

Antibody-based therapeutics



What criteria for efficacy, and how can they stay relevant if the virus evolves?

Rupert Beale

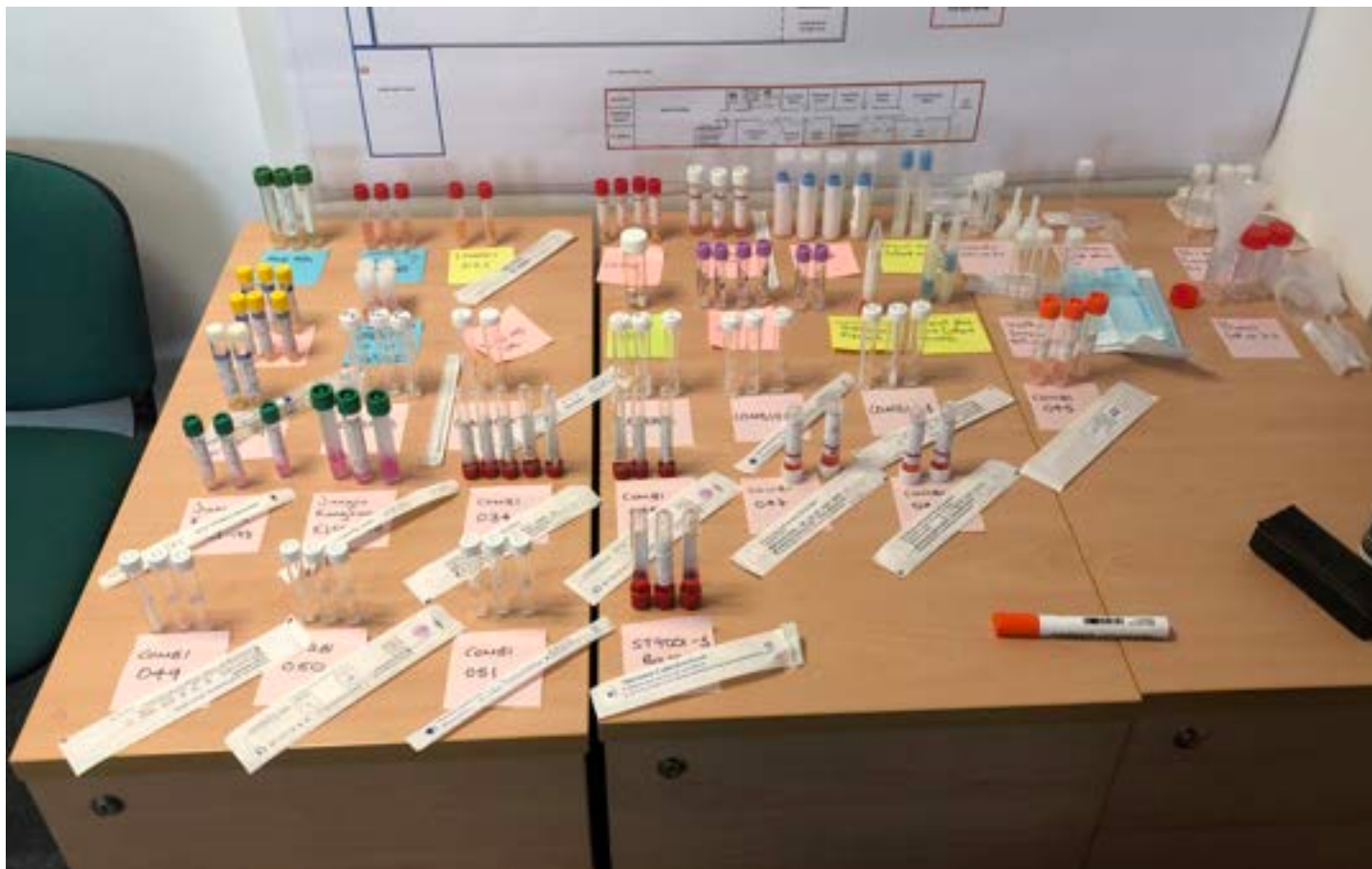
Cell Biology of Infection Laboratory

The Francis Crick Institute

UCL Division of Medicine

Consultant Nephrologist, Royal Free Hospital

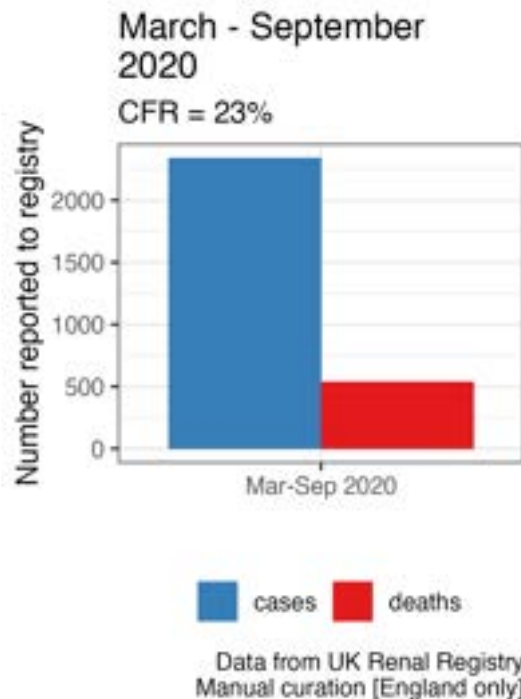




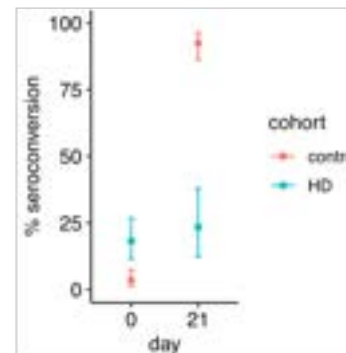
Tony Cox (MK Lighthouse Lab)

