Demographics, Hospital Outcomes and Vaccine Effect of S Gene Positive Cases in Scotland from April 01 2020

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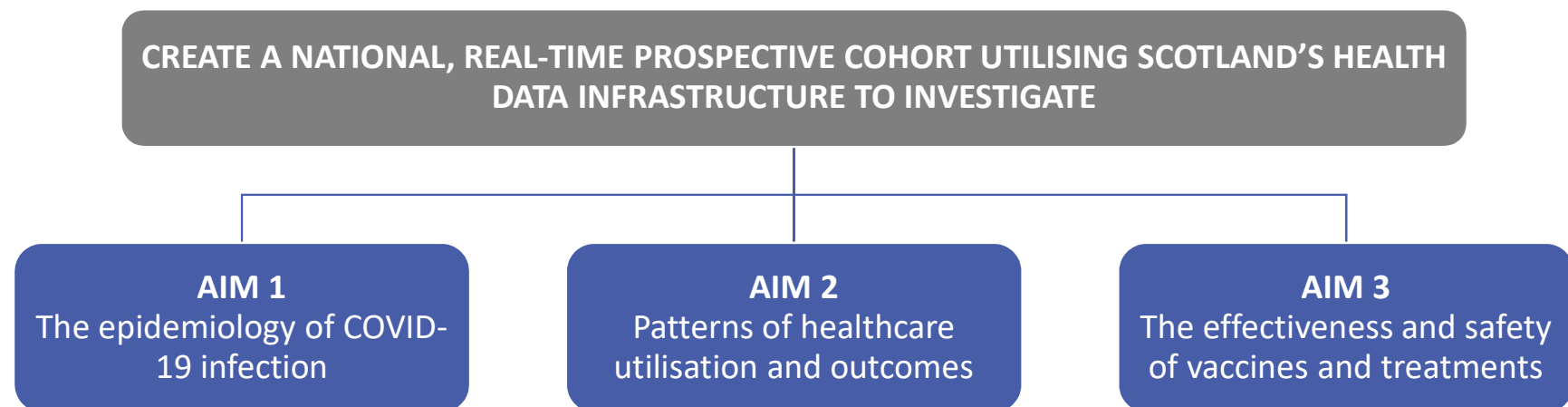CONFIDENTIAL PRELIMINARY DATA - PLEASE DO NOT SHARE

Updated results published in

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01358-1/fulltext
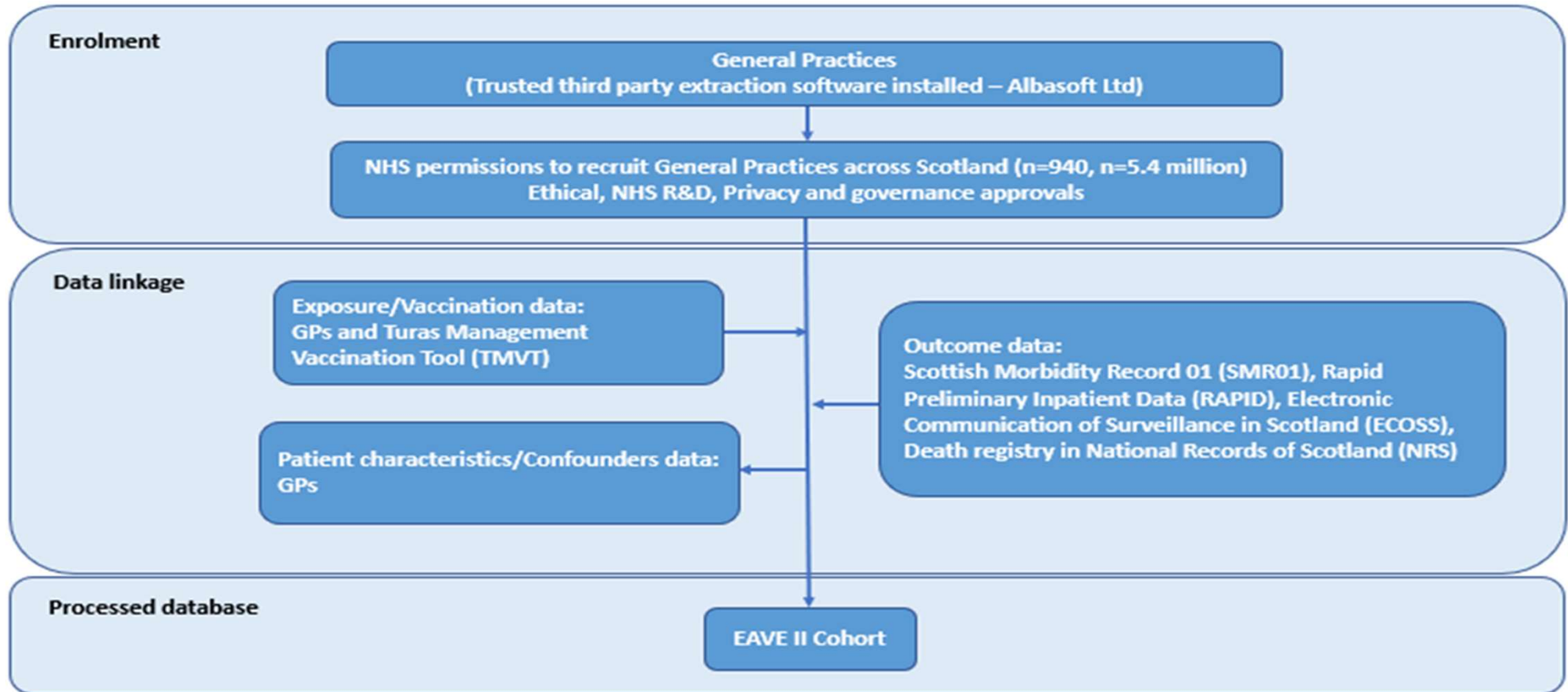
Background to EAVE II

