Dengue Epidemiology in the United States and U.S. Territories: Perspective as a Vaccine Preventable Disease

Steve Waterman, MD, MPH

Chief, Dengue Branch

San Juan, Puerto Rico

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Outline – Dengue in U.S. Territories

I Dengue Epidemiology Background
II Puerto Rico
II Other US Territories
III US Mexico Border Region
IV Florida
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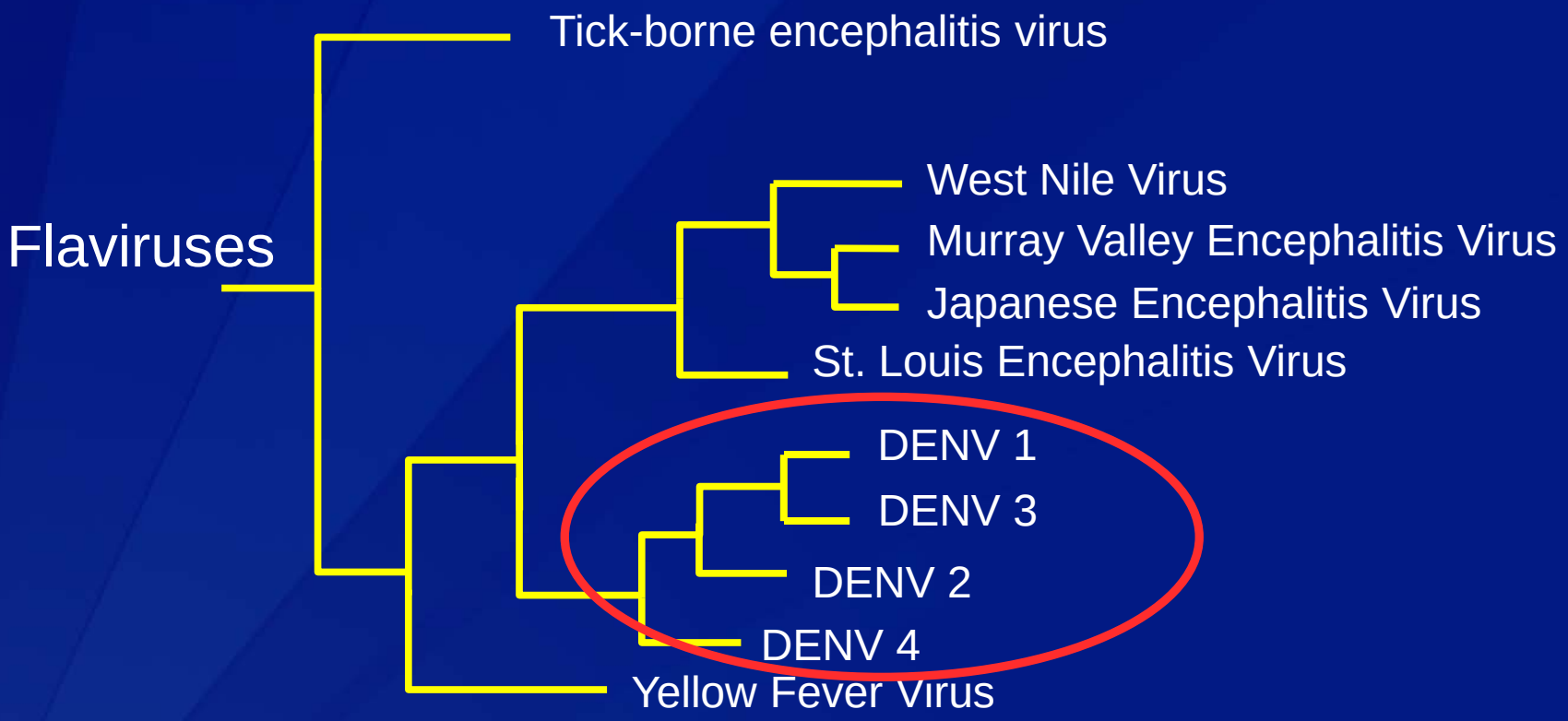
VI Summary

Dengue Viruses (DENV)

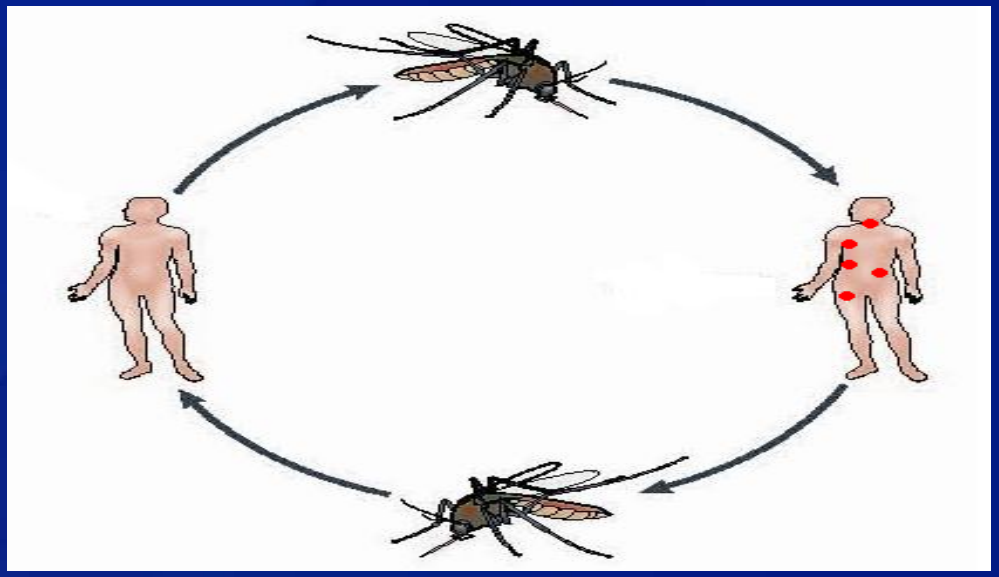


- Long-term protection to infecting virus-type
- No long-term cross protective immunity
- Can be infected up to 4 times during lifetime

