Predicting vaccine protection from SARS-CoV-2 variants.

Miles Davenport

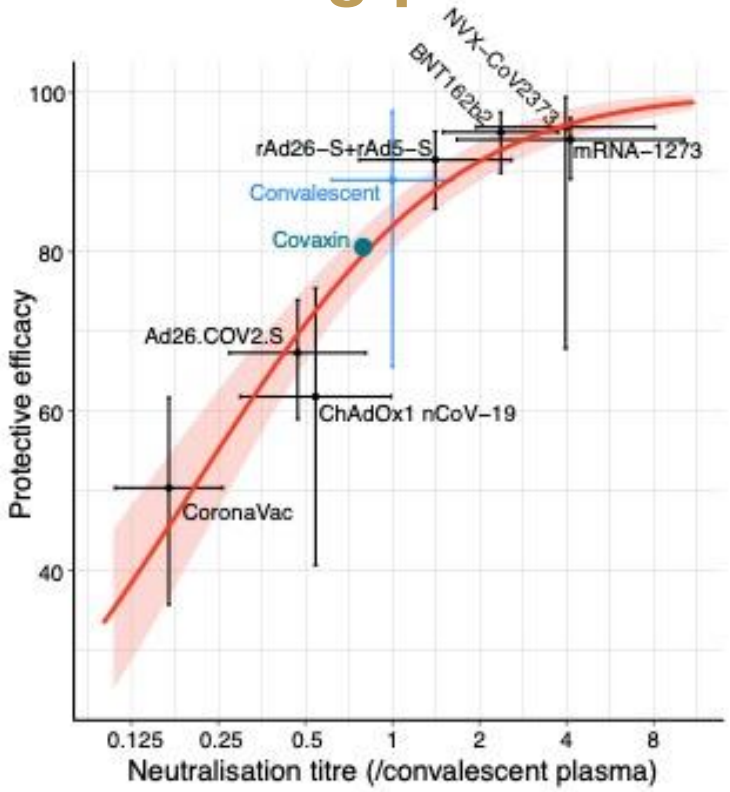
WHO COVID-19 Vaccines, **3 September 2021**

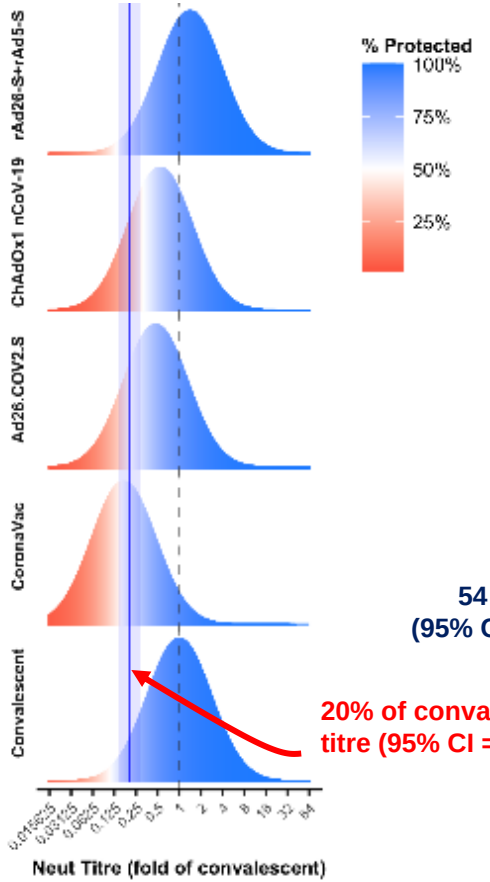
Declaration of potential conflicts:

Professor Davenport receives funding from:

- National Health and Medical Research Council (Australia)
- Medical Research Futures Fund (Australia)
- Australian Research Council
- University of New South Wales (Australia)
- National Institutes of Health (USA)
- eLife journal

Predicting protection;





54 IU/ml
(95% CI = 30-96)

20% of convalescent titre (95% CI = 14-28%)

Khoury, D……. Nature Medicine 2021

Predicting protection against SARS-CoV-2 VOC?

