# Applications in Climate and Society

## Impact of Increasing Temperatures on Malaria in the East African Highlands: A Systematic Review


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# Impact of Increasing Temperatures on Malaria in the East African Highlands: A Systematic Review

## Evidence Summary

*The included studies show that temperatures are increasing in the East African highlands. The studies also suggest that rising temperatures are strongly correlated with the rising cases of malaria transmission in humans.*

Historically, malaria has been absent from the East African highlands. However, recently the disease has made its way into the area and higher incidents of malaria are being reported from the highlands. The fact that highland inhabitants lack historical immunity against malaria makes them extremely vulnerable to the disease. This review assesses whether increasing malaria transmission is a consequence of rising temperatures due to climate change.

## Abstract

### Background

Malaria is a major public health concern for over half of the world caused by Plasmodium falciparum and transmitted by the transmitted by female *Anopheles* mosquito. It is known that both the mosquito and the pathogen are sensitive to temperature changes. Consequently, any fluctuations in temperatures caused by rising temperatures because of climate change are likely to affect the transmission of disease. Studies have also suggested that there are a rising number of malaria cases being reported from the East African highlands.

#### Objectives

To determine whether increasing malaria transmission is a consequence of rising temperatures due to climate change.

#### Search methods

Several online databases such as Science Direct, Web of Science, Med Line, Malaria Journal and Scopus were searched for relevant papers.

#### Selection criteria

The electronic databases were searched over the month of March 2015. The search strategy included both controlled vocabulary terms and keywords. The search was a focused keyword search using high-value phrases.

#### Data collection and analysis

Four review authors independently screened titles and abstracts found through electronic searches. If one of the authors considered the article potentially relevant, a full-text copy of the article was downloaded for further consideration. All full-text copies were independently examined to determine whether or not they met the inclusion criteria. Disagreements were resolved by discussion between the authors during weekly update meetings.

**Main results**

Studying the effects of climate on the entomological parameters of malaria transmission should be the initial step to understanding possible impacts of changing environments on this disease (Chaves et al. 2010). With both nonparametric and parametric statistical analyses, Pascual et al. (2005) found evidence for a significant warming trend in many study sites in the East African Highlands. Regions bordering areas with high endemicity of malaria, where temperatures at present limit the geographic distribution of malaria will be at risk in a warmer climate (Patz et al. 2005). Mathematical models not only demonstrate that increasing temperatures increase potential risk of malaria (Patz and Lindsay 1999); they also demonstrate that at low temperatures, small increases in temperature have a disproportionate effect on increasing malaria transmission (Patz et al. 2005). In the highland *Debre Zeit* sector of central Ethiopia, for example, an association has been documented between increasing malaria prevalence and incidence with concomitant warming trends from 1968 to 1993 (Patz et al. 2005). Coupled mosquito-human model of malaria by Alonso (2011) determined a significant increase in number of malaria cases between 1970 and 1990, attributing a high number of these malarial cases to warming in the highlands of East Africa. The altitude at which these temperatures occur will of course vary according to latitude, but generally areas above 1000-1500 m are considered vulnerable (Patz and Lindsay 1999). Abeku et al.  2003) showed that the epidemics of 1988 and 1991-92 that respectively affected the highlands and highland-fringe area in Ethiopia have been strongly related to temperatures (Abeku et al. 2003). Significantly high minimum temperatures and abnormally low frequency of low minimum temperatures preceded these epidemics (Abeku et al. 2003). However, it is important to note that is some controversy as not all studies attribute warming temperatures to increased malaria transmission. Hay et al (2002) show that at four sites in the highlands of East Africa there has been very little change in any meteorological variables during the past century or during the period of reported malaria resurgences. They also demonstrated the control of malaria implemented since the large epidemics of the 1940s have failed recently because of a rise in antimalarial drug resistance.

**Authors' conclusions**

The majority of the studies show that the increasing transmission of malaria on the East African highlands is strongly related to the rising temperatures, which is a direct consequence of climate change.

