Chapter 11
Impact of Climate Change on Vector-Borne Disease in the Amazon

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Abstract Impending changes in climate regimes coupled with anthropogenic changes in land use and land cover change pose the most pressing challenges to human societies and natural ecosystems. Global climate change is predicted to disrupt seasonal periodicities and long-term trends in rainfall and temperature, altering natural climate cycles and variation. The impact of environmental change on disease transmission will determine who, when, and where human livelihoods flourish and fail. Vulnerable populations will be particularly affected—i.e., chronically disadvantaged populations who are typically poor, have limited economic opportunities and access to services, and few (if any) options to improve their quality of life. Immediate action is needed to better understand, adapt, and respond to disease burdens that will be affected by changing climate.

Keywords Climate change • Vector-borne disease in the Amazon and climate change • Climate change in the Amazon • Amazon climate change and vector-borne disease • Disease burden and climate change

Impending changes in climate regimes coupled with anthropogenic changes in land use and land cover change (LUCC) pose the most pressing challenges to human societies and natural ecosystems. Global climate change is predicted to disrupt

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seasonal periodicities and long-term trends in rainfall and temperature, altering natural climate cycles and variation [1]. The impact of environmental change on disease transmission will determine who, when, and where human livelihoods flourish and fail. Vulnerable populations will be particularly affected—i.e., chronically disadvantaged populations who are typically poor, have limited economic opportunities and access to services, and few (if any) options to improve their quality of life. Immediate action is needed to better understand, adapt, and respond to disease burdens that will be affected by changing climate.

This chapter will discuss the impact of coupled climate–environment changes on disease transmission in the Amazon. The Amazon is the most bio-diverse region on the planet with over 50,000 plant, animal, fish, and reptile species and over one million insect species. It produces 20 % of the world's freshwater discharge, and contains over 100 billion tons of carbon [2, 3]. Maintaining the integrity of this ecosystem has local, regional, and global implications. Given the multi-scale impacts of the environment and the rapid demographic and economic changes occurring in the Amazon, we focus on vector-borne and zoonotic diseases (VBZD). The goals of this chapter are to (1) describe the unique nature of climate change in the Amazonia context; (2) discuss climate and environment factors that influence the VBZD–climate relationship; (3) provide malaria in the Peruvian Amazon as a specific example of a climate-sensitive VBZD; and (4) provide recommendations for research and action to address complexities of climate impacts on VBZD.

Climate Change in the Amazon

The Amazon basin is characterized by a pronounced east to west humidity gradient, with relatively dry conditions, seasonal precipitation, and occasional water stress in the eastern portions of the basin and more consistent, frequently flooded conditions to the west [2, 4]. The basin also experiences significant climate variability at inter-annual and inter-decadal time scales. The El Nino Southern Oscillation (ENSO) has a profound impact on precipitation, particularly in the eastern and northern Amazon, with warm phase ENSO (El Nino) associated with hot temperatures, suppressed wet season precipitation, and reduced stream flow [5, 6]. ENSO cycles have been shown to explain seasonal malaria in several areas of the Amazon, but with variable predictive accuracy [7–11]. Climate teleconnections associated with Atlantic Ocean sea surface temperatures (SST) also have a significant influence on precipitation. Oscillations in the tropical Atlantic SST gradient influence dry season precipitation in the eastern and southern portions of the basin [12], while the North Atlantic Oscillation (NAO) has been implicated in recent drought events [13]. These remote drivers of variability are overlain by a 28-year precipitation cycle that is characteristic to the Amazon but has not been fully explained, and some of the largest flooding events have resulted from coincident timing of La Nina with the wet phase of the 28-year cycle [5, 6]. Against this background, anthropogenic climate change already appears to be affecting the Amazon. Temperatures rose at a rate of 0.25° per decade between 1960 and 1998 [14], and projections from global climate models (GCMs) suggest that additional warming on the order of 2–5 °C is likely over the twenty-first century [1]. This already wide range is a basin average that includes a projection for greater warming in the Amazon interior during the dry season, and that could be amplified to a warming of up to 8 °C if significant biophysical feedbacks associated with forest dieback become active [15]. Projections for precipitation are even less certain. Observed precipitation trends in recent decades have been mixed, with evidence of a significant drying trend in the northern Amazon and a slight wetting trend in the southern Amazon [6], and with no evidence of a statistically significant trend in the eastern Amazon on the whole [14]. Nevertheless, there is reason to expect that a warming global climate, likely accompanied by continued deforestation within the basin, will alter precipitation patterns in coming decades. A number of GCMs, for example, suggest that El Nino events will become stronger and more frequent over the twenty-first century, which would be expected to effect a drying of the northern and eastern Amazon. In the less humid eastern portion of the basin such a reduction in precipitation could promote ecological change from forest to savannah-like conditions, which would reduce transpiration and enhance the drying trend [15, 16]. Deforestation could exacerbate these trends, as large scale removal of forest trees through burning and timber harvests reduces transpiration and can have a negative feedback on precipitation [17]. Somewhat paradoxically, while large scale deforestation is expected to lead to reduced precipitation and more frequent drought, the local effects of deforestation on the water cycle can lead to increases in flood intensity, as a reduction in transpiration leads to an increase in runoff [4]. The combined effects of climate change and deforestation, then, could well lead to long-term drying over the entire eastern Amazon but to more severe floods during high flow events.

