Climate Variability and Change and Its Effects on Malaria

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There is little scientific doubt that the earth is undergoing profound climate change, with much of it driven by human activity. The effects of climate change on the distribution of infectious disease remain less apparent than the fact of climate change itself. It is reasonable to expect that diseases that are mediated by climate, and whose distribution is partly governed by climate, will undergo changes in distribution as environmental conditions change. Malaria, a vectorborne disease, is highly subject to environmental and climatic influences. Nonetheless, it has proven difficult to generalize about the effects of climate change on malaria, and to predict future effects. The El Nino Southern Oscillation (ENSO) is one possible way of simulating the long-term effects of climate change on malaria, but efforts to do this have produced contradictory results that depend highly on location. In this paper, we synthesize and review the results of studies on the climate change-malaria distribution relationships, and discuss the possibility and need for developing malaria early warning systems.

Keywords: *Malaria, Medical geography, Epidemiology, Infectious disease, Climate change.*

The World Health Organization estimates that, between 2000 and 2009, there was an average of 236 million cases of malaria annually, leading to an average of 913,000 deaths per year (World Health Organization, 2010b). The disease is especially important for children in Africa, amongst whom it is responsible for 20% of deaths (World Health Organization, 2010a). With more than US$5 billion spent each year on malaria control, and estimated decreases in GDP of holoendemic countries of as much as 1.3% due to lost labor productivity, malaria is of great economic and public health importance (World Health Organization, 2010a; World Health Organization, 2010b).

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The disease is caused by four species of *Plasmodium* parasites – *P. falciparum, P. vivax, P. ovale* and *P. malariae* – and is transmitted by *Anopheles* mosquitoes. More recently, a fifth human pathogen, *P. knowlesii*, has been identified in Asia, but its significance is not fully understood. Both the vectors and parasites are affected by weather and so too, consequently, is malaria. Vector reproduction and survival probability are both dependent on temperature and rainfall. Vector biting rates depend on temperature (van Lieshout et al., 2004). Similarly, the rate of parasite replication within the mosquito is strongly influenced by ambient temperature (Paaijmans et al., 2009). Thus, weather is a major force dictating the spatial bounds, local intensity, and both the timing and duration of the transmission season of malaria.

Given these connections with weather, understanding both cyclical and secular climatic trends that may affect malaria incidence is central to our understanding both the current geography of the disease and the potential for future changes that may occur in response to these climatic trends. Arguably, the most notable driver of cyclical interannual climate variability is the El Niño Southern Oscillation (ENSO), in which the water temperature of the Pacific Ocean off the coast of Peru exhibits variability over irregular cycles of less than 10 years. This local temperature change profoundly influences weather in many areas of the world through "teleconnections"—long distance dependencies of weather on a localized area in the Pacific.

Longer-term climate change (*i.e.* secular trends) may catalyze dramatic changes in the distribution, variability and intensity of all vector-borne diseases in the future. The same is true of malaria. Because of malaria's profound effects on human mortality and morbidity, and consequent changes in quality of life and economic productivity, it is essential to develop the knowledge that is necessary to ascertain future patterns of malaria. Understanding these connections between climate and malaria offers the prospect of climate-based malaria prediction and early warning systems.

In this paper we will discuss the ecology of malaria and its links to weather; and review the current state of our understanding of the effects of ENSO and climate change on malaria and the evidence underlying this understanding.

MALARIA, ECOLOGY AND LIFE CYCLE

While a complete discussion of malaria's life cycle is beyond the scope of this review, the major elements of the life cycle deserve our attention for their dependence on weather and subsequent relevance to the association between weather and malaria.

