Is Climate Change Affecting Vector-borne Disease Transmission?

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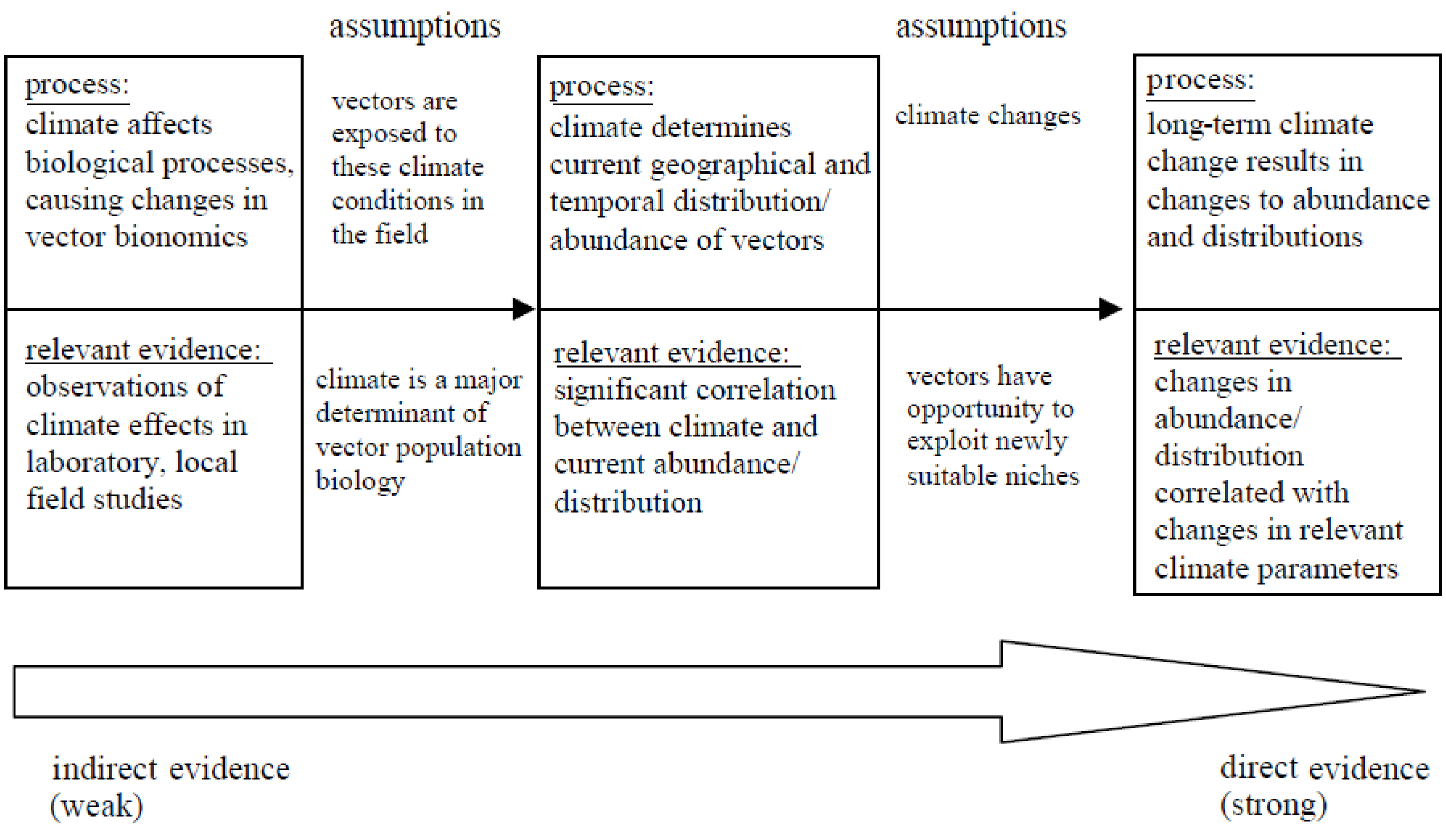
Why focus on vector-borne diseases?

- Many wide-spread and prevalent diseases are transmitted (vectored) by insects or ticks
- Several such diseases have undergone dramatic range extensions recently
- Vector-borne diseases are hypothesized to be especially sensitive to climate change, due to the relationship between temperature, precipitation, and vector abundance
- Models suggest potential dramatic increases in certain diseases, especially malaria

In principle, climate change may affect vector-borne diseases by:

- Increasing the duration of the transmission season
- Allowing transmission earlier in the season
- Allowing diseases to spread to new areas/populations as habitat becomes climactically suitable for vectors and (if needed) reservoir hosts

What kind of evidence supports a claim that climate change has influenced a vector-borne disease?



Kovats *et. al.* *Phil. Trans. R. Soc. Lond.* B (2001) **356**, 1057–1068

Factors that limit the ability to ascribe changes in disease frequency to climate change:

- Detailed studies of the historical limits to the range of vectors may be lacking
- Disease transmission may correspond to areas where vectors are abundant, and not to the margins of their range
- Vector-borne diseases are influenced (often strongly) by:
  - changes in land use (e.g. deforestation)
  - movement of human populations
  - implementation or collapse of abatement measures (vector control, access to medical services)
  - insecticide and drug resistance
  - surveillance, etc.

Claims that a disease has changed it's distribution due to climate change must exclude, as far as possible, other explanations for the change

The following diseases will be discussed, because they have been claimed to pose a great risk due to climate change (malaria), or because they have undergone recent range expansions:

- Malaria
- Chikungunya Fever/Dengue Fever

Malaria (2010)
~154-289 x 10^6 infections
~660,000 deaths

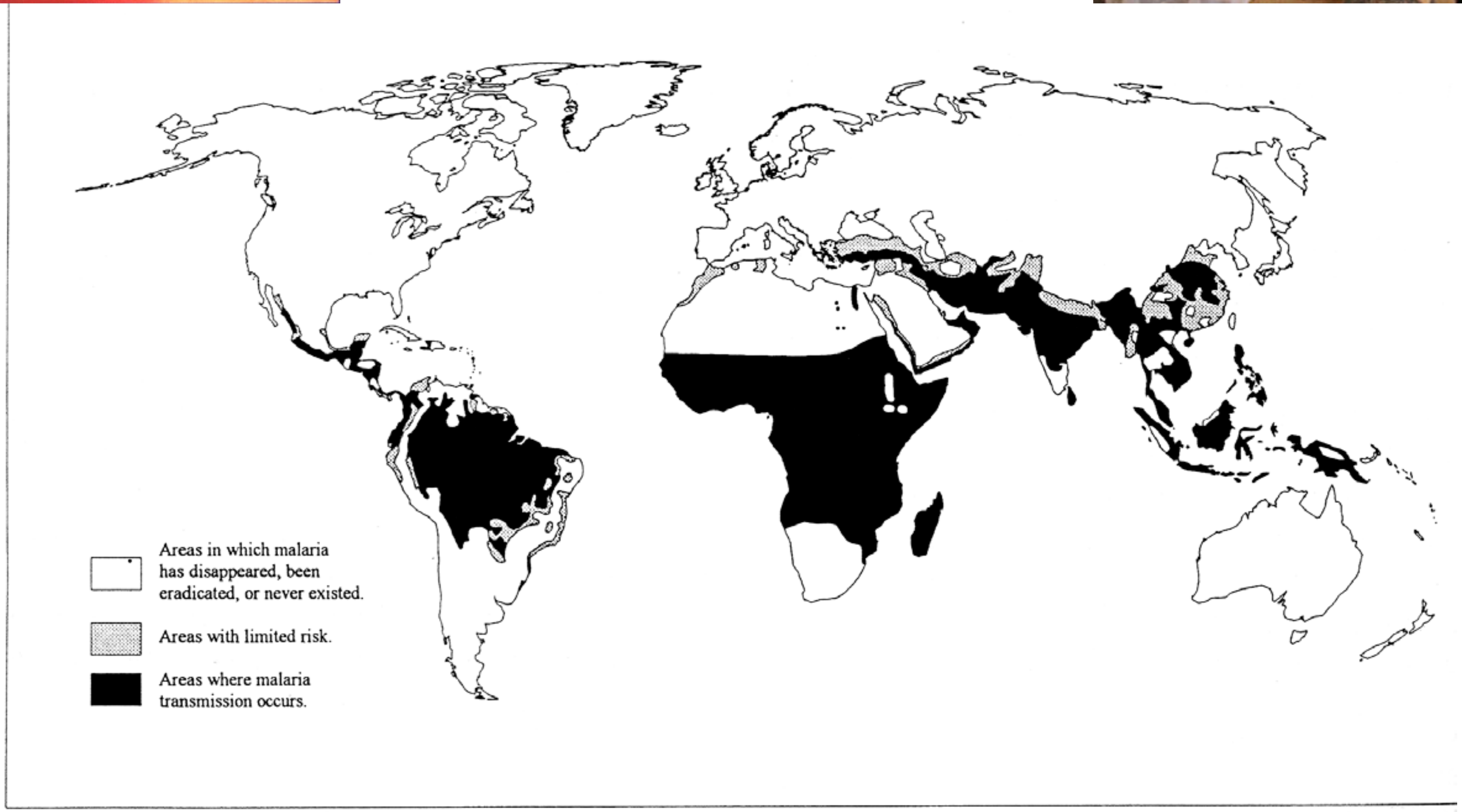


Figure 7.1. Worldwide distribution of human malaria (courtesy US Centers for Disease Control and Prevention).

