Evolving Epidemiology of Arboviruses

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Conflict of Interest Declaration

- Advisory boards:
  - Takeda (dengue vaccine)
  - Valneva (chikungunya vaccine)

- Speaker:
  - Valneva (JE vaccine)
  - Bavarian Nordic (rabies vaccine)

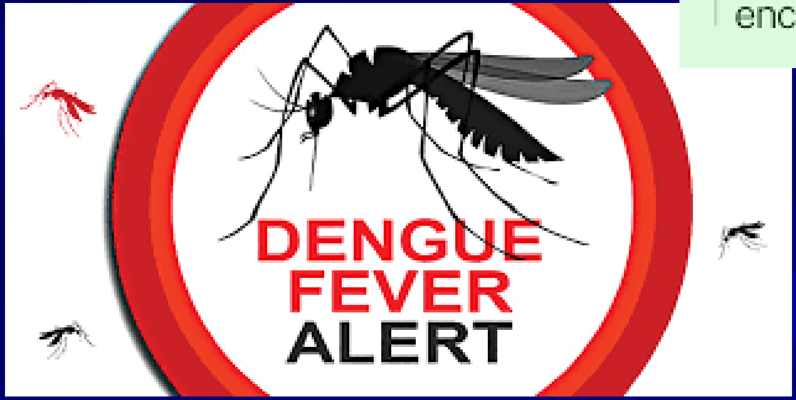
Presentation Objectives

- Review global warming data
- Analyze potential impact on major arboviral vectors (*Ae. aegypti* and *Ae. albopictus*)
- Changing epidemiology of dengue
- Brief review recent major arboviral epidemics

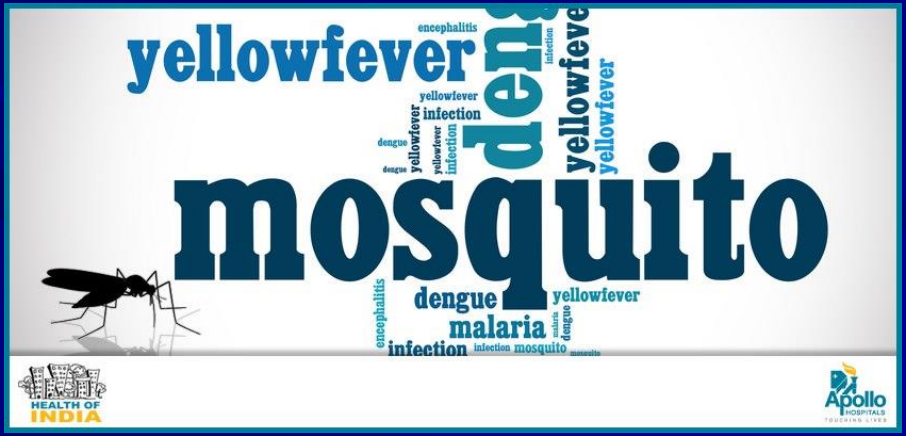

Eastern Equine Encephalitis
is spreading rapidly across the US. Learn how to naturally protect yourself from the EEE Virus with these facts & prevention tips!

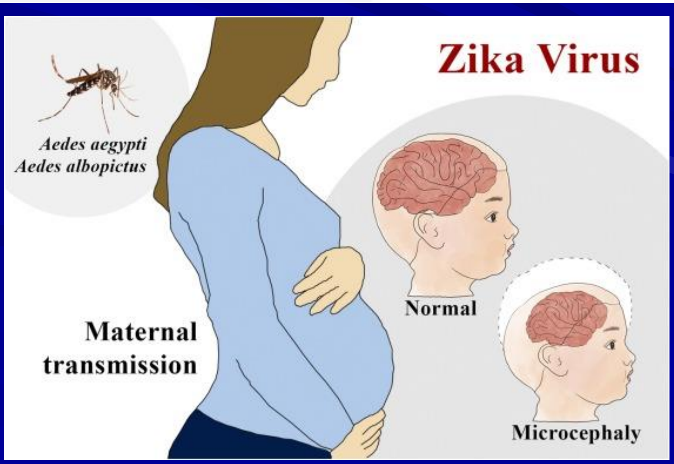

Health alert
Japanese encephalitis virus
NSW


WEST NILE VIRUS
How do you get it?
Mosquitoes bite infected birds, then bite humans.
What if you think you have it?
Only about 20% of people have any symptoms at all. Those are most often mild, flu-like complaints.
Symptoms usually show up 3 -14 days after being bitten by an infected mosquito.
Fewer than 1% of people get a serious illness that can be deadly.
If you develop severe headaches or confusion, see a health care provider right away.
How do you fight it?
Remember the 4 D's
Use an insect repellant such as DEET, picaridin or IR3535.
Drain standing water around your house routinely. Remember to drain tires, cans, flowerpots, clogged gutters, rain barrels, toys and puddles.
Mosquitoes are most active at dawn and dusk. Stay inside, or take precautions to prevent mosquito bites during these times.
Dress in long sleeves and pants in areas where mosquitoes are active.
CO
CDPHE

