Emerging Mosquito-Borne Diseases

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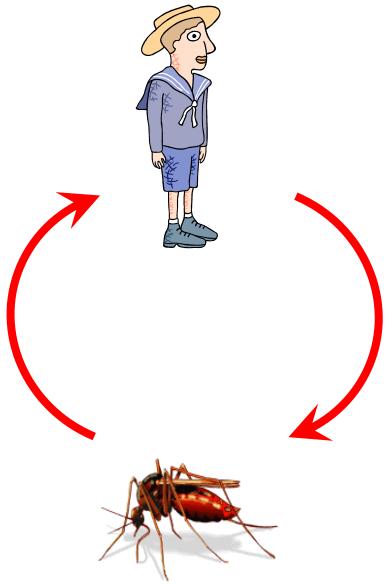
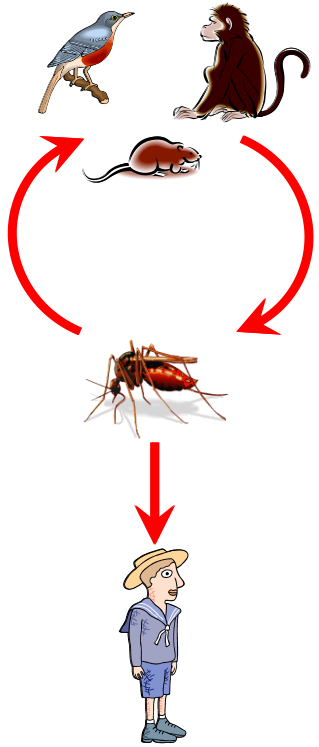
Basic Patterns of Mosquito-Borne Arbovirus Transmission

Scenario one:
Humans are the primary hosts

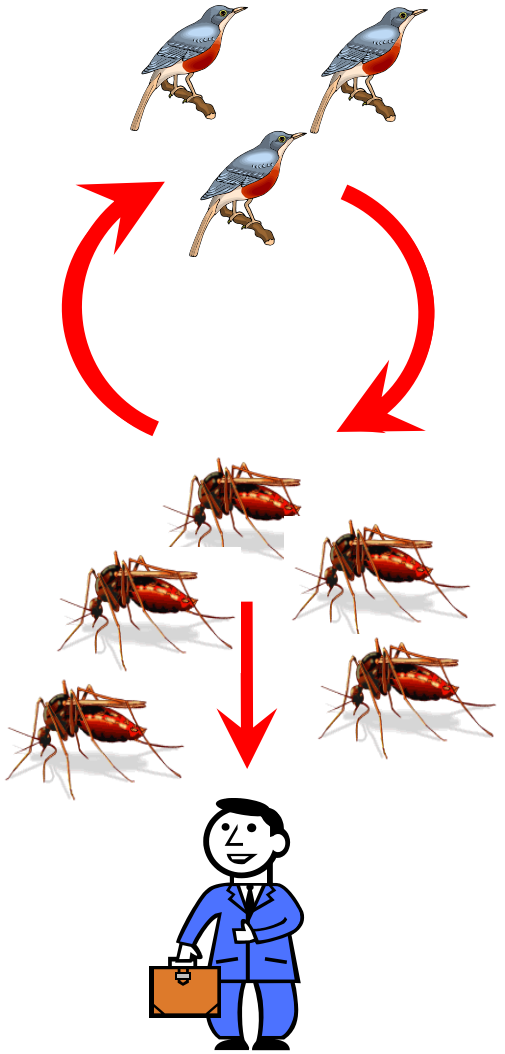


Scenario two:
Humans are incidental hosts

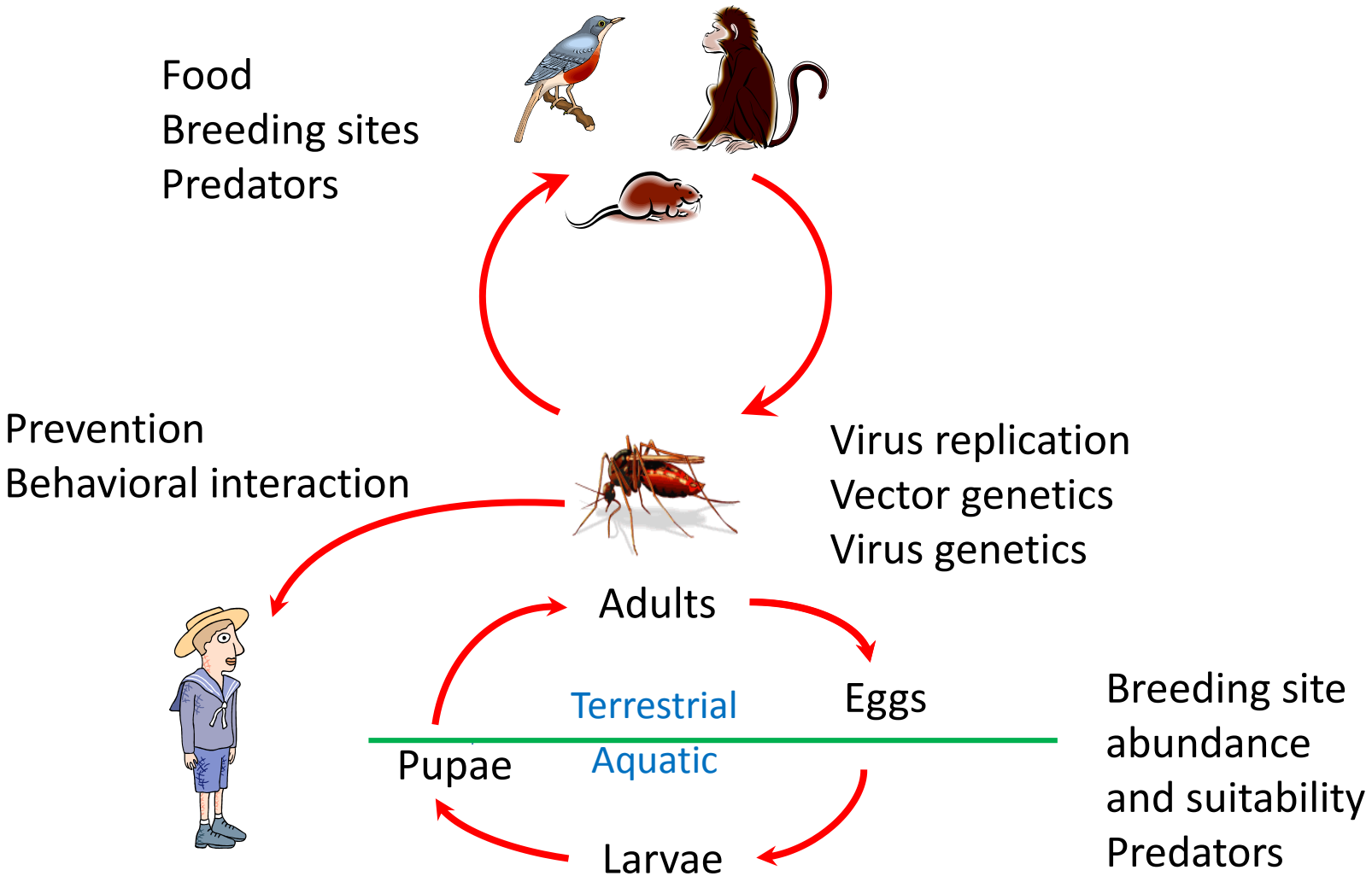


West Nile virus transmission

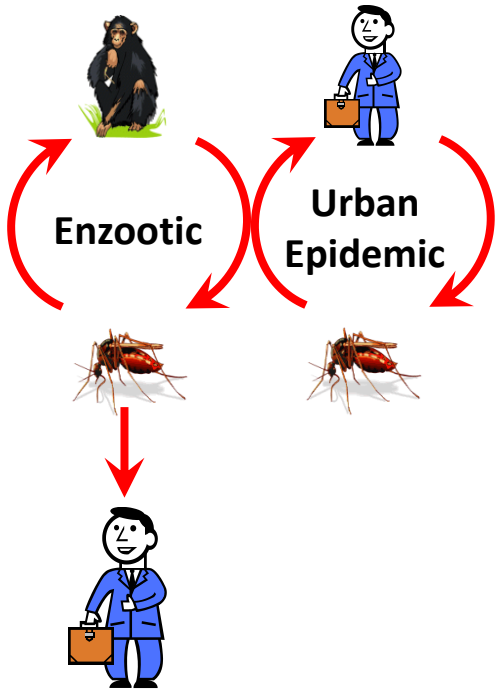
- *Culex* spp mosquitoes
- Virus overwinters in adult female hibernating mosquitoes in temperate climates
- Infected mosquitoes emerge in spring and start transmission cycle
- Birds amplifying host – many passerine species develop enormous viremias (>10^7 PFU/ml)
- Cycle continues throughout spring and summer
- Humans and horses are dead-end hosts



Climate/Weather and Anthropogenic Factors Affect Nearly All Factors Influencing Arboviral Transmission

