RESEARCH ARTICLE

A New Model for Predicting Infectious Disease Outbreaks

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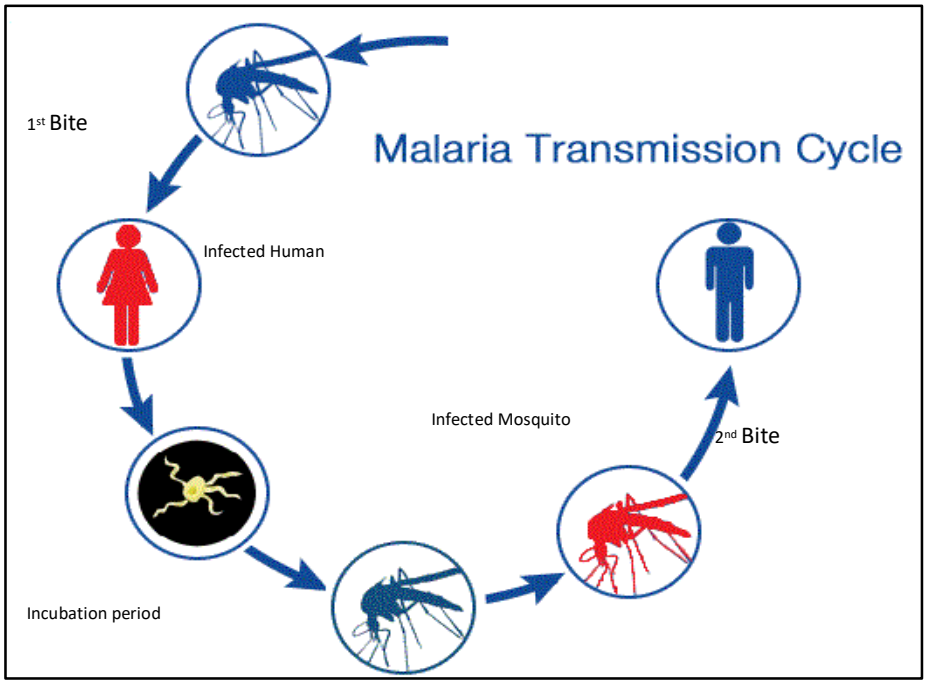
1.0 Abstract
This project integrated tools and hybrid methodologies historically used for early warning, intelligence, counter space, public health, informatics, and medical surveillance applications. A multidiscipline team assembled and explored non-medical prediction and analytical techniques that successfully predict critical events for low probability but high-regret national and global scenarios. The team then created novel approaches needed to fill nuanced and unique gaps for the infectious disease prediction challenge. The team adopted and applied those proven procedures to determine which would be efficacious in foretelling infectious disease outbreaks around the world. One outcome of that effort was a successful two-year development and validation project designated 'RAID' (Risk Awareness Framework for Infectious Diseases), which focused on malaria prediction. The project's objective was to maximize the warning (prediction) window of impending malaria epidemic outbreaks with sufficient time to allow meaningful preventive intervention before widespread human infection. It is generally recognized the more protracted the prediction window extends before an event, the more time available for health authorities to muster and deploy resources, which lessen morbidity, mortality, and harmful economic effects. Also, the value of early warning for an imminent epidemic must have mitigation options, or the warning window would have no beneficial impact on health outcomes. Finally, early notice is preferable over surprise epidemics, as unexpected waves of patients seeking acute care can easily overwhelm most local medical systems, as history repeatedly teaches. This cliché keeps repeating, with recurring Ebola epidemics and the recent COVID-19 pandemic as prominent exemplars. Predictive lead times need to be adequate for an intervention to be relevant. RAID's focus on malaria prediction met these criteria from a relevant clinical and humanitarian perspective.

Subsequent papers will address successful external generalization of these methods in predicting other similar infectious diseases. The model presented in this manuscript supports the conclusion that an additional two weeks advance notice could be available to public health authorities utilizing these techniques. This foreknowledge would allow the deployment of limited health resources into areas where they would do the most good and just in time. The geographical specificity was examined down to 5 km x 5 km grid squares overlaid anywhere in the world. Most of the model's input data were derived from remote sensing satellite sources that could combine with historical WHO (World Health Organization) or nation-reported existential pathogen loads to improve model accuracy; however, such data harmonization is not required. If ground sensors were integrated into the modeling, the confidence of the risk of infection would logically improve. The model provides a successful global risk assessment via commercially available remote space sensors, even without ground sensing.
RAID provides a necessary and useful preliminary means to predictive situational awareness. This improved predictive awareness is sufficiently granular to identify last chance windows for public health interventions globally. This need will become even more pronounced as infectious diseases evolve biologically and migrate geographically at ever-increasing rates.
Keywords: infectious disease prediction, malaria prediction, malaria, public health, medical modeling, medical prediction models

2.0 Introduction

Understanding infectious disease propagation is globally crucial for several reasons: (1) global warming is changing the landscape of "typical" diseases by geography and time of year; (2) greater mobility of the worldwide populace; and (3) mutation of infectious diseases from climate changes, deforestation, and antibiotic/anti-parasitic usage. These activities make the ability to predict the risk of infection more difficult than in years past. RAID focused on mosquito-borne disease that adversely and pervasively impacts global health and travel.

Mosquito-borne disease transmission is a seemingly simple process requiring two events. First, a female mosquito must bite an infected person and uptake the pathogen (five Plasmodium species are malarial parasites). Second, the now-infected mosquito then bites a susceptible person. For the first bite to occur, both infected people (i.e., pathogen pool, PP) and a sufficient number of mosquitoes in interest areas are required. For the second event to occur, the mosquito needs to live long enough after the pathogen's ingestion to become virulent (i.e., capable of transmitting the disease) and bite a susceptible person. However, in reality, this seemingly simple sequence is challenging to model accurately and assess in a timely fashion.



The Risk Awareness framework for Infectious Disease (RAID) project comprises a deterministic calculation to assess the local conditions of a specific area (5km x 5km) and establish the risk of a susceptible person contracting malaria (RCM) approximately two weeks before the virulent mosquito transferring the pathogen to a human via a bite. The RAID model uses the Diversity Prediction Theorem, unit analysis, and activity-based intelligence (ABI) principles to enable reliable predictive algorithms. Appendix A, B, and C contain short descriptions of these topics.

Malaria is a well-researched and long-studied infectious disease. Foundational equations and modeling techniques have risen out of much

research, data, and knowledge. Where possible, first principles are used to characterize malarial epidemic characteristics to identify an outbreak's prediction. When that knowledge was unavailable, the model received stochastic and empirical data creating the first infectious disease prediction model to use a hybrid approach via the Diversity Prediction Theorem (DPT). The team found coordinate transformation and dimensional analysis invaluable in reducing existing infectious disease models' complexity to create this new, arguably more predictive paradigm. The study of malaria outbreaks in the literature is depicted on a wide variety of axes (e.g., time, probability, temperature, etc.). To create an end-to-end evaluation of the local interactions leading to an outbreak, RAID standardized the x-axis to days, as the critical aspect of warning is time. Converting probability of survival from Marten's Equation[1] into a lifetime as a function of temperature for a specified segment of the population permitted the creation of what the team termed 'Vector Population Days' (VPD). VPD represents the days an adult mosquito is alive, virulent, and able to transmit malaria through a bite. As biting is a punctuated event, it occurs a discrete number of times within the lifetime of a mosquito and the VPD. The number of biting opportunities is called Virulent Biting Opportunities (VBO). VBO is used explicitly as the number of times the "dice are rolled" in calculating the Risk of Contracting Malaria (RCM).

This is a significant public health milestone. For the first time, real-time data for a specific area is compiled for predicting malarial infections up to fourteen days ahead of malarial epidemic surges. Due to the distributed nature of the data, this approach can be scaled globally. This fourteen-day warning period could provide adequate time for national and world health authorities to marshal resources to minimize morbidity and mortality in high-risk areas, lessening suffering, and economic consequences.

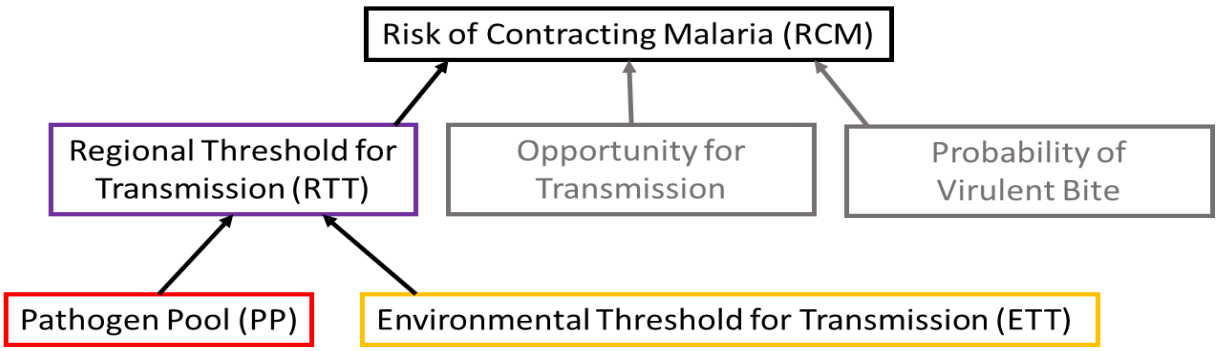
The model was validated using multiple malaria outbreak cases never used in model development. The team applied the model to these outbreaks retroactively to determine model validity and accuracy.

This paper documents the predictive warning of malaria outbreaks in the RAID model. Future manuscripts will describe how this model is applied to other viral and parasitic infections.

3.0 RAID Basics - Malaria

For local transmission of disease to occur, there must be sufficient "sick"/infectious people (i.e., pathogen pool, PP) in the area and an adequate number of mosquitoes to sustain a disease outbreak. As there is no current technique to monitor either factor globally, the model uses surrogate tests to determine if population and environmental conditions required for transmission are present. The correlation between surrogate conditions and the actual measurement of PPs and mosquitoes is discussed later in this paper. Following the Diversity Prediction Theorem, where aggregation of many independent evaluations is often more accurate than a single expert evaluation, the RAID algorithm relied on several proxy tests to determine the Pathogen Pool (PP), as well as the Environmental Threshold for Transmission (ETT) (i.e., environment conducive to support a sufficient mosquito population).

The figure below depicts how the combination of PP and ETT tests determined the Regional Threshold for Transmission (RTT). RTT represents the likelihood of the first bite of the necessary two-bite sequence.



Confidence levels for values were calculated based on the number and variability of tests across surrogates within each factor. For example, the more tests used, and the more tests found in agreement, the higher the confidence in the result. These confidence levels were not incorporated into the final RCM calculations but are described and available for context in RAID. The use of several tests also produced a more reliable algorithm, as it combines insight from disparate research approaches and ensures RAID's ability to make predictions with limited data.

3.1 Pathogen (Plasmodium) Pool (PP)

Three tests determine the value of PP in an area: (1) Annual Parasite Incidence (API), a commonly reported value stating the number of confirmed malaria cases during one year for a population per 1,000 people; (2) the Entomological Inoculation Rate (EIR) is the number of mosquito bites per night multiplied by the proportion of bites positive for sporozoites. EIR indicates an amount of live Plasmodium present in the grid; and (3) historical cases from the annual World Malaria Risk Chart from the International Association for Medical Assistance to Travelers (IAMAT) is a compilation of geographic endemicity from the Center for Disease Control (CDC), Malaria Atlas Project (MAP), and World Health Organization (WHO). All three tests (API, EIR, and historical cases) were equally weighted to determine if PP existed in the area of interest.

3.2 Environmental Threshold for Transmission (ETT)

Daily weather conditions are key factors in establishing a viable mosquito population to transmit malaria from person to person. The survival of both adult and larvae stages of Anopheles mosquitoes (the vector) is highly sensitive to temperature and water changes. Throughout scientific literature, numerous validated relationships correlate indicators of an ideal temperature range and standing water to increase malaria cases[2–4]. Rather than choosing the single 'best' of these relationships, five well-documented causative tests are used to add to the model's diversity. ETT is calculated from (1) a combination of temperature and rainfall; (2) a combination of temperature and soil moisture; (3) a combination of temperature and relative humidity; (4) Enhanced Vegetation Index (EVI); and (5) Normalized Difference Vegetation Index (NDVI). It should be noted that NDVI and EVI utilize spectral bands from remote imaging instruments to determine 'greenness' of an area, representing sufficient water and adequate temperature range to support mosquito proliferation. NDVI is a proportion of using Red and Near-Infrared spectral bands. EVI includes a third Blue band to provide more significant variation in densely forested areas and correct

soil background noise and atmospheric distortions. These may be derived from space-based global data streams, while EVI and NDVI are uniquely available from these near real-time space-based observations. For example, the presence of standing water is critical to the fecundity and survival of generations of Anopheles mosquito populations. If there is no water present, mosquito eggs cannot hatch and larval, unable to mature into the vector adult's paramount life stage. Without adult mosquitoes, there is very little chance of a *Plasmodium sp.* passing from one human to another and, in turn, a much lower risk of contracting malaria. Throughout our research, rainfall is often cited as a proxy to the presence of standing water. Other forms, such as irrigation ditches, slow-flowing streams, or flooded crop fields, also contribute to suitable habitats. A threshold of 80mm/month rainfall is necessary to establish and sustain an abundant mosquito population. The longer timeframe this amount of rainfall accumulates, the more extended the duration of the RCM. Please note, where rainfall is not able to be accurately collected, other surrogates, such as NDVI (.4), EVI (.2), relative humidity (60%), and soil moisture percentages (20%) are used.

Standing water is critical to the maintenance of the vector population, while temperature affects transmission effectiveness through its impact on EIP and Anopheles survival. Temperature influences multiple life stages of the mosquito, from larval duration through adulthood and biting rates. In addition, it affects the parasite maturation within the vector. This sensitive dependency can yield a large population of infected mosquitoes as a non-threat to a human population or as extremely dangerous in terms of RCM, in the span of 10°C.

