



**ENVIRONMENTAL
HEALTH
PERSPECTIVES**

<http://www.ehponline.org>

**Climate and Dengue Transmission:
Evidence and Implications**

Cory W. Morin, Andrew C. Comrie, and Kacey Ernst

<http://dx.doi.org/10.1289/ehp.1306556>

Received: 24 January 2013

Accepted: 18 September 2013

Advance Publication: 20 September 2013

Climate and Dengue Transmission: Evidence and Implications

Cory W. Morin,¹ Andrew C. Comrie,^{1,2} and Kacey Ernst²

¹School of Geography and Development, University of Arizona, Tucson, Arizona, USA

²Mel and Enid Zuckerman College of Public Health, University of Arizona, Tucson, Arizona, USA

Corresponding Author:

Cory Morin

The University of Arizona

School Geography and Development

P.O. Box 210076

Tucson, AZ 85721

E-mail: cmorin@email.arizona.edu

Phone: 603-498-1246

Short Running Title: Climate influences on dengue ecology

Acknowledgments: This research was supported in part by the National Oceanic and Atmospheric Administration (NOAA) Regional Integrated Sciences and Assessments (RISA) program, as well as grants IR56AI091843-01 and 1R01AI091843-01A1 from the National Institutes of Health.

Competing financial interests declaration: The authors have no competing financial interests.

Abstract

Background: Climate influences dengue ecology by affecting vector dynamics, agent development, and mosquito/human interactions. While these relationships are known, the impact climate change will have on transmission is unclear. Climate-driven statistical and process-based models are being used to refine our knowledge of these relationships and predict the effects of projected climate change on dengue fever occurrence, but results have been inconsistent.

Objective: We identify major climatic influences on dengue virus ecology and evaluate the ability of climate-based dengue models to describe associations between climate and dengue, simulate outbreaks, and project the impacts of climate change.

Methods: We review the evidence for direct and indirect relationships between climate and dengue generated from laboratory studies, field studies, and statistical analyses of associations between vectors, dengue fever incidence, and climate conditions. The potential contribution of climate driven, process-based dengue models is assessed, and suggestions are provided to improve their performance.

Discussion: Relationships between climate variables and factors that influence dengue transmission are complex. A climate variable may increase dengue transmission potential through one aspect of the system, while simultaneously decreasing potential through another. This complexity may at least partly explain inconsistencies in statistical associations between dengue and climate. Process-based models can account for the complex dynamics but often omit important aspects of dengue ecology, notably virus development and interactions between host species.

Conclusion: Synthesizing and applying current knowledge of climatic effects on all aspects of dengue virus ecology will help direct future research and enable better projections of climate change effects on dengue incidence.

Introduction

Climate change is one of the most important environmental changes populations will face in the coming decades. Understanding how it may impact human health and disease is complex and requires a thorough understanding of links between present climate and disease (Epstein 2005). Links between climate and diseases with various modes of transmission (vector-borne, water-borne, food-borne, soil-borne, and air-borne) have been identified (Colwell and Patz 1998; Epstein 2001) with the strongest associations being between climate and mosquito-borne diseases (Ebi et al. 2005; Rogers and Randolph 2000; Small et al. 2003). Though widely held as the world's most important arbovirus, only one review of potential climate change impacts on dengue transmission has been published, which focuses on tools currently used to establish climate-disease associations (Thai and Anders 2011).

Dengue is transmitted by *Aedes* genus mosquitoes, primarily *Ae. aegypti* and *Ae. albopictus*. Recent analysis indicates cases may be as high as 400 million per year (Bhatt et al. 2013). Climate affects dengue virus and vector populations both directly and indirectly (Gubler 2001). Temperature influences vector development rates, mortality, and behavior (Christophers 1960; Rueda et al. 1990; Tun-lin et al. 2000) and controls viral replication within the mosquito (Watts et al. 1987). Variability in precipitation influences habitat availability for *Ae. aegypti* and *Ae. albopictus* larvae and pupae. Temperature further interacts with rainfall as the chief regulator of evaporation, thereby also affecting the availability of water habitats. Indirectly, rainfall, temperature, and humidity influence land cover and land use, which can promote or impede the growth of vector populations. The incidence of dengue fever (DF) has been associated with vegetation indices, tree cover, housing quality, and surrounding land cover (Troyo et al. 2009; Van Benthem et al. 2005). Climate change can also alter how humans interact with the land,

altering its use and impacting mosquito population magnitude and species composition (Chang et al. 1997; Vanwambeke et al. 2007).

Although empirical relationships have been identified between climate conditions, DF, and dengue virus (DV) vectors, causal relationships have not been firmly established, limiting our ability to assess intervention strategies. In order to evaluate the potential impacts of climate change and better prepare mitigation strategies, this review examines the strength of the evidence supporting the complex relationships among climate/weather, *Aedes* mosquitoes, and the dengue virus. We explore the relative utility of statistical and process-based models and their ability to identify key associations between climate and disease and predict and simulate dengue transmission under projected climate change conditions.

Methods

We developed a framework of the hypothesized relationships between *Aedes* mosquitoes, dengue and climate/weather (Figure 1). Evidence for each of the links illustrated in the figure is reviewed based on 1) findings in published literature from laboratory and field studies conducted on the vector and virus, 2) results of predictive models driven by weather and climate data, and 3) investigations of DF transmission in relation to climate. The relative strengths and limitations of empirical and process-based models and their use of established climate – transmission relationships are assessed. Lastly, we make recommendations for future research that will enhance model performance and improve our ability to forecast and prepare for the effects of climate change on DF.

Results

Temperature and Virus Replication and Transmission

Temperature is a key component in the ecology of the DV as seen from its numerous interactions with other components of the disease system (Figure 1). Most directly, ambient temperature increases are associated with a faster rate of viral replication within the vector, and a shorter extrinsic incubation period (EIP, the time required for dengue virus to become transmissible to another host after initial infection of a mosquito). There are four major serotypes of the dengue virus; Dengue 1, Dengue 2, Dengue 3 and Dengue 4. Rohani et al. (2009) demonstrated that for both Dengue 1 and 4 the time between feeding and virus detection in the salivary glands of *Ae. aegypti* mosquitoes decreased from 9 days at 26°C and 28°C to 5 days at 30°C. Watts et al. (1987) more directly demonstrated that the EIP for Dengue 2 virus in *Ae. aegypti* mosquitoes is temperature dependent by allowing infected mosquitoes to feed on monkeys. The authors reported that the EIP was as short as 7 days at temperatures from 32-35°C, and 12 days or longer at 30°C, whereas no virus transmission occurred at 26°C within the 25-day period of the study (Watts et al. 1987). Additionally, the EIP was dependent on the density of the virus in the ingested blood, such that higher densities were associated with shorter EIPs (Watts et al. 1987). Using censored Bayesian time-to-event models to analyze data collected from many studies, Chan and Johansson (2012) estimated the average EIP to be 15 days at 25°C and 6.5 days at 30°C. Rohani et al. (2009) estimated shorter incubation periods (5-9 days), but these authors defined the end of the EIP as the time when the virus was detected in the mosquito, while Watts et al. (1987) defined it as the time when the mosquito transmitted the virus. Since temperature varies throughout the day in nature, Lambrechts et al. (2011) explored the susceptibility of *Ae. aegypti* to DV infections under different diurnal temperature ranges (DTR). They found that with

the same mean temperature, mosquitoes exposed to a greater DTR were less likely to become infected than those exposed to a smaller DTR; however, the EIP was unchanged (Lambrechts et al. 2011). Evidence suggests that even small increases in temperatures and narrower DTRs may facilitate dengue transmission by decreasing the EIP or increasing the susceptibility of mosquitoes to infection.

Temperature and Vector Ecology

Mosquitoes of the genus *Aedes*, primarily *Ae. aegypti*, are the vectors for dengue and therefore the ecology of the virus is intrinsically tied to the ecology of these mosquitoes. Temperature can exert considerable influence on mosquito population dynamics (Scott et al. 2000b). Egg and immature mosquito development, ovarian development, and survival at all stages of the mosquito life cycle are governed in part by temperature (Christophers 1960). In the laboratory setting, Rueda et al. (1990) found that immature *Ae. aegypti* development rates generally increased with incubation temperature until 34°C and then slowed. Survival through all developmental phases peaked at 27°C (~90%) with cooler temperatures being especially detrimental to survival (Rueda et al. 1990). Tun-lin et al. (2000) reported that *Ae. aegypti* egg, larvae, and pupae development increased at higher incubation temperatures and ceased below 8.3°C. Their estimated survival rates were also similar to Rueda et al. (1990) with the ideal range for survival (88-93%) occurring between 20-30°C (Tun-lin et al. 2000). The laboratory studies discussed above yielded consistent results with little variation between trials. In the field portion of their study, Tun-lin et al. (2000) found development accelerated in warmer water but it was often slower than in their laboratory trials at comparative temperatures. Results were also more variable in field trials compared with the laboratory portion of their study.

