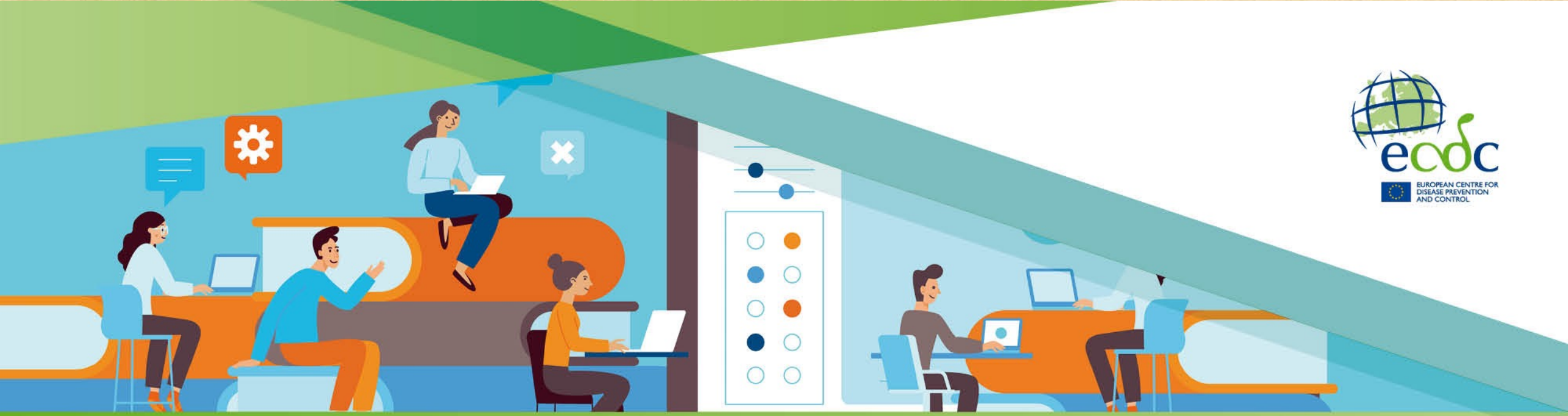

Genomics and epidemiology of polioviruses: How a virus resists eradication

Epidemiology and Genomic Surveillance

July 2027

Darlan da Silva Candido, PhD, Imperial College London

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Aim and learning objectives

Understand basic concepts of phylogenetic analysis of viral outbreaks and its applications to poliovirus epidemiology

Specific learning objectives

At the end of this session, you will be able to:

1. **Describe** the principles of viral phylogenetics and genomic epidemiology.
2. **Explain** how pathogen genome sequences can be used to investigate viral outbreaks, with examples from poliovirus and other viruses.
3. **Interpret** basic phylogenetic trees and identify the epidemiological information they provide.
4. **Apply** fundamental phylogenetic concepts to answer questions about outbreak transmission using real sequence data.
5. **Evaluate** simple phylogenetic outputs in a guided practical exercise and discuss their epidemiological implications.

Outline

This session consists of the following elements

1. The world of genomic epidemiology
2. Refresher on polioviruses
3. Polio example 1: Unravelling routes for international spread
4. Polio example 2: Assessing poliovirus surveillance and response
5. Basic phylogenetic concepts
6. Practical activity

1. The world of genomic epidemiology

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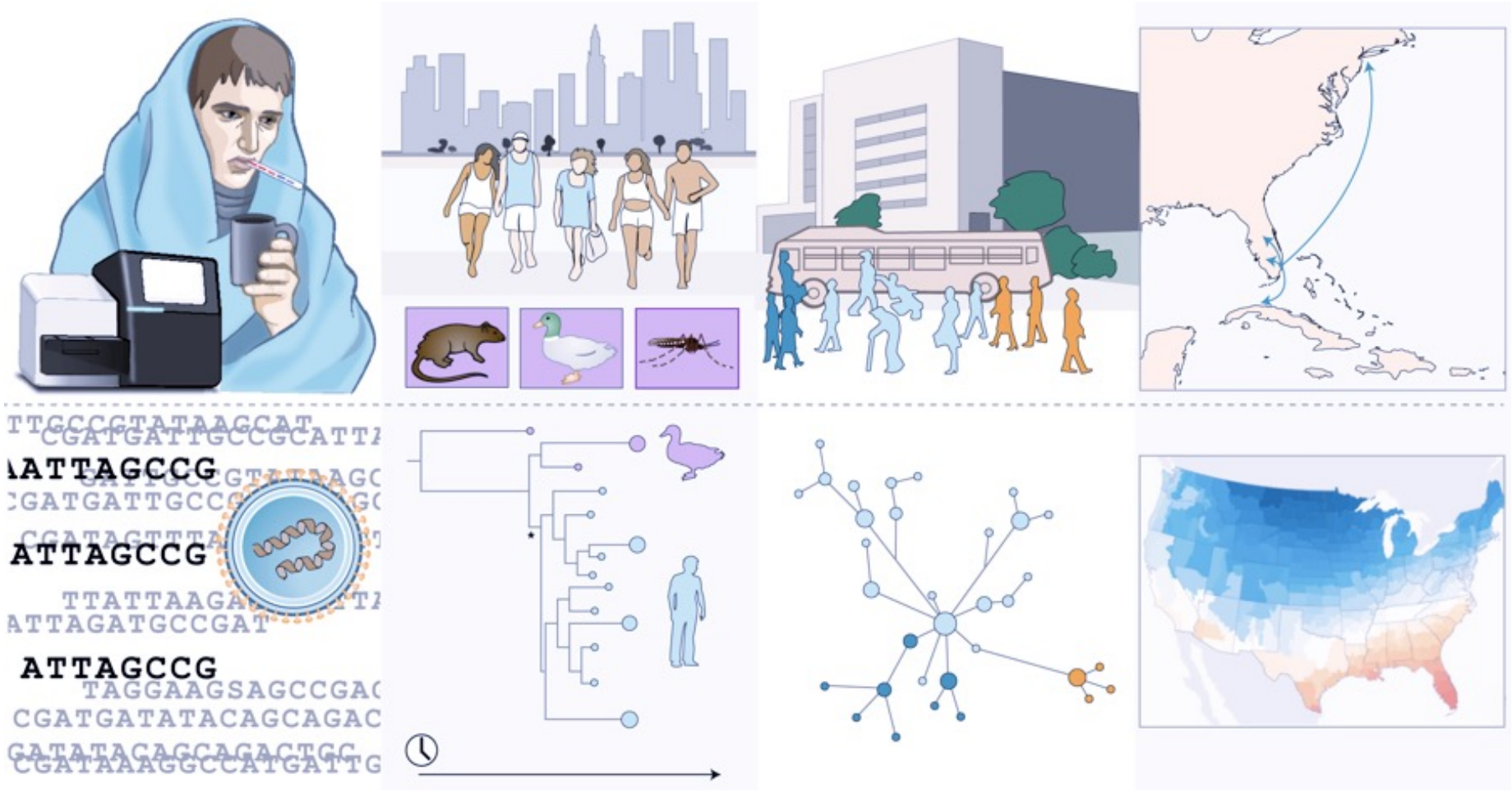
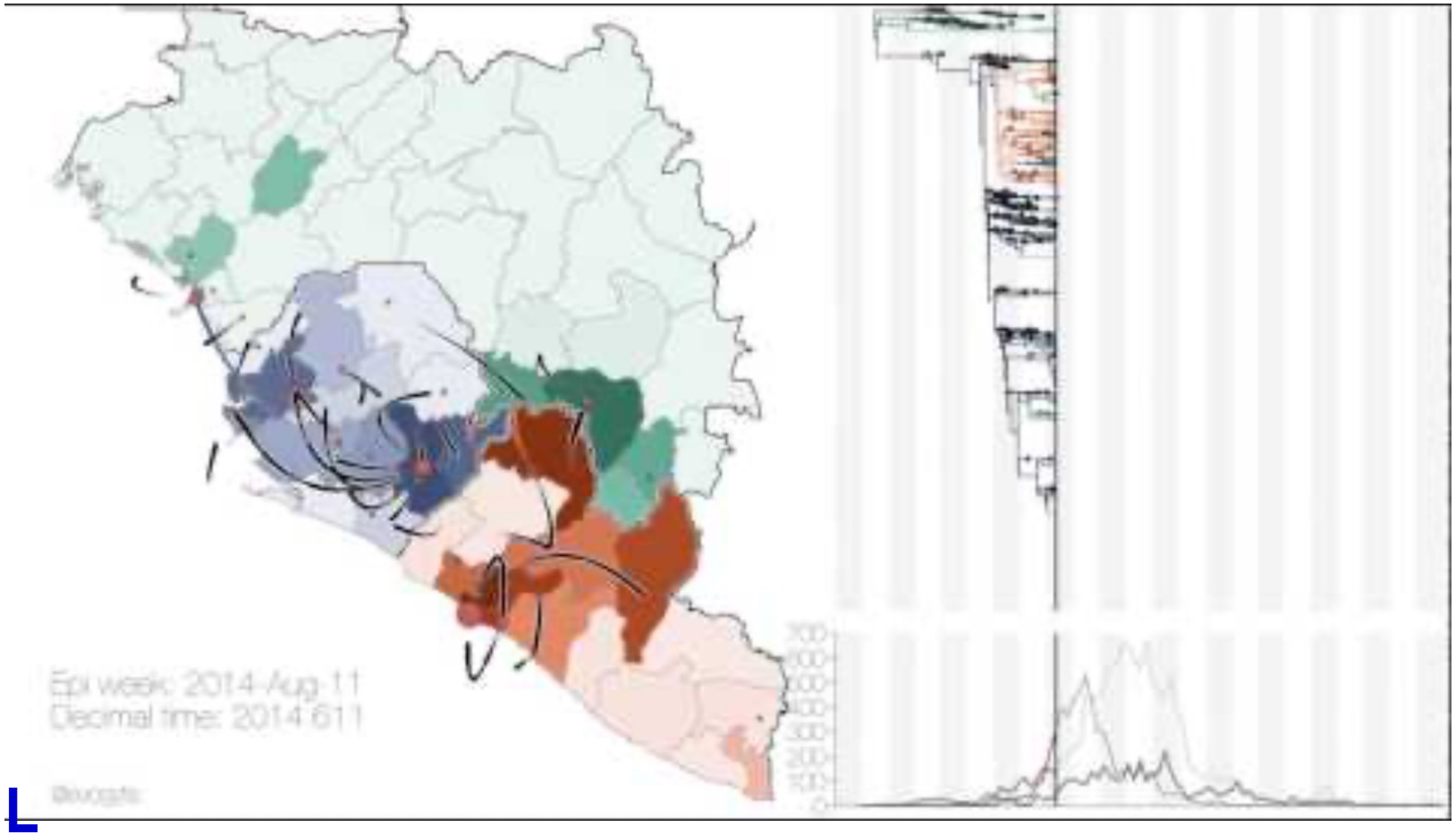
Why do we sequence pathogens?