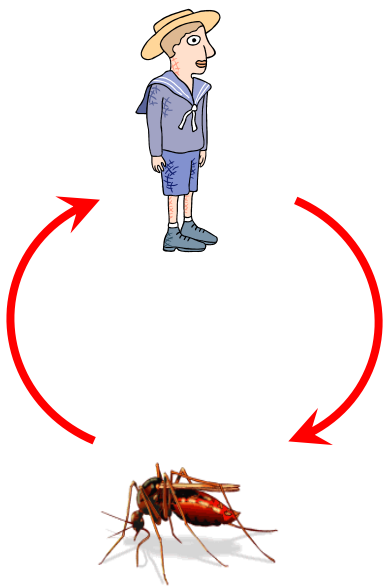


Scenario One: Humans Serve as the Primary Vertebrate Host



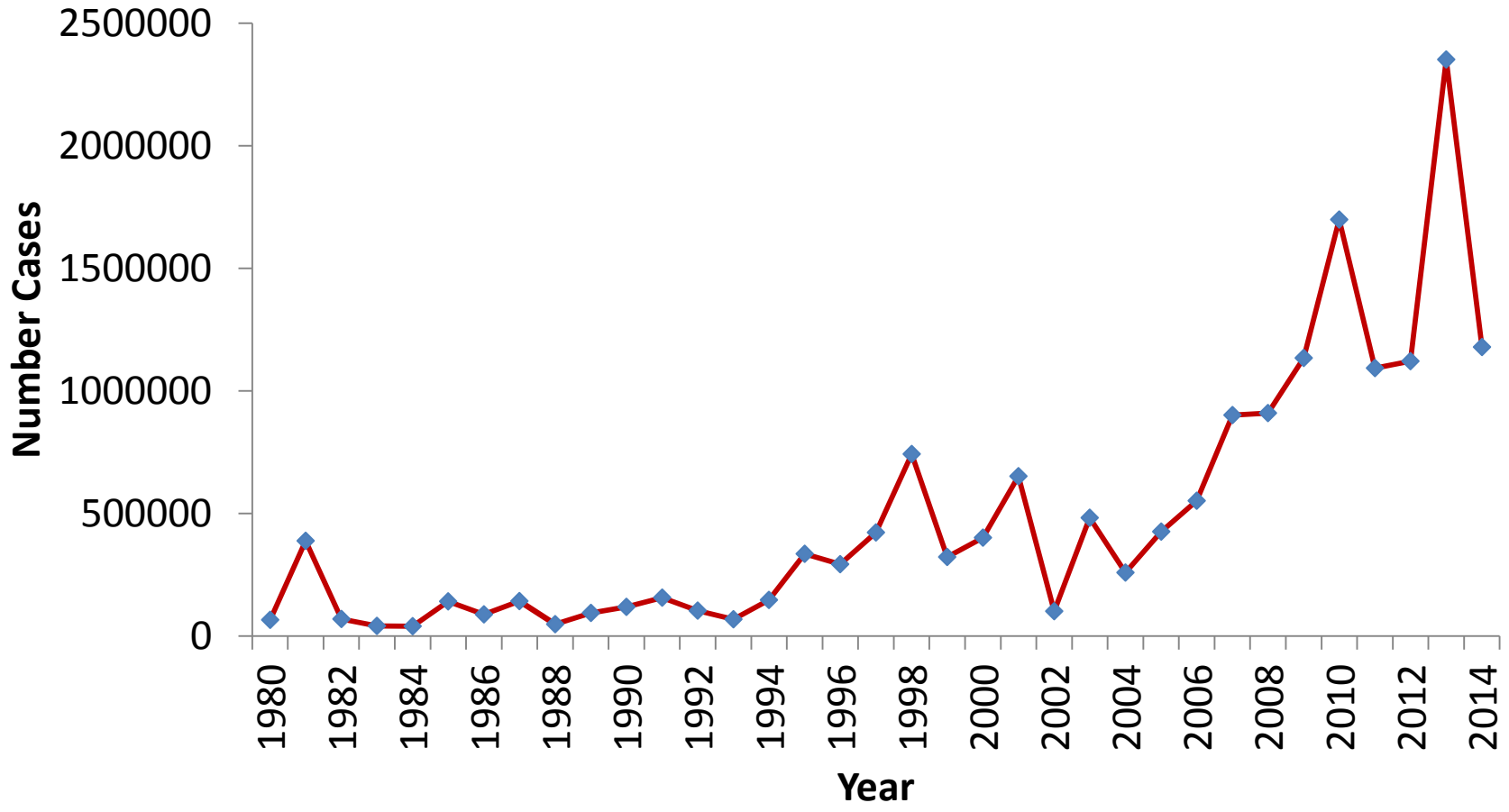
- Dengue
- Chikungunya
- Zika

Dengue



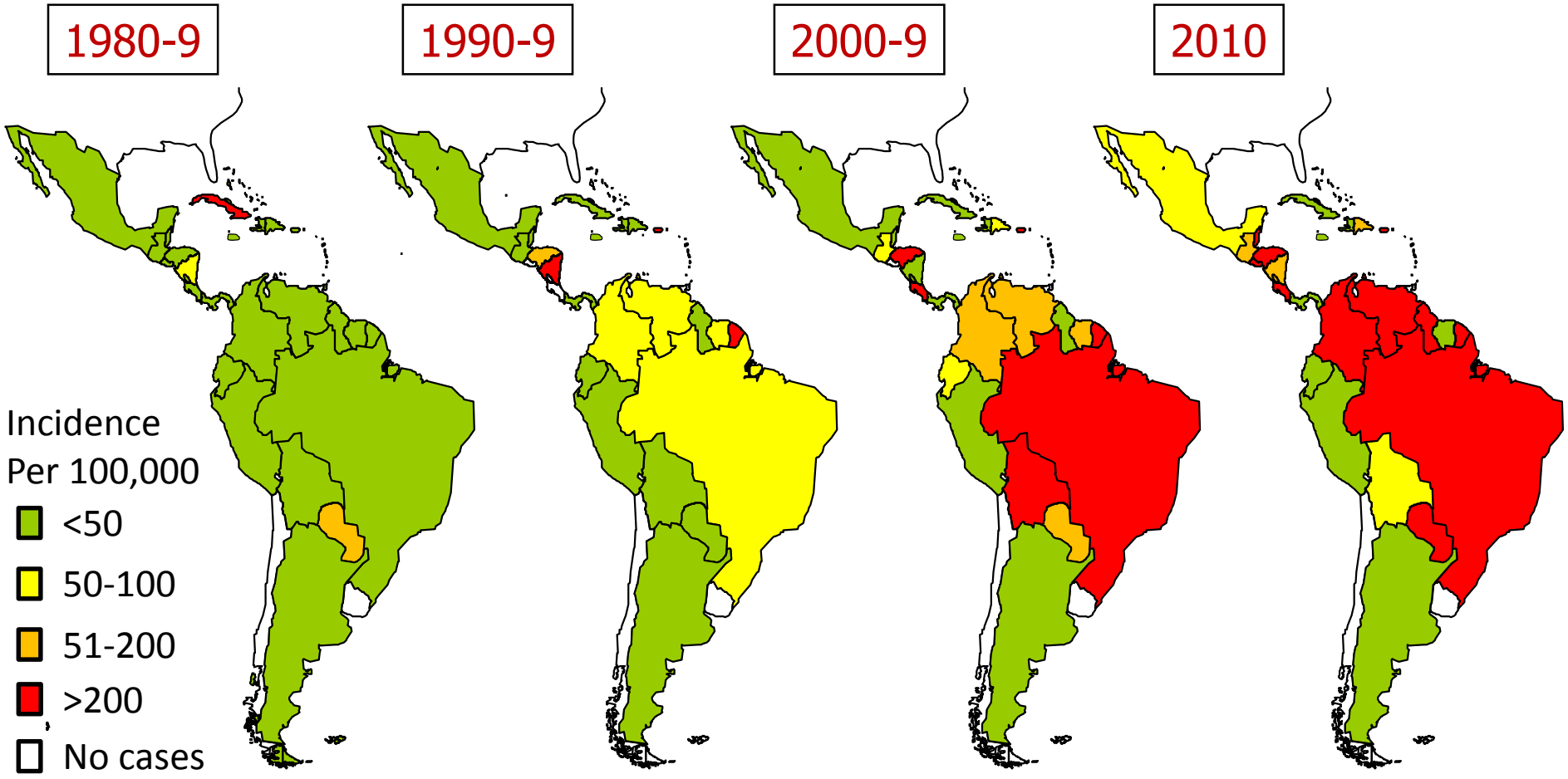
- Caused by four flaviviruses
- No known important animal reservoir
- Causes fever, rash, severe pain (“break bone fever”), shock, hemorrhage
- 400 million infections per year
- Subsequent infections increases liklihood of severe disease
- Spread by the *Aedes aegypti* mosquito
- *Aedes albopictus* can also sustain transmission

Dengue Incidence is Rapidly Increasing in the Americas



Source: Pan American Health Organization (PAHO)

Dengue Incidence in Latin America and the Caribbean, 1980-2010

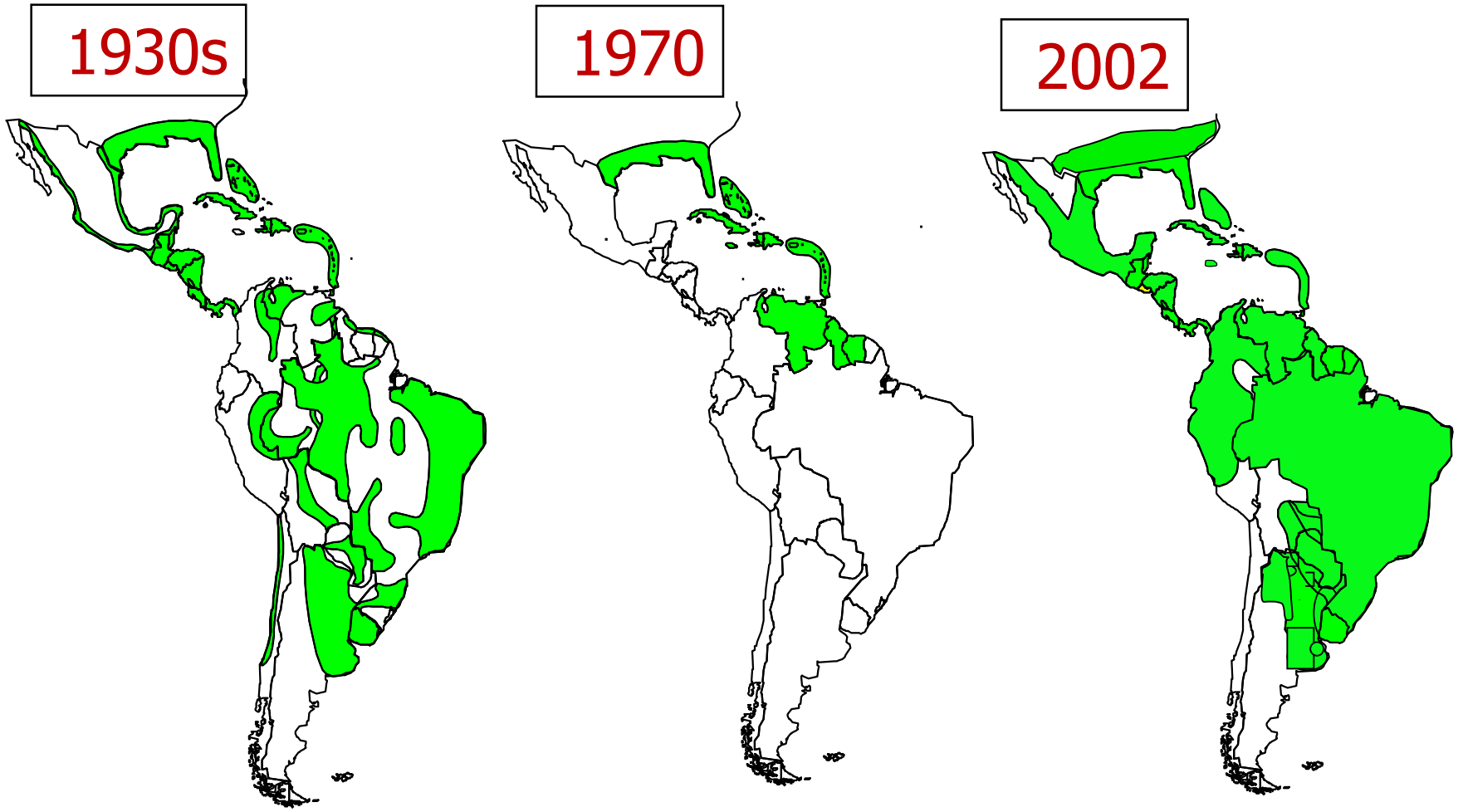


Source: PAHO

Aedes aegypti

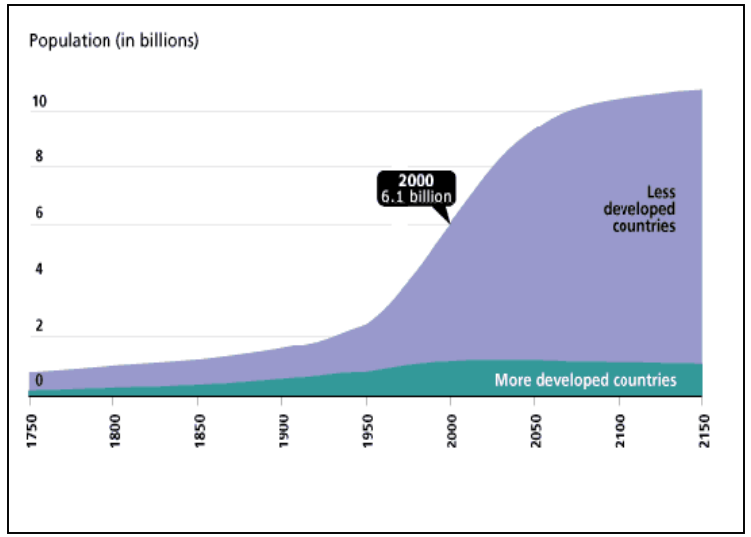
- Adapted to urban habitats
- Preferentially feeds on humans
- Can bite multiple humans in a single blood meal
- Feeds indoors
- Breeds in small containers
- Present throughout the tropical world

Reinfestation of *Aedes aegypti* after Cessation of Control Efforts from 1947-1970*

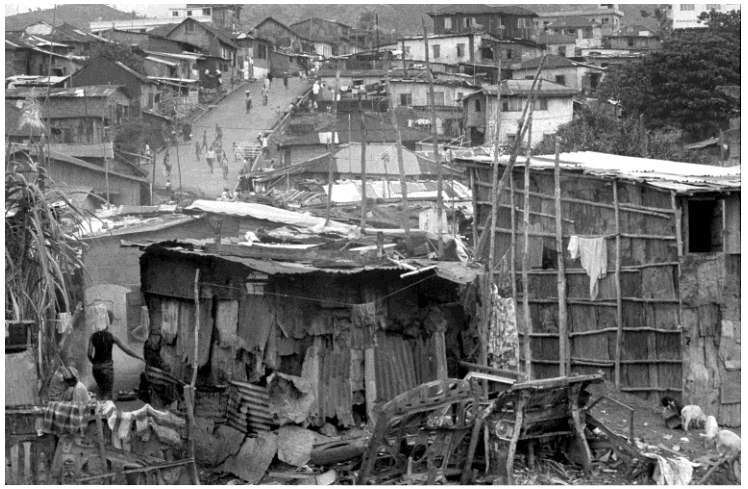


* Continental plan for eradication of the *Aedes aegypti.* PAHO Resolution–CD1.R1

Rapidly Increasing Human Population and Urbanization



- Population
  - 6.1 Billion in 2000
  - ~9.4 to 11.2 Billion in 2050



- Percent world population urban
  - 1950: 29%
  - 2007: 49%
  - 2030: 60%
  - Increase largely due to 3X increase in Asia and Africa

Can Dengue Reemerge in Temperate Climates?

