

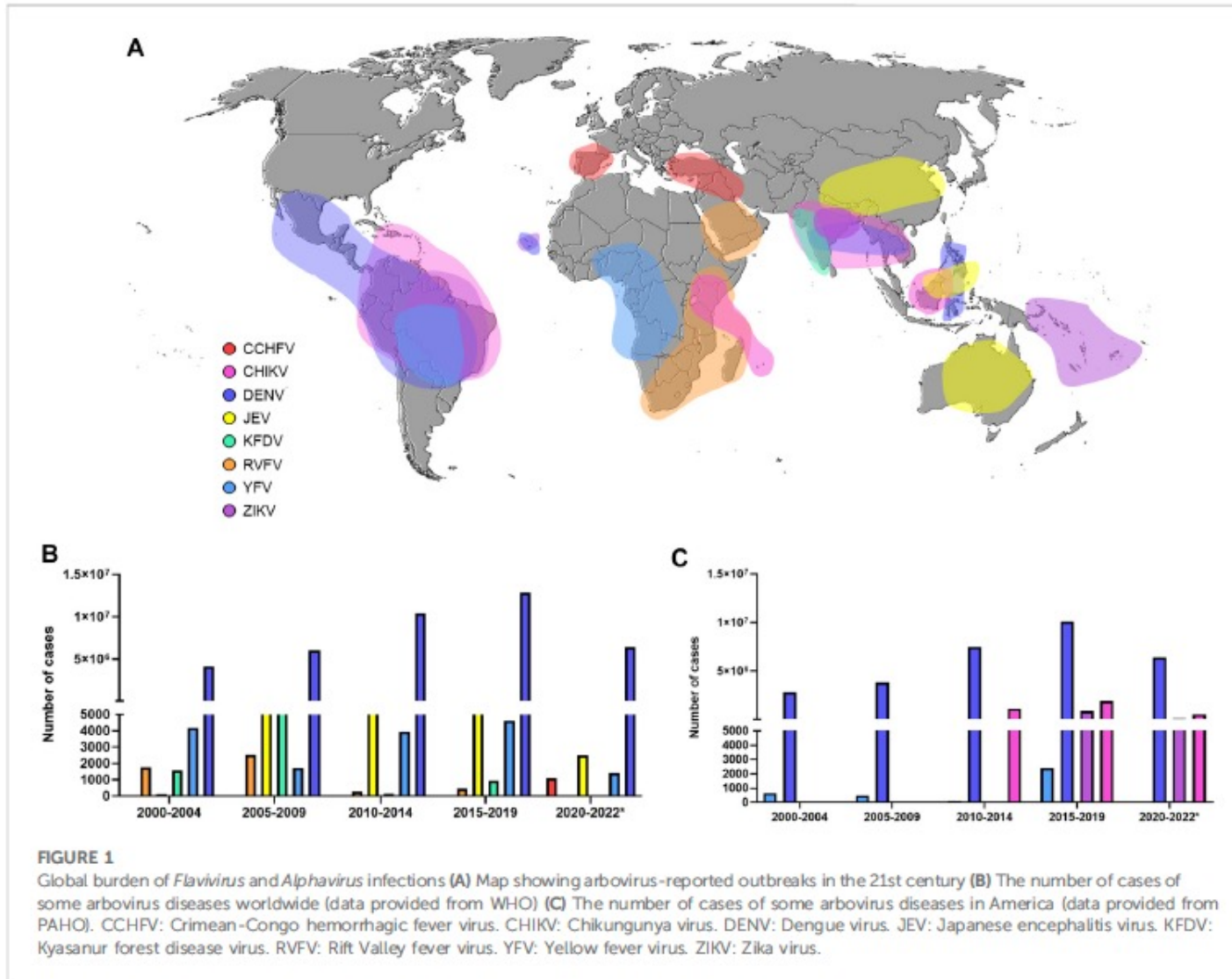


Introduction to Arboviruses & Arboviral Genomic Surveillance

Ruklanthi (Rukie) de Alwis

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Venue : Meeting Room 7C, Duke-NUS Medical School



- A range of arboviruses causing human diseases
- Different arboviruses circulating in different parts of the world
- Some arboviruses show geographical restriction
- Major arboviruses of concern belong to Flaviviruses and alphaviruses
- Dengue and Zika are flaviviruses