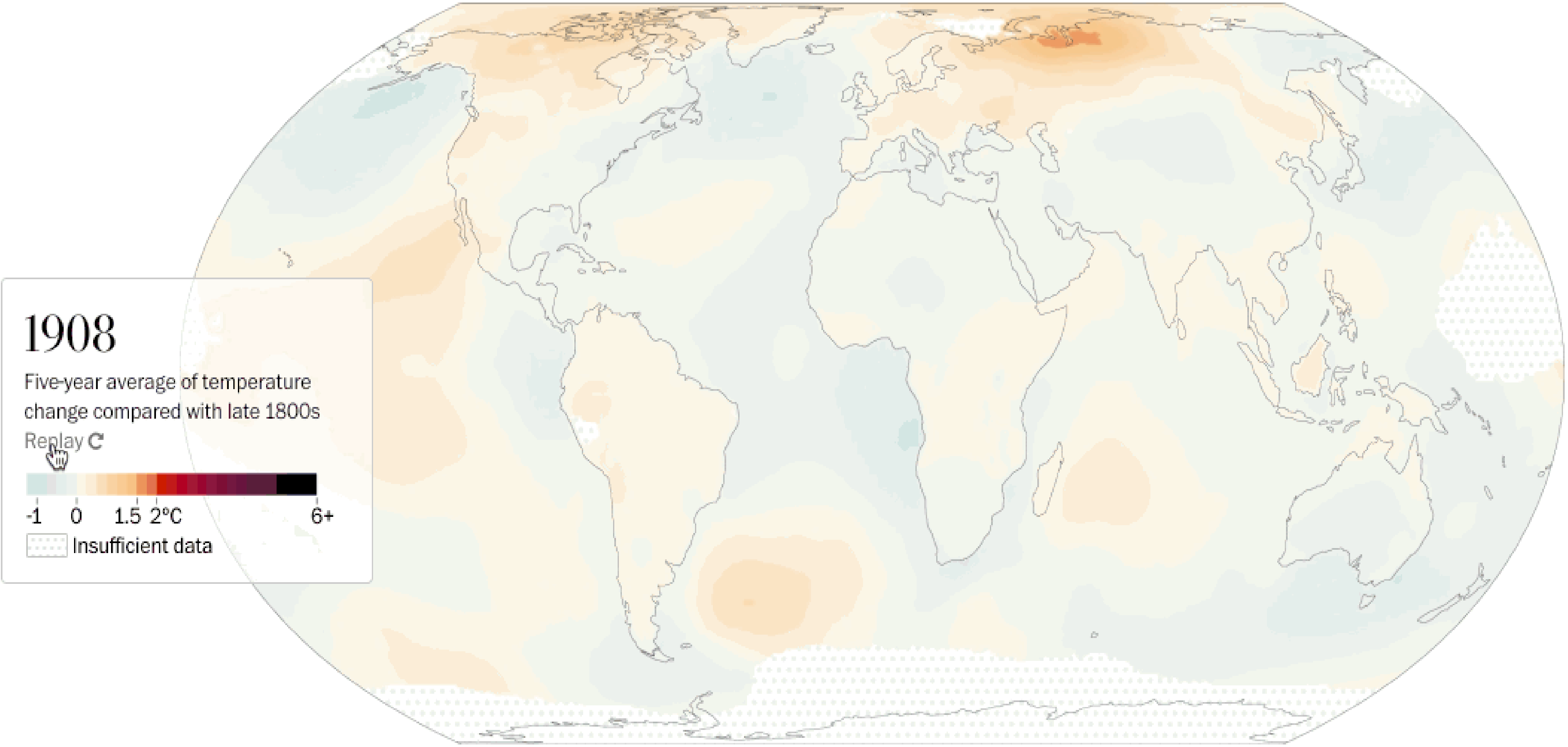

DENGUE FEVER ALERT


Chikungunya Outbreak Alert

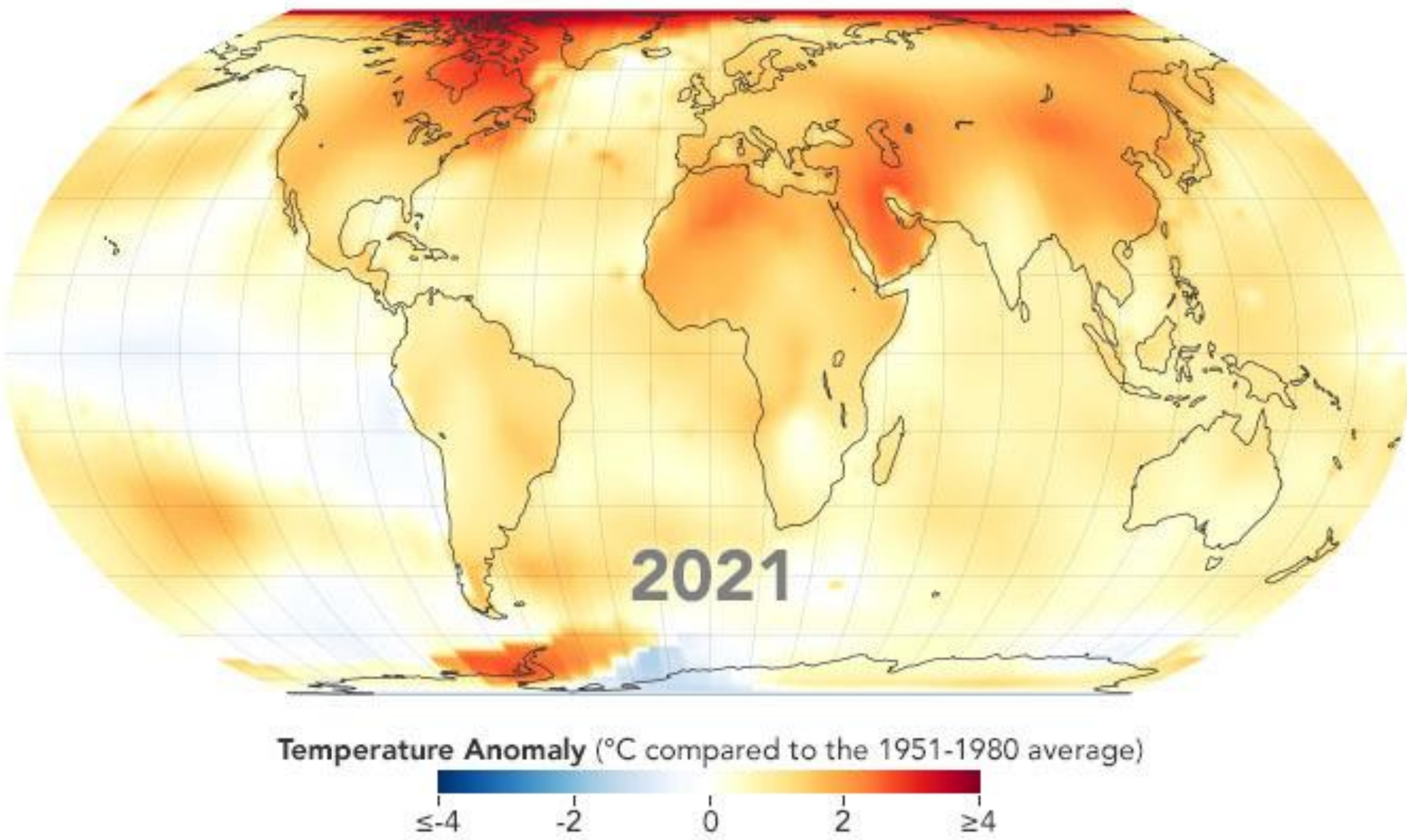

yellowfever
encephalitis
dengue
infection
mosquito
malaria
HEALTH OF INDIA
Apollo HOSPITALS


Zika Virus
Aedes aegypti
Aedes albopictus
Normal
Maternal transmission
Microcephaly

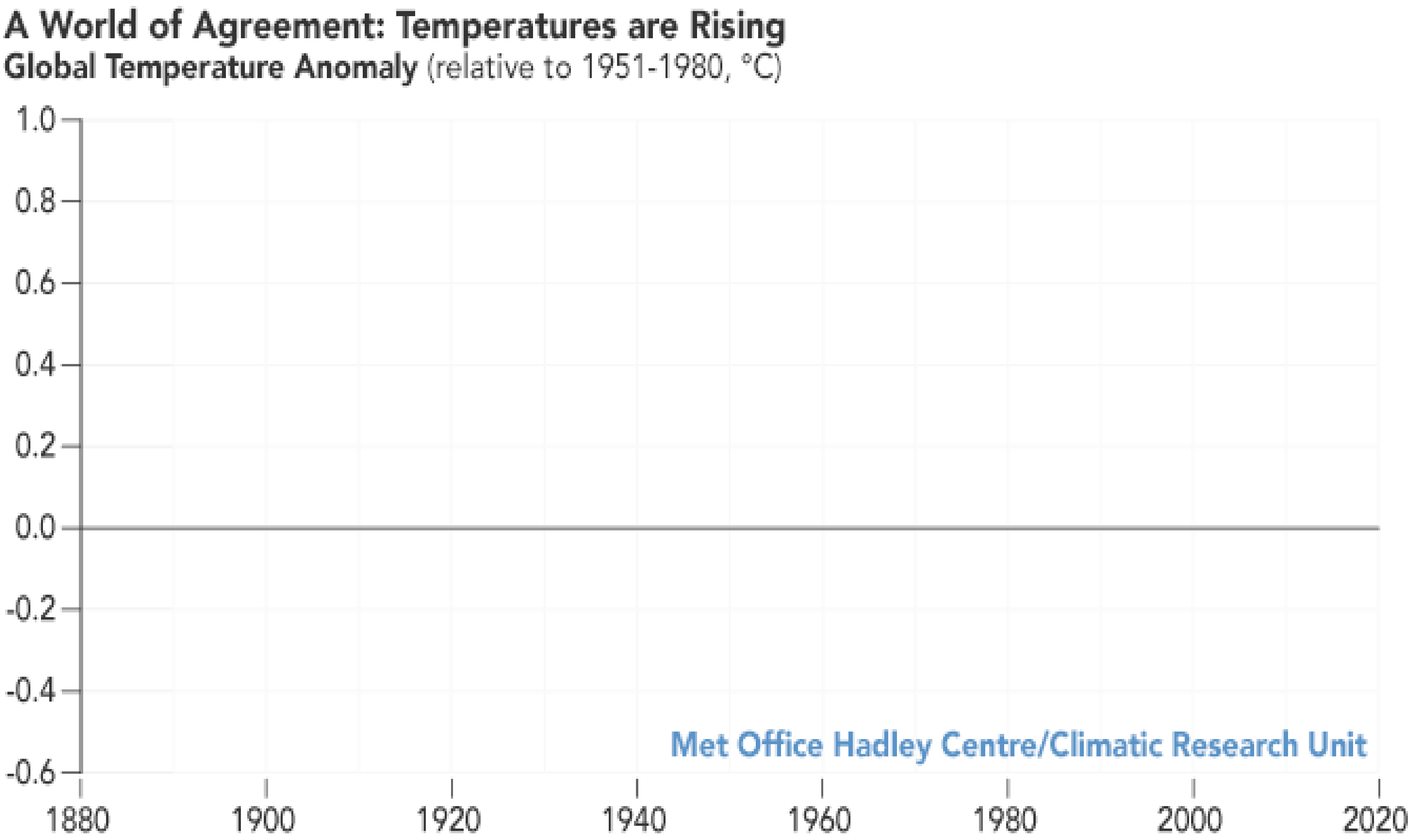
Five Year Average of Temperature Change Relative to Late 1800s



Washington Post



https://earthobservatory.nasa.gov/world-of-change/global-temperatures



https://earthobservatory.nasa.gov/world-of-change/global-temperatures

Aedes aegypti

Humans preferred mammalian host

Day time biting

Thrives in densely populated urban areas

Intolerant of winter temperatures (high egg mortality with frost)

Feed multiple times during one gonotrophic cycle (feeding, egg-producing cycle)

- https://www.ecdc.europa.eu/en/disease-vectors/facts/mosquito-factsheets/aedes-aegypti

Aedes albopictus

Asian tiger mosquito
Less common vector of dengue
Feeds on humans and other mammals
Increasing global distribution

Drought-resistant eggs
Can over winter (eggs laid in late summer undergo diapause until spring)
Higher temps accelerate larval development

https://www.ecdc.europa.eu/en/disease-vectors/facts/mosquito-factsheets/aedes-albopictus