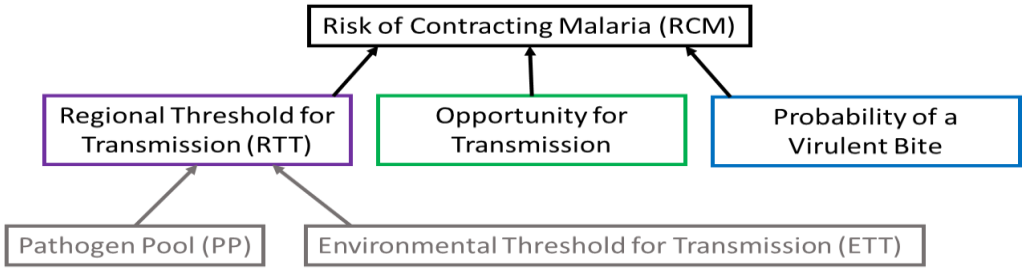
3.3 Regional Threshold for Transmission (RTT)

To determine the likelihood of a mosquito biting an infected person, the PP and ETT factors are used to calculate the Regional Threshold for Transmission (RTT) shown in the equation below. Before the RTT calculation is carried out, a mosquito presence map created by the Malaria Atlas Project is referenced to verify the Anopheles mosquito is found in the area of interest. This map can be found at https://malariaatlas.org. If the Anopheles mosquito is not present in the area, RTT is equal to zero, and there is no Risk of Contracting Malaria (RCM).

If the mosquito is present, RTT is calculated using the following equation developed empirically from documented outbreaks:

$$RTT = \left(\frac{(PP - 0.9)}{2.1}\right)^2 * \left(\frac{(ETT - 0.9)}{2.1}\right)$$

RTT is one of the three components needed to calculate RCM. The other two factors are the probability of virulent bite (i.e., the second bite) and transmission opportunity. The figure below displays the three major terms combining to produce an RCM value. One of RAID's primary innovations, Virulent Biting Opportunities (VBO), is contained within the “probability of a virulent bite."



3.4 Probability of a Virulent Bite

For a susceptible person to be bitten by a virulent mosquito, the mosquito must first bite an infected individual and live longer than the pathogen's incubation period within the mosquito. Before a female Anopheles mosquito takes her first bloodmeal (only female mosquitoes bite), she first emerges as an adult and finds a mate. For the malaria vector, the Anopheles mosquito, the time to first bite is approximated as the time to breed (they only mate once in their lifetime.) This can be treated as a constant two days. Time to breed subtracted from the mosquito's lifetime results in the total number of days the mosquito possesses the capacity to bite.

To determine an Anopheles mosquito's lifetime, the temperature-dependent (T in ℃) adult survival equation presented by Marten is used, as shown below[5].

$$Adult\ Survival\ (Anopheles\ gambiae) = e^{\frac{-1}{(-4.4+1.31T*(-0.03T^2))}}$$

The time between the first bite and when a mosquito becomes virulent is called the extrinsic incubation period (EIP). This delay represents the time for an ingested pathogen to mature/replicate and travel to the mosquito's saliva. The incubation periods for the primary three strains of malaria (*Pl. falciparum, Pl. vivax, and Pl. malariae)* are as follows[6–8]:

$$Pl.falciparum = \frac{11}{T-16}$$

$$Pl.vivax = \frac{105}{T-14.5}$$

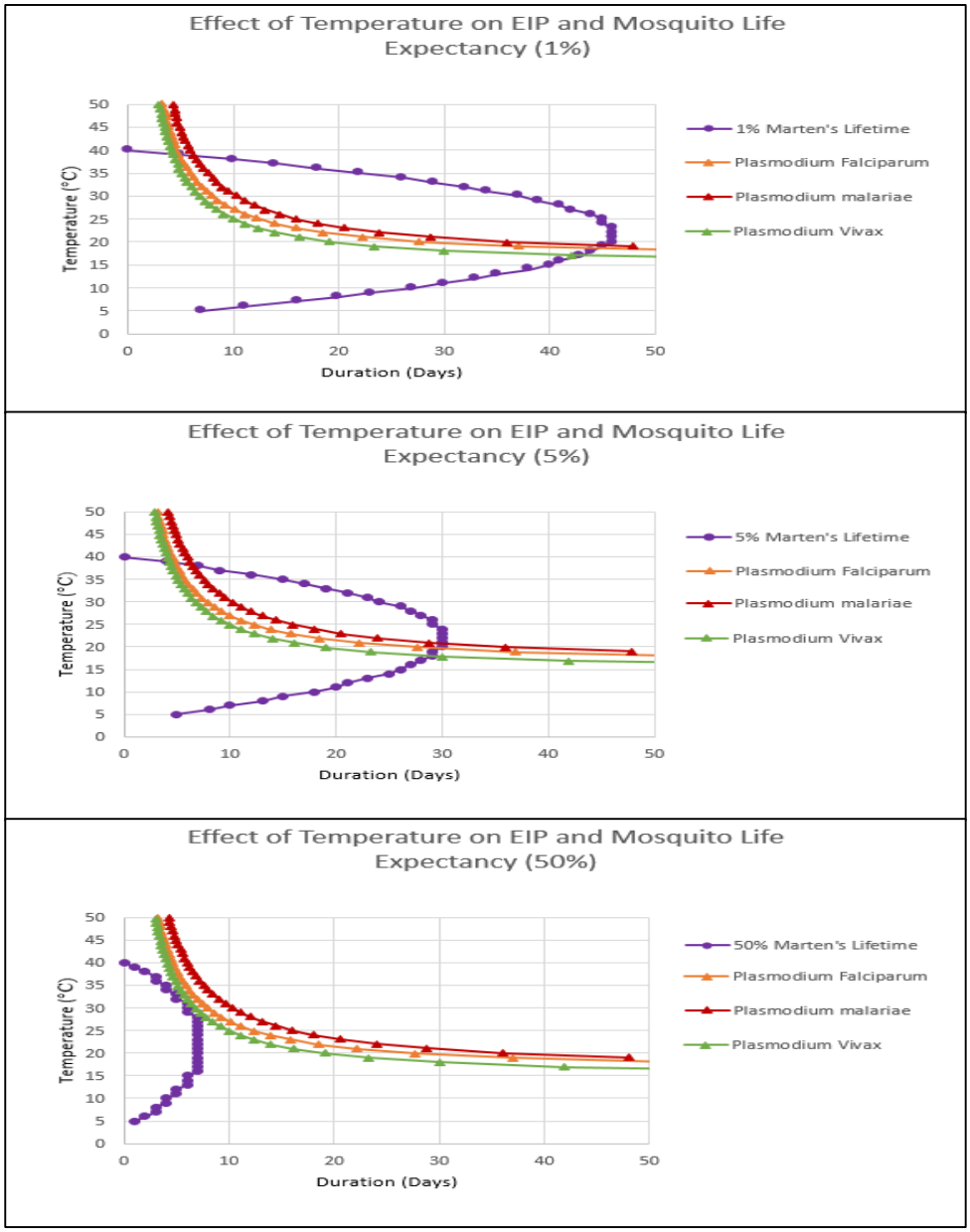
$$Pl.malariae = \frac{144}{T-16}$$

The difference between the adult lifetime (minus the two days to breed) and EIP gives the number of days the mosquito is infectious during her lifetime as it is conservatively assumed the mosquito contracts the pathogen on her first blood meal of an infected person. This value is called vector population days (VPD).

$$Vector\ Population\ Days\ (VPD) = Lifetime - Time\ to\ Breed - EIP$$

By calculating the number of days a chosen percentage of a mosquito population survives, we can determine the number of days a given population of mosquitoes may be virulent (i.e., transmit the pathogen to a susceptible human, via the "second" bite). Many population survival rates

were investigated, and the figures to the right depict three specific cases: 1%: top panel, 5%: middle panel, and 50%: bottom panel.

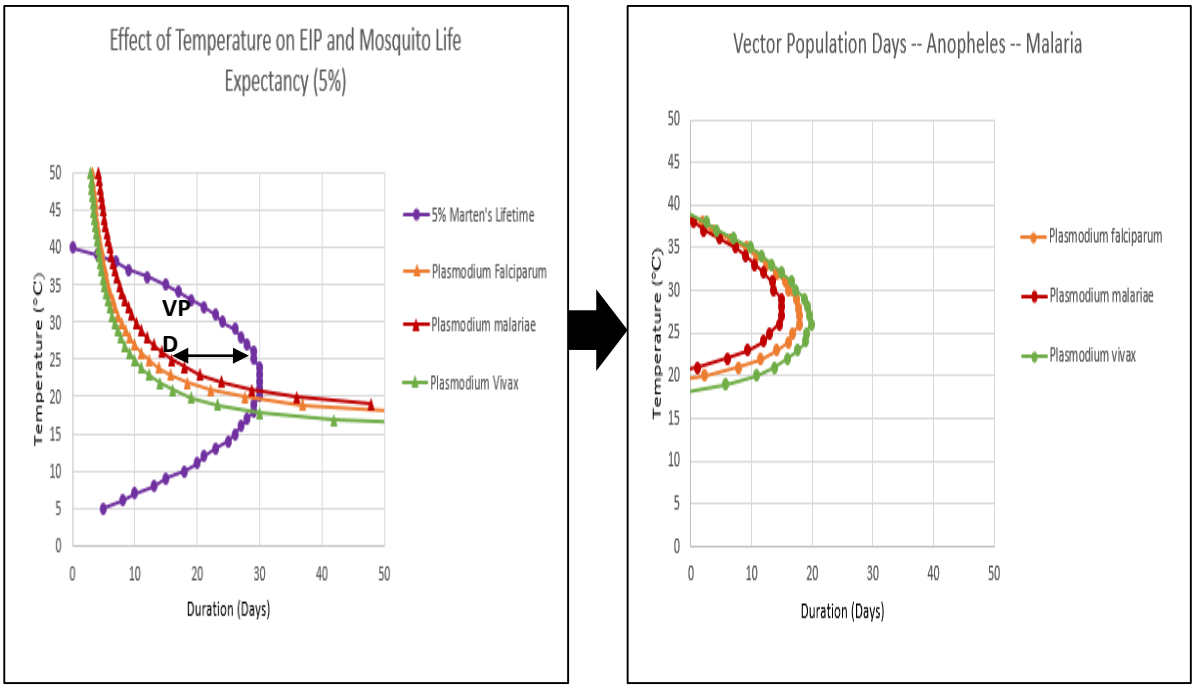


At 50%, VPD is zero-days, as the EIP lasts longer than the survival of 50% of mosquitoes across all temperatures (see lower panel). The "1% swarm" represents the time until only 1% of the swarm survives (i.e., 99% of the swarm dies) as a function of temperature. This is represented in the top panel and, if used, would create larger VPD values. Through discussion and research on mosquito lifetime with expert entomologists, a RAID uses a VPD threshold of 5%[9]. This implies sufficient active female mosquitoes to start the disease transmission process when 5% of a swarm is still alive.

Using the mosquito lifetime equation presented by Marten[5] the VPD for the lifetime comparable to 5% of the swarm surviving is shown below in the left panel. The plot highlights VPD as the time between each respective EIP curve and Marten's lifetime equation for a given temperature.

The panel on the right displays VPD values for each transmitting parasites calculated in the left panel. With the number of possible infectious days in a mosquito's lifetime (i.e., VPD) known, the number of times a mosquito may have the opportunity to bite a human to pass along the disease can be calculated. This term is referred to as virulent biting opportunities (VBO).

VBO divides the VPD by the frequency per day the mosquito takes a blood meal, as shown below.



$$VBO = \frac{VPD}{bloodmeal, (i.e., biting)\ frequency}$$

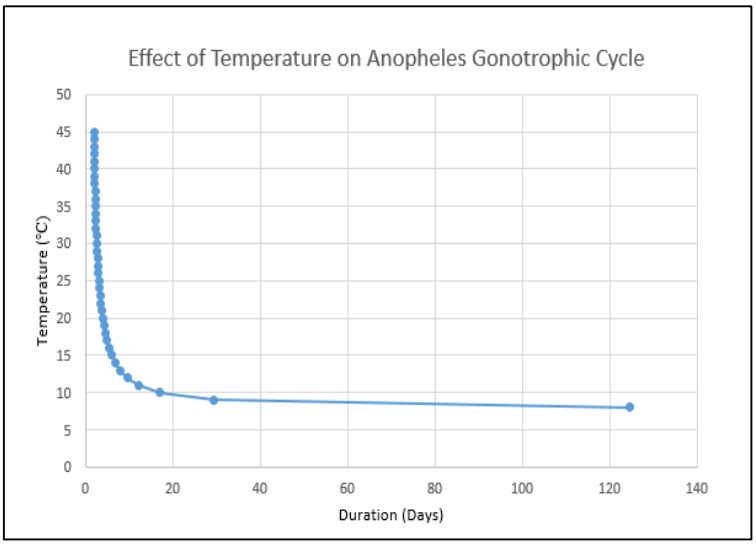
The frequency at which an Anopheles mosquito takes a bloodmeal is based on the gonotrophic cycle (i.e., the cycle of maturing and laying eggs), as the female does not bite during egg production. This is typically two to three days, but is dependent on temperature; as temperature increases, the cycle time decreases[10] (i.e., the number of virulent biting opportunities increases).

The equation for the gonotrophic cycle (gono) for the Anopheles mosquito is shown below in the panel on the left and plotted in the graph on the right.

