Public Health England

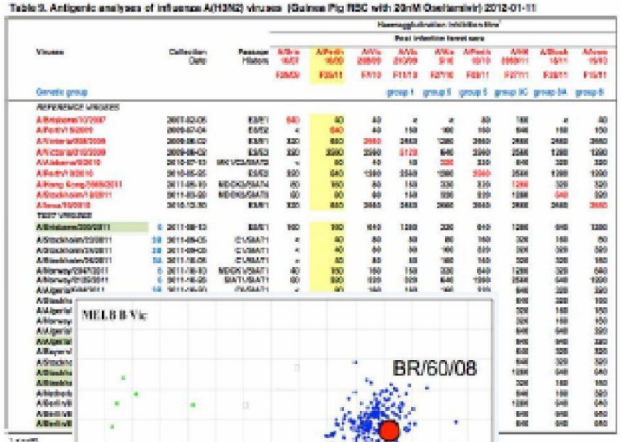
What information is needed to update vaccine strains

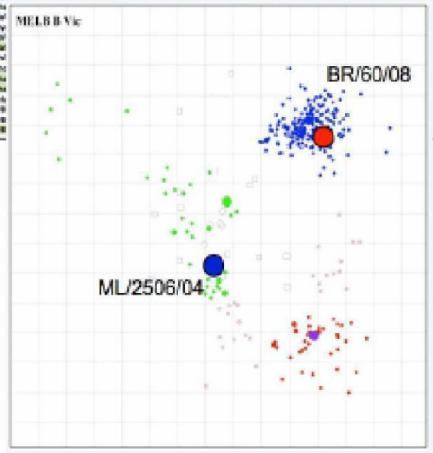
How might our experience with influenza help

5.1.2e

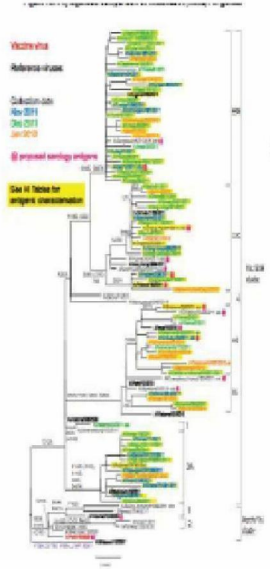
Virological Information for Strain selection

HI (and neutralisation) data)

