Malaria Risk Factors in the Peruvian Amazon: A Multilevel Analysis

by

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Thesis submitted in partial fulfillment of
the requirements for the degree of Master of Science
in the Duke Global Health Institute
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ABSTRACT

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Abstract

A multilevel analysis of malaria risk factors was conducted using data gathered from community-wide surveillance along the Iquitos-Mazan Road and Napo River in Loreto, Peru. In total, 1650 individuals nested within 338 households nested within 18 communities were included in the study. Personal travel (Odds Ratios [OR] 2.48; 95% Confidence Interval [CI] = 1.46, 4.21) and other house member's malaria statuses (OR = 2.54; 95% CI = 1.49, 4.32) were all associated with increased odds in having a malaria episode. Having a large household (>5 individuals) (OR = 0.33; 95% CI = 0.12, 0.93), presence of a community health post / secondary school (OR =0.26; 95% CI = 0.08, 0.80) and church (OR = 0.33; 95% CI = 0.30, 0.78) were associated with lower odds of having a malaria episode. Malaria clustering was evident as 54% of the malaria burden occurred in only 6% of the households surveyed.

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1. Introduction

With over 3.3 billion people in the world currently at risk of malarial infection (The World Health Organization (WHO), 2011), the control of the disease is one of global health's largest challenges (Tanner & Vlassoff, 1998). Considering the multiple layers of complexity that underlie malaria transmission, it may also be one of the global health's most daunting. Not only do malaria parasites and malaria vectors vary greatly by world region, vector density and vector breeding sites vary greatly from one community or household to the next. Across regions - large or small - changes in geography, weather patterns, drug resistance, population growth and mobility, deforestation, health treatment seeking behavior, access to resources, human activity patterns, and housing type affect the context in which the malaria exists; making it incredibly difficult to attack malaria with a one-size-fits-all-plan. Thus, governments, NGOs, and local communities throughout the Global South are struggling to find ways in which to stretch their limited resources to effectively *and* efficiently target the main drivers of malaria within their areas of concern. For these reasons and others, many studies choose to solely examine the most proximate factors associated with malaria rates. The distinct focus on such factors not only overshadows other important contextual interactions playing a role in the proliferation of one of the world's most deadly communicable diseases (Sachs & Malaney, 2002), but it may also mask any common social and socio-environmental contextual threads shared by communities spread throughout malaria zones.

Peru, a country that harbors 20% of South America's malaria burden, and the Amazon Basin, where two-thirds of all Peruvian cases of malaria are found, are no exception to having a regionally unique context for malaria to thrive; for, distance from and access to education and healthcare, community and household size, occupational opportunities, modes of transport,

population densities, and knowledge of malaria vary greatly from individual to individual making interventions beyond the most basic (i.e. bed net distribution) difficult to provide efficiently. But, the relatively large variation between communities outside of Iquitos, Peru, allows for a study of malaria risk factors that looks at more than just individual level risk factors for malaria. It may be that the individuals within a malaria region share common socio or socio-environmental link(s) in their malaria risk which, if identified, could provide a new target of focus for scientists and researchers looking to quell the malaria burden in regions beyond the Amazon jungle.

1.1 Malaria in Peru

The WHO defines malaria as "a life-threatening disease caused by [*Plasmodium*] parasites that are transmitted to people through the bites of infected [*Anopheles*] mosquitoes." Of the four *Plasmodium* parasites known to infect humans, *P. falciparum, P. vivax, P. ovale, and P. malariae, P. falciparum* is the most deadly. *P. vivax* and *P. falciparum*, the two types of parasites that exist in the northern most region of Peru, account for approximately 75% and 25% of the region's malaria infections, respectively (Price, Tjitra, Guerra, Yeung, White, & Anstey, 2007), and were responsible for over 1 million malaria cases in Latin America in 2010 (WHO, 2011).

Malaria incidence has risen dramatically in Peru over the past thirty years. In 1980, for example, only 14,000 cases of malaria were reported countrywide. In 1991, malaria in Peru represented just 3% of the malaria cases in all of South America, but that number quickly rose to 12% (208,543 cases) in 1995 and again to 19% in 1996 (Gunthman et al., 2001). Much of the increase occurred in the Department of Loreto in the Amazon Basin of Northern Peru (Parekh, Hernandez, Krogstad, Casaia, & Branch, 2007) where a similar rise in malaria cases has been seen. For example, in 1990, the Loreto Health Department reported only 641 cases of malaria, but by 1997 health officials reported 121,268 cases with recent estimates suggesting that Loreto

harbors around two-thirds of all malaria cases in Peru (Roper et al., 2000). Malaria infections in this region peak between February and July (Roshanravan et al., 2003); however, the incidence rate typically remains lower than 10% year round (Branch, 2005).

Although some researchers have associated the rise in malaria in the 1990's to the emergence of the *Anopheles darlingi* vector, others argue that the scarcity of pre-1990 data prohibit the conclusion that *A. darlingi* was absent from Peru before this period. It is likely that some of the increase in malaria would be a direct result of the decreased use of indoor residuals that occurred in the 1990s (Roper et al., 2000; Vittor et al., 2009). But it is also likely that the *A. darlingi* population increased along with the increased rate of deforestation (usually for logging or farming purposes) since *A. darlingi* thrives on the edges of forest and in previously cleared areas near forest edges – exactly where farms, households, and communities are located (Vittor et al., 2009; Yanociak, Paredes, Lounibos, & Weaver, 2006)!

Today, *A. darlingi* is South America's main malaria vector (including Loreto) and accounts for 90% of the entire mosquito population. *A. darlingi* carries both the *P. falciparum* and *P. vivax* malarial strains, prefers to feed on humans over animals, and is very attracted to areas of human settlement. *A. darlingi* has the ability to fly up to 7 kilometers and has a bimodal biting pattern which peaks at dusk and dawn (Caldas de Castro, Monte-Mor, Sawyer, & Singer, 2006; Roshanravan et al., 2003). As recent studies bring to light the spatial and temporal components of transmission that will undoubtedly affect every individual, household, and community, *A. darlingi* will likely be the main vector in the parasite-human interaction occurring in the Amazon.