Adult mosquito survival is important because only mosquitoes that live beyond the EIP can act as potential vectors. The first blood meal is generally taken three days post-eclosion (i.e., three days after emerging as an adult); therefore, assuming an EIP of 7 to 12 days (based on Watts et al. 1987), a minimum of 10 to 15 days is required for a newly emerged mosquito to become infectious. Mark-release-recapture studies have estimated that adult daily survival rates are between 0.86 and 0.91 (Rebollar-Tellez et al. 1995; Muir and Kay 1998). While these studies did not examine climatic influences on survivability, Christophers (1960) provides evidence of increased mortality with exposure to prolonged extreme heat (over 40°C) and cold (below 0°C) in a laboratory setting. Using the ranges of adult survival rates and the estimated minimum age to complete the EIP indicated above, 10.4% (0.86 daily survival with a 15 day EIP) to 38.9% (0.91 daily survival with a 10 day EIP) of mosquitoes will survive long enough to complete the EIP and become infectious to humans, assuming they are infected with dengue when they take their first blood meal. Larger diurnal temperature ranges (DTRs) result in a shorter mosquito life span than smaller DTRs around the same mean temperature, although larger DTRs may concurrently shorten the duration of the EIP demonstrating the complex nature of these relationships (Lambrechts et al. 2011). It was recently reported that less thermal energy is required for pupation when temperatures fluctuate around a low mean value than when the temperature is constant at that value, while more thermal energy is required when temperatures fluctuate around a higher mean value than when the temperature is constant around that value (Carrington et al. 2013). These results indicate that population models that assume the required thermal energy for pupation is constant could be over or underestimating development times leading to inaccurate simulations.

The female mosquito's reproductive cycle is also governed by ambient temperature: below 20°C, fertilization decreases (Christophers 1960). De Garin et al. (2000) established that increased minimum temperatures resulted in accelerated oviposition cycles and egg laying. Female *Ae. aegypti* require a blood meal for ovarian development, and feeding behavior is also influenced by temperature. Feeding activity is limited or ceases at temperatures below 15°C (Christophers 1960) and can also be limited at temperatures above 36°C (author's unpublished data). Multiplicity of feeding, i.e., the taking of blood meals from multiple hosts during a single gonotrophic cycle (cycle of blood feeding, ovarian development, and egg laying), has been associated with higher levels of transmission (Scott and Takken 2012). In a study by Scott et al. (2000a), the authors found that higher temperatures were associated with higher incidences of multiple blood feedings in Thailand, but not in Puerto Rico. Female size was also negatively correlated with temperature, and smaller females exhibited increased multiplicity of feeding in Thailand (Scott et al. 2000a).

The effect of temperature on the ability of the mosquito to reproduce has consequences for population dynamics and range limits. There is evidence of selection of breeding containers based on temperature and sun exposure. Barrera et al. (2006) found that *Ae. aegypti* preferred shaded containers and cooler water temperatures for egg laying in Puerto Rico. Yet, Wong et al. (2011) found that containers with more sun exposure were more likely to be inhabited in Iquitos, Peru. This may be because obtaining optimal water temperature for the mosquito required heating from direct sun exposure in one location, and protection from the sun in another. In both cases, however, water temperature was important for mosquito reproduction. Barrera et al. (2006) also found the presence of trees to be associated with *Ae. aegypti* pupal productivity, and suggested that although dense vegetation may promote growth by contributing organic material

to the habitat, it can also influence water temperature and evaporation by creating shade. This highlights how land cover and land use characteristics can influence microclimates and consequently mosquito populations. Using a statistical population model with known temperature limits and ecological parameters of the mosquito, Otero et al. (2006) calculated the limits of *Ae. aegypti* habitat range to be along the 15°C average annual temperature isotherm. An examination of the spatial distribution of adult *Ae. aegypti* with remotely sensed land-use/land-cover indicated that *Ae. aegypti* were more likely to be present in areas with structures and medium height trees than in areas with bare earth (Landau and van Leeuwen 2012).

Although there are similarities in the thermal characteristics of many of the variables associated with vector and viral development, the critical limiting values are not the same. Integrating all these variables together in one temperature-driven model can enable simulation of very complex dynamics. Figure 2 displays the varying effects of temperature on many of the variables discussed above. There is often little correlation in the individual responses of these variables to temperature. This indicates that while increasing temperatures may accelerate parts of the viral transmission cycle, other components may become limited by high temperatures. Thus the overall effect of warming on DV ecology will be context dependent.

Precipitation and Vector Ecology

While temperature has a direct biophysical influence on viral replication and vector development and survival, precipitation provides essential habitat for the aquatic stages of the mosquito life cycle. Containers, common in urban environments, are often an important habitat (Southwood et al. 1972). Hoeck et al. (2003) studied vector abundances related to climate in Tucson, Arizona, an urban area inhabited by *Ae. aegypti* and in close proximity to dengue endemic areas, but

where DF does not occur. Not surprisingly, increased collections of *Ae. aegypti* eggs and adults coincided with the monsoon rains. In a study conducted in neighborhoods near San Juan, Puerto Rico, Barrera et al. (2011) found that higher precipitation was associated with increased *Ae. aegypti* populations, and that man-made containers were the most important pupae habitat for producing adult mosquitoes. Intense rainfall, however, may wash out breeding sites and thus have a negative effect on vector populations.

Precipitation is often required to create and maintain breeding sites and has a strong influence on vector distributions. Kolivras (2010) estimated intra-annual climate-induced range changes of *Ae. albopictus* in Hawaii using a Geographic Information System (GIS), climate data, and known habitat of the mosquito. They concluded that mosquito ranges expand during La Nina conditions (generally wetter) and decrease during El Nino conditions (generally drier), which could increase future risk of DF given projected changes of El Nino Southern Oscillation (ENSO) cycles (Kolivras 2010). Drier conditions, however, can indirectly expand a vector's range. A study by Kearney et al. (2009) used a biophysical model in conjunction with an evolutionary response component to project alterations in the range of *Ae. aegypti* in Australia due to climate change, and concluded that habitat for the mosquito will likely expand as individuals increase household water storage in response to a drier climate. Drier conditions could also cause selection pressure towards greater egg resistance to desiccation (Kearney et al. 2009). Beebe et al. (2009) posited that installing domestic water reservoirs to combat drying from warmer temperatures and decreased precipitation actually provides additional breeding grounds for *Ae. aegypti* mosquitoes, whose range is predicted to expand with increasing temperature. Australia's risk of DF comes not only from the direct effects of climate change on mosquito population density, but also from the adaptive measures people take to mitigate its effects.

Climate, Habitat, and Vector Ecology

Precipitation and temperature work interdependently: increased temperatures accelerate evaporation rates and limit standing water as a potential habitat source for immature mosquitoes, although the eggs are resistant to desiccation over extended time periods (Christophers 1960) and thus climate effects on immature vector survival are a complex balance between precipitation and evaporation. Higher rates of precipitation combined with higher temperatures also result in increased humidity, which increases *Ae. aegypti* feeding activity, survival, and egg development (Christophers 1960). For instance, Nagao et al. (2003) reported that daily minimum temperature and an increase in precipitation from the previous month were both associated with increased larval abundances.

Within water habitats, competition for space and nutrients is a key determinant of population levels. As the water in containers evaporates, the density of immature mosquitoes may increase, enhancing competition and deterring potential egg laying. Barbosa et al. (1972) raised immature *Ae. aegypti* at various densities in laboratory conditions and found that higher densities resulted in slower development, greater mortality, and a lower body mass. Field studies have supported these findings (Seawright et al. 1977; Walsh et al. 2011). Southwood et al. (1972) demonstrated that mortality was density dependent for *Ae. aegypti* between the egg and second instar larval development stage. Similarly, Dye (1982) found that when competition existed among larvae, the younger instars suffered the greatest delay in development. At the greatest extreme, complete evaporation will result in complete mortality of larvae and pupae.

Much of the density dependence exhibited in these studies is the result of nutritional stress in the containers. This suggests that precipitation exerts less influence on density dependent mortality

than nutritional levels within the habitat. Keirans and Fay (1968) subjected laboratory-reared *Ae. aegypti* to varying levels of food rations and concluded that oviposition and pupation were delayed under food stress. Moore and Whitacre (1972) reported that nutritional levels regulate production of growth retardant factor (GRF), which can limit population growth. However, a conflicting study by Dye (1984) shows that use of GRF is strain dependent and probably plays little role in population control. Still other studies have provided evidence that nutrition to be important for *Ae. aegypti* larval development and survival. Tun-lin et al. (2000) discovered that containers with more organic matter resulted in larger mosquitoes, quicker development, and higher survival rates. Similarly, Barrera et al. (2006) studied larvae-inhabited containers in Puerto Rico and their results indicate the existence of food competition in most containers while containers with a larger water volume showed less effects from competition (such as retarded development and increased mortality). This may be explained by larger water bodies being less affected by evaporation resulting in lower larvae/pupae population densities. Their analysis also showed that the body mass of individual mosquitoes was decreased among mosquitoes in more crowded containers (Barrera et al. 2006). As noted previously, smaller body size is associated with increased transmission potential because of increased multiplicity of feeding in smaller mosquitoes compared with larger mosquitoes (Scott et al. 2000a).

