Present and Future arboviral threats: an overview

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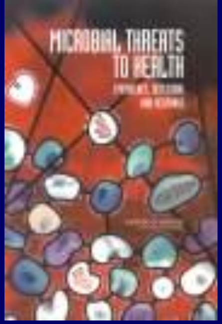
Arboviruses: A Global Public Health Threat, 20-22 June, 2018, Annecy, France

Emergence and Geographic Spread of *Aedes*-transmitted Viruses

Talk Outline

- Viruses involved
- Basic epidemiology
- Changing epidemiology
- Drivers of emergence
- Other viruses/ yellow fever
- Conclusions

Pandemic Threats to Health



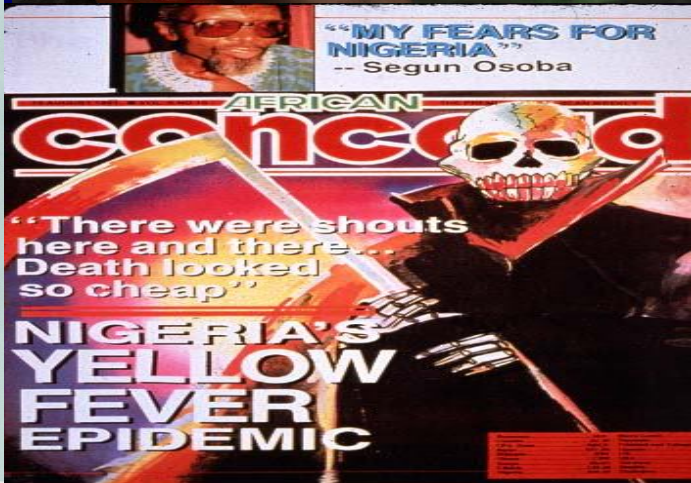
Respiratory Transmission


Pneumonic Plague


MERS

Pandemic Threats to Health

Vector-Borne Diseases



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Global Resurgence of Epidemic Arboviral Disease

BF - Barmah Forest
CE - California Encephalitis
Chik - Chikungunya
CCHF - Congo-Crimean Hemorrhagic Fever
DEN - Dengue
EEE - Eastern Equine Encephalitis
JE - Japanese Encephalitis
KFD - Kyasanur Forest Disease
LAC - LaCrosse Encephalitis

MAY - Mayaro
MVE - Murray Valley Encephalitis
ONN – O'nyong-nyong
ORO - Oropouche
RVF - Rift Valley Fever
RR - Ross River
SLE - St. Louis Encephalitis
SIN - Sinbis
TBE- Tick-Borne Encephalitis

VEE - Venezuelan Equine Encephalitis
WEE - Western Equine Encephalitis
WN - West Nile
WSL - Wesselsbron
YF - Yellow Fever
ZIK - Zika
Severe Febrile Thrombocytopenia Syndrome
Bourbon

Resurgent/Emergent Arboviral Diseases of Humans

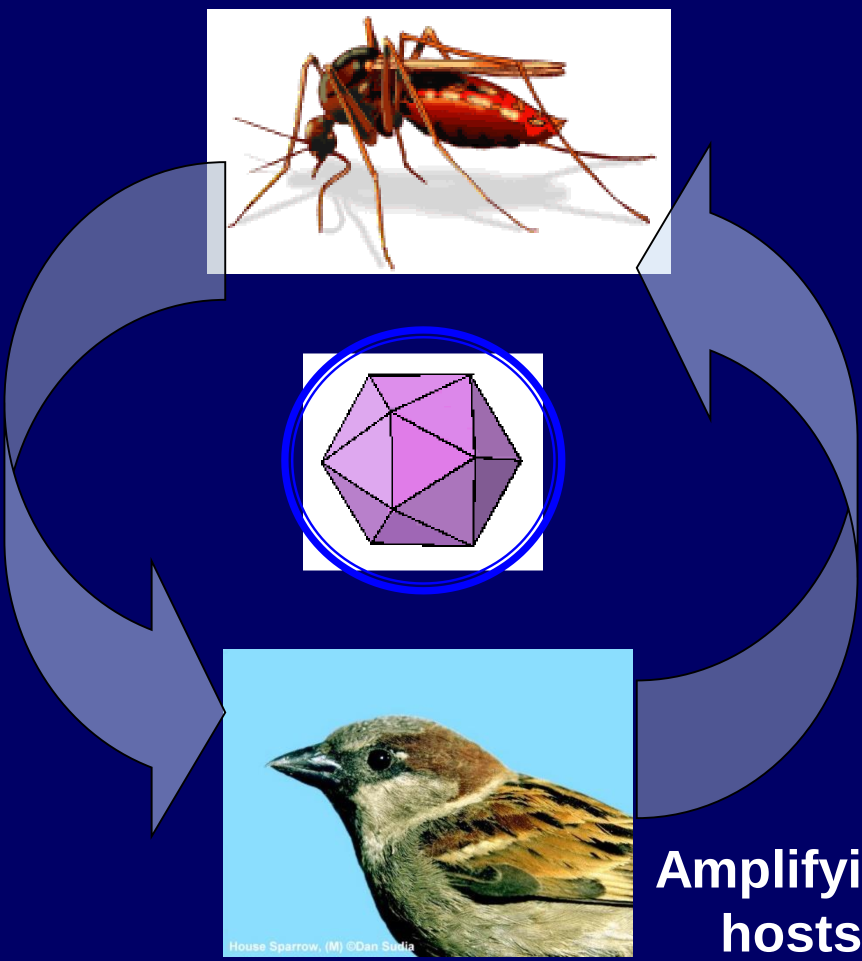
- Dengue Hemorrhagic Fever*
- West Nile
- Yellow Fever*
- Zika *
- Chikungunya*
- Japanese Encephalitis
- Venezuelan Equine Encephalitis*
- Mayaro*
- Epidemic Polyarthritis*
- Barmah Forest*
- Rift Valley Fever
- Usutu
- Kyasanur Forest Disease
- Oropouche
- California Encephalitis
- Crimean-Congo Hemorrhagic Fever
- Severe Febrile Thrombocytopenia Syndrome

*** *Aedes aegypti* transmitted**

West Nile Virus in the Western Hemisphere

West Nile Virus:
Basic Transmission Cycle

Enzootic (Maintenance/Amplification)



Amplifying hosts

Epidemic

Incidental hosts?

Epizootic

Epidemic/Epizootic West Nile Virus

1937

1950-93

Adapted from Gubler, 2007

Epidemic/Epizootic West Nile Virus

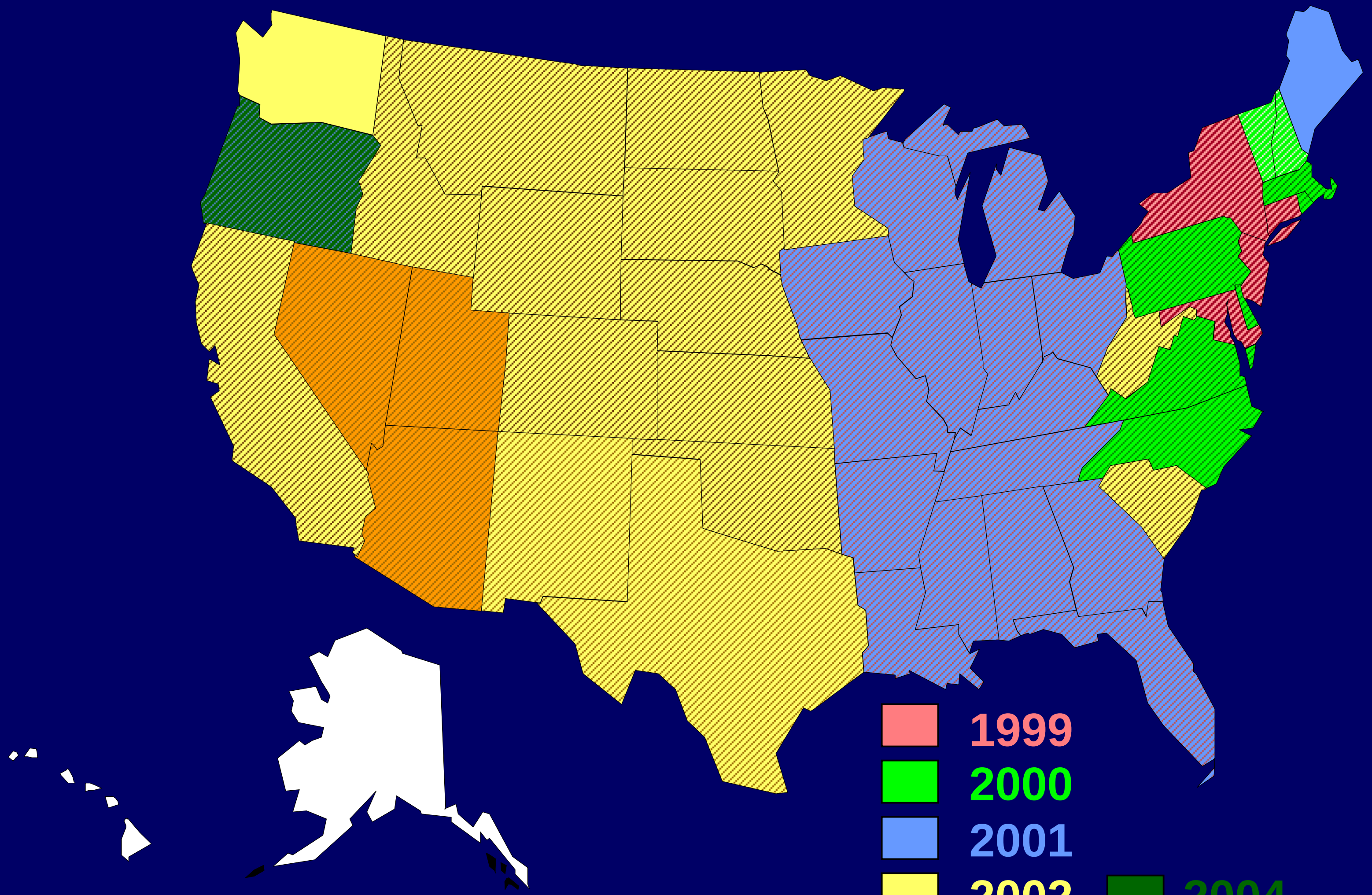
1937

1950-75

1994 - 1999

Adapted from Gubler, 2007

Reported WNV Activity, by State 1999-2004*



* Reported as of 1/31/2005

Epidemic/Epizootic West Nile Virus

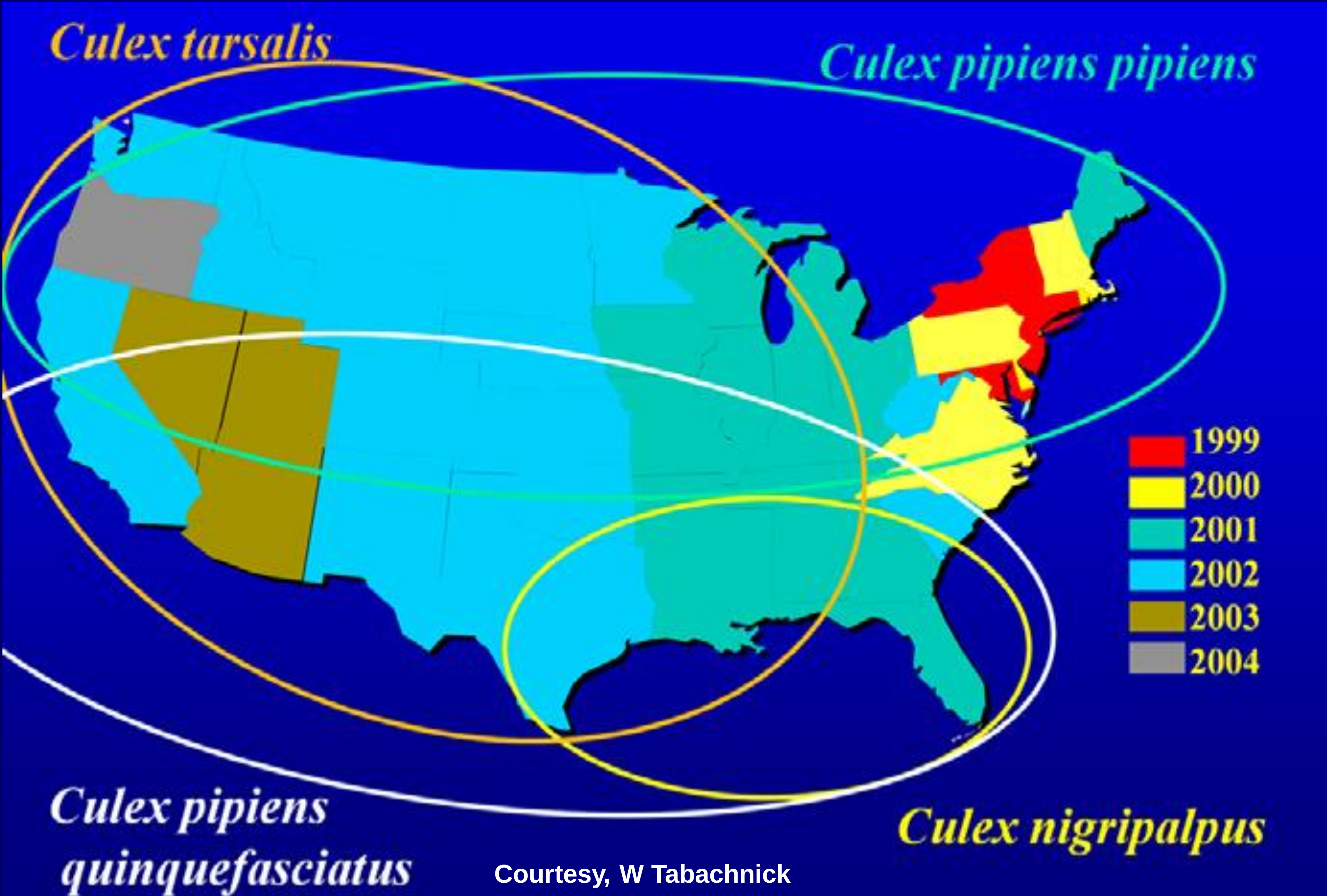
1937

1950-75

1994 - 2016

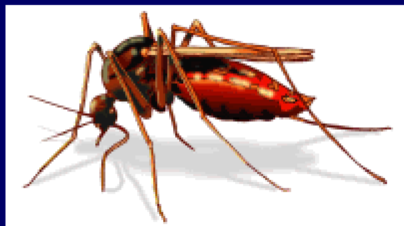
Adapted from Gubler, 2007

West Nile Virus in the US



Courtesy, W Tabachnick

Host-Use Patterns of Selected WNV-Positive Mosquito Species



Birds

- *An. barberi*
- *Cx. pipiens*
- *Cx. restuans*
- *Or. signifera*
- *Cs. melanura*

Unknown

- *Ae. atropalpus*

Mammals

- *Ae. cinereus*
- *An. punctipennis*
- *An. quadramaculatis*
- *Oc. atlanticus/tormentor*
- *Oc. canadensis*
- *Oc. cantator*
- *Oc. sollicitans*
- *Oc. taeniorhynchus*
- *Oc. triseriatus*
- *Oc. trivittatus*
- *Ps. columbiae*
- *Ps. ferox*

Opportunistic

- *Ae. albopictus*
- *Ae. vexans*
- *An. atropos*
- *An. crucians*
- *Cq. perturbans*
- *Cx. nigripalpus*
- *Cx. quinquefasciatus*
- *Cx. salinarius*
- *Oc. japonicus*
- *De. Cancer*

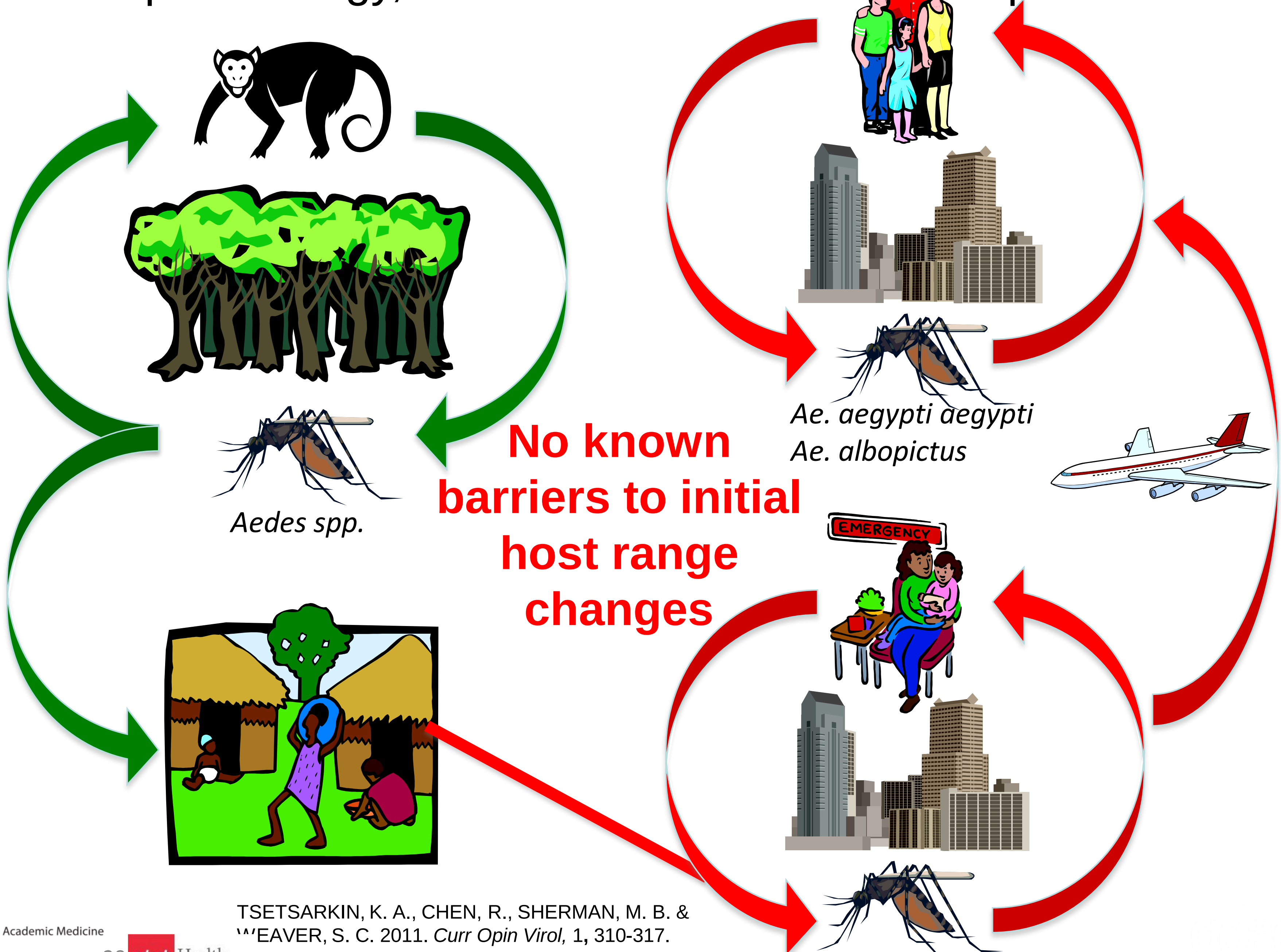
Amphibians/Reptiles

- *Ur. sapphirina*

Emergent Arboviruses Currently Causing Urban Epidemics

- Flaviviruses
  - Dengue
  - Zika
  - Yellow fever
- Alphaviruses
  - Chikungunya

Basic epidemiology, Sub-Saharan Africa/Asia/Tropical America



No known barriers to initial host range changes

TSETSARKIN, K. A., CHEN, R., SHERMAN, M. B. & WEAVER, S. C. 2011. *Curr Opin Virol,* 1**,** 310-317.

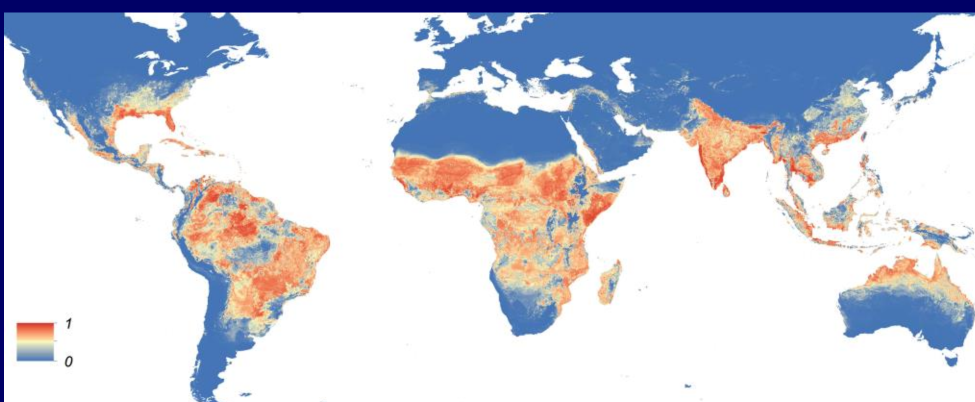
Urban *Aedes* Virus Vectors

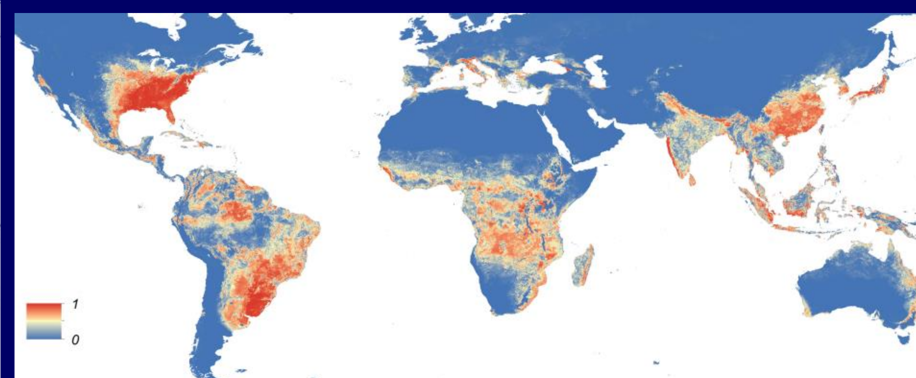
Ae.aegypti

Originated in sub-Saharan Africa, spread throughout the tropics centuries ago

Ae.albopictus

Originated in Asia, spread to the Americas, Africa and Europe beginning in 1985





Kraemer, M.U., et al., 2015. The global distribution of the arbovirus vectors *Aedes aegypti* and *Ae. albopictus*. Elife 4.

Other Potential Urban/Peridomestic Mosquito Vectors

Pacific and Asia

- *Aedes polynesiensis*
- *Aedes hensilii*
- *Aedes malayensis*
- *Aedes notoscriptus*
- Other *Aedes scutellaris* species

Africa

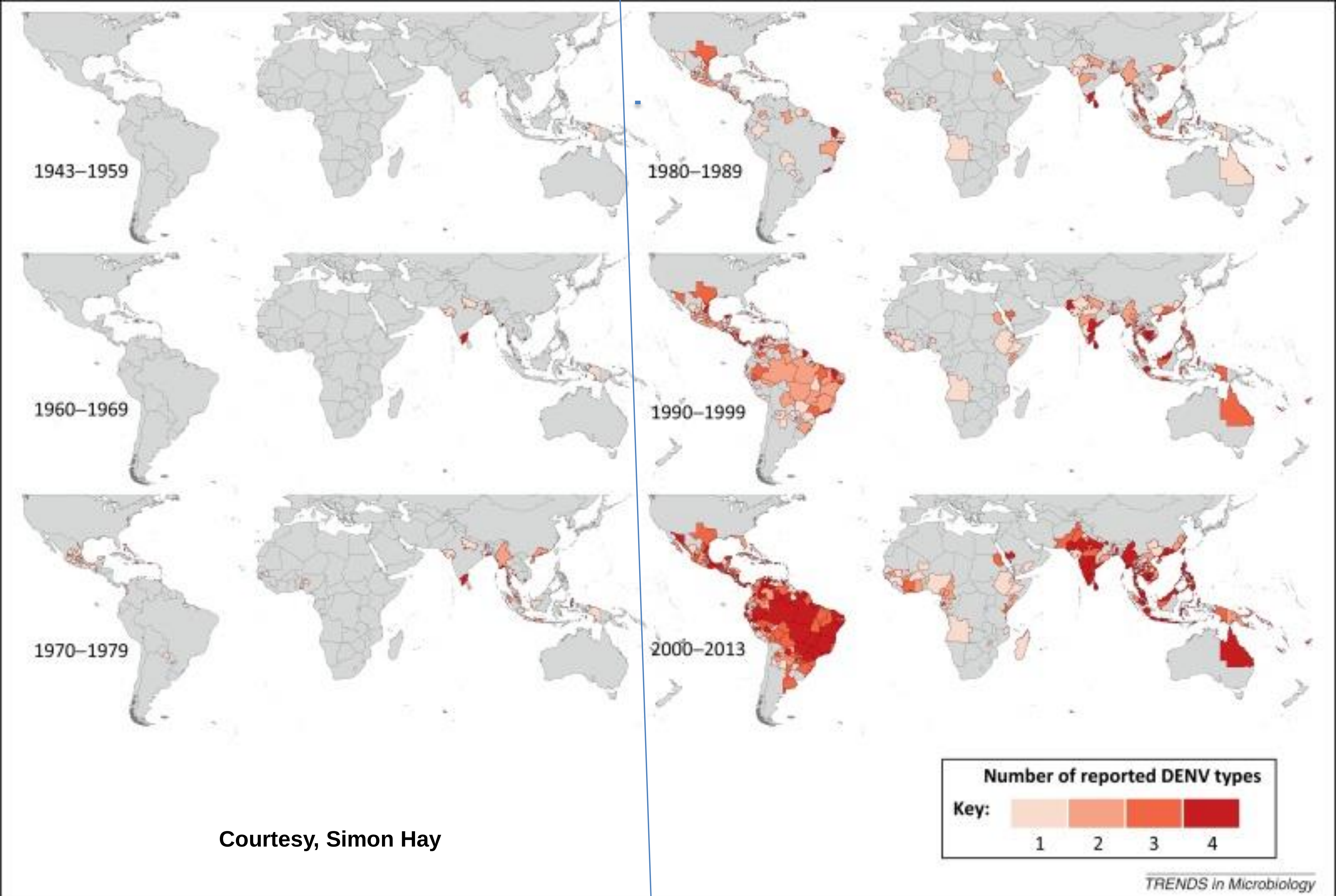
Aedes africanus complex species

Americas

Aedes mediovittatus

Other *potential mosquito vectors*

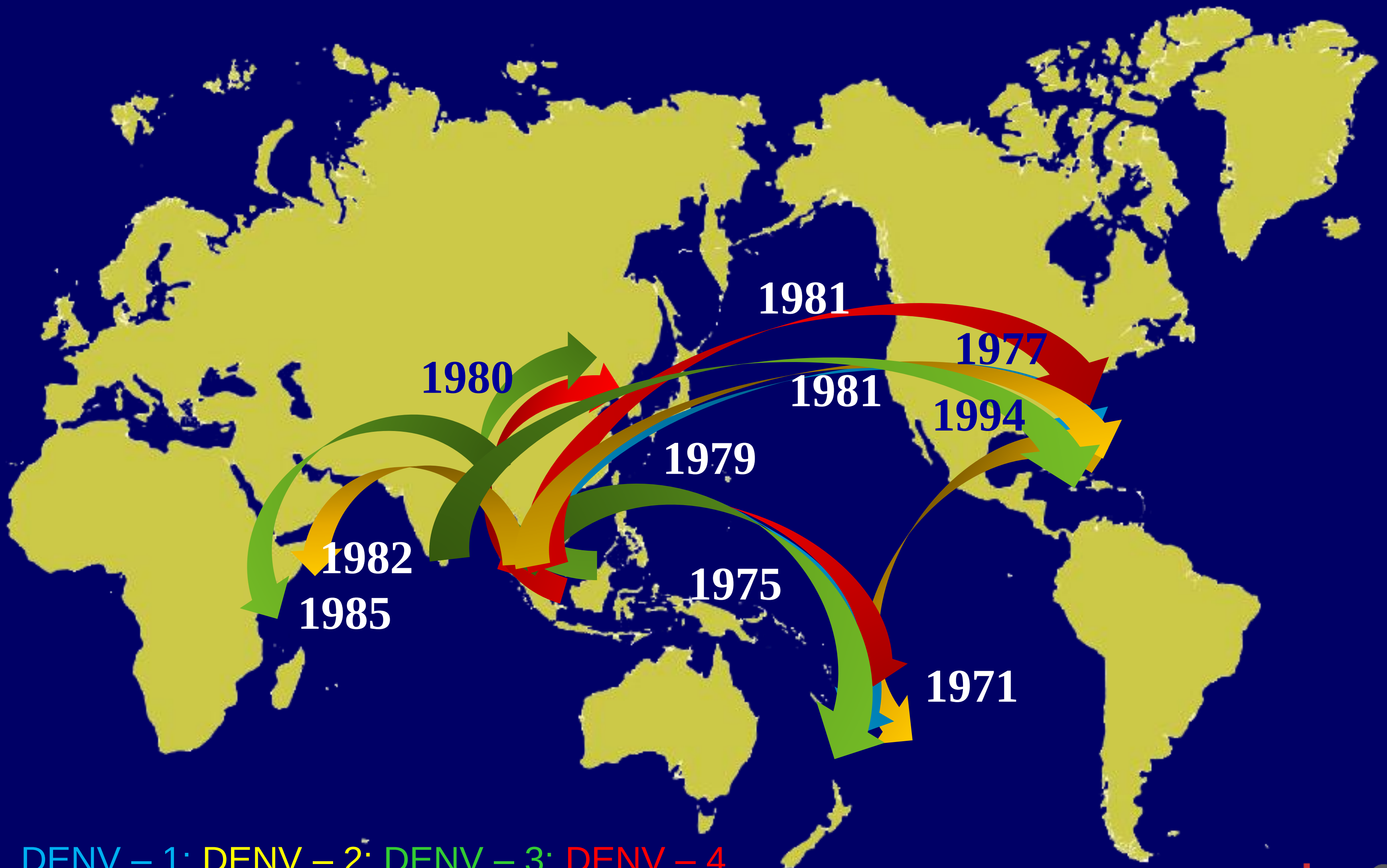
Global Spread of Dengue Viruses



Courtesy, Simon Hay

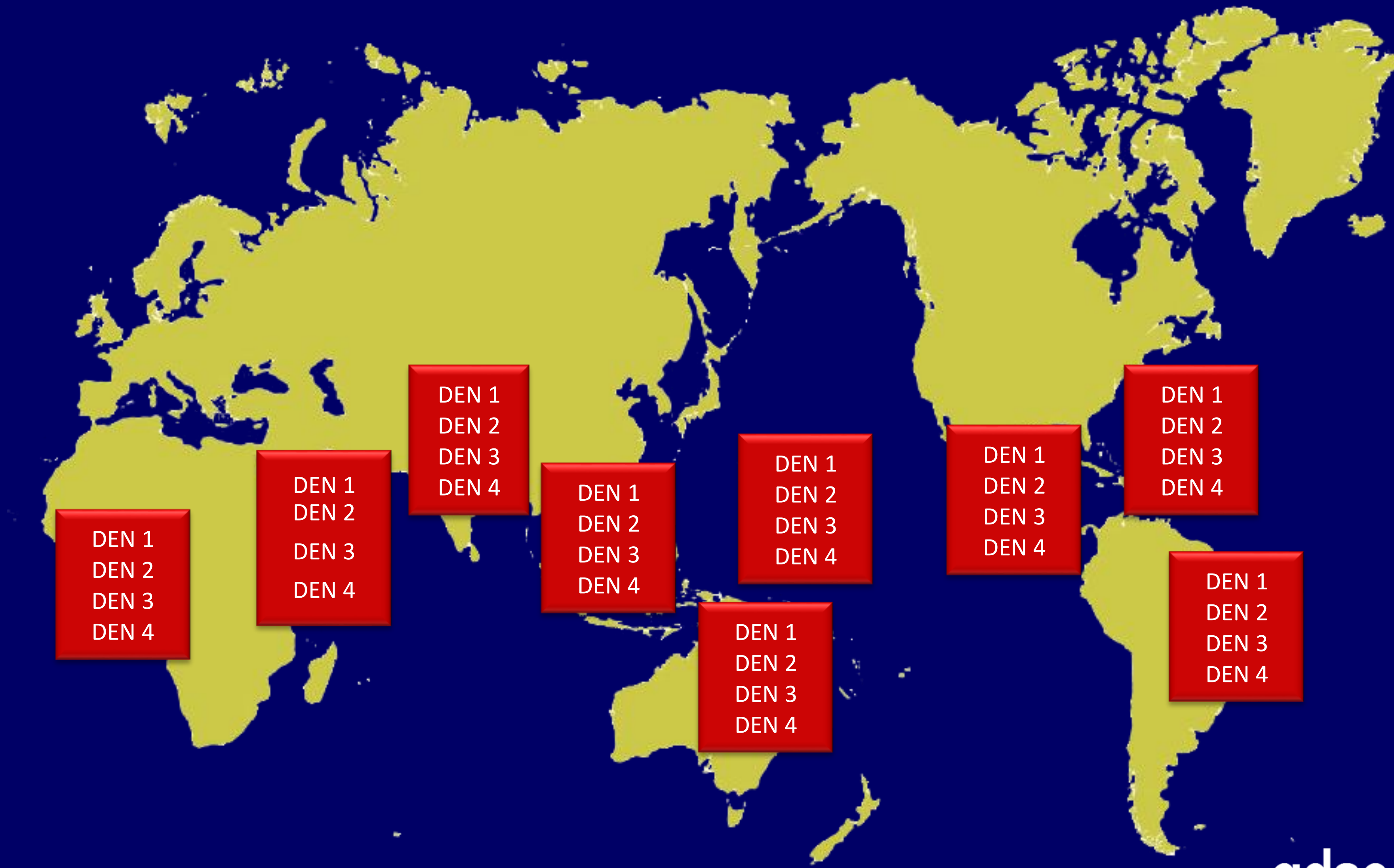
Global distribution of dengue virus serotypes, 1970

Global distribution of dengue virus serotypes 1970-2000

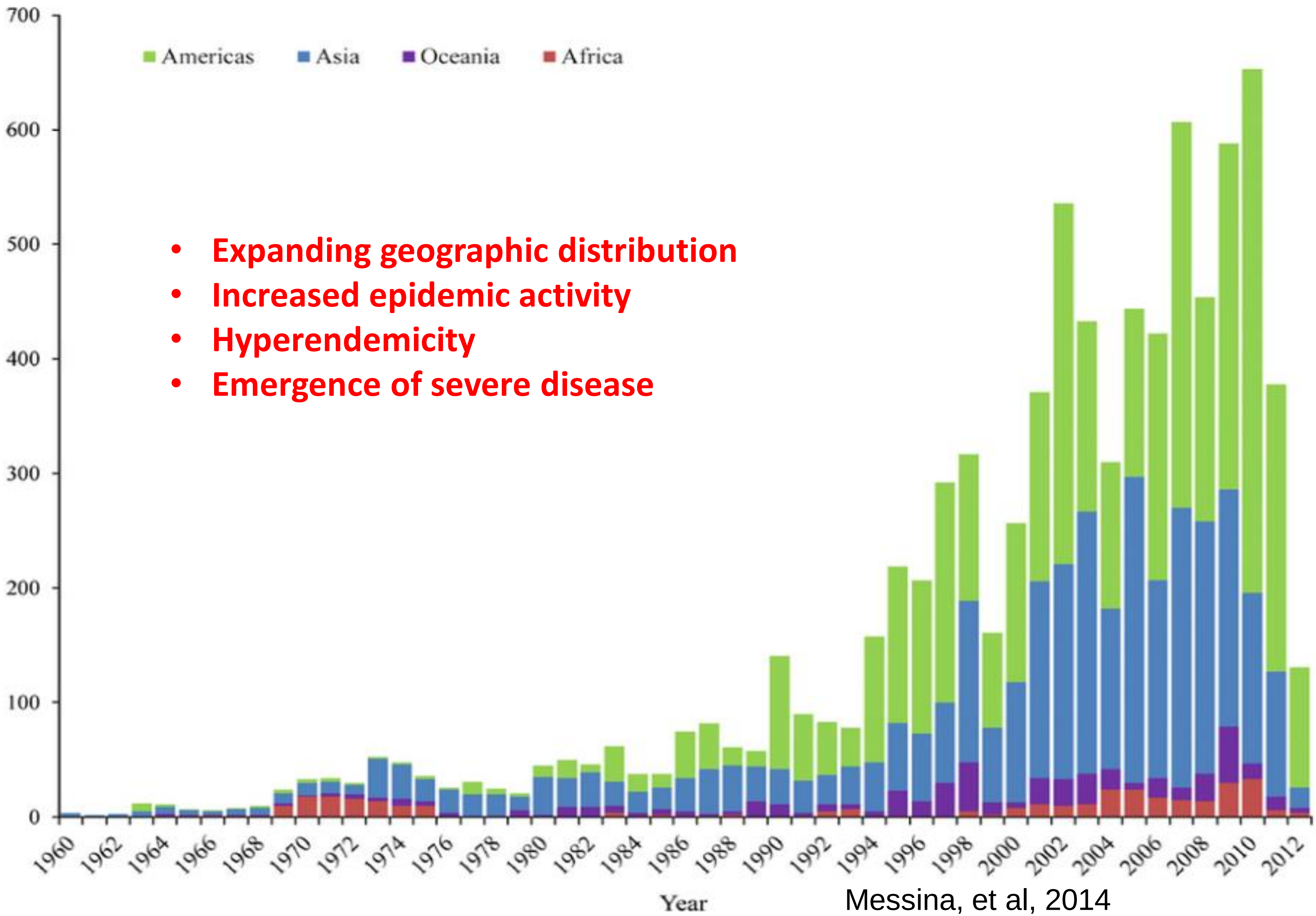


DENV – 1; DENV – 2; DENV – 3; DENV – 4

Global distribution of dengue virus serotypes, 2018

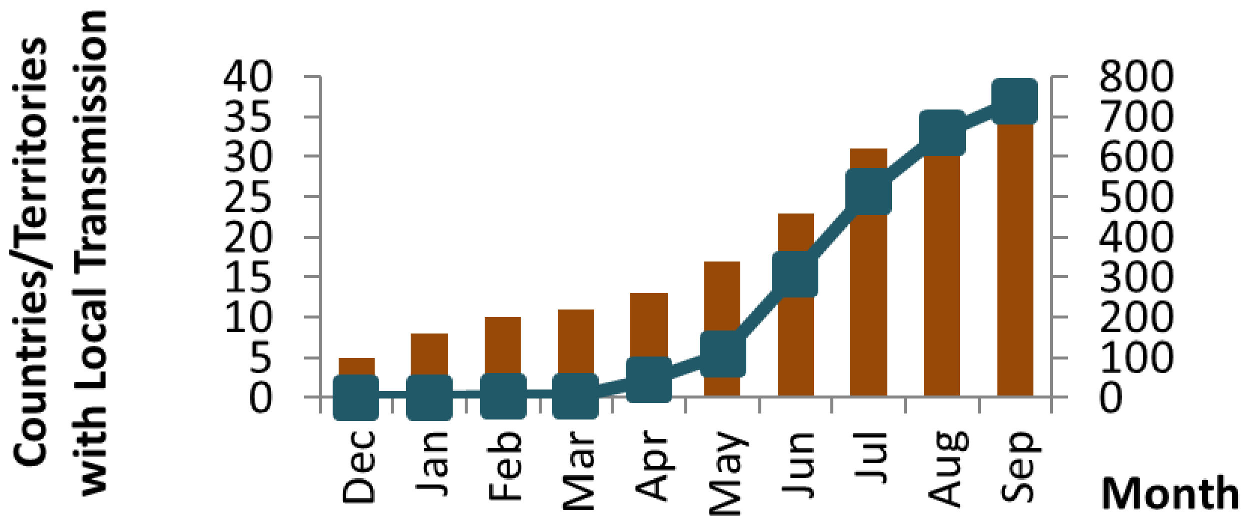


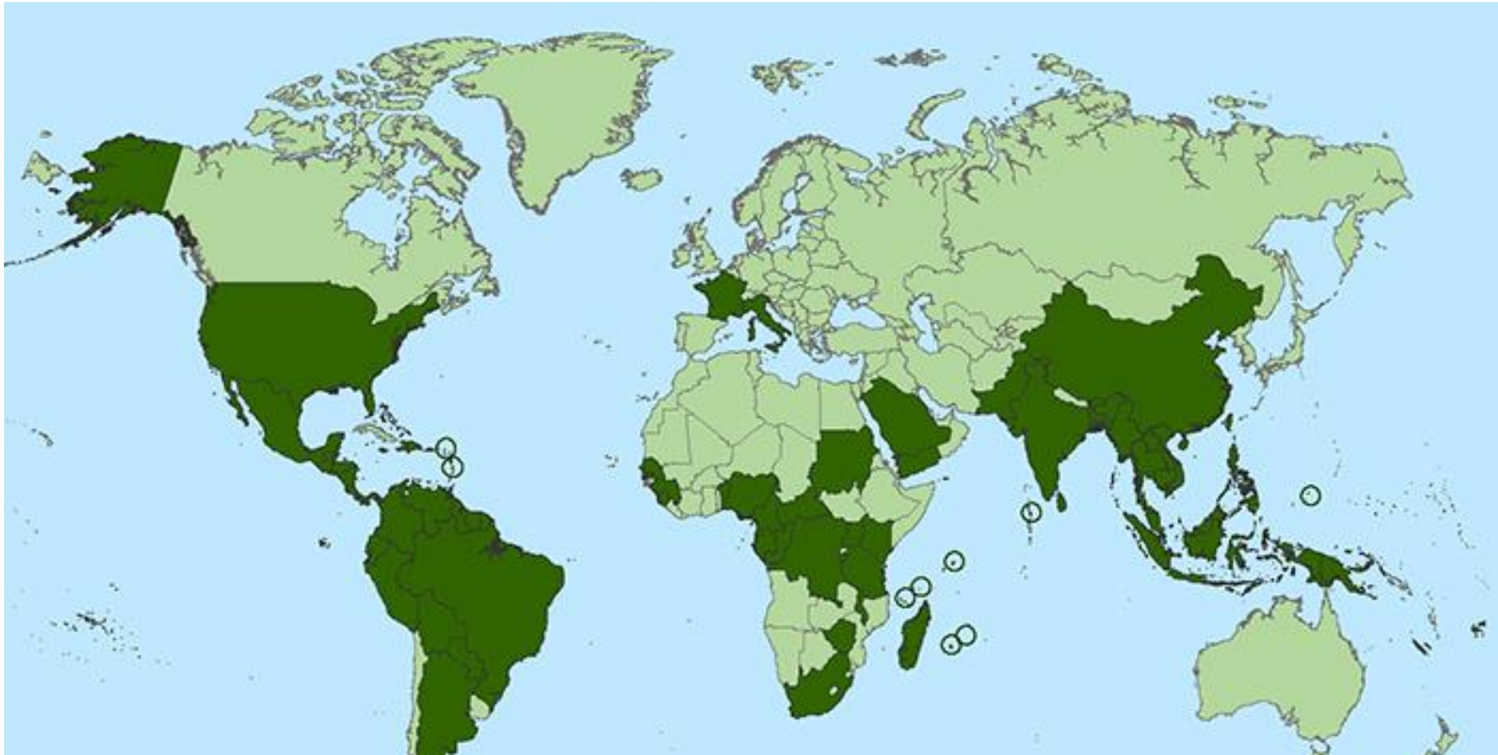
Pandemic dengue spread to 128 countries in 40 years



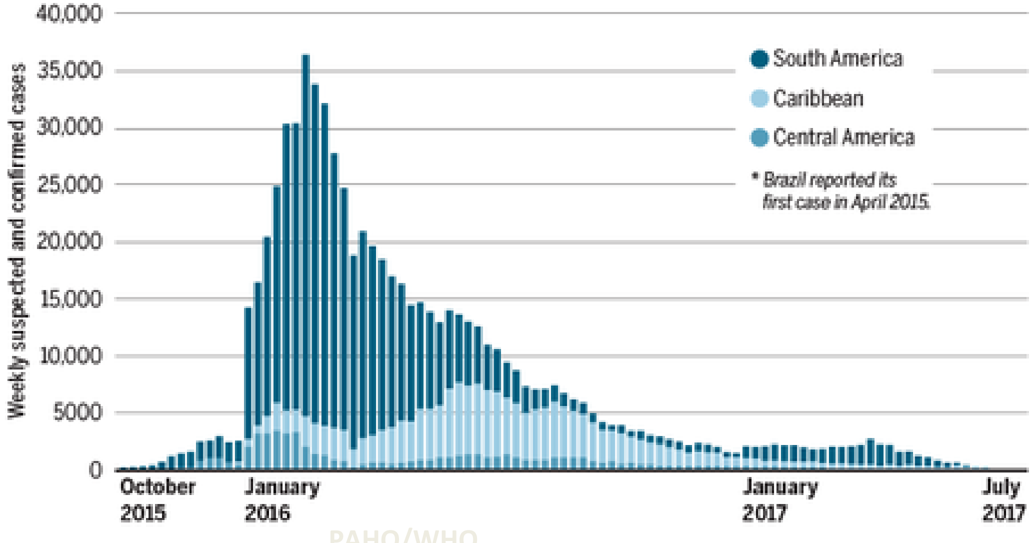
Messina, et al, 2014

Pandemic chikungunya spread to 37 countries in 10 years

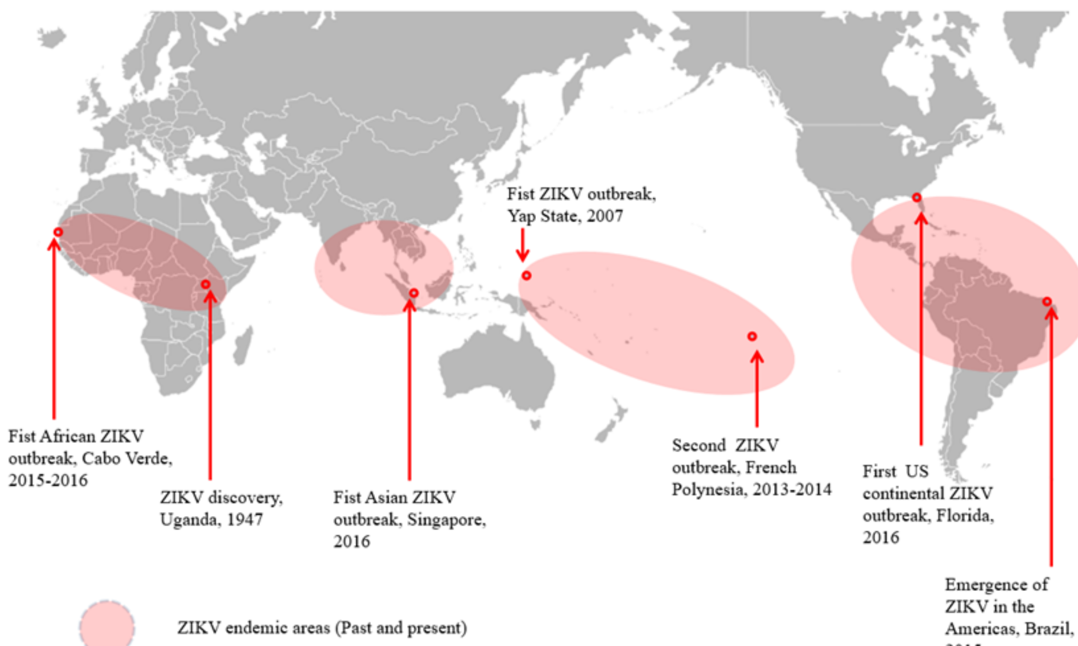




Pandemic Zika spread to 79 countries in 7 years



ZIKV endemic areas (past and present)



Why have we seen such a dramatic increase in epidemic arboviral diseases?

- Complacency, Lack of Political Will
- Policy Changes
- Changes in Public Health
- Changing Life Styles/Behavior
- Microbial Adaptation
- Technology
- Intent to Harm
- Climate Change?

The Global Threat of Urban Epidemics of Arboviral Diseases

- Unplanned urban growth unprecedented

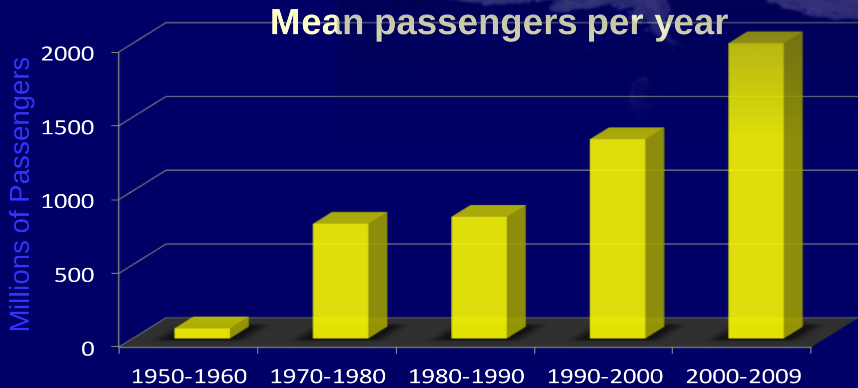
- Crowded tropical urban centers provide ideal ecological conditions to maintain viruses and mosquito vectors

- Changing Life styles; used auto tires, plastics, tins, etc, provide ideal mosquito breeding grounds

The Global Threat of Urban Arbovirus Epidemics

- Globalization and modern transportation provides ideal mechanism to move viruses and vectors among population centers

- In 2018, estimated 3+ billion passengers will travel by air



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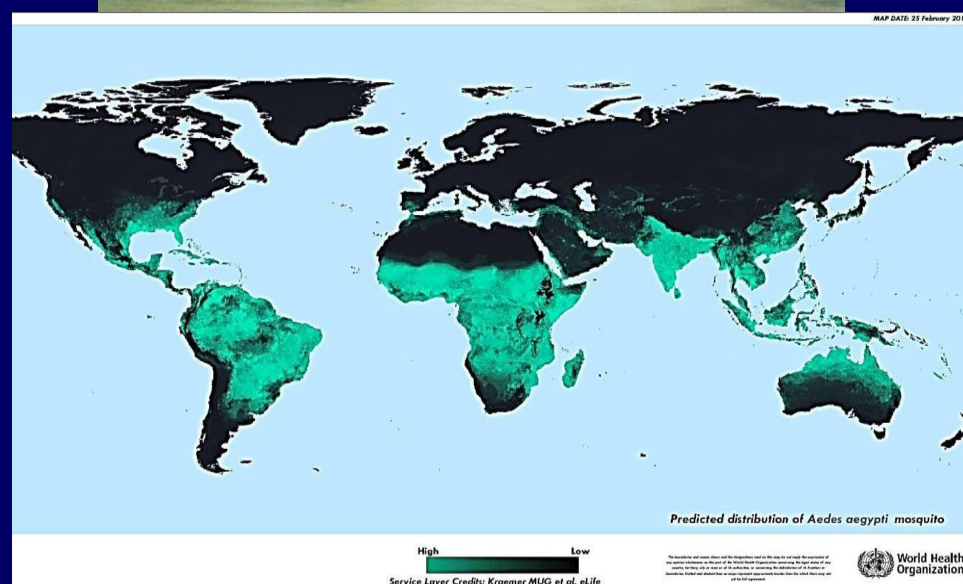
Why Have we Seen Such a Dramatic Geographic Expansion in Epidemic Epidemic Arboviral Diseases?

Major Drivers

- Demographic changes (Pop Growth)
  - Environmental change
    - Unprecedented urban growth
    - Changing lifestyles
- Increased transmission and emergence of viruses with greater epidemic potential
- Modern transportation (Globalization)
  - Increased movement of people, animals, commodities & pathogens
- Lack of effective vector control

Countries at Risk for Urban arbovirus epidemics; Global Predicted Distribution of *Aedes aegypti*

- *Aedes aegypti* and *Ae. albopictus* have global distribution in tropics & subtropics
- At risk population exceeds 3.6 billion people
- Vector control has been unable to prevent epidemic dengue, chikungunya and Zika



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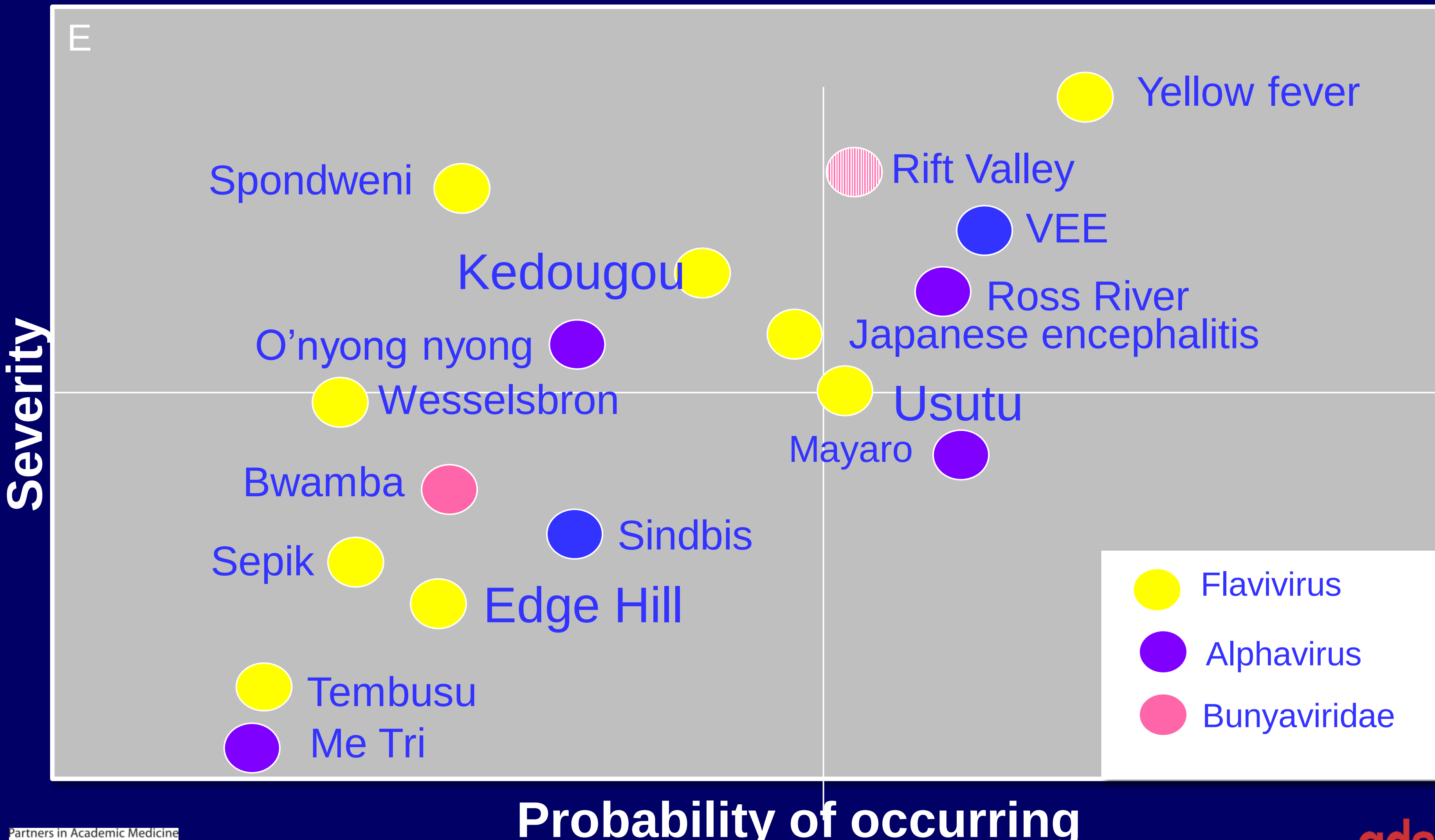
Other Arboviruses with Potential for Urban Emergence



Pandemic yellow fever: the next global threat?

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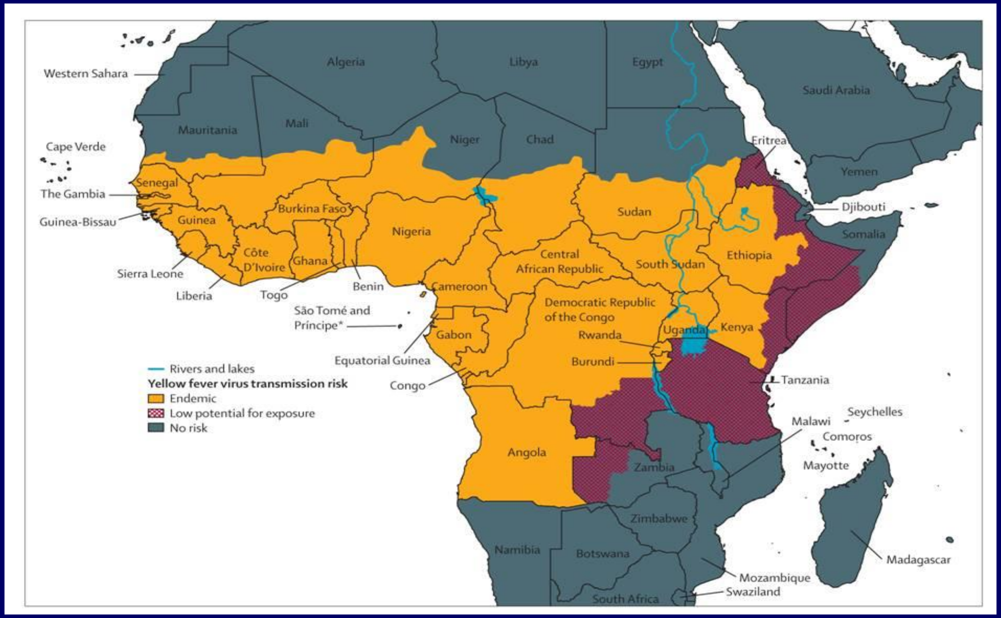
Global Distribution of Yellow Fever, 2017



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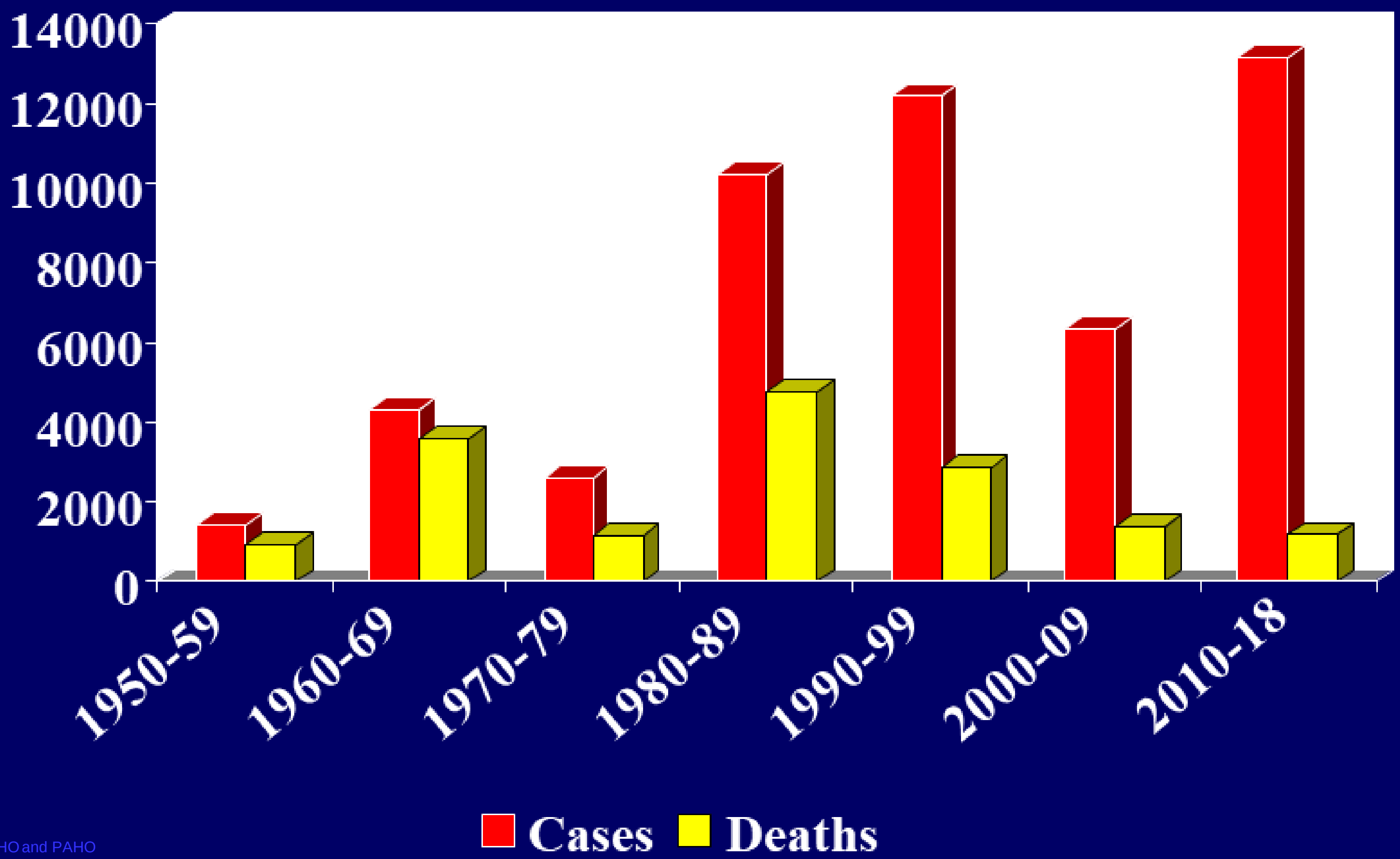
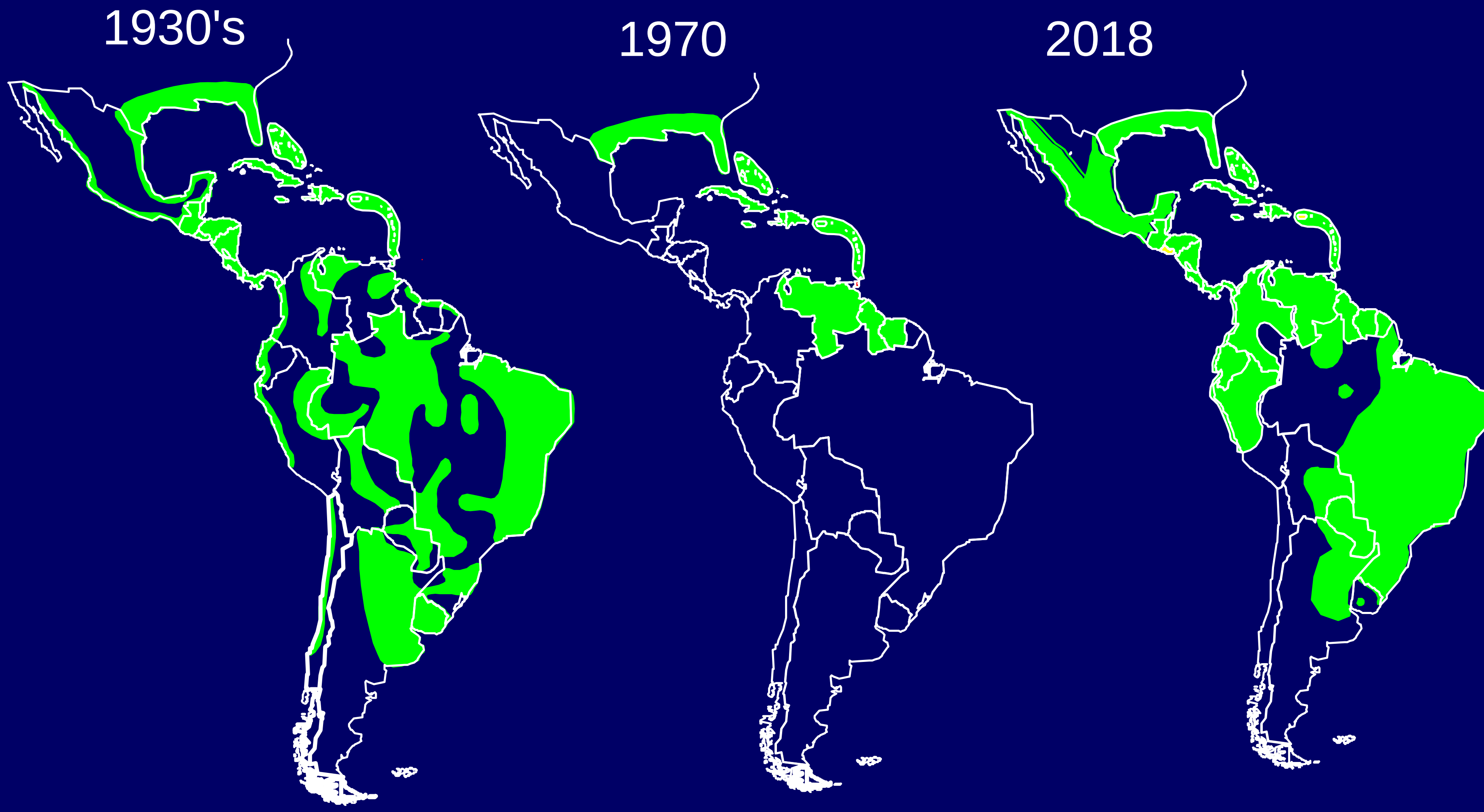
Number of Yellow Fever Cases and Deaths Reported to WHO, by Decade, 1950-May, 2018



Data from WHO and PAHO

Aedes aegypti Distribution in the Americas



Adapted from Gubler, 1998

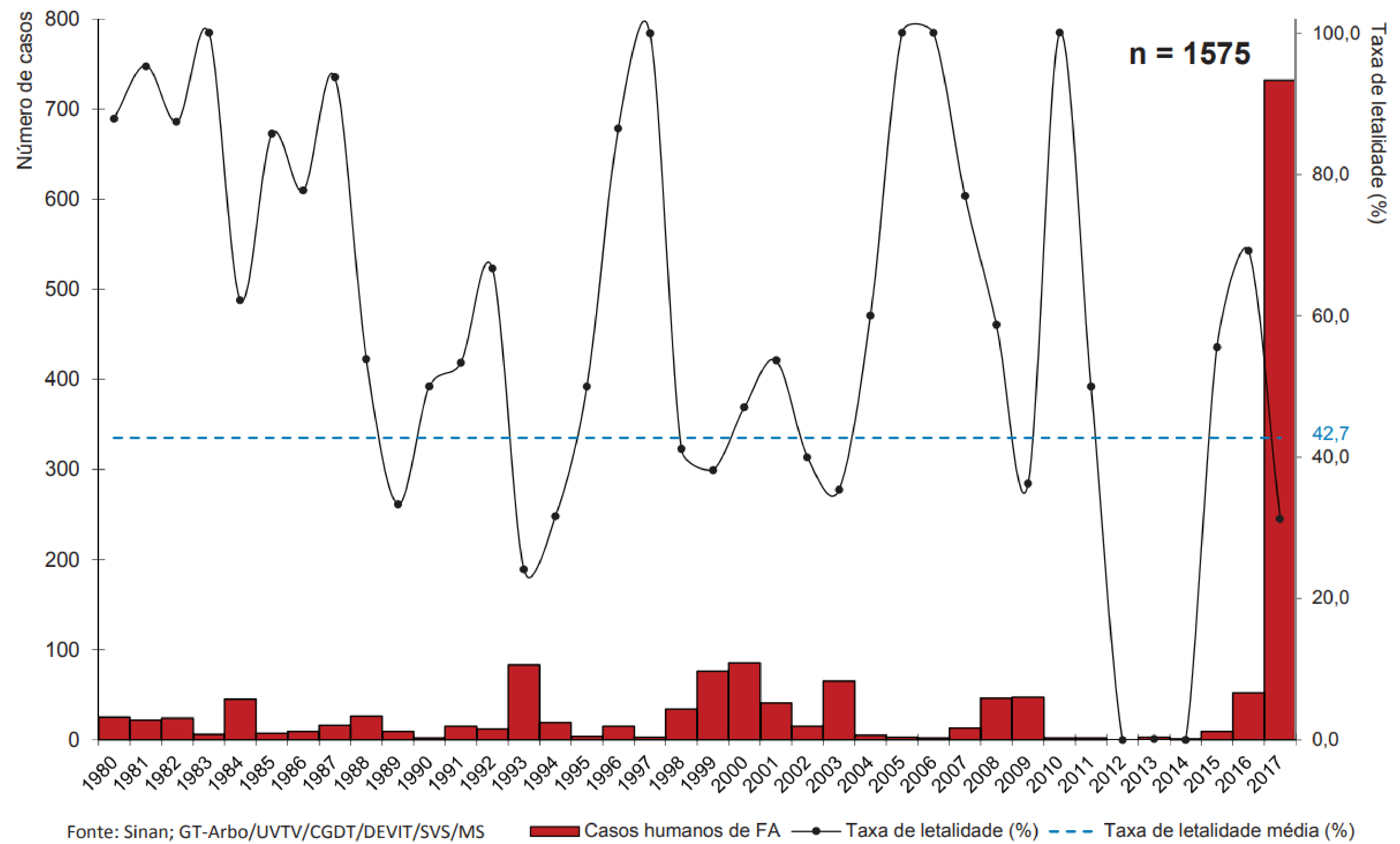
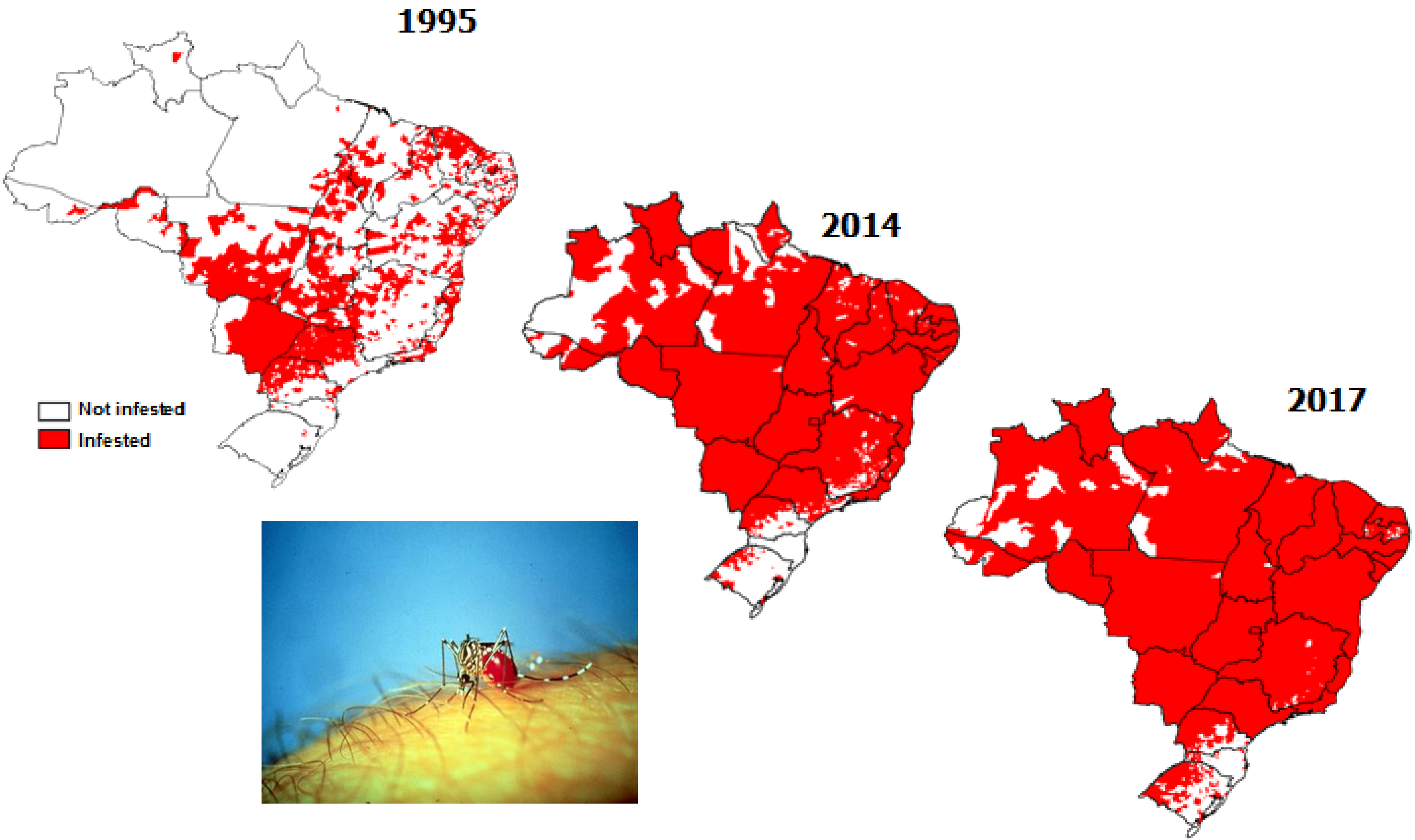
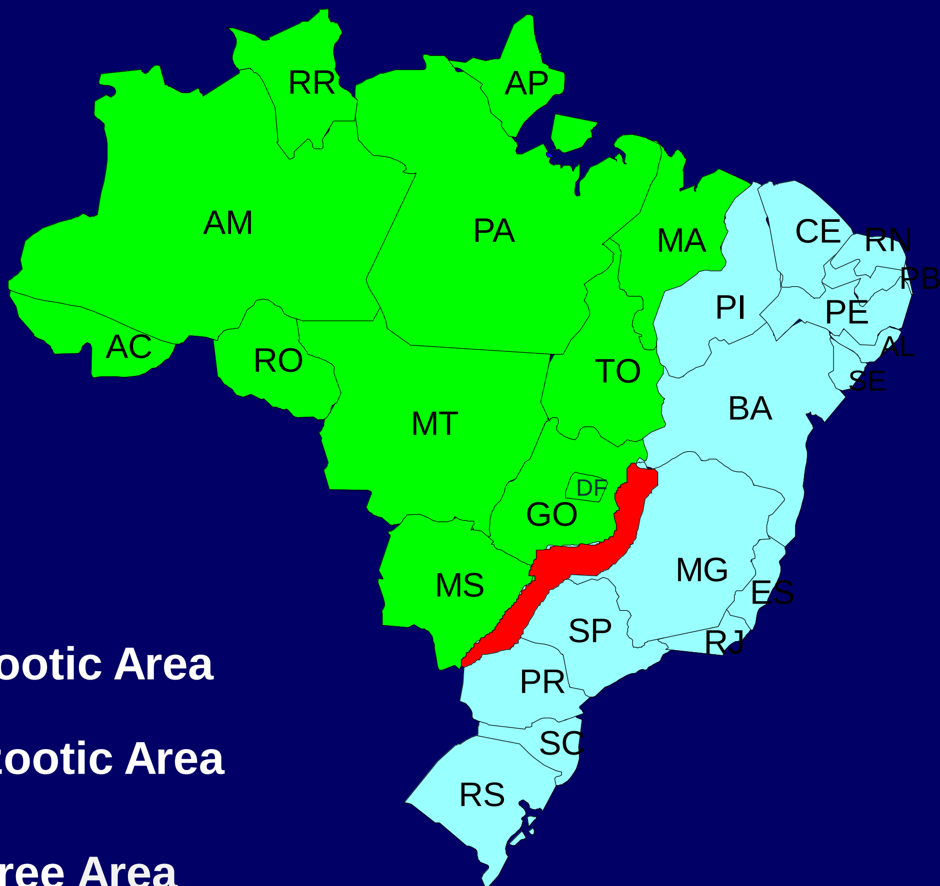


FIGURA 1 • Série histórica do número de casos humanos confirmados para FA e a letalidade, segundo o ano de início dos sintomas, Brasil, 1980 a junho de 2017.

Aedes aegypti, Brazil distribution



Epidemiologic Distribution of Yellow Fever, Brazil, 1997



Enzootic Area

Epizootic Area

YF Free Area

DADOS GERAIS:

ENDEMIC AREAS :

STATES: 12

POPULATION: 27.014.229

EPIZOOTIC AREA :

STATES – PARTS OF 3

POPULATION - 10.443.215

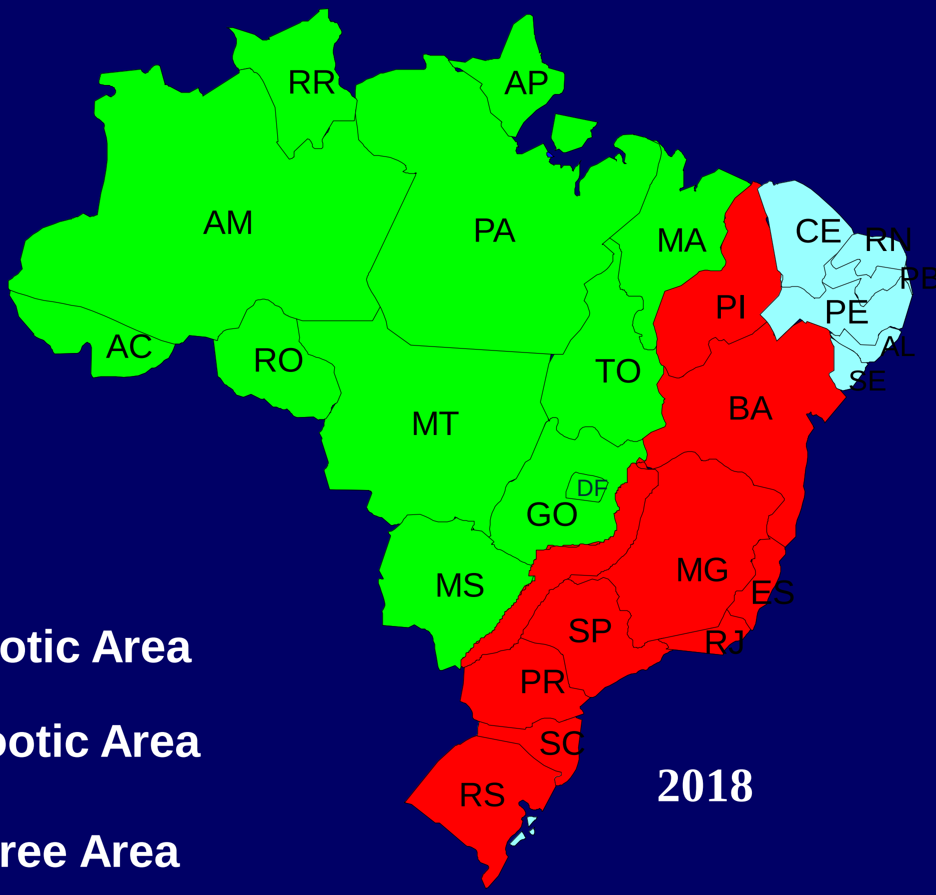
YF FREE AREA :

STATES: 15

Fonte:: SUCAM/MS

VASCONCELOS, P.F. (1997)

Epidemiologic Distribution of Yellow Fever, Brazil, 2018



Enzootic Area

Epizootic Area

YF Free Area

2018

DADOS GERAIS:

ENDEMIC AREAS :
STATES: 12
POPULATION: 27.014.229

EPIZOOTIC AREA :
STATES – PARTS OF 12
POPULATION - ??

YF FREE AREA :
STATES: 3

Fonte:: SUCAM/MS

Adapted from Vacconcelos, 1997

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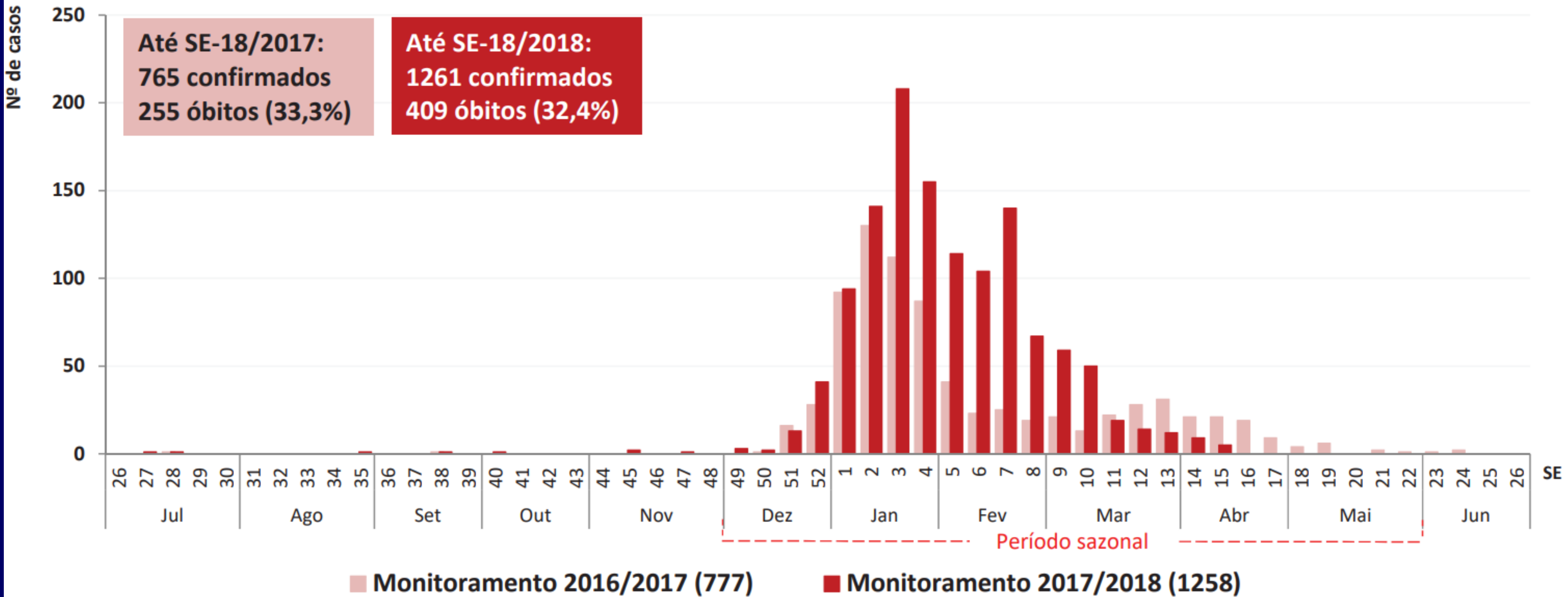
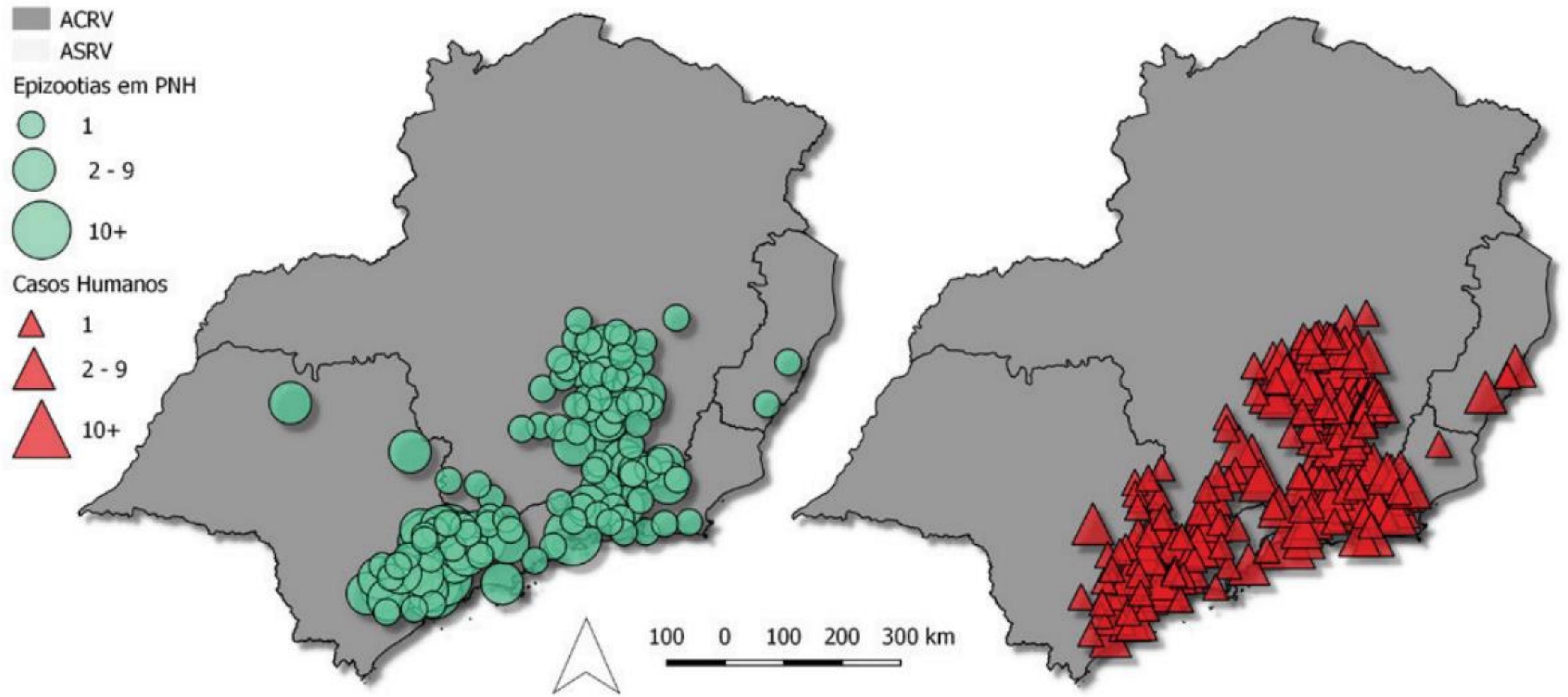


Fonte: CGDT/DEVIT/SVS/MS. *Dados preliminares e sujeitos à revisão.

FIGURA 6 • Distribuição dos casos confirmados à SVS/MS, por SE de ocorrência, nos períodos de monitoramento 2016/2017 (jul/16 a jun/17) e 2017/2018 (jul/17 a jun/18), Brasil, até a SE 18*.



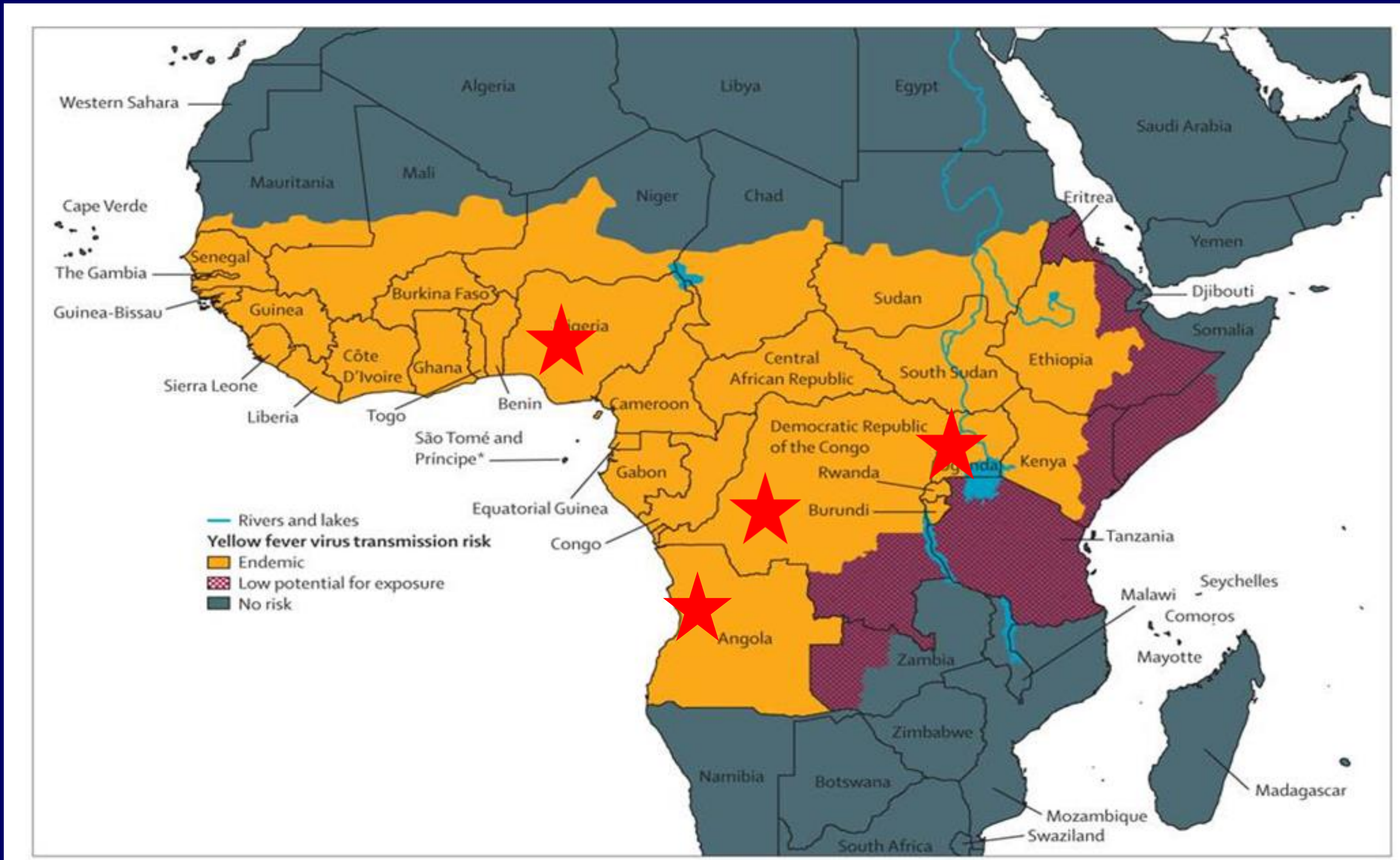
Fonte: CGDT/DEVIT/SVS/MS. Os pontos no mapa estão plotados no centroide do município e não georreferenciados no local de ocorrência do evento.

FIGURA 8 • Distribuição dos casos humanos e epizootias confirmadas para FA, por município do local provável de infecção, Região Sudeste, monitoramento 2017/2018 (jul/17 a jun/18), Brasil, até a SE 18.

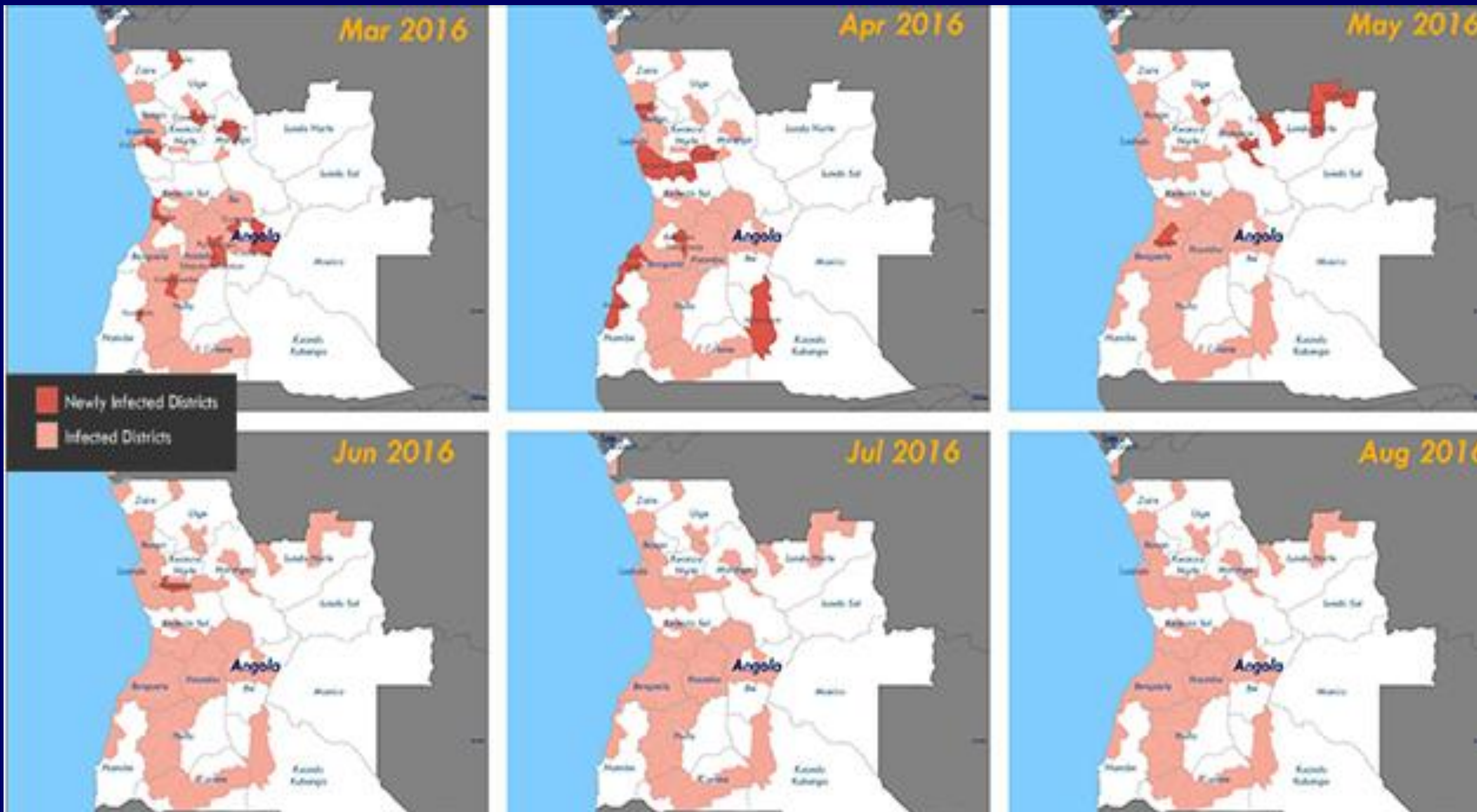
Imported Yellow Fever, 2018

Highest in decades

Epidemic Yellow Fever in Africa, 2016-2018



Epidemic Yellow Fever, Angola, 2016



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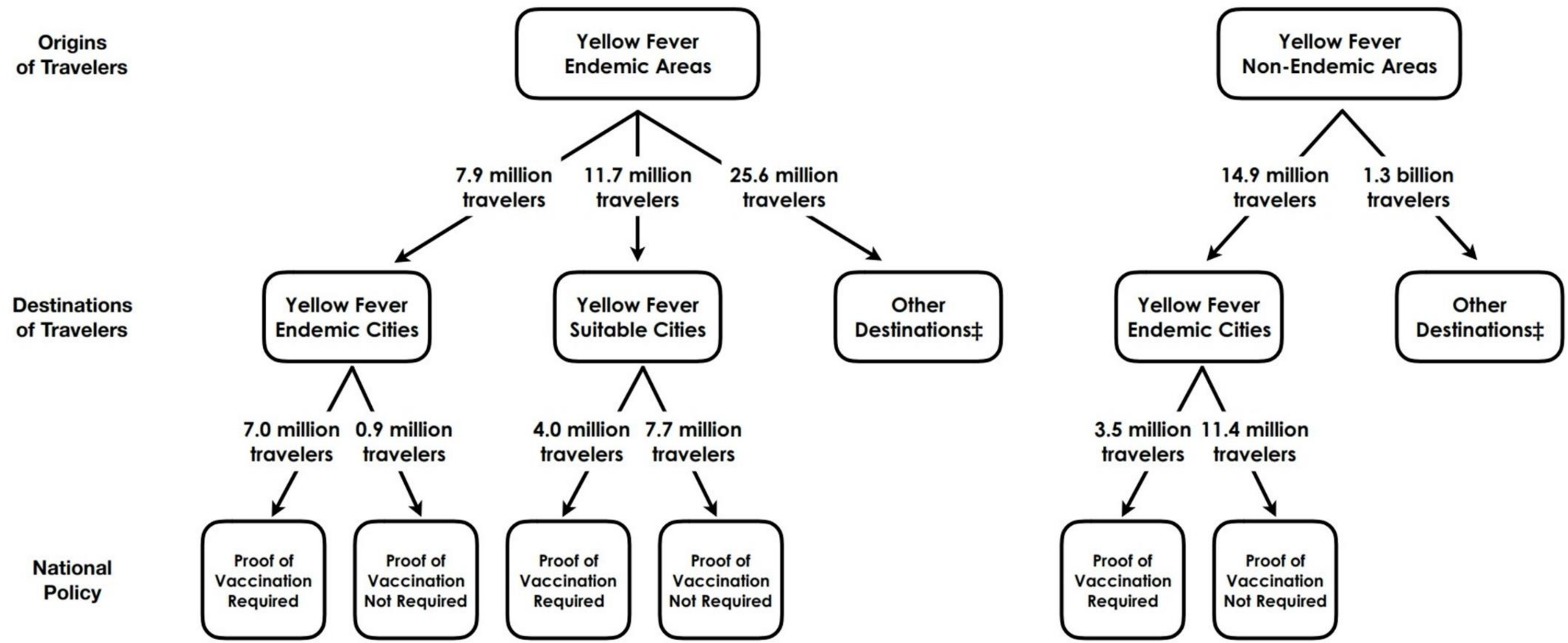
Imported Yellow Fever, China, 2016

