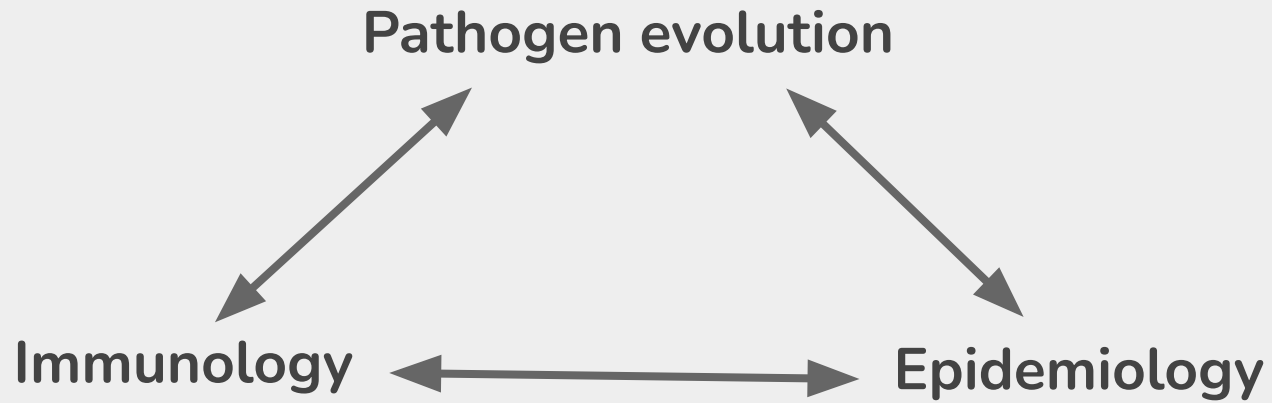
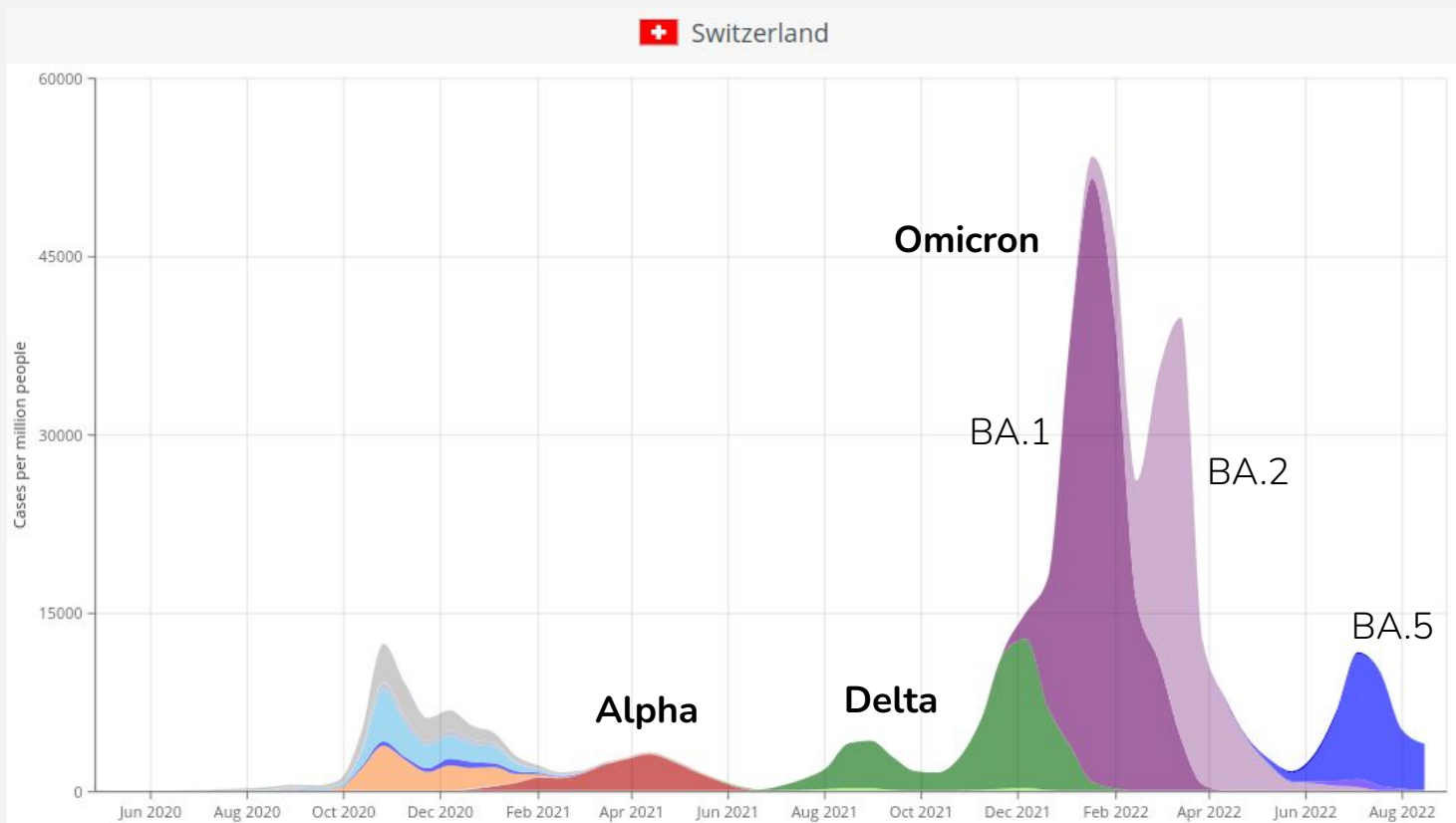