- Utilising linked data is crucial to monitor, understand and mitigate the effects of pandemics

- EAVE II aims to contribute to this effort for Scotland using a 'hibernating' NIHR funded platform originally created to respond to H1N1 pandemic (EAVE: **E**arly assessment of **A**nti-virals and **V**accine **E**ffectiveness)

- Funded by UKRI as part of its initial Rapid Response call

CREATE A NATIONAL, REAL-TIME PROSPECTIVE COHORT UTILISING SCOTLAND'S HEALTH DATA INFRASTRUCTURE TO INVESTIGATE

AIM 1
The epidemiology of COVID-19 infection

AIM 2
Patterns of healthcare utilisation and outcomes

AIM 3
The effectiveness and safety of vaccines and treatments
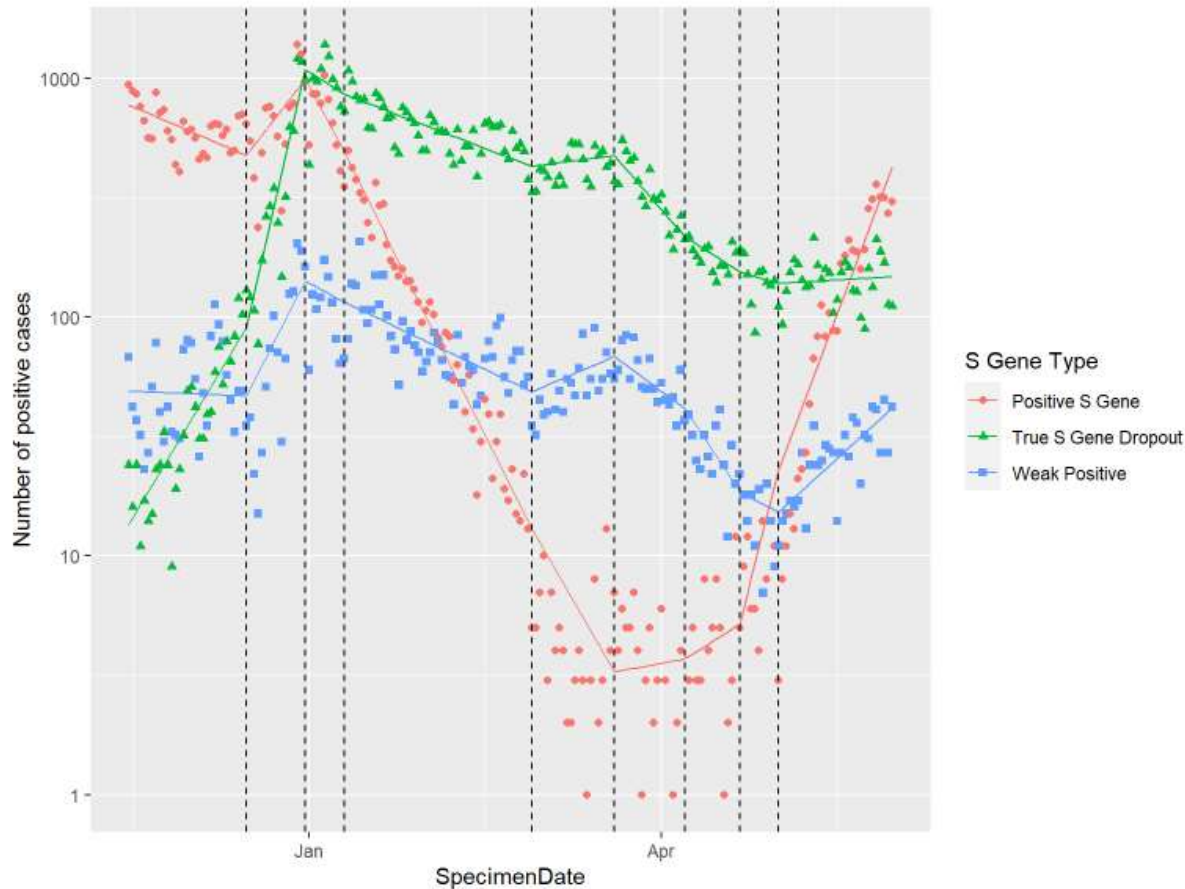
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Methods

- In Scotland testing is largely carried out in one Lighthouse lab (largely for community testing) and in a number of NHS labs.

