

## Migration as a mediator of climate-related infectious disease risk

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Over the past two decades, there has been a growing chorus of scientists stating that climate change, namely, the long-term rise in global temperature combined with more extreme observations of temperature and precipitation, is directly associated with infectious disease burden. The most sensitive diseases to climate change are believed to be vector- and water-borne infectious diseases, such as malaria, dengue, encephalitis, and a number of parasitic, viral and bacterial enteric infections (Epstein 2001, Patz, Campbell-Lendrum et al. 2005, Caminade, McIntyre et al. 2018). Due to the nature of climate change, these studies often fall into one of two categories: (1) Empirical data are collected to quantify the relationship between seasonal climate variation and presence of vectors, pathogens or both, with positive associations inferred to be associated with increased human disease due to climate change. (2) Other studies are largely exercises in deductive reasoning – e.g., since climate parameters constrain or expand the range of *Aedes* mosquitoes that spread Dengue and seasonal weather extremes influence Dengue incidence, it is logical to conclude that rising temperatures and more extreme conditions should result in greater risk (Patz, Epstein et al. 1996, Epstein 2001, Hales, de Wet et al. 2002). While the importance of seasonal climate and weather extremes on infectious disease risk cannot be debated, the contention that climate change is *directly* related to infectious disease risk, i.e., climate is a proximate determinant of infectious disease, is overstated.

For this Cyberseminar, I propose the following hypothesis: ***Migration and human mobility are the key underlying determinants driving infectious disease risk globally.*** In fact, I would further contend that the importance of migration in the maintenance of endemic disease and the emergence of new infections surpasses that of purported climate change. The impact of climate change on infectious diseases has been questioned due to the complex set of factors associated with disease (Rogers and Randolph 2000, Lafferty 2009). I offer three tenets to give credence to this claim that are described in this paper. First, there has been strong relationship described between climate change and migration. This relationship has been well-covered by the Cyberseminar; thus, I won't belabor this point except to say that for an infectious disease context, migration consists of a spatial reconfiguration of a person placed on a landscape for any amount of time. Therefore, migration includes concepts such as temporary travel, occupational mobility (daily commute or sub-annual contracts that involve temporary relocation), temporary movements for personal reasons, and permanent migration. Second, the proximate determinants of infectious disease epidemiology have a long history in defining properties of infection with a very specific approach to establish causality and define proximate and distal factors of disease. Note that epidemiologists

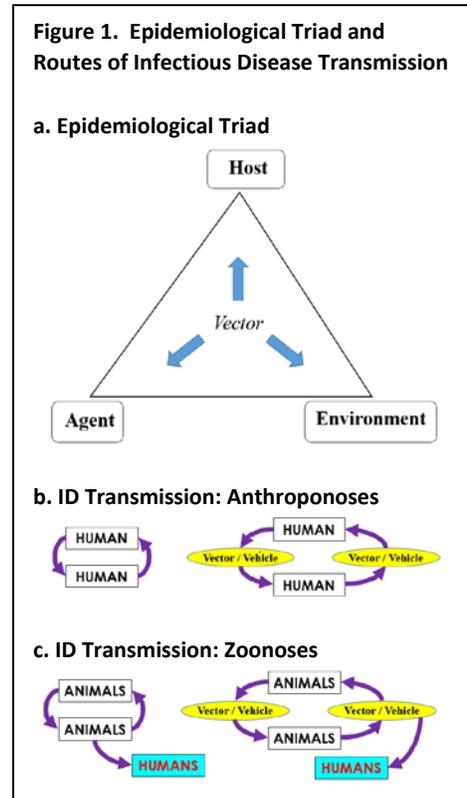
distinguish infection (presence of a pathogen in a host) and disease (presence of clinical symptoms). Third, drawing on research of malaria, I will discuss the importance of migration vs. climate on health.