- Understand changes in neutralisation titre
- Validate model on efficacy data

The problem of assays: *(Ancestral)*

No progress to standardized assay

Technical Name	Dosage	Dose 2 (Day)	Measured on Day	Assay*
mRNA-1273	100 µg	29	42	Live WT virus $PRNT_{80}$[1]
NVX-CoV2373	5 µg + 50 µg Matrix-M1 adjuvant	21	35	Live WT MN $IC_{>99}$[2]
BNT162b2	30 µg	21	28	Live fluorescent WT virus PRNT IC_{50}[3]
rAd26-S+rAd5-S	10^11 viral particles	21	42	Live WT virus MN IC_{50}[4]
ChAdOx1 nCoV-19	5x10^10 viral particles (SD)	28	42	Live WT virus MN IC_{50}[5]
Ad26.COV2.S	5x10^10 viral particles	N/A	29	Live WT virus PRNT IC_{50}[6]
CoronaVac	3 µg	14	28	Live WT virus MN IC_{50}[7]
BBV152	6 µg with Algel-IMDG	28	42	Live WT virus $PRNT_{50}$[8]
Convalescent Plasma	N/A	N/A	N/A	Live WT virus MN IC_{50}[9]

Assay variation:
Khoury et al, Nature Reviews Immunology (2020)

Khoury, D., *et al*, Nature Medicine 2021

Variants

Titre to ancestral

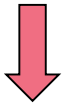
Titre to variant

Cromer et al, MedRxiv

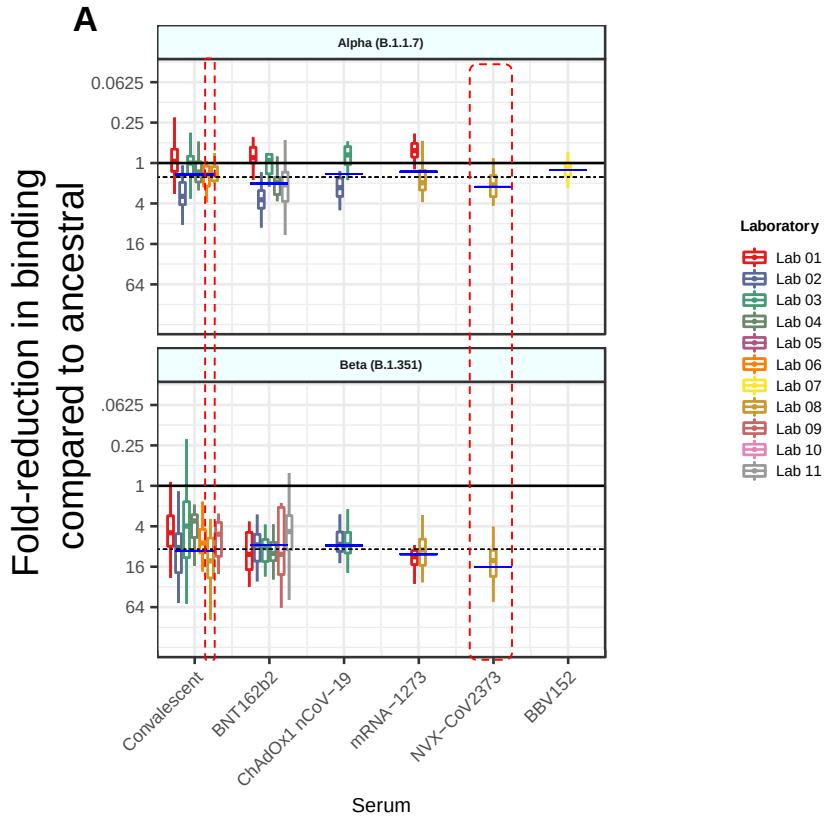
https://www.medrxiv.org/content/10.1101/2021.08.11.21261876v1