- True S Gene drop out corresponds to negative on the s gene and Ct values < 30 for at least one of the OR and N genes.

- Weak Positive is negative for S and Ct >= 30 for both OR and N genes

- S Gene Positive, Ct values < 30 for the S gene and valid Ctvalues for the other two genes.

- There are a number of lighthouse samples which do not yield an S gene categorisation, due to missing data in the Ct fields, and these are omitted. All the positive tests which are carried out in the NHS labs are omitted from this analysis also. From March 2021 very few positive cases per day in the NHS labs .

- Counts of the individuals testing positive are presented from November 16, 2020. The analysis was carried out using all data reported to Public Health Scotland by 17 th May 2021.

- The testing data are linked to the EAVE study data of GP clinical conditions for a clinical and demographic description of the individuals testing positive with the S Gene deletion in comparison to those who do not have this deletion. The laboratory data and GP data are then linked to hospital admissions and deaths (only 7 deaths among those tested positive since April 01 2021).

Methods

- A hospital admission is defined as an admission to hospital within 14 days of testing positive for covid 19. Individuals who tested positive within two days following the hospital admission are also counted. The time from test to hospital admission is the number of days from the date of the sample to the date of admission with individuals who tested positive on the two days following admission defined as having a time from test to admission of zero days. Individuals who were tested during a hospital stay, day 3 onwards, are excluded. Hospital acquired covid infections are not included in this analysis. Hospital admission data is largely complete up to the 14th May 2021.

- Data are linked to vaccination records Vaccination is coded at the date of the positive test

- The groups are uv - unvaccinated,

- v1_0-27 – one dose days 0 to 27 before date of sampling the specimen

- v1_28+ – one dose 28+ days before date of sampling the specimen

- v2_0-13 – two doses and dose 2 was administered on days 0 to 23 before date of sampling the specimen

- v2_14+ – two doses and dose 2 was administered on 14+ days before date of sampling the specimen

Trends in cases since Nov 16 2020

Cases from Lighthouse lab only – Community (Pillar 2) testing.

Vertical dotted lines in late Dec and January represent lockdowns, all others represent easing of restrictions (5 days after).

Only a handful of S Gene positive cases per day (<10) since March 2021

Rise in S Gene Positive started with the easing of restrictions at beginning of April

Sequence of join point models based upon over dispersed Poisson distribution

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Demographics

S Gene	Females	Males
Positive S Gene	2074	2131
True S Gene Dropout	4608	4443
Weak Positive	789	677

15531 cases with S gene information since April 01 2021 to 30th May 2021

14722 link into the EAVE cohort for clinical risk group information.

This shows the gender distribution of the cases for whom PHS has S gene status and who also link into the EAVE study cohort. This is a subset of all PCR cases reported to PHS. The subset is based upon those tested in the lighthouse labs and represents community testing. Not all will be symptomatic at the time of test.

