

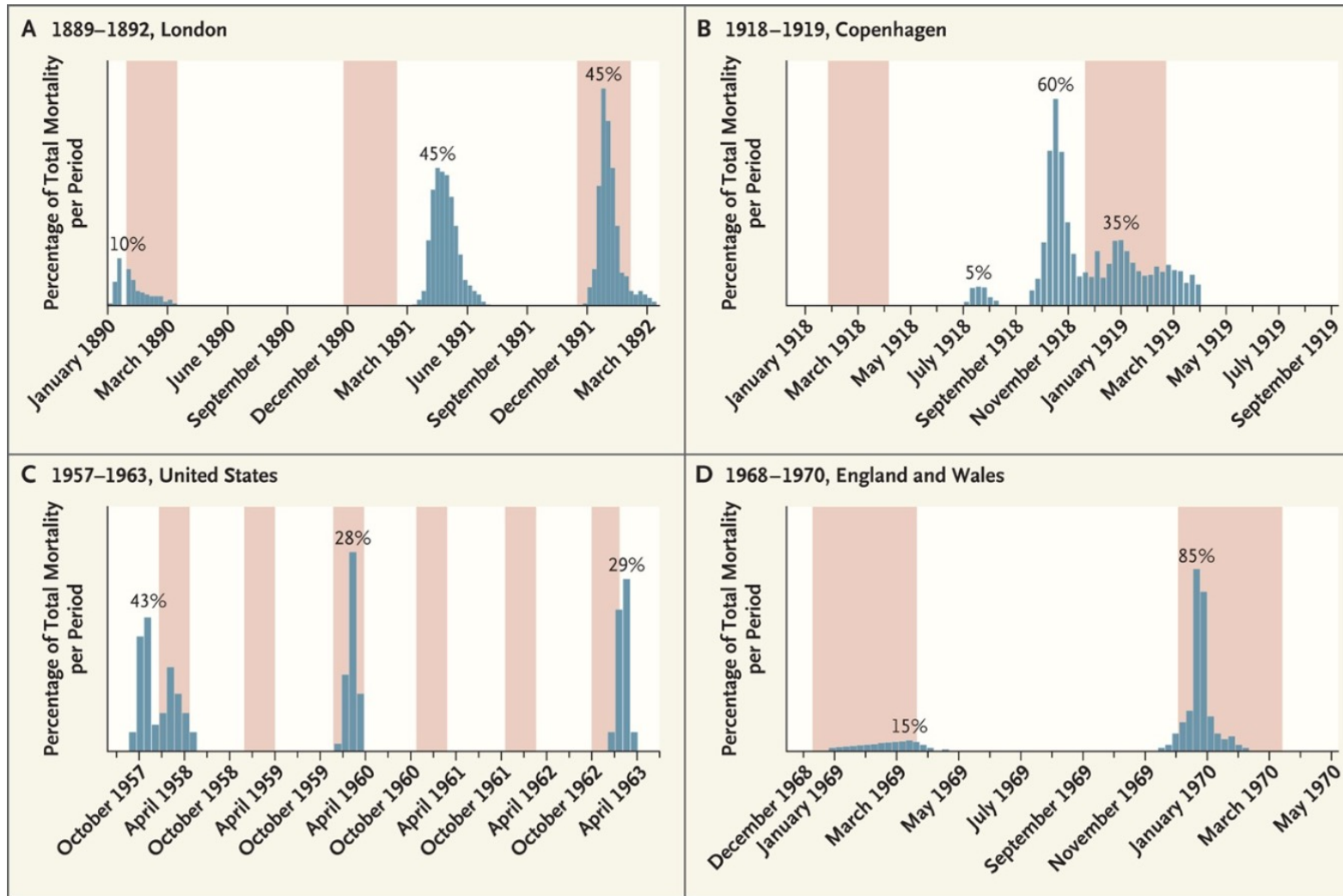
COVID-19: vers des épidémies saisonnières?

Arnaud Fontanet, Institut Pasteur & Cnam

Séminaire DES-C maladies infectieuses et tropicales

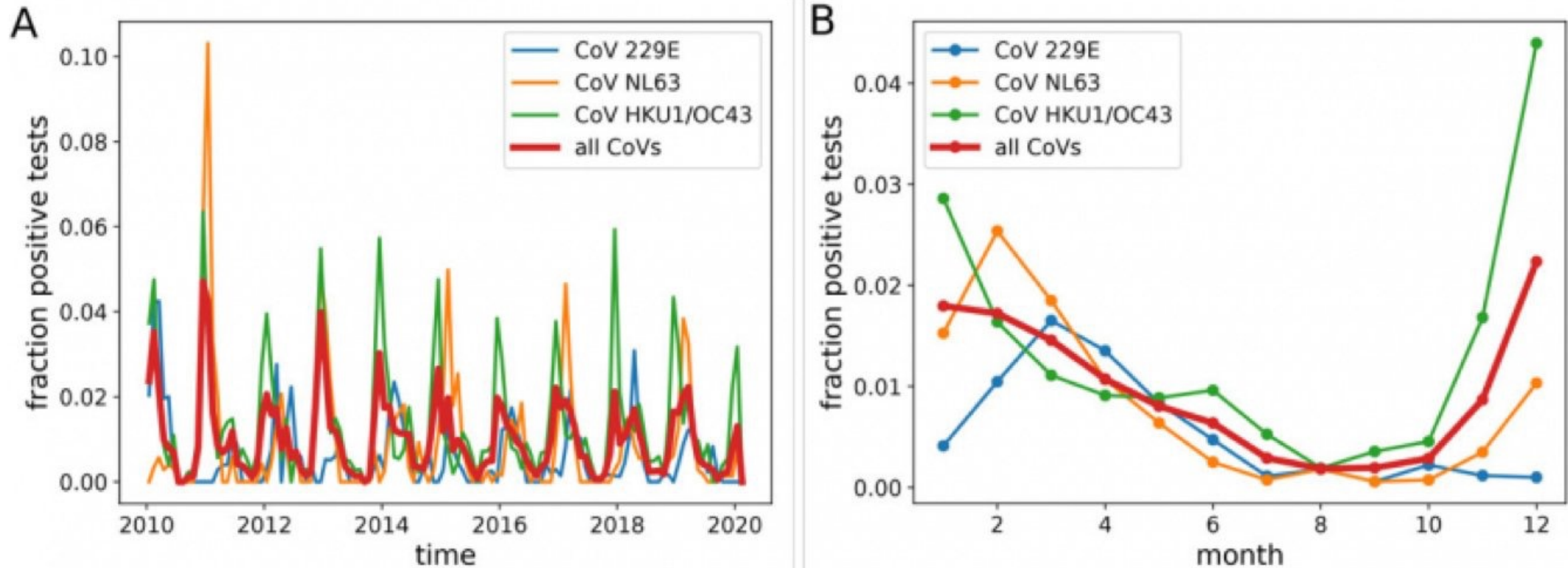
Hôpital Cochin - 28 mars 2022

Flu pandemic waves

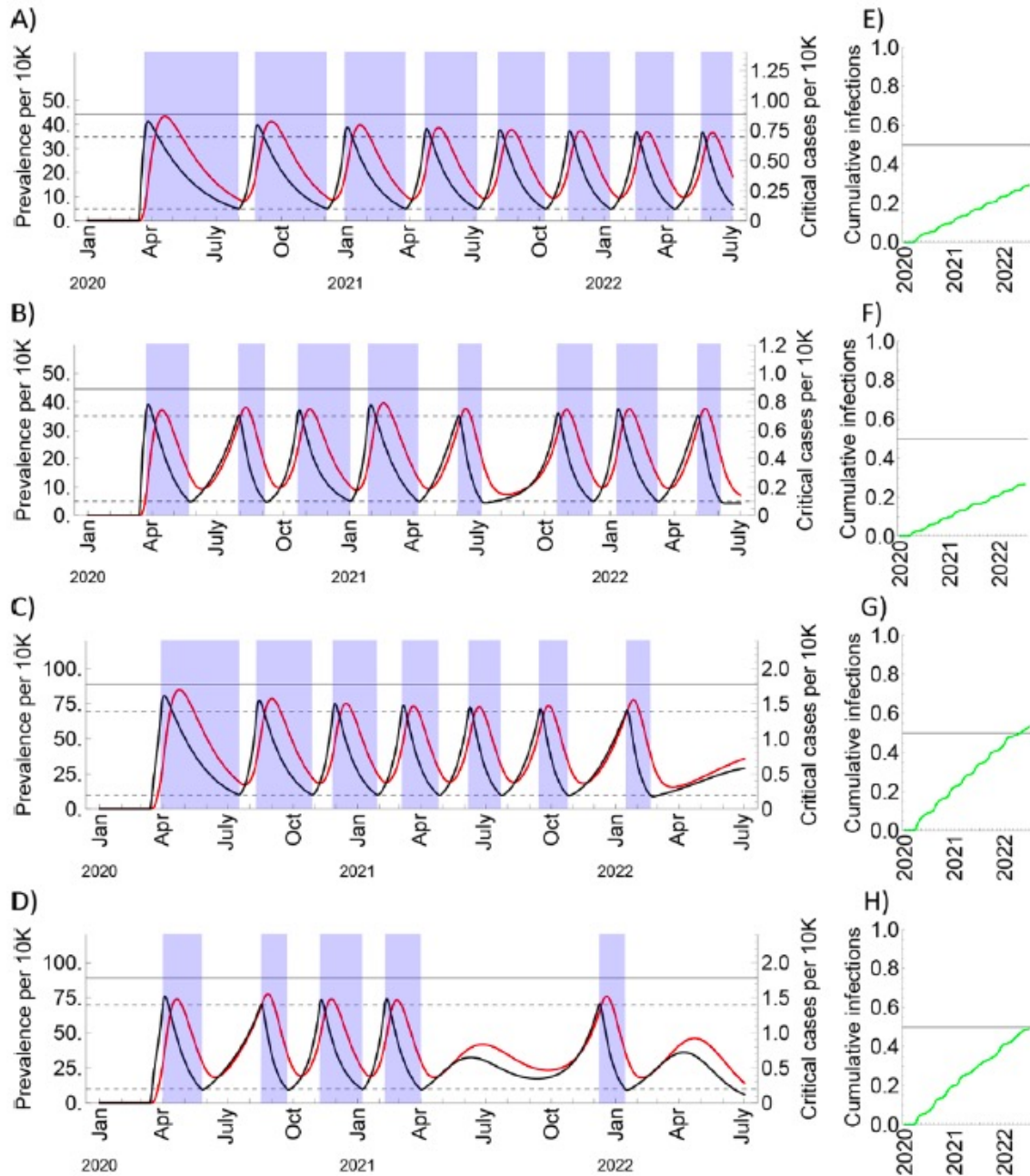


(Miller et coll., NEJM, 2009)

Human seasonal coronaviruses « season »



Seasonal Coronaviruses 2010-2020

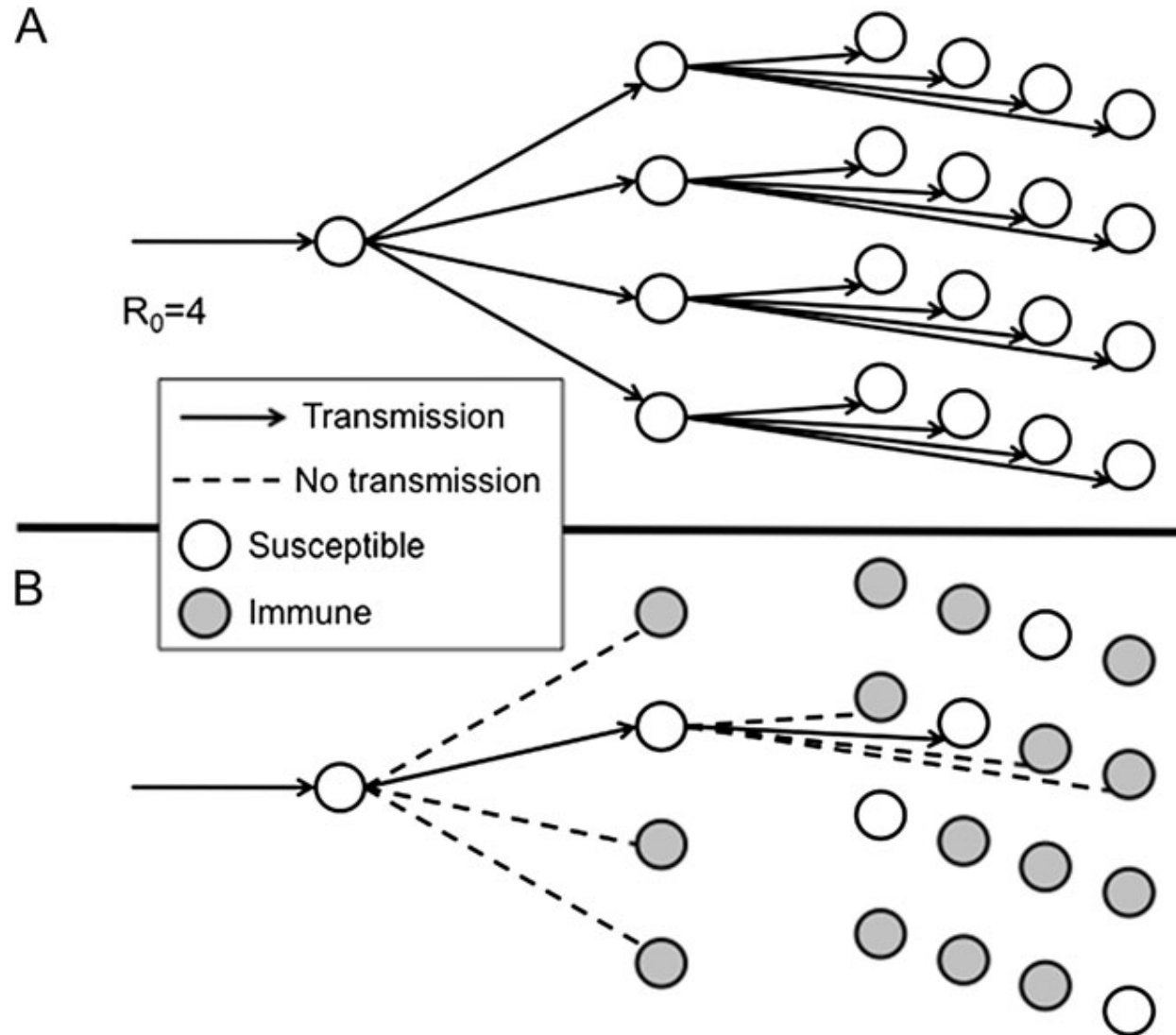


SARS-CoV-2 scenarios 2020-2022

Herd immunity acquisition by
alternating « social distancing »
and « non intervention »
periods

