RESEARCH

Measuring the contribution of mobility to malaria persistence

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Abstract

Background: ~~Human mobility is an important determinant of malaria distribution and can explain different patterns of (re)introduction, circulation and persistence of malaria. In order to understand the association between human mobility patterns and the probability of getting malaria, this study revisited a household survey conducted in 2015 in Alto Juruá region, Acre state, Brazil. This region registers one the greatest malaria burden in Brazil~~To achieve the goal of malaria elimination, it is important to determine the role of human mobility on maintaining parasite transmission. The Alto Jurua basin (Brazil) has one of the largest prevalence of malaria *vivax* and malaria *falciparum* in the Amazon. The goal of this work ~~is~~ was to estimate the contribution of human commutation ~~to~~ on the persistence of malaria in this region, using data from a origin-destination survey.

Methods: Data from the origin-destination survey was used to describe the intensity and motivation for commutation between rural settlements and urban areas in two municipalities, Mâncio Lima and Rodrigues Alves. The relative time-person spent in each locality per household was estimated. A logistic model was fitted to estimate the effect of commuting on the probability of getting malaria for a householder from a zone of residence commuting to another zone.

Results: Our main results ~~suggests~~ suggest that this population is not very mobile. 96% of households reported spending more than 90% of their ~~yearly~~ annual person-hour at localities within the same zone of residence. Study and work are the most prevalent ~~motivation to displace~~motivations for commuting, 40.5% and 29.5% respectively. Spending person-hours in urban Rodrigues Alves conferred relative protection to the residents of urban Mâncio Lima. On the other hand, spending time in ~~rural Rodrigues Alves increased the probability of malaria, but not significant in rural~~ urban Rodrigues Alves conferred protection against malaria for those living in urban Mâncio Lima. ~~For urban Rodrigues Alves residents,~~ The opposite effect occurs for those spending time in ~~urban and rural Mâncio Lima and rural Rodrigues Alves increased the probability of malaria, more so if going to the latter~~the rural areas of both municipalities.

Conclusion: ~~The results suggests that the~~ In the Alto Jurua region, the place one lives is a stronger determinant of ~~the~~ malaria risk than the place ones commute. These municipalities are a hotspot of *Plasmodium* transmission, thus, understanding the main fluxes is essential to planning control strategies because the probability of getting malaria ~~in Alto Juruá region and this can be a natural consequence of the low mobility and the local environment. The heterogeneity of malaria transmission in Brazil highlights the importance of microregion-targeted intervention since their risk signature within each municipality is quite different, despite being direct geographical neighbors. In addition, it~~ is dependent on the intensity of transmission of both, the area of origin and the area to which the displacement takes place. The natural conditions for the circulation of pathogens such as the *Plasmodium spp*, combined with the pattern of mobility of humans in the Amazon, make clear the need of disease control perspective change. It is essential that intersectoral public policies be the basis for health mitigation actions.

Keywords: malaria; household survey; mobility; commutation; logistic model

~~Content~~

Text and results for this section, as per the individual journal's instructions for authors.

Background

In 2015, Brazil has launched The Plan for Elimination of Malaria in alignment with the 2030 Sustainable Development Agenda [1]. Achieving this goal will require a better understanding of the local dynamics of malaria in the remaining hot spots of transmission. Malaria burden in Brazil is concentrated in the Amazon Basin [2]. Within this region, transmission is spatially heterogeneous [3, 4] with pockets of high malaria transmission associated with fish farming in rural and urban areas [5], arrival of susceptible individuals in new rural settlements in forest fringes, and illegal activities such as mining and logging [6, 7].

Risk factors for malaria have different levels of determination, from individual to household [8, 9, 10, 11, 12]. At the individual level, immunity, genetic background, nutrition, work activities, adherence to preventive practices, travel history, are important determinants of exposure and disease. At the household level, type of construction, distance to mosquito breeding sites, source of household income, preventive habits and customs are important determinants [9, 6]. At the eco-social (community) level, type of landscape, economic activities, human occupation and human mobility are important determinants [8, 13, 14].

The focus of this study is human mobility and its contribution to the persistence of malaria. Human movements, either seasonal or circular, or linear, within and across borders, are considered strong drivers of (re)introduction of malaria [13, 15]. In the Amazon region, drivers of mobility include seasonal economic activities, seeking search for urban services, illegal activitiestransportation of illegal commodities, among others [4, 16, 7]. Commuting requires long hours in small boats or 4x4 vehicles to cross rivers or poorly maintained dirty roads. The cost of travelling often imply staying away from home for daysto go banking or selling products. In Peru, Carrasco-Escobar et al. [8] found that human mobility was an important determinant of malaria persistence in riverine communities. Wesolowski et al (2012) [13] found influence of human mobility on the risk of malaria importation from transmission hot spots into low transmission areas in Kenya. The same scenario can be found in the Amazon Basin, for example, in Tocantins state, that is characterize by which is a low endemicity area with predominance of imported maintained by the importation of cases [14, 2].