Changing Global Distribution of *Ae. aegypti* & *Ae. albopictus*

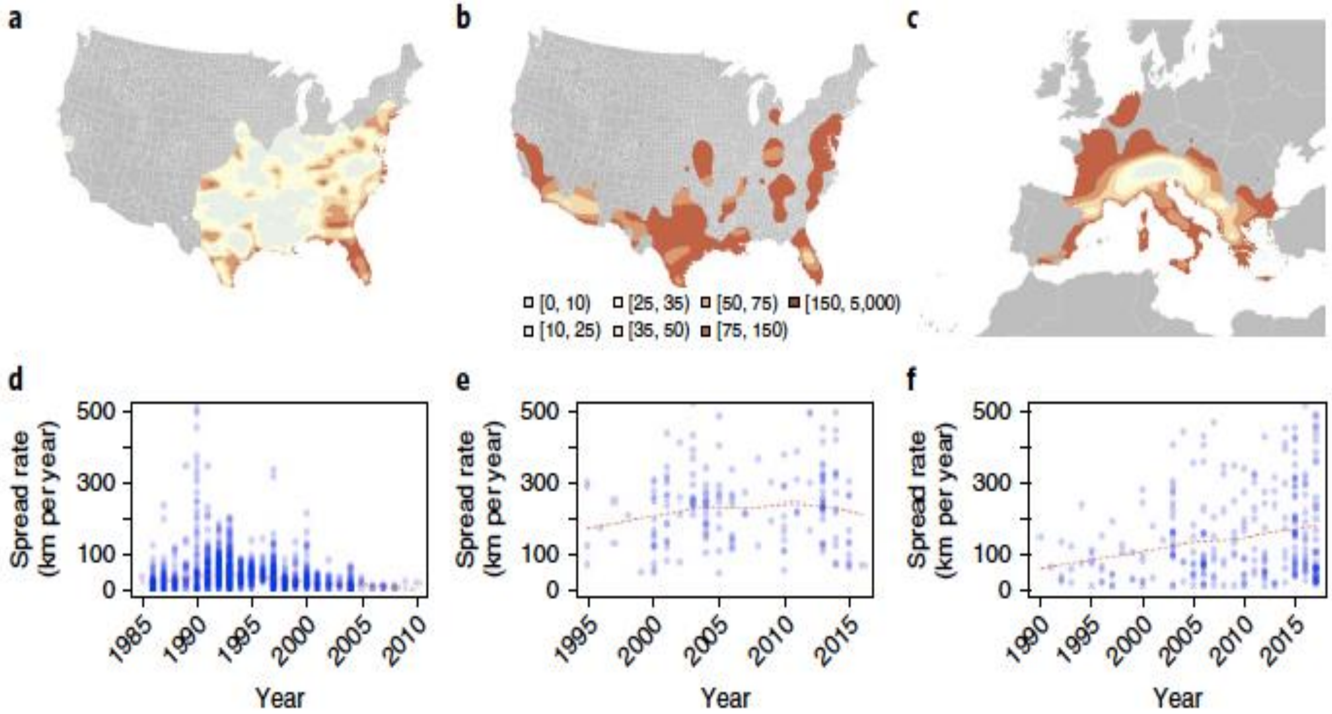


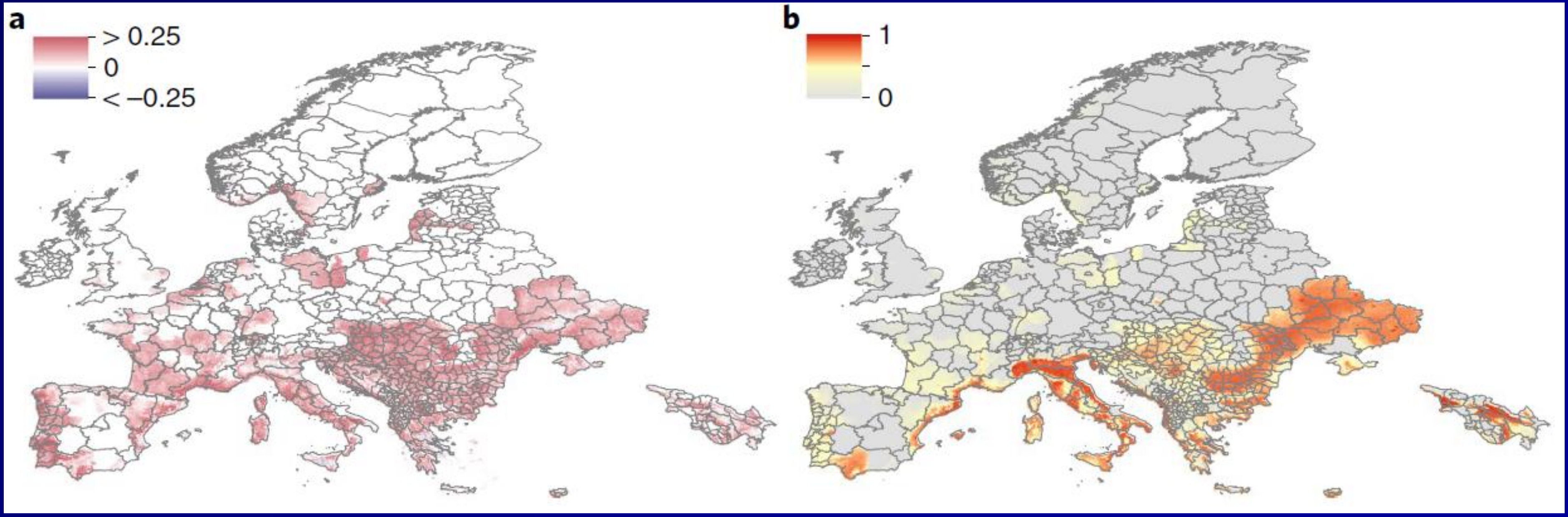
Fig. 1 | Reconstruction of *Ae. albopictus* and *Ae. aegypti* spread. a–c, Spread of *Ae. albopictus* (**a**) and *Ae. aegypti* (**b**) in the United States, and spread of *Ae. albopictus* in Europe (**c**). Estimates of speed of spread in km per year are based on thin spline regression on mosquito observations since their earliest

Kraemer MUG et al. Nat Microbiol 2019

Predicted spread of *Ae. albopictus* throughout southern Europe

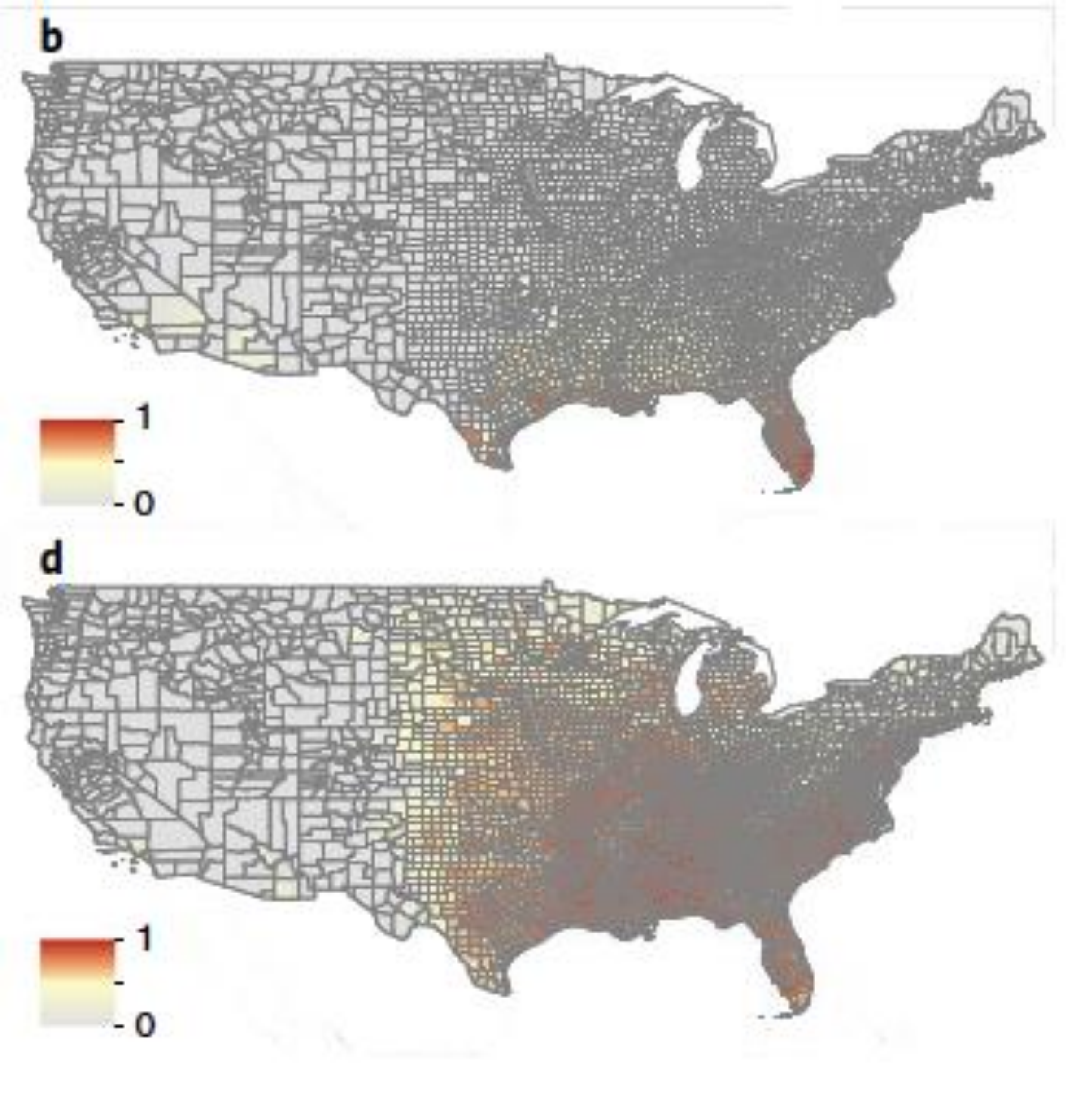
Expansion (red) and contraction (blue) of *Ae. albopictus* between 2020 and 2050 under the medium climate scenario RCP 6.0, with emissions peaking in 2080

Predicted distribution of *Ae. albopictus* and predicted habitat suitability for the presence of *Ae. albopictus* in 2050



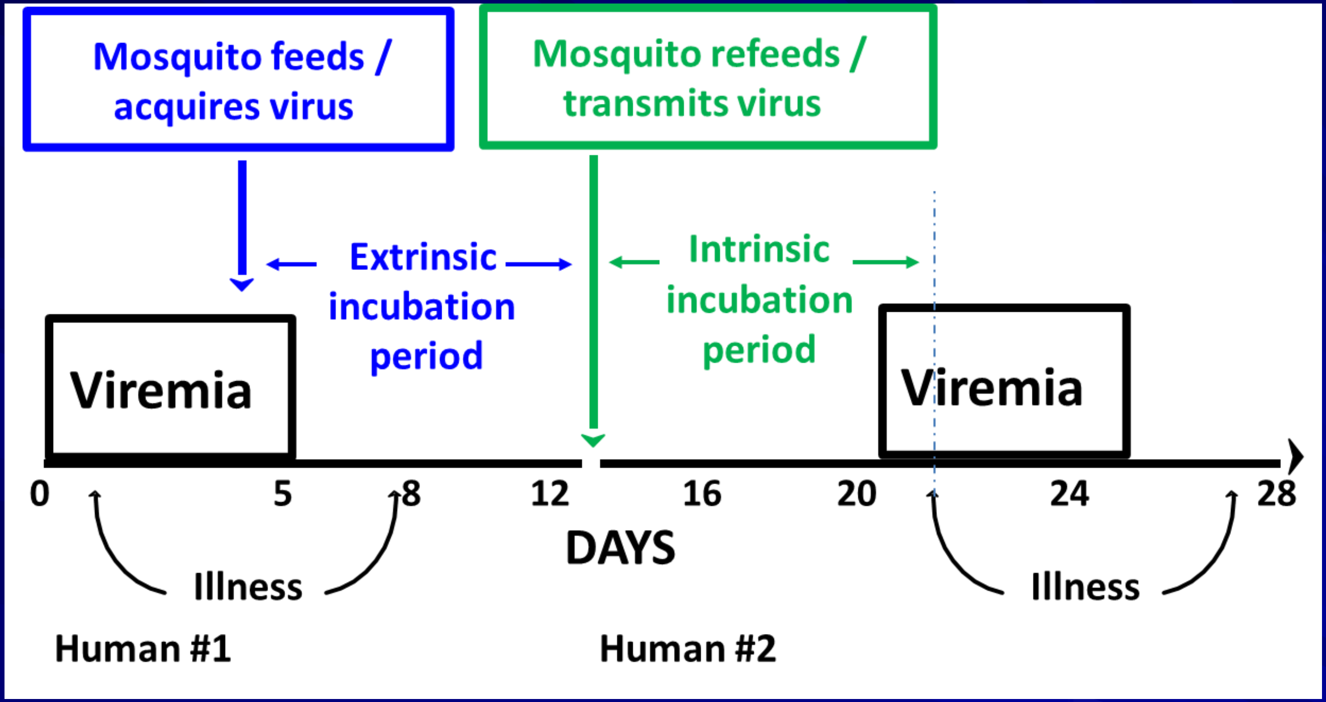
RCP, representative concentration pathway.
Kraemer MUG, et al. *Nat Microbiol* 2019;4:854–863.