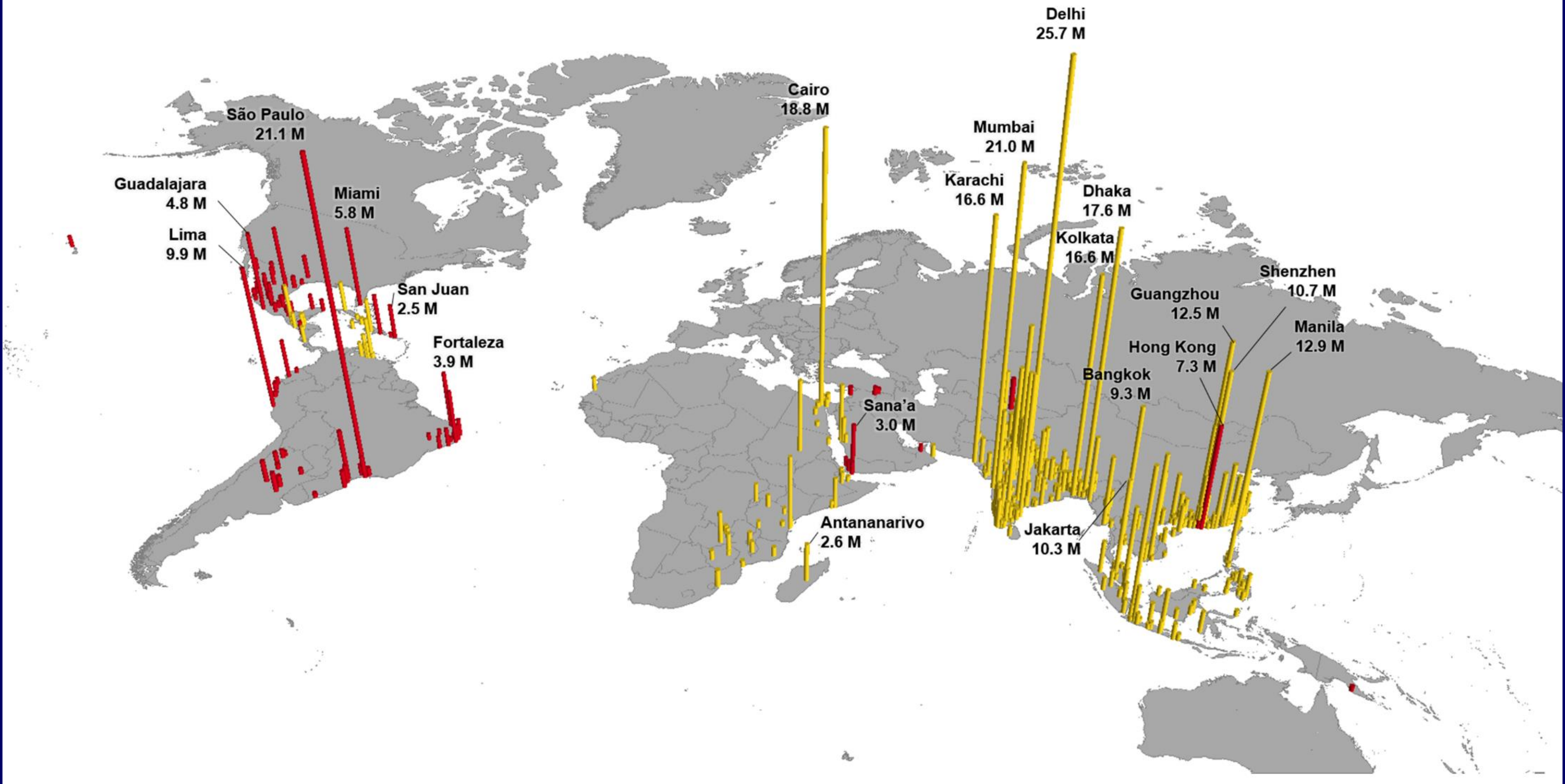
First time in History

Movements of international air travelers between yellow fever endemic* and non-endemic† areas of the world, 2016.



* Yellow fever endemic areas were defined as national and subnational regions where the World Health Organization recommends yellow fever vaccination.
† Cities were defined as yellow fever endemic if they landed within the geographic range of areas where the World Health Organization recommends yellow fever vaccination. Cities were defined as yellow fever suitable based on a global ecological model of dengue virus suitability. Traveler destinations are not in the same country as traveler origins.
‡ Other destinations were defined as: i) all regions not endemic or not suitable for yellow fever transmission and ii) areas endemic or suitable for yellow fever transmission but with population settlements of fewer than 300,000 residents. Our estimate of 1.3 billion travelers reflects the international movements of persons on flights[23] from yellow fever non-endemic to yellow fever endemic areas.

Global populations* living in yellow fever suitable cities and corresponding national yellow fever travel vaccination policy†



* Bars heights are proportional to resident population size, and represent 472 yellow fever suitable cities across 54 countries. In our urban scenario, there were six fewer yellow fever suitable destination cities, Satna, India (population 0·31 million residents); Ibb, Yemen (population 0·45 million residents); Al-Hudaydah, Yemen (population 0·57 million residents); Ta'izz, Yemen (population 0·69 million residents); Adan, Yemen (population 0·88 million residents), and Sana'a, Yemen (population 2·7 million residents).

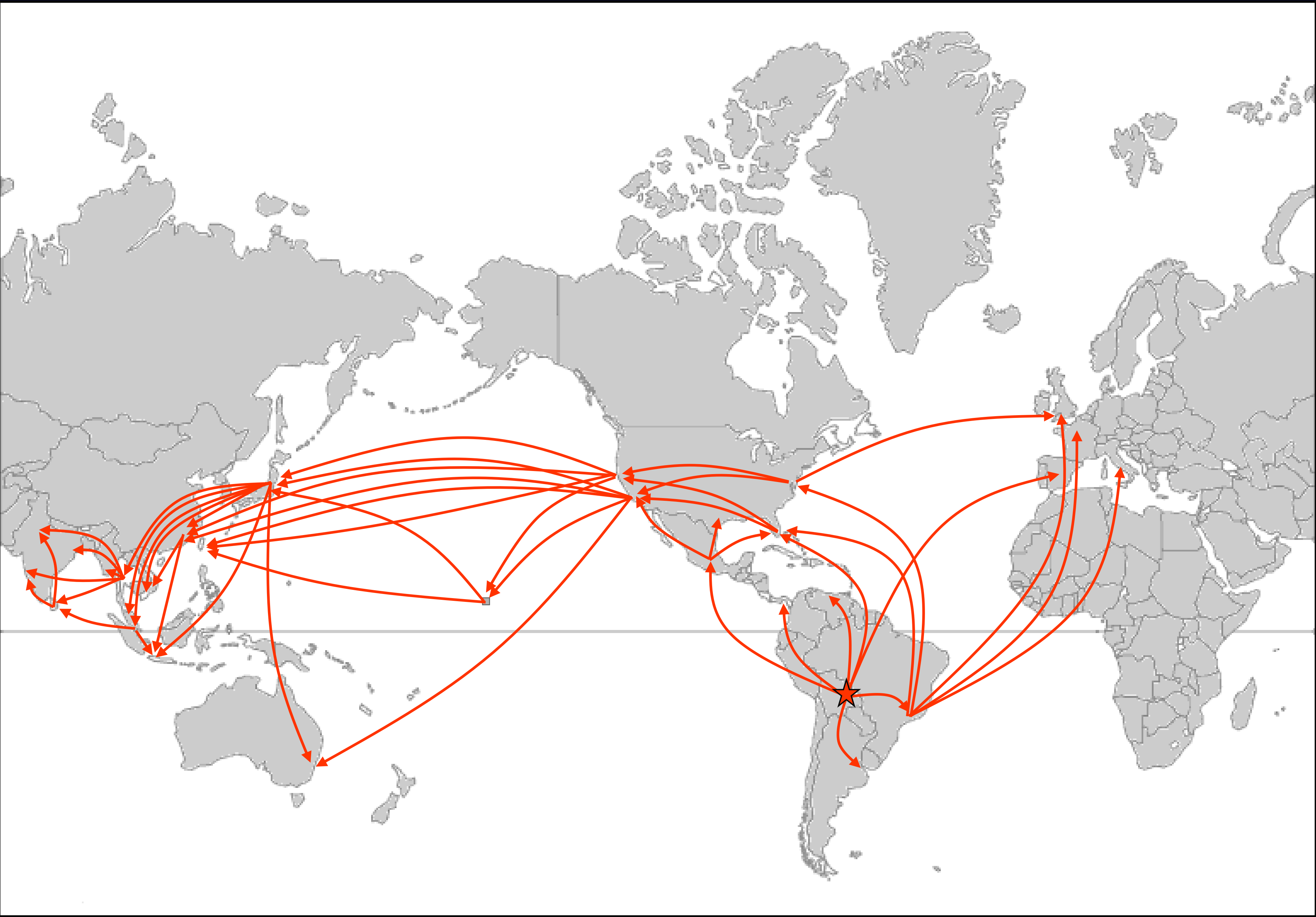
† Yellow bars represent cities where international travelers arriving specifically from yellow fever endemic countries are required to provide proof of yellow fever vaccination upon arrival. Red bars represent cities where international travelers are not required to provide proof of yellow fever vaccination, regardless of origin.

Brent, et al, 2018

Imported Yellow Fever, 2016-2018

Highest in decades

POTENTIAL GLOBAL SPREAD OF URBAN YELLOW FEVER



What is the Risk of Urban Epidemics of Yellow Fever Today?

Risk Factors

- Unplanned urban growth unprecedented
- Crowded tropical urban centers provide ideal ecological conditions to maintain viruses and mosquito vectors
- Globalization provides ideal mechanism to move viruses and vectors among population centers
- *Aedes aegypti* and *Ae. albopictus* have global distribution
- At risk susceptible population exceeds 3.6 billion people
- Low herd immunity in humans
- 10s of millions of travelers visit YF endemic countries annually
- IHR proof of vaccination not enforced
- Encroachment of humans on sylvatic cycle
- Vector control has been unable to prevent epidemic dengue, chikungunya and Zika
- Vaccine unavailable or inadequate supply

The risk of urban yellow fever epidemics is the highest in 70 years!

So why hasn't epidemic Yellow Fever occurred in Urban Centers of South America and Asia?

- **Mostly Speculation**
- **Number of hypotheses**

Why hasn't epidemic Yellow Fever occurred in Urban Centers of South America and Asia?

Hypotheses

- Plain old Luck
- Geographic and demographic obstacles in past
- Sylvatic foci are dynamic
- Barriers of YF immunity in border areas
- Aedes aegypti densities and competence are variable
- Acutely ill YF patients less exposure to mosquitoes
- Cross protective flavivirus immunity
- Good surveillance and rapid containment
- Effective mosquito control in areas at risk
- YFV urban cycle doesn't exist
- Evolutionary exclusion

Why hasn’t epidemic Yellow Fever occurred in Urban Centers of South America and Asia?

Most Important?

- Barriers of YF immunity in endemic countries
- Cross protective flavivirus immunity
- No YFV lineage adapted to Ae aegypti and human cycle

Urban Arboviral Disease Epidemics

Conclusions

- Risk of epidemic arboviral diseases is highest in history
- Vaccines are unavailable or in short supply
- Vector control has been ineffective in preventing epidemics
- We should expect more emergent epidemic viruses transmitted by Aedes Stegomyia mosquitoes
- Control is possible if we combine vaccines with best vector control tools

Global Dengue and *Aedes*-transmitted Diseases Consortium (GDAC)

GDAC Secretariat hosted by IVI

GDAC Director: In-Kyu Yoon

GDAC Consortium Management Committee (GCMC)

GDAC Chair: Duane Gubler

GDAC Technical Advisory Group (TAG)

Working Groups (for specific topics)

IVAC International Vaccine Access Center

SABIN VACCINE INSTITUTE

INTERNATIONAL VACCINE INSTITUTE

PDC PARTNERSHIP FOR DENGUE CONTROL

World Health Organization (Observer Partner)

GDAC Paradigm to Rollback Dengue and Other *Aedes*-Transmitted Diseases Using New Tools in the Control Pipeline

Integration and Synergy

Clinical management/ therapeutics

Community engagement

Vector Control

Vaccination

Improved Surveillance

Targeted Control program

International mobilization of resources

- Build public health capacity
- Fund program implementation
- Fund research