In the Brazilian Amazon, an important site of malaria transmission is the Alto Juruá region, in Acre [16]. *Plasmodium vivax* is the main pathogen, accounting for 70% of the reported cases followed by *Plasmodium falciparum* [2]. In 2018, the annual parasite index (API) was 121.7 positive exams per 1,000 inhabitants for *vivax* malaria and API = 30 for *P. falciparum*. *Vivax* malaria is considered a neglected tropical disease and its elimination is one of the goals of the 2030 Agenda [1].

Reis et al. [5] found a strong correlation between the time series of malaria incidence at the six Northwest municipalities of Acre: Cruzeiro do Sul, Mâncio Lima, Rodrigues Alves, Marechal Thaumaturgo, Porto Walter, and Tarauacá. All of them, but Tarauacá, are in the Alto Juruá region. The first three of these counties are connected by a single paved road while the remaining ones are only accessible by waterways. Reis et al. [5] postulate that connectivity and shared environmental [5, 17] postulated that shared environmental and social drivers could explain the synchronicity of malaria in this region contributing to the high receptivity and vulnerability to malaria.

A household survey conducted in 2015 in 40 localities in this region found a gradient of malaria prevalence along rural-urban gradients [9]. Although malaria did not cluster in any specific region, the odds of observing a household with malaria increased significantly along the urban-rural gradient, from 30% in urban households to ca. 65% in a riverine household. Lana et al. [9] also found increased odds of having malaria in rural households which were accessible by roads in comparison to those accessible by river only. These estimations did not take into account the time spent by individuals away from their place of residence.

The goal of this study is to revisit this household survey to estimate the contribution of human commutation to the persistence of malaria in the Alto Juruá region. We postulate that commutation between urban and rural areas is important to the maintenance of high malaria indices regionally. Understanding the dynamics of malaria along urban-rural axes is useful to increase the precision of the intervention strategies by directing efforts to the main risk groups and places.

To achieve this aim, we proposed a probabilistic model for estimating the contribution of mobility to the probability of getting malaria at household level using data from an origin-destination questionnaire that was part of the survey. First, we derive an estimate of the relative time spent in each locality by each the individual over one year. Second, we estimate the contribution of commuting on the probability of getting malaria.

Materials and methods

Study area

The study area comprises a set of 40 urban and rural localities in two municipalities at the Alto Juruá river basin, Acre state, Brazil: Mâncio Lima (ML) and Rodrigues Alves (RA). These are predominantly rural and forested municipalities, inhabited by indigenous populations, traditional extractivists of forest products, rural settlers and small scale agriculture and fish farming businesses. The main administrative center of the region, Cruzeiro do Sul, is 12 km away from the the RA town and 43 km from the ML town. Cruzeiro do Sul is 700 km away from Rio Branco, the state capital. (Fig. 1).

Mâncio Lima (ML) (7.5468°S, 73.3709°W) is the westernmost state municipality of Brazil. Population density is small (2.79 inhabitants/km^2), with 57.3% of the 15,206 inhabitants living in the town and the remaining 42.7% living in rural settlements scattered along dirt roads and along the Moa river and its effluents [18]. *P. vivax* is the most prevalent malaria parasite, being responsible for an API > 80 in the urban area with $API > 80$ every year since the SIVEP system was implemented in 2003. 2003, at least. Malaria transmission in this municipality has being partially attributed to fish farming, which contributes to the production of mosquitoes and increase the risk for the families working in this activity [17]. The largest peak of malaria activity was registered in 2005/2006 during a large malaria epidemics (API = 505), followed by a downwards trend after this date. In 2018, in the world and in Brazil , an increase of cases was observed and Brazil observed an increase in the number of malaria cases, which was in part attributed to the difficulty of access, implementation of comprehensive and integrated interventions mainly at the community level and inadequate investments [19]. ML followed the same pattern and a new peak was reached (*vivax* deterioration of the malaria control programs [19]. During this period, ML experienced a surge in the number of cases of vivax malaria, both in urban and rural settings (API = 359). In the rural areas of ML, the *vivax* API is always above 300, indicating high transmission. In 2006, it reached API = 1042, and in 2018, API = 504. Fish farming, proximity to flooded areas and living at the fringe of the forest working on logging activities are risk factors for malariain this area [9]. Urban malaria in ML is also significant (*vivax* API = 359 in 2018)and is associated with the presence of many small fish farms, often lacking proper environmental management [17]¿ 300).

Rodrigues Alves (RA) (7.8819°S, 73.3709°W) is predominantly rural (4.68 inhabitants/km^2). Only 30% of the 14,389 inhabitants live in the town, which is located by the Jurua river. RA town is small compared to ML's, has less public services. Residents often commute to CZS, which is only 12km away12 km apart, in search of urban services. It is located in a drier area, away from the flooded forest and fish farms are absent within the town's perimeter. Most of the population (70%) live lives in rural settlements scattered along a network of more than 1000 km of dirt roads. There are also several riverine localities that are accessible only by water along the Jurua river and its effluents during rainy the raining season [18]. As in ML, malaria *vivax* is the most prevalent with API always above 150 since 2004, presenting the peak in 2006 ($API = 994$) [2]. Fish farming, living close to flooded forests or at the fringe of the forest are also risk factors for malaria [9]. In RA, urban malaria is less frequent than in ML, varying from API = 40 to API = 70 during most of the time, except during the 2006 epidemic, when API was 290. In contrast, malaria was more frequent in rural RA than in rural ML up to 2018 ($API > 189$), with a peak in 2006 of 1135. Only after 2018, it decreased to $API = 227$.