Age Distribution of Cases (since April 01 2021)
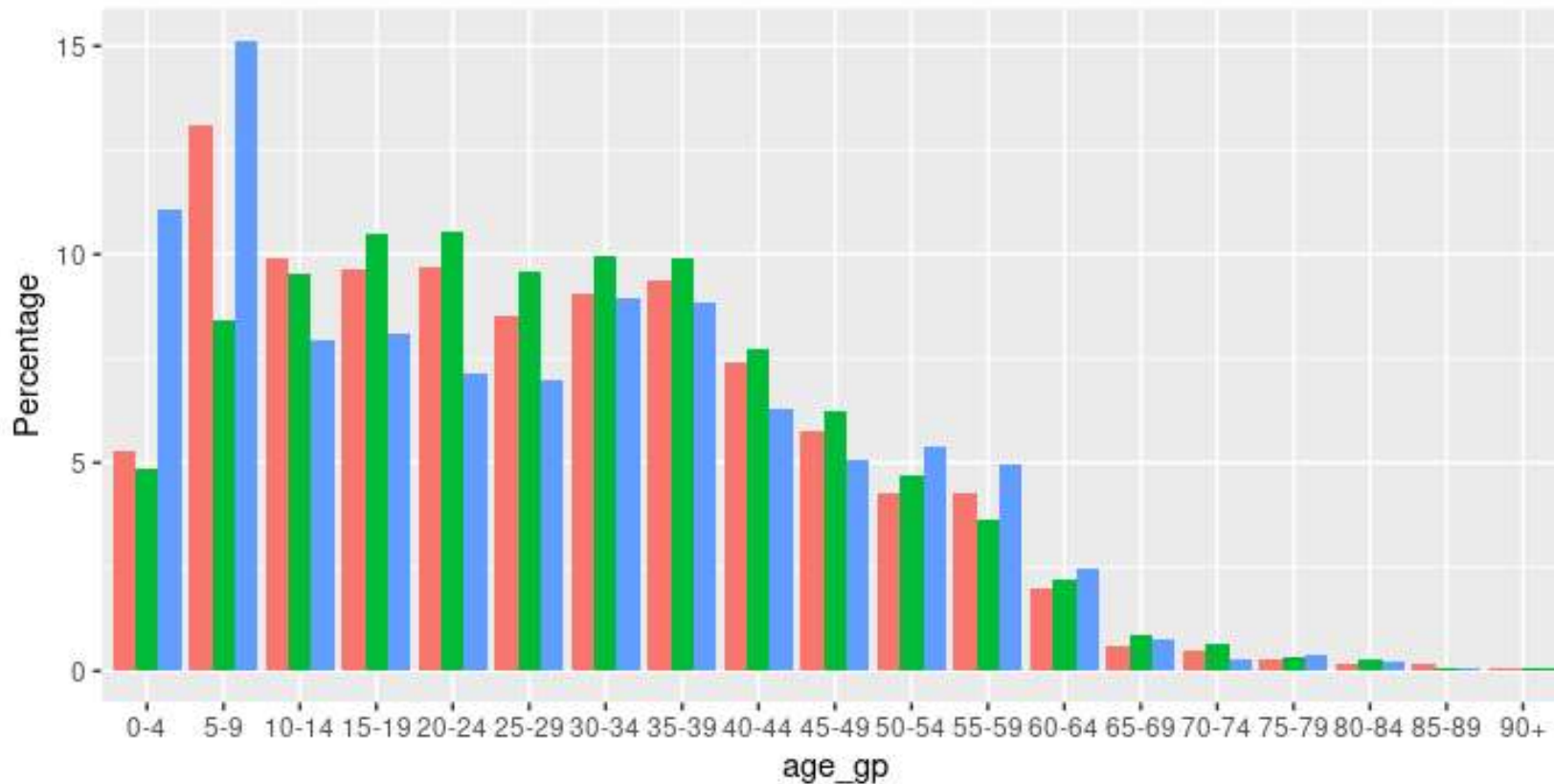
Weak positive on the S Gene have a greater proportion aged 0-9.

Positive S Gene a greater proportion aged 5-9

S Gene

- Positive S Gene
- True S Gene Dropout
- Weak Positive
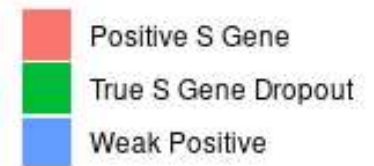
To 30th May 2021

The percentages add up to 100 over the age groups so represent the percentages of those testing positive (for each s gene status) who are in a specific age group.
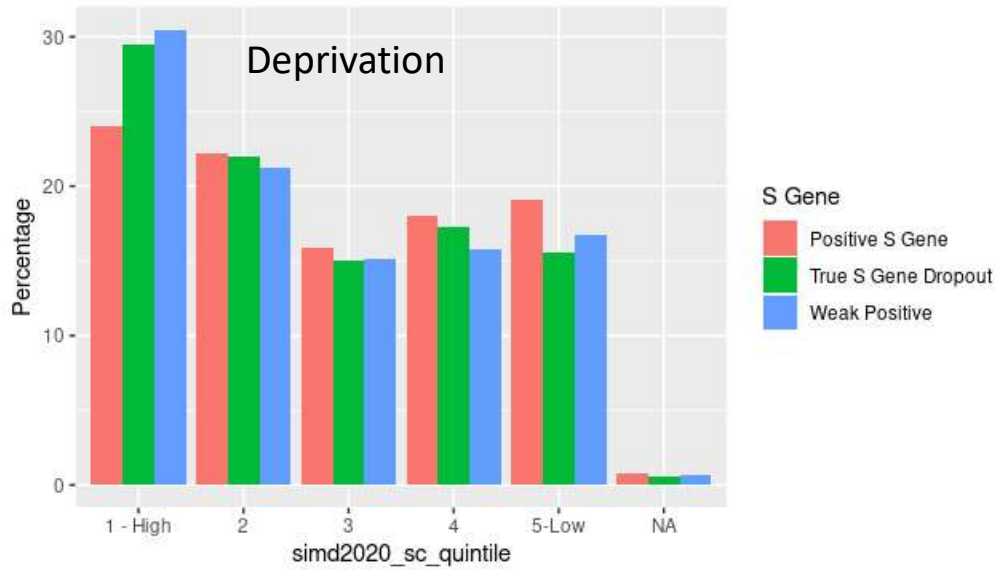
Deprivation