Additionally, Zahiri and Rau (1998) reported that female preferences for oviposition sites were affected by larval density. Specifically, female *Ae. aegypti* were more attracted to sites with higher larval densities up to a threshold level, after which they were repelled (Zahiri and Rau 1998). These results indicate that the effects of precipitation and evaporation on available water sources can regulate the size, population, and behavior of dengue vectors.

Climate factors may also provoke competition between species of mosquitoes. *Ae. aegypti* and *Ae. albopictus* are two DV vectors that often have overlapping habitat distributions. Juliano et al. (2002) studied egg mortality rates of these two species in varying laboratory environments and reported that while *Ae. aegypti* eggs thrived across ranges of humidity and temperature, *Ae. albopictus* eggs experienced high mortality at conditions under 95% humidity when temperatures were above 22°C. In their southern Florida cemetery survey of mosquito presence vs. absence, the authors found significantly lower *Ae. albopictus* presence after the dry season than during the wet season, while *Ae. aegypti* presence was consistent (Juliano et al 2002).

Vector Population and DF Incidence

Although often monitored to assess DV transmission risk, vector abundances are not always associated with DF incidence. In Sao Paulo, Brazil, Dibo et al (2008) reported that the average number of female mosquitoes was the best predictor of DF cases in humans, and that numbers of female mosquitoes and eggs, and the presence/absence of female mosquitoes were all positively correlated with temperature and precipitation (Dibo et al. 2008). Yet studies by Chadee et al. (2007) and Wu et al. (2007), using the Breteau index (number of containers inhabit by immature *Aedes aegypti* per 100 houses inspected), did not find statistically significant relationships between mosquito indices and DF cases, suggesting that the utility of surveying vector populations to evaluate DF risk may vary. Several factors may be responsible for this lack of association. Chadee et al. (2007) posited that the development of herd immunity may explain the decrease in the incidence of DF over the three year study period, despite a high mosquito index. Wu et al. (2007) found temperature to be a significant predictor of dengue incidence, and suggested that this relationship may exist because dengue replication within the mosquito is regulated by temperature and therefore so is the length of the EIP. It is possible that a given

temperature may be sufficient to support vector populations but inadequate to support viral replication, or that once a certain threshold of mosquito density is met, a further increase in density will have only a minimal impact on transmission.

Climate and Disease Occurrence

Numerous methods of statistical analysis have been used to estimate associations between climate variables and DF incidence, including cross correlations; Poisson, logistic, and multivariate regression; auto-regression, and wavelet analysis (Table 1). Many have been successful in identifying climate-dengue relationships and creating predictive models of dengue incidence based on climate associations. Variables that predict the intensity and timing of outbreaks include minimum, maximum, and mean temperature, relative humidity, and wind velocity, while the seasonal timing of epidemics is predicted by precipitation. Often these variables are predictive at specific time lags.

The sign and strength of climate-dengue associations depend largely on local climate context. In a study by Yu et al. (2010) in southern Taiwan, mean and maximum temperature were negatively associated with DF cases, which seems counterintuitive until the generally high temperatures in this region, which can often reach levels that damage mosquitoes and thus limit virus transmission ($>30^{\circ}\text{C}$), are considered. In contrast, in other regions low temperatures may be the limiting factor. Similarly, Pinto et al. (2011) did not find a high correlation between precipitation and dengue incidence in Singapore because rain occurs throughout the year, and thus it is not a significant limiting factor for mosquitoes. In Taiwan, Wu et al. (2009) found relative humidity to be negatively associated with dengue incidence. The authors hypothesized that although mosquitoes generally survive longer in humid conditions, they may bite more when water-

stressed, thus increasing transmission at lower humidity. These studies highlight the multiple avenues through which climate variables can influence dengue transmission.

Due to their influence on weather patterns, ENSO indices and sea surface temperatures also have been analyzed in relation to DF incidence. Hurtado-Diaz et al. (2007) and Colon-Gonzalez et al. (2011) have both found ENSO to be a good predictor of DF cases in Mexico. ENSO associations with dengue transmission have also been identified in the Caribbean (Amarakoon et al. 2008), Thailand (Cazelles et al. 2005; Tipayamongkhogul et al. 2009), Costa Rica (Fuller et al. 2009), Australia (Hu et al. 2010), and Vietnam (Thai et al. 2010). Studies in Noumea and Puerto Rico, however, have found little or only sporadic associations (Descloux et al. 2012; Johansson et al. 2009a). The inconsistent nature of these associations may reflect regional variation in the effects of ENSO on precipitation and temperature.

Unfortunately, because of data constraints, analyses are often performed using data aggregated over large spatial scales (e.g., country-level) or long time periods (e.g., monthly or annual). Johansson et al. 2009a found only weak associations between dengue, climate, and ENSO based on country-level analyses in Puerto Rico, Mexico, and Thailand. However, Johansson et al. 2009b reported that several climate variables were associated with dengue incidence when broken down by municipality in Puerto Rico. Importantly, the predictors and the strengths of their associations with DF varied among municipalities, highlighting the importance of local climate variation on dengue ecology. Other studies have also reported evidence of within-country or within-province variability in climate-dengue associations. In Indonesia, Arcari et al. (2007) found that variation in rainfall patterns among provinces was a large determinant of the strength and direction of associations between climate variables and DF incidence. Brunkard et al. 2008 reported that lag times for associations between climate variables and dengue varied

among locations along the Texas-Mexican border, while Tipayamongkholgul et al. 2009 reported that the explanatory power of ENSO and climate on DF incidence varied by province in Thailand.

Analyses based on long time scales and broad geographic areas may fail to identify the influence of processes that occur over daily or weekly time periods and geography and climate features that may vary substantially at the country and sub-country level. For instance Chowell et al. 2011 showed that dengue timing in Peru varied considerably between the coastal, mountain, and jungle regions. In particular, because suitable climatic conditions for dengue transmission existed during most of the year in jungle regions, these regions were often the source of DF outbreaks in neighboring regions. Hsieh and Chen (2009) analyzed a multi-wave outbreak of DF cases in Taiwan in 2007 and noted that after the initial wave of infection there were fewer infections in mid-August after two typhoons lowered temperatures, but the resulting moisture and reemerging high temperatures resulted in a second wave of DF cases in early fall (Hsieh et Chen 2009). These patterns were evident because data were analyzed over weekly and daily time periods. Unfortunately availability of data often forces researchers to scale up. For example, Barrera et al. (2011) attempted to perform a study at the census block level in San Juan, Puerto Rico, but because of small numbers of cases they had to analyze data at the municipality level instead.

The predictive power and robustness of predictive models would be improved with additional data over longer time periods. Gharbi et al. (2011), Hurtado-Diaz et al. 2007, and Tipayamongkholgul et al. 2009 created statistical predictive models that were trained on less than 10 years of data and could only be tested over one year. This makes it difficult to assess whether the relationships they observed will hold in time. Schreiber (2001) created a statistical model for Puerto Rico using data from 1988-2005, and found that validation statistics were reduced

considerably when data for one year were removed. In Mexico, Colon-Ganzales et al. (2011) noted an association between ENSO and DF incidence that was no longer evident when one large spike in DF cases was excluded from the analysis.

The incidence of dengue fever is subject to substantial over- and under-reporting due to changes in reporting/diagnosis criteria, misdiagnoses, and numerous subclinical (undiagnosed) cases. Descloux et al. (2012) avoided some of these issues by studying factors associated with time periods classified as epidemics or non-epidemics. It is also difficult to know where transmission occurs, especially given the 4-10 day incubation period between infection and the onset of symptoms. Introduction of new dengue virus serotypes into a population can also be a confounding factor because it will alter immunity and symptoms in response to an incident infection. Finally, efforts to control transmission may also confound associations between climate variables and the incidence of DF. Therefore, it is important to account for confounding by these and other factors before attempting to find associations with weather and climate.

Although the previously referenced studies suggest that climate strongly influences dengue transmission, some studies have found other factors to be of equal or greater importance. Wu et al. (2009) and Barrera et al. (2011) found the level of urbanization and number of artificial containers to be associated with vector populations and DF cases. Other studies have concluded that herd immunity, introduction of new or recycling of old viral serotypes, and changing demographics are partially or largely responsible for the variability in dengue transmission (Brunkard et al. 2008; Chadee et al. 2007; Keating 2001). Shang et al. (2010) found evidence that when climate conditions are favorable, imported cases of dengue can initiate local DF epidemics in Taiwan, thus suggesting a way in which climate and human behavior may interact to influence viral transmission.