Battle of the Models

Early models suggested climate change will drive vast expansions of areas at risk of malaria transmission, generating much attention in the scientific and popular media
Later models suggest very different outcomes

Climate-based models: identify climate features (usually just temperature and precipitation) currently associated with malaria transmission, generate risk maps based on predicted presence of similar climate features in new areas

Biology-based models: seek to account for temperature/climate effects on biological processes (development time, survivorship etc) and simulate transmission potential in relation to climate features

R_0 = theoretical number of new disease cases generated by introducing one infected person into a non-immune population

For a disease to be maintained in a population, R_0 must be ≥ 1

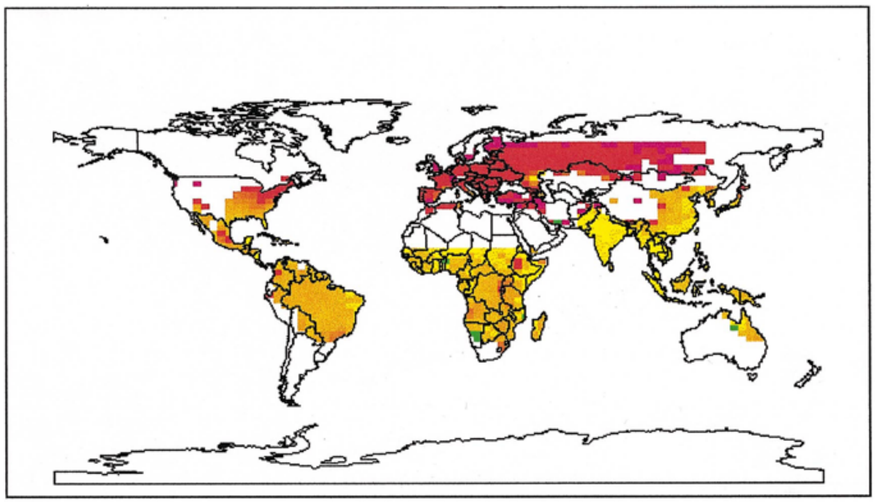
Biological models seek to predict R_0 under various climactic conditions, generate maps of expected increase or decrease in R_0

R = actual number of cases generated per infected patient

Influenced by immune status of the population, duration of time patient remains infectious, etc so changes with infection frequency

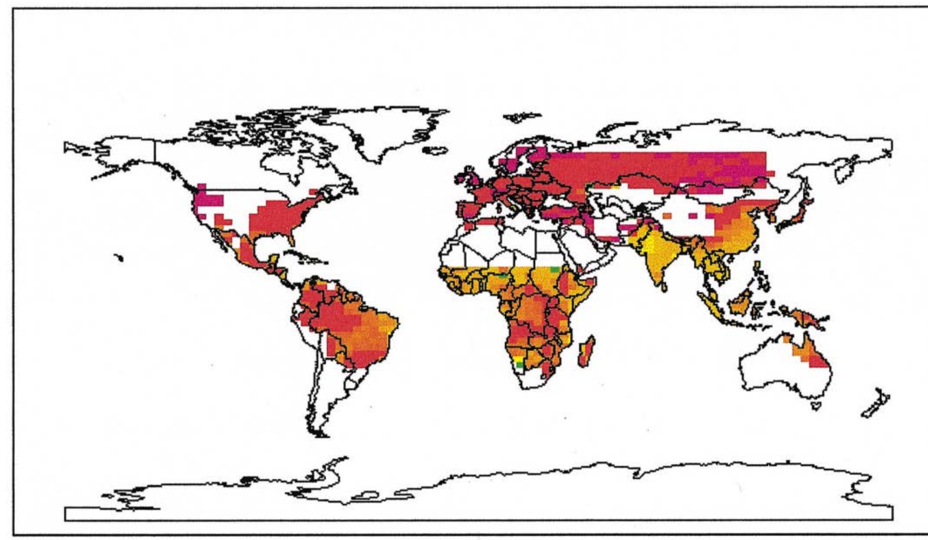
Harder to model but more realistic

Martens et al 1999 risk map: malaria (*P. falciparum + P. vivax*) increase in transmission potential under the HadCM2 and HadCM3 global climate models

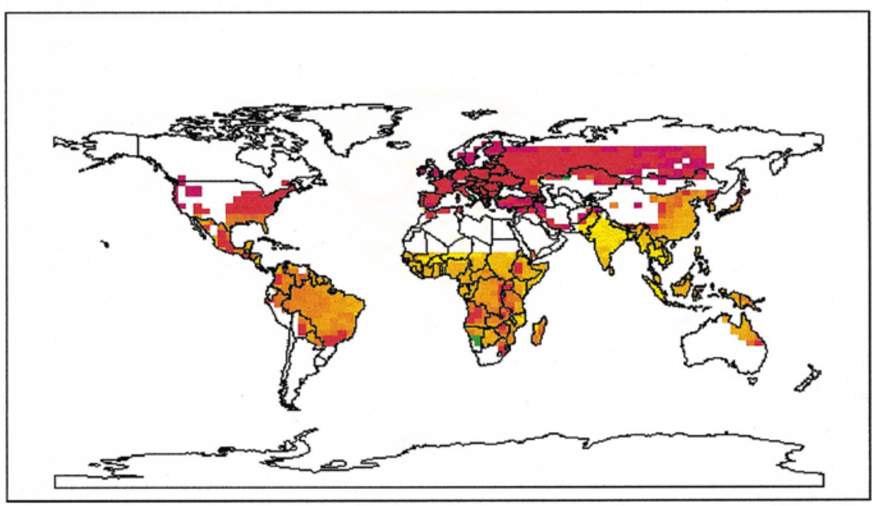


2020

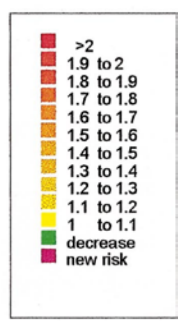
a)



2080

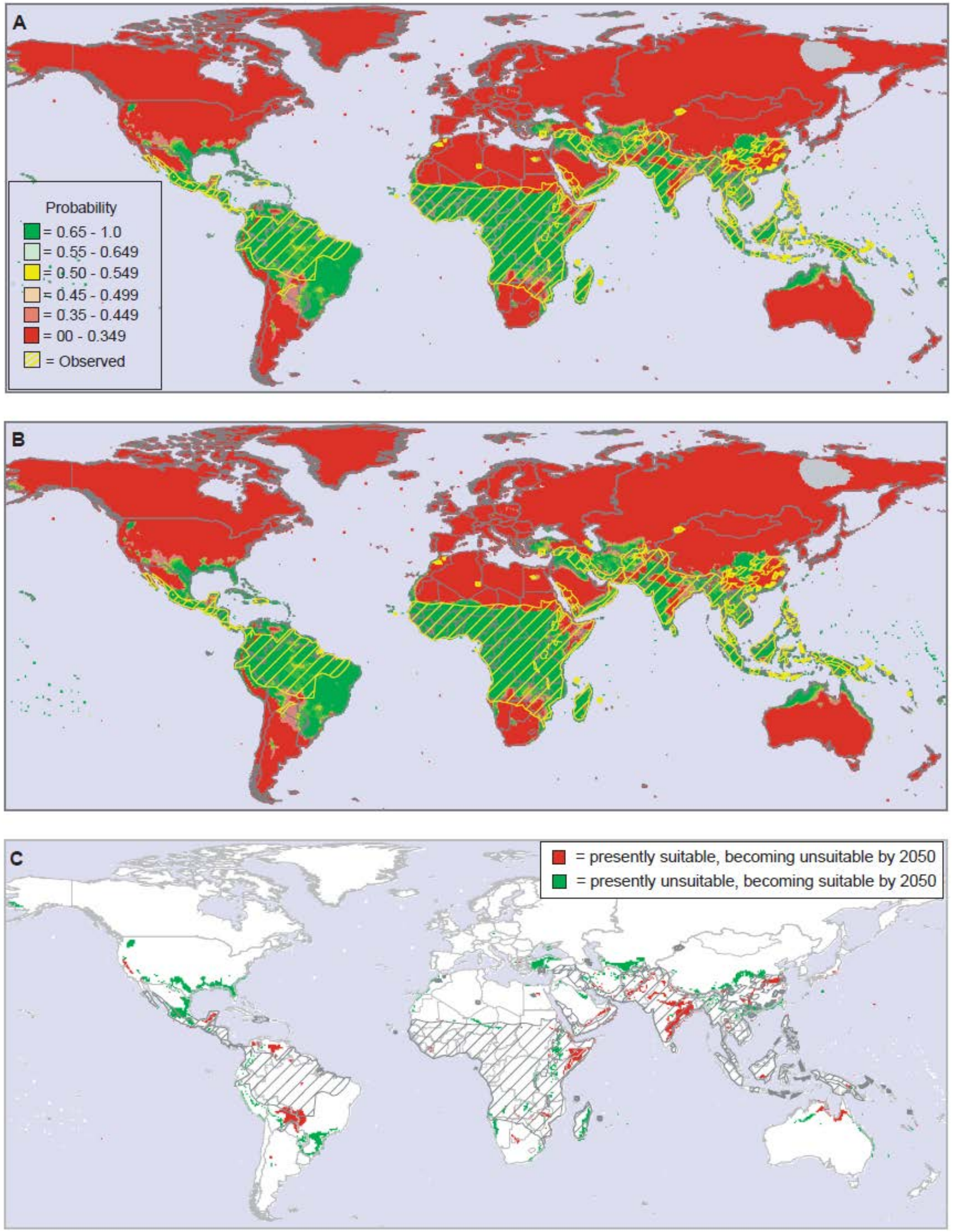


2050



Predicted 2080 increase (millions) in at-risk population:

	P. falcip.	*P. vivax*
HadCM2	260-320	100-200
HadCM3	300	150



Rodgers and Randolf (2000, Science 289) criticized earlier models for counting areas with R_0 < 1 as "increased transmission".

Developed R_0 based model that included only areas where $R_0 \geq 1$.

Very little change overall from present day

Net increase of 23 million people at risk under HadCM2 "medium-high" scenario, decrease of 25 million people under Had CM2 "high" scenario.

