

Epidemic Malaria Dynamics in Eastern Africa Highlands: The Role of Climate Change and Human Population Growth

Felipe Augusto Maurin Krsulovic^{1,2,*}, Timothy Peter Moulton³, Mauricio Lima^{1,2}, Fabian Jaksic^{1,2}

¹Department of Ecology, Faculty of Biological Sciences, Pontifical University Catholic of Chile, Santiago, Chile

²Center of Applied Ecology and Sustainability (CAPES), Santiago, Chile

³Department of Ecology, Faculty of Biological Sciences, University of the Estado do Rio de Janeiro, Rio de Janeiro, Brazil

Email address:

augustomaurin@gmail.com (F. A. M. Krsulovic)

*Corresponding author

To cite this article:

Felipe Augusto Maurin Krsulovic, Timothy Peter Moulton, Mauricio Lima, Fabian Jaksic. Epidemic Malaria Dynamics in Eastern Africa Highlands: The Role of Climate Change and Human Population Growth. *Ecology and Evolutionary Biology*. Vol. 6, No. 1, 2021, pp. 23-30. doi: 10.11648/j.eeb.20210601.15

Received: February 22, 2021; **Accepted:** March 4, 2021; **Published:** March 26, 2021

Abstract: During the last two decades, researchers have suggested that the increase of the malaria incidence rate in tea plantations in the Kericho district in Kenya was driven by climate change. Critics suggested that others variables could be involved in the increase of the malaria burden, such as HIV and human population size. Population ecologists have developed a simple framework which helps to explore the contributions of endogenous (density-dependency) and exogenous processes on population dynamics. Both processes may operate to determine the dynamic behavior of a particular population through time. Briefly, density-dependency (endogenous process) occurs when the per capita population growth rate (R) is determined by its previous population sizes. An exogenous process occurs when some variable affects another but is not affected by the changes it causes. In this study we re-explore the dynamics of the malaria incidence rate in Kericho tea plantations taking into account the HIV incidence rate, rural population size, temperature and rainfall. We found that malaria dynamics showed signs of a negative endogenous process between R and malaria infectious class. We found that there was weak evidence to support the climate change hypothesis and that rural population size and the HIV incidence could interact to positively force malaria models parameters explaining the positive malaria trend observed at Kericho tea plantations in Kenya from 1979 to 2002.

Keywords: Malaria Dynamics, Climate, HIV, Population Size

1. Introduction

During the last two decades, researchers have suggested that the increase of the malaria incidence rate in tea plantations in the Kericho district in Kenya was driven by climate change [1-10]. These studies gave way to extensive debates about the importance of climate in the malaria burden in these locations. Critics suggested that despite the relationship between malaria and climate is evident, principally between seasons, other variables could be involved in the increase of the malaria incidence in Kericho tea plantations [11-13]. Globally, malaria literature suggests that the positive trends in malaria could be also affected by HIV [14, 15], climate [1-10, 16], poverty level [16], health campaigns [16- 18] and human population size [19]. In this

study we re-analyze the data from period 1979 to 2002 (resurgence period) from Pascual et al study [4-6] and discuss the role of climate change, and other potential drivers for malaria dynamics in Kericho tea plantations.

Malaria endemicity and the burden of this disease have increased at the global level during the last centuries until 1955, when countries joined in a global effort to eradicate malaria [16, 17]. The use of quinine, chloroquine and indoor DDT reduced the malaria burden in many countries [14- 16]. After three decades of decline, around 1980, malaria started to rise and once again became a major health problem, principally in Sub-Saharan Africa [16, 20, 21].

During the same period (1980's decade), the Human Immunodeficiency Virus (HIV) started to spread globally [14, 15]. Kenya ranks in the top six HIV High Burden Countries [14]. HIV may increase malaria contagion, accelerate

progression rates from latent to infectious stage and may delay the recovery of infected individuals, which increases the period in which an infected individual may transmit malaria. In addition, individuals only acquire malaria immunological defenses following several episodes. By affecting the immunological system, HIV removes the acquired defenses increasing the susceptible pool (the population at risk) [22-26]. Additionally, studies already showed that prevalence of HIV in tea plantations could reach almost 40 % of the workers [26], suggesting that HIV increase could be involved on the increase of the malaria burden during the period ranging from 1979 to 2002 (Figure 1).

Malaria is a disease linked to climatological variables due to the aquatic life cycle of the *Anopheles sp.* larvae. Studies have pointed out that extreme climatological events (El Niño and La Niña) could affect malaria levels [27-29]. High temperatures accelerate larval development rate and the total number of eggs, boosting total mosquito biomass per season. Also, rain positively affects *Anopheles sp.* carrying capacity [30, 31]. Many studies have suggested that climate explains malaria seasonal fluctuations and anomalous outbreaks. Studies have shown an increase of temperature levels during the last decades in Kenya and suggested that temperature was the main driver of the increase of the malaria burden in the Kericho tea plantation (Figure 1) [1-10].

Kenya is a middle-income rural country [16]. The increase of human density in rural areas (i.e Kericho district) has many potential ecological effects that could increase the malaria burden. Increase of rural population size expands agriculture frontiers and in cities grow over natural rural areas. This expansion requires deforestation [16, 32-34]. Deforestation changes the aquatic food web structure where larvae develop part of their life-cycle, usually freeing larvae from predators. Deforestation may also increase the number of mosquito breeding sites and accelerates the mosquito life cycle by means of an increase in local temperature, resulting in high mosquito population biomass and plasmodium transmission in rural areas and small rural cities [4-6, 32, 33], like the Kericho district. Alonso et al [13] suggested that although temperature was the main driver of malaria dynamics in Kericho tea plantations, temperature could interact with rural population size and HIV prevalence, which we will consider in this study.

Climate change, HIV dispersion, rural population size are regional and global processes that could interact to explain the malaria dynamics in Kericho tea plantations [31]. Our main goal is to explore the potential interactions between climate, the HIV burden and rural population on the increase of the malaria burden in the period ranging from 1979 to 2002 in Kericho tea plantations.

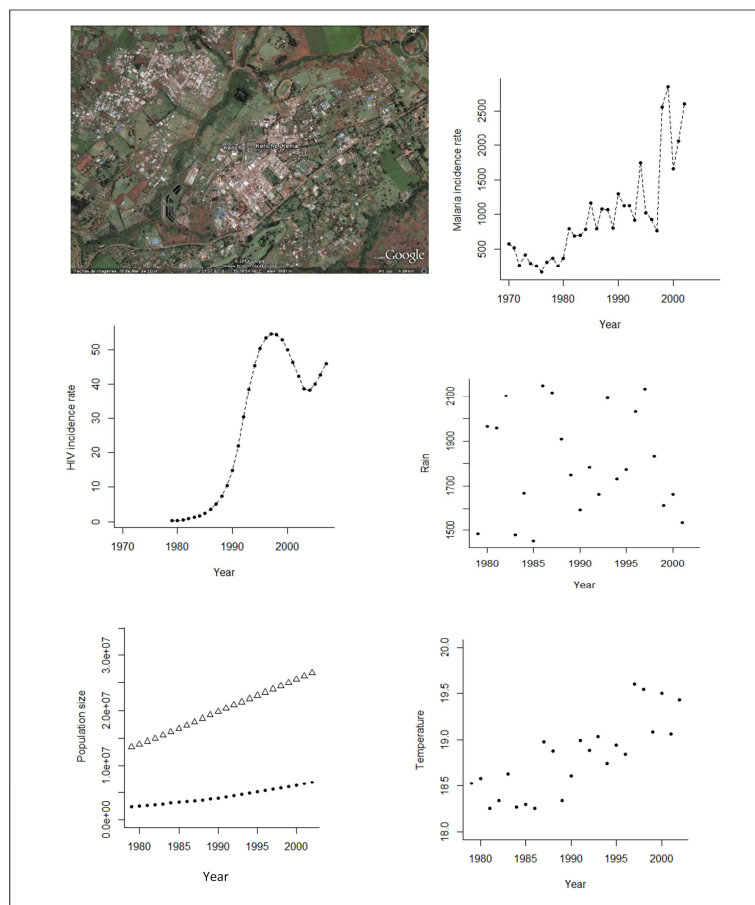


Figure 1. Location of Kenya Kericho district showing the degree of deforestation (rural land, light green) and shows a degree of urbanization in rural areas at Kericho district. We present the Pascual data of malaria incidence rate, rainfall and temperature during the years at Kericho tea plantations. The HIV incidence rate and rural population size at Kenya national level, as alternative drivers of malaria dynamics at Kericho tea plantations.

2. Methods

Population ecologists have developed a simple framework, which helps to explore the contributions of endogenous and exogenous processes on populations. Briefly, density-dependency (endogenous process) occurs when the per capita population growth rate (R) is determined by its previous population sizes. An exogenous process occurs when some variable affects another but is not affected by the changes it causes. Climate variables and governmental disease control policies are known examples of exogenous pulse/press perturbations with relation to diseases. Both processes may operate to determine the dynamic behavior of a particular population through time [34-36]. Therefore, a more complete understanding of the dynamics of a population is achieved when both endogenous and exogenous processes are considered. Using this framework, recent studies have captured the trends of measles, tuberculosis and pertussis at city, country and global scales [37-39].

The ecological principles mentioned above have analogies in epidemiological processes. Following the introduction of an infected individual in a naïve population, the infected class is expected to grow exponentially driven by R_0 , the basic reproductive number, since there are almost unlimited susceptible individuals (resources). Nevertheless, as the infected class grows, the susceptible pool is depleted and per infected transmission rate declines (R_0 becomes R_E , the realized reproductive number), a process known as self-limiting, analogous to the principle of intra-specific competition [37-39]. Higher infected class may increase contact rate enhancing transmission rate, analogous to the intra-specific cooperation principle. The realized that the per capita population rate of change (R) is the corner stone of the framework adopted in this study [36-43]. R can be estimated by the natural log differences between actual and past numbers of infected individuals, which are adopted in this work.

We used a simple linear regression between the malaria infectious class incidence rate and its rate of change to detect the sign and significance of the slope parameter, which suggest the principle; exponential (non-significant slope), cooperation (positive slope) and competition (significant negative slope). This exploratory process will suggest the basic model which could capture the general positive trend of malaria incidence rate in the Kericho tea plantations (from 1969 to 2002).

$$R_{It} = R_{max} - b * I_{t-1} \quad (1)$$

where R_{It} is the per capita growth rate, R_{max} is maximum population rate of change (analogous to R_0), b measures the impact of increasing incidence rate (I_{t-1}) on R_{max} . In advance, we found a negative correlation between R_{It} and I_{t-1} , which can be capture by the following Ricker model:

$$R_t = R_{max} \left(1 - \left(\frac{I_{t-1}}{K} \right) Q \right) \quad (2)$$

where R_{It} , R_{max} I_{t-1} are as above and K is the stable malaria

incidence carrying capacity. Q measures the degree of self-limiting around K . We also present the data from Pascual study using 4-month intervals. The goal is to identify distinct domain periods between R_{It} and I_{t-1} to help to interpret non-linear regression results.

The effect of exogenous variables on malaria dynamics will be assessed using Royama methodology [40], whom classified three basic exogenous effects on the logistic model (Eq.2): vertical, lateral and non-linear effects. Vertical effects occur when the exogenous variable affects proportionally both R_{max} and K , changing the intercepts (Eq. 3). Lateral effects occur when only the K is affected (Eq. 4), and the non-linear effects when the variable affects both R_{max} and K , but disproportionately (Eq. 5). These three types of exogenous effects can be tested as follows [34]:

$$R_t = R_{max} \left(1 - \left(\frac{I_{t-1}}{K + g * I_t} \right) Q \right) \quad (3)$$

$$R_t = R_{max} \left(1 - \left(\frac{I_{t-1}}{K} \right) Q + g * I_t \right) \quad (4)$$

$$R_t = R_{max} \left(1 - \left(\frac{I_{t-1}}{K} \right) Q + g * I_t \right) \quad (5)$$

where g is the linear coefficient that measures the effect of any exogenous variable on the self-limiting model parameters.

We include HIV incidence rate, Temperature ($^{\circ}\text{C}$), rain (mm) and rural population size as exogenous variables in Eq. 3, 4 and 5. We used the HIV national incidence rate and national rural population size from World Bank and World Health Organization websites, because there are no time series for these variables for Kericho area. We assumed that national trends are a proxy to what occurs at a smaller scale (Kericho tea plantation). We used Temperature and rain data from a Pascual study [4, 5].

In advance, using data from a period of four months between observations, we found three distinct logistic growth periods (see Figure 2). We also chose to analyze a shorter period (1978 to 1994), which corresponds to the second chronological logistic growth rate, avoiding the noise at the end of time series (1995-2002). We compared the results from both approaches (cut and uncut time series) looking for consistency between results. To address the effects of climate variables versus HIV and Human population size, we first analyzed models with and without climate variables. Secondly, we analyzed the effects of human population size and HIV without climate variables, and last, we analyzed the interaction of all variables on the logistic model parameters. The best model was selected based on the Akaike information criteria and R^2 (Coefficient of determination). Eqs. 1 to 5 were fitted using the nls library in R through non-linear regression analysis.

3. Results

We found that the malaria increase incidence rate could be capture by the logistic growth model (Table 1).

Table 1. The linear regression between the malaria incidence rate (I_{t-1}) and the per capita rate of change (R_I). The malaria dynamics showed signs of the self-limiting process during the study period (negative slope).

Response variable	Intercept	Pendent	Independent variable	P-value	R2
	(Rmax)				
R_{I_t}	0.488	-0.003	I_{t-1}	0.0028	0.307

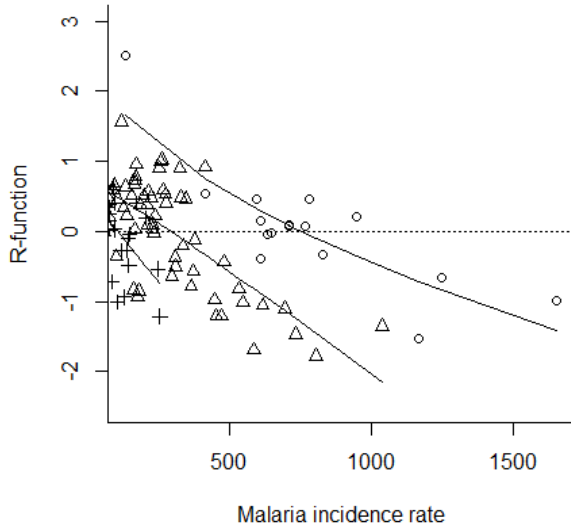


Figure 2. Distincts dynamical domains from 1969 to 2002. First period, cruces (1969-1979), second period, triangle (1979-1994). Last period, open circles (1994-2002). The figure shows the changes in the intercepts from 1969 to 2002 suggesting a lateral and a vertical changes from 1969 to 2002, respectively.

1978-2002

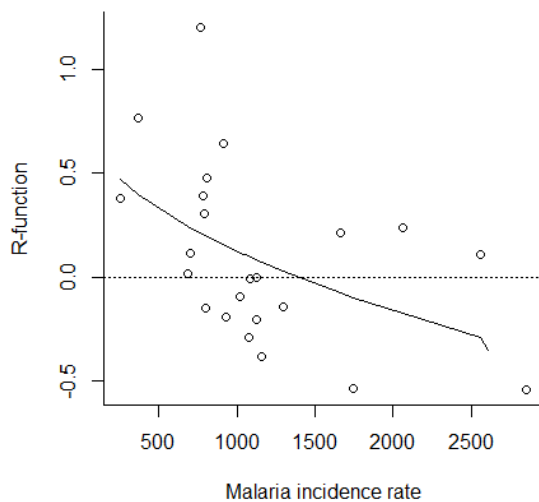


Figure 3. The relationship between the malaria incidence rate in Kericho tea plantations and the malaria per capita rate of change (R -function) from 1978 to 2002.

Also, the graphical relationship between R_I and I_{t-1} revealed three periods of logistic growth with increasing R_{max} and carrying capacities from 1979 to 2002 using 4 month- intervals between observations (Figure 2, 3 and 4 and Table 2). From the first to the second period of growth, we can observe a lateral effect. The R_{max} of the second period is

1.1 times higher than the first period and K is 2.5 times higher. Between the second and last period, we can observe a change which suggests a vertical or a nonlinear effect. R_{max} in the last period is 2.013 times higher than the second period, and K is 4 times higher.

1978-1994

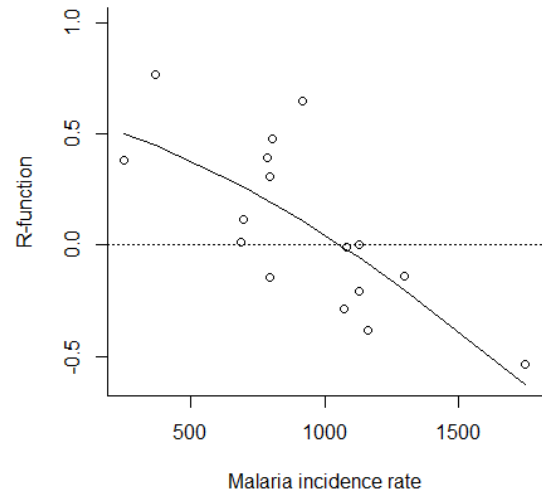


Figure 4. The relationship between the malaria incidence rate in Kericho tea plantations and the malaria per capita rate of change (R -function) from 1979 to 1994.

Table 2. The logistic model parameter estimations using four-months interval data from period 1969 to 2002. It shows an almost vertical dynamical change from 1979-1994 to 1994-2002 (Figure 1). Bold faces are for significant results.

Parameters						
Model	Variable	Period	Rmax	K	Q	R2
Logistic	Malaria	1969-1979	0.639	107.57	0.876	0.549
Logistic	Malaria	1979_1994	0.734	295	1.085	0.693
Logistic	Malaria	1994_2002	2.793	755	0.52	0.861

Models only including the interaction between rain and temperature had lower predictability and were less parsimonious than models with the interaction between climate variables and other variables, suggesting that climate had a low contribution to the increase of the malaria incidence rate in Kericho tea plantations from 1979 to 1994 and in 2002 (Table 3).

Uncut and cut time series had similar results. Models with the interaction (lateral and vertical) between rural population size and HIV incidence rate performed better than models with climate variables and the model without exogenous variables (Table 3). These results suggest that these variables could be involved in the malaria increase burden as exogenous forcing on malaria endogenous model parameters leading to an increase in the malaria burden. These results are consistent with regards to the graphical R behavior changes with infectious class (Figure 2, 3 and 4). The models with non-linear effects (Eq. 5) delivered worse results (R^2 and AIC) than vertical and lateral logistic models (not shown here).

Table 3. The lateral and vertical effects of the variables mentioned in the text for two periods of time (cut and uncut time series). We fixed R_{max} when assessing lateral effects and we fixed the non-linear parameter (Q) when evaluating vertical effects. R_{max} and Q were obtained from the malaria logistic model without exogenous variables for cut and uncut time series. AIC is the Akaike information criterion. The symbol (*) represents the interaction between variables. Results suggest a weak effect of climate variables and that the effects rural population size and incidence of HIV could interact to explain malaria model parameter changes.

Model	Variable	Period	Rmax	K	Parameters			
					a	Q	R2	AIC
Logistic	Malaria	1979_2002	0.872	1391		0.407	0.589	22.230
Lateral effect	HIV	1979_2002	0.872	837	1.97E+01	0.891	0.641	21.481
Lateral effect	Rain	1979_2002	0.872	-1857	1.88E+00	0.406	0.509	24.828
Lateral effect	Temperature	1979_2002	0.872	-1637	9.42E+02	0.780	0.509	20.263
Lateral effect	Rural population	1979_2002	0.872	-883	1.09E-04	1.021	0.650	19.905
Vertical effect	HIV	1979_2002	1.221	893	8.90E-03	0.470	0.610	21.754
Vertical effect	Rain	1979_2002	0.031	1309	4.30E-04	0.470	0.543	24.447
Vertical effect	Temperature	1979_2002	2.221	2000	-8.20E-01	0.470	0.394	26.616
Vertical effect	Rural population	1979_2002	0.355	37	7.42E-08	0.470	0.666	19.007
Lateral effect	Rain*Temperature	1979_2002	0.872	-388	3.20E-05	0.302	0.459	23.429
Lateral effect	Rain*Temperature*Rural	1979_2002	0.872	-428	2.62E-09	0.755	0.649	20.033
Lateral effect	Rain*Temperature*HIV	1979_2002	0.872	835	5.97E-04	0.858	0.629	20.920
Lateral effect	Rain*Temperature*Rural*HIV	1979_2002	0.872	850	2.49E-10	0.920	0.648	19.994
Lateral effect	HIV*Rural	1979_2002	0.872	850	8.19E-07	0.953	0.636	20.574
Vertical effect	Rain*Temperature	1979_2002	0.945	653	8.70E-07	0.470	0.547	21.675
Vertical effect	Rain*Temperature*Rural	1979_2002	0.447	1129	1.41E-11	0.470	0.680	20.464
Vertical effect	Rain*Temperature*HIV	1979_2002	1.157	894	2.52E-07	0.470	0.630	18.208
Vertical effect	Rain*Temperature*Rural*HIV	1979_2002	1.212	887	1.14E-15	0.470	0.650	18.239
Vertical effect	HIV*Rural	1979_2002	1.288	884	4.12E-10	0.470	0.633	20.712
Logistic	Malaria	1979_1994	0.572	1057		1.867	0.747	5.994
Lateral effect	HIV	1979_1994	0.572	887	1.36E+01	2.139	0.815	4.042
Lateral effect	Rain	1979_1994	0.572	368	3.82E-01	1.573	0.704	7.235
Lateral effect	Temperature	1979_1994	0.572	-3394	2.38E+02	2.021	0.720	7.662
Lateral effect	Rural population	1979_1994	0.572	-242	7.01E-05	2.691	0.827	0.847
Vertical effect	HIV	1979_1994	0.591	904	1.40E-02	1.867	0.856	-1.861
Vertical effect	Rain	1979_1994	0.122	461	2.41E-04	1.867	0.706	7.570
Vertical effect	Temperature	1979_1994	0.132	381	1.31E-04	1.867	0.650	5.948
Vertical effect	Rural population	1979_1994	0.655	860	4.51E-03	1.867	0.844	-0.777
Lateral effect	Rain*Temperature	1979_1994	0.572	414	1.90E-02	1.599	0.714	7.565
Lateral effect	Rain*Temperature*Rural	1979_1994	0.572	384	1.00E-09	1.813	0.765	4.805
Lateral effect	Rain*Temperature*HIV	1979_1994	0.572	884	4.16E-04	2.074	0.775	4.703
Lateral effect	Rain*Temperature*Rural*HIV	1979_1994	0.572	889	5.40E-05	1.980	0.783	3.459
Lateral effect	HIV*Rural	1979_1994	0.572	897	6.34E-07	2.113	0.856	4.160
Vertical effect	Rain*Temperature	1979_1994	0.079	365	1.43E-05	1.870	0.716	7.310
Vertical effect	Rain*Temperature*Rural	1979_1994	0.544	658	3.40E-10	1.870	0.789	1.386
Vertical effect	Rain*Temperature*HIV	1979_1994	0.578	909	3.80E-07	1.870	0.802	1.790
Vertical effect	Rain*Temperature*Rural*HIV	1979_1994	0.579	918	1.00E-14	1.870	0.811	2.022
Vertical effect	HIV*Rural	1979_1994	0.590	913	6.40E-10	1.870	0.803	-1.188

4. Discussion

The results suggest that other variables were more important than climate change in terms of the increase of malaria burden in Kericho tea plantations, as initially proposed in many studies from Kericho. In this study, we will discuss the manner in which the effects of HIV and rural population size could interact to explain the changes in model parameters.

Perhaps human population size could be the most important variable, because of its many effects. Rural population size increases the contact rate between infected and susceptible individuals by adding individuals inside the natural flying range of mosquitos in households, villages and small rural cities (such as the Kericho district); creates mosquitos breeding sites; leads to higher transport of

individuals between localities dispersing and amplifying the geographical range of malaria endemicity and increases pollution (favoring mosquito abundance) in rural areas [13, 16, 19, 31-34, 40-44]. All these effects could increase malaria transmission and burden in Kericho tea plantations.

The HIV spread completes the scenario. HIV grew exponentially for most part of the study period at the country level in Kenya. One potential effect of a higher malaria burden is that individuals only acquire malaria immunological defenses following several episodes of re-infection. The spread of HIV incidence in rural populations could remove this potential positive effect (i.e. herd immunity). The interaction between malaria and HIV is suspected to be synergetic, because malaria-infected individuals show an increase of the HIV host cells in the immunological system. This could produce a longer period of the acute phase of HIV, increasing infectivity between

individuals and susceptibility to future malaria infections. Besides the synergy, the effects of HIV seem to be greater than the effects of malaria on the spread of HIV, because the infection period and AIDS stage may last for years reducing the immune defense efficiency [24, 25]. The spread of HIV expands the population at risk of contracting malaria [13-16, 21-26]. The effects of HIV could aggravate the effects of increasing rural population size and regional ecological changes affecting the model parameters of malaria.

We could even propose a simpler model only including rural population size as a vertical effect. The increase of population size could allow the spread of HIV increasing the pool of the susceptible population at risk to contract malaria. Additionally, habitat degradation near Kericho district could favor *Anopheles* increase. We believe that habitat degradation driven by the mentioned effects of population size had stronger effects than climate change in the malaria dynamics in Kericho tea plantations.

We did not want to rule out climate change. We believe that climate could always provide an initial set of potential variables which could influence the dynamics of malaria. The main factor is probably temperature, which can accelerate larval development rate (including more life-cycles per season) and reduce the differences between seasons. Local rises in temperature could interact with deforestation and the effects of HIV to explain the higher malaria incidence rate peaks at the end of the time series from Kericho tea plantations [1-10]. For example, Alonzo [13] found that rise of temperature in Kericho tea plantations was indeed the main driver behind the rise of malaria burden. But they also suggested that temperature could interact with the increases of the HIV burden and human population size to explain the malaria positive trends, as we tested and confirmed in this study.

Despite the observed increases in temperature, the malaria incidence rate in Kericho tea plantations declined from 2002 to 2010, which is suspected to be related to investments in malaria control programs in Kenya [14-18, 20, 29-31, 43-44]. In 2000, several countries joined in a global effort to halt and begin to reverse the incidence of malaria by 2015 (Millennium Development Goals 6- Target 6C). Kenya received international funding and developed efficient national strategies to achieve the Millennium Development Goals. Kenya invested in Artemisinin-based Combination therapy (ACTs), increased the distribution of insecticide-treated mosquito nets (ITNs), rapid diagnostic tests (RDTs) and the application of Indoor Residual Spraying (IRS). Studies have demonstrated that investments in malaria commodities like ITNs, IRS, ACTs and RDTs reduced the malaria burden in many regions including the Sub-Saharan region. The increase of malaria commodities could explain the decreases of the incidence rate of malaria at district and at regional levels, despite the rises of temperature, population size and regional ecological changes [14-18, 20, 29-31, 43, 44].

Additionally, literature suggests that declining HIV could be also involved in the decrease of the malaria burden. Between 2001 and 2011, HIV incidence was reported to have

declined by >50% across 13 countries in sub-Saharan Africa. In 2004, USA made a massive investment to increase ART (Antiretroviral Therapy) coverage in Sub-Saharan Africa [2, 3]. ART is effective in preventing mother-to-child transmission and sexual transmission of HIV within couples. These correlated chronologies (malaria and HIV decline) may suggest that the malaria decline rate could also be related to HIV investments and interventions (ART coverage, education level, prevalence of male circumcision and condom use) along with the ITNs, ACTs and IRSs coverages during this period [14-18]. This suggests that efforts to control two linked diseases could interact in order to achieve the malaria Millennium Development Goals 6- Target 6C.

5. Conclusion

Here, we applied the Population Ecology Theory to re-explore malaria incidence rate dynamics in Kericho tea plantations. We present a distinct scenario to explain that others large-scale phenomena (HIV and rural population size) could have influenced the local malaria dynamics at a higher level than climate change from 1979 to 2002. Despite the many advances in malaria commodities, which could eradicate malaria from Kenya, the deforestation effects and high HIV burden could slow down the malaria burden decline and allow new epidemics episodes, under a potential scenario of any type of failure of the malaria control programs.