For the present study, we aggregated the data in four zones of residence: MLu = urban Mâncio Lima, MLr = rural Mâncio Lima, RAu = urban Rodrigues Alves, RAr = rural Rodrigues Alves. Hence, each locality of residence belongs to one, and only one, of the four zones.

Data

The Lana's 2015 survey assessed demographic and behavior traits associated with self-reported malaria at household level in the study site. The details are found in Lana et al. [9]. Briefly, a total of 520 households were surveyed, distributed in 40 localities: 9 in MLu (n = 190), 5 in RAu (n = 102), 13 in the MLr (n = 107) and 13 in RAr (n = 121).

A householder responded questions regarding him/herself and all the other members of the household, in total there is information about 2274 residents. Information on malaria was obtained with the question: "have you had at least one episode of malaria in the last 12 months?". The same question was posed for each householder. A total of 233 (44.8%) households reported at least one episode of malaria in the last 12 months, been 15.38% in MLu, 10.77% in MLr, 5.96% in RAu, and 12.69% in RAr [9].

One of the components of the survey was a origin-destination questionnaire. The householder responded how often she went in the last 12 months to other localities to study, work, and other reasons. The time spent at each destination per year was recorded. The same question was asked ~~for~~ about the other members of the household. After removing one household due to inaccurate information, the final data set for the analysis consisted of 519 households.

Mobility indicators

From the origin-destination data, we computed for each individual, the fraction of time spent in each destination. To harmonize differences in time units that emerged between responses, whenever possible, length of stay per trip was converted to hours and aggregated over the period of 12 months, providing a measure of total amount of hours per pair of origin-destination, per motive. In the case of pendular displacements for work and study, that is, same-day round-trips, we used standard work- and school-hours as described in more detail in the following paragraphs. In small set of responses (3/2274), the householder reported an area instead of a specific destination. A similarly small number of responses (6/2274) reported the locality but not the corresponding municipality. In these cases, we imputed the information based on the most likely destinations observed among neighbors.

Displacement for school attendance. The time spent at a destination for schooling was estimated assuming standard school hours, that is, $h_s = 4.5$ hours per day [20, 21] and $d_s = 200$ day-classes in a year [22], not accounting for extra times spent away waiting for transportation, attending extra-curricular activities, among other activities.

Formally, the total amount of time spent at a given locality l by individual i, $t^{(s)}_{i,l}$, is given by: $t^{(s)}_{i,l} = h_s \times d_s \times \mathscr{S}_{i,l}$ where $\mathscr{S}$ is a matrix where $\mathscr{S}_{i,l} = 1$ if the individual i attends classes at locality l, and 0 otherwise. If a household has n_h cohabitants, with n_s students, the total household's person-time spent at each destination for studying will be $T^{(s)}_{h,l} = \sum_{i=1}^{n_h} t^{(s)}_{i,l}$.

Displacement for work. Information on the average time spent and how frequently a householder went to a destination for work during the last 12 months was available for a fraction of the responses. In these cases, the amount of time $t^{(l)}_{w,i}$ spent at the destination received the reported value. When the destination was mentioned but the time spent was absent, we imputed this information using the maximum working hours in Brazilian labor law, $h_w = 40$ hours per week. There were 61/208 responses with partial information regarding time spent, reporting total number of days worked but not how many hours per day, and another 45/208 reporting regular workday. For the former, we assumed 8 hours for each reported day. For the later, we assumed 5 days over 52 weeks, with an assumed 8 hours per day. The total person-time spent at each locality l by the n_w workers in a household is $T^{(w)}_{h,l} = \sum_{i=1}^{n_h} t^{(w)}_{i,l}$, where $t^{(w)}_{i,l} = h_w \times d_w \times \mathscr{S}_{i,l}$ where $\mathscr{S}$ is a matrix where $\mathscr{S}_{i,l} = 1$ if the individual i works at locality l, and 0 otherwise.

Total displacement. The total time spent away from home to work or study was calculated at two spatial scales: first, we counted the time spent in every locality l, where locality is any settlement or neighborhood mentioned during the survey. Then we aggregated these localities by zone of residence (urban ML, rural ML, urban RA, rural RA, urban CZS, rural CZS, other). This way, we can observe local and regional mobility patterns. Only commutations for work and study were considered in this calculation since these are the main reasons for regular commuting.

The total person-time spent on each locality l by cohabitants of household h is simply the sum of the time spent away for study and for working, $T_{h,l} = T^{(s)}_{h,l} + T^{(w)}_{h,l}$. Complementary, we assume that the remaining time was spent at the locality of residence:

$$T_{h,l[h]} = n_h \times 24 \times 365 - \sum_{l \neq l[h]} \left(T^{(s)}_{h,l} + T^{(w)}_{h,l} \right). \tag{1}$$

Since households have different sizes, a normalized measure was computed by dividing $T_{h,l}$ by the total householders person-time (number of dwellers x 24 hs x 365 days):

$$\tau_{h,l} = \frac{T_{h,l}}{n_h \times 24 \times 365}. \tag{2}$$

The computation of the mobility at the zone of residence level was done by replacing the person-hour spent at each locality l by the sum over localities belonging to the same zone z, $T_{h,z} = \sum_{l \in z} T_{h,l}$.