DENV: Humans the Primary Host

Mosquito acquires virus during feeding, virus replicates in mosquito

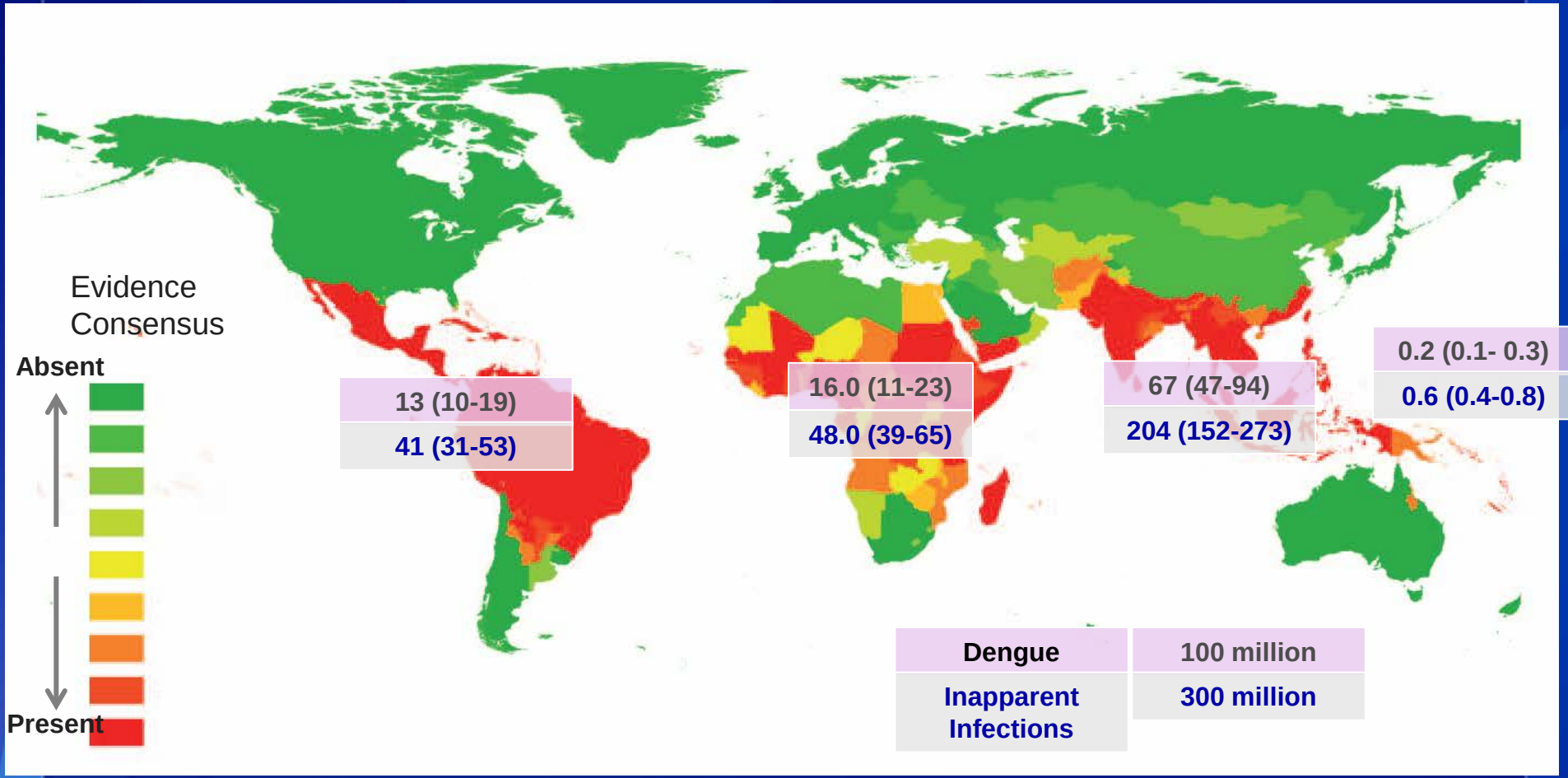
Mosquito infects susceptible person



Mosquito infects humans – virus in lymph nodes, other organs, blood

Mosquito acquires virus during feeding, virus replicates in mosquito

Dengue is a Global Problem



Adapted from Bhatt, S et al Nature 2013; 496: 504-507

Dengue Epidemiology Overview

- Dengue is an acute febrile illness (AFI) syndrome
- Incidence: high endemic + cyclical epidemics
- Highly seasonal
- Often several circulating DENV types
- Peak age of incidence may vary by region
- Severe dengue is natural progression of disease

Guidelines for Clinical Evaluation of Dengue Vaccine in Dengue Endemic Areas. Vaccine 2008;26:4113-4119

Risk factors for severe dengue

- Secondary infections
- Virus strain
- Host genetics
- Co-morbidities
- Young age
- Female

Dengue in the United States
A Risk-Assessment Framework

- **Vector present – endemic dengue**
  - Caribbean: Puerto Rico, Virgin Islands
  - Pacific Islands
- **Vector present – non-endemic – potential for transmission**
  - Outbreaks in: Texas (US - Mexico border), Florida, Hawaii
  - Many states (e.g., FL, GA, AL, LA, MI, SC, NC, TX, AZ, CA)
- **Vector not present**

History of Dengue in Puerto Rico

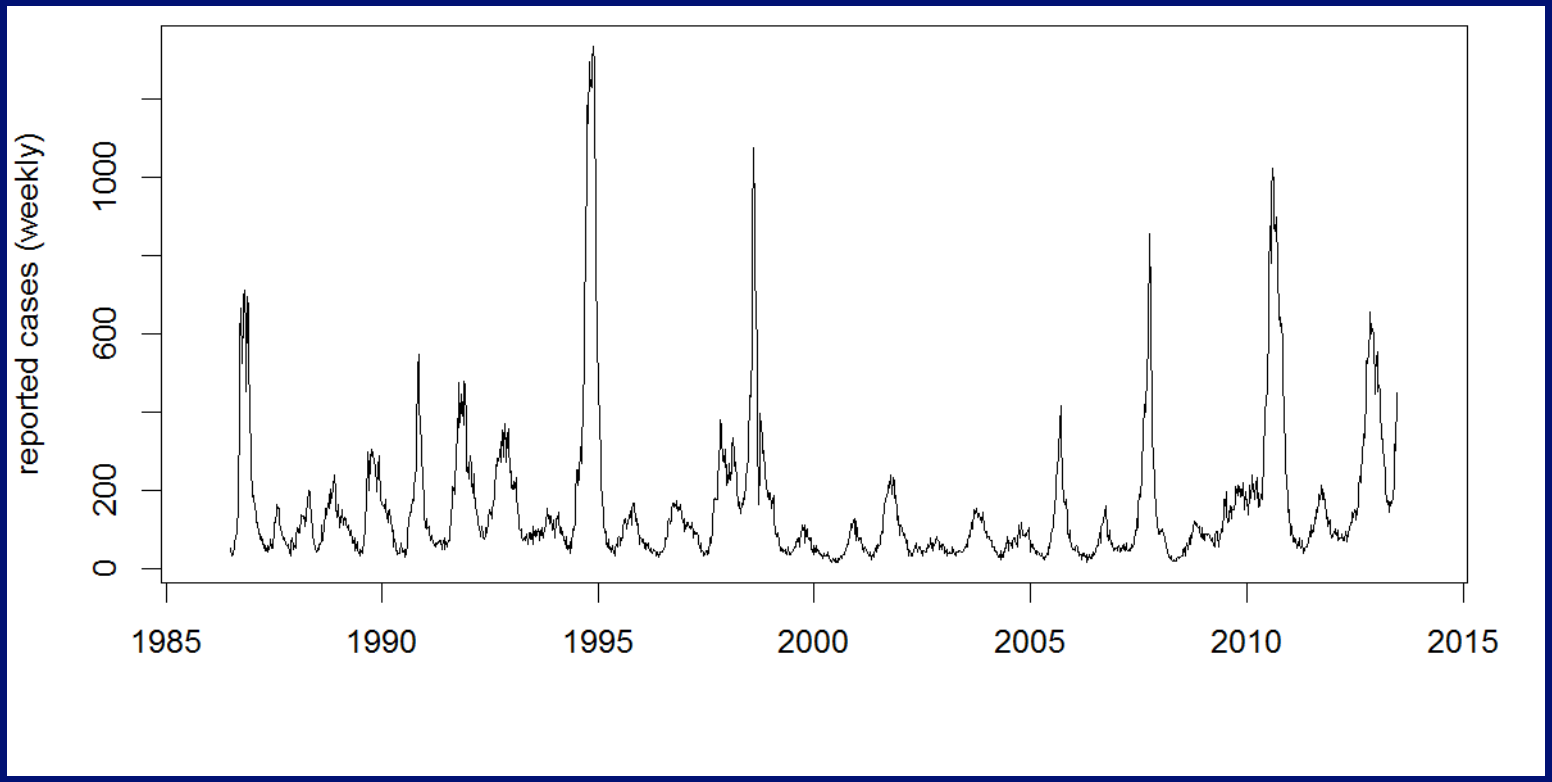
- **First major epidemics reported in 1915 and 1945**
- **In 1963, DENV first isolated in Puerto Rico**
- **First laboratory confirmed case of dengue hemorrhagic fever (DHF) reported in 1975**
- **First time more than one DENV type in circulation was in 1977 outbreak**
  - DENV- 1, 2 and 3 were detected
- **During 1969–1986, there were six large, island-wide outbreaks**