Grubaugh et al, Nature Microbiology, 2019

The 2013-2016 West African Ebola virus epidemic

- 1610 genomes (5% of all cases)
- Gravity model dynamics of spread: large and close populations
- Closing of borders was not effective
- Spatially dissociated collection of transmission clusters of varying size, duration and connectivity



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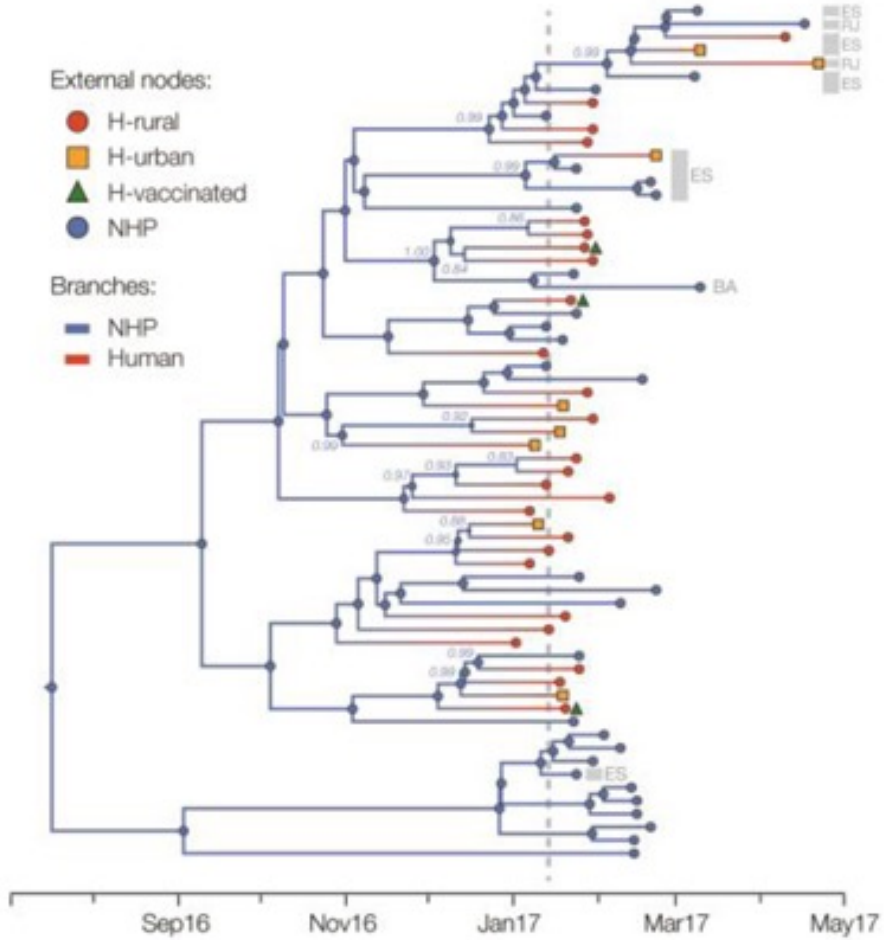
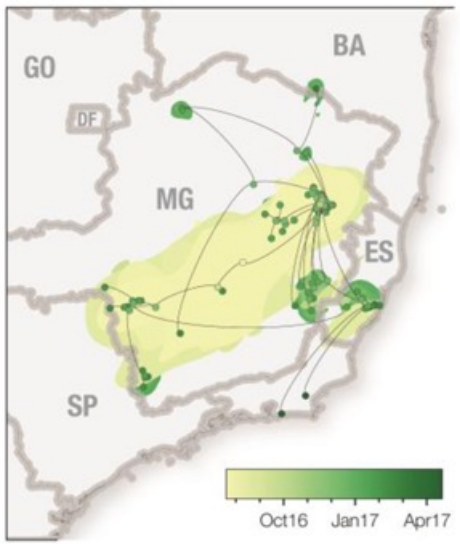
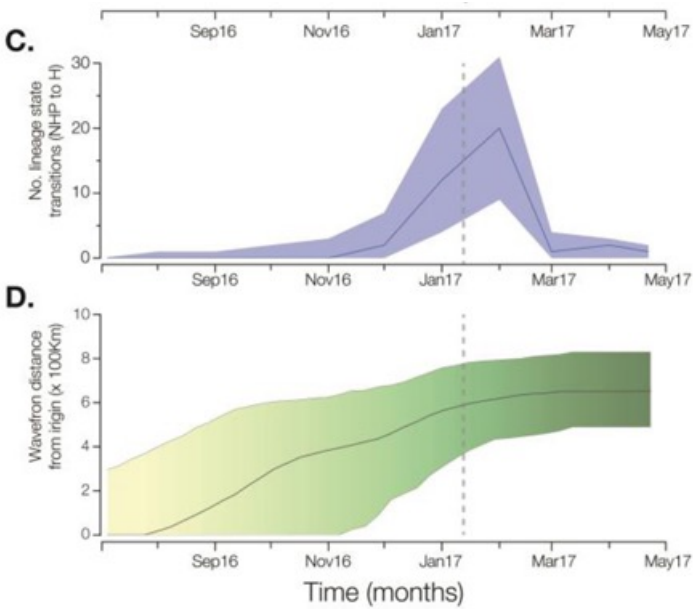
Dudas et al, Nature, 2017

The 2016-2017 Yellow fever outbreak in Brazil







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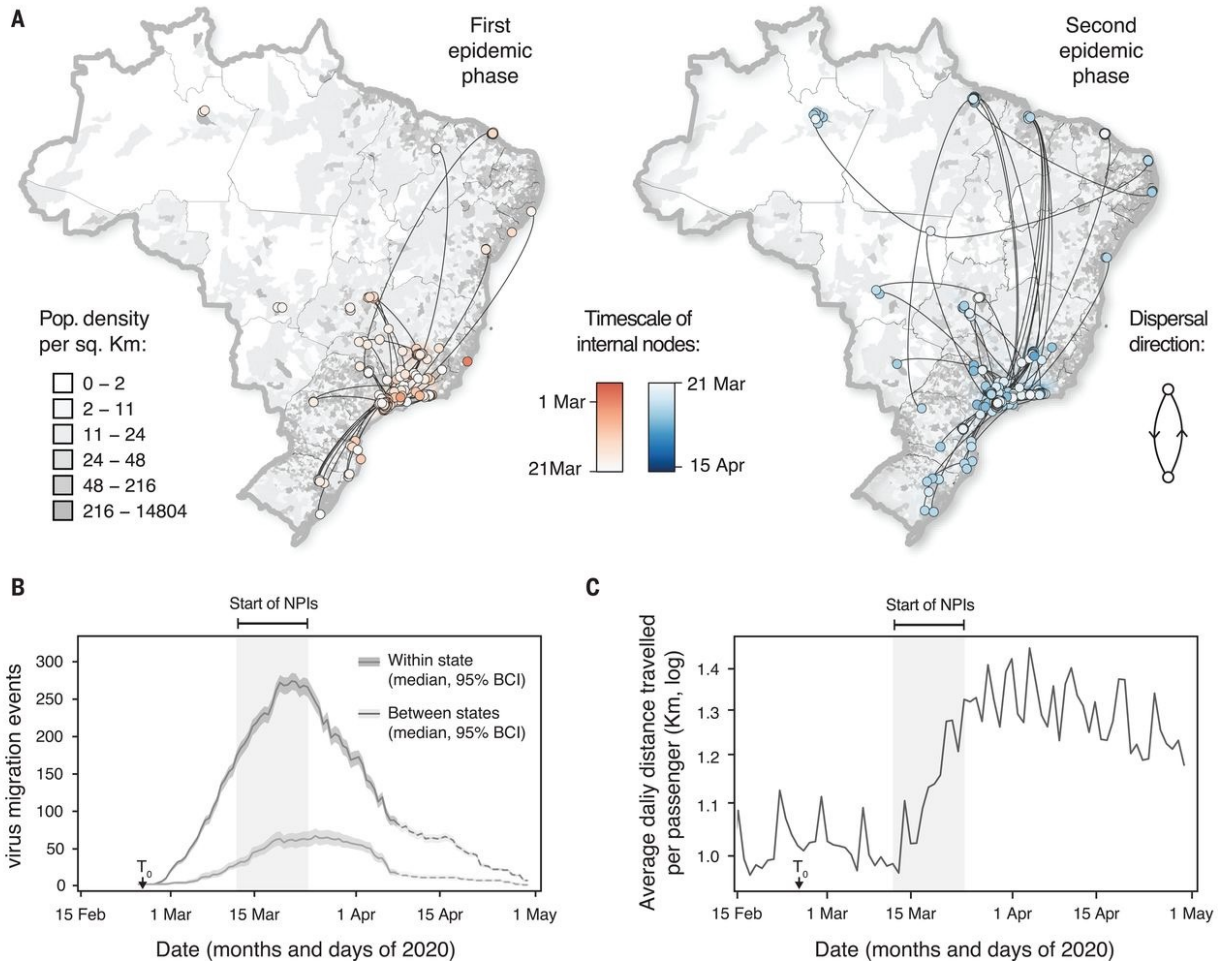
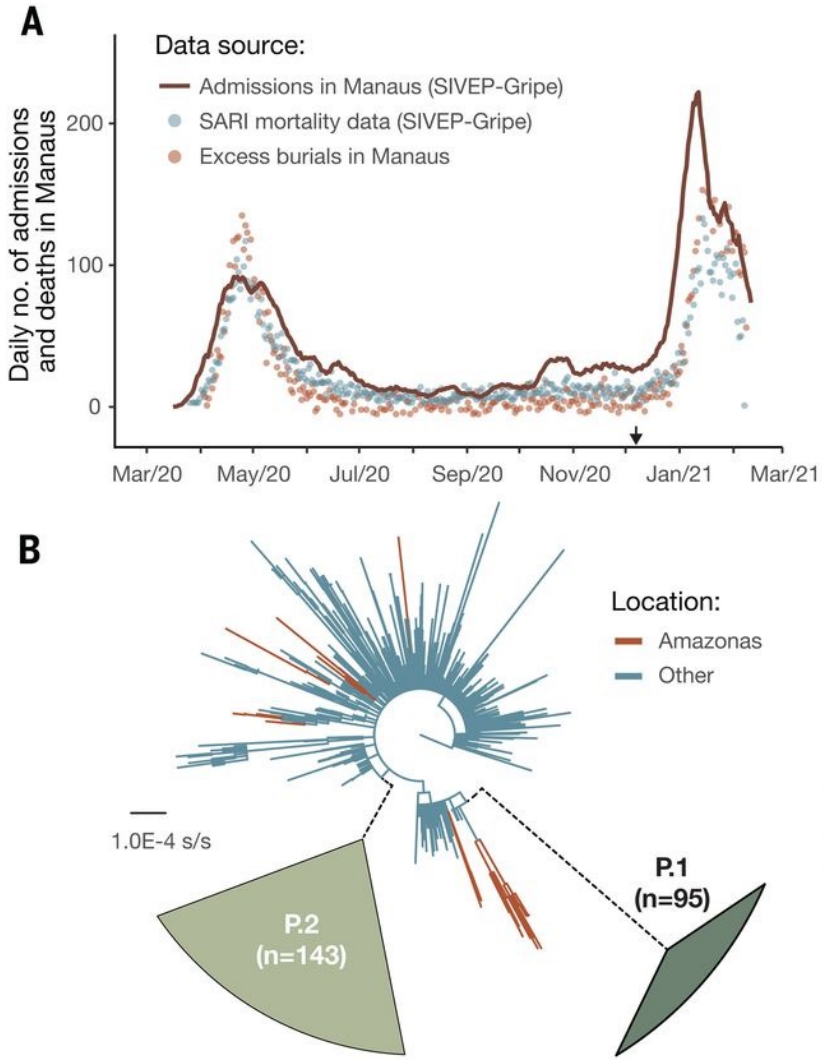
Faria et al, Science, 2018

The SARS-CoV-2 pandemic



Candido et al, Science, 2020



Faria et al, Science, 2021

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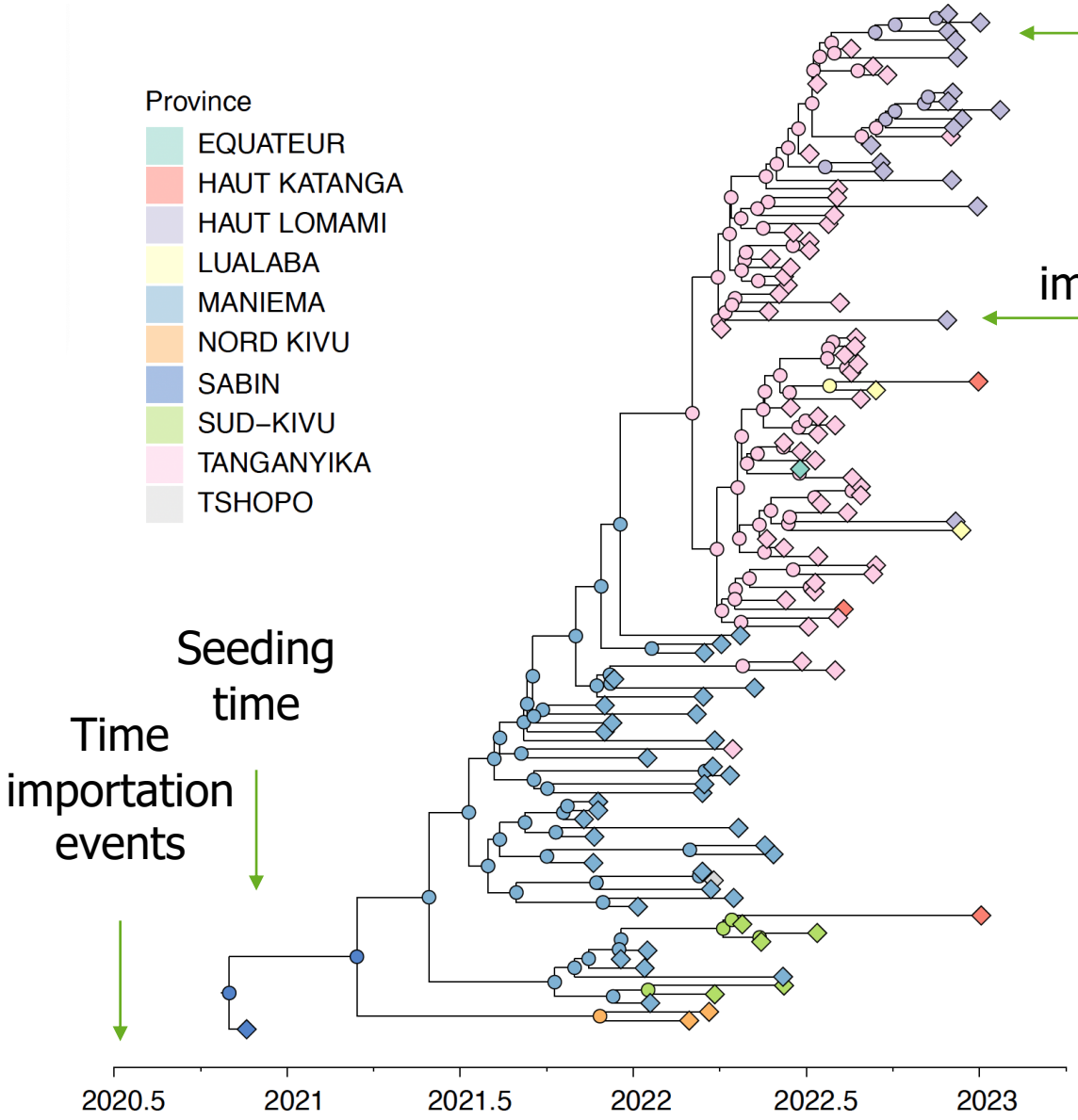
What can we learn from sequence data?