# **From Pandemic to endemic: the interplay of immunity, viral evolution, and seasonality**

Richard Neher @ Nordita

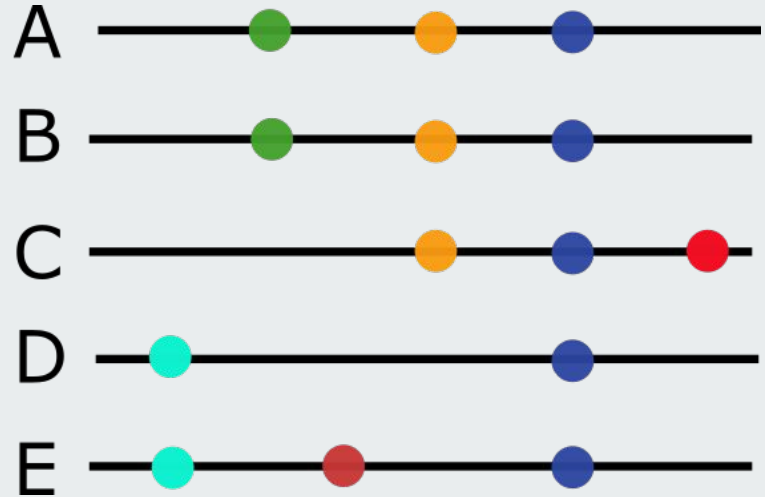


# Waves and variants from the past 3 years

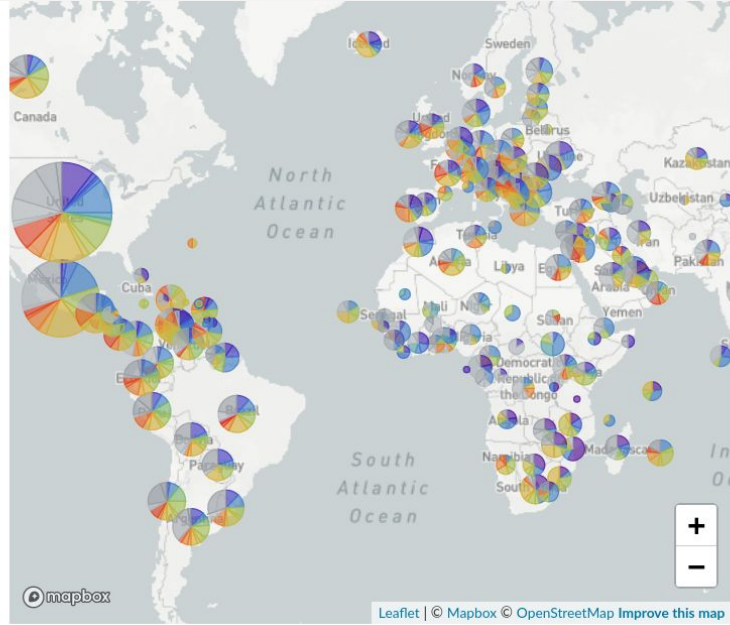
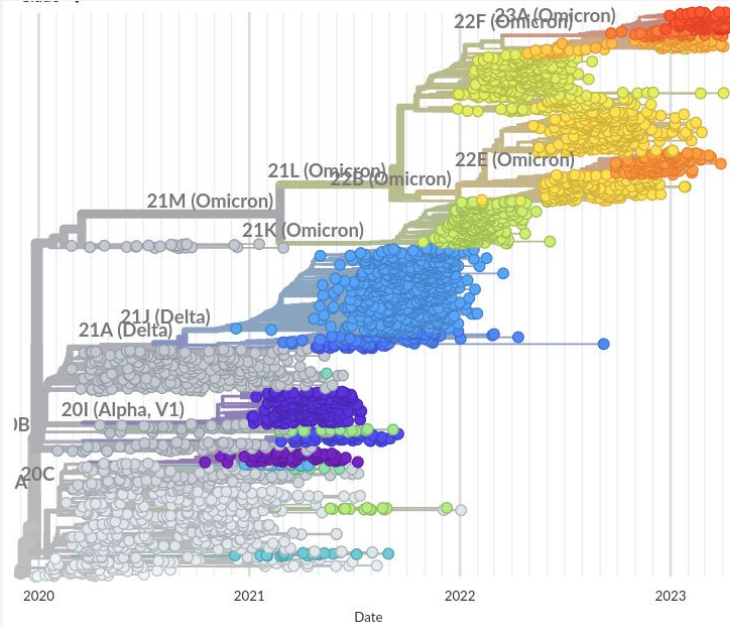


covariants.org

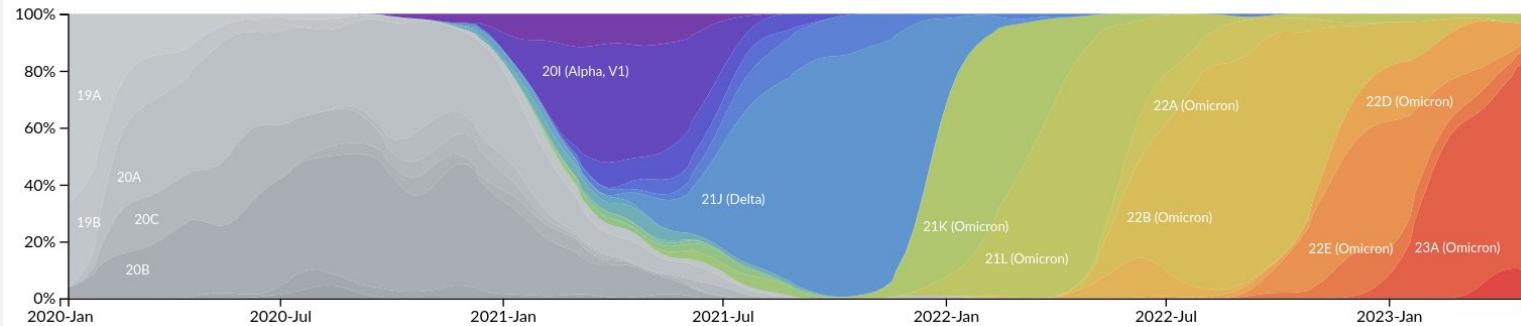
# Deciphering spread and change of SARS-CoV-2

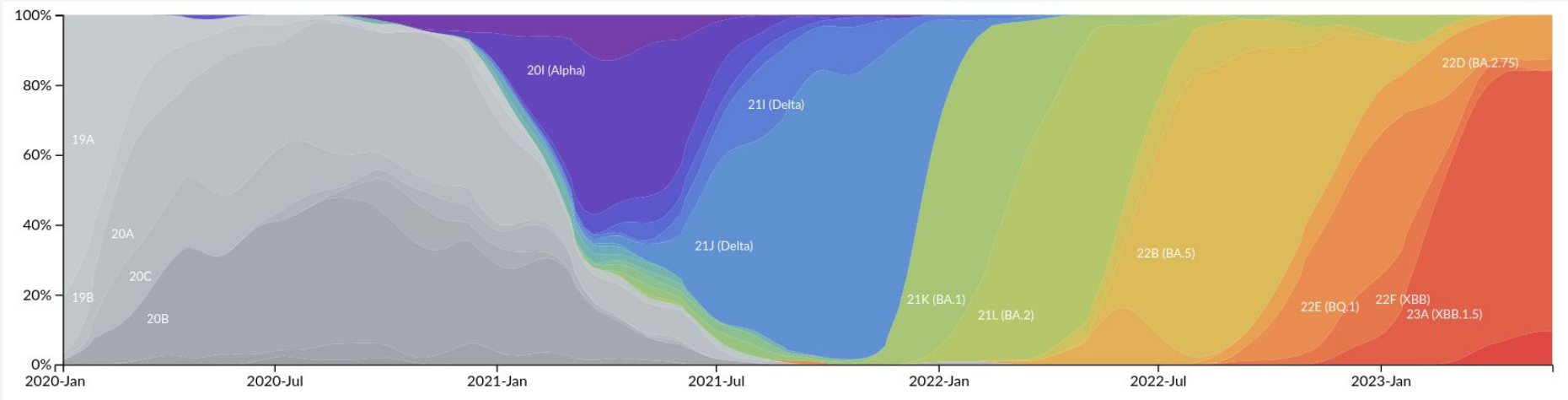


- Similar sequences imply they are closely related
- Allows to resolve dynamics on the scale of a month
- Most mutations hurt the virus, some increase transmissibility or lead to immune escape



Frequencies (colored by Clade )