SARS-CoV-2 in haemodialysis patients

Excess morbidity and mortality



Attenuated vaccine responses in HD to traditional vaccines



Novel pandemic H1N1 influenza vaccination
Chang et al. Vaccine 2012

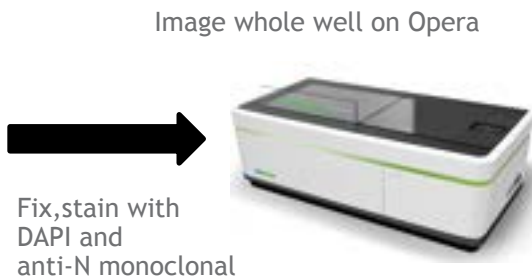
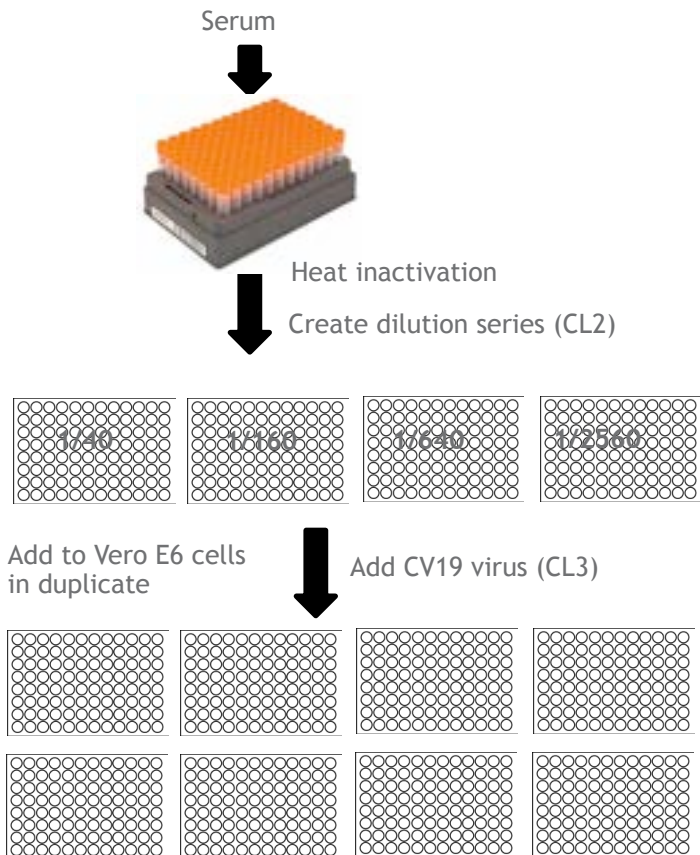
Haemodialysis excluded from phase 3 trials

- AZD1222 Voysey et al. *The Lancet* 2020
- BNT162b2 Polack et al. *NEJM* 2020
- mRNA-1273 Baden et al. *NEJM* 2021

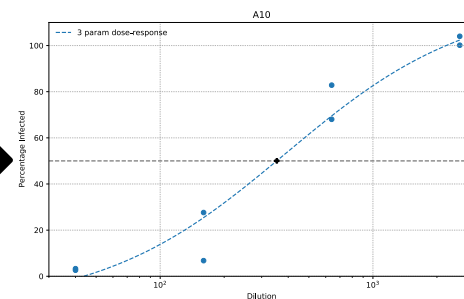
Crick 'Oscars'

