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15 / April / 2011

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**A HEALTH FACILITY-BASED ASSESSMENT OF MALARIA RISK
FACTORS IN URBAN MAPUTO, MOZAMBIQUE**

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A HEALTH FACILITY-BASED ASSESSMENT OF MALARIA RISK
FACTORS IN URBAN MAPUTO, MOZAMBIQUE

By

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2003

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Abstract

A Health Facility-Based Assessment of Malaria Risk Factors in Urban Maputo, Mozambique

By Lisa Schmidt

Background: Urbanization of sub-Saharan Africa has a major impact on malaria epidemiology. While much is known about malaria in rural areas of Mozambique, there is a lack of knowledge concerning urban malaria patterns. Malaria research and control strategies are based largely on experience gained in rural areas and need to be adapted to the urban environment. This study was done to determine malaria prevalence and risk factors in Maputo City.

Methods: A health-facility based survey was conducted to investigate the proportion of laboratory-confirmed malaria in patients presenting with fever or history of fever in Maputo, Mozambique. A total of 643 patients from 28 health facilities were analyzed in the study; each completed a questionnaire on malaria risk factors and gave a blood sample for microscopy and rapid diagnostic tests (RDTs). Logistic regression models were used to estimate the effect of potential malaria risk factors. Two potential confounders, travel outside Maputo City and bednet usage, were also incorporated into logistic regression models to control for their effect on an individual's risk of malaria.

Results: There were 103 (16.0%) patients who had a positive blood slide for malaria. When stratified by health facility location, the proportions were 10.1% (26/257), 15.1% (26/172), and 23.8% (51/214) in urban, peri-urban, and rural facilities, respectively. Risk factors that were significantly associated with malaria included: age greater than five years, documented fever at enrollment, living near a farm, health facility location, and living near water.

Conclusion: There is a high prevalence of malaria among febrile patients presenting to health facilities in Maputo. Prevention strategies should target adults as well as children and both urban and rural areas of the city should be addressed in malaria control interventions.

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Background

Geography/Climate

Mozambique is located on the eastern coast of Africa with Swaziland and South Africa to the south, Zimbabwe to the west, Zambia, Malawi, and Tanzania to the North and the Indian Ocean to the east [1]. Maputo City is situated in the southern part of the country at a latitude of 25°54'16"S and a longitude of 32°36'24" E [2]. The average elevation of the city is 47 meters [3]. Four rivers, Tembe, Umbeluzi, Matola and Infulene, drain into Maputo Bay, which is located on the east side of the city.

Mozambique has a tropical climate and two seasons: the wet season from October to March and the dry season from April to September [1]. Maputo Province receives an average of 793mm of rain each year while the average temperature ranges from 13 to 24°C in July and from 22 to 31°C in February [4].

Population

Maputo City has a population of 1,110,495 distributed among seven municipal districts: five on the mainland, the peninsula of Catembe, and the island of Inhaca. The city covers an area of 308 km², giving it a population density of about 3,605 persons per km² [5]. As the most densely populated urban area in the country, Maputo contributes to over 30% of the national GNP and has a population growth rate of 1.7% [6, 1].

Epidemiology/Malaria Burden

Malaria transmission in Mozambique is perennial with a seasonal peak that overlaps with the rainy period, extending from December to April. The intensity of transmission varies depending on annual rainfall, temperatures, and specific environmental conditions. *Plasmodium falciparum* is the most common parasite and is responsible for more than 90% of the malaria cases. *P. malariae* and *P. ovale* account for about 9% and 1%, respectively. The major vectors in Mozambique include *Anopheles gambiae s.s.*, *A. arabiensis*, *A. funestus s.l.*, and *A. Funestus s.s.*, with *A. arabiensis* being more prevalent in Maputo Province [7].

Malaria presents a major public health burden for the Mozambique health system. Forty-four percent of outpatient consultations and 57% of health facility admissions are due to malaria [1]. The situation is compounded by low health coverage; over 50% of the country's population is over an hour away from the nearest health facility [8]. In addition, weak health infrastructure and a shortage of health workers contribute to poor clinical and laboratory diagnostic capabilities and affect the efficiency and quality of the services health facilities offer. Malaria was determined to be the overall primary cause of death (29%), higher even than AIDS (27%), according to a post-census mortality survey (INCAM) carried out between 2007 and 2008 [7].

Costing

An exceptional increase in global financing for malaria control, particularly in sub-Saharan Africa, has launched a new phase in the fight against malaria. Global development assistance for health has quadrupled in the last two decades with

dramatic increases in support for malaria from 2003 through 2009 [18]. The vast majority of malaria-control funding is channeled through three sources: the Global Fund to Fight AIDS, Tuberculosis, and Malaria; the World Bank Malaria Booster Program; and the U.S. President's Malaria Initiative (PMI). Since 2004, Mozambique has received over \$1.5 billion in malaria aid from these three funders alone [10-14]. However, the NMCP and donors still need to make the most cost-effective use of available resources by targeting malaria control measures to those areas where they will have the greatest impact [15]. Emerging malaria risk factors and areas of high malaria transmission need to be identified in order for available funding to be used to significantly reduce malaria morbidity and mortality.

Urbanization

Mozambique is experiencing fast economic development, which has resulted in a recent increase in the urban population of Maputo City [2]. Rapid urbanization has been shown to alter the frequency and transmission dynamics of malaria with significant effects on disease-associated morbidity and mortality, which in turn have important implications for malaria control measures [16]. Previously, malaria transmission in Maputo City was assumed to be very low in comparison to the rest of the country. The 2007 Malaria Indicator Survey (MIS) showed malaria infections in almost 40% of children under five at the national level, with parasite prevalence varying greatly among provinces. The northern province of Nampula had the highest prevalence at 60.4% while Maputo and Maputo City represented the low end with prevalences of 3.9% and 5.7%, respectively. However, these data may not be an accurate representation of the current

burden of malaria. Maputo City is currently facing a number of challenges as a result of the pace and the extent of urbanization. Almost 75% of Maputo residents now live in informal settlements with slum characteristics: dense unregulated growth, lack of common infrastructure services such as water and electricity, and homes built of precarious materials and on unsuitable land at risk of recurrent flooding [17]. This lack of infrastructure, poor water drainage, and inadequate sanitation can increase vector breeding and human vector contact, and thus provide potential risk factors for increased malaria transmission.

Introduction

Malaria remains the leading cause of mortality and morbidity in sub-Saharan Africa, with 208 million cases and 863,000 deaths reported in 2008 [18]. Despite signs of decreasing malaria prevalence from the Mozambican Ministry of Health, malaria is still a major cause of concern, accounting for 29% of overall deaths and 42% of deaths in children under five [7]. According to the National Malaria Control Program, there were 4,020,574 malaria cases and 2,786 malaria deaths in 2009.