Malaria is transmitted by the bite of roughly 70 species of anopheline mosquitoes, with about 20 of these species being important malaria vectors, and the most important of these being members of the *Anopheles gambiae* complex (Centers for Disease Control and Prevention, 2010a; Craig et al., 1999; World Health Organization, 2010a). Mosquitoes lay their eggs in aquatic breeding sites, with different species preferring different conditions: for example, while *A. gambiae s.l.* prefers temporary rain-formed sites, *A. funestus* favors permanent bodies of water (Craig et al., 1999; Centers for Disease Control and Prevention, 2010a). Depending on temperature, the time to hatch can range from two days to three weeks, with warmer temperatures favoring shorting hatching times. The resulting larvae mature into pupae and then adults, at which point the aquatic portion of their life cycle ends. The time to maturation from egg to adult varies by species and temperature, but averages around 10 to 14 days in the tropics (Centers for Disease Control and Prevention, 2010a). While adult males do not feed on blood, adult females must take a blood meal to develop eggs. Thus, only female *Anopheles* mosquitoes play a direct role in malaria transmission. While taking a blood meal from an infected person, the mosquito ingests *Plasmodium* gametocytes. A period of sporogonic development occurs within the mosquito, called the extrinsic incubation period (EIP), during which ingested gametocytes develop into infective sporozoites. These sporozoites enter the salivary glands of the mosquito from where they can infect other people during each subsequent blood meal (Nelson and Williams, 2007).

Of the four *Plasmodium* species that are well understood, *P. falciparum* and *P. vivax* are the most important. *P. falciparum* is the most virulent and is responsible for the greatest share of malaria related morbidity and mortality. It is seen throughout the tropics and is the dominant species in Africa. *P. vivax* is probably the most common species. Due to the lower temperature requirements for sustained transmission, *P. vivax* maintains a more widespread distribution than does *P. falciparum* and it is found in tropical, sub-tropical and temperate areas in Africa, Asia and Latin America. It is the dominant species in Asia and Latin America. *P. ovale* exists in Africa and on western Pacific islands, but its importance is greatest in West Africa. Despite its worldwide distribution, *P. malariae* is the least prevalent species (Centers for Disease Control and Prevention, 2010b; Martens et al., 1999; Nelson and Williams, 2007; World Health Organization, 2010a).

WEATHER AND MALARIA

The basic reproductive number (R_0) is a measure of the number of infections that will result from each new infection, for a given disease and set of conditions. Thus, when R_0 exceeds 1.0, incidence will increase; when R_0 is below 1.0, incidence will decrease; and when R_0 equals 1.0, incidence will remain stable. For malaria, R_0 can be expressed as:

$$R_o = \frac{ma^2bce^{-\mu T}}{N\mu r}$$

where m and N are the numbers of vectors and humans, respectively; a is the rate at which vectors bite; b and c are the proportion of bites resulting in transmission from infectious mosquito to humans, and transmission from infectious humans to mosquito, respectively; μ is the mortality rate of vectors; T is the extrinsic incubation period; and r is rate at which humans recover from infection (Rogers et al., 2002; Parham and Michael, 2010). With this, we can now address the effects of weather on these underlying drivers of R_0.

Mosquito abundance is a function of survival and reproduction, both of which are climate-dependent. In their immature developmental stages, mosquitoes are bound to aquatic breeding sites, creating an association with rainfall and mosquito abundance. Still, the effect of rainfall on mosquito populations is complex. Higher rainfall is associated with higher humidity, which favors adult survival and helps prevent desiccation of breeding sites. Moreover, sufficient rainfall is required to create suitable breeding sites and to prevent the desiccation of these sites, but excessive rainfall can cause flooding and produce bodies of running water that are unsuitable for breeding and can destroy existing breeding sites (Craig et al., 1999; Martens et al., 1999).

While sufficient rainfall is required to support mosquito breeding and survival, the effects of temperature may be more important and are certainly better defined. Higher breeding site water temperatures are associated with decreases in the duration of the larval period and, therefore shorten development times (Craig et al., 1999; Paaijmans et al., 2010). Survival of adult mosquitoes is also temperature dependent with dramatic declines in survival occurring with temperatures in excess of 35°C, thermal death occurring at temperatures above the range of 40°C to 42°C and vector disappearance occurring with temperatures below 5°C (Martens et al., 1999; Craig et al., 1999). Finally, vector-biting rate is also a function of weather and increases linearly with temperature (Martens et al., 1999).

