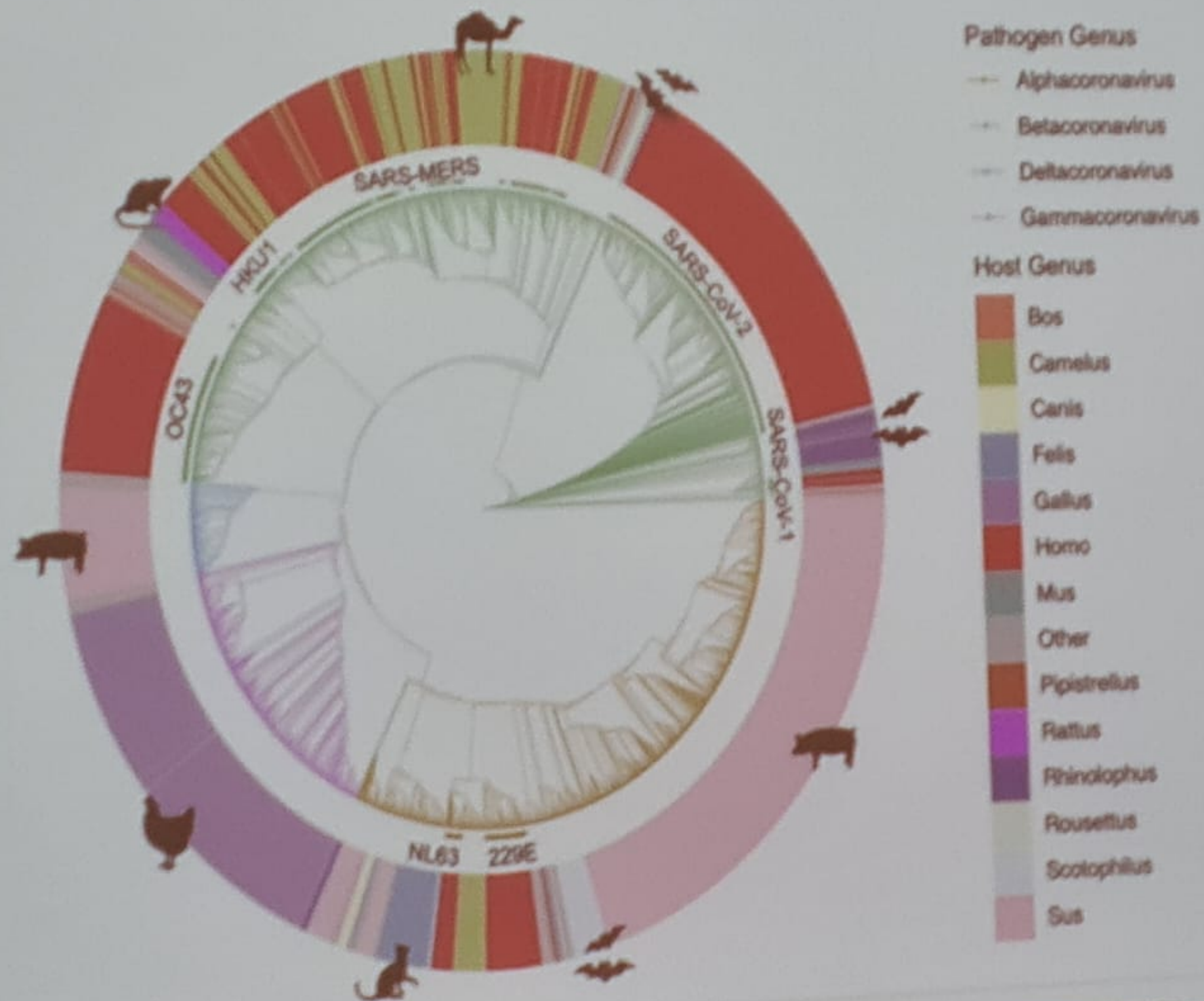


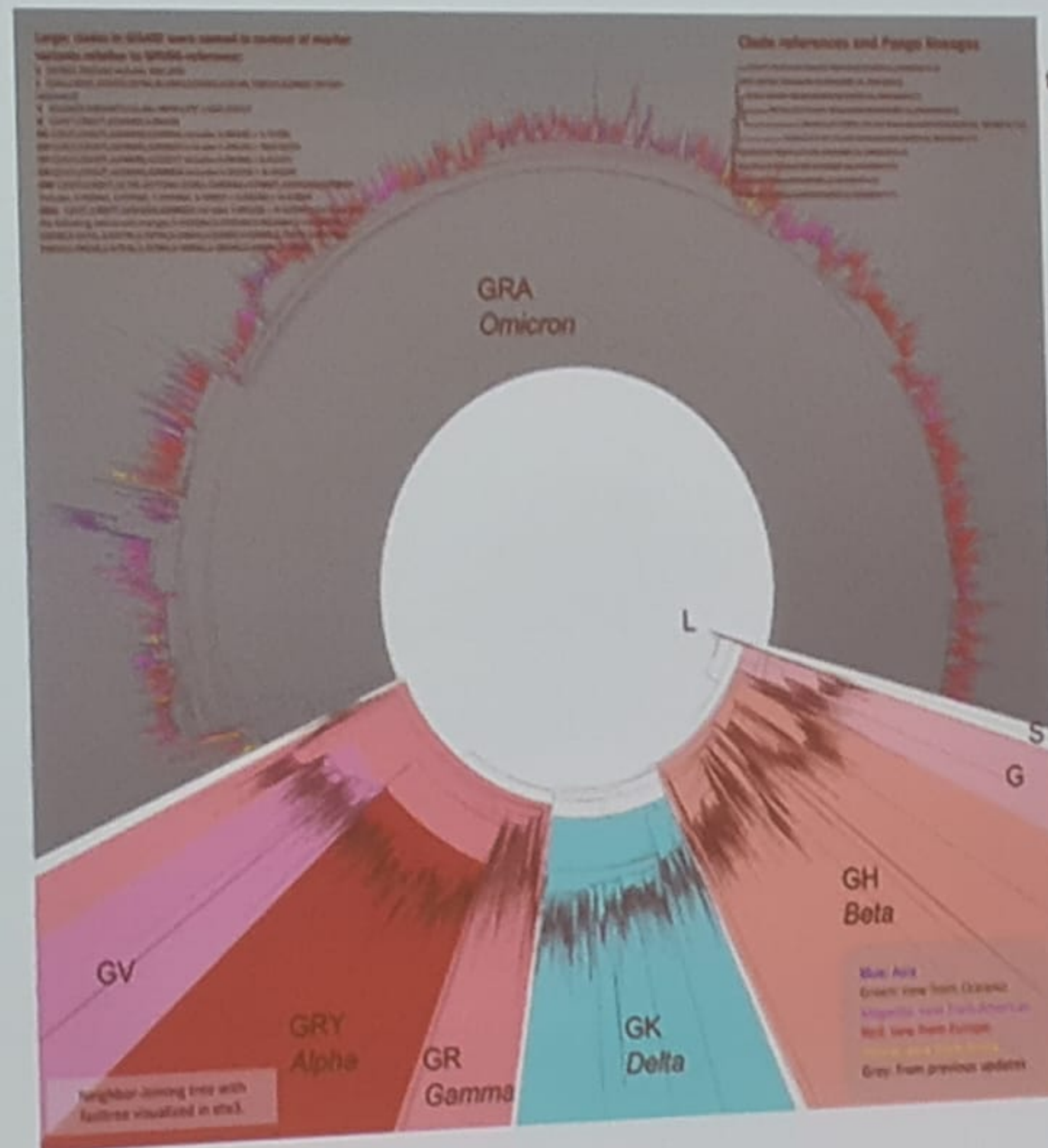
The virus is here to stay



Coronavirus evolution



SARS-CoV-2 evolution



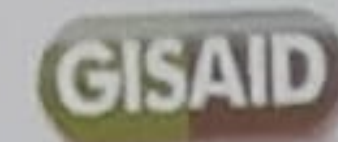
Sampled genome
tree derived from all
outbreak sequences
2022-08-23

Notable changes

11,576,799 full genomes (+98,433)
(excluding low coverage, out of
12,652,854 entries)

S clade [HBBN] 16,785 [6,397] (+1) (+0)
L clade [HBBN] 6,092 [1,477] (+0) (+0)
V clade [HBBN] 6,687 [81] (+0) (+0)
G clade [HBBN] 295,789 [322,308]
(+166) (+72)
GR clade [HBBN] 481,642 [250,686]
(+199) (+117)
GRY clade [HBBN] 1,036,207 [115,889]
(+46) (+0)
GV clade [HBBN] 523,792 [755,888]
(+137) (+72)
GV clade [HBBN] 172,574 [8,813]
(+2) (+0)
GR clade [HBBN] 6,108,343 [648,694]
(+504) (+60)