Current Epidemiology of Dengue in Puerto Rico

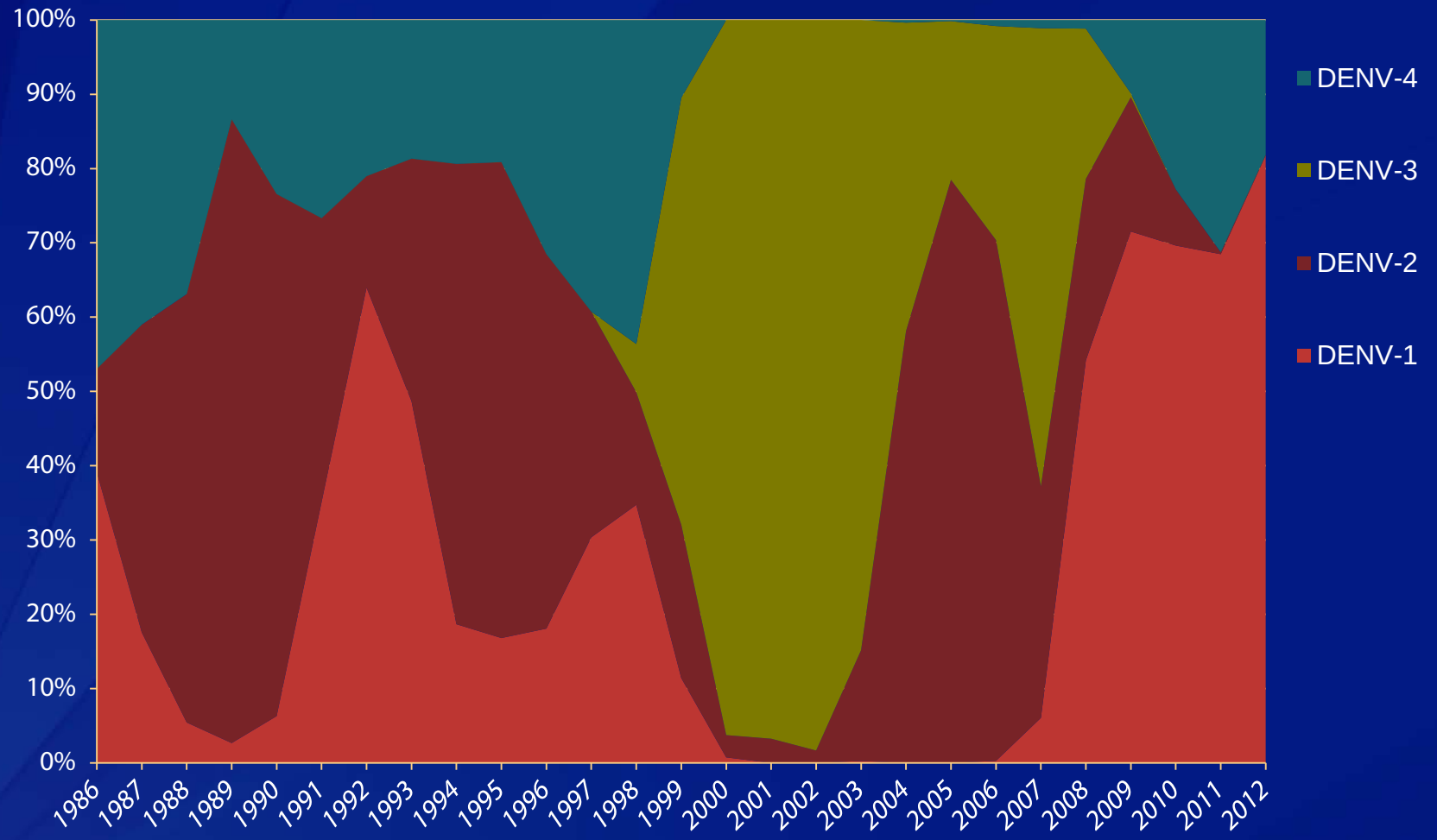
- **Only *Ae. aegypti* present**
- **Endemic**
  - 1960s–2013*: ~3,000–27,000 suspected cases per year
  - 3–4 DENVs co-circulating since 1980s
- **Seasonal**
  - Low incidence in Dec–Mar
  - High incidence in July–Sept
- **Geospatial clustering**
  - Higher population density = higher incidence
- **Burden of disease highest among 10–19 year-olds**
  - No difference by sex

*Chikungunya and Zika viruses first detected in May 2014 and November 2015, respectively