Positive S Gene a greater proportion from low deprivation groups – 15% of S- are low deprivation compared to 19% of S+

70% of cases have no clinical risk groups – similar pattern in all S Gene groups

75% are unvaccinated – similar pattern over all S Gene Groups but slightly lower in the S+

Number of Clinical Risk Groups

Vaccination Status

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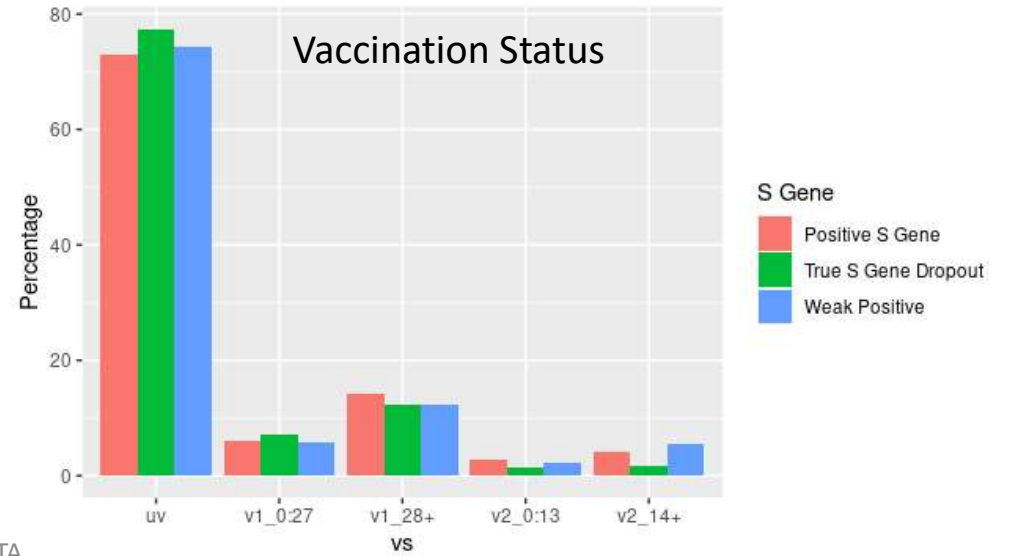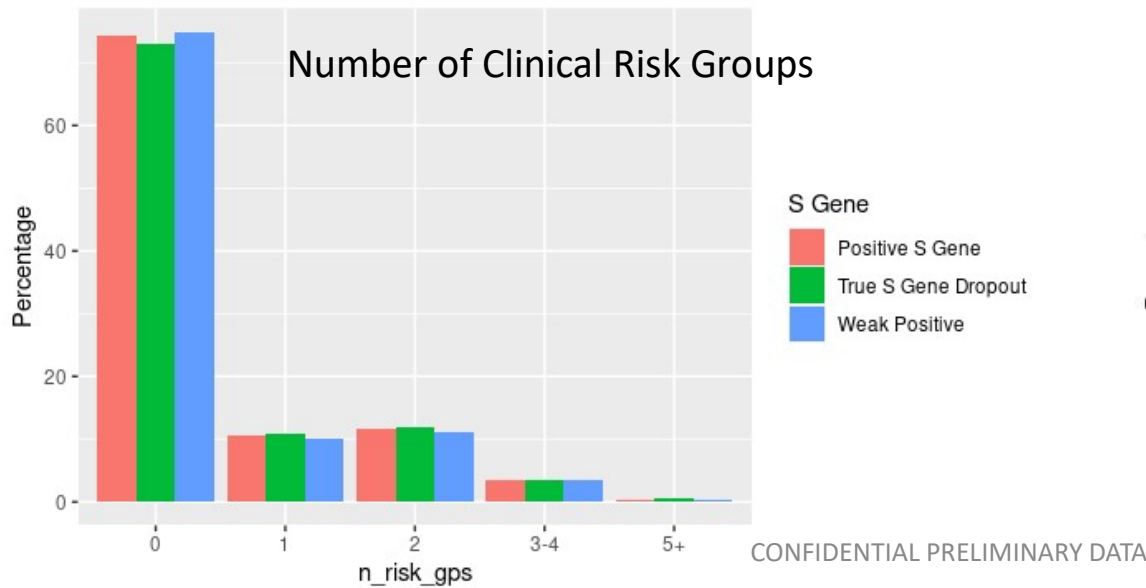
Daily Emergency Admissions to hospital with a positive test
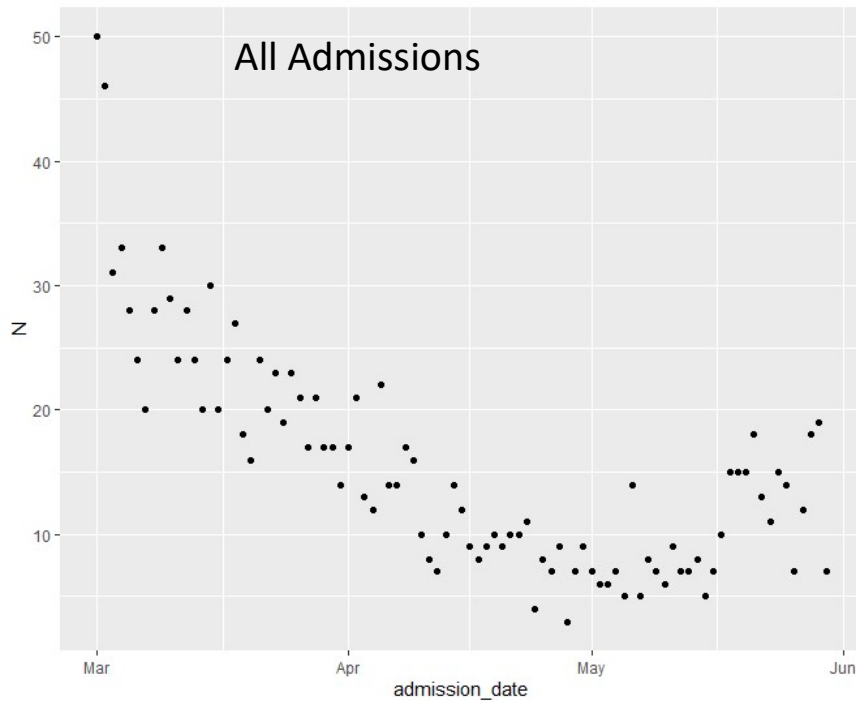
Admissions from community testing where S Gene is known and linking to EAVE (a subset of all admissions)