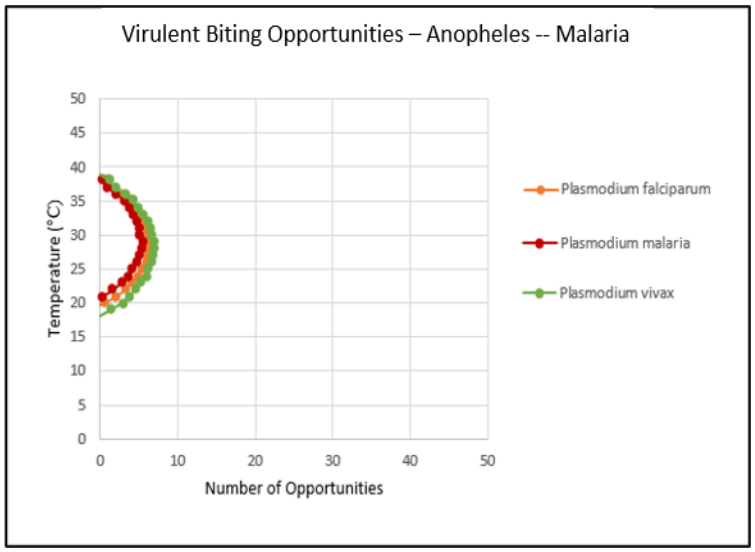
The resulting VBO equation is shown in the left panel figure, while the resulting VBO curves are plotted in the right panel.

$$gono(T) = 1 + \frac{37.1}{T - 7.7}$$

Where T = temperature ℃



$$VBO = \frac{VPD(T)}{gono(T)}$$



In the equation above, VPD and gono are highlighted as temperature-dependent (T) to emphasize the relationship between them. For example, as temperature increases, the gonotrophic cycle quickens, increasing the biting rate. However, at 25℃, the rise in temperature starts to reduce lifetime. This increase in temperature causes a "sweet spot" for disease transmission, which can be seen in the figure above to be around 27°C-29°C.

With representation for VBO values, the probability of a virulent bite occurring can be calculated with the equation below.

$$Probability\ of\ Virulent\ Bite = 1 - \left[1 - \left(Biting\ Rate * T_{\eta}\right)\right]^{VBO}$$

$$Where\ Biting\ Rate\,[4] = \frac{F_{gono}}{\left(1+\frac{37}{T-7.7}\right)} + \frac{1-F_{gono}}{(1.71+544347.6T)^{-3.93}}$$

$$F_{gono} = \min\left(max\left(\frac{-2}{3} + \frac{1}{30}T, 0, 0.5\right)\right)$$

$$T_{\eta} = Transmission\ efficiency\ of\ the\ second\ bite = 0.3$$

The second bite's transmission efficiency is the probability the pathogen is transferred from the virulent mosquito to the human. The first bite's transmission efficiency is assumed and equal to 1 in the RTT section of the equation, while the second is represented by a constant 0.3, based on literature[11].

3.5 Opportunity for Transmission

The final component of RCM is the opportunity of a virulent mosquito bite of a single susceptible person (SP). The equation below accounts for empirical insights about Anopheles biting preference and normalizes the effects of having many bloodmeal opportunities (larger populations decrease the probability of a single SP bite).

$$Opportunity\ for\ Transmission = \frac{Anopheles\ Preference}{\left(\frac{0.002 * Bloodmeals + 100}{100}\right)}$$

Where Anopheles Preference is the mosquito's preference of bloodmeal (dependent on species):

$$Anothropophilic\ (prefers\ to\ feed\ on\ humans) = 0.7$$

$$Opportunistic\ (no\ preference, bites\ available\ animal/human\ ) = 0.5$$

$$Zoophilic\ (prefers\ to\ feed\ on\ animals) = 0.3$$

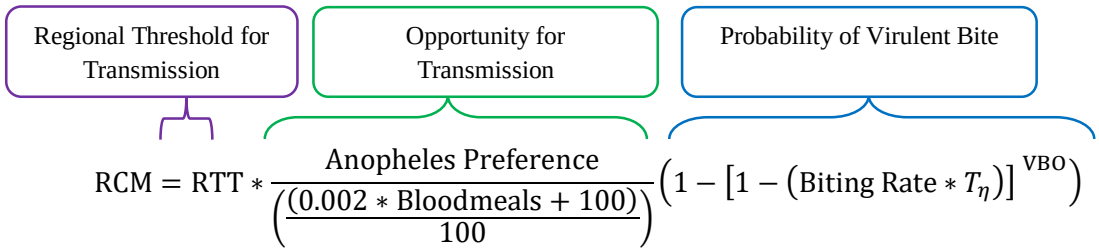
$$Bloodmeals = Population + Livestock + SP$$

The population is derived from the Gridded Population of the World from NASA Socioeconomic Data and Application Center while the livestock value is taken from the Food and Agriculture Organization of the United Nations Animal Production and Health Division Global Livestock Production and Health Atlas. SP is simply the number of susceptible persons in a 5 km x 5 km grid.

There are over 60 species of Anopheles mosquitoes with the ability to transmit malaria to humans. A species presence map shows the dominant vector from the Malaria Atlas Project is referenced for the bloodmeal preference. The opportunity-for-transmission factor considers the population of the area of interest. If there is a large population in the area, there is likely a lower risk for a single person contracting the disease than for a smaller population in the area

(i.e., fewer people to bite, the more likely the mosquito will bite the one susceptible person). Sources have reported that sweat, temperature, respiration rate, carbon dioxide, etc. may encourage the Anopheles mosquito to bite more. This potential effect is not accounted for in the RCM.

The compilation of RTT, opportunity for transmission, and probability of virulent bite produce the overall RCM equation shown below.



4.0 Model Output

This development combined the insights from hundreds of technical papers into a closed-form semi-empirical model leveraging real-time meteorological data, legacy public health information, and biologically-based mosquito disease dynamics. A full list of data sources used to create the RCM model can be found in Appendix D. The output of the RCM is a predictive risk value for contracting malaria with a 5km spatial resolution approximately two weeks in advance.

The team created an overall risk assessment score for each 5 km x 5 km geographical grid box of interest. The overall risk evaluation consisted of five different risk levels: Very Low, Low, Moderate, High, and Very High. The risk value incorporates all the factors previously (plasmodium presence, weather, ETT, data confidence, and RCM) discussed in a multidimensional weighted assessment within the model via first principles and other inserted data streams. The model continuously calculates a new risk value each day, creating a moving window of prediction. From the current day to the maximum prediction day, each day receives an updated calculated risk value (i.e., RCM) and confidence, akin to a weather storm forecast. Hurricane prediction becomes more accurate as the storm travels closer to any particular location, and the time to arrival shortens. The modeling predicts its outcome with continuous opportunities to self-update based on dynamic and sometimes chaotic weather patterns. Hurricane accuracy improves with monitoring the storm's track and calculating its next movements. Unlike storm modeling, the RAID infectious disease prediction remains geographically stationary across the area of interest, yet becomes increasingly more accurate through the time domain as prediction days count down from its maximum prediction down to the current day. As a hurricane track can provide a substantial warning to prepare for hurricanes, similarly RAID offers a significant warning to prepare for outbreaks and epidemics. The dynamic prediction window continuously updates each day in the 14-day prediction window, informing the health of shifting near-real-time risk.

5.0 Validation

Actual historical malaria outbreaks were selected to test model performance and validity. Validation scenarios selected only included outbreaks with data that the model was blind to and had never trained from. Further, none of the team reviewed or used the data in any aspect of model creation. Doing so would invalidate the model's legitimacy from the team's perspective. As such, the criteria for selecting validation sites and scenarios were: 1) the outbreak data were never used in any way to create any portion of the model, and 2) no one on the team knew the existence of these potential validation scenarios until they were presented to the team and entered into the model.

Validation Scenario #1 – Kenya (Dec 2015 – Jan 2016)

A validation case was conducted for an outbreak in Garba Tula, Kenya, occurring in Dec 2015. The team ran the RAID model from late 2015 to early 2016. The model provided increasing levels of risk and detailed the reasons for RAID's depiction of the outbreak.

Once fully calculated, the result of RCM is converted into a threat level of Low, Moderate, High, and Very High.

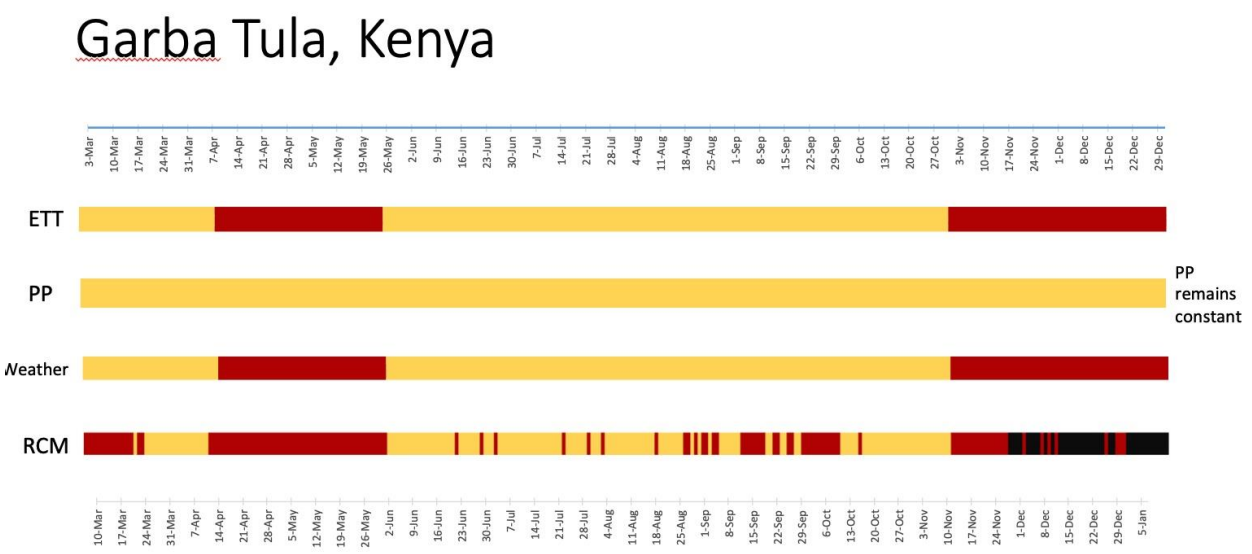
Green – All Clear There is a low probability that conditions will soon be present that would result in malaria contraction by susceptible individuals. RCM is less than .001.

Yellow – Alert (Monitor Situation) Risk of contracting malaria is moderate, and conditions may exist where malaria mitigation measures should be employed to prevent malaria contraction. RCM is between .001 and .025.

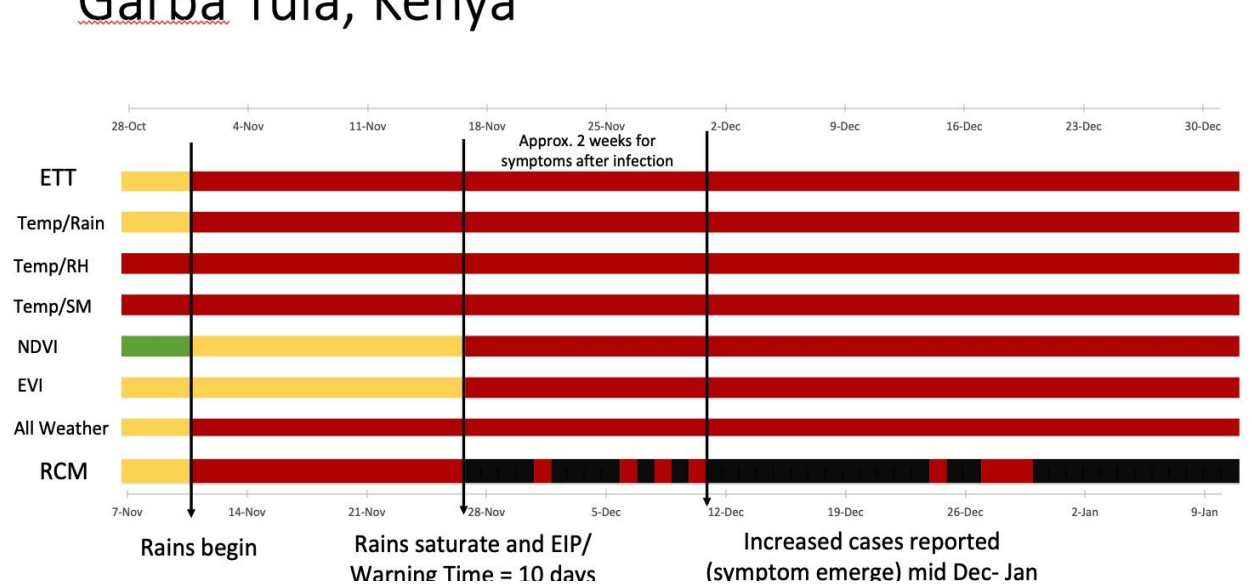
Red – Warning (Act) Risk of contracting malaria is high, and conditions exist where malaria mitigation measures must be employed to prevent the contraction of malaria. The local conditions will likely be stable transmission processes (i.e., endemic population). This level's first determination suggests the first virulent bite will likely occur in the next two weeks. RCM is between .025 and .25.

Black – Enhanced Warning (Act) Risk of contracting malaria is very high, and conditions exist where malaria mitigation measures must be employed to prevent malaria's rapid outbreak. The local conditions will likely be rapid transmission processes (i.e., epidemic population). RCM is greater than or equal to .25.

A full year was easily analyzed due to the automation of downloads from sensor feeds for model input. The first figure below depicts key RAID parameters over time and demonstrates the rise in RCM values in December 2015.