Climate Change and DF Incidence

The impact of climate change on DF has also been examined. The studies discussed in the previous section, concerning climate, vectors, and the virus, suggest that suitable climatic conditions are required for mosquito population development and subsequent infections. It follows, therefore, that changes in climate will alter the spatial and temporal dynamics of DV ecology, potentially increasing vector ranges, lengthening the duration of vector activity, and increasing the mosquito's infectious period by shortening the EIP. Conversely, increased temperatures in already warm locations may have negative effects on the range of virus transmission through decreased vector survival, reproduction, and immature habitat.

Jetten and Focks (1997) published one of the earliest papers connecting climate and future DV transmission risk. They used a modified vectorial capacity equation to estimate the vector population required to maintain dengue transmission. The equation included climate dependent variables such as the EIP, daily mosquito mortality, mosquito size, and the length of the gonotrophic cycle. Intergovernmental Panel on Climate Change (IPCC) projected temperature increases of 2°C - 4°C were applied to weekly-averaged data from weather stations in cities across the tropics. The study suggested that climate change would lead to an increase in the latitudinal and elevational extent of the disease, and a longer season of transmission (Jetten and Focks 1997).

Patz et al. (1998) used a similar vectorial capacity equation that was modified to estimate epidemic potential. The model used projected climate change data from a general circulation model (GCM) at 250 km x 250 km resolution to project future DF risk across the world, focusing on five climatologically contrasting cities. The model predicted large increases in the geographic

extent of DF and a longer disease season, especially in temperate regions at the fringes of the virus' range (Patz et al. 1998). The Jetten and Focks (1997) and Patz et al. (1998) studies both provided a good framework for future research on climate and DF risk, but estimates should be updated based on current GCM projections that have improved resolution and are based on standardized approaches.

Hales et al. (2002) conducted an early study using logistic regression to model disease range based on the statistical association of DF presence with water vapor and other climate variables. Based on GCM projections and human population demographics, the authors predicted that the magnitude and distribution of DF would increase and encompass a larger total population and percent of the population (Hales et al. 2002). Caution should be used when modeling DF incidence using statistical relationships with climate variables because the statistical model is trained with present climate data that may differ greatly from projected future climate regimes. The boundaries of statistical model predictions are limited to climate variable combinations that have already been experienced, and extrapolating outside those bounds may lead to inaccuracies.

Process-based models can be used to estimate the effects of climate change on DF incidence while avoiding some of the restrictions of statistical techniques. The container-inhabiting mosquito simulation model (CIMSIM) accomplishes this using a dynamic life-table model (Focks et al. 1993a and b). The model estimates the combined effects of temperature, precipitation, container types, and predation on mosquito survival and development (Focks et al. 1993a and b). This type of modeling has been applied using climate change scenarios to project changes in vector dynamics under future values of temperature and precipitation. Focks et al. (1995) paired CIMSIM with a dengue simulation model (DENSIM) to simulate dengue transmission between mosquito and human populations. This work was the first to use a

combined climate and epidemiological approach to study DV ecology. The authors have conducted a preliminary validation of the model in Honduras, but stress that, although initial results are promising, additional validation is needed. More recently, Shaeffer et al. (2008) used a matrix model driven by climate fluctuations to simulate the populations of two mosquito species of the genus *Aedes*. Using daily precipitation data, they were able to successfully replicate field populations of the mosquitoes over the first two years of the study period with relatively high accuracy (Shaeffer et al. 2008). However, although the model replicated the general dynamics, it over-estimated populations in the third year, possibly due to lower capture frequency or changing mortality rates. Hopp and Foley (2001) incorporated global average climate data that was linearly downscaled to 1° resolution into an *Ae. aegypti* population model. The authors reported that model-based estimates of mosquito density worldwide were in general agreement with the known mosquito range. In a follow up study, Hopp and Foley (2003) used numeric modeling to simulate the response of *Ae. aegypti* mosquitoes to climate change. They correlated modeled mosquito populations with DF incidence and used this relationship to predict future DF incidence by modeling new mosquito populations using projected future climate data (Hopp and Foley 2003). Although these studies show progress in our understanding of dengue ecology, they are still limited by equating DF incidence with vector populations, which have been shown to be unrelated in some studies (Chadee 2007; Wu 2007). Newer models and studies should build upon this framework to represent finer scales and better-detailed processes.

While process-based models can consider the complex dynamics of dengue ecology, they possess important limitations as predictive tools. Detailed knowledge of the processes within the system is required to build dynamic models. This is not true of statistical models, which are capable of establishing relationships even if the mechanisms responsible for the relationships are

not well understood. Indeed, associations identified based on statistical analyses can be used to inform the parameters used in process-based models, and process-based models can conversely identify field studies that might be useful. Additionally, process-based models of well understood systems will not perform well without appropriate input data. Information on climate, land cover, and demographic data must be available and accurate to produce useful results. Lastly, certain relationships between components of the model may change over time in ways that are difficult to predict. This includes possible evolution of the virus and the vector, changes in the land cover or land use of an area, and the behavior of human populations. Evaluating model results can also be difficult. Factors that may confound the association between climate change and dengue incidence include improvements in surveillance that increase the ascertainment of dengue cases, which makes it difficult to determine if increased cases are related to improved surveillance or increases in regional/ global temperatures. Therefore, although still an important and useful tool, the limitations of process-based models need to be considered, and while the models described above have been successfully used to simulate past vector dynamics and dengue epidemics, their utility for predicting future occurrences is untested.

Some studies suggest that climate change will not necessarily result in significant changes in the range and incidence of DF, especially in developed countries. Reiter et al. (2003) compared dengue incidence levels on either side of the Texas-Mexico border and concluded that although mosquito levels were similar, the risk of transmission was far lower in Texas than in Mexico because human-vector contact was reduced because of the prevalence of well-sealed air-conditioned buildings, less outdoor exposure, and socioeconomic factors (Reiter et al. 2003). Although not the focus of this review, the potential importance of socioeconomic factors should not be underestimated; clearly, these factors can have significant effects. In addition, we

recognize that both mosquitoes and the dengue virus may adapt to climate change in ways we cannot currently predict. However, the literature from other disease models suggests that the magnitude of these influences may vary by the intensity and types of climatic changes that occur in a given location. These changes may occur due to direct influences on the evolution of the vector and infectious agent but may also be related to changes in viral diversity associated with increasing or decreasing levels of transmission (Artzy-Randrup et al. 2010; Liu et al. 2011; Randolph and Rogers 2002; Rottschaefer et al. 2011).

Discussion

Previous studies have shown that climate exerts a critical influence on the spatial and temporal extent of DF. However, future studies need to better capture the effects of environmental factors on the ecology of the dengue virus. This section will briefly discuss two examples of environmental influences that need to be resolved in future studies of climate and DV transmission risk.

The assumption that a vector will always colonize new habitats if temperature tolerances allow is simplistic. Although mosquitoes transmitting disease are unlikely to be limited by host ranges (because they often feed primarily on humans), they may be limited by competition. For example in Florida, *Ae. aegypti* populations have been displaced spatially and/or temporally from some locations and replaced by *Ae. albopictus*, especially in rural settings (O'meara et al. 1995) which suggests that *Ae. albopictus* may be a better competitor for larval habitat under certain conditions (Juliano 1998; Juliano et al. 2002; Leisnham and Juliano 2009; Lounibos et al. 2010; Murrell et al. 2011). Although both of these mosquitoes are dengue vectors, their competence is variable. *Ae. albopictus* tends to be a more generalist feeder, but prefers human hosts for blood meals

when available (Delatte et al. 2010; Kamgang et al. 2012; Ponlawat and Harrington 2005; Richards et al. 2006; Valerio et al. 2010). Studies also suggest that *Ae. albopictus* is less susceptible to dengue infection and dissemination to the salivary glands (Chen et al. 1993; Gratz 2004; Lambrechts et al. 2010; Moore et al. 2007; Vazeille et al. 2003). Physical barriers such as large water bodies, mountains, or deserts may also restrict species dispersion (Venkatesan and Rasgon 2010).

The effect of climate on the virus itself also has received little attention in the literature. Vector abundance indices are generally taken as the only measure of dengue transmission potential. Because climate exerts a major influence on mosquito population dynamics, studies focusing on climate/disease associations often choose to model vectors. However, virus dynamics within the mosquito must also be considered. Thomas et al. (2011), for example, used the temperature dependence of the EIP to project dengue transmission rates in Europe under various climate scenarios. Optimal temperatures for development of the vector are not necessarily the same as those for the virus (Figure 2). As a result, large vector populations may not be sufficient for transmitting dengue virus if viral replication is inhibited or if the lifespan of the mosquito is shorter than the EIP. Consequently, vector abundance/density may not always be an appropriate proxy measure of transmission risk (Chadee et al. 2007; Wu et al 2007). The virus and vector may also adapt to changes in climate as they occur slowly over time, and thus, changes in the relationship between climate and disease transmission may also occur.