# INTRODUCTION:

Malaria is a major public health concern for over half of the world (Figure 1) and is the leading cause of death causing an estimated 627 000 deaths in 2012 (Thomson 2014). The disease is the most prevalent in the African continent, with incidents also reported from parts of South-Asia, South America, Oceania and Mexico (Figure 1).

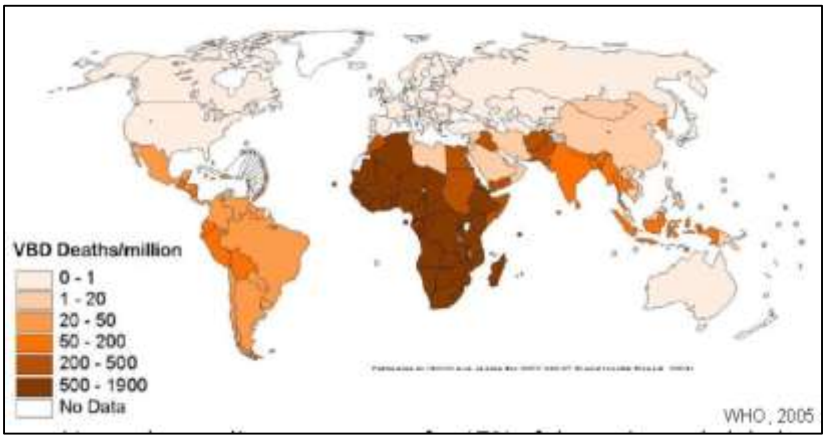


**Figure 1: Vector-borne disease mortality distribution, Source: Thomson 2014**

Malaria is caused by *Plasmodium falciparum* transmitted by female *Anopheles sp*. In Africa, the parasite is transmitted primarily by the *Anopheles gambiae* Giles complex and *Anopheles funestus* Giles (Minakawa 2002). The transmission of the disease is affected by a variety of factors (Githeko et al 2009; Shanks et al. 2002). This systematic review aims to study the effects of increasing temperature due to climate change on Malaria transmission in the East African Highlands.

**Why study the East African Highlands?**

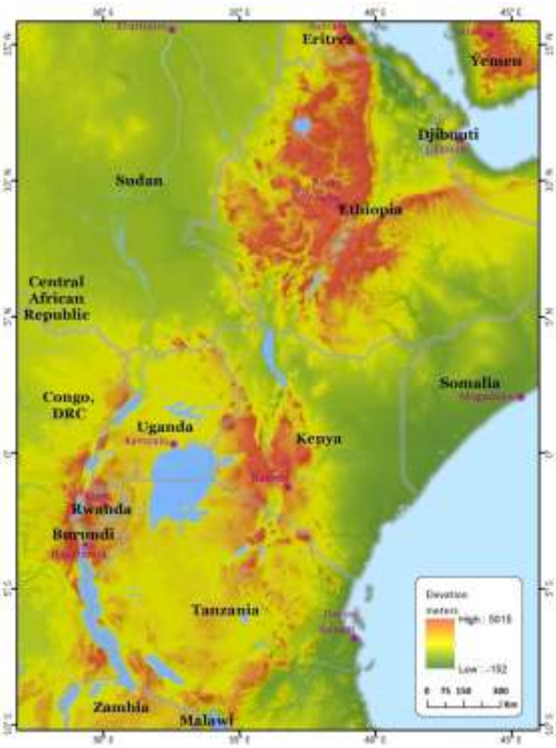


**Figure 2: Elevation in the East African Highlands**

The East African Highlands constitute a large area of land in East Arica consisting of Ethiopia, Kenya, Uganda, Rwanda, Burundi, Tanzania, and Mozambique. Defined as regions above 1,200 meters sea level and between 2°N and 10°S, the highlands comprise about 23% of East Africa. The topography of this region varies widely often within small geographic areas. Common landscapes include hilltops, steep and moderately sloping land, and narrow and wide flat plateaus and valley bottoms. Rivers and streams run along the valley bottoms in the valley ecosystem and swamps are a common feature. As a result of the varying of wind and rain patterns in the mountains, climate can change significantly within several kilometers (Pender and Ehui 2006). The Ethiopian highlands constitute 60% of all highlands in East Africa and the remaining area is distributed among the others (Hurni 1990).

