

## Research Paper

# *Kerteszia cruzii* and extra-Amazonian malaria in Brazil: Challenges due to climate change in the Atlantic Forest

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## ABSTRACT

*Kerteszia cruzii* is a sylvatic mosquito and the primary vector of *Plasmodium* spp., which can cause malaria in humans in areas outside the Amazon River basin in Brazil. Anthropogenic changes in the natural environments are the major drivers of massive deforestation and local climate change, with serious impacts on the dynamics of mosquito communities and on the risk of acquiring malaria. Considering the lack of information on the dynamics of malaria transmission in areas across the Atlantic Forest biome, where *Ke. cruzii* is the dominant vector, and the impact of climate drivers of malaria, the present study aimed to: (i) investigate the occurrence and survival rate of *Ke. cruzii* based on the distinct vegetation profiles found in areas across the coastal region of the Brazilian Atlantic Forest biome; (ii) estimate the extrinsic incubation period (EIP) and survival rates of *P. vivax* and *P. falciparum* parasites in *Ke. cruzii* under current and future scenarios. The potential distribution of *Plasmodium* spp. was estimated using simulation analyses under distinct scenarios of average temperature increases from 1 °C to 3.7 °C. Our results showed that two conditions are necessary to explain the occurrence and survival of *Ke. cruzii*: warm temperature and presence of the Atlantic Forest biome. Moreover, both *Plasmodium* species showed a tendency to decrease their EIP and increase their estimated survival rates in a scenario of higher temperature. Our findings support that the high-risk malaria areas may include the southern region of the distribution range of the Atlantic Forest biome in the coming years. Despite its limitations and assumptions, the present study provides robust evidence of areas with potential to be impacted by malaria incidence in a future scenario. These areas should be monitored in the next decades regarding the occurrence of the mosquito vector and the potential for malaria persistence and increased occurrence.

## 1. Introduction

Extra-Amazonian malaria, specifically autochthonous *Plasmodium* infection in the Atlantic Forest biome, occurs mainly in the eastern and south-eastern regions of Brazil (Pina-Costa et al., 2014). It is known as “bromeliad malaria” because the main mosquito vector species depends on bromeliads (Bromeliaceae) phytotelmas to lay eggs and develop immature life stages (Forattini, 2002). In these regions, *Kerteszia cruzii* (Dyar and Knab) is considered the primary vector of human and simian *Plasmodium* (Deane et al., 1970; Duarte et al., 2013; Kirchgatter et al., 2014). The most prevalent parasite species associated with human malaria across the Brazilian extra-Amazon region is *Plasmodium vivax* (Pina-Costa et al., 2014). However, a recent study demonstrated that *P.*

*falciparum* has a higher prevalence than *P. vivax* in *Kerteszia* species collected in forest fragments of the South-eastern Atlantic Forest in Brazil (Laporta et al., 2015).

*Kerteszia* species are sylvatic mosquitoes that occur from southern Mexico to southern Brazil (Carvalho-Pinto and Lourenço-de-Oliveira, 2004), including Venezuela (Berti et al., 2015), Ecuador (Linton et al., 2013), Colombia, Peru, Bolivia, Paraguay, Guiana, French Guiana, and Suriname (Marrelli et al., 2007). Most *Kerteszia* species occur in coastal areas of both the Pacific and Atlantic oceans, where bromeliads are abundant (Marrelli et al., 2007). However, there are reports of *Kerteszia* species in Northeast Brazil. Increased deforestation in the Atlantic Forest may have reduced the geographical distribution of some species (Laporta et al., 2011). *Kerteszia cruzii* females feed on blood of humans

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as well as of other mammals and birds (Consoli and de Oliveira, 1994). The infective biting rate was low in areas in which *Ke. cruzii* was found naturally infected with *Plasmodium* spp.; however, the high abundance of *Plasmodium* adults and high human biting rate sustain the endemic circulation of human *Plasmodium* in some areas across the Atlantic Forest domain (Lorenz et al., 2014).

It is well known that deforestation, temperature, and precipitation are major drivers of the dynamics of mosquito populations (Vasseur et al., 2014) and can affect the geographic dispersion of vector-borne diseases, such as malaria and arboviruses (Hales et al., 2002; McMichael, 2013; Liu-Helmersson et al., 2014). These factors influence the persistence and replication of *Plasmodium* parasites, the susceptibility of vectors to these parasites, the extrinsic incubation period (EIP) of the parasite in the mosquito population, the geographical distribution of the vector species, and seasonality of the vector-borne disease (Gubler et al., 2001). The EIP of a *Plasmodium* parasite is temperature dependent. High temperatures decrease the interval between the acquisition of infectious agents by a blood meal and the mosquito's ability to transmit the parasite to a new susceptible host, whereas low temperature increases this interval and decreases the vector competence of a mosquito population. Because of the effects of climate change on mosquito populations and vector-borne diseases, a predictive model considering the practical relevance of predicting the risk of malaria in a scenario of changes that may impact transmission rate and the geographical distribution of the *Plasmodium* infection must be proposed (Campbell et al., 2015). As there are very few models focused on the dynamics of malaria in the Atlantic Forest, where *Ke. cruzii* is the dominant vector, the present study aimed to: (i) investigate the occurrence and survival rate of *Ke. cruzii* based on the different vegetation types found along the Brazilian Atlantic coast; (ii) estimate the EIP and survival rates for *P. vivax* and *P. falciparum* pathogens in *Ke. cruzii* populations considering current and future climate change scenarios. We hypothesized that changes in temperature will affect the geographical distribution of the dominant vector and, consequently, the occurrence of malaria in areas outside the Amazon basin.

## 2. Materials and methods

### 2.1. Data acquisition

All records of *Ke. cruzii* in Brazil reported in scientific papers and databases in the last 60 years (from 1958 to 2019) were included in the present study. Data were exhaustively collected (Supplementary Table 1) using searches of the Google Scholar, PubMed, and Scielo databases through Boolean search (search terms: “*Anopheles*” OR “*Kerteszia*” AND “*cruzii*” AND “Brazil” OR “Brasil”). The presence data points used were the coordinates of the centroid of the municipality in which the presence of *Ke. cruzii* was registered or the coordinates of the collection site itself (when available). The distribution map proposed by Marrelli et al. (2007) was also used to model the occurrence of *Ke. cruzii*. To correlate the occurrences of *Ke. cruzii* with the vegetation profiles of the Atlantic Forest biome, a map of the species' geographic distribution area was compiled with the native vegetation profiles and associated ecosystems of the Atlantic Forest (IBGE, 2008).