As temperature affects vector development, so too does it affect parasite development. Transmission can only occur after the extrinsic incubation period during which ingested gametocytes develop into infective sporozoites (Nelson and Williams, 2007; Paaijmans et al., 2009). The length of this period is equal to $111/(T\text{-}T_{min})$, where T is the average ambient temperature in degrees Celsius, and T_{min} is the minimum temperature for development and is 14.5 and 16°C for *P. vivax* and *P. falciparum*, respectively (Gething et al., 2011). Thus, the time between a mosquito becoming infected and becoming infectious decreases dramatically with increasing temperatures. The maximum life span of most anophelines is approximately 56 days, so the opportunity for transmission is limited at temperatures below 18°C. Beyond this effect, evidence also suggests that daily temperature fluctuations also influence the extrinsic incubation period (EIP), with greater fluctuations decreasing the EIP when mean temperatures are below 20°C and increasing the EIP when mean temperatures exceed 22°C (Paaijmans et al., 2009; Craig et al., 1999).

Optimal conditions for malaria transmission, therefore, occur when temperature and precipitation are balanced so as to simultaneously favor short EIPs, high vector biting rates, and high mosquito abundance. Temperatures between 32°C and 33°C yield the most favorable balance and are therefore considered optimum for malaria (Craig et al., 1999; Parham and Michael, 2010). These temperatures must occur with adequate rainfall, thought to be at least 80 mm per month, for a minimum of three to four consecutive months (Craig et al., 1999; Martens et al., 1999). This minimum required duration of rainfall is greater in areas where temperatures rise slowly with changing seasons, and shorter in areas where temperatures remain high throughout the year (Craig et al., 1999). As such, the length of the malaria season is dictated by the length of the period during which these conditions coexist. The overall relationships between malaria and weather are summarized in Table 1. We can certainly say that malaria is related to weather. Relationships to climate change are more enigmatic.

Table 1: Summary of associations between weather and elements of the malaria transmission cycle

	Temperature	**Rainfall**	**Humidity**
Mosquito breeding	Higher breeding site water temperatures shorten development times	Regular rainfall favors breeding by creating aquatic sites Extensive rainfall can reduce breeding by destroying sites	High humidity prevents desiccation of aquatic sites and favors breeding
Mosquito survival	Survival declines above 35°C Thermal death occurs above 40°C to 42°C	Affects survival indirectly though the association between high rain fall and high humidity	High humidity favors mosquito survival
Mosquito biting rate	Biting rate increases with temperature	No association	No association
Parasite incubation period	The EIP decreases with increasing temperatures	No association	No association

EL NINO SOUTHERN OSCILLATION (ENSO)

The El Niño phenomenon and El Niño Southern Oscillation (ENSO) are periodic events that occur in irregular cycles in which the water off the coast of Peru alternates between unusually warm (El Niño) and unusually cool (La Niña) periods. It is a coupled atmosphere-ocean system with global effects on short term climate, and affects many parts of the earth through teleconnections. For example, during El Niño years, there is an excess of rainfall in Peru, but a deficit of rainfall in Venezuela. El Niño years are associated with drought in the southern cone of Africa, and warmer, wetter weather in the Pacific Northwest in the United States (Kovats et al., 2003). Kovats (2000) observed that, with a few exceptions, the most serious consequences of ENSO are more pronounced in developing countries than in the Global North. This includes a greater burden of natural disasters, including flooding, hurricanes/typhoons, and other weather-associated phenomena against which developing countries are less resilient.

Because there is a strong tie between climatic phenomena and malaria transmission, and because ENSO phenomena are both somewhat predictable and well recorded, ENSO can act as a short-term natural experiment in the effects of climate change on malaria transmission. A natural experiment is a situation when an event occurs in nature or society that imposes an exposure on a group of people and, therefore, allows for the observation of effect of this exposure on an outcome of interest. They offer an economic means of placing observational research into what could be most accurately termed a "pseudoexperimental" design, in which there is a control group as well as an exposed group. Conveniently, the ENSO phenomenon acts as a natural experiment that is analogous to studying the effects of climate change on infectious disease. There are both strengths and weaknesses to this approach, and those will be summarized at the end of this chapter.