### Migration and Climate Change – Role in the Proximate Determinants of Infectious Disease Epidemiology

Infectious disease (ID) epidemiology uses a clear model for conceptualizing disease risk, referred to the Epidemiological Triad (Figure 1). Here, infectious diseases are depicted as external agents that cause disease, such as a bacteria, viruses, parasites or fungi; hosts that define both where the agent naturally resides and reproduces as well as the susceptible animal or human that is infected by an agent; and environment, which is where host and agent interaction occurs that results in infection and disease. Two types of ID transmission are defined: Anthroponoses, which are either spread between humans (e.g., HIV) or with the aid of a vector (e.g., malaria); and Zoonoses, which cycle between animals, with humans as an incidental or dead-end host (e.g., the transmission cycle would end once a human is infected, such as with rabies or West Nile virus). Vectors are important in the ID process as they are organisms that can transmit the agent between hosts and may be involved in the lifecycle of the agent.

On the surface, it would appear that the Triad (and anthroponotic and zoonotic transmission pathways) depict environment, and therefore the effects of climate change, as a key element in any infectious disease process. However, besides the agent itself, four components define an ID process for which both environment and human migration play a critical role, albeit at different spatial scales. First, intrinsic properties of an agent define the mode of transmission as well as the eventual pathogenicity (ability to produce clinical symptoms) and virulence (proportion of clinical illnesses defined as severe). Properties include the molecular characteristics of an agent (i.e., morphology, size, antigenic make-up), number of hosts within which the agent can exist, and environmental conditions that define growth requirements within a host and conditions to survive outside a host. Note that intrinsic factors are NOT dependent on human migratory behavior, but can be influenced by climate parameters such as temperature and humidity, which may allow a particular pathogen to exist for longer times outside the host.

The second component of the ID process is host-agent interactions that will result in infection (in the host). This component defines properties such as infectivity of an agent (ability to invade and multiply in a host) and immunogenicity (ability of infection to induce immunity) as well as virulence and pathogenicity as factors moderating host-agent interactions. In order for these properties to be evaluated, an agent and host must come into contact, which is entirely predicted by the spatial distance between host and agent. However, host-agent spatial contact depends on both migration behavior and environmental conditions as environmental change may alter locations where a vector or agent exists on a landscape, while migration behavior will result in a human entering that space on a landscape. The question posed here is where migration and environmental change fall on the causal pathway linking humans and agents.



I contend that for the leading infectious diseases globally (i.e., highest morbidity and mortality), human migration is far more important due to the rapid change in human movement compared to relatively slow changes in the environment. We explore this in the next section.

The third component of the ID process, which is not dependent on either migration or environment, is the pathogenic mechanism of the agent that produces pathogenic effects (either independently or simultaneously). Mechanisms include tissue invasion, toxin production (e.g., tetanus), immunologic enhancement or allergic reaction (e.g., tuberculosis), persistent or latent infection, enhancement of host susceptibility (e.g., Reyes Syndrome and varicella), and immune suppression (e.g., AIDS, malnutrition).

The final component of an ID process is the reservoir, which can be a human, animal or environmental entity. The reservoir is where an agent normally resides, grows and multiplies. Note that hosts can also be reservoirs. Both spatial location and temporal environmental conditions are important factors in identifying reservoirs as well as the eventual interaction between a susceptible (non-infected) host and agent. Environmental conditions almost solely define extent of a reservoir except in circumstances when hosts and reservoirs are the same, such as for malaria, dengue, and shigella (i.e., humans are the only susceptible organisms).