Dengue in the Continental USA

- Dengue epidemics in US from 1700s until first half of the 1900s
- 807 returning travelers with dengue reported in 2013
- 8 outbreaks in Texas since 1980
- 2 outbreaks in Florida since 2009

Aedes aegypti

Aedes albopictus

A Tale of Two Cities:
Dengue Outbreak on the US-Mexico Border

	Brownsville	Matamoros
Positive serology	4%	32%
Breteau index	16	28
Air conditioning	85%	29%
Screens	61%	65%
Lot size (m^2)	1070	307

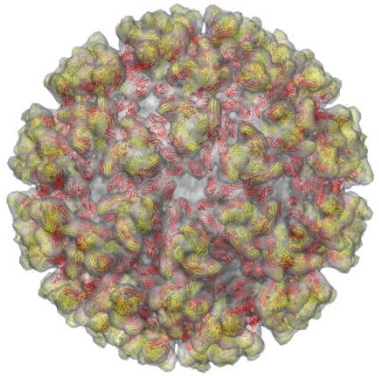
No air conditioning was a major risk factor for infection in Matamoros: OR 6.6 (1.9-17.9)

Lot size smaller than median was a risk factor for infection in Brownsville: OR 14.6 (1.2-172.3)

Am J Trop Med Hyg 2008;78: 364-9

Chikungunya Virus

- **Single-stranded RNA virus**
- **Genus *Alphavirus,* Family *Togaviridae***
- **Closely related to Mayaro, O'nyong-nyong, and Ross River viruses**
- **Three major genotypes**
  - West African
  - East/Central/South African (ECSA)
  - Asian

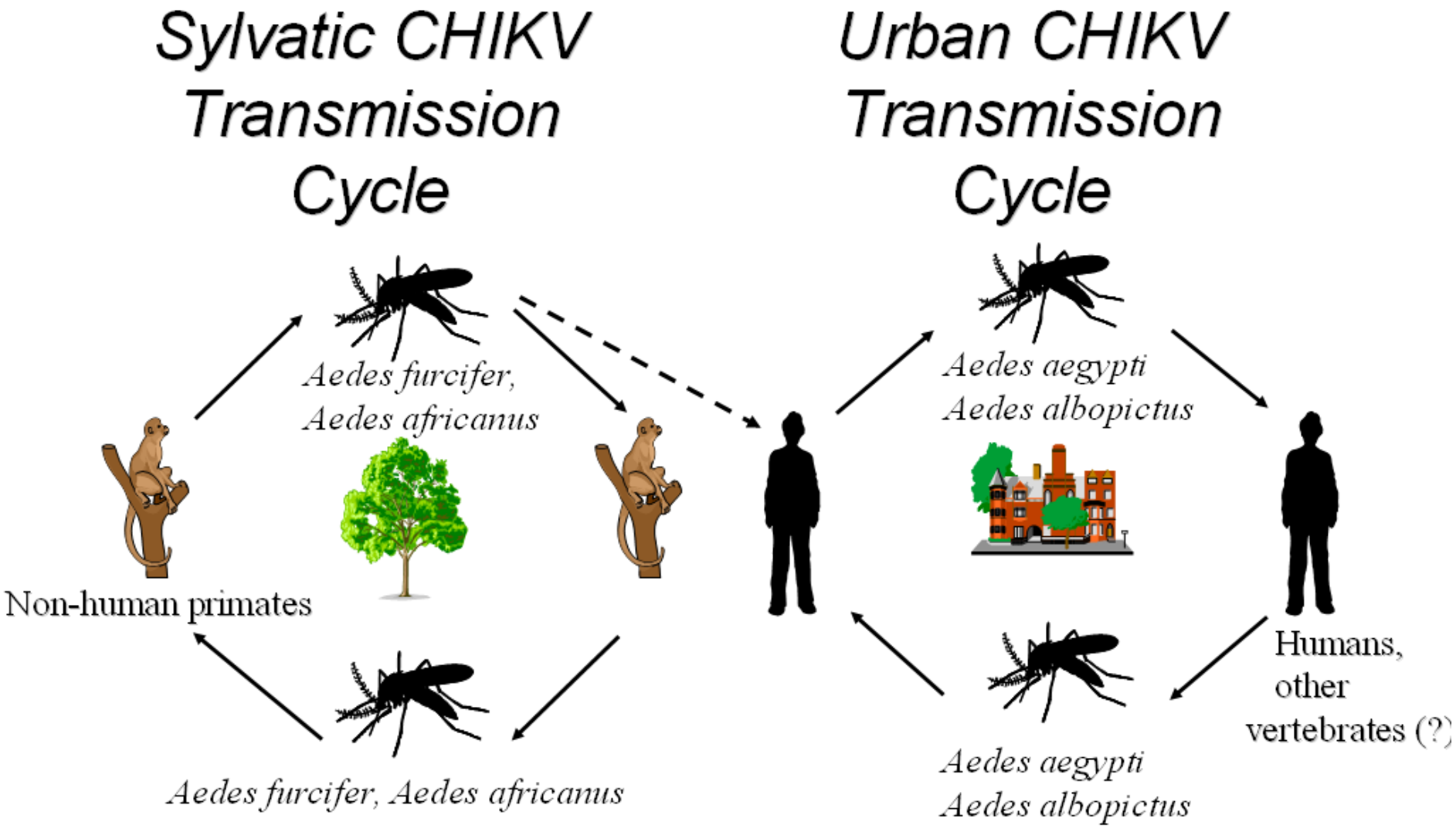


Organization of the chikungunya virus genome from: Expert R ev. Vaccines 11(9), (2012)
Cryo-EM from: Mukhopadhyay S et al., Structure 2006

Chikungunya Virus Infection

- Most (72%–97%) infected people develop clinical symptoms
- Incubation period usually 3–7 days (range 1–12 days)
- Primary clinical symptoms are fever and polyarthralgia

Chikungunya Transmission Cycles



Powers. Clin Lab Med. 2010 Mar;30(1):209-19.

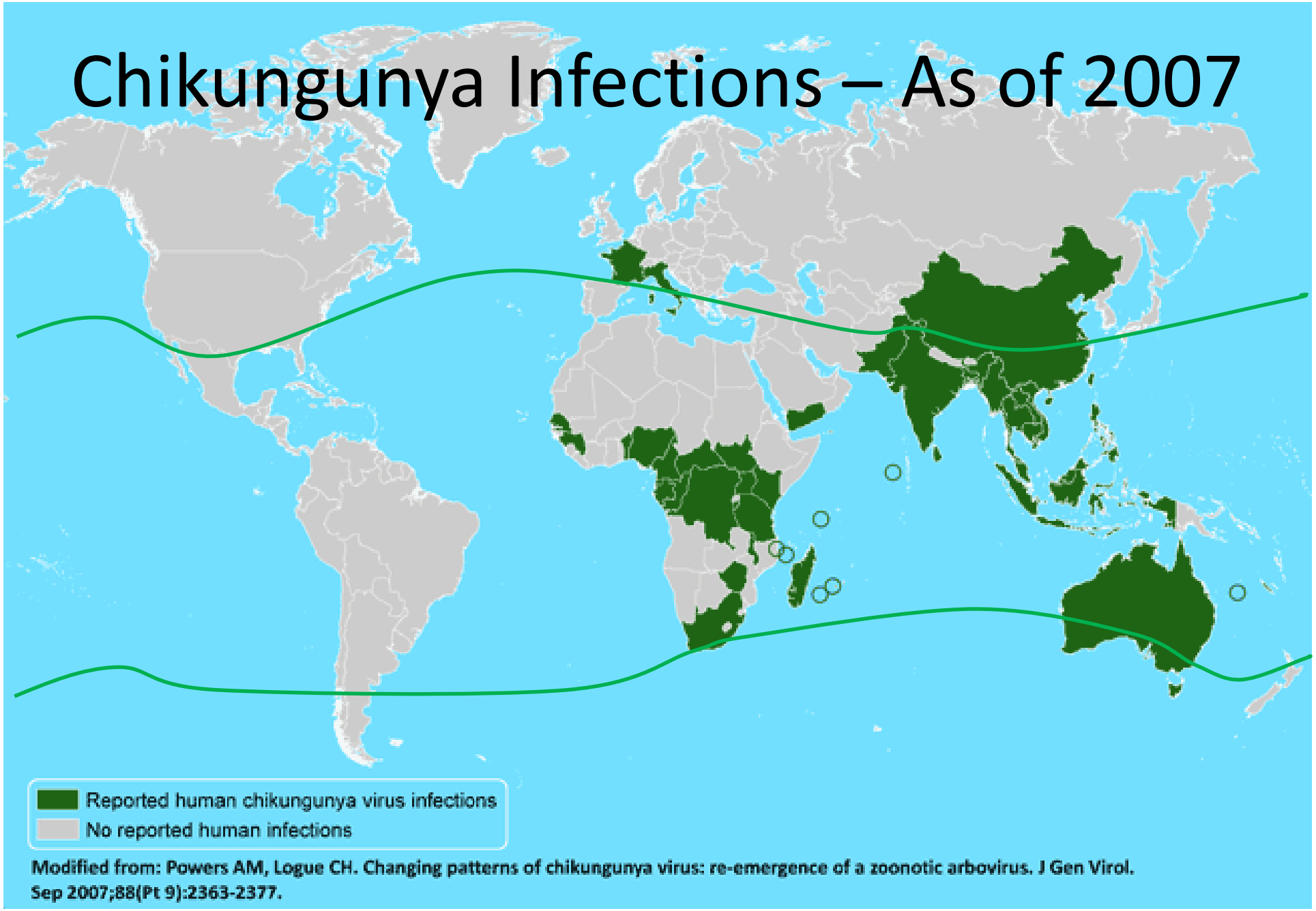
History of Outbreaks

- Discovery in 1953 in febrile woman in Tanzania
- First major documented emergence
  - Large urban outbreaks in India and Southeast Asia due to introduction of ECSA genotype in or around early 1950s
  - Resultant “Asian” genotype persisted in SE Asia
  - Numerous outbreaks documented in Africa and SE Asia subsequently

History of Outbreaks

- Second major emergence of ECSA genotype virus
  - Started in coastal Kenya in 2004
  - Spread to Comoros and then to La Reunion Island
    - Outbreaks of unprecedented size
    - Acquires E1-A226V mutation that increases fitness in *Aedes albopictus*
  - Spread to other islands in Indian Ocean and India where it has caused >1 million illnesses
  - Outbreaks in Italy and France initiated by travelers from India. Vectored by *Aedes albopictus.*

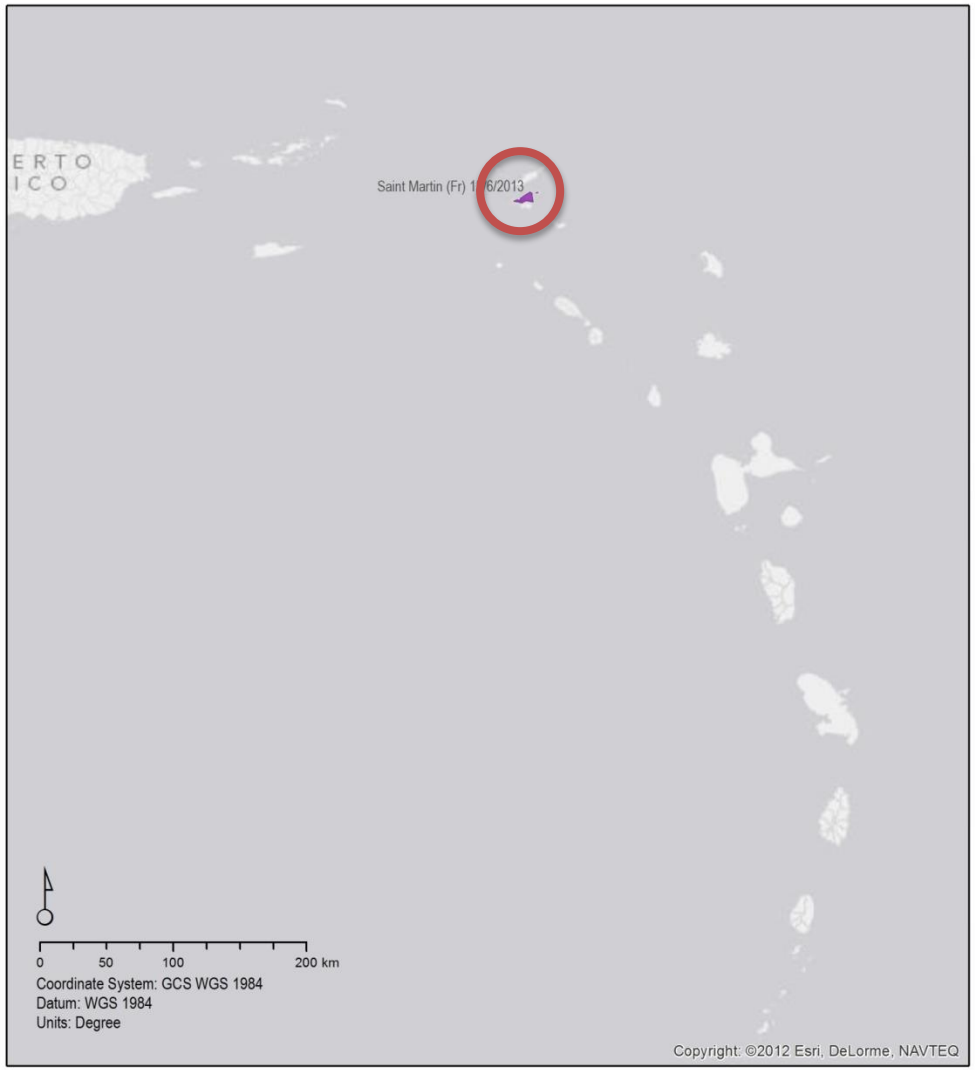
Chikungunya Infections – As of 2007



Modified from: Powers AM, Logue CH. Changing patterns of chikungunya virus: re-emergence of a zoonotic arbovirus. J Gen Virol. Sep 2007;88(Pt 9):2363-2377.