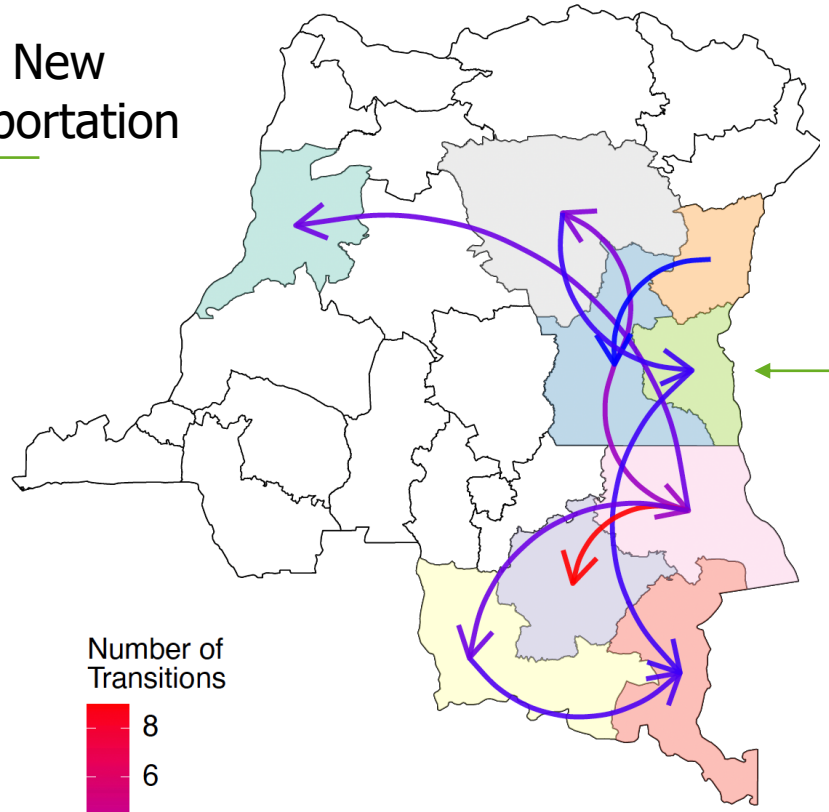


Local spread

New importation

Seeding time

Time importation events



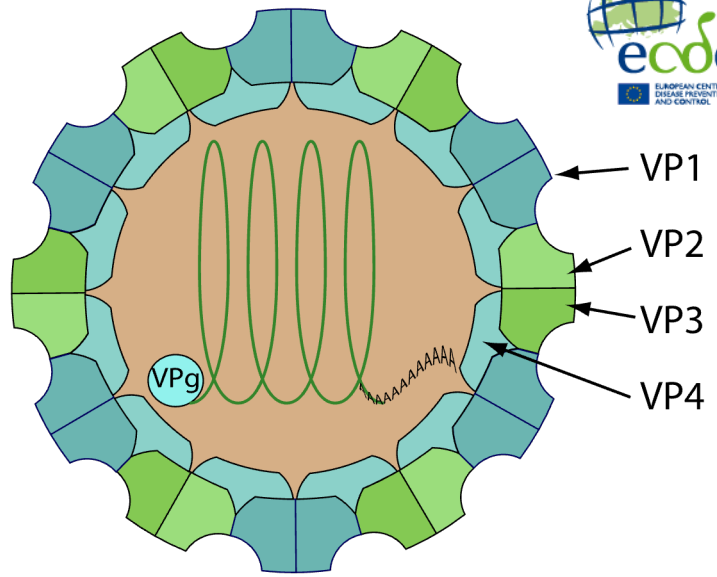
Origins and/or routes

Intensity

2. Refresher on polioviruses

The biology of polioviruses

- Causative agent of poliomyelitis (polio acute flaccid paralysis – AFP) ;
- Fecal-oral transmission;
- VP1 is the main capsid protein (~ 900 nucleotides);
- Evolutionary rate: approximately 1x10-2 substitutions/site/year;
- 3 serotypes: WPV1 , WPV2 (eradicated in 2015), and WPV3 (2019);
- Only 2 countries are endemic for WPV1: Pakistan and Afghanistan;
- 99.9% of transmission reduction;
- Vaccines: IPV (Salk) and OPV (Sabin);



OPV (Sabin)
• Attenuated; • Cheaper; • Easier to store, transport and administer; • Prevents transmission; • Genetically unstable;

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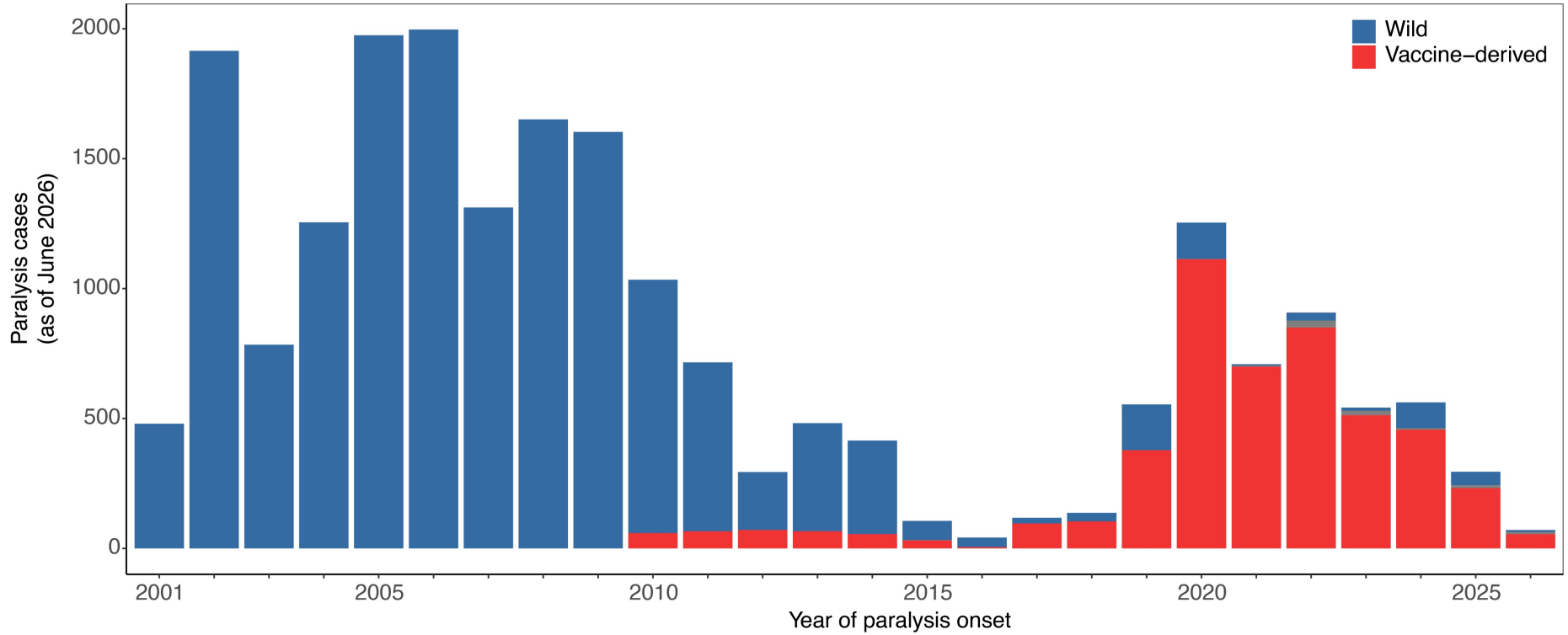
WHO; Jorba et al, *Journal of Virol*, 2008; GPEI; Macklin et al, *Science*, 2020; Jorgensen et al, *Virus Evol*, 2020;

Vaccine-derived poliovirus 2

- Public Health Emergency of International Concern (PHEIC);
- Outbreaks of acute flaccid paralysis caused by oral polio vaccination;
- Over 4400 cases of acute flaccid paralysis between May 2016 and May 2026;
- Over 100 outbreaks in 45 countries worldwide;
- VDPV 2: 6 or more mutations from Sabin 2;
- Sabin-like: up to 5 mutations from Sabin 2;



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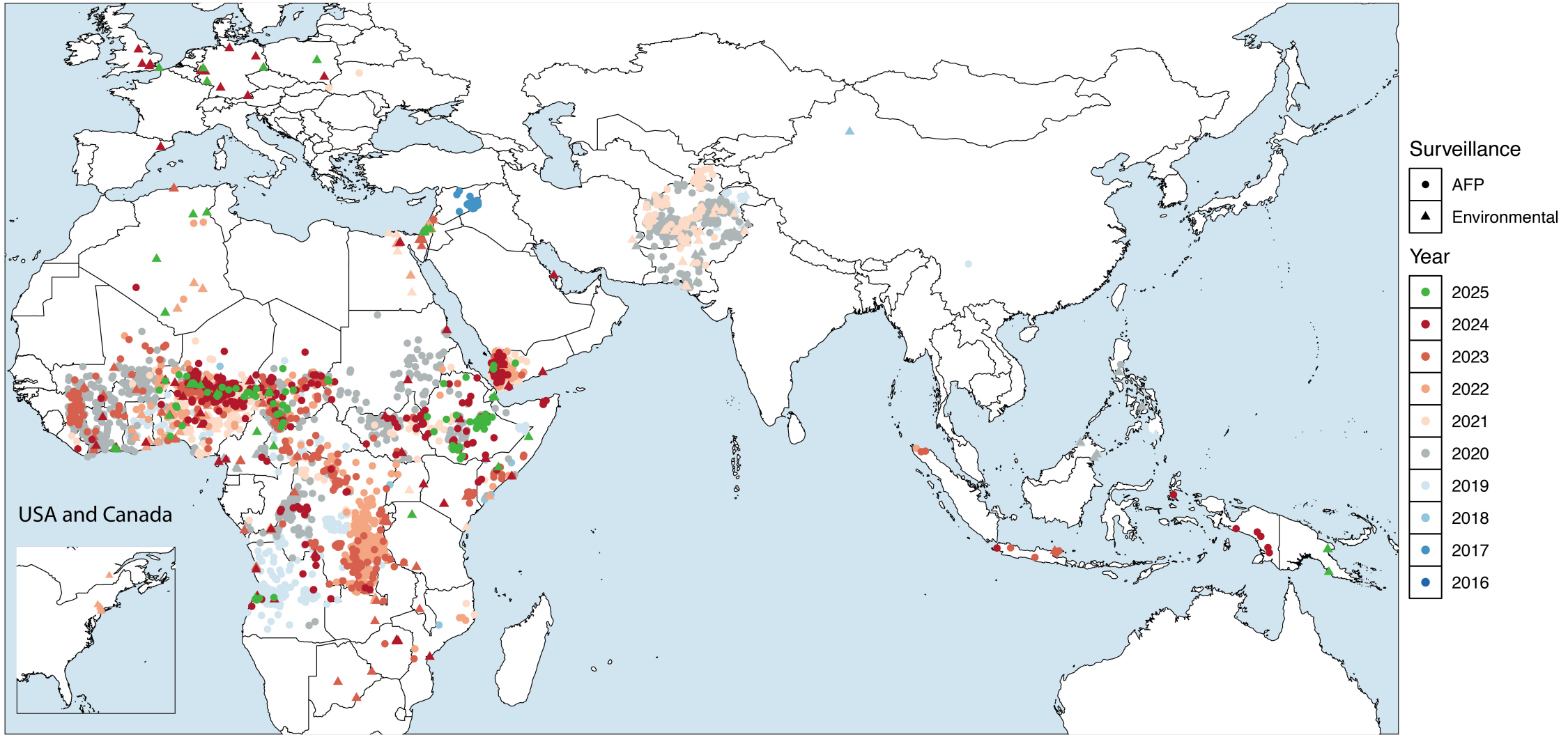
Candido et al, Nat Microbiol, 2025