(Kissler et al., Science, 2020)

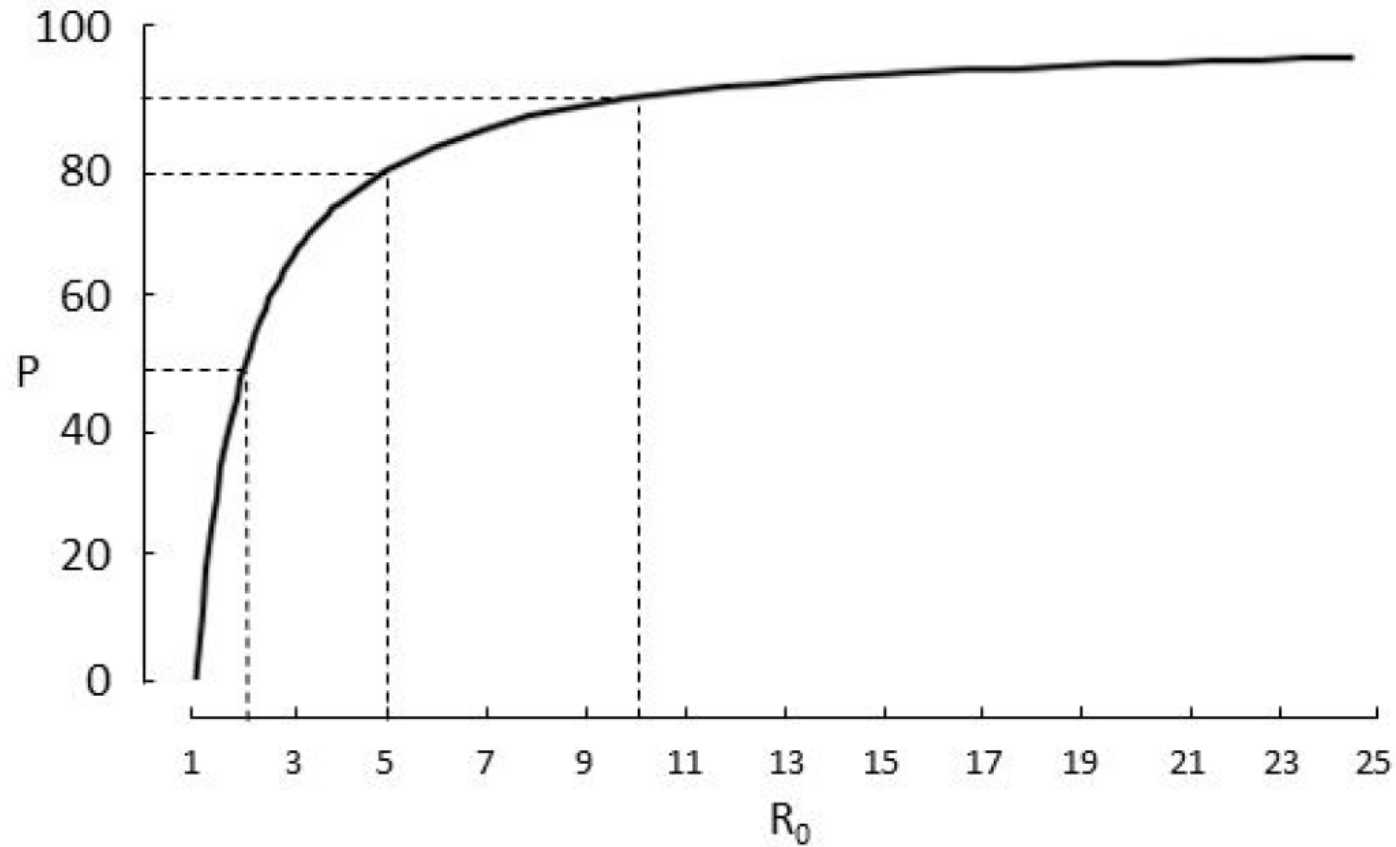
Herd immunity threshold



$$1 - 1/R_0$$

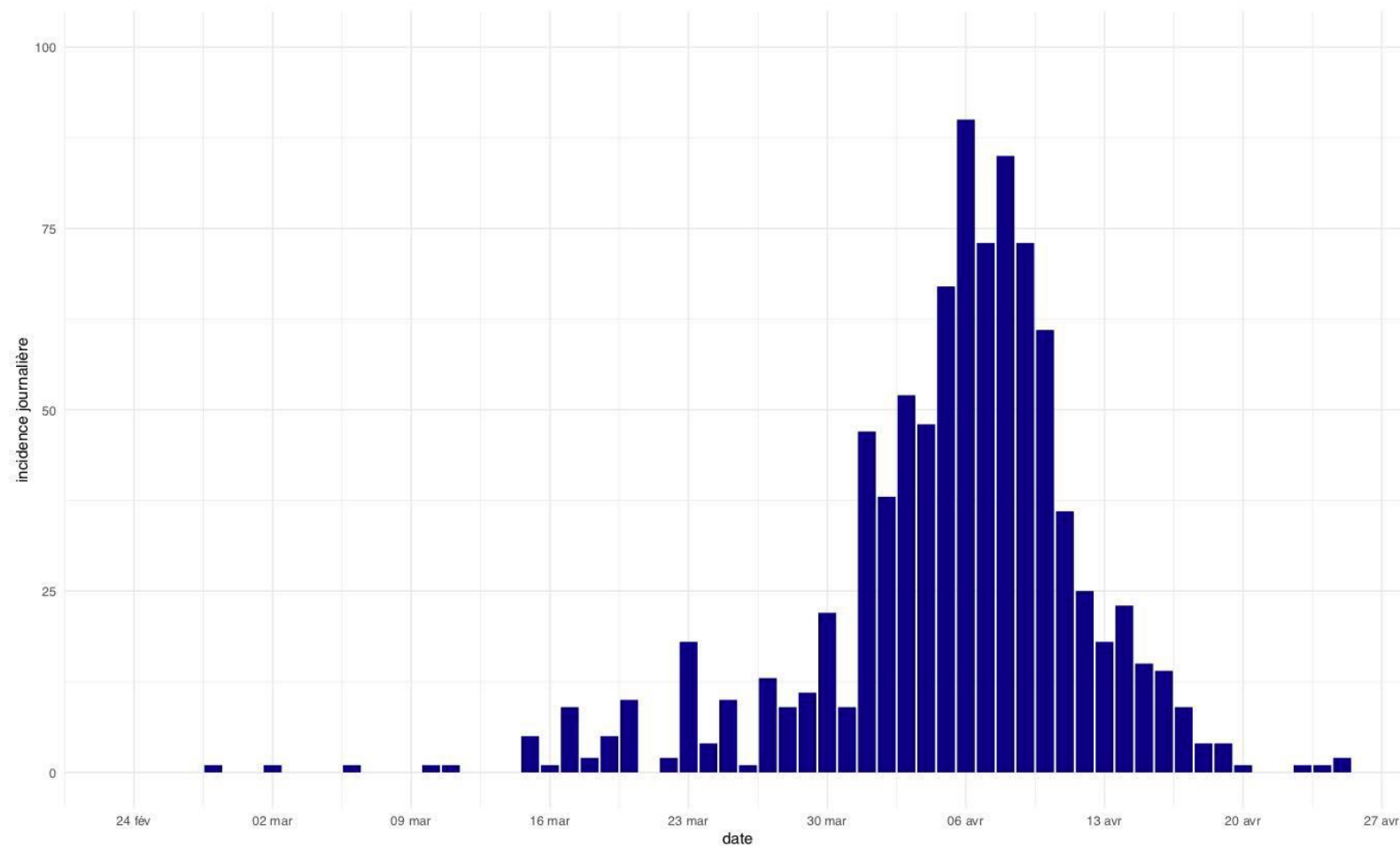
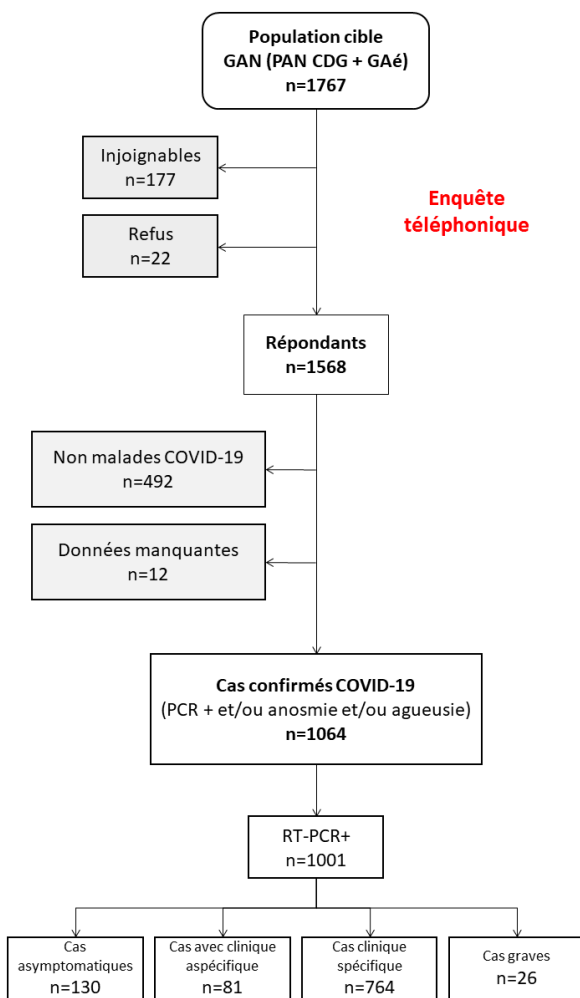
(Fine et al., CID, 2011)

Relation between R_0 and herd immunity threshold



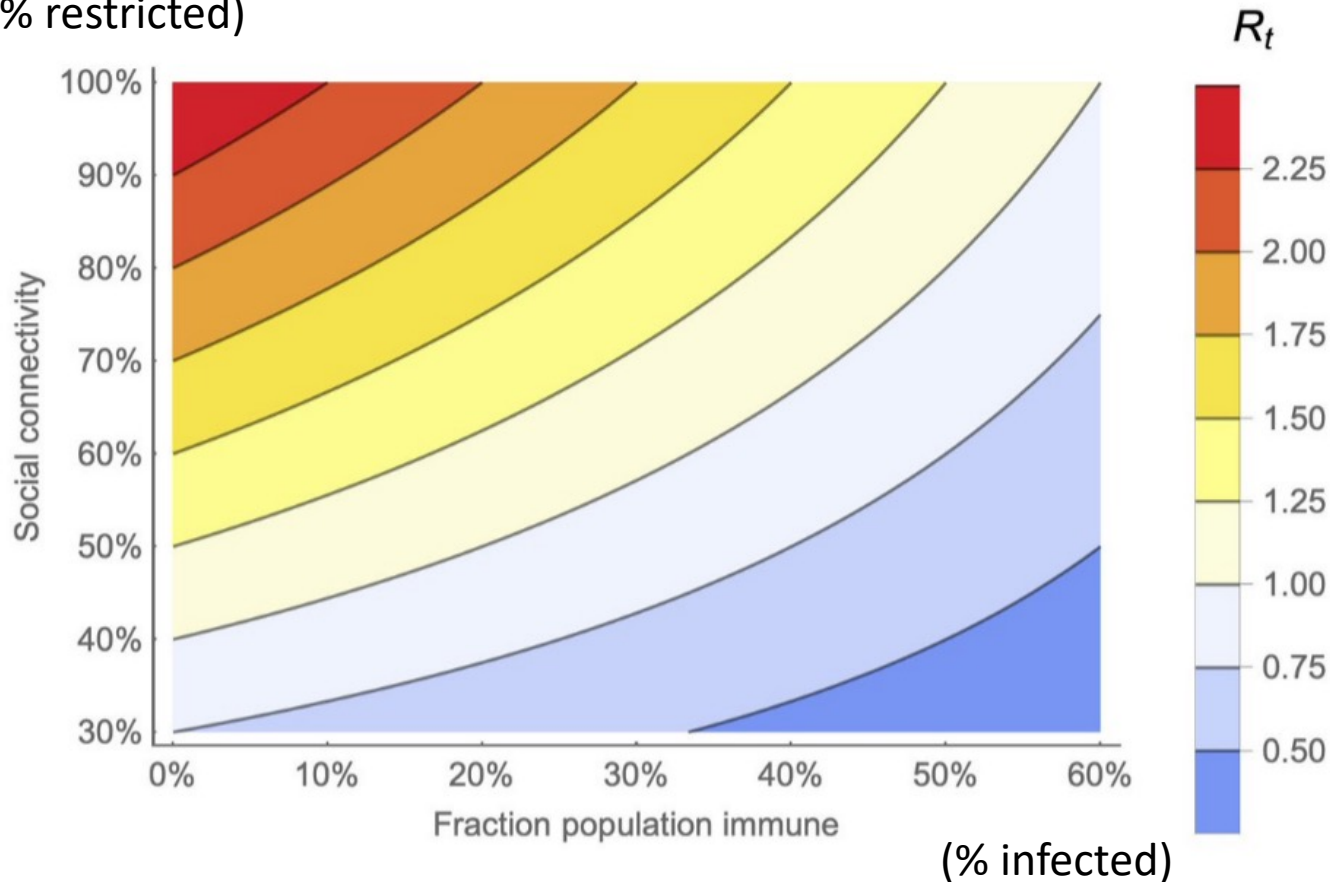
$$1 - 1/R_0$$

Charles de Gaulle aircraft carrier (n=1568)



R_t , immunity and social contacts

(1 - % restricted)



NATURE REVIEWS | IMMUNOLOGY

COVID-19 herd immunity: where are we?