On the ensemble average, the GCM simulations included in the fourth assessment of the Intergovernmental Panel on Climate Change (IPCC) project that dry seasons are likely to intensify across much of the basin and that water stress will, on average, increase in the eastern Amazon over the twenty-first century. This ensemble average must be interpreted with extreme caution, however, as individual ensemble members differ widely in the spatial and temporal character of projected precipitation change, and as all GCM simulations included in the ensemble are implemented at coarse spatial scale (typically at 1–5° resolution, or ~110–550 km) and with physics parameterizations that often neglect important biogeochemical feedbacks known to be important in the Amazon. As such the range of GCM projections for precipitation is best understood as an indicator of the potential sensitivity of Amazon precipitation to twenty-first century climate change.

Given these limitations, application of GCMs to predict specific impacts of climate on vector or animal seasonal and spatial distribution becomes problematic as the characteristics that define breeding, feeding, and living space are defined at smaller scales and with sensitivities that are often within the range of GCM uncertainty. For example, Ruiz et al. developed a system of coupled mathematical nonlinear models to help explain complexities between climate parameters and malaria transmission risk [10]. Their approach integrates human population with pre-imago (larva/pupa) and imago (adult) stages of *Anopheles* that respond to temperature, water availability, relative humidity (RH), and climate anomalies (e.g., *El Niño* events). While informative, the model parameterizes climate over an area larger than 20,000 km^2, which seriously limits the inference one can make about how climate is impacting the distribution of vectors.

Coupled Environment–Climate Impacts on VBZD

Given the biodiversity of the Amazon, it is not surprising that a number of VBZD circulate in the region. While climate change will surely affect the incidence of several pathogens, there exist several enabling factors that couple with climate parameters to exacerbate the effects of climate on human disease [4, 18–20]. Among these, LUCC and flooding are among the most important. LUCC, particularly deforestation, is a widely studied topic that remains void of a synthesized theoretical framework due to the vast differences in causes that can occur across temporal and spatial scales. For example, Walsh et al. [21] demonstrated variations in the relationship between geophysical and socio-demographic characteristics with cultivated land in Thailand when predicted land cover varied from 30 to 1,050 m pixels in size [21]. Similarly, Verberg and Veldkamp demonstrated that low-resolution approaches (i.e., large geographic areas) are ideal for identifying "hot zones" of land cover change, but high-resolution approaches (small geographic areas) provide insight into evolving land patterns and ecological consequences [22]. This is particularly relevant for VBZD—not only do researchers have difficulty applying GCM parameters to vector-borne disease predictions, but many studies have used coarse land cover grids to characterize vector habitats and disease risk, such as the 0.5° latitude–longitude grid in [23]. As described by Messina and Pan [20], this is an important ontological difference that exists between epidemiology and land change science that impedes understanding of proximate drivers of disease risk. That is, epidemiology often posits hypotheses anchored in traditional health and place organizational strategies, which incorporate land–climate data as discrete realizations of a continuous surface product. In contrast, land science operates using a geography, space, and time paradigm that do not provide appropriate individual-level variables necessary for inputs to epidemiology models. This confusion leads to issues of ecological fallacy as environmental variables are modeled at the individual level.

Another challenge posed by land–climate coupling is the intimate relationship between LUCC and human population dynamics. Studies of LUCC highlight important economic, social, cultural, political, and demographic factors influencing land change processes [24–28]. With continued high fertility rates and in-migration, population growth throughout the Amazon will continue, ensuring that LUCC will occur as people look to improve their livelihoods [29–32]. Livelihood choices are particularly overlooked as a root cause for VBZD risk—malaria is a prime example: studies that have shown a clear relationship between deforestation, vector density, and