1.2 Previously Identified Risk Factors in the Peruvian Amazon

Before Tanner and Vlassov's (1998) study which looked at treatment seeking behavior for those with symptoms of malaria, no published studies in the northern Peruvian Amazon were

available that examined risk factors associated with malarial acquisition risk for this region (Roper et al., 2000). More recent studies have tried to shine light on the complexity of the disease in Loreto. Researchers have since seen that age-specific human attack rates peaked in adult males, suggesting that occupation may be an important risk factor in malaria transmission (Roper et al., 2000). Chuquirayauri et al. (2011) examined risk factors for malaria acquisition in 9195 subjects in the Maynas Region surrounding Iquitos, Peru, and found that the odds of having a malaria episode were 31.1 times higher for those who had travelled one month outside their village before an episode occurred compared to individuals who had not travelled (after controlling for age, gender, education, health establishment, job type, and living with a logger or farmer). The same study found that agriculturists were 3.2 times as likely to have a malaria episode compared to individuals working in commerce. Those who lived with a logger or agriculturist were almost twice as likely to have a malaria episode as someone who did not live with individuals practicing these trades. While significant at the individual level, household and community variation in these results were not addressed nor was the potential clustering of malaria.

Recently, Branch et al. (2005) used active and passive malaria case detection in the suburbs of Iquitos, Peru, to explore local transmission patterns and clustering. They concluded not only that clustering of malaria existed by households in their study, but also that the effect of clustering made certain households more "contagious" or more likely to transmit malaria than others. Due to "highly-clustered asymptomatic infections," the authors concluded that passive case detection may not be an adequate measure of malaria incidence, and suggested that active case detection methods be used in similar settings. Furthermore, the authors suggested that future interventions target houses adjacent to those who were found to malaria parasites in their blood during the previous months' active surveillance round.

In an urban setting, such as this, where one health post is shared by all those in the study population and active surveillance techniques can be carried out with regularity and *relative* ease, the authors' conclusion are more than justified. In more remote and rural settings in the region, where distances among communities can vary greatly and any possible interventions are likely to encompass multiple communities with varying socio-environmental dynamics, the same conclusions may not hold. It is therefore necessary to identify the individual, household, and community level risk factors in more rural communities north of Iquitos to better understand what factors are most associated with malaria risk in these rural regions as well as to define how much variation in malaria risk can be explained by the included variables for individuals, households, and communities.

1.3 Individual Level Risk Factors and Interventions

Numerous studies exist that examine individual level risk factors for malaria. For example, there is strong evidence that age, gender, bed net usage, employment type, knowledge of malaria, and migration patterns are associated with malaria incidence (Peterson, Borrell, El-Sadr & Teklehaimanot, 2009). Using this information, and this information only, the most widely methods of malaria prevention suggested by health authorities to those living in low-resource, endemic malarial regions are the use of bed-nets and maybe indoor residual household spraying. On an individual level, "personal vector control" (bed nets, mosquito repellent, and avoidance of mosquitoes during the peak biting times of the *Anopheles* mosquito) can be very effective in reducing ones' risk of malarial infection if followed diligently on a daily basis (Martens & Hall, 2000). But even with the most consistent usage, the degree of efficacy of such personal protective methods may still differ greatly for each individual depending on a wide range of other factors including those beyond the control or outside the "scope" of the individual. (Not to mention that

in some of the most resource-limited environments, even the most highly effective or cost-efficient interventions may not be deliverable to all, if any, of those in need). While, individual level data is incredibly important in understanding malaria transmission, it does not fully describe the underlying parasite - mosquito – human relationship, nor does it provide all the necessary information in which to guide future efforts directed at combating transmission.

1.4 Supra-Individual Level Risk Factors

Equally important as the individual risk factors - and much more influenced by culture, regional and household economics, geographic location, and community support mechanisms - household and community level indicators are also associated with malaria transmission (Diez-Rouz, 1998; Mauny, Viel, Handschumacher, & Sellen, 2004). These "supra-level" risk factors provide the context in which malaria exists and may be key to understanding why malaria affects individuals differently. Location of households to vector breeding sites (Graves et al, 2009; Vittor et al., 2009), household SES status, and regional conflict are just a few examples (Messina et al., 2011). Others include the number of people or children living in the house, housing material type, education levels of heads of households, presence of livestock near home, etc. (Roberts et al., 1996). Risk factors at the community level that have been identified include: access to health resources and markets (Tanner & Vlassoff, 1998), the percentage of the population over age forty-five, and community wide fumigation campaigns (Peterson et al., 2009). Viewed concurrently with the individual level outcome of interest, supra-individual risk factors can be incredibly informative; for, it is well documented that social context can greatly affect ones' health and ones' health outcomes (Duncan, Jones, & Moon, 1993).

1.5 Importance of Considering Individual and Supra-Individual Risk Factors Concurrently

Depending on a study's objective, failure to consider covariates at the supra-individual level in conjunction with individual covariates can lead to an inadequate understanding of how and why transmission occurs. If the findings of an individual level study are interpreted wrongly, one may commit the Individualistic Fallacy, or "the fallacy of using individual-level observations to make inference on a higher, aggregated level" (Silver, 2000). By wrongly interpreting such results, the complex household and community level processes that also affect the heterogeneity of malarial risk in individuals can be lost (Guthman et al., 2001).