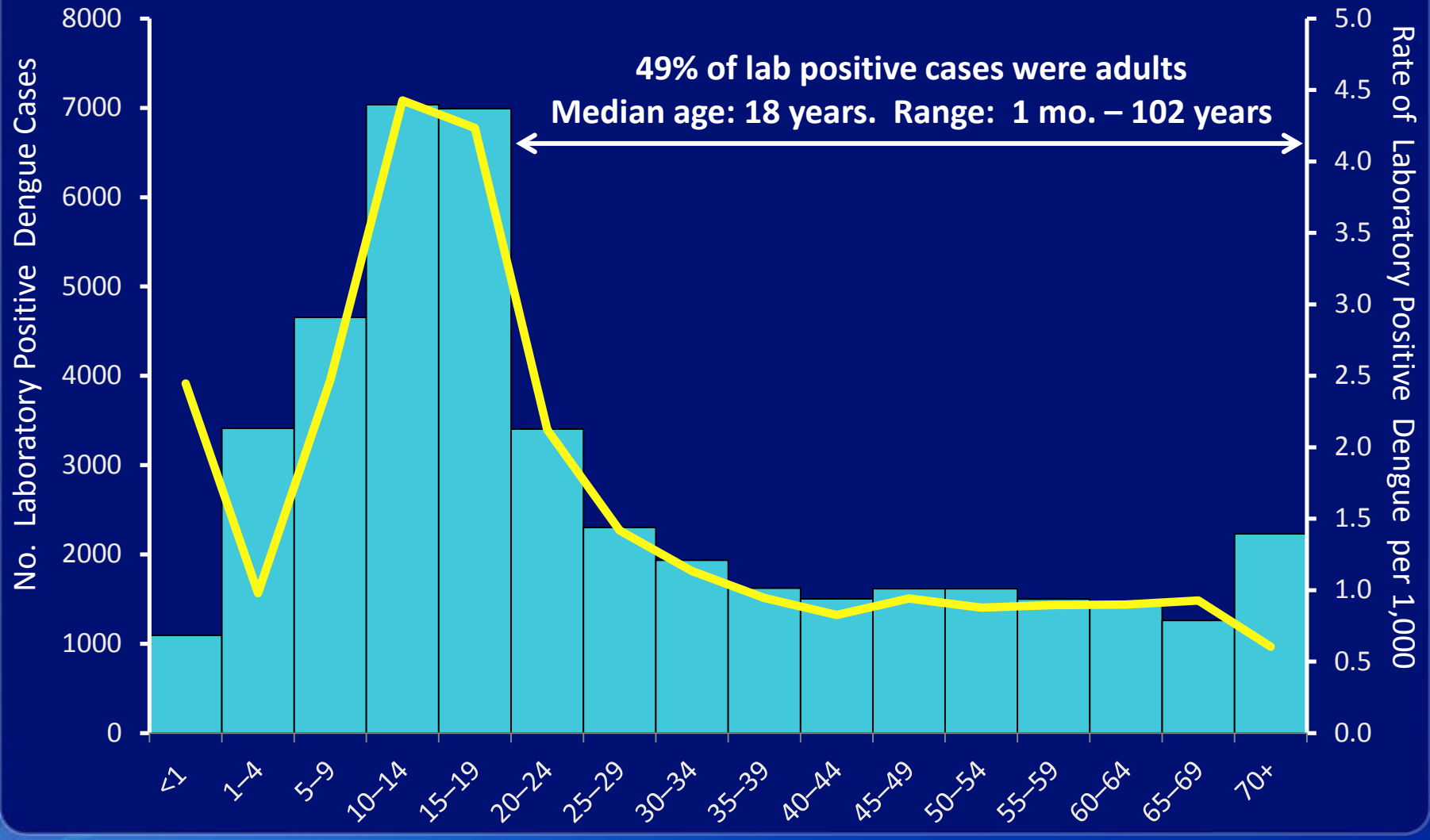
‘Suspect Dengue’ in Puerto Rico 1986-2013



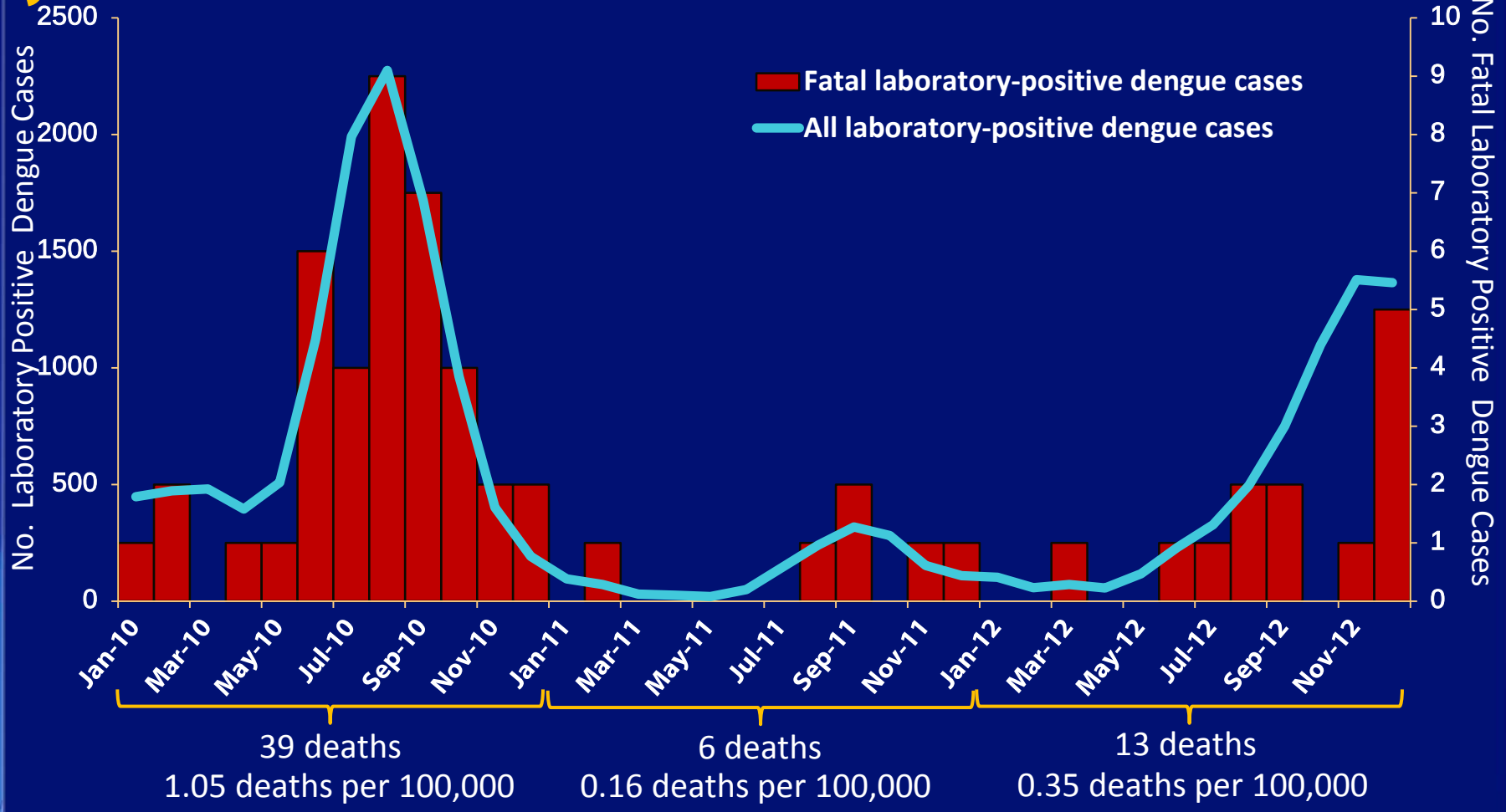
Percent of Dengue Virus Isolates by Type and Year — Puerto Rico, 1986–2012