Statistical model

A logistic model was fitted to the origin-destination data to estimate the effect of commuting on the probability of getting malaria for a householder living in a zone of residence z and commuting to a zone $z^{'}$. Let Y_h be the number of people in a household h with n_h cohabitants mentioning at least one episode of malaria in the past 12 months. If θ_h is the probability of a malaria case in the last 12 months at household h, Y_h can be modeled as a binomial process, dependent on the mobility pattern of its householders:

$$Y_h \sim Bin(n_h, \theta_h), \qquad h = 1, 2, \cdots, n = 519, \tag{3}$$

$$logit(\theta_h) = \sum_{l} \beta_z \tau_{h,z}, \tag{4}$$

with $\tau_{h,z}$ as given in Eq. (2) calculated by zone. The model has no intercept and each model coefficient β_z can be interpreted as the probability of getting malaria in the last 12 months when all people in a household spent their time at zone z.

Inference for the model coefficients is made under the Bayesian approach based on the approximation implemented in the R function *bayesglm* from the package arm [23]. In order to avoid numerical instability, relatively vague prior distributions are used for the model coefficients. These priors assume that the probability of getting malaria in the absence of commutation is approximately 12% ($logit^{-1}(-2) \approx 0.119$) varying from 1.8% to 49.0%. This is in accordance with the average annual parasite index observed in the area in 2015. Mathematically,

$$\beta_z \sim N(-2, 1), \qquad \forall z. \tag{5}$$

For any location l, the probability of a malaria case in the last 12 months is estimated as

$$\begin{aligned} \pi_l &= logit^{-1}\left(\sum_{z'} \bar{\tau}_{l,z'}\beta_{z'}\right) \\ &= \frac{e^{\sum_{z'} \bar{\tau}_{l,z'}\beta_{z'}}}{1 + e^{\sum_{z'} \bar{\tau}_{l,z'}\beta_{z'}}}, \end{aligned} \tag{6}$$

where $\bar{\tau}_{l,z'}$ is a normalized average of the ratio of person-time spent at zone z' by individuals from location l. That is

$$\bar{\tau}_{l,z'} = \sum_{h \in l} \frac{T_{h,z'}}{n_l \times 24 \times 365}, \tag{7}$$

where $n_l = \sum_{h \in l} n_h$ is the number of respondents in location l.

Scenarios

We used the fitted model to calculate the expected probability of getting malaria under different commuting scenarios. The baseline is zero mobility, that is, a scenario with nobody ~~living~~ leaving their home place. We compared this baseline with scenarios where individuals spent up to 50% of their time in rural or urban areas of ML and RA.

The calculated effect is obtained from the fitted model as the ratio $\tau_{z,z'}$ of person-hours spent at zone z' for a resident of z, the difference in malaria case probability:

$$\alpha_{z,z'} = logit^{-1}\left(\left(1 - \bar{\tau}_{z,z'}\right)\beta_z + \bar{\tau}_{z,z'}\beta_{z'}\right) - logit^{-1}\left(\beta_z\right). \tag{8}$$

The first term is the estimated malaria case probability given the mobility pattern scenario, while the second term is the probability without leaving the zone of residence (baseline). Therefore, it can be interpreted as the destination's malaria probability contribution at origin. To take into account statistical uncertainty, we generated 1000 samples from the posterior distribution of each parameter β_z obtained from the logistic model.

Along with R package arm [23] for statistical model previously cited, we used tidyverse [24] package for data processing, ggplot2 [25], and Inkscape [26] for plots and graphs styling, seriation [27] package for heatmap plot ordering, and cytoscape [28] for network representation.

Results

Mobility to places outside the study region

As a whole, the participants reported 19 destinations outside the study area that were visited in the last 12 months, being 17 in Brazil, 1 in Peru and 1 in Bolivia. In Brazil, the following destinations were cited: 9 in Acre, 1 in Rondônia, 1 in São Paulo, 1 in Rio de Janeiro, 1 in Rio Grande do Norte and 4 in Amazonas (~~Add. files 1~~see Additional file 1). Out of 519 households, only 92 reported at least one travel to localities outside the study area. Of those, only 10 households reported destinations outside the state of Acre. The main reasons for traveling to places outside the study area was seeking medical assistance, and leisure activities.

Mobility within the study region

In general, respondents showed a low rate of displacement to destinations outside their zone of residence, with 96% of households reporting more than 90% of their ~~yearly~~ annual person-hour spent at localities within the same zone (Fig. 2). In fact, 93.4% of the households reported at least 90% of person-hours spent in the same locality of residence. For reference, a typical Brazilian student will spend at least 10.23% of its ~~yearly~~ annual person-hours at school, while a 40h per week job results in at least about 22% of ~~yearly~~ annual person-hours at work.