Variants

Titre to ancestral



Titre to variant



Cromer et al, MedRxiv

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Variants

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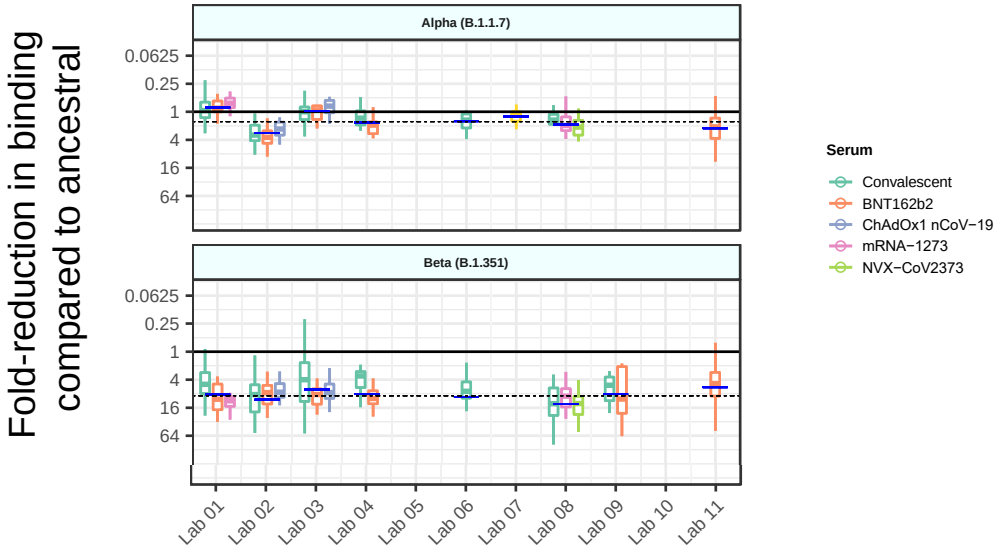


Cromer et al, MedRxiv

https://www.medrxiv.org/content/10.1101/2021.08.11.21261876v1

DROP in titre:

(regression model)

- Variant
- Lab
- ~~Vaccine~~ (compared to convalescent)

You should not rely on the results of any (single) neutralisation assay

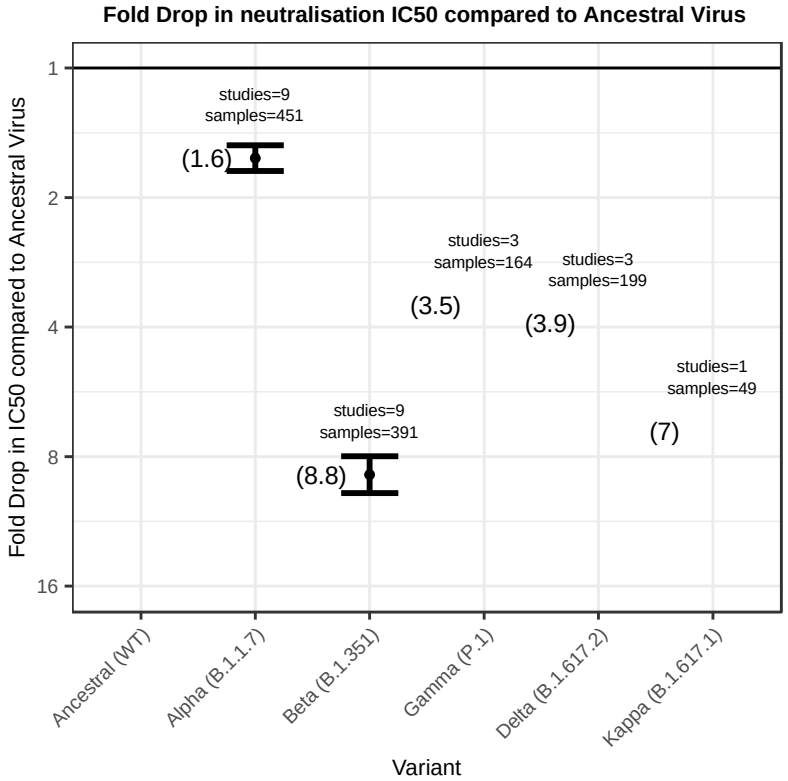
Cromer et al, MedRxiv

https://www.medrxiv.org/content/10.1101/2021.08.11.21261876v1

DROP in titre:

(regression model)

- Variant
- Lab
- ~~Vaccine~~ (compared to convalescent)