Because El Niño and La Niña are associated with location-specific inter-annual variations in climate (*i.e.* weather that is uncharacteristically warm and wet, warm and dry, or other possible combinations), areas that experience warming due to ENSO provide an opportunity to study the relationships between increases in temperature and the incidence of any disease. This may be done separately for warm-wet and warm-dry combinations. Other climatic attributes also change with the oscillation between El Niño and La Niña, including atmospheric pressure and wind patterns, but being less associated with malaria, they are outside the scope of this paper.

In this context, two robust methods exist to study relationships between ENSO-associated weather anomalies and disease incidence. The first is to observe a time series of temperature-incidence relationships at a given location. The other is to observe this relationship in a cross-sectional study in which the relationship between climate anomalies and disease may be studied at multiple locations, at a fixed time, through spatial analysis.

In this section, we review the evidence derived from the use of ENSO data and malaria. The results are geographically specific, both in terms of larger regions such as East Africa, and in terms of local variation. Malaria transmission is highly sensitive to microenvironments as small as 5 km x 5 km. Thus, malaria transmission may be present in the fields at point A, while at B, only a few kilometers away, malaria may not be present. This sensitivity to local conditions has been recognized for centuries, and was beautifully summed up by a British scientist who wrote in the 1930's that, "everything about malaria is so moulded and altered by local conditions that it becomes a thousand different diseases and epidemiological puzzles. Like chess, it is played with a few pieces, but is capable of an infinite variety of situations" (Hackett, 1937). While existing studies analyze the effects of ENSO at many scales, including the local, with fewer than 50 articles, it is impossible to develop an accurate tabulation of local conditions—very local conditions—and to develop generalizations about ENSO's effects on malaria distribution. There is a patchwork of studies ranging from the highly local (Omumbo et al., 2011) to areas as large as South America (Gagnon et al., 2002).

Thus, what actually happens to malaria incidence as climatic conditions change in response to ENSO cycles? Despite high hopes, inconsistent findings have revealed less about the effects of long term climate change than we hoped. This may partly result from ENSO-based deviations from the norm being relatively fleeting, while climate change is long term. Furthermore, there is a lack of consistency in malaria studies. The studies are summarized in the following pages.

South America

In South America as a whole (Gagnon et al., 2002), the conclusion reached from the most geographically inclusive study including Colombia and Venezuela, as well as a non-systematic sample of other countries was that the results are mixed. In French Guiana, El Niño results in warmer and dryer conditions, and had no apparent influence on malaria incidence. In Guyana, there was a clear influence of ENSO on malaria incidence, but the direction of the effect changed with different El Niño events. Thus, there is little conclusive in the case of Guyana. In Colombia, El Niño years bring warmer temperatures, and spatially heterogeneous changes in rainfall; here, Gagnon et al (2002) found that malaria incidence increased in only those regions of Colombia that experienced dry conditions during these warmer periods. Another study set in Colombia (Bouma and Dye, 1997) used mortality, rather than incidence data, and discovered that malaria mortality peaked 1 year after an El Niño event; however, this association weakened as the twentieth century progressed. In Peru, malaria incidence was found to be greater the year after a warm year, though this trend was not observed with all ENSO events. In Brazil, there was no identifiable relationship between El Niño and malaria incidence (Gagnon *et al.*, 2002)

Studies set in individual countries do not necessarily confirm the results summarized above, although the statistical methods are not consistent with Gagnon *et al.* (2002). A more nuanced analysis, using more sophisticated models and different time periods (Mantilla et al., 2009) demonstrated a shift from falciparum (*P. falciparum*) to vivax (*P. vivax*) malaria, which may behave differently under different climate scenarios. The direction of the relationship between incidence of malaria in general and ENSO was found to be dependent upon the region within Colombia. In a study in French Guiana (Hanf et al., 2011), ARIMA models found a significant relationship between the Southern Oscillation Index and malaria incidence, with a 3 month lag. This study used data from visits to one emergency department in one settlement, and it is unclear if emergency visits are correlated with population prevalence, or if diagnoses at this institution were accurate. Beyond that, the study's failure to consider the necessary spatial heterogeneity limited the authors' ability to draw conclusions. Furthering confusion is a contradicting result in which an analysis of data averaged over all of Colombia found a strong relationship between El Niño years and malaria incidence (Bouma et al., 1997). Similarly, using just two high prevalence areas of Colombia, in a simulation study calibrated to actual data, temperature was strongly related to falciparum malaria (Ruiz et al., 2006). Yet another study set in Colombia (Poveda et al., 2001) emphasized the interregional complexity of ENSO-malaria associations, and found that a 6 month lag after El Niño was strongly associated with malaria cases, and that ENSO as a whole spatially shifted the number of cases of malaria, but not the timing of outbreaks. Thus, a very confusing picture emerges concerning the ENSO-malaria link: not only does the association vary by location in Latin America but, also, different techniques and different data yield contradictory results.