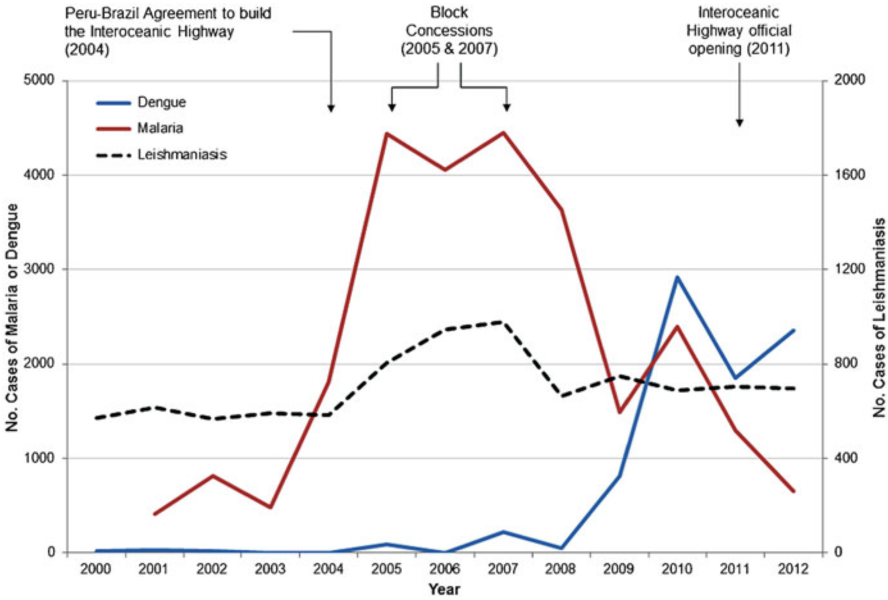

Fig. 11.1 Cases of malaria, dengue, and leishmaniasis in the region of Madre de Dios, Peru, between 2000 and 2012. Reported malaria cases are shown by the *red line*, dengue by *blue line*, and leishmaniasis by the *dotted black line*

malaria [33–35] are largely founded on the premise that ecological services are intimately tied to human dimensions of land cover change, as has been described by the Frontier Malaria Hypothesis [36, 37]. Castro et al. [37] clearly demonstrate the importance of Frontier Malaria as they related early features of colonization in Brazil with elevated malaria risk due to the establishment of new breeding sites for *Anopheles darlingi* and the introduction of a naïve human host. This is contrasted with recent research by Kosek and colleagues which demonstrated that epidemic malaria rates in northern Peru are associated with migration behaviors of families involved in occupational labor, primarily logging [38]. This human component of the land–climate relationship adds a layer of complexity that requires a comprehensive understanding of human livelihoods and vulnerability. Household livelihoods are tied to a number of factors that mediate household choices and, ultimately, drive malaria risk.

Perhaps the strongest mediating factor of VBZD in the Amazon is road construction and access. Roads alter the interface between humans and the environment by penetrating the forest like veins, pumping in migrants, occupational laborers, colonists, and altering species ecology and habitat. The multidimensional impact of roads is exemplified by the 2004 agreement between Brazil and Peru to construct the Interoceanic Highway connecting rural Amazonia farms in the western basin to Pacific and Atlantic Ocean ports. Construction began immediately with concession blocks awarded in 2005 and 2007. Figure 11.1 compares the timing of these large scale activities with malaria, dengue, and leishmaniasis disease rates reported by the Regional Ministry of Health of Madre de Dios (DIRESA-MDD) from 2000 to 2012.

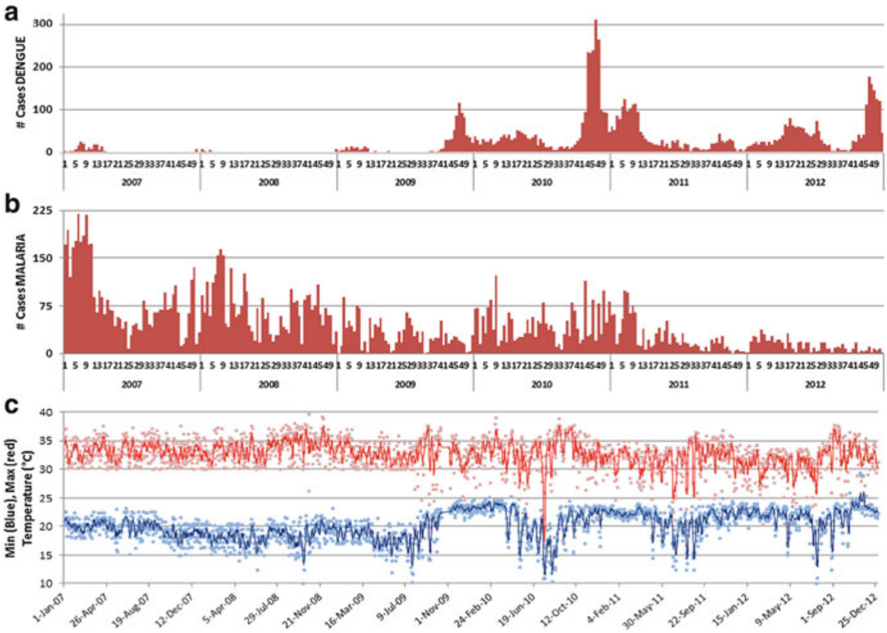

Fig. 11.2 Weekly surveillance case reports and daily minimum/maximum temperatures reported in Madre de Dios, Peru, between January 2007 and December 2012: (**a**) dengue cases; (**b**) malaria cases; and (**c**) temperature reported in Puerto Maldonado. Temperature reports were not available for the entire time series in Puerto Maldonado. For days with missing data, we used temperature reported from the Inapari weather station, which is approximately 180 km north

During construction, elevated rates of both malaria and leishmaniasis were experienced; in fact, between 2005 and 2008, reported cases were 470 % higher for malaria and 45 % higher for leishmaniasis compared to reported cases between 2000 and 2004. As road construction neared completion, reported cases of dengue skyrocketed, with cases primarily occurring in the city of Puerto Maldonado.