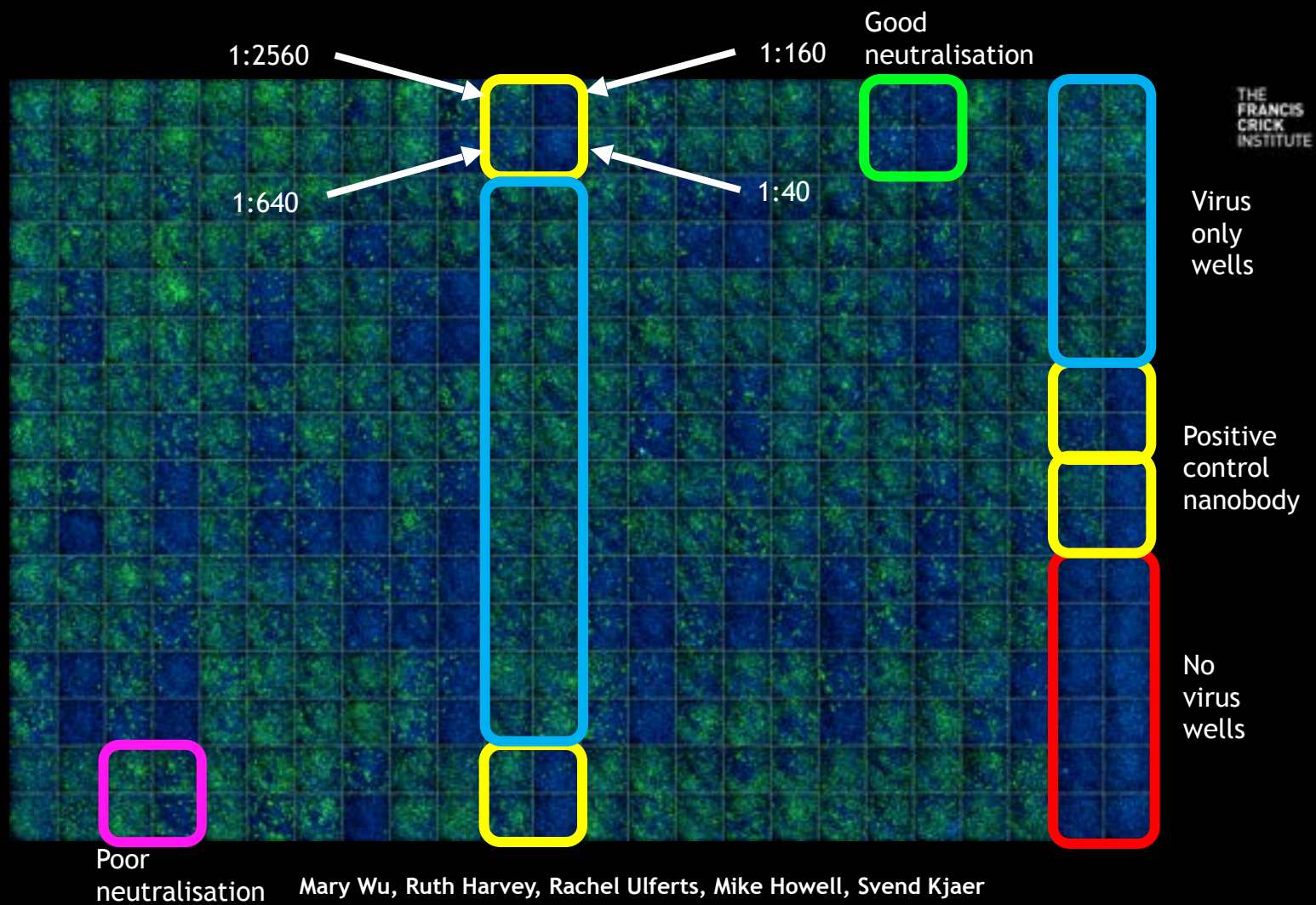


High-throughput quantification of neutralising antibodies



Fit curve for dilution IC₅₀








The Crick
@TheCrick

...

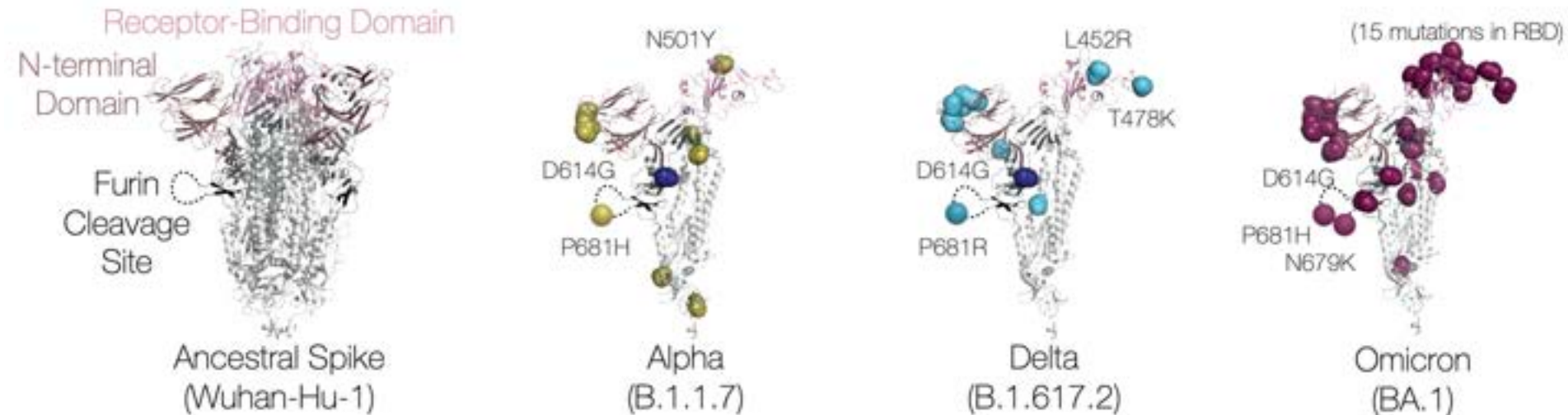


With the help of Arla and Curtis, two llamas from [@UniofReading](#), researchers at the Crick have established a nanobody production pipeline. Nanobodies are crucial to a number of Crick research projects, including efforts to tackle COVID-19

Read more 



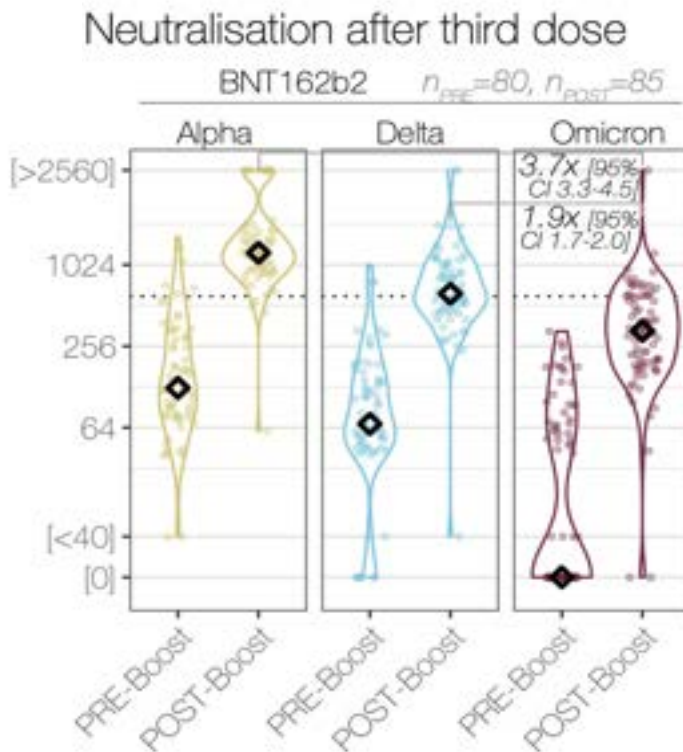
Measuring neutralising antibodies to variants of concern