The density of the vegetation cover on a given pixel of land was determined by the normalized difference vegetation index (NDVI) (Rouse et al., 1974) using the eq. (1):

$$\text{NDVI} = (\text{NIR} - \text{R}) / (\text{NIR} + \text{R}) \quad (1)$$

where NIR is the reflection in the near-infrared spectrum (band 4) and R is the reflection in the red range of the spectrum (band 3). The NDVI value for a given pixel always ranges from (−1) to (+1), but the absence of green leaves results in a value close to zero. An NDVI value of 0 indicates the absence of vegetation and a value of ~1 (0.8–0.9) indicates the highest possible density of green leaves in the pixel evaluated (Rouse et al., 1973).

To elaborate the occurrence map of *Ke. cruzii*, a mosaic was constructed using the QGIS geographic information system (Bossle, 2015) of the NDVI images from MODIS Satellite (250-m resolution, acquired in January 2018), available from the Brazilian Agricultural Research Corporation (EMBRAPA, 2018). Average temperature information was obtained from the WorldClim-Global and AMBDATA databases, which contain historical data from the last 50 years. These data were interpolated at a resolution of 30 arc sec (approximately 1 km). We did a regression analysis with the NDVI values and the frequency of *Ke. cruzii* occurrence to examine association between these two variables.

### 2.2. Data analysis

The association between temperature and malaria occurrence in the Atlantic Forest was investigated following Martens (1988) and Poveda et al. (2000). The probability of a daily survival rate of *Ke. cruzii* ( $p$ ) was estimated using eq. (2):

$$p = e^{-1/(-4.4 + 1.31T - 0.03T^2)} \quad (2)$$

where  $p$  is the daily survival probability rate and  $T$  is the average temperature. This procedure was performed for each location in which *Ke. cruzii* was registered. In the following round of analysis, the interpolated maps of the probability of daily survival rates of *Ke. cruzii* were generated using the inverse distance weighted (IDW) algorithm based on a 250 × 250 m grid. This algorithm was used because it calculates the values for all grid cells using the mean distance to the nearest points known as space weights. This method allows interpolation of the values of variables distributed in space taking into account the spatial dependence of the data.

To calculate the EIP for each *Plasmodium* species, autochthonous malaria cases registered from 2001 to 2017 in areas where *Ke. cruzii* occurred across the extra-Amazonian region were considered. Malaria data regarding the location of exposure to *Plasmodium* infection are publicly available in the Brazilian National Notifiable Diseases Information System (SINAN, 2018). The sites with registered malaria cases were georeferenced using the geographical coordinates of the municipality as the centroid of the pixel in which the presence of *P. vivax* and *P. falciparum* were registered. Few malaria cases with local geographical coordinates were available in the Brazilian malaria database; thus, when available, the case was georeferenced by the site. The EIP ( $n$ ) was calculated according to Martens (1988) using eq. (3):

$$n = D_m / (T - T_{min,n}) \quad (3)$$

where  $n$  is the EIP (in days);  $D_m$  is the number of days required for the development of the parasite given the sum of the temperatures of the parasite's development days, i.e., 105 °C for *P. vivax* (MacDonald, 1957) and 111 °C for *P. falciparum* (Kiszewski et al., 2004);  $T$  is average temperature; and  $T_{min,n}$  is minimum temperature required for parasite development, i.e., 14.5 °C for *P. vivax* and 16 °C for *P. falciparum* (Martens, 1998; Poveda et al., 2000). The procedures adopted for the spatialization of the temperature and malaria cases per parasite species were the same as those employed to elaborate the daily survival probability maps of *Ke. cruzii*. Assuming that the daily survival probability is an independent event (Poveda et al., 2000), the calculation of the parasite survival rate ( $sr$ ) is given by eq. (4):

$$sr = p^n \quad (4)$$

where  $p$  is the probability of daily survival of *Ke. cruzii* and  $n$  is EIP. To calculate the survival rate, map algebra (Tomlin, 1994) was applied in the ArcGIS software, with the daily survival probability maps of a mosquito vector being elevated by the EIP of both *P. vivax* and *P. falciparum* parasites.

Future climate data were integrated in the analysis using the MIROC-5 global climate model (Watanabe et al., 2011). We choose to use this model because the MIROC-5 also includes components of the Earth's system and climate change, in relation to anthropogenic

radiation. The advantage of using this model is that it increases the accuracy of short-term climate prediction, as it can be affected by both anthropogenic and intrinsic fluctuations of the climate system (Watanabe et al., 2011). To obtain future climate scenarios using the MIROC-5 model, it is necessary to choose a condition for the evolution of greenhouse gas emissions during the period of time for which the future climate is projected. The predictive modelling herein performed considered two different scenarios: low emissions (RCP 2.6) and very high emissions (RCP 8.5), detailed in the Special Report on Emissions Scenarios by the Intergovernmental Panel on Climate Change (Pachauri et al., 2014). In the first scenario assumed, the global temperature tend to increase by 1.0 °C and can reach a temperature anomaly of 0.4–1.6 °C in 2046–2065, and an additional 0.3–1.7 °C in 2071–2100 (Van Vuuren et al., 2007). In the second scenario, in which the high emission of greenhouse gas is assumed, the global temperature tends to increase from 2.0 to 3.7 °C and reach a thermal anomaly of 1.4–2.6 °C in 2046–2065 and of 2.6–4.8 °C in 2071–2100 (Chou et al., 2014).

### 3. Results

According to the literature, *Ke. cruzii* was registered in 94 localities from 1968 to 2019. Most of these localities were in dense ombrophilous forest regions, with NDVI of 0.8–0.9 (Fig. 1). Positive association between *Ke. cruzii* occurrence and high NDVI was found in the southern and south-eastern areas of Brazil, where there are many forest fragments with some representing the largest remnants of the Atlantic Forest. Regression analysis between NDVI values and the frequency of *Ke. cruzii* occurrence indicated association between these two variables ( $r^2 = 0.99$ ).