Age Distribution of Laboratory Positive Dengue Cases — Puerto Rico, 2010–2012

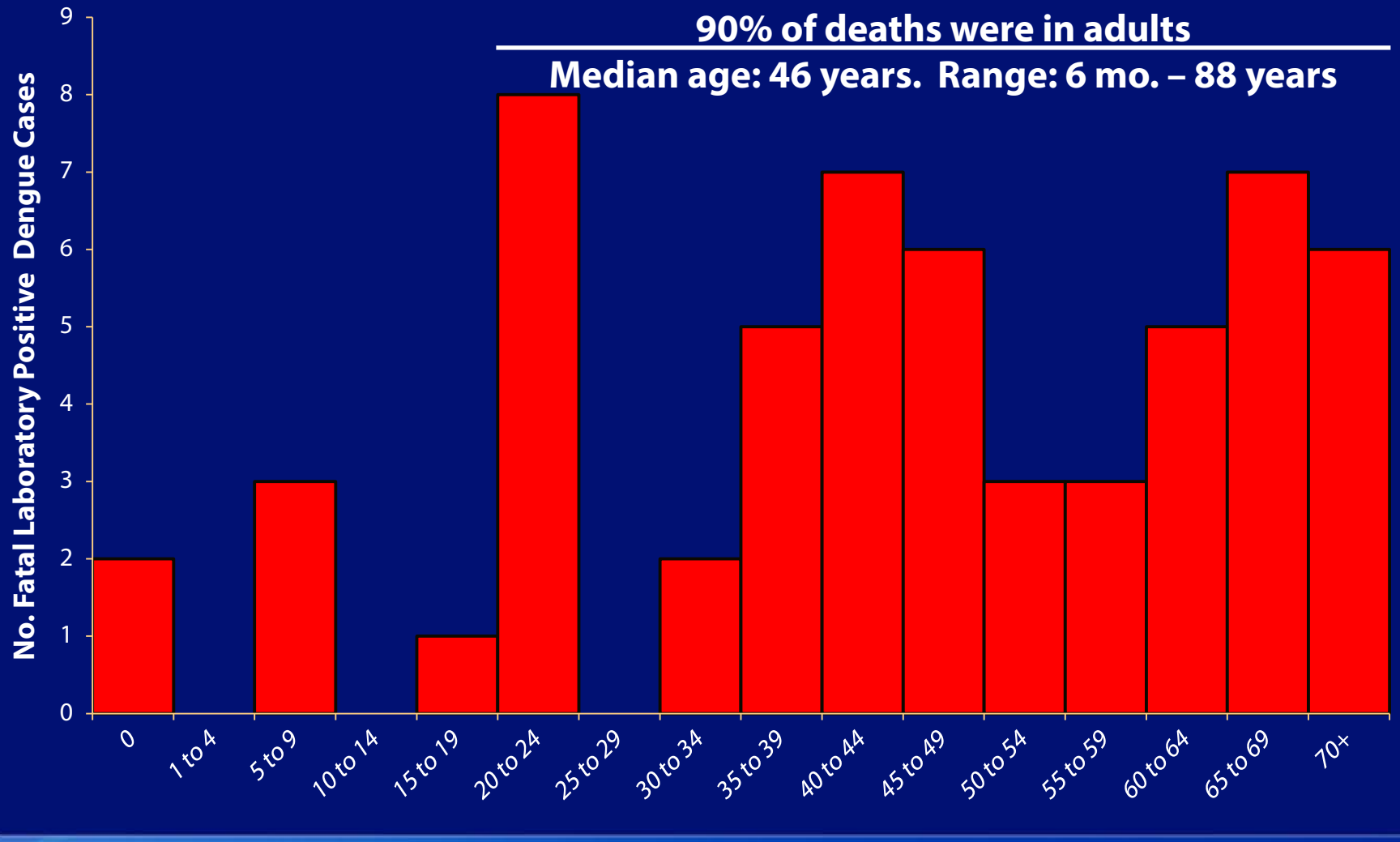


Laboratory Positive Dengue Cases and Fatal Cases by Month of Illness Onset, 2010–2012, Puerto Rico



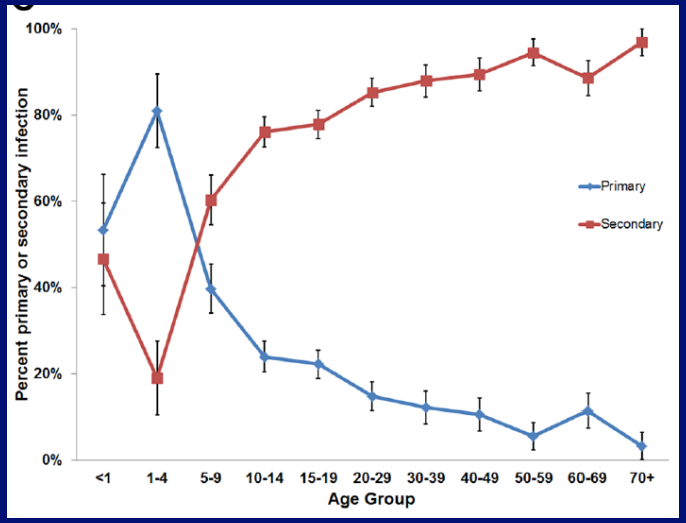
Tomashek et al., PLoS NTD, 2016.

Age Distribution of Fatal Laboratory-Positive Dengue Cases — Puerto Rico, 2010–2012



Seroprevalence of DENV infection and proportion of primary vs. secondary infections

- **2006: serosurvey among blood donors (only adults)[1]**
  - ~92% seropositive
    - ~96% secondary infections
- **2010: among lab-positive dengue cases[2]**
  - ~80% of all infections were secondary
  - Primary infection more common only among 1–4 year-olds
  - >80% of all adults had secondary infection



[1]Mohammed et al., Transfusion, 2012
[2]Sharp et al., PLoS NTD, 2013.