Predicted Habitat Suitability in 2050 of *Ae. aegypti (b)* and *Ae. albopictus (d)* in the United States



Kraemer MUG et al. Nat Microbiol 2019

Effects of Temperature on Vector-borne Pathogens

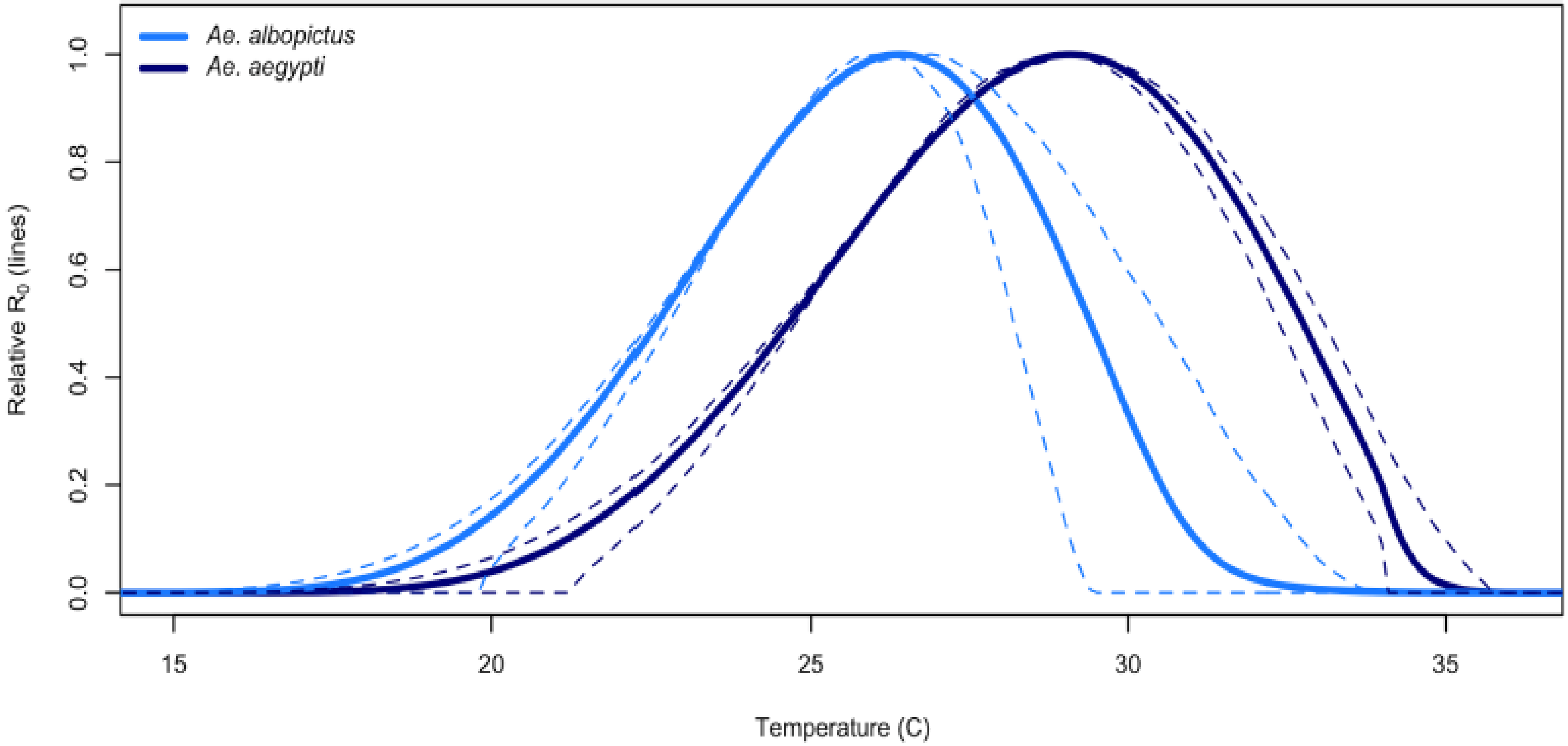


- Changes in temperature can alter:
  - Extrinsic incubation period of pathogens within vector
  - Transmission season
  - Pathogen distribution

Determinants of R_o for Mosquito-borne Diseases

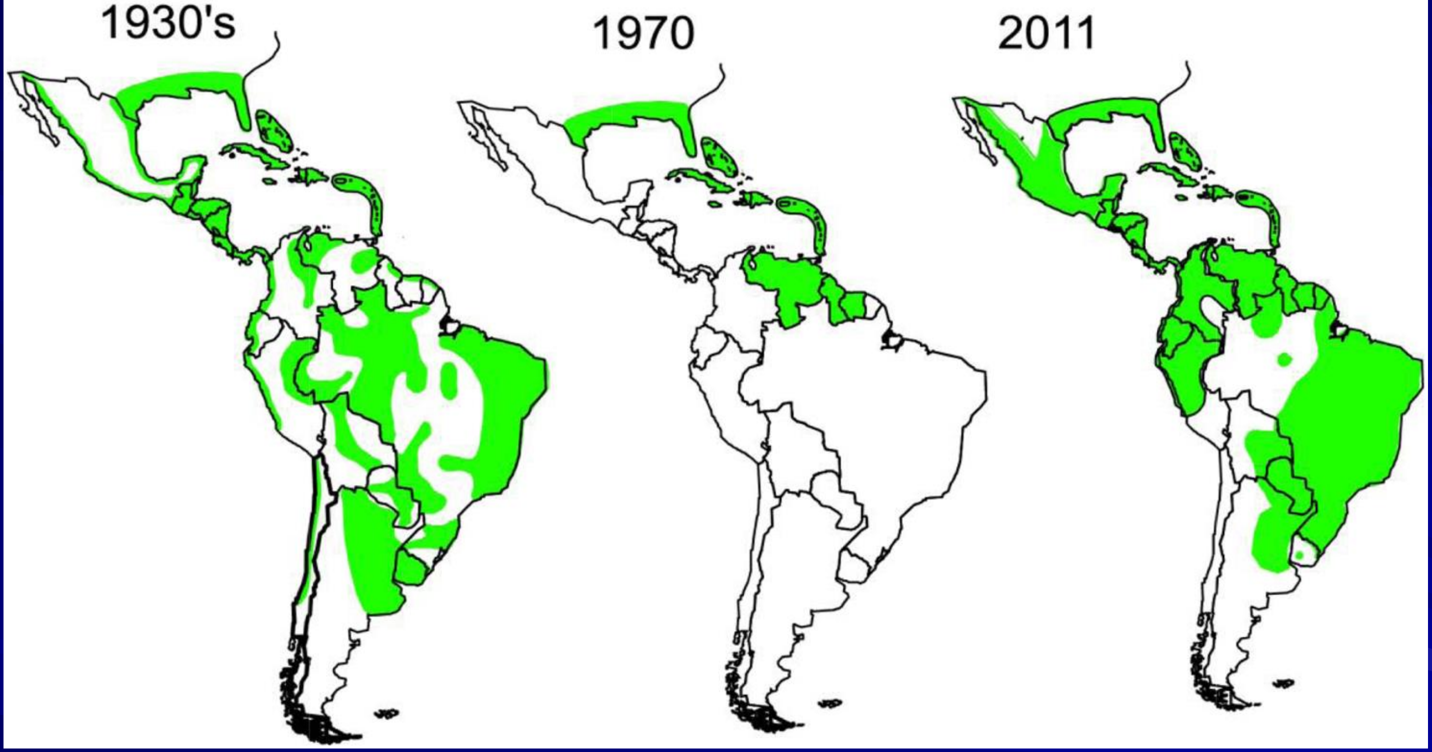
- **Vectorial capacity - capacity of a mosquito population to transmit a VBD**
  - **function of:**
    - **vector density (temperature, precipitation)**
    - **vector survival (temperature, precipitation)**
    - **extrinsic incubation period (temperature)**
    - **biting behavior (temperature, precipitation)**
- **Vector competence:**
  - **intrinsic ability of mosquito to amplify / transmit a pathogen (temperature)**
    - **1º genetically determined, result of vector and pathogen co-evolution**

Relative R_0 across Temperatures for *Ae. albopictus* and *Ae. aegypti*



Factors Contributing to Arboviral Emergence

Distribution of *Aedes aegypti*



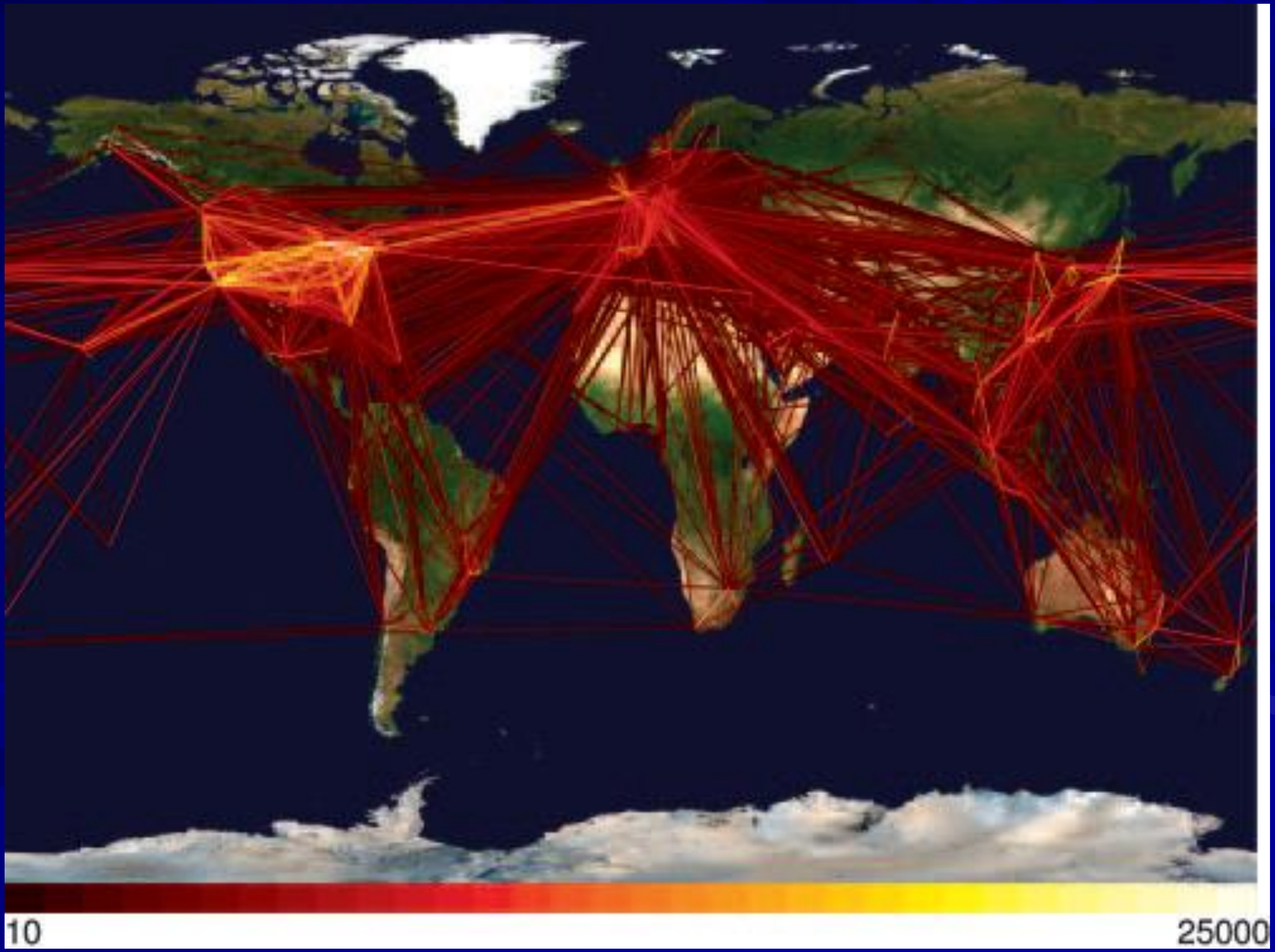
Limited mosquito vector control activities from 1970- 2000 Gubler DJ. Trop Med Health 2011

Factors Responsible for Spread of Arboviruses Transmitted by *Aedes* spp.