The probability of daily survival for *Ke. cruzii* was higher in warmer areas at lower latitudes, reaching 97% of the coastal areas of north-eastern Brazil, where bromeliads phytotelmas occur in sparse forest remnants (Fig. 2). The modelling analyses of the *Plasmodium* parasites showed that both *P. vivax* and *P. falciparum* had an increased trend in their survival rates (Figs. 3 and 5) and decreased EIP (Figs. 4 and 5) in future scenarios favouring warmer temperatures. For all sites, the EIP values predicted considering the current and future temperature scenarios decreased if the temperature was raised by 1–3.7 °C (Fig. 5). The decrease is greater for cooler areas (e.g., South region) than for the Northeast region. For example, in the Curitiba municipality (Parana State, Southern region), the EIP values for *P. vivax* were 33.6 days (current temperature), 26.3 days (for 1 °C increase), and 22.3 days (for 3.7 °C), whereas in warmer areas such as Recife (Pernambuco State, Northeast region), the EIP values ranged from 7.7 to 9.7 days

irrespective of changes in temperature. Under the scenario of increased temperature, *P. falciparum* had a greater change in EIP compared to *P. vivax*: on average, the former changed from 23.6 days (current temperature) to 15.3 days (3.7 °C increase), while the latter changed from 17.6 days (current temperature) to 12.6 days (3.7 °C increase).

The survival rate of both *Plasmodium* species increased under the raised temperature scenario, with the increase being greater for cooler sites (e.g. South region) and for *P. vivax*. On average, the survival rate of *P. vivax* will increase by 10% and 13% for the 1 °C and 3.7 °C rise scenario, respectively and *P. falciparum* will increase by 8% and 10.5% for a 1 °C and 3.7 °C rise, respectively (Fig. 5).

### 4. Discussion

Although higher temperatures may result in an increase in the population of vectors and parasites, this does not necessarily translate into an increase in a vector-borne disease incidence (Chua, 2012). Several factors are also important, including socioecological and environmental factors (water storage and disposal systems, agricultural practices, deforestation, population density, living conditions, control programs, and health infrastructure) (Reiter, 2001), human behaviour, human population immunity, and the parasite's levels of drug resistance (Chua, 2012). In addition, the estimated EPI and daily survival rate of *Ke. cruzii* solely based on temperature is too simplistic, as reported by Ohm et al. (2018). Our model, as well as most existing models, assumes that the only factor affecting EIP is the mean temperature. In addition to mean temperature, the EIP metrics is likely influenced by genetic diversity of the vector, diversity of the parasite, and variation in a range of biotic and abiotic factors that affect mosquito conditions (Ohm et al., 2018). Regarding the daily survival rate of *Ke. cruzii* many factors are correlated, such as female age, blood source availability, vector population density and the human-mosquito contact rate. Dalla Bona and Navarro-Silva (2010) found that parous females of *Ke. cruzii* had higher survival rates than nulliparous females. Regarding species of *Anopheles albittarsis* complex, 50% daily survival rates were shown to yield only 1% of the population that survived long enough to become infective (Kakitani and Forattini, 2000). Even so, our study provides additional insights for further modelling as there is not much information about the EPI in *Ke. cruzii* and survival rates in the Brazilian extra-Amazon region.

In Brazil, the geographic distribution range of *Ke. cruzii* is restricted to forest remnants across the Atlantic coast (Forattini, 2002; Marrelli et al., 2007). Species dispersal is modulated by the life history requirement for bromeliad phytotelma, blood, nectar, mating, resting sites, and environmental variables such as partial shade, warm

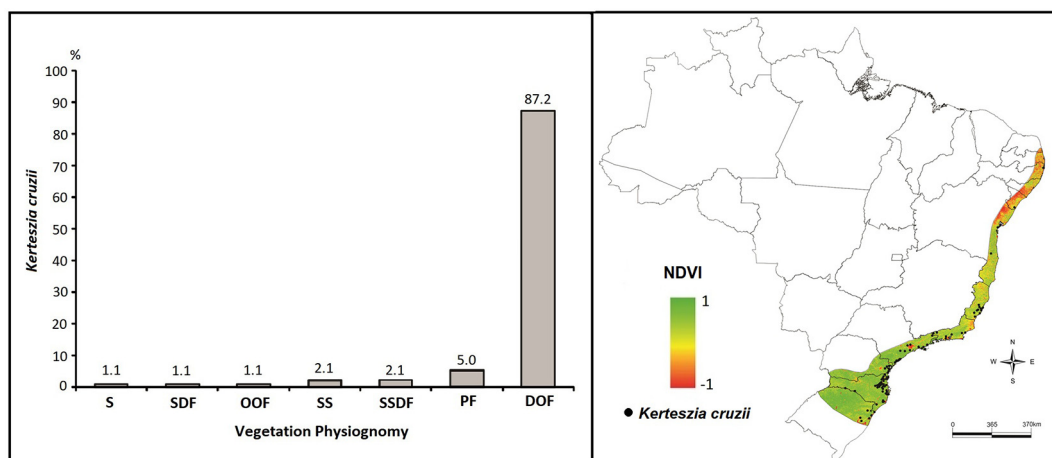


Fig. 1. Left: Remnants of Atlantic Forest determined by the NDVI metrics, where *Ke. cruzii* was registered (S = Savannas, SDF = Seasonal Deciduous Forest, OOF = Ombrophiles Open Forest, SS = Steppic-Savanna, SSDF = Seasonal Semi-Deciduous Forest, PF = Pioneer Formations, DOF = Dense Ombrophiles Forest). Right: NDVI values according to the vegetation physiognomies in the geographic distribution range of *Ke. cruzii* in Brazil.

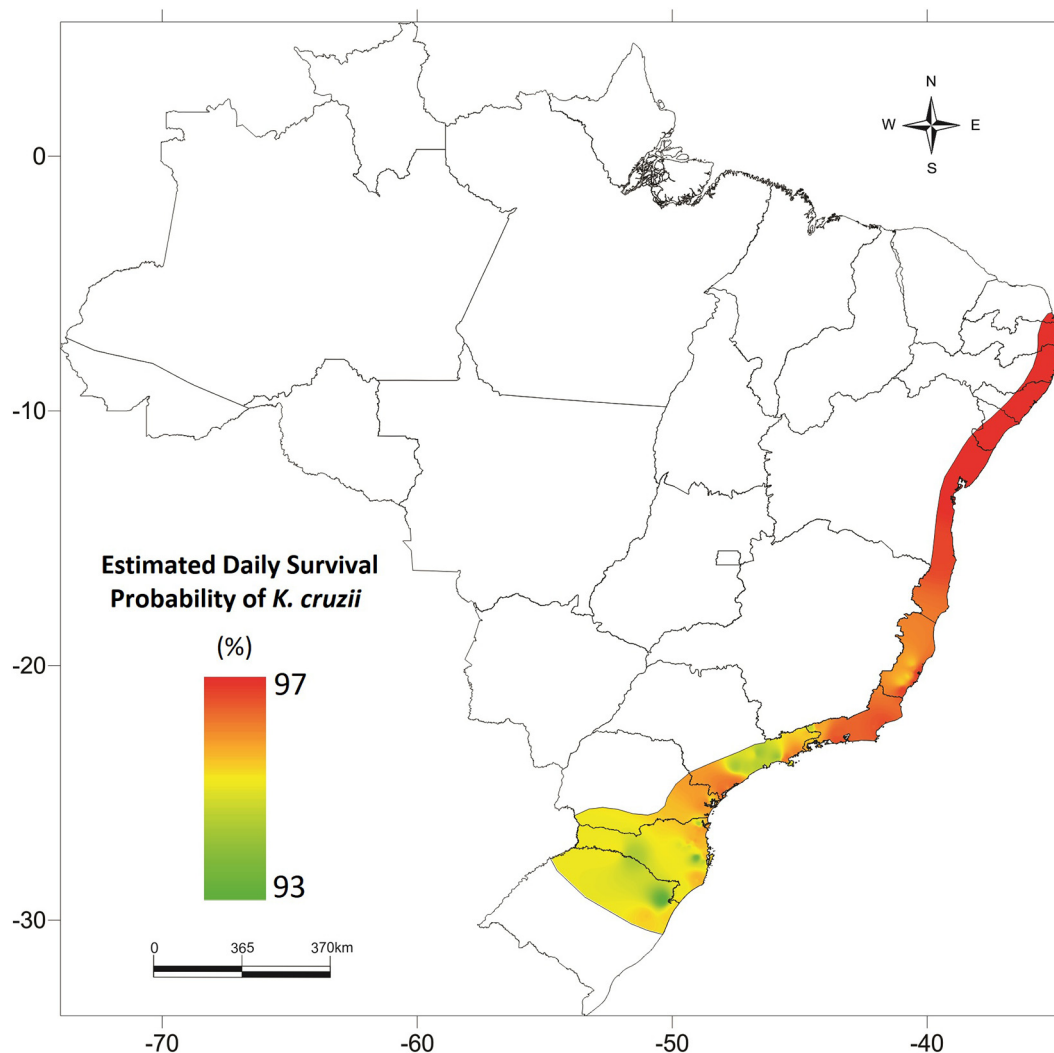


Fig. 2. Estimated daily survival probability (%) of *Ke. cruzii* in Brazil.

temperature, and high rainfall (Marrelli et al., 2007; Pina-Costa et al., 2014). These factors intrinsic to the microhabitat where they live highly constrain the occurrence of *Ke. cruzii* to the forest fringe of tropical rain forests (Forattini et al., 1993; Forattini, 2002). Our results from the spatial distribution of *Ke. cruzii* confirmed that the species is mainly associated with areas of ombrophilous dense forest located along the south and southeast coast, as found by Laporta et al. (2011). Because *Kerteszia* mosquitoes are concentrated in tropical rain forests with a high density of bromeliads (Guimarães et al., 2003), populations of these species can be negatively impacted by deforestation and degradation of the natural environment (Marrelli et al., 2007). Afrane et al. (2005) studied the effects of deforestation-caused microclimate change on the duration of the gonotrophic cycle of the malaria vector *Anopheles gambiae* and found that the duration of the first and second gonotrophic cycles was shortened by 1.5 d (17%) and 1.4 d (27%), respectively, in the deforested highland site. A shorter mosquito gonotrophic cycle implies an increased daily biting frequency and thus increased vectorial capacity; this may also occur with *Ke. cruzii* at some sites, even though it frequently occurs in peridomestic environments neighbouring forests. *Kerteszia* mosquitoes seem to not rest inside human houses after feeding on human blood (Forattini et al., 1993). Therefore, they are considered exophage vectors, at least in the Ribeira Valley and neighbouring regions (Forattini et al., 1986, 1993).

Despite the higher daily survival rate in areas along the northeast coast of Brazil, where the temperature is higher than in the southern

areas of the Atlantic Forest, *Ke. cruzii* distribution is highly heterogeneous, and the species is primarily restricted to forest fragments. However, even in forest remnants, the presence of *Ke. cruzii* is linked to the presence of particular species of bromeliad vegetation, such as those of the genera *Vriesia*, *Nidularium*, and *Aechmea* (Chaves et al., 2016). Chaves et al. (2016) observed that the landscape is an important modulating factor in the distribution of bromeliads in the Atlantic rainforest, influencing the abundance of *Kerteszia* species. Forest fragmentation is the major driver of habitat and natural vegetation loss, including of bromeliad plants, thus leading to a reduction in *Ke. cruzii* abundance (Medeiros-Sousa et al., 2019). In addition, habitat fragmentation can influence ecological and microclimatic factors, which explains the local variations in daily survival rate estimated for *Ke. cruzii* obtained in the present study. Conversely, differences in daily survival rate can be associated with genetic variations among populations or with the name *Ke. cruzii* encompassing a complex of putative species, as indicated by differences found in the polytene chromosome of females (Ramírez and Dessen, 2000) and sequence data (Rona et al., 2009; Dias et al., 2018). Another unusual fact that could indicate differences between *Ke. cruzii* populations is that this vector has never been described as malaria vector in North-eastern region of Brazil, unlike the South-eastern and Southern regions where it is the primary vector. Chu et al. (2019) studied the dominant malaria vector *Nyssorhynchus darlingi* and showed that genetic variation among mosquitoes from different localities results in plastic responses, which in turn have