Chikungunya Appears in the Western Hemisphere

- First cases reported:
  - St. Martin in December 5, 2013
  - Onsets actually in October 2013
- Asian genotype (recent outbreaks in Yap, Philippines, Indonesia, China)
  - Lacks E1-A226V mutation



Source: PAHO

Chikungunya: December 2013

New locations

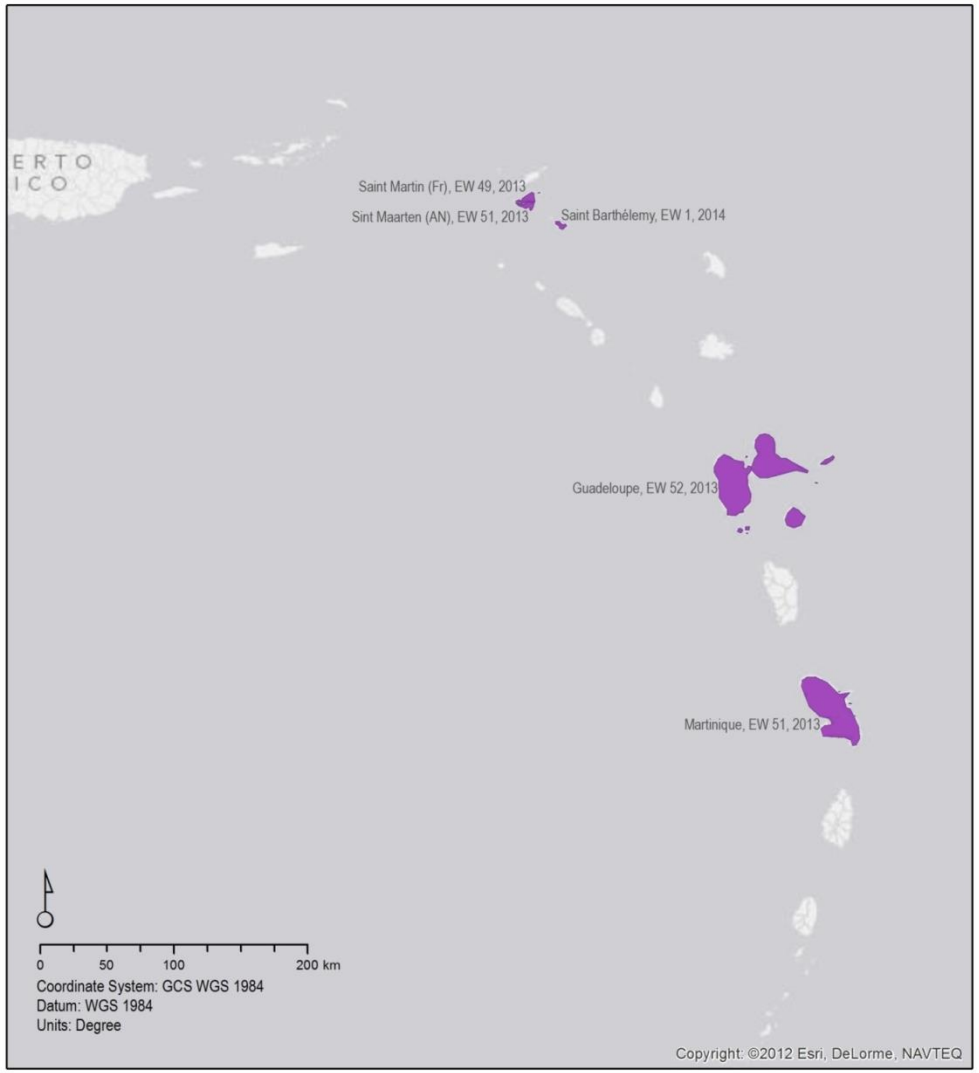
St. Martin

Martinique

Guadeloupe

St. Barthelemy

Sint Maartin



Source: PAHO

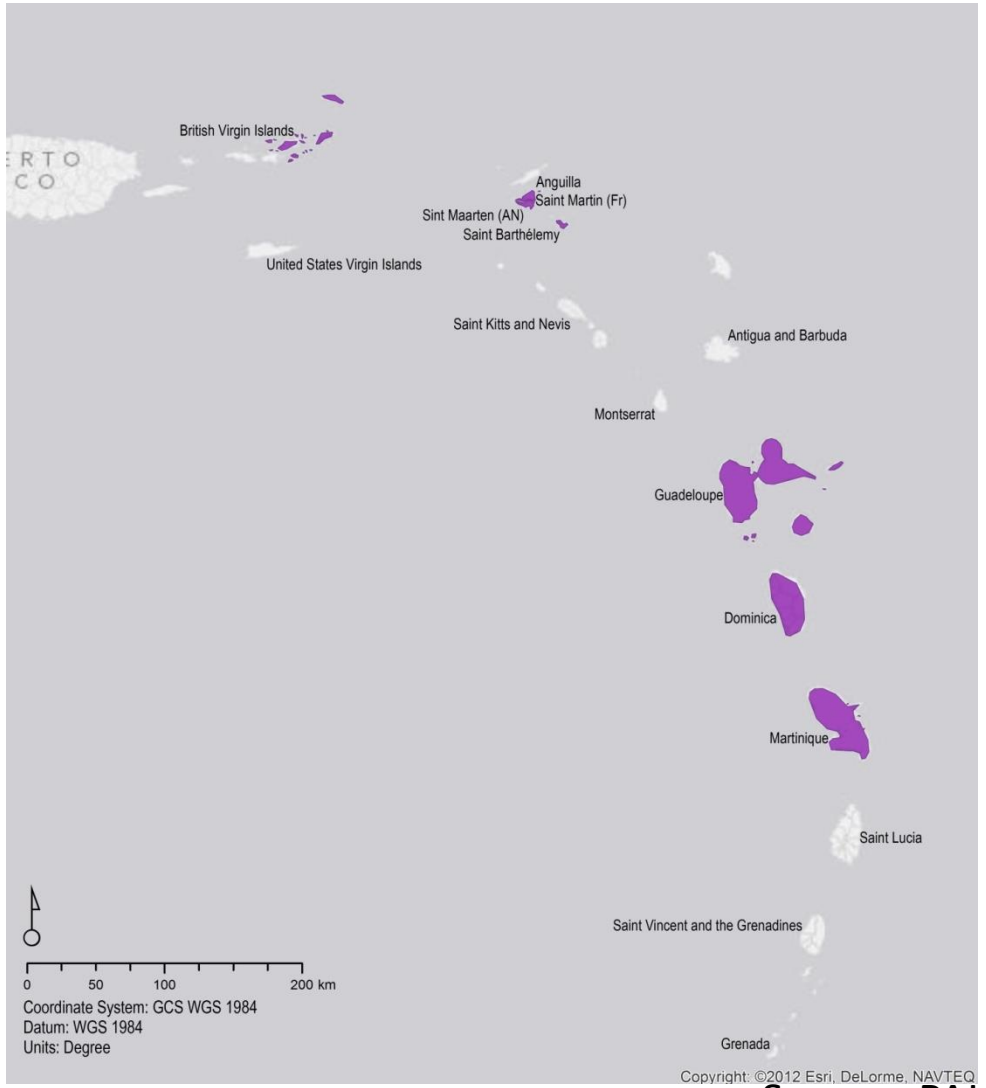
Chikungunya: January 2014

<u>New locations</u>

Br. Virgin Islands

Dominica

Anguilla



Source: PAHO

Chikungunya: Feb 2014

New locations

St. Kitts and Nevis

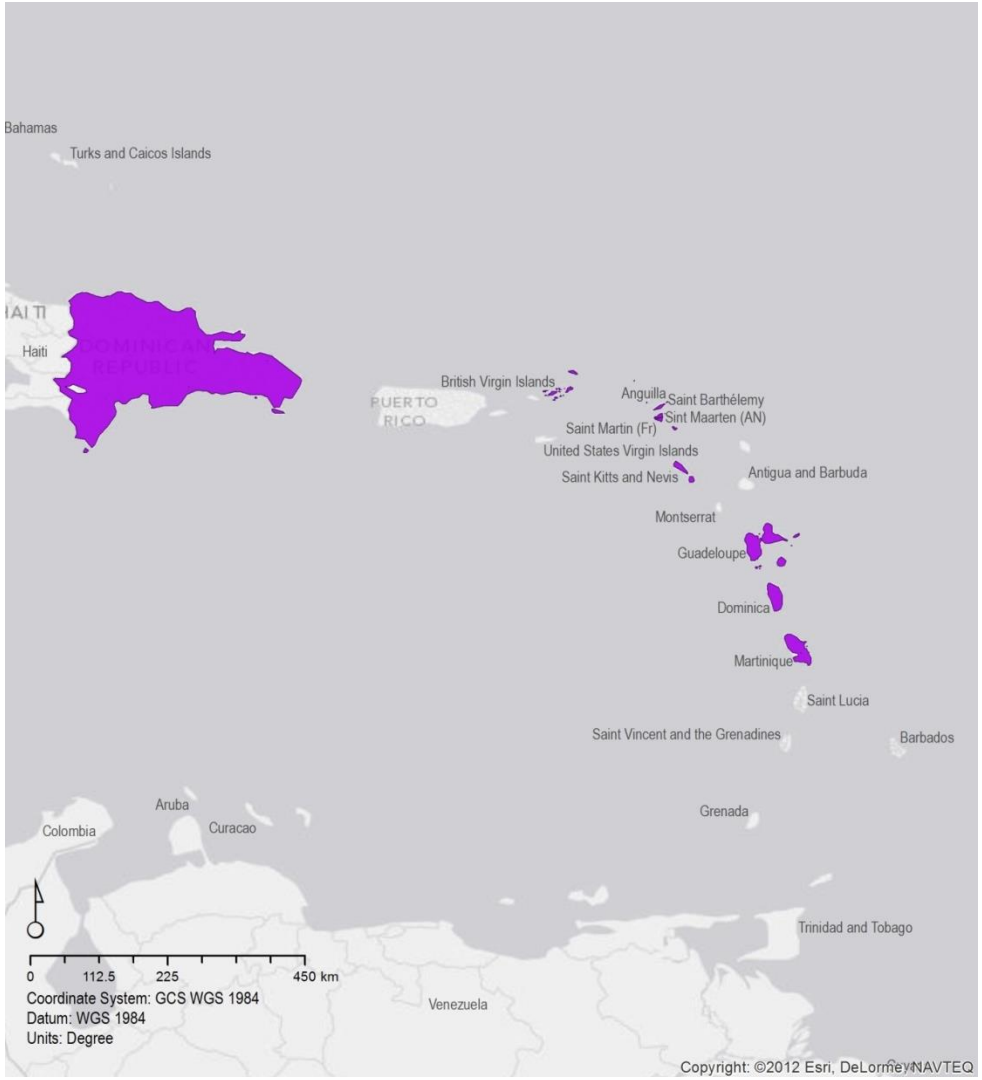
French Guiana

Source: PAHO

Chikungunya: March 2014

<u>New locations</u>

Dominican Republic



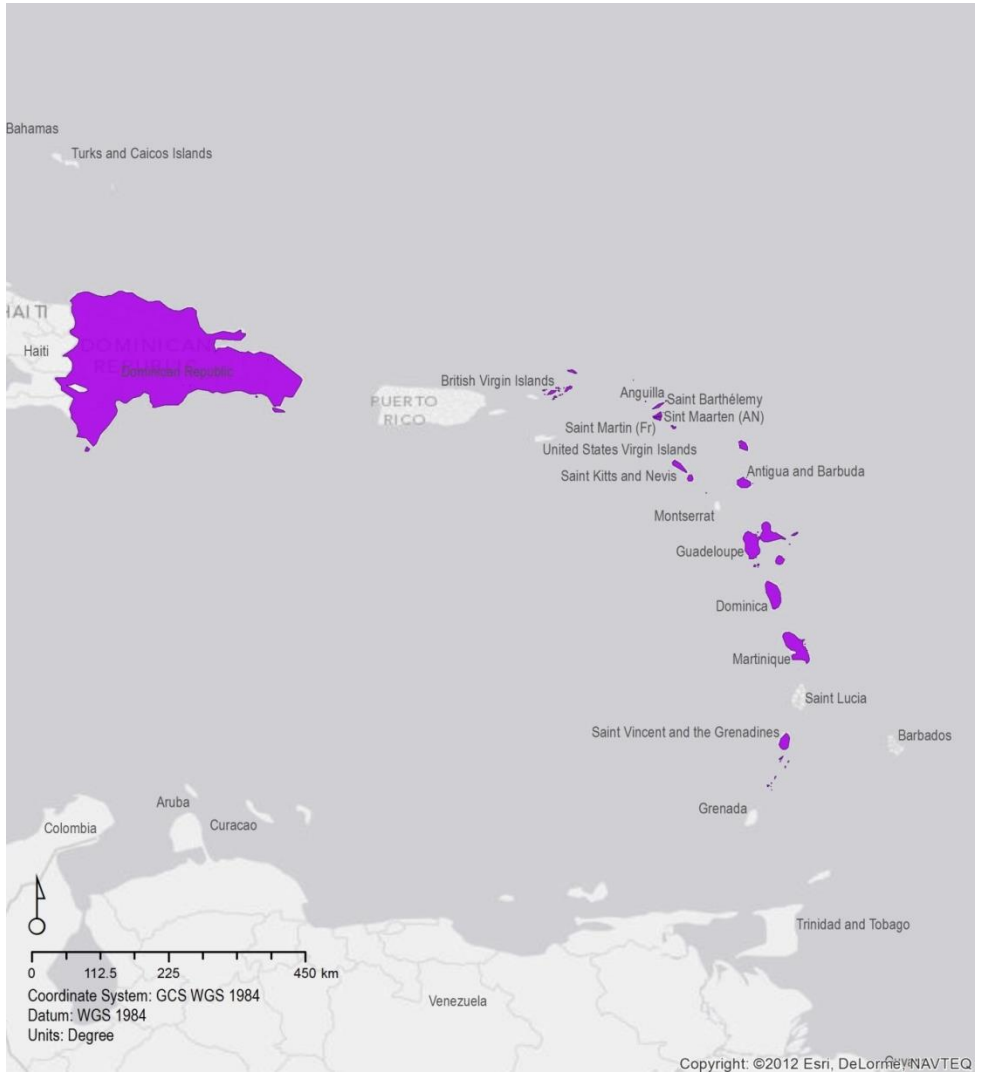
Source: PAHO

Chikungunya: April 2014

New locations

St. Vincent & Grenadines

Antigua & Barbuda



Source: PAHO

Chikungunya: May 2014

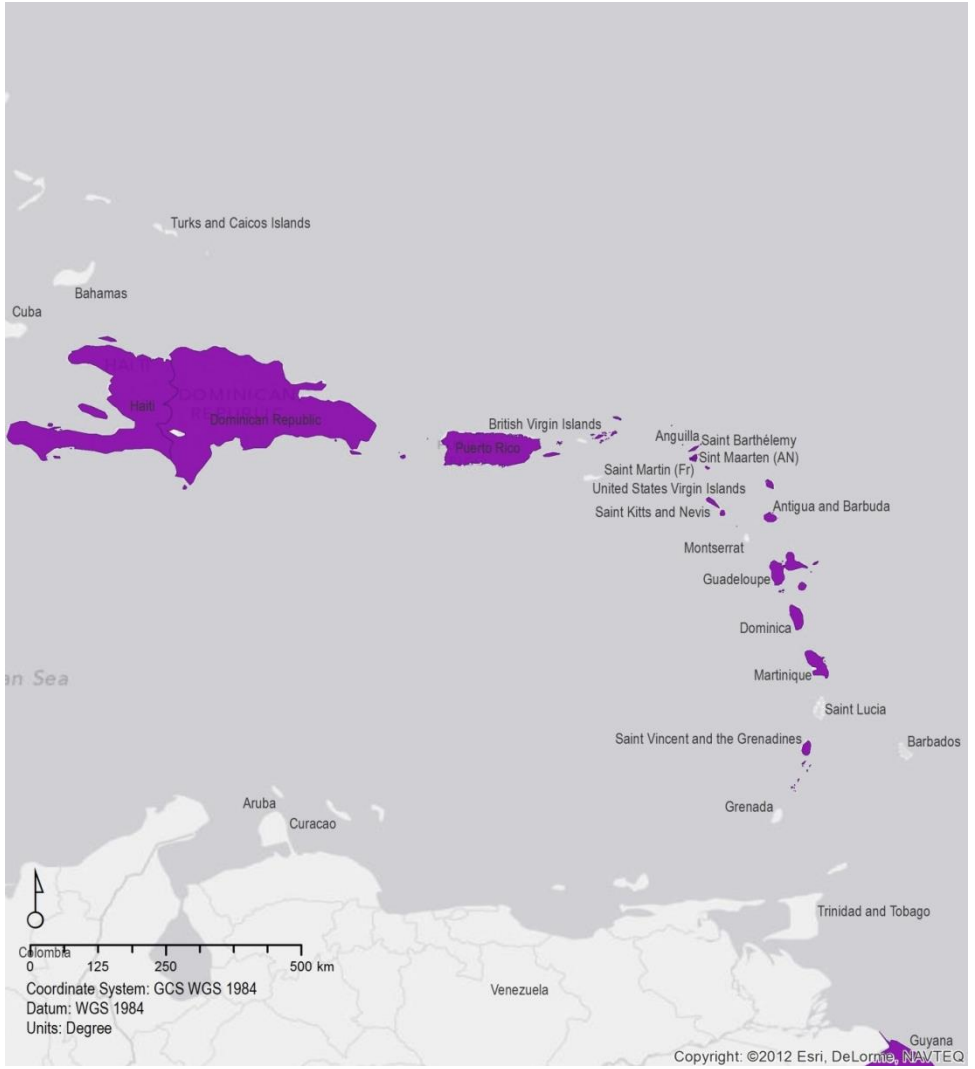