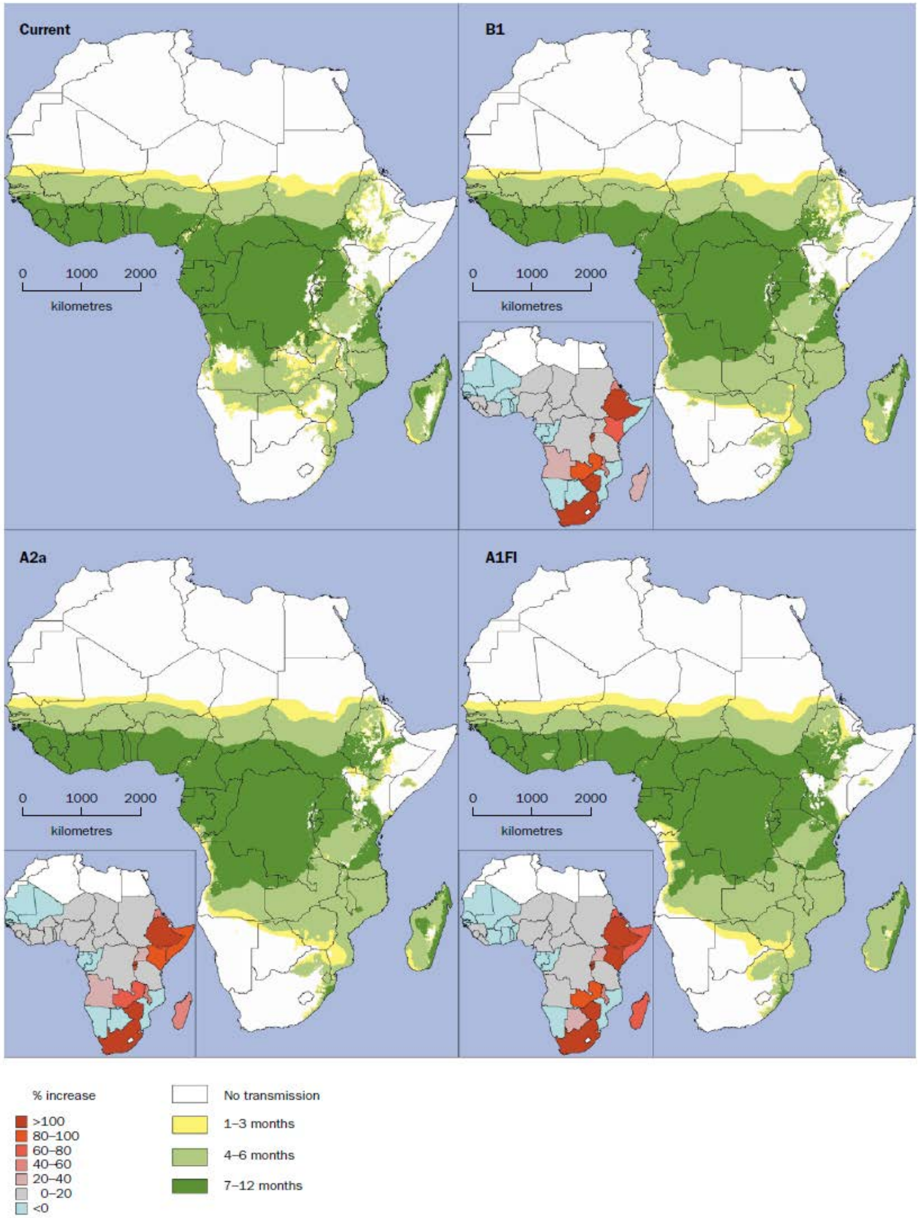


Figure 2: **Estimated number of months suitable for *Plasmodium falciparum* malaria transmission, and change in person-months of exposure by country at present and by 2100 using three HadCM3 scenarios (B1, A2a, A1FI)**
The scenarios project overall potential increases in person-months exposure by 2100 to be 16% (B1), 23% (A2a), and 28% (A1FI), respectively (constant population assumed).

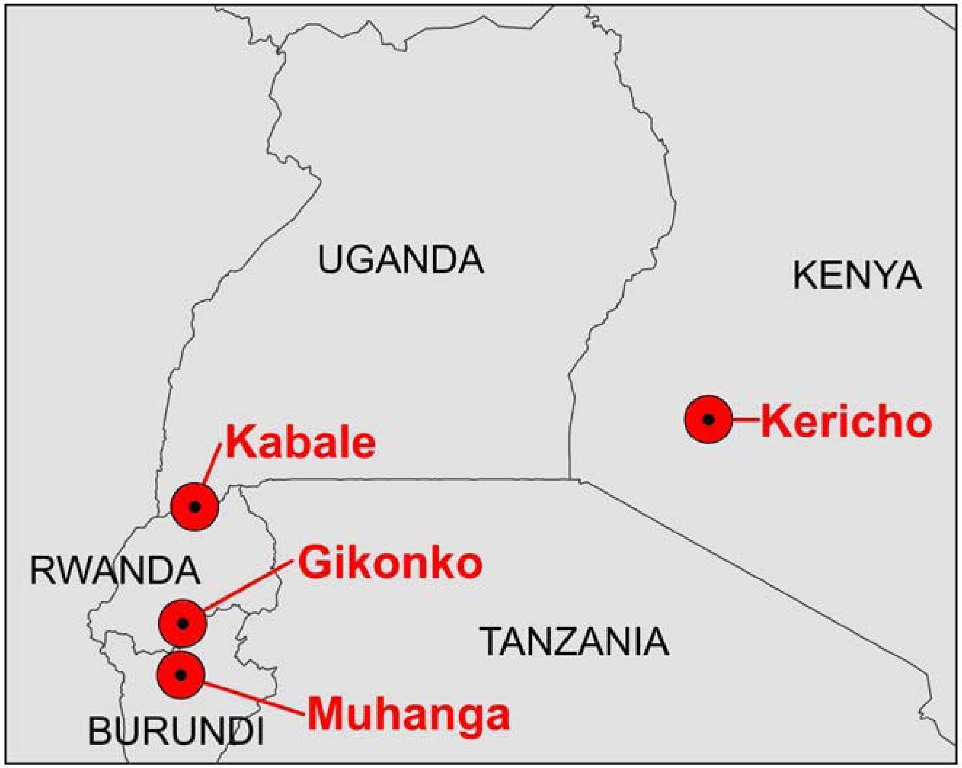
Tanser et al (2003) modeled duration of the transmission season (in moths) using the HadCM3 global climate model and 3 different rates of CO_2 increase.

Model based on temperature and precipitation, not R_0

Predicts increase in transmission season, especially in highlands of East Africa.

Malaria in Highland East Africa

Numerous studies of malaria incidence, meteorological data, especially at highland tea plantations (have on-plantation hospitals, keep good meterological records) (Stern et al 2011 PLoS One 6(9): e24524; Hay et al 2002 Nature 415:905-909)



But no correlation between temperature and malaria outbreaks, and malaria has returned to a low prevalence despite high temperatures.

Table 4. Robust Trend Tests for Malaria Series.

			t_{DAN} for a test of size				
Sample Period	**Slope β_{2i}**	**Change in Malaria Cases**	**1%**	**2.5%**	**5%**	**10%**	***J***
Unadjusted Data							
1966:1-1995:1	0.0810	29	**2.5660**	**3.2274**	**3.7938**	**4.2862**	0.3418
1966:1-2006:6	0.0834	40	2.4009	**2.8119**	**3.1433**	**3.4190**	0.2355
1966:1-2010:5	0.0436	23	0.9523	1.2006	1.4135	**1.5989**	0.3452
Deseasonalized Data							
1966:1-1995:1	0.0806	29	2.0569	**2.7454**	**3.3650**	**3.9238**	0.4303
1966:1-2006:6	0.0839	41	2.2154	**2.6583**	**3.0227**	**3.3305**	0.2716
1966:1-2010:5	0.0440	24	0.8577	1.1158	1.3432	**1.5450**	0.3921

Note: Significant t-statistics are marked in bold. t_{DAN} test is for significance of the trend and J is a test for a unit root in the residuals of the trend regression.
doi:10.1371/journal.pone.0024524.t004

Malaria outbreaks coincided with periods of hiring large numbers of workers, many of whom come from lowland areas with high malaria prevalence.

Outbreaks are associated with movement of people, not changes in temperature.

Malaria on the Rise as East African Climate Heats Up

In East Africa, warming as a result of climate change is paving the way for the spread of malaria

By Paul R. Epstein and Dan Ferber | April 1, 2011 | 1

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Editor's Note: The following is an excerpt from Changing Planet, Changing Health: How the Climate Crisis Threatens Our Health and What We Can Do about It *(University of California Press, April 4, 2011).*

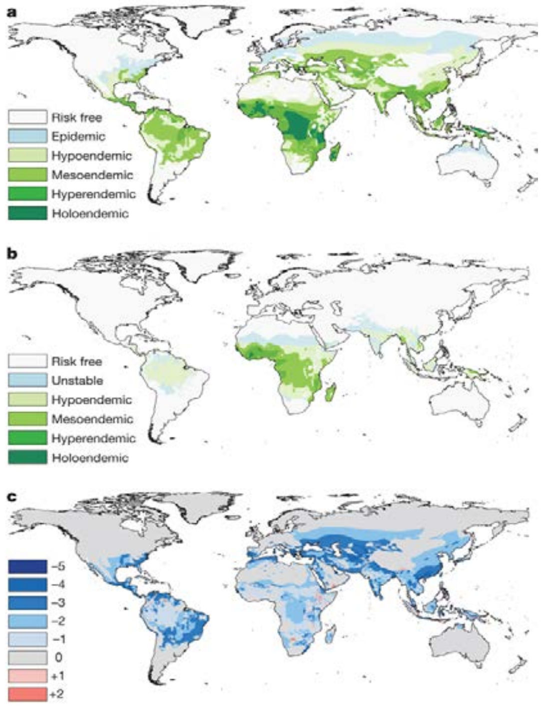
Elena Githeko was normally energetic and chatty. But on a Tuesday morning in 2003, Elena's mother, Anne Mwangi, found her daughter quiet and listless, her forehead warm with fever. Anne thought it was just the flu, so she did what any concerned mother would do: she stayed home from work to care for her daughter.

MALARIA MOVES: The mosquitoes that carry malaria are expanding their range as a result of warming average temperatures in East Africa. *Image: © iStockphoto.com / Henrik Larsson*

Not an *Anopheles*
Not a malaria vector!

Big Picture: malaria transmission (measured as R_0) has decreased significantly since 1900 despite increased temperatures

Changing global malaria endemicity since 1900.