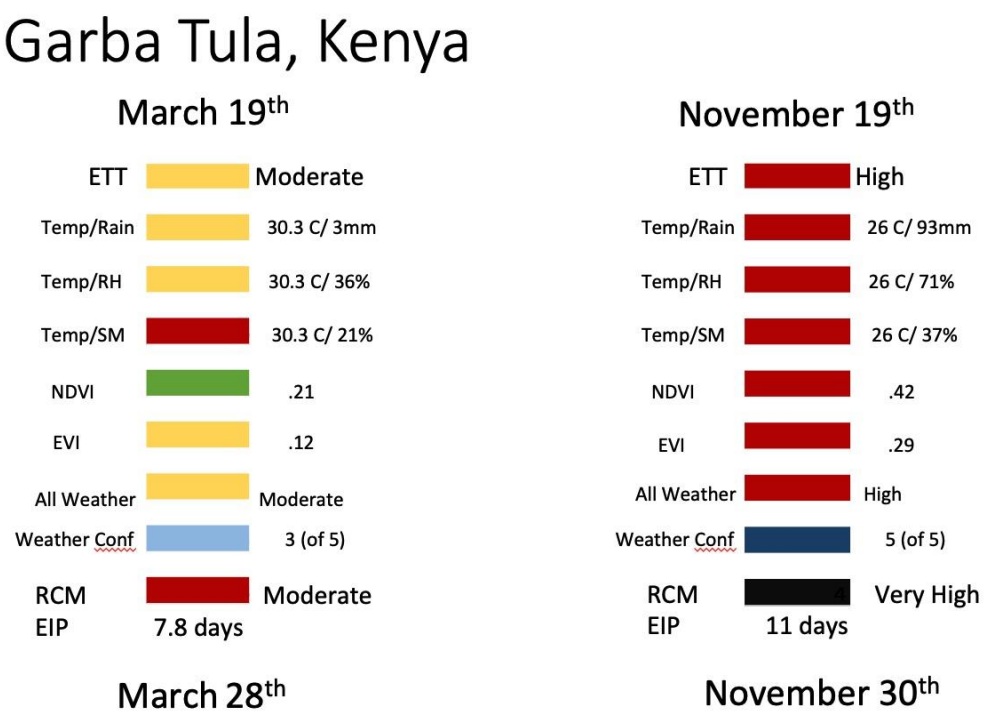


Taking a closer look at the December RCM values with reported cases and weather conditions reinforces the utility of RAID to predict outbreaks consistent with observed public health outcomes.



The graphic below compares outputs of RAID between March 19 and November 19. Note, the increasing risk factor is alarming as the country is heading into what will become a significant malaria epidemic.

The malaria outbreak in Kenya in Dec 2015 reported four deaths and 200 confirmed cases of malaria. The model correctly predicted an increased risk for this episode about two weeks before the new and unexpected illness wave. The entire district fits inside a single 5 km cell. In hindsight, malaria experts explained the unusual occurrence was likely caused by the El Nino rainy season.

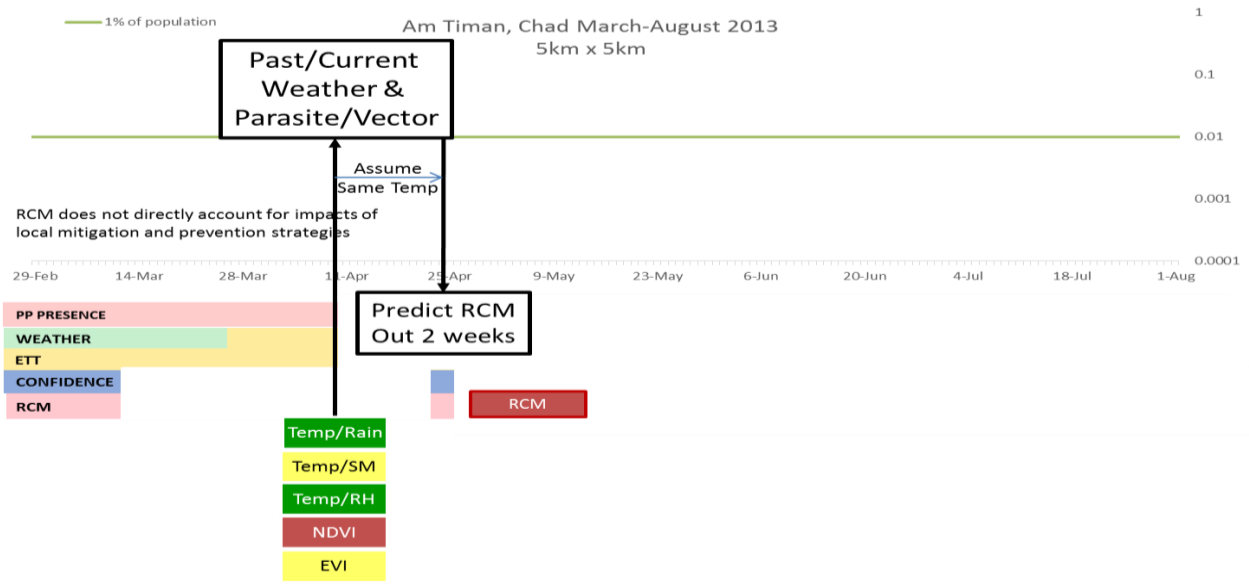


This validation scenario illustrates the model's specificity or the model's ability to identify times when the disease will not be spiking correctly. Understanding and testing any model's sensitivity and specificity are critical to model utility. These precise values will need to be further researched and determined based on real-world model operationalization and utilization.

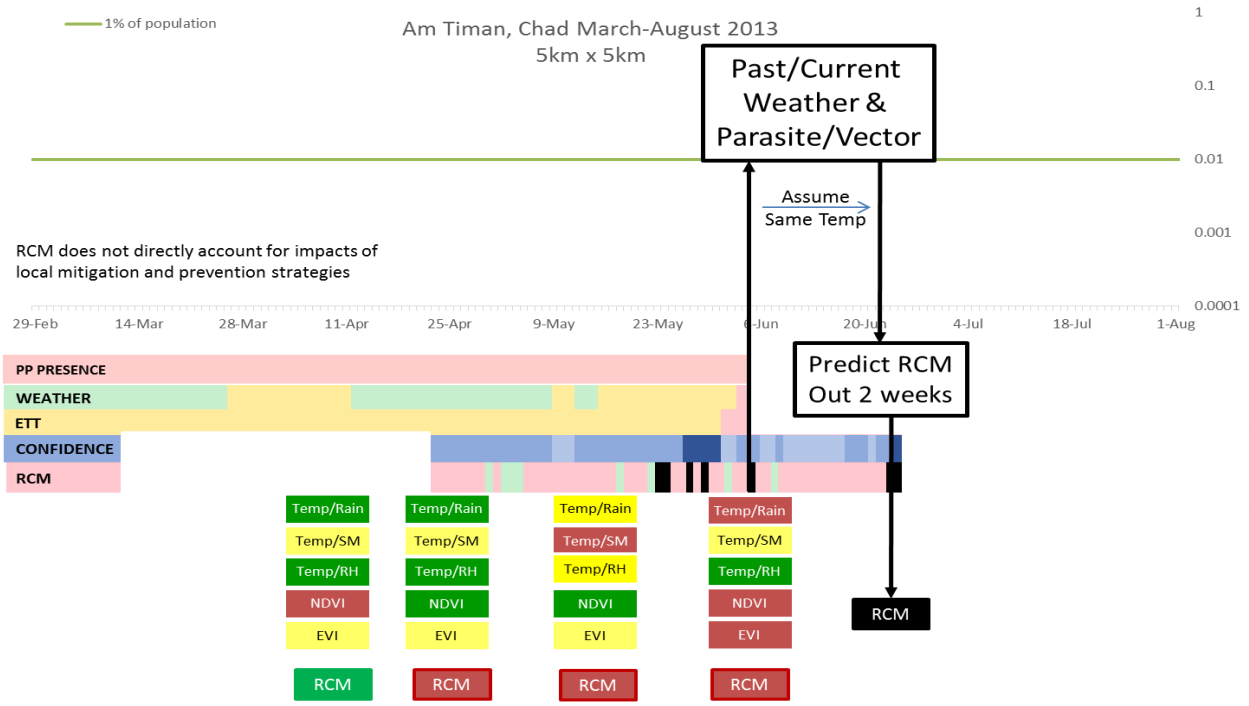
Validation Scenario #2 – Am Timan, Chad (March-August 2013)

Given the timeframe of the outbreak (August 2013), the team retrieved the relevant model inputs from historical data from March-August 2013.

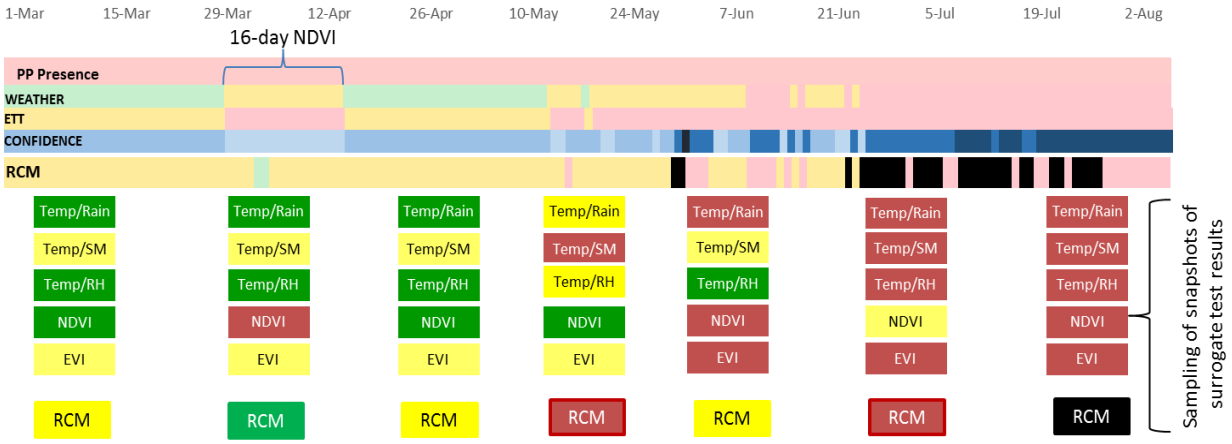
The following figures provide a rolling prediction of RCM based on the value of the critical factors of the RCM.



This first graph shows the model starting on April 11, calculating the RCM for April 25. As time progresses and new weather data is available, the RCM values are depicted below. While listed as High throughout May, such risk's confidence was not high, except in late May and again in late June. The characterization of the environment in Am Timan shows a constant high PP presence, indication an extended period of ideal outbreak weather would escalate the RCM values.



Because symptoms can take approximately 14 days to manifest in humans, we expect the observed caseloads to lag behind the date RCM predicts a virulent bite. Malaria cases in Am Timan reported throughout August continually climbed well above background endemic caseloads to over 14000 cases by the end of the month (compared to just over 1200 at the beginning of the month). It is evident that by late July, all RAID factors supporting RCM valuations are maximum due to weather changes. The consistent very high RCM and high confidence values for RCM starting in late June and persisting through late July are consistent with the progression of cases reported for the area.



6.0 Conclusion

This paper describes the motivation and techniques for creating a predictive awareness tool for malaria outbreaks via the 'RAID' modeling technique. Validation scenarios are presented confirming the initial achievements in predicting a true positive (sensitivity) and a second validation case showing specificity success. The team demonstrated that adopting tools from other analytical applications could be useful in certain types of infectious disease prediction models. The exemplar described herein presented a fourteen-day moving predictive window ahead of malaria spikes in clinical illness. The model also demonstrated one validation scenario where modeling correctly forecasts the decrease of clinical illness. This represents the first time such predictive modeling has been successfully applied. In no case did the team leave out any examined scenarios, or data that would not indicate the model does not work. Still, the team acknowledges that while the model is currently mature, further real-world testing is required to obtain rigorous sensitivity and specificity values in any ongoing effort to further refine and optimize the model. The team hopes to achieve further validation through further work with NFIM, academic, and other philanthropic groups. Malaria sickens an estimated 3.4 billion people in 92 countries. Over 1.1 billion are at high risk. Tools like this model could provide public health authorities with 14 days of predictive lead-time that could save millions of lives and allow decreased economic disease burdens. Future papers will describe how RAID has been successfully modified to predict Dengue Fever and Chikungunya virus outbreaks.

7.0 References

Appendix D contains references used in the development of RAID that were not specifically referenced in the paper's body.

1. Lunde TM, Bayoh MN, Lindtjørn B. How malaria models relate temperature to malaria trans- mission : Details of the Bayoh-Lunde model, mosquito biting rate, and parasite extrinsic incubation period. :3-7.

2. Mushinzimana E, Munga S, Minakawa N, et al. Landscape determinants and remote sensing of anopheline mosquito larval habitats in the western Kenya highlands. *Malar J*. 2006;5:13. doi:10.1186/1475-2875-5-13

3. Imbahale SS, Githeko A, Mukabana WR, Takken W. Integrated mosquito larval source management reduces larval numbers in two highland villages in western Kenya. *BMC Public Health*. 2012;12:362. doi:10.1186/1471-2458-12-362

4. Clennon J a, Kamanga A, Musapa M, Shiff C, Glass GE. Identifying malaria vector breeding habitats with remote sensing data and terrain-based landscape indices in Zambia. *Int J Health Geogr*. 2010;9:58. doi:10.1186/1476-072X-9-58

5. Lunde TM, Bayoh MN, Lindtjørn B. How malaria models relate temperature to malaria transmission. *Parasit Vectors*. 2013;6:20. doi:10.1186/1756-3305-6-20

6. Bomblies A, Eltahir E a B. Assessment of the impact of climate shifts on malaria transmission in the Sahel. *Ecohealth*. 2009;6:426-437. doi:10.1007/s10393-010-0274-5

7. Guerra C a., Gikandi PW, Tatem AJ, et al. The limits and intensity of Plasmodium falciparum transmission: Implications for malaria control and elimination worldwide. *PLoS Med*. 2008;5(2):0300-0311. doi:10.1371/journal.pmed.0050038

8. Kiszewski A, Mellinger A, Spielman A, Malaney PI a, Sachs SE, Sachs J. A global index representing the satability of malaria transmission. *Am J Trop Med Hyg*. 2004;70(5):486-498. doi:70/5/486

9. Thomas DM. Interviewee, Ecological Entomologist. July 13 2013.

10. Parham PE, Pople D, Christiansen-Jucht C, Lindsay S, Hinsley W, Michael E. Modeling the role of environmental variables on the population dynamics of the malaria vector Anopheles gambiae sensu stricto. *Malar J*. 2012;11:271. doi:10.1186/1475-2875-11-271

11. Ermert V, Fink a H, Morse a P, Paeth H. The impact of regional climate change on malaria risk due to greenhouse forcing and land-use changes in tropical Africa. *Env Heal Perspect*. 2012;120(1):77-84. doi:10.1289/ehp.1103681

Appendix A – Diversity Prediction Theorem

Predicting is an essential activity for models. There is often a focus on selecting the best model; however, a diverse suite of models (i.e., model of models) will always be more accurate than its average member. More analytically, the suite's squared error is equal to the average model's individual squared error minus the model legacies' diversity. This may be stated as:

$$(\text{model of models error})^2 = \sum(\text{model error})^2/\text{number of models} - \sum(\text{diversity of model of models})$$

This is known as the Diversity Prediction Theorem (DPT). This, in turn, means that the "model of models" error is equal to the average model's error minus the diversity of the models' suite. Therefore, as we get better models (e.g., less average error) with more diversity, the smaller the "model of models" error will be. Since it is challenging, if not impossible, to determine the best model, we opted for using this approach to advance the state of the art in disease outbreak prediction by combining a variety of community-accepted techniques.