A total of 62.2% and 18.6% of households from the urban areas of ML and RA had no householders displacing to outside their zone of residence for either work or study, respectively. Among the rural residents, the proportion is higher, reaching 84.4% and 81.0% in ML and RA, respectively.

Mobility motivation

~~Regular commutation for studying was reported by 210 (40.5%) households. This was the main reason for commuting (~~In Fig. 3 we present the distribution of time spent outside away from one's place of residence by motivation. In the panels in Fig. ~~3). More than 400 individuals (18.9% of sampled individuals and 23.5% of~~ 4 we present the amount of person-destination pairs ~~by motivation) attended educational facilities away from their locality. For these students, the time spent at the destination is ca. 10% of the year or 36.5 person-days, corresponding to 42.7% of the total person-hours spent out of household locality.~~ reported (Left panel) and the total fraction of time spent in each destination (Right panel). While the first provides information on the diversity of destinations, the second is fundamental to access actual impact in terms of exposure over the period of 12 months. Unfortunately, it was not possible to ascertain the time spent in trips motivated by seeking health services.

~~The second most common reason for traveling is work, reported by 153 (29.5%) households. This motivation accounted for 208 person-destination pairs (12.2%~~ In terms of person-destination pairs~~by motivation), representing 31.3% of the total person-hours spent away from their home locality. The time spent at the workplace presented roughly a bimodal distribution, with a group spending ca. 2.5% of the year at the destination (9 person-days) and another group spending ca. 25% of their time (90 person-day). Rural households reported 85 person-destination pairs for work related travel (from 62 out of 237 households), with 71 of those pairs having rural~~

areas as destination, 5 with urban destinations, and 9 with unspecified destination zone. For urban households, there were a total of 123 person destination pairs for work (91 out of 282 households), with 82 of those pairs having rural destinations, 10 to urban destinations, and 25 to destinations with unspecified zones.

Urban householders will predominantly go to rural areasfor work related reasons (71.5% of its work-related person-destination pairs), while commuting to other urban localities for study (83.9% of study-related person-destination pairs), it is clear that healthcare and study are the main drivers of displacement displacement, followed by work, leisure and banking. Participants listed rural localities as their main leisure destinations while referring to urban localities when the motivation was seeking healthcare, study or receiving social security benefits. In the case of study related displacement, the diagram shows that residents of urban localities are able to stay in urban areas. For rural residents that reported displacement for study, we see that those from ML have a similar amount of travelers to urban and rural areas, while those from RA stay in rural ones. On the other hand, rural householders that need to individuals that leave their locality for either work or study would mostly go to rural localities, with 83.5% of work-related and 67.9% of study-related person-destination pairs with rural destinations, respectivelyof residence for work almost always have rural destinations, regardless of their locality of residence.

From the total of 519 households, 292 (56.3%) reported displacement to another locality to seek health care assistance. From this total, 92 households (17.7%) reported displacement specifically for malaria treatment. In general, health related trips were more frequent among rural than urban households (178/237 and 114/282, respectively). For rural households, 78.7% of them reported at least one trip to urban localities. Conversely, there were no health related trips from urban households to rural localities reported. While reported health related trips from ML were almost all within the same municipality (159/229 household-destination pairs), from the 148 household-destination pairs originated in RA, most were distributed between RA (38.5%) and CZS (48.7%) localities. We could not calculate the time spent away for health related activities, since this information was not available.

A smaller fraction of trips was motivated by seeking urban services (mainly banking for retrieving social security benefits). This was reported by 238 (45.9%) households, most of them living in the rural areas. For rural households in ML, the destination was almost always localitiesWhen taking into account the actual amount of time spent outside locality of origin, the main motivations are work and study. Although we observe almost no flow from urban areas to rural ones for study, the opposite presents a considerable amount, particularly so for residents of ML. Conversely, in ML itself (94/100 household-destination pairs), while for those in RA the destination was again distributed between localities in RA (60/139) and CZS (65/139). A total of 265 (15.6%) person-destination pairs were driven by this necessity, but accounted for just 9.2% of the total time spent outside home. The median time dedicated to this activity was 9 person-day per year per destination (2.5% of the total time)terms of displacement for work, there is almost no observable flow to urban localities, while rural destinations attract residents of urban and rural localities from both municipalities with considerable total time spent at the destination.

Displacements for leisure accounted for 249 (14.6%) of the trips, representing 16.6% of the total amount of time spent out of household locality. The median time spent at each destination corresponded to 5.8% of the householder's year (ca. 18 person-day). For rural households, most household-destination pairs were to CZS (20/74), Rio Branco (19/74), capital of Acre state, ML (18/74), and RA (9/74) localities. For urban ones, most pairs were to Rio Branco (58/175), ML (43/175), RA (27/175), and CZS (23/175). There were 15 (2.9%) trips for miscellaneous motivations. A detailed description of the mobility motivation among respondents can be found in the Additional file 1.

Mobility and malaria

Figure summarizes the effect of traveling on the probability of malaria at each locality. It is a weighted directed graph (Fig.), where nodes represent the localities and directed edges represent the contribution of time spent at the destination on the probability of malaria at the origin (arrow). The thicker the line , the most darker the line color, the more important is the effect of commuting on malaria probability at the origin. Nodes are colored based on the estimated malaria probability using (Eq. 6). It is clear that all localities are well connected in this network.