GRA clade 4,883,730 (+87,135)
Other clade [HBBN] 45,127 [31,230]
(+44) (+34)

We gratefully acknowledge
the Authors from Originating
and Submitting laboratories
of sequence data on which the
analysis is based.



by BUKUS, A*STAR, Singapore

SARS-CoV-2 will keep evolving

Evolutionary potential of SARS-CoV-2



C WORLD WIDE MUTATION POTENTIAL

$$\begin{array}{ccc} 0.5 & 0.3-3 \times 10^5 & 0.1-1 \times 10^6 \\ \text{mutations} & \text{world wide} & \text{mutations transmitted} \\ \text{per} & \text{infections} & \text{per day world wide} \\ \text{infection} & \text{per day} & \\ \times & \approx & \end{array}$$

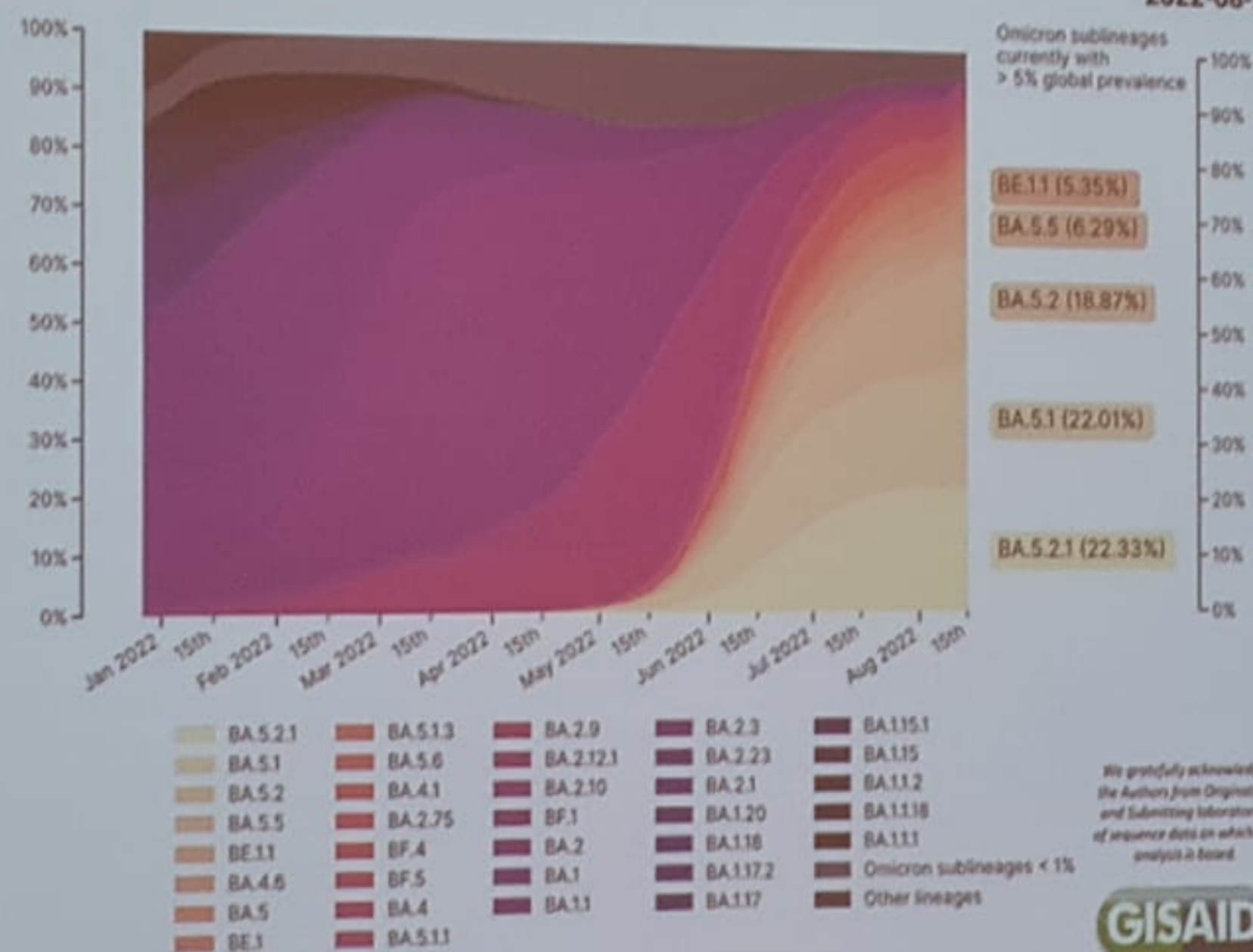
$$3 \times 10^4 \text{ bases} \times 3 \text{ alternative bases} \approx 10^5 \text{ possible single base mutations}$$