- Physical environment:
  - Climate change and perturbations of weather patterns
  - Artificial vector breeding sites (household water stores, manholes, used tires)
- Social, political, and economic:
  - Increased urbanization
  - Human population migrations in the Indian Ocean region
  - Delayed identification and control of initial outbreaks

Global Aviation Network

(Facilitates rapid spread of arboviruses via travelers)



PNAS 2004;101:15125

WHO Dengue Estimates

3.6 billion people at risk worldwide for dengue infection

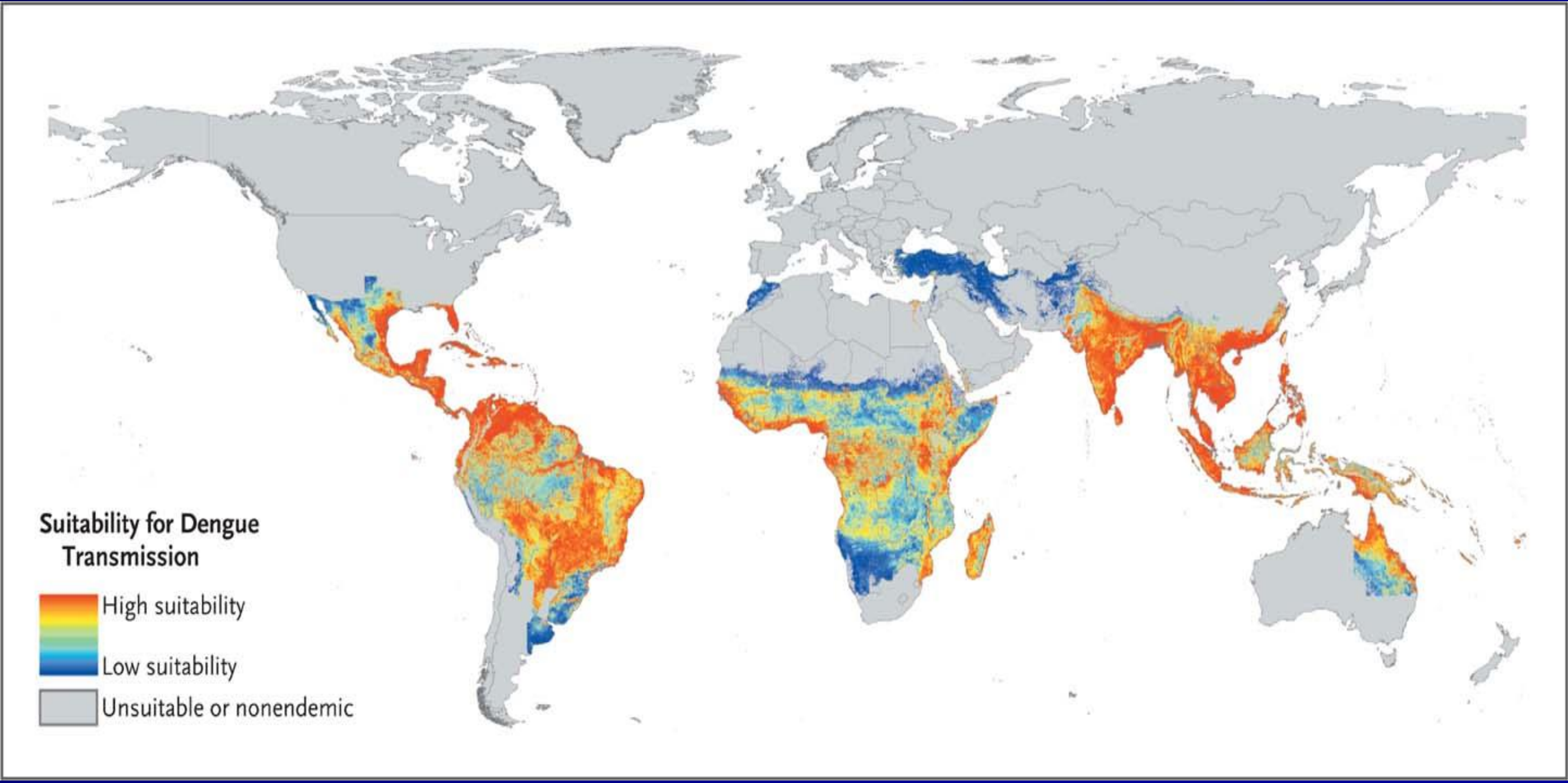
Estimated 390 million infections per year
About 96 million symptomatic cases annually

~500,000 DHF/DSS cases per year require hospitalization
~40,000 deaths (in 2017)

Global Burden Disease study estimated 400% increase between 2000 to 2013

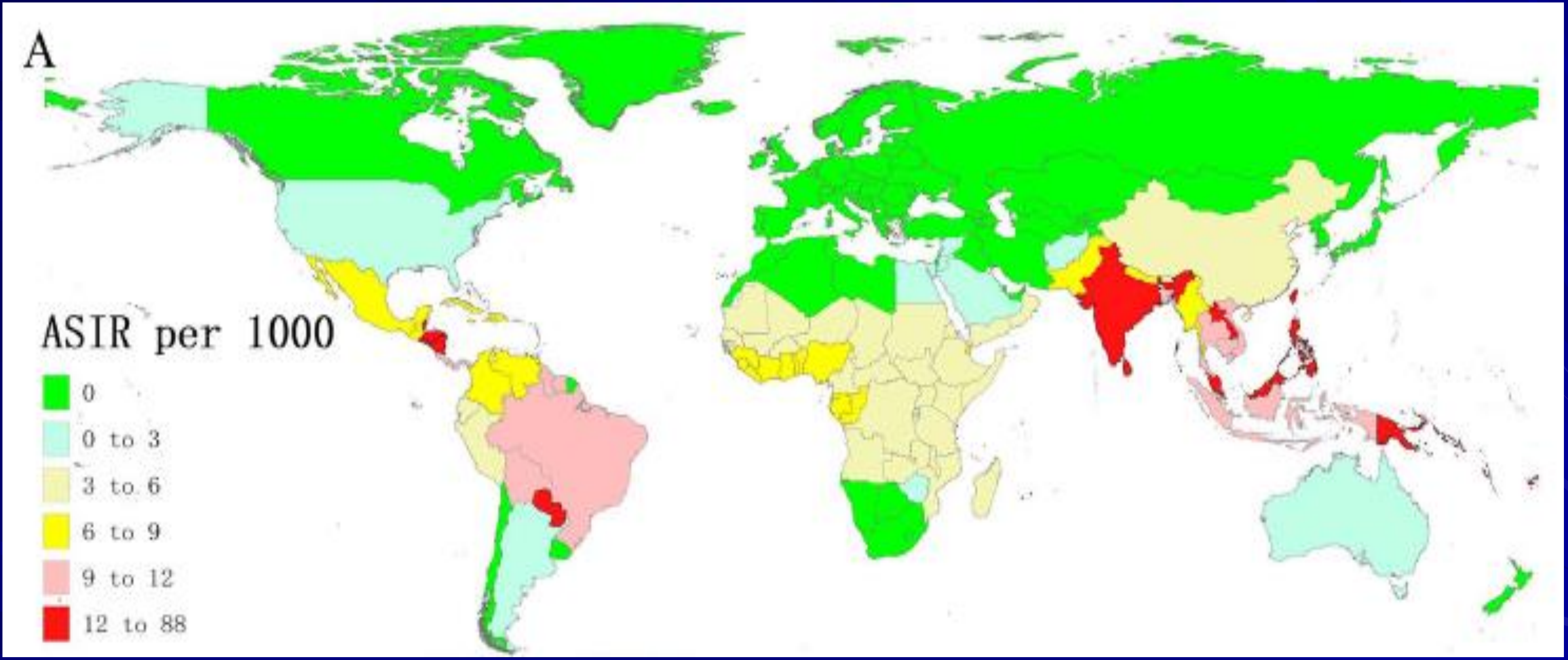
Stanaway JD et al. Lancet Infect Dis 2016
Zeng Z et al. Global burden of dengue. EClinMed 2021