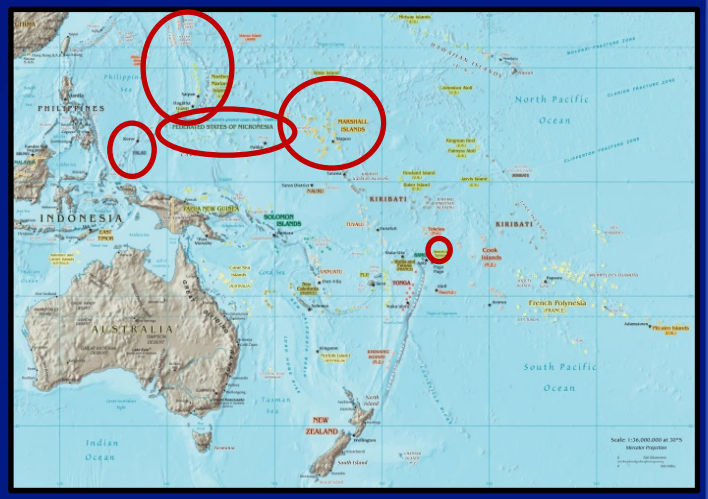
Dengue in US Virgin Islands

- **US Virgin Islands**
  - St. Croix, St. John, St. Thomas and Water Island
  - *Aedes aegypti* present throughout
  - Passive case reporting

- **Periodic outbreaks**
  - 1986-1987 (DENV-2, -4), St. Johns
  - 1990 (DENV-1, -2, and -4), all islands
  - 2004 (DENV-2), St. Thomas
  - 2005 (DENV-2), St. Croix
  - 2012 (DENV-1, -4), St. Croix
    - School survey: ~20% acute/recent infections

Dengue in the US-affiliated Pacific Islands† and Territories*

- *Ae. albopictus* and *aegypti* both present, as well as less common vectors (e.g., *Ae. hensilii*, *Ae. marshellensis*)
- Periodic outbreaks detected since 1958 (Guam[1])
  - Unclear which, if any, are endemic
- Often only one DENV type circulating at a time
- 2010 serosurvey in American Samoa (adults only): 96% seropositive[2]



*American Samoa, Guam, Northern Mariana Islands; †Palau, Republic of the Marshall Islands, Federated States of Micronesia

[1]Hammon et al., *Am J Trop Med Hyg*, 1958.

[2]Lau, EID, 2013.

Dengue Outbreak in American Samoa, 2015

- May–November: 479 suspected dengue cases
  - ~1% of population
- Incidence highest among individuals aged <25 years
- Only DENV detected by RT-PCR was DENV-3
- 4 fatal cases
  - CFR = ~1%
- Most common vectors were *Ae. polynesiensis* and *aegypti*

Dengue in the U.S. – Mexico Border Region

Locally-acquired Dengue in Texas

- **Historical outbreaks[1]**
  - **First outbreak 1885-86: >70% of Austin residents affected**
  - **Last 1922: ~500,000 cases throughout the state**

[1]Ehrenkranz et al., *NEJM* 1971.

Locally-acquired Dengue in South Texas

- 3 outbreaks prior to 1999
  - 1980: 28 cases in Brownsville and nearby Texas border towns; DENV-1
  - 1986: 9 cases, Brownsville (4), Corpus Christi (3), Laredo (2); DENV-1
  - 1995-6: 7 cases Brownsville (3), McAllen (4): DENV-2, 4

MMWR 45(39) 1996

Dengue in Laredo, Texas /Nuevo Laredo, Tamaulipas, Mexico, 1999

- Seroprevalence
  - Mexico (n=288)
    - IgM – 16.0%
    - IgG – 47.8%
  - U.S. (n=228)
    - IgM – 1.3%
    - IgG – 22.5%

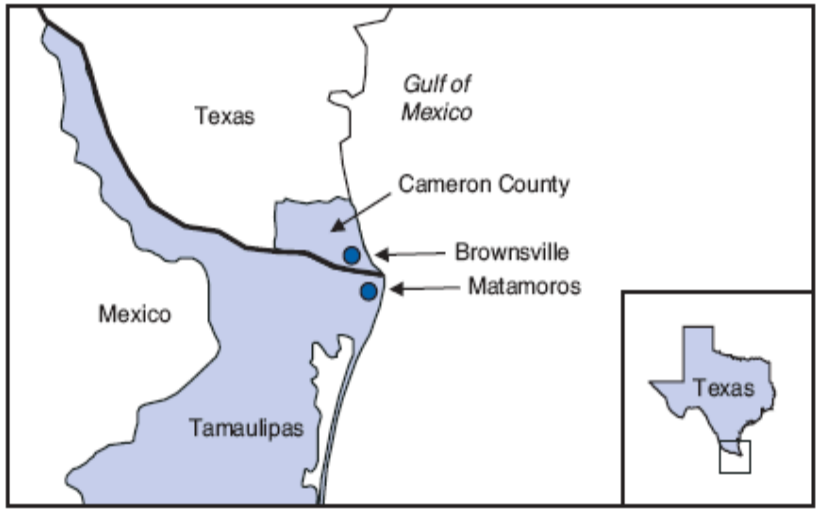
- Evidence of local transmission
- Lack of air conditioning a risk factor for dengue infection

Reiter et al. *Emerging Infectious Diseases* 2003

Dengue/Dengue Hemorrhagic Fever in Cameron County, Texas and Matamoros, Tamaulipas, Mexico, 2005

- **Seroprevalence**
  - **Mexico (n=132)**
    - **IgM – 22.8%**
    - **IgG – 76.6%**
  - **U.S. (n=141)**
    - **IgM – 2.5% (0-5.4, 95% CI))**
    - **IgG – 38.2% (26.7-49.8, 95% CI)**
- **DENV-2, SE Asia strain**
- **Clinical classification**
  - **Mexico – > 6800 cases, > 50% hospitalized, estimate 1/3 with DHF**
  - **U.S. – 25/28 (89%) hospitalized; 16 DHF cases**
- **Evidence of local transmission**

FIGURE 1. Jurisdictions affected by dengue fever outbreak — Texas–Mexico border, 2005



Ramos et al *Am J Trop Med Hyg 78(3) 2008; MMWR 56 2007*

Dengue in Cameron County, 2013

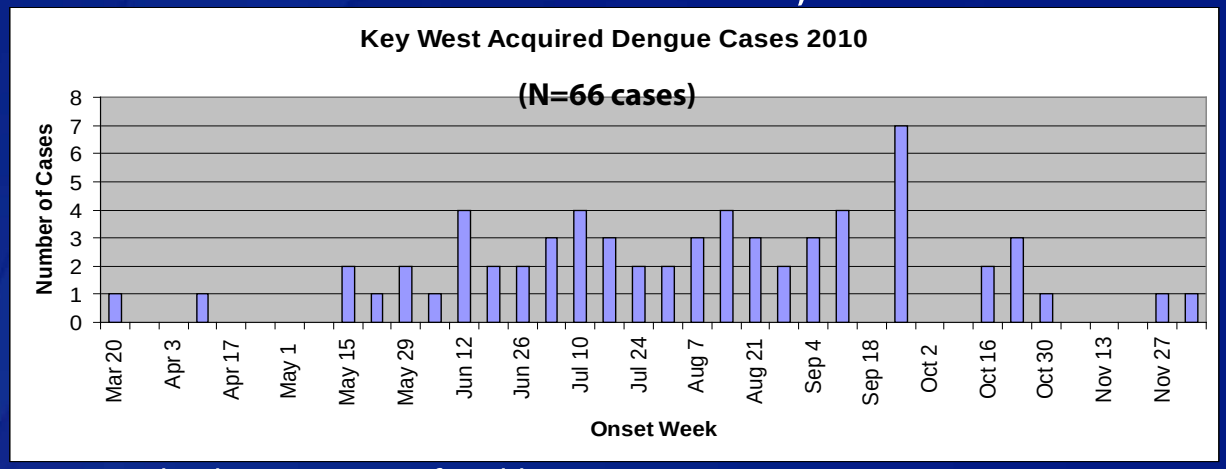
- DENV-1, 3
- 53 laboratory positive cases from enhanced surveillance
- 55% hospitalized
- 49% locally acquired
- Cluster survey – 6 (12%) of 51 household members of dengue cases with recent dengue and no travel