every single base mutation is being generated de-novo and transmitted to a new host every day



Ongoing evolution of Omicron

Timecourse of Omicron variant sublineage distribution
2022-08-23



See <https://www.who.int/en/emergencies/tracking-sars-cov-2-variants/> for variant information and definitions.

We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence data on which the analysis is based.

GISAID

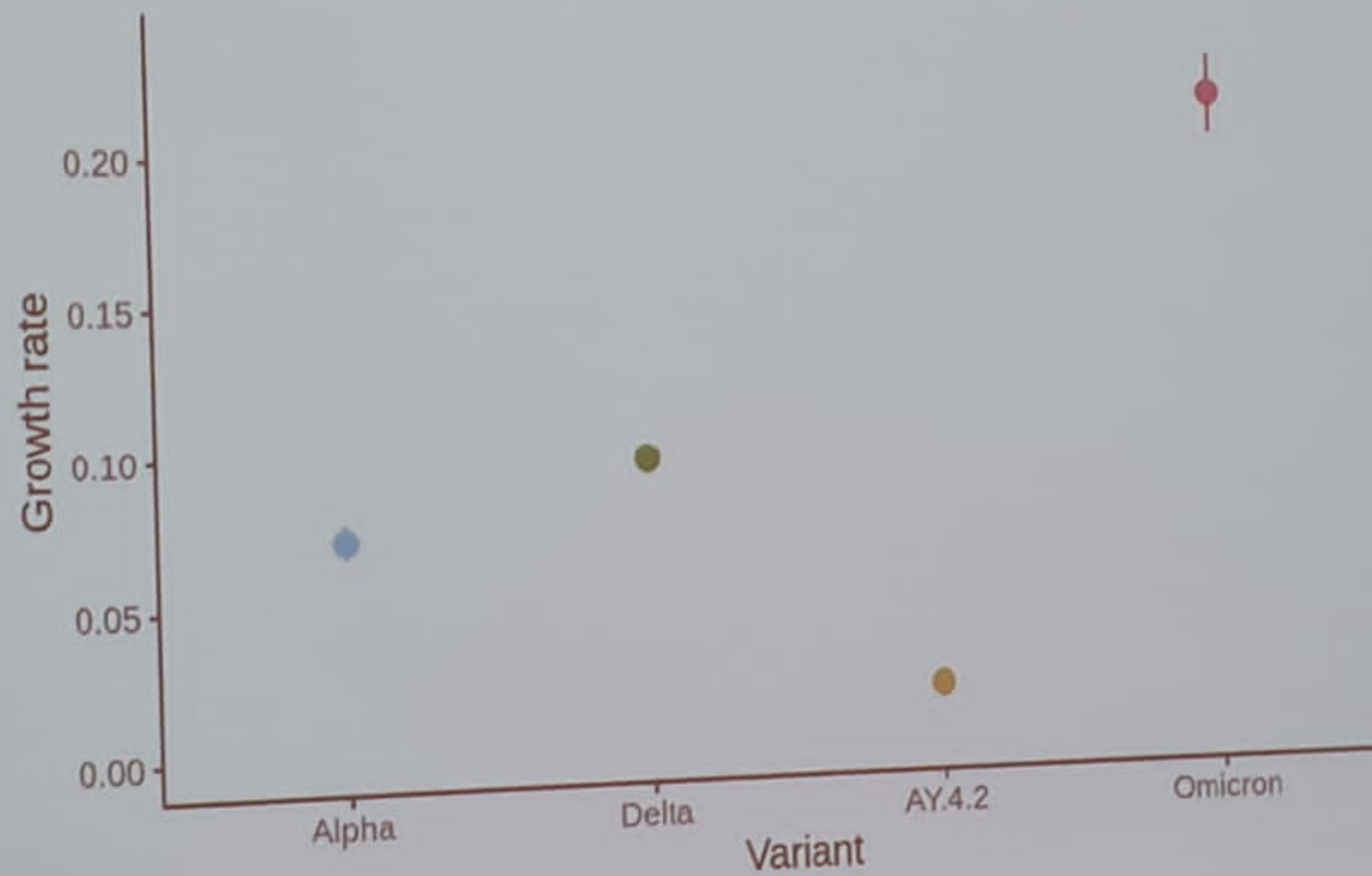
by GISAID, A*STAR Singapore

The main driver of evolution is transmission



Obermeyer et al. 2022. 10.1126/science.abm1208

Evolution is not predictable: growth rates



Evolution is not predictable: severity effects



Many paths to achieve higher transmissibility

- Better affinity to cell receptor(s)
- Shorter generation time
- Increased virus productivity
- Escape from immunity
- Binding to new receptors
- Improved processes during the virus life-cycle
- Longer infection
- Longer persistence in the environment
- ...