Future studies should focus on addressing these issues. Vector dispersal ability should be evaluated by inventorying the species currently inhabiting areas of concern and then assessing the likelihood of invasion by the new vector. Current mosquito population models can be made more sophisticated by including a viral component, as done by Focks et al (1995). This entails

calculating viral development within mosquitoes and ensuring that models are sensitive to adult survival and biting behavior in relation to temperature and humidity. The resulting models would be capable of estimating populations of infectious mosquitoes, and not simply total mosquito populations. Lastly, climate data can be incorporated into vectorial capacity models, as was done in earlier studies (Jetten and Focks 1997; Patz et al. 1998).

Many specific questions still need to be addressed. For instance, do key processes identified in developing nations hold the same importance in developed nations? What is the best method of assessing climate effects on DF transmission risk? Will human processes supersede environmental factors in dictating disease prevalence in some areas? And finally, can we enhance our understanding of DV ecology by studying disease systems, and if so, how might we apply this knowledge to mitigate the effects of DF on human populations?

Conclusions

While there has been much speculation on the connection between climate and DF occurrence, this review has highlighted the need for research that produces more precise and stable results. Although climate variables strongly influence dengue virus and its vectors, caution must be taken when using only one element or connection to predict disease occurrence. Climate influences disease ecology at many levels, and the many nonlinearities and feedbacks present in the system create complex dynamics that are not easily modeled or understood. In addition, human factors, including behavior, immunity, and socioeconomic influences, also contribute to the complexity of these relations. Nonetheless, it may be possible to extract basic patterns and general predictions that could provide useful information for mitigating the effects of climate change on DF occurrences.

Capturing all aspects of the disease is a daunting task, but newer techniques may help overcome the difficulties. Process-based models that incorporate a more holistic view of the viral ecology should be implemented as new information on the topic is obtained and computing power increases. In addition, the use of interdisciplinary approaches will ensure that studies focus on the interactions between the components of the disease system, in addition to studying each component in isolation. In conclusion, a better understanding of the influences of climate on disease ecology is needed to improve projections of future disease risk, thus enabling better preparation and improved strategies to limit DV transmission.

References

- Amarakoon D, Chen A, Rawlins S, Chadee DD, Taylor M, Stennett R. 2008. Dengue epidemics in the Caribbean-temperature indices to gauge the potential for onset of dengue. *Mitig Adapt Strat Global Change* 13:341-357.
- Arcari P, Tapper N, Pfueller S. 2007. Regional variability in relationships between climate and dengue/DHF in Indonesia. *Singapore J Trop Geo* 28:251-272.
- Artzy-Randrup Y, Alonso D, Pascual M. 2010. Transmission intensity and drug resistance in malaria population dynamics: implications for climate change. *PLoS One* 5:e13588; doi:10.1371/journal.pone.0013588 [Online 26 October 2010].
- Barbosa P, Peters TM, Greenough NC. 1972. Overcrowding of mosquito populations: response of larval *Aedes aegypti* to stress. *Environ Entomol* 1:89-93.
- Barrera R, Amador M, Clark GG. 2006. Ecological factors influencing *Aedes aegypti* (Diptera : Culicidae) productivity in artificial containers in Salinas, Puerto Rico. *J Med Entomol* 43:484-492.
- Barrera R, Amador M, MacKay AJ. 2011. Population dynamics of *Aedes aegypti* and dengue as influenced by weather and human behavior in San Juan, Puerto Rico. *PLoS Negl Trop Dis* 5:e1378; doi:10.1371/journal.pntd.0001378 [Online 20 December 2011].
- Beebe NW, Cooper RD, Mottram P, Sweeney AW. 2009. Australia's dengue risk driven by human adaptation to climate change. *PLoS Negl Trop Dis* 3:e429; doi:10.1371/journal.pntd.0000429 [Online 5 May 2009].
- Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. 2013. The global distribution and burden of dengue. *Nature*; doi:10.1038/nature12060 [Online 7 April 2013].
- Brunkard JM, Cifuentes E, Rothenberg SJ. 2008. Assessing the roles of temperature, precipitation, and ENSO in dengue re-emergence on the Texas-Mexico border region. *Salud Publica Mexico* 50:227-234.
- Carrington LB, Armijos MV, Lambrechts L, Barker CM, Scott TW. 2013. Effects of Fluctuating Daily Temperatures at Critical Thermal Extremes on *Aedes aegypti* Life-History Traits. *PLoS One* 8:e58824; doi:10.1371/journal.pone.0058824 [Online 8 March 2013].

- Cazelles B, Chavez M, McMichael AJ, Hales S. 2005. Nonstationary influence of El Nino on the synchronous dengue epidemics in Thailand. *PLoS Med* 2:e106; doi:10.1371/journal.pmed.0020106 [Online 26 April 2005].
- Chadee DD, Shivnauth B, Rawlins SC, Chen AA. 2007. Climate, mosquito indices and the epidemiology of dengue fever in Trinidad (2002-2004). *Ann Trop Med Parasitol* 101:69-77.
- Chan M, Johansson MA. 2012. The incubation periods of dengue viruses. *PLoS One* 7:e50972; doi:10.1371/journal.pone.0050972 [Online 30 November 2012].
- Chang MS, Hii J, Buttner P, Mansoor F. 1997. Changes in abundance and behaviour of vector mosquitoes induced by land use during the development of an oil palm plantation in Sarawak. *T Roy Soc Trop Med H* 91:382-386.
- Chen W, Wei H, Hsu E, Chen E. 1993. Vector competence of *Aedes albopictus* and *Ae. aegypti* (Diptera: Culicidae) to dengue 1 virus on Taiwan: development of the virus in orally and parentally infected mosquitoes. *J Med Entomol* 30:524-530.
- Chen SC, Liao CM, Chio CP, Chou HH, You SH, Cheng YH. 2010. Lagged temperature effect with mosquito transmission potential explains dengue variability in southern Taiwan: insights from a statistical analysis. *Sci Total Environ* 408:4069-4075.
- Chowell G, Sanchez F. 2006. Climate-based descriptive models of dengue fever: the 2002 epidemic in Colima, Mexico. *J Environ Health* 68:40-44.
- Chowell G, Cazelles B, Broutin H, Munayco CV. 2011. The influence of geographic and climate factors on the timing of dengue epidemics in Peru, 1994-2008. *BMC Infect Dis* 11:164; doi:10.1186/1471-2334-11-164 [Online 8 June 2011].
- Christophers, SR. 1960. *Aedes Aegypti: The Yellow Fever Mosquito*. London: The Syndics of the Cambridge University Press.
- Colon-Gonzalez FJ, Lake IR, Bentham G. 2011. Climate variability and dengue fever in warm and humid Mexico. *Am J Trop Med Hyg* 84:757-763.
- Colwell RR, Patz JA. 1998. *Climate, infectious disease and health: an interdisciplinary perspective*. Washington, DC: American Academy of Microbiology.
- de Garin AB, Bejaran RA, Carbajo AE, de Casas SC, Schweigmann NJ. 2000. Atmospheric control of *Aedes aegypti* populations in Buenos Aires (Argentina) and its variability. *Int J Biometeorol* 44:148-156.

- Delatte H, Desvars A, Bouetard A, Bord S, Gimonneau G, Vourc'h G, et al. 2010. Blood-feeding behavior of *Aedes albopictus*, a vector of chikungunya on La Reunion. *Vector Borne Zoonotic Dis* 10:249-258.
- Descloux E, Mangeas M, Menkes CE, Lengaigne M, Leroy A, Tehei T, et al. 2012. Climate-based models for understanding and forecasting dengue epidemics. *PLoS Negl Trop Dis* 6:e1470; doi:10.1371/journal.pntd.0001470 [Online 14 February 2012].
- Dibo MR, Chierotti AP, Ferrari MS, Mendonca AL, Neto FC. 2008. Study of the relationship between *Aedes (Stegomyia) aegypti* egg and adult densities, dengue fever and climate in Mirassol, state of Sao Paulo, Brazil. *Mem Inst Oswaldo Cruz* 103:554-560.
- Dye C. 1982. Intraspecific competition amongst larval *Aedes-aegypti* - food exploitation or chemical interference. *Ecol Entomol* 7:39-46.
- Dye C. 1984. Competition amongst larval *Aedes-aegypti* - the role of interference. *Ecol Entomol* 9:355-357.
- Ebi KL, Hartman J, Chan N, McConnell J, Schlesinger M, Weyant J. 2005. Climate suitability for stable malaria transmission in Zimbabwe under different climate change scenarios. *Climatic Change* 73:375-393.
- Epstein PR. 2001. Climate change and emerging infectious diseases. *Microbes Infect* 3:747-754.
- Epstein PR. 2005. Climate change and human health. *New Engl J Med* 353:1433-1436.
- Focks DA, Haile DG, Daniels E, Mount GA. 1993a. Dynamic life table model for *Aedes-aegypti* (Diptera, Culicidae) - analysis of the literature and model development. *J Med Entomol* 30:1003-1017.
- Focks DA, Haile DG, Daniels E, Mount GA. 1993b. Dynamic life table model for *Aedes-aegypti* (Diptera, Culicidae) - simulation and validation. *J Med Entomol* 30:1018-1028.
- Focks DA, Daniels E, Haile DG, Keesling JE. 1995. A simulation-model of the epidemiology of urban dengue fever - literature analysis, model development, preliminary validation, and samples of simulation results. *Am J Trop Med Hyg* 53:489-506.
- Fuller DO, Troyo A, Beier JC. 2009. El Nino Southern Oscillation and vegetation dynamics as predictors of dengue fever cases in Costa Rica. *Environ Res Lett* 4:140111-140118.