The rapid growth of urban areas, fueled by high rates of rural-urban migration, together with the recognition of risk of epidemics and the importance of urban malaria control for economic development, has led to renewed interest in urban malaria transmission [19]. Few studies have been done on the malaria epidemiology in Maputo and accurate data on the incidence, distribution, and risk factors of malaria in this urban setting is needed in order to effectively define and assess control programs [20]. The objective of this study was to determine malaria prevalence and risk factors in Maputo City.

Research Question

Malaria research and control strategies are based largely on experience gained in rural areas and need to be adapted to the urban environment. While much is known about malaria in rural areas of Mozambique, there is a lack of knowledge concerning urban malaria patterns. This health facility-based assessment was conducted to determine what proportion of patients with fever or history of a fever had lab-

confirmed malaria and what potential malaria risk factors exist in the urban setting of Maputo City.

Methods

Study sites

All registered health facilities in Maputo City were included as study sites, resulting in 30 public health facilities (HFs) being selected to participate in the survey. Health facilities were categorized as urban, peri-urban or rural based on their distance from the city center and on suburban administrative boundaries. The Central Hospital of Maputo, located in the middle of the city (25°58'6" S, 32°35'19" E) was used as the city center [21]. Urban health facilities were located within a radius of approximately two miles from the Central Hospital; peri-urban facilities were located between two and five miles from the Central Hospital; and rural facilities were those located more than five miles from the Central Hospital, but within the administrative boundaries of Maputo City. Health facilities included hospitals, health clinics and health posts.

Survey teams

Twelve interviewers and three phlebotomists participated in the survey. All were former Mozambican Ministry of Health staff with experience in malaria case management and all were fluent in Portuguese and able to converse in other local languages. Before beginning field work, survey teams completed a one-week training on the survey methodology, data collection, rapid diagnostic tests (RDTs) and blood slide preparation. Survey staff were divided into three teams, each consisting of one team leader, three nurses or nurse assistants, one phlebotomist and a driver. Each team was responsible for visiting one health facility per day over a 2-week period, for a

total a 10 health facilities per team. The survey instrument and methodology were pilot tested at a health facility outside Maputo City.

Survey procedure

The survey was conducted using the previously developed Rapid Urban Malaria Appraisal (RUMA) protocol. This methodology provides a standardized and cost-effective tool with which to evaluate the burden of malaria in an urban area [22-26]. Teams arrived in the morning, introduced themselves to the head of the health facility and asked permission to conduct the survey during the working day. Persons seeking care from out-patient departments or emergency rooms were screened by team members for eligibility and recruited for participation. Inclusion criteria included documented fever (defined as axillary temperature ≥ 37.5 °C) at the time of enrollment or a history of fever in the previous 24 hours among patients who weighed more than 5 kg and who were presenting at the health facility for the first time with their current illness. Once screened, a brief consent in Portuguese was read to all eligible persons. Participants were enrolled in the evaluation if the participant or participant's guardian agreed.

A standardized RUMA questionnaire was administered which included questions on demographic characteristics, presence of malaria signs and symptoms, malaria risk factors, bednet ownership and usage, household indoor residual spraying (IRS), anti-malaria treatment prior to seeking care at the health facility, location of residence and recent travel history. A finger-prick blood sample was collected and used for an RDT and for thick and thin blood smears. ICT Malaria P.f.[®] rapid diagnostic tests were

performed according to manufacturer's directions. National guidelines were followed and artemether-lumefantrine was used to treat any patient with a positive RDT. Health facility staff performed follow-up and evaluation on all patients, regardless of RDT results.

Laboratory procedures

The Parasitology Laboratory at the National Institute of Health in Mozambique stained the thick and thin smears. Magnification of 100x was used to examine slides and to determine malaria positivity and speciation. Trophozoites and gametocytes were counted per 300 white blood cells and parasitemia was estimated assuming 8,000 white blood cells/ μ L. Smears were read by two independent microscopists. Each was blinded to the other's result and a third reader examined slides in cases where the two readings differed (by positivity, species, or >50% of parasitemia). The final reading for each slide was determined by using the geometric mean of the two closest results. A malaria case was defined as the presence of asexual parasites in a health facility patient with current fever or history of fever in the previous 24 hours.

Ethics

This protocol was deemed non-research and granted approval of public health evaluation by the Institutional Review Board at the Centers for Disease Control and Prevention (CDC). No human subject research was conducted and IRB review was not required. Protocol was also approved by the ethics committee of the Mozambican Ministry of Health [21].

Analysis

Data were double entered into Epi Info 2000 (CDC, Atlanta, Georgia) for initial data cleaning and were analyzed using SAS 9.2 statistical software (SAS Institute, Cary, North Carolina). Univariate analyses using logistic regression models were performed on selected environmental, socioeconomic, and malaria prevention variables. Each variable's association with laboratory-confirmed malaria was assessed using likelihood ratio statistics to identify variable significance, with the probability of committing a type-1 error (α) set at 0.05. The corresponding odds ratios (OR) and 95% confidence intervals (CIs) were used to assess the relationship between each potential risk factor and the risk of acquiring malaria.

Laboratory-confirmed malaria was the outcome of interest. Seven exposure variables were identified as potential risk factors based on current scientific literature and on their independent association with the outcome. All exposure variables were categorical and those that were analyzed included: age group (AG), defined as less than five or greater than/equal to five; health facility stratum (HF), defined as urban, peri-urban, or rural; documented fever at the time of enrollment (DF); patient's home within 250 meters of a standing water source (HNW); patient's home within 250 meters of a farm (HNF); patient works or accompanies a caregiver to a farm (WF); and type of material the walls of the home are made of (HW), defined as metal/reed or stone. Whether a patient worked or accompanied a caregiver to a farm was thought to measure similar environmental factors as whether or not a patient's home was within 250 meters of a farm and the former was therefore excluded from further analyses.

The initial multivariate model contained the aforementioned six exposure variables (where two dummy variables were used to define the three-category predictor health facility strata), two potential confounder variables, and 16 potential interaction terms. Confounders were chosen a priori based on recent studies conducted in sub-Saharan Africa which assessed potential malaria risk factors in urban settings. Travel and bednet usage were analyzed as potential confounders. Travel was defined as any trip taken outside of Maputo city within the last three months. Having slept under a bednet the previous night was considered as a proxy for bednet usage. Two-way interaction terms were included to evaluate multiplicative interaction among two potential risk factors and among potential risk factors and confounders ($\alpha=0.05$).