Arnaud Fontanet^{1,2} and Simon Cauchemez³

VOLUME 20 | OCTOBER 2020

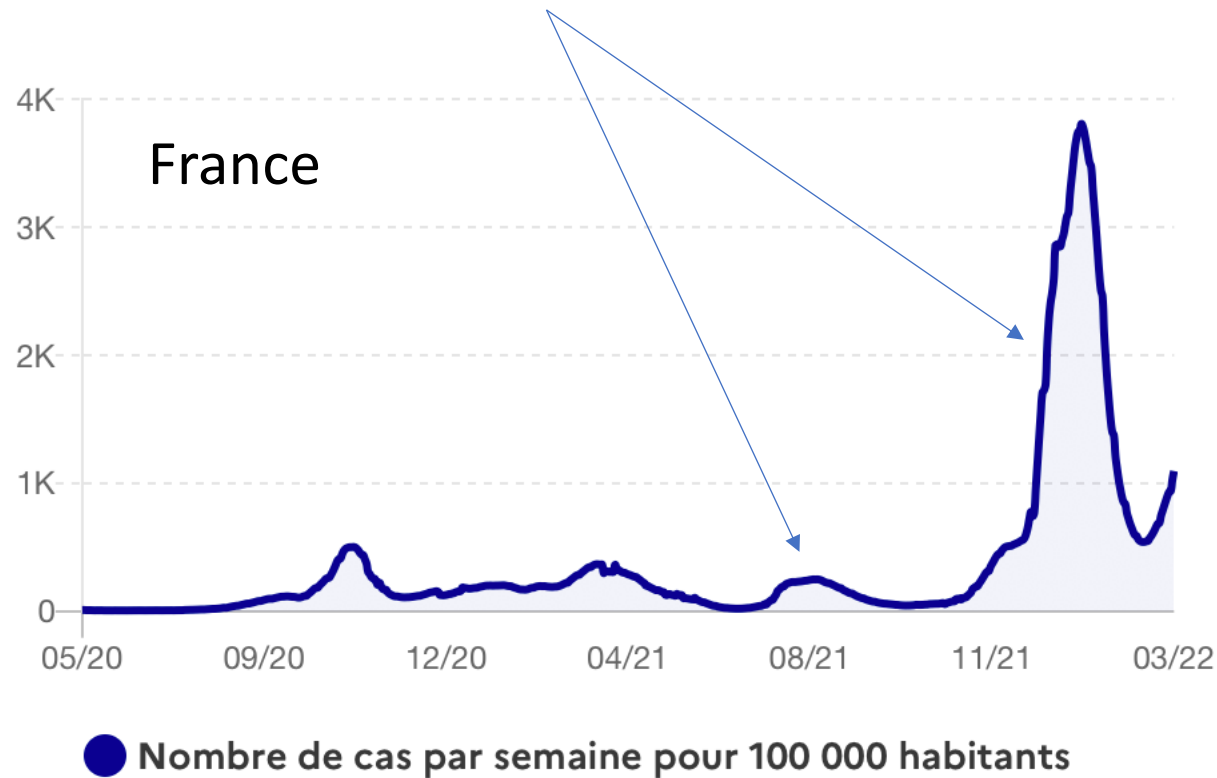
$$R_t = R_0 * (1 - \% \text{ infected}) * (1 - \% \text{ restricted})$$

→ With R_0 of 2.5, to keep $R_t < 1$:

- lots of immunity
- very strong social distancing
- or something in between for each

Is there a seasonal effect?

Yes, Delta during summer and fall

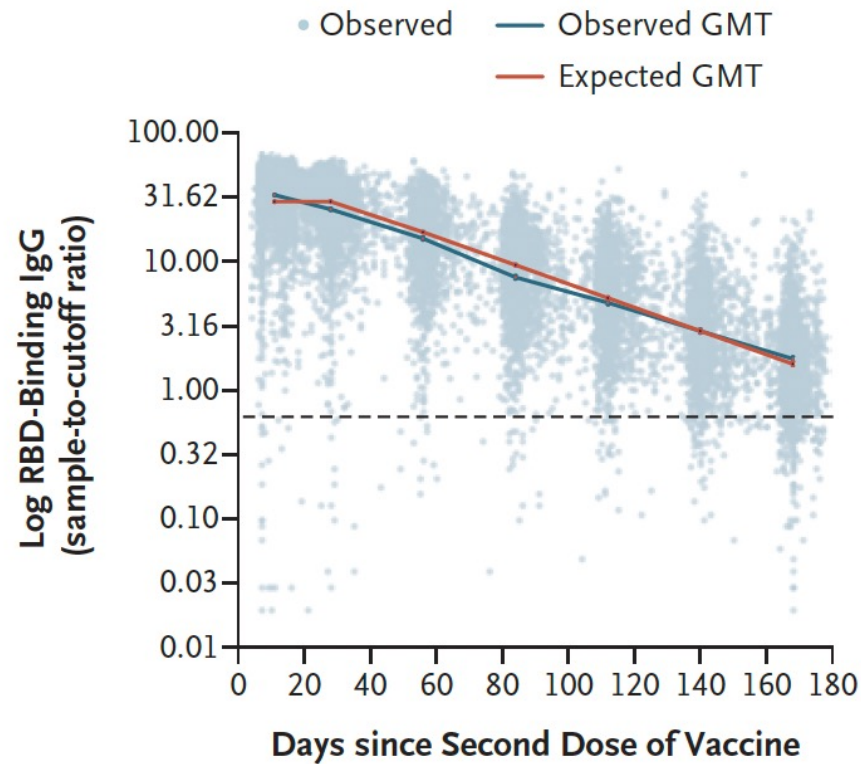


$$R_t = R_0 * (1 - \% \text{ infected}) * (1 - \% \text{ restricted})$$

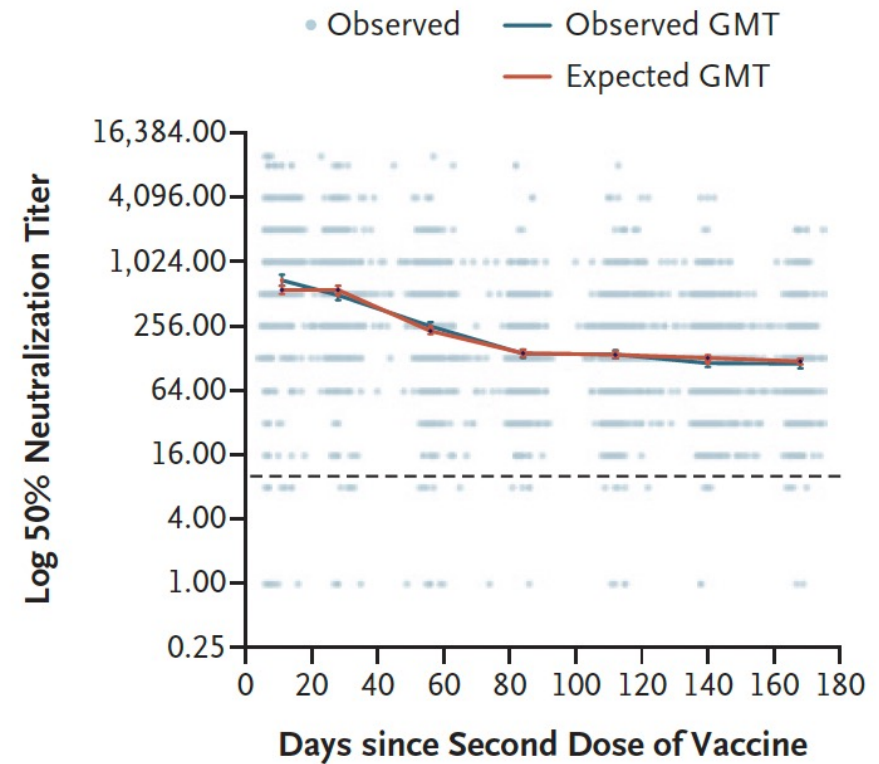
Seasonal effect acts on R_0 :
+33% during winter compared to summer

Anti-RBD IgG and neutralising Ab post 2nd dose BNT162b2 Health care workers (n=4,868), Israel, Dec 2020 - Jul 2021

A IgG in Overall Population (n=4,868)



B Neutralizing Antibody in Overall Population (n=1,269)

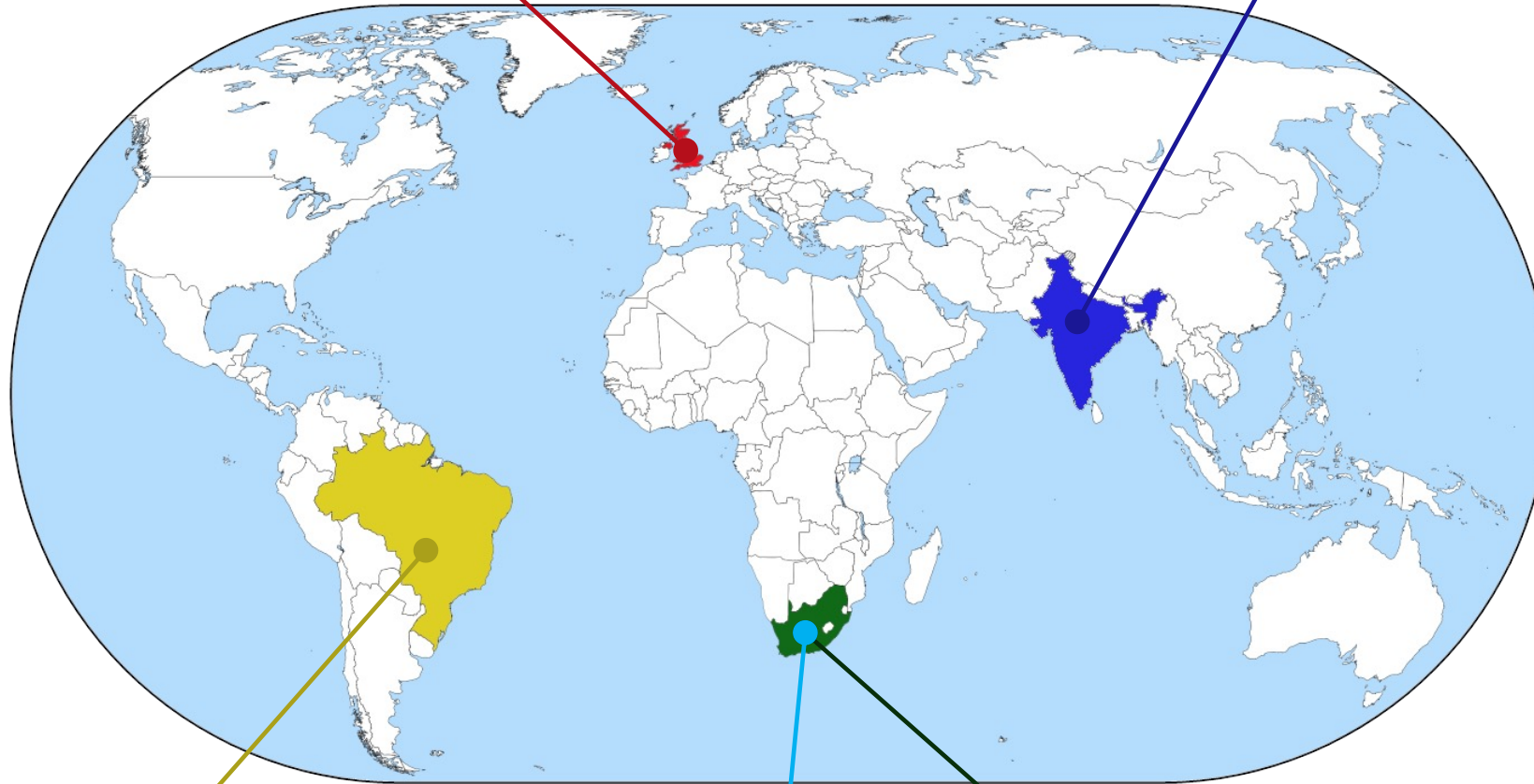


(Levin, NEJM, 2021)

Variants of concern (VOC)

Lineage B.1.1.7 (VOC Alpha, « UK » variant)

Lineage B.1.617.2 (VOC Delta, « Indian » variant)