Thomas et al. Emerg Inf Dis 2016

Locally-acquired Dengue in Florida, 2009-2010

- **27 cases in Monroe County (Key West) in 2009**
  - DENV-1
  - 2009 Onset: July 19–Oct 18, 2009

- **Serosurvey in Key West Sept 2009**
  - 5% had acute/recent dengue
- **66 cases in Monroe County in 2010**
  - 2010 Onset: March 20–Nov 30, 2010



Data: Florida Department of Health

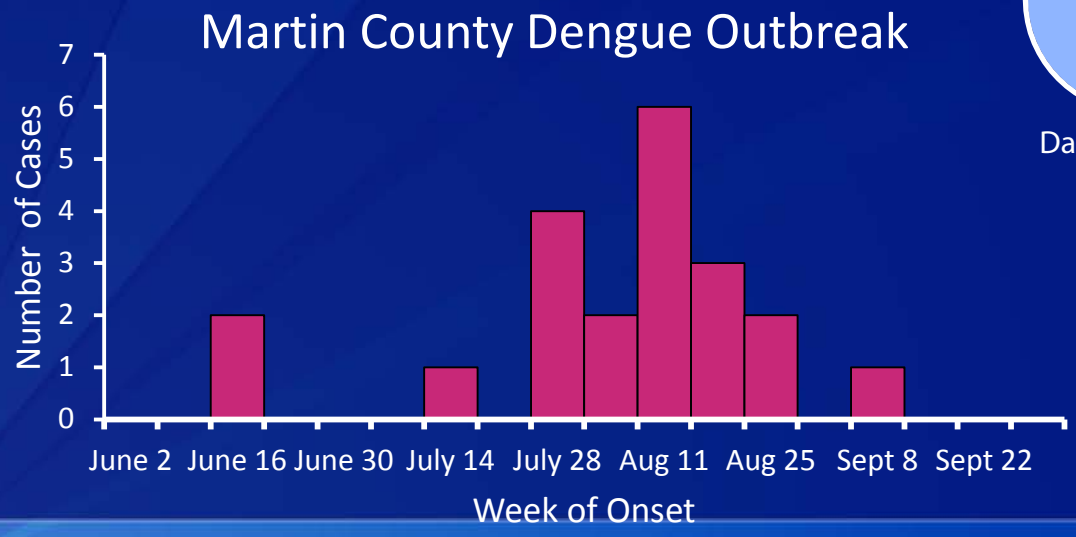
Locally-acquired Dengue in Florida, 2010-2012

- **2 sporadic cases in 2010**
  - Miami-Dade (1) and Broward (1) counties
- **7 sporadic cases in 2011**
  - Miami-Dade (3), Palm Beach (2) Hillsborough (1), and Martin (1) counties
- **4 sporadic cases in 2012**
  - Miami-Dade (2), Seminole (1) and Osceola (1) counties

Locally-acquired Dengue in Florida, 2013

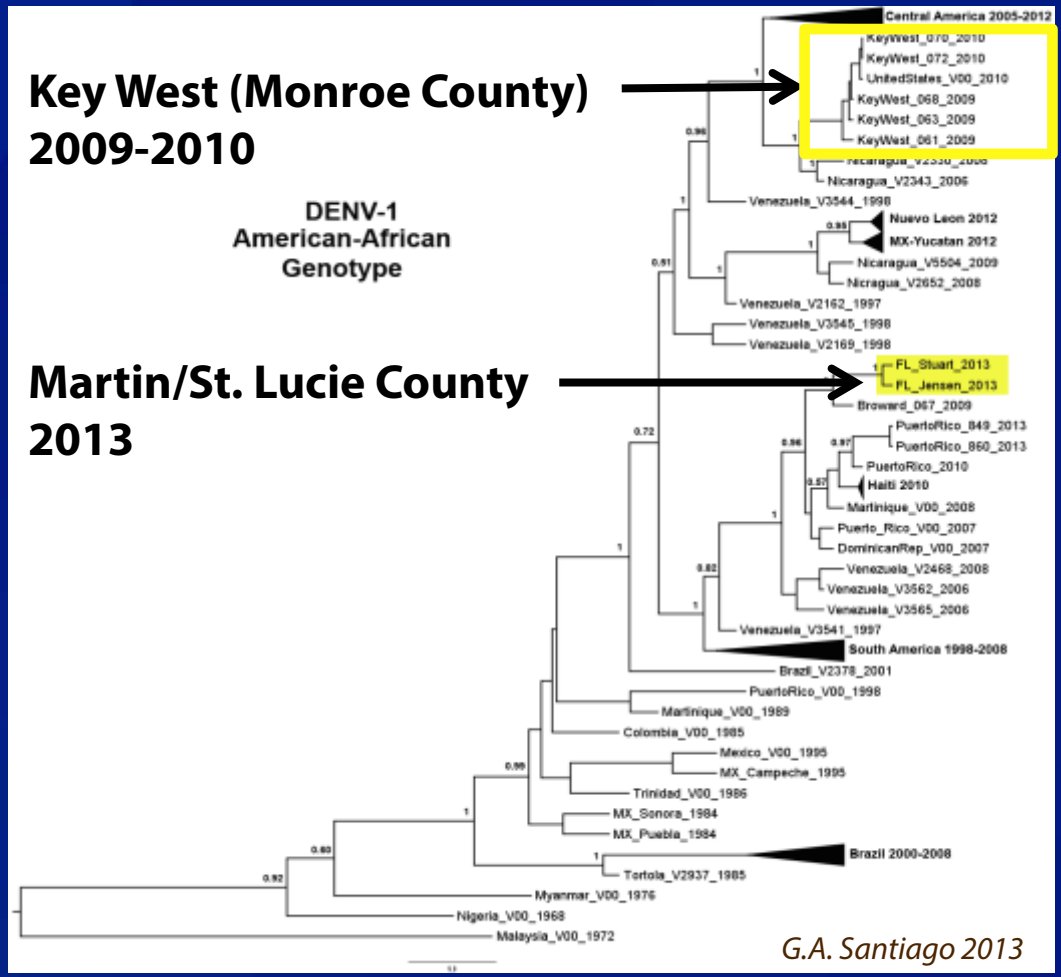
- **21 cases Martin/St Lucie county**
  - All DENV-1
  - Onset : June 16 –present
  - Median age: 48 years (range: 4 to 63)
  - 57% male and >85% non-Hispanics
- **1 case in Miami-Dade county**
  - DENV-4