Antigenic distance of SARS-CoV-2 variants



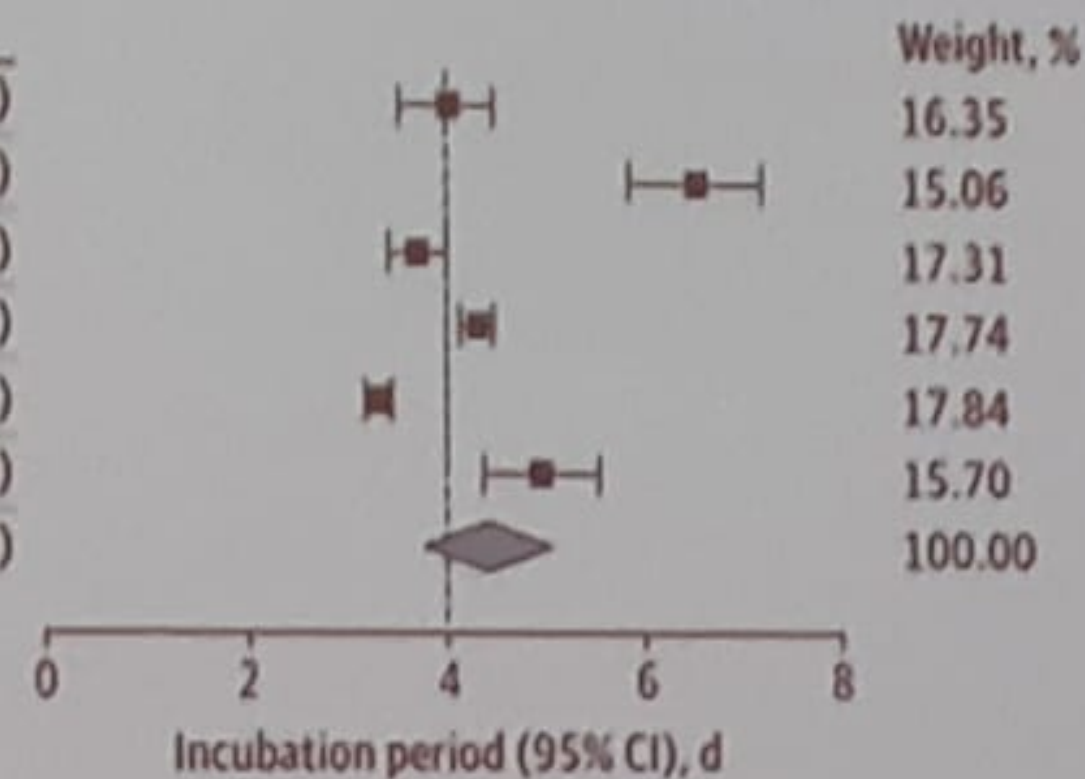
Incubation Times Decrease in VOCs

Variant	Days	95% CI
Original Wu-1	5.2	
Alpha	5.00	4.94 – 5.06
Beta	4.50	1.83 – 7.17
Delta	4.41	3.76 – 5.05
Omicron	3.42	2.88 – 3.96