<u>New locations</u>

St. Lucia

Haiti

Puerto Rico

Guiana



Source: PAHO

Chikungunya: June 2014

New locations

Aruba

El Salvador

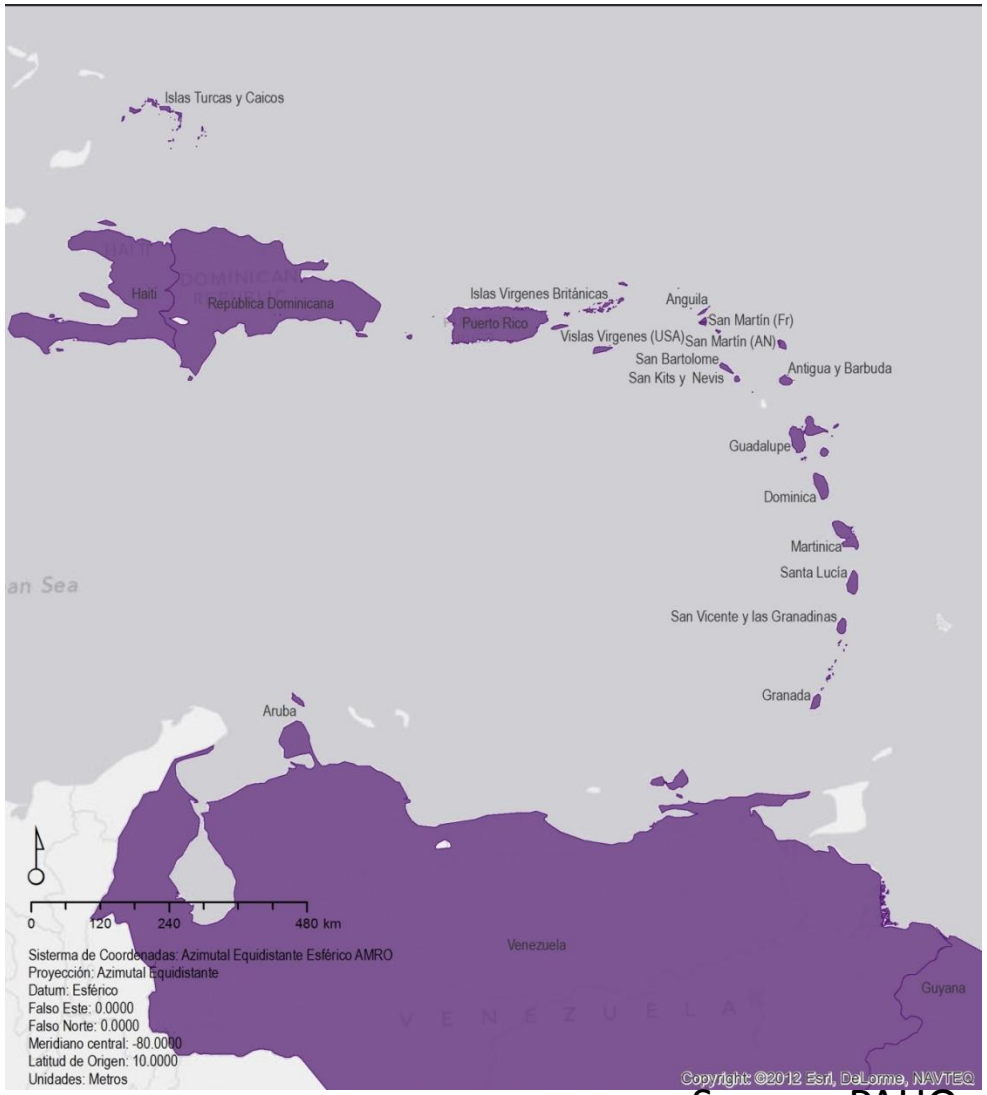
Grenada

Suriname

Turks and Caicos

U.S. Virgin Islands

Venezuela



Source: PAHO

Chikungunya: July 2014

<u>New areas</u>

Bahamas

Barbados

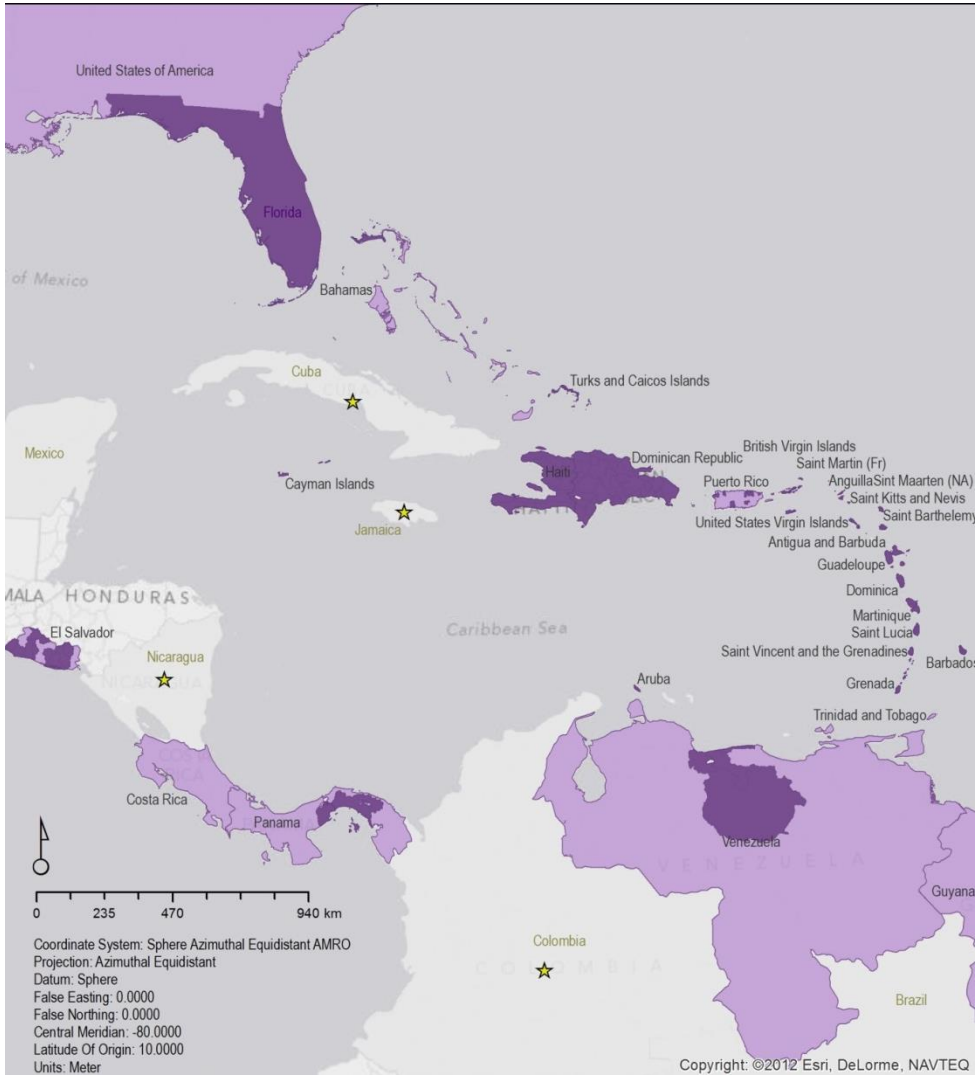
Cayman Islands

Trinidad and Tobago

Panama

Costa Rica

United States



Countries with autochthonous transmission

Sub-national areas with autochthonous transmission

Source: PAHO

Chikungunya: August 2014

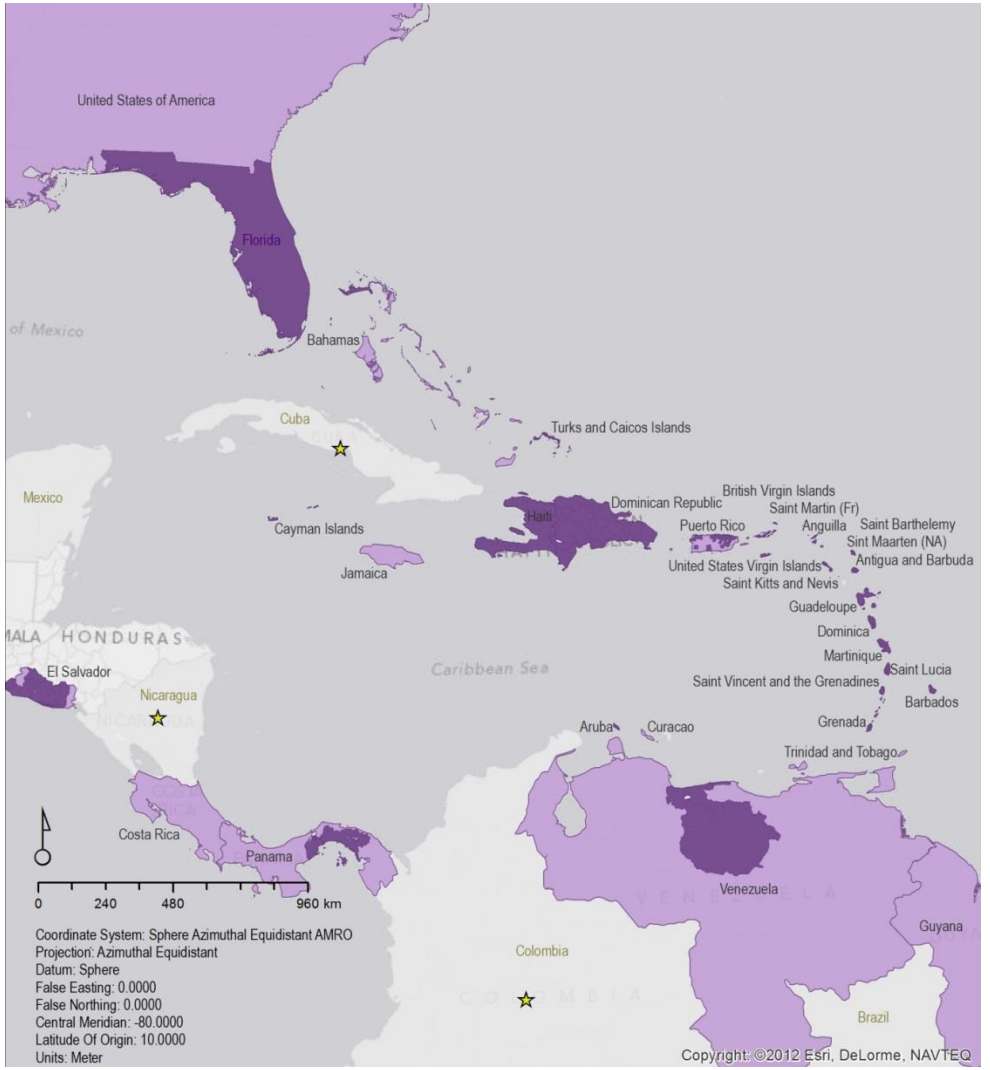
New Areas

Curacao

Jamaica

Countries with autochthonous transmission

Sub-national areas with autochthonous transmission



Source: PAHO

Chikungunya: September 2014

<u>New areas</u>

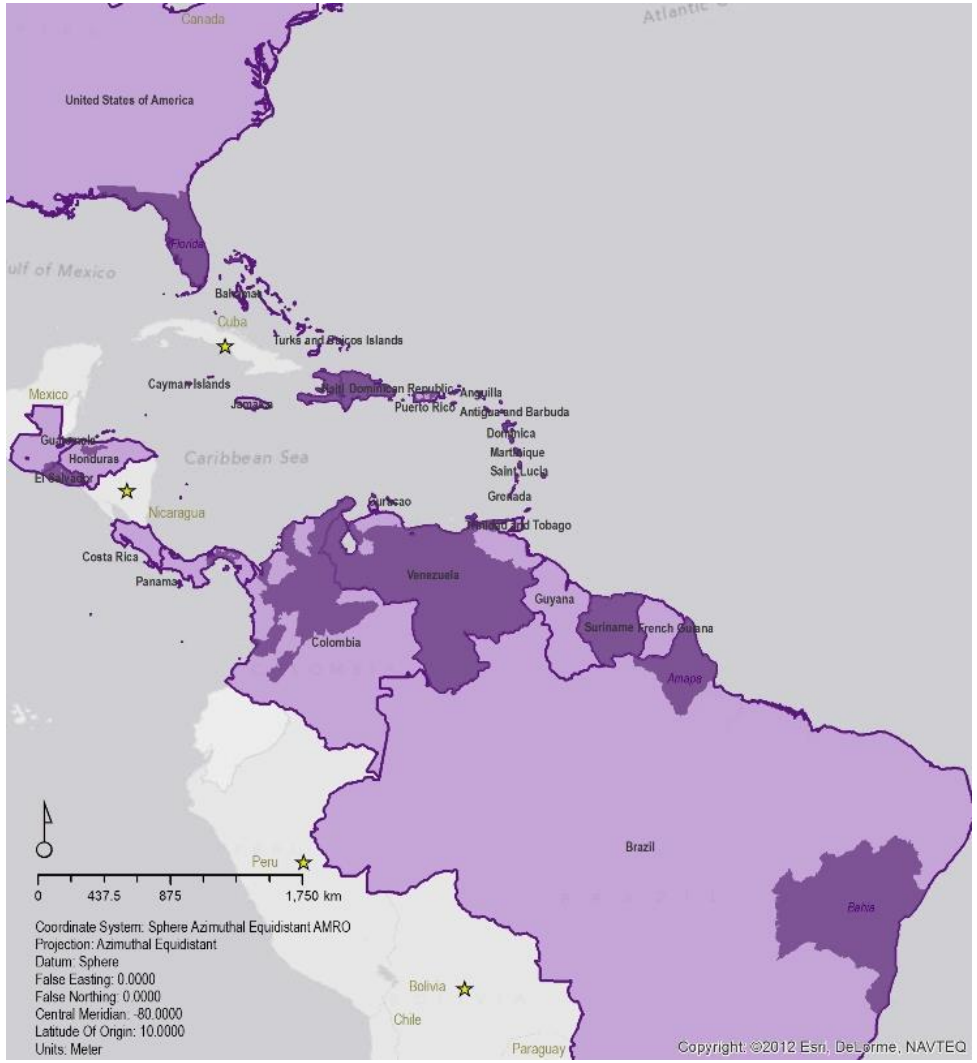
Brazil

Colombia

Guatemala

Honduras

Nicaragua



Countries with autochthonous transmission

Sub-national areas with autochthonous transmission