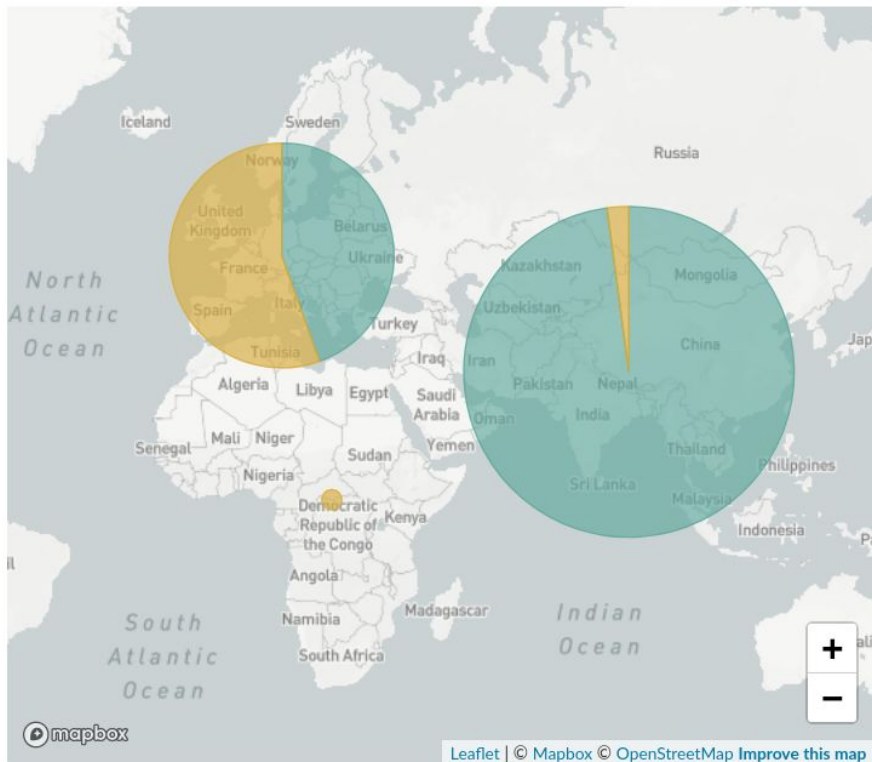
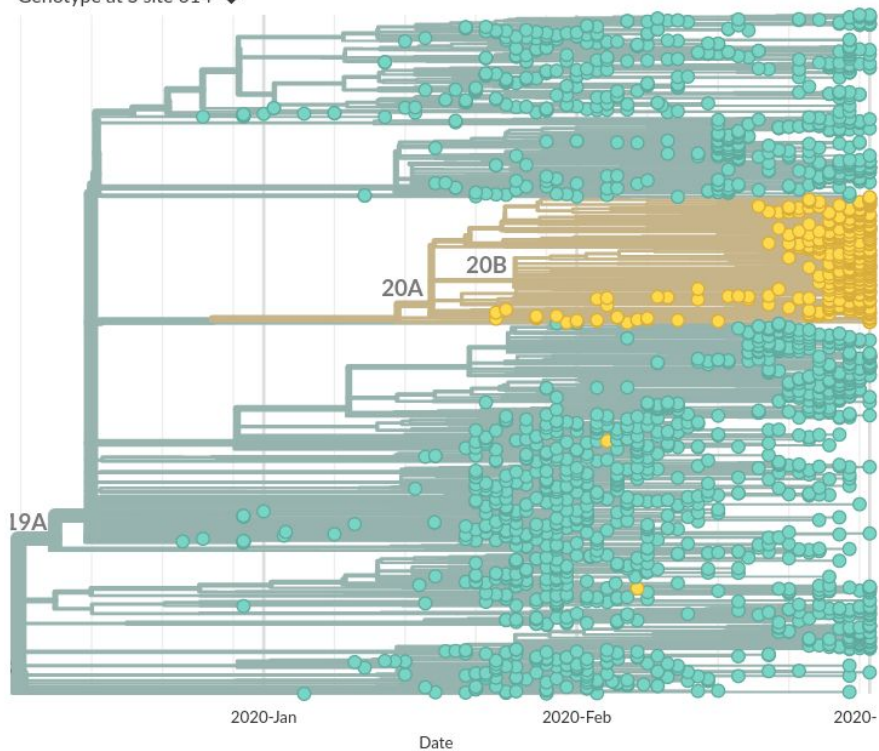


✘ Ancestral → Alpha → Beta → Delta → Omicron

✔ Ancestral → Alpha  
 Ancestral → Beta  
 Ancestral → Delta  
 Ancestral → Omicron