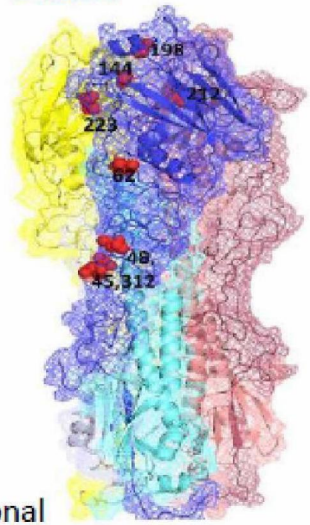




Antigenic cartography



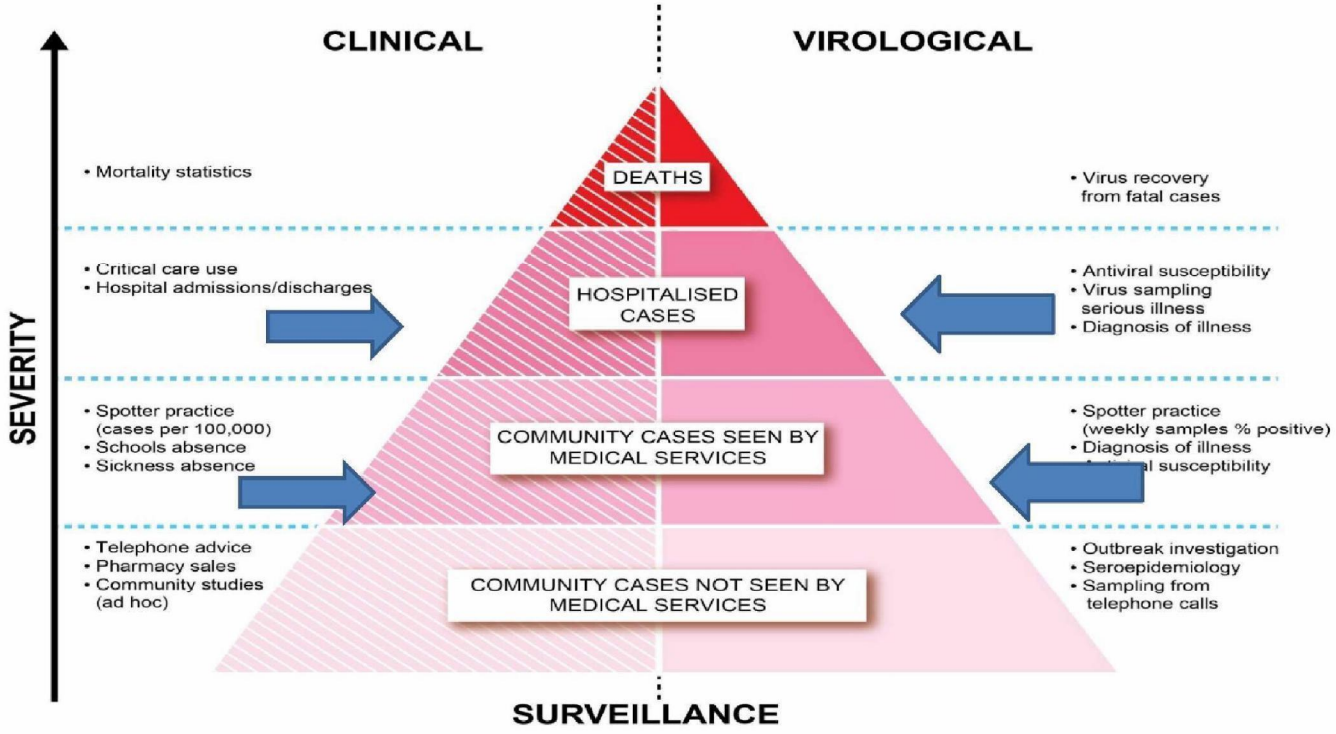
Sequence analysis



Structural/functional
significance of mutations

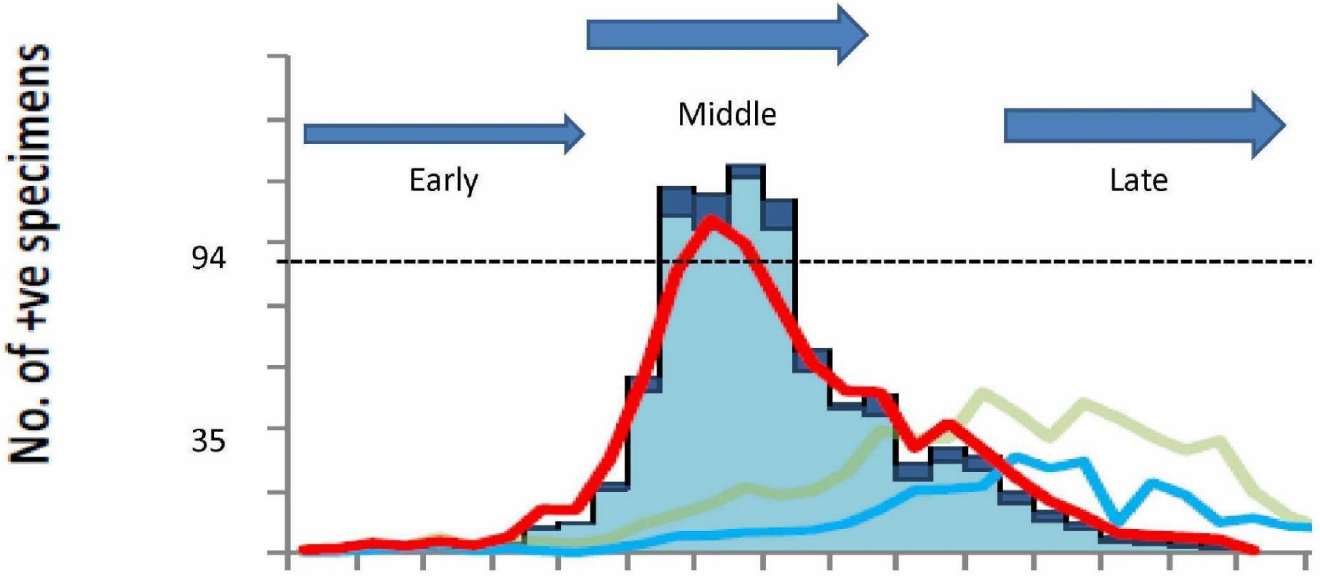
De volgende pagina is verwijderd i.v.m. 5.1.2a

Disease Monitoring (ILI/SARI/ARI)