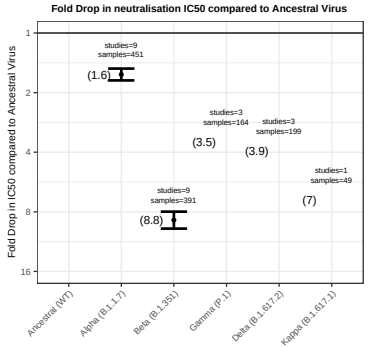
Cromer et al, MedRxiv

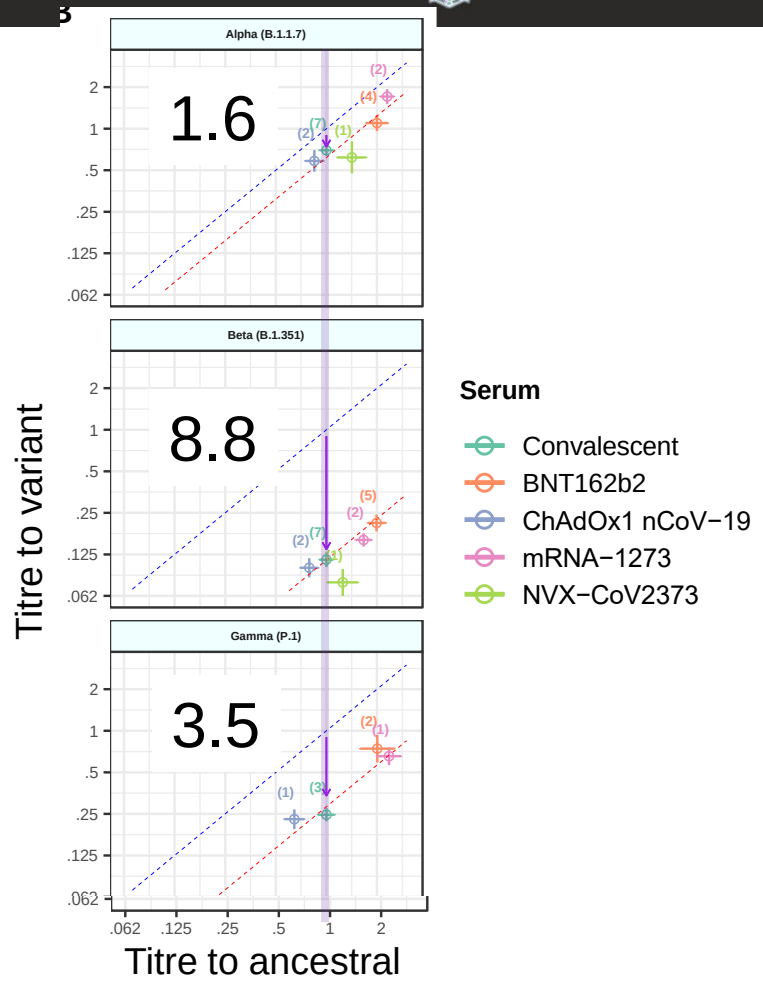
https://www.medrxiv.org/content/10.1101/2021.08.11.21261876v1

DROP in titre:

(regression model)

- Variant
- Lab
- ~~Serum~~ (convalescent / vaccine X)