Collinearity was assessed using a SAS macro to identify condition indices (CIs) and variance decomposition proportions (VDPs) deviating from set standards. After collinearity assessment, a hierarchical backwards elimination technique was used to first test for the significance of remaining interaction terms ($\alpha=0.05$), followed by significance tests for those exposure variables (among age, fever at enrollment, health facility location, household location relative to water and farms, and household wall material) that were not contained in any significant interaction terms, while controlling for potential confounding of bednet usage and travel. For interaction assessment, product terms involving an exposure variable and a potential confounder were tested first, followed by an assessment of product terms involving two exposure variables. Since only two potential confounders were considered, both were controlled for throughout all multivariate analyses. An adjusted odds ratio was determined for each

variable in the model. Edited output from collinearity and interaction assessments can be found in the attached appendix.

Results

Demographics

Twenty-eight of the 30 health facilities participated in the study; one facility was closed during the time of the survey and one facility did not have any patients who met the case definition. Of the 28 participating health facilities, 10 were urban, 7 were peri-urban, and 11 were rural. A total of 4,604 out-patients presented on the day of the survey and 718 (15.6%) were considered eligible to participate. Of all eligible patients, 703 (15.3%) provided informed consent and complete clinical and laboratory information and were enrolled in the study (Figure 2).

Table 1 provides information on the demographic characteristics of all enrolled patients. Among all patients, 281 (40.0%) were seen at urban health facilities, 200 (28.5%) at peri-urban facilities, and 222 (31.6%) at rural facilities. Approximately 58% of the study population was female and 643 (91.5%) were residents of Maputo City. The age of study participants ranged from three months to 84 years; the median age was 18 and almost one third (29.5%) of the participants were children under five years of age.

Laboratory results

In the 703 enrolled patients, two malaria species were identified; *P. falciparum* was found in 111 (15.8%) patients and *P. ovale* was found in six (0.9%) patients. No cases of *P. vivax* or *P. malariae* were identified. Since the presence of gametocytes alone is not necessarily indicative of acute malaria infection, asexual parasites had to be present in order to be considered a malaria case [21]. One hundred and eleven malaria cases were identified in the study population; 105 patients had positive slides for *P.*

falciparum only, two patients for *P. ovale* only, and four for both *P. falciparum* and *P. ovale*. Of the 643 patients residing in Maputo City, there were 103 (16.0%) positive malaria cases; 98 (95.1%) for *P. falciparum*, 2 (1.9%) for *P. ovale* and 3 (2.9%) for both (mixed infection). Twelve (1.9%) of these patients had a positive microscopy result for gametocytes; ten for *P. falciparum* and two for *P. ovale*.

RDT sensitivity and specificity were also assessed. Of the 111 malaria cases, 99 had positive RDT results, corresponding with a sensitivity of 89.2%. RDT results were negative in 574 of the 592 non-cases, yielding a specificity of 97.0%.

Analysis of potential risk factors

All univariate and multivariate analyses were restricted to patients who resided in Maputo City (n=643). Univariate analysis showed several significant associations between potential risk factors and acquisition of malaria (Table 2). Patients five years of age or older were almost twice as likely to have a positive malaria status as patients under five years of age (OR=1.99; 95% CI: 1.17-3.37; p=0.0113). Two hundred ninety-nine (46.94%) patients had a documented fever at enrollment, which was also associated with malaria (OR=2.22; 95% CI: 1.43-3.44; p<0.0001). Malaria prevalence rates differed among health facility stratum; 26 (10.12%), 26 (15.12%) and 51 (23.83%) cases occurred at urban, peri-urban, and rural health facilities, respectively. There was a significant association only between rural and urban health facilities (OR=2.78; 95% CI: 1.66-4.64; p<0.0001) when using urban health facilities as the reference group.

Environmental risk factors of living within 250 meters of water, living within 250 meters of a farm, and working or accompanying a caregiver to a farm were all

significantly associated with malaria. In addition, household wall material, when comparing metal or reed houses to stone houses, was also a significant risk factor for malaria (OR=1.83; 95%CI: 1.11-3.02; p=0.0188).

The multivariate logistic regression analysis began with the assessment of collinearity in the initial model containing six exposure variables, two potential confounders and sixteen product terms. Collinearity was present, which resulted in three product terms being dropped from the initial model: sleeping under a bednet the previous night and household wall material, health facility strata and household wall material, and age group and travel outside Maputo City. Due to collinearity, interactions involving these variables were unable to be assessed. The other 13 product terms remained in the model and were assessed for interaction using backwards elimination techniques. No significant interaction was found among product terms involving an exposure variable and a potential confounder. Among product terms involving two exposure variables, only HF*HNF was found to have significant interaction (p=0.027).

The final model included age, fever at enrollment, health facility location, and household location relative to water and farms as malaria risk factors. Both potential confounders, bednet usage and travel outside of Maputo City, and the aforementioned significant product term were included in the final model as well. Estimated odds ratios for each variable, adjusted for all other variables in the model, are presented in Table 3. Age greater than five years, fever at enrollment, and living close to a farm were all positively associated with the risk of malaria. Evidence of interaction was found between health facility location and living within 250 meters of a farm. When

controlling for other variables in the model, the association between living within 250 meters of water and malaria status progressively increased from urban to peri-urban to rural health facilities (ORs=0.45, 1.56, and 3.39, respectively). The strongest association between health facility stratum and malaria cases was due to the combined effects of living within 250 meters of a farm and presenting at a rural health facility (OR=11.02; 95% CI: 2.61-46.48).

Discussion

This study demonstrates that almost 16% of febrile patients presenting for care at public health facilities have laboratory-confirmed malaria, suggesting that the malaria prevalence in Maputo City may be higher than expected. The adaptation of malaria vectors to urban areas has been well documented in recent years [16]. However, transmission patterns have been shown to vary greatly by area, season, and age group. Only 5.2% of febrile patients presenting to health facilities in Dar es Salaam, Tanzania, had positive malaria blood slides while in Yopougon, Côte d'Ivoire, the malaria prevalence among fever cases was 22% [24, 25]. Malaria transmission also varies among different geographical areas within the same city. In Kinshasa, Democratic Republic of the Congo, prevalence in school children ranged from 14% in a central urban area to 65% in peri-urban areas [22]. Maputo showed a similar, but less extreme, trend with malaria prevalence ranging from 10.1% to 15.1% to 23.8% in urban, peri-urban, and rural health facilities, respectively.

The high degree of heterogeneity among different urban environments makes it challenging to carry out effective malaria control strategies. In malaria settings where transmission is high, preventive measures such as ITN usage, IRS campaigns, and IPTp accessibility are essential to significantly reduce malaria morbidity and mortality. In low transmission settings, prompt recognition and case management are crucial, in addition to prevention. It is essential that all infections are detected, including those in asymptomatic carriers with low parasite densities since they represent a parasite reservoir that is capable of effectively transmitting the infection [27]. The malaria

epidemiology of each area therefore needs to be considered and control strategies should be tailored appropriately.

