Mahidol University
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Epidemiology of Dengue

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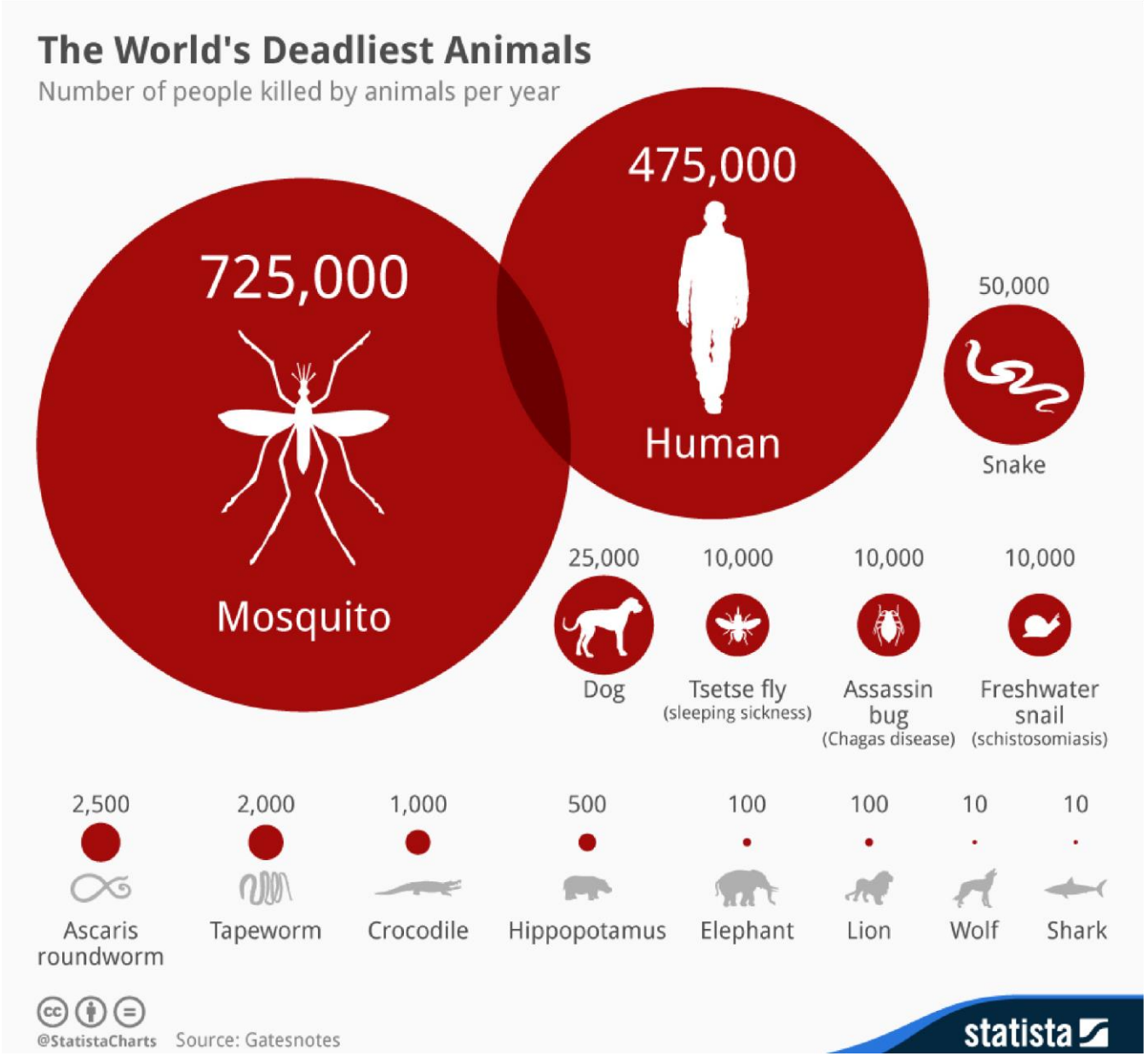

https://www.statista.com/chart/2203/the-worlds-deadliest-animals/

Mosquito-borne Diseases

	Predominant vectors by genus	Estimated or reported number of cases per annum
Malaria	*Anopheles*	212 million (range 148–304 million)
Dengue	*Aedes*	96 million (range 67–136 million)
Lymphatic filariasis	*Aedes*, *Anopheles*, and *Culex*	38·5 million (range 31·3–46·7 million)
Chikungunya	*Aedes*, *Anopheles*, *Culex*, and *Mansonia*	693 000 (Americas)
Zika virus	*Aedes*	500 000 (Americas)
Yellow fever	*Aedes* and *Haemagogus*	130 000 (range 84 000–170 000) (Africa)
Japanese encephalitis	*Culex*	42 500 (range 35 000–50 000
West Nile fever	*Culex*	2588

Data are from WHO.[1,2]

Table 1: **Number of cases of the major mosquito-borne diseases of global health significance per year**

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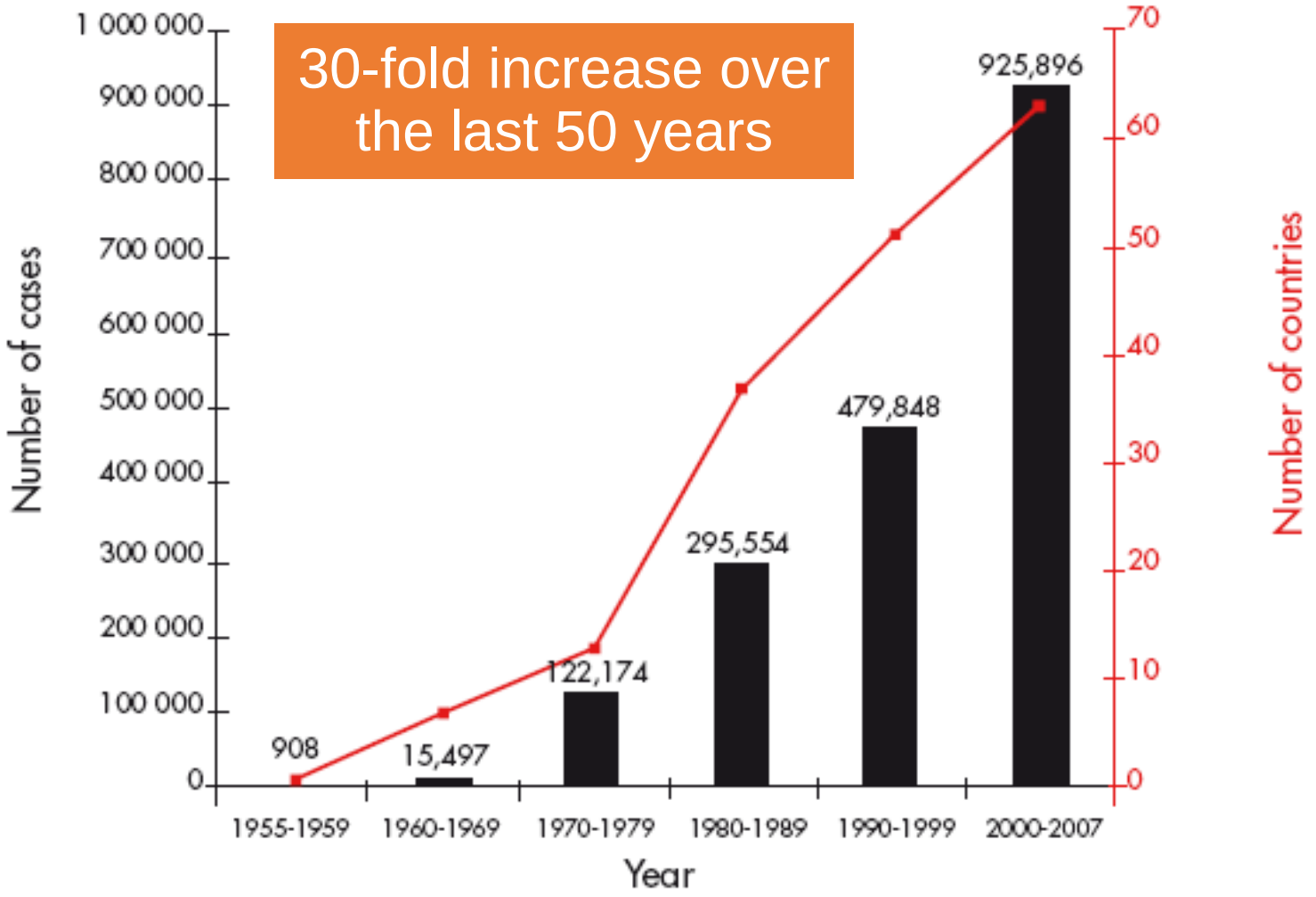
Franklinos LHV, Jones KE, Redding DW, Abubakar I. The effect of global change on mosquito-borne disease. Lancet Infect Dis. 2019 Sep;19(9):e302-e312.

“Dengue is the most rapidly spreading mosquito borne viral disease in the world.”

-WHO, 2014 -

Figure 1.2 Average annual number of dengue fever (DF) and dengue haemorrhagic fever (DHF) cases reported to WHO, and of countries reporting dengue, 1955–2007



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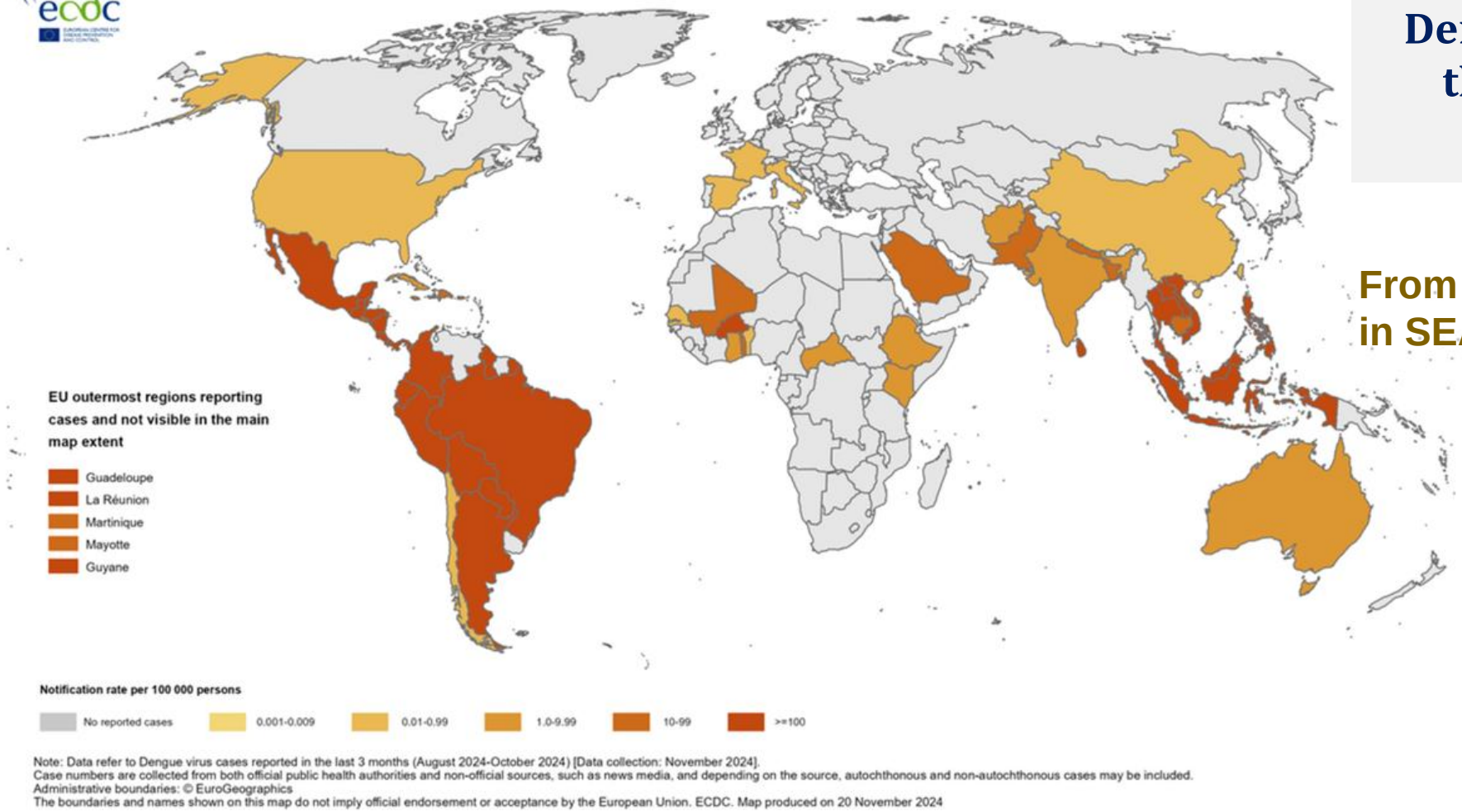
WHO: Dengue guidelines for diagnosis, treatment, prevention and control 2009

Dengue virus disease case notification rate per 100 000 population, August to October 2024



Note: Data refer to Dengue virus cases reported in the last 3 months (August 2024-October 2024) [Data collection: November 2024].
Case numbers are collected from both official public health authorities and non-official sources, such as news media, and depending on the source, autochthonous and non-autochthonous cases may be included.
Administrative boundaries: © EuroGeographics
The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on 20 November 2024

Dengue is one of the top ten threats to public health.