Progressive reduction in incubation times

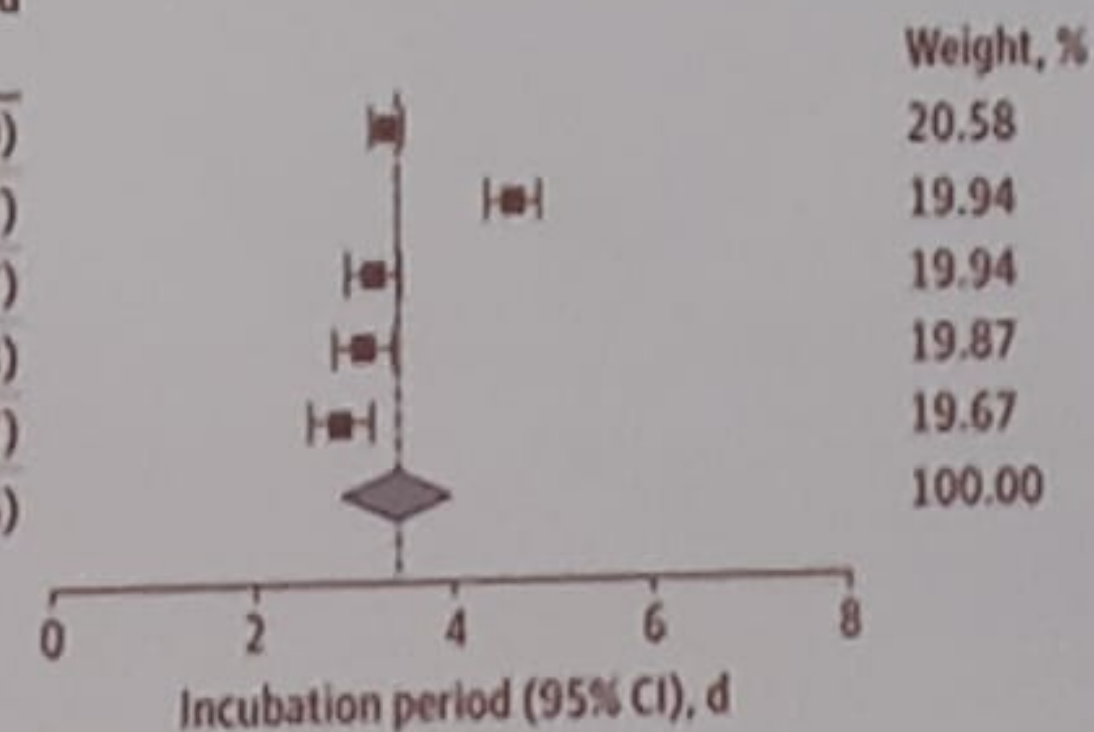
A Delta

Study	Incubation period (95% CI), d
Zhao et al, ¹⁵² 2021	4.00 (3.52-4.48)
Li et al, ⁶³ 2022	6.50 (5.86-7.20)
Ogata et al, ⁸⁰ 2022	3.70 (3.40-4.00)
Grant et al, ³⁵ 2022	4.30 (4.12-4.48)
Del Águila-Mejía et al, ²⁶ 2022	3.30 (3.16-3.44)
Tanaka et al, ¹¹² 2022	4.97 (4.36-5.52)
Overall, DL ($I^2 = 96.8\%$, $P < .001$)	4.41 (3.76-5.05)

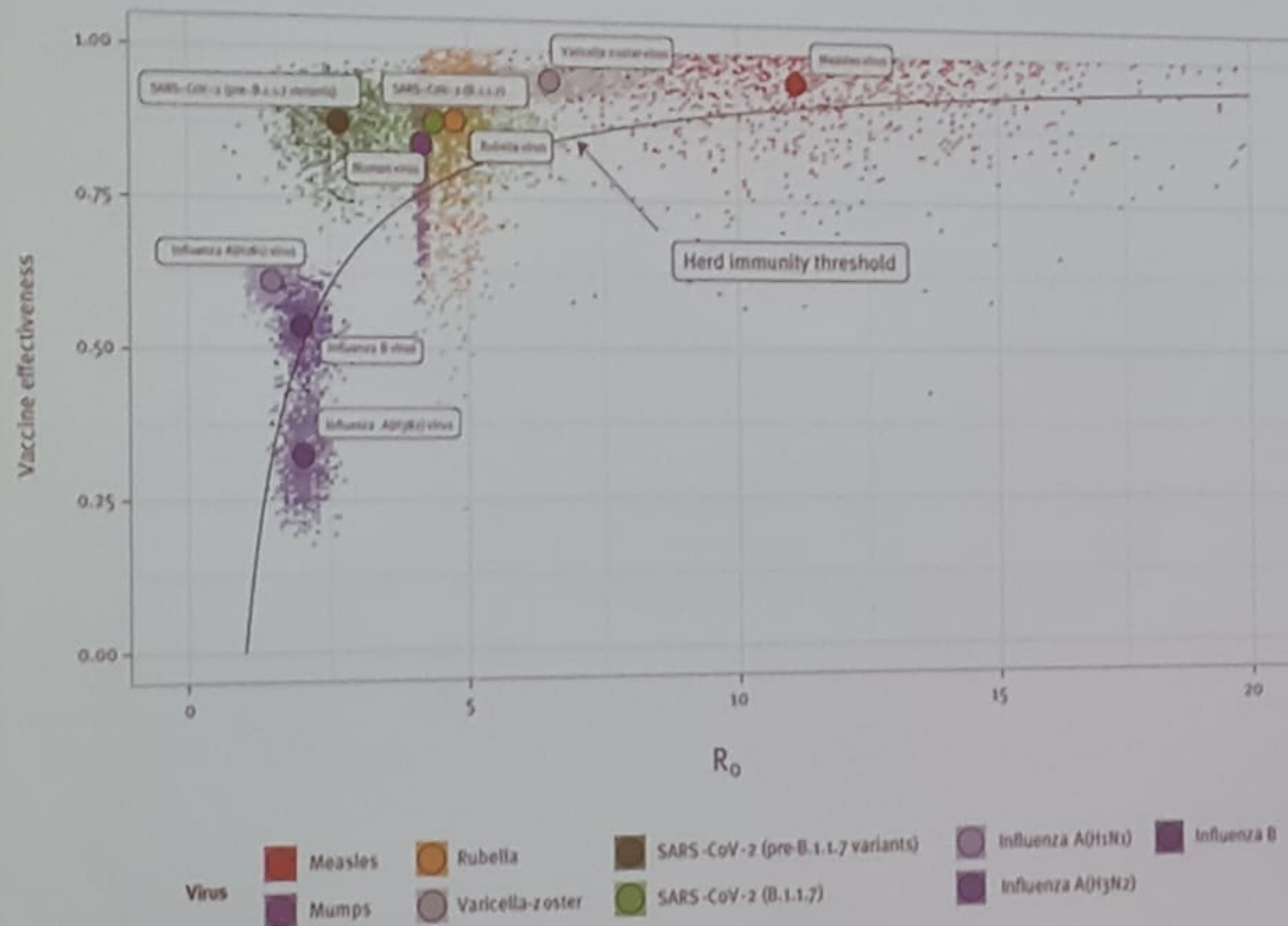


B Omicron

Study	Incubation period (95% CI), d
Brandal et al, ²⁰ 2021	3.33 (3.17-3.50)
Lee et al, ⁵⁹ 2021	4.60 (4.33-4.87)
Backer et al, ¹⁷ 2022	3.20 (2.93-3.47)
Del Águila-Mejía et al, ²⁶ 2022	3.10 (2.82-3.38)
Tanaka et al, ¹¹² 2022	2.87 (2.56-3.17)
Overall, DL ($I^2 = 95.8\%$, $P < .001$)	3.42 (2.88-3.96)



Herd Immunity?