The prevalence of malaria among health facility patients was almost twice as high in older children and adults as in children under five. A higher incidence of malaria in older children or adults suggests delayed or non-existent acquisition of immunity and is typically found in areas with very low levels of malaria transmission [15]. In areas with higher transmission levels, like Maputo City, these results could indicate a recent increase in malaria prevalence or a mixed transitional pattern of high/low malaria transmission levels [25]. They may also be a result of using health facility data; adults are more likely to present at a health facility and seek care for a fever than young children. Regardless, the high prevalence of malaria in adults should be considered when developing malaria control strategies. ITN distribution campaigns and other preventative measures that reach older population groups may need to be developed in order to focus control efforts on adults as well as children.

Fever is no longer a reliable sign for the diagnosis of malaria [23]. In this study, almost 84% of febrile patients did not have malaria, indicating a need for improved differential diagnosis of fever. Malaria overdiagnosis, and the consequent neglect of alternative diagnoses, has become more widely recognized and efforts are being made to properly detect malaria parasitaemia. The current malaria diagnosis guidelines by the World Health Organization (WHO) recommend that in all settings, clinical suspicion of malaria should be confirmed with a parasitological diagnosis [28]. Mozambique has adopted this case management policy and recommends laboratory confirmation for all

suspected malaria cases [21]. Correct diagnoses will help avoid unnecessary antimalarial drug use and increased drug resistance, which are concerns since *P. falciparum* resistance to chloroquine has been already been reported throughout most of Mozambique [8]. Inaccurate diagnosis also results in an unnecessary number of return health visits, putting an increased burden on financial and health resources and undermining patients' trust in health facility care.

The use of RDTs as a diagnostic tool can be an effective way of decreasing overdiagnosis of malaria. While light microscopy is still considered the "gold standard" for routine parasite-based diagnosis, it can be unreliable and wasteful unless performed by expert microscopists under ideal conditions [29, 30]. RDTs, which can be used by any health care worker and do not need extra infrastructure, are now being thought of as a viable option for diagnosing malaria [30]. Malaria antigens currently targeted by RDTs are histidine rich protein 2 (HRP2), Plasmodium lactate dehydrogenase (pLDH) and Plasmodium adolase [31]. HRP2 is unique to *P. falciparum* and is the antigen detected by the ICT diagnostic test used in this study. RDTs from this assessment yielded a sensitivity of 89.2% and a specificity of 97.0%. These results support recent trials that have shown HRP2 antigen-based RDTs to have high sensitivity and specificity for the diagnosis of *P. falciparum* infection [32]. However, the performance of RDTs is highly correlated with appropriate training and supervision of health care workers; increasing the use and accessibility of RDTs will only result in improved diagnostics if it is coupled with adequate staff training and supervision.

Neither the univariate nor multivariate analyses found evidence of an inverse association between the preventative intervention of bednet usage and malaria parasite infection. This result was unexpected; numerous studies have shown significant reductions in malaria parasite infection prevalence among those who slept versus did not sleep under ITNs [33-36]. In Maputo City, less than 15% of patients reported owning an ITN and less than 50% lived in homes that had received IRS spraying. This could, in part, be contributed to a lack of access to malaria prevention measures or a lack of concern that malaria transmission in the city is a problem. However, it should also be noted that 100% of those who reported owning an ITN also reported sleeping under it the previous night. While these findings may be partially attributed to the Hawthorne effect of patients giving the response they felt the health facility staff would want to hear, they are still promising. The effectiveness of ITNs as malaria prevention tools depends on their 'regular' and 'proper' use and could contribute to the success of an urban ITN distribution campaign [37].

These results also highlight a need to consider the reallocation of funds and resources to Maputo City. Over five million LLINs were distributed in Mozambique between 2007 and 2009, but only 1.2% of those were distributed in Maputo City, which is home to almost 7% of the country's population [7]. Mozambique is currently shifting towards a new ITN distribution policy which focuses on universal coverage. Distribution campaigns are unable to target all areas of the country simultaneously and these findings should be taken into account to help prioritize which areas campaign distributions will address first. The prevalence of malaria and the population affected

should be determined at the provincial level to better guide the planning and implementation of this process.

This assessment has a number of limitations. First, three product terms were excluded from analysis due to collinearity, which subsequently prevented interaction from being assessed among these terms. Second, the survey methodology is a cross-sectional design and it is not possible to determine how malaria prevalence and risk factors vary over time due to seasonality, the dynamics of urbanization and the evolution of malaria transmission. Third, the study was health facility-based and thus was not necessarily representative of the total population; a trend in the health facility burden does not always imply a corresponding trend in the community burden. Additionally, cases of febrile illness that present at a formal health clinic represent only a small portion of those that exist in the community which could lead to an underestimation of the true burden on malaria [38]. Finally, no GIS coordinates for the individual health facilities were available at the time of publication. GIS mapping of the health facility locations would allow for construction of malaria risk maps, which could help identify specific high risk areas and target potential vector breeding sites.

In conclusion, the proportion of febrile patients with laboratory-confirmed malaria in the city of Maputo is higher than previously expected. This assessment provides important data on malaria risk factors and should be acknowledged when deciding on appropriate malaria control strategies, such as the reallocation of resources to urban areas, increased ITN coverage and targeting an older population. Further studies, in Maputo as well as in other urban areas, need to be conducted to support

these findings and to gain a better understanding of the process of urbanization in order to develop suitable malaria interventions and preventative measures for large urban centers in the future.