Global Dengue Risk

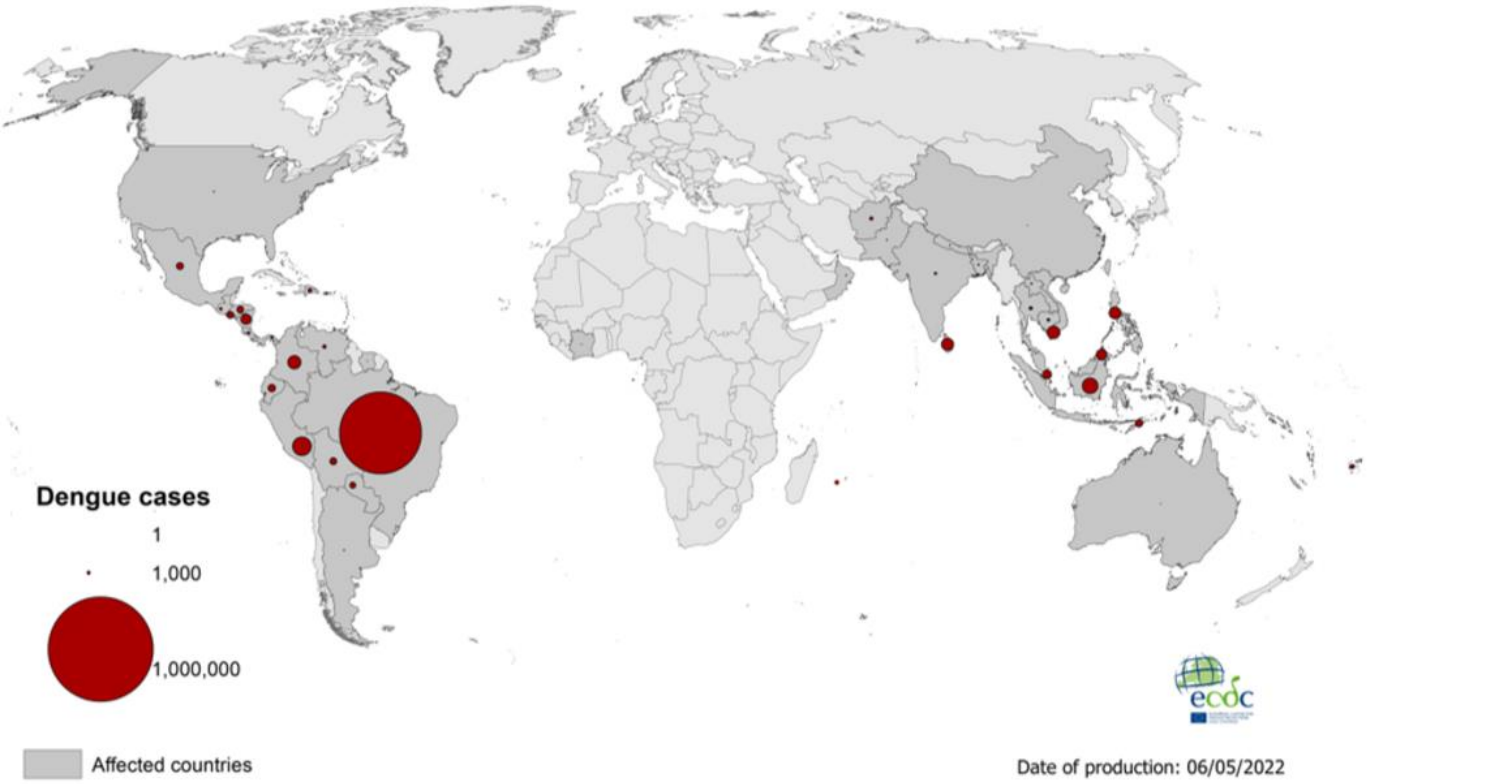


Simmons CP et al. N Engl J Med 2012;366:1423-1432

Age-Standardized Incidence Rate in 2019

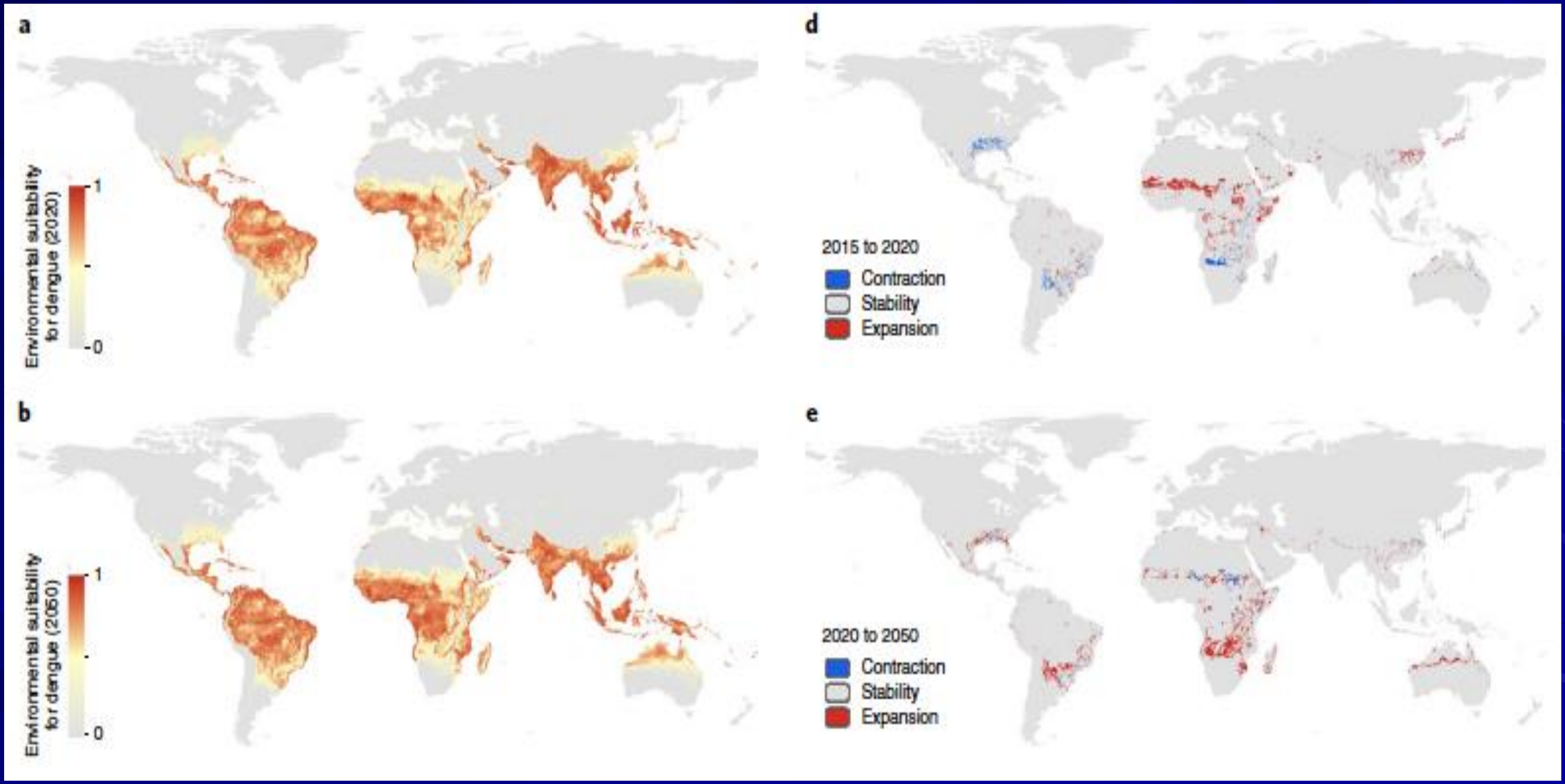


Yang X et al. Dengue and evolving pattern over 30 years JTM 2021



Geographical distribution of dengue cases reported worldwide in 2022, as of 5 May 2022 (ECDC)

Environmental Suitability and Expansion of Dengue (2015-50)



Messina JP et al. Dengue global burden. Nat Microbiol 2019

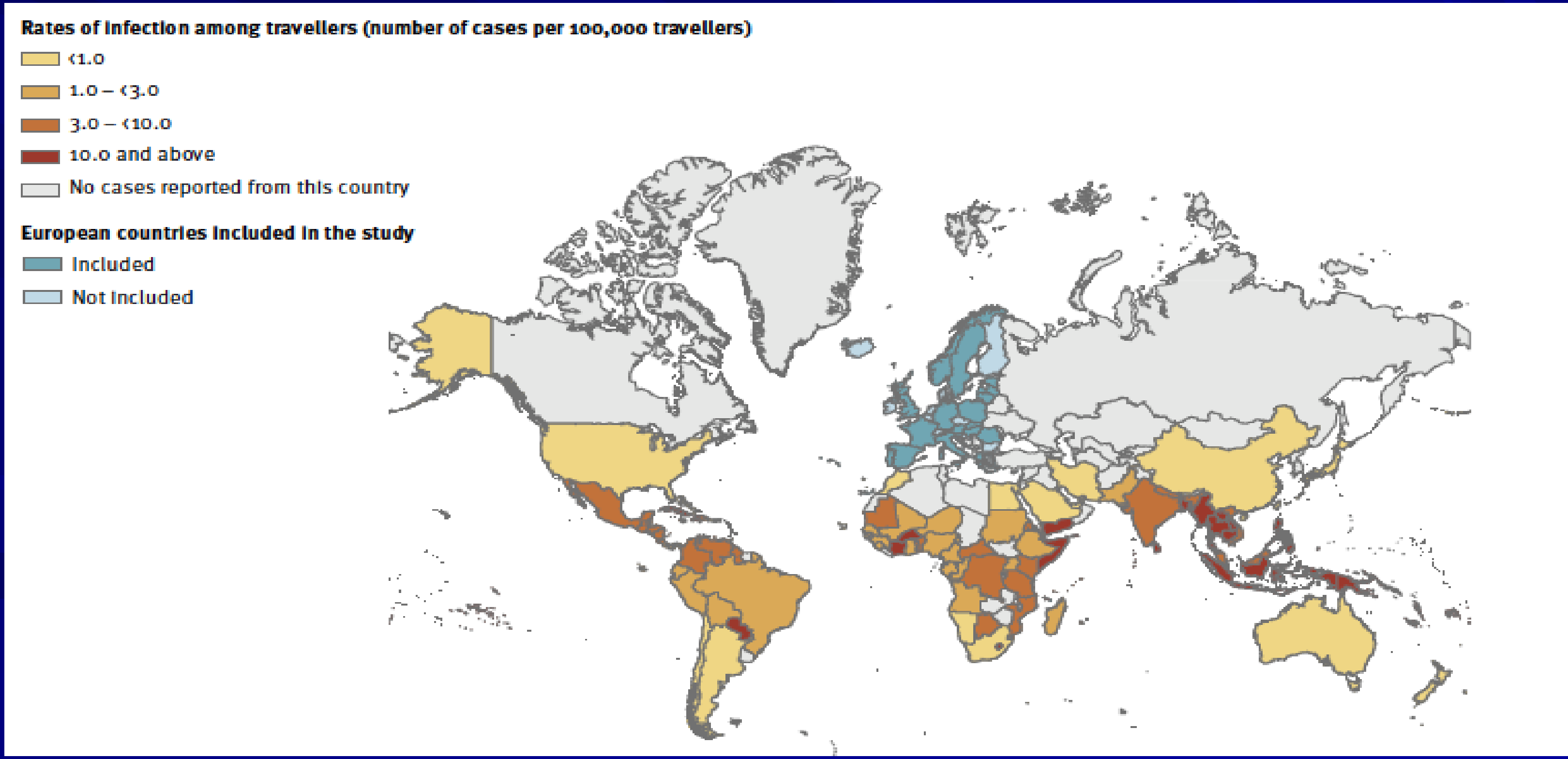
Dengue and Travel

Dengue Seroconversion in Travelers

Author, country	Study time period	Number of travelers	Median travel duration	Incidence rates (per 1,000 person-months)
Cobelens et al. Netherlands	1991-1992	447	28 d	11
Potasman et al. Israel	Pre-1999	104	6.1 mo	30
Ratnam et al. Australia	2006-2008	387	21 d	10.2
Baaten et al. Netherlands	2009-2010	1207	21 d	14.6
Hesse et al. US military	2008-2011	1000	7.1 mo	1.76
Olivero RM et al. USA	2009-2010	589	21 d	28.7

Dengue among European Travelers (2015-2019)

- 11,478 travel-related dengue cases reported to the ECDC European Surveillance System 71% acquired in Asia, 18% Latin America & Caribbean)
- 9 autochthonous outbreaks in Europe (6 France, 3 Spain) and several more in 2020-2021 (7 France; 1 Italy)