Asia

Only a few studies have been completed in Asia exploring the ENSO-malaria link. As published in a brief research note (Bouma and van der Kaay, 1994), a small study in West Rajasthan, India, found that malaria peaked during two non-successive years of high rainfall during El Niño events. This can be considered more a case report than a systematic study, and no relationship with temperature was apparent. In Sri Lanka, a time series analysis of malaria and climatic data discovered (Zubair et al., 2008) that the relationship between El Niño and climate actually reversed itself around 1930, suggesting a temporal shift in the dynamics of climate: while there was no relationship between ENSO and malaria epidemics between 1930 and 1980, El Niño years were associated with malaria epidemics prior to 1930 and, confusingly, La Niña years were associated with malaria epidemics after 1980. The reasons for this shift are unknown. In Anhui Province, China, the increased rainfall and temperature found during El Niño years correlated with increases in malaria (Bi et al., 2005). We found no synthesis of ENSO-malaria linkages for Asia, and the studies were in different areas. Little conclusive can therefore be said about ENSO and malaria in Asia.

Africa

The ENSO-malaria association has been equally confusing in Africa. Africa is ecologically heterogeneous, including human ecology. It is, therefore, impossible to generalize about climate, land use and land form, human activity patterns, and malaria prevalence patterns. For example, falciparum malaria is intense in West Africa, Cameroon, Gabon, and both central and eastern areas of the continent. Transmission has typically been altitude-dependent in Kenya, and this has been the focus of much debate about rainfall-temperature-malaria associations. Much of the debate uses the East African highlands as the setting. In one part of highland Tanzania, the hypothesis that malaria incidence would have increased during the 1997-98 El Niño period was rejected by a study that found the opposite (Lindsay et al., 2000). However, while acknowledging the differential effects of ecosystem on malaria in Highland Kenya, a more biologically sophisticated study using an entomologic survey, malaria antibody levels and case counts found a strong positive association between El Niño and malaria. The region covered in this study, of course, does not overlap that of the preceding study (Hay et al., 2002b)

Results from analyses of the ENSO-malaria link in Africa are no more consistent than research conducted elsewhere in the world. As Africa's climate is as varied as elsewhere, it has been impossible to generalize about the specific local effects of the periodic climate changes associated with El Niño. This underlies the complexity of the El Niño-malaria relationships. One reason for the great attention given to malaria in highland Kenya is its status as a marginal area for malaria endemicity. Marginal areas appear more subject to rapidly transitional and short term changes in malaria incidence due to the lack of immunity in the population living in areas of unstable malaria.

Several factors limit ENSO's utility as an analogue of climate change. The main reason, however, is that the rapid short term changes associated with El Niño do not mirror longer-term climate change. It can be argued that the effects of longer term climate change are more subject to human and natural adaptations than are the effects of the rapid short-term changes associated with El Niño. And as such, public health authorities will be better able to adapt to more long-term and predictable climate change than to the shorter-term change associated with El Niño.

With this in mind, what do empirical studies of the ENSO phenomenon tell us about climate change and malaria? Our argument is that the data derived from the analysis of ENSO events and malaria incidence is inconsistent and contradictory. Analyses conclude that it is difficult or impossible to develop generalizations concerning the impact of specific attributes of ENSO events such as increases in temperature and rainfall. ENSO events pose their own challenges in terms of increased frequency of extreme weather events such as hurricanes and rainfall, and the resultant flooding and landslide.