Public Health England

Schematic sampling and sequencing Strategy



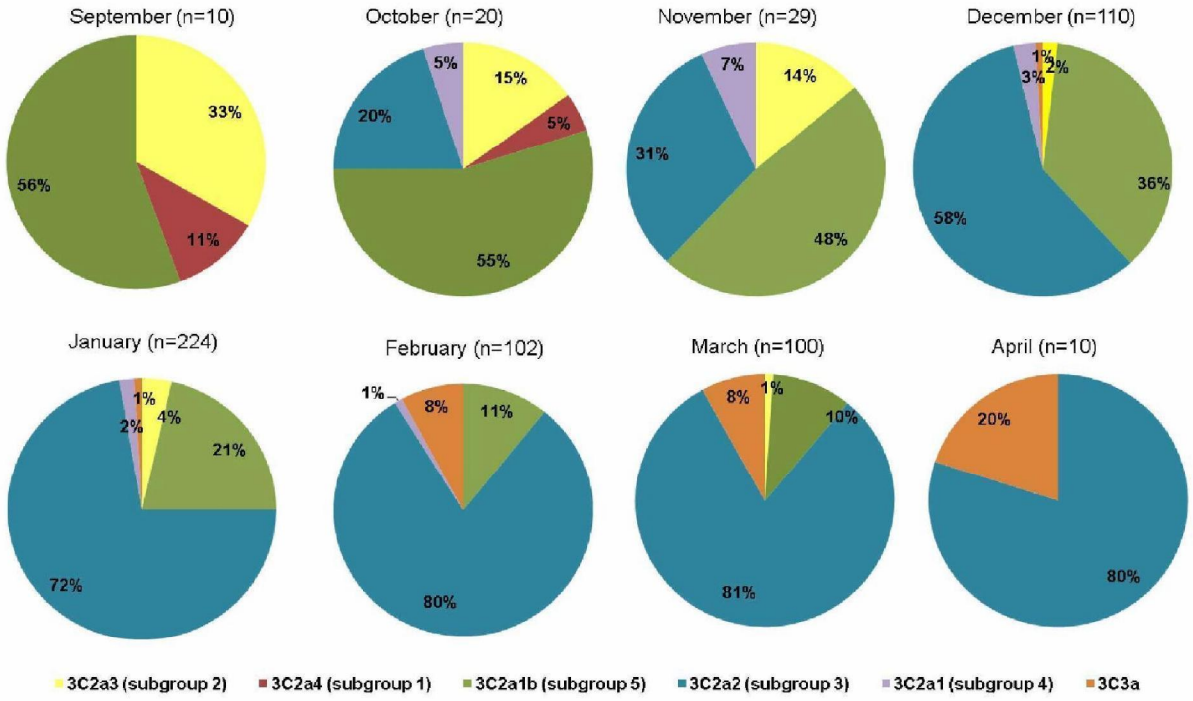
Criteria for sequencing

Sentinel
Vaccine failures

Non-sentinel
Vaccine failures, fatalities, ECMO
Suspicion of drug resistance/immunocompromised
Recent travel
Suspected mismatch to molecular detection methods