Gossner CM et al. Eurosurveillance 2020; ECDC 5 May 2022

Probable local transmission in Miami, Florida

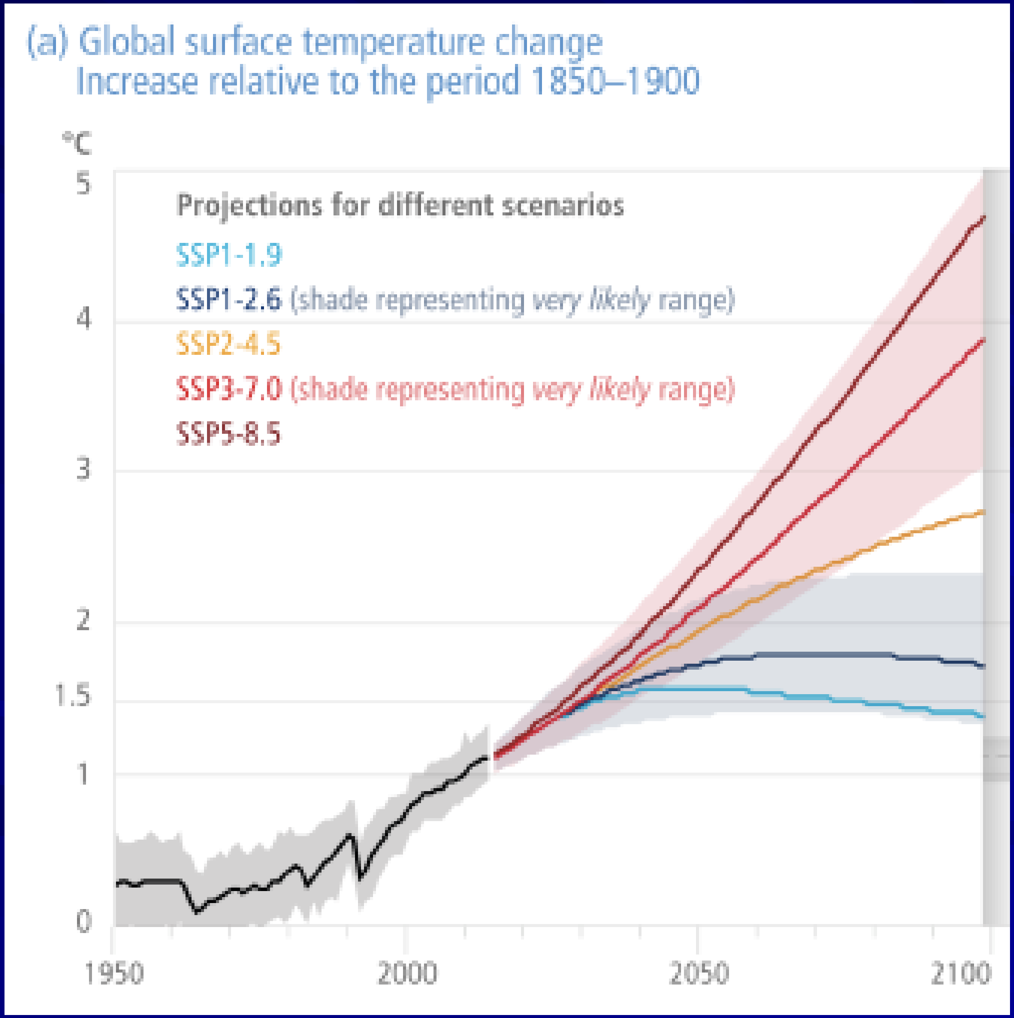
The NEW ENGLAND JOURNAL of MEDICINE

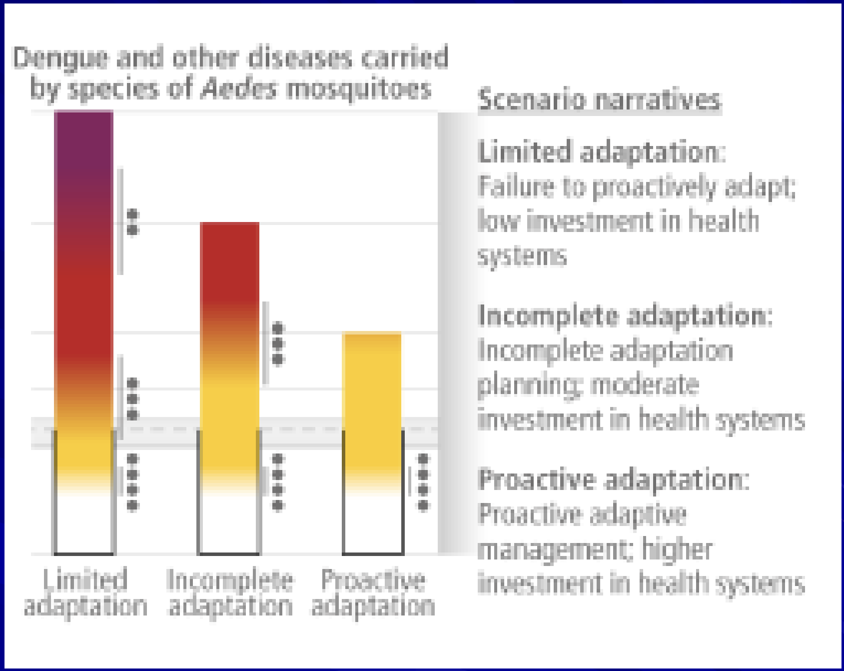
CORRESPONDENCE

Fatal Dengue Acquired in Florida

- Past travel to Honduras but no recent travel
- Locally acquired dengue in FL (phylogenetics suggested imported Cuban DENV strain)
- Fatal outcome for a missed diagnosis
    - Sharp et al, *NEJM,* 2021

Potential Future Scenarios Global Warming and Dengue





Intergovernmental Panel on Climate Change: Climate Change 2022: Impact, Adaptations, and Vulnerability

Chikungunya Global Spread

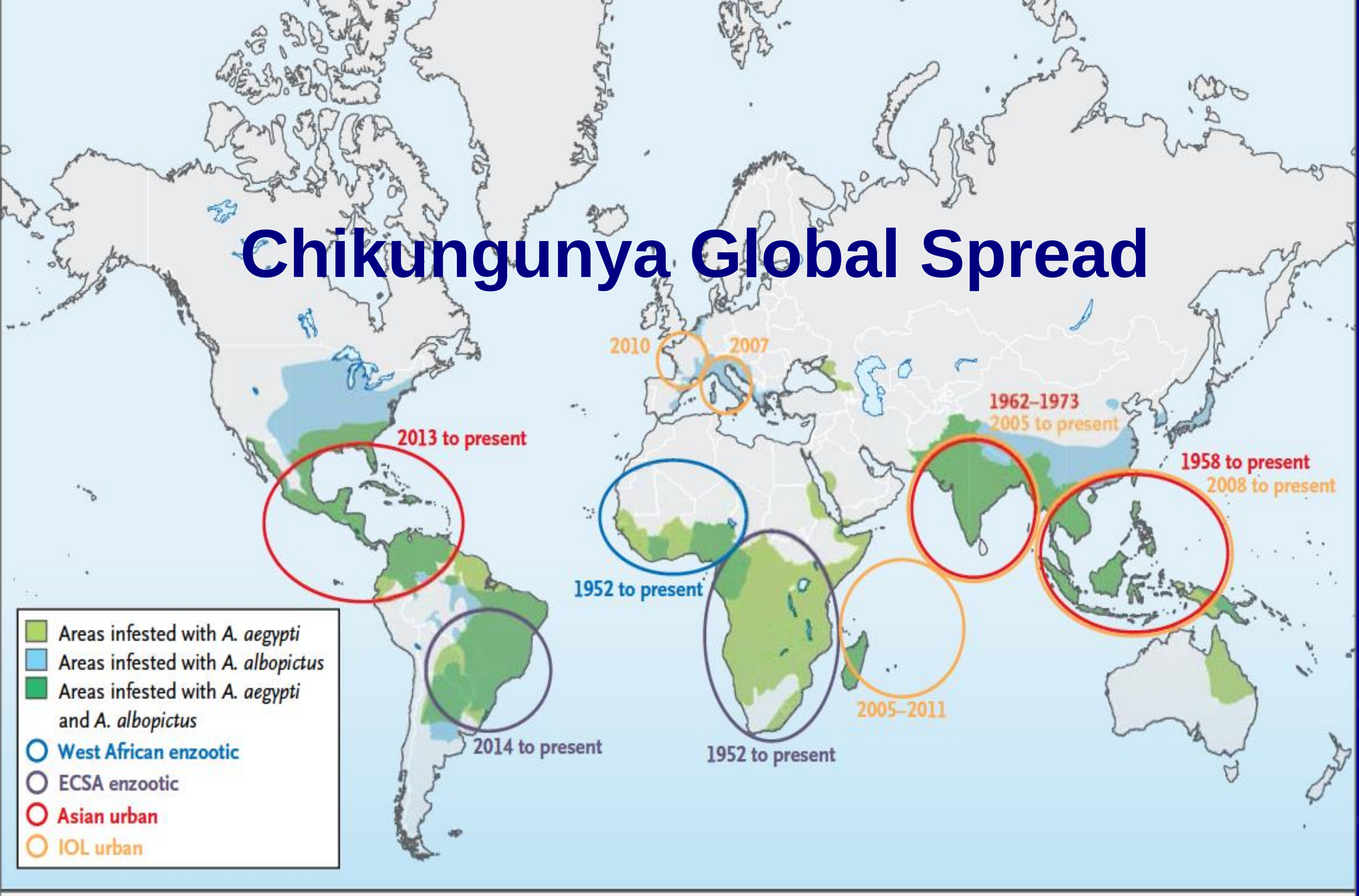


Figure 2. Origin, Spread, and Distribution of Chikungunya Virus and Its Vectors.

Weaver and Lecuit NEJM 2015

Chikungunya in the Americas

More than 1.7 million estimated cases reported to PAHO

Pan American Health Organization

World Health Organization
Regional Office for the Americas

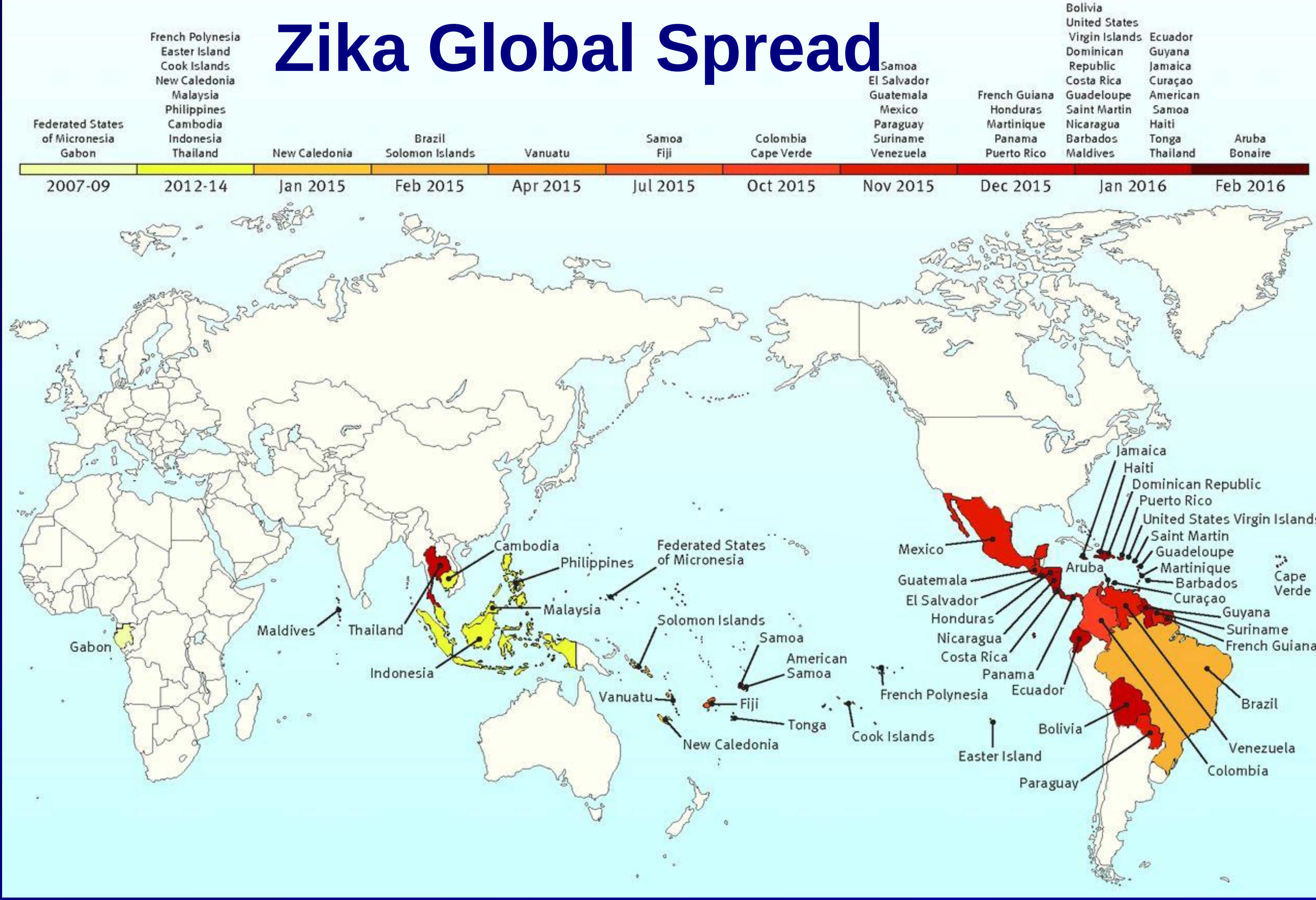
Countries/territories with autochthonous transmission or imported cases of Chikungunya in the Americas, EW 49, 2013 - EW 5, 2016