Studies that examine risk factors for disease only at the "supra-individual" level (i.e. household, neighborhood, community) are also at risk of committing additional fallacies similar in nature to the Individualist Fallacy. The Ecologic Fallacy occurs when aggregated level measures (like those at the community level) are inferred to accurately reflect an individual's risk of outcome (Blakely & Woodward, 2000), which disregards the heterogeneity that exists between individuals within every community. Clearly, not all individuals within a group are identical to the point in which their risk of outcome represents all others (Ecologic Fallacy), nor are higher-level grouping inclusive enough that their risk represents all (Individualistic Fallacy).

1.6 How Might the Ecologic and Individualistic Fallacy Affect our Interpretation of Study Results?

In their study, "Health Risk Behaviors and Health Perceptions in the Peruvian Amazon," Nawaz, Rahman, Graham, Katz, & Jekel (2001) found that men were not only more likely to report having malaria than females, but also that females who did report having malaria were much less likely to have received treatment than men who reported a malaria episode. The findings by Nawaz et al. are informative because they expose the gender differences in health

reporting behaviors *and* treatment seeking behaviors. Imagine how limited the results could have been had Nawaz et al. failed to consider gender - an individual level covariate that is likely to be considered in even the most basic of epidemiologic research – into their study. The conclusion at the aggregate level would miss entirely the heterogeneity of risk that existed between males (by underestimating their risk) and females (by overestimating their risk) in the same community - an Ecologic Fallacy and classic confounding problem.

If, however, Nawaz et al. had assumed everyone in the community had equal access to the community treatment facility they may have very well assumed that both men and women visited the health facility with equal frequency, and as a consequence, the heterogeneity of treatment seeking behavior at the individual level (based on a community level measure) would have been lost - the Individualistic Fallacy. It must be noted that Nawaz et al. was chosen purely for the simplicity in pointing out where analytical fallacy *can* occur, not because Nawaz et al. attempted to draw greater conclusion than their study design allowed. Put simply, by taking analytical approaches with limited emphasis on the multiple levels of covariates that affect ones' disease risk or by applying the results of a study too broadly or too narrowly can lead to faulty understanding of study's results.

1.6 Multilevel Modeling

Multilevel models (also referred to as hierarchical models or random effects models) are a proven, statistical technique that can be applied to complex data containing nested variables, or variables that are hierarchical in nature (Leyland & Groenewegen, 2003). The purpose of multilevel modeling is to "analyze simultaneously the influence of individual factors and environmental factors" affecting a particular outcome of interest (Mauny et al., 2004). Used originally in the social sciences - when researchers sought to explain variations in test scores

between children in different classrooms and different schools - multilevel modeling use has been increasing public health research over the past ten years (Mauny et al., 2004). Much of the increasing use of multilevel modeling is due to the advances in computing power and statistical packages such as Stata (StataCorp LP, College Station, TX), SAS (SAS Institute Inc., Cary, NC), and SPSS (SPSS Inc., Chicago, IL) that allow researchers to examine the complex relationships affecting their outcomes of interest simultaneously.

Mauny et al. (2004) called for the usage of multilevel modeling for malaria studies in their article "Multilevel modeling and malaria: a new method for an old disease." Modeling malarial risk using a hierarchical structure, as the authors saw it, was a natural extension of the methodology used by social scientists, because parasitological diseases, like malaria, are influenced by a range of factors "defined at different levels." The use of multilevel modeling techniques allows researchers to understand the influences and variations of effects between all nested factors (individuals nested in households nested in communities) concurrently, and thus, allowing researchers to more precisely define any interactions taking place between the various levels.

1.7 Malaria Clustering

Infectious diseases, including vector-borne parasitic infections, often present themselves in what has been called the eighty-twenty rule, or the phenomena where the overwhelming majority of a disease burden or transmission potential (approximately 80%) is located within a small subset of a population (approximately 20%). Multilevel modeling has become an increasingly used tool for understanding malaria clustering within various spatial paradigms. For example, Roberts et al. (1996) found evidence of clustering in Belize where 8% of the households harbored 50% of the malaria burden. In the highlands near Tigray, Ethiopia, 50% of malarial

cases were found in just 18% of the houses (Ghebreyesus et. al, 1999), driving home the argument that an individual's risk of malaria is driven by factors beyond the individual personal characteristics.

According to Woolhouse et al., (1997) "the [eighty-twenty] rule implies that control programs targeted at the 'core' 20% group are potentially highly effective and, conversely, that programs that fail to reach all of this group will be much less effective than expected in reducing levels of infection in the population as a whole." Carter, Mendis, & Robert's (2000) WHO bulletin, "Spatial Targeting of Interventions Against Malaria" demonstrates that a household spraying intervention targeting households most at risk of malaria infection first, and continuing on to the next highest risk households second and so on, can be much more efficient compared to a intervention randomly introduced across the larger population subset. According to the authors, what could be achieved with a campaign targeted at 8%, 18%, and 75% of targeted households in the Ethiopian highlands would be accomplished with 18%, 50%, and 91% treatment coverage, respectively, if treatment were to be randomized across all households.

Common to both Belize and the Ethiopian highlands is that malaria exists in a hypoendemic state**.** Defined years ago by Metselaar and Van Thiel (1959), hypoendemic malaria is as a situation where malaria prevalence is < 10%. Today hypoendemic malaria is better understood as an "unstable" malaria transmission state. Unlike highly endemic malaria settings - where the "super infection and exposure acquired immunity blur the proportional relationship between inoculation rates and case incidences" (Carter et al., 2000) - hypoendemic or low transmission settings make it much easier to pick up on disease clustering. This may explain why multilevel models have been used rather sparingly in malaria research as the majority of studies take place in areas with much higher, epidemic malaria levels. The distinction in the varying levels of endemicity that lend to the ability or inability to detect clustering when present is

important; as, it suggests that the most promising campaigns towards eliminating transmission are in low endemicity settings where variations of risk in individuals, households or specific communities may be easier to spot. Such may be the case in Northern Peru, where even in the most epidemic years (1995 -1998) malaria incidence has not reached levels regularly experienced in some parts of South East Asia or Sub-Saharan Africa (Guarda, Asayag, Witzig, 1999).

