COVID-19 research: SARS-CoV-2 variants

Achievements, lessons learned and next steps

Global Research and Innovation Forum
24th-25th February 2022

World Health Organization

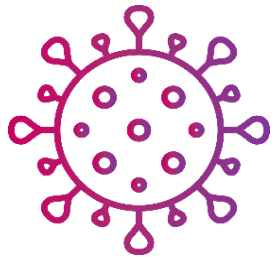
R&DBlueprint
Powering research
to prevent epidemics

Understanding the phenotypes of the successive variants of SARS-CoV-2

A huge amount of viral sequencing data has been generated during this COVID pandemic.

Some virus variants have emerged with phenotypes that have enabled them to spread across the world.

To help what to expect in the future we need to understand what underlies the phenotypes of the successful variants.



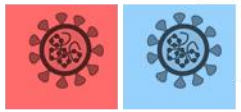
G2P-UK

Successive variants of SARS-C0V-2

Wuhan like virus

D614G

Alpha

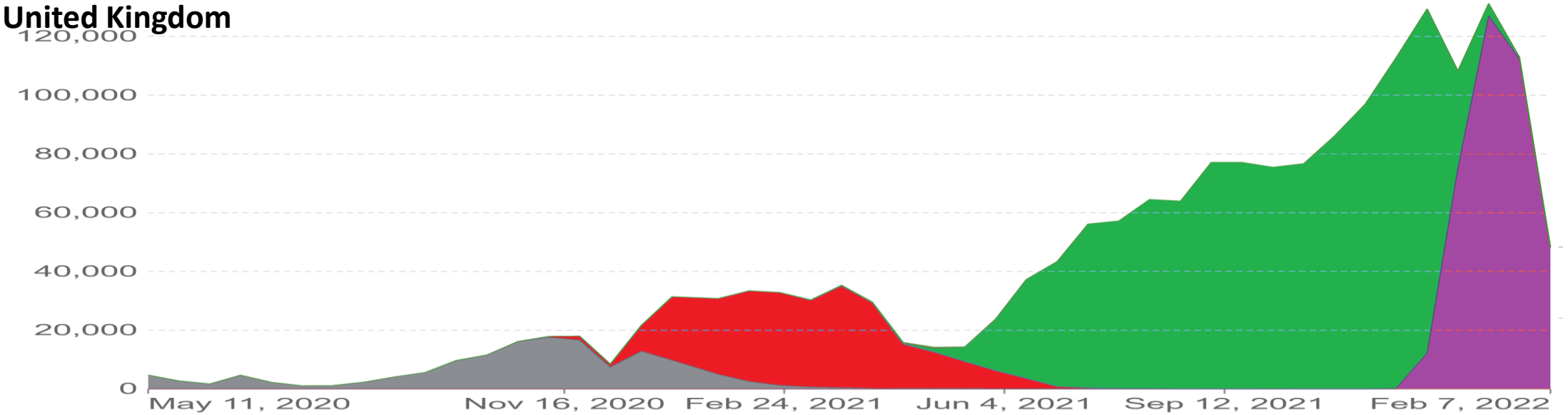


Beta /Gamma
Local circulation

Delta

Omicron

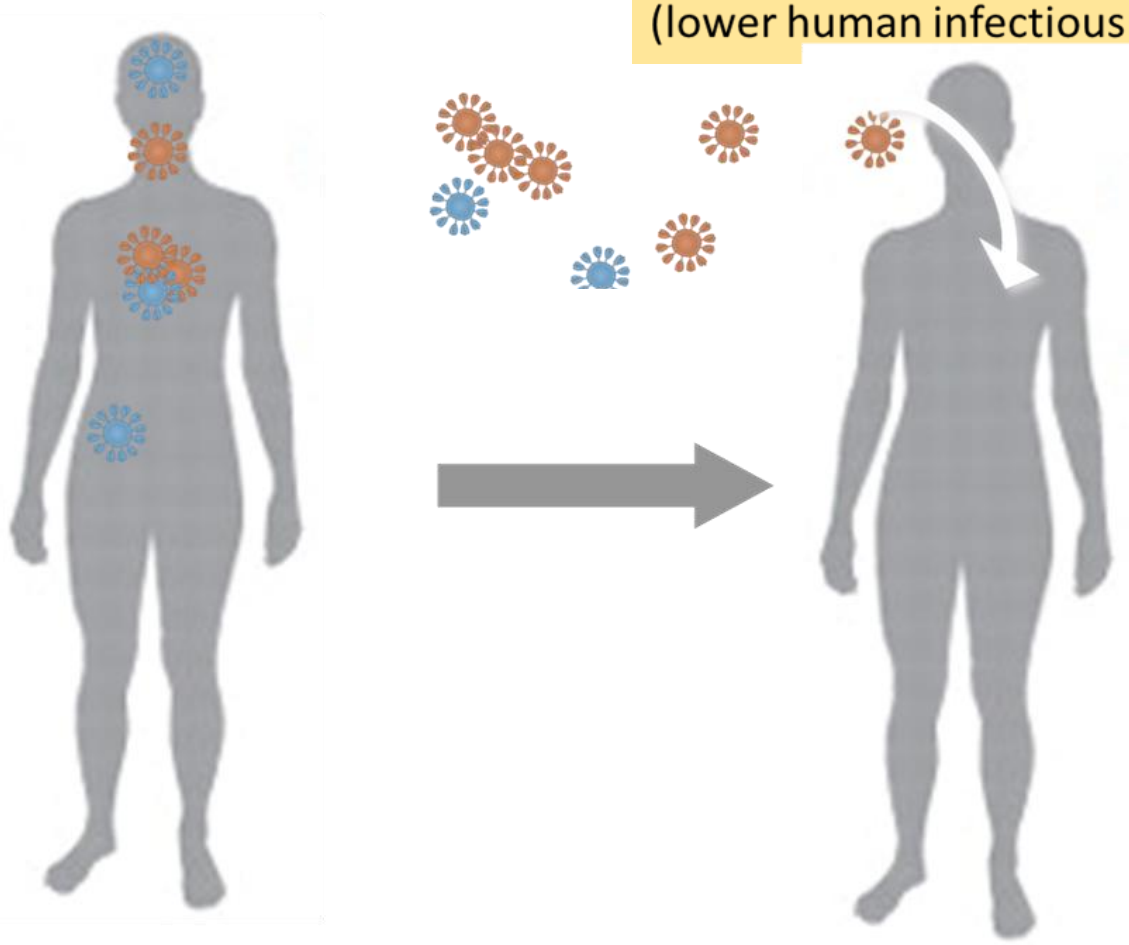
United Kingdom



Early variants had increased transmissibility

Higher or longer virus shedding

Different disease or tropism

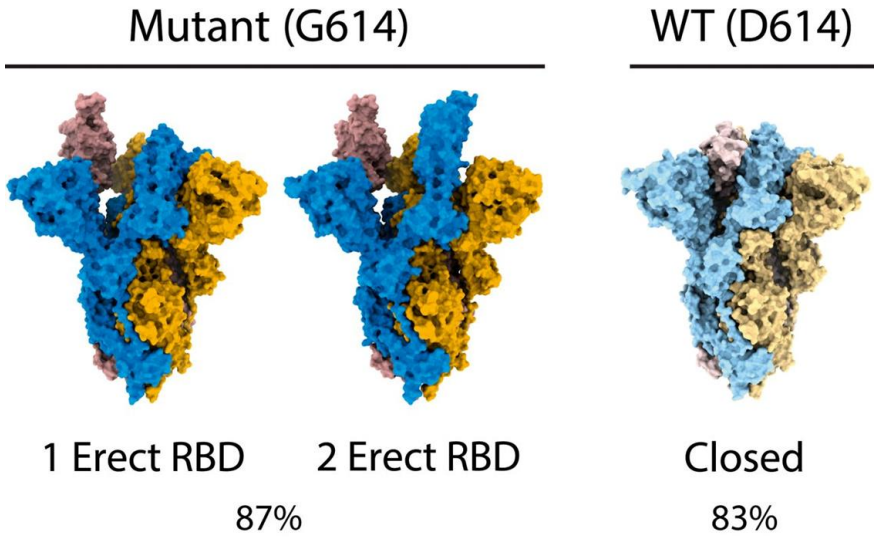


More efficient entry
(lower human infectious dose)