# METHODOLOGY:

**Overview**

The methodology adopted in this paper mirrors the work of Cochrane. Cochrane is an independent, non-profit organization that conducts systematic reviews and publishes them in The Cochrane Library. The authors drew on the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2008), which describes in detail the process of preparing systematic reviews. Cochran's tool for assessing risk of bias was also used for this paper.

**Research questions and goals**

Research Null Hypothesis: Rising temperatures caused by climate change will not cause any change in malaria transmission in the East African highlands.

**Research questions**

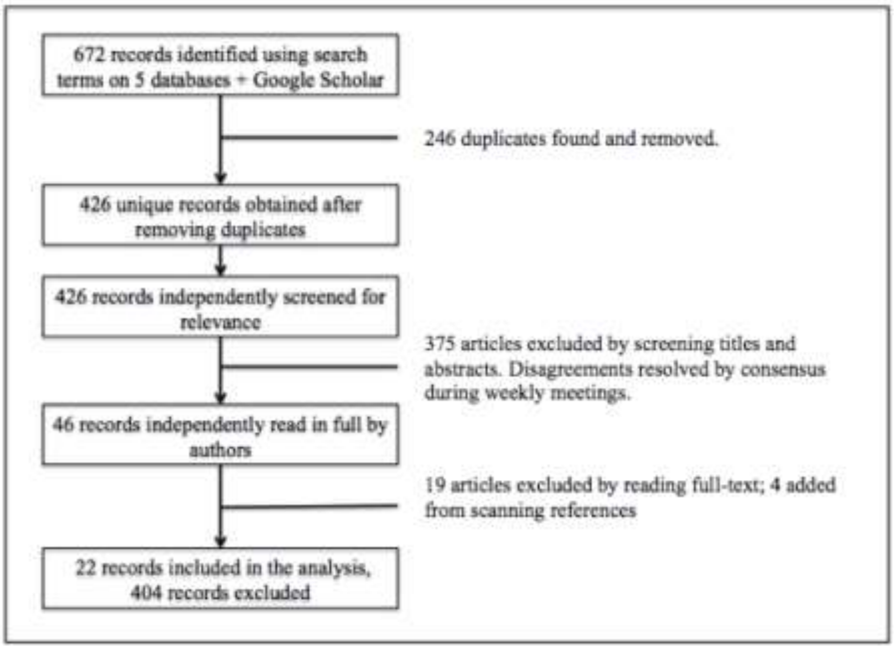
1. Why are the highlands particularly susceptible to a malaria emergency?
2. How does temperature affect malaria transmission?
3. How have temperatures impacted malaria transmissions in different regions of East African Highlands in the past?

**Prior expectation of results**

Although the authors of this paper did have a prior expectation for the relationship between climate change and malaria transmission in the highlands of East Africa, this did not affect the selection process, as studies that also discussed why climate might not be causing increased malaria transmission in the East African highlands were also included.

**Search methods for identification of studies**

The flow diagram below summarizes the study selection process used in this systematic review.



The following databases were searched for potential studies:

- ScienceDirect (360 articles)
- MEDLINE (24 articles)
- Web of Science (11 articles)
- Malaria Journal (256 articles)
- Scopus (21 articles)

The authors independently searched the electronic databases over the month of March 2015, compiling titles on a shared spreadsheet. The search strategy included both controlled vocabulary terms and keywords. One portion of the search was a focused keyword search using high-value phrases. A standardized search phrase was used throughout the search process:

*Malaria AND East* Africa* Highland* AND (temperature OR climate) AND transmission*

Owing to the fact that using only the term "East* Africa* Highland*" could possibly miss out important studies on individual questions, the authors explicitly added the following countries in the search phrase, replacing East* Africa* Highland*: Ethiopia, Kenya, Tanzania, Rwanda, Burundi, Uganda, and Madagascar.