- Gharbi M, Quenel P, Gustave J, Cassadou S, La Ruche G, Girdary L, et al. 2011. Time series analysis of dengue incidence in Guadeloupe, French West Indies: forecasting models using climate variables as predictors. *BMC Infect Dis* 11:166; doi:10.1186/1471-2334-11-166 [Online 9 June 2011].
- Gratz NG. 2004. Critical review of the vector status of *Aedes albopictus*. *Med Vet Entom* 18:215-227.
- Gubler DJ, Reiter P, Ebi KL, Yap W, Nasci R, Patz JA. 2001. Climate variability and change in the United States: potential impacts on vector- and rodent-borne diseases. *Environ Health Persp* 109:223-233.
- Hales S, Dewet N, Maindonald J, Woodward A. 2002. Potential effect of population and climate changes on global distribution of dengue fever: an empirical model. *Lancet* 360:830-834.
- Hii YL, Rocklov J, Ng N, Tang CS, Pang FY, Sauerborn R. 2009. Climate variability and increase in intensity and magnitude of dengue incidence in Singapore. *Global Health Action* 2; doi:10.3402/gha.v2i0.2036 [Online 11 November 2009].
- Hoeck PAE, Ramberg FB, Merrill SA, Moll C, Hagedorn HH. 2003. Population and parity levels of *Aedes aegypti* collected in Tucson. *J Vector Ecol* 28:65-73.
- Hopp MJ, Foley JA. 2001. Global-scale relationships between climate and the dengue fever vector, *Aedes aegypti*. *Climatic Change* 48:441-463.
- Hopp MJ, Foley JA. 2003. Worldwide fluctuations in dengue fever cases related to climate variability. *Climate Res* 25:85-94.
- Hsieh YH, Chen CW. 2009. Turning points, reproduction number, and impact of climatological events for multi-wave dengue outbreaks. *Trop Med Int Health* 14:628-638.
- Hu W, Clements A, Williams G, Tong S. 2010. Dengue fever and El Nino/Southern Oscillation in Queensland, Australia: a time series predictive model. *Occup Environ Med* 67:307-311.
- Hurtado-Diaz M, Riojas-Rodriguez H, Rothenberg SJ, Gomez-Dantes H, Cifuentes E. 2007. Short communication: impact of climate variability on the incidence of dengue in Mexico. *Trop Med Int Health* 12:1327-1337.
- Jetten TH, Focks DA. 1997. Potential changes in the distribution of dengue transmission under climate warming. *Am J Trop Med Hyg* 57:285-297.

- Johansson MA, Cummings DAT, Glass GE. 2009a. Multiyear climate variability and dengue-El Nino Southern Oscillation, weather, and dengue incidence in Puerto Rico, Mexico, and Thailand: a longitudinal data analysis. *PLoS Med* 6:e1000168; doi:10.1371/journal.pmed.1000168 [Online 17 November 2009].
- Johansson MA, Dominici F, Glass GE. 2009b. Local and global effects of climate on dengue transmission in Puerto Rico. *PLoS Negl Trop Dis* 3:e382; doi:10.1371/journal.pntd.0000382 [Online 17 February 2009].
- Juliano SA. 1998. Species introduction and replacement among mosquitoes: interspecific resource competition or apparent competition? *Ecology* 79:255-268.
- Juliano SA, O'Meara GF, Morrill JR, Cutwa MM. 2002. Desiccation and thermal tolerance of eggs and the coexistence of competing mosquitoes. *Oecologia* 130:458-469.
- Jury MR. 2008. Climate influence on dengue epidemics in Puerto Rico. *Int J Environ Health Res* 18:323-334.
- Kamgang B, Nchoutpouen E, Simard F, Paupy C. 2012. Notes on the blood-feeding behavior of *Aedes albopictus* (Diptera: Culicidae) in Cameroon. *Parasit Vectors* 5:57; doi:10.1186/1756-3305-5-57 [Online 21 March 2012].
- Kearney M, Porter WP, Williams C, Ritchie S, Hoffmann AA. 2009. Integrating biophysical models and evolutionary theory to predict climatic impacts on species' ranges: the dengue mosquito *Aedes aegypti* in Australia. *Funct Ecol* 23:528-538.
- Keating J. 2001. An investigation into the cyclical incidence of dengue fever. *Soc Sci Med* 53:1587-1597.
- Keirans JE, Fay RW. 1968. Effect of food and temperature on *Aedes aegypti* (L.) and *Aedes triseriatus* (Say) larval development. *Mosq News* 28:338-341.
- Kolivras KN. 2010. Changes in dengue risk potential in Hawaii, USA, due to climate variability and change. *Climate Res* 42:1-11.
- Lambrechts L, Scott TW, Gubler DJ. 2010. Consequences of the expanding global distribution of *Aedes albopictus* for dengue virus transmission. *PLoS Negl Trop Dis* 4:e646; doi:10.1371/journal.pntd.0000646 [Online 25 May 2010].
- Lambrechts L, Paaijmans KP, Fansiri T, Carrington LB, Kramer LD, Thomas MB, et al. 2011. Impact of daily temperature fluctuations on dengue virus transmission by *Aedes aegypti*. *Proc Natl Acad Sci USA* 108:7460-7465.

- Landau KI, van Leeuwen WJD. 2012. Fine scale spatial urban land cover factors associated with adult mosquito abundance and risk in Tucson, Arizona. *J Vector Ecol* 37:407-418.
- Leisnham PT, Juliano SA. 2009. Spatial and temporal patterns of coexistence between competing *Aedes* mosquitoes in urban Florida. *Oecologia* 160:343-352.
- Liu K, Tsujimoto H, Cha S, Agre P, Rasgon JL. 2011. Aquaporin water channel AgAQP1 in the malaria vector mosquito *Anopheles gambiae* during blood feeding and humidity adaptation. *Proc Natl Acad Sci USA* 108: 6062-6066.
- Lounibos LP, O'Meara GF, Juliano SA, Nishimura N, Escher RL, Reiskind MH, et al. 2010. Differential survivorship of invasive mosquito species in south Florida cemeteries: do site-specific microclimates explain patterns of coexistence and exclusion? *Ann Entomol Soc Am* 103:757-770.
- Lu L, Lin H, Tian L, Yang W, Sun J, Liu Q. 2009. Time series analysis of dengue fever and weather in Guangzhou, China. *BMC Public Health* 9:395; doi:10.1186/1471-2458-9-395 [Online 27 October 2009].
- Moore CG, Whitacre DM. 1972. Competition in mosquitos .2. Production of *Aedes-aegypti* larval growth retardant at various densities and nutrition levels. *Ann Entomol Soc Am* 65:915-918.
- Moore PR, Johnson PH, Smith GA, Ritchie SA, Van Den Hurk AF. 2007. Infection and dissemination of dengue virus type 2 in *Aedes aegypti*, *Aedes albopictus*, and *Aedes scutellaris* from the Torres Strait, Australia. *J Am Mosq Control Assoc* 23:383-388.
- Muir LE, Kay BH. 1998. *Aedes aegypti* survival and dispersal estimated by mark-release-recapture in northern Australia. *Am J Trop Med Hyg* 58:277-282.
- Murrell EG, Damal K, Lounibos LP, Juliano SA. 2011. Distributions of competing container mosquitoes depend on detritus types, nutrient ratios, and food availability. *Ann Entomol Soc Am* 104:688-698.
- Nagao Y, Thavara U, Chitnumsup P, Tawatsin A, Chansang C, Campbell-Lendrum D. 2003. Climatic and social risk factors for *Aedes* infestation in rural Thailand. *Trop Med Int Health* 8:650-659.
- O'meara GF, Evans LF, Gettman AD, Cuda JP. 1995. Spread of *Aedes-albopictus* and decline of *Aedes-aegypti* (Diptera, Culicidae) in Florida. *J Med Entomol* 32:554-562.