1.8 Study Objective

The goal of this study is to understand individual, household, and community level risk factors that may interact to explain malaria risk variation at different levels of malaria clustering.

2. Materials and Methods

2.1 Study Area

The study was conducted north of Iquitos, Peru, in 11 communities along 42 kilometers of the Iquitos – Mazan Road and 7 communities along 200 kilometers of the Napo River. All the communities are located within the Maynas Provincial District within the Department of Loreto. This region has a tropical climate with an average temperature of 27 degrees Celsius. Average yearly rainfall is approximately 2490 millimeters. The rains peak in March and are lowest in August. Malaria in Loreto is present all 12 months of the year with reports ranging from 3000 – 9000 cases monthly (Roshanravan et al., 2003).

2.2 Data Collection

During the month of August 2012, a group of trained interviewers visited study households as part of a routine surveillance. All individuals and households that participated in the study were given unique study identifiers used to link individuals to a particular household and community. All heads of households that were present when the field team visited their homes were asked questions from a standard form. Questions centered around household demographics, type and date of malaria infections, other illnesses, deaths, reproductive history, migration history, economic activities and government assistance. Furthermore, biometric data including anthropometrics, blood smear for malaria diagnosis, and blood drops to test the amount of hemoglobin for anemia screening were collected from all individuals present in the home and enrolled in the study. Spatial and environmental data included GPS household locations, environmental land use and climate. The following analysis is a cross-section of a three-year longitudinal study done in conjunction with Duke Global Health Institute (Durham, North Carolina) and PRISMA Benefica (Iquitos, Peru).

During this same period, the author met with community leader(s) from each community and, using a standard form, asked questions regarding the infrastructure present in the community, assistance received by the community or residents, and the cost to acquire and sell goods both in the community and at the nearest market. The author also recorded the GPS coordinates of all relevant infrastructures.

2.3 Study Participants

In 16 of the 18 communities surveyed, all households with individuals present at the time of surveillance were asked to participate. In the two largest communities, interviewers were instructed to choose a house at random to begin the surveillance, and from the chosen house, continue with neighbors on outward until 40 households had been surveyed. For the community-level survey, the author sought to speak with the community mayor, municipal agent, or lieutenant governor, and if none of the aforementioned were available, the longest residing community resident. Every effort was made to include more than one person in the survey and to have both a male and female participate.

Inclusion criteria for the data analysis included all persons aged ≥ 1 year whose malaria status from the previous six months were known at the time of the interview. Individuals with unknown malaria statuses were still accounted for in other covariate measures (i.e. the number of people living in the home).

2.4 Dependent Variable

The outcome of interest was the probability of having a self-reported malaria episode (*P. vivax* and/or *P. falciparum)* during the six-month follow-up surveillance. The dependent variable, malaria status, was coded as a binary dummy variable to represent either ≥ 1 malaria infections or 0 infections.

2.5 Individual Level Independent Variables

Age categories were created for participants aged 1-5, 6-14, 14-25, 25-49, and 50+ to correspond with socially important age groups in the region: not enrolled in school, enrolled in school, young adults, working age, & older individuals, respectively. Whether or not the individual had travelled to another community within the past six months was included as a yes-no dummy variable as was the gender variable *male*.

2.6 Household Level Independent Variables

Yes-no dummy variables were created for whether or not another individual in the household had visited a different community in the past 6 months, if the household was large (> 5 individuals), whether children (< 6 years of age) lived in the household, and whether another individual in the household had ≥ 1 malaria episodes in the previous six months. Using principal component analysis, an SES score was derived based on information about the household living conditions (housing wall-type, housing roof-type, housing floor-type, and presence of a household electricity) and the household assets (tv, radio, canoe, bike, motorbike, land telephone, mobile phone, refrigerator, sewing machine, gas cooker, coal cooker, and car). All households without a SES score (due to missing data) were given a value equal to their community mean SES score. The SES score was divided into quintiles so that SES quintile dummy variable could be used in the analysis.

2.7 Community Level Independent Variables

Yes-no dummy variables were created for the presence of pre-school and the presence of a primary school in each community. The presence of the health post and secondary school were perfectly correlated, so one variable was created to represent these variables simultaneously. Dummy variables were also created for the presence of a church, whether or not the community

was located directly on a river's edge, and if the time to nearest market was greater or less than 60 minutes.

2.8 Statistical Analysis

All statistical analyses were conducted using StataCorp, 2011. (Stata Statistical Software: Release *12*. College Station, TX: StataCorp LP.) First, univariate analyses were carried out by regressing single independent variables against the dependent variable. Based on the univariate analyses and hypothesized relationships, variables were coded for use (described above) in the multivariate analysis. Four models were run: an empty model with the dependent variable only, a model containing the dependent and individual level variables, a model containing the dependent and all individual and household level covariates, and a full-model containing the dependent and individual, household, and community level covariates. Models were run using Stata's `gllamm` (generalized linear latent and mixed models) command using 8-point adaptive quadrature.

The three-level random intercept logit model where individual *i* is nested in household *j* which are nested in community *k* is as follows (Rabe-Hesketh & Skrondal, 2005):

$$\text{logit}\ \{\text{PR}\ (y_{ijk} = 1 \mid x_{ijk}, \zeta_{\text{jk}}, \zeta_{\text{k}})\} = \beta_1 + \beta_2 x_{2ijk} + \ \ldots \beta_{11} x_{11k} + \zeta_{jk} + \zeta_k$$

ζ_{jk} = Random intercept for household *j* in community *k*
ζ_{k} = Random intercept for community *k*

Percentage of between models variance explained by each model was calculated as follows (Peterson et al., 2009):

$$((\Omega_a - \Omega_b) / \ \Omega_a) * 100$$

Ω_a = Random effect term from lower level model
Ω_b = Random effect term from higher level model

3. Results

The final sample included 1650 individuals (*i*) nested in 338 households (*k*) nested in 18 communities (*j*).