PW Gething *et al. Nature* **465**, 342-345 (2010) doi:10.1038/nature09098

nature

ECOLOGY LETTERS

Ecology Letters, (2013) **16**: 22–30 doi: 10.1111/ele.12015

Optimal temperature for malaria transmission is dramatically lower than previously predicted

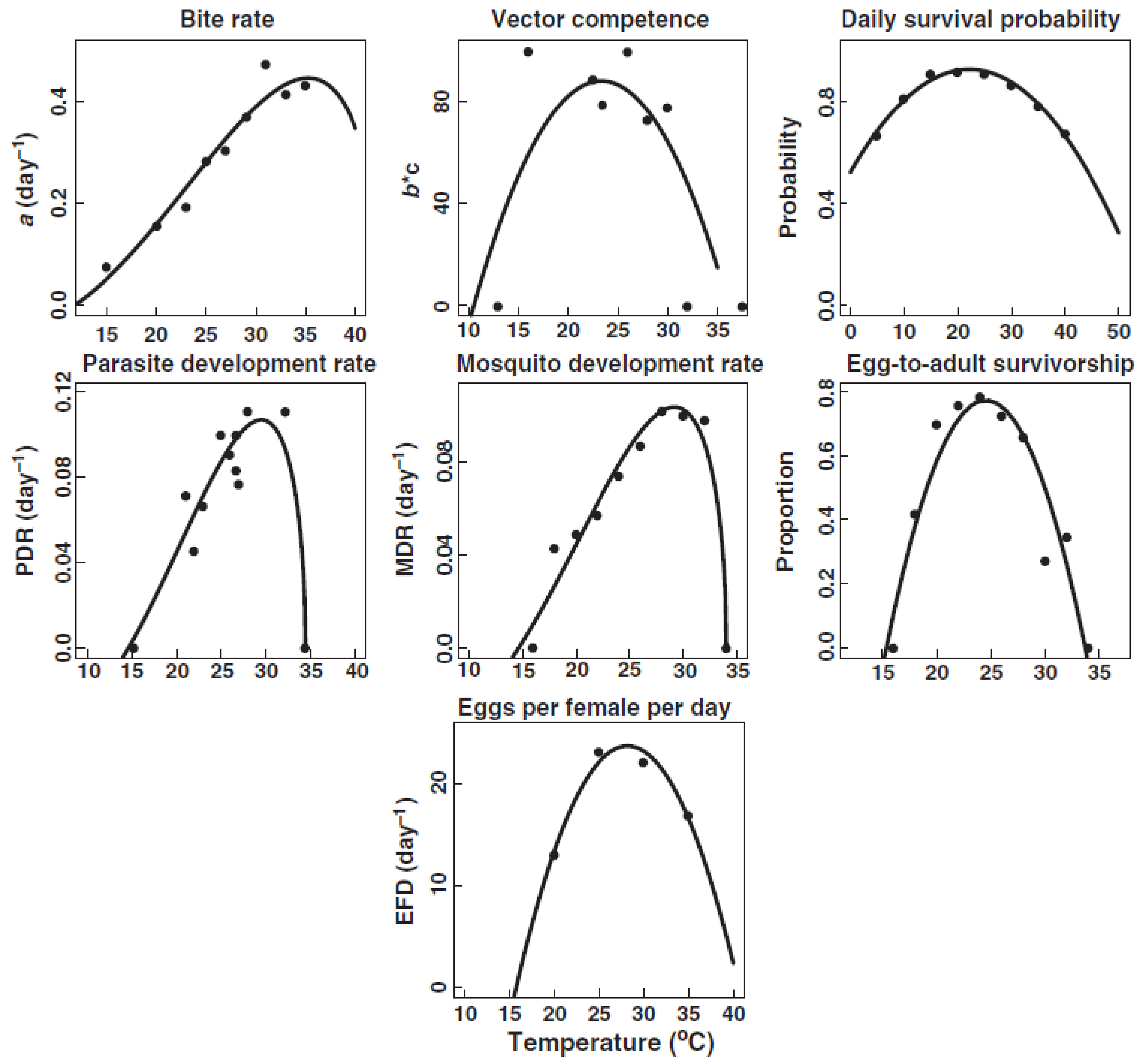
Erin A. Mordecai,[1,*] Krijn P. Paaijmans,[2] Leah R. Johnson,[3] Christian Balzer,[1,†] Tal Ben-Horin,[4] Emilyde Moor,[5] Amy McNally,[5] Samraat Pawar,[6] Sadie J. Ryan,[7] Thomas C. Smith[1] and Kevin D. Lafferty[1,8]

$$R_0 = \left(\frac{Ma^2 bce^{-\mu EIP}}{Nr\mu} \right)^{1/2}$$

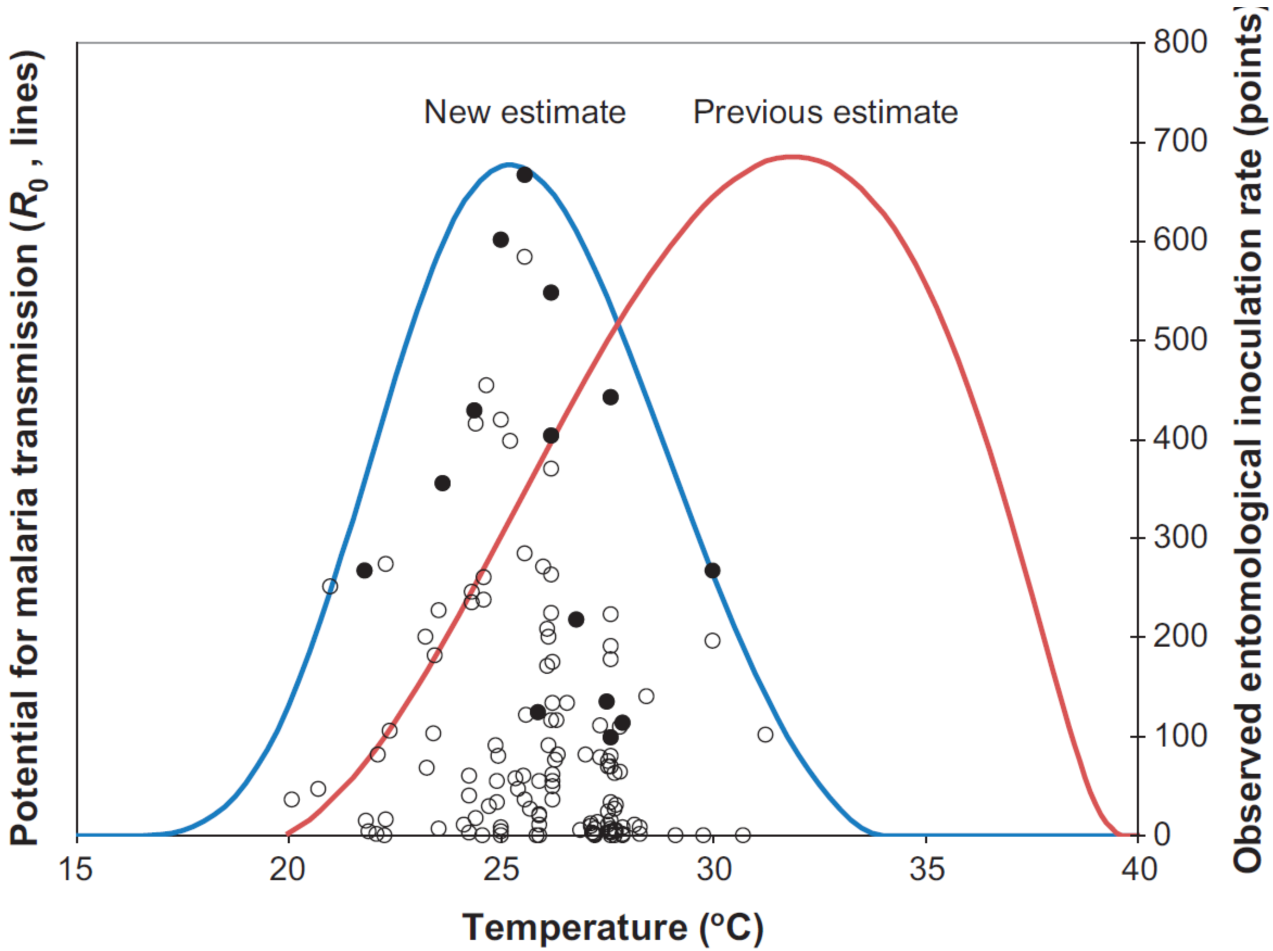
M	mosquito density
a	per mosquito human biting rate
bc	vector competence
μ	adult mosquito mortality rate
EIP	extrinsic incubation period (time from infective blood meal to sporozoite infection in salivary glands
N	human density
r	rate at which humans recover and acquire immunity

All parameters shown in bold are temperature dependent

Experimental determination of T for parameters in model:



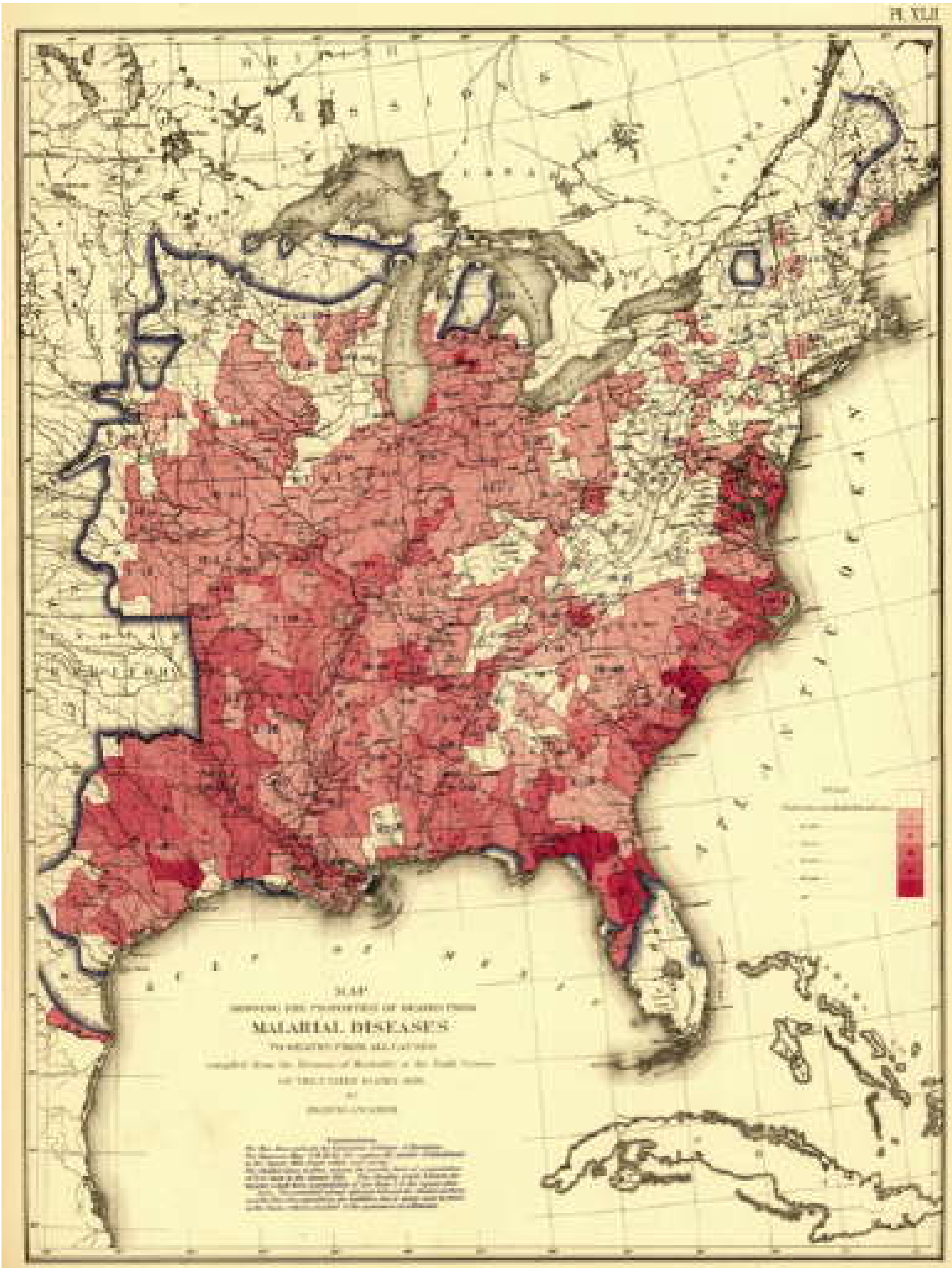
Optimal temperature for malaria transmission is 25°, not 32-33°



Model validation against field data:
Entomological Inoculation Rate (EIR) ~ R_0
Open circles: field observed EIR; Closed circles: highest observed EIR when several measurements available for a given temperature

Is climate change likely to increase the risk of malaria epidemics in the US?

Question assumes that present day climate excludes or limits malaria transmission within the US.



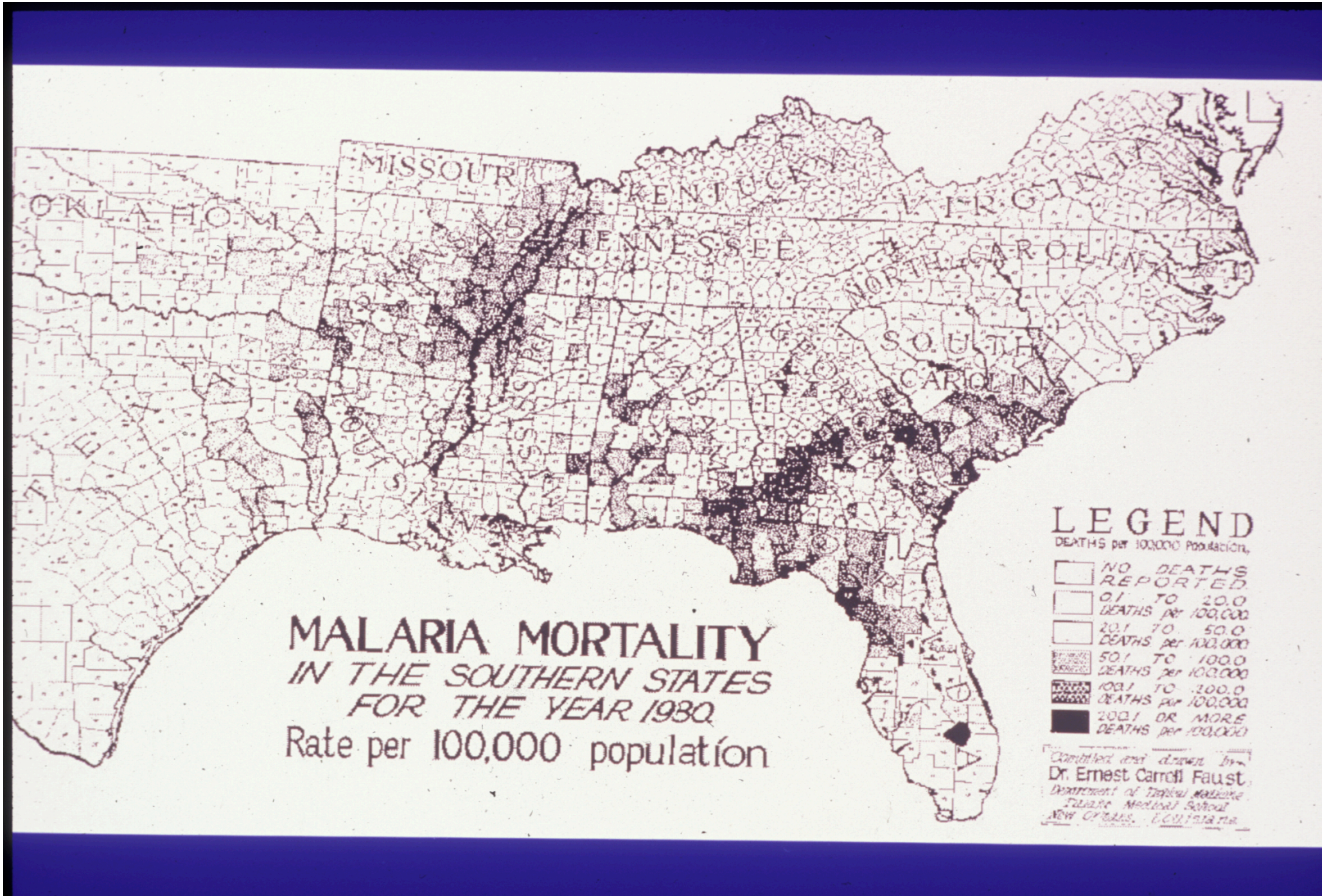
Both *Plasmodium falciparum* and *Plasmodium vivax* malaria were formerly widespread in the US and southernmost Canada! (1870 map)

Malaria peak in US ~ 1875

1914 ~600,000 cases
~25,000 deaths

Take-home message:
The US already has both the climate and native vectors to support high rates of malaria transmission

US malaria 1930: in retreat but not gone yet



Why did malaria transmission disappear in the US?

Population movement from rural to urban areas
Improved housing and nutrition
Better socioeconomic conditions and living standards
Access to medical services, quinine for treatment

1930s: Tennessee Valley Authority integrated mosquito control with hydroelectric generation by varying water levels to flush larvae

1940s:

- Malaria Control in War Areas (MCWA) program (1942-1945), forerunner of the CDC
- CDC (1946-present
- Development of chloroquine (available 1946)
- Development of DDT (1939)

Malaria eliminated in the US 1951

Opinion of Dr. Andrew Spielman, Harvard University:

“The single biggest factor was the Rural Electrification Program”

Based on his experience of finding malaria gone from the Louisiana Bayou area before any effort at DDT spraying or other control measures were implemented

Why?

Prior to availability of electricity:
- People were outdoors in the evening (socializing)
- Windows wide open at night to allow cooling breeze

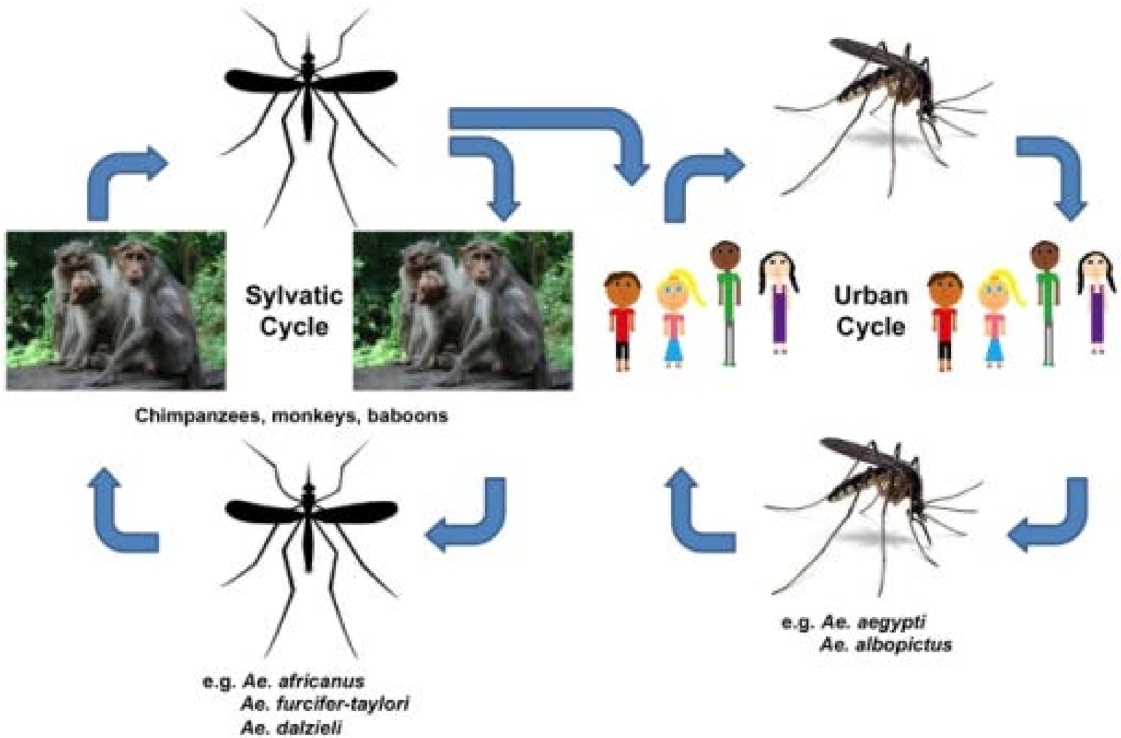
After arrival of electricity:
- People stayed indoors in evening to listen to radio, later television
- Electric fans for “breeze”, later air conditioning, favored closed windows

So, in the US malaria disappeared due to:

1. Changes in human behavior (related to access to electricity)
2. Access to medical services and antimalarial drugs
3. Direct interventions such as elimination of mosquito breeding sites, use of insecticides (DDT)

1 & 2 in particular are unlikely to be affected by warming climate, or to be affected in a manner counter to malaria transmission due to people staying indoors to avoid heat.