# Early 2020: Little population immunity, selection for transmissibility

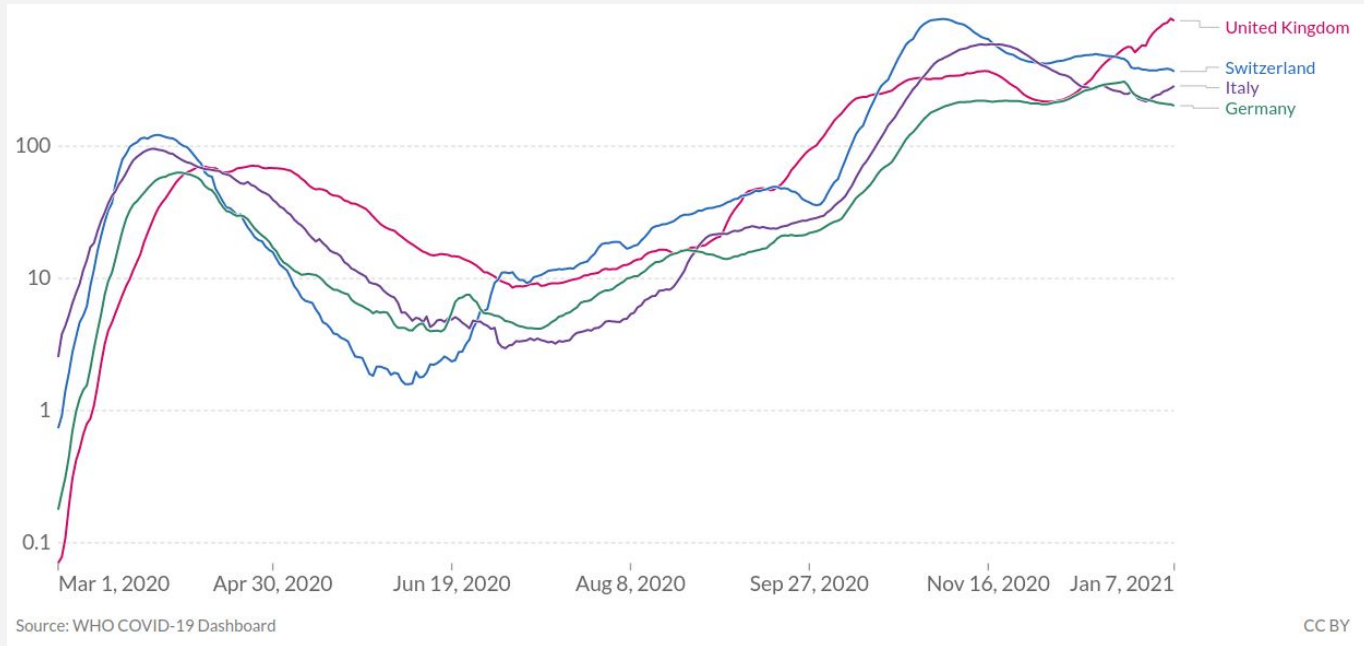
Genotype at S site 614 ▾



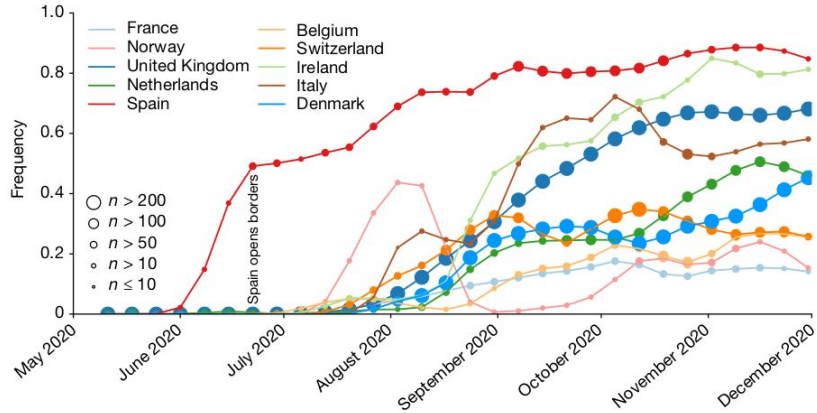
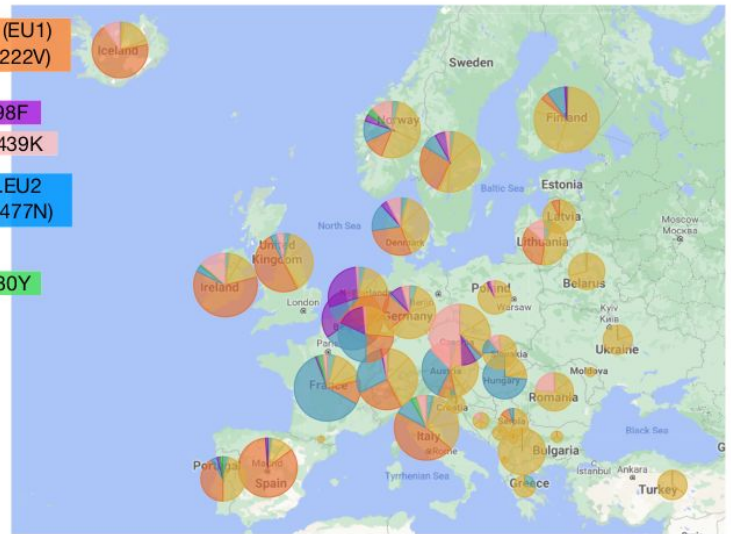
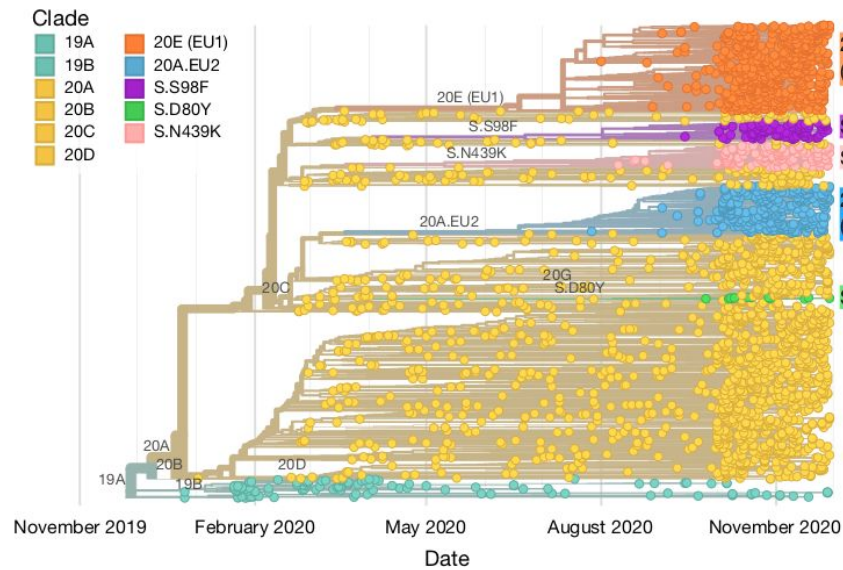
Outbreak in Europe rapidly dominated by more transmissible D614G variants

# Summer and Fall 2020

- Limited evolutionary change
- Dispersal of lineages in Europe after the borders reopened
- Gradual increase over the summer until pressure on hospitals was high in fall

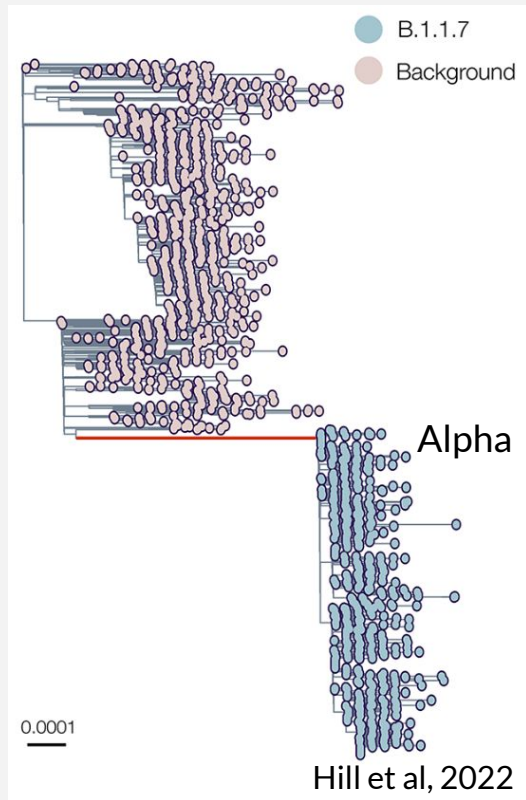




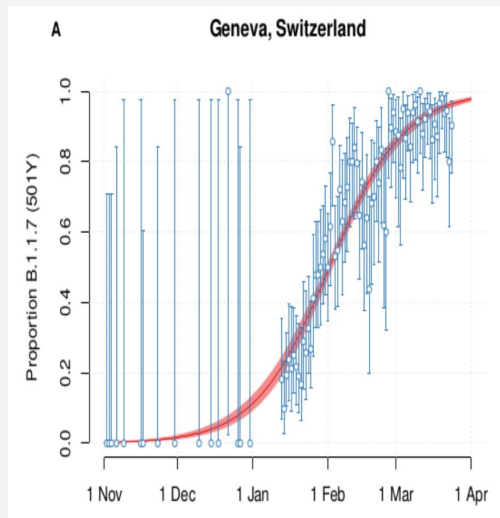


- Variant was first dominant in Spain
- Dispersed by tourists across Europe
- But it probably didn't make a big difference

# December 2020: Variants of Concern



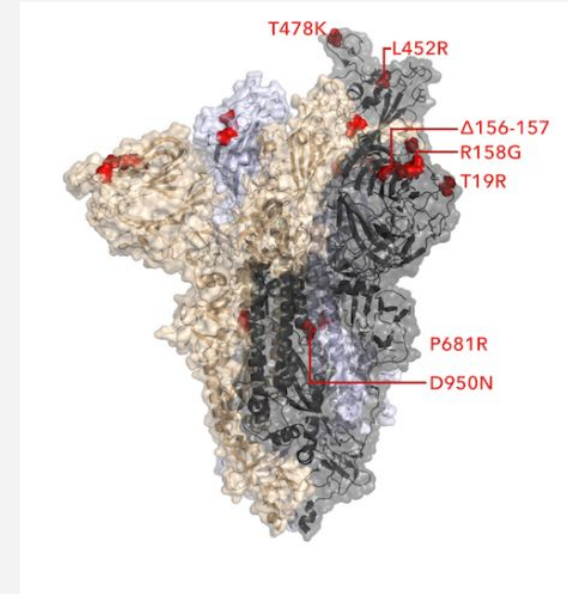
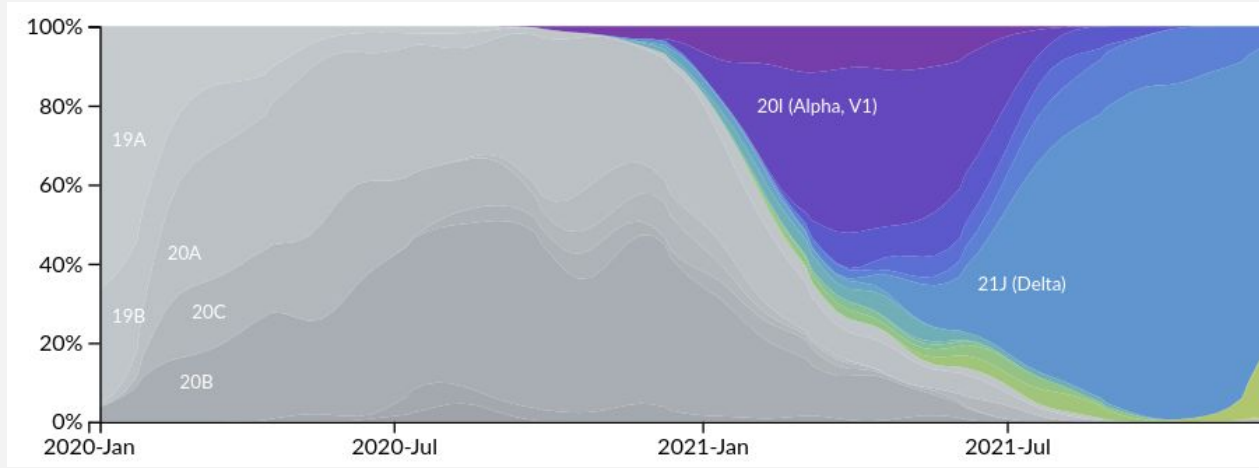
- Sudden emergence of variants with a large number of mutations  
In Spike: Delta 69/70, N501Y, A570D, P681H, T716I, S982A, D1118H, E1202Q
- No observed intermediates
- Almost simultaneous occurrence of
  - Alpha
  - Beta
  - Gamma
- They share several mutations, suggesting they are adaptive