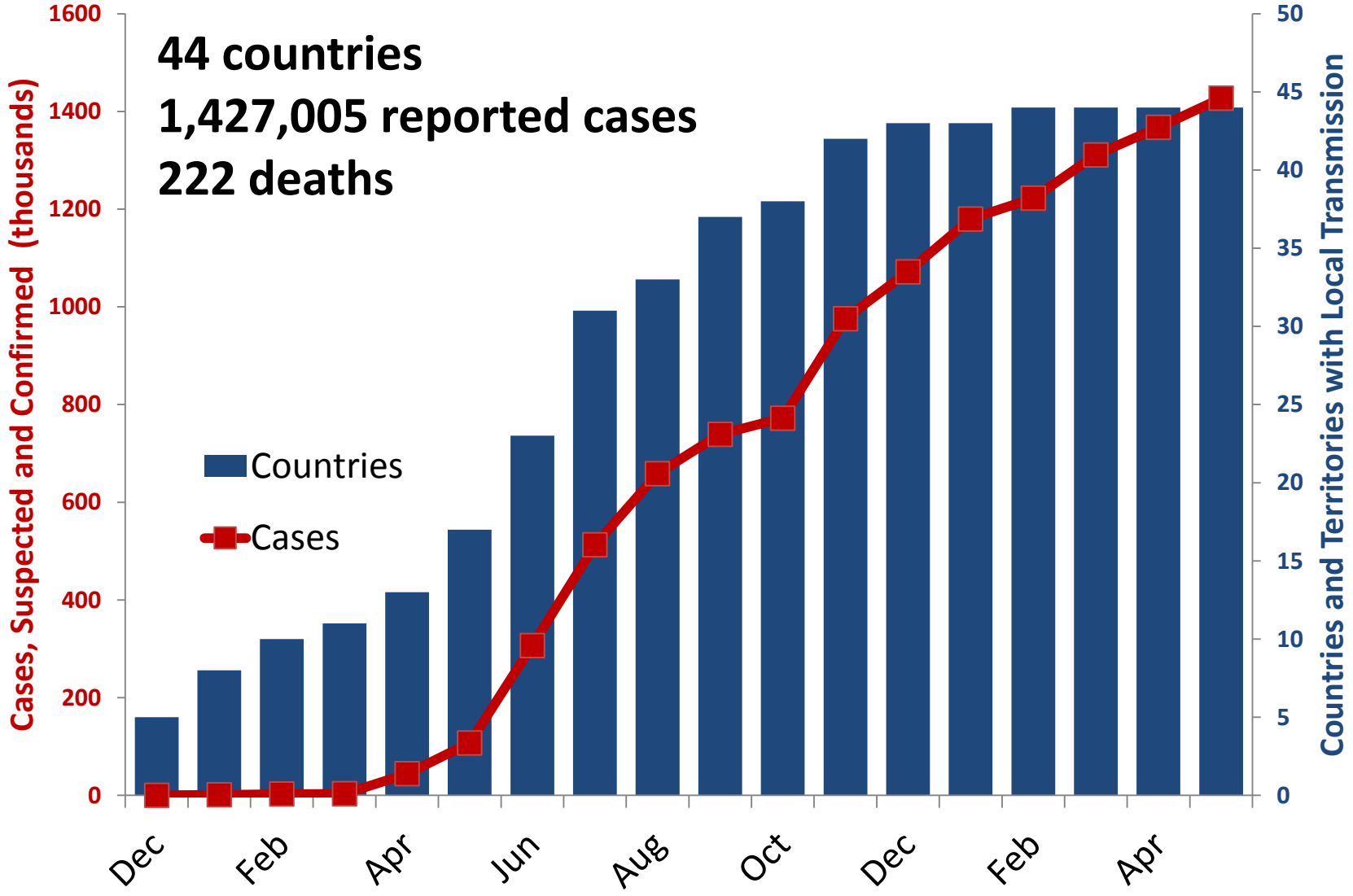
Source: PAHO

Chikungunya June 2015

Countries with autochthonous transmission

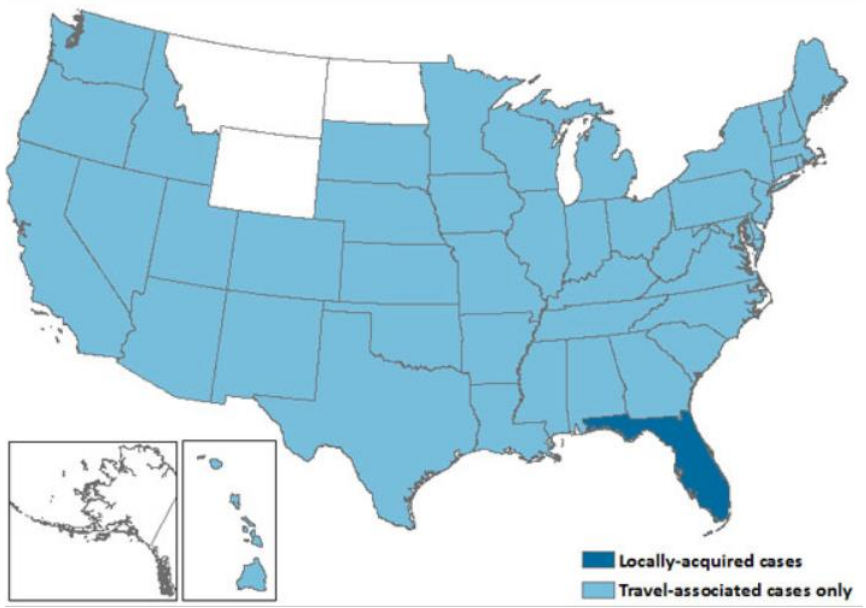
Sub-national areas with autochthonous transmission

CHIK in the Americas
December 2013 – May 2015



Source: PAHO report posted to http://www.paho.org/hq/index.php?option=com_topics&view=article&id=343&Itemid=40931

Chikungunya in the United States



(As of March 24, 2015)

Historically, from 2006–2013:

- An average 28 people/year with positive tests for recent CHIKV infection
- (Range 5–65 per year)

Current Outbreak, CONUS

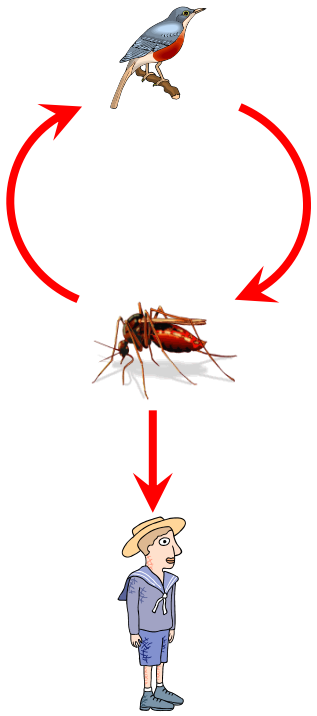
- 47 states reporting cases, and the District of Columbia
- 2,549 travel-associated cases
  - 18% from FL
  - 30% from NY
- 12 locally-acquired cases (FL)

http://www.cdc.gov/chikungunya/geo/index.html

Zika Virus

- Mild dengue-like illness
- Human-mosquito-human transmission
- *Aedes aegypti* primary vector
- Discovered in Zika Forest in Uganda