There is a strong connectivity between zones of residence. Figure ?? shows the A detailed description of the estimated probability of getting malaria considering the typical median time spent at each destination is provided in the supplementary material (see Additional file 2), since the values reported in the network are the median of the posterior distribution. This calculation does not differentiate between residing or visiting a locality. Probability is highest in rural RA, followed by rural ML. Urban ML shows a slightly less risk compared to its urban counterpart. Only urban RA presented very low probability of malaria. Spending time in rural Cruzeiro do Sul also had a protection effect, although not statistically significant (not shown).

Scenarios

The results of the logistic model are presented in Table 1. The coefficients correspond to the marginal effect of spending 100% of the person-time of a household at a rural or urban zone at ML, RA or CZS. Those can be used to estimate the probability of malaria case in each zone without displacement. This is computed from the inverse of the logit function (Eq. 6) with $\bar{\tau}_{z,z} = 1$, and $\bar{\tau}_{z,z'} = 0$ for $z' \neq z$.

Figure 6 shows how the probability of getting malaria for urban residents changes as they spend more time in the other zones of residence. Spending person-hours in RAu conferred relative protection to the residents of MLu. On the other hand, spending time in RAr increased the probability of malaria, but not significant in MLr. For RAu residents, spending time in MLu, MLr and RAr increased the probability of malaria, more so if going to the latter.

Discussion

Mâncio Lima and Rodrigues Alves are important targets for malaria prevention. In 2015, the official system reported for ML and RA a an *falciparum* API = 48 and 64 and *vivax* API = 294 and 220, respectively [2]. It was a relatively good year considering the historical trend of these municipalities, but a bad year considering the Amazon Basin as a whole. Conditions Risk factors for malaria transmission exist both in urban and rural areas, and the such as the presence of fish farming, proximity to flooded areas, living at the forest fringe working on logging activities [9], summed to the few health teams have to move around to distant places in search of cases. Understanding how mobile is this population can bring new approaches to the control of malaria in this region.

The Our analysis suggests that the population of Mâncio Lima and Rodrigues Alves is not very mobile, with most of the residents rarely leaving their home place. When they do, the majority of destinations are within their municipalities. The major commutation hub is CZS, the regional administrative center. Low mobility can be attributed to the majority of the movements being restricted to places within the municipalities or to CZS. This implies that importation of malaria cases from other regions by traveling residents is unlikely. Similarly, the cost of fuel, the scarcity of routes between most rural localities, as well as the difficulty of using the existing ones year around. For example, dirt roads often close during the rainy season while small rivers become too shallow to be navigable by larger boats during the dry season [9]. However, it is important to mention that some types of commutations, as those motivated by illegal activities (hunting, drug trafficking) may have be omitted by the interviewees. Moreover, it is possible that a household survey may have failed to capture truly mobile populations, that is, those without fixed residence, or that were away from home during the survey. To capture hidden populations, other study designs are required, like snowball sampling or respondent-driven-sampling.

Importation of malaria cases by the commutations of residents is likely to be low. On the other hand, exportation of cases to other municipalities by residents of ML and RA is also unlikely. On the other hand, residents from the neighbor municipalities (e. gML and RA should be monitored. Exportation depends on the rate of travelling and the probability of being infected. Although travelling is infrequent, malaria prevalence is high. Guajará in the Amazon state)or the state capital (Amazônia state), and Rio Branco (Add. files 1) , have their probability of importation increased by their residents traveling to ML and RA [5, 2].

Low mobility can be explained by the lack of routes between localities, like dirt roads that close during the rainy season or small rivers that become navigable only by small boats Acre state) (see Additional file 1) are at risk of malaria importation due to their connectivity with the studied population [5, 2]. Low rate of mobility should not be disregarded in a malaria control program. In such situation, active testing of travellers should be considered to avoid reinfection in these as well as in other areas of the Amazon. Some studies characterize the strains of *Plasmodium* in circulation, and have shown the importance of long journeys on infection importation [29, 30]. Saita et al.[31] found a positive association between malaria prevalence during the dry season [9]. Moreover, travelling is very costly for this low-income population, the price of fuel in in the Thai-Myanmar border and road quality, a proxy of mobility rate.

In the Alto Juruáregion being the highest in Brazil.

Our analysis suggests that, in this region, the place one lives is a stronger determinant of the , overall, the probability of getting malaria is more associated with the place of residence than the place one goes for study or work. This can

~~be a natural consequence of the low mobility of this population and the local environment. The highest probability of malaria was found in rural~~ of displacement. This is explained by the low rate of mobility. Still some types of commutations present higher risk than others. We have shown that a resident of urban RA ~~, followed by rural ML, and urban ML. The lowest was urban RA. The hypothetical scenarios analysed show that in order to have~~ has an increase of only 5% in ~~the~~ their probability of getting malaria ~~for a resident of urban RA would require more than~~ by spending 30% of ~~its time being spent at~~ their time in rural RA~~or~~ , but as high as 50% if spending the same time in ML localities (Fig. 6). ~~Fish farming is an important activity associated with increased malaria risk in the~~ The effectiveness of the malaria control program can be improved by placing testing sites along these routes.