An important question is whether climate variability was related to these temporal patterns. Figure 11.2 compares the weekly surveillance reports for malaria and dengue from the DIRESA-MDD to daily minimum and maximum temperatures between 2007 and 2012. Dengue cases peaked in late 2009, 2010, and 2012, with a slight increase in late 2011 as well (i.e., November and December). Cases also appear to peak in early each year, roughly mid-January to March. This was true each year except 2012 when the peak appears to be shifted to April and May. Malaria trends are much more difficult to describe as they appear to have two distinct peaks in 2007 and 2008, but following widespread efforts to control malaria, the pattern begins to lack seasonality. Meteorological conditions appeared relatively stable between 2007 and mid-2009, but became much more erratic between 2010 and 2012 with less variance between minimum and maximum temperatures. The higher minimum temperature after 2010 may have contributed to the rise in dengue cases seen regionally. There does not seem to be a strong signal between malaria and temperature during the high risk periods. However, finding an increase in malaria with overall VBZD is not expected at this gross-scale of analysis. Malaria infections in the Amazon are more long-lived in the human host than dengue (i.e., due to the nature of *Plasmodium vivax*), making it difficult to detect a strong signal between malaria and temperature at any given point in time. Also, this type of analysis lacks fine-scale resolution data on human mobility, urbanization, and land cover to fully evaluate the relationship. A specific demonstration of malaria associated with climate change will be discussed in the following section.

Epidemiology of Climate-Associated Vector-Borne Disease

Malaria is a prime example of a climate-sensitive VBZD disease. Malaria is endemic in over 100 countries with over 3.3 billion people at risk and, in 2010, caused an estimated 216 million episodes and 655,000 deaths [39]. It is transmitted by the female *Anopheles* mosquito and is the result of infection due to the presence of *Plasmodium* parasites (primarily, *P. vivax*, *P. falciparum*, *P. malariae*, and *P. ovale*) that cause fever, chills, fatigue, and headache, among other symptoms. In the Amazon, approximately 75 % of malaria is caused by *P. vivax*. Although less lethal when considering the acute infection, symptoms can be severe. There can be long-term pathology and *P. vivax* inflicts major impacts on human development ranging from impaired child growth and cognitive development, malnutrition, lower productivity in people of all ages, and disincentives for investment by industry and government [40–46]. As mentioned previously, malaria epidemiology in the Amazon can broadly be classified as either Frontier Malaria or occupational and migratory malaria. *Frontier Malaria* involves three stages of malaria risk in forest environments that follow stages of the frontier settlement process: [1] *Epidemic*, early years of agricultural colonization with high vector density, exposure, human population mobility, and weak institutional presence; [2] *Transition*, 3–10 years after settlement whereby land practices exhibit lower deforestation rates, population mobility slows, and residents begin to understand exposure risks; and [3] *Endemicity*, characterized by the integration of health services and infrastructure leading to improved socioeconomic status, such as urbanization, economic investments, and improvements in housing and income levels that result in less population mobility and environmental change [47, 48]. Occupational malaria refers to the idea that livelihood choices that involve human mobility for resource extraction, agriculture, or other activities far from one's home places that individual at greater risk for infection than if the individual stayed at home. Note that neither of these approaches directly integrate climate as a proximate determinant of infection.

Anopheles mosquitos are the vector capable of transmitting malaria. Only about 40 *Anopheles* species (of over 450) can transmit malaria to humans and only approximately 27 are effective transmitters [49, 50]. In the Amazon, the primary malaria vector is *A. darlingi* Root, 1926 [51–55]. *A. darlingi* is highly dependent on water for its survival and breeding, is a typical riverine species that inhabits jungle and forest environments, and is mostly distributed in low altitude regions (<500 m above sea level) with high relative humidity [56, 57]. Vector competence is highly dependent on temperature and humidity, as *P. falciparum* and *P. vivax* are unable to develop at temperatures below 16 °C and 14.5 °C, respectively, but accelerate development when temperatures exceed 35 °C [50, 58–61]. High relative humidity (above 75 %) prolongs vector life and extends transmission (once infected), but below 35 % RH shortens their life span and prevents Plasmodium development. Vector density is directly proportional to the rate of malaria transmission, both from mosquitoes to humans and vice-versa [59]. Breeding site characteristics for *Anopheles* vary by species, but all depend on the presence of water for an average of 12–14 days to allow time to growth from egg to adult emergence.

