AN AGENT BASED MODEL TO ASSESS MALARIA TRANSMISSION DRIVERS IN THE ECUADORIAN AMAZON

by

Maria Liseth Velasco Delgado

Dr. William Pan, Advisor

April 24th, 2020

Masters project submitted in partial fulfillment of the requirements for the Master of Environmental Management degree in the Nicholas School of the Environment of Duke University

ABSTRACT

Through intensive malaria control initiatives, Ecuador almost eradicated malaria. Recent data shows that between 2015 and 2018 malaria cases quadrupled in indigenous communities in the Amazon region bordering the Peruvian Amazon, with trends similar to the increased incidence in Peruvian indigenous communities. Studies show that malaria transmission is spatial, and infections occur in high transmission areas where hosts and vectors move through geographical barriers. A series of agent-based models were developed to assess the drivers of malaria transmission in six Achuar indigenous communities. The models are then used to test the effectiveness of a malaria control intervention using bed nets. To understand movement behavior this study surveyed 48 Achuar households in 2019 and compared it to data from 63 households from 2016. As expected, the agent-based simulations show that malaria incidence is influenced by local-scale human movement and bed net interventions have an effect in decreasing malaria risk.

EXECUTIVE SUMMARY

Malaria cases in the Ecuadorian Amazon have increased since 2015, with trends corresponding to outbreaks in the Peruvian Amazon. The purpose of this study is to understand the factors that are driving an increase in malaria cases in the Achuar indigenous territory in the Pastaza province in the Ecuadorian Amazon near the border with the Peruvian Amazon. This is the first research project that focuses on the Achuar indigenous people in Ecuador.

To understand the behaviors that increase the risk of malaria transmission, we visited six Achuar indigenous communities during the summer of 2020. We adapted a survey from a 2016 survey elaborated by researchers from the Universidad San Francisco de Quito (USFQ) and randomly selected survey participants in each of the visited communities. Each survey collected: (i) education and occupation information for each member of the household; (ii) movement information for travel with a motive for leisure and visiting family, for education purposes, and work; and (ii) information on malaria cases for everyone in the family, including movement information if traveled three months prior diagnosis. We also obtained data from surveys administered in 2016 by USFQ researchers. Survey results were then analyzed using RStudio version 1.2.5019 to assess changes in malaria prevalence over time, the effect of human movement on malaria cases, and the effect of education on malaria control. Since malaria transmission is spatial and uneven, an Agent Based Model (ABM) was developed using parameters based on results from data analysis. The purpose of the ABM is to simulate malaria transmission dynamics in small communities and assess the effectiveness of intervention strategies. An ABM was chosen for this analysis because it allows for accounting for a high level of individual details from small datasets.

In total, our dataset included information from 327 people distributed in 45 households in six communities in 2019, and 325 distributed in 52 households in four communities in 2016. Most men in the study area work in fishing and agriculture and women usually take care of the land around the house and the children. Our dataset also included information for 143 travel events in

2019. We obtained information for 102 malaria cases in 2019 and 77 malaria cases in 2019. We observed that malaria prevalence increased for most communities in the study area between 2016 and 2019. We assessed the relationship between travel to Peru and malaria risk per family, but no significant relationships were observed. However, people in 2019 crossed the border with Peru more than people in 2016. We also observed no significant effect of the education of women on reducing malaria cases. Through ABM simulations we observed that intervention strategies with insecticide-treated bed nets could be a useful approach for malaria control if used effectively. Cumulatively, results suggest that malaria cases have increased in the past three years, as well as human movement between communities, and this relationship should be further studied in future research.

BACKGROUND

At present there are 91 countries with active malaria transmission, which can be translated to approximately 3,200 million people actively exposed to malaria. The majority of cases and deaths have been reported in Sub-Saharan Africa, but Latin American are also affected (WHO, 2017).

In 2015 the World Health Organization classified Ecuador to be in the pre-elimination stage for malaria, after almost eradicating malaria between 2000 and 2014, decreasing the number of cases from 104,528 to 241 (WHO, 2016). In indigenous communities, Ecuador reported a decrease of cases between 2013 and 2014, from 544 to 368 cases. The decrease of malaria incidence with respect to the year 2000 was remarkable, making Ecuador one of the countries with the most significant trends in malaria burden decline in the Amazon region.

The introduction of tools such as insecticide-treated bed nets (ITNs), rapid diagnostic tests, and artemisinin-based combination therapy (ACT) successfully decreased malaria incidence and mortality worldwide (WHO, 2016b). International financing accounted for 78% of funding for malaria control in endemic countries in between 2005 and 2014. In 2013 the Global Fund contributed a million dollars to malaria control in Ecuador, while the Ecuadorian government invested an extra two million (WHO, 2015). However, in 2016 and following years international financing for malaria control in Ecuador was nonexistent (WHO, 2019).

After several years of low malaria incidence, the Ecuadorian government disintegrated the “Servicio Nacional de Control de Malaria”, the department in charge of eradicating malaria in the country. This department had heavily focused in the following fundamental aspects: early diagnosis, treatment of cases, control of anopheles population, and strengthening community epidemiological surveillance and community education (SNEM 2013, 22). After the closure, recently formed health districts received prevention and control responsibilities not only for malaria but for other vector borne diseases, such as Dengue, Zika, and Chikungunya (Mosquera et al., 2018). Shortly after, in 2015, malaria cases started to increase, and in 2016 a total of 1,191 confirmed cases were reported, increasing to 1,806 confirmed cases in 2018 (WHO, 2019).

In the past decade Ecuador also observed an increase in imported cases, a person who was infected while traveling outside the area of diagnosis, from 10 in 2013 to 153 in 2018 (WHO, 2019). Imported cases, from national or international migration, have recently become more problematic and lead to a faster transmission of infectious diseases. Migration, along with social and ecological factors, allows for malaria to be observed in non-endemic areas.

In recent years, similar trends have been observed between an increase in malaria incidence in indigenous communities in the central Ecuadorian Amazon region and human movement to and from indigenous communities in the Peruvian Amazon. In 2018, three provinces in the Amazon region had the highest malaria incidence per 1000 inhabitants. The province of Pastaza had the highest incidence at 2.3, followed by Orellana and Morona Santiago with incidences of 1.8 and 1.4 respectively (MSP, 2018). In the first seven months of 2018, a total of 255 confirmed cases of malaria were reported, with 243 being *P. vivax* and 12 being attributed to *P. falciparum* (MSP, 2018).

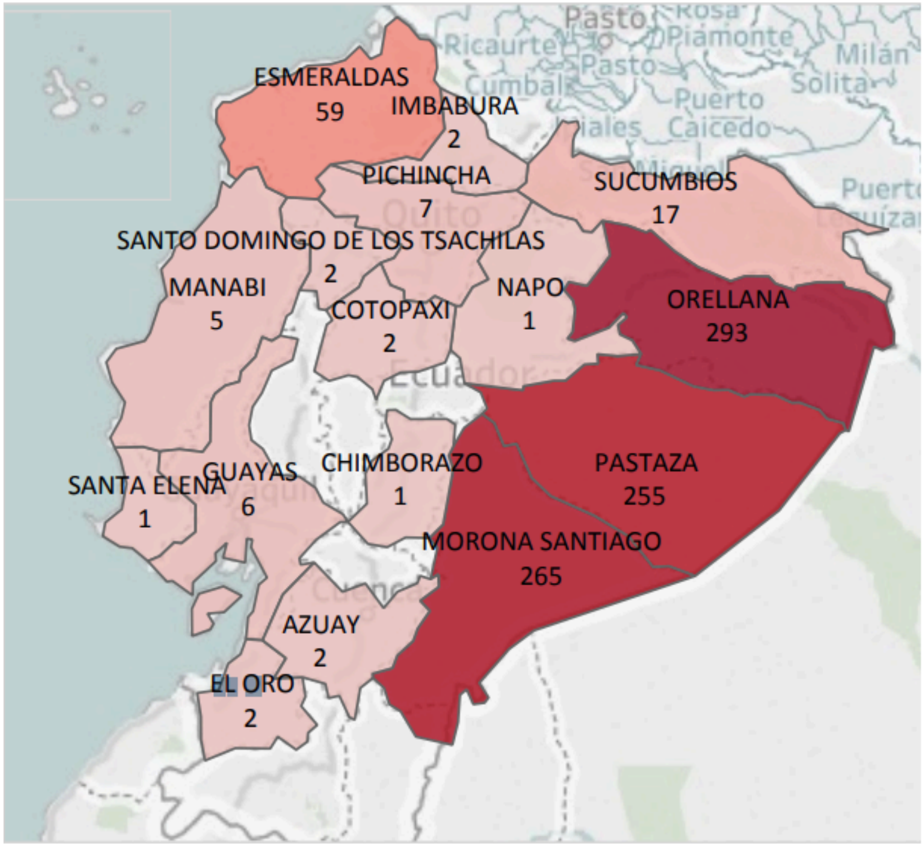

Figure 1. Confirmed cases of malaria per province in Ecuador for the epidemiological week 31/2018. Retrieved from (MSP. 2018)

In general, this study is motivated by a lack of research in malaria transmission in Ecuador. When searching "Malaria in Ecuador" through the Duke University Library Database, a total of 1,197 results for peer-reviewed publications appear since 2016, however most of these are descriptive studies focusing on risk factors associated with malaria, along with its prevalence. Narrowing down the search to a more specific group incorporating the words "indigenous communities" results in only 214 studies since 2016, most of them focusing again on risk factors in indigenous communities. However, no previous studies have focused on transmission in the Ecuadorian Achuar territory, which accounts for more than 90% of cases in Ecuador (MSP, 2018).

This study follows the guidelines established by the anthropologist Dr. Eduardo Menendez and Dr. Young, who define the process of infectious disease research as a composite of social relationships Menendez states that the objective of an infectious disease researcher is to understand the social and cultural drivers not just of the disease, but surrounding the disease (Menendez, 2001). Young, in his paper "The anthropologies of illness and disease" proposes diseases to be studied under three dimensions: 1) the biological dimension of disease, 2) the cultural dimension of disease, and 3) the social relationships surrounding the disease (Young 1982, 11:8).