-WHO, 2019-

From 2015 to 2019, dengue cases in SEA region increased by 46%.

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European Centre for Disease Prevention and Control
https://www.who.int/southeastasia/health-topics/dengue-and-severe-dengue

Dengue Situation in Thailand

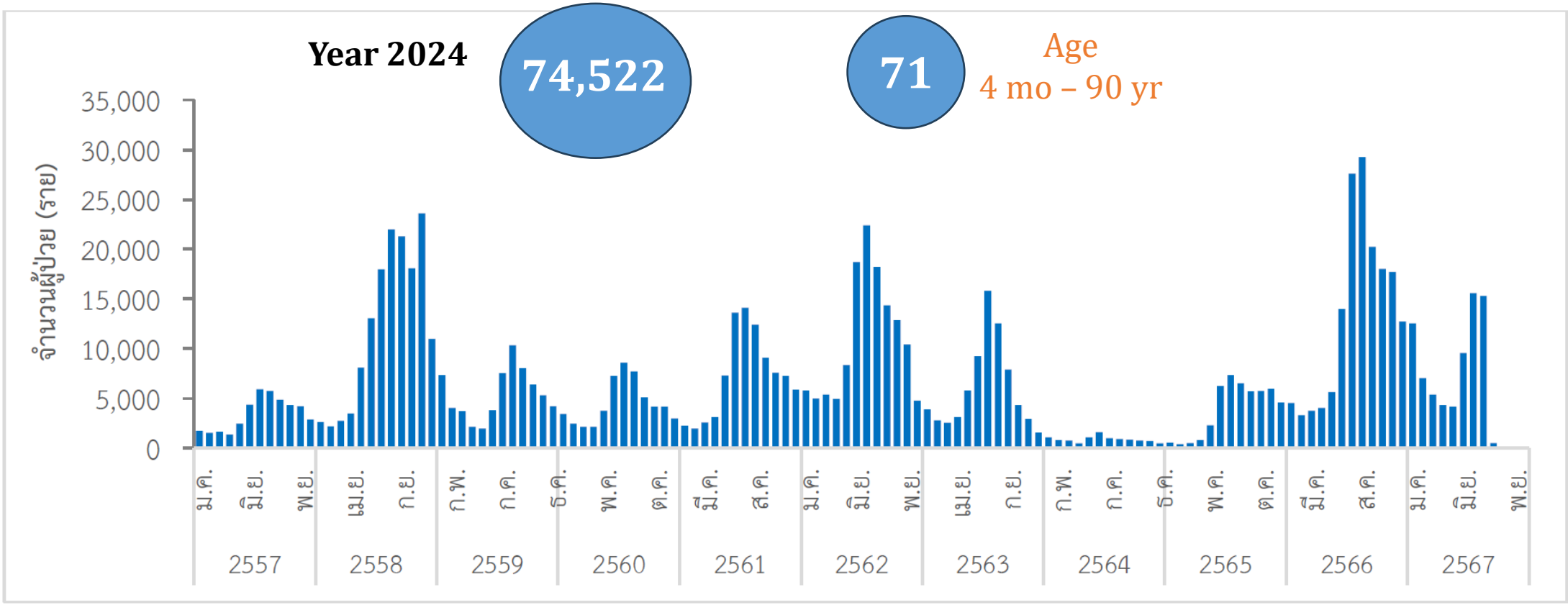
Dengue cases **Death**

Year 2024

74,522

71

Age
4 mo – 90 yr



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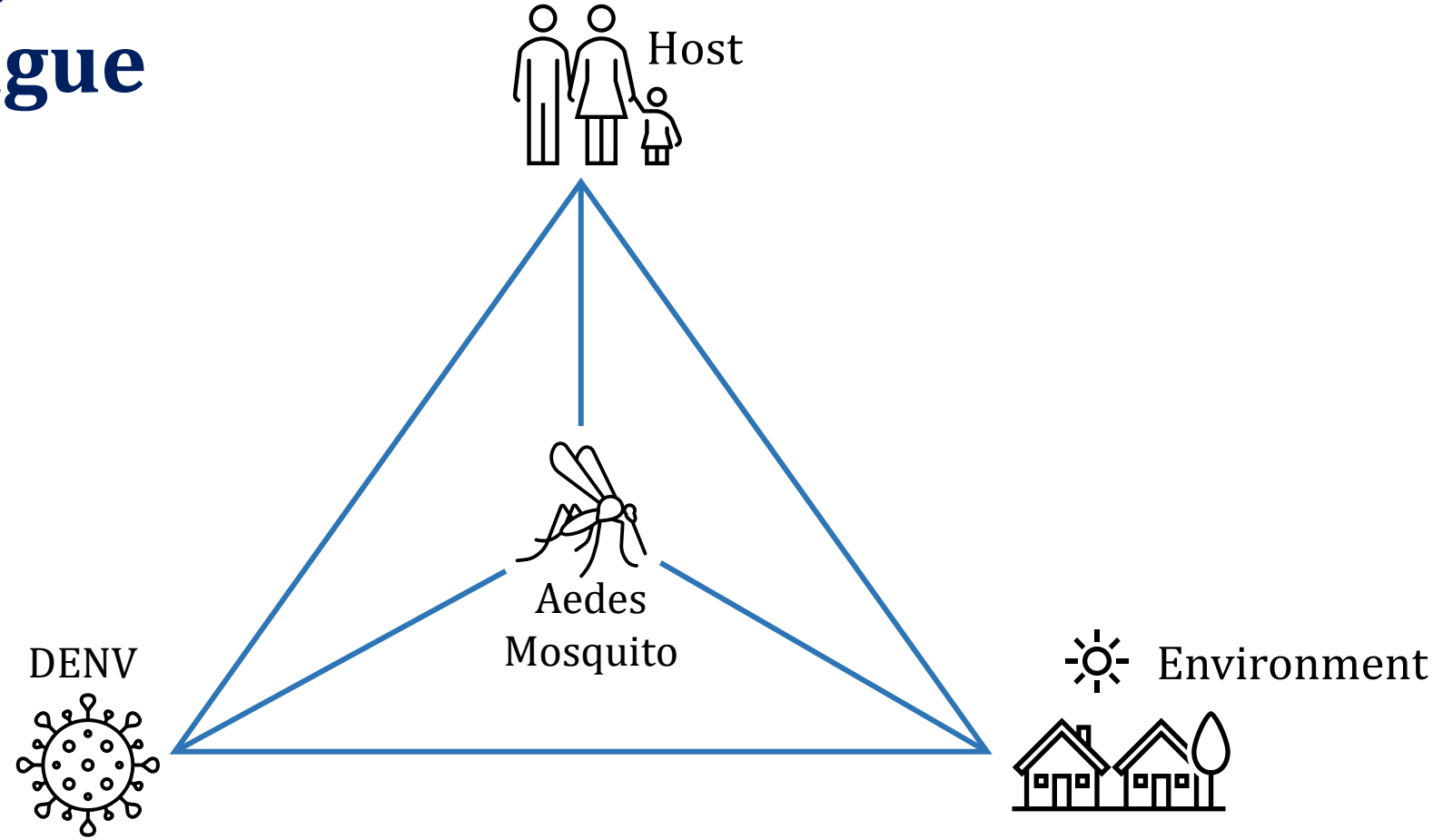
Epidemiological Triad of Dengue



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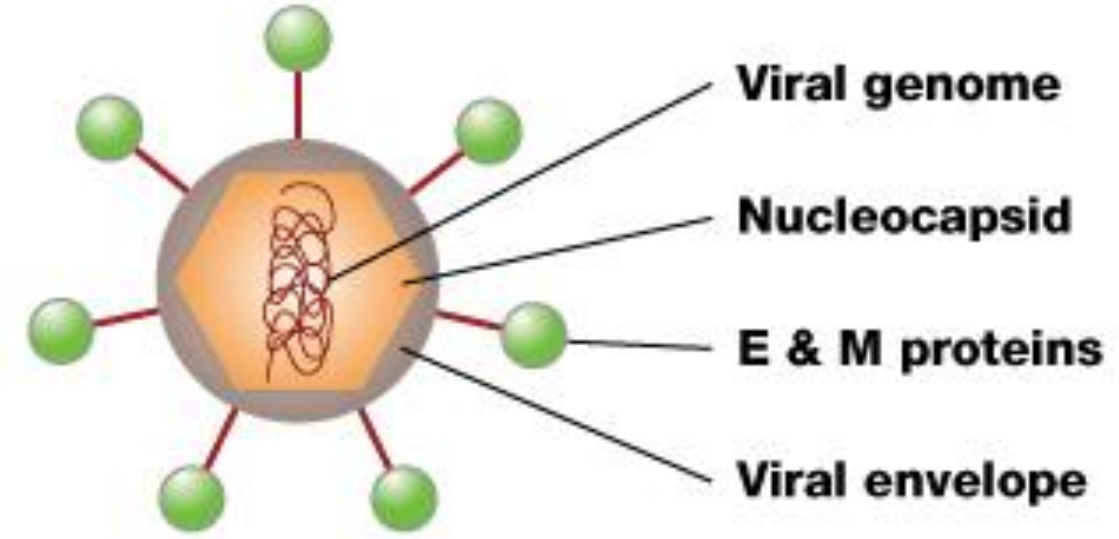
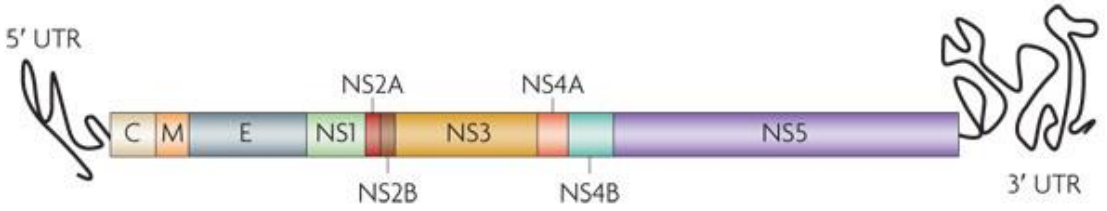
Dengue Virus

- Genus *Flavivirus*
- **4 Serotypes**
  - DENV1
  - DENV2
  - DENV3
  - DENV4
- Each serotype has different interactions with the antibodies in human