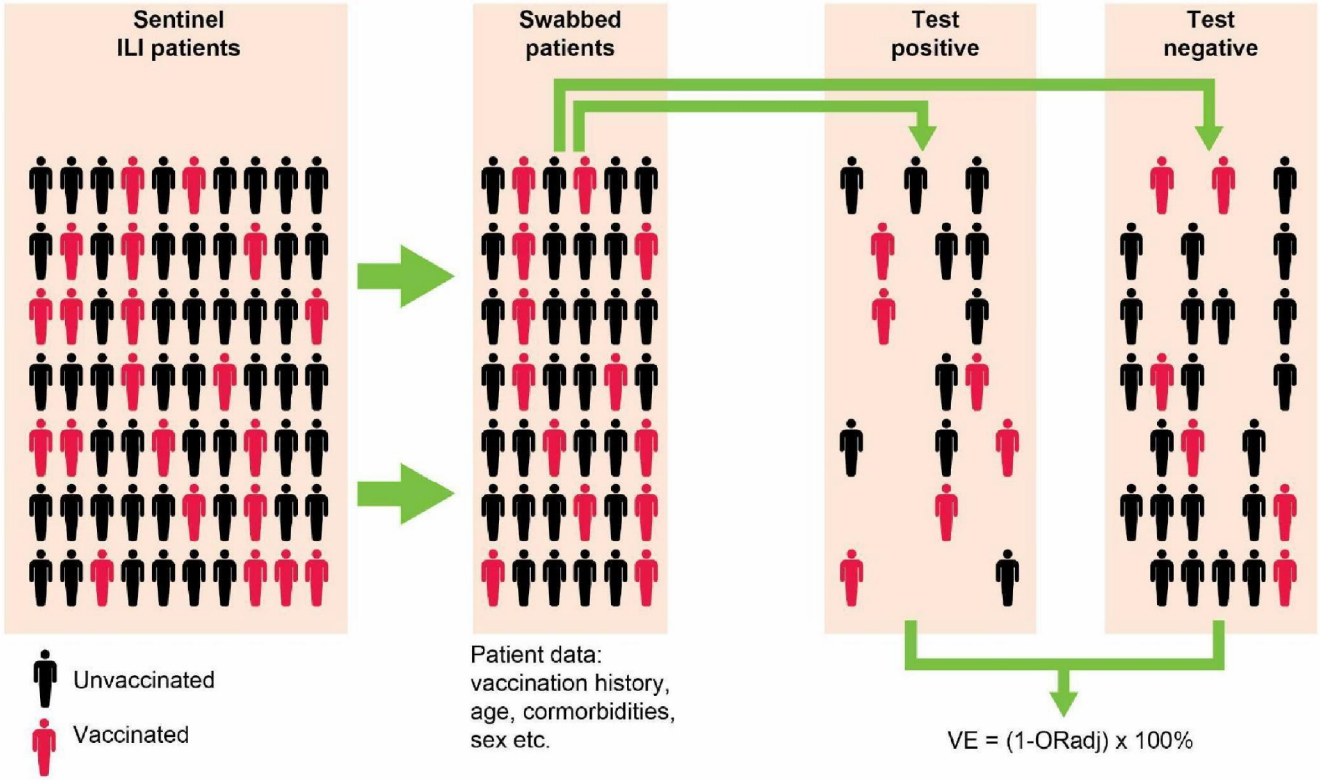
Locally set capacity

Temporal analysis
e.g H3N2 Variation



Vaccine Effectiveness

Test Negative Case Control Design (TNCC)



Process for Strain selection

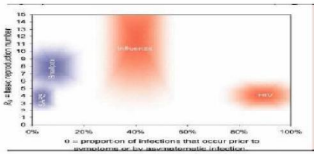
- GOAL Best match to circulating strains

- Globally Harmonised process. One decision for N & S hemisphere.
- Regular timing to coincide with vaccine campaigns
- Data coming from multiple and expert laboratories
- Experienced multidisciplinary team to make choices
- Transparant process
- Clear timelines for industry
- Process of vaccine candidate evaluation

What might be different in a pandemic with a new virus ?

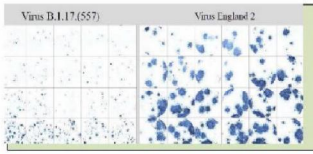
Iceberg ratio unclear

Broadly based Sampling Symptomatic and asymptomatic



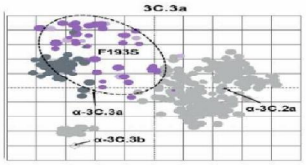
Relationship between transmission and infection

All ages



Relationship between genotype and phenotype

What criteria to assess differences between strains



Nature of protective immunity

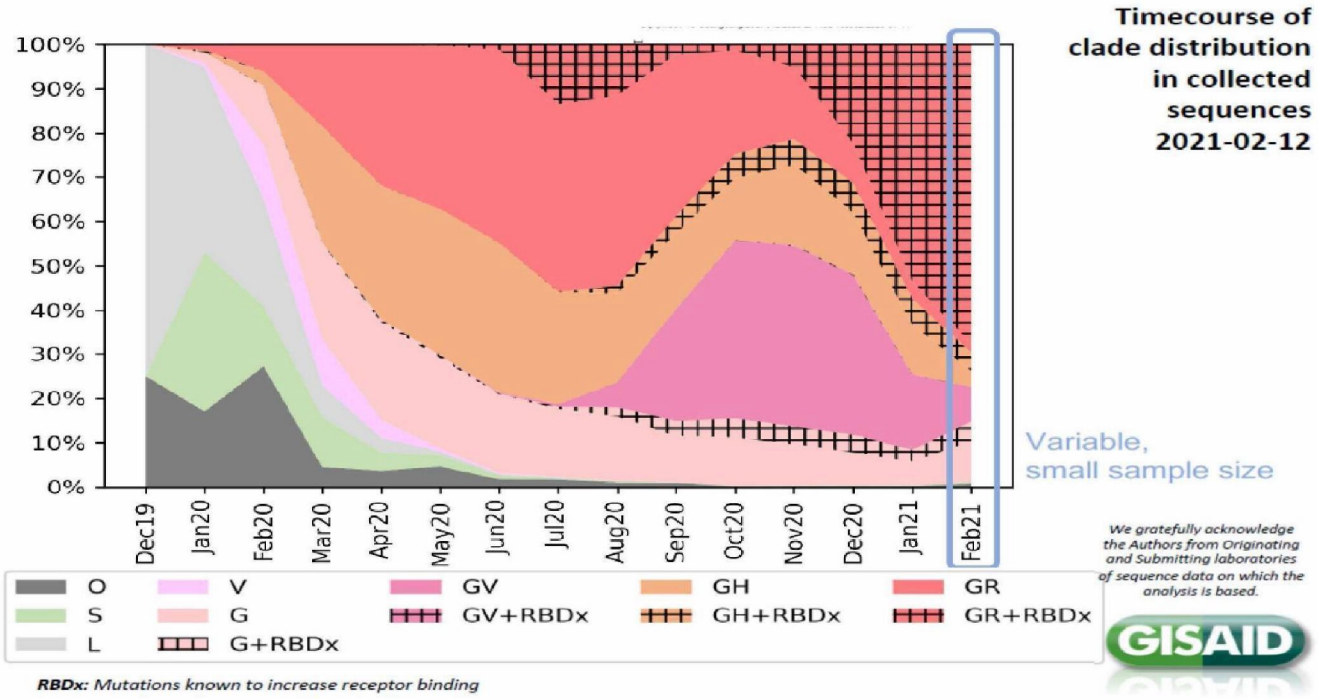
Correlates of protection?
Antigenic distance