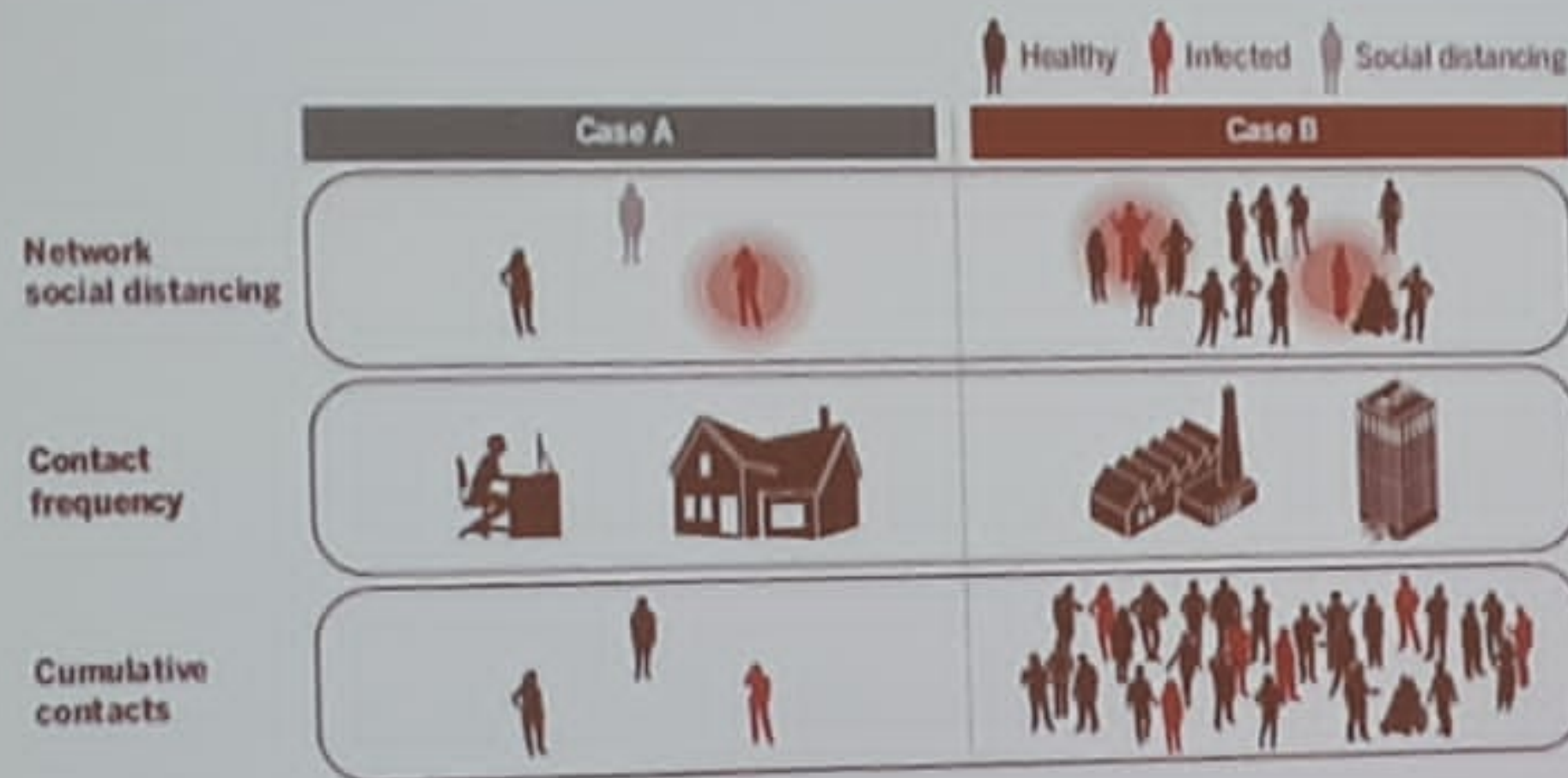
$$HIT = 1/E \cdot (1 - (1/R_e))$$

E = vaccine effectiveness

R_e = effective transmission rate

An homogeneous population at all levels (age structure, contacts, immunization, etc.) is assumed

Population structure and herd immunity



← Tweet

↳ Muge Cevik is retweeted



Muge Cevik
@mugcevik

Responding to @mugcevik @TheHyacinth y A role

That's why it doesn't matter what the overall vaccination rate is. As long as high risk communities w/ disproportionate risk remain unvaccinated we'll continue to see high rates of hospitalisations in many countries. It doesn't mean vaccines no longer work, in fact the opposite!