- Circulating in Western Pacific in recent years
- First detected in Western Hemisphere in Brazil in 2015; spreading

Scenario Two:
Humans are Incidental Hosts

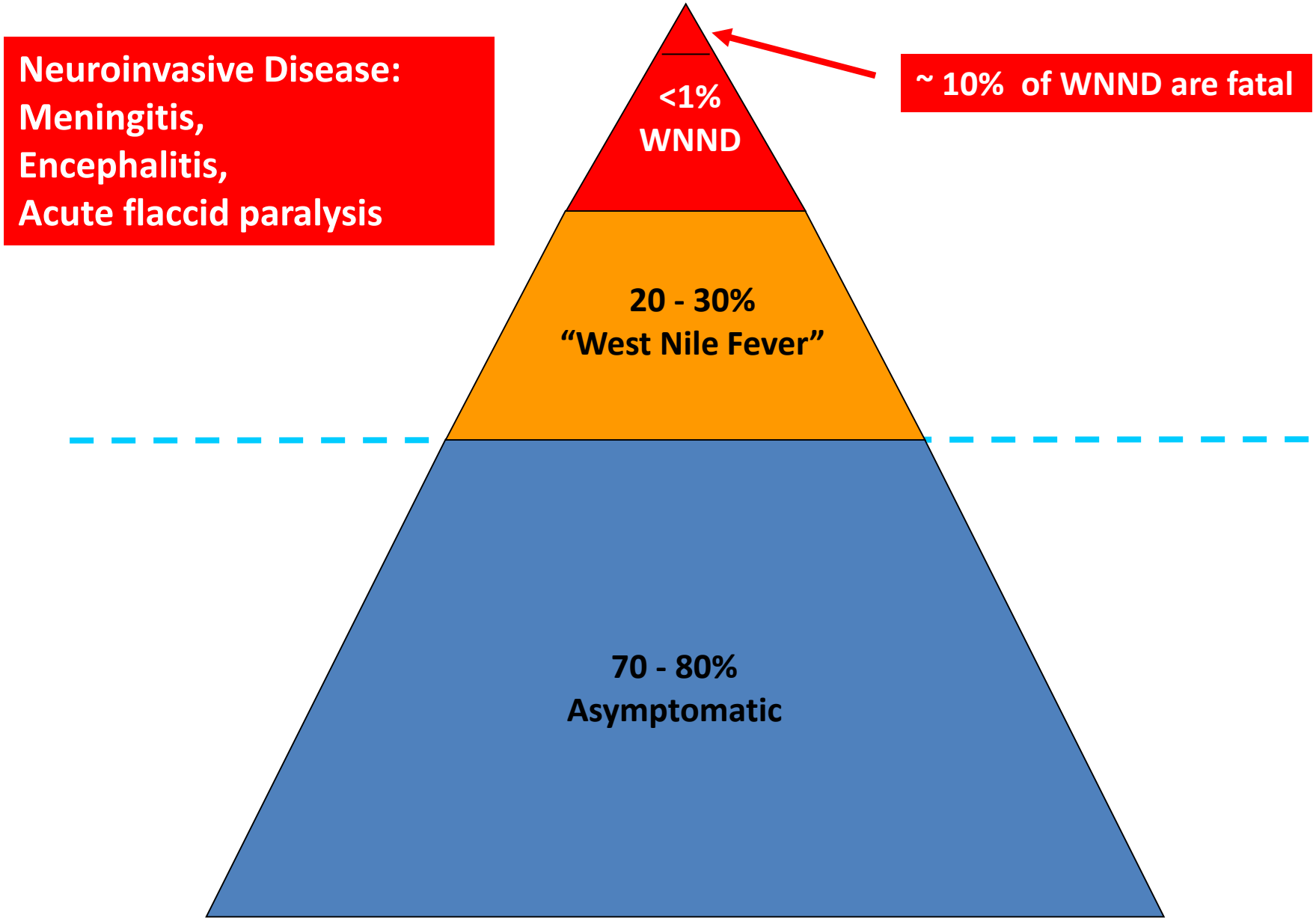


- West Nile virus

West Nile Virus

- Flavivirus
- Birds are vertebrate hosts; *Culex* mosquitoes vectors
- Introduced into New York City area in 1999
- No means of natural transport to Western Hemisphere
- Emergence during a heat wave
- Genetics suggests separate introductions in Europe and USA of lineage 1 WNV from Africa
- At least two sequential genetic mutation events of consequence
  - NY99 strain: NS3 T249P mutation increases viremia and mortality in birds
  - WN02 strain: E-V159A mutation changes viral transmission dynamics in birds and mosquitoes
- Continued co-evolution: Birds becoming less susceptible to illness and death, but viruses creating higher viremia

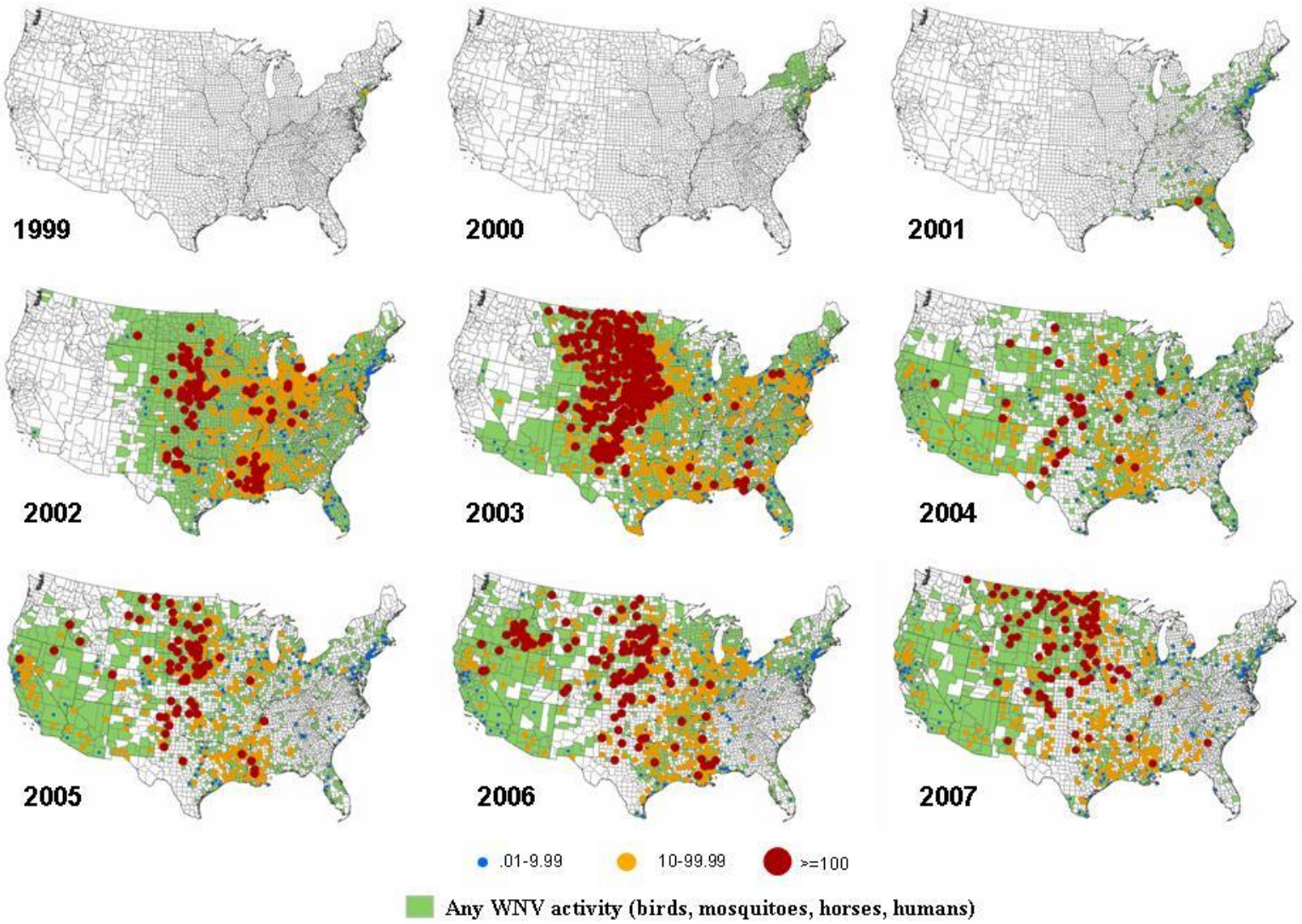
Clinical spectrum of human WNV infections