The framework employed is based on the realized per capita population rate of change (R_1), which is surrounded by plausible ecological principles and is hence an advantageous starting point to explore disease dynamics. Any government may disentangle R_1 in its components (new per capita infections and per capita mortality), explore which of them are most important for R_1 trends and explore the contributions of endogenous and exogenous processes. Hence, we suggest that this approach, based on simple principles based on population ecology theory, could be included as a supplement to WHO reports with minimal cost- and time-demanding efforts, which could provide insights and hypotheses and may facilitate the testing and estimation of the drivers of disease dynamics.

Data Accessibility Statement

Malaria incidence rate, rain and temperature are available in published studies [4-6]. HIV and human population size data were obtained from World Bank (<https://www.worldbank.org/>) and WHO (<https://www.who.int/>) web sites.

Acknowledgements

FAMK receives a postdoctoral scholarship from FONDECYT (Folio: 319001). TPM receives a productivity scholarship from CNPq (PQ 302121/2019-6). FMJ and ML receive receives funding: ANID PIA/BASAL FB0002.

References

- [1] S. I. Hay, D. J. Rogers, G. D. Shanks, M. F. Myers, R. W. Snow, Malaria early warning in Kenya. *TRENDS in Parasitology* 17, 95–99 (2001).
- [2] G. Zhou, N. Minakawa, A. K. Githeko, G. Yan, Association between climate variability and malaria epidemics in the East African highlands. *PNAS* 101, 2375–2380 (2004).
- [3] S. I. Hay, J. Cox, D. J. Rogers, S. E. Randolph, D. I. Stern, G. D. Shanks, M. F. Myers, R. W. Snow, Climate change and the resurgence of malaria in the East African highlands. *Nature* 415, 905–909 (2002).
- [4] M. Pascual, J. A. Ahumada, L. F. Chaves, X. Rodo, M. Bouma, Malaria resurgence in the East African highlands: Temperature trends revisited. *PNAS* 103, 5829–5834 (2006).
- [5] M. Pascual, B. Cazelles, M. J. Bouma, L. F. Chaves, K. Koelle, Shifting patterns: malaria dynamics and rainfall variability in an African highland. *Proc. R. Soc. B* 1-17, (2007).
- [6] M. Pascual, A. P. Dobson, M. J. Bouma, Underestimating malaria risk under variable temperatures. *PNAS* 106, 13645–1364 (2009).
- [7] J. A. Patz, M. Hulme, C. Rosenzweig, T. D. Mitchell, R. A. Goldberg, A. K. Githeko, S. Lele, A. J. McMichael, D. L. Sueur, Regional warming and malaria resurgence. *Nature* 420, 627–628 (2002).
- [8] D. I. Stern, P. W. Gething, C. W. Kabaria, W. H. Temperley, A. M. Noor, E. A. Okiro, G. D. Shanks, R. W. Snow, S. I. Hay, Temperature and malaria trends in highland East Africa. *PLoS ONE*, (2011).
- [9] J. A. Omumbo, B. Lyon, S. M. Waweru, S. J. Connor, M. C. Thomson, Raised temperatures over the Kericho tea estates: revisiting the climate in the East African highlands malaria debate. *Malaria Journal* 10, 1–16 (2011).
- [10] S. S. Imbahale, W. R. Mukabana, B. Orindi, A. K. Githeko, W. Takken, Variation in Malaria Transmission Dynamics in Three Different Sites in Western Kenya. *Journal of Tropical Medicine*, 1–8 (2012).
- [11] D. Ruiz, C. Brun, S. J. Connor, J. A. Omumbo, B. Lyon, M. C. Thomson, Testing a multi-malaria-model ensemble against 30 years of data in the Kenyan highlands. *Malaria Journal* 13, 1-14 (2014).
- [12] G. D. Shanks, S. I. Hay, J. A. Omumbo, R. W. Snow, Malaria in Kenya's Western Highlands. *Emerging Infectious Diseases* 11, 1425-1432 (2005).
- [13] D. Alonso, M. J. Bouma, M. Pascual, Epidemic malaria and warmer temperatures in recent decades in an East African highland. *Proc. R. Soc. B* 278, 1661–1669 (2011).
- [14] UNAIDS. "Global report: UNAIDS report on the global AIDS epidemic". Eds. (Geneva, UNAIDS, 2013).
- [15] UNAIDS. "Global AIDS update". Eds. (Geneva, UNAIDS, 2016).
- [16] World Malaria Report 2019. Geneva: World Health Organization; 2019.
- [17] J. F. Trape, G. Pison, A. Spiegel, C. Enel, C. Rogier, Combating malaria in Africa. *Trends in Parasitology* 18, (2002).
- [18] S. Bhatt et al, The effect of malaria control on *Plasmodium falciparum* in Africa between 2000 and 2015. *Nature* 526, 207–211 (2015).
- [19] P. Martens, L. Hall, Malaria on the Move: Human Population Movement and Malaria Transmission. *Emerging Infectious Diseases* 6, (2000).
- [20] Ministry of Health. "The epidemiology and control profile of malaria in Kenya: reviewing the evidence to guide the future vector control". Eds. (National Malaria Control Programme, Ministry of Health, 2016).
- [21] I. Bates et al, Vulnerability to malaria, tuberculosis, and HIV/AIDS infection and disease. Part 1: determinants operating at individual and household level. *The Lancet Infectious Diseases* 4, (2004).
- [22] D. L. Doolan, C. Doban, K. Baird, Acquired Immunity to Malaria. *Clinical Microbiology Reviews* 22, (2009).
- [23] D. F. Cuadros, A. J. Branscum, P. H. Crowley, HIV–malaria co-infection: effects of malaria on the prevalence of HIV in East sub-Saharan Africa. *International Journal of Epidemiology* 40, (2011).
- [24] L. Abu-Raddad et al, Dual Infection with HIV and Malaria Fuels the Spread of Both Diseases in Sub-Saharan Africa. *Science* 314, (2006).
- [25] E. L. Korenromp, G. Brian, B. G. Williams, S. J. de Vlas, E. Gouws, C. F. Gilks, P. D. Ghys, L. Bernard, B. L. Nahlen, Malaria Attributable to the HIV-1 Epidemic, Sub-Saharan Africa. *Emerging Infectious Diseases* 11, (2005).
- [26] G. Foglia et al, High prevalence of HIV infection among rural tea plantation residents in Kericho, Kenya. *Epidemiol Infect.* 136 694-702, (2008).
- [27] A. S. Gagnon, K. E. Smoyer-Tomic, A. B. G. Bush, The El Niño Southern Oscillation and malaria epidemics in South America. *Int. J. Biometeorol* 46, (2002).
- [28] R. S. Kovats, M. J. Bouma, S. Hajat, E. Worrall, A. Haines, El Niño and health. *The Lancet*, (2003).
- [29] M. T. White, J. T. Griffin, T. S. Churcher, N. M. Ferguson, M. G. Basáñez, A. C., Modelling the impact of vector control interventions on *Anopheles gambiae* population dynamics. *Parasit Vectors*. 28, 4-153 (2011).
- [30] R. C. Reiner Jr, C. Guerra, M. J. Donnelly, T. Bousema, C. Drakeley, D. L. Smith, Estimating malaria transmission from humans to mosquitoes in a noisy landscape. *J. R. Soc. Interface* 12, (2015).
- [31] NMCP. "Kenya Malaria Indicator Survey 2015". Eds. (Rockville, NMCP, KNBS, ICF International, 2015).
- [32] C. C. P. Loiola, C. J. M. da Silva, P. L. Tauil, Controle da malária no Brasil: 1965 a 2001. *Pan Am J Public Health* 11, (2002).
- [33] S. Amaral, G. Câmara, A. M. V. Monteiro, Análise Espacial do Processo de Urbanização da Amazônia. *INPE*, (2001).
- [34] T. Royama. "Analytical population dynamics". Eds. (Chapman and Hall, 1992).