Replied to tweet

6:47 p.m. · 29 ago, 2021 · Twitter for iPhone



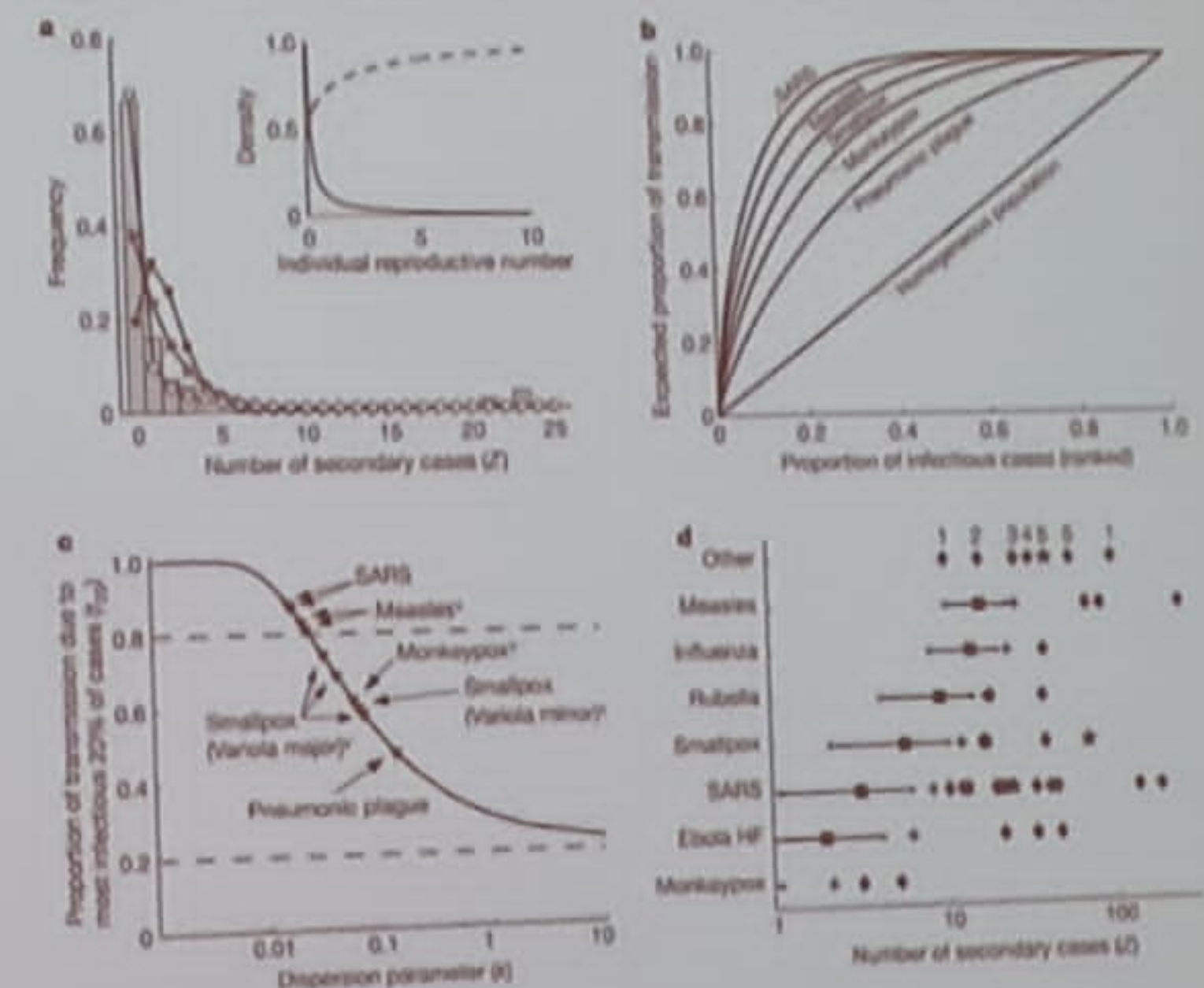
Meaghan Kall
@kallmemeg

The virus's job is to find susceptible populations & rip through them.

If all the susceptible people are in one area and/or socialise together, then you'll keep seeing high case numbers.

This is also why it's impossible to estimate a single overall herd immunity threshold

Figure 1: Evidence for variation in individual reproductive number v .