Global burden of VDPV 2



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Candido et al, Nat Microbiol, 2025

3. Polio example 1: Unravelling routes for international spread

Candido et al, Nat Microbiol, 2025

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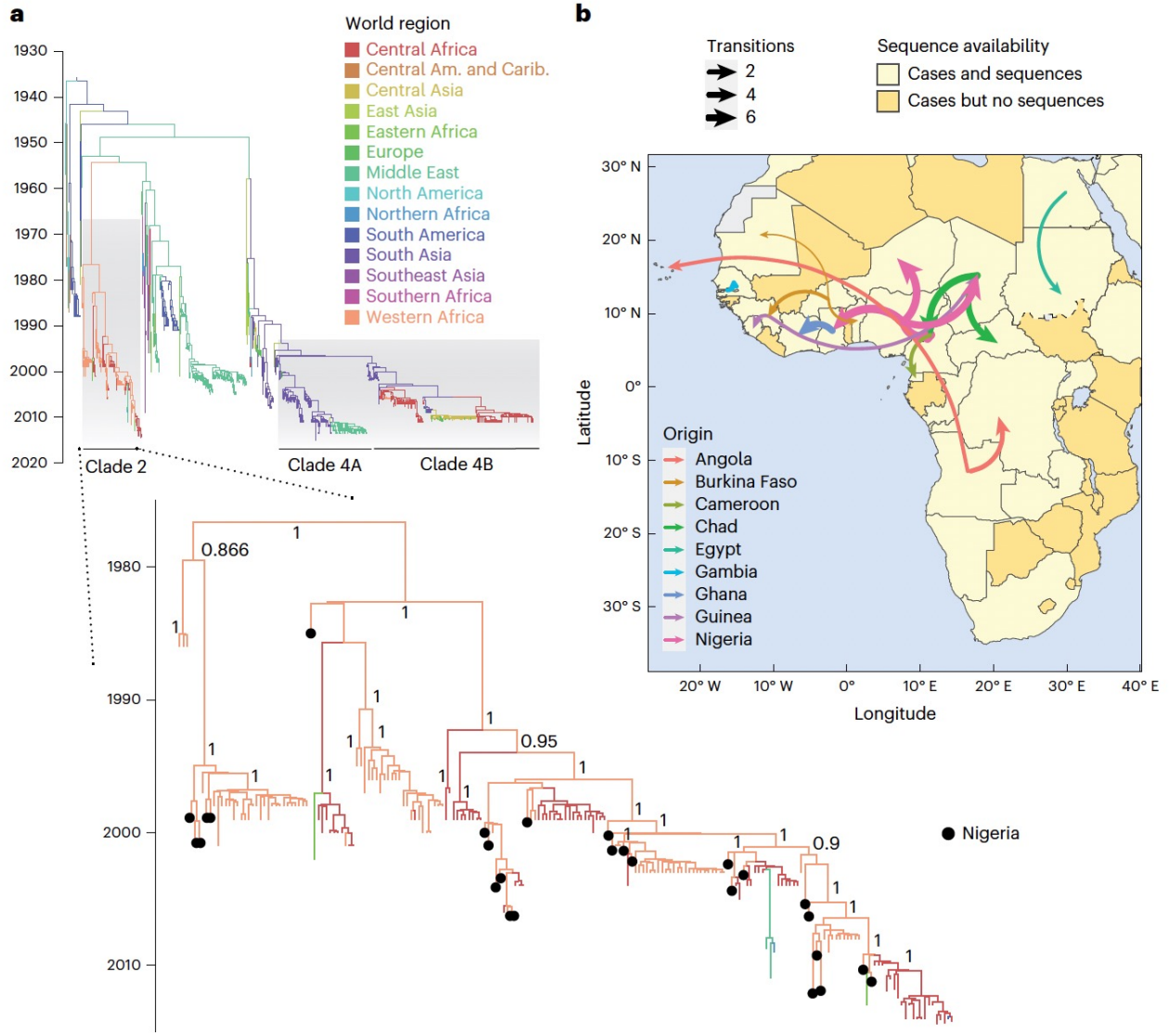
Global phylogeography of WPV1 spread

- 1,534 WPV1 sequences with collection date and country information (Publicly available);
- 38 newly generated historical; sequences (MHRA);
- Importing and exporting from immediate neighbours (77.7%);
- Nigeria is the main exporter within clade 2 (BF=19);
- Gatekeepers: Chad (6.24 exports), Ghana (3.41) , and Angola (2.56);
- No reversed directionality of movement;



Candido et al, Nat Microbiol, 2025

4. Polio example 2: Assessing poliovirus surveillance and response

Chopra et al, under review

Kieran Chopra, MRes
PhD candidate
Imperial College London

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RDC-MAN-3 outbreak in the DRC

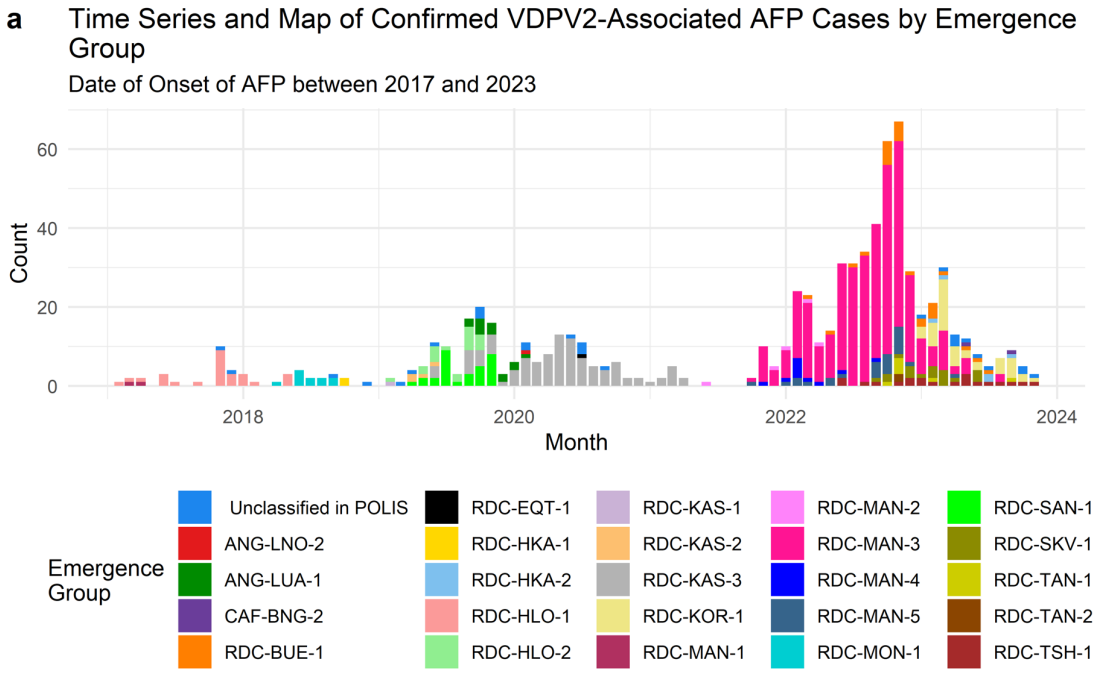
Between 2017 and early 2024, 757 confirmed VDPV2 cases were reported in the DRC

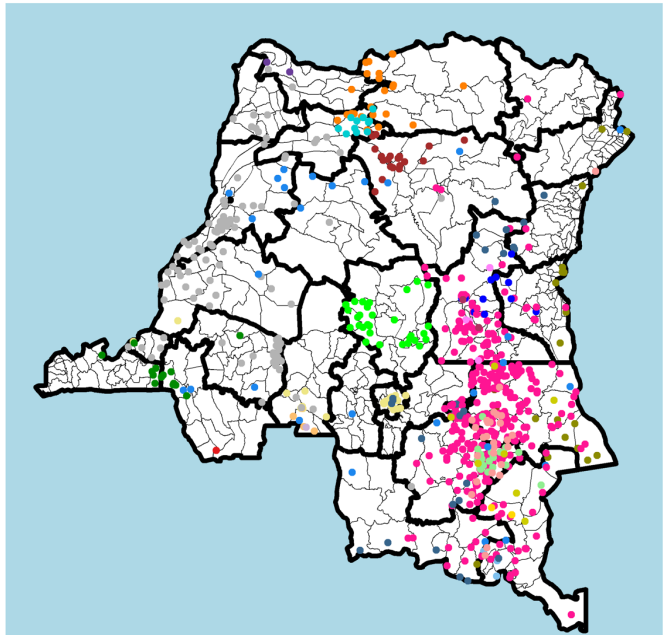
349 of which were from the RDC-MAN-3 outbreak

10 provinces with RDC-MAN-3 poliomyelitis cases spanning eastern DRC

130 sequences from RDC-MAN-3 (33%) polio outbreak in DRC

Sequences generated by Direct Detection Nanopore Sequencing (DDNS)

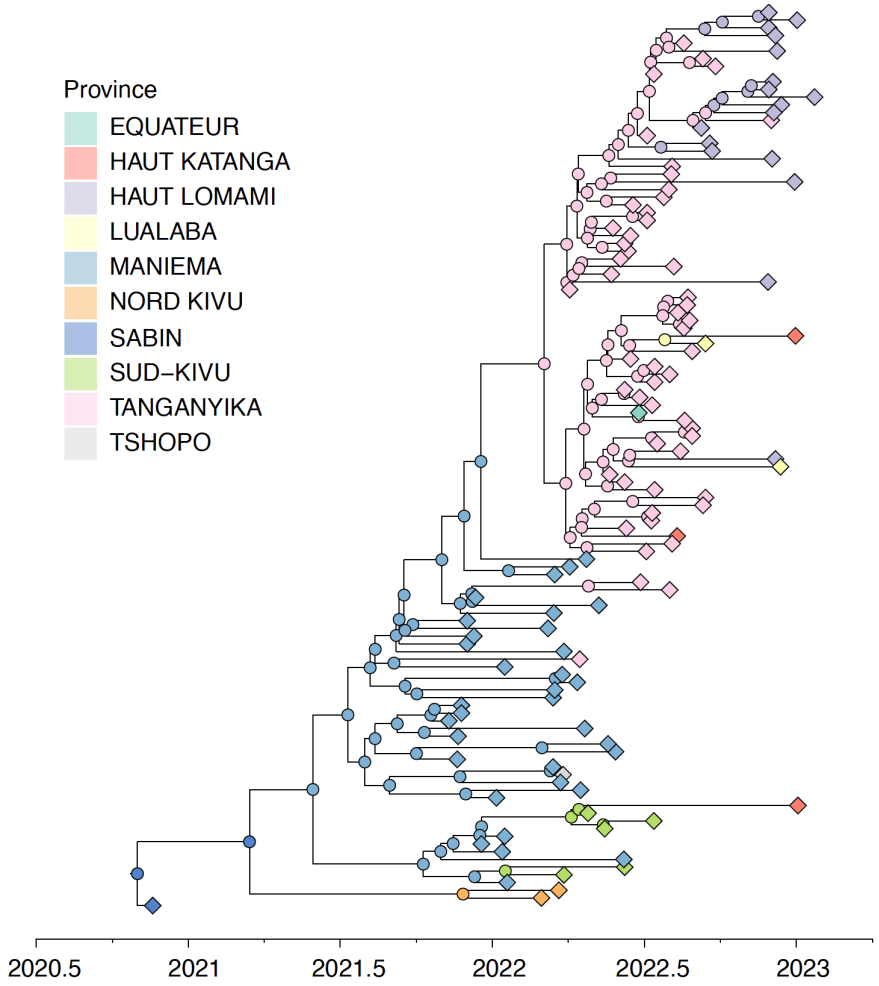


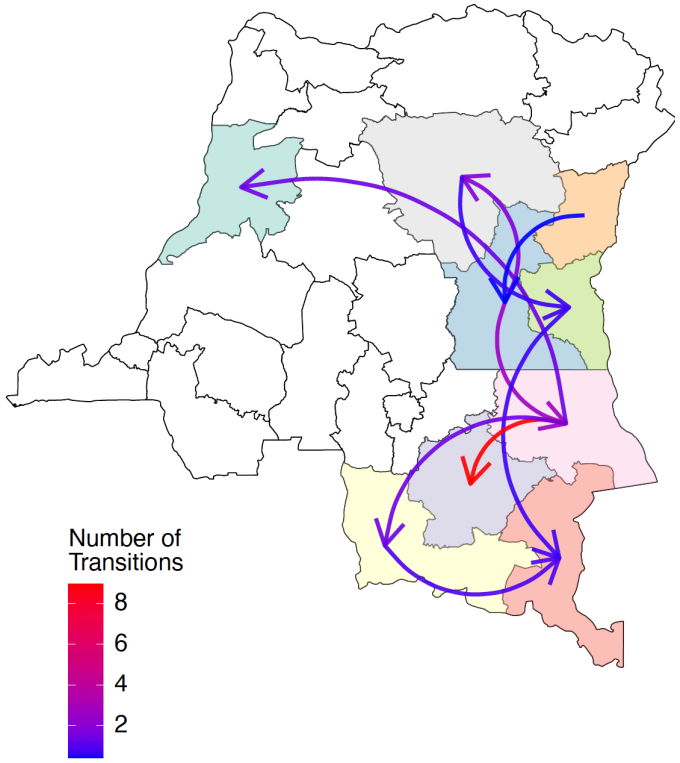


Chopra et al, Under review

Unveiling routes for spread

- Undetected transmission by about 1 year;
- Majority of transmission is local (within ADM1)
- 19.9 (69.5%) jumps between neighbours vs 8.74 (30.51%) between non-neighbours
- Outbreak likely spread to Haut Lomami before Haut Lomami was vaccinated