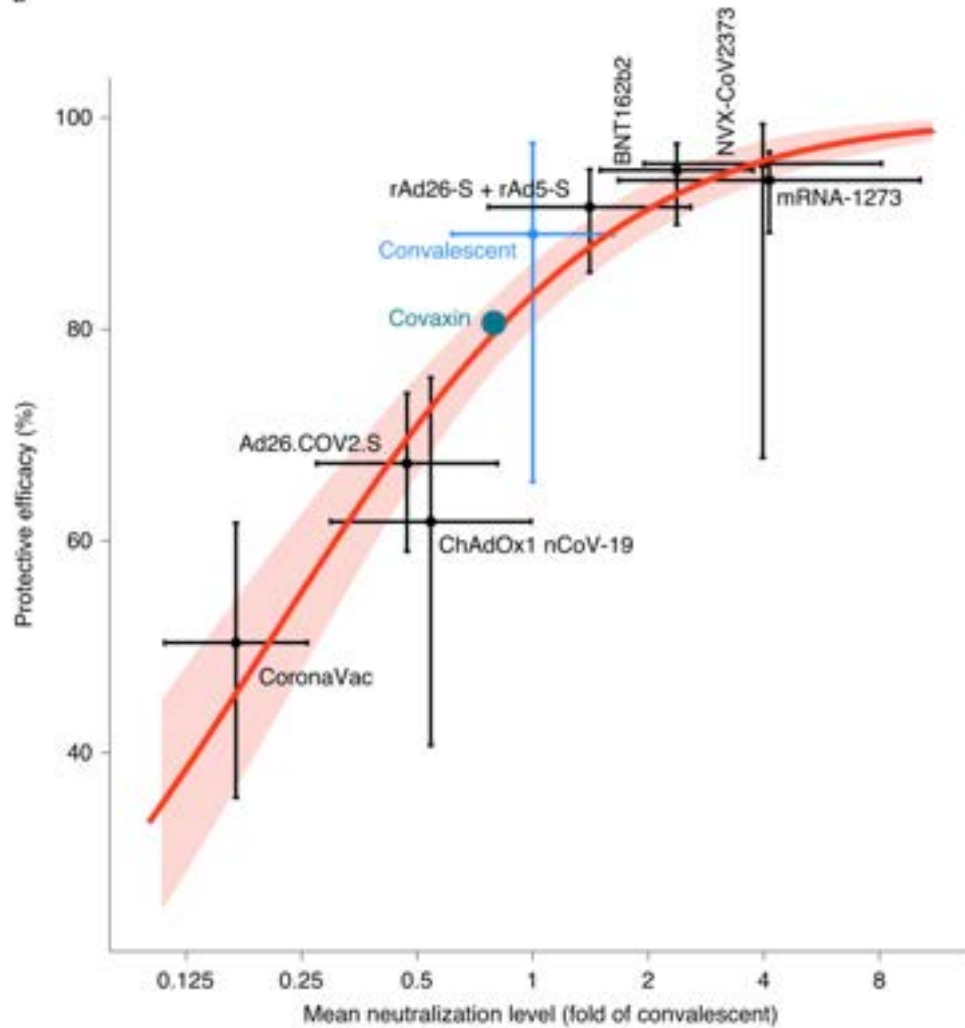


nAb responses before and after third doses in laboratory and healthcare workers - *Legacy Study, Crick and UCLH*