To objective of this research project is to answer questions that arise from a lack of previous research, specifically to answer questions that seek to understand the dynamics that have allowed malaria transmission to increase, including: How has human movement between Achuar communities within Ecuador and across the Ecuador-Peru border influence malaria transmission?

INTRODUCTION

Malaria

Malaria is a vector-borne disease caused by a parasite of the *Plasmodium* group and transmitted by female Anopheles mosquitoes. There are five parasite species of *Plasmodium, P. knowlesi, P. ovale, P. malariae, P. falciparum, and P. vivax* (Recht et al., 2017). The last two parasites, *P. vivax and P. falciparum* are responsible for the majority of the malaria cases in the Amazon.

The malaria parasite has a complex lifecycle that involves a human host and the Anopheles mosquito. For *Plasmodium* to infect a host, the parasites need to go through a complex 14-16-day development cycle inside a mosquito. After a female consumes a blood meal infected with the parasite, it ingests gametocytes that will turn into gametes in the insect's midgut and 16-20 hours later the gametes will transform into motile ookinetes. Approximately 24 hours after an infected blood meal, the ookinetes will cross the midgut epithelium and reach the basal side of the midgut. In the following 10 days the ookinetes will reproduce through meiosis and produce thousands of sporozoids, which will mature and migrate to the salivary glands, ready to infect a new host following blood feeding (Blandin et al., 2004) (Fig 2).

The human stages develop after an infected female Anopheles mosquito injects approximately 10-100 sporozoites into the human host. Within 30 minutes the sporozoites will migrate to the liver and will start replicating into hepatocytes for approximately 2-10 days. Replicated hepatocytes release thousands of merozoites that will then enter the bloodstream and invade red blood cells. In the blood, merozoites divide into schizonts over a period of days. Rupture of infected blood cells containing schizonts result in malaria-like symptoms such as fever and release of new merozoites. Merozoites from ruptured schizonts then enter new blood cells and the process is repeated, producing fever cycles in the host (Pouniotis et al., 2004) (Fig 2).

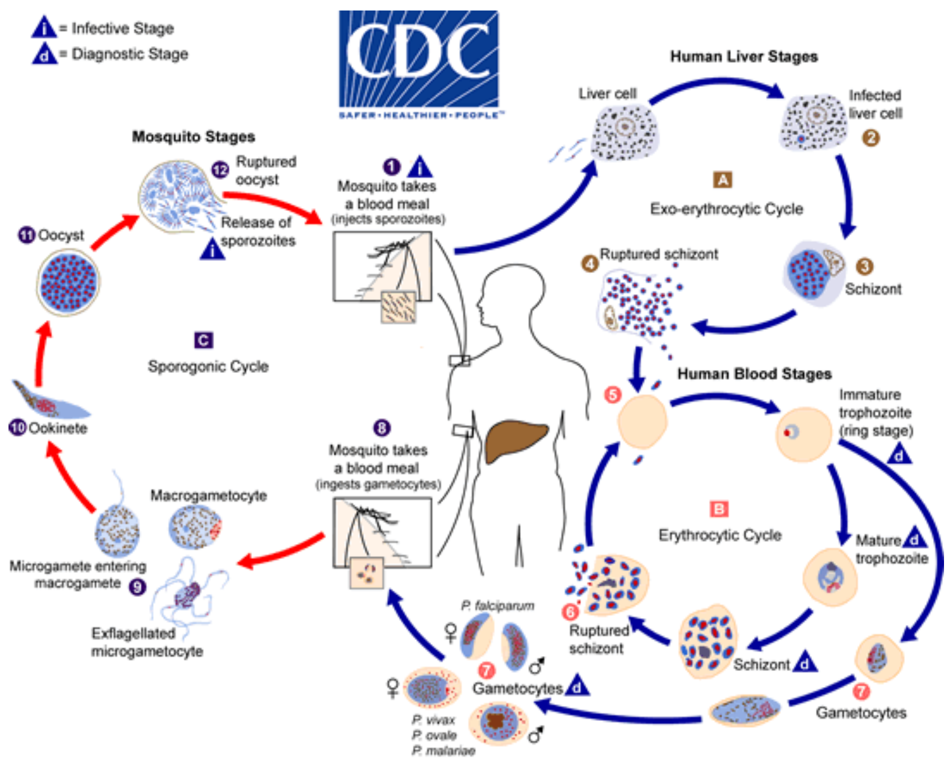

Figure 2. Plasmodium life cycle (CDC, 2019)

According to the WHO, in 2017 *P. Falciparum* caused 99.7% of malaria cases in Africa, and most of the cases in Asia and the Middle East. In the Americas, *P. vivax* caused 74.1% of the cases in 2017. *P. vivax* compared to *P. falciparum* is more resilient to lower temperatures and higher altitudes (WHO, 2017).

P. falciparum has long been associated with more severe disease, and higher mortality and morbidity. However, contrary to common belief, *P. vivax* can be as severe as *P. falciparum*, especially because its faster growth capacity in mosquitoes and the presence of hypnozoites that allow for the parasite to stay dormant in the liver, allow for relapses and high transmission (Recht et al., 2017).

Malaria is endemic to tropical and subtropical regions. From and environmental perspective, malaria transmission is influenced by warm temperatures, humidity, rainfall, and presence of ambient water bodies. Studies have also shown clusters of malaria transmission, considered “hot spots” (Parker et al., 2013). In low-transmission areas, such as the Ecuadorian Amazon, malaria hot spots have been observed in proximity to forests, swamps, rice fields and other agricultural fields, and marshes (Ernst, 2006; Kreuels, 2008).

Diagnosis

The WHO suggests that in endemic countries, malaria should be suspected in people presenting high fevers and no other obvious cause. For suspected cases diagnosis is usually done through light microscopy or rapid diagnostic tests. Examination of thin and thick blood films by a microscopist will reveal malaria infection and the type of parasite. Rapid diagnostic tests are only used in areas where microscopy is not readily available (WHO, 2015).

Health impacts

Malaria symptoms are cyclical and occur through “malaria attacks” that last 6-10 hours. These attacks consist of: (i) a cold stage where shivering and a sensation of cold is experienced, (ii) a hot stage with fevers, headaches, vomiting, and seizures (in young children), and (iii) a sweating stage where body temperature returns to normal accompanied by fatigue (CDC, 2019).

Severe malaria could occur when infection is complicated by immunocompromised organisms, some health effects include: severe anemia, acute kidney injury, abnormalities in blood coagulation, hypoglycemia, acute respiratory syndrome, and cerebral malaria with loss of consciousness, seizures, and other neurologic abnormalities. All of these symptoms are a medical emergency and should be treated urgently (CDC, 2019 a).

Treatment

Natural immunity to malaria is possible is some cases, but it takes years and repeated infections to acquire. In areas with high malaria transmission such as sub-Saharan Africa where transmission is so intense that a person will be bitten by hundreds of infectious mosquitoes during wet seasons, people are continuously infected with malaria and the majority of adults acquire partial immunity over time. However, infants, young children and pregnant women don't have partial immunity (Doolan et al., 2009). Three types of acquired immunity to malaria have been observed: anti-disease immunity, anti-parasite immunity, and premunition. A person with anti-disease immunity can still be infected by *plasmodium* but may develop mild symptoms or be asymptomatic. Anti-parasite immunity doesn't prevent parasite infection but affects the density of parasites, resulting in mild or no symptoms. Premunition occurs after several stages on anti-parasite immunity and "provides protection against new infections by maintaining a low-grade and asymptomatic parasitemia" (Doolan et al., 2009). However, these levels of immunity are usually never reached in regions with low or seasonal exposure to *Plasmodium* (Miller et al., 1994).

Nonimmune people have a higher of developing illness after being bitten by an infected mosquito. The WHO recommends that a subject with suspected clinical malaria should be tested for malaria in a reliable diagnostic center and if positive treatment should be started based on clinical indicators and travel history. For *P. vivax* and *P. ovale* infections the recommended treatment is an chloroquine, but and artemisinin-based combination therapy (ACT) should be given in regions with chloroquine resistant *P. vivax*. If ACT is not available, quinine can also be used, and all these treatments should be combined with primaquine. Chloroquine cannot be used for P. falciparum because of its resistance to the antimalarial drug, the WHO recommends treating with artemether and lumefantrine. There is also possibility of mixed *P. falciparum – P. vivax* infections, and for these cases the treatment for *P. falciparum* will usually attack P. vivax (WHO, 2015).

For vulnerable groups, such children and pregnant women, malaria infection is a medical emergency and be rapidly fatal, especially in remote areas, such as indigenous communities, where accessing malaria treatment is limited.

Other impacts of malaria

Besides the health impacts, malaria has an economic burden in countries were the disease is endemic. Malaria endemic countries have lower economic growth than non-endemic countries. Between 1965 and 1990, malaria countries experience an average growth of GDPpc (Gross Domestic Product per capita) of 0.5% per year, compared to 2.3% for non-malaria counties (Gallup & Sachs, 2001). A high prevalence of malaria represents high government expenditures for prevention and treatment, including medical costs and vector control interventions. Malaria household expenditures, including expenses for consultation fees, medicine, and transport, also have a big economic impact, affecting poor households the most. Ettling et al. (1994) reported that malaria expenditures correspond to 28% of total household income for low income households, compared to 2% for middle income households.

The indirect costs of malaria also have an economic burden in endemic countries. The opportunity cost of productive labor time due to illness, which includes time seeking treatment, morbidity time, and the cost of mortality, impact the cost of malaria per household. Chima et al. (2003) reported that “the average work time lost per malaria episode for an adult in Malawi ranges from 1 to 5 days” and 52% of adults with malaria reported that their work or education had been affected because of malaria infection. In addition, healthy adults report lower productivity due to time spent caring for sick household members, especially children (Chima et al. 2003).

Achuar Nationality

The Achuar nationality is one of the Jivaroan ethnic groups in the Ecuadorian Amazon. The entire Achuar nationality expanded through Ecuador before 1941, but after the war between Peru and Ecuador, most commonly known as “La Guerra del 41”, Ecuador lost most of its Amazonian territory to Peru, and until today the Achuar territory is located on both sides of the border between Peru and Ecuador. However, the Achuar nationality is demarcated by the protocol of Rio de Janeiro (1942) as part of a single cultural unit and not affected by geographical boundaries (Espinosa, 1998). The Achuar identity is now based on the fact that their people have stayed for several generations in one specific area.