Evasion of innate immune response

Evasion of acquired immune response

Genetic determinants of increased transmissibility

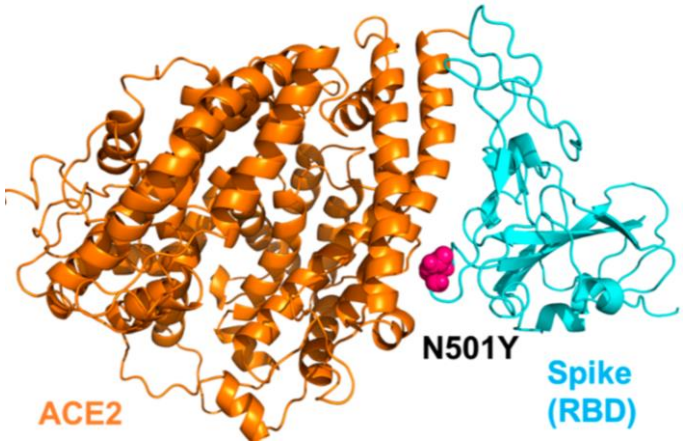


- Increased exposure of receptor binding domain:

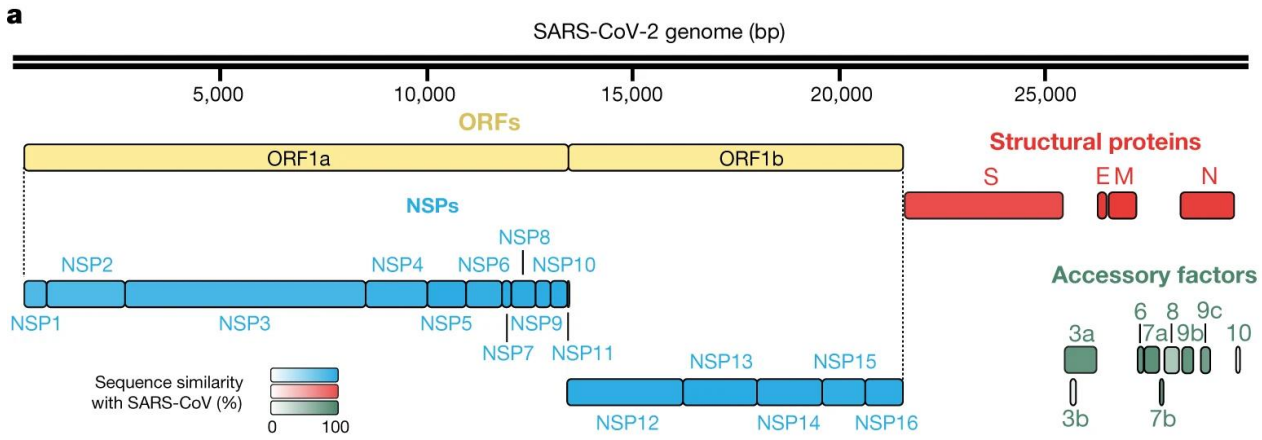
Spike D614G

- Increased affinity for ACE2:

Spike N501Y



Mutations in variants outside Spike gene also impact the virus

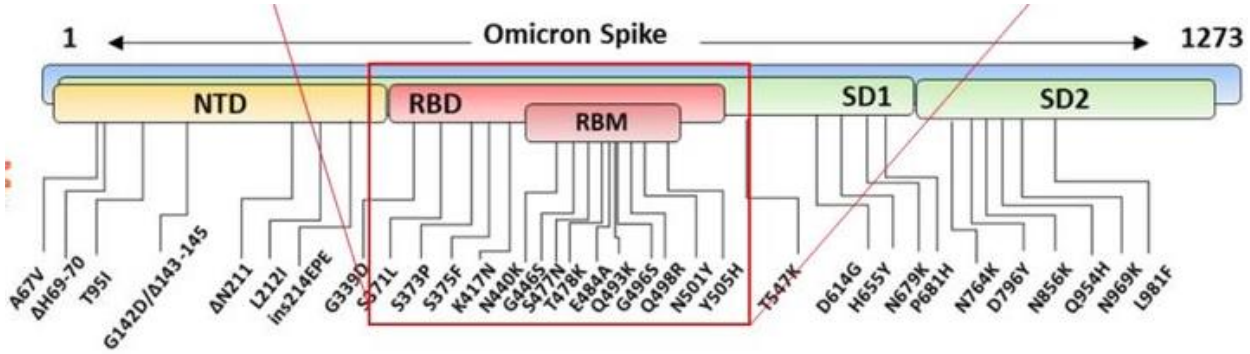


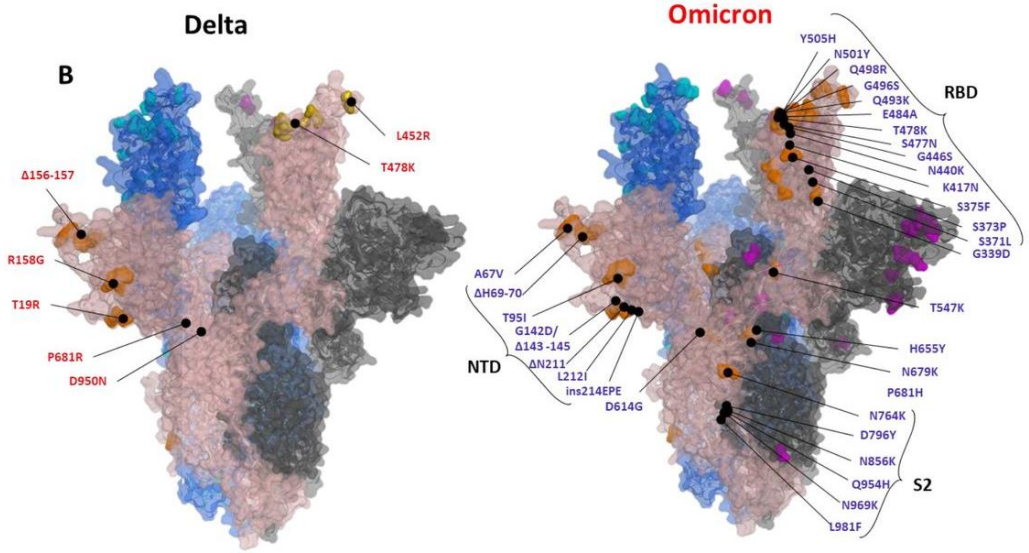
Mutations in N gene that affect innate immune control and virion assembly have arisen

We understand very little of the impact of mutations that have arisen elsewhere in the genome

Omicron carries an unprecedented number of mutations in Spike

This raises concerns for the effectiveness of vaccines that use Spike based on the first wave virus