For both the weather and plasmodium pool surrogates, DPT was used to combine multiple triggers into one test instead of selecting the best single indicator (or model). This qualitative approach mirrors a Kalman filter that uses all data to produce the most accurate prediction of the future rather than a single measurement. Just as with DPT, a Kalman filter weighs more accurate individual estimates heavier, yet includes all estimates to produce a better representation of all available data.

It is not just a hunch that a group of people makes better decisions than a monolithic team. The DPT states the team's predictive capability is determined equally by the quality of the individuals and the diversity in their backgrounds. This means a more diverse group, with moderately smart people, will outperform a single brilliant person. As a result, a meeting slated for establishing future key actions is better if there is a little disagreement rather than no disagreement. This diversity in opinion hints at a better eventual outcome.

Primary sources for this summary are:

1. Ioannides Y and Page S. The Difference: How the Power of Diversity Creates Better Groups, Firms, Schools, and Societies. Journal of Economic Literature. 2007.
2. Page S. *The Hidden Factor: Why Thinking Differently Is Your Greatest Asset.* Chantilly, VA: The Great Courses. 2011.

Appendix B – Activity-Based Intelligence Principles

The RAID Team applied and refined Activity-Based Intelligence (ABI) methodologies and heuristics that focus primarily on interactions, choke points, and transactions rather than objects. These techniques include:

- geo-reference to discover (location is a critical dimension of data meaning) as per local RCM calculations,
- sequence neutrality (most recent data is not necessarily the most credible data) as per DPT,
- data neutrality (source of data does not rule out use) as per DPT, and
- knowledge management (data is collected with its interface to the user in mind), as per the VBO development.

In researching the utility of early warning through predictive awareness, the RAID team studied the basics of this field and summarized several general warning lessons applicable to RAID.

- Education about a warning system is needed before an event.
- Alerting needs to attract attention.
- People seek social confirmation of warnings before taking protective action.
- Messages should contain information that is important to the population.
- Wording should consider the demographics of affected populations.
- Be precise: explain when, where, what, and why.
- Warnings and alerts should be consistent both during escalation and during downgrading.

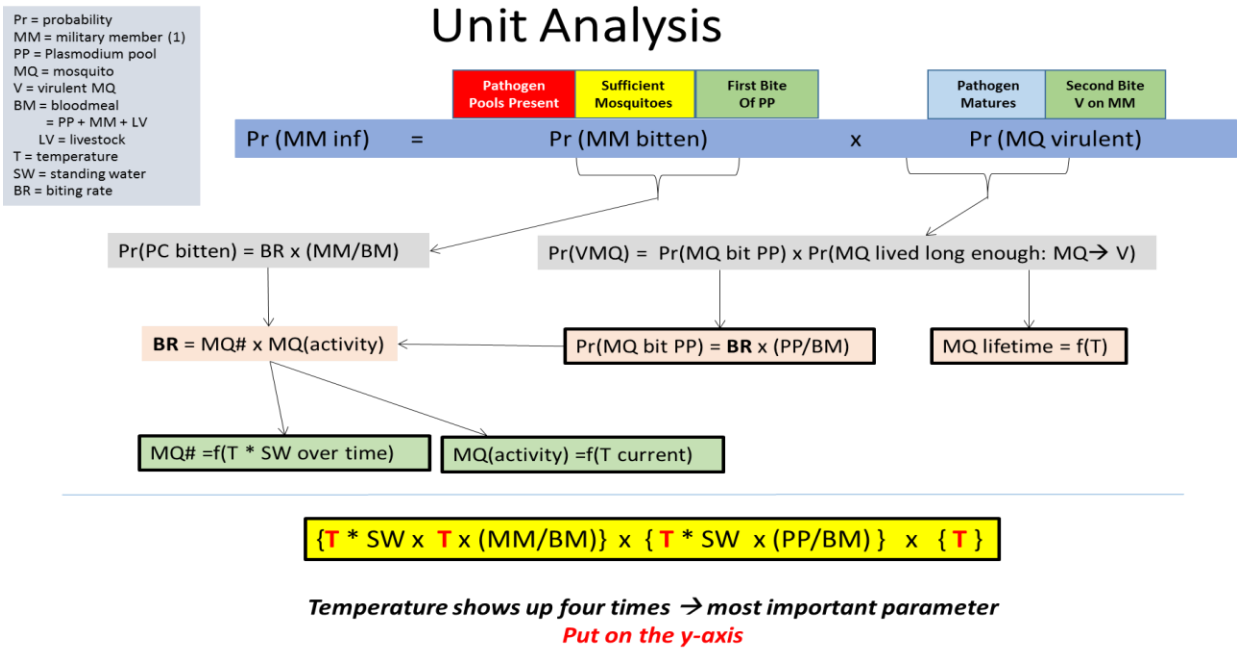
Primary sources for this summary are:

1. Public Response to Alerts and Warnings Using Social Media: Report of a Workshop on Current Knowledge and Research Gaps, NAS, 2013. ISBN 978-0-309-29033-3.
2. Geotargeted Alerts and Warnings: Report of a Workshop on Current Knowledge and Research Gaps, NAS, 2013. ISBN 978-0-309-28985-6.

Appendix C – Unit Analysis

Coordinate transformations and dimensional analysis are valuable in reducing the complexity of existing models and creating new models. The analysis of malaria outbreaks in literature has been depicted on a wide variety of axes (e.g., time, probability, temperature, etc.). To create an end-to-end evaluation of the local interactions that predicts an outbreak (i.e., warns of the impending event,) the x-axis was standardized to days since the key aspect of warning is time.

To determine the y-axis, each aspect of the local interactions (e.g., biting rate, biting preference, mosquito lifetime, sporogony cycle, gonotrophic cycle, etc.) was analyzed to determine the most significant parameter(s) for RCM. The figure below shows the unit analysis highlighting temperature as a driving factor.



Temperature had a higher-order effect on the probability of a susceptible person becoming infected; temperature was used four times in the final calculations. The temperature and standing water combination threshold were the second most critical; this combination appeared twice. All other parameters only exhibited linear effects (i.e., showed up once) on results. In summary, temperature appeared in the two most important terms with an exponential impact in both, corroborating the decision to focus local interactions around Marten's temperature-dependent survivability curve. This realization catalyzed the conversion of Marten's probability of survival equation into a lifetime as a function of temperature for a specified segment of the

population. This permitted the creation of the Vector Population Days (VPD) term, representing possible virulent biting days.

Appendix D – References Used for RAID Development Not Referenced Specifically in Paper

1. Abate A, Degarege A, Erko B. Community knowledge, attitude and practice about malaria in a low endemic setting of Shewa Robit Town, northeastern Ethiopia. BMC Public Health. 2013;13(1):312. doi:10.1186/1471-2458-13-312

2. Abeku T a., De Vlas SJ, Borsboom G, et al. Forecasting malaria incidence from historical morbidity patterns in epidemic-prone areas of Ethiopia: A simple seasonal adjustment method performs best. Trop Med Int Heal. 2002;7(10):851-857. doi:10.1046/j.1365-3156.2002.00924.x

3. Adimi F, Soebiyanto RP, Safi N, Kiang R. Towards malaria risk prediction in Afghanistan using remote sensing. Malar J. 2010;9:125. doi:10.1186/1475-2875-9-125

4. Al-Taiar A, Jaffar S, Assabri A, et al. Who develops severe malaria? Impact of access to healthcare, socio-economic and environmental factors on children in Yemen: A case-control study. Trop Med Int Heal. 2008;13(6):762-770. doi:10.1111/j.1365-3156.2008.02066.x

5. Andrick B, Clark B, Nygaard K, Logar a., Penaloza M, Welch R. Infectious disease and climate change: detecting contributingfactors and predicting future outbreaks. IGARSS'97 1997 IEEE Int Geosci Remote Sens Symp Proceedings Remote Sens - A Sci Vis Sustain Dev. 1997;4:1947-1949. doi:10.1109/IGARSS.1997.609159

6. Araújo MDS, Gil LHS, de Almeida e Silva A. Larval food quantity affects development time, survival and adult biological traits that influence the vectorial capacity of Anopheles darlingi under laboratory conditions. Malar J. 2012;11:261. doi:10.1186/1475-2875-11-261

7. Asih PB, Rozi IE, Herdiana H, et al. The baseline distribution of malaria in the initial phase of elimination in Sabang Municipality, Aceh Province, Indonesia. Malar J. 2012;11:291. doi:10.1186/1475-2875-11-291

8. Ayele DG, Zewotir TT, Mwambi HG. Prevalence and risk factors of malaria in Ethiopia. Malar J. 2012;11:195. doi:10.1186/1475-2875-11-195

9. Badolo A, Traoré A, Jones CM, et al. Three years of insecticide resistance monitoring in Anopheles gambiae in Burkina Faso: resistance on the rise? Malar J. 2012;11:232. doi:10.1186/1475-2875-11-232

10. Baeza A, Bouma MJ, Dobson AP, Dhiman R, Srivastava HC, Pascual M. Climate forcing and desert malaria: the effect of irrigation. Malar J. 2011;10:190. doi:10.1186/1475-2875-10-190

11. Baliraine FN, Afrane Y a, Amenya D a, et al. A cohort study of Plasmodium falciparum infection dynamics in Western Kenya Highlands. BMC Infect Dis. 2010;10:283. doi:10.1186/1471-2334-10-283

12. Basurko C, Hanf M, Han-Sze R, et al. Influence of climate and river level on the incidence of malaria in Cacao, French Guiana. Malar J. 2011;10:26. doi:10.1186/1475-2875-10-26

13. Bayoh MN. Studies on the development and survival of Anopheles gambiae sensustricto at various temperatures and relative humidities. Published online 2001:134. http://etheses.dur.ac.uk/4952

14. Beck LR, Lobitz BM, Wood BL. New Sensors and New Opportunities. Emerg Infect Dis. 2000;6(3):217-226.

15. Beier JC, Killeen GF, Githure JI. Short report: Entomologic inoculation rates and Plasmodium falciparum malaria prevalence in Africa. Am J Trop Med Hyg. 1999;61(1):109-113.

16. Bekele D, Belyhun Y, Petros B, Deressa W. Assessment of the effect of insecticide-treated nets and indoor residual spraying for malaria control in three rural kebeles of Adami Tulu District, South Central Ethiopia. Malar J. 2012;11:127. doi:10.1186/1475-2875-11-127

17. Berberian G, Rosanova MT. [Impact of climate change on infectious diseases]. Arch Argent Pediatr. 2012;110(3):39-45. doi:10.1590/S0325-00752012000100009

18. Berg J, Breederveld D, Roukens AH, et al. Knowledge, attitudes, and practices toward malaria risk and prevention among frequent business travelers of a major oil and gas company. J Travel Med. 2011;18(6):395-401. doi:10.1111/j.1708-8305.2011.00555.x

19. Blanford JI, Blanford S, Crane RG, et al. Implications of temperature variation for malaria parasite development across Africa. Sci Rep. 2013;3:1300. doi:10.1038/srep01300

20. Bomblies A, Duchemin JB, Eltahir E a B. Hydrology of malaria: Model development and application to a Sahelian village. Water Resour Res. 2008;44:1-26. doi:10.1029/2008WR006917

21. Booman M, Sharp BL, Martin CL, Manjate B, La Grange JJ, Durrheim DN. Enhancing malaria control using a computerised management system in southern Africa. Malar J. 2003;2:13. doi:10.1186/1475-2875-2-13

22. Breeveld FJ, Vreden SG, Grobusch MP. History of malaria research and its contribution to the malaria control success in Suriname: a review. Malar J. 2012;11:95. doi:10.1186/1475-2875-11-95

23. Briët OJT, Galappaththy GNL, Amerasinghe PH, Konradsen F. Malaria in Sri Lanka: one year post-tsunami. Malar J. 2006;5:42. doi:10.1186/1475-2875-5-42

24. Briët OJT, Galappaththy GNL, Konradsen F, Amerasinghe PH, Amerasinghe FP. Maps of the Sri Lanka malaria situation preceding the tsunami and key aspects to be considered in the emergency phase and beyond. Malar J. 2005;4:8. doi:10.1186/1475-2875-4-8

25. Ceccato P, Vancutsem C, Klaver R, Rowland J, Connor SJ. A vectorial capacity product to monitor changing malaria transmission potential in epidemic regions of Africa. J Trop Med. 2012;2012. doi:10.1155/2012/595948

26. Chen H, Githeko AK, Zhou G, Githure JI, Yan G. New records of Anopheles arabiensis breeding on the Mount Kenya highlands indicate indigenous malaria transmission. Malar J. 2006;5:17. doi:10.1186/1475-2875-5-17