Family is the basis of the social organization of Achuar communities, and each family has great self-sufficient capacity. They are characterized for their subsistence economy, based on work for self-consumption in fishing, hunting, and agriculture with a combination of crops. The main crops in the area are yuca, potato, corn, plantains, pineapple, sugar cane, and medicinal herbs. Most families also have a henhouse near their home that provides meat and eggs. Economic activities are usually divided by sex and women’s responsibilities are only to stay home raising the children and caring for the garden and henhouse. The jefe, the man of the family, usually goes to “la selva” (the rainforest) for hunting and to the river for fishing accompanied by any sons above 14 years old. Other economic activities involve teachers, artisans, tourism officials, and natural medicine practitioners (EcuRed, 2020).

The standard Achuar home is shaped as an oval to resemble a boat upside down, without outer walls and with a high roof to allow good ventilation. The roof is often made out of palm tree fronds and the floor is usually just the bare ground (EcuRed, 2020). Due to the lack of walls for protection, several households have bed nets to protect them from mosquitoes when sleeping. A typical Achuar home can be observed in Figure 3.

Figure 3. Picture of an Achuar home in Wachirpas (Maria Velasco, 2019)

Culture is very important between the Achuar people. They follow ancestral customs such as polygamy, painting their bodies for hunting, and drinking chicha, a drink made from fermented yuca, and guayusa, an herbal drink. Daily activities usually start around 3am, women have to wake up early to make Guayusa for men, which they immediately drink while meeting to discuss community issues. During the first hours of daylight people go to perform their daily activities, including agriculture and fishing, and in the late afternoon the men go back to the community centers for recreational activities while women look after children. Around 6pm community members return to their homes to spend family time and rest (ForosEcuador, 2018).

The Achuar people are very mythical and spiritual, with a strong ideology surrounding the linkages between natural resources, supernatural beings, and social relationships. They associate the spiritual sphere with their health, and each person must stay in harmony with the supernatural beings of nature, the environment, their community, and family to maintain good health (Rio Corrientes GAD, 2016). They have a great respect for nature and consider that this is what provides subsistence and the perpetuation of the Achuar ethnicity. They also practice natural medicine and consider the jungle the primary source for healing any illness.

Agent Based Models

The transmission process of malaria is spatial and uneven, infections occur in certain high transmission areas, and hosts and vectors move through geographic barriers, but the biophysical, geomorphological, and hydrological characteristics of the environment make transmission uneven within regions. Transmission involves complex network interactions that are not easy to simulate with traditional mathematical models built with differential equations. In ordinary models for malaria, such as the one formulated by Ross and MacDonald categorize individuals in homogenous groups controlled by differential equations (Smith, 2004; 2012). The simplicity of these models complicates representing factors such as individual-based behaviors and environmental heterogeneities that are crucial in determining malaria transmission. To account for the limitations of ordinary mathematical models, an Agent Based Model was developed for this analysis.

Agent Based Models (ABM) are a new emerging type of simulation techniques that allows for accounting for a high level of individual details of features of transmission of vector-borne diseases (Pizzitutti et al., 2015). ABMs represent individuals as agents interacting with each other, and with a representation of the characteristics of the natural environment. Agent based models describe the behavior of individual agents and simulate population dynamics from the interactions between individuals with each other and with their local environment (Grimm et al., 2005).

For infectious diseases such malaria, ABMs have been used because they provide a better understanding of the host-vector system (Ferrer et al., 2012). In the past agent based models have been used to study the relation between hydrologic dynamics and mosquito density, to simulate the effect of interventions on controlling mosquito habitats, to understand the spatial distribution of mosquitoes in water pools, to model the influence of migration on malaria transmission, and to model the relation between asymptomatic infections and migration to malaria transmission (Pizzitutti et al., 2015, 2018, 2019). The agents selected for models can be either humans, mosquitoes, or both; and simulations can include interventions, spatial mapping, host infectivity, mortality, and climate change (Smith et al., 2018).

METHODS

Study area

The study area for this analysis is composed of 6 Achuar communities in the province of Pastaza in the central Ecuadorian Amazon closely situated near the Peruvian border. The communities: Sharamentza, Kapawi, Wachirpas, Suwa, Napurak, and Kusutkau, are situated close to the river Pastaza and surrounded by agricultural fields and tropical primary and secondary rainforest patches (See Figure 4).

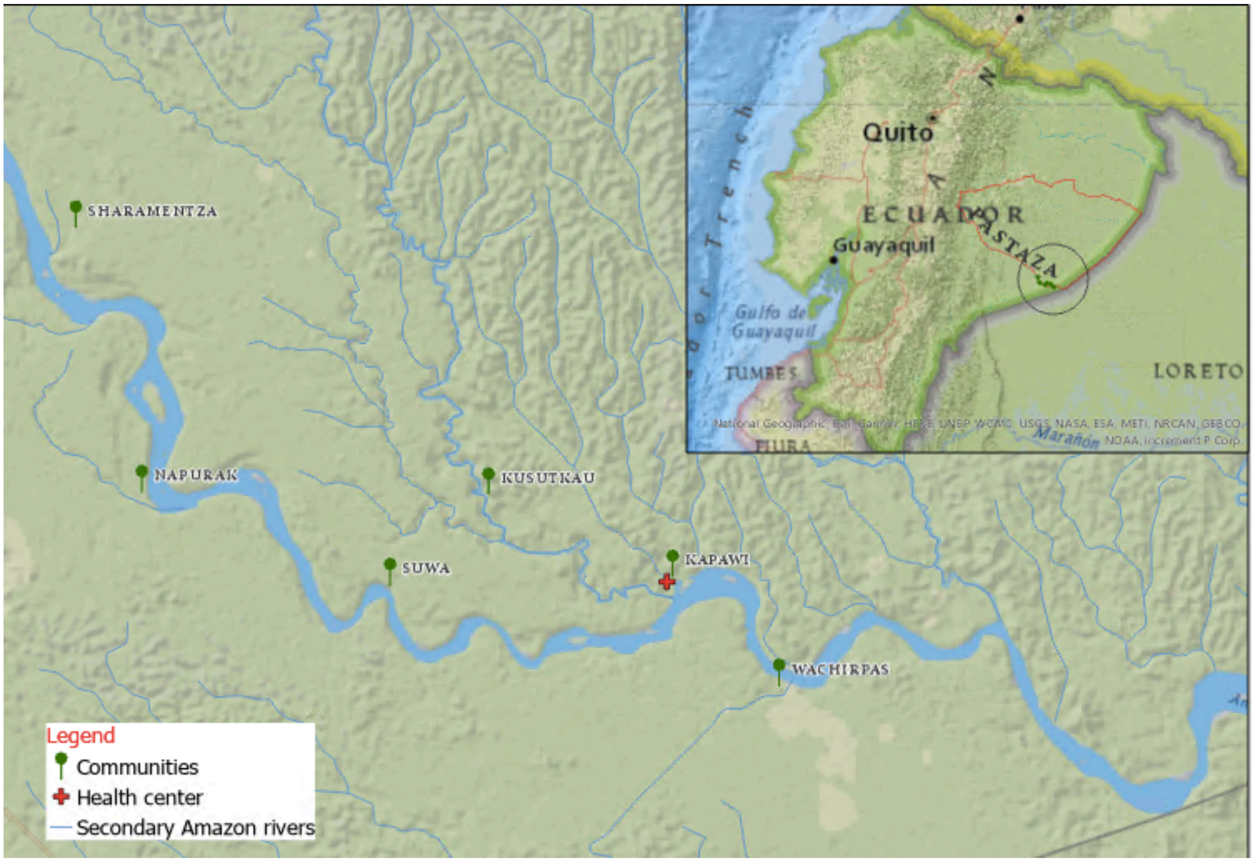

Figure 4. Achuar indigenous communities study sites

The Pastaza province is located in the Ecuadorian Amazon bordering Peru, it has an area of 29,641.37 square kilometers (11,444/60 sq mi) which places it as the province with the most extensive territorial range of the country.

Pastaza is a territory primarily populated by the Shuar and Achuar nationalities, with a population of 83,933 people with 39.8% self-identifying as indigenous peoples (INEC, 2012) and 46.3% living in rural areas (INEC, 2001). The province is divided in four administrative counties: Arajuno, Mera, Santa Clara, and Pastaza, this last one is responsible for 73.9% of the total population, 7865 individuals of the nationality Achuar, and is where our study communities are located (INEC, 2012).

The area is characterized by a tropical humid climate, known as the amazon rainforest, where both primary and secondary forests patches can be observed. The climate is high in humidity and with an average temperature of 25.6° C (Fig. 5). The region has rainfall year-round.

February is usually the driest month with an average precipitation of 203mm (0.8 in) and a high average in the month of June with 350 mm (13.8 in) of precipitation (Fig. 4) (Climate-data.org, 2020). These subtropical hydrometeorological characteristics make the study area the perfect habitat for the anopheles mosquito to reproduce.