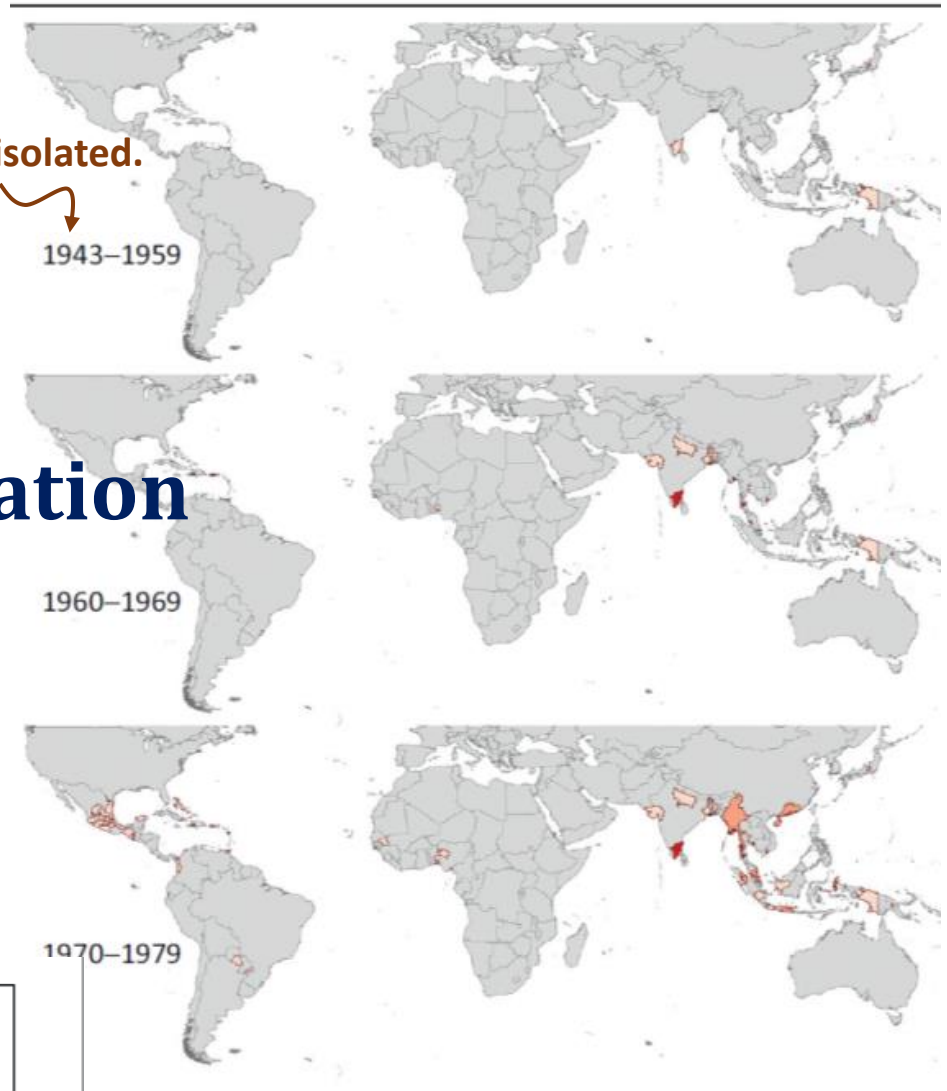


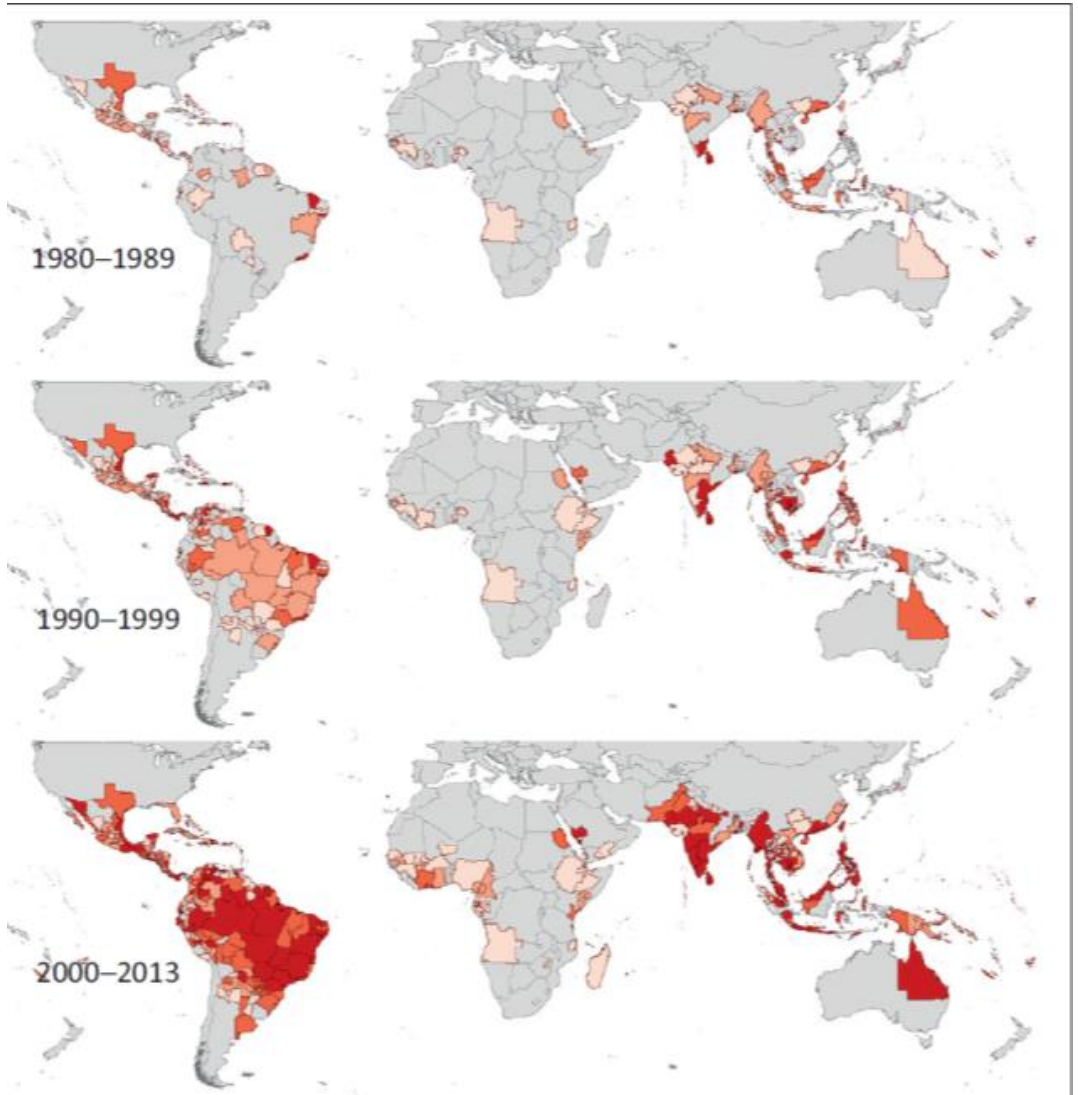


Scitable by Nature Education. Dengue Virus (2014)

DENV was firstly isolated.

DENV Co-circulation





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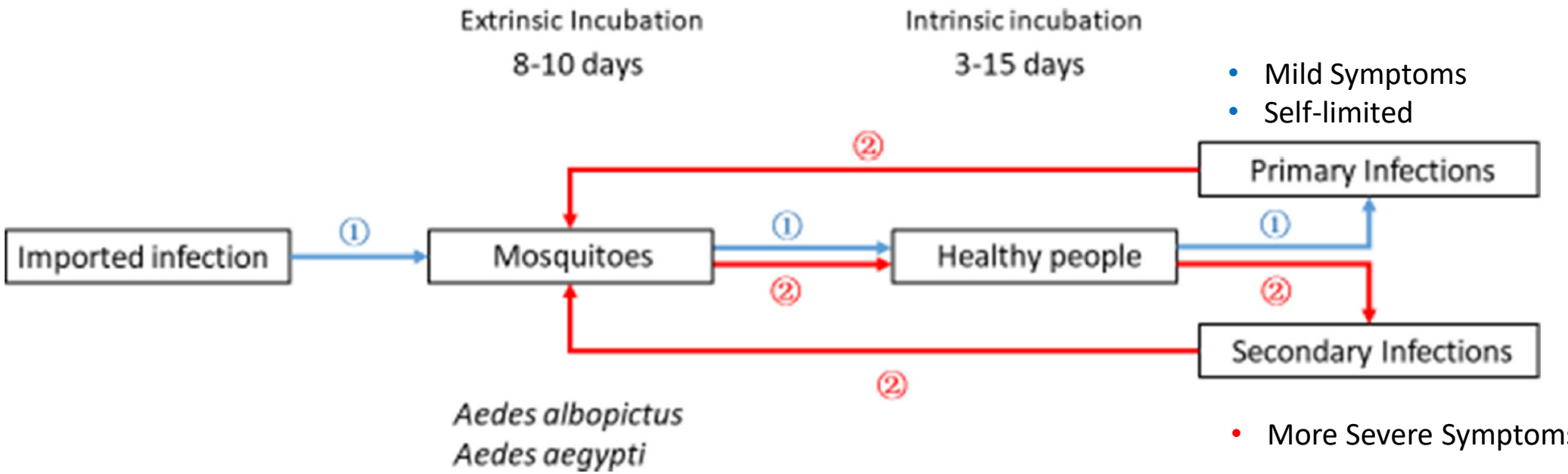
Messina JP, et al. Global spread of dengue virus types: mapping the 70 year history. Trends Microbiol. 2014

Dengue virus transmission cycle



- Mild Symptoms
- Self-limited

- More Severe Symptoms

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Jing Q, Wang M. Dengue Epidemiology. Global Health Journal, 2019

Dengue Virus Infection

Table 1 | Estimated burden of dengue in 2010, by continent

	Apparent	Inapparent
	Millions (credible interval)	Millions (credible interval)
Africa	15.7 (10.5–22.5)	48.4 (34.3–65.2)
Asia	66.8 (47.0–94.4)	204.4 (151.8–273.0)
Americas	13.3 (9.5–18.5)	40.5 (30.5–53.3)
Oceania	0.18 (0.11–0.28)	0.55 (0.35–0.82)
Global	96 (67.1–135.6)	293.9 (217.0–392.3)

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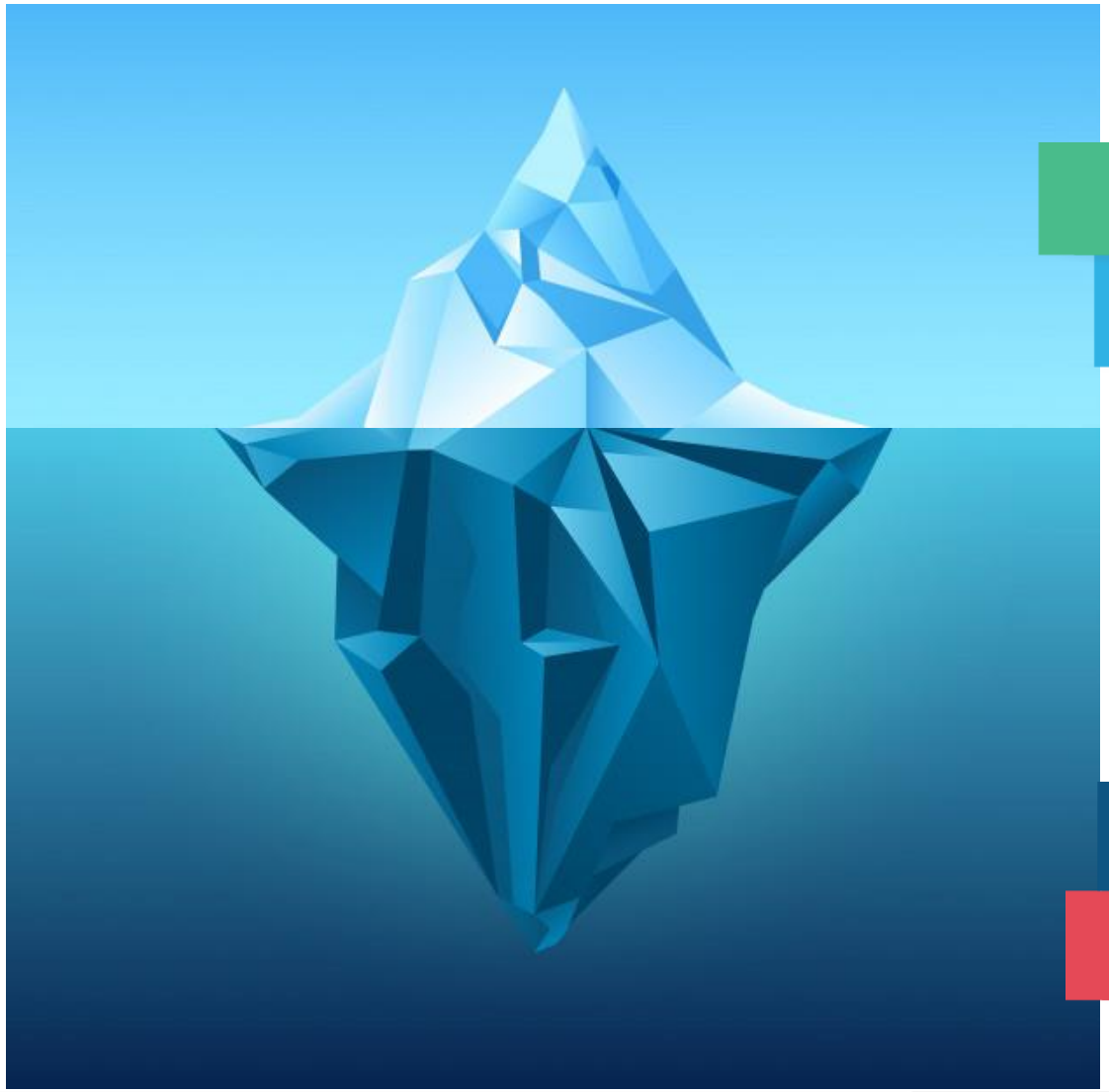
Bhatt S., et al. The global distribution and burden of dengue. Nature 2013

Dengue Surveillance Data



Common data sources

- Hospital-based
- Passive report

Underestimated

- Asymptomatic infection
- Mild symptoms

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How much is the number of dengue infections underestimated?