Cromer et al, MedRxiv

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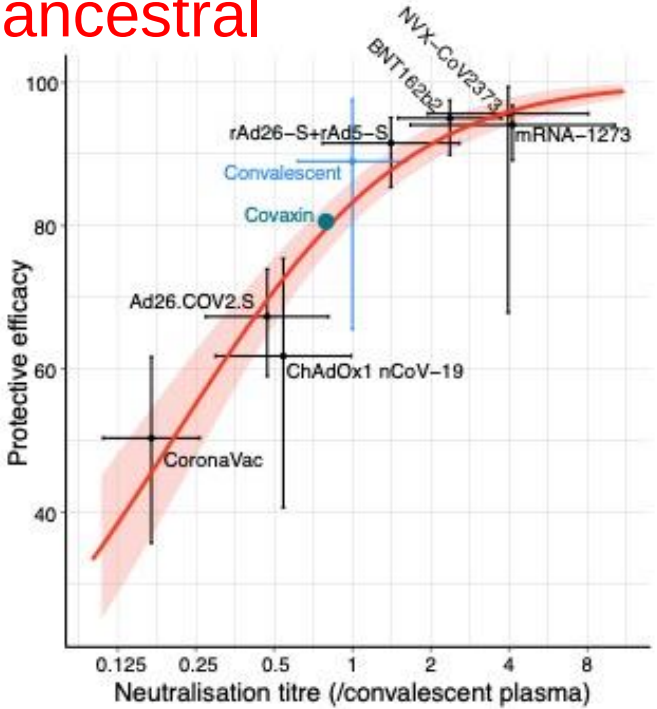
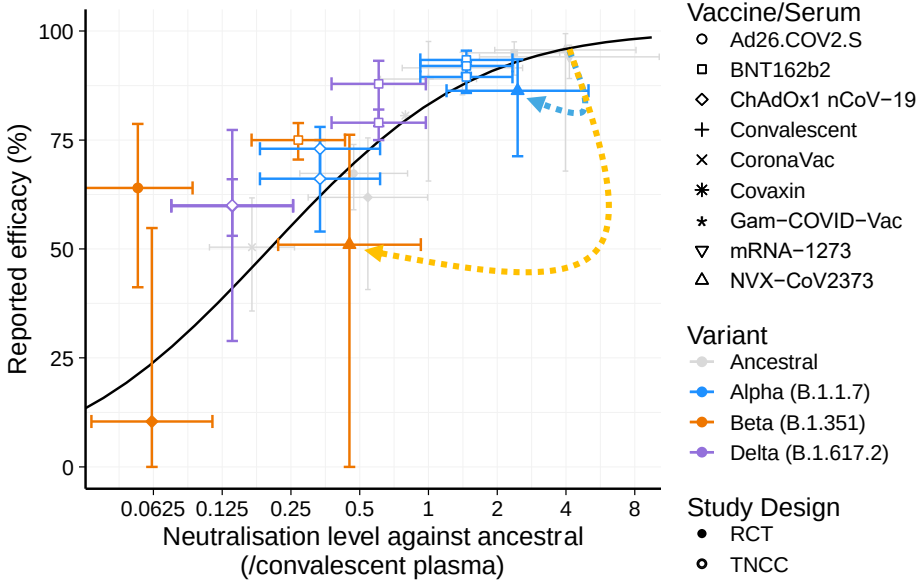
Scaling existing model

Cromer et al, MedRxiv
https://www.medrxiv.org/content/10.1101/2021.08.11.21261876v1

ancestral



1) Move ‘dots’