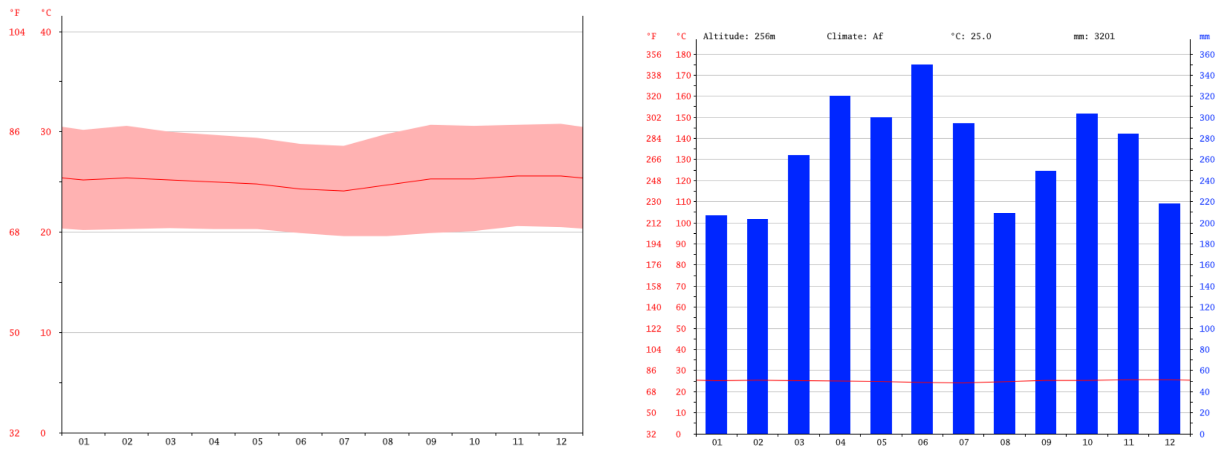

Figure 5. Average temperature and average precipitation in Pastaza. Retrieved from Climate-data.org (2020)

Study design

The analysis for this report was conducted in three time-steps. First, the study area was visited during the summer of 2019 with the purpose of administering a survey to understand the behaviors that increase risk of malaria transmission. Survey data and additional data retrieved from researchers from the Universidad San Francisco de Quito was then analyzed using RStudio version 1.2.5019 (2009-2019 RStudio Inc.). Finally, an agent based model was developed in NetLogo version 5.1 (Wilensky, 1999).

Survey Design

The survey was adapted from a 2016 survey elaborated by researches from Universidad San Francisco de Quito. It was administered to the jefe of the household and households were randomly selected to avoid selection bias. The sample size was 45 households: five in Sharamentza, eight in Kapawi, eight in Wachirpas, eight in Suwa, six in Napurak, and ten in Kusutkau

The survey was composed of three separate sections:

(i) The first section asked personal information including number of adults and children in the household, education level for family members, occupation of each family member, and the number of times the jefe crossed the border with Peru in the past year. For the purpose of this analysis, anyone above the age of 14 is considered an adult.

(ii) The second section collected information on travel for work, pleasure, and studies. This section asked where the jefe travels per year for each of the stated motives, how long he stay in that place, travel time, and how many family members accompany the jefe for each trip.

(iii) The las section collected information on malaria cases for everyone in the household. This section asked the number of total cases over time in the household. Only for cases diagnosed within a year of administration of the survey, we asked information on whether and where people had traveled three months prior infection.

Additional data

We also obtained behavior and malaria incidence data from the study area collected in 2016. A team from the Universidad San Francisco de Quito (USFQ) from Quito, Ecuador, administered a more complex version of the survey used for this analysis in 2016 in six Achuar communities in the Ecuadorian Amazon. The researchers visited the following communities: Kapawi, Wayusentza, Kusutkau, Suwa, Ishpingo, and Wachirpas. For the purpose of this analysis

Wayusentza and Ishpingo were dropped since they were not included in the previously stated study area.

Statistical Analysis

Descriptive statistics were calculated using RStudio version 1.2.5019 (2009-2019 RStudio Inc.) to describe the final sample population for the 2016 and 2019 cohorts.

Agent Based Model

The agent based model present here is used to simulate malaria transmission dynamics in small indigenous communities and assess the effectiveness of intervention strategies such as the distribution of insecticide treated bed nets (ITNs) and malaria treatment.

The agent based model developed for this analysis includes two autonomous decision-making agents, human and mosquitoes. The two agents are designed to assess the situation and make a decision following a set of predetermined. In Figures 6 and 7 the flow charts of decisions humans and mosquitoes have to follow in this model are shown.

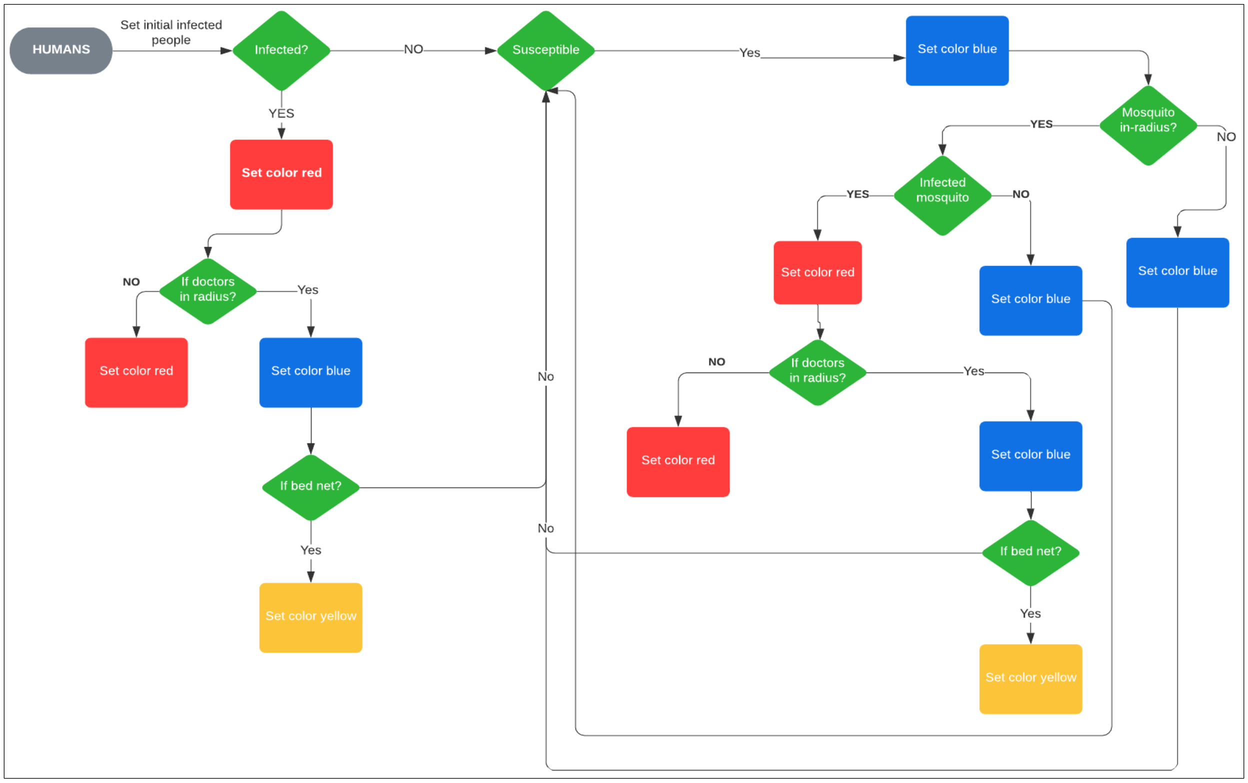

Figure 6. Set of rules for the human agent

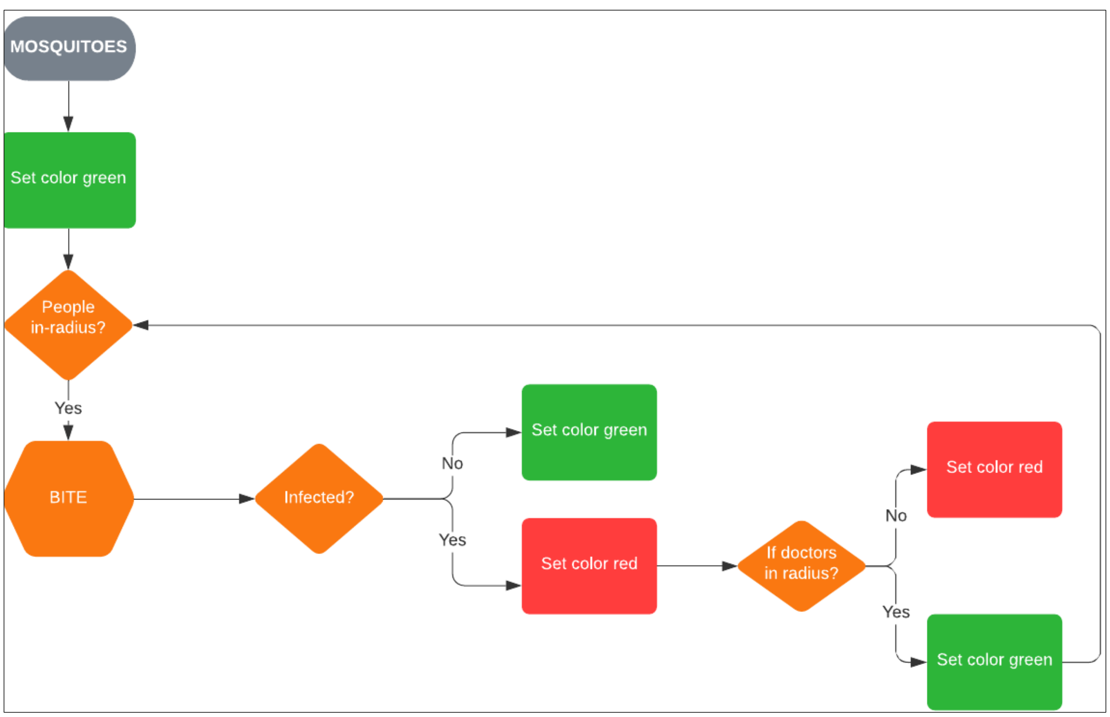

Figure 7. Set of rules for the mosquito agent

For the purpose of this report five models were developed with the same agents following the same set of rules but different parameters. Each model assesses movement between one of the study communities and Kapawi. During fieldwork in the summer of 2019 we learned that Kapawi is the only community with a health center (see Figure 4), meaning that most people have to travel to Kapawi for malaria diagnosis and treatment, or for any other health concern. The developed models where: (i) Movement between Sharamentza and Kapawi, (ii) movement between Wachirpas and Kapawi, (iii) movement between Suwa and Kapawi, (iv) movement between Napurak and Kapawi, and (v) movement between Kusutkau and Kapawi.

Four different parameters were set before simulations were run. Table 3 shows the values assigned to the four parameters for each model. Observational data was fitted to the model parameters following guidelines from Thiele et al. (2014) and values for each parameter were extrapolated from statistical analysis of survey data.

(i) Number of initial infected people, a parameter set depending on the number of houses surveyed in each community.