3.1 Individual Level

90 subjects (5.5%) self-reported 101 malaria incidences. 80, 9, and 1 subject reported 1, 2, and 3 incidences, respectively. Average age of individuals was 24.9 years (SD =19.9). The youngest participant was aged 1 and the eldest participant was aged 88 years. See Table 1. 1648 participants reported sleeping under a bed net the previous night. Two individuals did not report bed net usage. 14 of those who did sleep under a bed net (0.85%) reported that the bed net had been treated with insecticide.

Table 1: Individual Level Variables

	Individuals (N = 1650)	
	River (%)	Road (%)
	(n = 799)	(n = 851)
Individual Variables		
Gender		
Female	366 (46)	410 (48)
Male	433 (55)	441 (51)
Age Category		
Age 1 - 5	123 (16)	150 (17)
Age 6-14	204 (26)	179 (21)
Age 15-24	159 (20)	155 (18)
Age 25-49	216 (27)	221 (26)
Age 50+	97 (12)	146 (17)
Personal Travel		
No	585 (74)	715 (83)
Yes	214 (27)	136 (16)
Other Malaria in Household		
No	661 (83)	672 (78)
Yes	138 (17)	179 (21)
Family Travel		
No	303 (38)	487 (57)
Yes	496 (63)	364 (42)

3.2 Household Level

The average household size was 5.1 persons (SD = 2.4) with a range of 13 (1-14). On average there were 0.3 cases of malaria per household. See Table 2. Malaria was highly clustered. 6% of the malaria burden fell in just 54% of the houses. In total, 100% of the malaria burden occurred in just 67 (20%) of the households. See Figure 1.

Table 2: Household Level Variables

	Households (N = 338)	
	River (%)	Road (%)
	(n = 156)	(n = 182)
Household Variables		
HH Size		
≤ 5	19 (12)	31 (17)
≥ 6	137 (88)	151 (83)
Children Present		
No	59 (38)	72 (39)
Yes	97 (63)	110 (60)
SES Status		
Quintile 1	54 (35)	20 (11)
Quintile 2	49 (32)	15 (08)
Quintile 3	38 (25)	24 (13)
Quintile 4	8 (05)	65 (36)
Quintile 5	7 (05)	58 (32)