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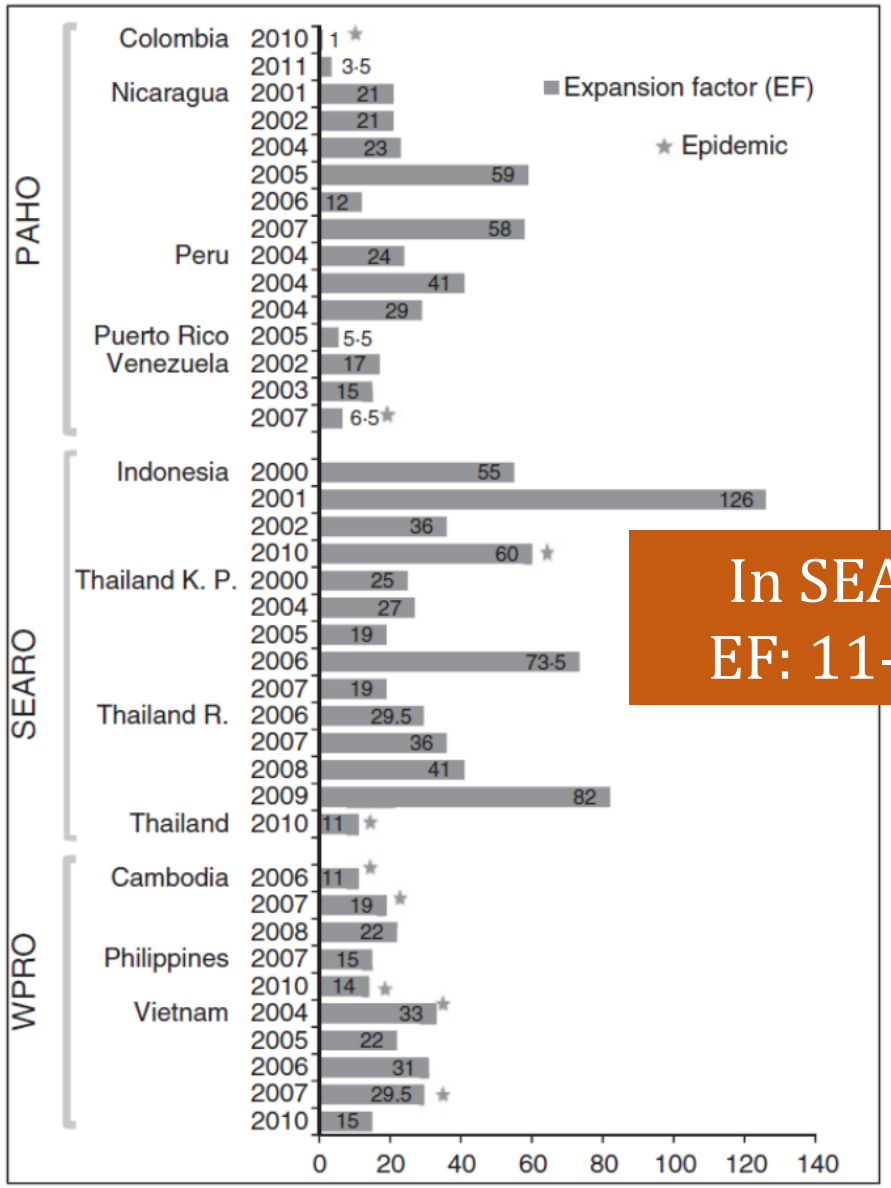

In SEARO
EF: 11-126

Expansion Factor (EF)

$$\frac{Cumulative\ incidence_{Cohort}}{Cumulative\ incidence_{National\ report}}$$

nEF = CI-active data/CI passive National data)

CI_{Active}: Cumulative Incidence = [(n° symptomatic–not hospitalized laboratory confirmed cases/cohort size)/10^3]

$CI_{Passive}$: Cumulative Incidence = [(n° symptomatic notified clinical cases/NATIONAL population, all age)/10^3]

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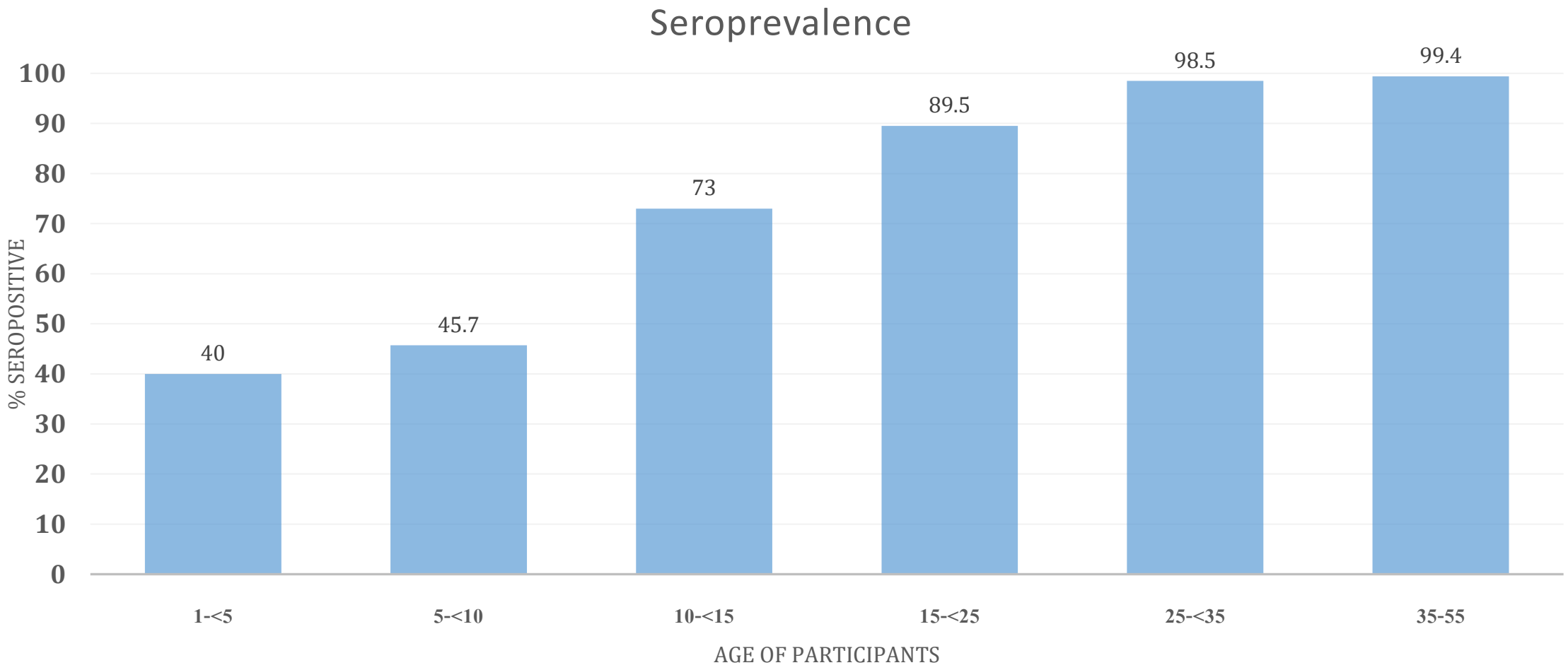
Toan NT., et al. Dengue epidemiology in selected endemic countries: factors influencing expansion factors as estimates of underreporting. Tropical Medicine and International Health. 2015

Proportion of Population had been infected with Dengue: A study in 2,000 Thai people



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Limkittikul K, et al. Dengue virus seroprevalence study in Bangphae district, Ratchaburi, Thailand: A cohort study in 2012-2015. PLoS Negl Trop Dis. 2022 Jan 4;16(1):e0010021.

Can Asymptomatic individual transmit dengue virus?

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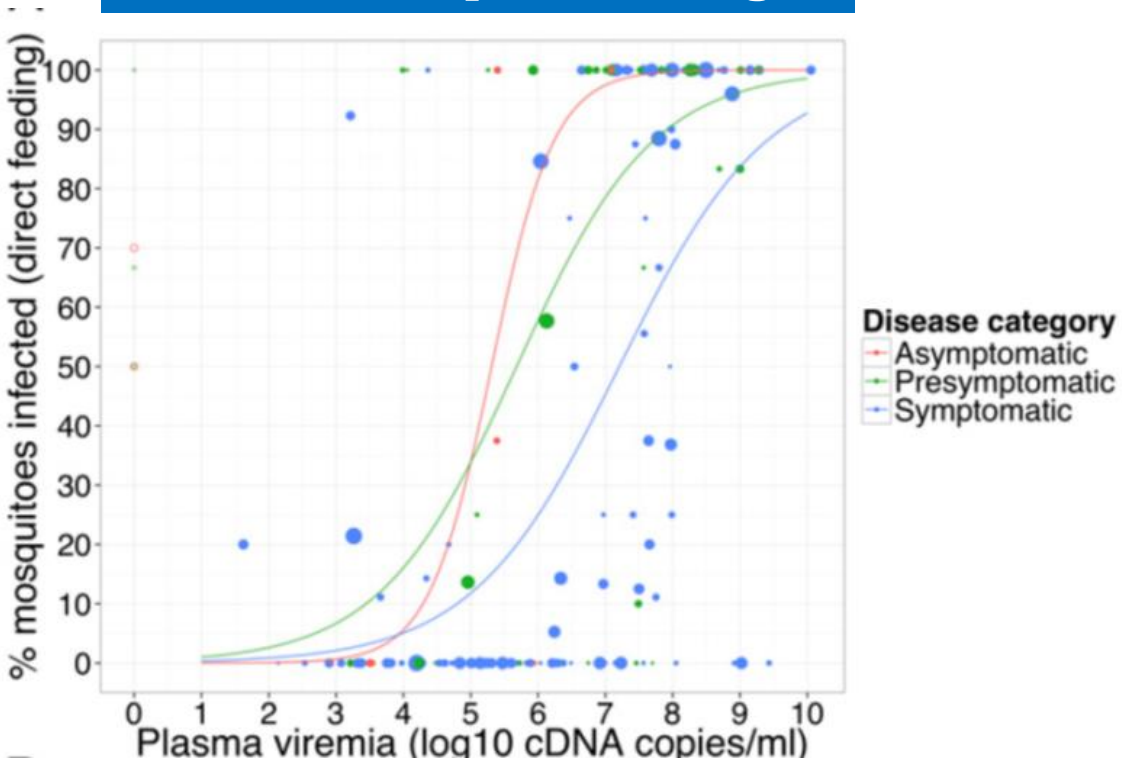
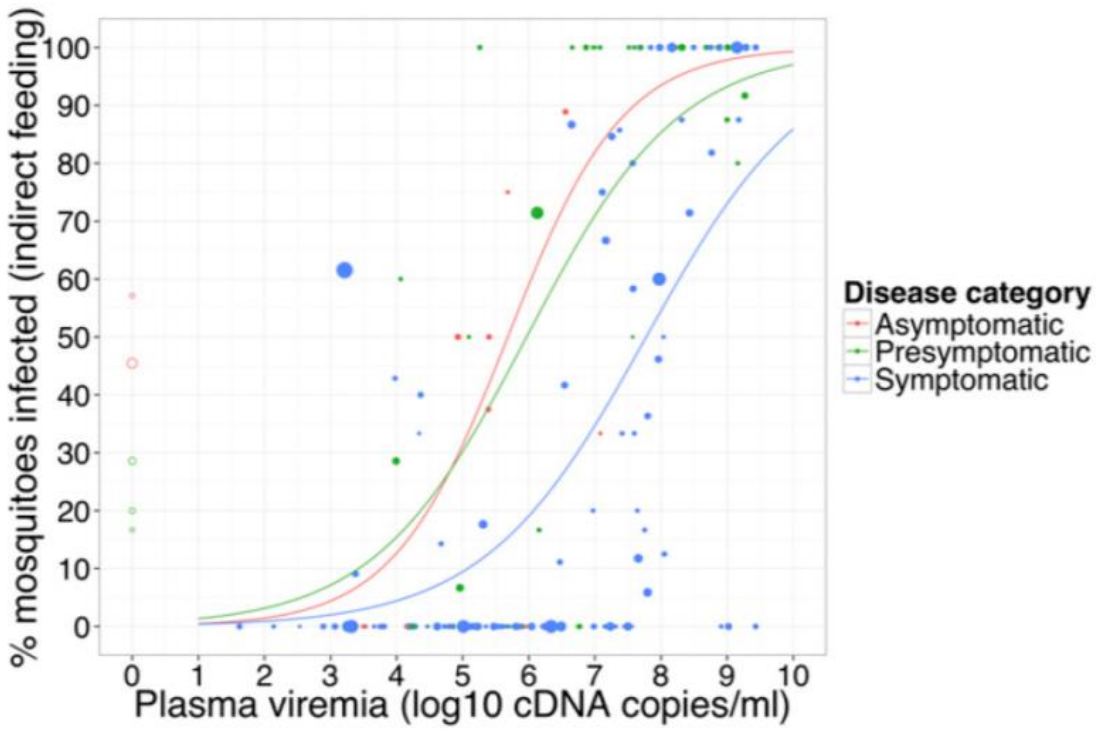
Mosquito infectivity by disease category and viral load

Direct mosquito feeding



Indirect mosquito feeding



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Duong V, et al. Asymptomatic humans transmit dengue virus to mosquitoes. Proc Natl Acad Sci U S A. 2015

Infectivity of Asymptomatic Individuals

Table 1. Multivariate regression analysis of successful human-to-mosquito DENV transmission

	Direct feeding		Indirect feeding	
Factor	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Serotype	N.S.			
DENV-1			3.66 (1.76–7.63)	<0.001
DENV-2			1.74 (0.72–4.19)	0.213
DENV-4			Ref.	
Gender			N.S.	
Male	2.08 (1.07–4.04)	0.032		
Female	Ref.			
Viremia, +1 $\log_{10}$ copies/mL	2.05 (1.64–2.56)	<0.001	1.81 (1.52–2.16)	<0.001
Disease category				
Asymptomatic	10.05 (1.76–57.51)	0.010	6.72 (1.90–23.9)	0.003
Presymptomatic	4.84 (2.02–11.58)	<0.001	4.19 (1.94–9.05)	<0.001
Symptomatic	Ref.		Ref.	

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Do DENV serotypes infection correlated with dengue symptoms?