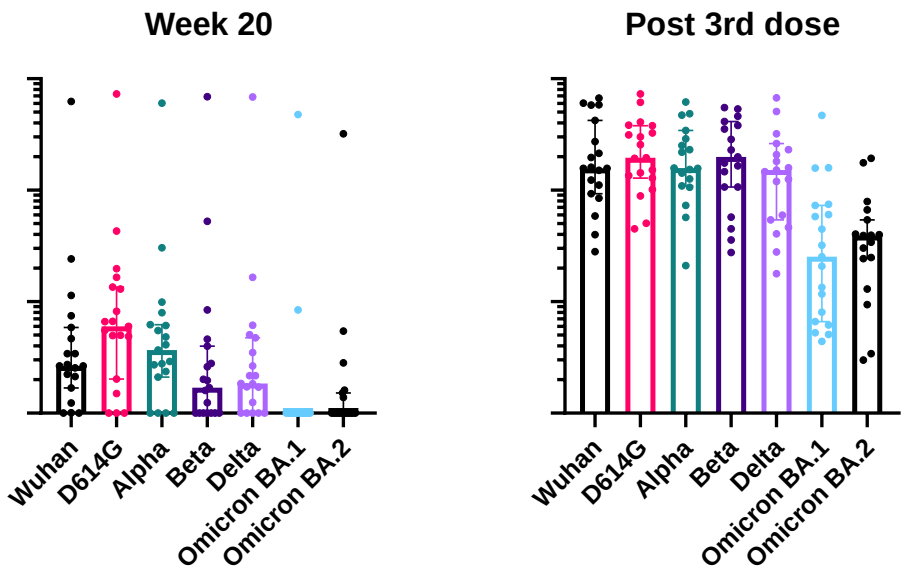




Omicron is less well neutralized by antibodies raised to the vaccine

Antibody titres are restored after a 3rd dose boost

Vaccine remains effective against severe disease



Bailey et al. Pirbright Institute , with UK-HSA consensus study

Table 2. Hazard ratios and vaccine effectiveness against hospitalisation (all vaccine brands combined). OR = odds ratio, HR = hazards ratio, VE = vaccine effectiveness

Dose	Interval after dose (weeks)	OR v symptomatic disease	HR vs hospitalisation	VE vs hospitalisation
1	4+	0.74 (0.72-0.76)	0.57 (0.38-0.85)	58% (37-72)
2	2 to 24	0.81 (0.8-0.82)	0.45 (0.36-0.56)	64% (54-71)
2	25+	0.94 (0.92-0.95)	0.6 (0.49-0.74)	44% (30-54)
3	2 to 4	0.32 (0.31-0.33)	0.26 (0.19-0.35)	92% (89-94)
3	5 to 9	0.42 (0.41-0.43)	0.29 (0.23-0.37)	88% (84-91)
3	10+	0.5 (0.49-0.51)	0.34 (0.26-0.44)	83% (78-87)

UK-HSA technical briefing 34

Omicron infection is associated with milder disease

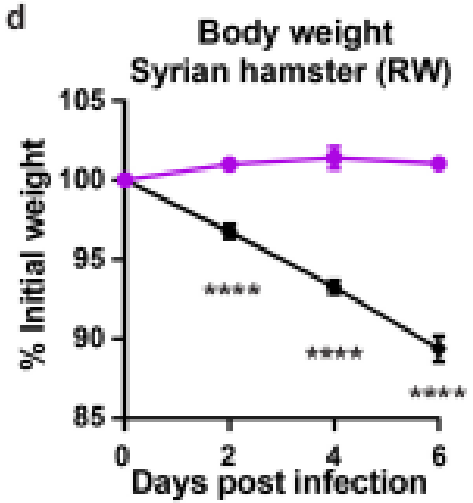
SARS-CoV-2 variants of concern and variants under investigation in England: Technical briefing 36

Table 3. Odds of ICU-HDU admission among hospitalised Omicron cases versus Delta cases, acute NHS trusts, England

Odds of admission to ICU/HDU OR= Odds Ratio CI= Confidence Interval										
	Number admitted to ICU/HDU	Total hospitalisations	Unadjusted OR	95% CI		P>z	Adjusted OR†	95% CI		P>z
Delta*	31	361	1.00				1.00			
Omicron*	13	439	0.32	0.17	0.63	0.001	0.51	0.22	1.15	0.103

* sequenced linked cases/SGTF status if sequence data not available

†adjusting for: age (<40y, 40 to 49, 50 to 64, ≥65y), sex, vaccination status on admission (unvaccinated, D1 only, 2 Doses only, 3D+), levels of comorbidity (1, 2 or ≥3 conditions), ethnicity and hospital random effects



Omicron

D614G

Halfmann et al Nature 2022

Research gaps: questions for the future

- **Are antigenic distance and milder disease separable phenotypes ?**

- How will heterogeneous immunity across the world impact future evolution?
- Will future variants co-circulate, will they recombine?
- Will the virus reside in animal reservoirs?
- How will we track the growth of the next variants if there is less testing and sequencing?

Lessons learned

Rapid responses to emerging variants can be strengthened by working together in consortia

Collaborations between academics and government institutes can enable a strong interdisciplinary approach