Closer look at Flaviviruses

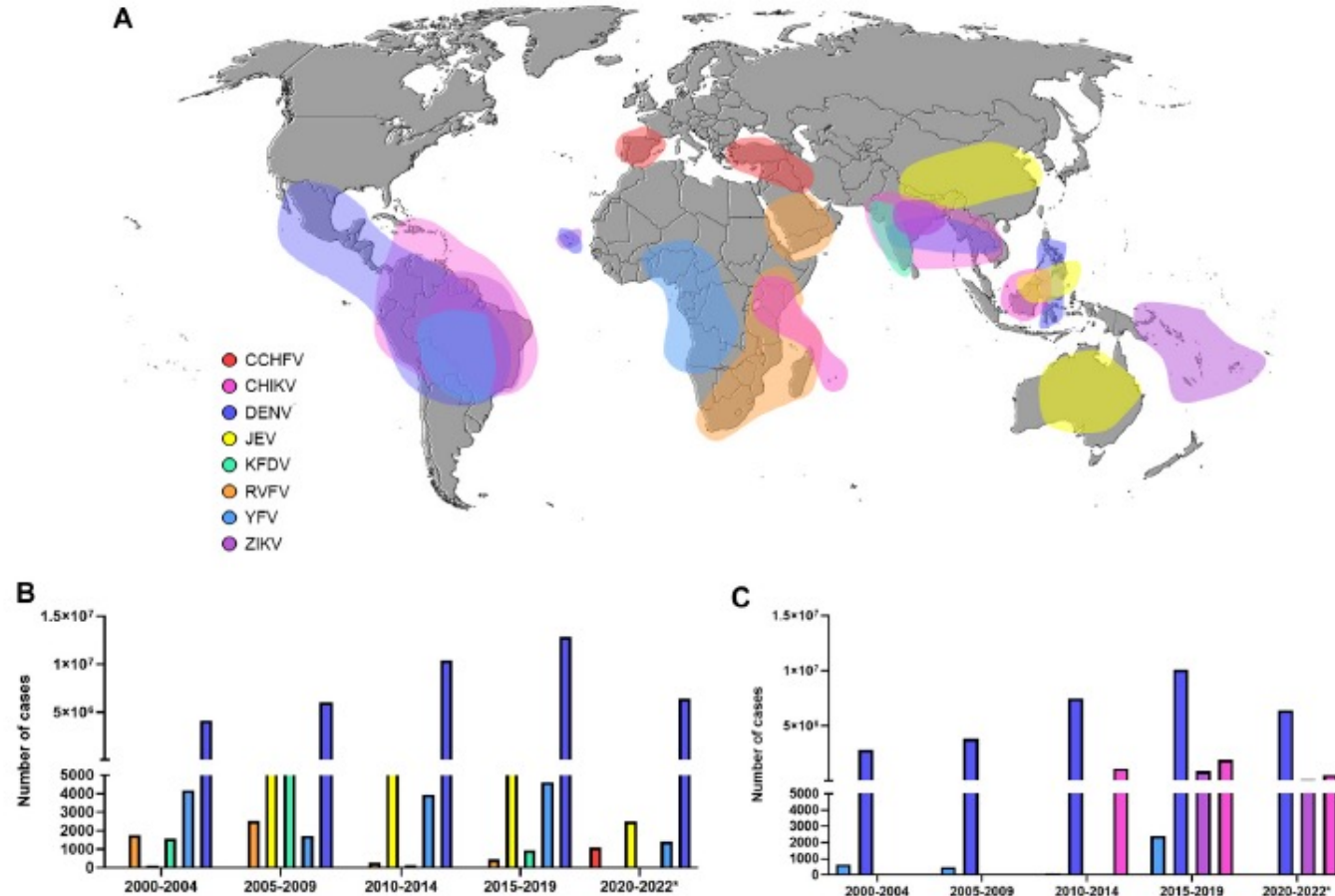
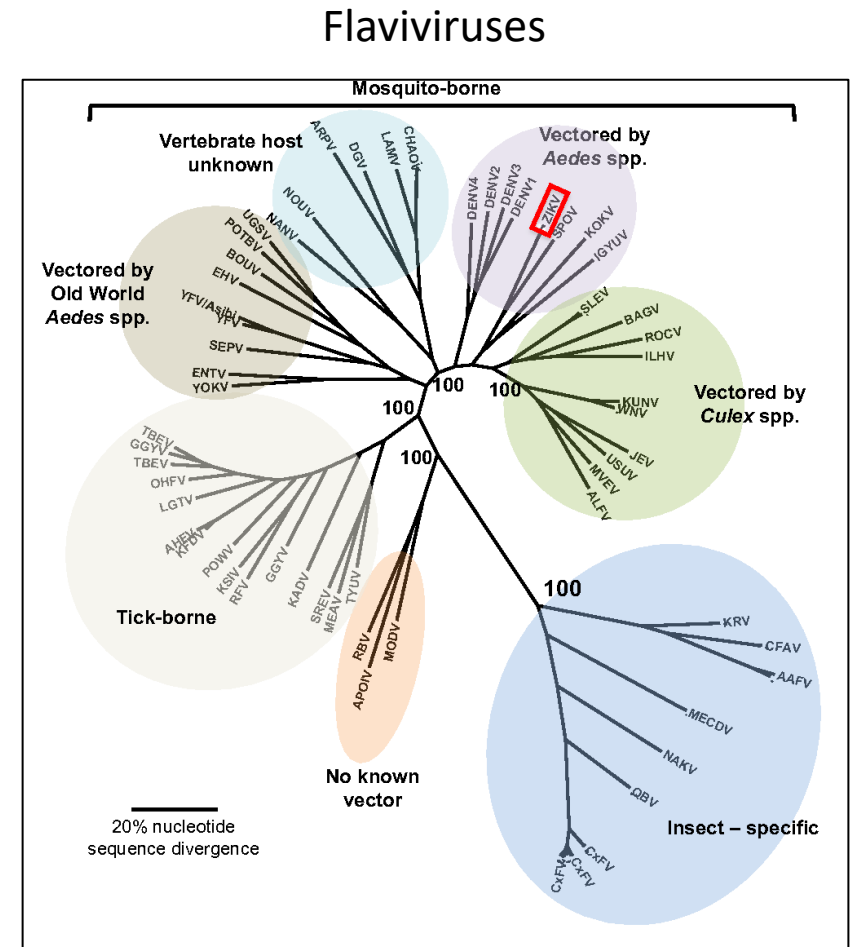
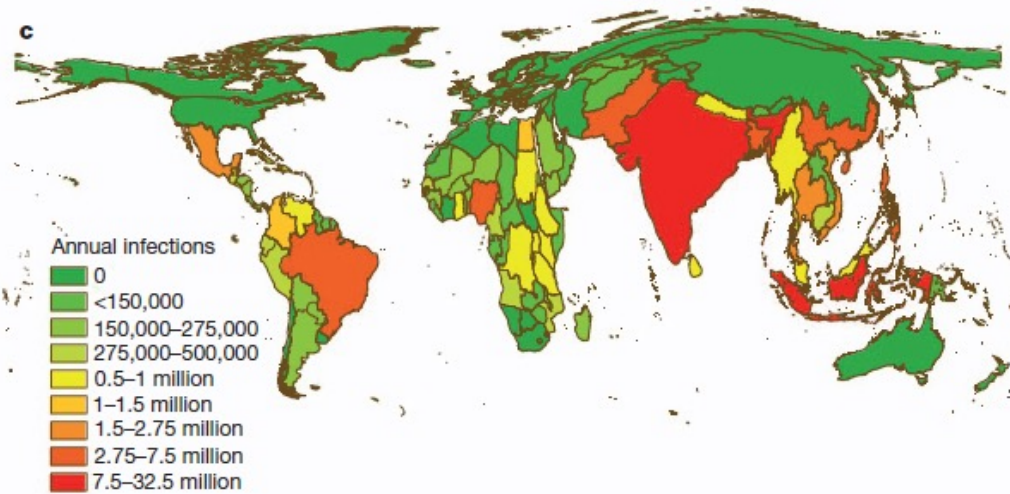