All Admissions

Positive S gene cases dominate admissions from May 15 onwards
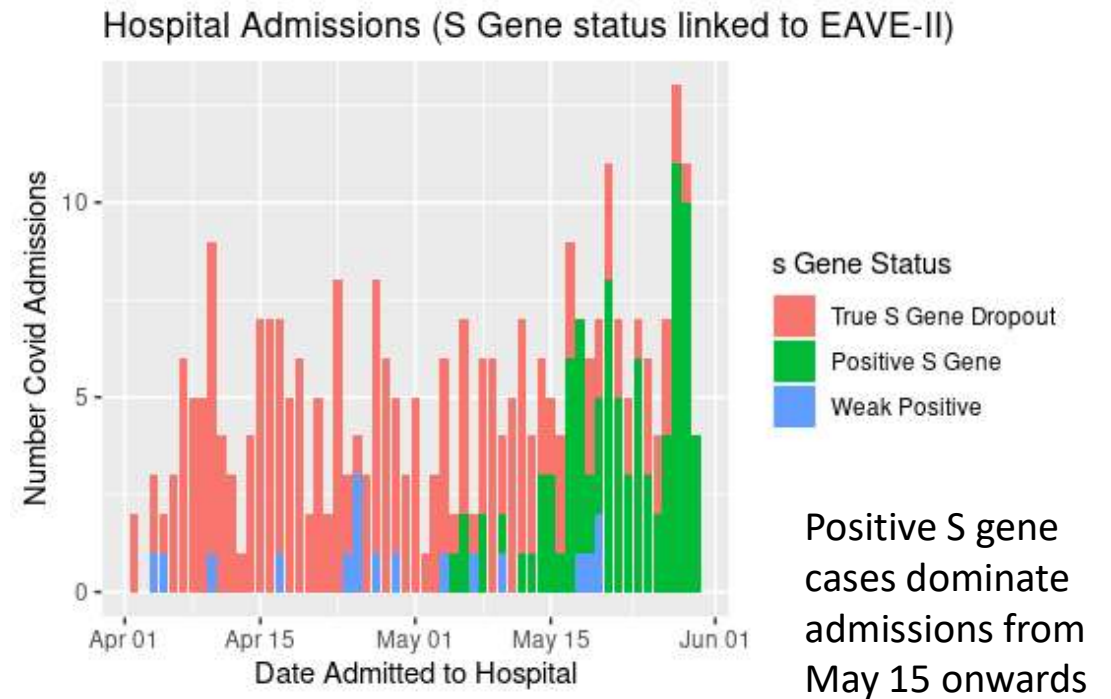
Date of positive test within 14 days prior to admission date and up to 2 days after
Reason for admission is unknown other than an emergency admission
The left graph represents all admissions including those tested in NHS labs; The right graph is a subset of all admissions following community testing in a lighthouse lab.