- Doubling every 1-2 weeks
- Mostly regional, not global
- Moderately more severe
- Beta was immune evasive

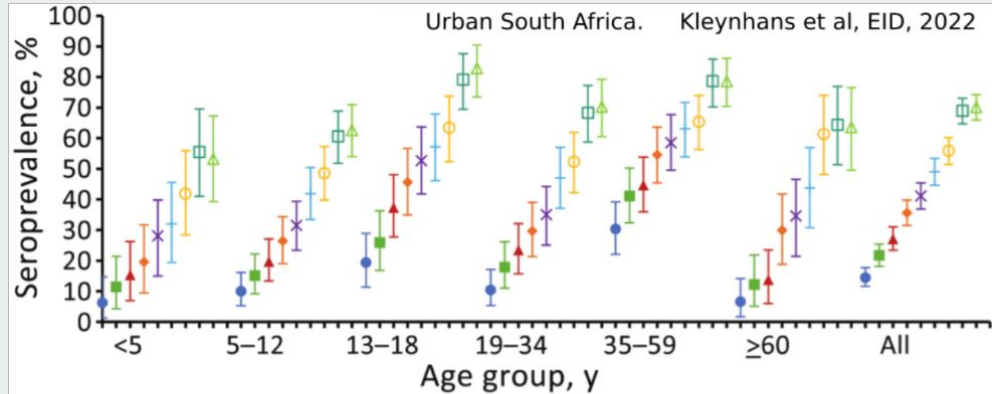
By Christian Althaus

# 2021: Delta – global dominance

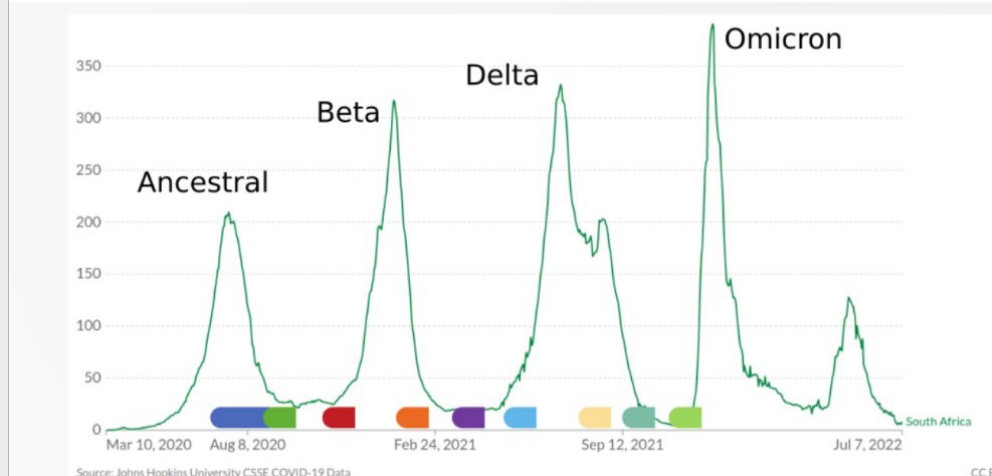


- A number of mutations that increase transmissibility
- Moderately reduce immune recognition (less than Beta)

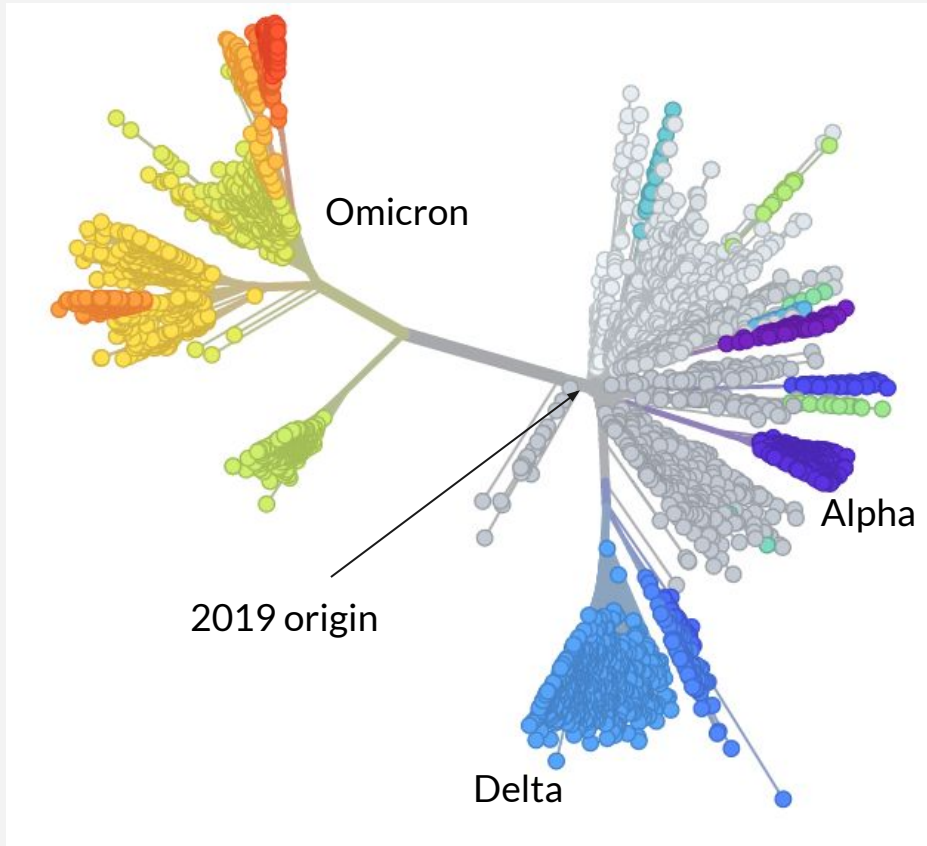
# Seroprevalence: by end of 2021 most people had immunity



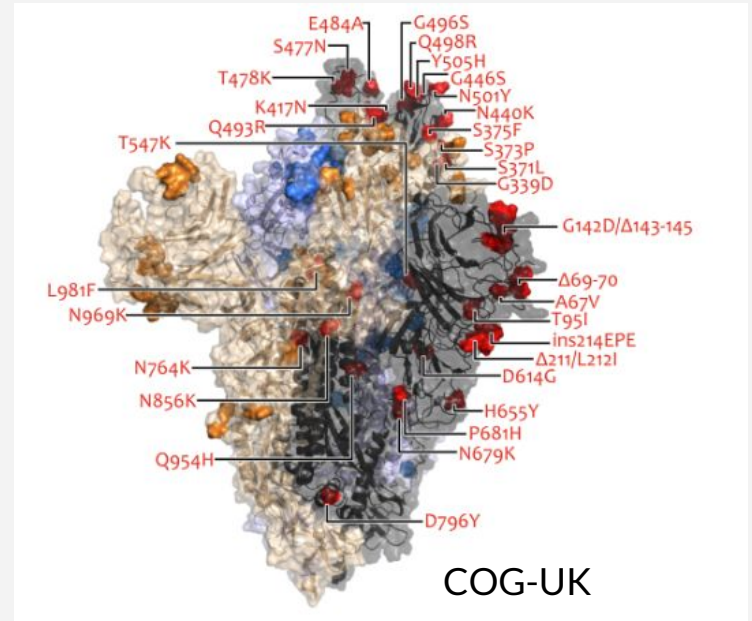
- In some places, most immunity stemmed from infection, in other from vaccination
- Since Nov 2021, most have experienced one or several Omicron infections