(ii) Initial number of mosquitoes, a parameter set randomly to 25.

(iii) Mosquito bite likelihood, a parameter extrapolated from the prevalence of malaria for each community in the 2019 cohort.

(iv) Travel tendency, a parameter extrapolated by analyzing where people from the six communities traveled to and how many times, they visited Kapawi in relation to other communities.

Table 1. Values of the Model Parameters

Model	Number of initial infected people	Initial number of mosquitoes	Mosquito bite likelihood	Travel tendency
Sharamentza-Kapawi	5	25	0.7	0.15
Wachirpas-Kapawi	8	25	0.4	0.12
Suwa-Kapawi	8	25	0.2	0.27
Napurak-Kapawi	6	25	0.4	0.15
Kusutkau-Kapawi	10	25	0.2	0.35

The models also assess the effectiveness of ITNs and treatment medication for malaria control. Each of the five models was run for three different intervention simulations: (i) No intervention, (ii) only medicine intervention, (iii) medicine and ITNs intervention. Each simulation was then ran 100 times to obtain an average number of people infected with malaria at the end of a period of 365 days.

RESULTS

Statistical Analysis

In total, our dataset included information from 52 households from the 2016 surveys and 45 households from the 2019 surveys.

2019 population description

In total, our dataset from surveys performed in 2019 included information from 45 households with population of 327 people including adults and children from six Achuar indigenous communities. Specific distribution of households and number of adults and children per community is shown in Table 2.

Table 2. Survey distribution (2019 cohort)

Community	Number of surveyed households	Sample size (number of total people included in the survey)
Sharamentza	5	26 (13 adults and 13 children)
Kapawi	8	52 (21 adults and 31 children)
Wachirpas	8	59 (31 adults and 28 children)
Suwa	8	74 (31 adults and 43 children)
Napurak	6	35 (15 adults and 20 children)
Kusutkau	10	81 (29 adults and 52 children)

Regarding occupation, most men usually work in fishing and agriculture, but a few of them are teachers. 44.4% of jefes identified fishing as their primary job, 31% work in agriculture, 17.7% work as teachers, 4.4% are artisans, and 2.2 work in natural medicine (Figure 8). Women usually work in the house and in agriculture since most families have crops in their property. 66.7% of women work agriculture, 15.6 identified as housework as their primary activity, and 6.6% work in fishing. There is no occupation data for 11.1% of women (Figure 8).

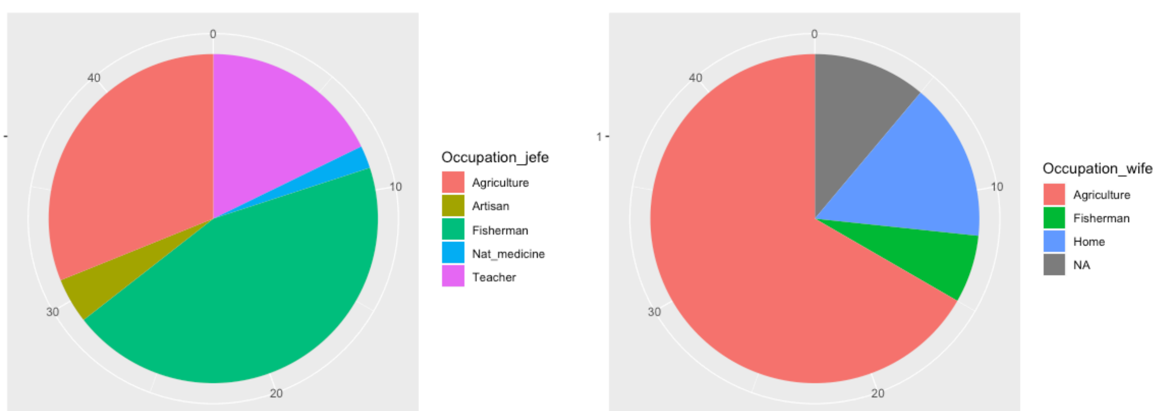

Figure 8. Occupation distribution for jefe (left) and wife (right) for all six communities in 2019

People reported they traveled to other Achuar communities for work, to visit family and friends, and for leisure activities such as to participate in sports competitions. A total of 143 travel events were reported, with 72.7% of those being because for leisure and visiting family purposes, and 27.3% being for work related purposes. There were no reports of travel for education purposes. Travel destinations for each of the six communities can be observed in Figure 9.

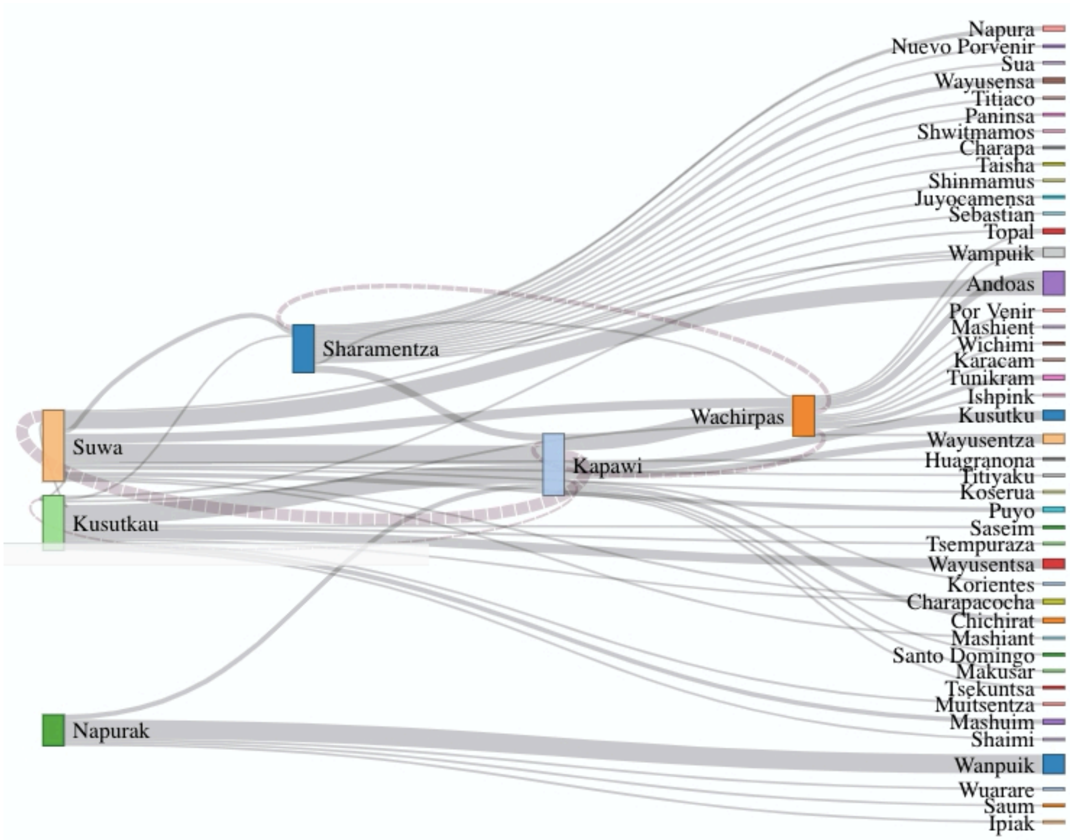

Figure 9. Travel destinations for all six communities in 2019

2016 population description

In total, the dataset from surveys performed in 2016 included information from 52 households with population of 325 people including adults and children from four Achuar indigenous communities. Specific distribution of households and number of adults and children per community is shown in Table 3.

Table 3. Survey distribution (2016 cohort)

Community	Number of surveyed households	Sample size (number of total people included in the survey)
Kapawi	15	82 (33 adults and 49 children)
Wachirpas	18	107 (50 adults and 57 children)
Suwa	7	47 (17 adults and 30 children)
Kusutkau	12	89 (31 adults and 58 children)

Malaria prevalence

In total, our 2019 dataset included information for 102 malaria cases, 45.1% of these cases were in children from 0-14 years old, and 54.9% were in adults above 14 years old. The sex distribution of cases was higher for males, who encapsulated 64.7% of the cases (Table 4). The 2016 dataset included information for 77 malaria cases, with a higher percentage of children infected compared to 2019. In 2016 children corresponded to 63.6% of cases within the las 12 months, while adults corresponded to 36.4% of cases.

Variable	All		0 - 14 years		> 14 years	
	N	Proportion(%)	N	Proportion(%)	N	Proportion(%)
Age	102	100%	46	45.1%	56	54.9%
Sex						
Female	36	35.3%	15	41.7%	21	58.3%
Male	66	64.7%	31	47.0%	35	53.0%
Diagnosis <12 months						
Yes	74	72.6%	40	54.1%	34	45.9%
No	28	27.4%	6	21.4%	22	78.6%
Travel < 3 months						
Yes	15	14.7%	3	20.0%	12	80.0%
No	62	60.8%	40	64.5%	22	35.5%

Table 4. Summary of malaria cases from the 2019 dataset. N = sample size.

Prevalence of malaria increased for most communities in the study area between 2016 and 2019 (Figure 10). Kapawi had the greatest increase, malaria prevalence increased by 177.8% between 2016 and 2019, from 18 per 100 people to 50 per 100 people. Wachirpas had an increase in prevalence of 69% going from 26 cases per 100 people to 50 cases per 100 people. Malaria prevalence increased by 41% in Kusutaku, from 12 per 100 people in 2016 to 17 per 100 people in 2019. For Suwa, malaria prevalence actually decreased by 42.3% between 2016 and 2019, from 26 to 15 per 100 people. Fluctuations in malaria risk couldn't be assessed for Sharamentza and Napurak, since no 2016 was available for these communities. Based on survey data malaria prevalence was estimated to be 69 per 100 people for Sharamentza, and 37 per 100 people for Napurak.