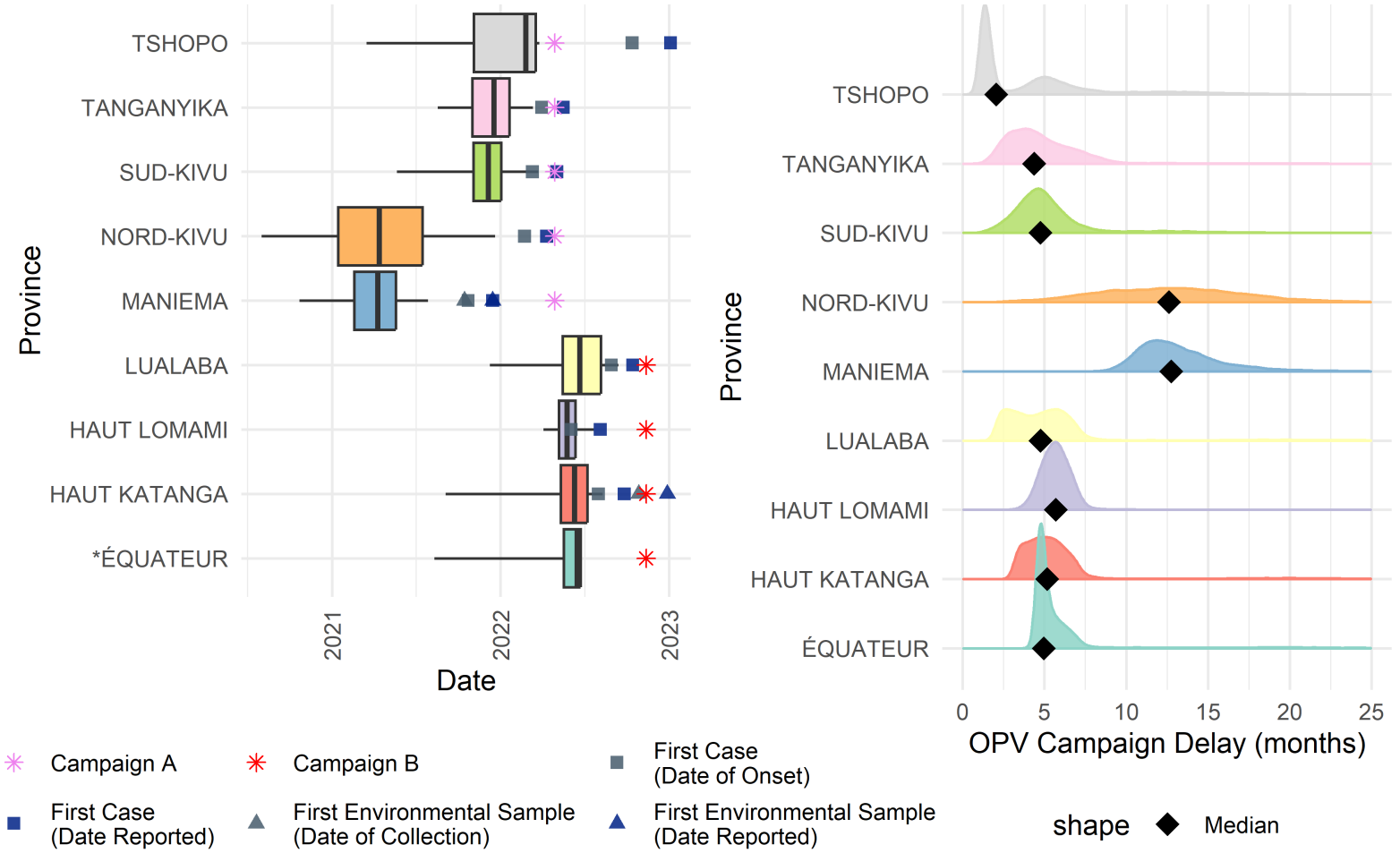




Chopra et al, Under review

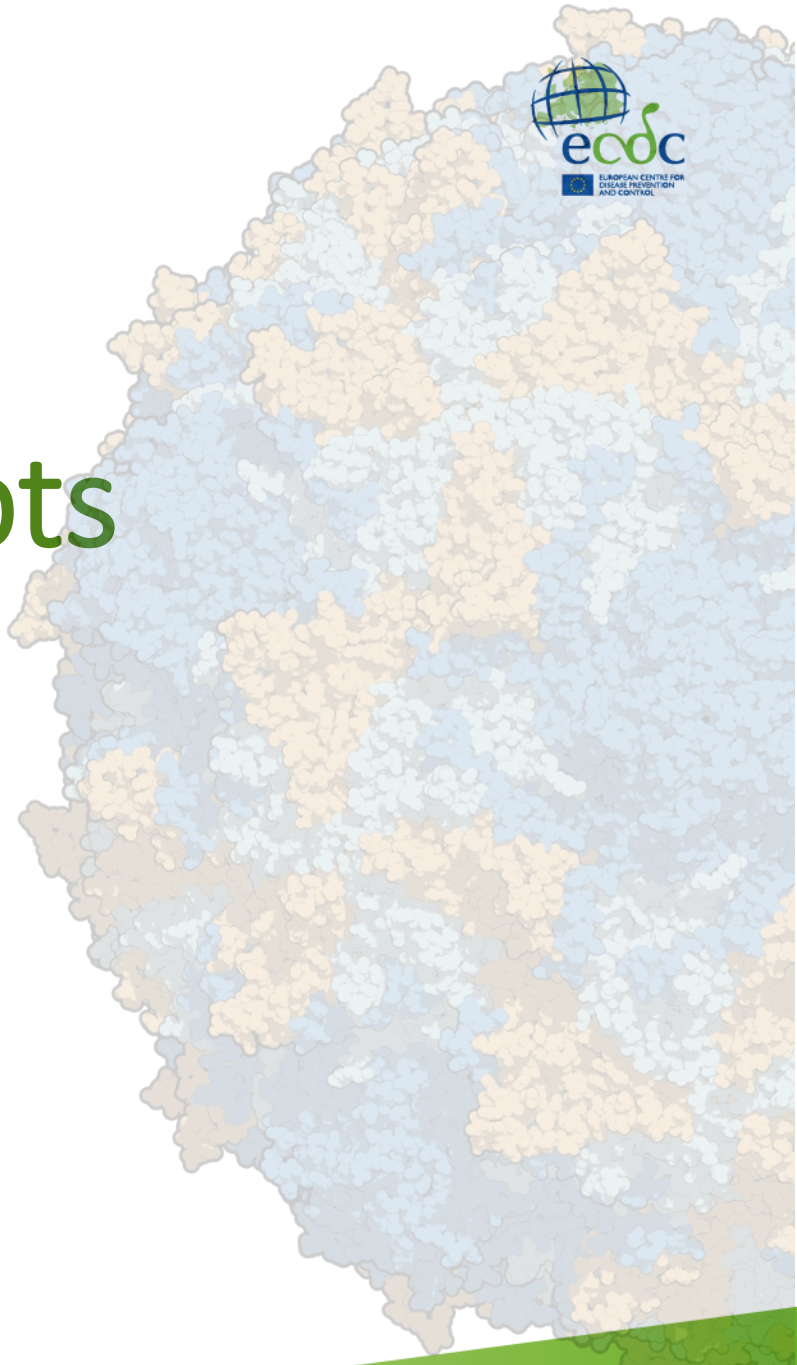
Chasing the virus: vaccination response

- All first importations into new provinces happened before vaccination responses in that area started
- The median delay between introduction and response per province is of at least 5 months but can be as high as 1 year;



Chopra et al, Under review

5. Basic phylogenetic concepts



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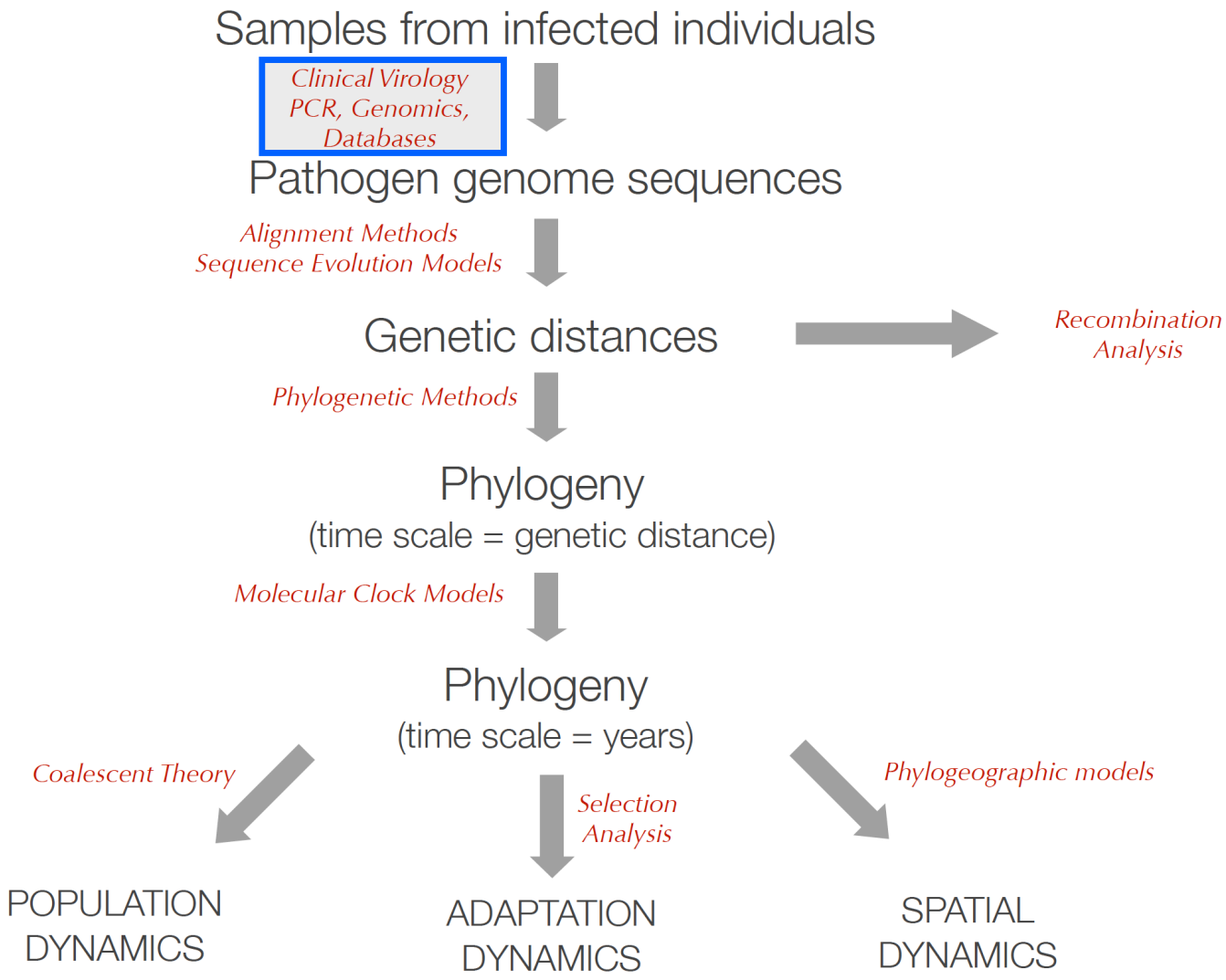
What is our objective? What are we trying to answer?