# November 2021: Omicron

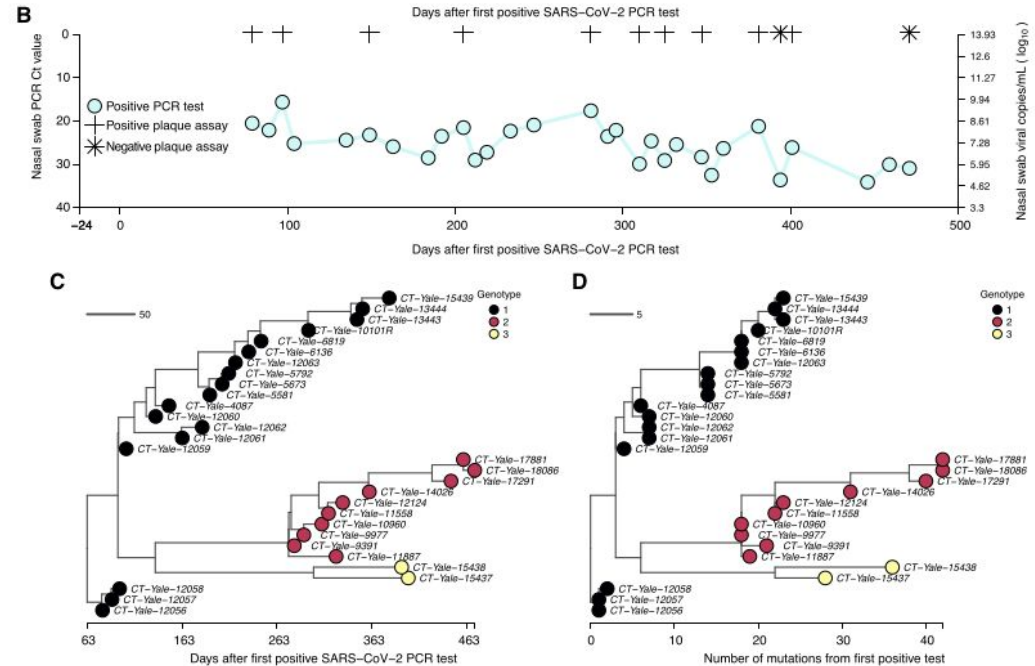


- Heavily mutated sister variant of previous VOCs
- Several distinct variants
- High rate of reinfections
- Very rapid spread



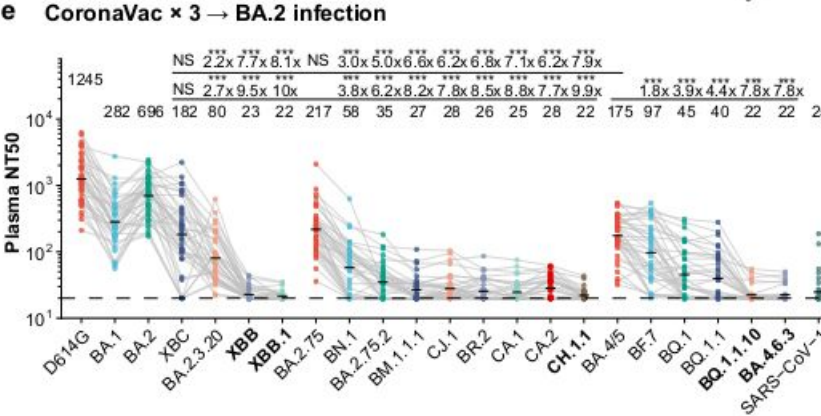
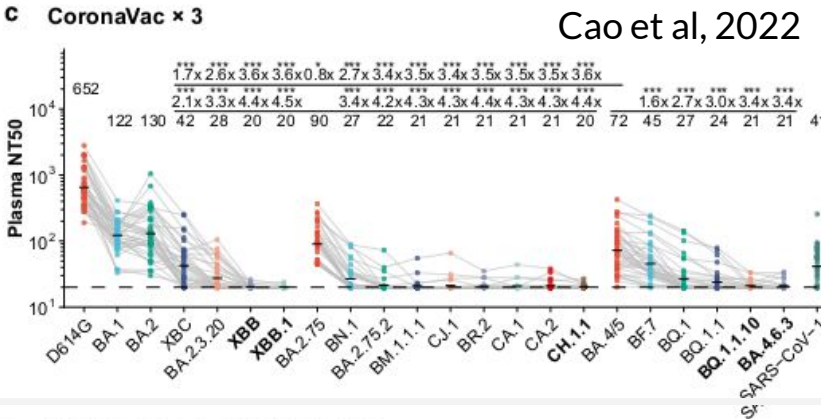
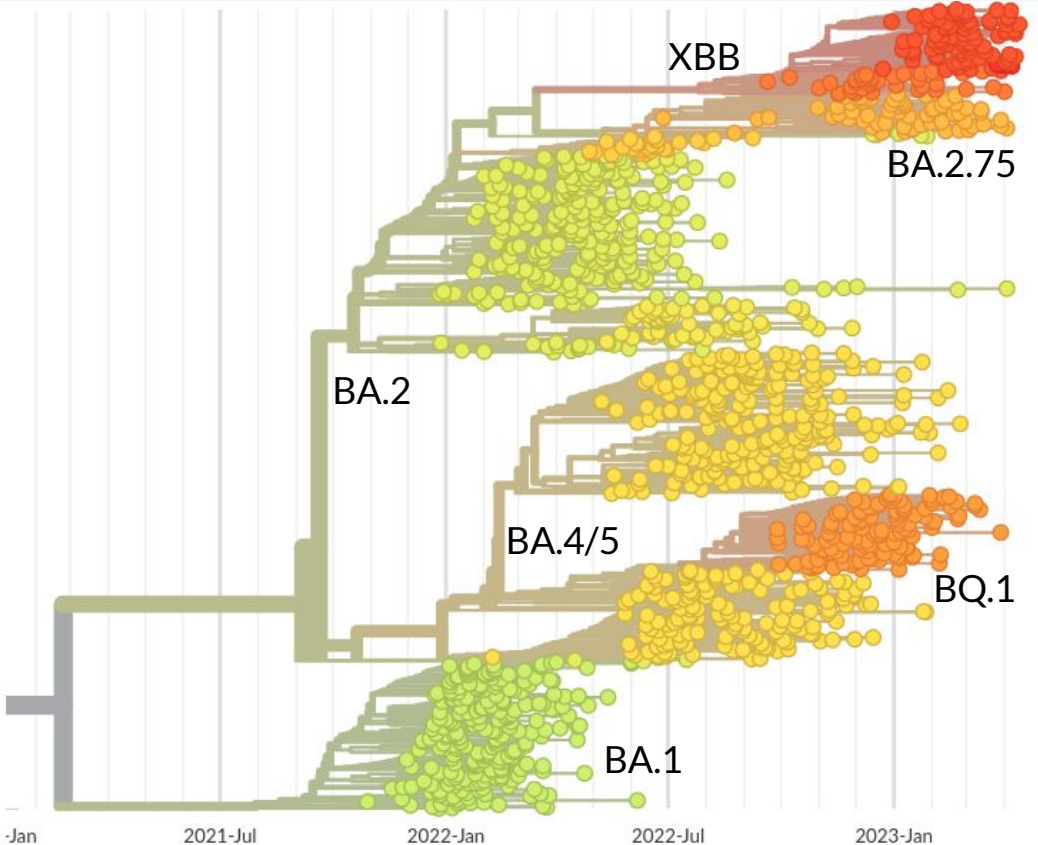
# Emergence of VOCs: probably chronic infections