Chikungunya Fever



A sylvatic cycle with simian reservoirs exists in Africa, but humans are competent reservoirs and can sustain virus transmission resulting in epidemic outbreaks

What are the symptoms?

- Sudden onset of **high fever (>102^{o}F)**.
- **Severe joint pain** mainly in the arms and legs.
- **Headache**
- **Muscle pain**
- **Back pain**
- **Rash** (~50% of cases)

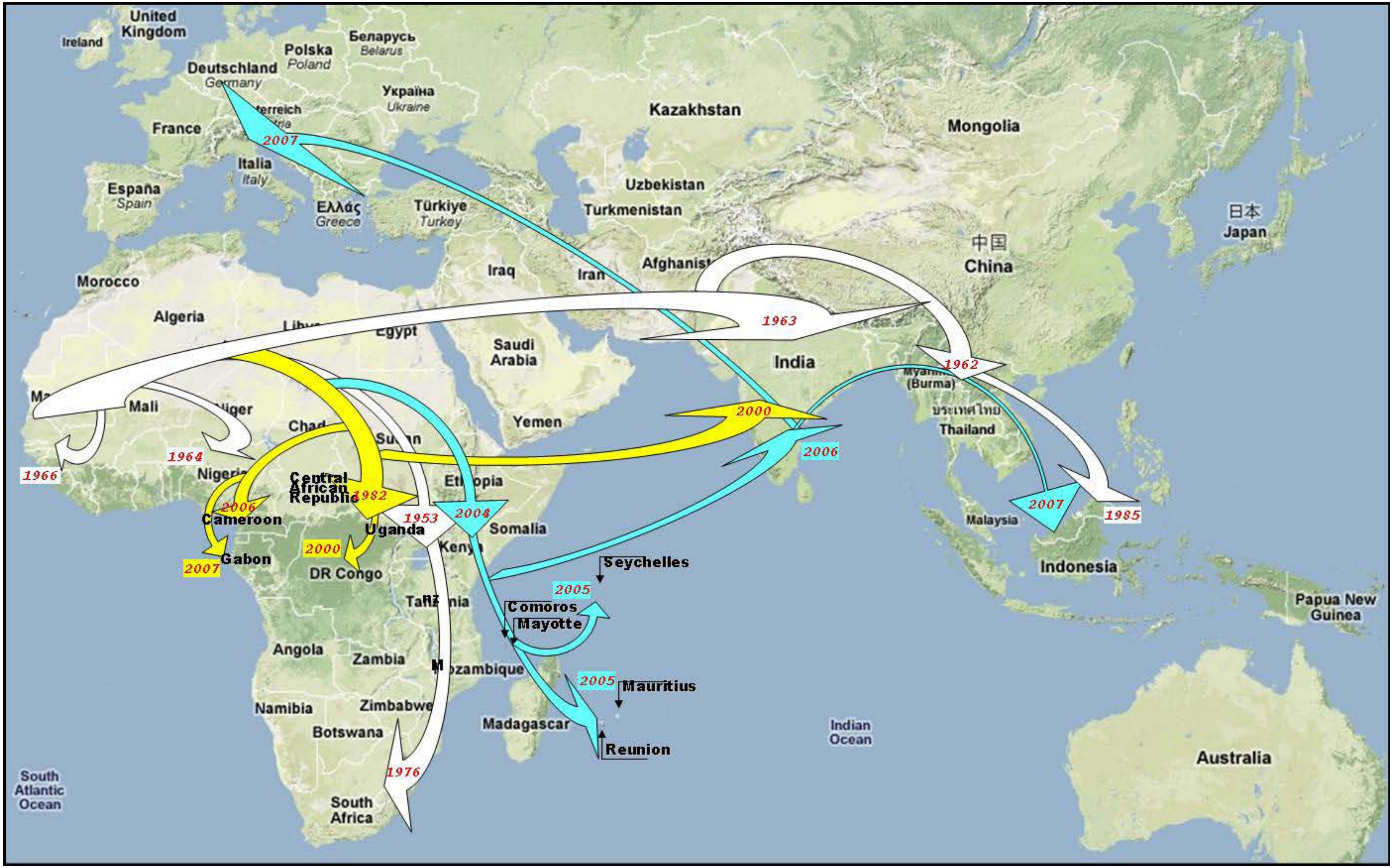
Symptoms appear on average 3 to 7 days after being bitten by an infected mosquito.

Most patients feel better after a few days or weeks. Some people may develop longer-term joint pain.

Complications are rare, but more common in:

1. **Infants (<1 year)**
2. **Elderly (>65 years)**
3. People with **other chronic conditions** such as: diabetes, hypertension, etc.

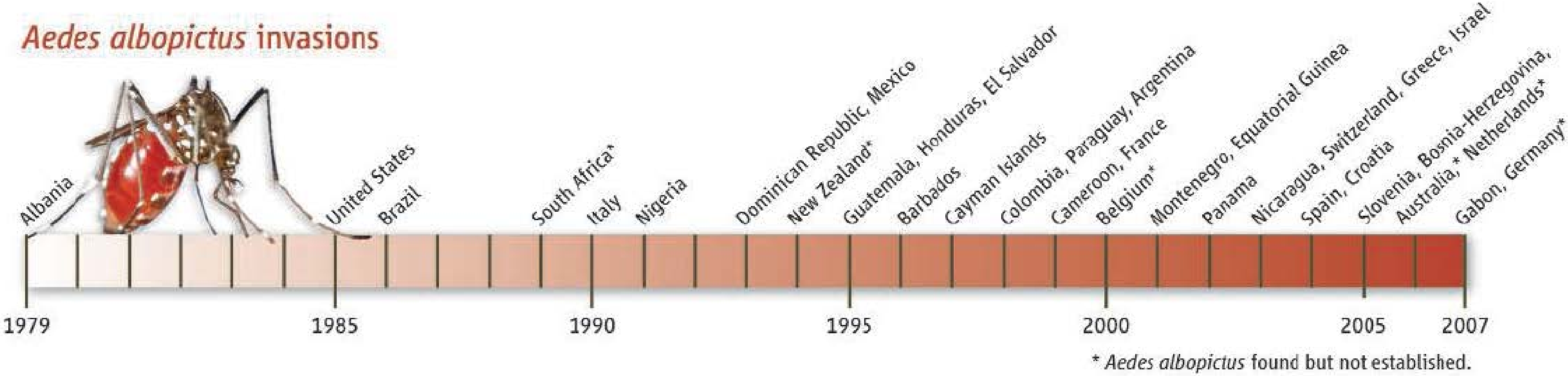
Movement of CHIKV



Could the jump to Italy reflect the warming European climate?

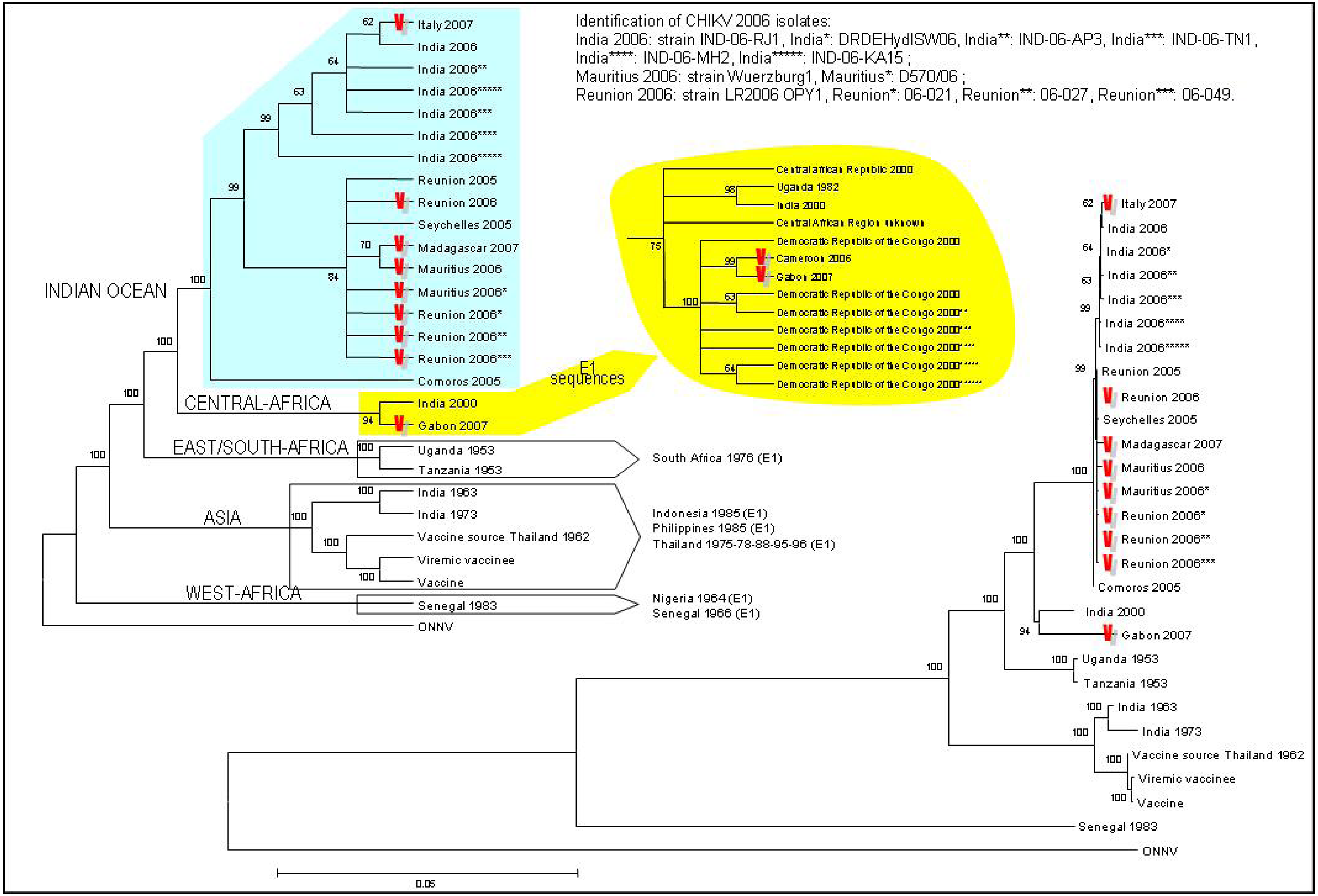
Chikungunya virus is efficiently vectored by *Aedes aegypti* (left), historically less well by *Aedes albopictus* (right)

Aedes albopictus is a supreme invasive species, moving around the world in recent decades.