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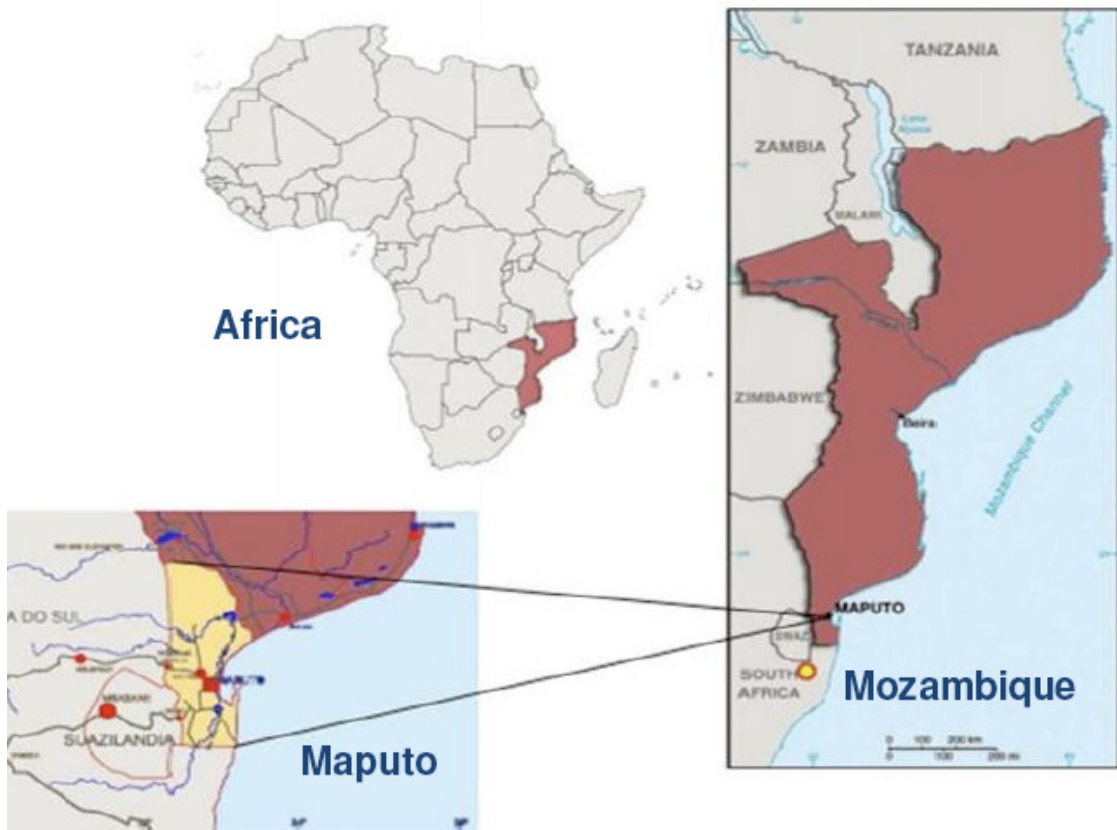
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Figure 1: Map of Maputo, Mozambique¹



¹Map from UN HABITAT for a Better Urban Future

Figure 2: Longitudinal component patient profile

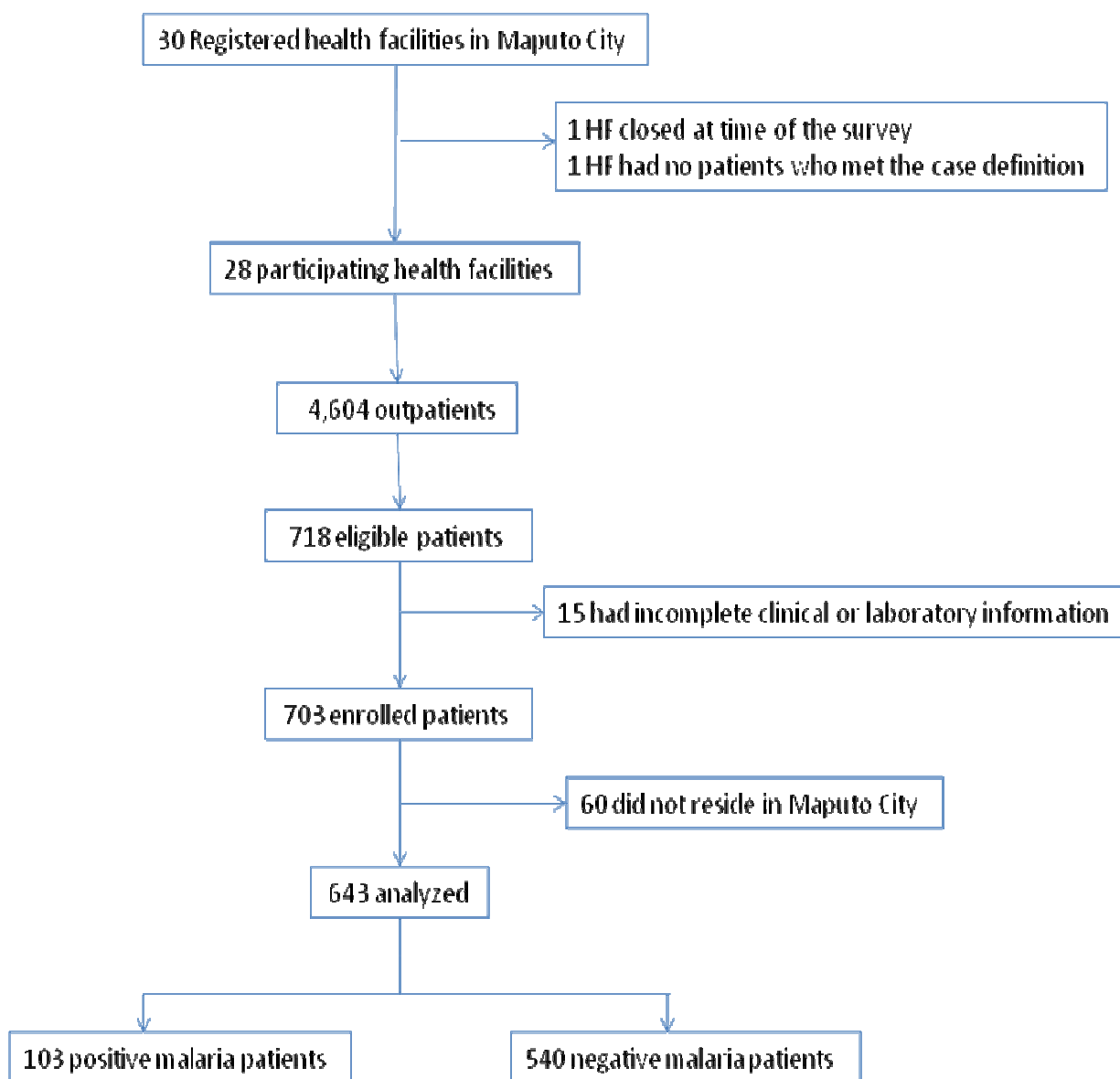


Table 1. Selected characteristics of enrolled patients, Maputo, Mozambique^a

	Eligible Patients (n=703)	
	No.	%
Age		
(mean, median)	20.6, 18.2	3 mo-84.6 yrs
Children under 5	207	29.5
Gender		
Male	290	41.9
Female	403	58.2
Health facility stratum		
Urban	281	40.0
Peri-urban	200	28.5
Rural	222	31.6
Resident of Maputo City		
Yes	643	92.1
No	55	7.9
Documented fever at enrollment		
Yes	328	47.1
No	368	52.9
Education level		
None	82	11.7
Primary school (grades 1-5)	244	31.9
Primary school (grades 6-7)	188	26.7
Secondary school (grades 8-10)	124	17.6
Secondary school (grades 11-12)	63	9.0
Professional	3	0.4
Superior	11	1.6
Don't know	8	1.1
Home close to water (<250 meters)		
Yes	112	16.1
No	584	83.8
Home close to field (<250 meters)		
Yes	165	23.8
No	528	76.2
Work and/or accompany caregiver to field		
Yes	122	18.2
No	549	81.8
Housing material (walls)		
Metal	16	2.3
Reeds	98	14.0
Wood	5	0.7
Maticada	2	0.3
Stone/brick	578	82.7
House received IRS		
Yes	315	46.7
No	348	51.6
Slept under bednet previous night		
Yes	284	40.9
No	410	59.1
Slept under ITN previous night		
Yes	93	13.4
No	552	79.5