27. Chen S, Blanford JI, Fleischer SJ, Hutchinson M, Saunders MC, Thomas MB. Estimating west nile virus transmission period in pennsylvania using an optimized degree-day model. Vector Borne Zoonotic Dis. 2013;13(X):489-497. doi:10.1089/vbz.2012.1094

28. Chitnis N, Cushing JM, Hyman JM. Bifurcation Analysis of a Mathematical Model for Malaria Transmission. SIAM J Appl Math. 2006;67(1):24-45. doi:10.1137/050638941

29. Chitnis N, Hardy D, Gnaegi G, et al. Modeling the effects of vector control interventions in reducing malaria transmission, morbidity and mortality. 2010;9(Suppl 2):O7. doi:10.1186/1475-2875-9-S2-O7

30. Chiyaka C, Tatem a J, Cohen JM, et al. The Stability of Malaria Elimination. Science (80-). 2013;339:909-910. doi:10.1126/science.1229509

31. Cho P-Y, Lee S-W, Ahn SK, et al. Evaluation of circumsporozoite protein of Plasmodium vivax to estimate its prevalence in the Republic of Korea: an observational study of incidence. Malar J. 2013;12:448. doi:10.1186/1475-2875-12-448

32. Cibulskis RE, Aregawi M, Williams R, Otten M, Dye C. Worldwide incidence of malaria in 2009: estimates, time trends, and a critique of methods. PLoS Med. 2011;8(12):e1001142. doi:10.1371/journal.pmed.1001142

33. Cohen JM, Ernst KC, Lindblade K a, Vulule JM, John CC, Wilson ML. Local topographic wetness indices predict household malaria risk better than land-use and land-cover in the western Kenya highlands. Malar J. 2010;9:328. doi:10.1186/1475-2875-9-328

34. Cohen JM, Smith DL, Cotter C, et al. Malaria resurgence: a systematic review and assessment of its causes. Malar J. 2012;11:122. doi:10.1186/1475-2875-11-122

35. Craig MH, Snow RW, le Sueur D. A climate-based distribution model of malaria transmission in sub-saharan Africa. Parsitol today. 1999;15(99):105-111.

36. Cuamba N, Mendis C. The role of Anopheles merus in malaria transmission in an area of southern Mozambique. J Vector Borne Dis. 2009;46(June):157-159.

37. Cui X, Parker DJ, Morse AP. The Drying Out of Soil Moisture following Rainfall in a Numerical Weather Prediction Model and Implications for Malaria Prediction in West Africa. Weather Forecast. 2009; 24:1549-1557. doi:10.1175/2009WAF2222240.1

38. Daash A, Srivastava A, Nagpal BN, Saxena R, Gupta SK. Geographical

information system (GIS) in decision support to control malaria--a case study of Koraput district in Orissa, India. J Vector Borne Dis. 2009;46(1):72-74. http://www.ncbi.nlm.nih.gov/pubmed/19326711

39. Dambach P, Sié A, Lacaux JP, Vignolles C, Machault V, Sauerborn R. Using high spatial resolution remote sensing for risk mapping of malaria occurrence in the Nouna district, Burkina Faso. Glob Health Action. 2009; 2:1-8. doi:10.3402/gha.v2i0.2094

40. Das A, Anvikar AR, Cator LJ, et al. Malaria in India: the center for the study of complex malaria in India. Acta Trop. 2012;121(3):267-273. doi:10.1016/j.actatropica.2011.11.008

41. David N, Agricultural N, Zonal B, Sciences E. Characterisation of Anopheles Mosquitoes breeding habitats in lowland rice fields in Uganda. Nat Sci. 2011;9(6):44-58.

42. Davis RG, Kamanga A, Castillo-Salgado C, Chime N, Mharakurwa S, Shiff C. Early detection of malaria foci for targeted interventions in endemic southern Zambia. Malar J. 2011;10:260. doi:10.1186/1475-2875-10-260

43. Deressa W, Ali a., Enqusellassie F. Self-treatment of malaria in rural communities, Butajira, southern Ethiopia. Bull World Health Organ. 2003;81(01):261-268.

44. Derua Y a, Alifrangis M, Hosea KM, et al. Change in composition of the Anopheles gambiae complex and its possible implications for the transmission of malaria and lymphatic filariasis in north-eastern Tanzania. Malar J. 2012;11:188. doi:10.1186/1475-2875-11-188

45. Devi NP, Jauhari RK. Climatic variables and malaria incidence in Dehradun, Uttaranchal, India. J Vector Borne Dis. 2006;43(1):21-28. http://www.ncbi.nlm.nih.gov/pubmed/16642782

46. Dhiman S, Gopalakrishnan R, Goswami D, Rabha B, Baruah I, Singh L. Malaria incidence among paramilitary personnel in an endemic area of Tripura. Indian J Med Res. 2011;133(June):665-669.

47. Diabaté A, Yaro AS, Dao A, Diallo M, Huestis DL, Lehmann T. Spatial distribution and male mating success of Anopheles gambiae swarms. BMC Evol Biol. 2011;11:184. doi:10.1186/1471-2148-11-184

48. Dongus S, Nyika D, Kannady K, et al. Participatory mapping of target areas to enable operational larval source management to suppress malaria vector mosquitoes in Dar es Salaam, Tanzania. Int J Health Geogr. 2007;6:37. doi:10.1186/1476-072X-6-37

49. Donnelly MJ, McCall PJ, Lengeler C, et al. Malaria and urbanization in sub-Saharan Africa. Malar J. 2005;4:12. doi:10.1186/1475-2875-4-12

50. Donovan C, Siadat B, Frimpong J. Seasonal and Socio-Economic Variations in Clinical and Self-Reported Malaria in Accra , Ghana : Evidence From. 2012;46(2).

51. Eisele TP, Keating J, Swalm C, et al. Linking field-based ecological data with remotely sensed data using a geographic information system in two malaria endemic urban areas of Kenya. Malar J. 2003;2:44. doi:10.1186/1475-2875-2-44

52. Ernst KC, Lindblade K a., Koech D, et al. Environmental, socio-demographic and behavioural determinants of malaria risk in the western Kenyan highlands: A case-control study. Trop Med Int Heal. 2009;14(10):1258-1265. doi:10.1111/j.1365-3156.2009.02370.x

53. Fillinger U, Ndenga B, Githeko A, Lindsay SW. Integrated malaria vector control with microbial larvicides and insecticide-treated nets in western Kenya: A controlled trial. Bull World Health Organ. 2009;87(November 2008):655-665. doi:10.2471/BLT.08.055632

54. Fuller DO, Ahumada ML, Quiñones ML, Herrera S, Beier JC. Near-present and future distribution of Anopheles albimanus in Mesoamerica and the Caribbean Basin modeled with climate and topographic data. Int J Health Geogr. 2012;11:13. doi:10.1186/1476-072X-11-13

55. Fuller DO, Parenti MS, Hassan AN, Beier JC. Linking land cover and species distribution models to project potential ranges of malaria vectors: an example using Anopheles arabiensis in Sudan and Upper Egypt. Malar J. 2012;11:264. doi:10.1186/1475-2875-11-264

56. Gadiaga L, Machault V, Pagès F, et al. Conditions of malaria transmission in Dakar from 2007 to 2010. Malar J. 2011;10:312. doi:10.1186/1475-2875-10-312

57. Garamszegi LZ. Climate change increases the risk of malaria in birds. Glob Chang Biol. 2011;17:1751-1759. doi:10.1111/j.1365-2486.2010.02346.x

58. Garros C, Van Nguyen C, Trung HD, Van Bortel W, Coosemans M, Manguin S. Distribution of Anopheles in Vietnam, with particular attention to malaria vectors of the Anopheles minimus complex. Malar J. 2008;7:11. doi:10.1186/1475-2875-7-11

59. Gemperli A, Sogoba N, Fondjo E, et al. Mapping malaria transmission in West and Central Africa. Trop Med Int Heal. 2006;11(7):1032-1046. doi:10.1111/j.1365-3156.2006.01640.x

60. Gething PW, Elyazar IRF, Moyes CL, et al. A Long Neglected World Malaria Map: Plasmodium vivax Endemicity in 2010. PLoS Negl Trop Dis. 2012;6(9). doi:10.1371/journal.pntd.0001814

61. Gething PW, Patil AP, Smith DL, et al. A new world malaria map: Plasmodium falciparum endemicity in 2010. Malar J. 2011;10(1):378. doi:10.1186/1475-2875-10-378

62. Graves PM, Osgood DE, Thomson MC, et al. Effectiveness of malaria control during changing climate conditions in Eritrea, 1998-2003. Trop Med Int Heal. 2008;13(2):218-228. doi:10.1111/j.1365-3156.2007.01993.x

63. Grover-Kopec E, Kawano M, Klaver RW, Blumenthal B, Ceccato P, Connor SJ. An online operational rainfall-monitoring resource for epidemic malaria early warning systems in Africa. Malar J. 2005;4:6. doi:10.1186/1475-2875-4-6

64. Grover-Kopec EK, Blumenthal MB, Ceccato P, Dinku T, Omumbo J a, Connor SJ. Web-based climate information resources for malaria control in Africa. Malar J. 2006;5:38. doi:10.1186/1475-2875-5-38

65. Gu W, Novak RJ. Agent-based modelling of mosquito foraging behaviour for malaria control. Trans R Soc Trop Med Hyg. 2010;103(11):1-14. doi:10.1016/j.trstmh.2009.01.006.Agent-based

66. Guerra C a, Hay SI, Lucioparedes LS, et al. Assembling a global database of malaria parasite prevalence for the Malaria Atlas Project. Malar J. 2007;6(June 2009):17. doi:10.1186/1475-2875-6-17

67. Guerra C a, Snow RW, Hay SI. A global assessment of closed forests, deforestation and malaria risk. Ann Trop Med Parasitol. 2006;100(3):189-204. doi:10.1179/136485906X91512

68. Gurarie D, Karl S, Zimmerman P a., King CH, Pierre TG, Davis TME. Mathematical modeling of malaria infection with innate and adaptive immunity in individuals and agent-based communities. PLoS One. 2012;7(3):1-13. doi:10.1371/journal.pone.0034040

69. Guthmann JP, Llanos-Cuentas a, Palacios a, Hall a J. Environmental factors as determinants of malaria risk. A descriptive study on the northern coast of Peru. Trop Med Int Health. 2002;7(6):518-525. doi:10.1046/j.1365-3156.2002.00883.x

70. Haghdoost AA, Alexander N, Cox J. Modelling of malaria temporal variations in Iran. Trop Med Int Heal. 2008;13(12):1501-1508. doi:10.1111/j.1365-3156.2008.02166.x

71. Hamusse SD, Balcha TT, Belachew T. The impact of indoor residual spraying on malaria incidence in East Shoa Zone, Ethiopia. Glob Health Action. 2012;5:11619. doi:10.3402/gha.v5i0.11619

72. Hanafi-Bojd A, Vatandoost H, Oshaghi M a, et al. Spatial analysis and mapping of malaria risk in an endemic area, south of Iran: a GIS based decision making for planning of control. Acta Trop. 2012;122(1):132-137. doi:10.1016/j.actatropica.2012.01.003

73. Hanf M, Adenis A, Nacher M, Carme B. The role of El Niño Southern Oscillation (ENSO) on variations of monthly Plasmodium falciparum malaria cases at the Cayenne General Hospital, 1996-2009, French Guiana. Malar J. 2011;10:100. doi:10.1186/1475-2875-10-100

74. Haque U, Soares Magalhães RJ, Mitra D, et al. The role of age, ethnicity and environmental factors in modulating malaria risk in Rajasthali, Bangladesh. Malar J. 2011;10:367. doi:10.1186/1475-2875-10-367

75. Hathaway AK, Coldren R, Webby R. Title: The Impact of Altitude on Influenza Authors: Kyle Hathaway, Rodney Coldren, Richard Webby.

76. Hay SI, George DB, Moyes CL, Brownstein JS. Big Data Opportunities for Global Infectious Disease Surveillance. PLoS Med. 2013;10(4):2-5. doi:10.1371/journal.pmed.1001413

77. Hay SI, Omumbo J, Craig MH, Snow RW. Earth observation, geographic information systems and Plasmodium falciparum malaria in sub-Saharan Africa. Adv Parasitol. 2000;47:173-215. doi:http://dx.doi.org/10.1016/S0065-308X(00)47009-0

78. Hay SI, Rogers DJ, Toomer JF, Snow RW. Annual Plasmodium falciparum entomological inoculation rates (EIR) across Africa: literature survey, Internet access and review. Trans R Soc Trop Med Hyg. 2000;94:113-127. doi:10.1016/S0035-9203(00)90246-3

79. Herrel N, Amerasinghe FP, Ensink J, Mukhtar M, van der Hoek W, Konradsen F. Breeding of Anopheles mosquitoes in irrigated areas of South Punjab, Pakistan. Med Vet Entomol. 2001;15(3):236-248. http://www.ncbi.nlm.nih.gov/pubmed/11583440

80. Herrmann SM, Mohr KI. A continental-scale classification of rainfall seasonality regimes in Africa based on gridded precipitation and land surface temperature products. J Appl Meteorol Climatol. 2011;50:2504-2513. doi:10.1175/JAMC-D-11-024.1

81. Howard N, Shafi A, Jones C, Rowland M. Malaria control under the Taliban regime: insecticide-treated net purchasing, coverage, and usage among men and women in eastern Afghanistan. Malar J. 2010;9:7. doi:10.1186/1475-2875-9-7

82. Huang F, Zhou S, Zhang S, Wang H, Tang L. Temporal correlation analysis between malaria and meteorological factors in Motuo County, Tibet. Malar J. 2011;10:54. doi:10.1186/1475-2875-10-54

83. Iqbal J, Sher a., Hira PR, Al-Aniezi a. Drug-resistant Plasmodium falciparum infection in immigrants and non-immune travellers. Clin Microbiol Infect. 2002;8:734-738. doi:10.1046/j.1469-0691.2002.00451.x

84. Jacob BG, Muturi EJ, Mwangangi JM, et al. Remote and field level quantification of vegetation covariates for malaria mapping in three rice agro-village complexes in Central Kenya. Int J Health Geogr. 2007;6(Ivm):21. doi:10.1186/1476-072X-6-21

85. Jima D, Getachew A, Bilak H, et al. Malaria indicator survey 2007, Ethiopia: coverage and use of major malaria prevention and control interventions. Malar J. 2010;9:58. doi:10.1186/1475-2875-9-58

86. Jones AE, Morse AP. Application and validation of a seasonal ensemble prediction system using a dynamic malaria model. J Clim. 2010;23:4202-4215. doi:10.1175/2010JCLI3208.1

87. Jones AE, Wort UU, Morse AP, Hastings IM, Gagnon AS. Climate prediction of El Niño malaria epidemics in north-west Tanzania. Malar J. 2007;6:162. doi:10.1186/1475-2875-6-162

88. Jongwutiwes S, Buppan P, Kosuvin R, Seethamchai S. Plasmodium knowlesi Malaria in Humans and Macaques, Thailand. 2011;17(10):1799-1806.