- Otero M, Solari HG, Schweigmann N. 2006. A stochastic population dynamics model for *Aedes aegypti*: formulation and application to a city with temperate climate. *Bull Math Biol* 68:1945-1974.
- Patz JA, Martens WJM, Focks DA, Jetten TH. 1998. Dengue fever epidemic potential as projected by general circulation models of global climate change. *Environ Health Perspect* 106:147-153.
- Pinto E, Coelho M, Oliver L, Massad E. 2011. The influence of climate variables on dengue in Singapore. *Int J Environ Health Res* 21:415-426.
- Ponlawat A, Harrington LC. 2005. Blood feeding patterns of *Aedes aegypti* and *Aedes albopictus* in Thailand. *J Med Entomol* 42:844-849.
- Randolph SE, Rogers DJ. 2002. Remotely sensed correlates of phylogeny: tick-borne flaviviruses. *Exp Appl Acarol* 28:231-237.
- Rebollar-Téllez EA, Loroño-Pino MA, Rodriguez-Angulo EM, Farfan-Ale JA. 1995. Blood-feeding frequency and life expectancy of *Aedes aegypti* (Diptera: Culicidae) in an urban area of Merida city, state of Yucatan, Mexico. *Rev Biomed* 6:135-141.
- Reiter P, Lathrop S, Bunning M, Biggerstaff B, Singer D, Tiwari T, et al. 2003. Texas lifestyle limits transmission of dengue virus. *Emerg Infect Dis* 9:86-89.
- Richards SL, Ponnusamy L, Unnasch TR, Hassan HK, Apperson CS. 2006. Host-feeding patterns of *Aedes albopictus* (Diptera : Culicidae) in relation to availability of human and domestic animals in suburban landscapes of central North Carolina. *J Med Entomol* 43:543-551.
- Rogers DJ, Randolph SE. 2000. The global spread of malaria in a future, warmer world. *Science* 289:1763-1766.
- Rohani A, Wong YC, Zamre I, Lee HL, Zurainee MN. 2009. The effect of extrinsic incubation temperature on development of dengue serotype 2 and 4 viruses in *Aedes aegypti* (L.). *Southeast Asian J Trop Med Public Health* 40:942-950.
- Rottschaefer SM, Riehle MM, Coulibaly B, Sacko M, Niare O, Morlais I. 2011. Exceptional diversity, maintenance of polymorphism, and recent directional selection on the *APLI* malaria resistance genes of *Anopheles gambiae*. *PLoS Biol* 9:e1000600; doi:10.1371/journal.pbio.1000600 [Online 8 March 2011].

- Rueda LM, Patel KJ, Axtell RC, Stinner RE. 1990. Temperature-dependent development and survival rates of *Culex-quinquefasciatus* and *Aedes-aegypti* (Diptera, Culicidae). *J Med Entomol* 27:892-898.
- Schaeffer B, Mondet B, Touzeau S. 2008. Using a climate-dependent model to predict mosquito abundance: application to *Aedes (Stegomyia) africanus* and *Aedes (Diceromyia) furcifer* (Diptera: Culicidae). *Infect Genet Evol* 8:422-432.
- Schreiber KV. 2001. An investigation of relationships between climate and dengue using a water budgeting technique. *Int J Biometeorol* 45:81-89.
- Scott TW, Amerasinghe PH, Morrison AC, Lorenz LH, Clark GG, Strickman D, et al. 2000a. Longitudinal studies of *Aedes aegypti* (Diptera: Culicidae) in Thailand and Puerto Rico: blood feeding frequency. *J Med Entomol* 37:89-101.
- Scott TW, Morrison AC, Lorenz LH, Clark GG, Strickman D, Kittayapong P, et al. 2000b. Longitudinal studies of *Aedes aegypti* (Diptera : Culicidae) in Thailand and Puerto Rico: population dynamics. *J Med Entomol* 37:77-88.
- Scott TW, Takken W. 2012. Feeding strategies of anthropophilic mosquitoes result in increased risk of pathogen transmission. *Trends Parasitol* 28:114-121.
- Seawright JA, Dame DA, Weidhaas DE. 1977. Field survival and ovipositional characteristics of *Aedes-aegypti* and their relation to population-dynamics and control. *Mosq News* 37:62-70.
- Shang CS, Fang CT, Liu CM, Wen TH, Tsai KH, King CC. 2010. The role of imported cases and favorable meteorological conditions in the onset of dengue epidemics. *PLoS Negl Trop Dis* 4:e775; doi:10.1371/journal.pntd.0000775 [Online 3 August 2010].
- Small J, Goetz SJ, Hay SI. 2003. Climatic suitability for malaria transmission in Africa, 1911-1995. *Proc Natl Acad Sci USA* 100:15341-15345.
- Southwood TRE, Murdie G, Yasuno M, Tonn RJ, Reader PM. 1972. Studies of the life budget of *Aedes aegypti* in Wat Samphaya, Bangkok, Thailand. *Bull World Health Organ* 46:211-226.
- Su GLS. 2008. Correlation of climatic factors and dengue incidence in Metro Manila, Philippines. *Ambio* 37:292-294.
- Thai KT, Cazelles B, Nguyen NV, Vo LT, Boni MF, Farrar J, et al. 2010. Dengue dynamics in Binh Thuan province, southern Vietnam: periodicity, synchronicity and climate variability. *PLoS Negl Trop Dis* 4:e747; doi:10.1371/journal.pntd.0000747 [Online 13 July 2010].

- Thai KT, Anders KL. 2011. The role of climate variability and change in the transmission dynamics and geographic distribution of dengue. *Exp Biol Med* 236:944-954.
- Thomas SM, Fischer D, Fleischmann S, Bittner T, Beierkuhnlein C. 2011. Risk assessment of dengue virus amplification in Europe based on spatio-temporal high resolution climate change projections. *Erdkunde* 65:137-150.
- Tipayamongkholgul M, Fang CT, Klinchan S, Liu CM, King CC. 2009. Effects of the El Niño-Southern Oscillation on dengue epidemics in Thailand, 1996-2005. *BMC Public Health* 9:422; doi:10.1186/1471-2458-9-422 [Online 20 November 2009].
- Troyo A, Fuller DO, Calderon-Arguedas O, Solano ME, Beier JC. 2009. Urban structure and dengue fever in Puntarenas, Costa Rica. *Singap J Trop Geogr* 30:265-282.
- Tun-Lin W, Burkot TR, Kay BH. 2000. Effects of temperature and larval diet on development rates and survival of the dengue vector *Aedes aegypti* in north Queensland, Australia. *Med Vet Entomol* 14:31-37.
- Valerio L, Marini F, Bongiorno G, Facchinelli L, Pombi M, Caputo B, et al. 2010. Host-feeding patterns of *Aedes albopictus* (Diptera: Culicidae) in urban and rural contexts within Rome province, Italy. *Vector Borne Zoonotic Dis* 10:291-294.
- Van Benthem BHB, Vanwambeke SO, Khantikul N, Burghoorn-Maas C, Panart K, Oskam L, et al. 2005. Spatial patterns of and risk factors for seropositivity for dengue infection. *Am J Trop Med Hyg* 72:201-208.
- Vanwambeke SO, Lambin EF, Eichhorn MP, Flasse SP, Harbach RE, Oskam L, et al. 2007. Impact of land-use change on dengue and malaria in northern Thailand. *Ecohealth* 4:37-51.
- Vazeille M, Rosen L, Mousson L, Failloux AB. 2003. Low oral receptivity for dengue type 2 viruses of *Aedes albopictus* from Southeast Asia compared with that of *Aedes aegypti*. *Am J Trop Med Hyg* 68:203-208.
- Venkatesan M, Rasgon JL. 2010. Population genetic data suggest a role for mosquito-mediated dispersal of West Nile virus across the western United States. *Mol Ecol* 19:1573-1584.
- Walsh RK, Facchinelli L, Ramsey JM, Bond JG, Gould F. 2011. Assessing the impact of density dependence in field populations of *Aedes aegypti*. *J Vector Ecol* 36:300-307.
- Watts DM, Burke DS, Harrison BA, Whitmire RE, Nisalak A. 1987. Effect of temperature on the vector efficiency of *Aedes aegypti* for dengue 2 virus. *Am J Trop Med Hyg* 36:143-152.

- Wong J, Stoddard ST, Astete H, Morrison AC, Scott TW. 2011. Oviposition site selection by the dengue vector *Aedes aegypti* and its implications for dengue control. *PLoS Negl Trop Dis* 5:e1015; doi:10.1371/journal.pntd.0001015 [Online 12 April 2011].
- Wu PC, Guo HR, Lung SC, Lin CY, Su HJ. 2007. Weather as an effective predictor for occurrence of dengue fever in Taiwan. *Acta Trop* 103:50-57.
- Wu PC, Lay JG, Guo HR, Lin CY, Lung SC, Su HJ. 2009. Higher temperature and urbanization affect the spatial patterns of dengue fever transmission in subtropical Taiwan. *Sci Total Environ* 407:2224-2233.
- Yu HL, Yang SJ, Yen HJ, Christakos G. 2011. A spatio-temporal climate-based model of early dengue fever warning in southern Taiwan. *Stoch Environ Res Risk Assess* 25:485-494.
- Zahiri N, Rau ME. 1998. Oviposition attraction and repellency of *Aedes aegypti* (Diptera: Culicidae) to waters from conspecific larvae subjected to crowding, confinement, starvation, or infection. *J Med Entomol* 35:782-787.