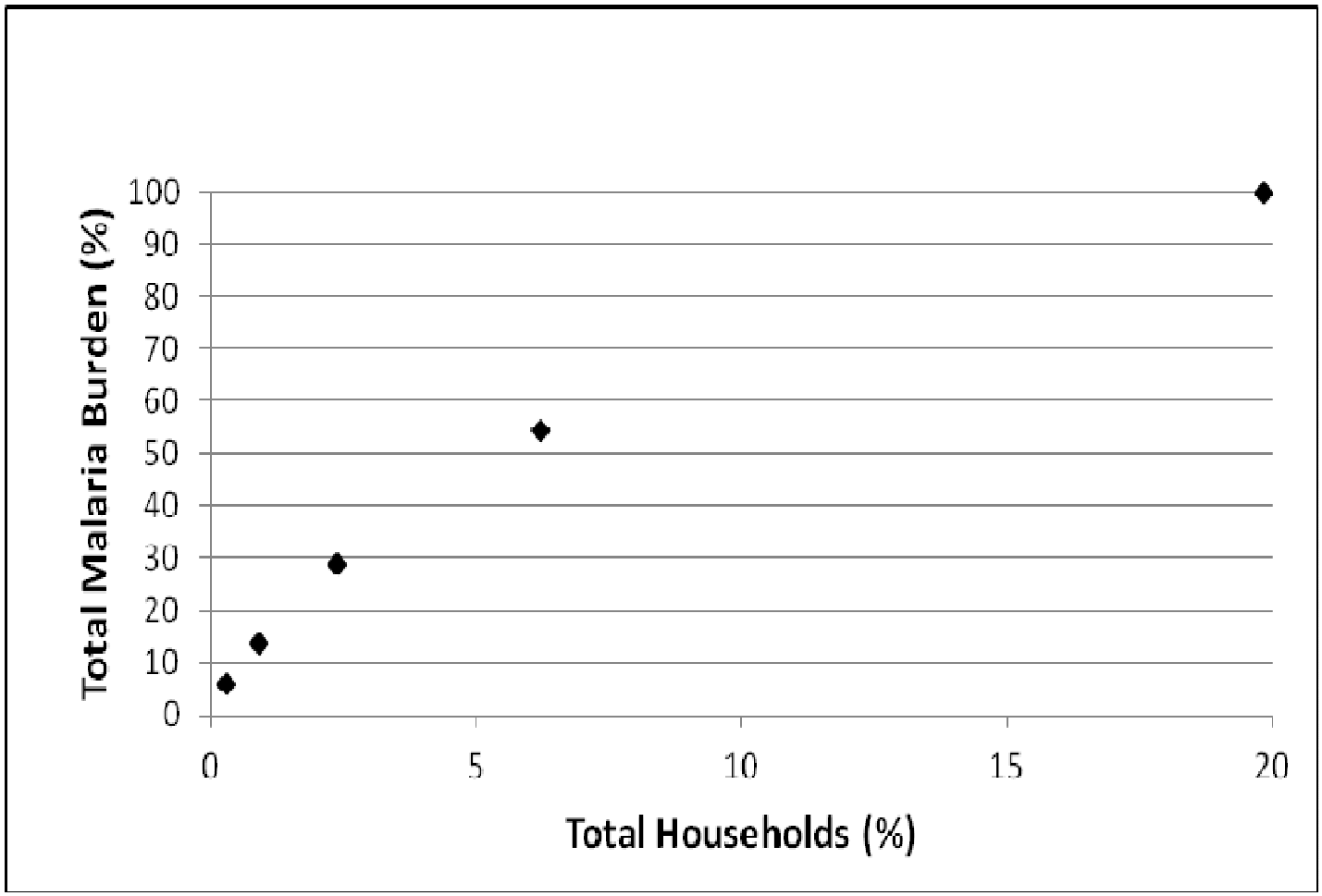

Figure 1: Malaria Clustering by Household

3.3 Community Level

The mean number of houses sampled per community was 18.7 (SD = 13.4) with a range of 48 (1-49). The mean number of participants sampled per community was 94.1 (SD =72.6) with a range of 208 (8 - 216). See Table 3.

Table 3: Community Level Variables

	Communities (N = 18)	
	River (%)	Road (%)
	(n = 7)	(n = 11)
Pre-school		
No	4 (57)	9 (82)
Yes	3 (43)	2 (18)
Primary School		
No	0 (00)	2 (18)
Yes	7 (100)	9 (82)
Secondary School/Health Post		
No	4 (57)	10 (91)
Yes	3 (43)	1 (09)
Church		
No	4 (57)	8 (73)
Yes	3 (43)	3 (27)
River		
No	0 (00)	7 (64)
Yes	7 (100)	4 (36)
Market Distance		
≤ 60 min	1 (14)	2 (18)
> 60 min	6 (86)	9 (82)

3.4 Final Model

See Appendix A – C for the following tables of results: Table 5: Univariate Analysis, Table 6: Individual Covariates Model, and Table 7: Individual & Household Covariates Model.

Using a p-value cutoff of 0.05, two individual level variables were significantly associated with higher odds of having at least one malaria episode: if the individual travelled in

the previous six months and if another individual in the house reported malaria. At the household level, household size (> 5 people) was associated with lower odds of having at least one malaria episode. At the community level, the presence of a church and the presence of a health post, were associated with having lower odds of having at least one malaria episode over follow up. See Table 4 for a full list of covariates and their respective odds ratios. For the reduction of household and community level variance accounted for by each the four models see Appendix D.

Table 4: Empty & Full Models

	Log Odds = β		Odds ratios = exp(β)		P-values
	Est	(SE)	OR	(95% CI)	
Empty Model Fixed Part					
β_1 [_cons]	-3.36	(0.33)	0.03	(0.02, 0.07)	0.000
Full Model Fixed Part					
Individual Level Covariates					
β_1 [_cons]	-3.25	(1.16)	0.04	(0.00, 0.38)	0.005
β_2 [Age 6 -14]	0.95	(0.46)	2.58	(1.05, 6.35)	0.039
β_3 [Age 15-24]	0.49	(0.48)	1.64	(0.64, 4.19)	0.301
β_4 [Age 25-49]	0.65	(0.46)	1.91	(0.77, 4.72)	0.163
β_5 [Age 50+]	0.19	(0.56)	1.21	(0.41, 3.59)	0.735
β_6 [Male]	0.00	(0.23)	1.00	(0.63, 1.58)	0.993
β_7 [Individual Travel]	0.91	(0.27)	2.48	(1.46, 4.21)	0.001
β_8 [Other Family Member with Malaria]	0.93	(0.27)	2.54	(1.49, 4.32)	0.001
β_9 [Other Family Member had Travelled]	-0.01	(0.27)	0.99	(0.58, 1.70)	0.983
Household Level Covariates					
β_{10} [Large Family]	-1.11	(0.53)	0.33	(0.12, 0.93)	0.035
β_{11} [Kids Living in Home]	-0.27	(0.29)	0.77	(0.43, 1.36)	0.360
β_{12} [SES Quintile 2]	1.03	(0.41)	2.79	(1.24, 6.27)	0.013
β_{13} [SES Quintile 3]	0.44	(0.47)	1.56	(0.62, 3.93)	0.349
β_{14} [SES Quintile 4]	0.91	(0.49)	2.47	(0.95, 6.44)	0.064
β_{15} [SES Quintile 5]	1.02	(0.50)	2.76	(1.04, 7.36)	0.042
Community Level Covariates					
β_{16} [Pre-school]	1.11	(0.68)	3.02	(0.80, 11.45)	0.103
β_{17} [Primary School]	0.65	(0.81)	1.92	(0.39, 9.34)	0.421
β_{18} [Secondary School / Health Post]	-1.35	(0.57)	0.26	(0.08, 0.80)	0.018
β_{19} [Church]	-1.10	(0.44)	0.33	(0.14, 0.78)	0.012
β_{20} [River]	-0.48	(0.37)	0.62	(0.30, 1.26)	0.186
β_{21} [Distance to Market > 60 min]	0.03	(0.46)	1.04	(0.42, 2.55)	0.940

4. Discussion

The study used a multilevel modeling tool to identify individual, household, and community level indicators associated with having a malaria episode over the six month follow-up period (February – July 2012) in rural Loreto, Peru. In the final model, personal travel and living with someone who reported a malaria incidence were associated with higher odds of a malaria episode. The presence of a church and secondary school/hospital in the community were associated with lower odds of having malaria as was sharing a house with more than 4 other individuals. Evidence of malaria clustering at the household level existed.

The simultaneous inclusion of individual, household, and community level covariates into the hierarchical model was important to better characterize malaria risk for individuals in the study area. The presence of a primary school and children living in the home were both significant in the univariate analysis but were no longer significant once included in the full model. However, the presence of a church, hospital/secondary school, individual travel, and other malaria in the home remained highly significant in the full model confirming their strong relationship with malaria risk and the need for more multilevel modeling in future research. The final full-model accounted for 100% of between household variance and nearly 87% of the between community variance.