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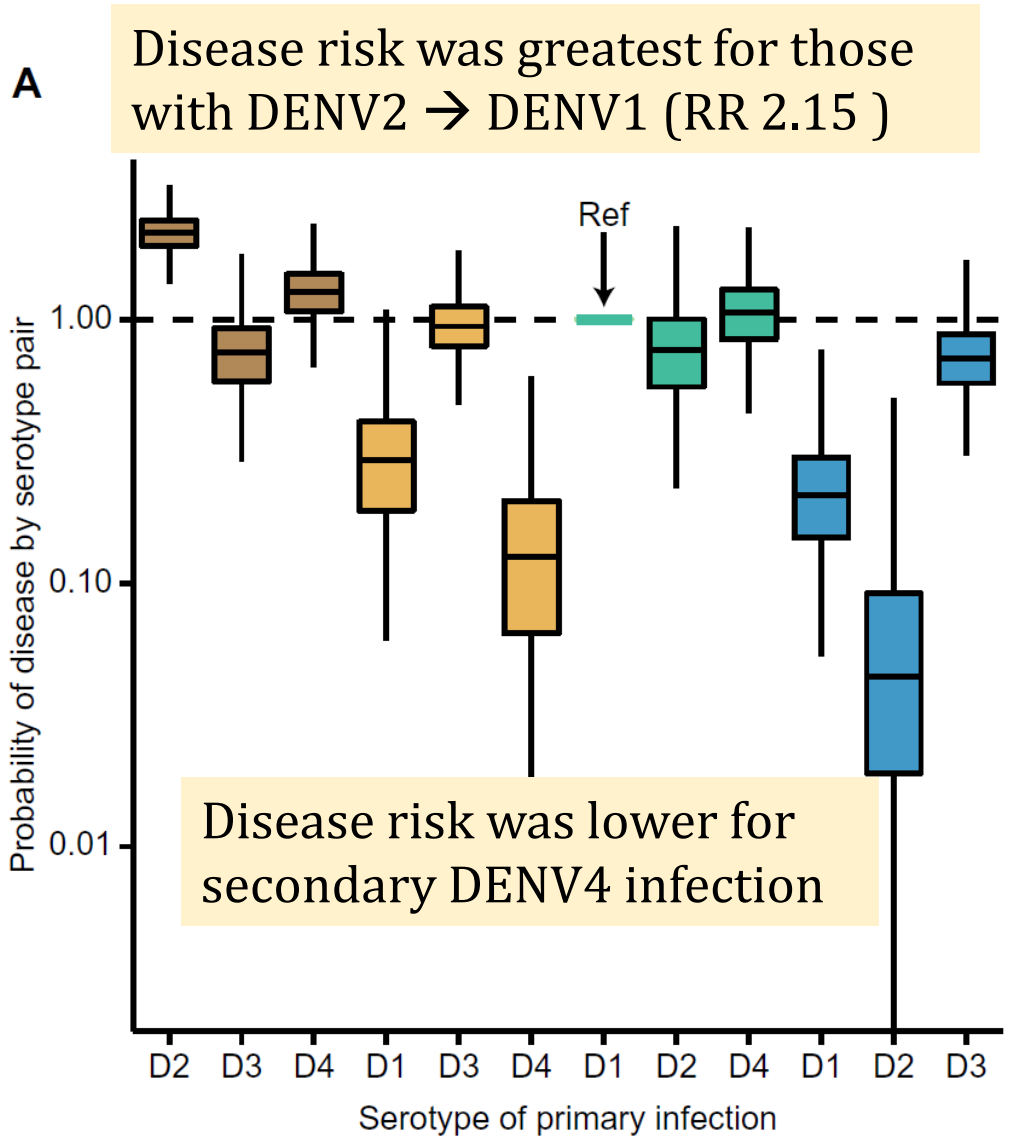

Data on dengue case and virus isolates from the QSNICH (1994-2014)

N= 15,281 cases aged 1-14 years

Used mathematical framework to estimate primary infection and model disease transmission process

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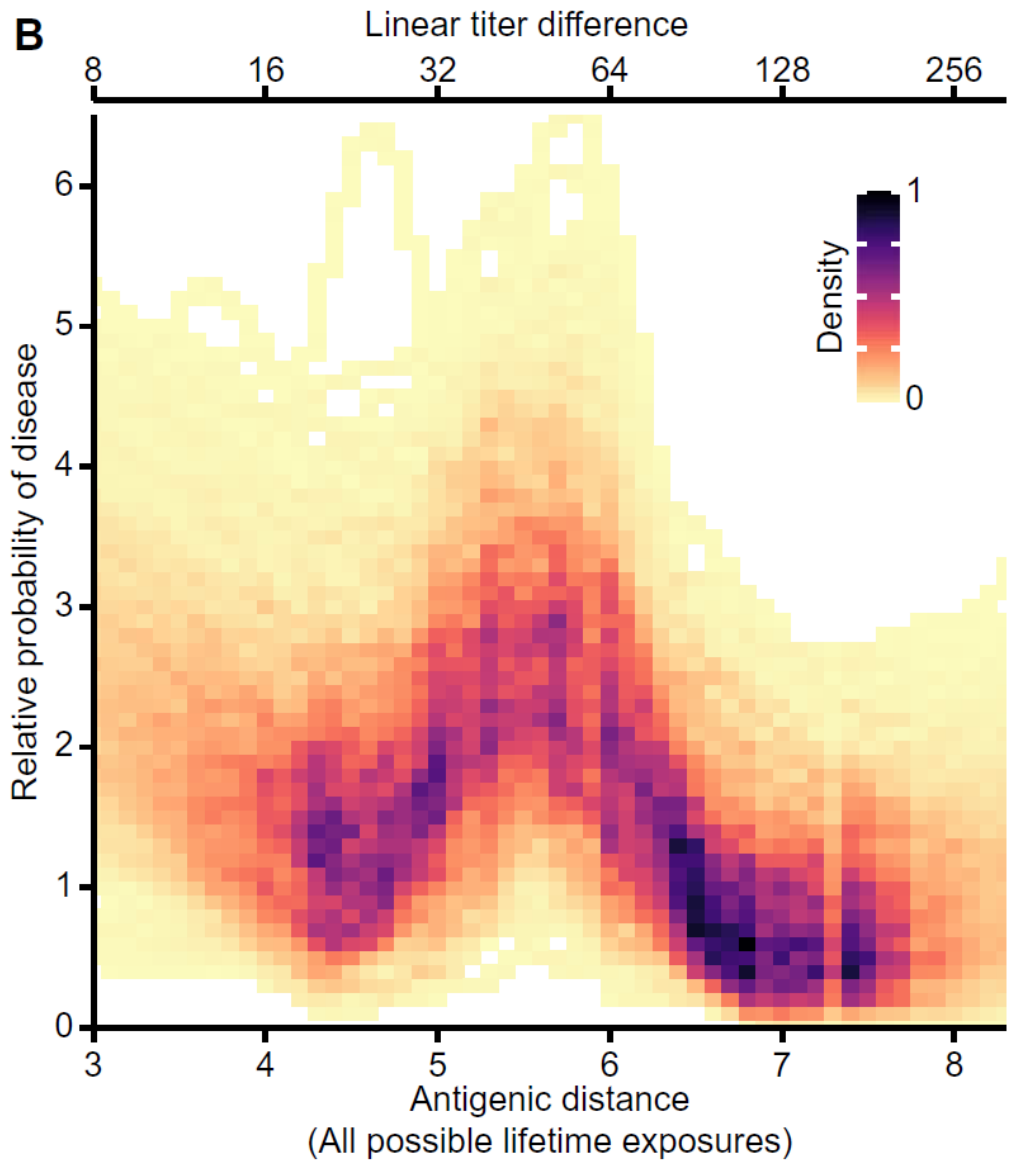
Wang L., et al. Antigenic distance between primary and secondary dengue infections correlates with disease risk. Sci. Transl. Med. 2024



Disease risk is maximized at intermediate antigenic distance between the two infecting viruses.

Changing antigenic profile of circulating viruses within a serotype shifts the disease risk of the population.

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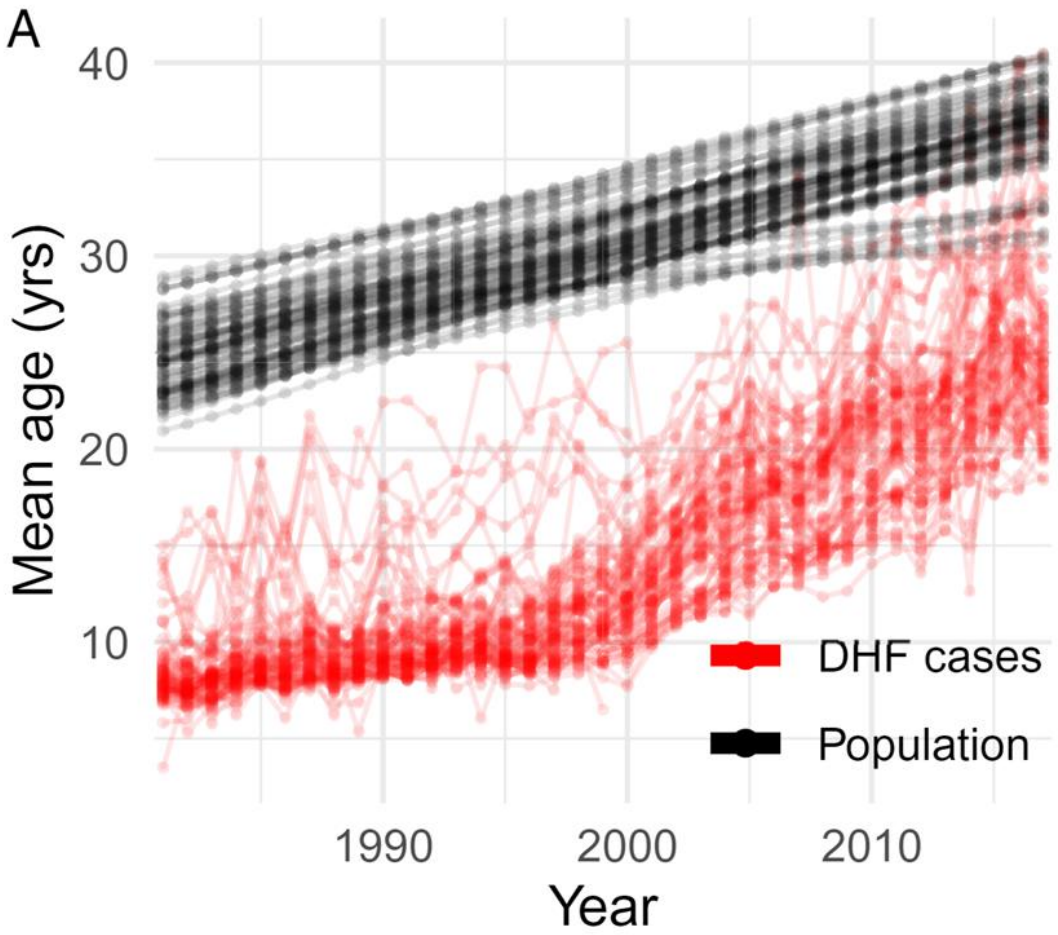
Wang L., et al. Antigenic distance between primary and secondary dengue infections correlates with disease risk. Sci. Transl. Med. 2024

Shift in Susceptible Population



Mean age of dengue cases in Thailand

- 8.1 years in 1981
- 24.3 years in 2017

Potential contributors:

- Change in age structure
- Change in number of infection overtime
- Change in per-serotype hazard overtime

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Huang AT, et al. Assessing the role of multiple mechanisms increasing the age of dengue cases in Thailand. Proc Natl Acad Sci U S A. 2022

Is it possible to have arboviruses Co-infection?