Environmental determinants of larval and adult *Anopheles* habitat also vary by country [61]. For example, *A. darlingi* density has been reported to peak following maximum precipitation [62], the dry season [63], and wet–dry transition periods [34, 64]. Recently Barros et al. identified "microdams" (small obstructions to river flow such as tree trunks, branches, etc., that cause water to pool) to explain elevated adult and larval *A. darlingi* density during the dry season [65]. Ecologically altered landscapes (deforested, secondary forest, grass/cropland) [34, 53], forest fringes [66, 67], microclimate variation [62], as well as natural and artificial bodies of water (fish farms, rice fields, irrigation canals, etc.) [34] have all been identified as important breeding sites for anophelines, particularly *A. darlingi*.

Although climate change is not directly integrated into the human components of transmission, climate, coupled with land and flooding, is directly correlated with *Anopheles* species composition and abundance. Floods can significantly alter the epidemiology of disease transmission. Flood areas are predictable topographical features of the landscape where usual seasonal fluctuations are related to the usual patterns of infection. However, large floods, such as those that occurred throughout a large part of the western Amazon in 2012, dramatically increased the number of reported cases following several years of progress in reducing malaria burden. Between 2000 and 2006, reported cases of malaria in the region of Loreto averaged around 44,000 cases annually. During the ensuing years, reported cases dropped by about 10,000 each year and remained at 10,000–11,000 cases in 2010 and 2011. February and March of 2012 were among the wettest months in the Peruvian Amazon, resulting in one of the largest historical floods in Loreto. By the end of 2012, the number of reported cases of malaria had reached 25,000. Cases peaked between April and August, with an abnormally high second peak between October and November.

Climate and environment changes were associated with increases in malaria cases in the Peruvian Amazon region in three ways. First, elevated rainfall and high temperatures likely contributed to an expanded transmission season. With more water available, mosquito density could remain sufficiently high throughout the year, rather than dissipating between September and January. Second, flood waters altered the interface between people and *Anopheles* exposure. Families were displaced and moved into temporary housing, often without bednets or other protective measures they may have against biting insects. Even animals, such as rodents, mice, and snakes, were similarly displaced from forested areas and moved into the populated communities. Third, public health efforts became focused on providing services to displaced families, and distracted from the prior surveillance interventions that gave some protection against VBZD transmission. All available resources were being used for dealing with injuries, snakebites, acute infections, and sanitation problems. This allowed malaria cases to go undetected and likely untreated, further enabling the increase of malaria transmission.

Malaria-Climate Change Case Study

During the 1990s, Loreto experienced an epidemic malaria outbreak that peaked at 121,268 cases in 1997 [68]. Cases were initially reported in the towns of Rumococha and Zungarococha in 1991, located about 10 and 20 km from the central city of Iquitos, respectively. Malaria rates subsequently transitioned to endemic levels ranging from 30,000 to 50,000 cases annually between 2000 and 2008, and then rapidly fell to approximately 10,000 cases annually in 2010 and 2011. The transition from epidemic malaria was aided by policies of the Peruvian Ministry of Health that focused intervention efforts on case detection, treatment, and bednet distribution. Specifically, the Ministry of Health focus is on febrile individuals because malaria infection is much more likely in individuals with fever than in individuals without fever. Individuals are instructed and reminded to go to their community health center if they have a fever, headache, or other symptoms that might indicate they have malaria. Individuals suspected to have malaria are diagnosed with a blood smear that is read by a trained microscopist. If the test is positive, treatment is prescribed *at no cost*, and treatment is specific to the malaria species found (i.e., *P. falciparum* or *P. vivax*). Malaria treatment drugs are not available in private pharmacies. In 2012, the number of malaria cases in Loreto unexpectedly rose to approximately 25,000 cases following massive flooding that significantly displaced a large proportion of the population.

A clinical study initiated in 2003 by Branch and colleagues in Zungarococha [69] is a microcosm of the underlying transition observed and new malaria epidemic. Zungarococha has an average population of around 2,200 persons across a 4 km^2 area that is organized into four villages. Beginning in 2004, the population was followed each full year until 2012. Although population size has been relatively stable, population turnover has been rapid. Seventy five percent of the 2,340 residents in 2012 who were older than 4 years old in 2012 participated in the 2007 (pop. 2,145) study. Most of the population works within the community in occupations related to local farming (agriculture and fish) and trading.