**Inclusion Criteria**

**Types of studies:** The present review only included peer-reviewed original articles in English language. Thus, reviews, books, meta-analyses and conference abstracts were excluded.

**Target population:** Studies involving all years of age, ethnicities, nationalities, health conditions, and both genders were considered.

**Target countries:** Studies including the following countries: Ethiopia, Kenya, Tanzania, Rwanda, Burundi, Uganda, and Madagascar.

**Research factors:** Only studies in which temperature was considered as an independent climate factor affecting transmission, vector or pathogen populations were considered. This means that studies that considered temperature and precipitation together without independently considering the effect of temperature, or studies that did not analyze temperature's effect in the specific areas of Malaria transmission, vector or pathogen populations, were excluded.

**Searching other resources**:
The reference list of articles that was read in full was screened for more potential articles. The search terms were also entered into Google Scholar to extract more potential articles. The authors of some papers were also contacted through Research Gate, to allow extraction of additional data and information needed to carry out our analysis. However, none of the lead authors gave us any reply.

**Selection of studies**
All review authors independently screened titles and abstracts found through electronic searches. If one of the authors considered the article potentially relevant, a full-text copy of the article was downloaded for further consideration. In total we retrieved the full-text of 46 studies that were potentially relevant to the review. The authors then independently examined all full-text copies to determine whether or not they met our inclusion criteria. Disagreements were resolved by discussion and consensus between the authors during weekly update meetings.

**Exclusion of studies**
The present review strictly excluded studies that missed/ lacked any aspect of the inclusion criteria. The lack of time and resources was an important reason behind these strict criteria. Unlike most systematic review processes, this review was conceptualized and completed over a short period of two months as part of a Masters program at Columbia University.

**Data extraction and management**
The data was then extracted onto a standardized data extraction form, created on GoogleDocs. We compared extracted data and reconciled differences.

**Data synthesis**
Studies were grouped according to indicators such as study site, type of temperature information used (minimum, maximum, mean temperature), measure of malaria transmission (cases, hospital admission rate). The hypothesized direction of effect between climate change, temperature, and malaria differed between studies, with some studies expecting an increase in end point (malaria transmission) and others citing high uncertainty with the data and model results.

# DISCUSSION:

# The Highlands effect

**Why is malaria in highlands a potential disaster?**
Historically, due to low temperatures at higher altitudes, malaria has been naturally excluded from the East African highlands, where malaria transmission was mainly sporadic and unstable (Lindsay and Martens 1998). However, this is changing and rising incidents of the disease in East African highlands are being reported (Chaves et al. 2010; Heimeidan 2012; Shanks et al. 2002), indicating a change in the disease dynamics due to external factors.

Topography plays a significant role in malaria transmission because cooler temperatures slow the development of Anopheline vectors and the transmission of *Plasmodium* parasites. In contrast to the lowland region, where there is wide distribution of mosquito breeding areas due to poor water drainage; however, breeding havens in the topographical diverse and variable highlands are limited to the only the valley bottoms. This is because steep gradients in the hillsides stimulate efficient drainage. Suitability for mosquito breeding is also dependent on the actual shape of the highlands within smaller spatial scales. For example and depending on the variation in shape of a local valley, the risk of malaria can substantially decrease within just a few hundred meters from established breeding grounds (Mushinzimana et al. 2006).

Further, the fact that highland inhabitants lack immunity against the disease makes them extremely vulnerable to the disease. The region has the world's highest population growth rate (United National Development Fund in Himeidan and Kweka 2012), thereby exacerbating the disease vulnerability by its rapidly increasing human populations. This could potentially lead to an impending emergency situation, as the opening of the East African highlands to malaria would add many more deaths to the already staggering number of people who die each year due to malaria, primarily in sub-Saharan Africa (Sachs and Malaney 2002). Estimates by Bouma et al. (2011) suggest that 66% of the population in Ethiopia, Kenya and Tanzania live in the vulnerable altitude between 1000 and 2500 m. In light of this, it becomes absolutely necessary for global relief organizations and local governments to take notice of impending crises. This includes studying the effects of climate variables like temperature on malaria so as to develop a malaria epidemic early warning system in areas where communities are at risk of sudden increase in transmission due to slight changes in climatic factors.