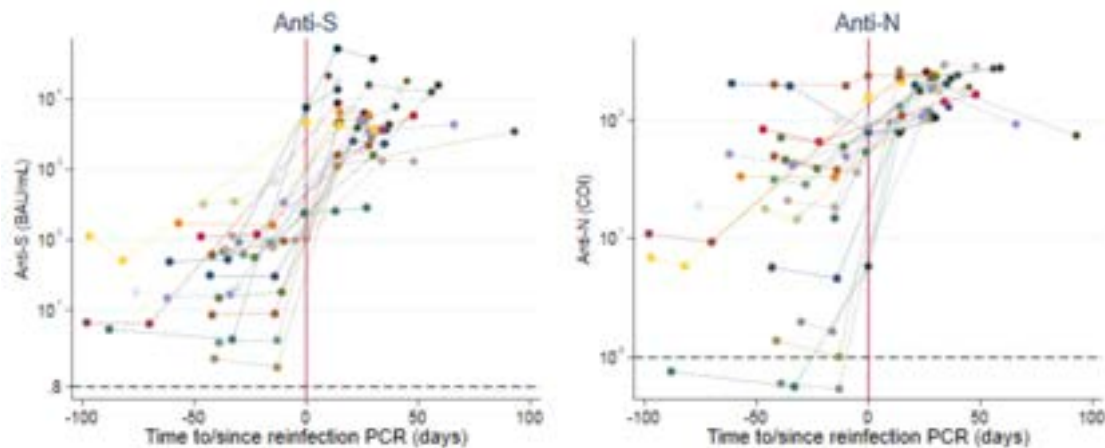


Figure 2

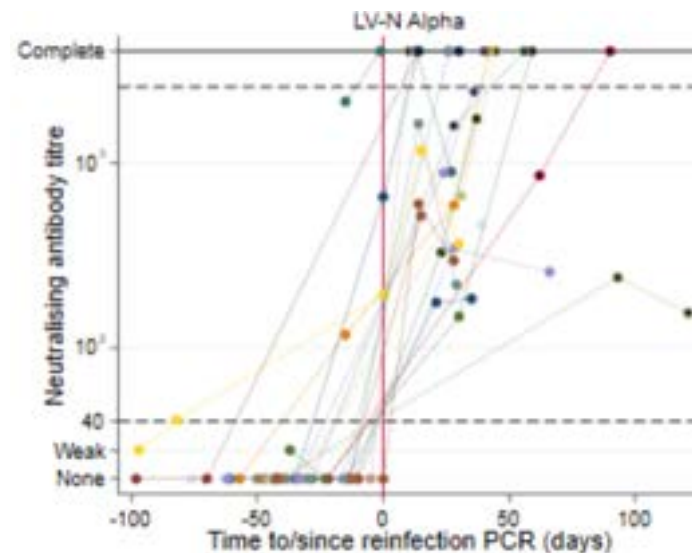
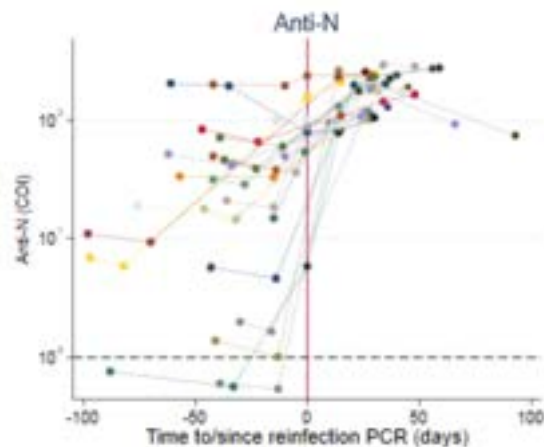
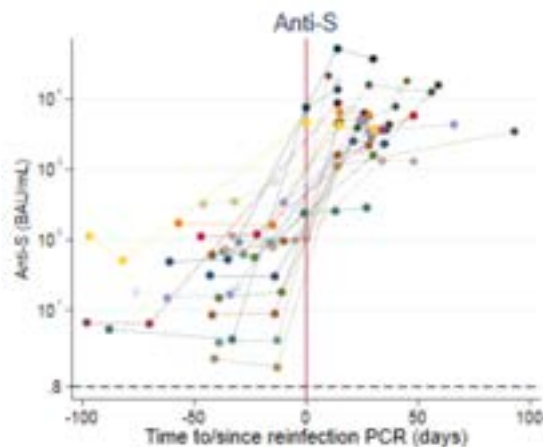


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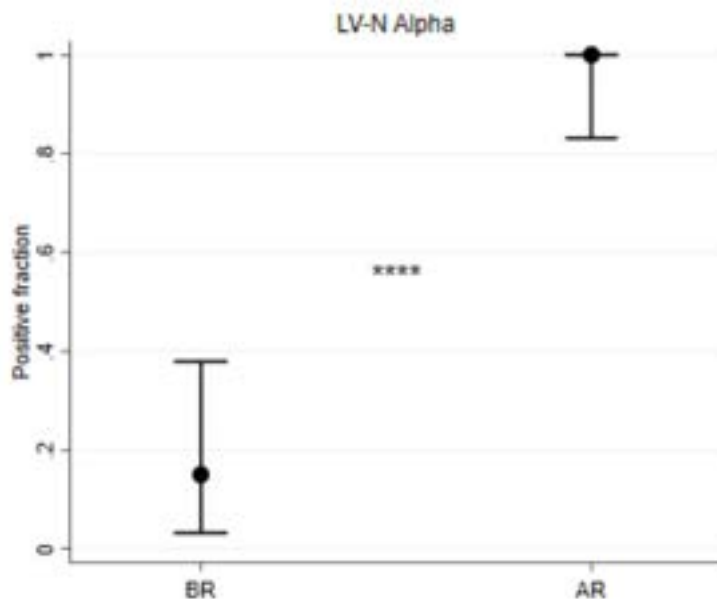
Re-infection cases from SIREN