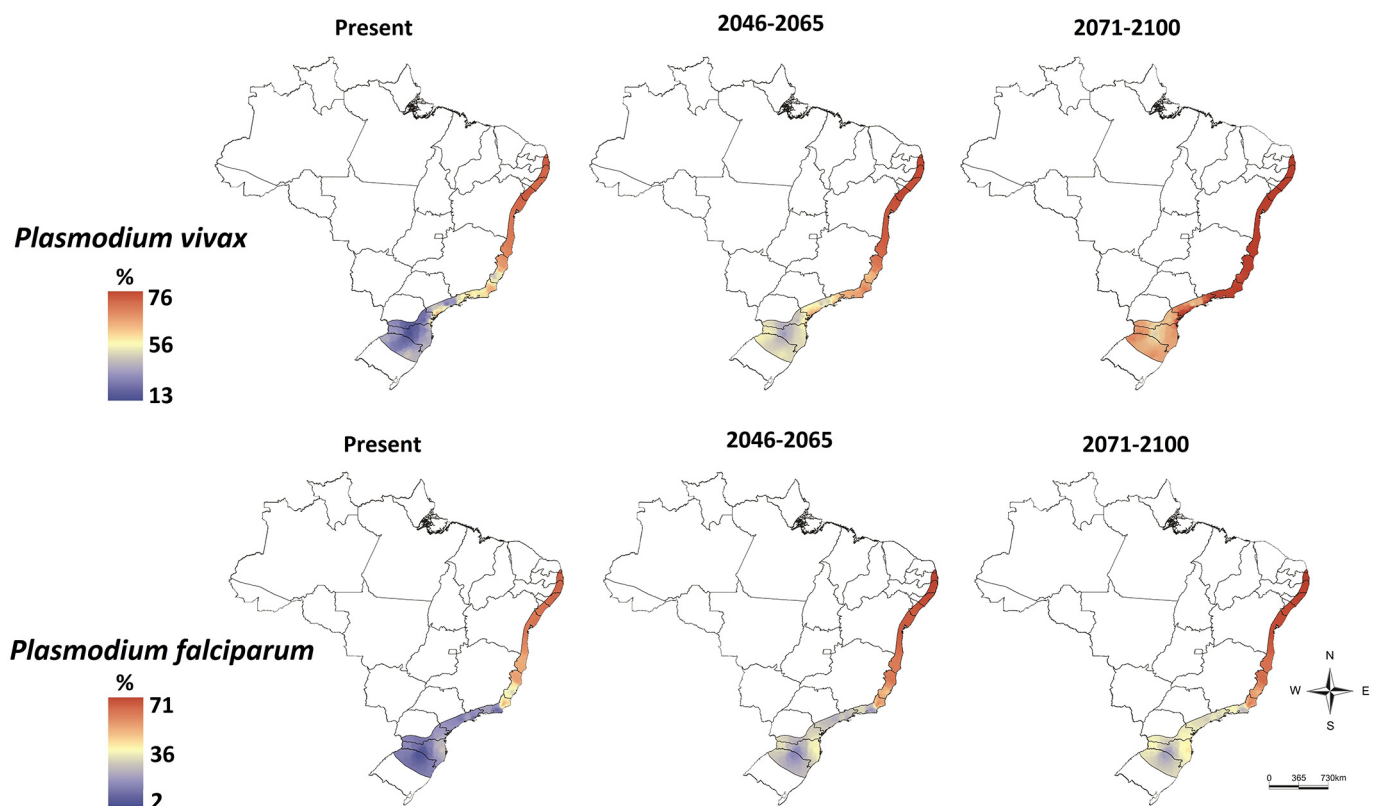


Fig. 3. Estimated extrinsic incubation period (EIP) for *P. vivax* and *P. falciparum* at geographic area of *Ke. cruzii* distribution based on MIROC-5 global climate model. The maps show the probability under two climate change scenarios: RCP 8.5 (2046–2065) and RCP 2.6 (2071–2100).