One of the reasons that a great deal of attention has been devoted to El Niño and its effects on malaria transmission is hope that El Niño, and its accurate forecasting could assist in the development of early warning systems for malaria epidemics. This would offer a significant tactical advantage by providing individuals, groups, and governments with the advance warning needed to prepare for outbreaks and increases in malaria incidence. This will be dealt with later in the paper.

CLIMATE CHANGE AND VARIABILITY

Atmospheric carbon dioxide, methane and nitrous oxide block outgoing radiation and warm the global climate. Burning fossil fuels, agriculture and changes in land use have increased the atmospheric concentrations of these greenhouse gases to levels believed to be the highest in more than 10,000 years, and the resulting radiative forcing has produced observable warming. Anthropogenic greenhouse gas concentrations are expected to continue rising and, with them, so too are global temperatures: global mean temperatures are projected to increase by 2°C to 4.5°C during the twenty-first century (Solomon et al., 2007). While the effects of climate change are expected to be wide-reaching, changes in temperature, precipitation and humidity are most important for our discussion of malaria. Projections suggest that, beyond overall warming, climate is expected to change in ways that should favor malaria, including increased daily minimum temperatures, fewer frost days, greater mean water vapor, and increased precipitation in many regions. Conversely, predictions of drought and increased extreme precipitation events suggest that climate change might curb malaria in some areas.

Still, obstacles limit our ability to predict the future of malaria. First, the precise nature of climate change remains itself unsettled and different predicted climate change scenarios yield different (and sometimes contradictory) predictions for malaria. Second, climate predictions lack the spatial resolution to describe the local and micro scales on which malaria operates. Third, while direct connections between weather and malaria are generally well understood, it is less clear how these connections translate to malaria incidence in the context of complex real world systems. And, fourth, climate change is only one factor affecting the future of malaria, and our inability to predict and control for these other factors means that most climate change-based predictions must unrealistically treat all other variables as constants.

Given these difficulties and uncertainties, the precise effects that climate change will exert on malaria incidence and distribution remains an unsettled question. Studies suggesting an increased burden from malaria with climate change have predicted latitudinal or altitudinal expansion of the disease, increases in both the intensity and duration of malaria seasons in currently endemic regions, and the potential for the more dangerous *P. falciparum* to replace *P. vivax* in some areas. Conversely, other studies have suggested the potential for range contraction due to drought or predictions that improvements in abiotic factors (*e.g.* increased use of bed nets) will overwhelm any possible effects of climate change.

Effect on the spatial extent of malaria transmission

In many cases, the latitudinal limits of malaria are drawn by climatic conditions, most notably, temperature and precipitation. Climate change may alter the distribution of malaria causing expansions into areas where conditions become sufficiently favorable to support transmission, and contractions from areas where conditions become sufficiently adverse. With increased temperatures malaria is predicted to expand into northern South Africa by the end of the twenty-first century (Tanser et al., 2003; Thomas et al., 2004); during the same period, the combination of decreased precipitation and excessively high temperatures are expected to yield contractions in south-central Africa (Thomas et al., 2004), West Africa (Tanser et al., 2003; Thomas et al., 2004), Namibia and Mozambique (Tanser et al., 2003). Similarly, climate-based models of malaria vectors in Africa suggest a shift in the distribution of important malaria vectors, most notably *Anopheles gambiae*, towards eastern and southern Africa, with declining vector abundance in West Africa (Tonnang et al., 2010).

Beyond these shifts in the latitudinal extent of malaria, changes are also predicted in the altitudinal extent of the disease. With every 1,000 meters of elevation, temperatures decrease by an average of 6°C because of the adiabatic lapse rate (Patz and Olson, 2006). As such, temperatures in highland areas are often inadequate to support sustained malaria transmission. In highland areas where the disease is limited only by low temperatures, warming could raise the elevation ceiling for malaria, and climate-based models regularly predict increased highlands malaria with warming, with the east African highlands receiving the most attention (Martens et al., 1999; Martens et al., 1995; Tanser et al., 2003; Thomas et al., 2004). Observational studies may support these predictions, as increased highlands malaria has been noted in parts of east Africa in recent years. Still, the degree to which these observed increases are attributable to warming is controversial: while some studies have found evidence supporting this connection (Pascual et al., 2006; Patz and Olson, 2006; Ndyomugyenyi and Magnussen, 2004; Loevinsohn, 1994), others believe these increases are better explained by increased drug resistance, human migration, and declines in health services and control measures (Hay et al., 2002a; Bodker et al., 2003).