89. Kampango a., Cuamba N, Charlwood JD. Does moonlight influence the biting behaviour of Anopheles funestus? Med Vet Entomol. 2011;25:240-246. doi:10.1111/j.1365-2915.2010.00917.x

90. Kamuliwo M, Chanda E, Haque U, et al. The changing burden of malaria and association with vector control interventions in Zambia using district-level surveillance data, 2006-2011. Malar J. 2013;12:437. doi:10.1186/1475-2875-12-437

91. Karunamoorthi K. Vector control: A cornerstone in the malaria elimination campaign. Clin Microbiol Infect. 2011;17:1608-1616. doi:10.1111/j.1469-0691.2011.03664.x

92. Khan W a, Sack D a, Ahmed S, et al. Mapping hypoendemic, seasonal malaria in rural Bandarban, Bangladesh: a prospective surveillance. Malar J. 2011;10(1):124. doi:10.1186/1475-2875-10-124

93. Khan W a, Sack D a, Ahmed S, et al. Mapping hypoendemic, seasonal malaria in rural Bandarban, Bangladesh: a prospective surveillance. Malar J. 2011;10:124. doi:10.1186/1475-2875-10-124

94. Kibret S, Alemu Y, Boelee E, Tekie H, Alemu D, Petros B. The impact of a small-scale irrigation scheme on malaria transmission in Ziway area, Central Ethiopia. Trop Med Int Heal. 2010;15(1):41-50. doi:10.1111/j.1365-3156.2009.02423.x

95. Kim YM, Park JW, Cheong HK. Estimated effect of climatic variables on the transmission of plasmodium vivax malaria in the republic of Korea. Environ Health Perspect. 2012;120(9):1314-1319. doi:http://dx.doi.org/10.1289/ehp.1104577

96. Kirby MJ, Lindsay SW. Responses of adult mosquitoes of two sibling species, Anopheles arabiensis and A. gambiae s.s. (Diptera: Culicidae), to high temperatures. Bull Entomol Res. 2004;94:441-448. doi:10.1079/BER2004316

97. Korgaonkar NS, Kumar A, Yadav RS, Kabadi D, Dash AP. Mosquito biting activity on humans & detection of Plasmodium falciparum infection in Anopheles stephensi in Goa, India. Indian J Med Res. 2012;135(January):120-126. http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3307172&tool=pmcentrez&rendertype=abstract

98. Kotwal RS, Wenzel RB, Sterling R a, Porter WD, Jordan NN, Petruccelli BP. An outbreak of malaria in US Army Rangers returning from Afghanistan. JAMA. 2005;293(2):212-216. doi:10.1001/jama.293.2.212

99. Lachish S, Knowles SCL, Alves R, Wood MJ, Sheldon BC. Fitness effects of endemic malaria infections in a wild bird population: The importance of ecological structure. J Anim Ecol. 2011;80:1196-1206. doi:10.1111/j.1365-2656.2011.01836.x

100. Lardeux FJ, Tejerina RH, Quispe V, Chavez TK. A physiological time analysis of the duration of the gonotrophic cycle of Anopheles pseudopunctipennis and its implications for malaria transmission in Bolivia. Malar J. 2008;7:141. doi:10.1186/1475-2875-7-141

101. Lautze J, McCartney M, Kirshen P, Olana D, Jayasinghe G, Spielman A. Effect of a large dam on malaria risk: The Koka reservoir in Ethiopia. Trop Med Int Heal. 2007;12(8):982-989. doi:10.1111/j.1365-3156.2007.01878.x

102. Le Menach a., Tatem a. J, Cohen JM, et al. Travel risk, malaria importation and malaria transmission in Zanzibar. Published online 2011:1-7. doi:10.1038/srep00093

103. Lee P-W, Liu C-T, do Rosario VE, de Sousa B, Rampao HS, Shaio M-F.

Potential threat of malaria epidemics in a low transmission area, as exemplified by São Tomé and Príncipe. Malar J. 2010;9:264. doi:10.1186/1475-2875-9-264

104. Loiseau C, Harrigan RJ, Robert A, et al. Host and habitat specialization of avian malaria in Africa. Mol Ecol. 2012;21:431-441. doi:10.1111/j.1365-294X.2011.05341.x

105. Lunde TM, Bayoh MN, Lindtjørn B. How malaria models relate temperature to malaria transmission. Parasit Vectors. 2013;6:20. doi:10.1186/1756-3305-6-20

106. Machault V, Orlandi-Pradines E, Michel R, et al. Remote sensing and malaria risk for military personnel in Africa. J Travel Med. 2008;15(4):216-220. doi:10.1111/j.1708-8305.2008.00202.x

107. Machault V, Vignolles C, Pagès F, et al. Spatial heterogeneity and temporal evolution of malaria transmission risk in Dakar, Senegal, according to remotely sensed environmental data. Malar J. 2010;9:252. doi:10.1186/1475-2875-9-252

108. Malone JB, Poggi E, Igualada F-J, et al. Malaria environmental risk assessment in Eritrea. IGARSS 2003 2003 IEEE Int Geosci Remote Sens Symp Proc (IEEE Cat No03CH37477). 2003;2(C):1000-1003. doi:10.1109/IGARSS.2003.1293991

109. Manh C Do, Beebe NW, Van VNT, et al. Vectors and malaria transmission in deforested, rural communities in north-central Vietnam. Malar J. 2010;9:259. doi:10.1186/1475-2875-9-259

110. Manimunda SP, Sugunan AP, Sha WA, Singh SS, Shriram AN, Vijayachari P. Tsunami, post-tsunami malaria situation in Nancowry group of islands, Nicobar district, Andaman and Nicobar islands. Indian J Med Res. 2011;133(January):76-82.

111. McKelvie WR, Haghdoost AA, Raeisi A. Defining and detecting malaria epidemics in south-east Iran. Malar J. 2012;11:81. doi:10.1186/1475-2875-11-81

112. Mckenzie FE, Bossert WH. A TARGET FOR INTERVENTION IN PLASMODIUM FALCIPARUM INFECTIONS. Am J Trop Med Hyg. 1998;58(6):763-767.

113. Mendis K, Rietveld A, Warsame M, Bosman A, Greenwood B, Wernsdorfer WH. From malaria control to eradication: The WHO perspective. Trop Med Int Heal. 2009;14(7):802-809. doi:10.1111/j.1365-3156.2009.02287.x

114. Messina JP, Taylor SM, Meshnick SR, et al. Population, behavioural and environmental drivers of malaria prevalence in the Democratic Republic of Congo. Malar J. 2011;10:161. doi:10.1186/1475-2875-10-161

115. Midekisa A, Senay G, Henebry GM, Semuniguse P, Wimberly MC. Remote sensing-based time series models for malaria early warning in the highlands of Ethiopia. Malar J. 2012;11:165. doi:10.1186/1475-2875-11-165

116. Montgomery BC, Grieco J, Masuoka PM, et al. A remote sensing analysis of vector abundance and malaria riskassociated with selected villages in southern Belize, C.A. IGARSS '98 Sens Manag Environ 1998 IEEE Int Geosci Remote Sensing

Symp Proceedings (Cat No98CH36174). 1998;2:1053-1054. doi:10.1109/IGARSS.1998.699670

117. Montosi E, Manzoni S, Porporato A., Montanari A. An ecohydrological model of malaria outbreaks. Hydrol Earth Syst Sci. 2012;16:2759-2769. doi:10.5194/hess-16-2759-2012

118. Mordecai E a., Paaijmans KP, Johnson LR, et al. Optimal temperature for malaria transmission is dramatically lower than previously predicted. Ecol Lett. 2013;16:22-30. doi:10.1111/ele.12015

119. Morrow MG, Johnson RN, Polanco J, Claborn DM. Mosquito vector abundance immediately before and after tropical storms Alma and Arthur, northern Belize, 2008. Rev Panam Salud Publica. 2010;28(May 2008):19-24. doi:10.1590/S1020-49892010000700003

120. Moss WJ, Hamapumbu H, Kobayashi T, et al. Use of remote sensing to identify spatial risk factors for malaria in a region of declining transmission: a cross-sectional and longitudinal community survey. Malar J. 2011;10(1):163. doi:10.1186/1475-2875-10-163

121. Moutinho PR, Gil LHS, Cruz RB, Ribolla PEM. Population dynamics, structure and behavior of Anopheles darlingi in a rural settlement in the Amazon rainforest of Acre, Brazil. Malar J. 2011;10(June):174. doi:10.1186/1475-2875-10-174

122. Myers MF, Rogers DJ, Cox J, Flahault a, Hay SI. Forecasting disease risk for increased epidemic preparedness in public health. Adv Parasitol. 2000;47:309-330.

123. Najera J a, Kouznetzsov RL, Delacollette C. Malaria epidemics, detection and control, forecasting and prevention. Malar epidemics Detect Control Forecast Prev. 1998;81:52. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=fulltext&AN=19980808001&D=cagh2

124. Ndiath MO, Brengues C, Konate L, et al. Dynamics of transmission of Plasmodium falciparum by Anopheles arabiensis and the molecular forms M and S of Anopheles gambiae in Dielmo, Senegal. Malar J. 2008;7:136. doi:10.1186/1475-2875-7-136

125. Ndugwa RP, Ramroth H, Müller O, et al. Comparison of all-cause and malaria-specific mortality from two West African countries with different malaria transmission patterns. Malar J. 2008;7:15. doi:10.1186/1475-2875-7-15

126. Ngomane L, de Jager C. Changes in malaria morbidity and mortality in Mpumalanga Province, South Africa (2001- 2009): a retrospective study. Malar J. 2012;11:19. doi:10.1186/1475-2875-11-19

127. Njabo KY, Cornel J, Bonneaud C, et al. Nonspecific patterns of vector, host and avian malaria parasite associations in a central African rainforest. Mol Ecol. 2011;20:1049-1061. doi:10.1111/j.1365-294X.2010.04904.x

128. Olayemi IK. Survivorship Of Anopheles gambiae In Relation To Malaria Transmission In Ilorin, Nigeria. Online J Heal Allied Sci. 2008;7(3):3-7.

129. Ortega LI. Malaria Situation in South East Asia Region Regional Adviser , Malaria Milestones and trend of malaria in South East Asia , 1948-2011. :1-15.

130. Paaijmans KP, Cator LJ, Thomas MB. Temperature-Dependent Pre-Bloodmeal Period and Temperature-Driven Asynchrony between Parasite Development and Mosquito Biting Rate Reduce Malaria Transmission Intensity. PLoS One. 2013;8(1):1-7. doi:10.1371/journal.pone.0055777

131. Paaijmans KP, Read AF, Thomas MB. Understanding the link between malaria risk and climate. Proc Natl Acad Sci U S A. 2009;106:13844-13849. doi:10.1073/pnas.0903423106

132. Parham PE, Michael E. Modeling the effects of weather and climate change on malaria transmission. Environ Health Perspect. 2010;118(5):620-626. doi:10.1289/ehp.0901256

133. Patil AP, Okiro E a, Gething PW, et al. Defining the relationship between Plasmodium falciparum parasite rate and clinical disease: statistical models for disease burden estimation. Malar J. 2009;8:186. doi:10.1186/1475-2875-8-186

134. Pattanayak SK, Yasuoka J. Deforestation and malaria: Revisiting the human ecology perspective. People, Heal For A Glob Interdiscip Overv. 2005;(919):19pp. doi:10.4324/9781849771627

135. Peeters Grietens K, Xuan XN, Van Bortel W, et al. Low perception of malaria risk among the Raglai ethnic minority in south-central Vietnam: implications for forest malaria control. Malar J. 2010;9:23. doi:10.1186/1475-2875-9-23

136. Pindolia DK, Garcia J, Wesolowski A., et al. Human movement data for malaria control and elimination strategic planning. Published online 2012:1-17. doi:10.1186/1475-2875-11-205

137. Pindolia DK, Garcia AJ, Wesolowski A, et al. Human movement data for malaria control and elimination strategic planning. Malar J. 2012;11(1):205. doi:10.1186/1475-2875-11-205

138. Qi Q, Guerra C a, Moyes CL, et al. The effects of urbanization on global Plasmodium vivax malaria transmission. Malar J. 2012;11(1):403. doi:10.1186/1475-2875-11-403

139. Raiesi A, Nikpour F, Ansari-Moghaddam A, et al. Baseline results of the first malaria indicator survey in Iran at the health facility level. Malar J. 2011;10:319. doi:10.1186/1475-2875-10-319

140. Raso G, Schur N, Utzinger J, et al. Mapping malaria risk among children in Côte d'Ivoire using Bayesian geo-statistical models. Malar J. 2012;11:160. doi:10.1186/1475-2875-11-160

141. Reid HL, Haque U, Roy S, Islam N, Clements AC. Characterizing the spatial and temporal variation of malaria incidence in Bangladesh, 2007. Malar J. 2012;11(1):170. doi:10.1186/1475-2875-11-170

142. Reiner RC, Perkins TA, Barker CM, et al. A systematic review of mathematical models of mosquito-borne pathogen transmission: 1970-2010. J R Soc Interface. 2013;10:20120921. doi:10.1098/rsif.2012.0921

143. Resseguier N, Machault V, Ollivier L, et al. Determinants of compliance with malaria chemoprophylaxis among French soldiers during missions in inter-tropical

Africa. Malar J. 2010;9:41. doi:10.1186/1475-2875-9-41

144. Rob Marchant Cassian Mumbi1 SB, Yamagata T. Review Paper The Indian Ocean dipole – the unsung driver of climatic variability in East Africa. Afr J Ecol. 2006;45:4–16.