Time to Covid Hospitalisation

| To 30th May | Person Years | | Number Admitted to | Rate per 100 |
S Gene	Exposure	N	Hospital	person years
True S Gene Dropout	532.71	8900	200	37.54
Positive S Gene	93.40	3776	88	94.22
Weak Positive	79.49	1414	17	21.39

The table shows the exposure from April 01 to 30th May for all testing positive; N is the number of individuals and the rate is the number admitted divided by the person years.

The cumulative incidence curves below show that admissions to hospital tend to be greater for those whose virus is S+ compared to those whose virus is S-
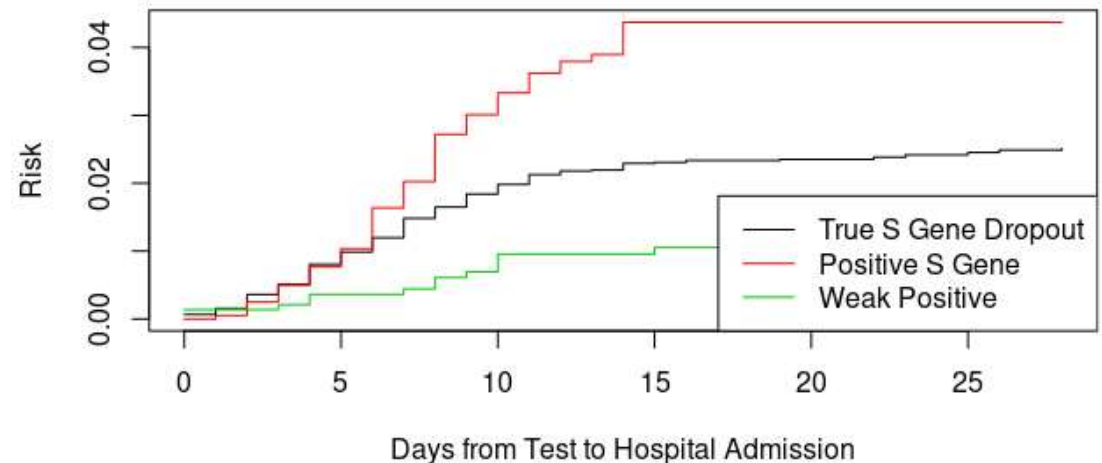
Cox Regression 30th May

		HR	LCL	UCL
S Gene Status	**S Gene Dropout**	1.00		
	Positive	2.39	1.72	3.31
	Weak Positive	0.65	0.39	1.06
Number of clinical	**0**	1.00		
Risk Groups	**1**	1.66	1.20	2.28
	2	1.96	1.43	2.68
	3-4	3.19	2.13	4.77
	5+	6.26	3.26	12.01
Vaccination Status	**Unvaccinated**	1.00		
	v1_0:27	0.74	0.50	1.10
	v1_28+	0.37	0.25	0.55
	v2_0:13	0.29	0.13	0.66
	v2_14+	0.34	0.17	0.68

CONFIDENTIAL PRELIMINARY DATA
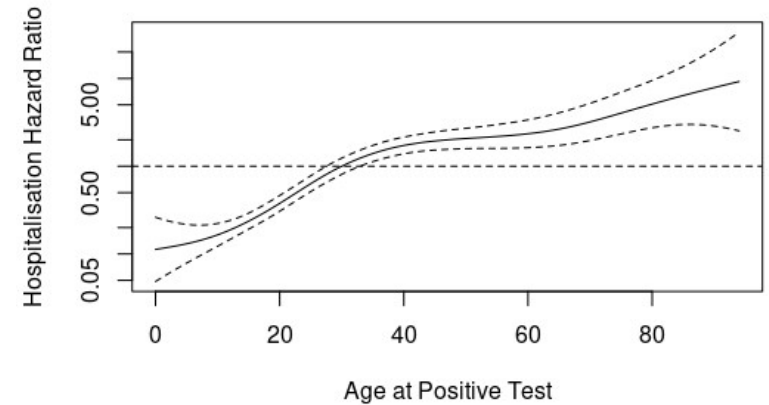
While hazard ratio of hospital admission increases with Age this is not nearly as steep as before vaccination

Positive S gene hazard ratio of hospitalisation for covid is 2.4 (95% CI 1.7, 3.3)

Increased hazard with increased co morbidities

Vaccinated 28+ or 2 doses less likely to be admitted

No temporal trend since April 01.