# Temperature and Malaria

#### Temperature projections with climate change

With changing climate due to anthropogenic influences, global and regional temperatures are expected to rise. The earth has significantly warmed in the recent years — the temperatures in 2000-2005 were 0.7°C higher than those in the period 1850-1899 and are likely to warm further at a rate of 0.2°C per decade (IPCC 2007). Climate change is likely to lead to both latitudinal and altitudinal temperature increases (Afrane 2012). These rising temperatures will consequently affect the dynamics of the disease especially in the African continent

### Effect of temperature on malaria transmission

Of these, changes in the climatic parameters such as temperature and precipitation are likely to affect disease transmission potential by altering the vector's "biting rates, the duration of their gonotrophic cycles, their fecundity, and the survival and development of the immature mosquitoes and the adult" (Afrane 2012).

### Effect of temperature on development of vector larvae

Several studies (Koenraadt 2006 in Afrane et al 2012; Githeko et al 2009) have shown that the development of vector larvae is strongly impeded at low temperatures. The development of *A. gambiae* larvae stops below 16°C and temperatures below 14°C leads to their deaths.

### Effect of temperature on adult mosquito development and transmission

The rate at which the adult mosquitoes feed on human blood is also determined by ambient temperatures. Githeko et al. (2009) explain that the female mosquitoes feed on human blood every 4 days at 17˚C. With a temperature increase to 25°C, the mosquito feeds on blood at shorter intervals of 2 days (Githeko et al. 2009). This is because increased temperatures lead to accelerated digestion of the mosquito's blood meal (Afrane 2012). Consequently, this causes faster parasite sporogonic development in turn leading to increased disease transmission efficiency (Afrane 2005 In Afrane 2012). Further, a drop in temperature has been consistently shown to be associated with interruption of transmission in malaria (Abeku et al. 2004; Chaves et al 2010), and daily survival of adults reaches zero at around 40°C (Lindsay and Martens 1998).

### Effect of temperature on parasite development

Plasmodium, the malaria parasite, is also very sensitive to changes in temperature. The time taken by the parasite to reach maturity within the female mosquito is reduced several folds with very small increase in external temperatures (Githeko et al. 2009). Small increases in temperature near the lower limit for parasite and mosquito development would probably produce greater mosquito densities, higher biting rates and more rapid parasite development in the mosquito (Lindblade et al. 2000). The effect of temperature is greatest on transmission at lower temperatures (17-21°C); thereafter, the rate of reduction on the period of the development and maturity of the parasites is low (Githeko and Ndegwa 2001). Temperatures above 34°C generally have a negative impact on the survival of both vectors and parasites (Afrane 2012). According to Githeko et al. (2009), the threshold temperature for malaria transmission is 18°C mean annual temperature. Below this temperature malaria transmission is not possible as the vector dies even before the malaria parasite can mature and be transmitted.