FIGURE 1
Global burden of *Flavivirus* and *Alphavirus* infections (A) Map showing arbovirus-reported outbreaks in the 21st century (B) The number of cases of some arbovirus diseases worldwide (data provided from WHO) (C) The number of cases of some arbovirus diseases in America (data provided from PAHO). CCHFV: Crimean-Congo hemorrhagic fever virus. CHIKV: Chikungunya virus. DENV: Dengue virus. JEV: Japanese encephalitis virus. KFDV: Kyasanur forest disease virus. RVFV: Rift Valley fever virus. YFV: Yellow fever virus. ZIKV: Zika virus.

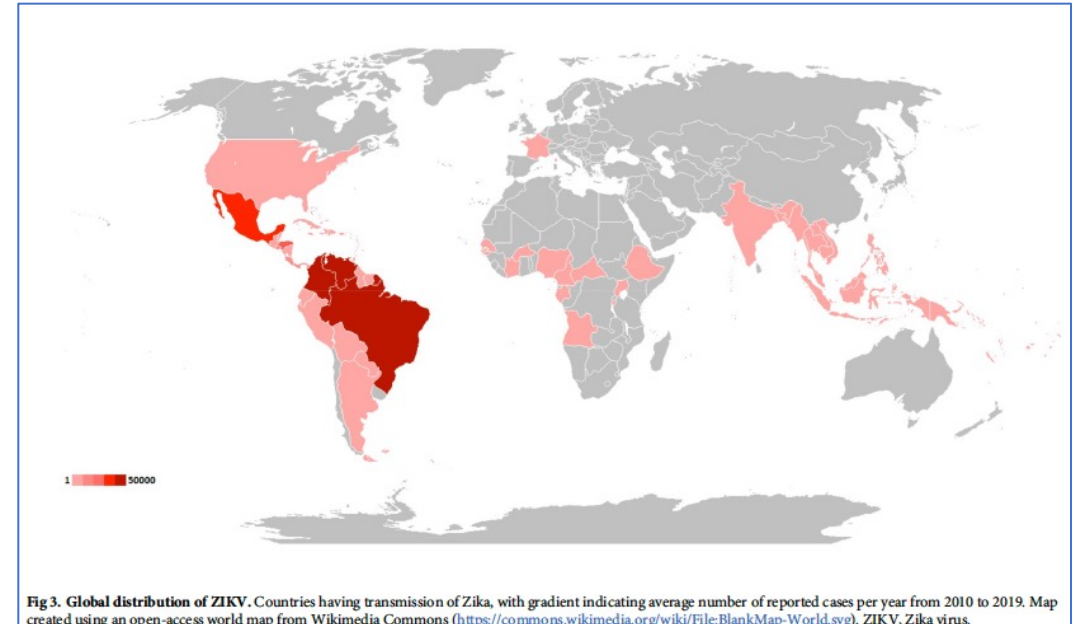


Dengue – Global burden



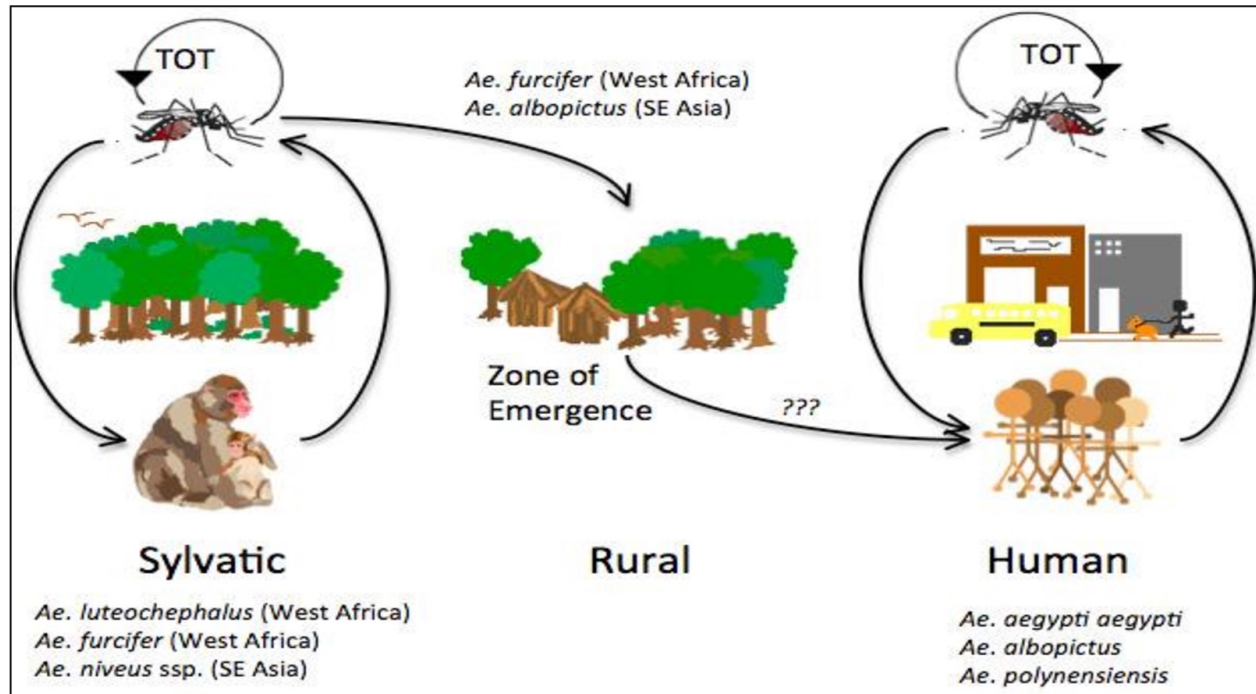
- Disease – broad spectrum (rash, fever to hemorrhaging, shock)
- 390 million infections, 96 million cases yearly
- Arbovirus – *Aedes aegypti* & *albopictus*
- Location – tropical & subtropical regions