- Identify pathogen
- Understand pathogen diversity
- Outbreak origins
- Number of introductions
- Time importation events
- Estimate growth rate

Analysis pipeline



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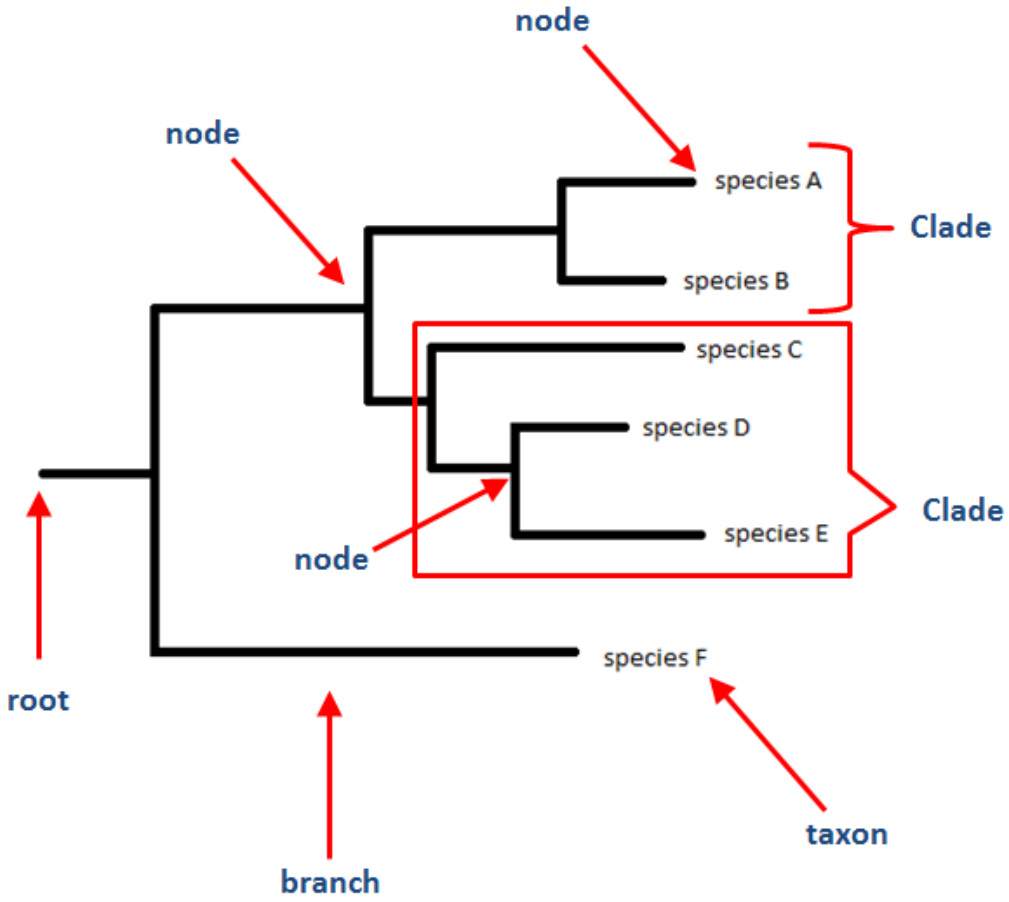
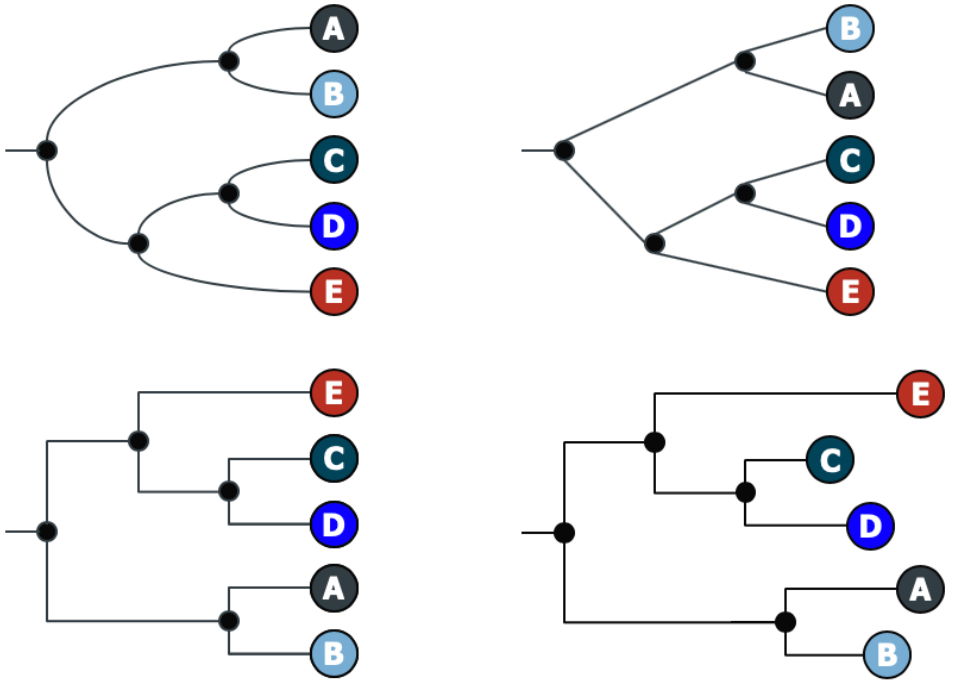
Phylogenetic tree

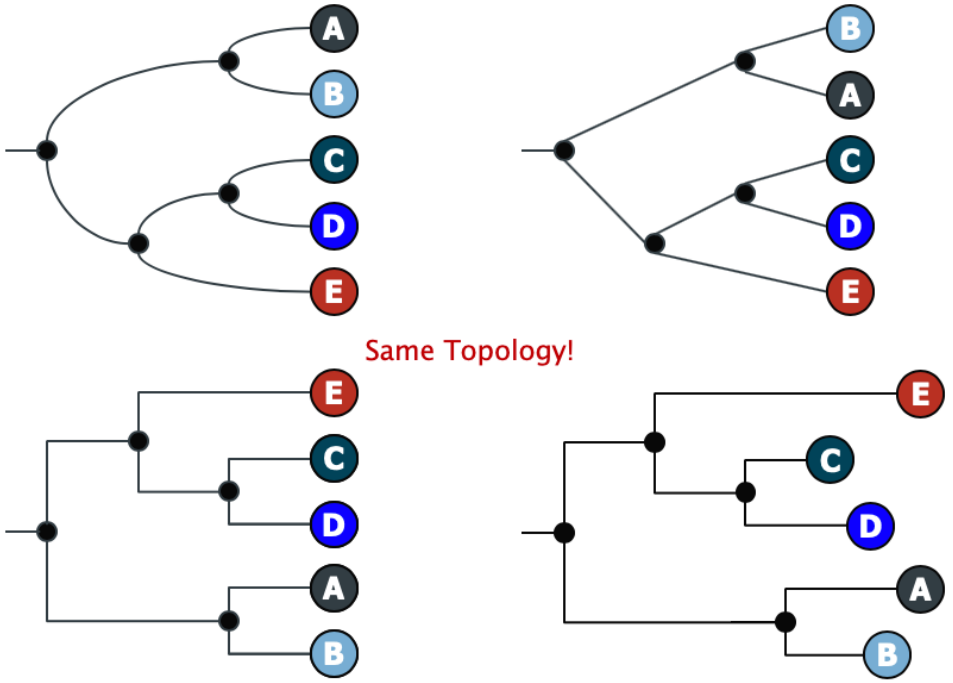


Tree topology



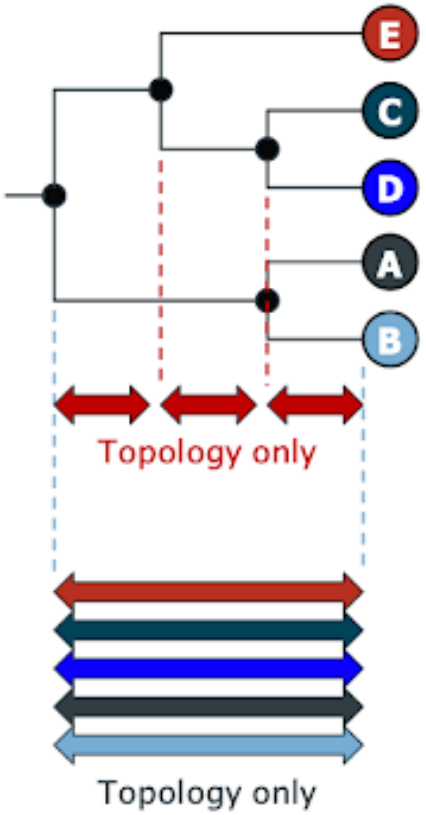
Source: http://cabbagesofdoom.blogspot.com/2013/04/how-to-read-phylogenetic-tree.html

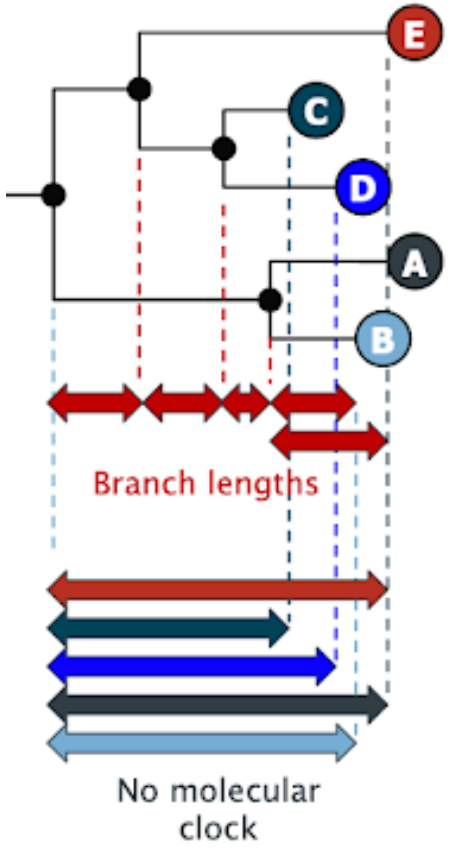
Tree topology

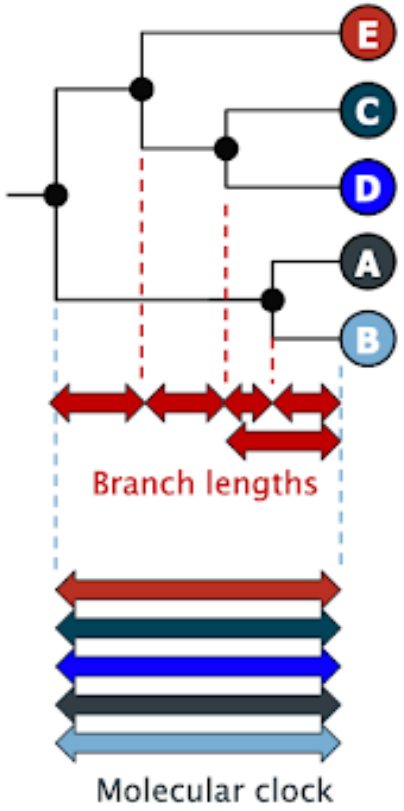


Source: http://cabbagesofdoom.blogspot.com/2013/04/how-to-read-phylogenetic-tree.html