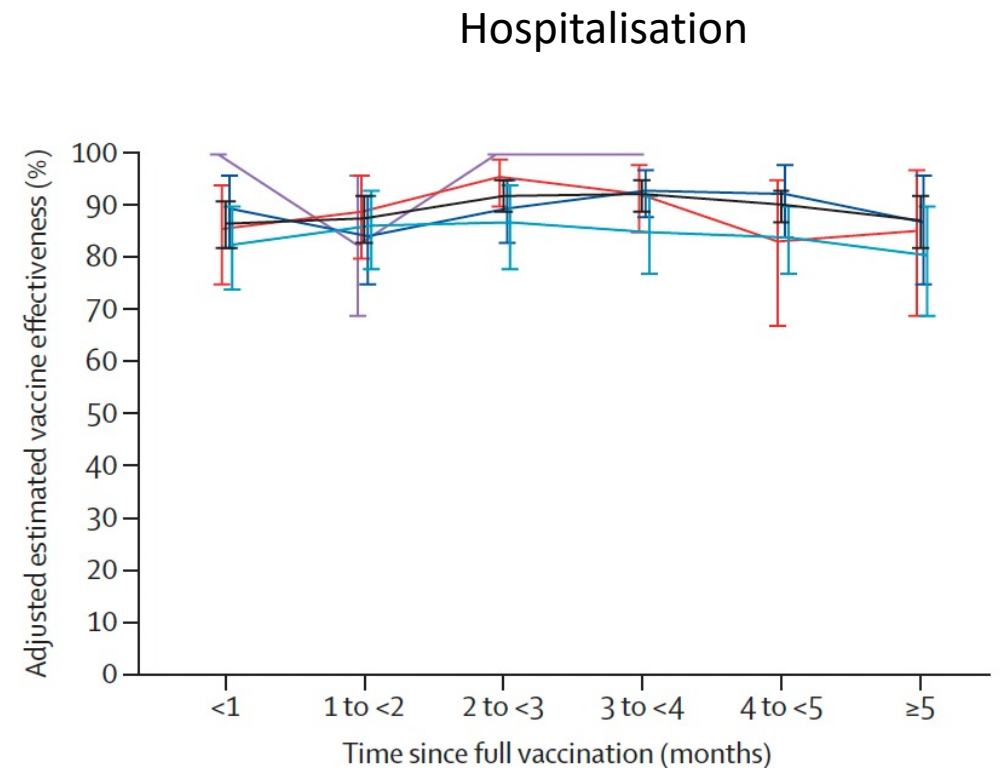
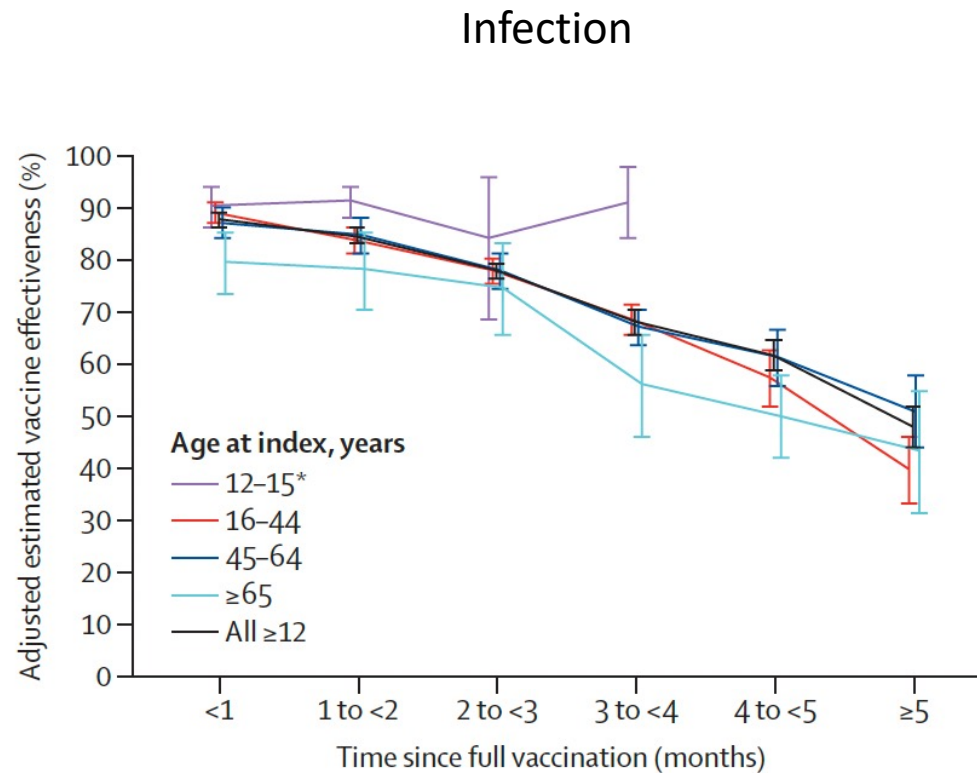
Lineage P.1 (VOC Gamma, « Brazilian » variant)

Lineage B.1.351 (VOC Beta, « South-African » variant)

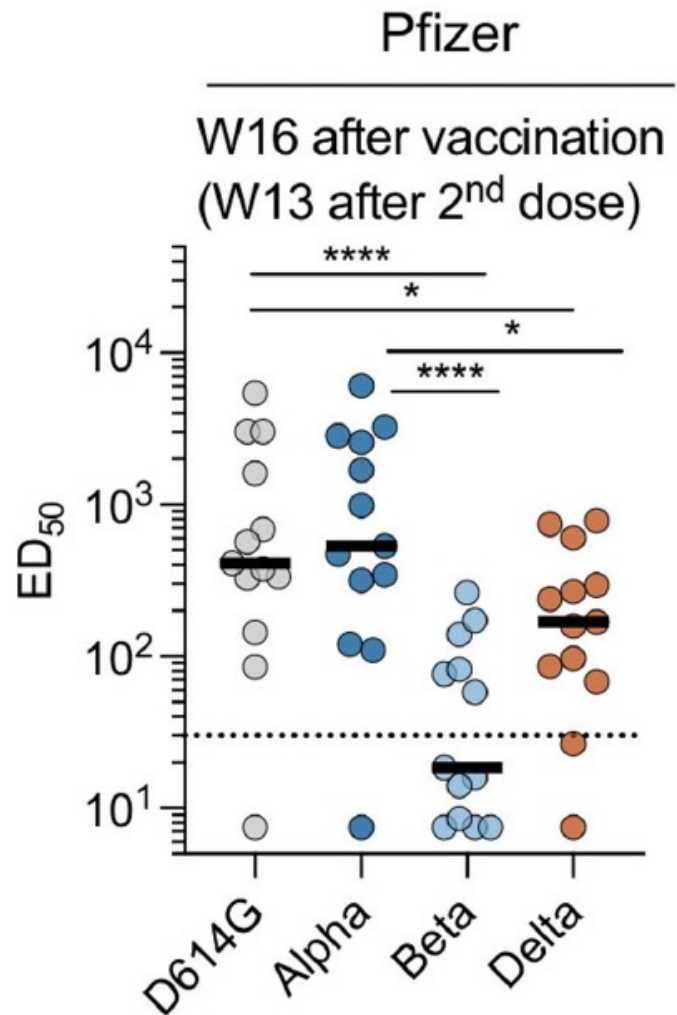
Lineage B.1.1.529 (VOC Omicron)

(<https://www.ecdc.europa.eu/en/covid-19/variants-concern>)

Vaccine efficacy against infection and hospitalisation by age and month since 2nd dose, BNT162b2 Retrospective cohort (n=1,043,289), Dec 2020-Aug 2021, United States

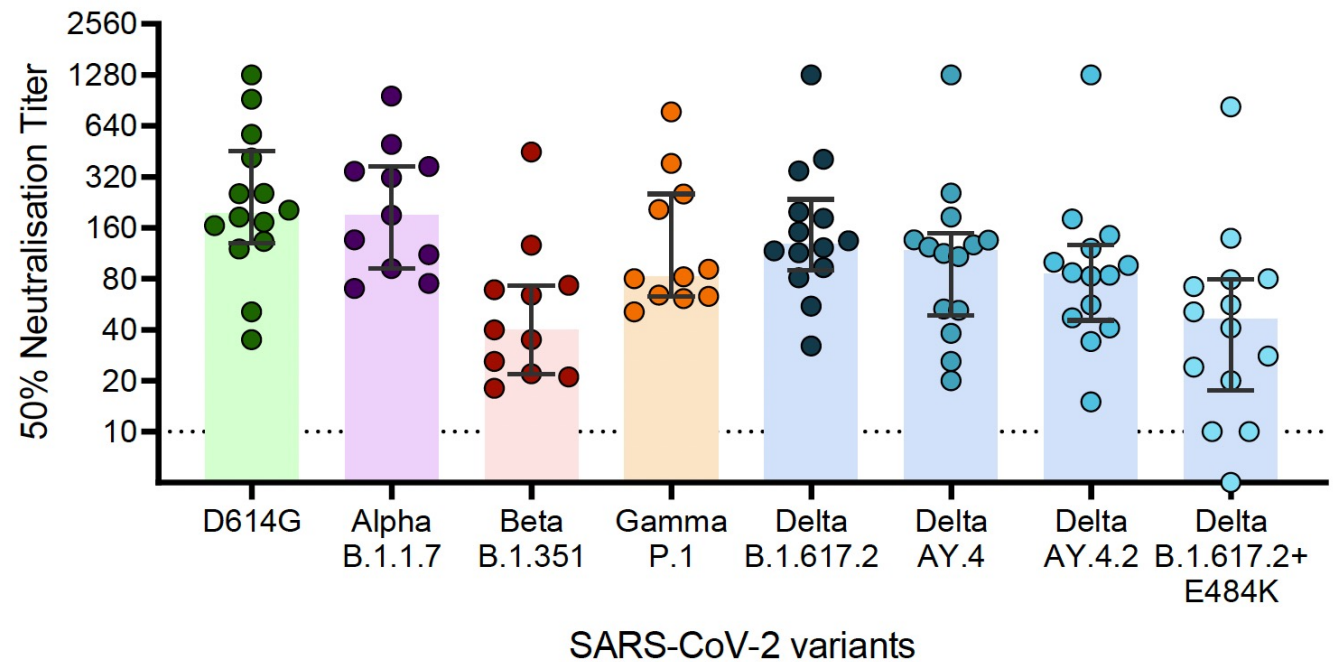


SARS-CoV-2 variants neutralization post 2nd dose



(Planas, Nature, 2021)

2 months after 2nd dose BNT162b2

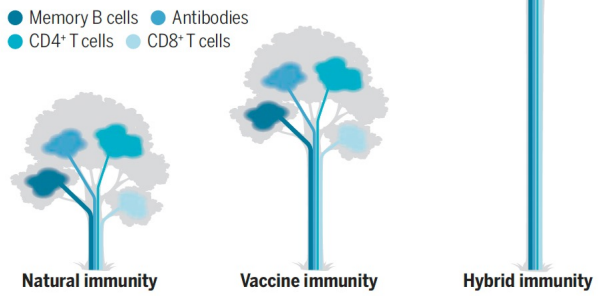


(Lassaunière, medRxiv, 2021)

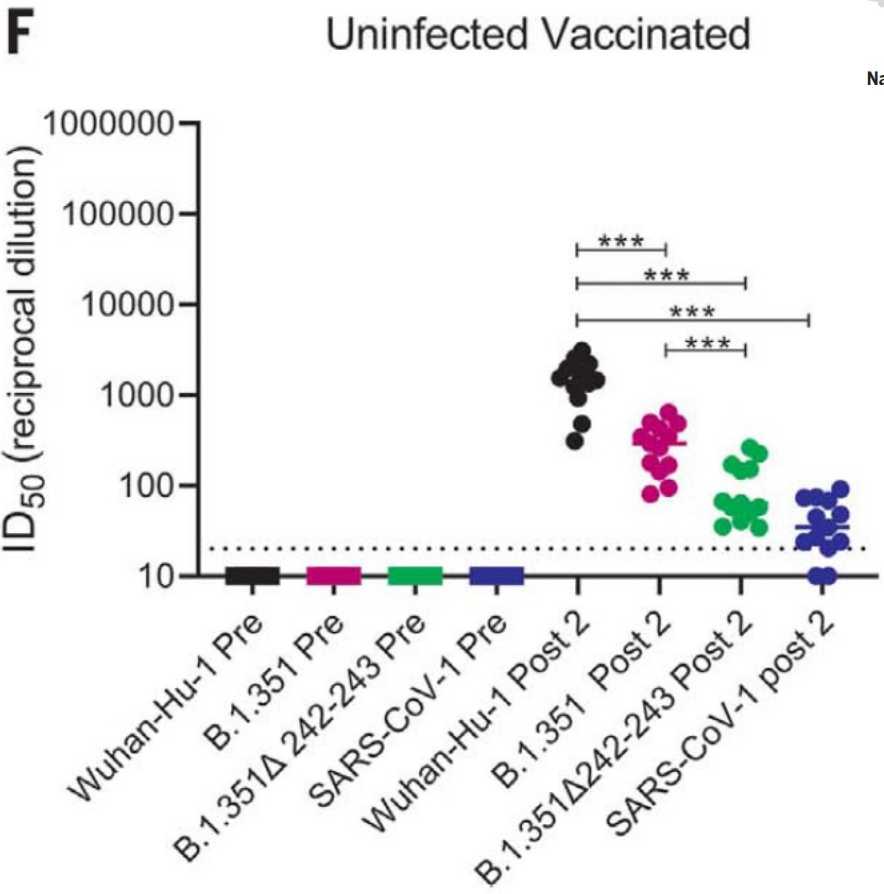
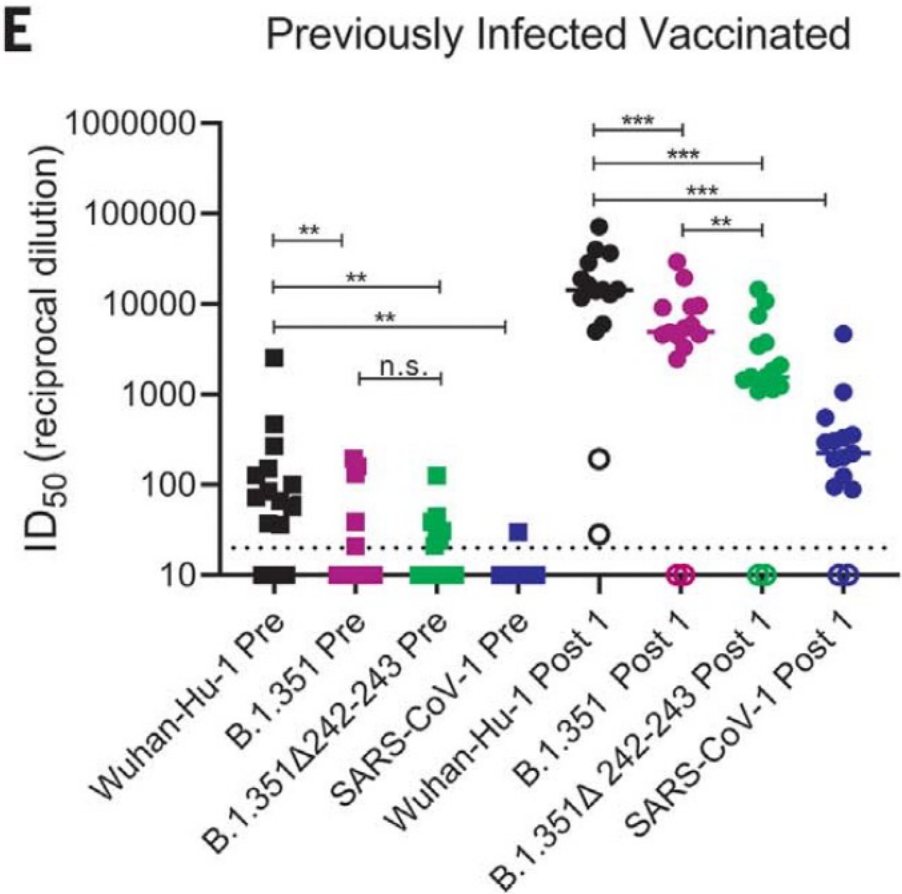
Neutralising Ab One dose + infection compared to two doses without infection

Hybrid vigor immunity with COVID-19 vaccines

Hybrid vigor can occur when different plant lines are bred together and the hybrid is a much stronger plant. Something similar happens when natural immunity is combined with vaccine-generated immunity, resulting in 25 to 100 times higher antibody responses, driven by memory B cells and CD4⁺ T cells and broader cross-protection from variants.