Table 1: Studies identifying relationships between climate variables and DF cases.

Source	Location	Study Type / Model	Identified Climate Predictors/Associations
Amarakoon et al. 2008	Caribbean	Time Series Analysis, Correlation	ENSO, Temperature
Arcari et al. 2007	Indonesia	Multivariate Regression, Correlation	Temperature, Rainfall
Barrera et al. 2011	Puerto Rico	Longitudinal Study	Rainfall
Brunkard et al. 2008	Mexico	Time Series Analysis, Autoregressive Model	Temperature, Rainfall, Sea Surface Temperature
Cazelles et al. 2005	Thailand	Wavelet Analysis	ENSO
Chadee et al. 2007	Trinidad	Correlation	Precipitation
Chen et al. 2010	Thailand	Correlation, Poisson Regression	Minimum Temperature, Rainfall, Relative Humidity
Chowell et al. 2011	Peru	Time Series, Spatial Analysis	Mean Temperature
Chowell and Sanchez 2006	Mexico	Correlation, Multiple Linear Regression	Max Temperature, Evaporation, Precipitation
Colon-Gonzalez et al. 2011	Mexico	Multiple Linear Regression	Minimum Temperature, ENSO
Descloux et al. 2012	Australia	Multivariate Non-linear Model	Temperature, Relative Humidity, Precipitation
Fuller et al. 2009	Costa Rica	Statistical Model	ENSO
Gharbi et al. 2011	Guadeloupe	Seasonal Autoregressive Integrated Moving Average Model	Relative Humidity, Mean Temperature, Minimum Temperature
Hii et al. 2009	Singapore	Time Series Poisson Regression	Mean Temperature, Precipitation
Hsieh and Chen 2009	Taiwan	Correlation, Multi-phase Richards Model	Temperature, Rainfall
Hurtado-Diaz et al. 2007	Mexico	Time Series Analysis, Autoregressive Model	Sea Surface Temperature, Minimum Temperature, Rainfall
Johansson et al. 2009a	Mexico Puerto Rico Thailand	Wavelet Analysis	ENSO, Temperature, Precipitation (All Sporadically)
Johansson et al. 2009b	Puerto Rico	Regression Model	Temperature, Precipitation
Jury 2008	Puerto Rico	Multiple Statistics	Temperature, Precipitation

Source	Location	Study Type / Model	Identified Climate Predictors/Associations
Keating 2001	Puerto Rico	Multivariate Linear Regression	Temperature
Lu et al. 2009	China	Time Series Analysis, Poisson Regression	Minimum Temperature, Minimum Humidity, Wind Velocity
Pinto et al. 2011	Singapore	Correlation, Poisson Regression	Minimum and Maximum Temperature
Schreiber 2001	Puerto Rico	Multivariate Regression	Temperature, Energy, Moisture Variables
Su 2008	Philippines	Correlation, Regression	Precipitation
Tipayamongkholgul et al. 2009	Thailand	Poisson Autoregressive Model	ENSO
Thai et al. 2010	Vietnam	Wavelet Analysis	ENSO
Wu et al. 2007	Taiwan	Time Series, Autoregressive Integrated Moving Average Models	Monthly Temperature Variation, Relative Humidity
Wu et al. 2009	Taiwan	Spatial Analysis, GIS	Temperature
Yu et al. 2011	Taiwan	Spatio-Temporal Analysis, Stochastic Bayesian Maximum Entropy Analysis	Multiple Climate Variables

GIS: Geographic Information Systems

ENSO: El Nino Southern Oscillation

Figure Legends

Figure 1: Diagram of biophysical influences on dengue virus ecology showing the interactions between climate variables, vectors, and the virus. Numbers identify relationships between variables. Habitat availability for mosquito larvae is influenced by temperature through evaporation and transpiration (1) and incoming precipitation (2). Temperature is a major regulator of mosquito development (3), viral replication within infected mosquitoes (4), mosquito survival (5), and the reproductive behavior of mosquitoes (6). Habitat availability is required for immature mosquito survival (7) and reproduction of adult mosquitoes (8). Faster mosquito development and increased survival will accelerate mosquito reproduction (9 and 10). Increased mosquito reproduction enhances the likelihood of transmission by increasing the number of blood feedings (11), while faster viral replication increases transmission by shortening the extrinsic incubation period (12). Lastly, increased survival of the adult mosquito increases the amount of viral replication (13).

Figure 2: Effects of temperature on variables associated with dengue fever transmission. Days required for immature *Ae. aegypti* development (blue squares) (Rueda et al. 1990), length of the extrinsic incubation period of dengue-2 virus (black circles) (Watts et al. 1987), percent of *Ae. aegypti* mosquitoes that completed a blood meal within 30 minutes after a blood source was made available (green diamonds) (author's unpublished data), and percent of hatched *Ae. aegypti* larvae surviving to adulthood (red triangles) (Rueda et al. 1990).

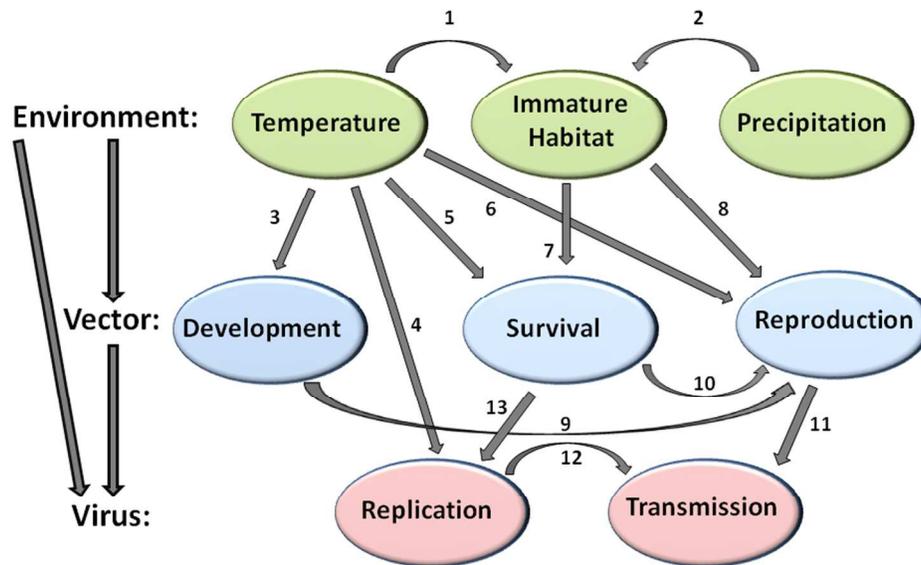


Figure 1

152x91mm (300 x 300 DPI)

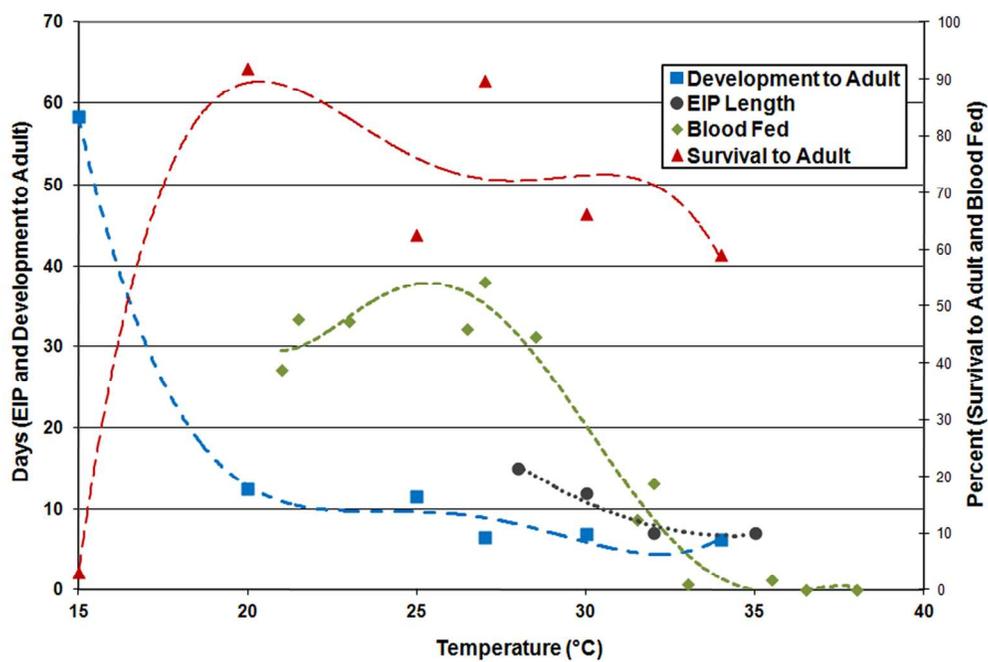


Figure 2
162x110mm (300 x 300 DPI)