Zika – Global burden

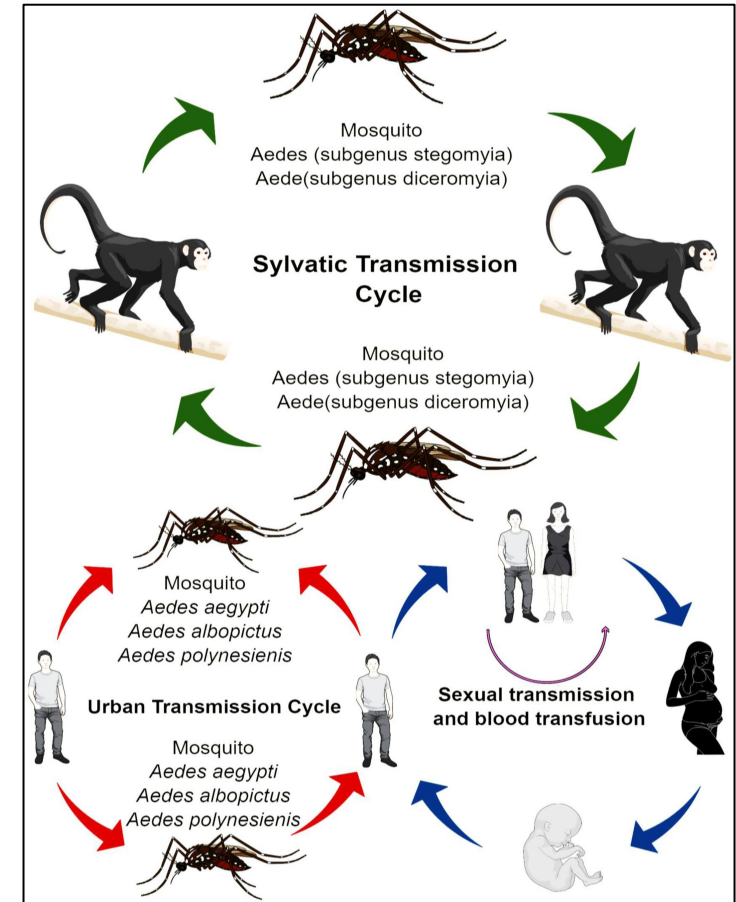


- Disease
 - Mostly asymptomatic or mild fever
 - Chronic disease – congenital, neurological
- Global burden of cases not well characterized
- Arbovirus – *Aedes aegypti* & *albopictus*