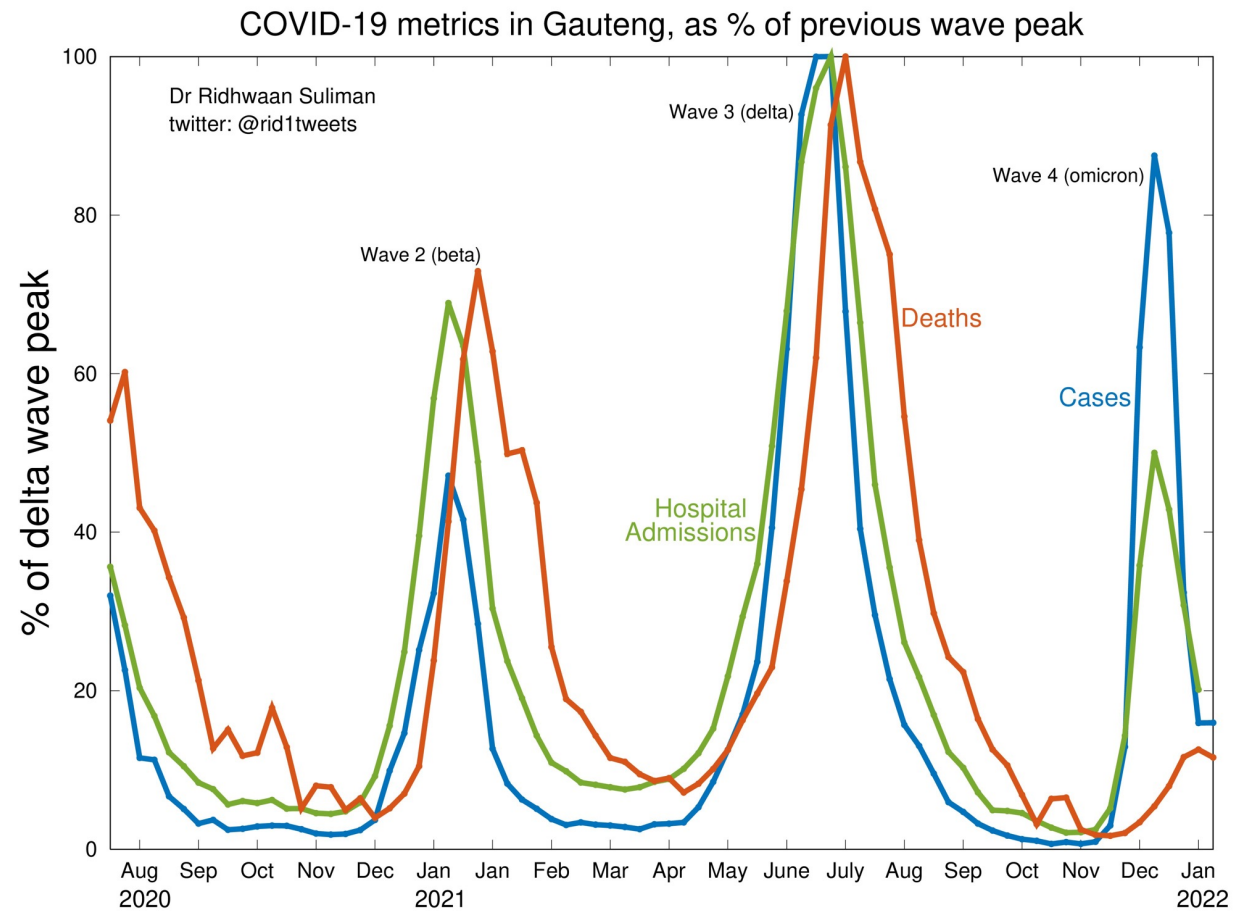


(Crotty, Science, 2021)

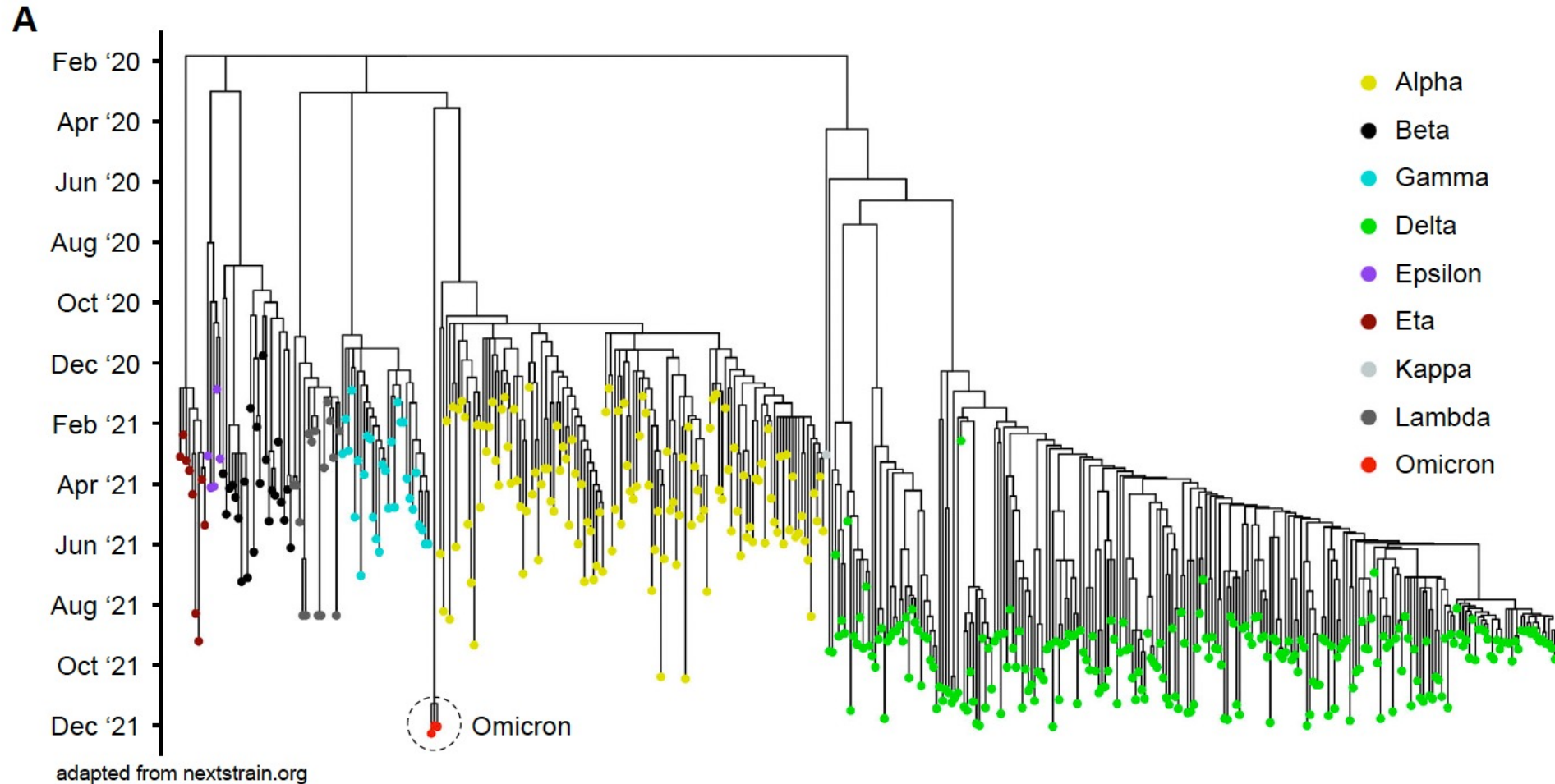


(Stamatatos, Science, 2021)

South Africa, comparison of COVID-19 waves



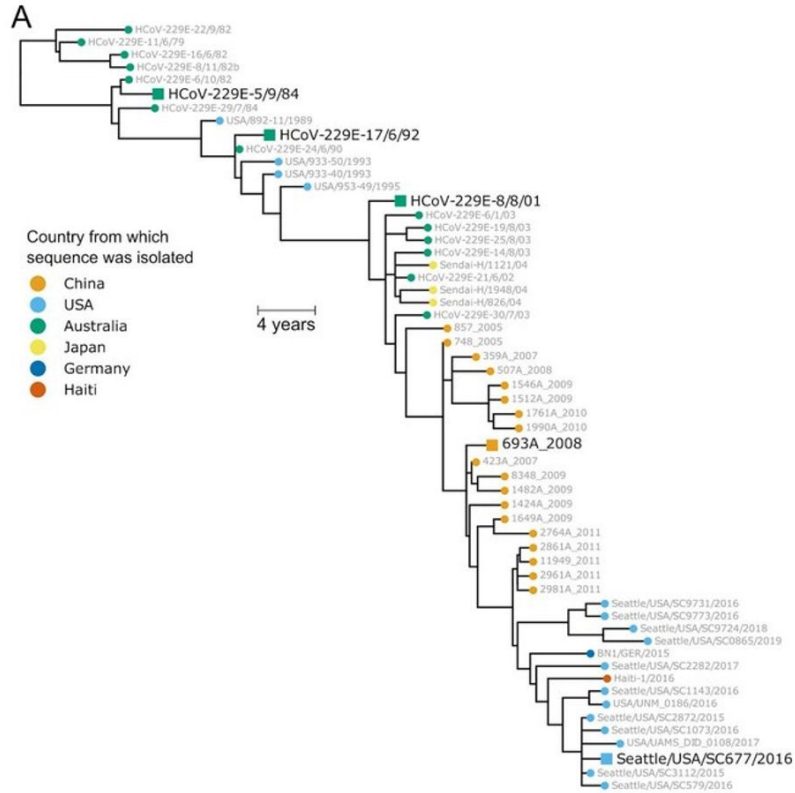
SARS-CoV-2 phylogeny



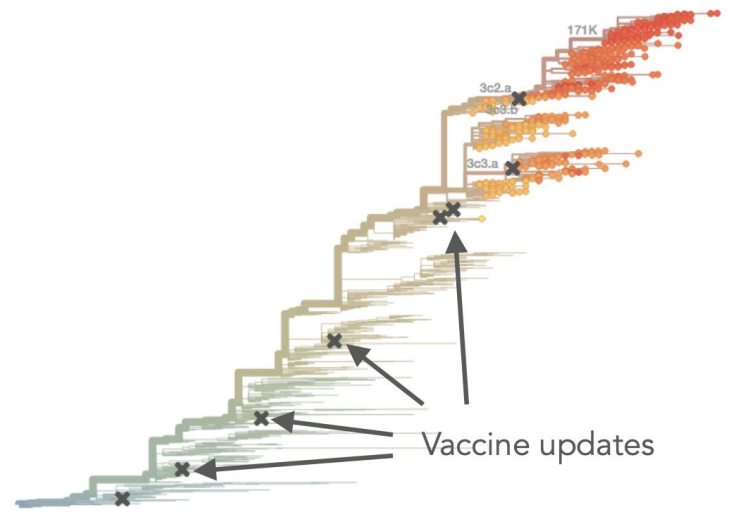
(Garcia-Beltran)

Variant emergence : mutations & selection

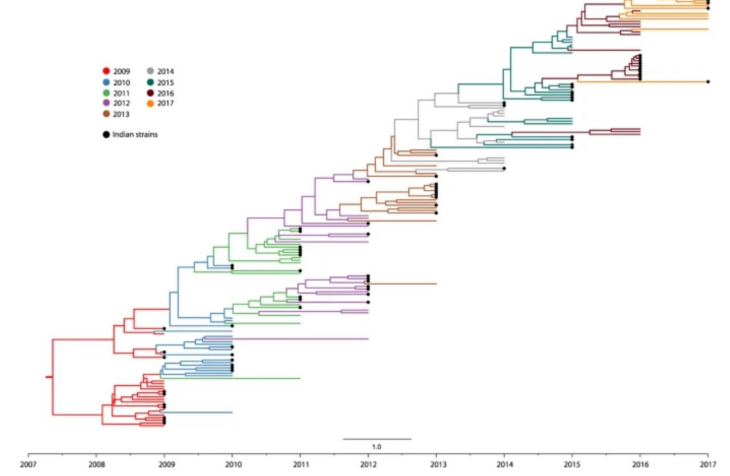
Human coronavirus 229E:



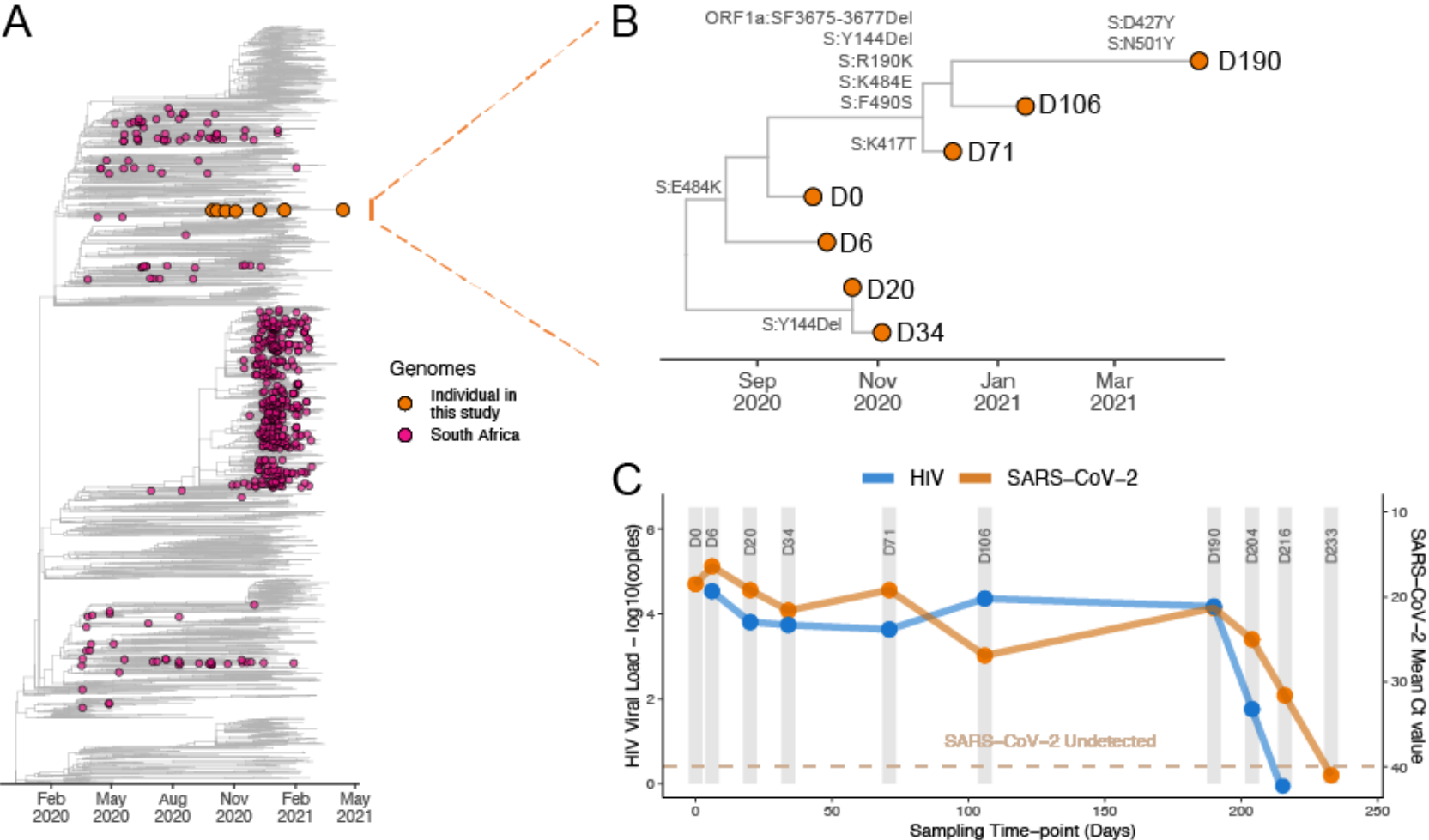
Influenza A/H3N2 (2005–17):