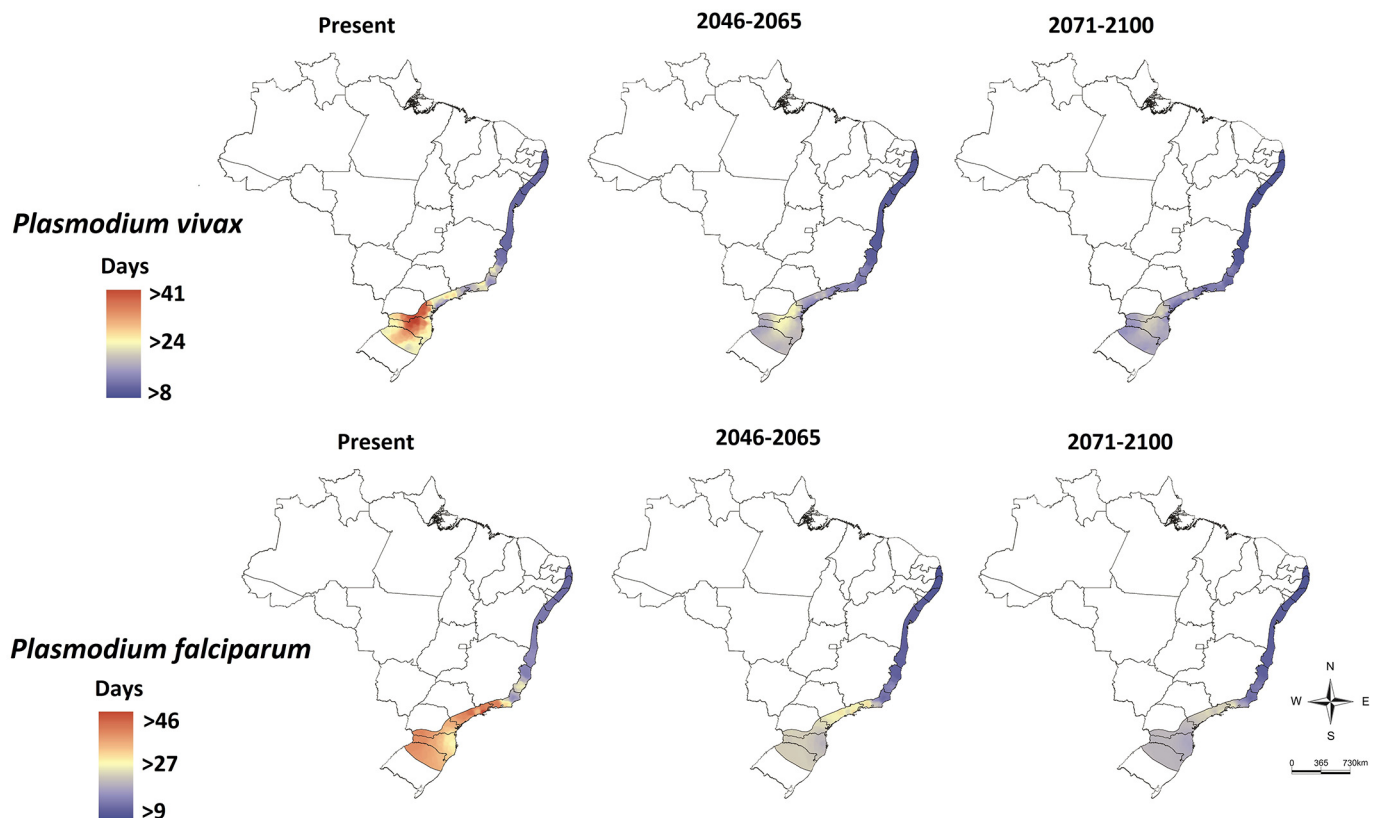
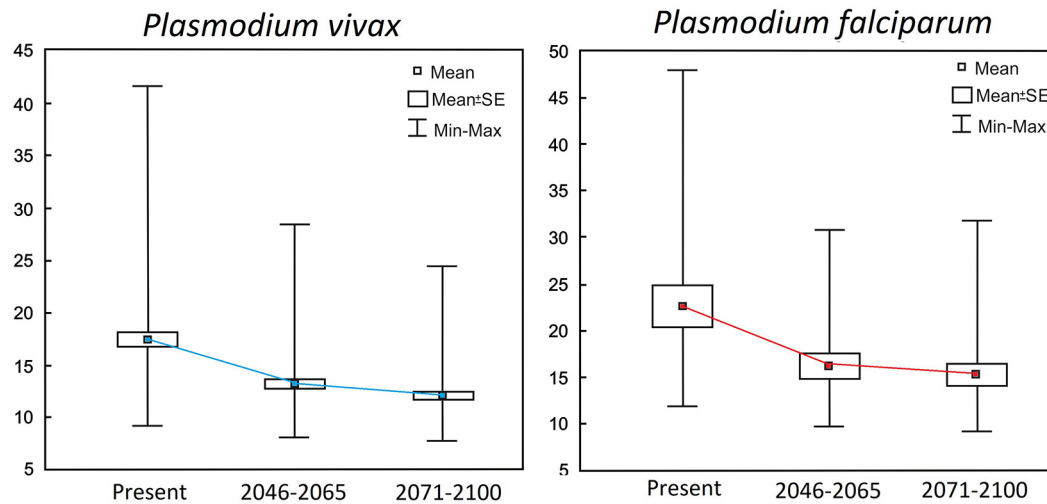


Fig. 4. Estimated survival rate of *P. vivax* and *P. falciparum* at geographic area of *Ke. cruzii* distribution based on MIROC-5 global climate model. The maps show the probability under two climate change scenarios: RCP 8.5 (2046–2065) and RCP 2.6 (2071–2100).