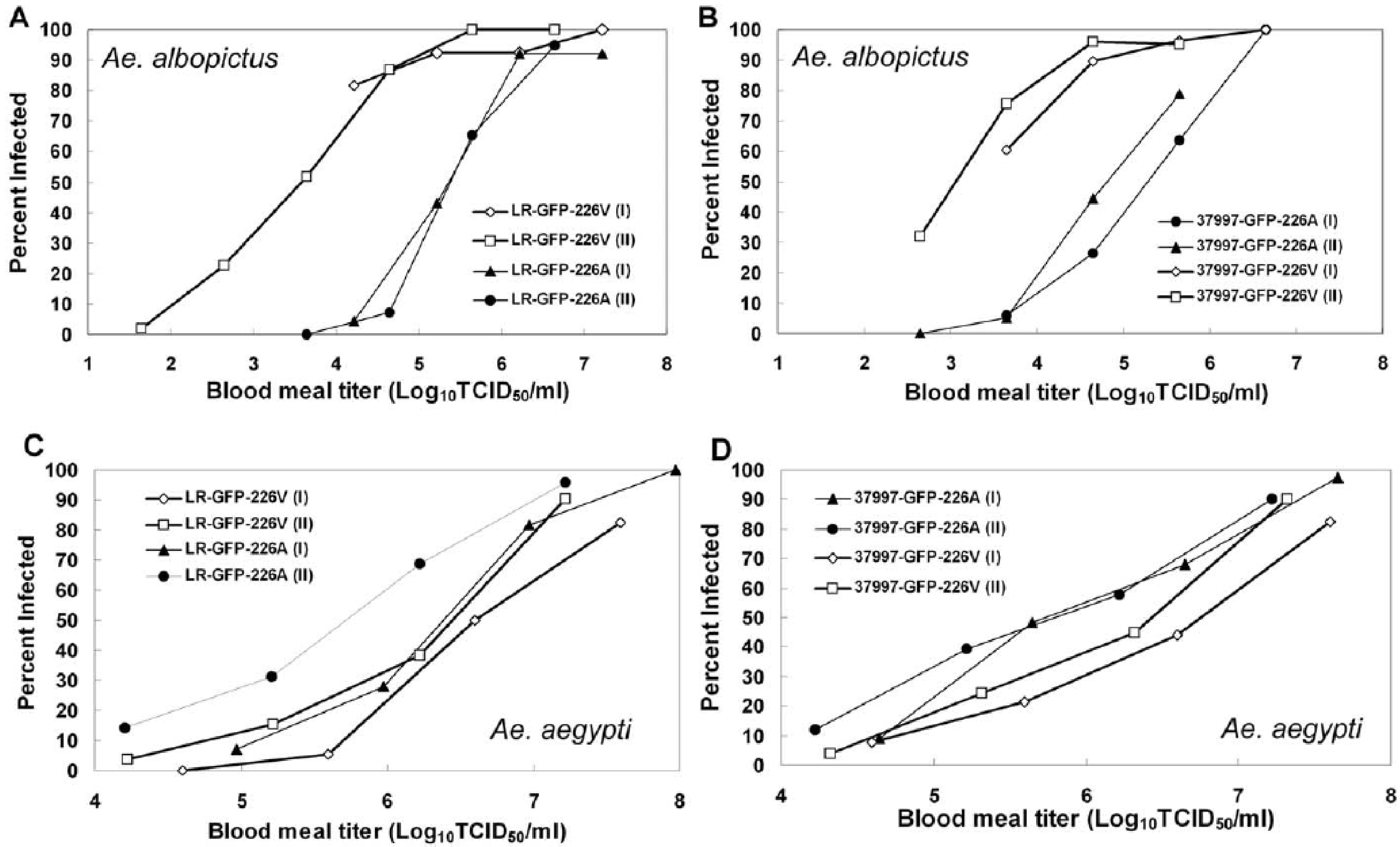


The natural range of *Aedes albopictus* extends to Northern Japan, so it is tolerant of a wide temperature range from subtropical to cool temperate.

A specific mutation, A226V is shared (shown in blue) by all Indian Ocean outbreak isolates and the Italy isolate, but not African or Asian isolates

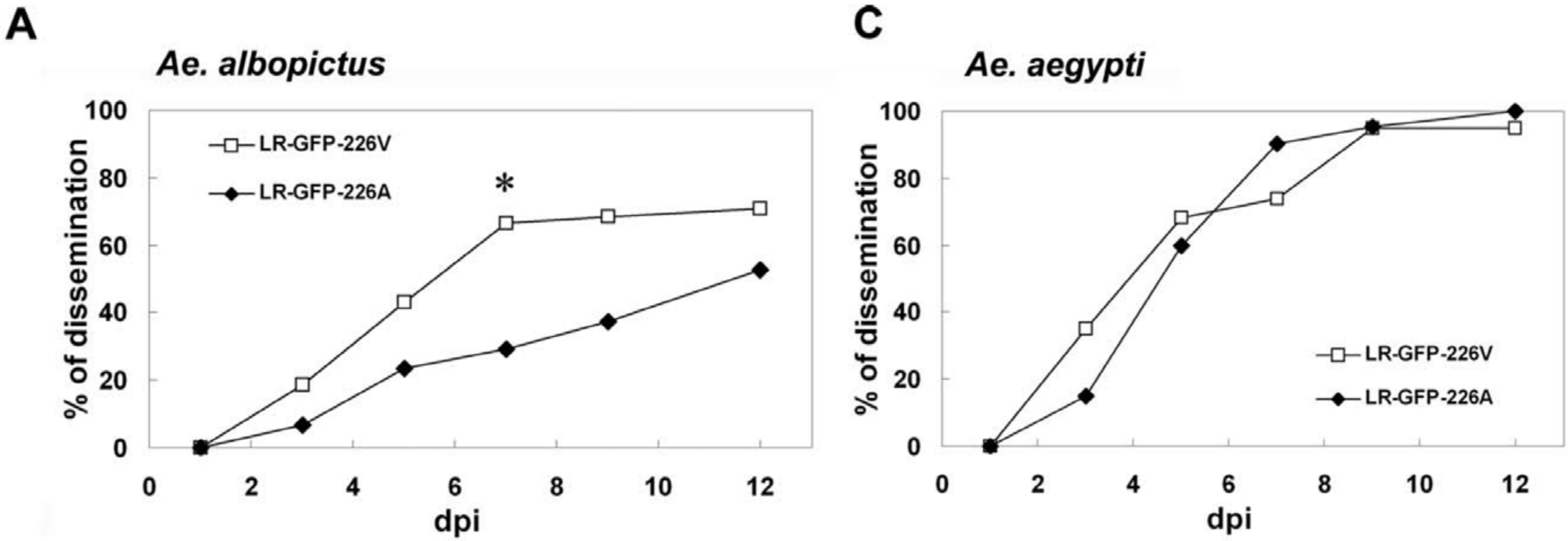


A single amino acid change, A226V, in an envelope glycoprotein enhances midgut infectivity in *Aedes albopictus*



Tsetsarkin et al 2007 Plos Pathogens 3(12):e201

The same mutation enhances dissemination of the virus into salivary glands in *Aedes albopictus* but not *Aedes aegypti*



Tsetsarkin et al 2007 Plos Pathogens 3(12):e201

The Indian Ocean and Italian epidemics of Chikungunya Fever appear to have resulted from a two-step process:

1. Invasion of areas around the Indian Ocean and Europe by *Aedes albopictus*, a species already well adapted to the existing climate;
2. Mutation of the virus resulting in improved infection and dissemination in a new vector, *Aedes albopictus*, compared to the ancestoral vector *Aedes aegypti*