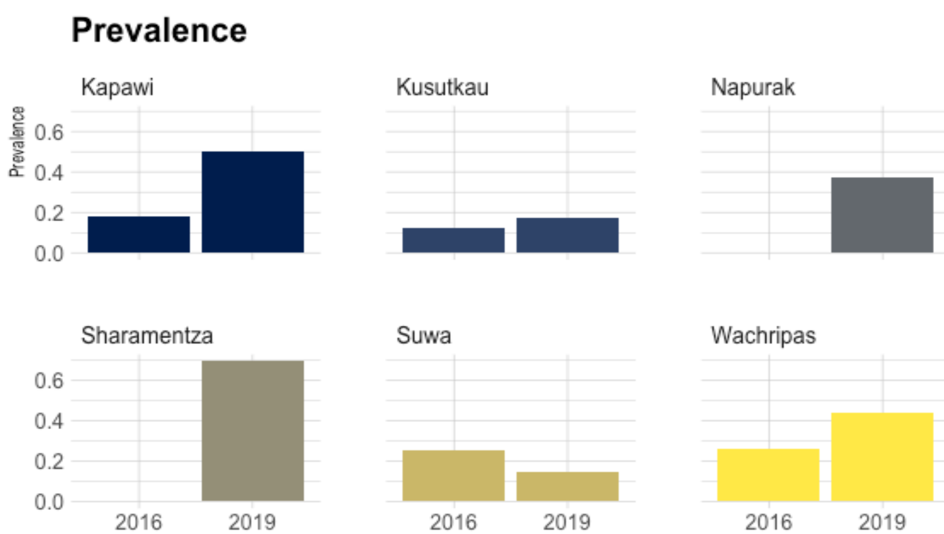

Figure 10. Estimated malaria prevalence for Achuar indigenous communities from 2016 and 2019 survey data.

Movement and malaria

In 2019, out of a total of 108 total cases of malaria, 74 cases occurred 12 months prior data collection (Figure 11), 15 of those cases had traveled within three months of infection. Most cases traveled to other Achuar communities within Ecuador, but three traveled to Puyo, and urban area in Pastaza, and five traveled to Peru.

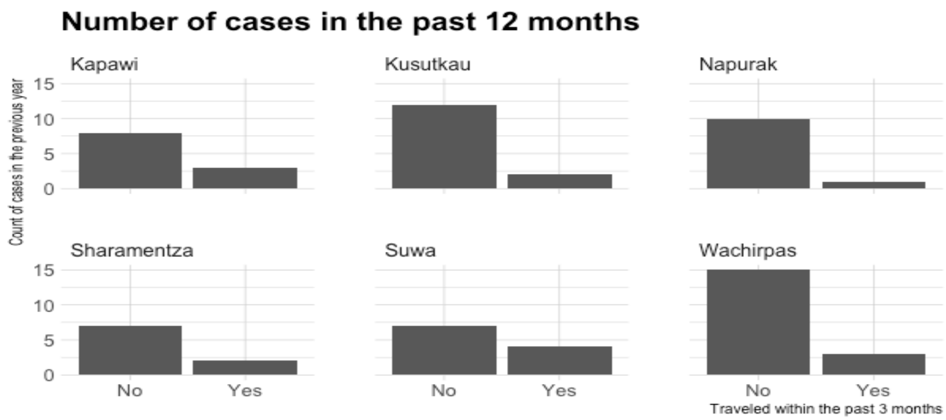

Figure 11. Comparison of cases that traveled vs. not traveled three months prior malaria diagnosis.

From the total 74 malaria cases that occurred within a year from data collection, 15 traveled 3 within three months before diagnosis. Travel destination for cases diagnosed within 12 months of data collection are shown in Figure 12. Cases from Suwa traveled the most out of the six communities, three cases to Andoas in Peru and one to Wachirpas. Other communities that traveled to Peru were Wachirpas to Tititaku, and Sharamentza to an unkown location in Peru. In total 20% of the cases that traveled 3 months prior being diagnoses with malaria had traveled to areas in Peru.

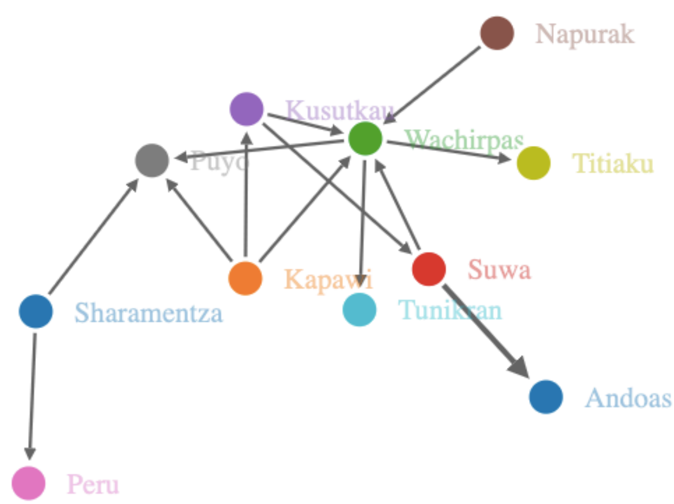

Figure 12. Travel network for cases of malaria that traveled 3 months prior diagnosis.

The relationship between the number of times the jefe crosses the border and the number of malaria cases in the family was also assessed for the 2019 dataset. The average number of times a jefe crossed the border in 2019 was estimated to be 1.69, with a maximum value of 12 and a minimum value of zero, 40% of people reported they didn't cross the border with Peru at all. We conducted a two-sample unpaired t-test to observe the different in average of malaria risk for families with the jefe crossing the border less than 2 times a year (low border crossing incidence) and more than 3 times a year (high border crossing incidence). The test showed no significant difference between the two groups (p-value= 0.5645) and estimated an average risk of malaria per family of 41.8% for families with low border crossing incidence and 36.09% for families with high border crossing incidence.

In 2016, people crossed the border with Peru less times a year compared to 2019, 82.7% of survey respondents reported to not have crossed the border at all. The two-sample unpaired t-test for the 2016 didn't show a significant difference (p-value= 0.4305) in average distribution of malaria risk for families with the jefe crossing the border less than 2 times a year (low border crossing incidence) and more than 3 times a year (high border crossing incidence).The average malaria risk for families with low border crossing incidence was estimated to be 21.7%, and 9.83% for families with high border crossing incidence.

Effect of education on malaria control

We also tried to observe the relationship between education and malaria risk. In total we obtained education data from 19 men and 19 women. The distribution of education for men was: 21.6% had a low level of education (0-3rd grade), 31.6% had a medium level of education (4-8th grade), and 47.4% had a high level of education (9th-12th grade). For women the distribution of education was: 68.4% had a low level of education (0-5th grade) with 79.9% of women in that group having received no education at all. Only 31.6% of women had a high level of education (6th-12th grade), with just one woman having graduated from high school.

An unpaired two sample t-test was conducted to observe the difference in means between rate of malaria cases in the family for low education compared to high education. For men, no significant relationships were observed. For women, since they're the ones raising the children and staying in the house, we hypothesized that education level of the mother would have an effect on the rate of malaria cases per family. However, no significant difference in means (p value=0.7853) between malaria rate for low education and high education was observed. Figure 13 shows the relationship between the mother's education and malaria risk in the family.

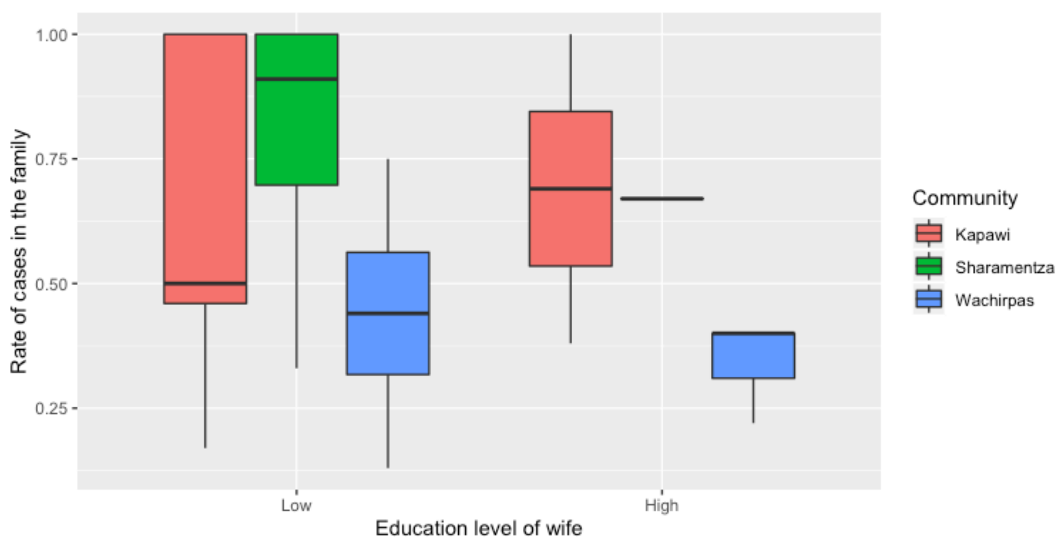

Figure 13. Boxplots for education and rate of malaria cases in the family for Kapawi, Sharamentza, and Wachirpas. In this graph a low level of education is defined as 0 – 5th grade, and a high level of education is defined as 6th – 12th grade.

Agent Based Model

The number of malaria cases between the two communities at the end of a 365-day period after running 100 simulations of each of the models is presented in table 5. For the no intervention approach for the models for all 5 models, prevalence at the end of 365 days was almost 100%. Interventions with medicine decreased prevalence all models, with the Suwa-Kapawi model having the most significant decrease at 43.8%, and the Napurak-Kapawi model having the least significant decrease at 12.6%. An intervention with insecticide treated bed nets along with medicine distribution was successful in decreasing malaria prevalence for all five models. The average decrease in prevalence when moving from a no intervention strategy to a more complex strategy including medicine and ITNs is estimated to be 79.8%. The average decrease in prevalence when comparing a strategy just distributing medicine and a strategy for distributing both medicine and ITNs is 72.3%.

Table 5. Malaria prevalence per 100 people at the end of a 365-day period for each model. Prevalence is an average of 100 simulations.