## Extrinsic incubation period



## Survival rate

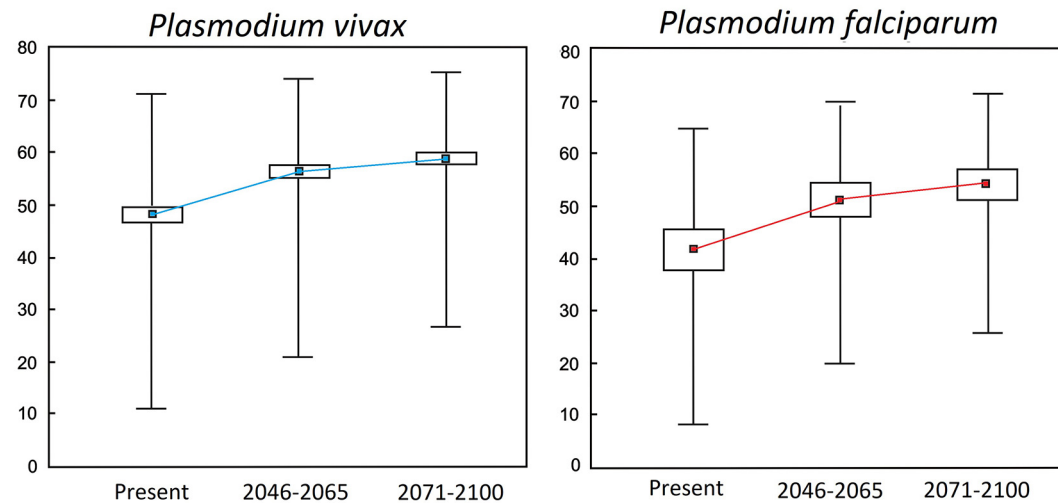


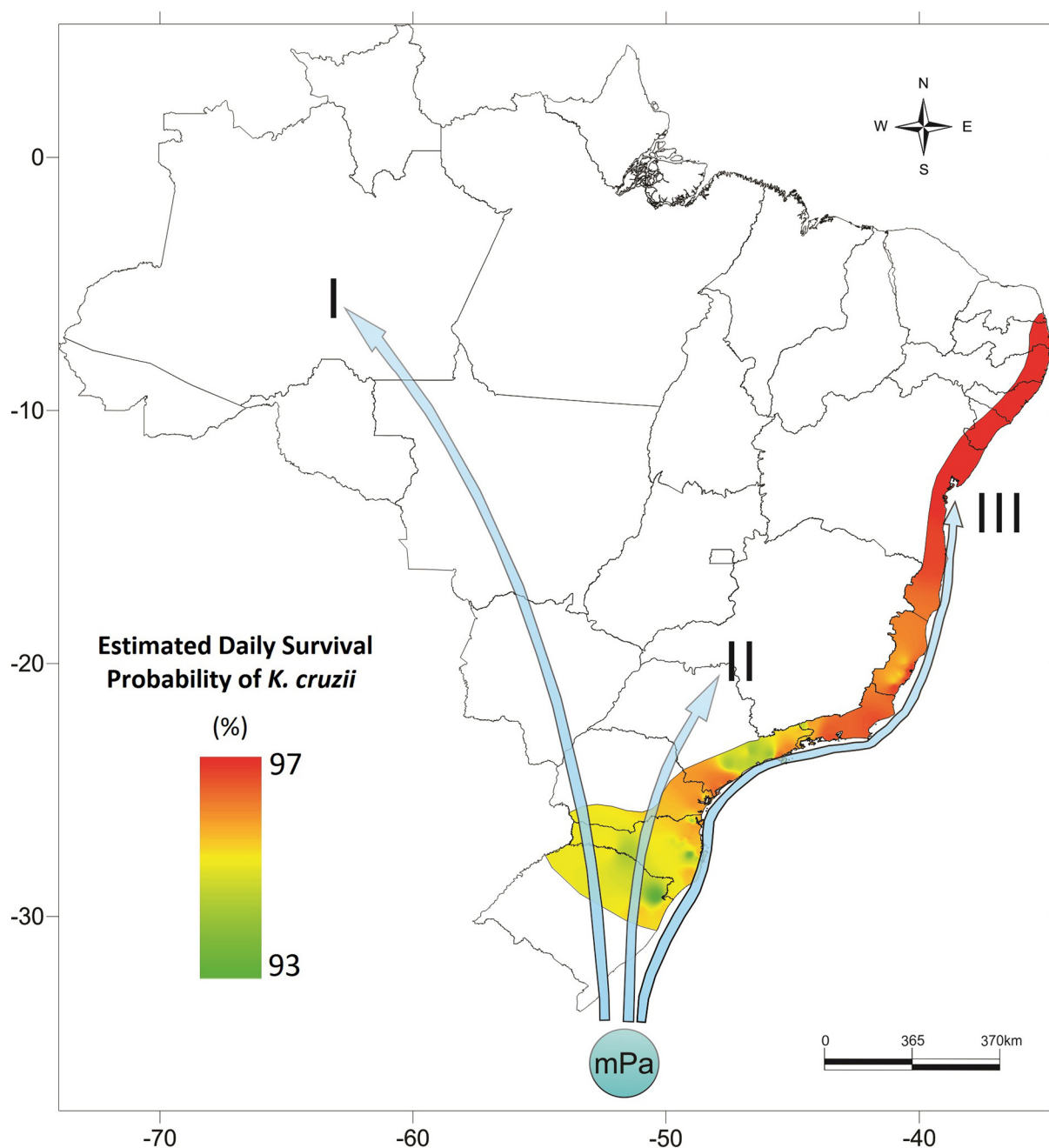
Fig. 5. Extrinsic incubation period (EIP) and survival rate for *P. vivax* and *P. falciparum* at present and future scenarios. RCP 8.5 (2046–2065) and RCP 2.6 (2071–2100).

implications for malaria transmission under the climate change scenario.

Other environmental factors, such as high elevation mountainous areas in the Southeast region and strong influence of the Atlantic polar mass (mPA) in the southern areas (Fig. 6), may explain the low survival of *Ke. cruzii* in some areas. The mPA, for instance, is a transient system that can invade the Brazilian territory from the south by three main routes: two routes through the interior of the continent and one that propagates along the Atlantic coast (Borsato and Mendonça, 2015). When the coastal branch of the mPA surpasses the Southeast region, the atmospheric system becomes tropicalized because of the influence of latitude and intense incidence of sun rays (Parmenter, 1976). These geographical peculiarities may be responsible for the spatial variation in the estimated daily survival probability of *Ke. cruzii* in Brazil. In addition, several studies have associated the survival rate of *Anopheles* with *Plasmodium* infection. For instance, Anderson et al. (2000) showed that infection by *P. falciparum* sporozoites significantly reduced the survival of blood-feeding *Anopheles gambiae*. This hypothesis is supported by the findings of previous studies that focused on the blood-feeding behaviour of infected and uninfected anopheline mosquitoes.

They showed that the presence of sporozoites in the salivary glands decreases the female's ability to feed on blood because the female has to increase the probing time to obtain a bloodmeal; this elicited a greater degree of defensive behaviour of hosts under attack (Rossignol et al., 1984; Ferguson et al., 2012).

Regarding *Plasmodium* parasites, the EIP was shorter when the baseline temperature was high (i.e., above 25 °C), such as in Northeast Brazil. Lindsay and Martens (1998) showed that malaria transmission is more effective in areas with temperature  $\geq 20$  °C, and that transmission is either interrupted or reduced at temperatures  $\leq 18$  °C because few females will survive the 56 days required for the sporogony stage at low temperatures (Cox et al., 1999). The effect of temperature on EIP indicates that the potential increase in malaria transmission in localities where the temperature can decrease to  $\leq 20$  °C, such as in the southern region of Brazil, is less effective and can occur when temperature increases (i.e., summer). It is worth mentioning that the principal factor for the decrease of *Kerteszia* population is the forest loss and fragmentation, as seen before, thus this increase in the malaria risk will occur mainly near areas with large extension of forest fragments, like protect areas. In the present study, we simulated an increase of 1–3.7 °C in the



**Fig. 6.** Interference zones of the Atlantic polar air mass (mPa) in Brazil. This air mass moves across the Brazilian territory from the South by three main routes: two routes move across the continental area, and one route along the Atlantic coast.

average temperature, but this can vary depending on the greenhouse gases emission rates. Rueda et al. (1990) showed that at above 34 °C, the development time of *Culex quinquefasciatus* and *Aedes aegypti* from egg hatching to adult emergence decreased by 4 and 5 days, respectively. Mosquito tolerance to temperature is limited to a certain range, with increased death when temperature either increases or decreases outside the maximum and minimum limits. Thermal death occurs around 40–42 °C and daily survival is zero at 40 °C (Jepson et al., 1947). When mosquitoes are exposed to temperatures above 40 °C, the prevalence of *Plasmodium* infection in the population will decline. However, *P. vivax* can persist in human populations as hypnozoites, which explains malaria being a global health problem throughout human history (Cowman et al., 2016), including in areas north of the Arctic circle (Packard, 2005). Moreover, temperature is not the only limiting factor for anophelines. In Senegal, malaria prevalence in the

human population was shown to decrease by more than 60% with temperature increase and precipitation decrease (Githeko et al., 2000). It is important to consider the effect of climate change on rainfall, which is critical to the formation and persistence of mosquito breeding sites (Afrane et al., 2012), including bromeliads for *Kerteszia* species.