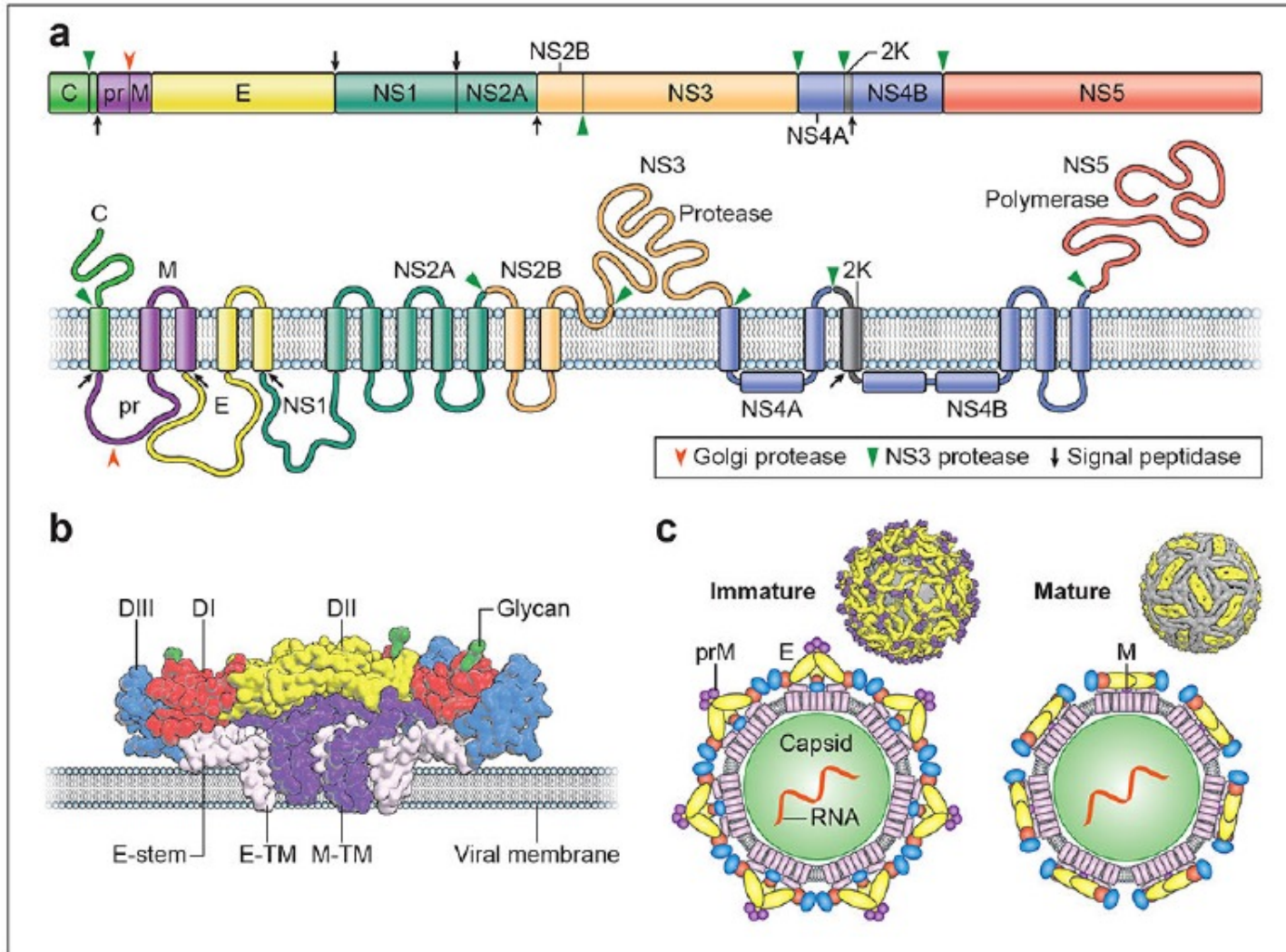
Transmission cycles of DENV



Transmission cycles of ZKV



Dengue and Zika virus structure & genome



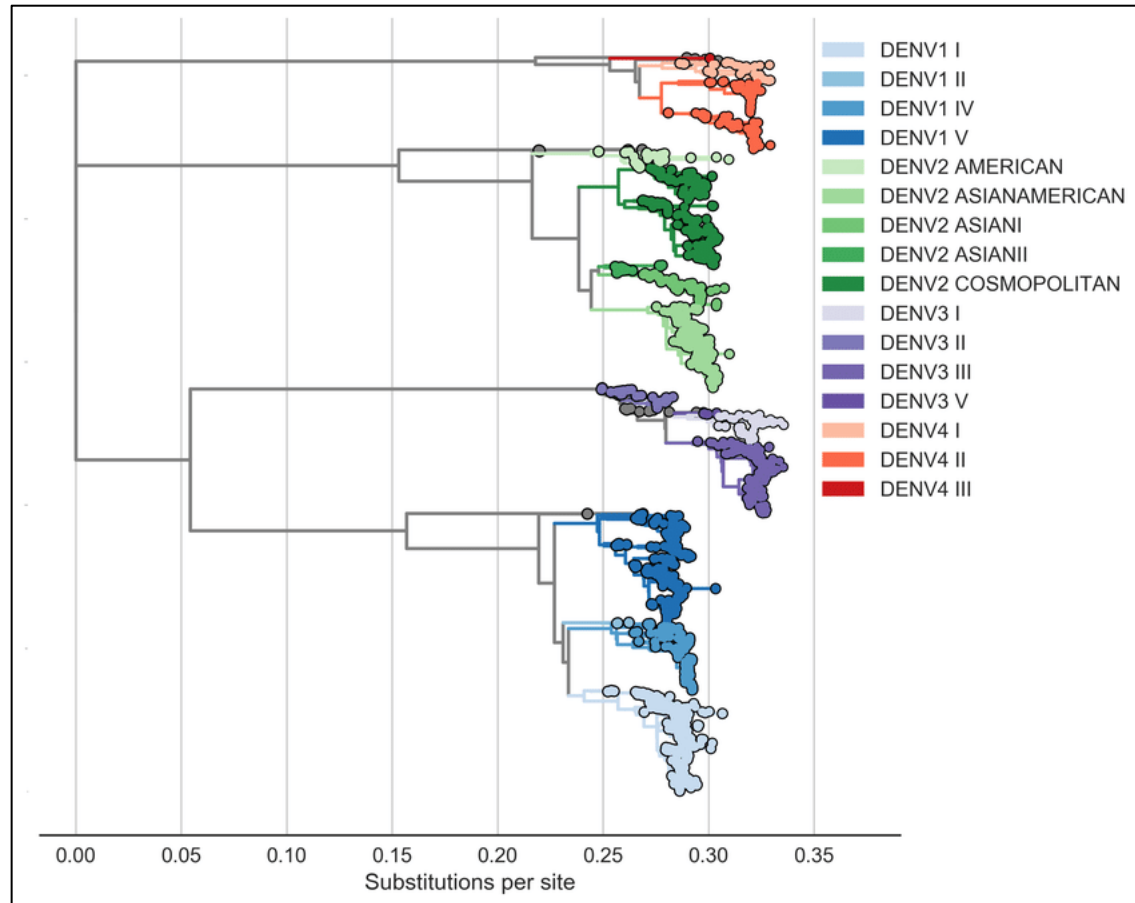
- Dengue and Zika have complex viral structures with surface glycoproteins assembled into an icosahedral virus
- Envelope or E protein is the target of neutralizing antibodies
- Enveloped virus
- 11 Kb Genome encoding 3 structural & 7 non-structural proteins.
- 1 long single stranded RNA strand genome and translated to one long polypeptide

TABLE 4 Methods for the diagnosis of human *Flavivirus* infections.