Differences in malaria prevalence along rural-urban gradients can be explained by ecological, social,and behavioral factors [9, 7, 31, 8]. In general, urban areas present conditions, like housing, drainage network, pavement, and easier access to health care, that contribute to reduce malaria prevalence, when compared to rural areas [32]. According to Braz et al.[33], malaria in Amazon Basin showed a spatial dependency with characteristics that differ between municipalities, states and international borders, which reinforces the importance of monitoring malaria clusters and integrative control actions. The Alto Juruá ~~region. Fish~~ as a whole is highly receptivity to malaria, since most of the population live at the forest fringe. This forest floods seasonally, creating favorable breeding conditions for the vector [34]. Fish farming also contributes to maintaining a high abundance of vectors in urban and peri-urban areas. Fish ponds started to be built around the year 2000 ~~in this region, with a large part being completed in~~ as an important local economic activity. A large fraction of the ponds were completed by 2005 [35]~~. According to Reis et al.[5], the municipalities like ML~~, ~~RA, CZS and Tarauacá, that built~~ with more than 80 fish ponds / year ~~between 2003 to 2006, showed higher malaria rates.~~

~~Differences in malaria probability between study zones can be explained by ecological differences as well as human work/occupation and way of life [9, 7]. Reis et al. [17] showed that fish ponds without adequate management contribute to increased *Anopheles* abundance. This contributed to make urban ML a significant area for malaria transmission~~[5]. Fish farming contributed to keep urban ML as significant area of malaria transmission, despite the efforts to remove natural breeding sites. The same ~~does~~ phenomenon did not happen in urban ~~RA~~RA, as the conditions for fish farming were not so suitable.

Studies carried out in Colombia, Peru and Namibia using molecular markers to measure gene flow between different study areas have suggested the presence of malaria corridors that allow the slow and progressive movement of parasite populations throughout endemic areas with few evidence of direct human displacement between them [36, 8, 29, 30]. This is an important issue to consider in Alto Juruá region when we observed the differences of prevalence throughout the urban and rural zones and the neighbor municipalities. The studied rural localities in rural ML are traditional communities living along the Moa and Azul rivers. Their way of life is mainly based on ~~extractivism activities~~ traditional extractivism of forest products and subsistence agriculture. Their mobility is very low and strictly by boat [9].

~~Rural~~ Conversely, rural RA has several newly implemented settlements, what means new population that probably was not exposed to malaria. Arriving recently in a rural settlement is ~~a risk factor~~ an known risk for symptomatic malaria [6]. This region has more people commuting, mainly to work. Work follows a pattern most related to agricultural populations that is dependent to seasons even as Saita et al.[31] found.

The study has ~~some~~ other limitations. This is a cross-sectional survey, which provided only one measure in time. The interviews were performed in a self-reported questionnaire, memory bias is possible to affect the responses, since the time of events reported was up to 12 months before the day of the interview. Another limitation is the fact that we do not account for time of day spent in each locality, which can affect the probability of malaria infection due to vector's activity preferences. Seasonality attributed to malaria transmission dynamic may have an important influence in this study as reported in the literature [32, 37, 34, 31, 3].

Conclusion

The natural conditions ~~of~~ for the circulation of pathogens such as the ~~*Plasmodiuns*~~*Plasmodium spp*, combined with the ~~circulation and permanence of humans in certain Amazonian regions~~pattern of mobility of humans in the Amazon, make clear the need of disease control perspective change. ~~This context reminds us to think on how to coexist with malaria, since there is no vaccine against the disease and people will continue to live in those highly endemic places. How to actually manage the environment and also malaria cases to reduce transmission? The environment already faces collective and individual challenges, as characterized in Lana et al. Lana2017. In terms of cases clinical management and surveillance, the message is a general consensus: to guarantee quick access to diagnosis and treatment, in addition to rolling out active case detection. However, how to facilitate access to health care in regions as remote and difficult to access as those found in the riverine region of Mâncio Lima? Or in some rural settlements in Rodrigues Alves where the road is often interrupted due to rainy season? How to make these environments less infection-prone and more accessible while respecting the equally important forest conservation?~~

~~The results of this study suggest that mitigation actions in the Alto Juruá region should focus on those with high malaria incidence at the localities of residence, not so much at localities of visit/transit. Important to mention that this is different for states like Tocantins, where most reported cases are imported [14, 2]. The spatial heterogeneity highlights the importance of microregion-targeted intervention since their risk signature within each municipality is quite different, despite being direct geographical neighbors. In addition, it is~~ It is essential that intersectoral public policies be the basis for health mitigation actions. Places that have fish farmings need to have adequate policies to support this economic activity. This policy must contemplate the entire process, from the concession of the fish pond, through training for maintenance, as well as the final destination of the product. Thus, it avoids the abandonment of the fish ponds by those owners who are unaware of the risks related to malaria and who are often unable to afford maintenance costs, which is common in the region [38] and (personal communication). Especially to places close of forest fringe, most of them are recent settlements, should have more active case monitoring to improve the opportunity of response on diagnoses and treatment, what can reduce the malaria transmission in those places. Acre state was the reference in those protocols and won for 3 consecutive years (2011-2013), the Malaria Champion of the Americas award [39]. The problem now is the changes on theses policies and the investments in Malaria Control Program. Another important action that must be considered is to include malaria as a transverse activity in the school curriculum in the region, as well as in other regions of the Amazon Basin. In workshops held with teachers in the region, we identified that schools work more on diseases such as dengue, than malaria (manuscript in preparation), which in terms of disease burden, impacts the region much more (~~manuscript in preparation~~submitted manuscript).