Our findings demonstrate that the survival rate estimated for *P. vivax* and *P. falciparum* across Atlantic Forest can differ considerably depending on the temperature change scenario. Considering that *P. vivax* was found to be tolerant to a wide range of temperature, the probability of it persisting in areas of the Brazilian coast is greater than that of *P. falciparum*. Similar findings were reported by Sarkar et al. (2019), who showed that the transmission risk suitability for *P. vivax* is higher than that for *P. falciparum* in the Himalayan region. A temperature window of approximately 32–33 °C in which endemic transmission and spread rate in disease-free regions are optimized was

observed by Parham and Michael (2010). This window was the same for *P. falciparum* and *P. vivax*, but mosquito density played a stronger role in driving the rate of malaria spread than the *Plasmodium* species. The second major finding of our study is that, according to the scenarios produced by MIROC-5, the temperature conditions in the Northeast and part of the Southeast will be favourable for the circulation of *P. vivax* even in a scenario of warmer temperatures. Certainly, the presence of the parasite will also be determined by the occurrence of vector species that can be infected and propagate the parasite to susceptible hosts.

The global constraint of temperature variation in the transmission of both studied *Plasmodium* species demonstrated by previous studies was similar to our findings, with *P. vivax* being more resilient to changes in temperature than *P. falciparum* (Gething et al., 2011). The similarities between the results of the present study and those of the modelling study of Gething et al. (2011) can be explained by the higher genetic diversity of *P. vivax* compared to that of *P. falciparum* (Neafsey et al., 2012). Neafsey et al. (2012) estimated the genetic diversity of *P. vivax* to be approximately twice as high as that found in *P. falciparum* using SNP data comparison. This indicates a distinct history of global colonization and/or a more stable demographic history for *P. vivax* compared to that of *P. falciparum*, which is thought to have undergone a recent population bottleneck (Neafsey et al., 2012). The SNP diversity as well as additional microsatellite and gene family variability data suggest a capacity for greater functional variation in the global population of *P. vivax* (Neafsey et al., 2012).

Human extra-Amazonian malaria is often associated with *P. vivax* (Marrelli et al., 2007; Kirchgatter et al., 2014), but Lorenz et al. (2015) noted an unusual pattern of malaria infections predominantly by *P. falciparum* in the Northeast and Southeast regions. Our study confirmed that the estimated survival rate of *P. falciparum* is indeed higher in these areas. Additionally, a high prevalence of *P. falciparum* was recently found in the blood of asymptomatic donors living in the Southeast Brazilian Atlantic Forest (Maselli et al., 2014). Laporta et al. (2015) showed that *P. falciparum* actively circulates, in higher proportion than *P. vivax*, among *Anopheles* mosquitoes in parts of the Southeast Brazilian Atlantic Forest. In the past, bromeliad malaria was an endemic disease of great epidemiological importance in the south-eastern and southern regions of Brazil (Medeiros-Sousa et al., 2019). Although it is now under control as a result of substantial efforts, it has not been totally eliminated and there are still transmission foci in various places. Nevertheless, many of these foci have probably not come to the attention of health authorities because of the high proportion of asymptomatic and oligosymptomatic cases. Furthermore, the malaria symptoms can be confused with those of other diseases (Alencar Filho et al., 2014; Maselli et al., 2014). Despite all efforts and accumulated knowledge in the literature, it remains difficult to identify the main cause of a malaria outbreak (Massad et al., 2008) and to determine the most efficient techniques for protecting humans from these parasites. We herein showed that temperature increases may directly interfere with the distribution of *Plasmodium* parasites in the next decades, changing the current epidemiological scenario of extra-Amazonian malaria.

## 5. Conclusions

Despite its limitations and assumptions, our study is an important first step in understanding the actual distribution of the primary malaria vector, *Ke. cruzii*, along the Brazilian coast and the impact of increased temperatures on *Plasmodium* parasites. Two conditions need to be satisfied for *Ke. cruzii* occurrence and survival: warm temperatures and the presence of Atlantic Forest. Although the estimated daily survival probability of *Ke. cruzii* is expected to be higher in the Northeast region because of temperatures, this mosquito does not settle abundantly in this area because of a lack of rainforest. Meanwhile, the southern region still has areas with Atlantic Forest, but these areas are strongly influenced by the Atlantic polar mass, decreasing local

temperature.

Regarding the *Plasmodium* parasites, both species showed a tendency to decrease their EIP and increase their estimated survival rates in a scenario with higher temperatures. The drop in EIP is relatively low if the baseline temperature is already high, such as in the Northeast region. This indicates the potential rise in malaria cases in places where the current temperatures are below 20 °C, such as in southern areas. Additionally, we showed that the estimated survival rates of *P. vivax* and *P. falciparum* considerably differ along the Brazilian coast. The first species seems to be generalist and its probability of survival is greater along the Brazilian coast, whereas the second species remains more localized in the Northeast and Southeast regions.

Our results suggest that extra-Amazonian high-risk areas for malaria may change in the coming years, becoming more pronounced in the southern region of the country. This is the first predictive study of these parasites outside the Amazonian region. These findings are particularly concerning given that malaria symptoms can be confused with those of other diseases and the lack of experience in the health community to diagnose malaria in non-endemic areas. In this way, we specify which areas should be carefully monitored in the next decades, not only by researchers but also by health and control services.

## Credit Author Statement

**Thiago S Azevedo:** Conceptualization, Methodology, Investigation, Software. **Camila Lorenz:** Data acquisition, Investigation, Writing - Original Draft Preparation. **Francisco Chiaravalloti-Neto:** Visualization, Writing - Reviewing and Editing. **Maria Anice Mureb Sallum:** Supervision, Writing - Reviewing and Editing.

## Declaration of Competing Interest

The authors declare that they have no competing interests.

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## Appendix A. Supplementary data

Supplementary material.

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