	Model				
Intervention	Sharamentza - Kapawi	Wachirpas - Kapawi	Suwa-Kapawi	Napurak - Kapawi	Kusutkau-Kapawi
No intervention	100	100	97.6	100	99.2
Medicine	87.2	73.9	54.8	87.4	74.4
Medicine and ITNs	20.5	17.1	24.6	20.7	17.3

To show fluctuations in malaria cases over a period of a year, the model produced a graph for malaria cases for each of the interventions (Figure 14). Cases for the five models with no intervention show and logistic growth, cases initially increase rapidly but then the rate growth plateaus when most people are infected and there's no new people coming in. For a strategy with medicine, there is also an initial rapid increase in cases when people are first bitten by infected mosquitoes, but then it becomes cyclical when people start receiving treatment. The model for controlling malaria cases with medicine and ITNs distribution shows an initial rapid increase like the two previous models, but then it peaks, and cases start to decrease when people receive bed nets.

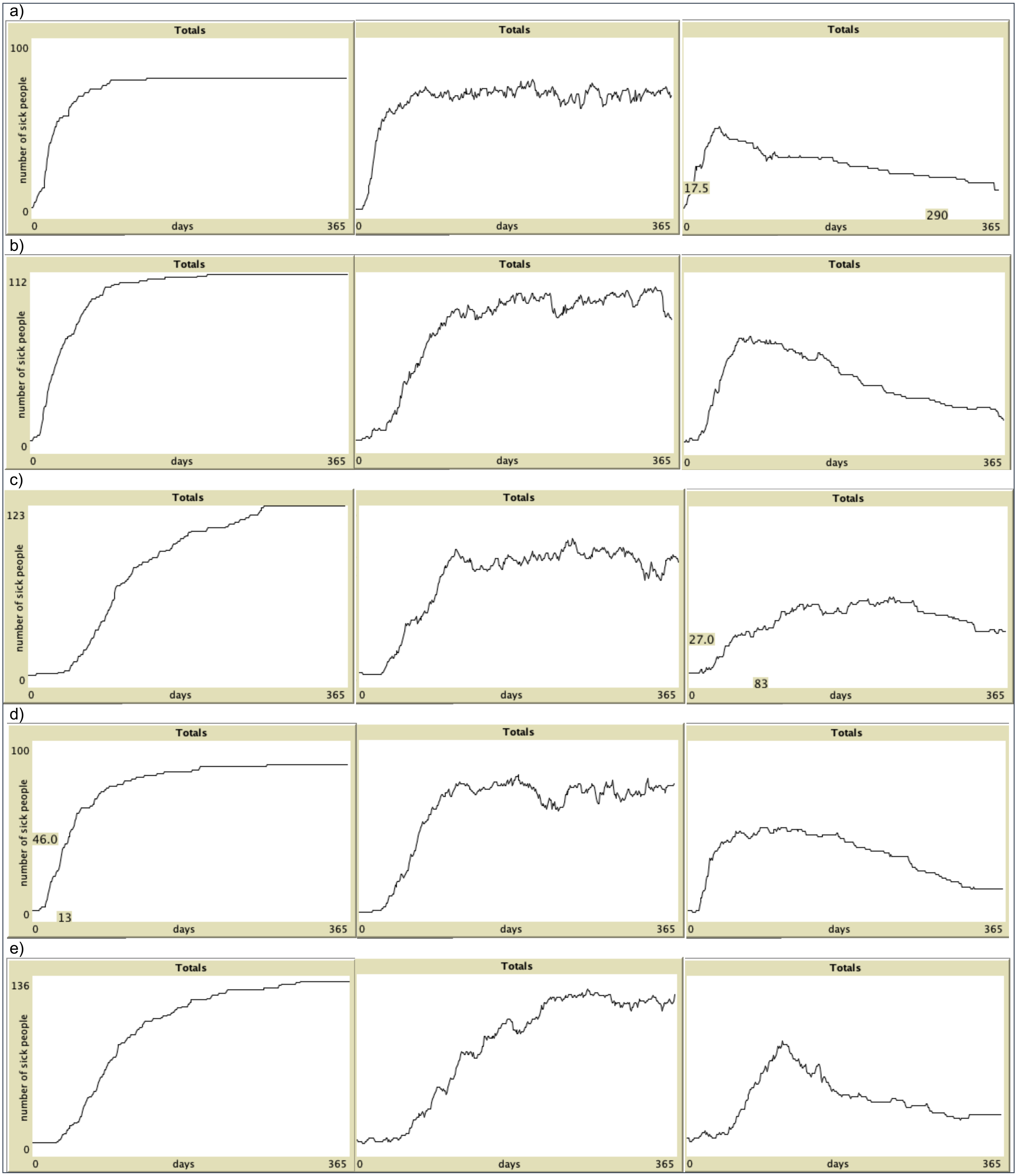

Figure 14. Netlogo output for malaria cases fluctuations over a period of 365 days for model (a)Sharamentza-Kapawi, (b)Wachirpas-Kapawi, (c)Suwa-Kapawi, (d)Napurak-Kapawi, (e)Kusutkau-Kapawi

DISCUSSION

This is the first study on malaria prevalence in Achuar indigenous communities in Ecuador, so no comparisons can be done to previous studies. Our analysis showed that between 2016 and 2019 malaria prevalence increased for three of six communities visited Kapawi, Kusutkau, and Wachirpas. The analysis also reports a high prevalence of malaria for communities for which no 2016 case data was available. In 2019, malaria prevalence in Sharamentza was 69 cases per 100 people, which is three times higher than the 23 per 100 people prevalence observed for the entire province of Pastaza (MSP, 2018). Overall, average prevalence in the study area increased by 88.7% from 20.5 per 100 people in 2016 to 38.7 in 2019. These findings are supported by data obtained the Ecuadorian Ministry of Public Health (MSP) that reported malaria cases in Pastaza increased by 62% between 2016 and 2019, from 348 cases to 564.

To understand the increased transmission of malaria it is important to understand the effects on globalization on human movement. However, it is also important to consider the dynamics within the Achuar nationality that leads to people exposing themselves to travels within and outside of the country, increasing their vulnerability not only to by the vector transmitting malaria, but to other situations that have a significant health impact.

Analysis of the 2019 dataset showed that a 100% of survey respondents traveled to at least one other Achuar community a year, and most people traveled to six different communities every year, more than once a year to each community. The least number of days someone reported to stay in another community, for leisure or work, was one, while the maximum number of days was a month.

Through conversations with locals we learned that almost everyone in Achuar communities have traveled or travel frequently to Peru, especially to Achuar communities in the department of Loreto, where people have family members. Achuar people from Peru also travel frequently to Ecuador not only to visit friends and family, but also for commerce. The number of people who cross the Ecuador-Peru border increased between 2016 and 2019, from 17.3%

respondents reporting to have crossed the border at least once a year in 2016 to 60% of respondents reporting to have crossed the border at least once a year in 2019. Statistical analysis showed no significant relationship between the number of times the jefe crossed the border and the risk of malaria per family. However, this could be attributed to the small size of the sample size and recall bias for both number of cases in the family and number of times a person traveled to Peru. It is also important to consider the possibility to developing partial immunity to malaria (Doolan et al., 2009), and the possibility of people outside of the family becoming a secondary infection of the case who traveled. Our study also looked at travel destination for each malaria case diagnosed 12 months prior data collection. Out of the total 74 cases that occurred in the past year, only 15 had traveled. This could be attributed to adults traveling more than children and children becoming secondary infections of symptomatic or asymptomatic adults. This assumption is supported by the observation that out of the 15 cases who traveled 3 months prior data collection, only two of those were children.

Several studies have identified low levels of education and low gestation age of women (age at first pregnancy) to be risk factor for infectious diseases such as malaria (Fana et al., 2015; Agomo & Oyibo, 2013; Schultz et al., 1994). Regidor et al. (2002) observed that for both men and women and education level lower than elementary school is correlated to higher likelihood of mortality due to infectious diseases. In our study we asked education questions for the jefe and his wife at three of the communities: Sharamentza, Kapawi, and Wachirpas. We observed that men had a higher level of education than women, and for this study we focused on analyzing the relationship between education level of the mother and rate of malaria cases in the family. We focused on women since they are in charge of caring for the children most of the day while the jefe is at work or attending community meetings. Iriemenam et al. (2011) and Abdullahi Fan et al. (2015) observed that education of women of child-bearing age could be a tool for malaria control. Malaria risk was overall higher for families with a mother having education lower than 5th grade, but not significant (p-value=0.7953). These findings are aligned with Agomo & Oyibo (2013) observation that women's education was not significantly associated with malaria infection and explain it by the possibility that other interventions such as massive malaria control strategies through television and radio have been effective in decreasing malaria cases.

The outputs of the agent based model shows that intervention strategies are expected to be successful for malaria control if executed suitably. For all simulations for all communities, a model of intervention distributing medicine to malaria cases successfully decreased average malaria prevalence for a year by 23.9% compared to a no intervention scenario. By going one step further and distributing both medicine and insecticide treated be nets, average malaria prevalence was decreased by 79.8% when compared to a no intervention scenario.

The outputs of the agent based model shows that intervention strategies are expected to be successful for malaria control if executed suitably. For all simulations for all communities, a model of intervention distributing medicine to malaria cases successfully decreased average malaria prevalence for a year by 23.9% compared to a no intervention scenario. By going one step further and distributing both medicine and insecticide treated be nets, average malaria prevalence was decreased by 79.8% when compared to a no intervention scenario.

Malaria transmission depends on the parameters that limit agent interactions (human-mosquito and mosquito-human interactions). The model results showed that the number of initial sick people didn't have an effect as significant in malaria cases at the end of a 365-day period, instead mosquito bite likelihood and travel tendency had more power in changing malaria prevalence. These results are validated by statistical analysis of survey data that showed a relationship between human movement and malaria risk.

In the Amazon basin region, malaria transmission is seasonal with high peaks in cases connected with periods of riverine flooding (Pizzitutti et al., 2018). We observed that our agent based model linked malaria cases with seasonality, as figure 14 shows various peaks of high malaria cases. An agent based model, such as the one developed for this analysis could predict seasonality of malaria and fluctuations in cases.

CONCLUSIONS & LIMITATIONS

There are several limitations to this study's design. First, the study accounts only for infections occurring when people travel to Achuar communities in Peru or other Achuar communities in Ecuador, but it doesn't account for imported cases of people traveling from Peru to Ecuador and starting local transmission there. A more extensive survey that includes a section for visitors coming from Peru may shed light on the effect of migration from Peru to Ecuador on malaria risk.