^aData collected from all registered health facilities in Maputo City, 2009

Table 2. Univariate analysis of potential malaria risk factors for residents of Maputo, Mozambique presenting at health facilities (n=643)^a

	Analyzed patients (n=643)			
	Prevalence of variable in comparison group	Prevalence of malaria in comparison group	OR	95% CI
Age group (>=5 vs <5)	456 (71.0%)	84 (18.42%)	1.99	1.17-3.37
Gender (ref=male)	368 (58.0%)	56 (15.2%)	0.84	0.55-1.28
Health facility stratum				
Peri vs Urban	172 (26.8%)	26 (15.1%)	1.58	0.88-2.83
Rural vs. Urban	214 (33.3%)	51 (23.8%)	2.78	1.66-4.64
Reside in Maputo City (ref=no) (n=703)	643 (92.1%)	103 (16.0%)	1.31	0.58-2.97
Documented fever at enrollment (ref=no)	299 (46.9%)	64 (21.4%)	2.22	1.43-3.44
Education (ref=any education)	78 (12.3%)	10 (12.8%)	0.79	0.39-1.59
Home within 250 meters of water (ref=no)	100 (15.7%)	24 (24.0%)	1.83	1.09-3.07
Home within 250 meters of farm (ref=no)	144 (22.6%)	29 (27.1%)	2.49	1.59-3.91
Work or accompany caregiver to farm (ref=no)	112 (18.2%)	26 (23.2%)	1.81	1.09-2.99
House wall material (ref=metal/reed vs. stone)	109 (17.2%)	26 (23.9%)	1.83	1.11-3.02
House received IRS (ref=yes)	318 (52.4%)	54 (17.0%)	1.14	0.74-1.76
Any bednet in home (ref=yes)	298 (46.5%)	48 (16.1%)	1.01	0.66-1.53
ITN in home (ref=yes)	561 (87.3%)	88 (15.7%)	0.83	0.45-1.52
Slept under bednet previous night (ref=yes)	377 (59.4%)	64 (17.0%)	1.18	0.77-1.83
Slept under ITN previous night (ref=yes)	506 (80.0%)	80 (15.8%)	0.84	0.46-1.54
Received previous anti-malaria tx (ref=yes)	508 (79.4%)	77 (15.2%)	0.77	0.46-1.27
Traveled outside Maputo in last 3 months (ref=no)	118 (18.4%)	26 (22.0%)	1.63	0.99-2.69

^aData collected from all registered health facilities in Maputo City, 2009

Table 3. Multivariate analysis of potential malaria risk factors for residents of Maputo, Mozambique presenting at health facilities (n=643)^a

	Analyzed patients (n=643)	
	OR ^b	95% CI
Age group (>=5 vs <5)	2.28	1.28-4.06
Documented fever at enrollment (ref=no)	2.63	1.62-4.27
Home within 250 meters of farm (ref=no)	2.12	1.26-3.59
Traveled outside Maputo in last 3 months (ref=no)	2.00	1.16-3.44
Slept under bednet the previous night (ref=no)	0.94	0.59-1.52
Health facility stratum ^{**}		
Peri vs. Urban, home > 250 meters from water	0.86	0.43-1.71
Rural vs. Urban, home > 250 meters from water	1.47	0.78-2.76
Peri vs. Urban, home within 250 meters of water	2.96	0.62-13.99
Rural vs. Urban, home within 250 meters of water	11.02	2.61-46.48
Home within 250 meters of water ^{**} (ref=no)		
Urban	0.45	0.12-1.70
Peri-urban	1.56	0.52-4.71
Rural	3.39	1.46-7.86

^aData collected from all registered health facilities in Maputo City, 2009

^bAdjusted ORs

^{**}Stratum-specific adjusted ORs due to interaction

APPENDIX

Univariate Analysis

```

proc logistic data=filemap;
  class agegroup (ref='<5 years') / param=ref;
  Model microanyass (Event='Positive') = agegroup;
  Title "Univariate analysis - Age Group";
run;

```

Model Fit Statistics			
Criterion	Intercept Only	Intercept and Covariates	
AIC	567.464	562.358	
SC	571.928	571.288	
-2 Log L	565.464	558.358	
Type 3 Analysis of Effects			
Effect	DF	Wald Chi-Square	Pr > ChiSq
agegroup	1	6.4180	0.0113

Analysis of Maximum Likelihood Estimates						
Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept		1	-2.1736	0.2421	80.5932	<.0001
agegroup	>5 years	1	0.6855	0.2706	6.4180	0.0113

Odds Ratio Estimates			
Effect	Point Estimate	95% Wald Confidence Limits	
agegroup >5 years vs <5 years	1.985	1.168	3.373

Univariate Analysis – Edited SAS Output

Variable	-2 Log L (Intercept only)	-2 Log L (Intercept and variable)	-2 Log L Reduced - (-2 Log L Full)	df	p-value
Age group	565.46	558.36	7.11	1	0.0077
Health facility stratum	565.81	549.54	16.27	1	0.0003
Documented fever at enrollment	557.08	544.01	13.06	1	0.0003
Home within 250 meters of farm	563.71	548.85	14.86	1	0.0001
Home within 250 meters of water	564.06	558.79	5.27	1	0.0217
Home wall material	563.00	557.81	5.19	1	0.0227
Traveled outside Maputo in last 3 months	564.76	561.22	3.54	1	0.0599
Slept under bednet previous night	559.71	559.34	0.36	1	0.5463

Collinearity Assessment

```

** Variables in the model:
    - E1 - agegroup
    - E2 - tempgroupnum
    - E3 - usstratanum
    - E4 - homewaternum
    - E5 - homemachanum
    - E6 - homewallbin
    - C1 - bednetundern
    - C2 - traveln

** Full Model including all variables and all relevant interaction
terms:

%include "H:\Modeling\collinearity_macro 09.sas";

proc logistic data=filemap covout outest=infomat;
  model microanyass (Event='Positive')= usurban usperi agegroupnum
  tempgroupnum homewaternum homemachanum homewallbin bnundern
  traveln
    bnundern*usurban bnundern*usperi bnundern*agegroupnum
    bnundern*tempgroupnum bnundern*homewaternum
    bnundern*homewallbin bnundern*homemachanum
    traveln*usurban traveln*usperi traveln*agegroupnum
    traveln*tempgroupnum
    usurban*homewallbin usperi*homewallbin
    usurban*homewaternum usperi*homewaternum
    usurban*homemachanum usperi*homemachanum
    homewallbin*homewaternum homewallbin*homemachanum
    homewaternum*homemachanum agegroupnum*tempgroupnum/covb;
  title "Collinearity - Full Model";
run;

%collin (covdsn=infomat);
run;