Branch lengths







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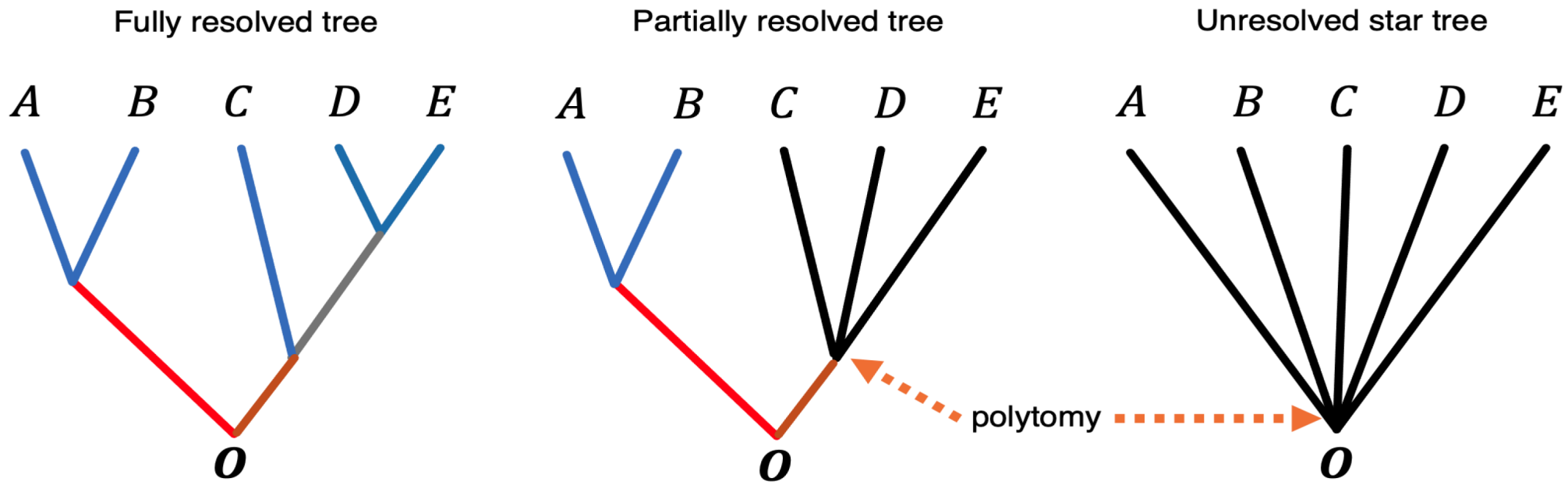
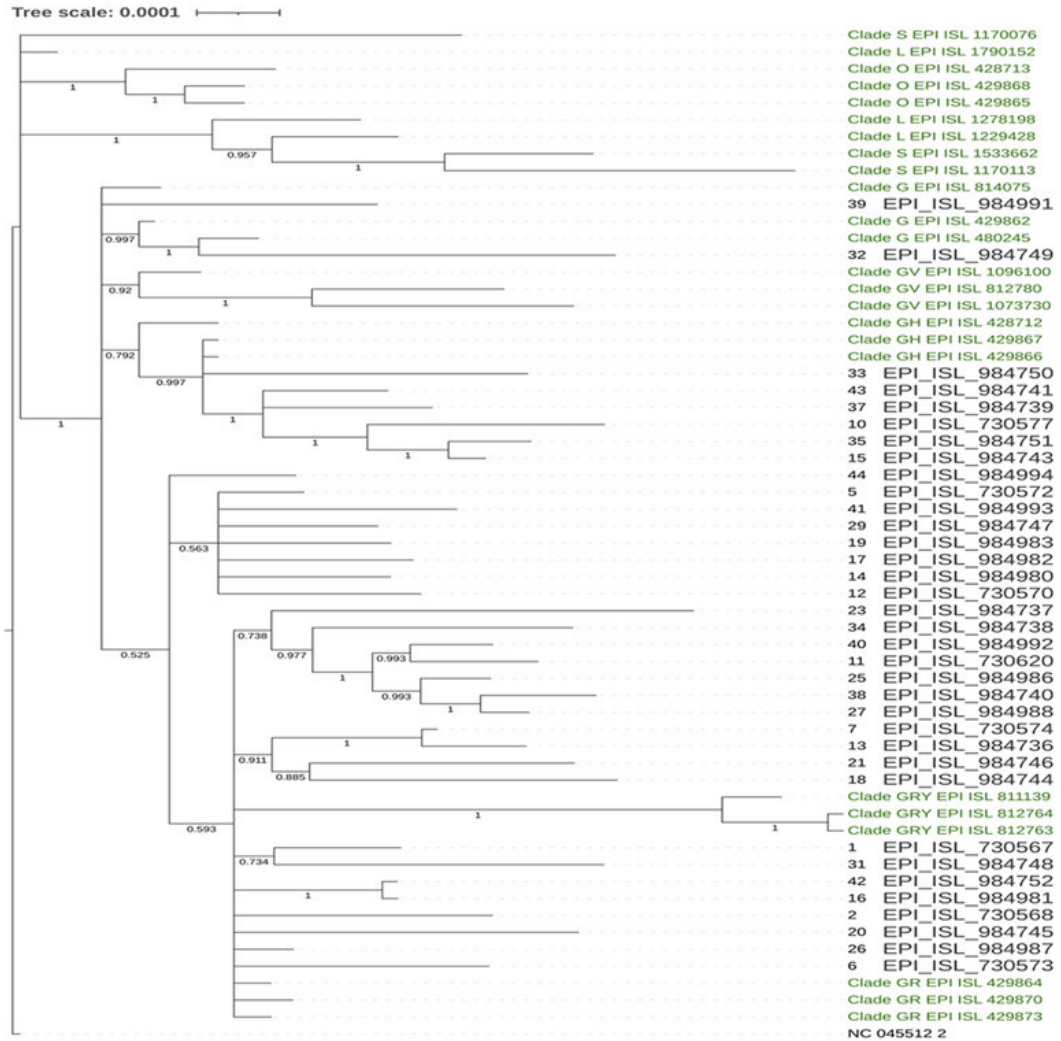
Source: http://cabbagesofdoom.blogspot.com/2013/04/how-to-read-phylogenetic-tree.html

Resolution of phylogenetic relationships



Jhwueng DC & Liu FC, Diversity, 2022

Polytomies: SARS-CoV-2



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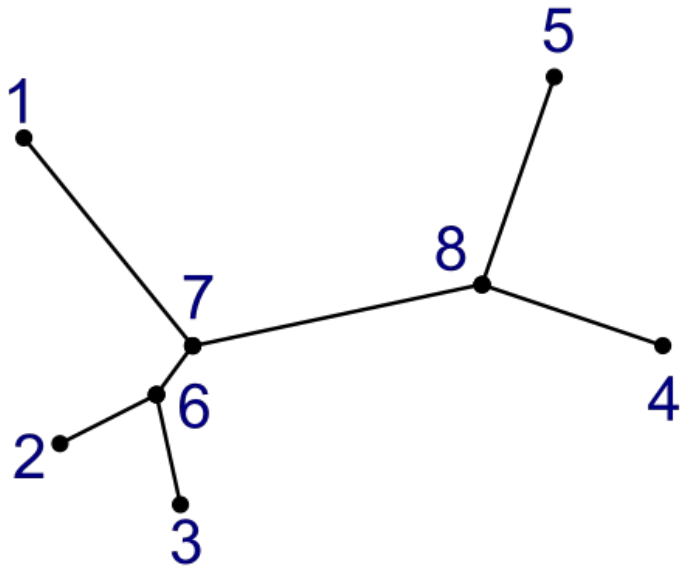
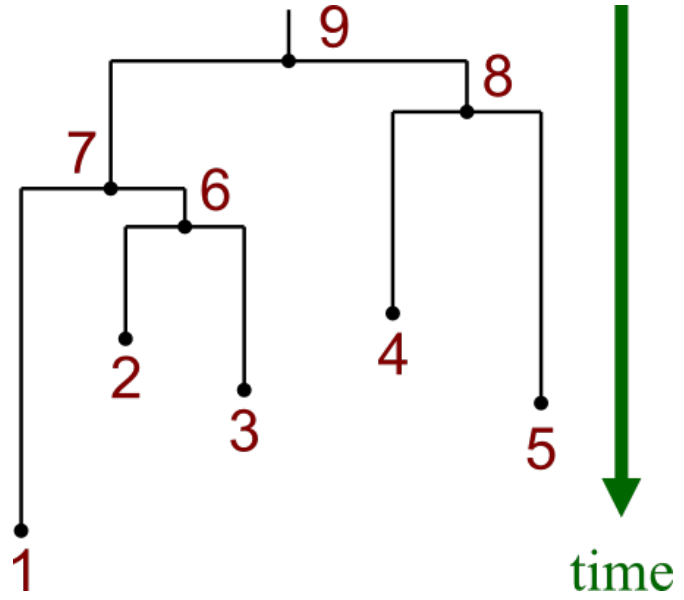
Sahin E et al, Journal of Med Vir, 2021

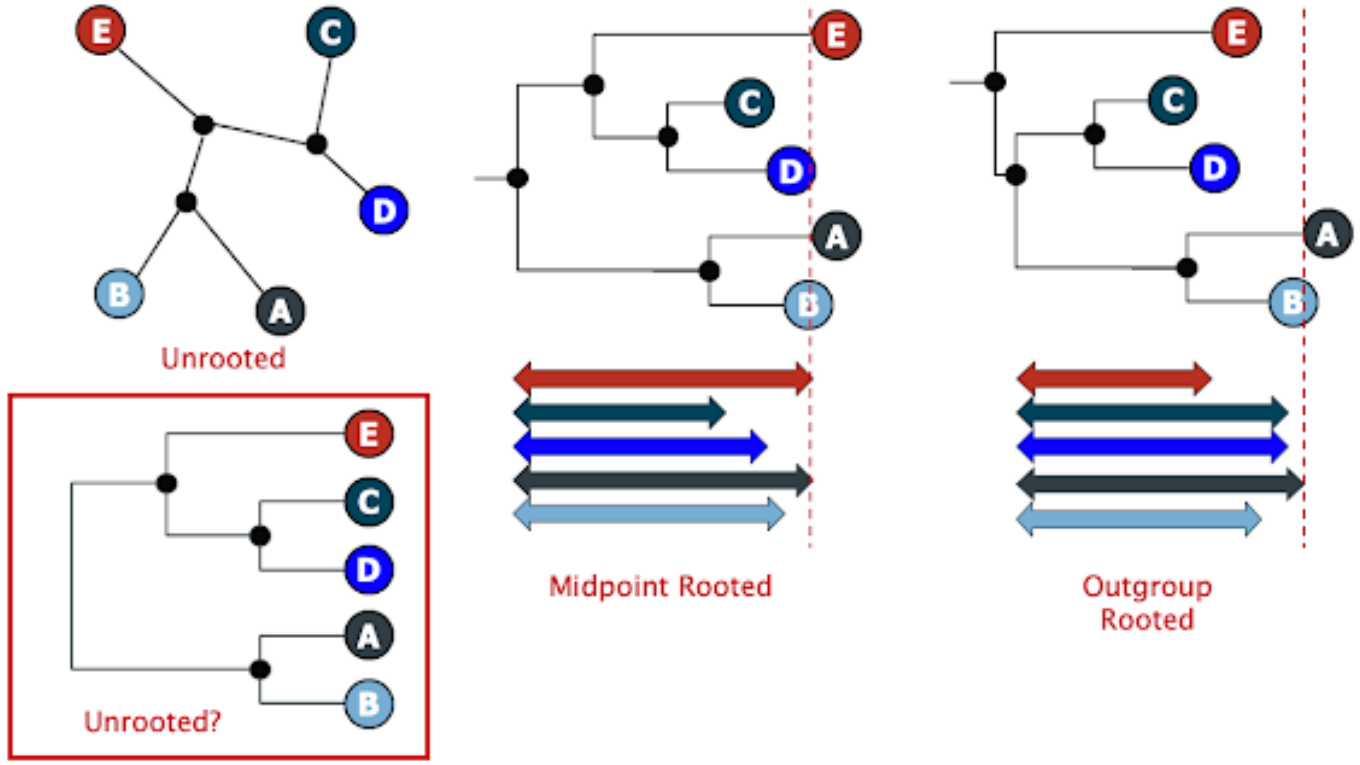
Rooted vs unrooted tree





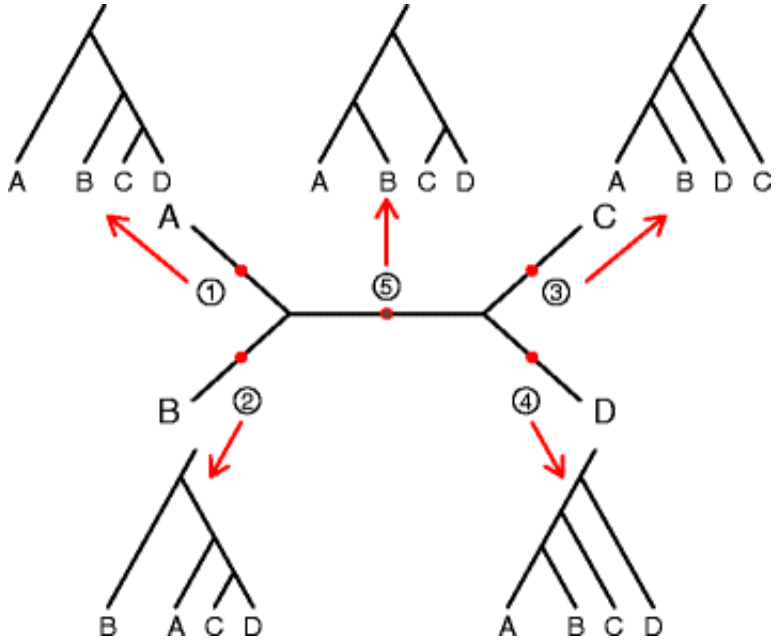
Source: https://pages.cs.wisc.edu/~aasmith/biolec/trees.html