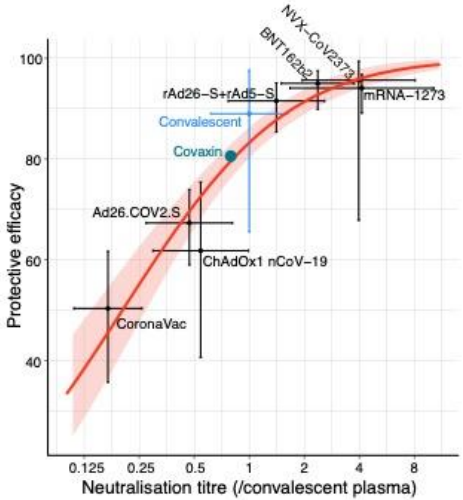


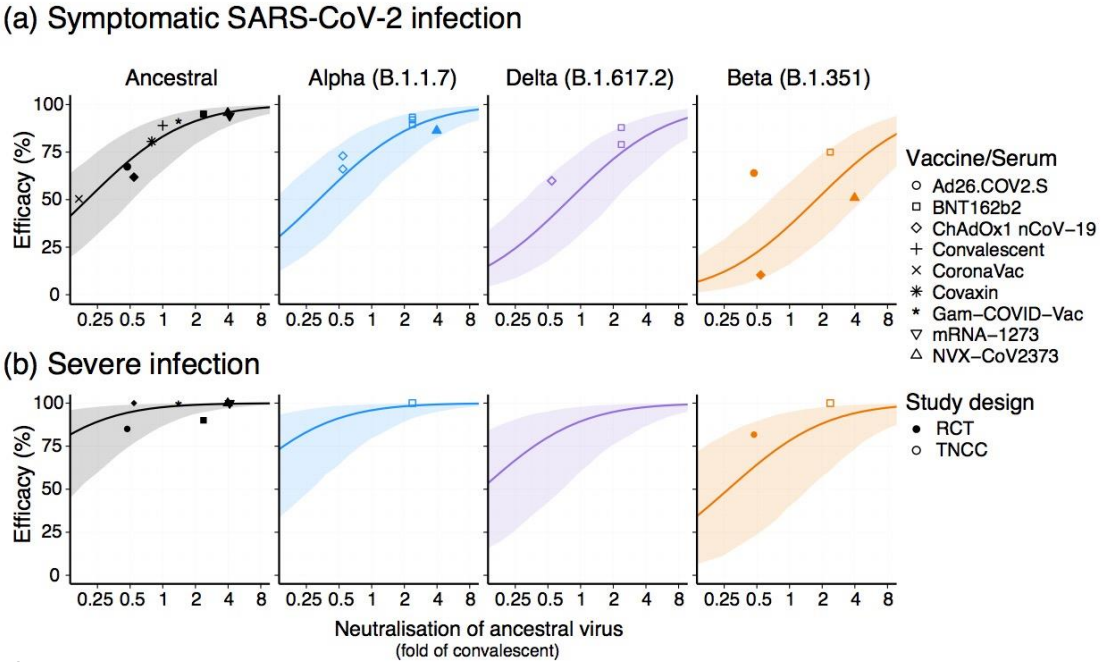
Scaling existing model

ancestral

2) Move ‘curves’

13/14 VOC efficacy
22/23 Ancestral + VOC





Cromer et al, MedRxiv

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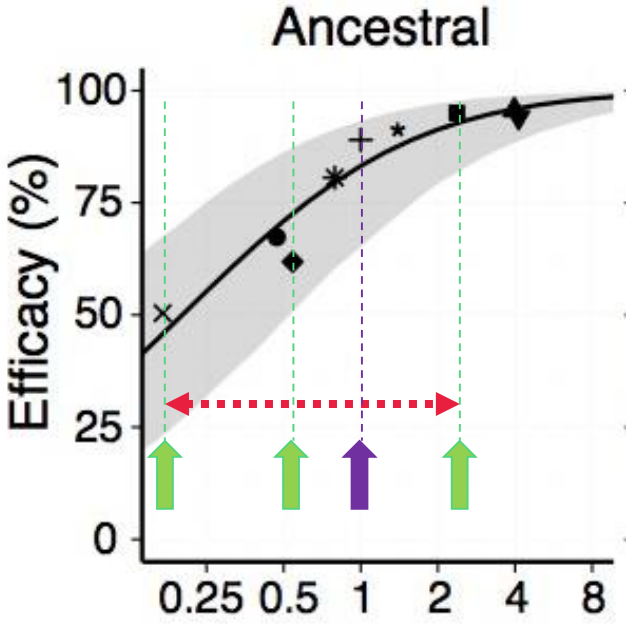
Predicting efficacy

New vaccine:

- Estimate neutralisation against ancestral virus

Benchmark in SAME ASSAY:

- Intnl Standards
- Coronavac
- ChAdOx1 nCoV19
- Convalescent (1-2 months)
- BNT162b2



Neutralisation of ancestral virus
(as fold convalescent)