Where are we with SARS Cov 2 ?
Sequence First Surveillance

- Paradigm shift….Genomic surveillance (WGS)
- Global database (GISAID)
- Lack of proportionate sampling
- Lack of systematic sampling
- Temporal analysis in infancy
- Limited phenotype work
- Link between genotype and phenotype to be developed

- When to worry about variants
- How to assess their importance

SARS Cov-2 Tracking Virus Evolution (>500,000 genomes)



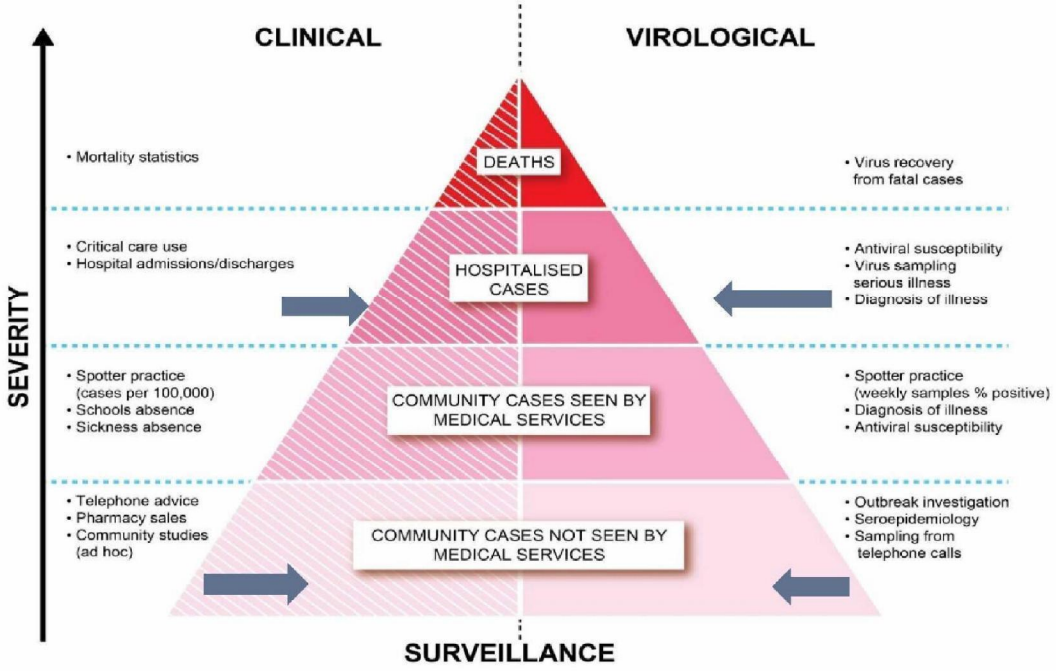
Laboratory based case confirmation
Symptomatic vs Asymptomatic
Summary of performance characteristics
Clinical Case Definitions

	Influenza		**COVID-19**	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
ILI	45-55	85-95	20-51	60-90
ARI	94	27	86	23
SARI	45-70	45-70	40-55	33-60