The Zungarococha study was designed as a year-round active case surveillance coupled with passive detection in the community health center [69]. Active case detection involved a minimum of six visits to each household during the (6-month) rainy season and testing a blood sample for malaria from all persons in the house

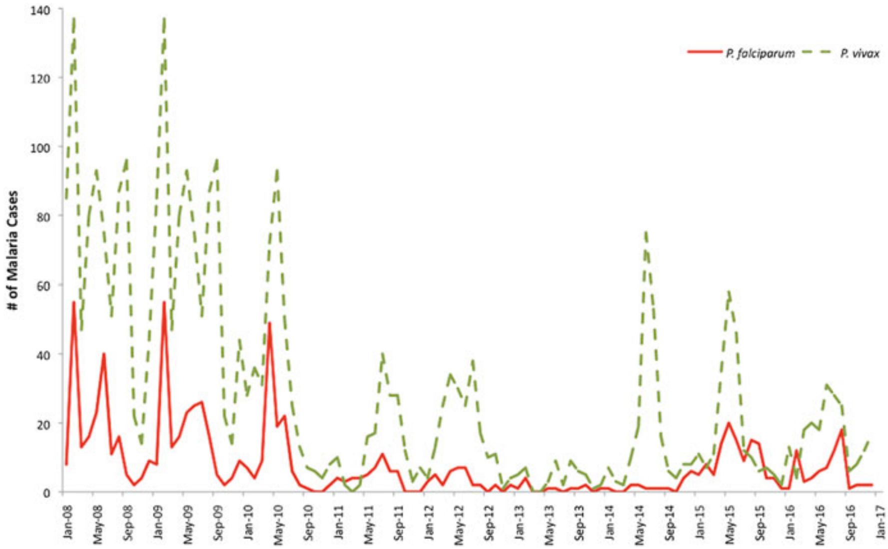

Fig. 11.3 Number of *P. falciparum* (*solid red line*) and *P. vivax* (*hatched green line*) in Zungarococha detected with active case surveillance between 2004 and 2012. Population size under surveillance varied from 2,145 to 2,340; however, the major flood event in April 2012 limited some surveillance and detection until June 2012

regardless of symptoms. Additionally, any person reporting to the community health center with fever or other malaria-like symptoms was tested for malaria parasites. More than 91 % of the community participated in the study each year (2004–2012).

Figure 11.3 shows the number of *P. falciparum* and *P. vivax* cases each month detected in Zungarococha. Strong seasonal patterns were observed between 2004 and 2006, followed by sharp declines in 2007 and 2008. These declines can be partly explained by increased treatment of symptomatic and asymptomatic cases identified during active case detection as well as some persons developing immunity [69–73]. Between 2009 and 2010, *P. falciparum* was nearly eradicated and *P. vivax* infections were at historically low levels in 2009.

In 2010 and 2011, *P. vivax* cases spiked during the normal transmission season (April–July), but by mid-2011 it was apparent that *P. falciparum* was also returning. Between 2011 and 2012, there was a dramatic increase in malaria infections, which resulted in the MOH declaring a new malaria epidemic in Loreto (Fig. 11.3). What happened during this interval? How was the climate changing? Were there coupled climate effects? While the study cannot answer all these questions, there are three distinct changes that occurred over the 8-year interval to begin understanding the underlying drivers. First, as mentioned previously, population turnover was rapid. Between 2004 and 2010 a large proportion of the population migrated out of Zungarococha, being replaced primarily by new births and unexposed new in-migrants to the community. For example, after 2010, the study enrolled 124 new individuals who either immigrated or were born into the community. The number of susceptible persons to malaria (either never been infected or infected more than 5 years prior) likely reached a maximum in 2009 and 2010 following several years of declining rates (Branch, unpublished).

Second, significant climate variation was experienced in the form of temperature change and water stress, resulting in some regions of the Amazon to have extensive droughts in 2005 and 2010 followed by a major flood in 2012. Notably, the 2005 drought at the time was considered one of the worst on record, but impacted primarily the southwest Amazon basin, leaving Loreto with relatively normal rainfall levels [74]. However, Loreto felt the full effect of the 2010 drought, which was much worse than 2005 and brought higher temperatures, fewer clouds, and less rainfall [75]. This was followed by one of the worst floods in the history of the Amazon that began in late 2011 with elevated precipitation. In Zungarococha, improved case detection and treatment, development of immunity, and extensive drought conditions likely translated into fewer infected persons and both fewer susceptible and infected *Anophelines*. This would reduce the force of infection over time. The higher temperatures over time might have caused a more rapid development of malaria in *Anopheles* mosquitoes. Because this is a riverine environment, there were at least some mosquito breeding sites available. As rivers began to swell in late 2011 and reached flood levels in 2012, *Anopheles* densities increased throughout the year, extending the malaria transmission season into usual non-malaria months of September, October, November, December, and January in Zungarococha, during which 24 and 33 cases of *P. falciparum* and *P. vivax* were found, respectively. Figure 11.4 shows the time series of *P. falciparum* cases and air temperature detected prior to, during, and after the drought in Zungarococha (2007–2013). As the figure shows, following the drought, there was high malaria incidence coupled with an expanded malaria transmission season.