```

Collinearity Assessment – Edited SAS Output

Collinearity diagnostics for nonlinear models using the information matrix: Eigen values, condition indexes, and Variance Decomposition Proportions (VDPs)

	Full Model	A	B	C
EIGENVAL	0.001	0.002	0.0016	0.0026
CONDINDX	137.982	87.761	92.6666	71.4087
Intercept	0.874	0.862	0.924	0.945
usurban	0.017	0.612	0.128	0.246
usperi	0.031	0.473	0.033	0.108
agegroupnum	0.000	0.003	0.622	0.210
tempgroupnum	0.015	0.031	0.086	0.158
homewaternum	0.027	0.064	0.003	0.020
homemachanum	0.052	0.018	0.070	0.120
homewallbin	0.848	0.656	0.052	0.116
Bnundern	0.809	0.040	0.243	0.486
traveln	0.009	0.170	0.645	0.292
usurban*BNundern	0.039	0.026	0.034	0.091
usperi*BNundern	0.008	0.012	0.017	0.035
agegroupnum*BNundern	0.003	0.001	0.136	0.207
tempgroupnum*BNundern	0.005	0.013	0.015	0.085
homewaternum*BNundern	0.007	0.006	0.001	0.001
homewallbin*BNundern	0.793	--	--	--
homemachanum*BNundern	0.063	0.001	0.025	0.023
usurban*traveln	0.002	0.125	0.081	0.137
usperi*traveln	0.003	0.073	0.012	0.063
agegroupnum*traveln	0.004	0.001	0.497	--
tempgroupnum*traveln	0.010	0.023	0.066	0.090
usurban*homewallbin	0.001	0.538	--	--
usperi*homewallbin	0.020	0.419	--	--
usurban*homewaternum	0.031	0.063	0.000	0.005
usperi*homewaternum	0.012	0.043	0.002	0.004
usurban*homemachanum	0.000	0.014	0.029	0.033
usperi*homemachanum	0.005	0.008	0.014	0.011
homewaternum*homewallbin	0.011	0.026	0.003	0.012
homemachanum*homewallbin	0.016	0.014	0.028	0.086
homewaternum*homemachanum	0.001	0.002	0.001	0.005
agegroupnum*tempgroupnum	0.002	0.002	0.007	0.000

A - Model without homewallbin*bnundern

B - Model without homewallbin*bnundern, usstratanum*homewallbin

C - Model without homewallbin*bnundern, usstratanum*homewallbin, agegroupnum*traveln

Interaction Assessment

** FULL MODEL after collinearity assessment:

```
proc logistic data=filemap covout outest=infomat;
  class usstratanum (ref='1');
  model microanyass (Event='Positive')= usstratanum agegroupnum
  tempgroupnum homewaternum homemachanum homewallbin bnundern
  traveln
    bnundern*usstratanum bnundern*agegroupnum
    bnundern*tempgroupnum bnundern*homewaternum
    bnundern*homemachanum traveln*usstratanum
    traveln*tempgroupnum usstratanum*homewaternum
    usstratanum*homemachanum homewallbin*homewaternum
    homewallbin*homemachanum homewaternum*homemachanum
    agegroupnum*tempgroupnum/covb;
  title "Full Model";
run;
```

Model Fit Statistics		
Criterion	Intercept Only	Intercept and Covariates
AIC	550.256	532.370
SC	554.673	651.622
-2 Log L	548.256	478.370

Analysis of Maximum Likelihood Estimates						
Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept		1	-1.5389	1.5896	0.9372	0.3330
usstratanum	2	1	-0.4656	1.0079	0.2134	0.6441
usstratanum	3	1	0.1133	0.9773	0.0134	0.9077
agegroupnum		1	0.3606	1.0122	0.1269	0.7216
tempgroupnum		1	0.8898	1.4401	0.3818	0.5366
homewaternum		1	1.3618	1.8079	0.5674	0.4513
homemachanum		1	0.1204	1.5660	0.0059	0.9387

Analysis of Maximum Likelihood Estimates						
Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
homewallbin		1	-0.2384	0.4474	0.2838	0.5942
BNundern		1	-0.2092	0.6803	0.0946	0.7584
traveln		1	-0.3193	0.4850	0.4333	0.5104
BNundern*usstratanum	2	1	-0.4411	0.3778	1.3635	0.2429
BNundern*usstratanum	3	1	-0.0610	0.3441	0.0315	0.8592
agegroupnum*BNundern		1	0.0794	0.6123	0.0168	0.8969
tempgroupnu*BNundern		1	0.3579	0.5246	0.4655	0.4950
homewaternu*BNundern		1	-0.4458	0.6544	0.4641	0.4957
homemachanu*BNundern		1	0.0390	0.5517	0.0050	0.9437
traveln*usstratanum	2	1	0.5447	0.4434	1.5093	0.2192
traveln*usstratanum	3	1	0.2181	0.4127	0.2794	0.5971
tempgroupnum*traveln		1	-0.5138	0.6056	0.7197	0.3962
homewater*usstratanu	2	1	0.2856	0.4934	0.3351	0.5627
homewater*usstratanu	3	1	0.9868	0.4386	5.0627	0.0244
homemacha*usstratanu	2	1	-0.0612	0.4570	0.0179	0.8935
homemacha*usstratanu	3	1	-0.3440	0.3777	0.8297	0.3624
homewater*homewallbi		1	-0.1768	0.7152	0.0611	0.8048
homemacha*homewallbi		1	0.4855	0.6274	0.5988	0.4390
homewater*homemachan		1	-0.5165	0.6413	0.6486	0.4206
agegroupn*tempgroupn		1	0.5393	0.6140	0.7715	0.3798

Edited SAS Output from Backwards Elimination

Model	-2 Log L	-2 Log L Reduced - (-2 Log L Full)	df	p- value	Wald X ² p value of least significant term
Exposure/Confounder Interactions					
Full	478.370	--	--	--	0.944
bnundern*homemachanum dropped	478.375	0.005	1	0.944	0.899
bnundern*agegroup dropped	478.391	0.016	1	0.899	0.863
bnundern*usstratanum dropped	480.382	1.991	2	0.370	0.744
bnundern*tempgroupnum dropped	480.488	0.106	1	0.745	0.602
traveln*usstratanum dropped	483.972	3.484	2	0.175	0.655
traveln*tempgroupnum dropped	484.173	0.201	1	0.654	0.396
bnundern*homewaternum dropped	484.897	0.724	1	0.395	0.990
Exposure/Exposure Interactions					
homewallbin*homewaternum dropped	484.897	0.000	1	1.000	0.975
usstratanum*homemachanum dropped	485.865	0.968	2	0.616	0.458
homewaternum*homemachanum dropped	486.412	0.547	1	0.460	0.383
homewallbin*homemachanum dropped	487.165	0.753	1	0.386	0.292
agegroup*tempgroupnum dropped	488.261	1.096	1	0.295	0.738
usstratanum*homewaternum dropped	495.484	7.223	2	0.027	--