It is important to note the several assumptions that had to be made for the agent based model, which are great limitation of this study. First, the model assumes that if people don't receive medication infections could last up to a year since the parasite if not killed, remains dormant in the human body with the risk of developing disease months later (Markus 2012). The models also assume that people who receive medication recover immediately. Another assumption made for these models is that ITNs are 100% effective in protecting from malaria infections and will prevent future exposure to the malaria vector. However, because ITNs are usually not used properly and are only used when people are sleeping and nor throughout the entire period of time the anopheles mosquito is the most active, ITNs don't fully protect hosts from exposure. Finally, this study doesn't account for seasonal variation and mosquito distribution is highly variable depending on temperature and precipitation, creating seasons of high and low malaria risk.

The results of this analysis can help policy makers and healthcare providers better understand social risk factors of malaria transmission between Achuar indigenous communities, and effectiveness of malaria intervention strategies to plan for feasible control and prevention strategies.

REFERENCES

Agomo, C. O., & Oyibo, W. A. (2013). Factors associated with risk of malaria infection among pregnant women in Lagos, Nigeria. Infectious diseases of poverty, 2(1), 19.

Blandin, S., Shiao, S. H., Moita, L. F., Janse, C. J., Waters, A. P., Kafatos, F. C., & Levashina, E. A. (2004). Complement-like protein TEP1 is a determinant of vectorial capacity in the malaria vector Anopheles gambiae. Cell, 116(5), 661-670.

CDC - Malaria - About Malaria - Disease. (2019 a). Retrieved from https://www.cdc.gov/malaria/about/disease.html

CDC. (2019 b). DPDx – Laboratory Identification of Parasites of Public Health Concern. Retrieved February 24, 2020 from https://www.cdc.gov/dpdx/malaria/index.html

Chima, R. I., Goodman, C. A., & Mills, A. (2003). The economic impact of malaria in Africa: a critical review of the evidence. Health policy, 63(1), 17-36.

Climate-org (2020). Retrieve February 22, 2020 from https://en.climate-data.org/south-america/ecuador/provincia-de-pastaza/namu-180090/

Doolan, D. L., Dobaño, C., & Baird, J. K. (2009). Acquired immunity to malaria. Clinical microbiology reviews, 22(1), 13-36.

EcuRed (2020). Achuar. Retrieved February 24,2020 from https://www.ecured.cu/Achuar#Econom.C3.ADa

Ernst, K. C., Adoka, S. O., Kowuor, D. O., Wilson, M. L., & John, C. C. (2006). Malaria hotspot areas in a highland Kenya site are consistent in epidemic and non-epidemic years and are associated with ecological factors. Malaria journal, 5(1), 78.

Espinosa, O. (1998). Los pueblos indígenas de la Amazonía peruana y el uso político de los medios de comunicación. América Latina Hoy, 19, 91-100.

Ettling, M., McFarland, D. A., Schultz, L. J., & Chitsulo, L. (1994). Economic impact of malaria in Malawian households. Tropical medicine and parasitology: official organ of Deutsche Tropenmedizinische Gesellschaft and of Deutsche Gesellschaft fur Technische Zusammenarbeit (GTZ), 45(1), 74-79.

Fana, S.A., Bunza, M.D.A., Anka, S.A. et al. Prevalence and risk factors associated with malaria infection among pregnant women in a semi-urban community of north-western Nigeria. Infect Dis Poverty 4, 24 (2015). https://doi.org/10.1186/s40249-015-0054-0

Ferrer, J., Albuquerque, J., Prats, C., López, D., & Valls, J. (2012). Agent-based models in malaria elimination strategy design. EMCSR 2012.

ForosEcuador (2019) “Pueblos y Nacionalidades Indígenas del Ecuador - Idioma, ubicación y características Foros Ecuador 2019.”Retrueved from http://www.forosecuador.ec/forum/ecuador/educación-y-ciencia/171842-pueblos-ynacionalidades-indígenas-del-ecuador-idioma-ubicación-y-características.

Gallup, J. L., & Sachs, J. D. (2001). The economic burden of malaria. The American journal of tropical medicine and hygiene, 64(1_suppl), 85-96.

INEC. (2001). “Censo de población y vivienda 2001”.

INEC. (2012). “Censo de población y vivienda 2010”.

Iriemenam, N. C., Dosunmu, A. O., Oyibo, W. A., & Fagbenro-Beyioku, A. F. (2011). Knowledge, attitude, perception of malaria and evaluation of malaria parasitaemia among pregnant women attending antenatal care clinic in metropolitan Lagos, Nigeria. Journal of vector borne diseases, 48(1), 12.

Kreuels, B., Kobbe, R., Adjei, S., Kreuzberg, C., von Reden, C., Bäter, K., ... & May, J. (2008). Spatial variation of malaria incidence in young children from a geographically homogeneous area with high endemicity. The Journal of infectious diseases, 197(1), 85-93.

Markus, M. B. (2012). Dormancy in mammalian malaria. Trends in parasitology, 28(2), 39-45.

Menéndez, Eduardo (2001) “Técnicas cualitativas, problematización de la realidad y mercado de saberes.” Cuaderno de Antropología Social 13.

Miller, L. H., Good, M. F., & Milon, G. (1994). Malaria pathogenesis. Science, 264(5167), 1878-1883.

Mosquera M, Zuluaga L, Tobón A. Challenges for the diagnosis and treatment of malaria in low transmission settings in San Lorenzo, Esmeraldas, Ecuador. Malar J [Internet]. BioMed Central; 2018;17(1):1–9. Available from: https://doi.org/10.1186/s12936-018-2591-z

MSP. (2018). Infome Malaria (SE) 31. Retrieved February 22 2020 from https://www.salud.gob.ec/wp-content/uploads/2016/09/Malaria-SE-31_2018-1.pdf

NetLogo Home Page. (n.d.). Retrieved March 24, 2019, from http://ccl.northwestern.edu/netlogo/

Parker, B. S., Paredes Olortegui, M., Peñataro Yori, P., Escobedo, K., Florin, D., Rengifo Pinedo, S., … Kosek, M. (2013). Hyperendemic malaria transmission in areas of occupation-related travel in the Peruvian Amazon. Malaria Journal, 12(1), 178. https://doi.org/10.1186/1475-2875-12-178

Pizzitutti, F., Mena, C. F., Feingold, B., & Pan, W. K. (2019). Modeling asymptomatic infections and work-related human circulation as drivers of unstable malaria transmission in low-prevalence areas: A study in the Northern Peruvian Amazon. Acta tropica, 197, 104909.

Pizzitutti, F., Pan, W., Barbieri, A., Miranda, J. J., Feingold, B., Guedes, G. R., ... & Mena, C. F. (2015). A validated agent-based model to study the spatial and temporal heterogeneities of malaria incidence in the rainforest environment. Malaria journal, 14(1), 514.

Pizzitutti, F., Pan, W., Feingold, B., Zaitchik, B., Álvarez, C. A., & Mena, C. F. (2018). Out of the net: An agent-based model to study human movements influence on local-scale malaria transmission. PLOS ONE, 13(3), e0193493. https://doi.org/10.1371/journal.pone.0193493

Pouniotis, D. S., et al. "Malaria parasite interactions with the human host." Journal of postgraduate medicine 50.1 (2004): 30.

Recht, J., Siqueira, A. M., Monteiro, W. M., Herrera, S. M., Herrera, S., & Lacerda, M. V. G. (2017). Malaria in Brazil, Colombia, Peru and Venezuela: current challenges in malaria control and elimination. Malaria Journal, 16(1), 273. https://doi.org/10.1186/s12936-017-1925-6

Regidor, E., De Mateo, S., Calle, M. E., & Domínguez, V. (2002). Educational level and mortality from infectious diseases. Journal of Epidemiology & Community Health, 56(9), 682-683.

Río Corrientes GAD. (2016). “NACIONALIDAD ACHUAR | GAD Río Corrientes.” Retrieved from https://gadprriocorrientes.gob.ec/?page_id=176.

Schultz LJ, Steketee RW, Chitsulo L, et al. Malaria and childbearing women in Malawi: knowledge, attitudes and practices. Tropical Medicine and Parasitology : Official Organ of Deutsche Tropenmedizinische Gesellschaft and of Deutsche Gesellschaft fur Technische Zusammenarbeit (GTZ). 1994 Mar;45(1):65-69.

Smith, D. L., & McKenzie, F. E. (2004). Statics and dynamics of malaria infection in Anopheles mosquitoes. Malaria journal, 3(1), 13.

Smith, D. L., Battle, K. E., Hay, S. I., Barker, C. M., Scott, T. W., & McKenzie, F. E. (2012). Ross, Macdonald, and a theory for the dynamics and control of mosquito-transmitted pathogens. PLoS pathogens, 8(4).

Smith, N. R., Trauer, J. M., Gambhir, M., Richards, J. S., Maude, R. J., Keith, J. M., & Flegg, J. A. (2018). Agent-based models of malaria transmission: a systematic review. Malaria Journal, 17(1), 299. https://doi.org/10.1186/s12936-018-2442-y

SNEM, Servicio Nacional De Control De Enfermedades Transmitidas Por Vectores. (2013). Proyecto de Vigilancia y Control de Vectores para la Prevencion de la Transmision de Enfermedades Metaxenicas en el Ecuador 2013-2017. Primera edición. Guayaquil, Ecuador.

Thiele, J. C., Kurth, W., & Grimm, V. (2014). Facilitating parameter estimation and sensitivity analysis of agent-based models: A cookbook using NetLogo and R. Journal of Artificial Societies and Social Simulation, 17(3), 11.

WHO. Eliminating Malaria.; 2016 (b)

WHO. World malaria report. Geneva: World Health Organization; 2015.

WHO. World malaria report. Geneva: World Health Organization; 2015.

WHO. World malaria report. Geneva: World Health Organization; 2016.

WHO. World malaria report. Geneva: World Health Organization; 2019.

Wilensky, U. (1999). NetLogo.

Young, Allan (1982) THE ANTHROPOLOGIES OF ILLNESS AND SICKNESS. Vol. 11. Cleveland Ohio 44106: Annual Reviews.