This type of transmission season expansion can have long lasting consequences on VBZD epidemiology and evolution. Under normal seasonal conditions, there is a barrier to the spread and evolution of the malaria parasite by there being several months that are not hospitable to the malaria parasite and/or the mosquitos; however, when transmission occurs continuously throughout the year, the malaria parasite can evolve to become more virulent [76]. Also, if high vector density persists throughout the year, this could facilitate reemergence of the disease as infected individuals reenter the area. The effect could make a balanced endemic transmission system change to one that either has higher endemic transmission or results in a new epidemic. In Zungarococha, the endemic transmission and near eradication that existed before 2011 became classified as epidemic in late 2011 due to the high number of *P. falciparum* cases in May 2011 (20 cases).

Third, the 2012 flood altered the structural response to malaria. In March 2012, the regional government of Loreto declared a state of emergency as several thousand people were displaced from their homes. At the regional level, the ability of the MOH to conduct passive detection of individuals with fever was significantly diminished. Local clinics and hospitals were distracted by injuries and illnesses other than malaria during these months (Sihuincha, unpublished). In Zungarococha, study protocols faltered as only 1,154 individuals were contacted and tested during

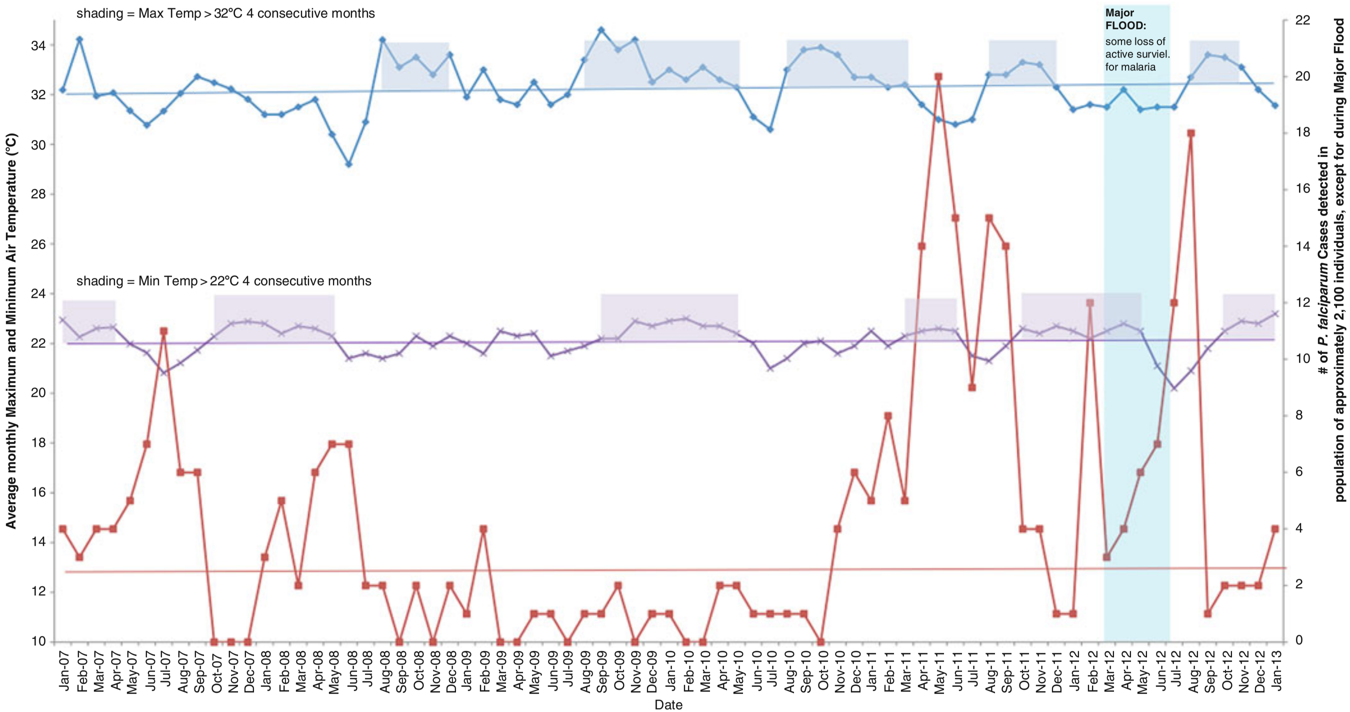

Fig. 11.4 Average monthly temperature maximum (*top blue line*) and minimum (*middle purple line*), and monthly *P. falciparum* malaria cases detected in Zungarococha. Temperature measures were collected by the National Weather Station located within the district of Zungarococha and provided by Dr. Moises Sihuincha and colleagues

this period, compared to an expected minimum of 1,800. Approximately 600 individuals were absent from their homes and could not be located; 532 individuals who returned to their homes by June 2012 were asked if they were diagnosed with malaria while they were away, but none reported a diagnosis or treatment. In prior years, the study found that approximately 30 % of the malaria infections detected were asymptomatic [69–73], all of which were treated with antimalaria drugs to help stop transmission. Even throughout active surveillance, the extent of the Iquitos flood likely resulted in some missed malaria detection due to displacement of individuals and distraction of health centers to focus on acute injuries, bites, and illnesses associated with the flood.