WHO Consultation Adapting GISRIS for Winter 20/21
In preparation

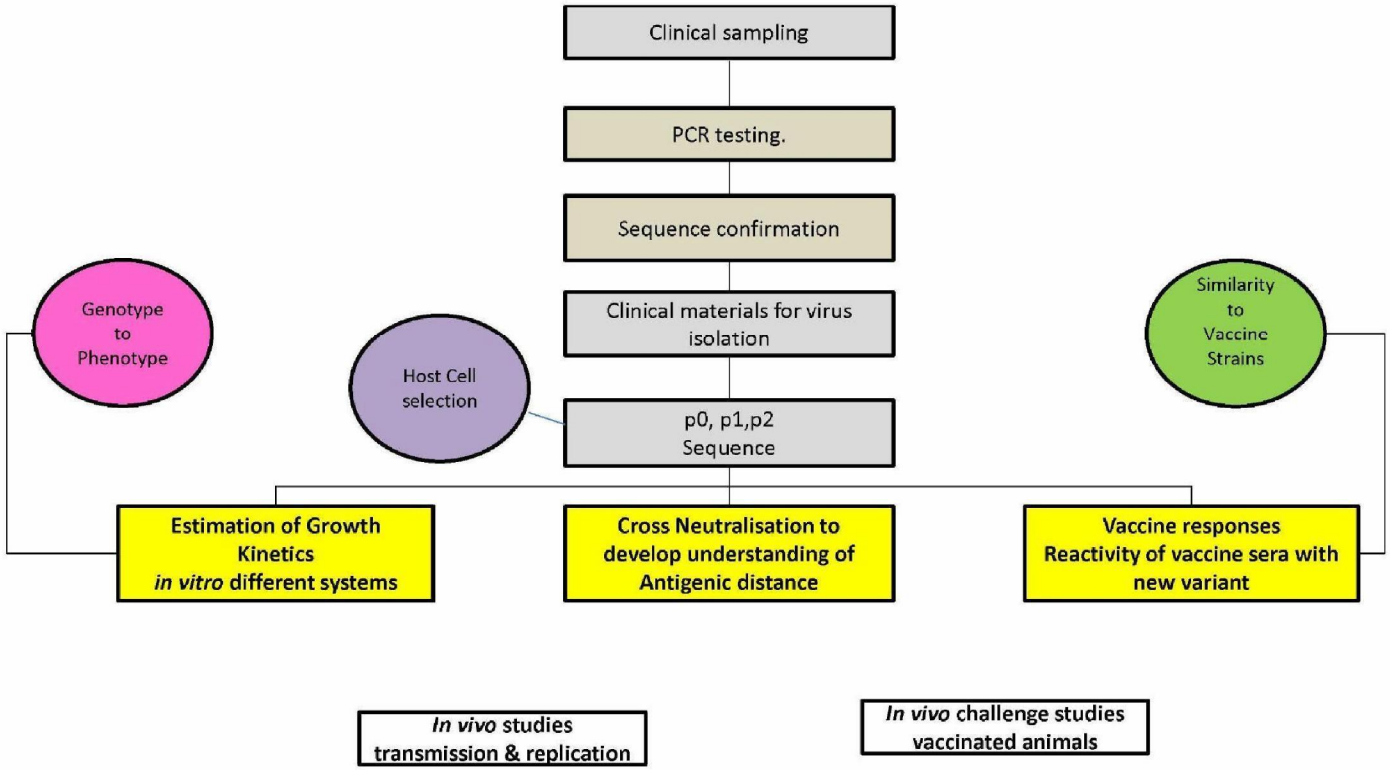
Public Health England

Adapt surveillance systems

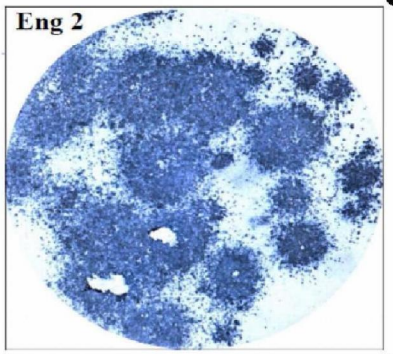


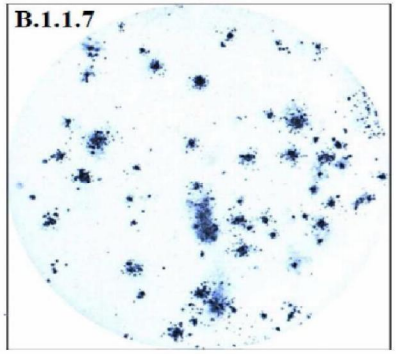
Zambon M. Influenza surveillance and laboratory diagnosis, in Textbook of Influenza (second edition), 2013.

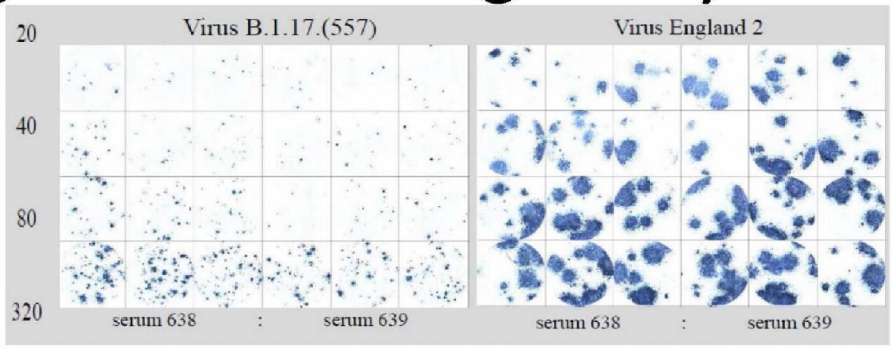
Pathways for virological characterisation