The net effect of climate change may be for expansion into previously non-malarial areas to be balanced by retreats from previously endemic areas; however such a range shift is unlikely to be neutral and would almost certainly increase malaria cases and deaths. In malarial areas, protections exist to minimize the burden of the parasite: people regularly exposed to malaria acquire immunity (Dobson, 2009; Lindsay and Martens, 1998), health services institutions implement prevention measures and provide antimalarial drugs, and cultural protections develop over generations. The incidence of malaria in a newly exposed population lacking these protections should, therefore, be far greater than the incidence in an endemic, but otherwise similar area (Lindsay and Martens, 1998). Consequently, we should expect the increases in incidence from range expansions to outweigh the decreases in incidence from contractions (Dobson, 2009). Moreover, shifts away from the tropics and toward more temperate areas would mean a shift away from areas with high species diversity to areas of lower species diversity; and, as areas with lower species diversity will have fewer species upon which vectors may feed , such a shift could result in humans receiving a greater proportion of mosquito bites and, consequently, higher malaria incidence (Dobson, 2009).

Effect on the intensity of malaria

Beyond its effect on the spatial extent of malaria, climate change may also influence the incidence of malaria in areas where the disease is already present. Here, the effect of climate change may be to alter the intensity or the duration of the malaria season. In areas where malaria already occurs, warming may produce conditions even more favorable to transmission, thereby increasing the incidence of infection; in areas where malaria already occurs, warming may allow transmission during months currently too cold to support malaria, thereby extending the malaria season. Models by Martens *et al* (1999) predict an increase in transmission potential in almost all currently malaria regions. Tanser *et al* (2003) developed a range of predictions based on three climate change scenarios and predicted a 16-28% increase in the number of person-months of malaria exposure in Africa by the year 2100, with 28-42% of this increase being due to increases in the duration of malaria transmission seasons.

Conversely, some areas that currently experience malaria may see decreased precipitation and, in turn, reduced vector populations and reduced malaria. Areas that experience sufficient reductions in precipitation during some months may benefit from a shorter malaria season. Climate-based models have predicted declines in transmission in parts of the Sahel and Kalahari regions (Martens et al., 1999), Madagascar and southern east-Africa (Thomas et al., 2004), parts of West Africa, Namibia and Mozambique (Tanser et al., 2003), and parts of South and Central America, Pakistan, north-west India, and in areas bordering deserts (van Lieshout et al., 2004).

Changes in burden of malaria may also occur from changes in the proportion of infections caused by different *Plasmodium* species. Since warmer temperatures favor *P. falciparum*, we might expect warming associated with long term climate change to result in an increase in the proportion of infections caused by *P. falciparum*. Because of its greater virulence, an increase in the proportion of infections caused by *P. falciparum* would result in greater morbidity and mortality from malaria. A study of malaria in Pakistan suggests that such a change may have already occurred, finding that climatic trends, especially increasing temperatures, were likely responsible for a dramatic increase in the proportion of cases caused by *P. falciparum* during recent decades (Bouma et al., 1996).

Quantitative predictions

Quantitative predictions of the cumulative effects of these changes vary with the climate change scenario used and the parameterization of the predictive model. Using the Modelling framework for the health Impact Assessment of Man-induced Atmospheric changes (MIASMA) and mean monthly temperature and precipitation from five climate change scenarios from HadCM2 and HadCM3 GCMs, Martens *et al* (1999) estimated between 260 and 320 million additional people at risk for *P. falciparum* and an additional 100 to 200 million at risk for *P. vivax* due to climate change by 2080. Van Lieshout *et al* (2004) developed similar estimates using the MIASMA model with HadCM3 climate data, and estimated that the population at risk for at least one month per year would increase by 220 to 400 million by the 2080s; their estimates of changes in the size of population at risk for at least three months per year, however, ranged from a decrease of roughly 150 million to an increase of 100 million. Rogers and Randolph (2000) expressed similar uncertainty, with HadCM2-based estimates ranging from 25 million fewer to 23 million additional people exposed to malaria in 2050.