One of the strongest associations with malaria risk was personal travel. Travel and migration have both been associated with higher reported malaria incidence in previous studies. In this region of Peru, the main occupations are farming and logging. Both occupations require individuals to travel away from their homes and to work in areas with recently cleared forest –the same location that the main mosquito vector in the region, *A.darlingi*, prefers to live and breed. Loggers in particular often stay at their work site for multiple weeks. It is likely many of the loggers are without bed nets during their time spent at logging camps. They also lack easy access

to health resources during this time, as many of the logging sites are days or weeks away from their homes by boat. It is important to note that gender was not significant. While some loggers and farmers will take their wives and children with them when they travel to worksites, if this accounts for the reasonably equal malaria rates between men and women remains to be seen.

Our study identified clustering of malaria at the household level, which was confirmed in our model. One conclusion drawn by Branch et al. (2005) is that individuals within the home are contagious to their family members as well as those living in nearby houses. This too, could explain near equal male and female malaria rates, if male workers are responsible for bringing malaria into the home. In small communities such as these, and considering *Anopheles* mosquitoes can fly upwards to 7 km, it is unclear as to whether residing with someone with malaria would put one at greater risk than, say, having a neighbor who is infected. It could very well be that all those in the household are more susceptible for reasons not accounted for in the multilevel model, such as distance of house from a mosquito breeding site or education levels of the heads of household. Controlling for education would also give more weight to the notion that self-reporting is an accurate measure of malaria status for all individuals.

Furthermore, the degree in which the clustering occurred remains to be determined fully. While having 100% of a disease burden in 20% of the homes in an important finding this phenomenon is also a function of the level at which a disease is present in the population. In this particular study, only 101 cases of malaria were present in the 338 houses surveyed, meaning with absolutely zero clustering at the household level, 30% of the burden would have been found in 100% of the houses. How much greater the clustering of malaria was than what would occur randomly is undetermined at this time.

The presence of a health post/secondary school in ones' community of residence decreased the odds of having a malaria episode. Health posts/secondary schools were located in

four of the five biggest communities in our sample. Access to a health post could imply easier access (and faster symptom to treatment time) for individuals with malaria. Proper treatment not only prevents relapses in *P. vivax* infections (as *P. vivax* has the ability to sit dormant in the liver and occur at later periods), but also lessens the time the individuals would be considered "contagious" to all others. The decreased odds could also be associated with how with the convenient sampling was conducted in 2 of the communities, or simply a result of not accounting for community population.

The presence of a church and having a large household (> 5 individuals living in the home) were both associated with lower odds of malaria infection. The relationship here is more unclear. Church and large family structure could be indicators of stronger social networks for the individuals and communities. These could then translate into better/easier access to resources. Clearly, a closer examination as to why these are significant is warranted.

4.1 Study Strengths

The study was one of the first multilevel models used to examine malaria risk in Peru or South America. The large variations between communities and low malaria transmission made it an ideal place to conduct the study and to examine clustering. To the knowledge of the author, few studies, if any, look at the presence of infrastructure and its association with malaria risk. The strong relationship between field team members, and the routine nature of the study, likely helped in gaining acceptance in the households, access to community leaders, and ultimately, accurate reports of behavior.

4.2 Study Limitations

The study relied strictly on self-reported measures. It is unclear if malaria incidences are likely to be over-reported or under-reported compared to the actual number of cases or cases

reported to a health facility. Nor is it certain whether or not individuals are likely to misreport their malaria status randomly if ones' education level would play a key role. Unfortunately, at the time of analysis, education information on the heads of household was not available. Due to the information available and coding of the variables, any temporal relationships that existed between malaria incidences and covariates such as travel or malaria status of other individuals were lost. The lack of education and employment information are likely to be partially accounted for through SES score and perhaps travel history. Lastly, incomplete information on animal possession at the time of analysis prevented its inclusion into the principal component analysis for SES.

4.3 Conclusions & Implications for Future Research

The use of a multilevel model is an enhancement to previous models in the region. By better defining who may be at a greater risk and the varied socio and socio-environmental context in which these individuals reside is important if future interventions are to more efficiently and effectively target those at the greatest risk within the larger population. However, this study is just the beginning in that it identified many, but not all, factors associated with malaria risk. Future studies should look to account for important, yet missing, covariates from the study's final model including employment, temporal trends in travel and their relation to malaria, as well as temporal trends in other house member's malaria statuses.

This study examined risk factors over the previous six months. While many covariates were significant in this particular study, whether or not the same covariates would remain significant in data from other years remains to be seen. Including data from multiple years would give better indication of what factors are significant over a longer time frame.

Lastly, behind each of the covariates and the respective odds for malaria incidence is a much more complex picture that needs to be examined – especially at the community level. Now that infrastructure has been identified as a factor that could be acting on disease transmission it must be looked at in greater detail. For example, can it be determined what characteristics are unique about a community with a church that influences malaria prevalence in each setting. As it is very unlikely the church is more than an indicator for something else that is acting more directly on malaria in the community. Ultimately, by better characterizing communities and households – and not just individuals – we can then begin to compare socio contextual trends and infrastructure commonalities across malaria zones. These could be key in strengthening the effect of current malaria interventions.