- Chronic infections are common in immunocompromised
  - Immune suppression
  - Advanced HIV
- Often hardly symptomatic
- Rapid evolution is common
  - some times very diverse variants
- Likely the source of Alpha and Omicron, maybe more
- Since Omicron, evolution is more stepwise and gradual

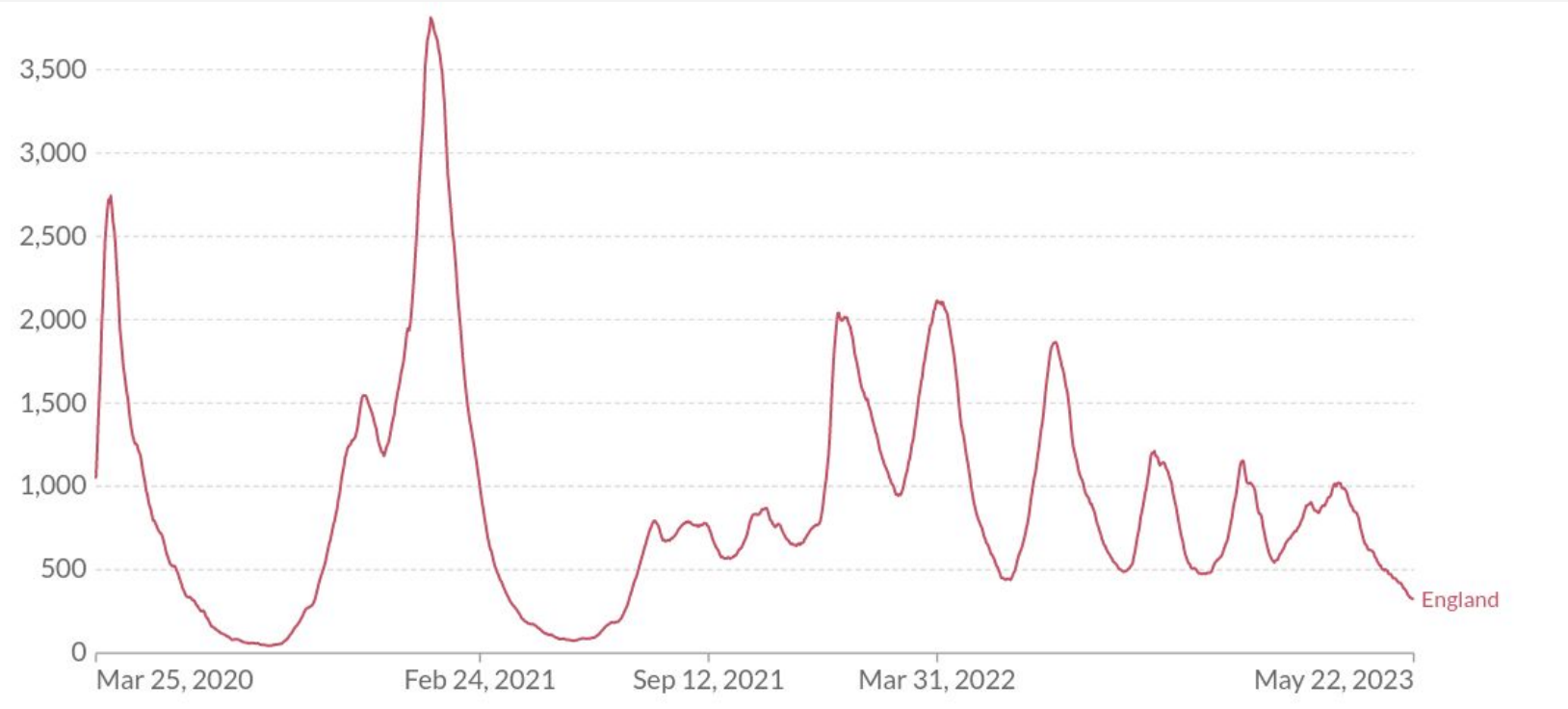


Chaguzo et al, 2023

# 2022 and ongoing: Variant soup



# From waves to more continuous circulation



Hospitalization numbers in England (via [Our World in Data](#))



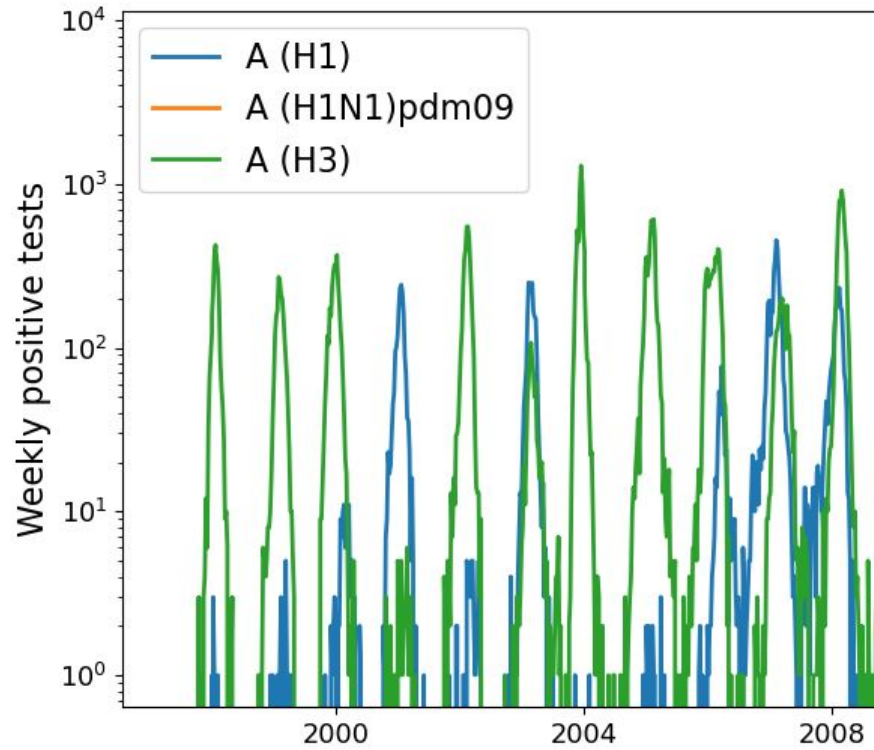
## Rapid immune escape/waning leads to short intrinsic period

$$T \approx \frac{2\pi}{\sqrt{\nu\gamma(R_0 - 1)}}$$

- $\nu$  is infectious period
- $\gamma$  immune escape/waning
- $\nu=1/5$ days
- $\gamma=1$ /year
- $\rightarrow T=0.3$  years