Neutralising antibodies absent/minimal

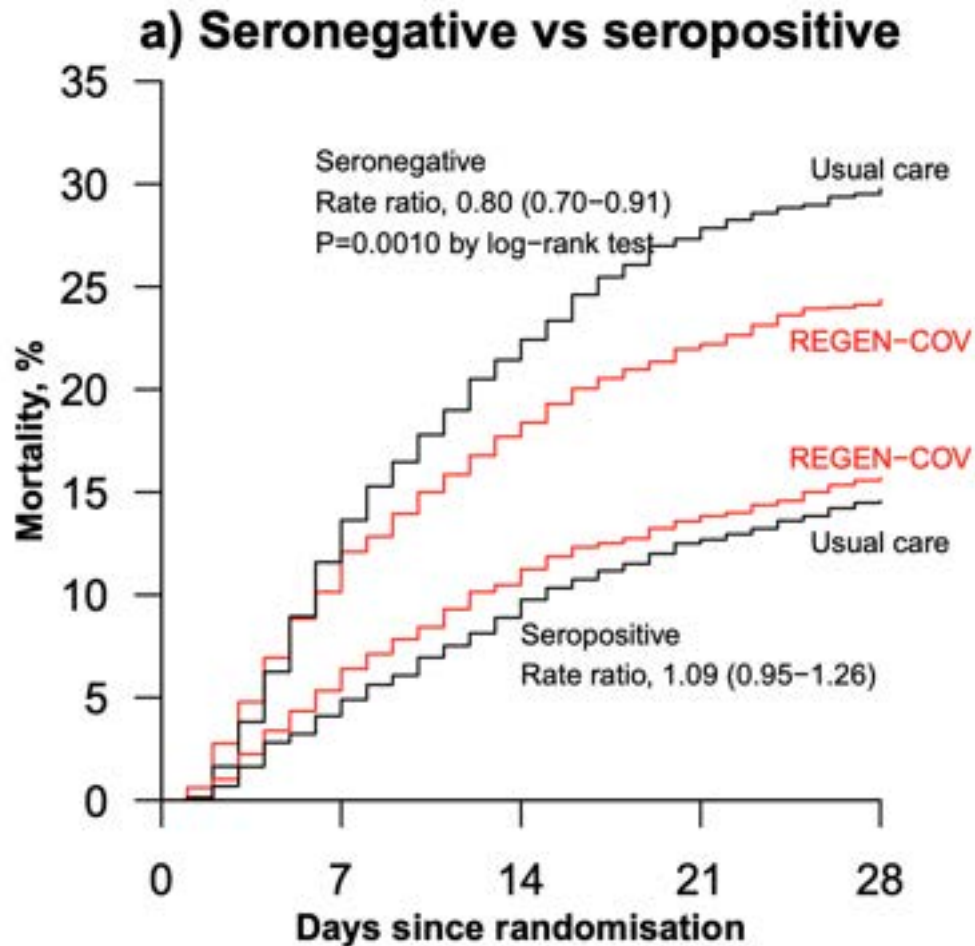


Neutralising antibodies >1:40 are a correlate of protection after infection (similar to influenza A)

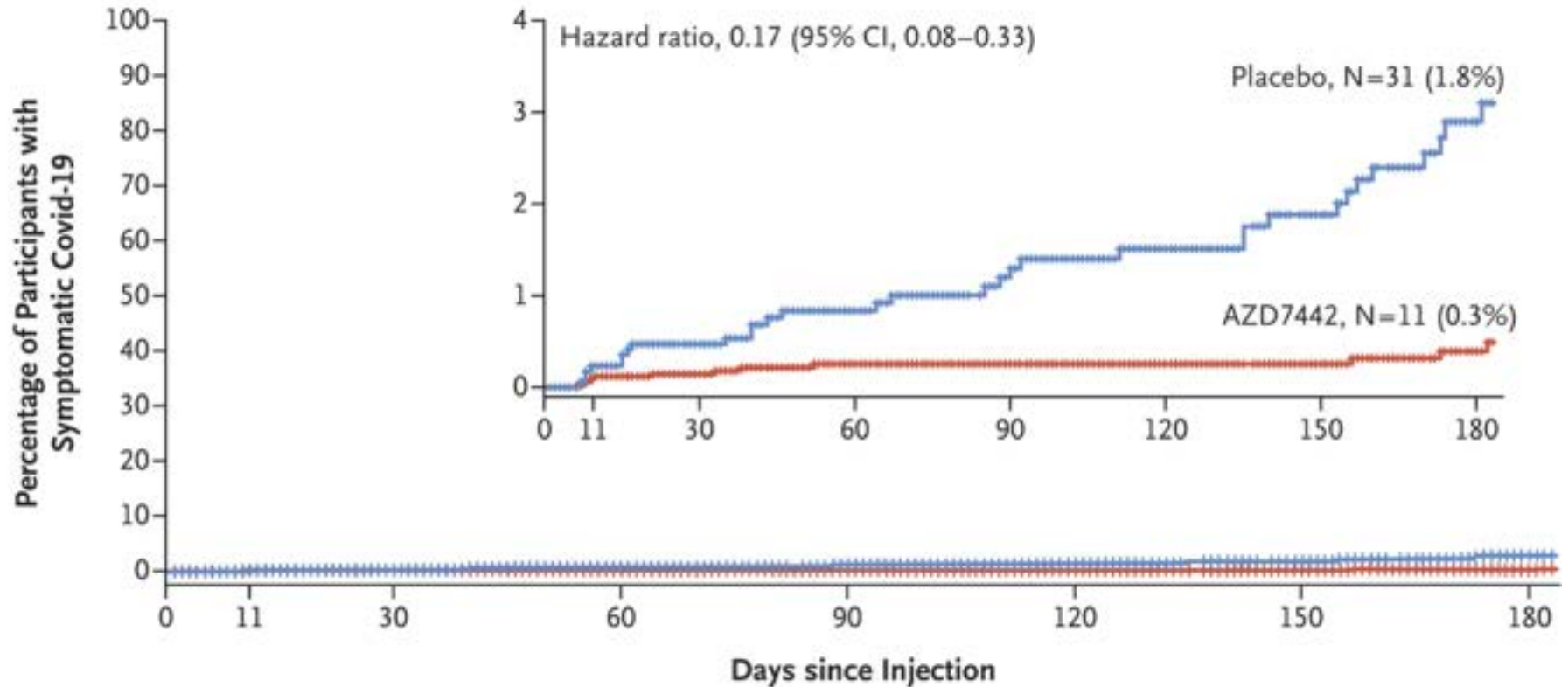


In preparation:
Delta era is different,
correlate more likely
 $\approx 1:200$, anti-S titres \approx useless

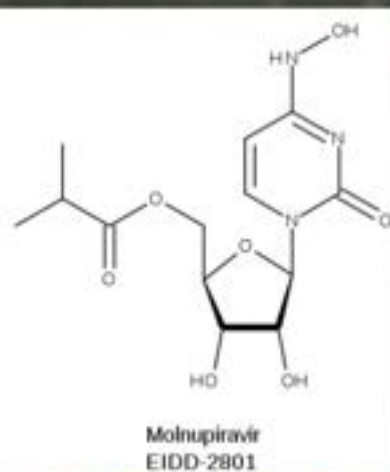
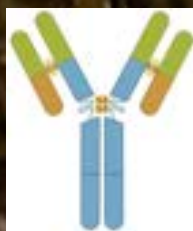
Efficacy of therapeutic neutralising antibodies