## **Migration and Health**

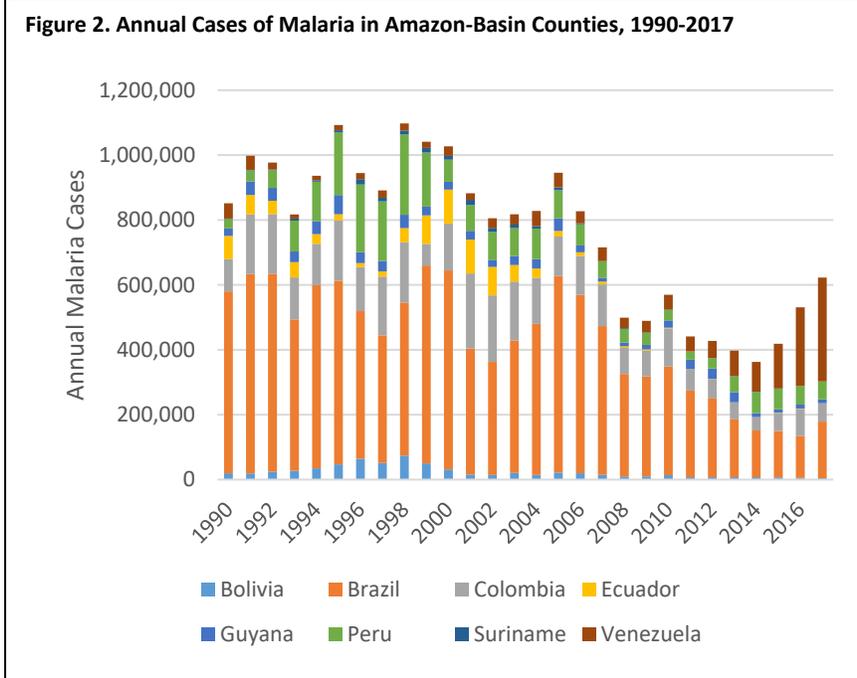
### **Malaria**

Malaria is a vector-borne disease caused by infection with one of four *Plasmodium* parasites. It is transmitted between humans by infected female *Anopheles* mosquitoes. Mosquitoes can only become infected and transmit if they take a blood-meal from a human infected with malaria; therefore, humans are the reservoir and host. Several studies have demonstrated a strong correlation between environmental conditions and malaria risk, including temperature influencing growth rates of vectors and the *Plasmodium* parasite (Bayoh and Lindsay 2003), while rainfall is associated with water pooling and larval production. Several studies have also hypothesized that vector range would expand to higher altitudes due to climate change (REF); however, recent studies have shown this effect to be minimal (e.g., (Rogers and Randolph 2000) or that expansion to higher altitudes may occur during simultaneous contraction at lower altitudes (Lyimo, Takken et al. 1992, Kulkarni, Desrochers et al. 2016).

The contention that global climate change is causing outbreaks of malaria is not strongly supported by evidence, particularly at global scales. For example, the World Health Organization (WHO) reports that over the past two decades malaria cases and deaths have declined (World Health Organization (WHO) 2017), with a 50% decline reported since 2010 alone. However, since 2000, data from NOAA indicate that average global temperature has increased by 0.5°C (Blunden, Arndt et al. 2018). While we must be careful in drawing local inference from global trends, clearly there is a nuance missing when connecting disease risk to climate.

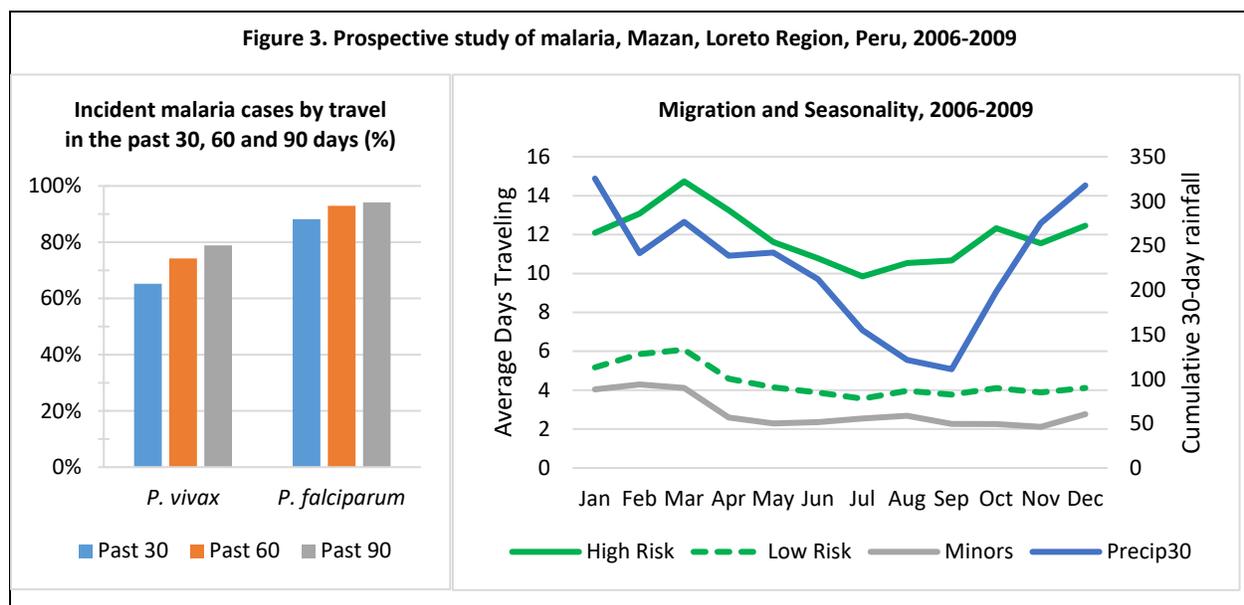
At local levels, the role of climate clearly plays a role, but mostly through processes associated with human mobility. In the Amazon, malaria cases declined dramatically from the mid-1990s until 2011, prompting the withdrawal of the Global Fund to Fight Aids, TB and Malaria from Latin America (Figure 2). However, in 2011 the Amazon region also experienced one of the largest floods to affect the region in over 30 years. In 2012, Venezuelan economic policies began to entice migration away from the country, which occurred much more frequently after the death of Chavez and subsequent inflation. Since 2011, cases in Peru and