Here, we presented a specific case where malaria incidence responds positively to the climate–VBZD relationship through an expanded transmission season, flooding that contributed to *A. darlingi* breeding habitat and density, and disruption of active and passive case detection. Having an ongoing active case surveillance protocol in each year between 2004 and 2012 enabled us to observe this relationship. With more study, improved clarity of the associations between climate change and VBZD can be obtained. It is noteworthy that the climate–VBZD relationship does not have to increase disease incidence. For example, after the floods there was an increased detection of dengue virus infections in many communities, including Zungarococha. Dengue is spread by *Aedes aegypti*, which is considered hardier, more resistant to heavy rains, and more capable of breading in small, artificial containers of water compared to anopheles [77]. Therefore, we might observe competition between vectors, resulting in differential VBZD risk. We are only at the beginning of understanding this complex climate–environment and disease relationship and ways they will impact the way we live, flourish, and fail.

Future Directions in Research

There have been several attempts to describe a generalized framework for understanding environmental relationships with disease transmission [18–20, 78]. Undoubtedly, studying VBZD is complex. Transmission results from interaction between humans, vectors, and pathogens that are mediated by environmental conditions operating at multiple geographic and temporal scales, which are likewise impacted by people [34, 49, 79–81]. Frontier Malaria is a clear example of how these interactions persist in the Amazon and how climate variation and change can significantly alter the natural course of disease transmission. Changes in climate not only alter the expected seasonal temperature and rainfall patterns, land–climate coupling means that if certain thresholds are breached, local and regional impacts in land surface characteristics and surface hydrology are also significantly affected. This was the case in Zungarococha, where declining malaria rates were impacted by major flooding, which caused a multitude of problems: extended vector breeding habitat over space and time, altered socio-demographic behavior of individuals, and weakening of the health system to respond to malaria. Admittedly, positive human behavioral response can occur, such as increased awareness of the infection, prevention, or participation in intervention strategies; however, in resource-poor environments, the likelihood of these types of positive responses is, unfortunately, minimal.

One of the most challenging aspects of VBZD prevention and control is the interdisciplinary nature of transmission and causation. Collaborations between researchers in physical science, epidemiology, and social science to better understand disease dynamics have advanced considerably in recent years. These collaborations have been encouraged by interdisciplinary funding opportunities supported by NIH, NSF, NASA, and other funding agencies, and they have yielded significant improvements in integrated assessments of disease process, predictability, and prevention. For the most part, however, these collaborations have involved diverse experts bringing their traditional analytical tools and study designs to the problem of VBZD, with minimal feedback across disciplines that limit more effective integration of techniques. For example, the epidemiological triangle of disease causation (agent–host–environment) often characterizes disease risk as discrete events between agents and hosts. Environment, which is often a distant third wheel, is usually categorized as the place where agent–host interactions occur. This is where a large disconnect exists between epidemiology and land/climate scientists. In epidemiology, environment is a discrete space (e.g., community, political/administrative boundary) that is statistically modeled as a predictive variable of infection. However, land/climate scientists recognize that environmental characteristics are derived from modeled products (e.g., satellite imagery) and the inputs used in epidemiology are actually continuous in space and time. The severing of a continuous ecological biome to examine discrete events can result in ecological fallacies or at least spurious relationships between environment and disease.

In general, the application of satellite imagery to VBZD represents a core science of opportunity. While data from satellite sensors are of interest to VBZD risk monitoring and prediction, these sensors were almost never designed with any specific consideration for what measurement characteristics would be most useful for VBZD research or surveillance. Similarly, climate models are almost never optimized for VBZD applications in their resolution, periods of analysis, or even in the process simulations and model outputs. Of course, some limitations in these physical science techniques are difficult to overcome—high-resolution satellite-derived soil moisture measurements are extremely expensive and sometimes impossible to obtain, and climate models are computationally intensive and are plagued by possibly irreducible uncertainties for both seasonal prediction and future climate change projections. Recognizing this, epidemiologists might need to alter the study designs and/or surveillance networks to take full advantage of the model results and satellite observations that are available. This suggests that collaborations that currently occur primarily at the scale of small research teams need to be moved upstream into satellite mission design, climate model development, and planning for health monitoring systems, so that the interdisciplinary nature of VBZD problems is recognized in the design of the required research tools as well as in their application.

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