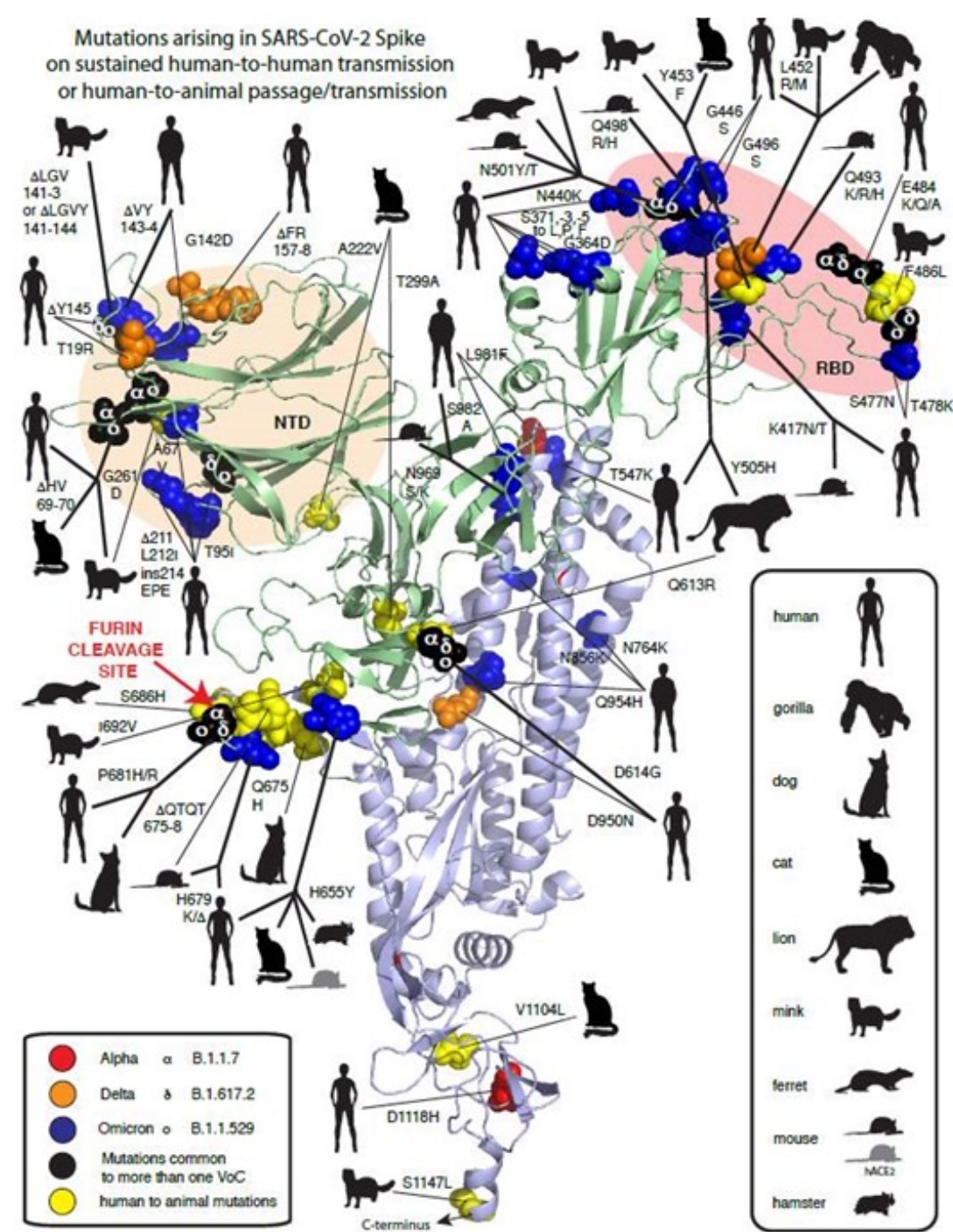
A/H1N1p



Variant emergence: chronic infection in immunosuppressed individuals

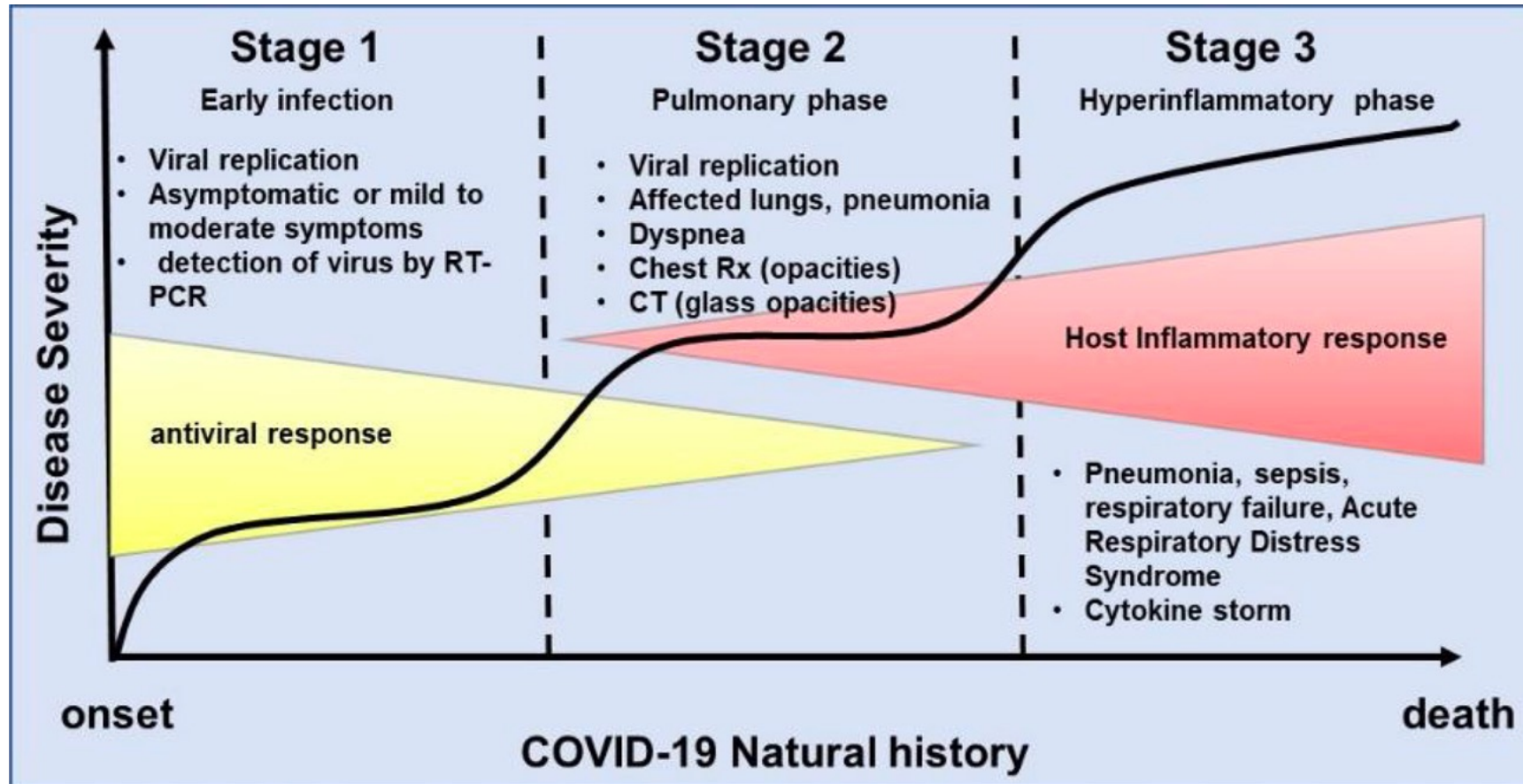


Variant emergence: zoonotic pathway



(Garry, Cell)

Forces driving variant selection



Selection pressure



Transmission

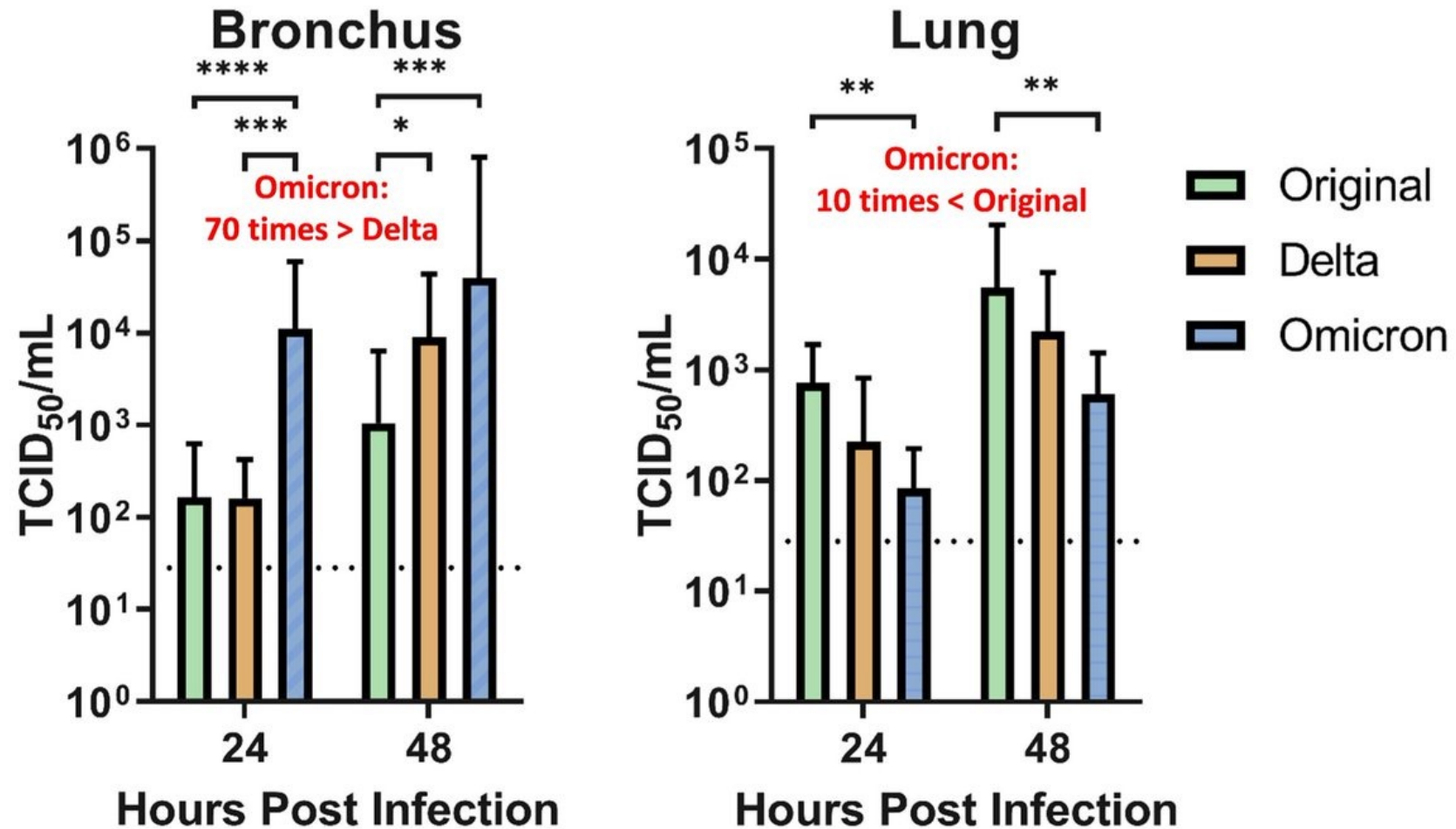
Contagiosity and immune escape



Severity

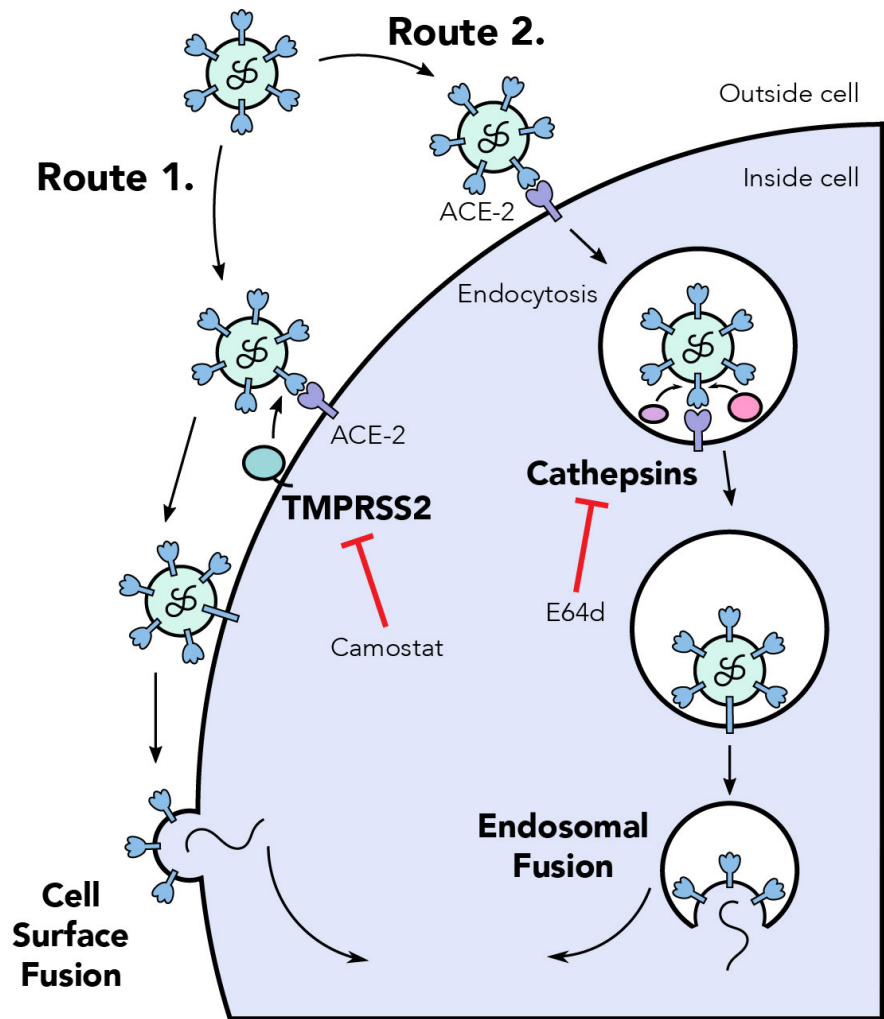
(Gouvea dos Santos, Biomedicine and Pharmacotherapy, 2021)