Venezuela doubled in less than two years (World Health Organization (WHO) 2017, Daniels 2018). Outbreaks followed in Colombia where cases doubled by 2016 (to 83,227) and Ecuador which experienced a 5-fold increase (World Health Organization (WHO) 2017). The outbreaks in Peru were initiated by floods that cause internal displacement of over 70,000 people and complete disruption of the health system. However, by 2012, environmental conditions were normal, yet disease momentum had begun and



population mixing due to continued internal mobility resulted in widespread transmission. Outbreaks in Venezuela were initiated primarily due to a breakdown of the health system; however, Colombia and Ecuador outbreaks were almost solely driven by migration, both across international borders (from Peru and Venezuela) as well as internal migration. Current malaria burden in the Amazon exceeds every year over the past 11 years.

At an even smaller spatial scale, we conducted a study to better understand the role of travel and migration on the incidence of new malaria infections in a the town of Mazan (population ~5000) in the Loreto Region of Peru between 2006 and 2009 (Chuquiyauri, Paredes et al. 2012). This was a prospective cohort study that tested people weekly for malaria as well as tested people within three days of returning



from any overnight travel. Among all incident *Plasmodium vivax* cases, 65% occurred in people who returned from travel in the past 30 days, while for *Plasmodium falciparum*, the more deadly of the malaria species, 88% of cases were from people who traveled in the past 30 days (Figure 3). Travel was primarily due to occupation, with loggerman, fisherman and miners comprising the high risk group of travelers (Figure 3), while low-risk was associated with people involved in agriculture, outdoor work (construction), students, and other non-migratory work. Travel was also strongly associated with season. Mining (small-scale gold mining) primary occurred during low water season for the river so that miners could overturn sandbanks for gold prospecting. Loggerman almost always traveled during and after peak river height due to the ease of transporting large trees downstream for processing. Peak river height usually followed peak rainfall periods that occurred between December and January (Figure 3).

In sum, factors predicting malaria risk have strong correlations with temperature and rainfall; however, known relationships between malaria and climate have not resulted in global increases in malaria risk. Migration and travel are the leading factors associated with incident malaria, while seasonal trends in rainfall and river height are strong predictors of when migration decisions are made for certain occupations. Thus, a causal pathway for human malaria infection in the Amazon can be conceptualized as climate change, variation and extremes influence mobility decisions, which then produce risk factors of infection.

### **Summary**

Migration and mobility are the key determinants in predicting when and where a potential human host (susceptible) will be to become infected. The contention that climate change directly impacts infectious disease is likely an overstatement, particularly for vector-borne diseases. There are simply too many important underlying mediating factors that proximate transmission, including migration behavior, livelihood strategies, community resilience, and proximate factors of ID risk, among others. Part of lack of understanding or direct integration of migration behavior into infectious disease research is the absence of demographers and other social scientists from epidemiological risk assessment.

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