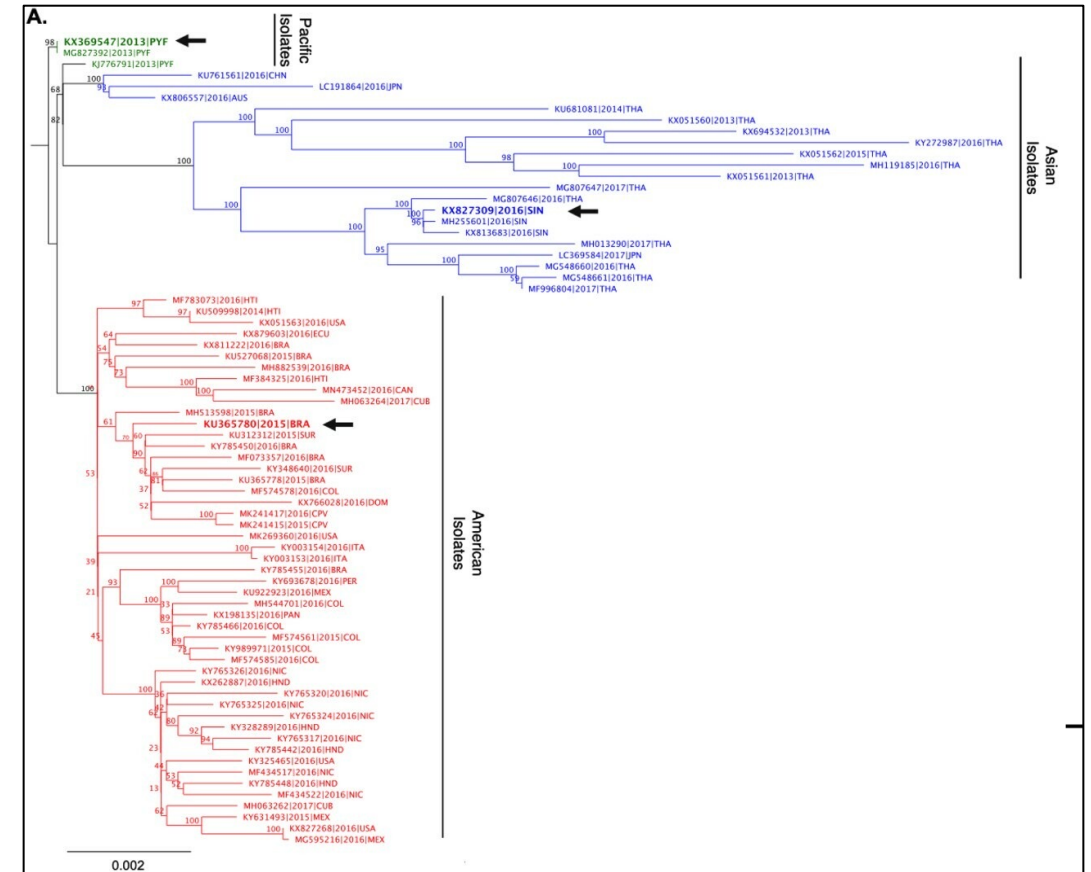
Methods	Advantages	Limitations	References
Virus isolation	<ul style="list-style-type: none"> • Direct pathogen detection • Most specific and conclusive diagnosis 	<ul style="list-style-type: none"> • Time consuming • Laborious • Requirement of acute sample • Biosafety Laboratory considerations of level 2–4 	<ul style="list-style-type: none"> • (Goncalves et al., 2017) • (Musso and Desprès, 2020) • (Samuel Sulca Herencia, 2019)
RT-PCR	<ul style="list-style-type: none"> • Detection of viral nuclei acids • High sensitivity and specificity • Rapidity 	<ul style="list-style-type: none"> • Require careful handling to prevent cross-contamination • Require specialized instrumentation • Expensive 	
Viral antigen capture	<ul style="list-style-type: none"> • Detection of acute of DENV based on the capture of soluble NS1 • Easy to perform 	<ul style="list-style-type: none"> • Only available for DENV • Less accurate than viral isolation • Requirement of acute sample 	
Serology	<ul style="list-style-type: none"> • Detection through the capture of IgG/IgM or virus neutralization assays • Qualitative and quantitative serological diagnosis tests 	<ul style="list-style-type: none"> • Limited specificity and sensitivity • False interpretation of DENV diagnostic might occur during the secondary DENV infection 	

Phylogeny of DENV and ZKV

DENV viruses (based on whole genomes)



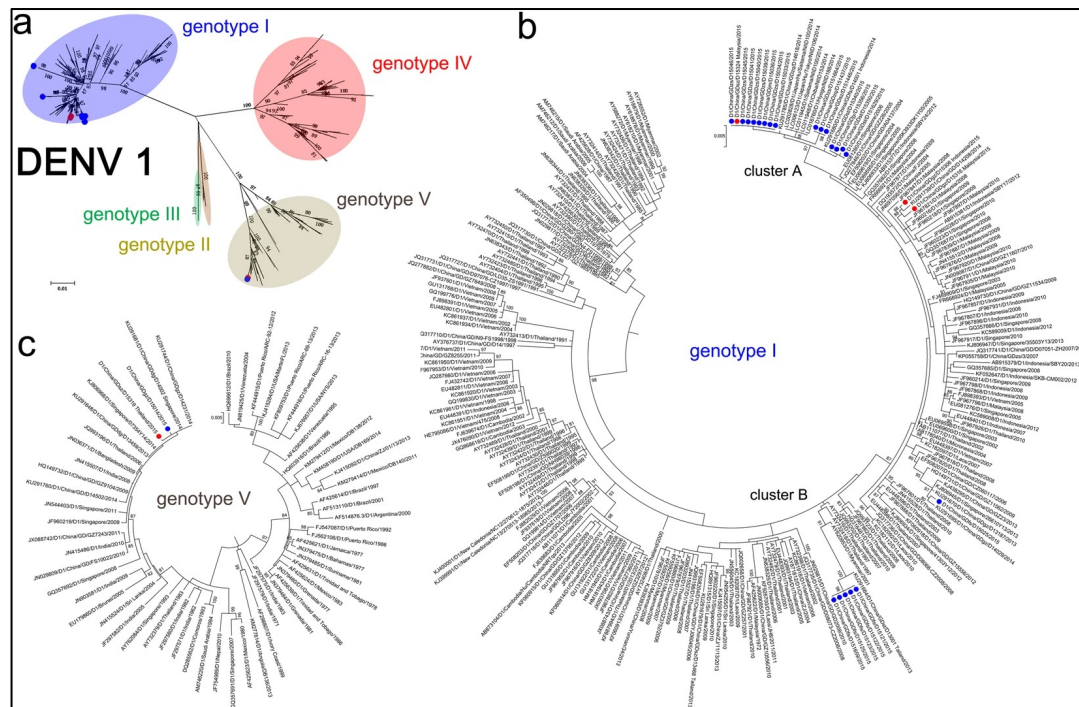
ZKV viruses (based on whole genomes)