145. Robert V, Trape JF, Rogier C. Malaria parasites: Elimination is not eradication. Clin Microbiol Infect. 2011;17:1597-1599. doi:10.1111/j.1469-0691.2011.03657.

146. Roca-Feltrer A, Carneiro I, Armstrong Schellenberg JRM. Estimates of the burden of malaria morbidity in Africa in children under the age of 5 years. Trop Med Int Health. 2008;13(6):771-783. doi:10.1111/j.1365-3156.2008.02076.

147. Russell TL, Lwetoijera DW, Maliti D, et al. Impact of promoting longer-lasting insecticide treatment of bed nets upon malaria transmission in a rural Tanzanian setting with pre-existing high coverage of untreated nets. Malar J. 2010;9:187. doi:10.1186/1475-2875-9-187

148. Sainz-Elipe S, Latorre JM, Escosa R, et al. Malaria resurgence risk in southern Europe: climate assessment in an historically endemic area of rice fields at the Mediterranean shore of Spain. Malar J. 2010;9:221. doi:10.1186/1475-2875-9-221

149. Santelli AC, Ribeiro I, Daher A, et al. Effect of artesunate-mefloquine fixed-dose combination in malaria transmission in amazon basin communities. Malar J. 2012;11:286. doi:10.1186/1475-2875-11-286

150. Saxena R, Nagpal BN, Srivastava A, Gupta SK, Dash a P. Application of spatial technology in malaria research & control: some new insights. Indian J Med Res. 2009;130(August):125-132.

151. Shaman J, Lipsitch M. Fostering Advance in Interdisciplinary Climate Science Sackler Colloquium: The El Nino-Southern Oscillation (ENSO)-pandemic Influenza connection: Coincident or causal? Proc Natl Acad Sci. Published online 2012:1-3. doi:10.1073/pnas.1107485109

152. Sinka ME, Bangs MJ, Manguin S, et al. A global map of dominant malaria vectors. Parasit Vectors. 2012;5(1):69. doi:10.1186/1756-3305-5-69

153. Siri JG, Lindblade K a, Rosen DH, et al. Quantitative urban classification for malaria epidemiology in sub-Saharan Africa. Malar J. 2008;7:34. doi:10.1186/1475-2875-7-34

154. Smith DL, Battle KE, Hay SI, Barker CM, Scott TW, McKenzie FE. Ross, Macdonald, and a theory for the dynamics and control of mosquito-transmitted pathogens. PLoS Pathog. 2012;8(4). doi:10.1371/journal.ppat.1002588

155. Smith DL, Drakeley CJ, Chiyaka C, Hay SI. A quantitative analysis of transmission efficiency versus intensity for malaria. Nat Commun. 2010;1(8):108. doi:10.1038/ncomms1107

156. Smith DL, McKenzie FE, Snow RW, Hay SI. Revisiting the basic reproductive number for malaria and its implications for malaria control. PLoS Biol. 2007;5(3):0531-0542. doi:10.1371/journal.pbio.0050042

157. Snow RW, Guerra CA, Noor AM, Myint HY, Simon I. Europe PMC Funders Group The global distribution of clinical episodes of Plasmodium falciparum malaria. 2011;434(7030):214-217. doi:10.1038/nature03342.The

158. Teklehaimanot HD, Lipsitch M, Teklehaimanot A, Schwartz J. Weather-based prediction of Plasmodium falciparum malaria in epidemic-prone regions of Ethiopia I. Patterns of lagged weather effects reflect biological mechanisms. Malar J. 2004;3:41. doi:10.1186/1475-2875-3-41

159. Teklehaimanot HD, Schwartz J, Teklehaimanot A, Lipsitch M. Weather-based prediction of Plasmodium falciparum malaria in epidemic-prone regions of Ethiopia II. Weather-based prediction systems perform comparably to early detection systems in identifying times for interventions. Malar J. 2004;3:44. doi:10.1186/1475-2875-3-44

160. Thenkabail, P. S., Gamage, M. S. D. N. and Smakhtin VU. The Use of Remote Sensing Data for Drought Assessment and Monitoring in Southwest Asia.; 2004.

161. Tikar SN, Mendki MJ, Sharma a K, et al. Resistance status of the malaria vector mosquitoes, Anopheles stephensi and Anopheles subpictus towards adulticides and larvicides in arid and semi-arid areas of India. J Insect Sci. 2011;11(85):85. doi:10.1673/031.011.8501

162. Torr SJ, Della Torre A, Calzetta M, Constantini C, Vale GA. Towards a fuller understanding of mosquito behaviour: use of electrocuting grids to compare the odour- orientated responses of. Med Vet Entomol. Published online 2008:93-108.

163. van der Hoek W, Konradsen F, Perera D, Amerasinghe PH, Amerasinghe FP. Correlation between rainfall and malaria in the dry zone of Sri Lanka. Ann Trop Med Parasitol. 1997;91(8):945-949. http://www.ncbi.nlm.nih.gov/pubmed/9579215

164. Van Genderen PJJ, Van Thiel PP a M, Mulder PGH, Overbosch D. Trends in knowledge, attitudes, and practices of travel risk groups toward prevention of hepatitis A: Results from the Dutch Schiphol Airport Survey 2002 to 2009. J Travel Med. 2012;19:35-43. doi:10.1111/j.1708-8305.2011.00578.x

165. Vittor AY, Pan W, Gilman RH, et al. Linking deforestation to malaria in the Amazon: Characterization of the breeding habitat of the principal malaria vector, Anopheles darlingi. Am J Trop Med Hyg. 2009;81(August 2001):5-12.

166. Wallinga J, van Boven M, Lipsitch M. Optimizing infectious disease interventions during an emerging epidemic. Proc Natl Acad Sci U S A. 2010;107(2):923-928. doi:10.1073/pnas.0908491107

167. Whitman TJ, Coyne PE, Magill AJ, et al. An outbreak of Plasmodium falciparum malaria in U.S. marines deployed to Liberia. Am J Trop Med Hyg. 2010;83(2):258-265. doi:10.4269/ajtmh.2010.09-0774

168. Woyessa A, Deressa W, Ali A, Lindtjørn B. Prevalence of malaria infection in Butajira area, south-central Ethiopia. Malar J. 2012;11:84. doi:10.1186/1475-2875-11-84

169. Yé Y, Hoshen M, Kyobutungi C, Louis VR, Sauerborn R. Local scale prediction

of plasmodium falciparum malaria transmission in an endemic region using temperature and rainfall. Glob Health Action. 2009;2:1-14. doi:10.3402/gha.v2i0.1923

170. Yé Y, Kyobutungi C, Louis VR, Sauerborn R. Micro-epidemiology of Plasmodium falciparum malaria: Is there any difference in transmission risk between neighbouring villages? Malar J. 2007;6:46. doi:10.1186/1475-2875-6-46

171. Zhang Y, Liu Q-Y, Luan R-S, et al. Spatial-temporal analysis of malaria and the effect of environmental factors on its incidence in Yongcheng, China, 2006–2010. BMC Public Health. 2012;12:544. doi:10.1186/1471-2458-12-544

172. Zhou G, Munga S, Minakawa N, Githeko AK, Yan G. Spatial relationship between adult malaria vector abundance and environmental factors in western Kenya highlands. Am J Trop Med Hyg. 2007;77(1):29-35.

Appendix E – Model Input Data Sources

Data Source	Parameter(s)	Resolution	Short Description
NOAA Global Forecast System (GFS)	Temperature (K) Wind Speed/Direction (m/s, Knots), only in testing Relative Humidity (%) Soil Moisture (%) (0-10 cm below ground Daily summed precipitation (mm)	0.5 and 1-deg data. (0.5 deg available for Aug 2013)	Best available operational analysis for the 2013 Chad case. NOAA National Center for Environmental Prediction's operational Global Forecast System (GFS). Available through NOAA servers and web servers at the Center for Ocean-Land-Atmosphere Studies (COLA) located at George Mason University. Fields downloaded include temperature, horizontal (u- and v-component) winds, soil moisture, precipitation, and relative humidity. Analyses and forecasts available 2-4X/day at 0.5-1-deg resolution.
European Center for Medium Range Weather Prediction Interim Reanalysis (ERA)	Soil Moisture (%) (0-7 cm below ground) Soil Moisture (%) (0-7 cm below ground)	0.75-deg 0.75-deg	Atmospheric reanalysis produced by the European Centre for Medium-Range Weather Forecasts (ECMWF). Used for soil moisture. 4X/day values downloaded and averaged. Global fields were retrieved and tailored to region of interest.
NOAA CPC African Rainfall Climatology, Version 2 (ARC2)	Daily summed precipitation accumulation (mm)	0.1-deg	This data is a result of a project to create a satellite-estimated precipitation climatology over the Africa domain. This method uses 3-hourly GPI and GTS data, exclusively. For creation of the climatological GPI, 3-hourly Meteosat data was obtained directly from Eumetsat's archived data group, while daily-updating products use 3-hourly data pulled from NOAA's Meteosat data feed. Data is available through NOAA CPC ftp site (binary downloads) and Columbia University's International Research Institute for Climate and Society
North American Land Data Assimilation System (NLDAS)	Daily summed precipitation (mm)	0.125-deg	NASA-led land data assimilation data set, which includes 0.125-deg, hourly **precipitation** accumulation over the Continental U.S.
NASA MERRA Renalysis	Temperature (K) Wind Speed/Direction (m/s, Knots), only in testing		Global, NASA based reanalysis using the GEOS-5 Global Circulation Model. Resolution is .6 deg in longitude and .5 deg in latitude. This data set was also used to produce seasonal climatologies covering 30 years.

	Relative Humidity (%) Daily summed precipitation (mm)		
NOAA-CIRES 20th Century Reanalysis			For analysis of 40-year seasonal mean monthly temperatures, cloud cover, relative humidity for Chad case
NOAA CPC Unified Precipitation			Monthly-averaged fields used to compute 30-year averages to obtain a regional climatology of cloud cover and temperature changes expected from season-to-season. This precipitation data set was used for the Chad and Liberia cases.
Gridded Population of the World (GPW)	Human Population		Available through NASA's Socioeconomic Data and Applications Center (SEDAC). Estimates every 5 years projected out to 2015.
Malaria Atlas Project EIR 2010 Map	EIR	5km	Entomological Inoculation Rate (EIR) of *Plasmodium falciparum* global map. EIR is the number of mosquito bites per night times the proportion of bites positive for sporozoites
Malaria Atlas Project Dominant Anopheles Species Map	Anopheles species	5km	A map with the dominant or combination of dominant vector species found in 5km pixels. Vector identification is used to calculate the RCM for a given region.
MODIS Spectral Image	EVI, NDVI	5km	NDVI (Normalized Difference Vegetation Index) is a vegetative index that measures an area's vegetative health or greenness. Photosynthetic vegetation will absorb solar radiation but strongly reflect near-infrared waves. NDVI = (NIR-Red)/(NIR + Red). EVI (Enhanced Vegetation Index), incorporates the blue spectral band to increase sensitivity to highly vegetative areas and reduce atmospheric influences. MODIS has a 250m resolution, which is aggregated to 5km.
Food and Agriculture Organization of the United Nations Animal Production and Health Division Global Livestock Production and Health Atlas	Livestock Population	5km	GLiPHA is an interactive, electronic atlas containing global animal production and health statistics. Sub-national statistics relating to the livestock sector can be viewed cartographically against a back-drop of selected maps, such as livestock densities, land-use, and topography. GLiPHA draws on data managed within the Global Livestock Impact Mapping (GLIMS), a global, sub-national data warehouse containing a multitude of livestock-sector related information.

International Association for Medical Assistance to Travellers World Malaria Risk Chart	Plasmodium species, Historical Transmission Risk	Country (some regional)	Geographical distribution of principal malaria vectors, *Plasmodium falciparum* drug-resistant areas, and guidelines for suppressive medication by country.
World Health Organization 2012 World Malaria Report	API	Sub-national	The World Malaria Report 2012 summarizes information received from 104 malaria-endemic countries and other sources and updates the 2011 report analyses. It highlights the progress made towards the global malaria targets set for 2015 and describes current challenges for global malaria control and elimination. Annual Parasite Incidence (API) is the confirmed cases during one year for population surveillance per 1000 people
Center for Disease Control Health Information for International Travel 2014	Plasmodium Species	Country (some regional)	CDC Health Information for International Travel (commonly called the Yellow Book) is published every two years by CDC as a reference for those who advise international travelers about health risks. The Yellow Book is written primarily for health professionals.
AVHRR Spectral Image	NDVI	5km	NDVI (Normalized Difference Vegetation Index) is a vegetative index that measures the vegetative health or greenness of an area. Photosynthetic vegetation will absorb solar radiation but strongly reflect near-infrared waves. NDVI = (NIR-Red)/(NIR + Red). AVHRR has a 1km resolution, which is aggregated to 5km.
Malaria Atlas Project Parasite Rate (*Pl. falciparum* and *Pl. vivax*)	Parasite Rate	5km	Global distribution of Parasite Rate (PR) for the two most prevalent Plasmodium species. PR is the proportion of the human population found to carry asexual blood-stage parasite