Grounds for skepticism

Beyond the uncertainty expressed in these models, those who are skeptical of predictions of an increased burden of malaria due to climate change cite other factors that favor more optimistic predictions. These include demographic, land-use, and ecologic changes, and improvements in treatment and prevention (*i.e.* improvements in the public health infrastructures). During the twentieth century, these factors overwhelmed the effects of observed warming, and the extent and intensity of malaria declined in response. Consequently, some authors argue that we can expect improvements in malaria to continue in the face of continued warming (Gething et al., 2010; Reiter, 2001). Similarly, these authors assert that non-climatic factors better explain recent increases in malaria observed in some areas (e.g. Sri Lanka and the highlands of New Guinea, Madagascar and east Africa). They argue that population growth, migration, insecticide and drug resistance, and breakdowns in the health infrastructure are the underlying drivers (Reiter, 2001).

SUMMARY AND CONCLUSIONS

Malaria is deeply connected to weather. Temperature directly governs the rate of parasite development; and temperature, precipitation and humidity govern vector reproduction, survival and behavior. Considering these connections, and the sensitivity of malaria to atmospheric conditions, concerns about the effects that climate will exert on the future of malaria are justified. Still, attempts to understand the effects of ENSO on malaria, attempts to use ENSO-related changes as a proxy by which to study climate change, and attempts to develop accurate predictions of the effects of climate change on malaria have yielded inconsistent and unsatisfying results.

The use of the ENSO phenomenon as a natural experiment is appealing, but the results of analyses of the ENSO-malaria connection yield contradictory results and offer little clarity. There is insufficient evidence that ENSO can be accurately used as a proxy for longer term climate change in the prediction of malaria, based on existing empirical evidence. In addition, human adaptations to longer term climate change, ranging from the development of public health measures to housing construction and residential relocation cannot be predicted on the basis of short term changes. Public health, environmental planning, and engineering measures can at least partially mitigate the effects of climate change on malaria, yet these are impossible to consider in shorter term studies of ENSO and its effects on malaria. Put another way, the human propensity for long term adaptation to change will be a mitigating response to climate change, but the nature of those changes are impossible to specify before the fact.

While it seems clear that climate change will exert some influence on malaria incidence and distribution, the exact degree and nature of the changes are difficult to predict and remain controversial. When considered in the context of uncertain ecologic and demographic changes, specific predictions become even more difficult. Still, common themes have emerged from the research. It is likely that climate change will allow malaria to extend into areas where its presence is currently limited by lower temperatures and where insufficient resources exist to maintain adequate control measures. This includes, most notably, parts of eastern and southern Africa, and highlands regions bordering malarial areas in Africa, Asia and South America. Conversely, range reductions are likely to occur in areas with marginally sufficient and decreasing precipitation, including the Sahel region of West Africa. In addition to these changes, many areas will experience either increases or decreases in the length or intensity of their malaria season. We believe that, on balance, the evidence suggests that climate change will produce real and meaningful changes in the extent, intensity and season-length of malaria, but that probable improvements in malaria prevention technologies, and ecologic and demographic changes are likely to exert greater influence over the future of the disease.

Finally, because of the very local nature of malaria's sensitivity to ecological conditions, including atmospheric conditions, specific predictions of the influence of climate change are difficult to make. Predictions that are "coarse", either spatially or temporally, mask local spatial variation; yet existing models are probably accurate only at coarser levels. Climate change comprises more than global warming: it includes changes in precipitation, wind magnitude and direction, humidity, and other factors that all, in turn, influence the landscape. All of these together determine specific local habitats for anopheline vectors and their replication. It is prudent to be cautious and concerned about the potential for climate change to alter the distribution of malaria, yet it is difficult to generalize more than this on the global level. Hopefully, geographically and temporally specific models of both climate and malaria occurrence will improve and will facilitate more accurate prediction.

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