Data source:
PAHO/WHO. Number of reported cases of Chikungunya Fever in the Americas
http://www.paho.org/chikungunya

Map production:
PAHO-WHO AD CHA IR ARO

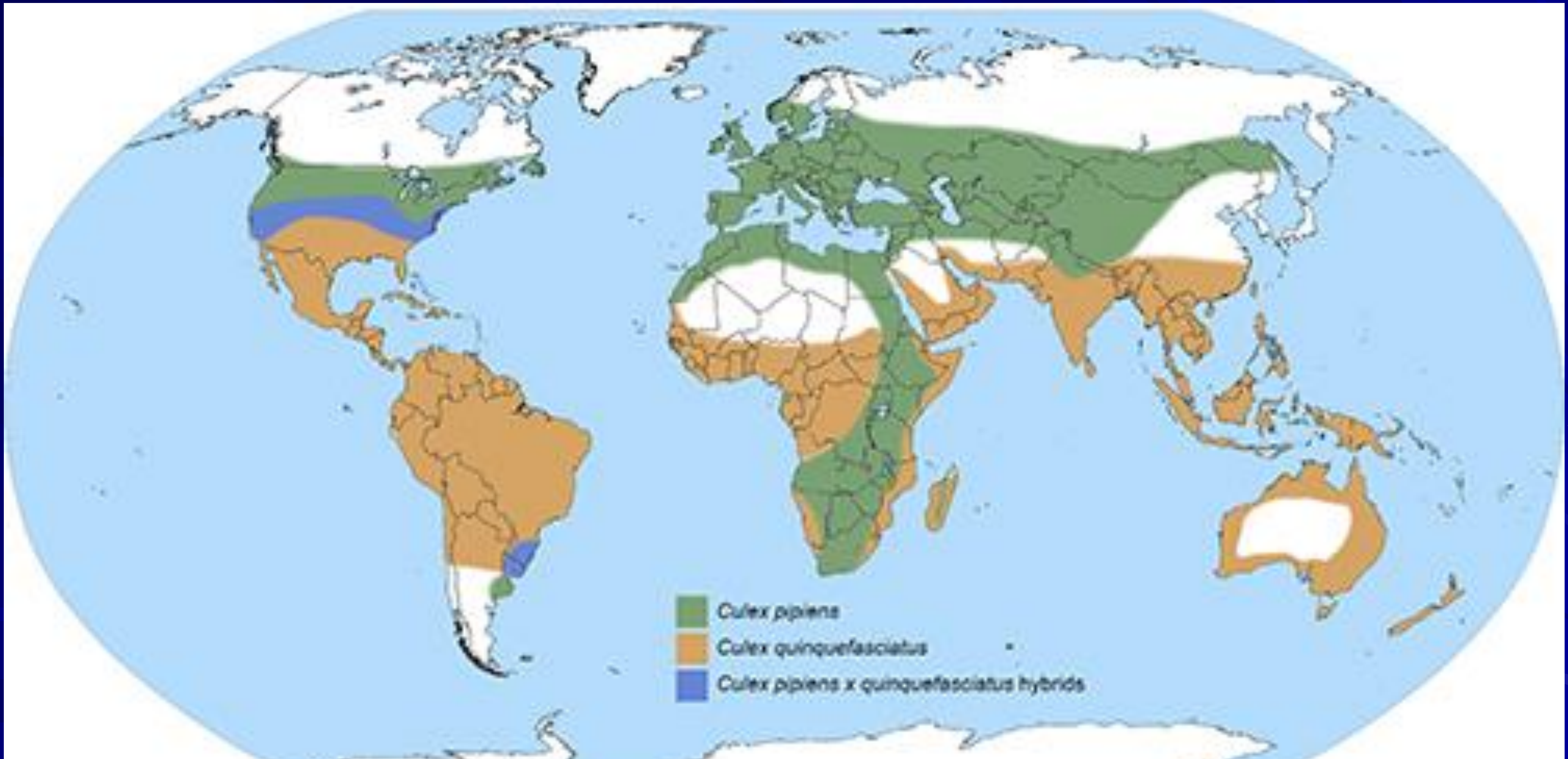
* Note: Entire countries have been shaded on the map though there is no evidence of country-wide virus presence.

Zika Global Spread



Basarab M et al. Zika virus. BMJ 2016

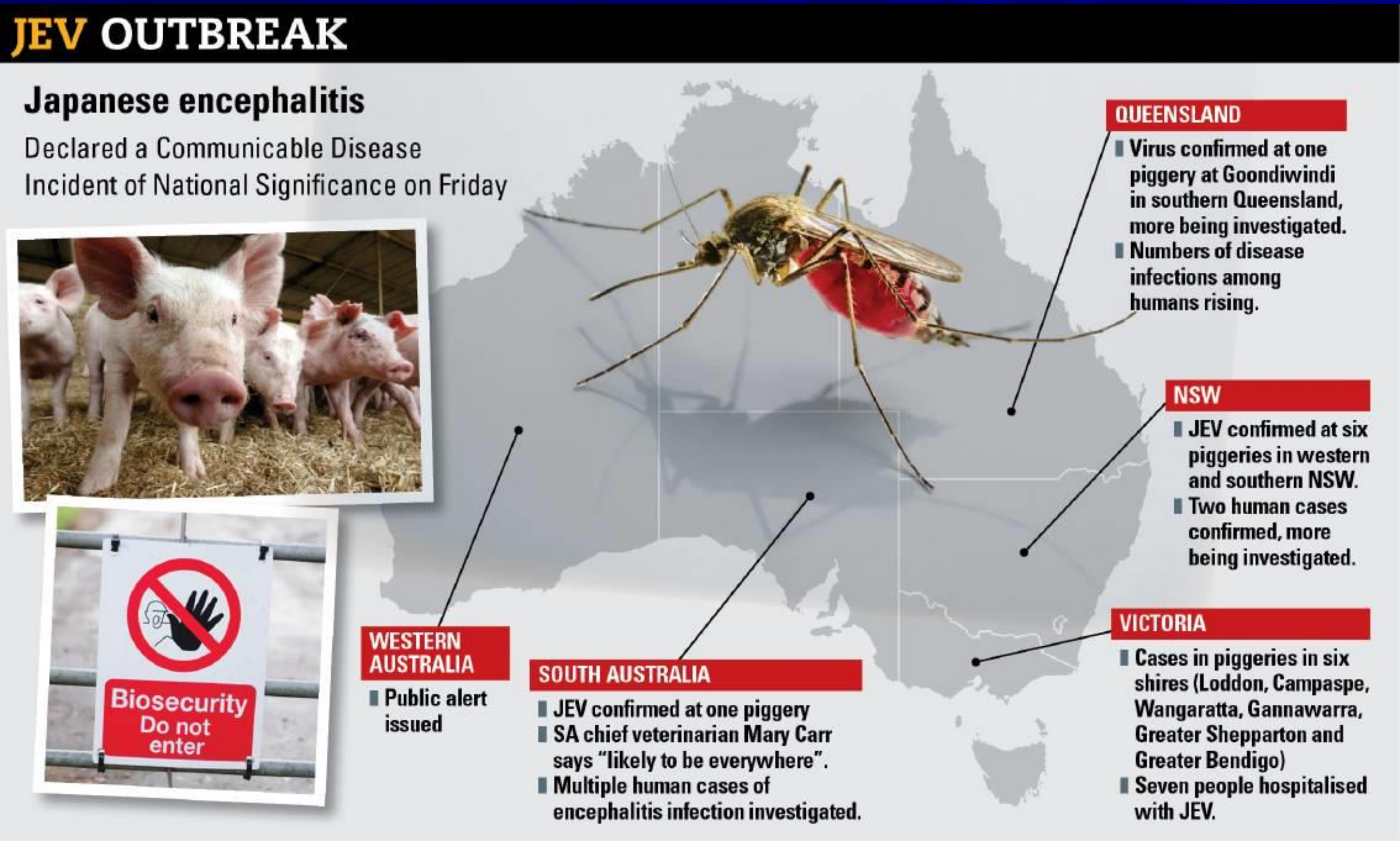
Culex spp. may also be expanding their distribution



Map redrawn after Ciota and Kramer 2013 by Nathan D. Burkett-Cadena, U. Florida

Potential for increased transmission of WNV, JE, SLEV, RVFV

Japanese Encephalitis in Australia



JE in Australia

Australia records fifth Japanese encephalitis death

The latest confirmed death has prompted health authorities to remind GPs of their role in vaccination uptake.

- By 25 May, 42 human cases (30 confirmed; 12P)
- https://www.health.gov.au/health-alerts/japanese-encephalitis-virus-jev/about

Conclusions

- Dengue global burden progressively rising
  - With a brief slowdown during the COVID-19 pandemic
- Predicted climate change in coming decades likely to lead to expanded distribution of competent vectors
- Substantial potential for arbovirus introduction and spread in Western Europe, the US, and other temperate climates in decades to come
- Greater risk for travelers and dengue outbreaks in formerly non-endemic geographic regions

Any Questions?