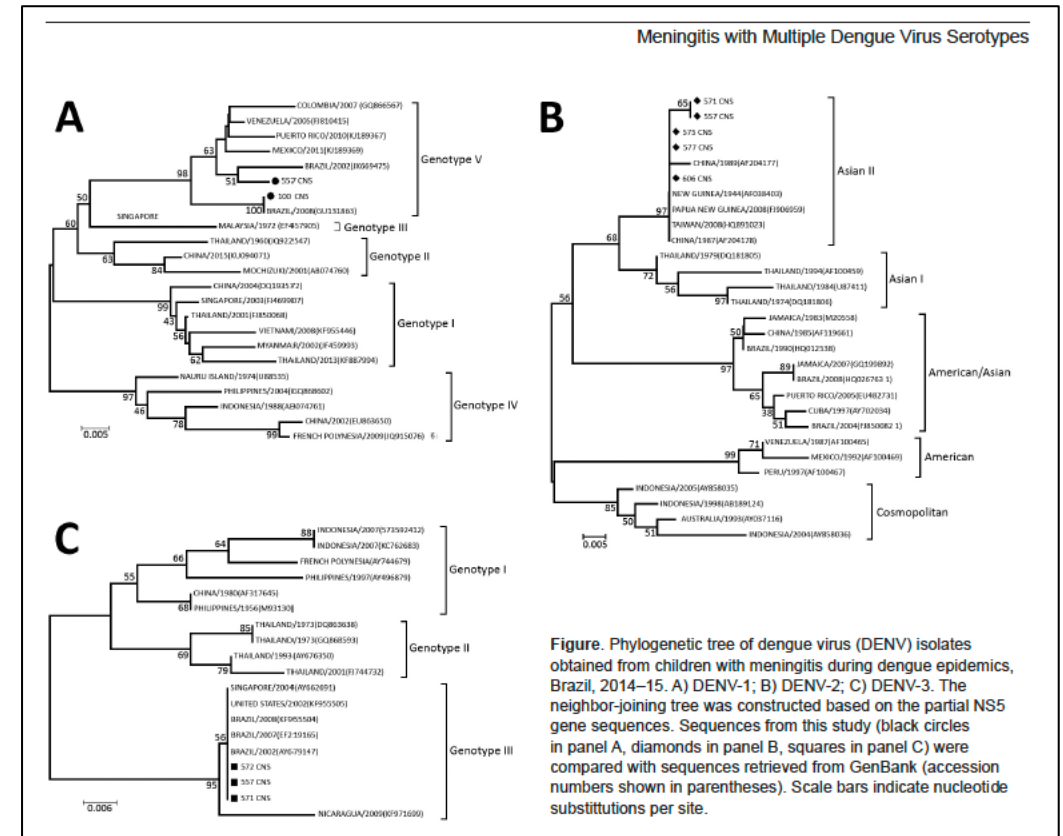
De Alwis R et al, 2021, EMI

Historically mostly E and NS5 protein sequenced

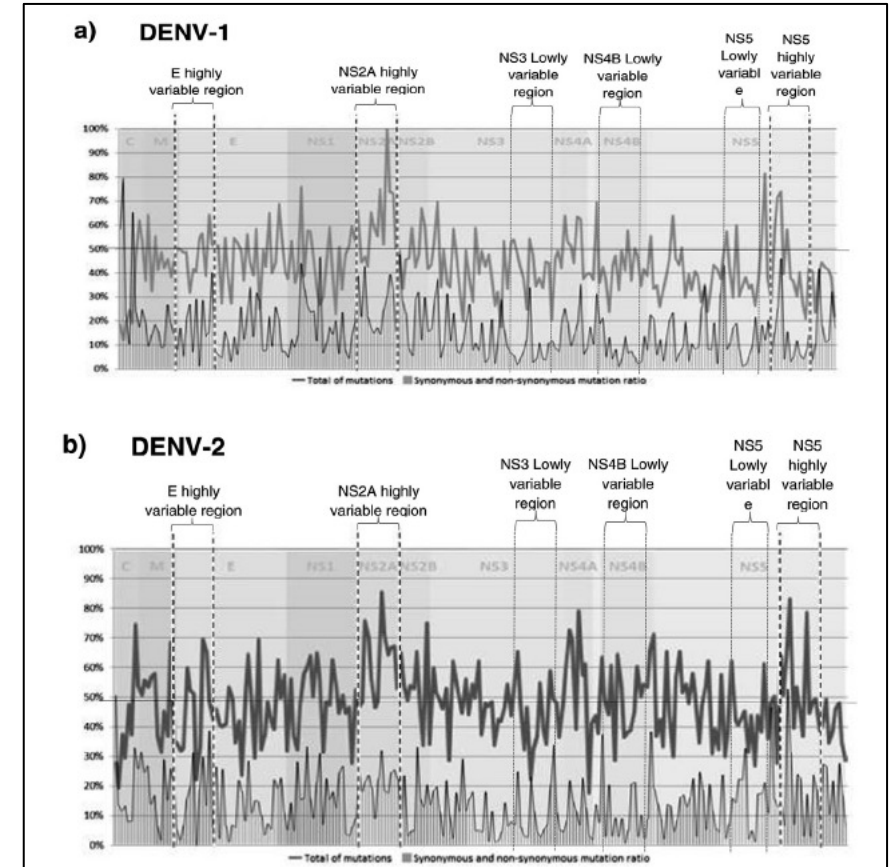
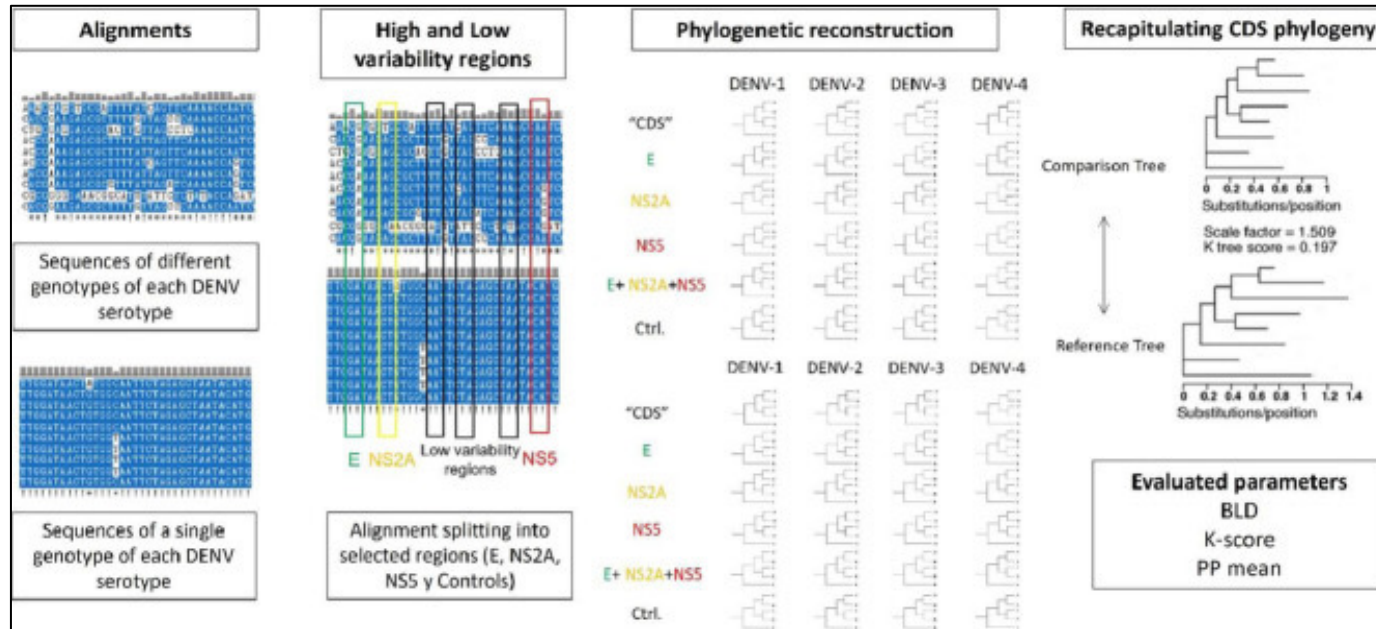
DENV phylogeny based on E protein sequences