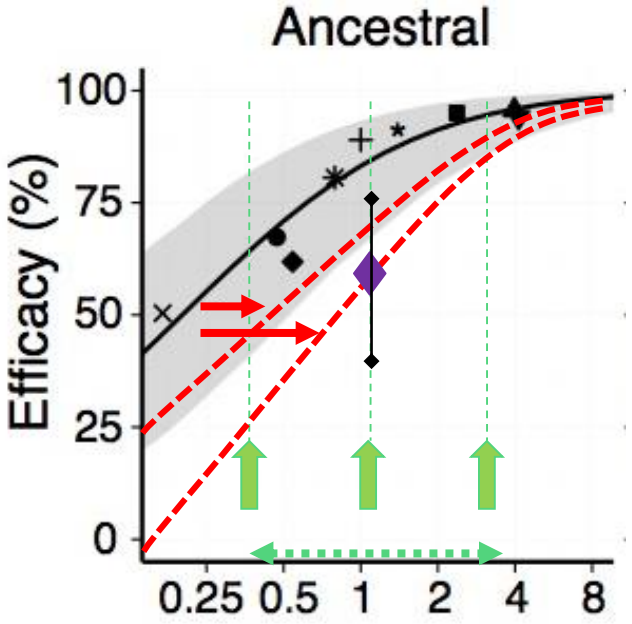
Predicting efficacy

New vaccine:

- Estimate neutralisation against ancestral virus

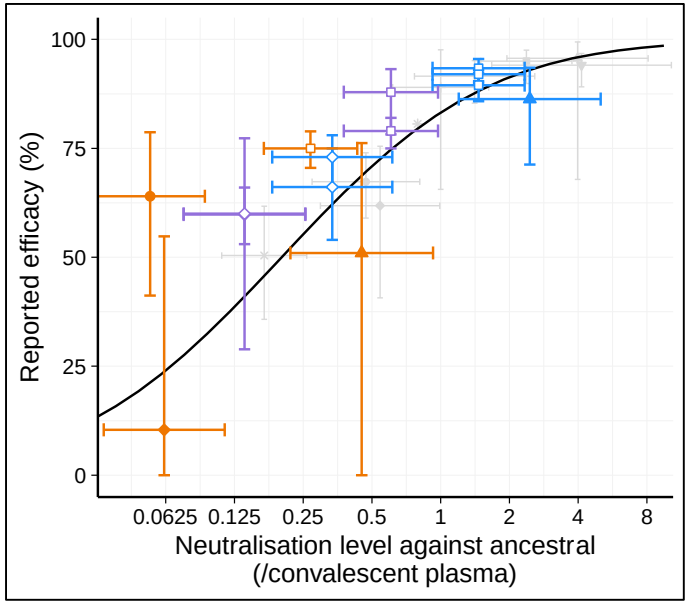
New variant:

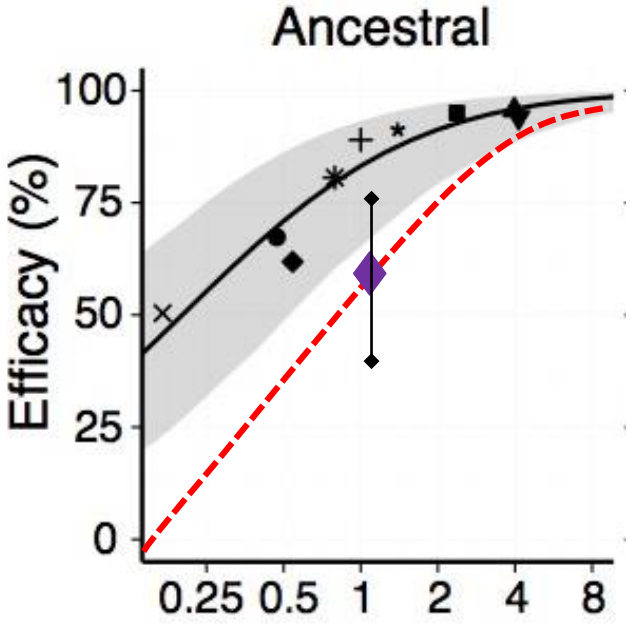
- Estimate fold-drop (from ancestral) (across several assays)



Neutralisation of ancestral virus (as fold convalescent)

Predicting efficacy





Neutralisation of ancestral virus
(as fold convalescent)

Details of primary sources of all studies analysed:

Cromer, D. *et al*,

SARS-CoV-2 variants: levels of neutralisation required for protective immunity. MedRxiv

https://www.medrxiv.org/content/10.1101/2021.08.11.21261876v1

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Funding:
NHMRC (Australia)
MRFF

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