Rooting methods

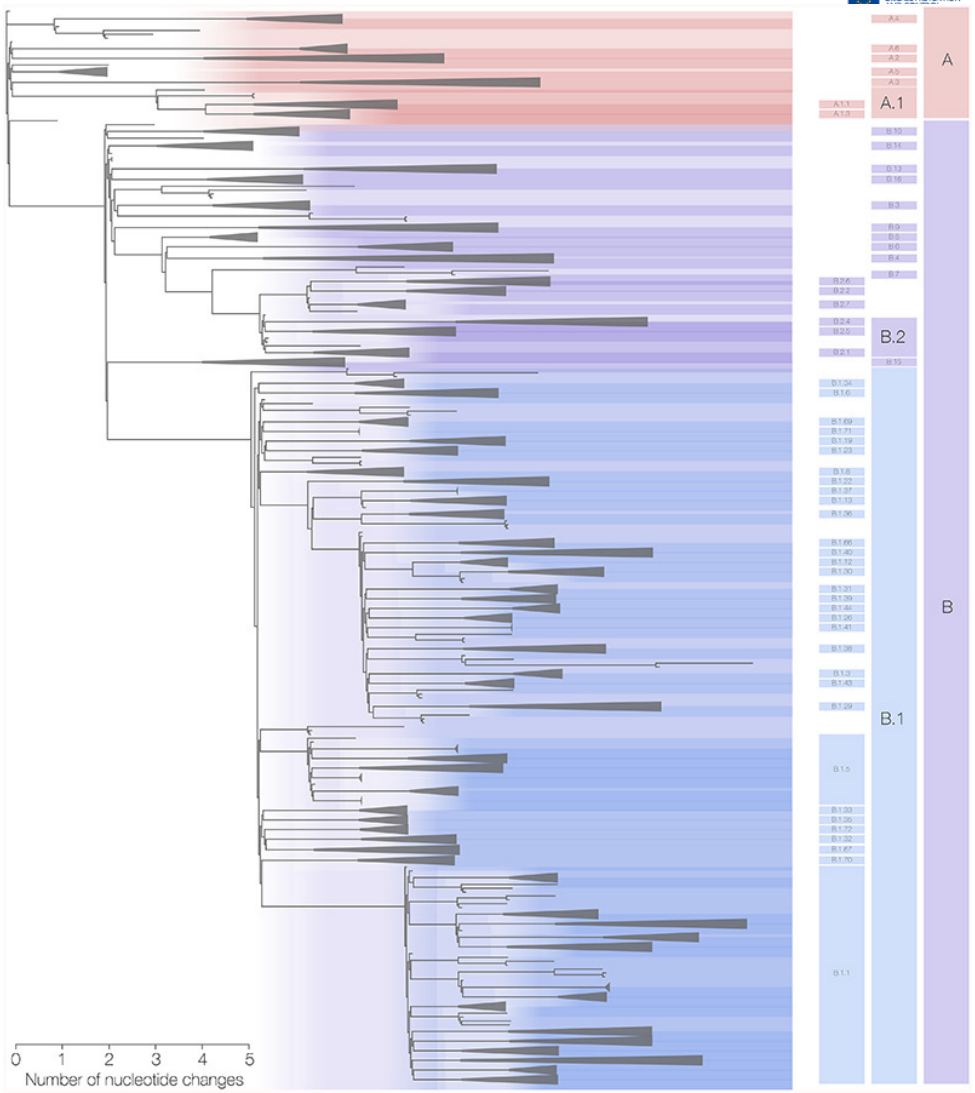


Source: http://cabbagesofdoom.blogspot.com/2012/06/how-to-root-phylogenetic-tree.html

Why is rooting important?



Number of branches:
2n-3



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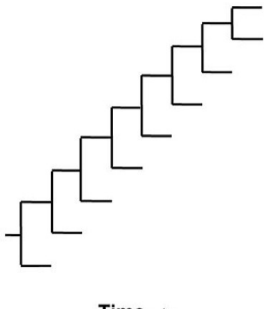
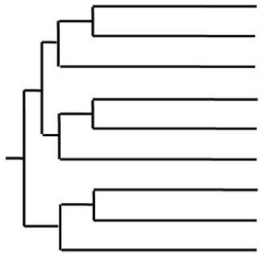
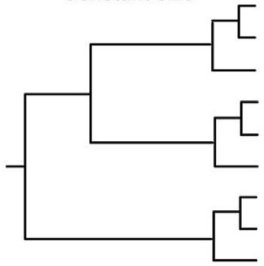
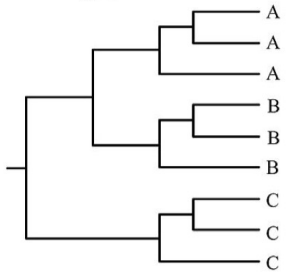
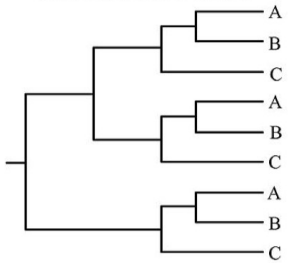
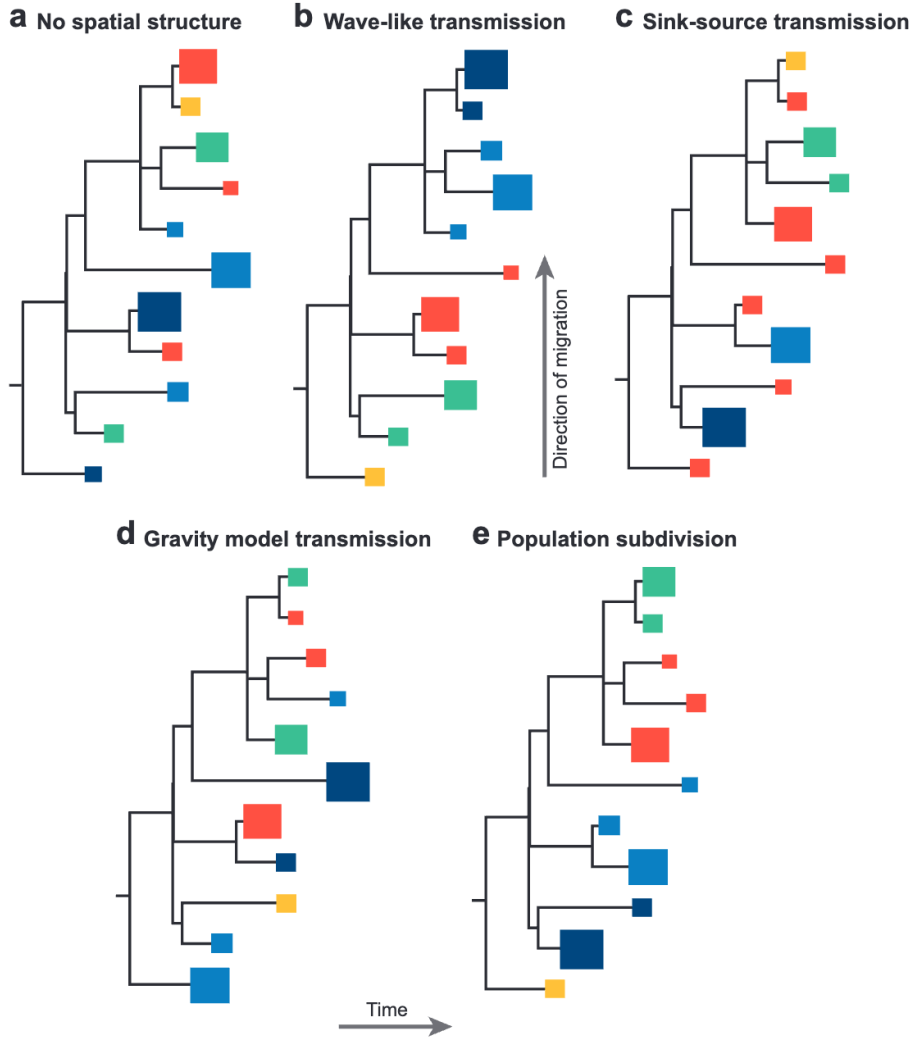
Tian Y & Kubatko L, BMC Ecol Evol, 2017

Rambaut A et al, Nat Microb, 2020

What else can tree structure tell us?

	Continual Immune Selection	Weak or Absent Immune Selection	
		Tree shape controlled by non-selective population dynamic processes	
		Population size dynamics	Spatial dynamics
Idealized Phylogeny Shapes		Exponential growth  Constant size 	Strong spatial structure  Weak spatial structure 
Examples	Human influenza A virus intra-host HIV	inter-host HIV inter-host HCV	Measles, rabies inter-host HIV
Tree Inferences	Detection of antigenic escape mutations	Estimation of population growth rates	Estimation of population migration rates



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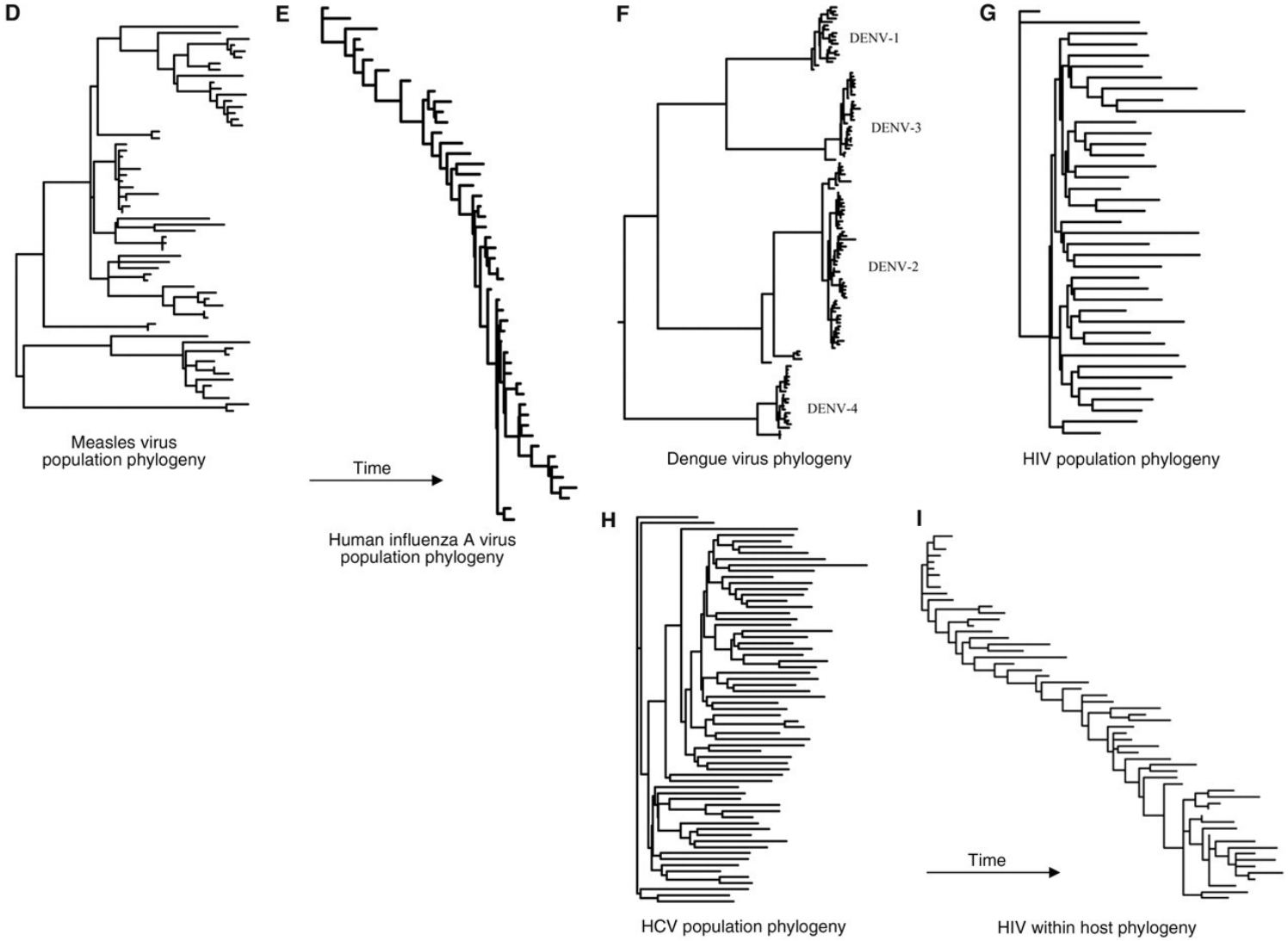
Grenfell et al. (2004) *Science* 303:327–332, Holmes (2008) Annual Reviews Microbiology 62:307-328

Strong immune selection?



Grenfell et al. (2004) *Science* 303:327–332