Appendix A

Table 5: Univariate Analysis

	Log Odds		Odds ratios		P-values
	Est	(SE)	OR	(95% CI)	
Age 6 - 14	0.93	(0.44)	2.54	(1.08, 5.98)	0.033
Age 15 - 24	0.95	(0.45)	2.59	(1.08, 6.21)	0.034
Age 25 - 49	0.84	(0.43)	2.31	(0.98, 5.41)	0.055
Age 50+	0.84	(0.47)	2.32	(0.92, 5.85)	0.074
Male	0.11	(0.22)	1.12	(0.73, 1.71)	0.613
Individual Travel	0.92	(0.23)	2.52	(1.62, 3.91)	0.000
Other Family Member with Malaria	1.21	(0.22)	3.36	(2.17, 5.20)	0.000
Other Family Member had Travelled	0.19	(0.22)	1.21	(0.79, 1.86)	0.375
Large Family	-0.98	(0.36)	0.38	(0.19, 0.76)	0.006
Kids Living in Home	-0.52	(0.22)	0.60	(0.38, 0.92)	0.021
SES Quintile 2	1.06	(0.38)	2.90	(1.36, 6.17)	0.006
SES Quintile 3	0.37	(0.42)	1.45	(0.64, 3.31)	0.376
SES Quintile 4	0.96	(0.38)	2.62	(1.23, 5.56)	0.012
SES Quintile 5	0.67	(0.40)	1.96	(0.89, 4.30)	0.095
Pre-school	-0.51	(0.22)	0.60	(0.39, 0.92)	0.018
Primary School	-0.10	(0.61)	0.90	(0.27, 2.95)	0.863
Health Post / Secondary School	-0.76	(0.23)	0.47	(0.30, 0.74)	0.001
Church	-0.76	(0.22)	0.47	(0.30, 0.72)	0.001
River	-0.10	(0.25)	0.91	(0.56, 1.48)	0.701
Distance to Market > 60 min	-0.16	(0.28)	0.85	(0.49, 1.48)	0.566

Appendix B

Table 6: Individual Covariates Model

	Log Odds = β		Odds ratios = exp(β)		P-values
	Est	(SE)	OR	(95% CI)	
Empty Model Fixed Part					
β_1 [_cons]	-3.36	(0.33)	0.03	(0.02, 0.07)	0.000
Individual Level Model Fixed Part					
Individual Level Only					
β_1 [_cons]	-3.96	(0.98)	0.02	(0.00, 0.05)	0.000
β_2 [Age 6 -14]	0.99	(0.45)	2.68	(1.10, 6.49)	0.029
β_3 [Age 15-24]	0.61	(0.47)	1.84	(0.73, 4.62)	0.195
β_4 [Age 25-49]	0.76	(0.46)	2.15	(0.88, 5.23)	0.092
β_5 [Age 50+]	0.80	(0.49)	2.22	(0.85, 5.80)	0.104
β_6 [Male]	0.01	(0.22)	1.01	(0.64, 1.58))	0.968
β_7 [Individual Travel]	0.94	(0.26)	2.55	(1.52, 4.26)	0.000
β_8 [Other Family Member with Malaria]	0.96	(0.25)	2.61	(1.60, 4.27)	0.000
β_9 [Other Family Member had Travelled]	-0.26	(-0.26)	0.77	(0.46, 1.27)	0.305

Appendix C

Table 7: Individual & Household Covariates Model

	Log Odds = β		Odds ratios = exp(β)		P-values
	Est	(SE)	OR	(95% CI)	
Empty Model Fixed Part					
β_1 [_cons]	-3.36	(0.33)	0.03	(0.02, 0.07)	0.000
Individual and Household Fixed Part					
Individual Level Covariates					
β_1 [_cons]	-3.63	(0.76)	0.03	(0.01, 0.12)	0.000
β_2 [Age 6 -14]	0.94	(0.46)	2.55	(1.03, 6.32)	0.043
β_3 [Age 15-24]	0.52	(0.48)	1.68	(0.65, 4.31)	0.279
β_4 [Age 25-49]	0.65	(0.47)	1.91	(0.77, 4.76))	0.164
β_5 [Age 50+]	0.27	(0.55)	1.31	(0.44, 3.88)	0.625
β_6 [Male]	0.03	(0.23)	1.03	(0.64, 1.62))	0.910
β_7 [Individual Travel]	0.81	(0.27)	2.26	(1.33, 3.82)	0.002
β_8 [Other Family Member with Malaria]	0.87	(0.27)	2.39	(1.42, 4.04)	0.001
β_9 [Other Family Member had Travelled]	-0.15	(-0.27)	0.86	(0.50, 1.46)	0.570
Household Level Covariates					
β_{10} [Large Family]	-0.87	(0.52)	0.42	(0.15, 1.15)	0.092
β_{11} [Kids living in home]	-0.32	(0.29)	0.72	(0.41, 1.27)	0.259
β_{12} [SES Quintile 2]	1.14	(0.44)	3.11	(1.32, 7.31)	0.009
β_{13} [SES Quintile 3]	0.65	(0.49)	1.91	(0.73, 4.95)	0.185
β_{14} [SES Quintile 4]	1.13	(0.49)	3.11	(1.19, 8.09)	0.020
β_{15} [SES Quintile 5]	1.19	(0.52)	3.30	(1.19, 9.18)	0.022

Appendix D

Table 8: Household Level Random Effects & Between Model Variance Reduction

			Percentage Reduction From:		
Model	Random Effect	(SD)	Empty Model	Individual	Individual + Household
Empty	1.29	(0.56)	0.00	-	-
Individual Only	1.60E-16	(2.22E-08)	100.00	0.00	-
Individual + Household	7.12E-22	(2.21E-11)	100.00	100.00	0.00
Individual + Household + Community	1.70E-19	(3.75E-10)	100.00	99.89	-23751.02

Table 9: Community Level Random Effects & Between Model Variance Reduction

			Percentage Reduction From:		
Model	Random Effect	(SD)	Empty Model	Individual	Individual + Household
Empty	0.76	(0.44)	0.00	-	-
Individual Only	0.49	(0.28)	35.30	0.00	-
Individual + Household	0.59	(0.34)	22.68	-19.51	0.00
Individual + Household + Community	0.10	(0.16)	86.64	79.34	82.71

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