**What do different studies say about the impact of temperature (due to climate change) on disease transmission?**

Studying the effects of climate on the entomological parameters of malaria transmission should be the initial step to understanding possible impacts of changing environments on this disease (Chaves et al. 2010). With both nonparametric and parametric statistical analyses, Pascual et al. (2005) found evidence for a significant warming trend in many study sites in the East African Highlands. Regions bordering areas with high endemicity of malaria, where temperatures at present limit the geographic distribution of malaria will be at risk in a warmer climate (Patz et al. 2005). Mathematical models not only demonstrate that increasing temperatures increase potential risk of malaria (Patz and Lindsay 1999); they also demonstrate that at low temperatures, small increases in temperature have a disproportionate effect on increasing malaria transmission (Patz et al. 2005). In the highland *Debre Zeit* sector of central Ethiopia, for example, an association has been documented between increasing malaria prevalence and incidence with concomitant warming trends from 1968 to 1993 (Patz et al. 2005). Coupled mosquito-human model of malaria by Alonso (2011) determined a significant increase in number of malaria cases between 1970 and 1990, attributing a high number of these malarial cases to warming in the highlands of East Africa. The altitude at which these temperatures occur will of course vary according to latitude, but generally areas above 1000-1500 m are considered vulnerable (Patz and Lindsay 1999). Abeku et al. (2003) showed that the epidemics of 1988 and 1991-92 that respectively affected the highlands and highland-fringe area in Ethiopia have been strongly related to temperatures (Abeku et al. 2003). Significantly high minimum temperatures and abnormally low frequency of low minimum temperatures preceded these epidemics (Abeku et al. 2003). However, it is important to note that is some controversy as not all studies attribute warming temperatures to increased malaria transmission. Hay et al (2002) show that at four sites in the highlands of East Africa there has been very little change in any meteorological variables during the past century or during the period of reported malaria resurgences. They also demonstrated the control of malaria implemented since the large epidemics of the 1940s have failed recently because of a rise in antimalarial drug resistance.

## RISK OF BIAS:

Systematic reviews are usually reserved for synthesizing information from clinical research. Therefore, considering this topic does not fit into the arena of clinical research, it was difficult to implement standard methods for assessing risk of bias on included studies. However, an adapted and abbreviated version of the Cochrane Collaboration’s tool for assessing risk of bias was used in order to evaluate included studies that contained an empirical process.

Some of the sources were not included because they did not contain an empirical process or an explanation of methods and data collection in the paper. These mainly consisted of book chapters, papers, and articles that aimed to synthesize information about or describe in theoretical/hypothetical terms the relationship between climatic variables and malarial transmission.

The following domains were excluded in the summary table: random sequence generation, allocation concealment, blinding of participants and personnel, and blinding of outcome assessment. These factors were irrelevant to this type of literature. Furthermore, it seemed that although adding an assessment of vector related data reliability would have been informative, because of the scope of our research question, which included malarial transmission and vector-pathogen population changes, the data was too diverse to compare across studies.

**Incomplete Outcome Data**

There was low-risk of incomplete outcome data in most studies. There was some uncertainty about outcome data in one study (Munikawa et al., 2002) because during the identification of specimens via the rDNA-polymerase chain reaction method, samples that could not be identified after three trials were marked as unknown, and there was no indication of what percentage of the sample was constituted by these unidentified specimens.

**Selective Outcome Reporting**

There was low-risk of selective reporting across all trials.

**Climate Information Reliability**

This domain was added to the risk of bias assessment because the use of climate information was a central element in the research question. Climate information inherently focuses on averaged values and is difficult to collect with local reliability. In general, studies were said to have low-risk of climate information reliability bias if data was collected at the same sight as the vector information was collected and a method of verifying the accuracy of the data was explicitly stated in the paper. Studies that used interpolated data from gridded data sets, reanalysis data, or monthly mean data were assigned a high-risk label because of the uncertainty of the fidelity of this data on shorter time scales (diurnal variations) and smaller spatial domains, which need to take topography variations into account.  A detailed break down of the risk of bias of climate information reliability can be found in Figure 4.

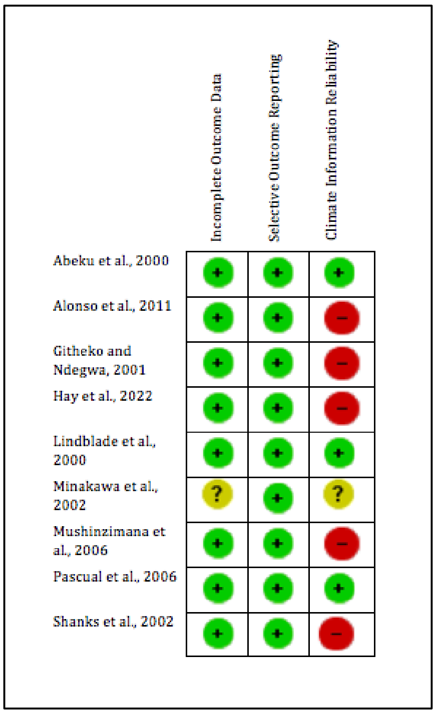



**Figure 3: Risk of bias summary: author's judgments about risk of bias items for included studies with empirical processes**