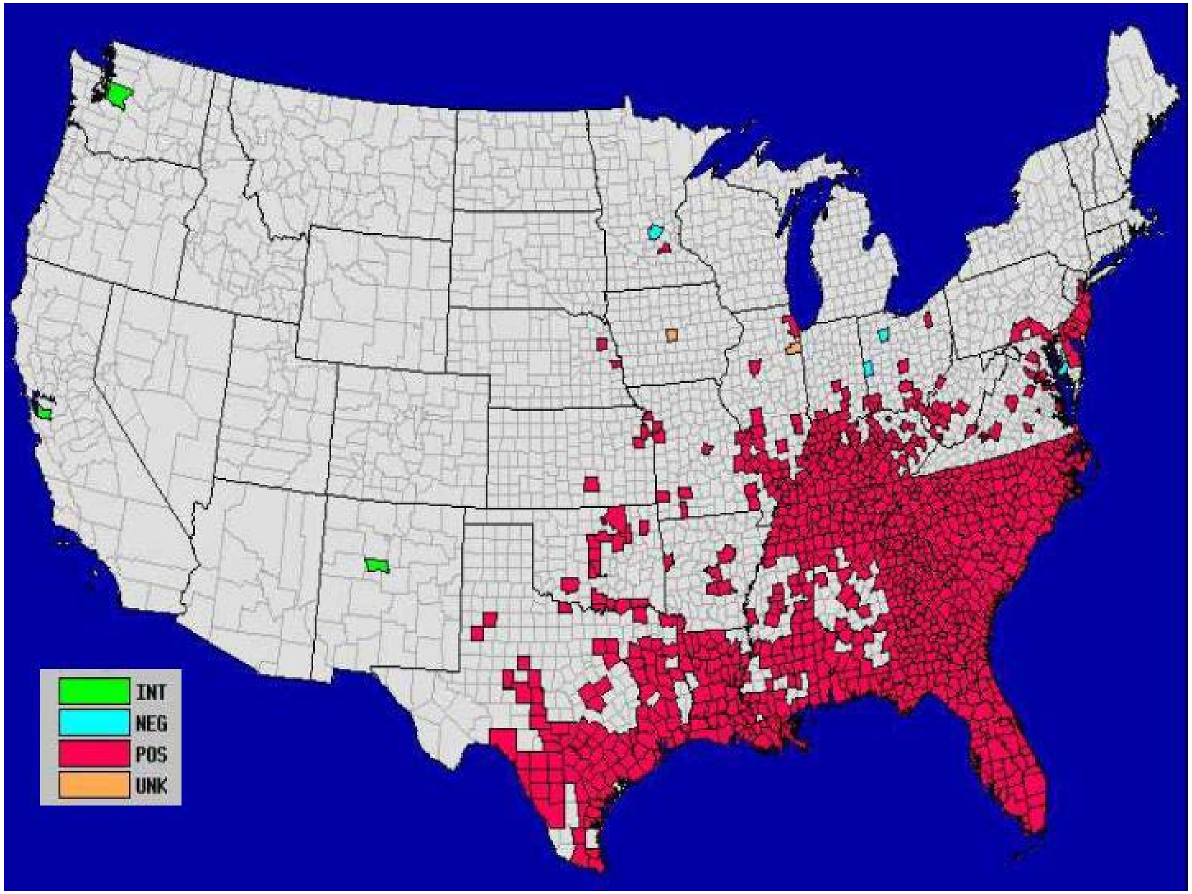
Since *Aedes albopictus* prefers habitats that are more temperate than are colonized by *Aedes aegypti*, the Chikungunya virus has been able to move into new territories independently of climate change.

Is any of this applicable to the US?

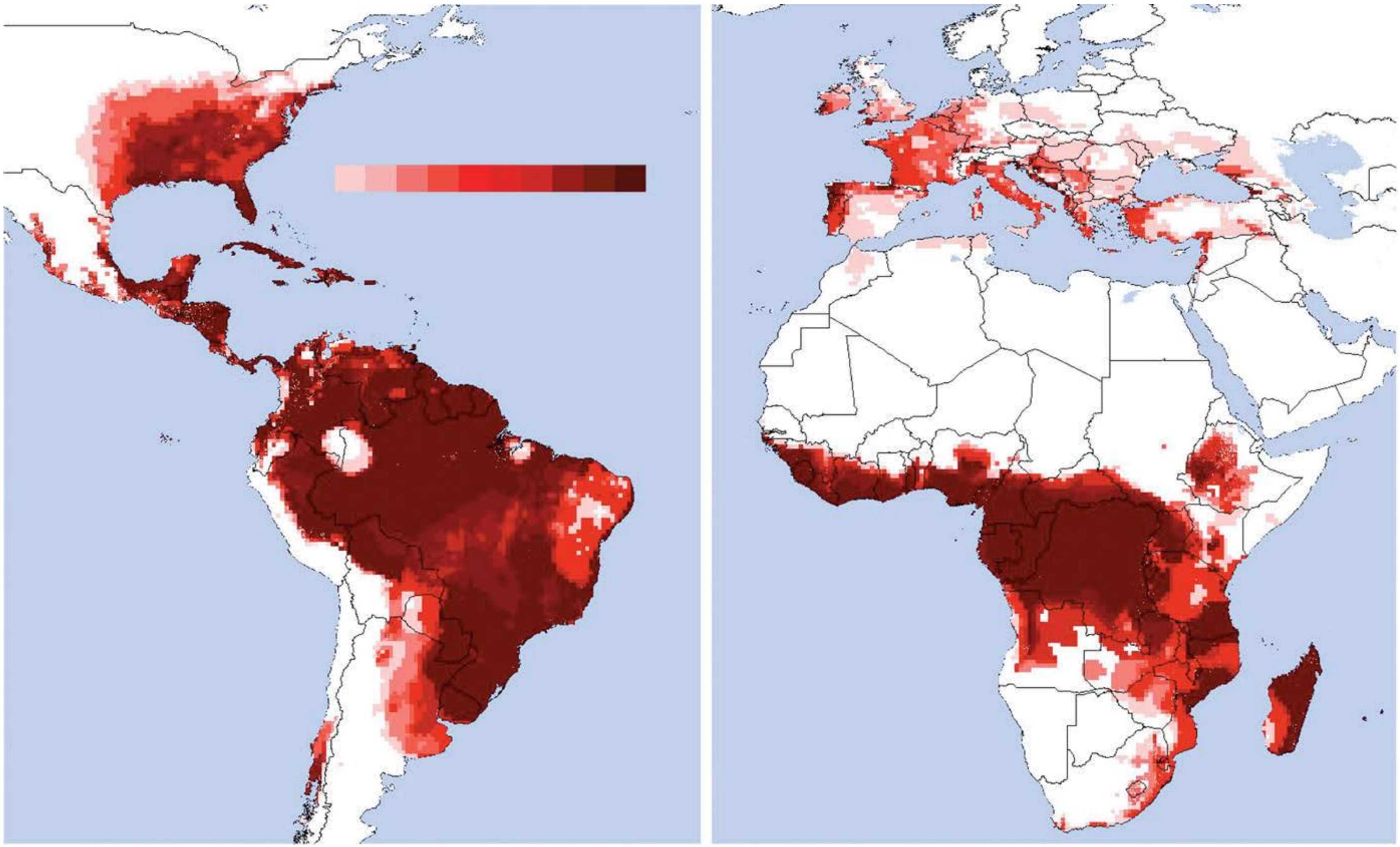
Aedes albopictus was first detected in the US in 1983, likely imported with tires from Northern Japan being sent to Houston TX for retreading.

By 2000 it had spread through the South, the Gulf States, and up the Eastern US and the Mississippi Valley

Since then, it has formed locally established populations in California



Climate models suggest that *Ae. albopictus* will be able to extend its range North and West in North America, and widely across Europe, as the climate warms. Much of Africa is already suitable habitat.



Benedict et al 2007, Vector Borne Zoonotic Dis

But that's not all!

In 1998 another invasive mosquito, *Aedes japonicus*, was found in Connecticut. Since then it has established up and down the Eastern US, from Georgia and South Carolina up North to Ontario!

Establishment and Abundance of a Recently Introduced Mosquito Species *Ochlerotatus japonicus* (Diptera: Culicidae) in the Southern Appalachians, USA

Author(s): Sarah N. Bevins
Source: Journal of Medical Entomology, 44(6):945-952. 2007.

Establishment of *Ochlerotatus japonicus* (Diptera: Culicidae) in Ontario, Canada

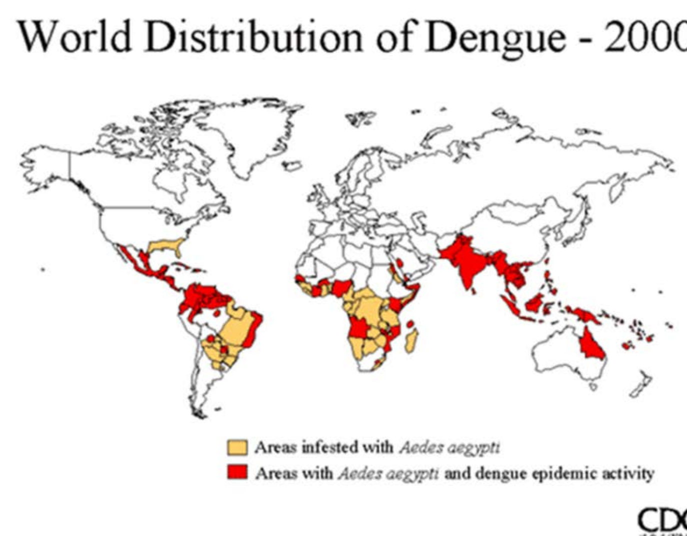
Author(s): Aynsley Thielman and Fiona F. Hunter
Source: Journal of Medical Entomology, 43(2):138-142. 2006.

Aedes albopictus and Aedes *japonicus* are competent vectors of Chikungunya virus and Dengue virus

The stage is already set for either virus to spread widely in the US and into Canada, irrespective of any climate change

The effect of climate change would be to extend the range of these vectors to the North and West, resulting in small increases in the population put at risk

Dengue distribution in the New World



Dengue fever

Also called breakbone fever
Sudden onset of high fever, extreme headache, extreme myalgia, photophobia
Not fatal, resolves in about 10 days
4 known serotypes

Dengue hemorrhagic fever

Complication resulting in profuse bleeding internally and from eyes, nose, mouth, other orifices
Thought to be due to prior exposure to serotype 2, followed by exposure to any of the other serotypes
Now well established throughout SE Asia and in Caribbean

Conclusions:

- Models of malaria distribution make very different predictions based on biological assumptions, whether or not human behaviors (including anti-malaria activities) are included
- Basic biological attributes, particularly the optimal temperature for malaria transmission, may need to be reconsidered and applied to new models
- Malaria seems to be strongly influenced by non-climate-based factors (such as behavior)
- Field observations do not support a strong influence of changing climate on disease occurrence

- Other mosquito-borne diseases (Chikungunya, Dengue, West Nile) have undergone epidemic outbreaks in new areas, but these outbreaks are related to movement of highly invasive mosquito vectors into new areas with favorable climates rather than climate change.

- In the American (and European) contexts, invasive species have already colonized the landscape and are poised to vector introduced pathogens. Native anophelene mosquitoes are competent malaria vectors, and are already widely distributed.

- Climate change may allow gradual expansions of the range occupied by these vectors, increasing the at-risk population.
- Climate change may also increase the variety of vectors that can successfully invade.

- Attention should be paid to prevention of further introductions of invasive species.

- Climate change seems unlikely to significantly expand the population at risk of plague in the near future (~50 years), though the area affected may change slightly.