Omicron multiplies in the bronchi, not the lungs

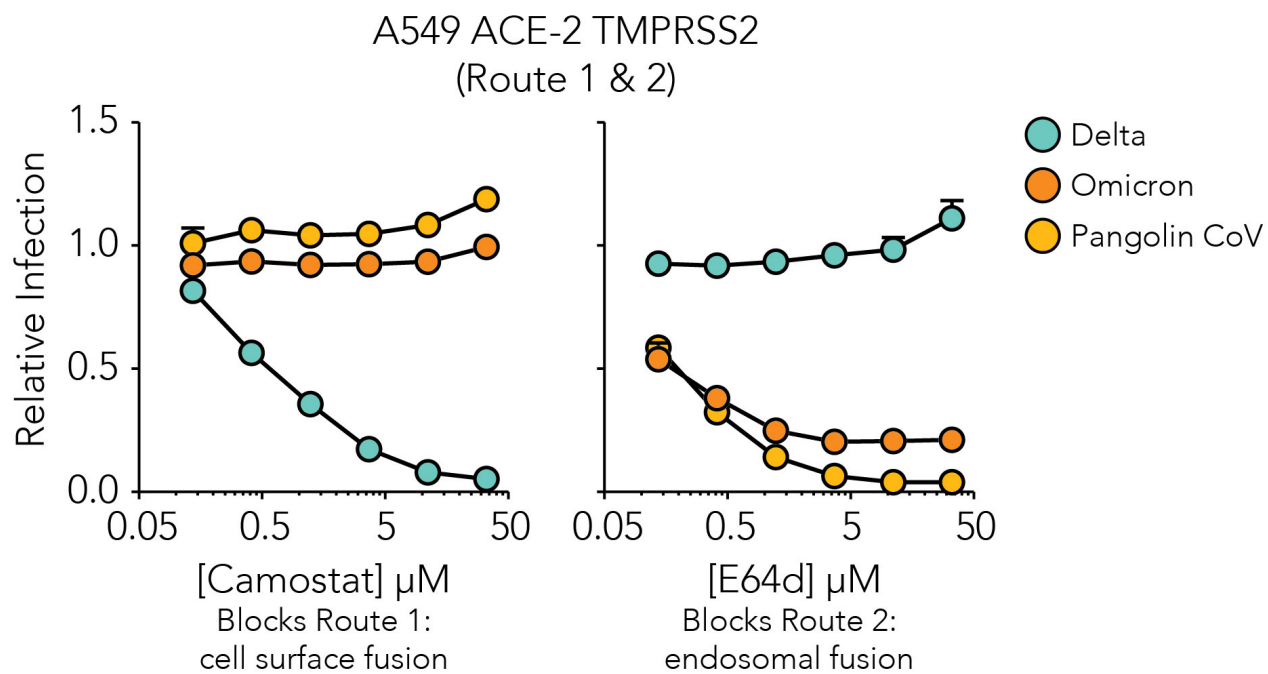


(Nicolls & Peiris)

Omicron double entry routes



Thanks to Georgina Brown for use of this cartoon



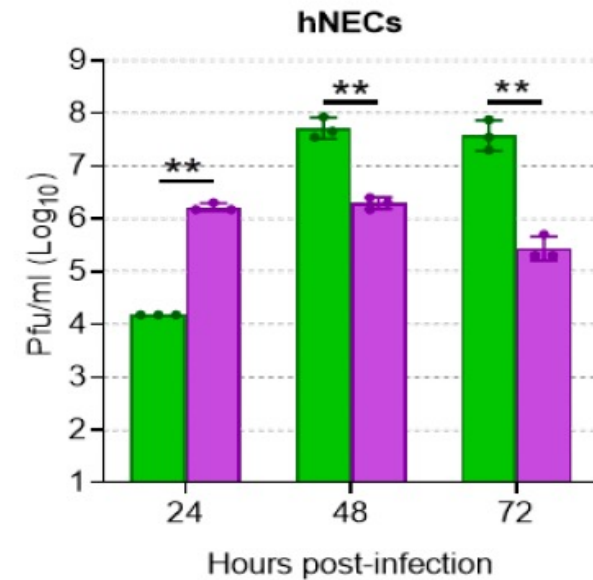
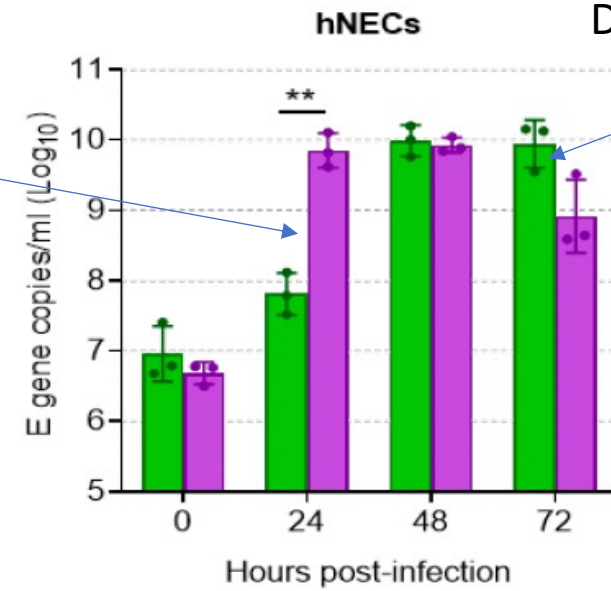
Data: Joe Grove @GroveLab

(Joe Grove)

Multiplying in nasal epithelium cells

Omicron > Delta at 24h

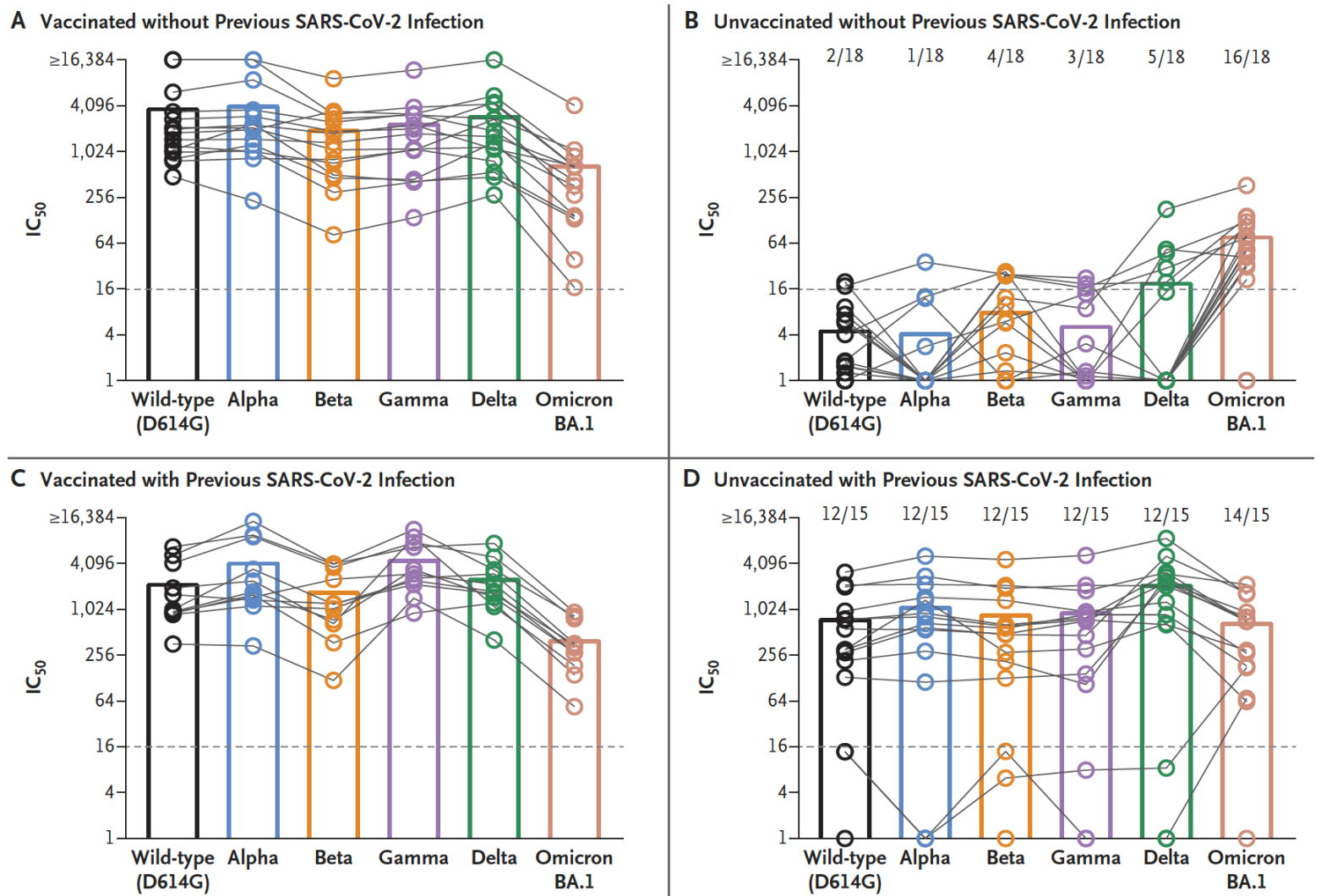
Delta > Omicron at 72h



● Delta 1 ● Omicron 1

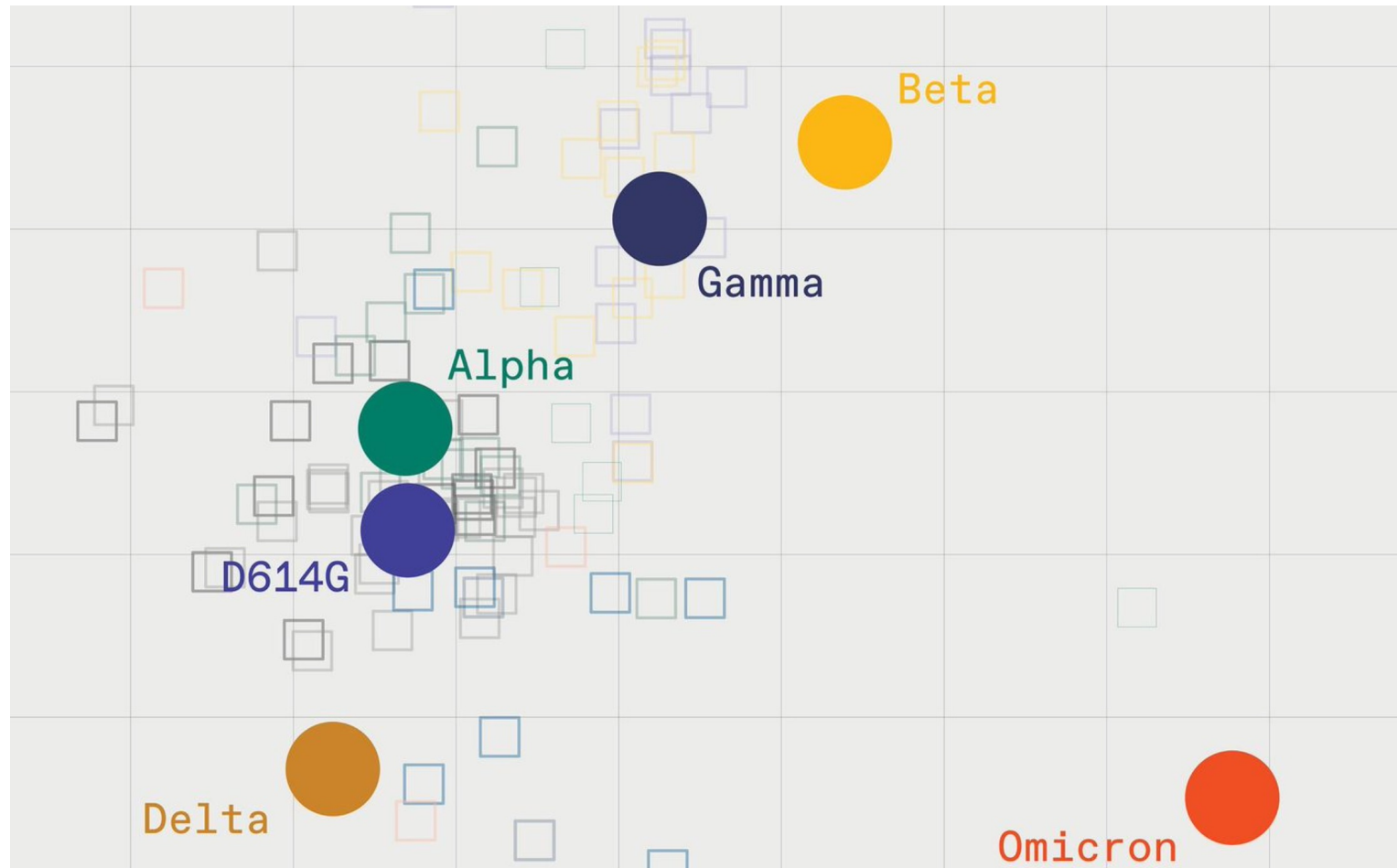
(Peacock & Barclay)