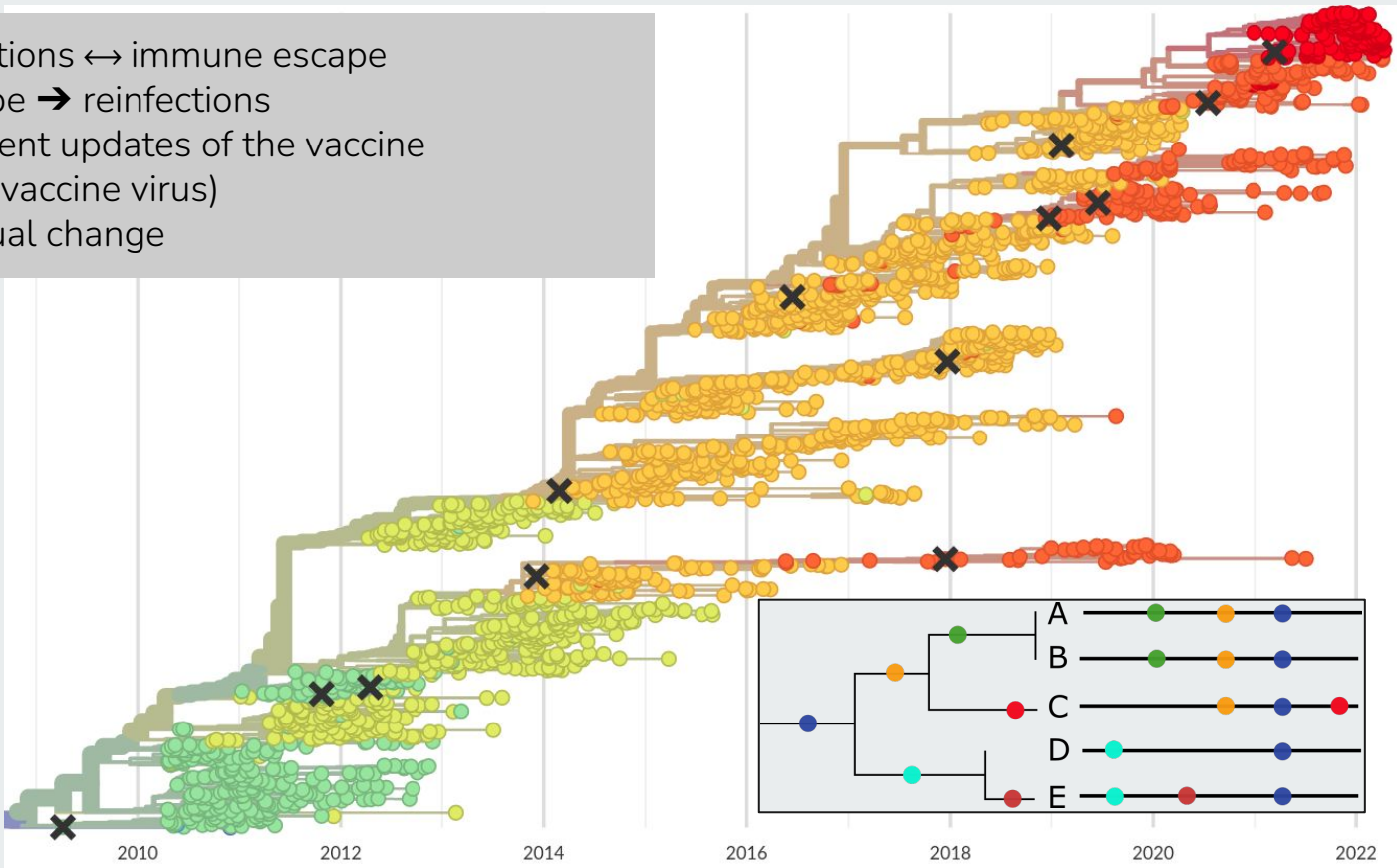
- Period much shorter than 1 year  $\rightarrow$  model “equilibrates” faster than seasonal forcing
- Only moderate modulation by seasonal forcing.
- If rate of waning/escape goes down, we expect more pronounced seasonal forcing

# Influenza subtype dynamics in 2009

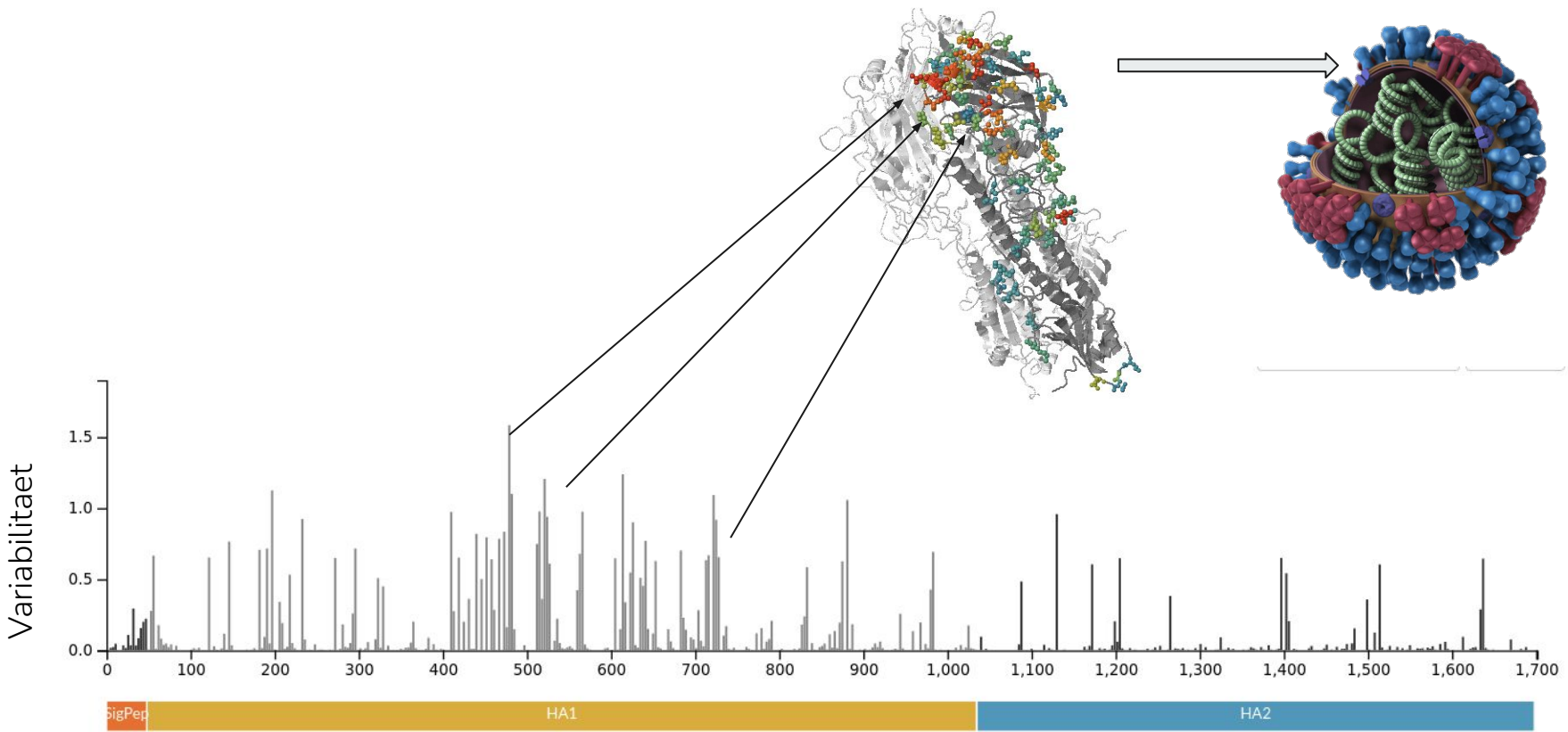


# Pandemic to endemic: example influenza

- mutations ↔ immune escape
- escape → reinfections
- frequent updates of the vaccine (X ==vaccine virus)
- gradual change



# Influenza surface proteins change rapidly – similar to SARS-CoV-2



# Acknowledgements

- Nextstrain team (my lab and Trevor Bedford's lab)
  - Ivan Aksamentov, Cornelius Roemer, Emma Hodcroft, Moira Zuber
  - John Huddleston, Jover Lee, Tom Sibley, James Hadfield
- Sequence data contributors around the world (shared via GISAID or INSDC)