Data: Florida Department of Health



Locally-acquired Dengue in Florida, 2013

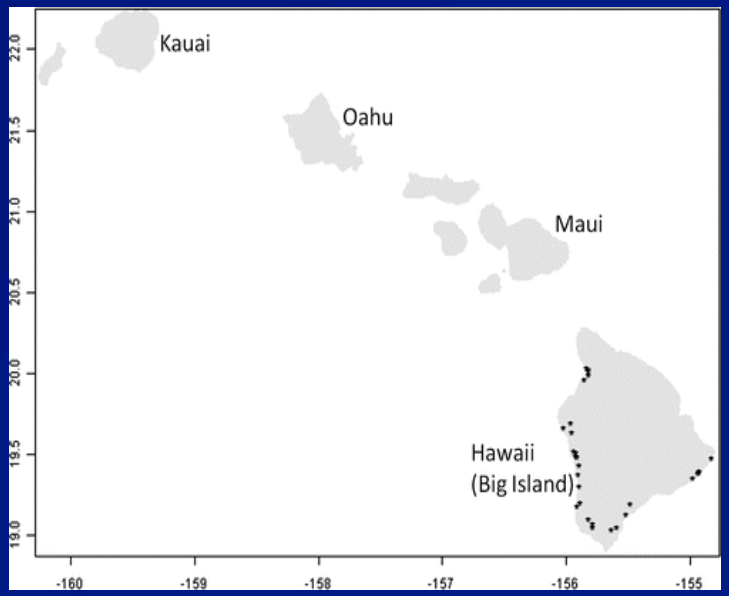
- **Sequence analysis done at CDC-DB**
  - Is this Key West DENV-1 strain? No



Data: CDC Dengue Branch and Florida Department of Health

Locally-acquired Dengue in Hawaii

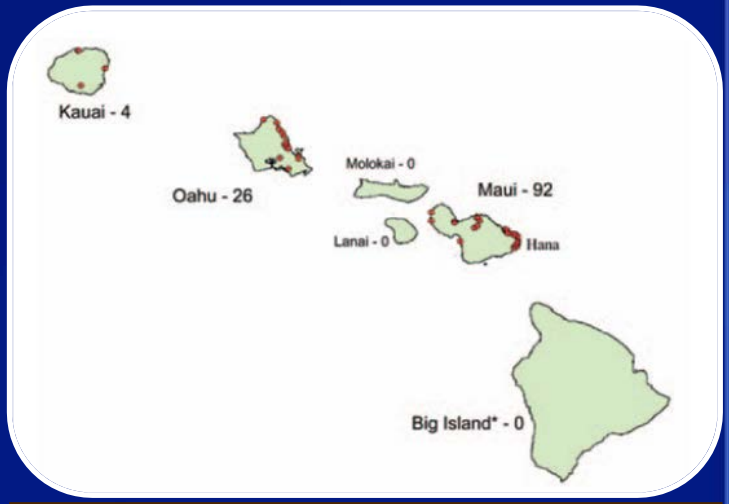
- **Historical outbreaks**
  - **First outbreak in late 1840s**
  - **1903**
  - **1943-44, Oahu**
    - **DEN1**
    - **1500 cases**
  - **Aedes aegypti introduced first**
  - **Aedes albopictus introduced in early 20th century**

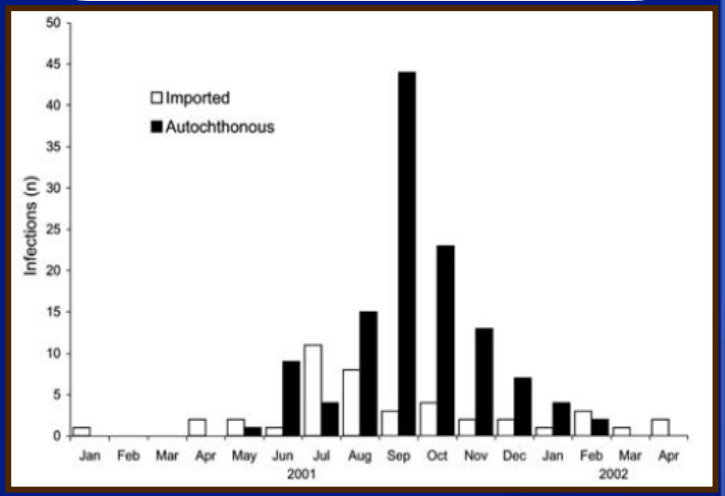


Anderson and Kaplan. History of Aedes mosquitoes in Hawaii. Journal Am Mosq. Control Assoc. 2013

Locally-acquired Dengue in Hawaii, 2001

- **2001 outbreak**
  - Maui, Oahu, Kauai
  - 1644 suspected cases; 122 positive
  - 39% attack rate, Nahiku, Maui
  - DENV-1 genotype IV Tahitian strain
  - Median age: 41 years (range 1—77)
  - Three hospitalized; no DHF/DSS cases
  - *Aedes albopictus*





Bottom image, [1]Effler P, *et al.EID* 2005.
Top image, [2]Smith et al., *EID* 2005.

Locally-acquired Dengue in Hawaii, 2011

- **2011 outbreak in Oahu**
  - **January – March 2011**
  - **5 laboratory positive cases**
  - **DENV-1**
  - **Index case: traveler from Philippines**
  - **All cases from same neighborhood**
  - **No DHF/DSS cases or deaths**

Locally acquired Dengue in Hawaii, 2015-16

- **2015-2016 outbreak on Island of Hawaii (Big Island)**
  - **264 lab confirmed infections**
  - **Median age: 29 years (range 0-80)**
  - **14% hospitalized**
  - **DENV-1, Asian strain**
  - **Predominantly *Aedes albopictus***

MMWR 2016 65(2): 34-35

Summary

- Dengue is highly endemic in Puerto Rico with simultaneous circulation of multiple serotypes
  - Limited seroprevalence data strongly suggests most of population has had at least one dengue infection by the second decade of life
  - During large outbreaks 100's of hospitalizations and tens of deaths occur
- Dengue is common and may be endemic in the Virgin Islands and American Samoa and other US Pacific territories
  - Seroprevalence data limited

Summary

- South Texas with repeated small dengue outbreaks and local transmission since the 1980s
  - Seroprevalence data > 10 years old suggests border crossing sub-population with significant past exposure to dengue
- Other US –Mexico border states at risk for dengue but no evidence of local transmission to date
- South Florida - repeated small dengue outbreaks since 2009
- Hawaii has had two outbreaks and a small cluster of cases since 2001
  - Primarily *Aedes albopictus* transmitted

Acknowledgements

- CDC Dengue Branch Epidemiology Activity, Tyler Sharp, Kyle Ryff
- Hal Margolis
- Puerto Rico, US Virgin Islands, Texas, Florida, Hawaii, America Samoa Departments of Health