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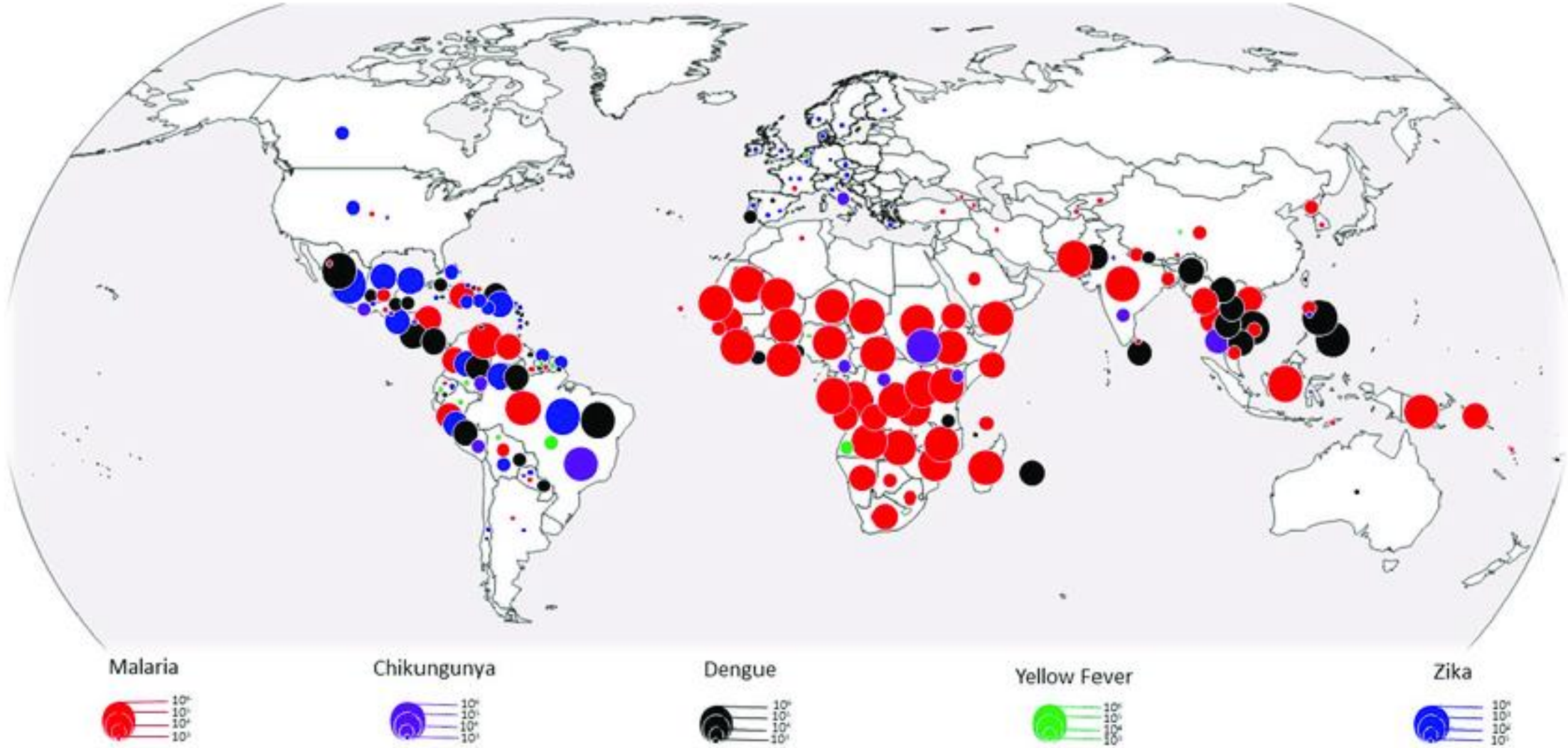

Re-emergence of significant mosquito-borne diseases, including outbreaks, reported native and imported cases (2017-2019)

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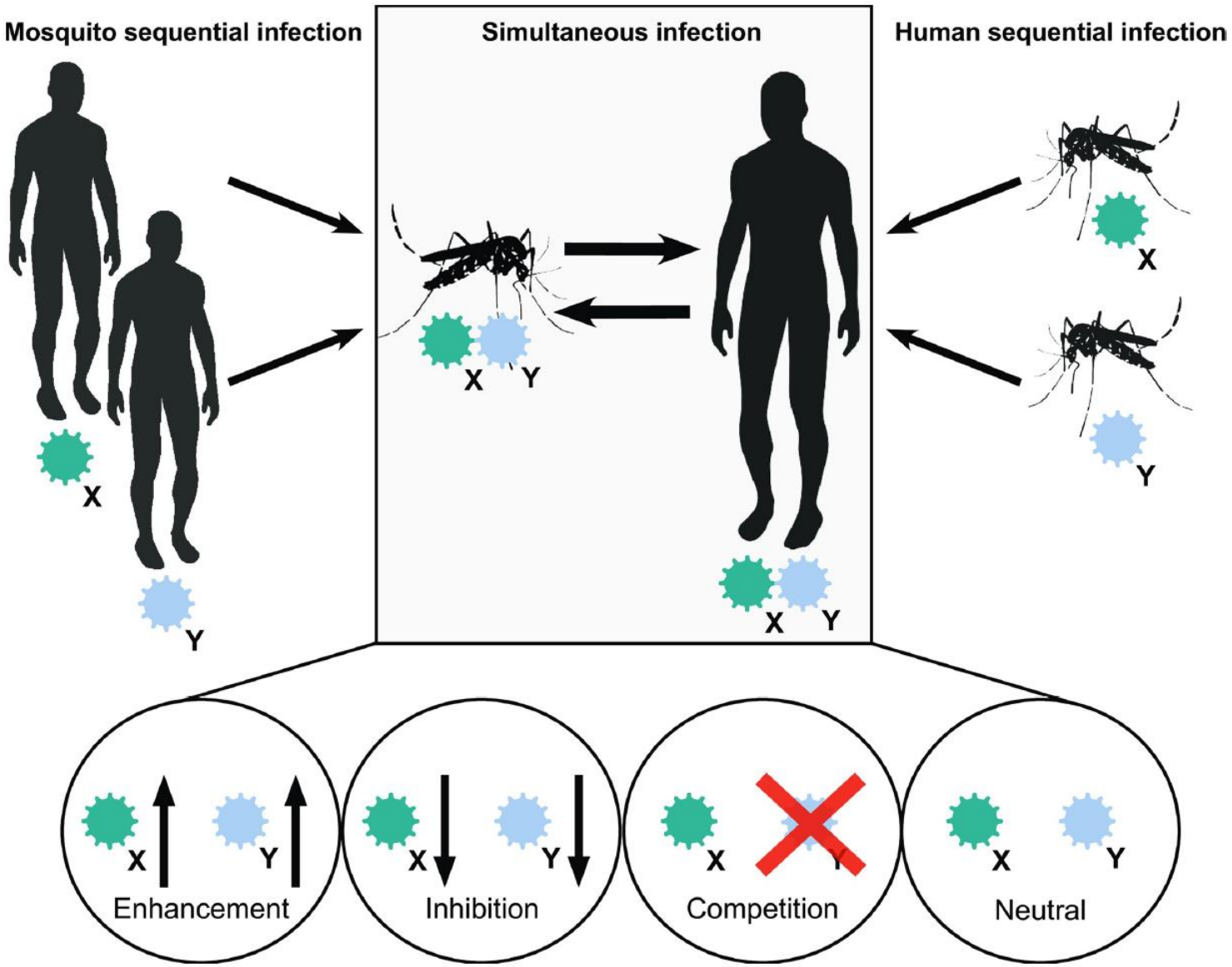
Dahmana H., et al. Mosquito-Borne Disease Emergence/Resurgence and How to Effectively Control It Biologically. Pathogens 2020



Arbovirus Co-infection

4 potential outcomes of co-infection

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Vogels CBF, et al. Arbovirus coinfection and co-transmission: A neglected public health concern? PLoS Biol. 2019

What are factors associated with dengue transmission?

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Know the Vectors

Aedes aegypti

Aedes albopictus

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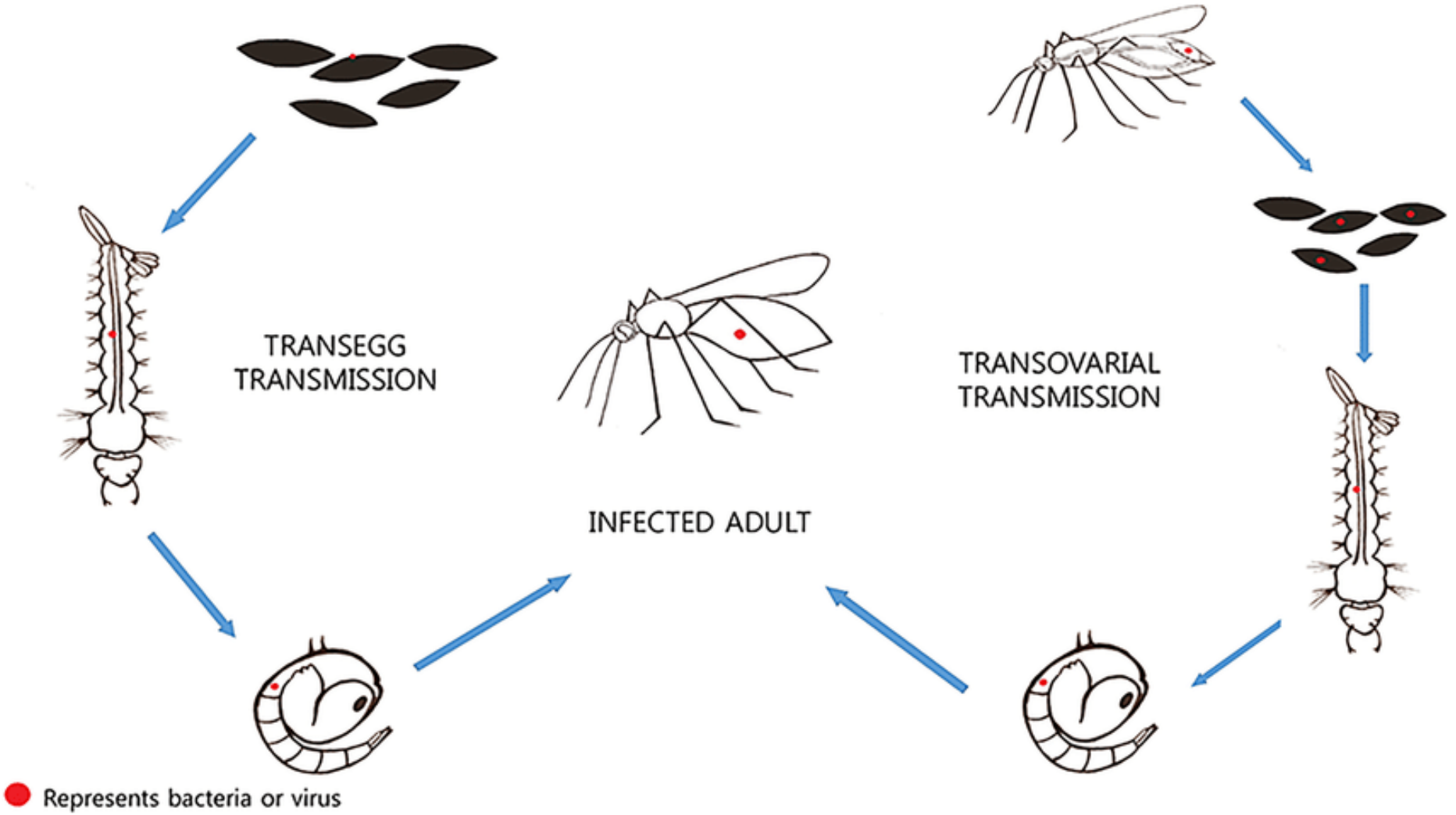
https://www.cdph.ca.gov/Programs/CID/DCDC/pages/Aedes-aegypti-and-Aedes-albopictus-mosquitoes.aspx

Vertical Transmission



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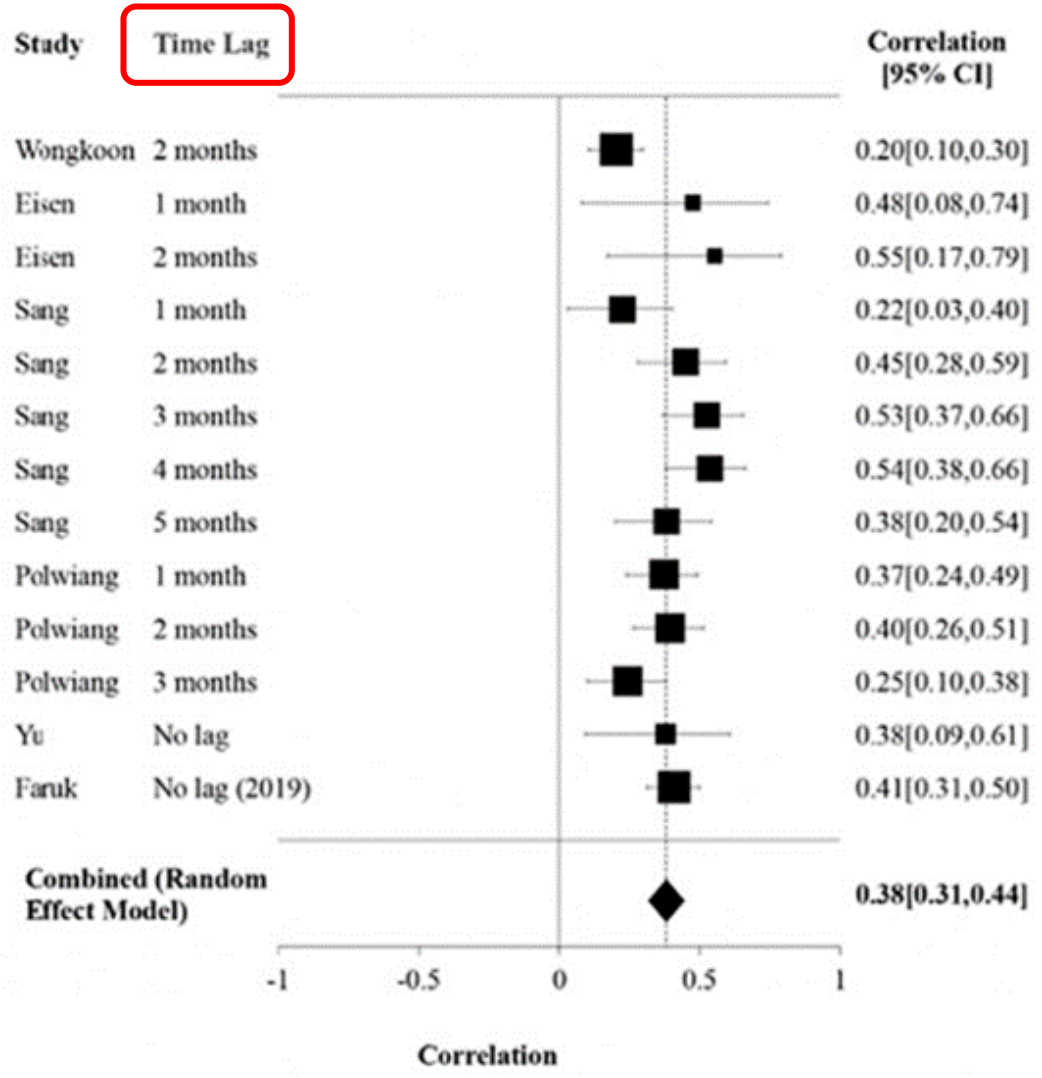
K.Kaavya, et al. Role of vertically transmitted viral and bacterial endosymbionts of Aedes mosquitoes. Does Paratransgenesis influence vector-borne disease control? Symbiosis. 2022

Environment

Precipitation

- Breeding sites
- Survival of larva



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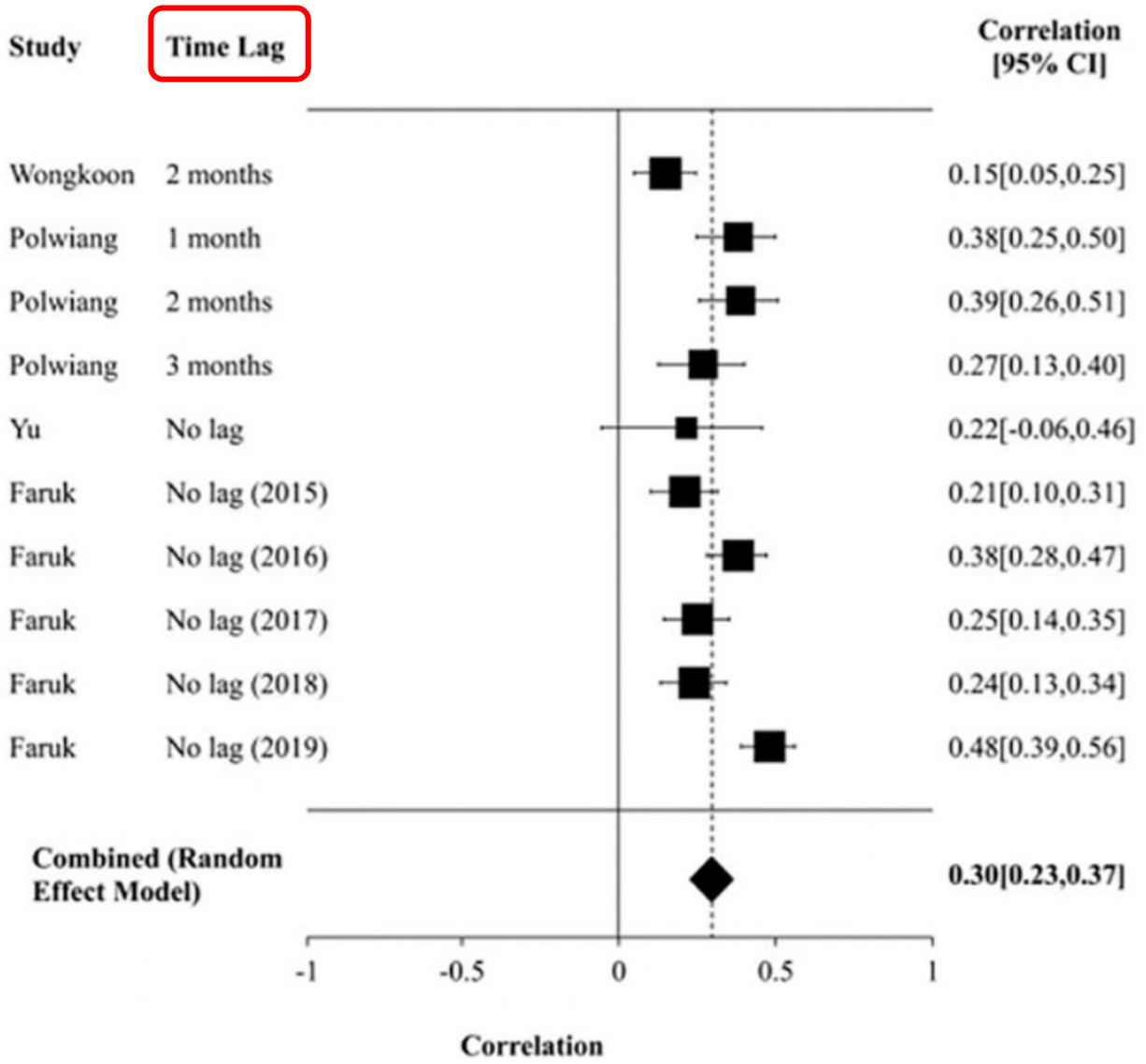
Abdullah NAMH, et al.The association between dengue case and climate: A systematic review and meta-analysis. One Health. 2022

Environment

Humidity

- Breeding sites
- Survival of adult mosquitoes



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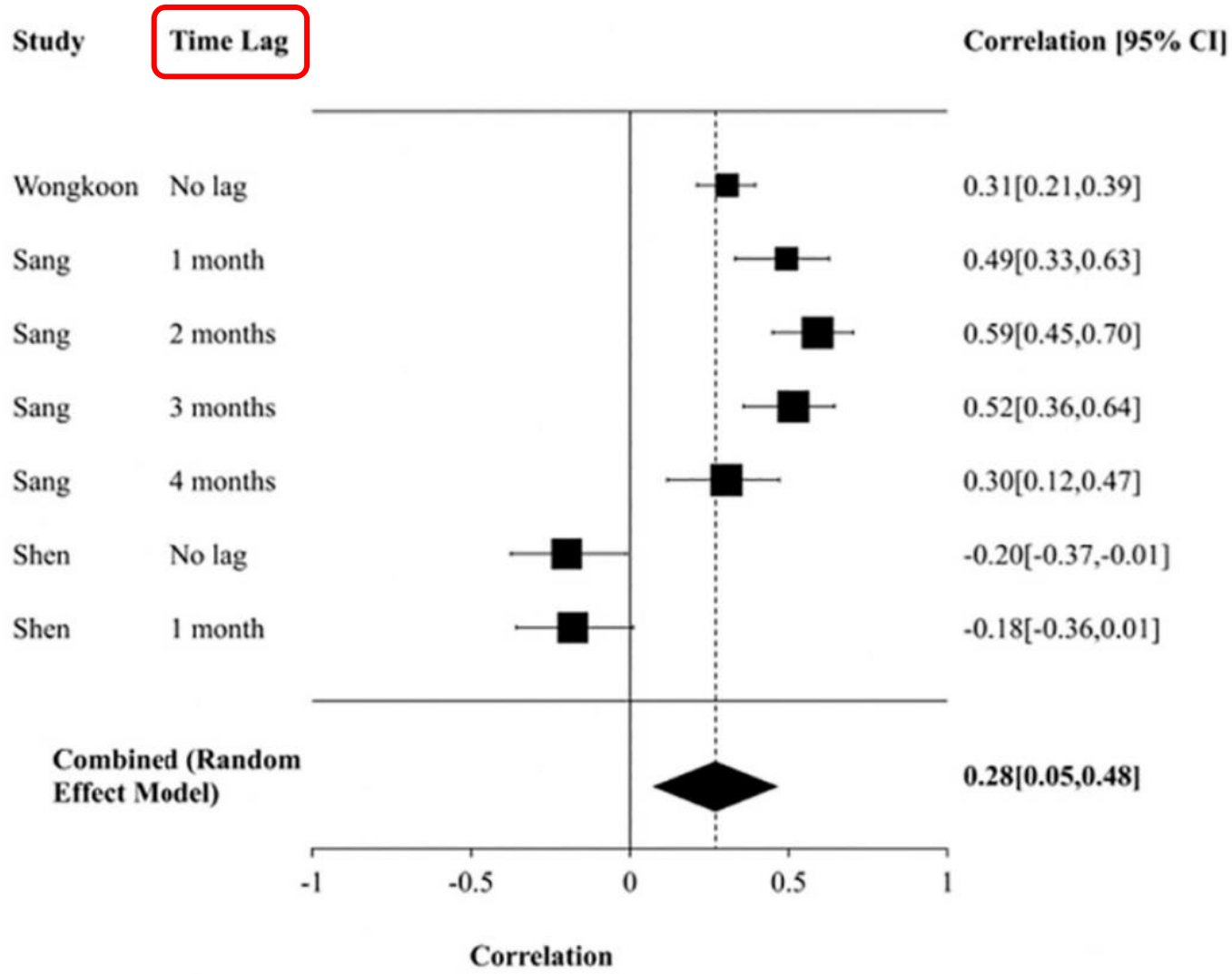
Abdullah NAMH, et al.The association between dengue case and climate: A systematic review and meta-analysis. One Health. 2022

Environment

Temperature

- Optimal temperature for extrinsic incubation is 18c -31c
- Survival of adult mosquitoes



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Climate Change and Mosquito population

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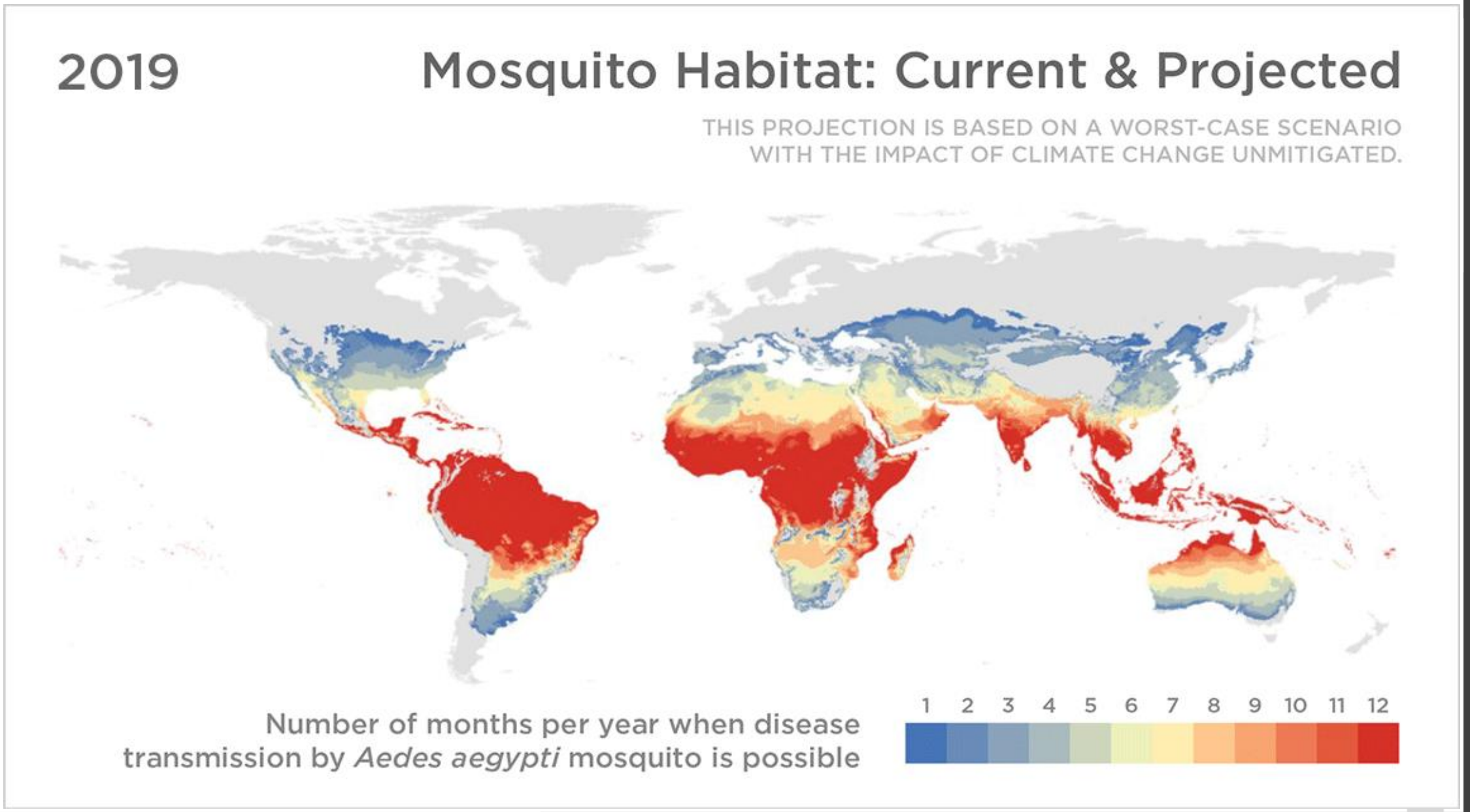

Source: Sadie J. Ryan, Colin J. Carlson, Erin A. Mordecai, and Leah R. Johnson
Credit: Koko Nakajima/NPR

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https://www.npr.org/sections/goatsandsoda/2019/03/28/707604928/chart-where-disease-carrying-mosquitoes-will-go-in-the-future

Prediction

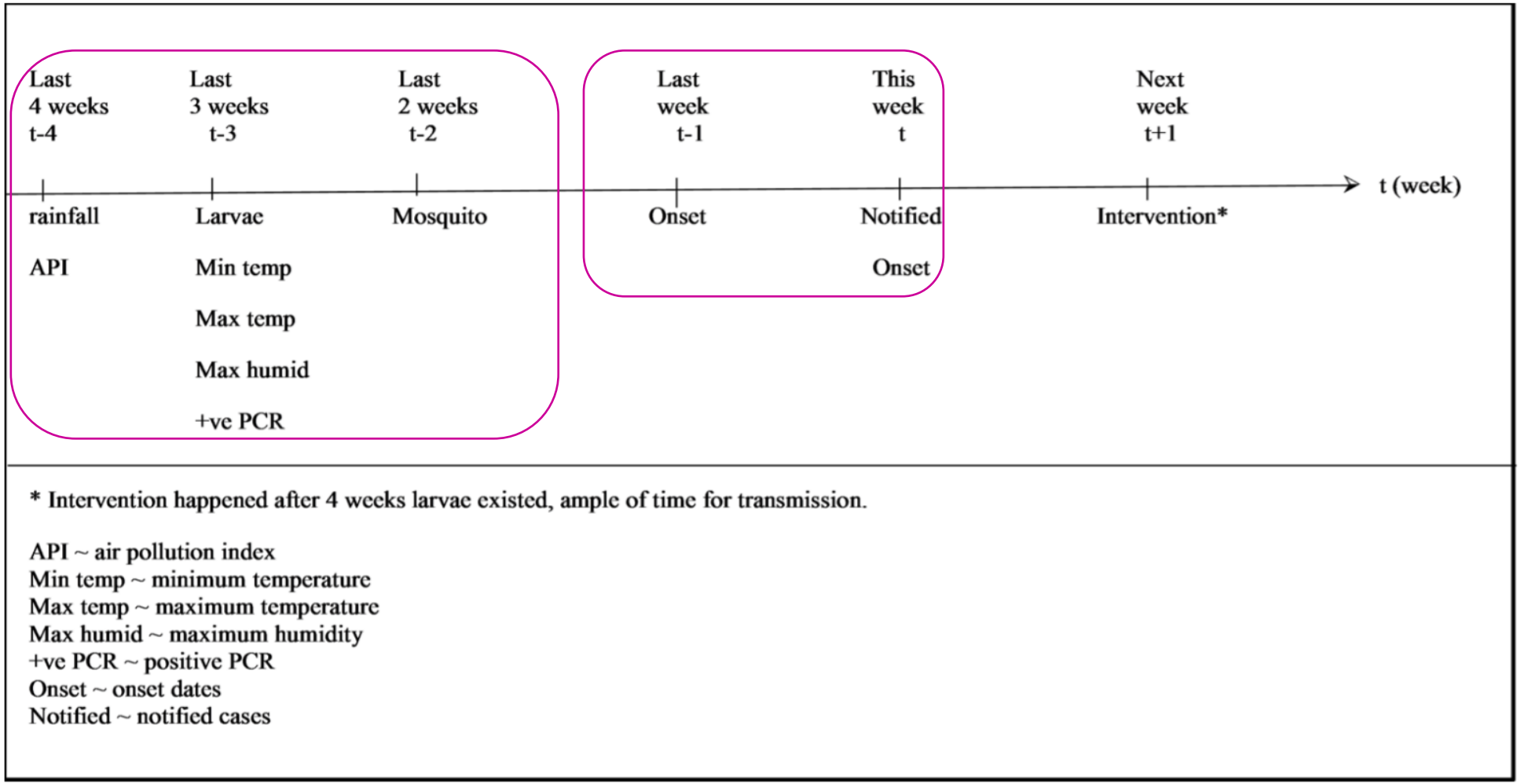

Fig 5. Conceptual relationship: Epidemiological, entomological & environmental factors based on weeks.

https://doi.org/10.1371/journal.pone.0193326.g005

Ahmad R, et al. Factors determining dengue outbreak in Malaysia. PLoS One. 2018

Dengue Control Methods

	Community-centric	Intersectoral involvement
Community involvement	Awareness campaign	Community education, Community empowerment
Chemical controls	Abate sand, repellant	**Insecticides**, Insect Growth Regulators
Physical controls	Lid-covered water container, Solid waste management	Modified water drainage
Biological controls	Guppy fish, tilapia, turtle, copepod	Modified mosquitoes, Wolbachia

Integrated Vector Control

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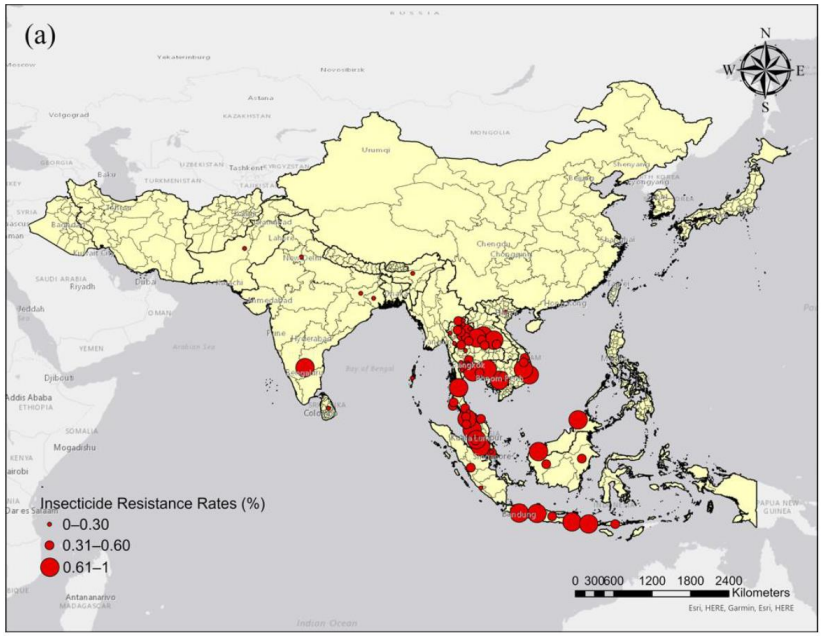
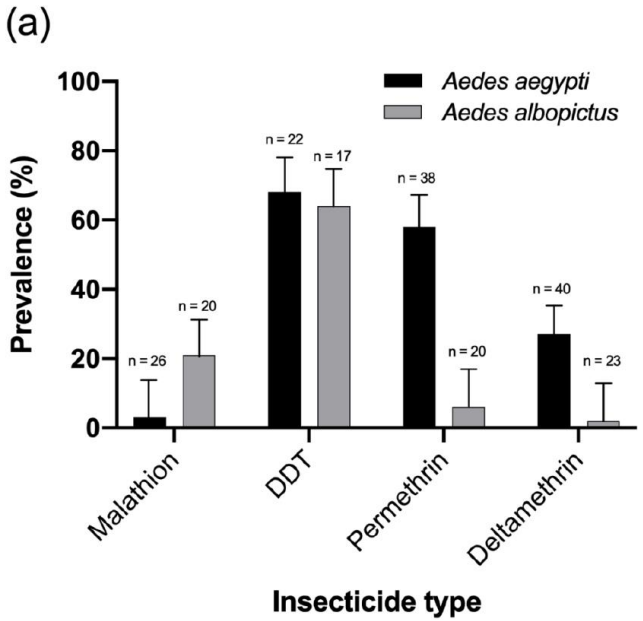
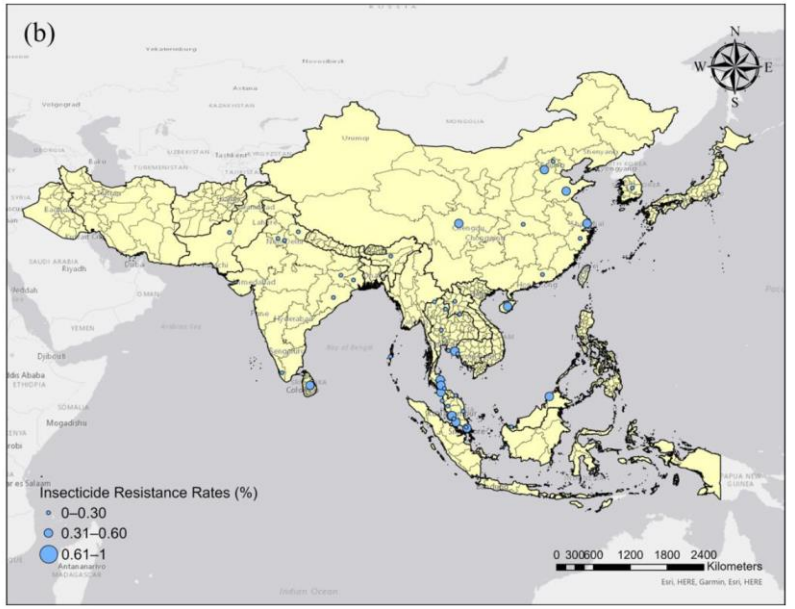
Insecticide Resistance

Ae. aegypti





Ae. albopictus



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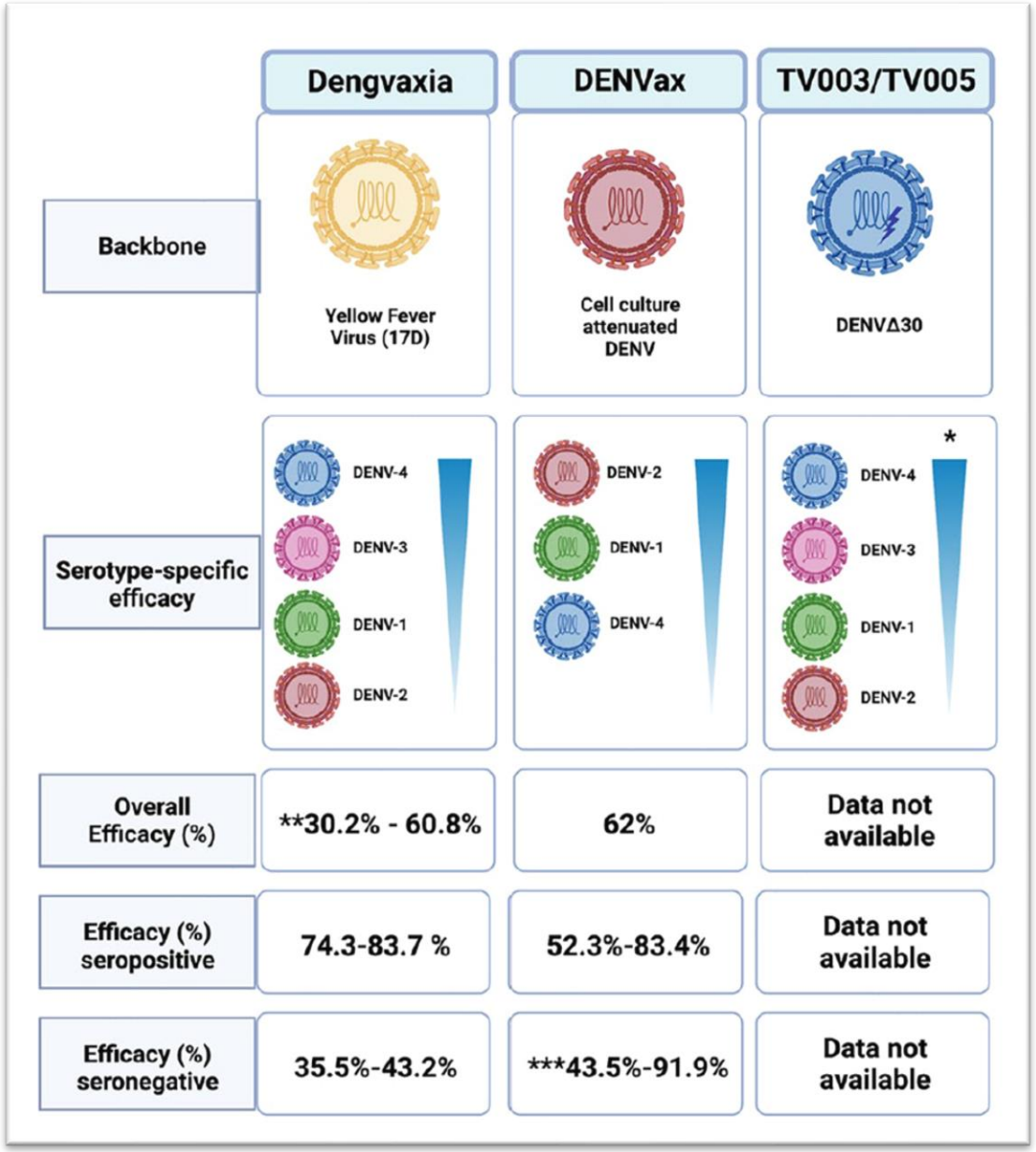
Zulfa, R. et al. Updating the Insecticide Resistance Status of Aedes aegypti and Aedes albopictus in Asia: A Systematic Review and Meta-Analysis. Trop.Med. Infect. Dis. 2022.

Dengue Vaccines



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Torres-Flores JM, Reyes-Sandoval A, Salazar MI. Dengue vaccines: An update. BioDrugs. 2022 May;36(3):325-36.

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