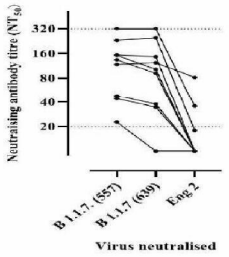


Assay developments: assess growth and antigenicity

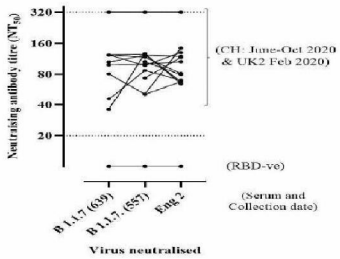






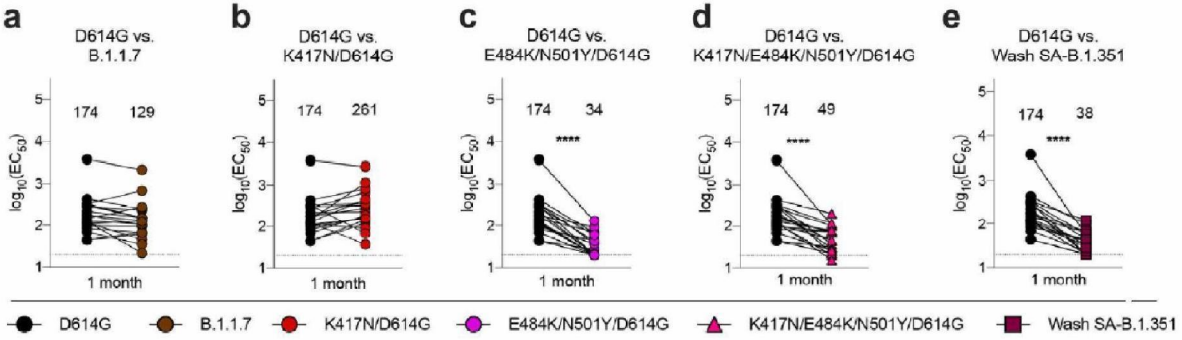


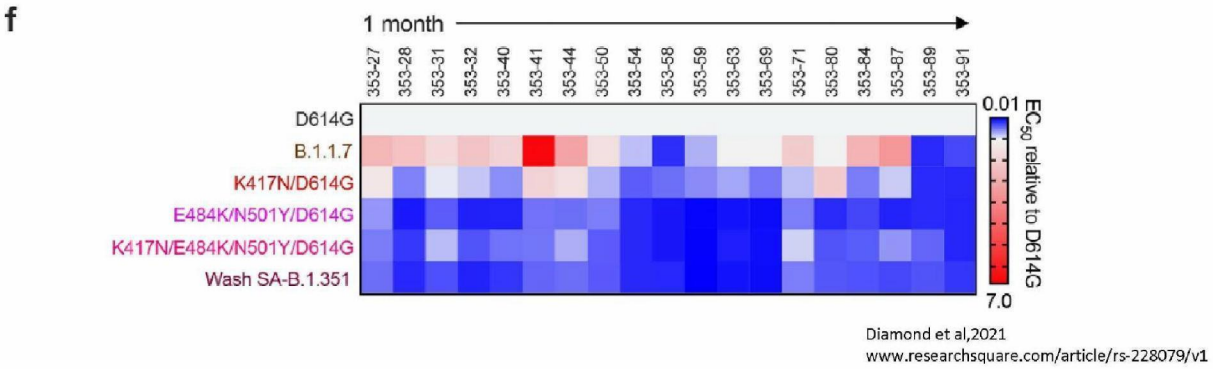
A. Panel of **Nine RBD positive/eq** Sera from Individuals infected with ***B.1.17*** tested against B.1.17(557), B.1.1.7 (639) & England 2 viruses in a Focus Reduction Neutralisation



Cross reactivity of sera elicited against SARS-CoV-2 strains circulating during 2020