| | Risk of Bias Label | Evidence from Study | Author's assessment Explanation |
|---|---|---|---|
| Abeku et al., 2000 | Low-risk | "three thermometers were placed in each village, attached 2 m from ground." "We discarded all daily village temperature measurements for which the range was greater than the mean plus twice the standard deviation of the ranges." "Overall, 4.0% of daily village measurements of T[illegible] and 2.8% of dv measurements of T[illegible] were disregarded" | -reliable time scale (daily)<br>-collected from same location as vector information<br>-method of verification stated |
| Alonso et al., 2011 | High-risk | "we consider a local temperature time series generated by dovetailing the records from two local meteorological stations adjacent to the tea plantation" "we subdivided the monthly cumulative rainfall equally into daily values to estimate the amount of rainfall per day, since all our rates in the model equations are expressed per day" | -monthly mean data used |
| Githeko and Ndegwa, 2001 | High-risk | "maximum and minimum temperature data from January 1970-June 2000 for the grid 33.75E-39E, 2.8N-2.8S was downloaded and plotted to show long-term trends in anomalies and to detect association" [using NCARR Reanalysis data] "we chose a simple, feasible scenario where due to the creation of extra breeding sites (and therefore, an increase in the number of biting adult mosquitoes), the value of man-biting rates were doubled by rainfall." | -reanalysis data used<br>-gridded data set |
| Hay et al., 2002 | High-risk | "reliable data for diurnal temperature range spanned the 1950-1995 period" "meteorological data were obtained from a global 0.5x0.5 degree gridded data set of monthly terrestrial surface climate for the 1901-1995 period" | -gridded data set |
| Lindblade et al., 2000 | Low-risk | "three thermometers were placed in each village "We discarded all daily village temperature measurements for which the range was greater than the mean plus twice the standard deviation of the ranges." "Overall, 4.0% of daily | -reliable time scale (daily)<br>-collected from same location as vector information<br>-method of verification stated |
| Minakawa et al., 2002 | Unclear | "the temperature, rainfall, and evapotranspiration data were obtained from the ACT database with a spatial resolution of 0.05 degrees" | -unsure of the details of this dataset |
| Mushinzimana et al., 2006 | Low-risk | "Ikonos and Landsat Thematic Mapper 7 satellite images were acquired for a study area in Kakamega, western Kenya. The retrieved data from the remote sensors were compared to the ground results on aquatic habitats and land-use. The probability of finding aquatic habitats and habitats with Anopheles larvae were modeled base on digital elevation model and land-use types." | -collected from same location as vector information<br>-method of verification stated |
| Pascual et al., 2006 | High-risk | "the monthly temperature time series were extracted for the Climate Research Unit (CRU, Norwich, U.L.) global grid of 0.5 degree resolution (data set CRU TS 2.1). The four grid points chosen for the analysis respectively contain the following locations of interest" | -monthly mean data used<br>-gridded data set |
| Shanks et al., 2002 | High-risk | "Two meteorologic datasets were compiled. Point locality measurements of mean monthly temperature and monthly total rainfall (mm) were obtained from the Tea Research Foundation meteorologic station on the Kericho tea estates for the 1966-1995 period. Climate data were also obtained from a global 0.5 x 0.5 degree gridded dataset of monthly terrestrial surface climate for the 1966-1995 period (CRU)" | -gridded data set<br>-monthly mean data used |

**Figure 4: Explanation of Climate Information Reliability Risk of Bias**

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## Excluded Studies

| **References** | **Reason for Exclusion** |
|---|---|
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