- [35] A. A. Berryman, P. Turchin, Identifying the density-dependent structure underlying ecological time series. *Oikos* 92, (2001).
- [36] A. A. Berryman. "Principles of population dynamics and their application". Eds. (Stanley hornes, 1999).
- [37] M. Lima, A link between the North Atlantic Oscillation and measles dynamics during the vaccination period in England and Wales. *Ecology Letters* 12, (2009).
- [38] M. Lima et al, Whooping cough dynamics in Chile (1932–2010): disease temporal fluctuations across a north-south gradient. *BMC Infectious Diseases* 15 (2015).
- [39] F. A. M. Krsulovic, M. Lima, Tuberculosis Epidemiology at the Country Scale: Self-Limiting Process and the HIV Effects. *PLoS ONE* 11, (2016). doi:10.1371/journal.pone.0153710.
- [40] African Centre for Technology Studies. "Climate change and development consultation on key researchable issues". Eds. (ACTS, 2005).
- [41] Y. B. Amrish et al, Factors associated with high heterogeneity of malaria at fine spatial scale in the Western Kenyan highlands. *Malaria Journal* 15, 1-9 (2016).
- [42] E. H. Yousif, E. J. Kweka, Malaria in East African highlands during the past 30 years: impact of environmental changes. *Frontiers in Physiology* 3, 1-11, (2012).
- [43] NCPD. "KENYA POPULATION SITUATION ANALYSIS". Eds. (NCPD, 2013). pp. 1-338.
- [44] S. Bhatt et al, Coverage and system efficiencies of insecticide-treated nets in Africa from 2000 to 2017. *eLife*, 1-37, (2015).