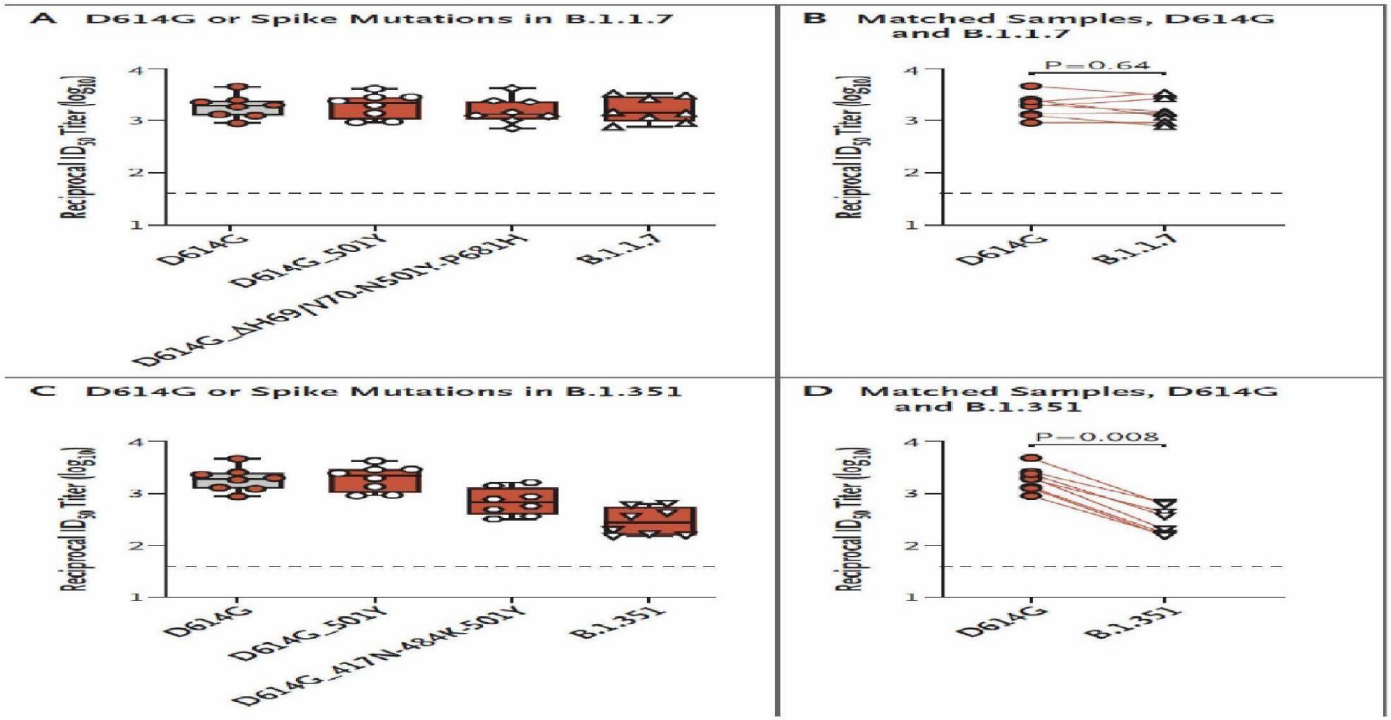
Develop metrics of antigenic distance





Diamond et al,2021
www.researchsquare.com/article/rs-228079/v1

Post vaccine analysis
mRNA-1273

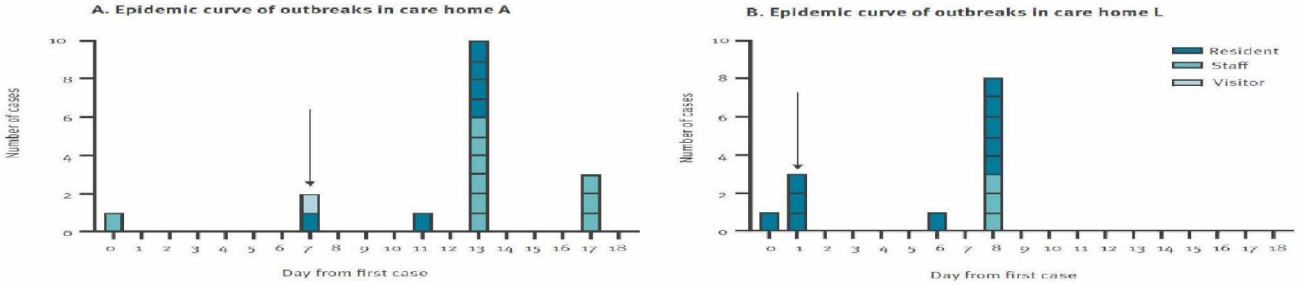


NEJM Wu et al, 2021

Duration of Protection : Field work and outbreak Investigations link *in vitro* to *in vivo*

FIGURE 1

Epidemic curves of outbreaks in care home A (A) and care home L (B), London, United Kingdom, September and October 2020



TABLE

Severe acute respiratory syndrome coronavirus 2 attack rate by susceptibility status in two care home COVID-19 outbreaks, London, United Kingdom, September and October 2020

Category	Residents (n = 103)			Staff (n = 106)			Overall	Attack rate	Attack rate percentage
	Status pre outbreak	PCR positive during outbreak	PCR negative during outbreak, seroconversion	Status pre outbreak	PCR positive during outbreak	PCR negative during outbreak, seroconversion			
Not susceptible	44[a]	0	NA	44	1	NA	88/209	1/88	1.1%
Susceptible	40	13	2	33	5	2	73/209	22/73	30.1%
Unknown	19	3	NA	29	7	NA	48/209	10/48	20.8%

Protective Effect of Previous Exposure

96.2%

Jeffrey-Smith et al, Eurosurveillance, 2021

How can we adapt ?

Influenza

- WHO VCM strain selection
- GISRIS lab network
- ILI case definition
- Expert influenza laboratories
- HA & NA sequencing
- Structural predictions
- Standard cell lines & reagents
- HI/Neuts
- Animal models
- Field correlate of protection
- TNCC VE methods
- IFPMA

SARS CoV 2

- WHO create process
- Adapt GISRIS
- COVID case definition
- Expert CoV reference laboratories
- WGS
- Structural predictions
- Standard cell lines and reagents
- Live virus/pseudotype neut
- Animal models
- ? Field correlates
- Adapt VE measurements
- Manufacturer liaison

Next steps

- Improve temporal analysis of variants based on WGS
- Develop genotype to phenotype understanding
- Field studies correlates of protection
- Concepts of antigenic distance
- Vaccine Effectiveness analysis