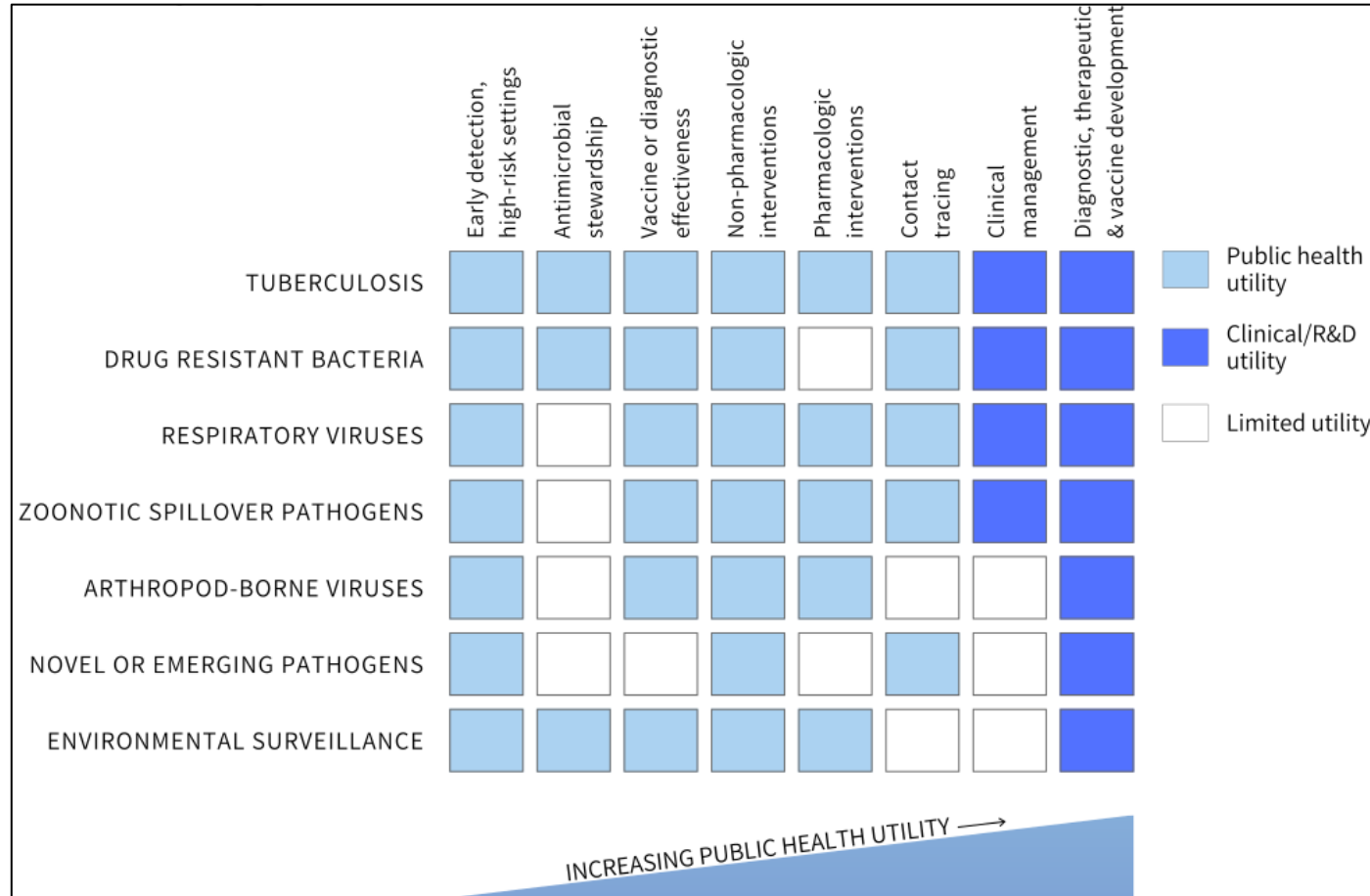


DENV phylogeny based on NS5 sequences



High genome diversity at locations of E, NS2 and NS5





Discussion

Pronyk P et al 2023 Cell Genomics

Thank you