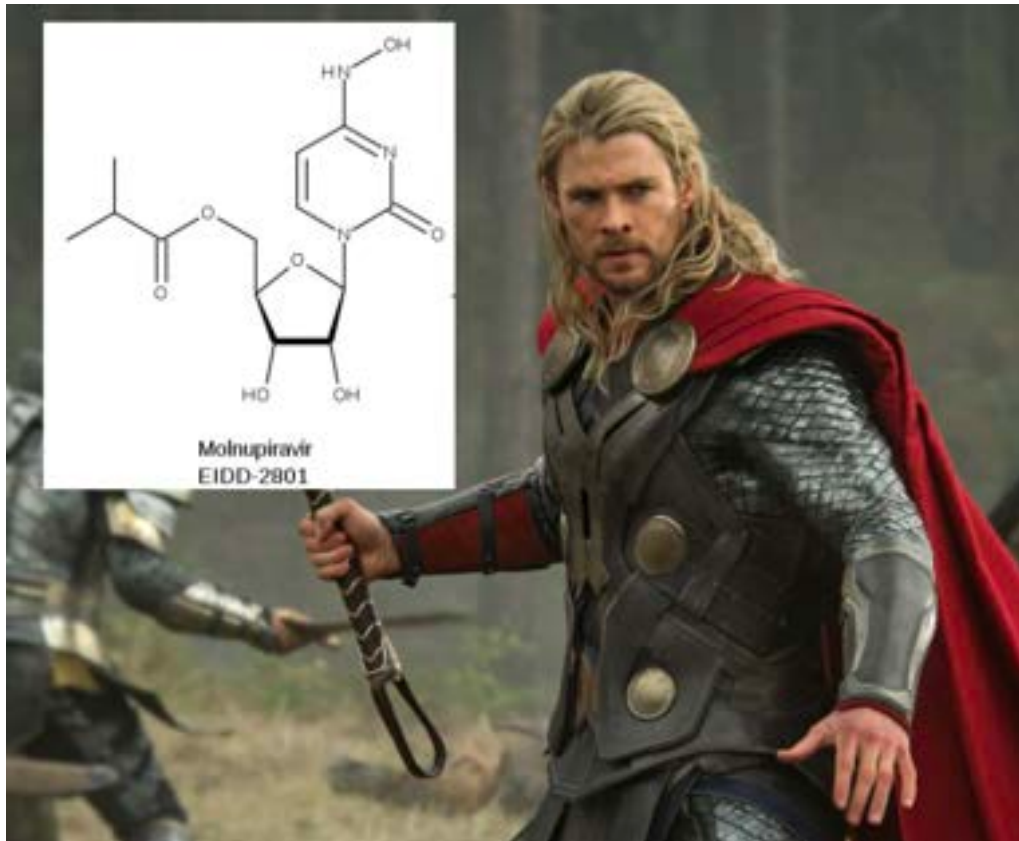
Efficacy of prophylactic neutralising antibodies