Neutralisations titers post BA.1 Omicron infection by past history of infection and vaccination



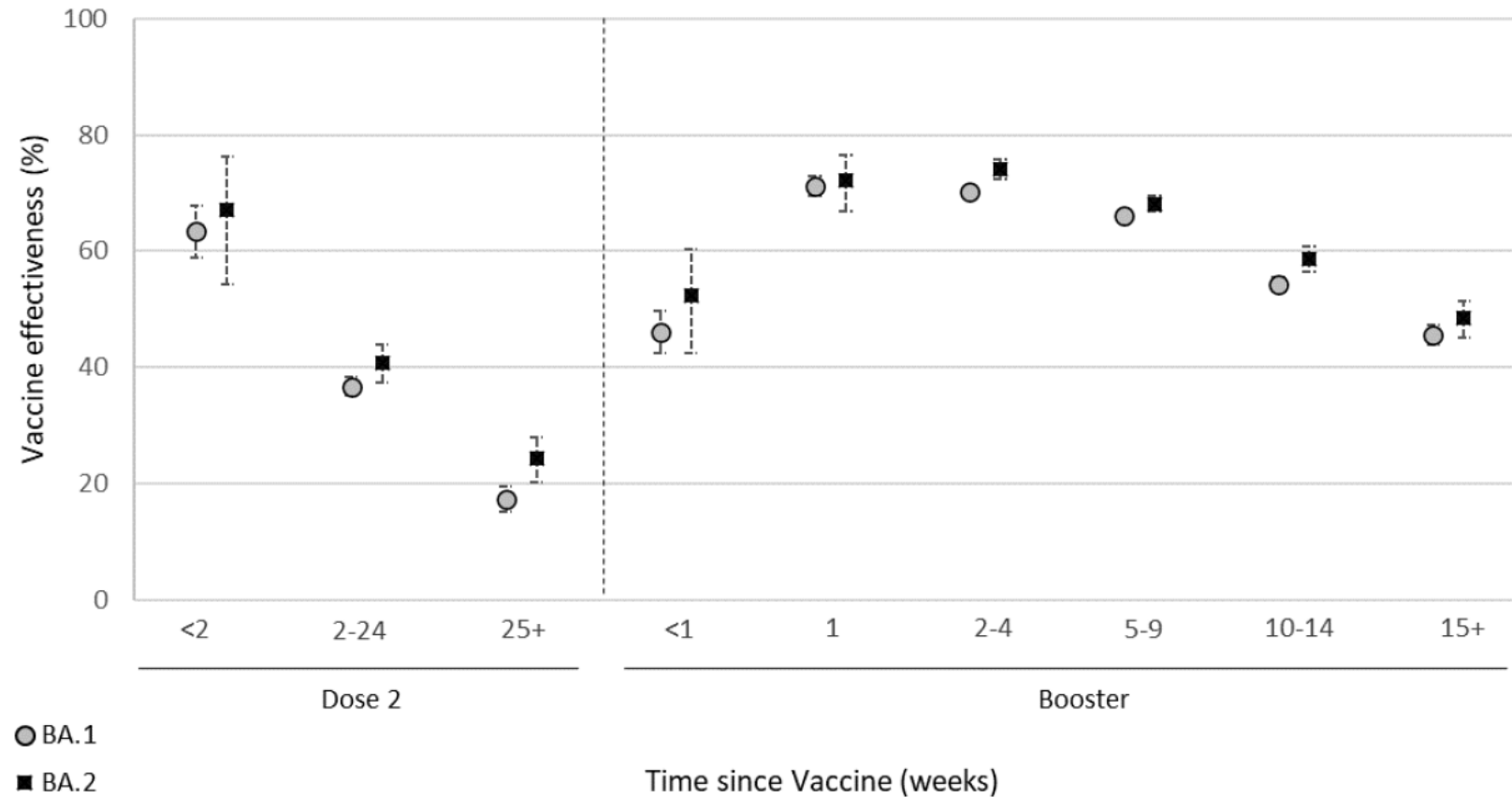
(Rössler, NEJM, 2022)

Antigenic map - Omicron

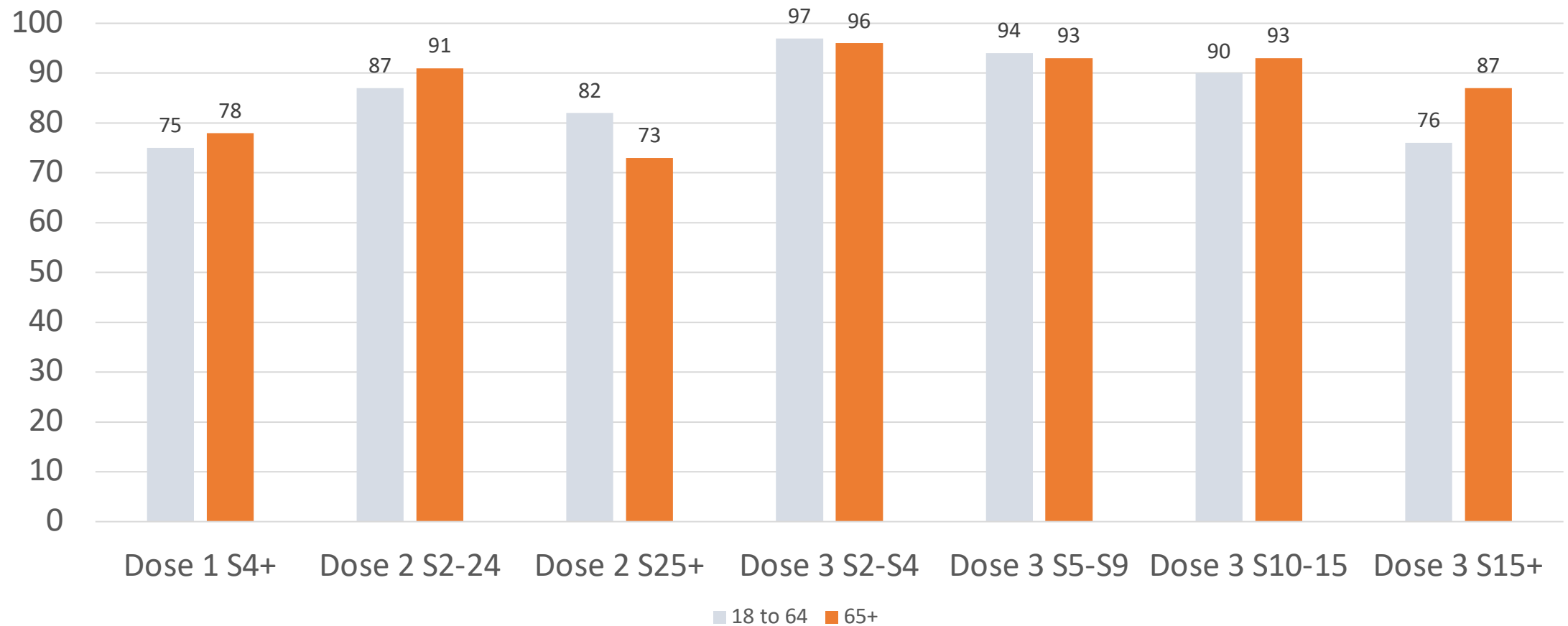


(Wilks & Smith, 2022)

Vaccine Efficacy against symptomatic infection (BA.1 & BA.2) Omicron variant – England – March 2022

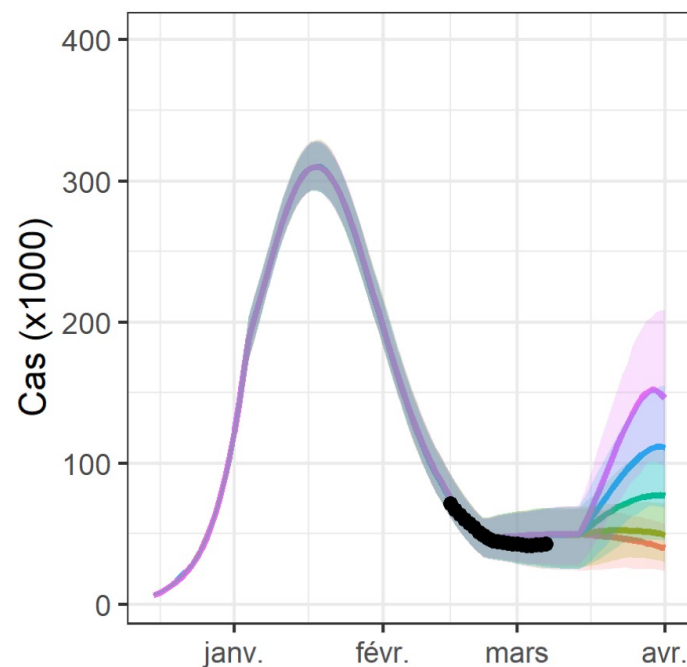


Vaccine efficacy (%) against hospitalisation Omicron variant – England – March 2022

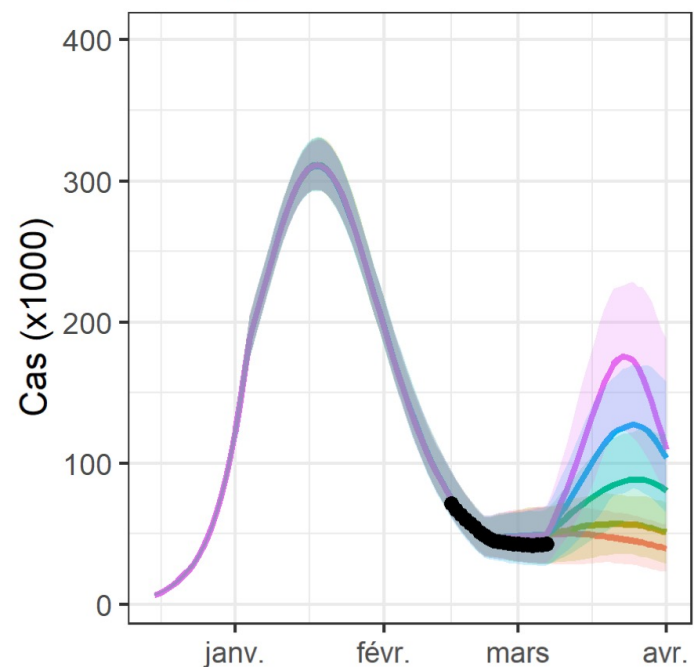


BA.2 projections – April 2022

A Changement le 14 mars



B Changement le 7 mars



Augmentation des taux de transmission



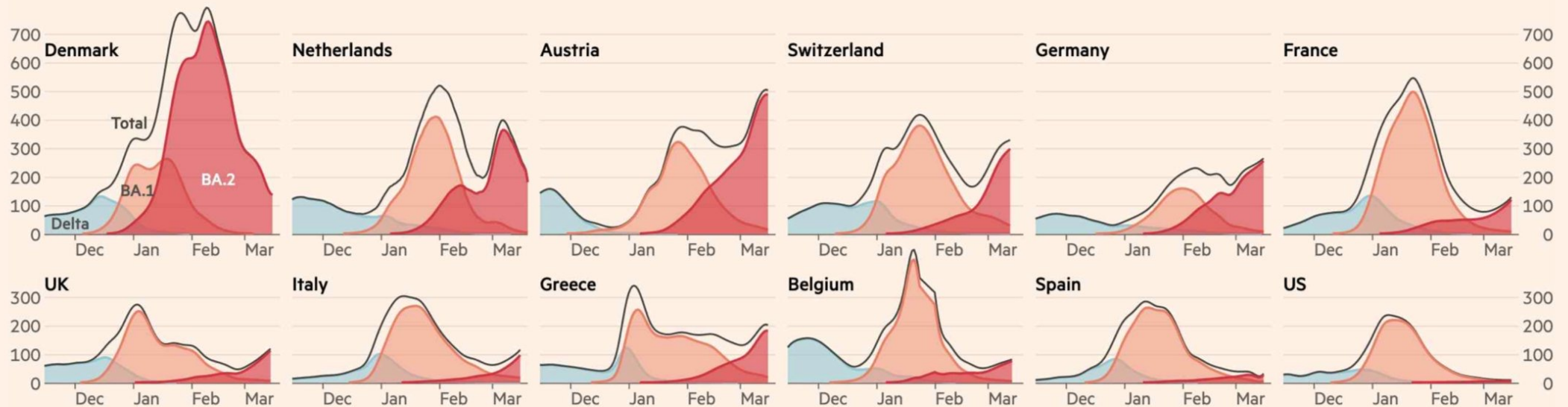
● Données non disponibles lors de la calibration

(Bosetti et al, 2022)

European situation – BA.1 & BA.2

The BA.2 Omicron sublineage has displaced the original strain and is driving new surges in cases across Europe, with Denmark and the Netherlands now past their BA.2 peaks

7-day average of new confirmed cases per 100k people, by variant*



*Each variant's share of all cases estimated using method from Tom Wenseleers / @TWenseleers, then applied to case rates
Source: FT analysis of data from Johns Hopkins CSSE, World Health Organization
FT graphic: John Burn-Murdoch / @burnmurdoch
© FT

(26 March 2022)

In summary

- Most likely there will be new variants
- We cannot rule out a highly transmissible variant that would also be severe
- Still, we will be better protected with time against severe forms of disease thanks to cumulative layers of past infections and vaccinations
- SARS-CoV-2 may ultimately join the group of seasonal human coronaviruses
- Should we let children get their first immunity through natural infection or early immunisation will depend on the severity of infections in very young