Dynamic protection

LIVING PROTECTED ALONGSIDE SARS-CoV-2 A POSSIBLE COVID-NORMAL FUTURE LIFE, ONCE IMMUNE



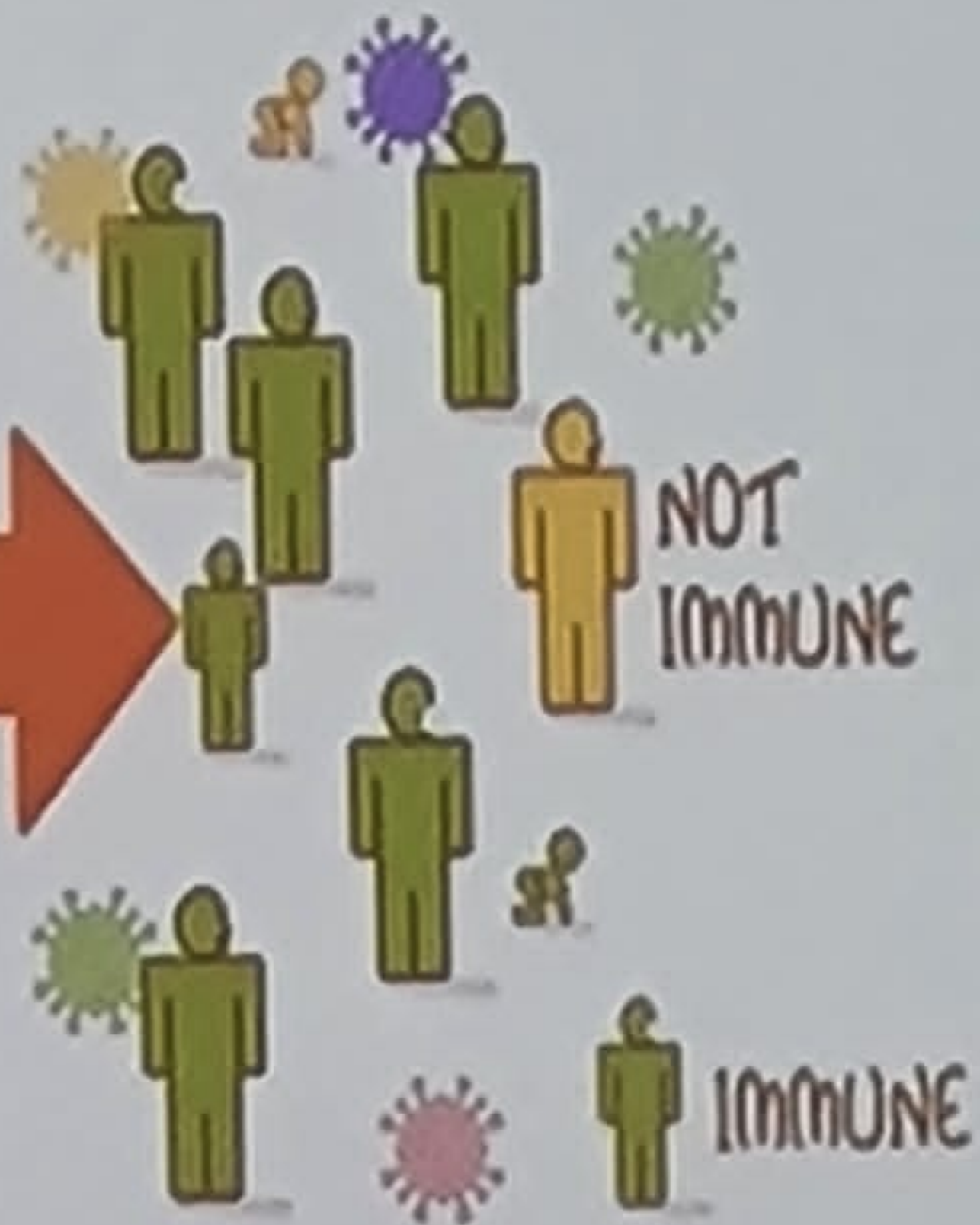
Dynamic protection

LIVING PROTECTED ALONGSIDE SARS-CoV-2 A POSSIBLE COVID-NORMAL FUTURE LIFE, ONCE IMMUNE



DEATHS

CONDITIONS

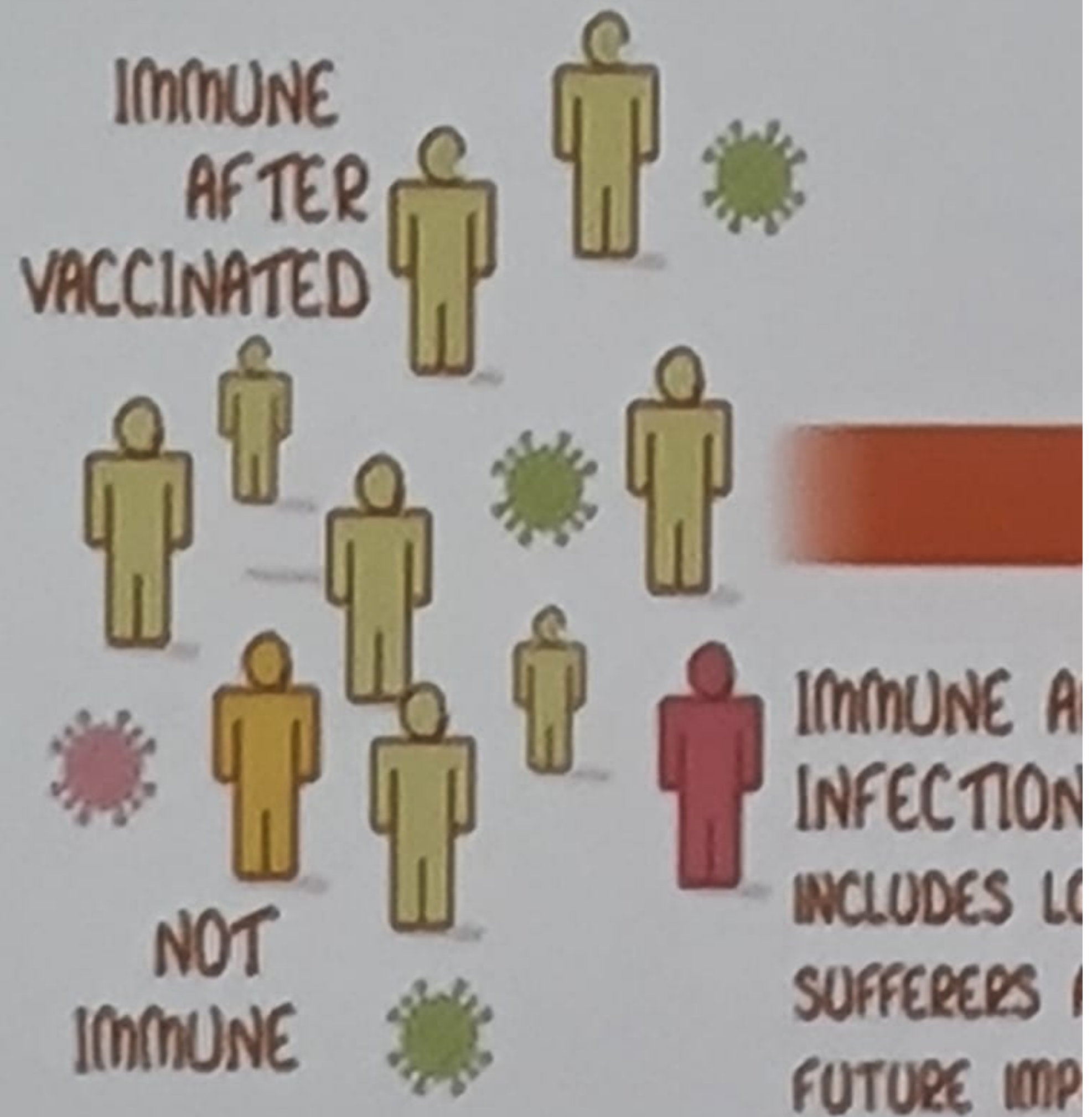


DISTANT FUTURE:

- IMMUNITY BOLSTERED BY NEW VACCINES, BOOSTERS & ONGOING INFECTIONS
- ? ONGOING SAFEGUARDS
- ANTIVIRALS

THE FUTURE

ONCE EVERY ELIGIBLE PERSON
WHO WANTS TO BE VACCINATED
HAS BEEN



Conclusions

- The virus is here to stay.
- SARS-CoV-2 will keep evolving.
- The main driver of evolution is transmission.
- There are many possible paths to achieve a higher transmission.
- We cannot predict which of these will follow the virus.
- It is not possible to eliminate the virus by attaining herd immunity.
- A combination of measures, adjusted for an evolving situation, should be adopted in order to control as much as possible virus evolution and disease effects.