Tixagevimab/Cilgavimab



Molnupiravir
EIDD-2801

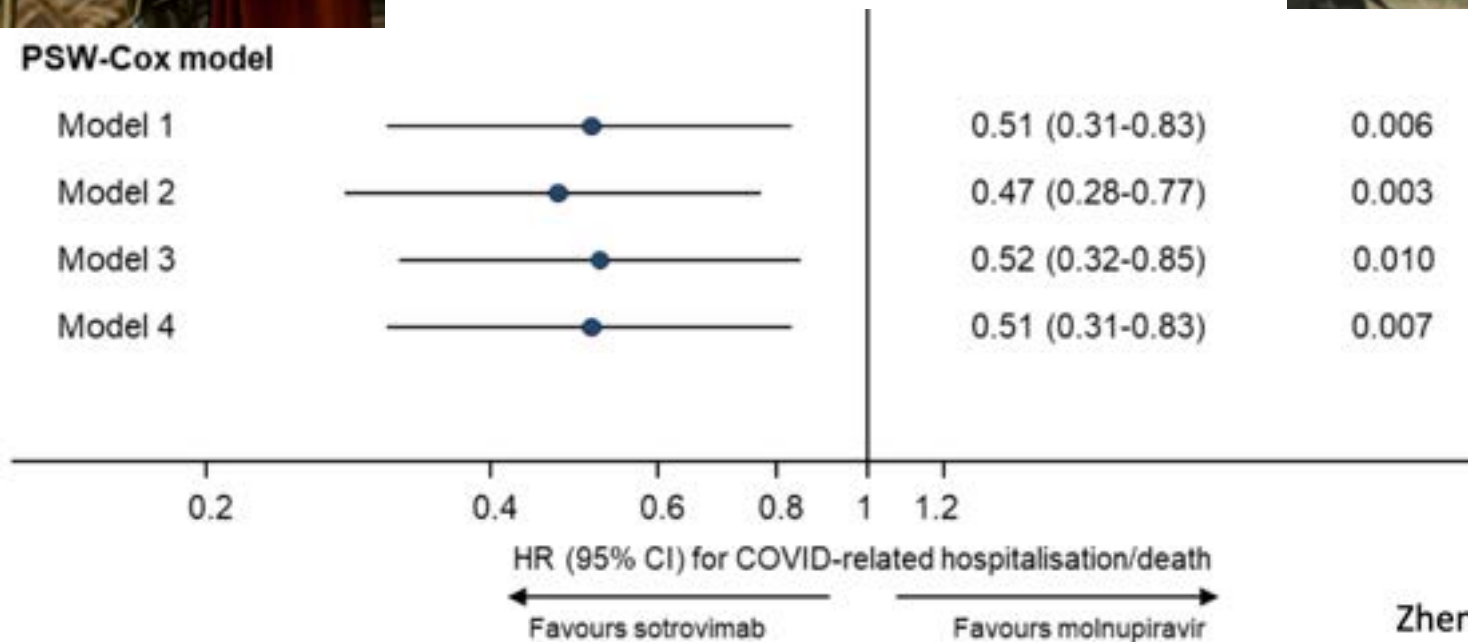




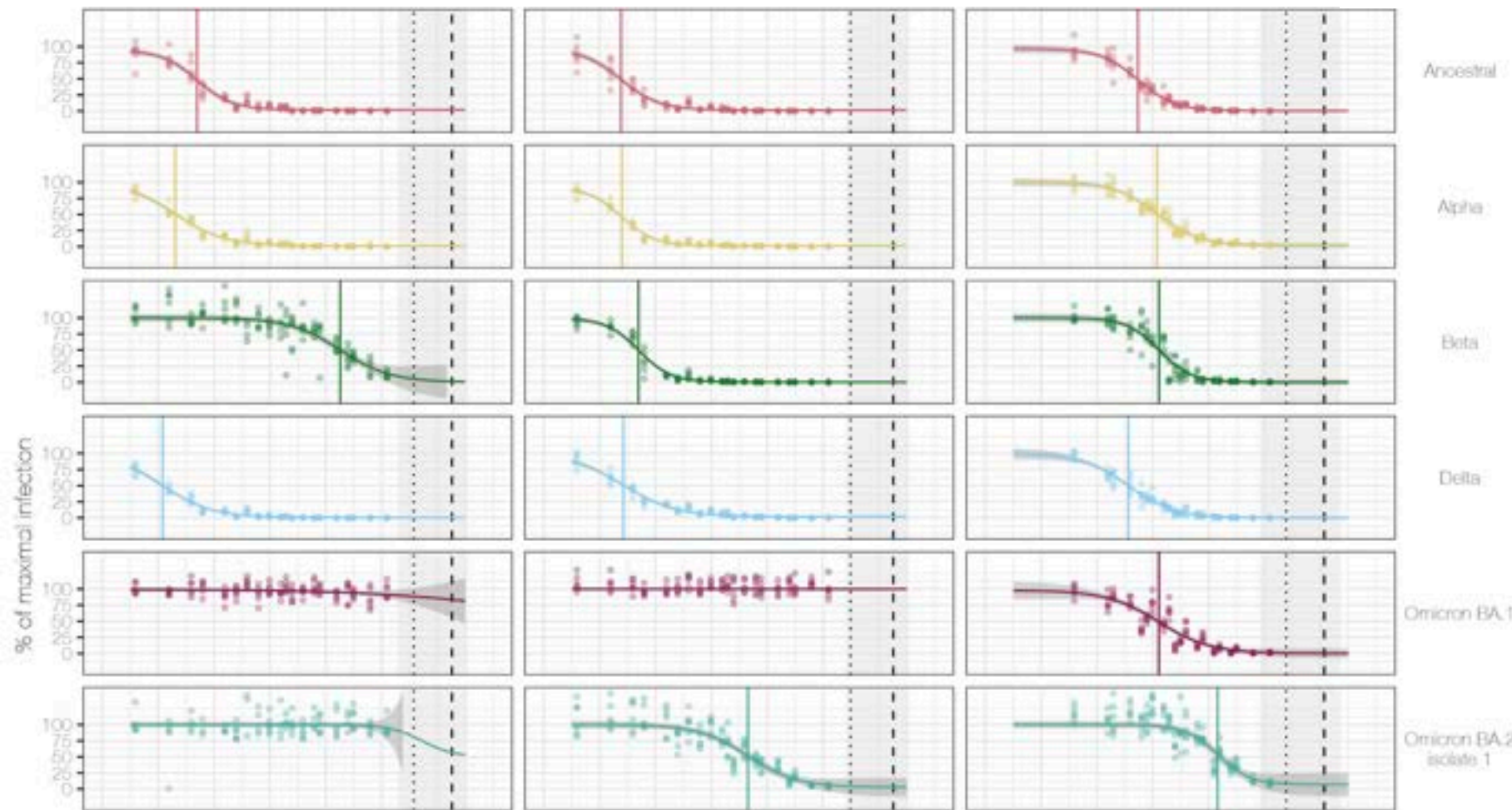
Odin more powerful
than Thor?



PSW-Cox model



Three different therapeutic monoclonals



Conclusions

- Neutralising antibodies are the main *mechanism* of protection against SARS-CoV-2
- Neutralising monoclonal antibodies can be powerful drugs and prophylactics
- Very likely 'Pathogen X' would be susceptible if respiratory RNA virus
- May not be so clear cut for other pathogens
- Unknown: how much neutralisation you need for what variant of what virus
- Unknown: how long will protection last?
- Start treating neutralising antibodies a bit like antibiotics

Acknowledgements

Cell Biology of Infection

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Dialysis patients

Dialysis staff around the UK

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Cambridge

Rona Smith
Rachel Jones

Oxford

Sushma Shankar
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Joseph Beckett
Fadi Issa

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G2P-UK



COVID-19
GENOMICS
UK CONSORTIUM

NIHR

University College London Hospitals
Biomedical Research Centre



UK Health
Security
Agency



HEALTH SERVICES
LABORATORIES

Kidney
Wales
Aren
Cymru



Kidney Research UK

Wessex Kidney Patients Association



nkf
NATIONAL KIDNEY
FEDERATION



Imperial College
London