Declarations

Ethics approval and consent to participate

Ethical considerations. The study protocol was approved by the Ethical Review Board of the National Public Health School, Brazil (Number 861.871), and written informed consent was obtained from each adult participant.

Consent for publication

All participants signed an informed consent for publication.

Availability of Data and Materials

The dataset supporting the conclusions of this article is available in the ~~additional file 2~~Additional file 3.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

RML and CTC developed the questionnaire, the study designed, conducted the household survey and consolidated the database. MFCG and RML organized the database for the analysis. MFCG and LSB analyzed the data. RML, MFCG and CTC wrote the manuscript. All authors revised the manuscript.

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Figures

Figure 1 Map of the study area in the Alto Juruá region, Acre state, Brazil. The black dots represent the surveyed communities. These communities are connected by dirt roads (red lines) and rivers (blue lines). Source: ~~Instituto Brasileiro de Geografia e Estatística (~~IBGE ~~)~~ [18], PRODES [40], TerraClass [41], ANA [42] and the household survey described in Lana et al. [9]

Figure 2 Heatmap of person-hours annual ratio spent in each zone by locality of residence. Color gradient based on log-scale of the ratio, ranging from white (< 0.0001) to dark blue (1). Locality (rows) and zone (columns) names are colored by their type: urban (blue), rural (brown), or nonspecific (gray). Localities' names have a prefix of M.L or R.A. to indicate the corresponding municipality, ML or RA. The suffixes u and r in each destination zone indicate urban and rural zones in the corresponding municipality, respectively.

Figure 3 Fraction of time spent in the last 12 months per destination, by respondent. Each curve correspond to a specific travel motivation: social security (red), study (green), work (blue) and leisure (pink). Main plot represent the kernel density distribution, while the inset shows the histogram with number of respondents per bin of size 0.05.

Figure 4 Alluvial diagram of reported displacements. Left panel presents the number of reported destinations per respondent, stratified by municipality and type of origin (red: rural, blue: urban), motivation, and destination type. Right panel presents the total fraction of hours spent in destination per respondent, stratified by municipality and type of origin (red: rural, blue: urban), motivation, and destination type.

~~Points represent~~ Please refer to the ~~median and vertical lines the 95% CI over 1000 samples of the posterior distribution~~online article for high resolution image.

Figure 5 Mobility and malaria probability network. Each node represent a locality surveyed or reported as a place of work/study. Localities outside of the surveyed area where aggregated by municipality (ML, RA, or CZS) and zone type (rural, urban, or nonspecific) and are gray shaded. Nodes' shape represent rural (triangles), urban (squares), and unspecified (diamonds) zones. Nodes from surveyed area are displayed according to their geolocation. Nodes representing aggregated localities are displayed in the corresponding municipality. Nodes are colored according to the estimated malaria case probability based on typical mobility pattern, with a gradient from light yellow (0) to dark red (0.25). Edge's direction and color reflect the ~~yearly~~ annual person-hours ratio contribution of the locality of edge's origin to the probability of observing a malaria case at locality of edge's destination, with gradient from light blue (0) to dark purple (0.06).
~~Points represent~~ Please refer to the ~~median and vertical lines the 95% CI over 1000 samples of the posterior distribution~~online article for high resolution image.

~~Points represent~~ Please refer to the ~~median and vertical lines the 95% CI over 1000 samples of the posterior distribution~~online article for high resolution image.

Figure 6 The expected probability of getting malaria under different commuting scenarios. Contribution at urban areas from ML and RA based on percentage of person-hours spent at different destination zones. Results obtained from 1000 samples of the posterior distribution of exposure effect of each zone, and simulating single-destination mobility profiles.

Table 1 Logistic model results

Zone	Coefficients	Std. error	p value
MLr	-1.28428	0.10405	< 0.001
MLu	-1.44798	0.10605	< 0.001
RAr	-0.91538	0.09384	< 0.001
RAu	-2.52504	0.18589	< 0.001
CZS	-3.11453	3.95460	0.4309
CZSr	-16.23128	7.72548	0.0356

Additional Files

Additional file 1
The additional file named Addfile1.~~csv is a table that contains~~ zip contains the table with information about origin-destination pairs by a total of hours, motivation, and type of zone destination and the pdf file with the quantitative description of mobility motivation.

Additional file 2
The additional file named Addfile2.pdf presents the estimated malaria case probability based on typical person-hour origin-destination matrix and the estimated effect of each locality to the probability of observing a malaria case. Points represent the median and vertical lines the 95% CI over 1000 samples of the posterior distribution.

Additional file 3
The additional file named Addfile3.zip presents the dataset used to conduct the analysis.