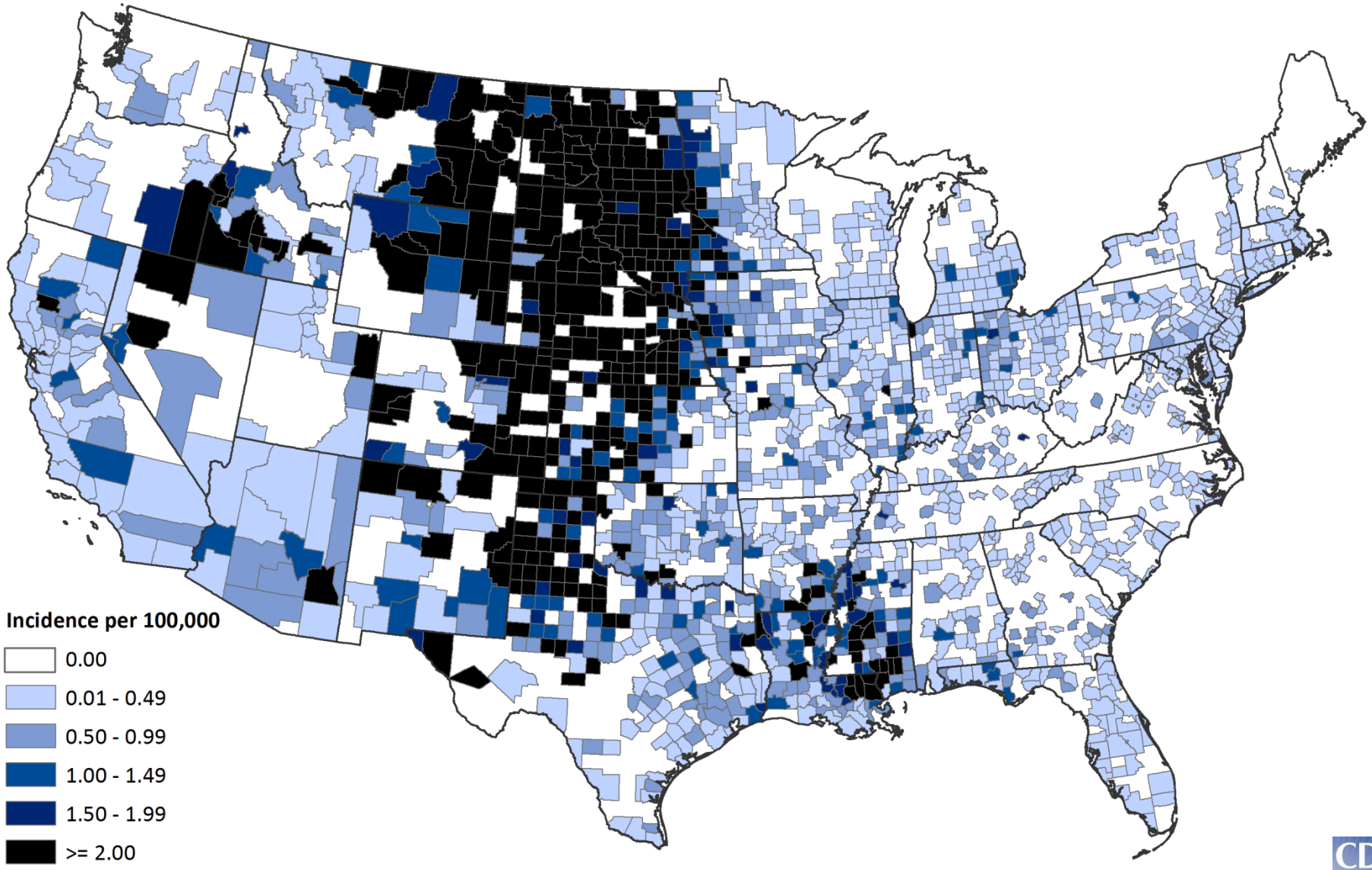
Estimated Number of West Nile Infections and Illnesses, 1999-2014

- 18,788 neuroinvasive disease cases reported
- For every reported neuroinvasive disease case,
  - 30 - 70 non-neuroinvasive disease cases
    - 560,000 - 1.3 million non-neuroinvasive disease cases
  - 150 - 300 infections
    - 2.8 - 5.6 million infections

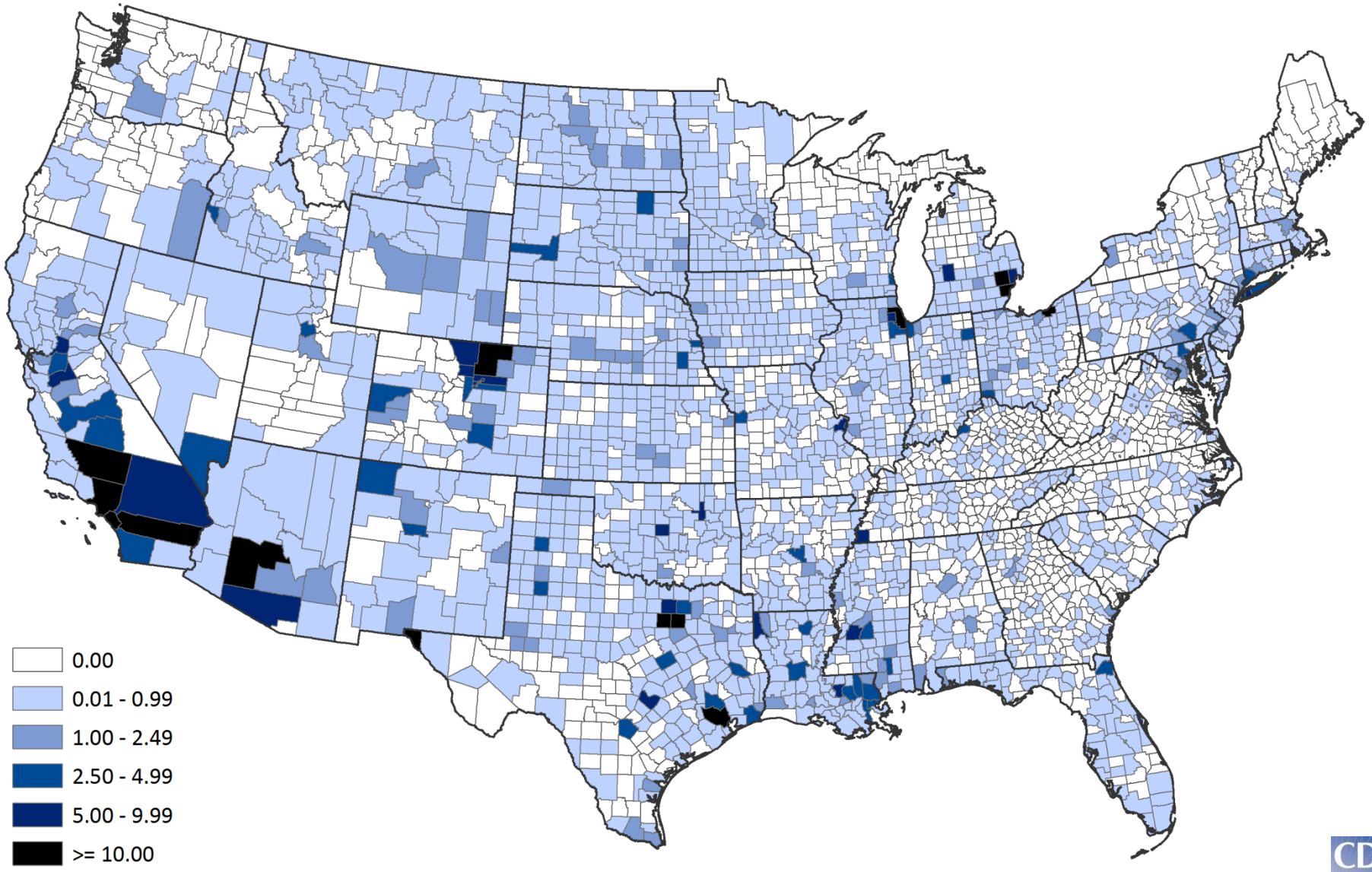
WNV Neuroinvasive Disease Incidence, by County, US, 1999-2007



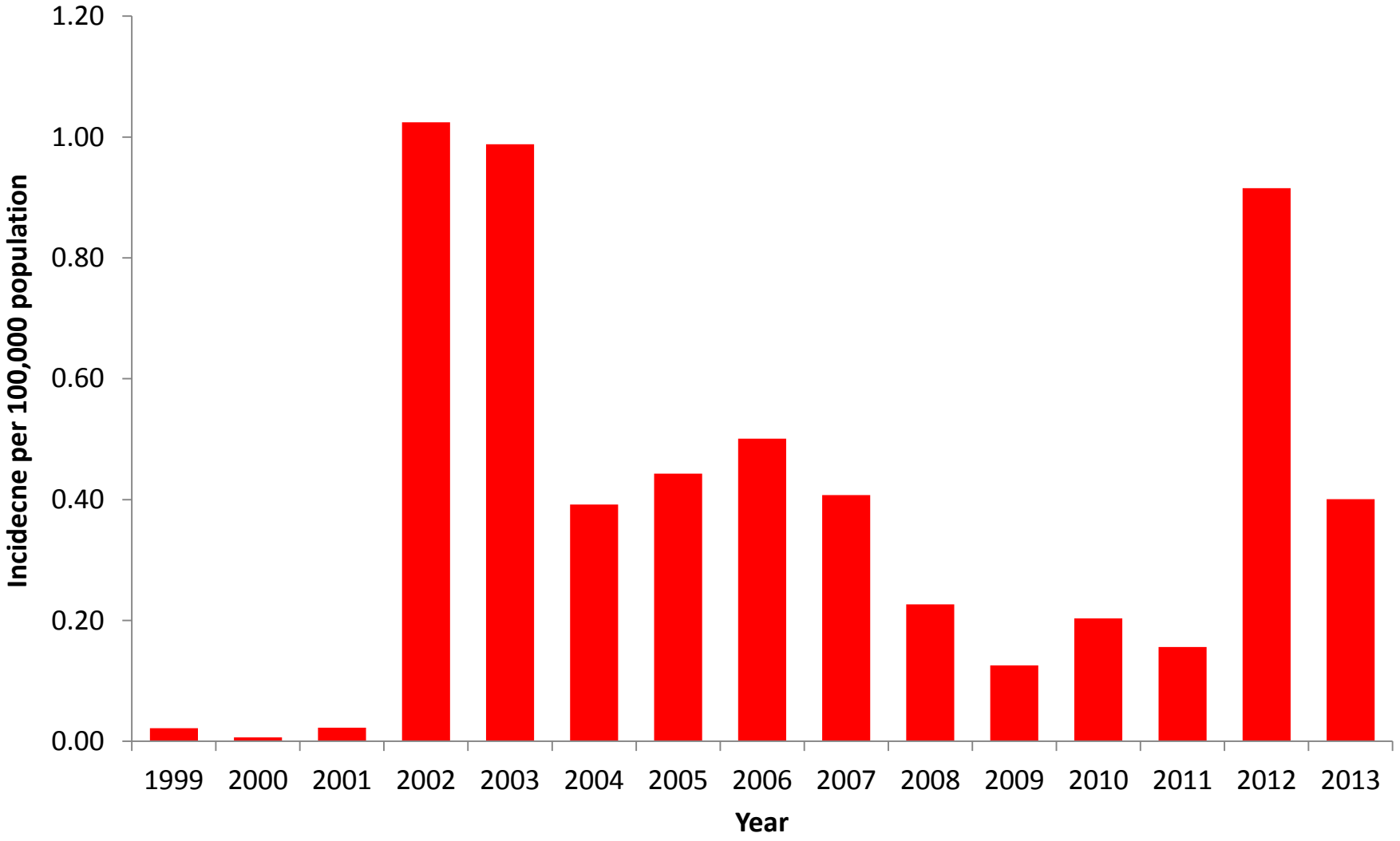
Average annual incidence of WNV severe neurological disease by county – United States, 1999–2013



Average annual number of WNV neuroinvasive disease cases by county – United States, 1999-2013



Average annual incidence of WNV neuroinvasive disease – United States, 1999–2013



Increasing Temperature Does Two Bad Things to Infected Mosquitoes

- Shortens time from infection to infectiousness (extrinsic incubation period)
- Increases viral replication in mosquitoes, making them more infectious

- E-V159A mutation in WN02 strain may augment this effect

Conclusions

- Climate and weather affect many factors that influence viral amplification, and hence outbreaks.
  - Heat waves appear to promote West Nile outbreaks
- Anthropogenic factors – travel and trade, land use, lifestyle, urbanization – are the major contributing factors to mosquito-borne disease emergence
  - Influence of climate change unclear
  - Models that consider climate change impacts on mosquito-borne disease emergence must consider anthropogenic factors that promote or prevent emergence

The findings and conclusions in this presentation are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention