Introduction to Vector-Borne Diseases

UChicago Center in Paris

Paris, France

January 2025

Mechanisms of disease transmission

- **Directly-transmitted** diseases – transmitted via exchange of bodily fluids
  - Droplet (> 5 microns) spread or direct contact, includes sexually-transmitted pathogens
  - Ex: Smallpox *(Variola* spp.), HIV, Mononucleosis (*Epstein Barr virus*)
- **Indirectly-transmitted** diseases – transmitted via droplets retained in air
  - Droplets < 5 microns in diameter
  - Ex: Measles, COVID (*SARS-CoV-2*)
- **Vertically-transmitted** pathogens – transmitted mother-to-child *in utero*
  - Ex: HIV, *Herpes simplex virus*, *Cytomegalovirus*, Rubella, Zika
- **Environmentally-transmitted** pathogens – transmitted outside host (e.g. water, food)
  - Ex: Cholera *(Vibrio cholerae*), Salmonellosis (*Salmonella* spp. bacteria)
- **Vector-borne** diseases (a type of indirect transmission) are transmitted via blood-feeding arthropod (mosquitoes, ticks, fleas)
  - Ex: malaria, arboviruses (dengue, yellow fever), sleeping sickness, plague

Pathogens exhibit **diverse transmission mechanisms** that require tailored modeling structures

- **Vector-borne** diseases (a type of indirect transmission) are transmitted via blood-feeding arthropod (mosquitoes, ticks, fleas)
  - Euclidean **vector**: a quantity with a magnitude and direction

  - Epidemiological **vector**: an agent that carries and transmits an infectious patient into another living organism

Pathogens exhibit **diverse transmission mechanisms** that require tailored modeling structures

- **Vector-borne** diseases (a type of indirect transmission) are transmitted via blood-feeding arthropod (mosquitoes, ticks, fleas)
  - Malaria: Mosquito-borne protozoan *Plasmodium spp.*
  - "Arboviruses": Mosquito-borne viruses, including Dengue, Zika, Yellow fever virus, West Nile virus, Chikungunya virus
  - Sleeping sickness, also known as African trypanosomiasis: tsetse fly vector and protozoan pathogen (trypanosome)
  - Chagas disease: kissing bug vector and trypanosome pathogen
  - Plague: flea vector and bacterial pathogen (*Yersinia pestis)*

Pathogens exhibit **diverse transmission mechanisms** that require tailored modeling structures

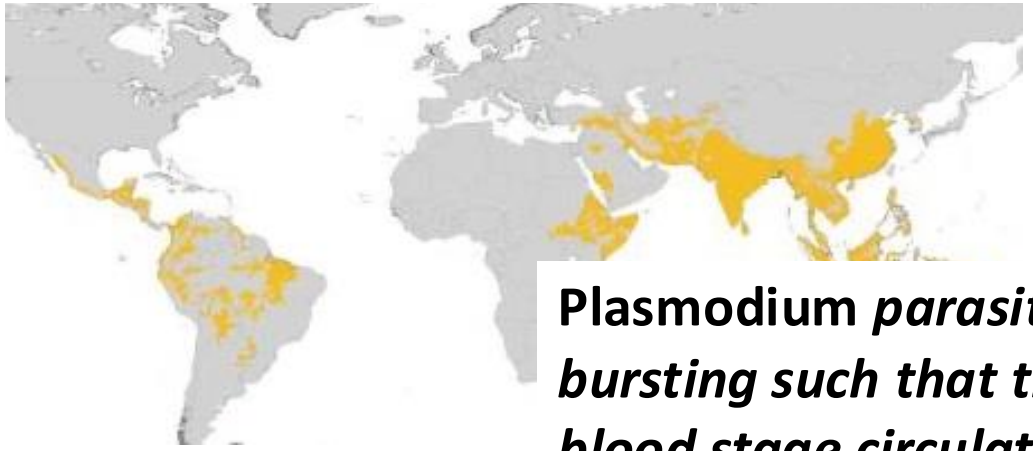
- **Vector-borne** diseases (a type of indirect transmission) are transmitted via blood-feeding arthropod (mosquitoes, ticks, fleas)
  - Malaria: Mosquito-borne protozoan *Plasmodium spp.*
  - "Arboviruses": Mosquito-borne viruses, including Dengue, Zika, Yellow fever virus, West Nile virus, Chikungunya virus
  - Sleeping sickness, also known as African trypanosomiasis: tsetse fly vector and protozoan pathogen (trypanosome)
  - Chagas disease: kissing bug vector and trypanosome pathogen
  - Plague: flea vector and bacterial pathogen (*Yersinia pestis)*

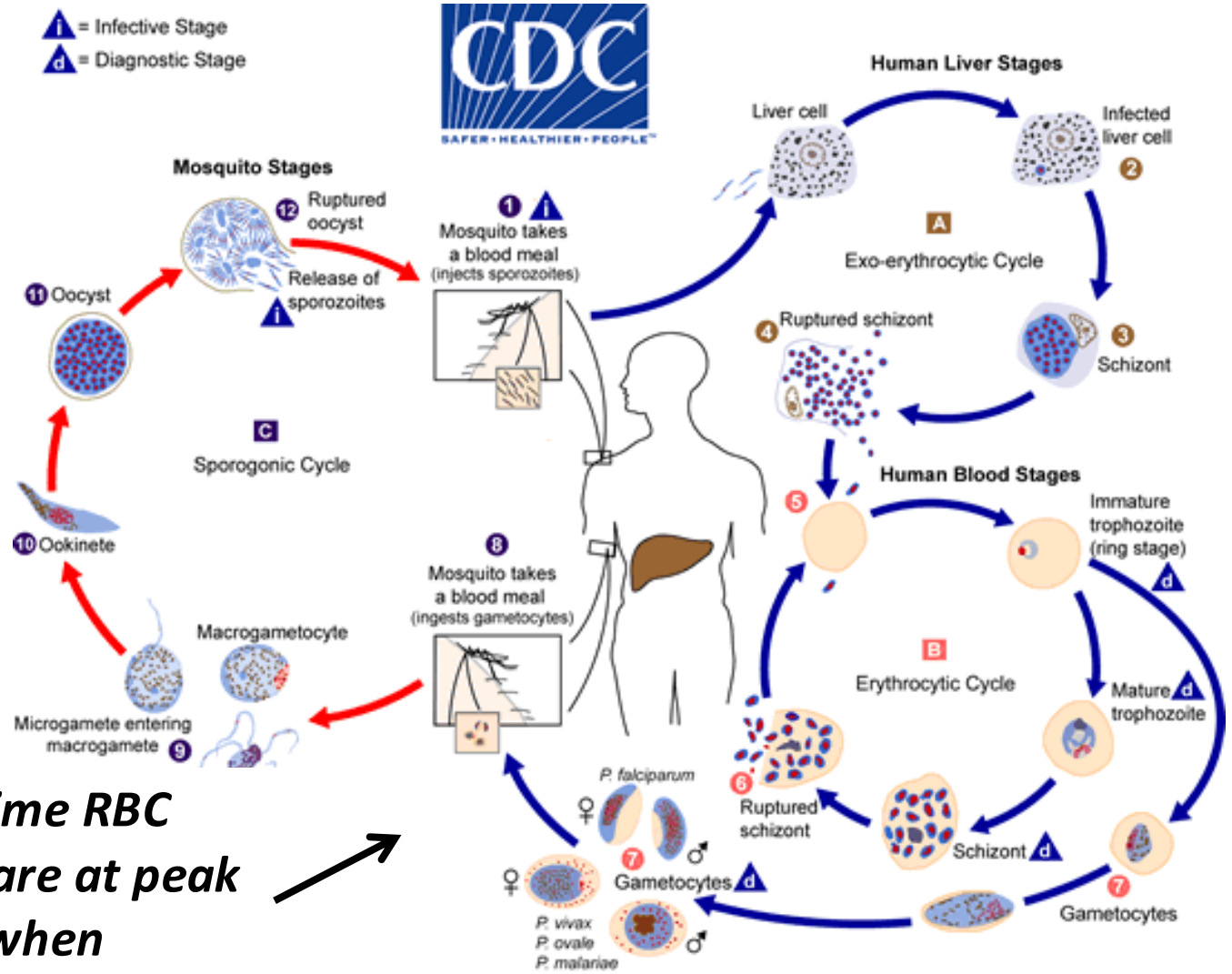
Malaria

- 4 main human ***Plasmodium* parasites** (*falciparum, vivax, malariae, ovalae*).
- Over 200 *Plasmodium* spp. globally, infecting birds, reptiles, and other mammals (rodents, bats, primates)

Distribution *Plasmodium falciparum*

Distribution *Plasmodium vivax*





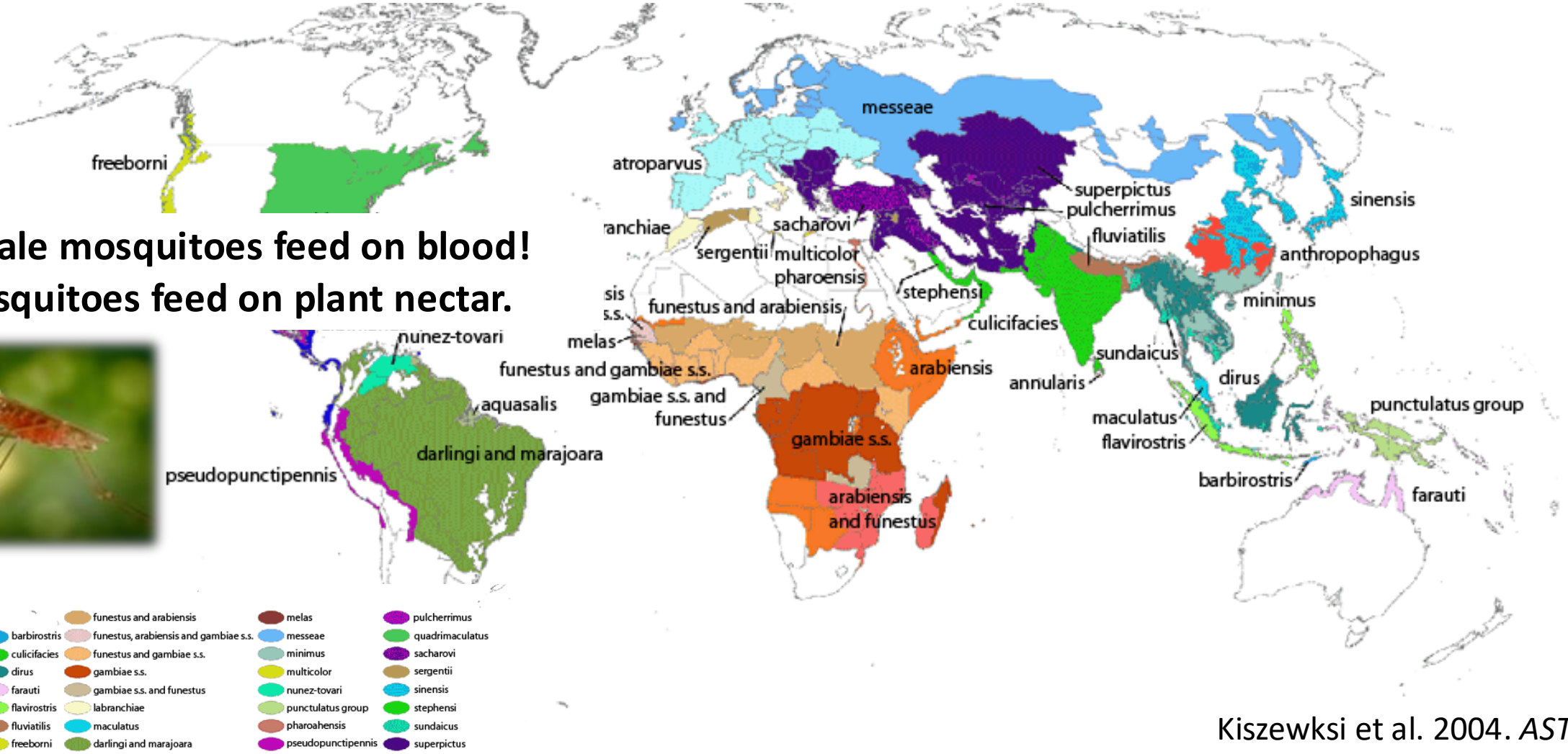
Plasmodium *parasites time RBC bursting such that they are at peak blood stage circulation when mosquito vectors are feeding at dusk!*

Guerra et al. 2006. *Trends i*

Malaria

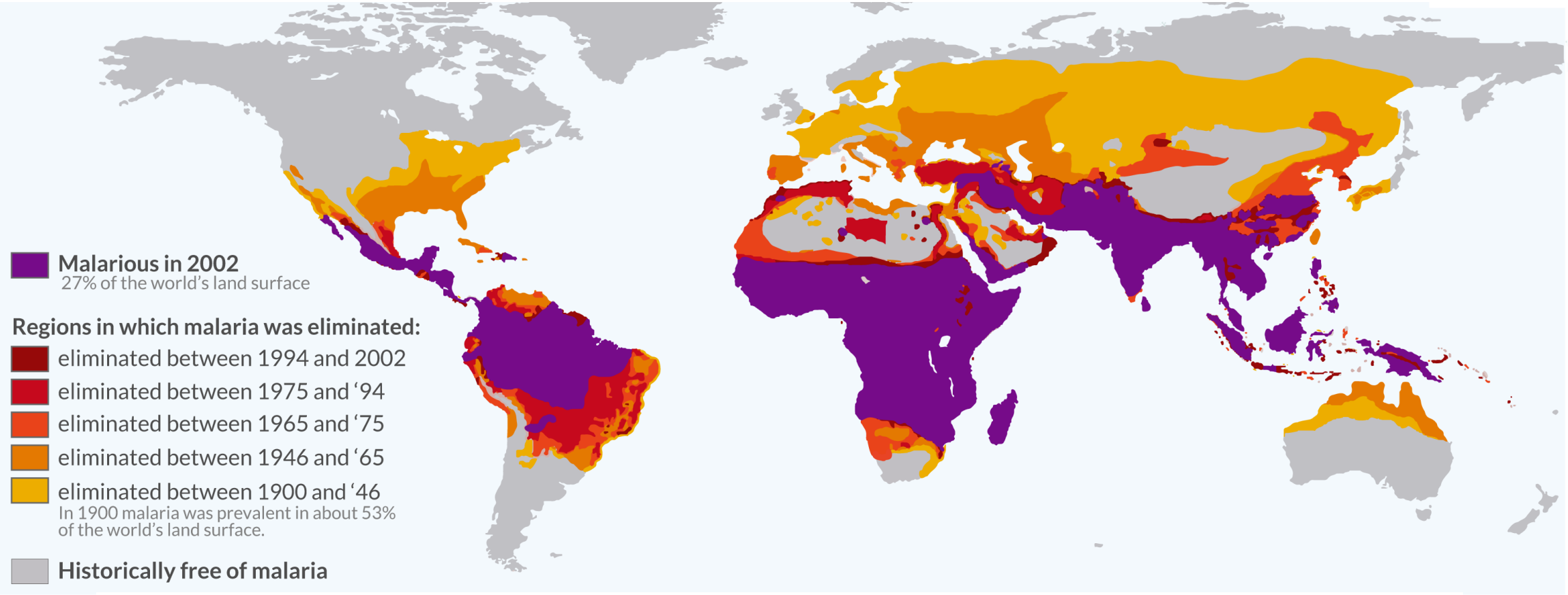
- 4 main human ***Plasmodium* parasites** (*falciparum, vivax, malariae, ovalae*).
- Over 200 *Plasmodium* spp. globally, infecting birds, reptiles, and other mammals (rodents, bats, primates)
- >400 global species of ***Anopheles* mosquito**, >100 that can transmit human malaria
- ~30-40 *Anopheles* spp. most commonly implicated in human malaria transmission!

Only female mosquitoes feed on blood!
Male mosquitoes feed on plant nectar.



Kiszewksi et al. 2004. *ASTMH.*

Malaria has been eliminated from many regions where it was previously endemic, including the US.

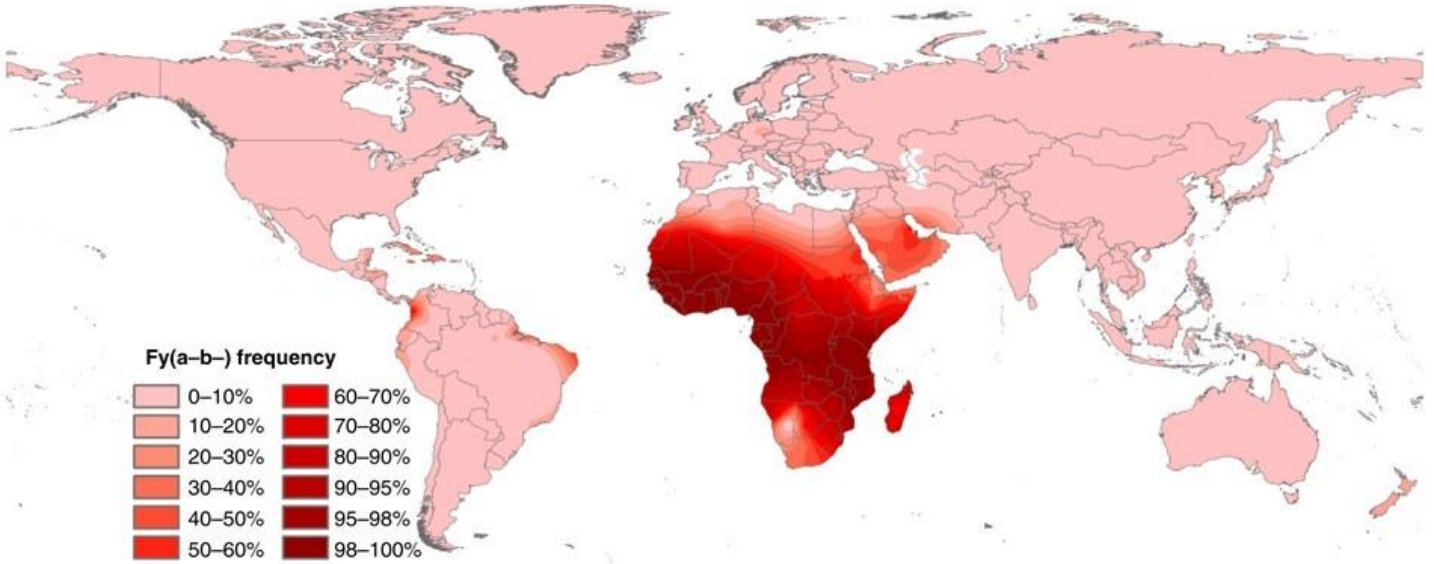


Still one of the leading causes of child mortality globally – responsible for about half a million childhood deaths a year, 80% in Africa.

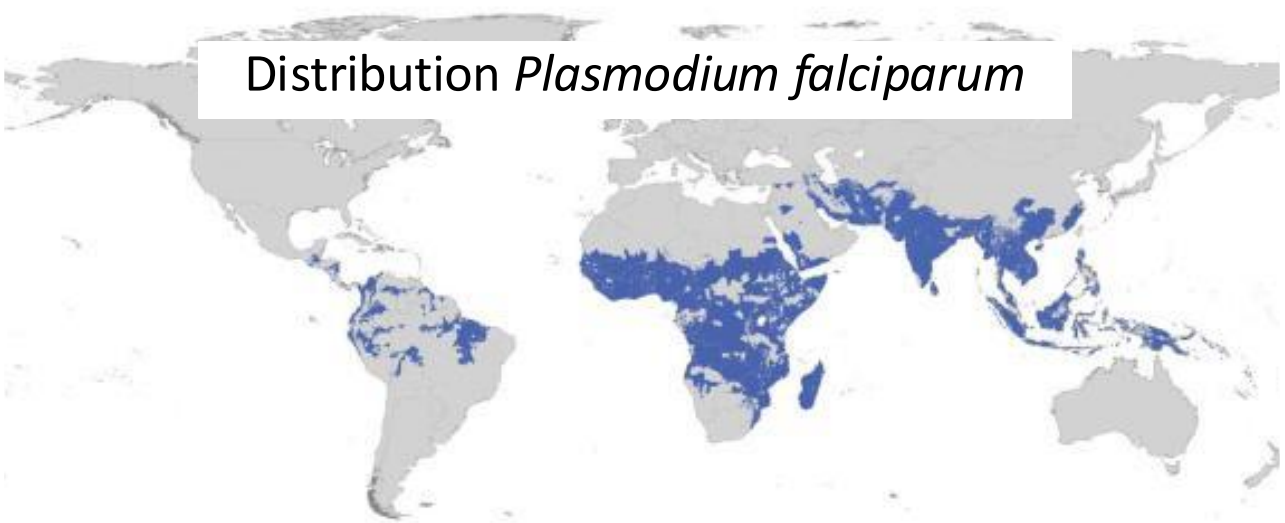
OurWorldinData.org

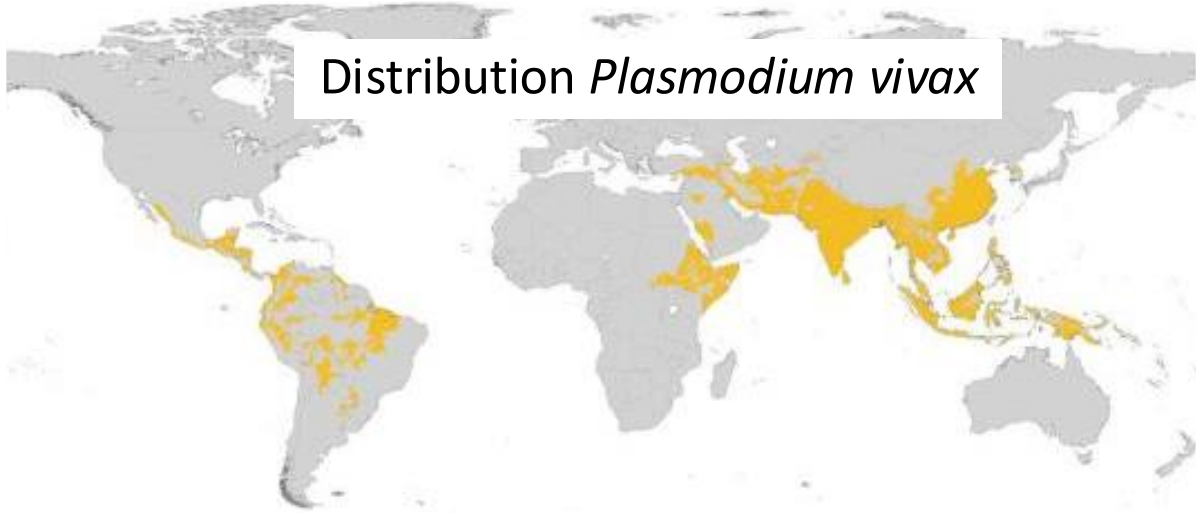
Malaria has also shaped human DNA.

Duffy antigen



- Modeled distribution of Duffy-negative human population





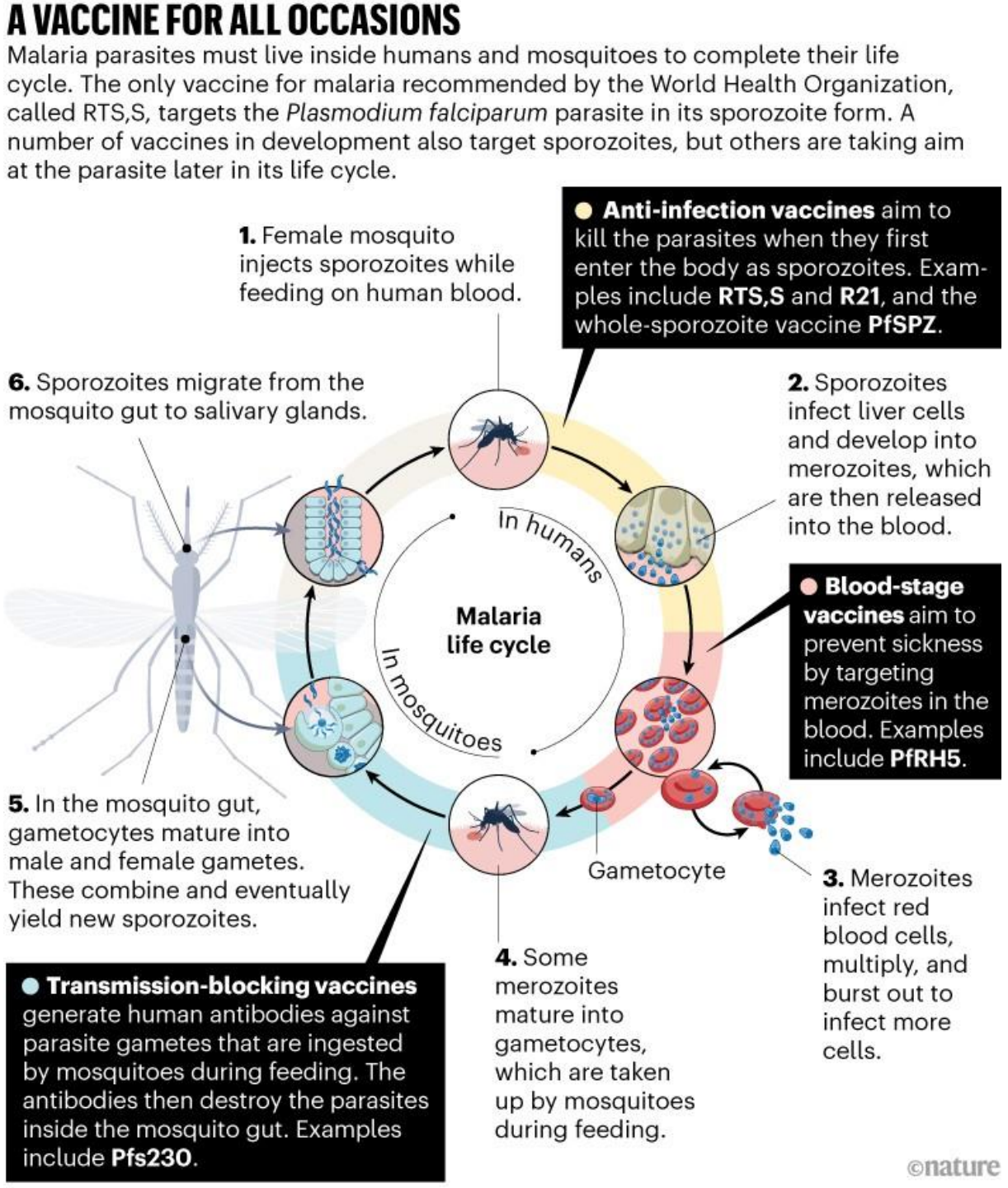
Guerra et al. 2006. *Trends in Parasitology*
Howes et al 2011. *Nature Communications.*

Challenges to malaria elimination?

- High parasite diversity: sexual reproduction in 4+ *Plasmodium* species
  - Fast evolution of resistance *(e.g. to drugs)*
- Many possible vectors! Potentially additional possible reservoirs!
- Latent cases as burden is reduced
- Vaccine candidates: what life stage to target?

Malaria vaccines

- Only two currently licensed
- *Mosquirix*/RTS,S pre-erythrocytic vaccine licensed in 2022
  - Requires at least 3 doses in children <2
  - Does not eliminate pathogen but reduces severe malaria burden and burden of hospitalization by ~30%
- *R21/Matrix-M* pre-erythrocytic vaccine licensed in 2023
  - Requires at least 3 doses in children <2
  - Does not eliminate pathogen but reduces severe malaria burden and burden of hospitalization by 77%



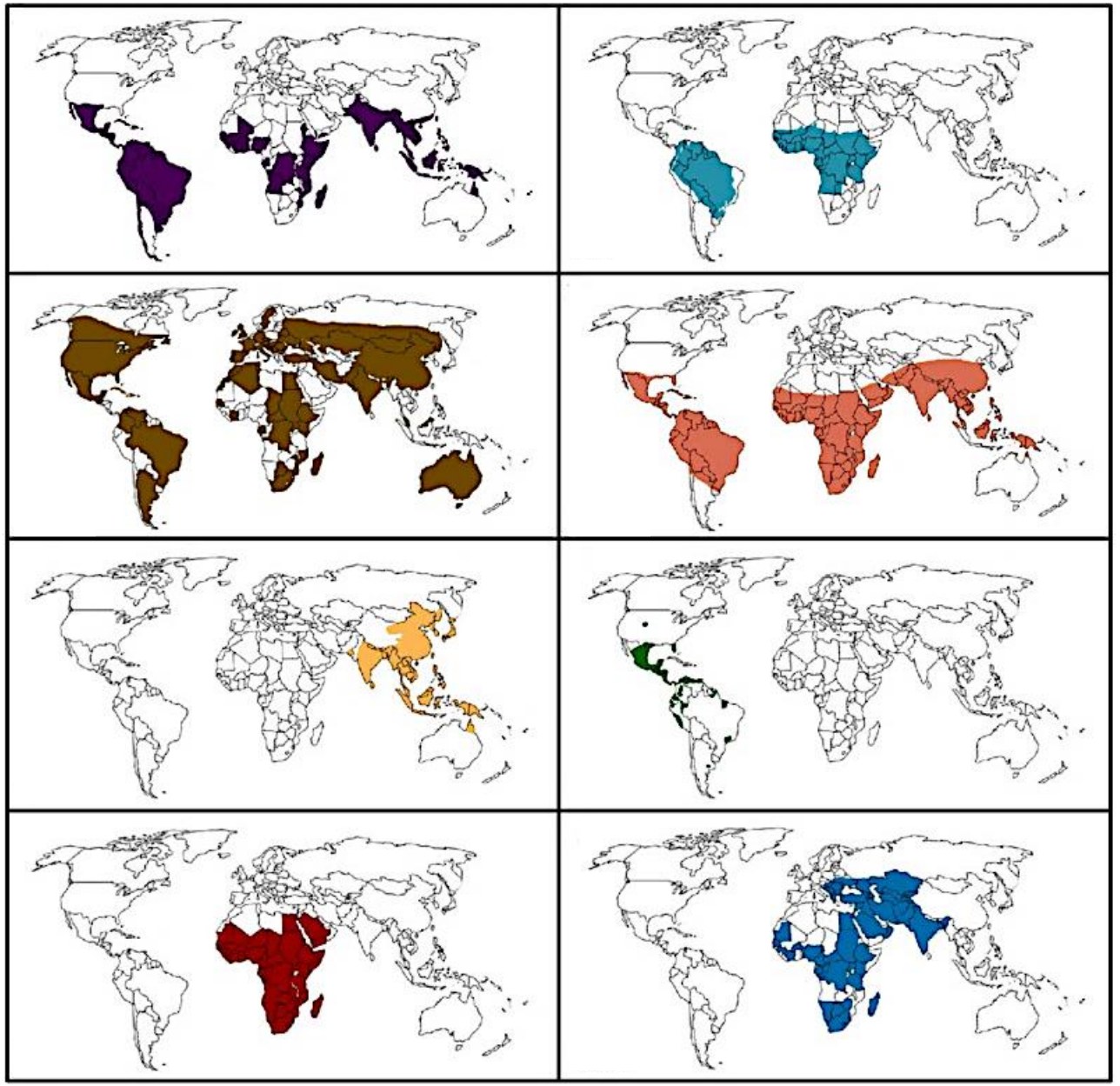
Pathogens exhibit **diverse transmission mechanisms** that require tailored modeling structures

- **Vector-borne** diseases (a type of indirect transmission) are transmitted via blood-feeding arthropod (mosquitoes, ticks, fleas)
  - Malaria: Mosquito-borne protozoan *Plasmodium spp.*
  - "Arboviruses": Mosquito-borne viruses, including Dengue, Zika, Yellow fever virus, West Nile virus, Chikungunya virus. ***Arbovirus is not a phylogenetic term!***
  - Sleeping sickness, also known as African trypanosomiasis: tsetse fly vector and protozoan pathogen (trypanosome)
  - Chagas disease: kissing bug vector and trypanosome pathogen
  - Plague: flea vector and bacterial pathogen (*Yersinia pestis)*

Important arbovirus distributions

Aedes spp.

Dengue virus



Yellow fever virus

Aedes spp.

Culex pipiens

West Nile virus

Chikungunya virus

Aedes spp.

Culex pipiens

Japanese encephalitis virus

Venezuelan equine encephalitis virus

Culex -> *Aedes*

Culex and *Aedes*

Rift-Valley fever virus

Crimean-Congo hemorrhagic fever virus

Hyalomma ticks

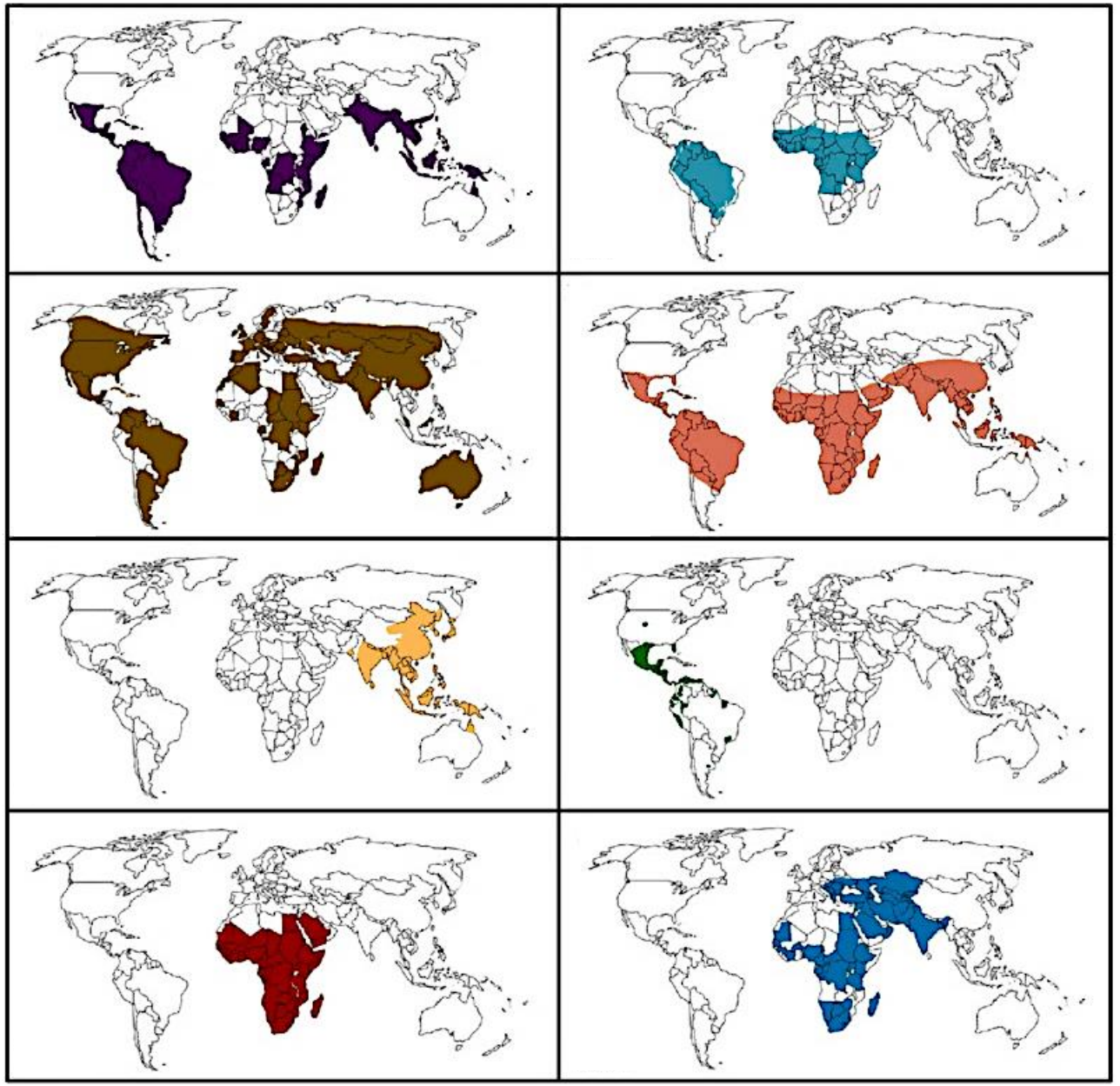
Iranpour. 2016. *Expert Reviews in Molecular Medicine*

Flaviviruses

Important arbovirus distributions

Aedes spp.

Dengue virus



Yellow fever virus

Aedes spp.

Culex pipiens

West Nile virus

Chikungunya virus

Aedes spp.

Culex pipiens

Japanese encephalitis virus

Venezuelan equine encephalitis virus

Culex -> *Aedes*

Culex and *Aedes*

Rift-Valley fever virus

Crimean-Congo hemorrhagic fever virus

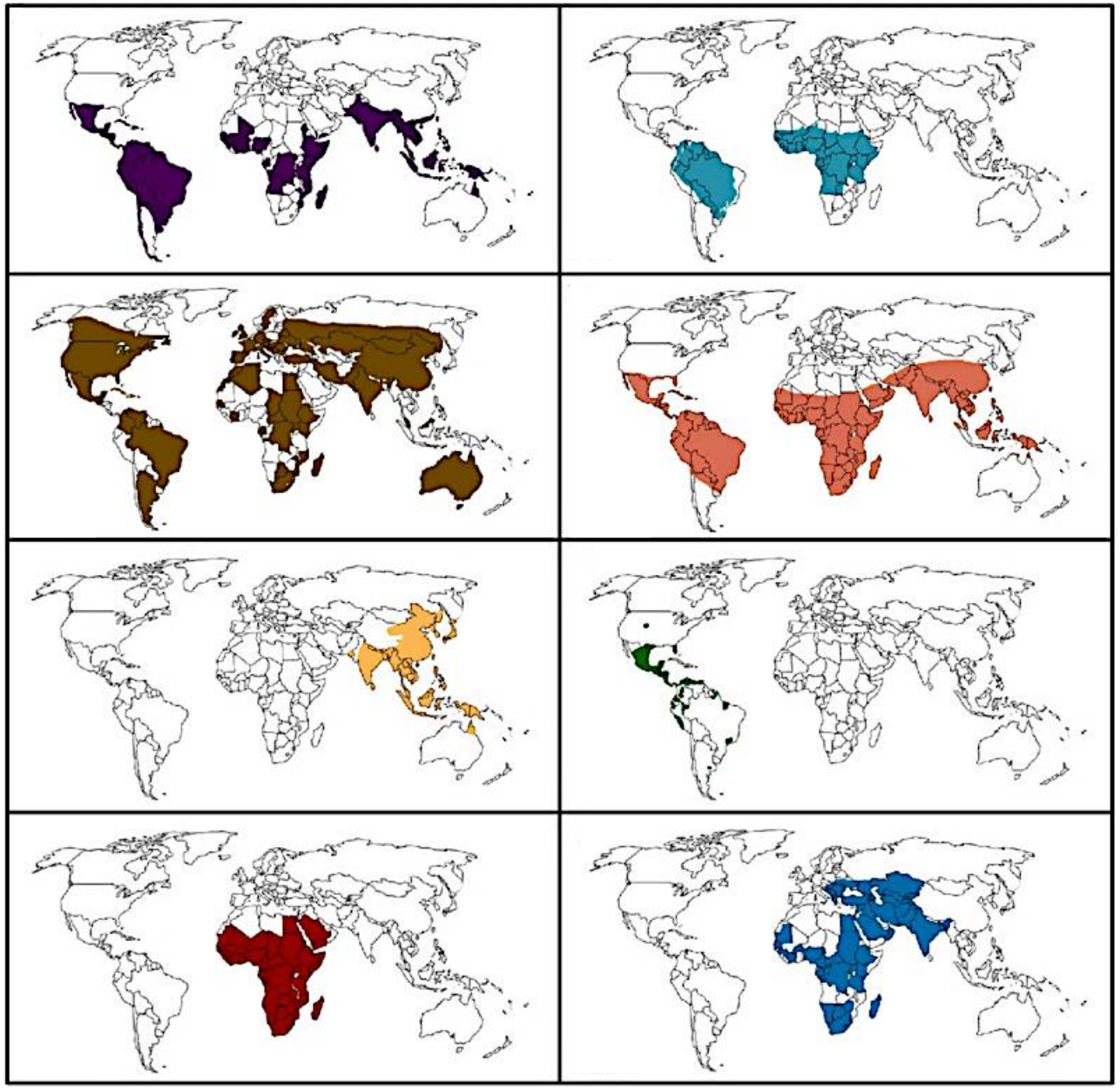
Hyalomma ticks

Iranpour. 2016. *Expert Reviews in Molecular Medicine*

Alphaviruses (Togaviridae)

Important arbovirus distributions

Aedes spp.	Dengue virus		Yellow fever virus	*Aedes* spp.
Culex pipiens	West Nile virus		Chikungunya virus	*Aedes* spp.
Culex pipiens	Japanese encephalitis virus		Venezuelan equine encephalitis virus	*Culex* -> *Aedes*
Culex and *Aedes*	Rift-Valley fever virus		Crimean-Congo hemorrhagic fever virus	*Hyalomma* ticks

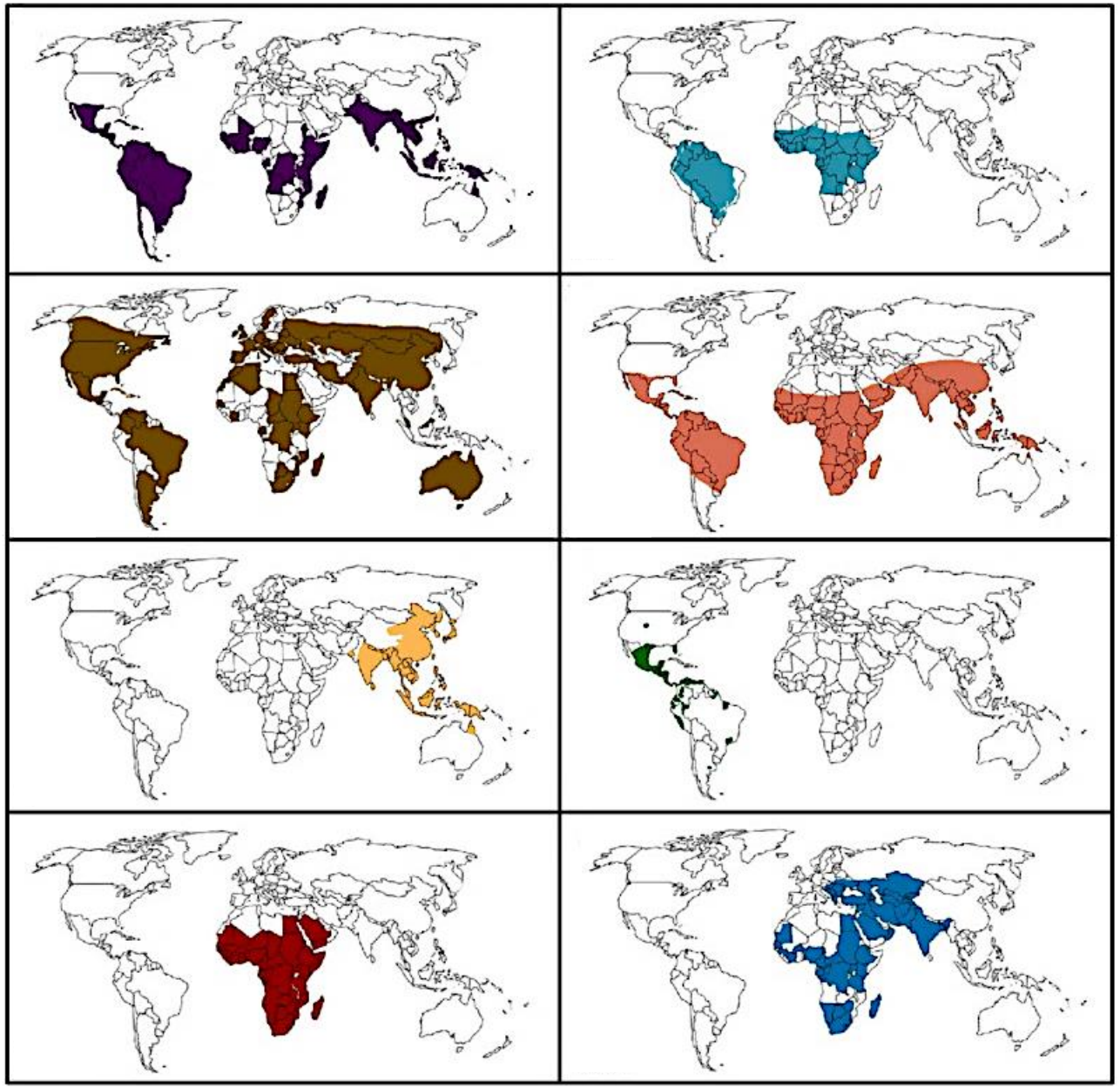


Iranpour. 2016. *Expert Reviews in Molecular Medicine*

Bunyaviruses

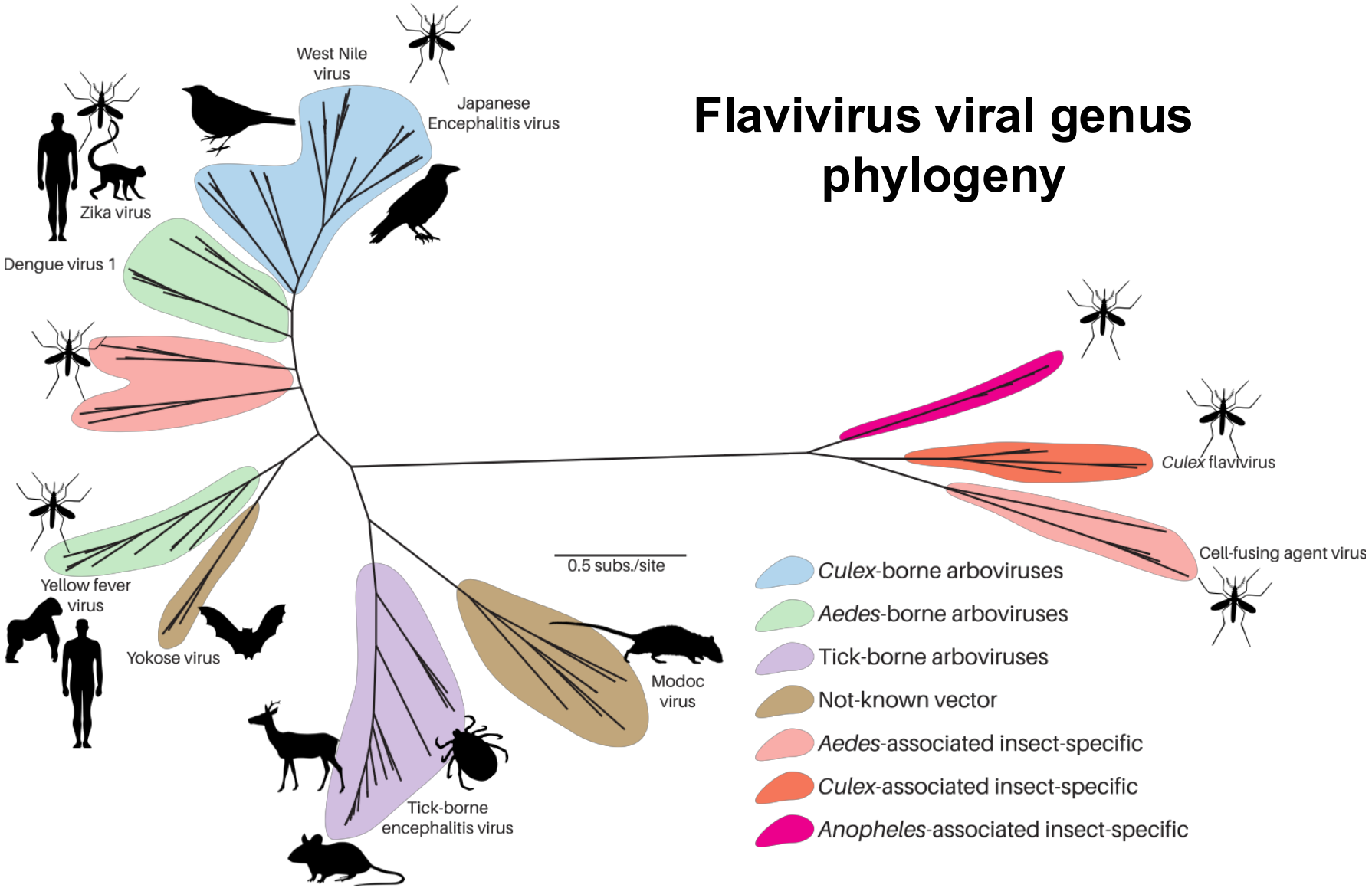
Important arbovirus distributions

***Aedes* spp.**	**Dengue virus**		**Yellow fever virus**	 ***Aedes* spp.**
Culex pipiens	**West Nile virus**		**Chikungunya virus**	 ***Aedes* spp.**
Culex pipiens	**Japanese encephalitis virus**		**Venezuelan equine encephalitis virus**	 ***Culex* -> *Aedes***
Culex* and *Aedes	**Rift-Valley fever virus**		**Crimean-Congo hemorrhagic fever virus**	 ***Hyalomma* ticks**



Iranpour. 2016. *Expert Reviews in Molecular Medicine*

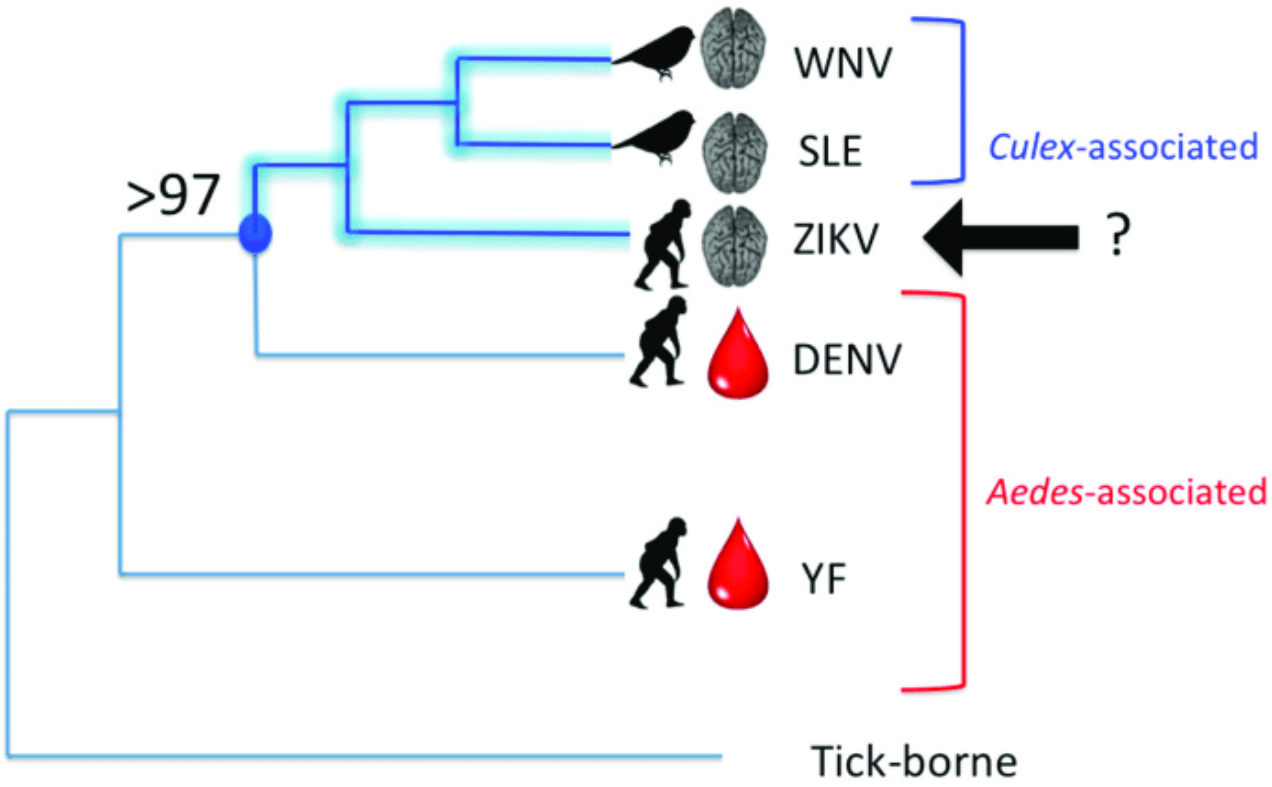
Arboviruses infect a wide range of hosts and vectors

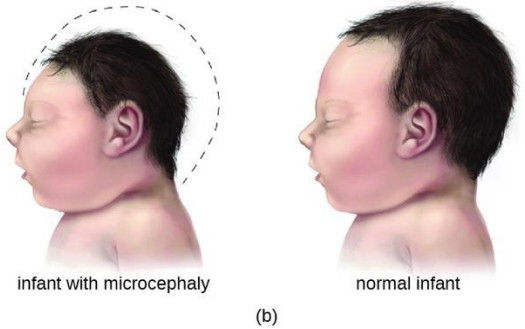


Flavivirus viral genus phylogeny

Sebastian Lequime. 2020.

Is flavivirus pathogenesis correlated with vector identity?





Hunter. 2017. *Frontiers in Micro*

A brief introduction to dengue.

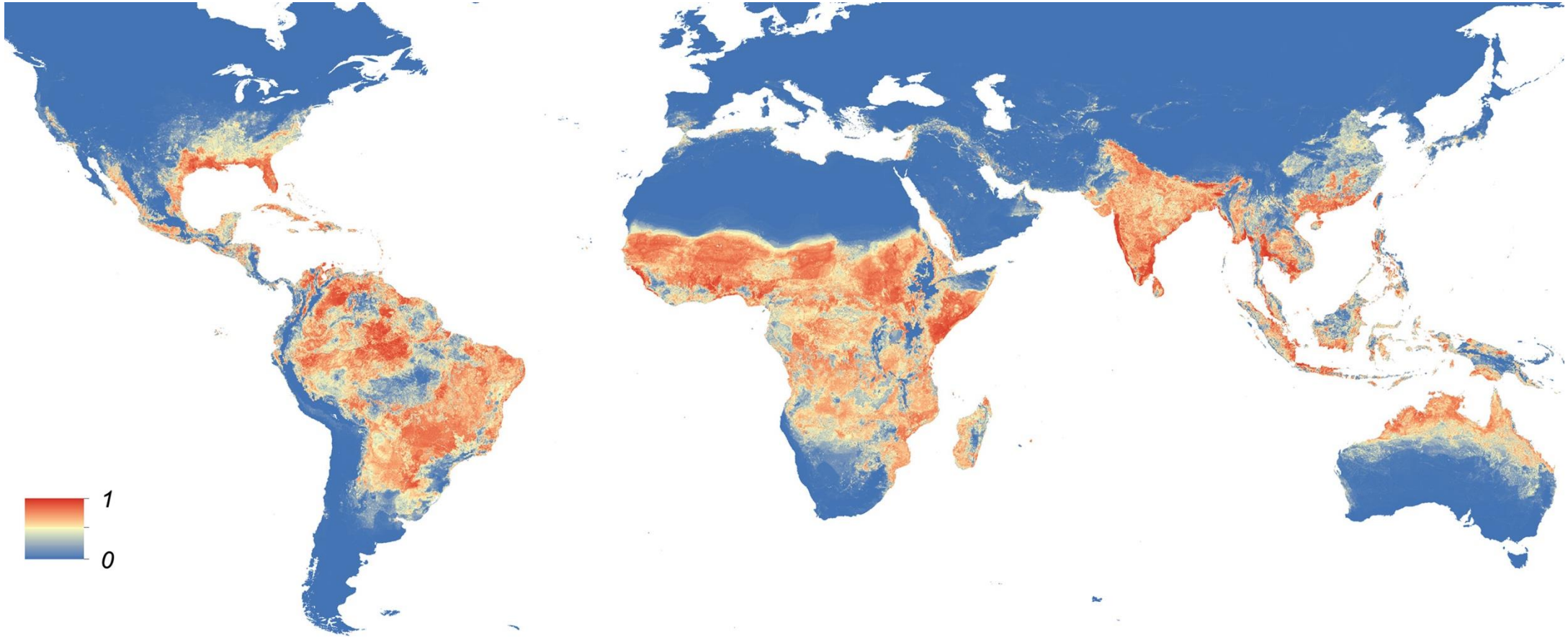
- Dengue is an arbovirus disease caused by one of four known serotypes of dengue **flavivirus** (DENV-1, -2,-3,-4).
- DENV is vectored by mosquitoes in the genus *Aedes.*
- 40% of the world's population resides in dengue-endemic regions, though historically the burden has been highest in Southeast Asia.
- Most (70+%) of dengue cases are asymptomatic, but a small proportion develop into dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS).
- Most severe cases occur in secondary infections resulting from **antibody-dependent enhancement (ADE)**, a phenomenon whereby pre-existing immunity to a single serotype facilitates infection by a subsequent serotype.

WHO 2012

Dengue vaccines

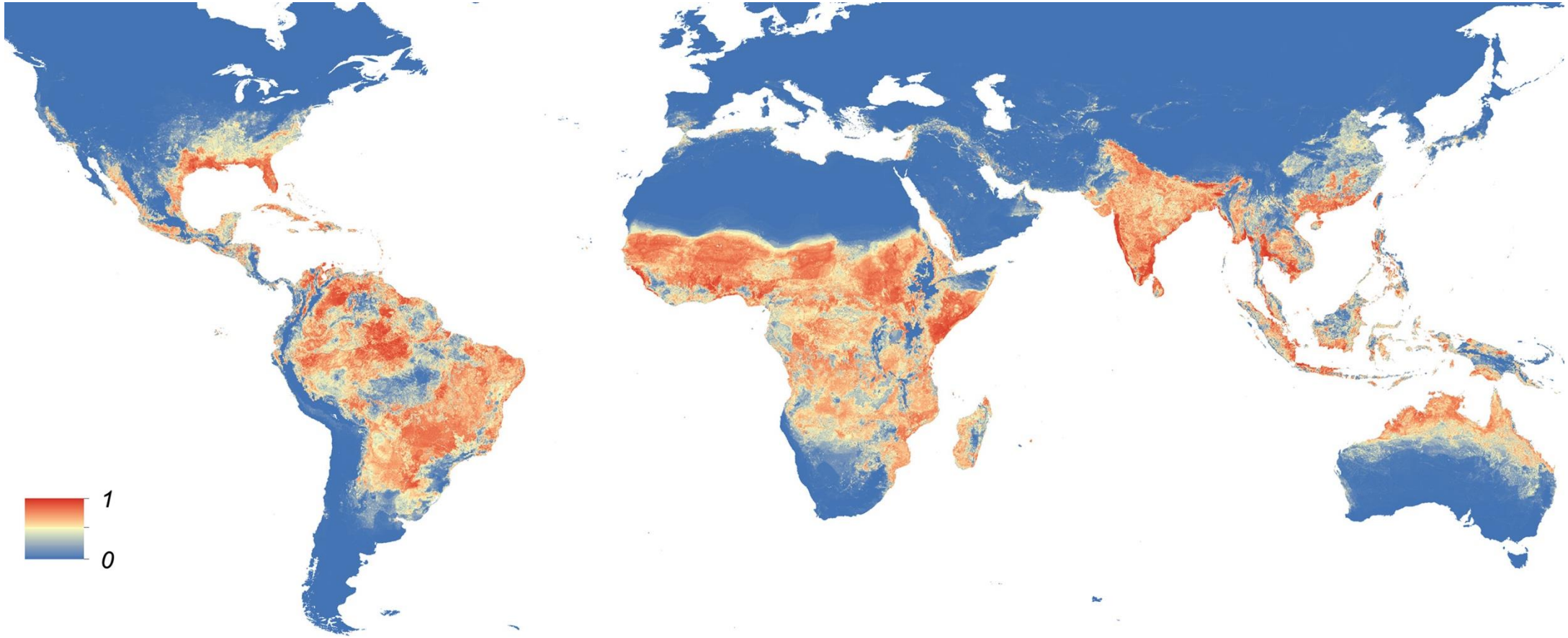
- Two licensed vaccines in circulation – both tetravalent live attenuated vaccines which confer immunity to all 4 serotypes simultaneously
- Dengvaxia – by Sanofi Pasteur
  - First licensed in 2016 but controversy developed after severe cases developed in those who were previously naïve in Philippines
  - Now recommended only in those who test seropositive
  - This policy has greatly diminished demand. Vaccine no longer widely used.
- Qdenga – TAK-003 – by Takeda
  - Pre-qualified for use in May 2024
  - Appears to be efficacious in both seronegative/seropositive individuals, though is ineffective at preventing infection for DENV-3/4 in seronegatives and lack of enhanced pathogenicity cannot be ruled out.
  - WHO recommends use in children 6-16 in high transmission settings only at this stage.
- NIH NIAID vaccine **TV005** also showing promise but not yet licensed.

Global distribution of *Aedes aegypti*

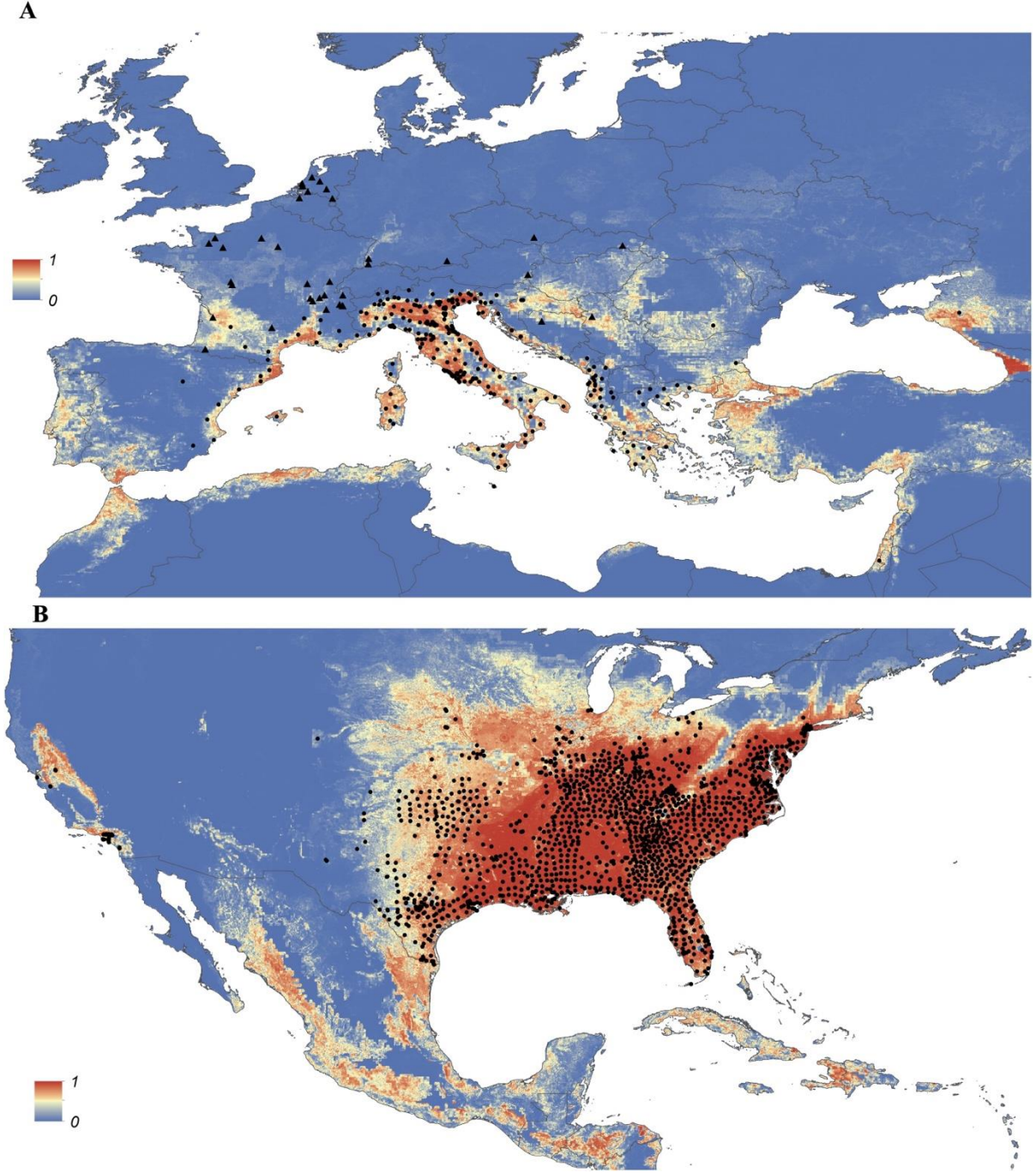


Kraemer et al. 2015

Global distribution of *Aedes albopictus*



Kraemer et al. 2015



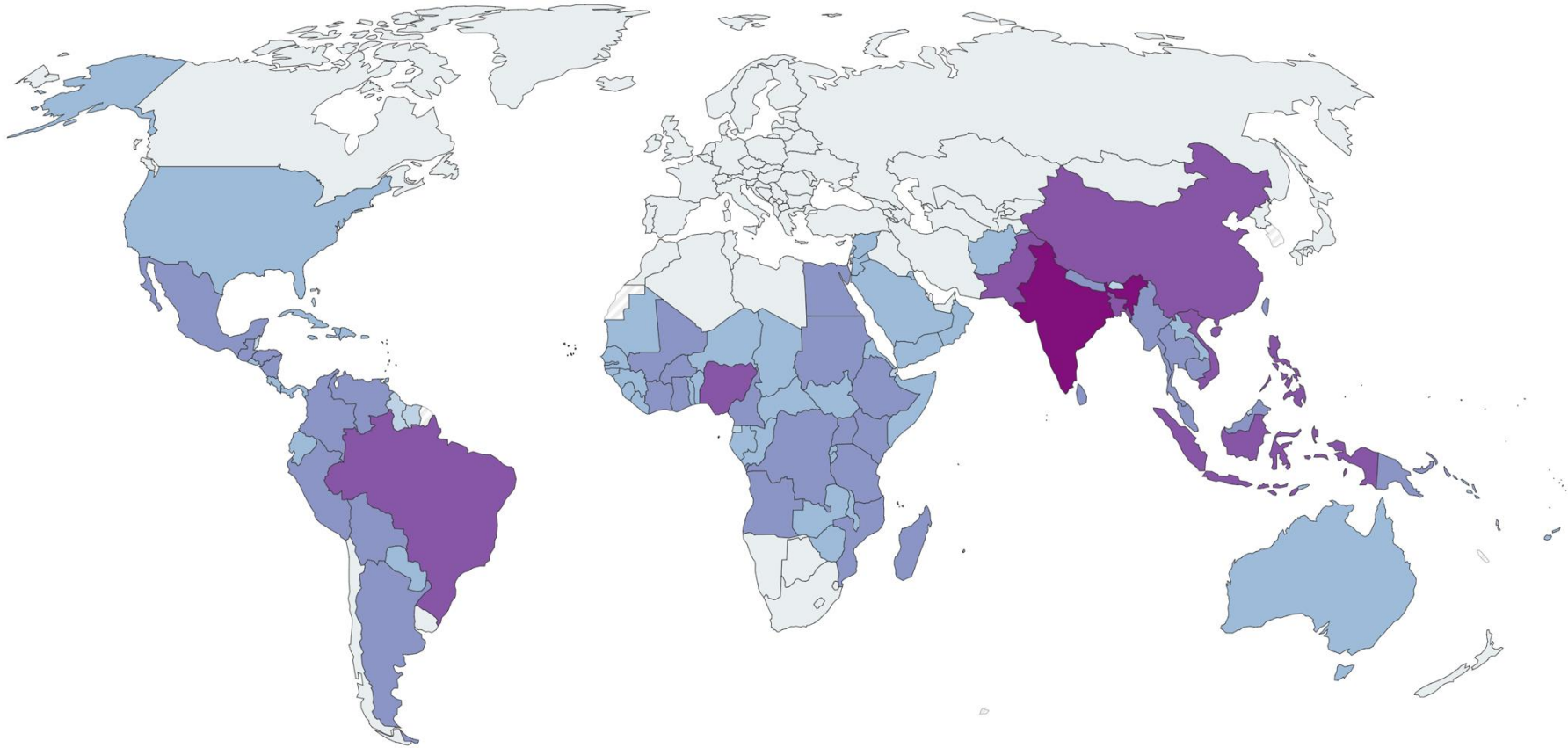
Detailed probability of occurrence of *Aedes albopictus* in Europe and US, areas where the mosquito is most rapidly expanding its range

Kraemer et al. 2015

Dengue fever infections, 2019

Our World in Data

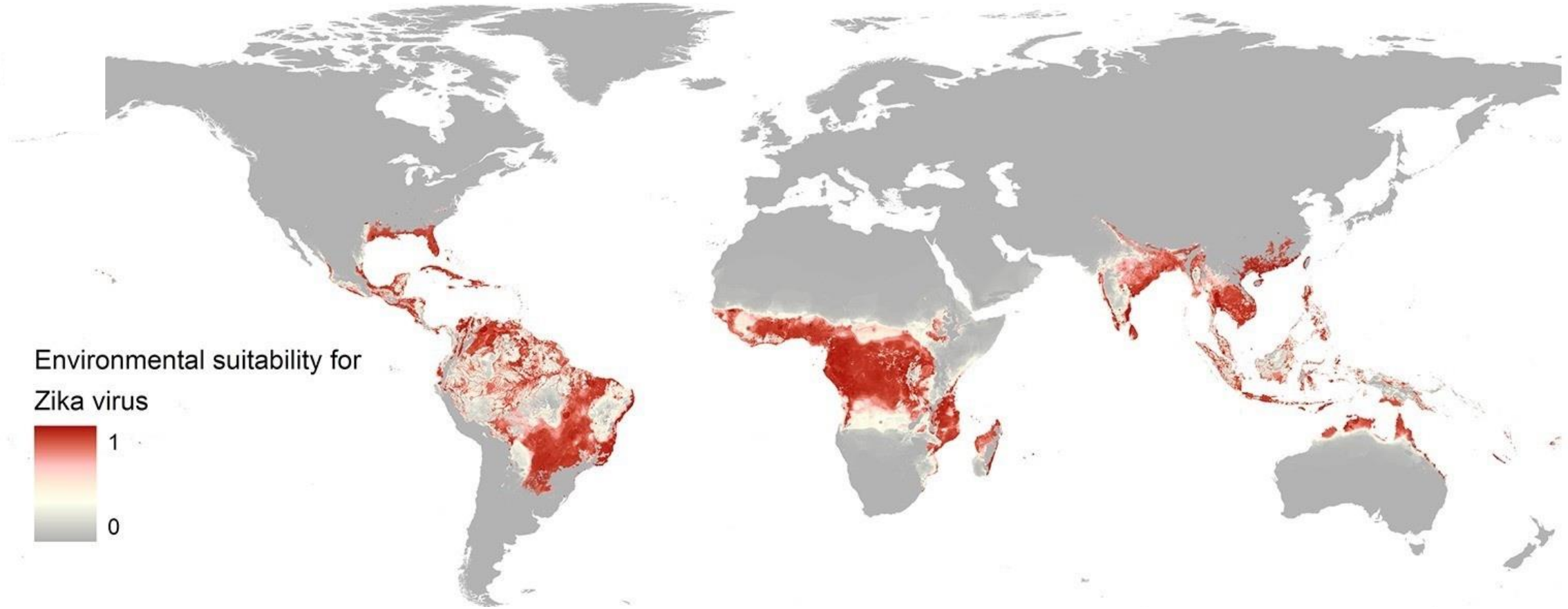
Estimated annual number of new dengue infections. Dengue is a viral infection transmitted through the bite of infected mosquitoes; symptoms include fever, headaches, and nausea. Most infections are asymptomatic or mild, but dengue can occasionally be severe or fatal.



Data source: IHME, Global Burden of Disease (2019)

OurWorldInData.org/burden-of-disease | CC BY

Zika is also vectored by *Aedes aeygpti* and its relatives

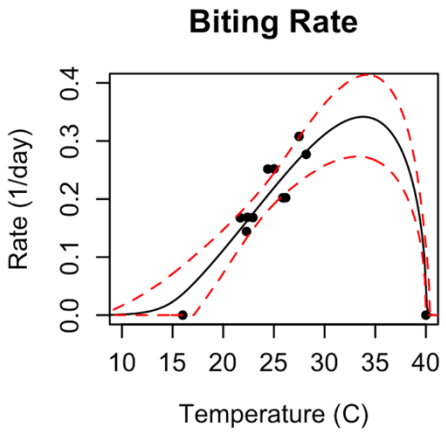


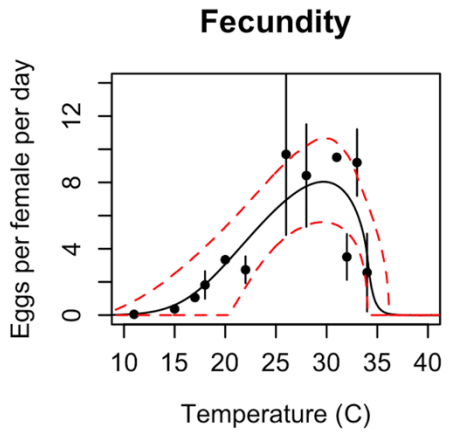
Messina et al 2016. *eLife*

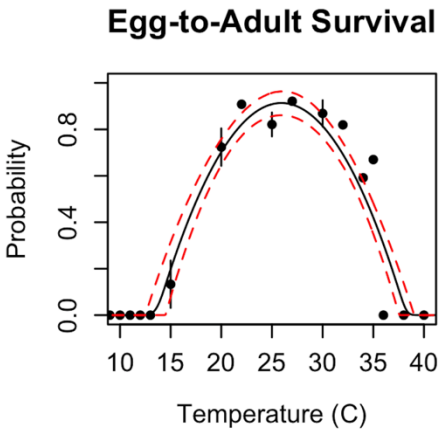
Arboviruses and climate change

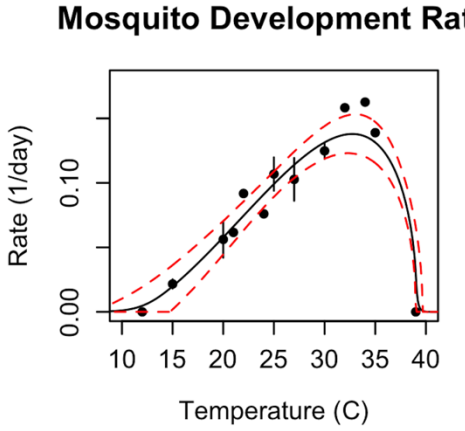
- Mosquito development rates are highly sensitive to temperature.
- As a result, many arboviruses are climate-constrained in distribution but ranges are expanding with climate change.

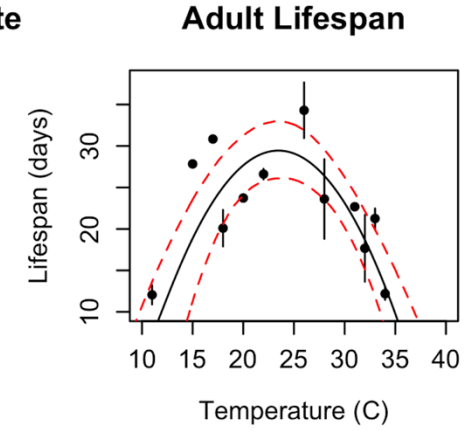
Thermal performance curves for *Aedes aegypti*

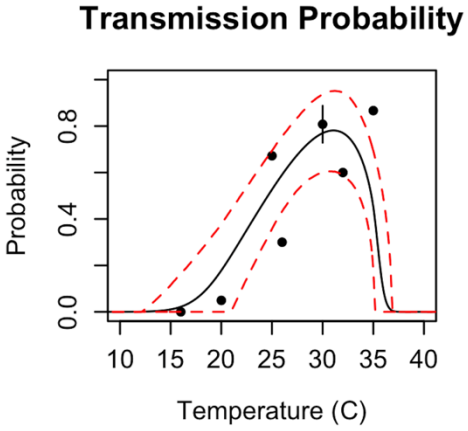


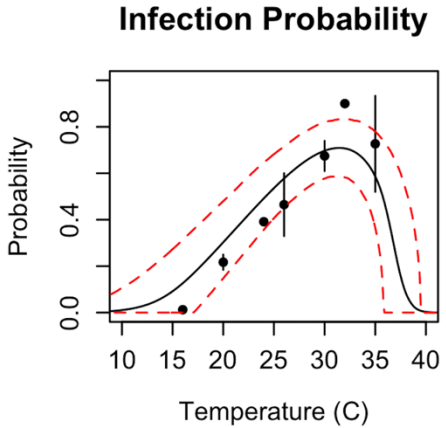


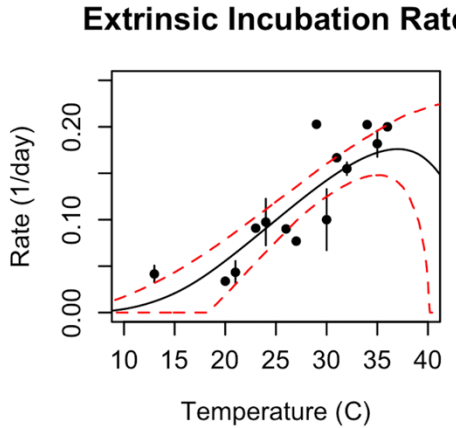






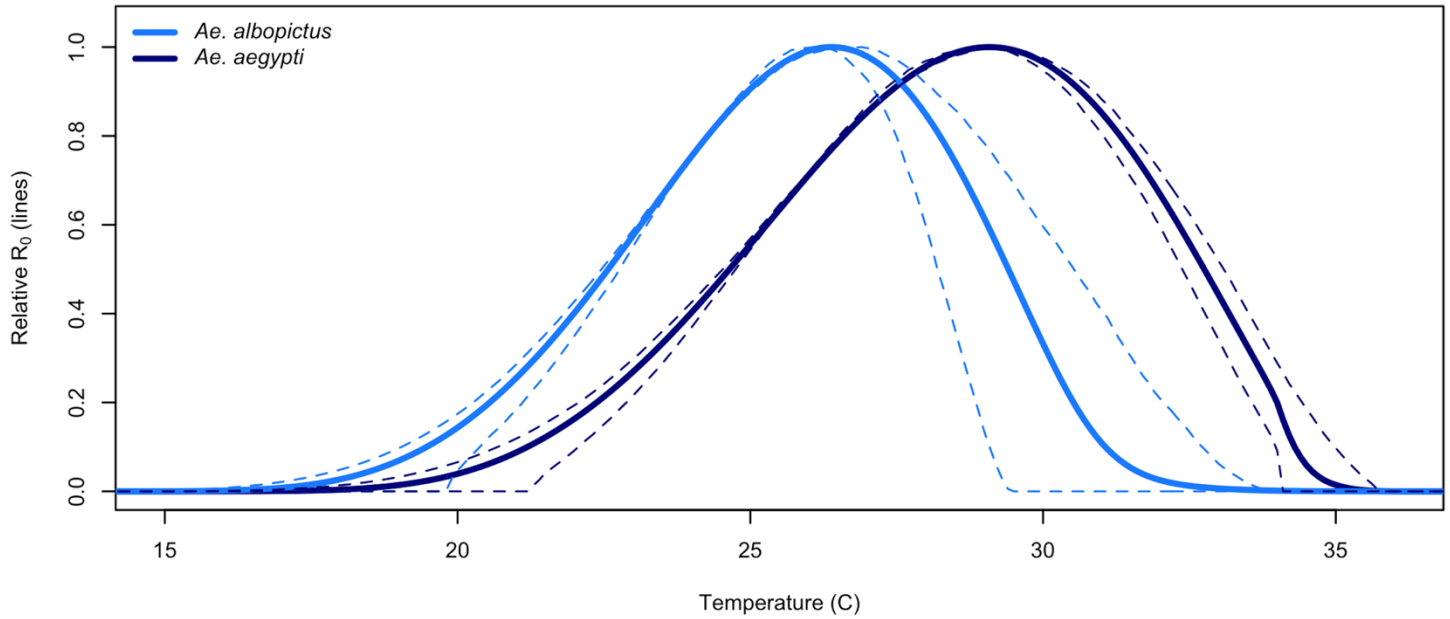


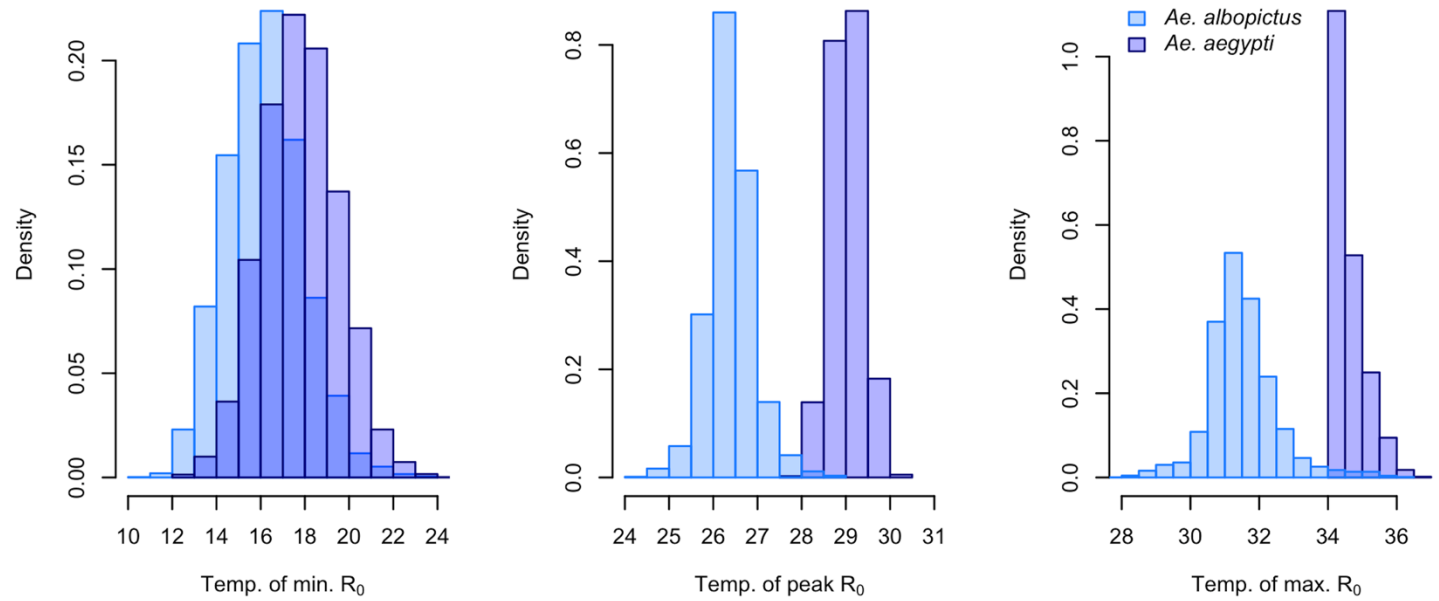




Mordecai et al 2017. *PLoS NTDs.*

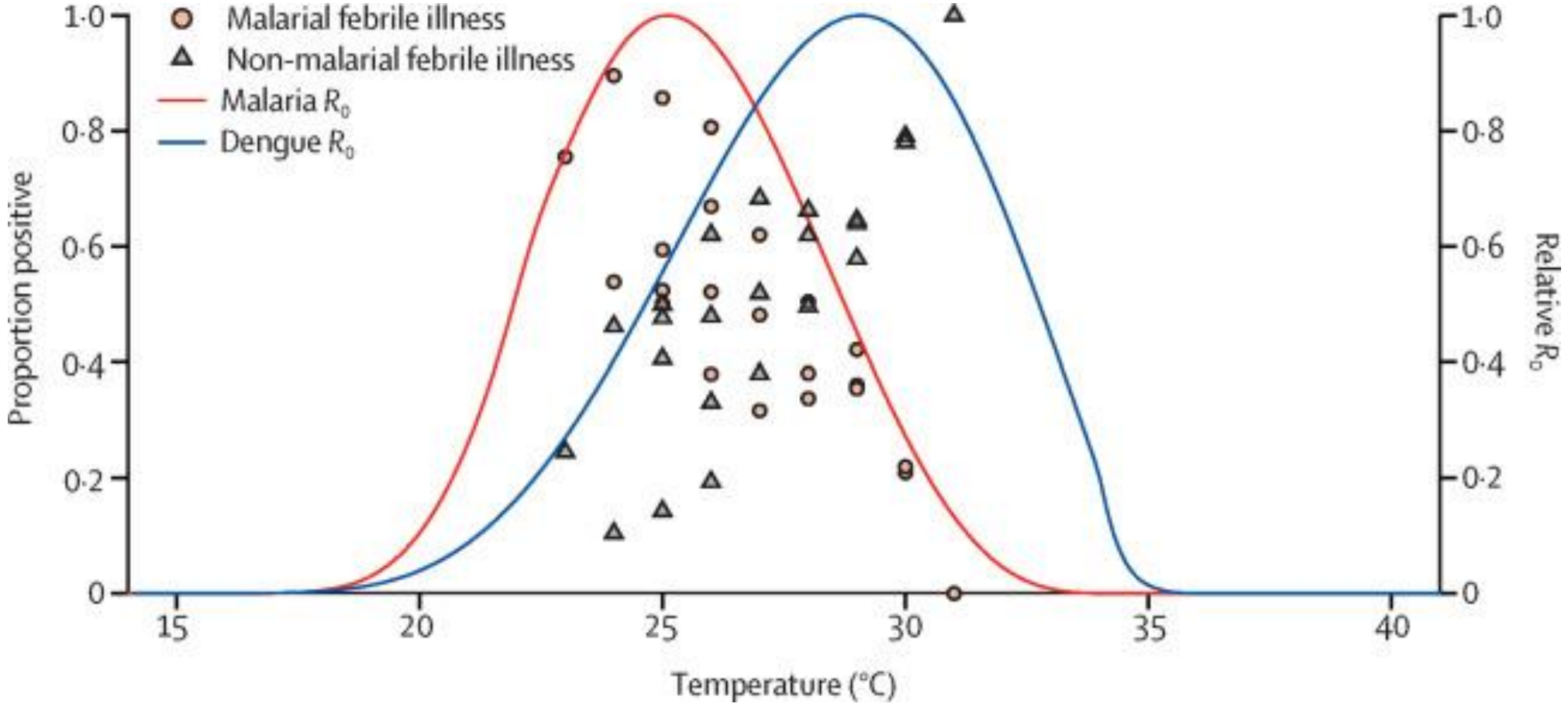
Different vectors respond to temperature in different ways.





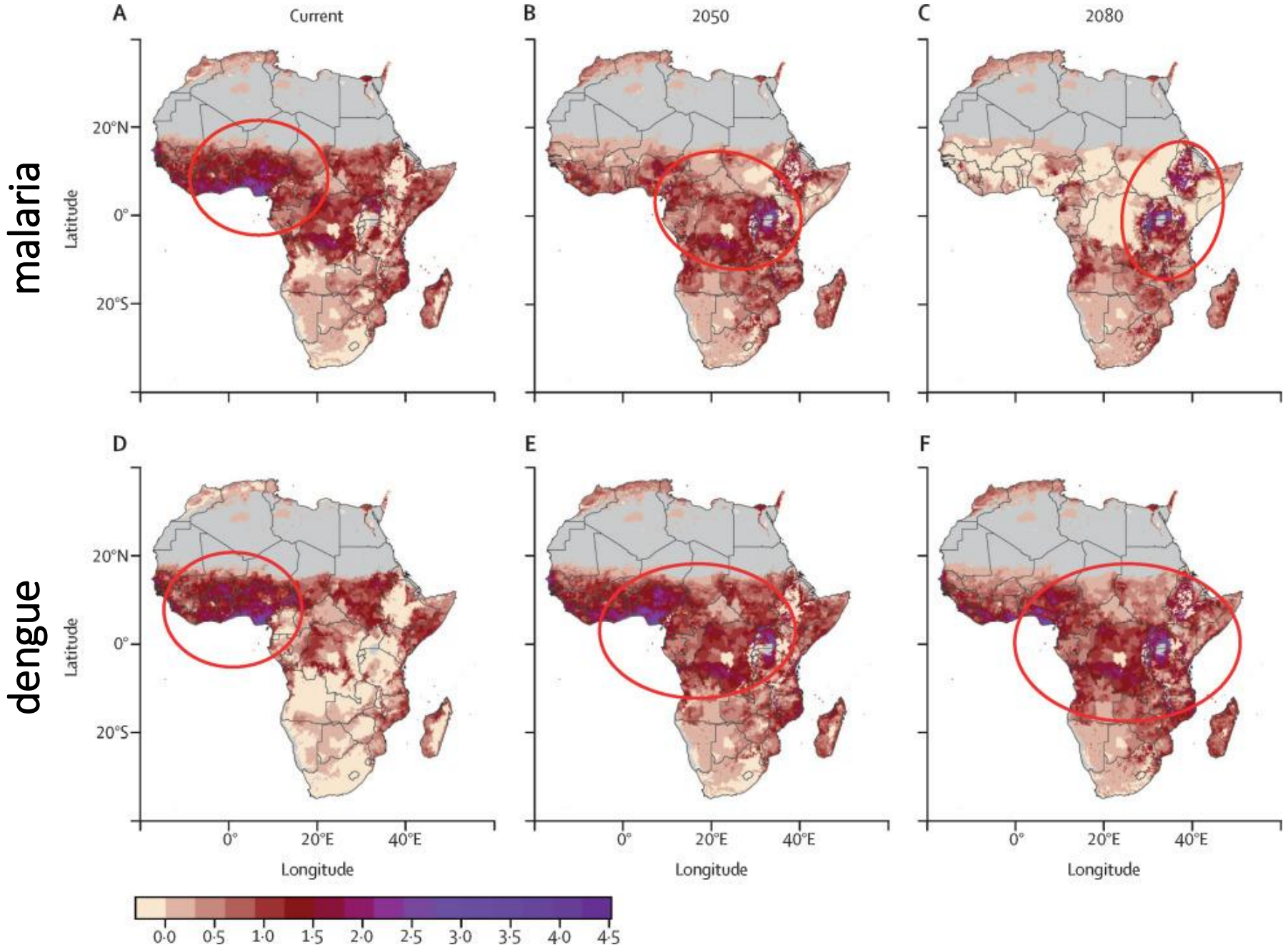
Mordecai et al 2017. *PLoS NTDs.*

These vector differences have important consequences for disease dynamics.



Mordecai et al 2020. *The Lancet Planetary Health.*

These vector differences have important consequences for disease dynamics.



Mordecai et al 2020. *The Lancet Planetary Health.*

Pathogens exhibit **diverse transmission mechanisms** that require tailored modeling structures

- **Vector-borne** diseases (a type of indirect transmission) are transmitted via blood-feeding arthropod (mosquitoes, ticks, fleas)
  - Malaria: Mosquito-borne protozoan *Plasmodium spp.*
  - "Arboviruses": Mosquito-borne viruses, including Dengue, Zika, Yellow fever virus, West Nile virus, Chikungunya virus
  - Sleeping sickness, also known as African trypanosomiasis: tsetse fly vector and protozoan pathogen (trypanosome)
  - Chagas disease: kissing bug vector and trypanosome pathogen
  - Plague: flea vector and bacterial pathogen (*Yersinia pestis)*

Plague is BOTH vector-borne and zoonotic!