Multivariate Analysis – Final Model

** Obtaining multivariate ORs for the final model;

```
proc logistic data=filemap covout outest=infomat;
  class traveln (ref="2");
  model microanyass (Event='Positive')= usrural usperi agegroupnum
    tempgroupnum homewaternum homemachanum bnundern traveln
    usrural*homewaternum usperi*homewaternum/covb;
  title "Final Model Multivariate ORs";
run;
```

Analysis of Maximum Likelihood Estimates						
Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept		1	-2.8769	0.4888	34.6448	<.0001
usrural		1	0.3883	0.3199	1.4731	0.2249
usperi		1	-0.1497	0.3502	0.1829	0.6689
agegroupnum		1	0.8235	0.2947	7.8070	0.0052
tempgroupnum		1	0.9652	0.2480	15.1500	<.0001
homewaternum		1	-0.7908	0.6733	1.3793	0.2402
homemachanum		1	0.7523	0.2681	7.8733	0.0050
BNundern		1	-0.0572	0.2411	0.0563	0.8125
traveln	1	1	0.3467	0.1382	6.2948	0.0121
usrural*homewaternum		1	2.0118	0.7997	6.3281	0.0119
usperi*homewaternum		1	1.2340	0.8604	2.0569	0.1515

Odds Ratio Estimates			
Effect	Point Estimate	95% Wald Confidence Limits	
agegroupnum	2.279	1.279	4.060
tempgroupnum	2.625	1.615	4.268
homemachanum	2.122	1.255	3.589
BNundern	0.944	0.589	1.515
traveln 1 vs 2	2.000	1.164	3.438

Obtaining OR estimates for health facility stratum and home distance from water

$$\begin{aligned}
 \text{aOR (Periurban vs Urban, living near water)} \\
 &= \exp[\beta_2 + \delta_2(\text{HNW})] \\
 &= \exp[-0.1497 + 1.2340(1)] \\
 &= \exp[1.0843] \\
 &= 2.96
 \end{aligned}$$

$$\begin{aligned}
 \text{aOR (Periurban vs Urban, living far from water)} \\
 &= \exp[\beta_2 + \delta_2(\text{HNW})] \\
 &= \exp[-0.1497 + 1.2340(0)] \\
 &= \exp[-0.1497] \\
 &= 0.86
 \end{aligned}$$

$$\begin{aligned}
 \text{aOR (Rural vs Urban, living near water)} \\
 &= \exp[\beta_3 + \delta_3(\text{HNW})] \\
 &= \exp[0.3883 + 2.0118(1)] \\
 &= \exp[2.4001] \\
 &= 11.02
 \end{aligned}$$

$$\begin{aligned}
 \text{aOR (Rural vs Urban, living far from water)} \\
 &= \exp[\beta_3 + \delta_3(\text{HNW})] \\
 &= \exp[0.3883 + 2.0118(0)] \\
 &= \exp[0.3883] \\
 &= 1.47
 \end{aligned}$$

$$\begin{aligned}
 \text{aOR (living near water, urban)} & \\
 &= \exp[\beta_4] \\
 &= \exp[-0.7908] \\
 &= 0.45
 \end{aligned}$$

$$\begin{aligned}
 \text{aOR (living near water, peri-urban)} & \\
 &= \exp[\beta_4 + \delta_2] \\
 &= \exp[-0.7908 + 1.2340] \\
 &= \exp[0.4432] \\
 &= 1.56
 \end{aligned}$$

$$\begin{aligned}
 \text{aOR (living near water, rural)} & \\
 &= \exp[\beta_4 + \delta_3] \\
 &= \exp[-0.7908 + 2.0118] \\
 &= \exp[1.221] \\
 &= 3.39
 \end{aligned}$$

Where β_2 = estimated coefficient of peri HF
 β_3 = estimated coefficient of rural HF
 β_4 = estimated coefficient of HNW

δ_2 = estimated coefficient of periHF*HNW
 δ_3 = estimated coefficient of ruralHF*HNW

** Using contrast statements to obtain adjusted ORs for the effect of usstratanum;

```

proc logistic data=filemap covout outest=infomat;
  class traveln (ref="2");
  model microanyass (Event='Positive')= usrural usperi agegroupnum
  tempgroupnum homewaternum homemachanum bnundern traveln
  usrural*homewaternum usperi*homewaternum /covb;
  contrast 'Peri vs. Urban when living near water' usperi 1
  usperi*homewaternum 1/estimate=both;
  contrast 'Rural vs. Urban when living near water' usrural 1
  usrural*homewaternum 1/estimate=both;
  contrast 'Peri vs. Urban when not living near water' usperi 1
  usperi*homewaternum 0 /estimate=both;
  contrast 'Rural vs. Urban when not living near water' usrural 1
  usrural*homewaternum 0/estimate=both;
  title "Final Model with Dummy Variables";
run;

```

** Using contrast statements to obtain adjusted ORs for the effect of homewaternum;

```
proc logistic data=filemap covout outest=infomat;
  class traveln (ref="2");
  model microanyass (Event='Positive')= usrrural usperi agegroupnum
  tempgroupnum homewaternum homemachanum bnundern traveln
  usrrural*homewaternum usperi*homewaternum /covb;
  contrast 'Live near water vs far - Urban' homewaternum 1
  /estimate=both;
  contrast 'Live near water vs far - Peri' homewaternum 1
  usperi*homewaternum 1/estimate=both;
  contrast 'Live near water vs far - Rural' homewaternum 1
  usrrural*homewaternum 1 /estimate=both;
run;
```

Contrast Rows Estimation and Testing Results

	Estimate	S.E.	95% CI	Wald Chi- Square	Pr > ChiSq
Peri vs. Urban when living near water	2.96	2.35	0.62-13.99	1.87	0.1716
Rural vs. Urban when living near water	11.02	8.09	2.61-46.48	10.69	0.0011
Peri vs. Urban when not living near water	0.86	0.30	0.43-1.71	0.18	0.6689
Rural vs. Urban when not living near water	1.47	0.47	0.78-2.76	1.47	0.2249
Live near water vs far - Urban	0.45	0.31	0.12-1.70	1.38	0.2402
Live near water vs far - Peri	1.56	0.88	0.52-4.71	0.62	0.4320
Live near water vs far - Rural	3.39	1.45	1.46-7.86	8.10	0.0044