Cox Regression 30th May impact of s gene status on vaccine effect

		HR	LCL	UCL
Unvaccinated	S Gene Dropout	1.00		
or dose 1 < 28 days	Positive	2.14	1.49	3.09
	Weak Positive	0.57	0.32	1.02
Vaccinated	S Gene Dropout	0.32	0.21	0.50
D1 28+ Dose 2	Positive	0.51	0.31	0.83
	Weak Positive	0.56	0.20	1.63
Number of clinical	0	1.00		
Risk Groups	1	1.64	1.19	2.26
	2	1.96	1.43	2.68
	3-4	3.15	2.10	4.71
	5+	6.42	3.35	12.31

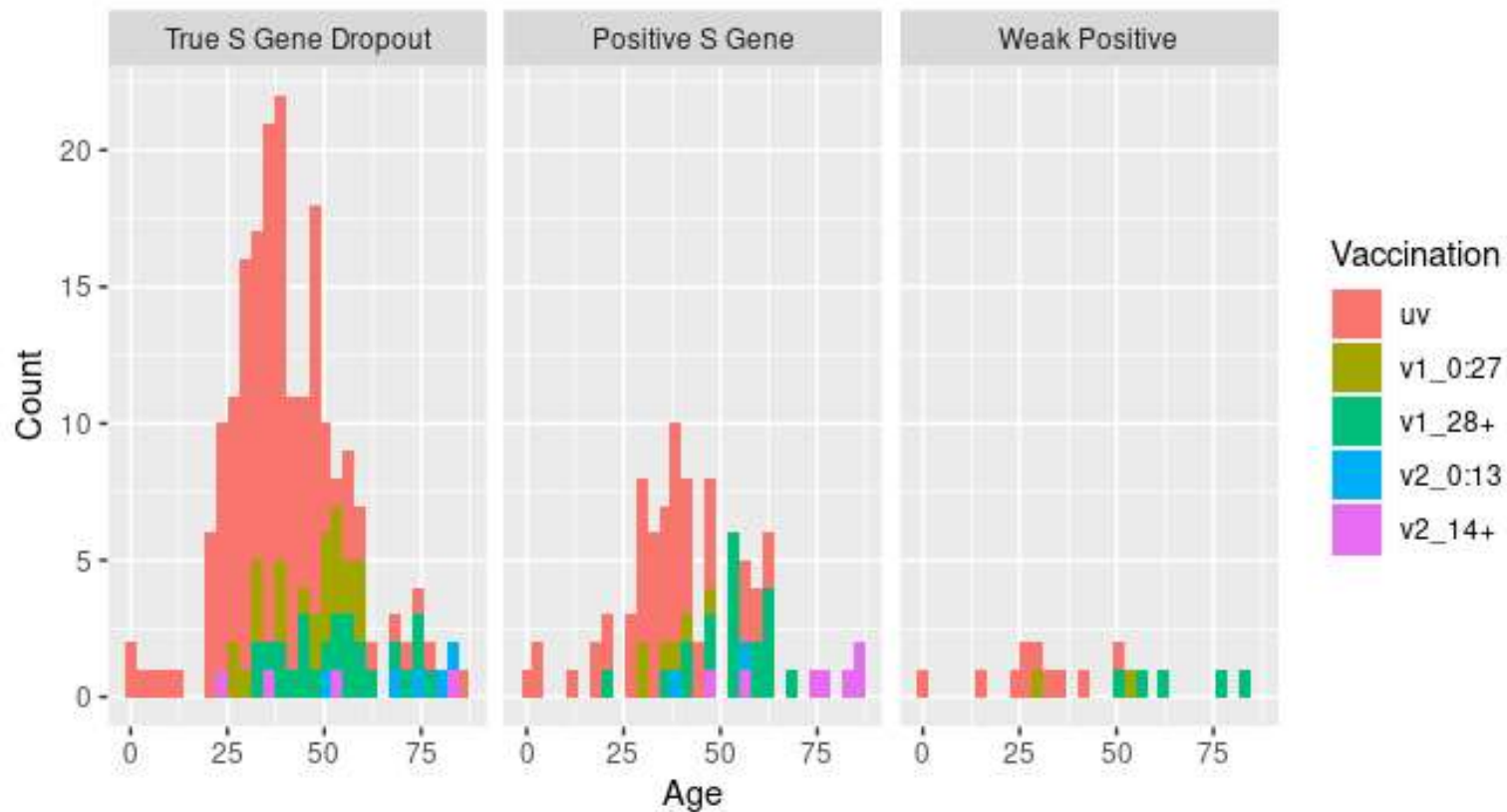Imprecise analysis as the number of events is some of the vaccination by s gene groups is small

Vaccination recoded as
  Unvaccinated and dose 1 0-27 days combined
  Dose 1 28+, and Dose 2 combined

Interaction test for vaccine status and S gene
p = 0.22

S gene dropout
68% (50, 79) vaccine effect on hospitalisation

S gene positive 49% (17, 69)
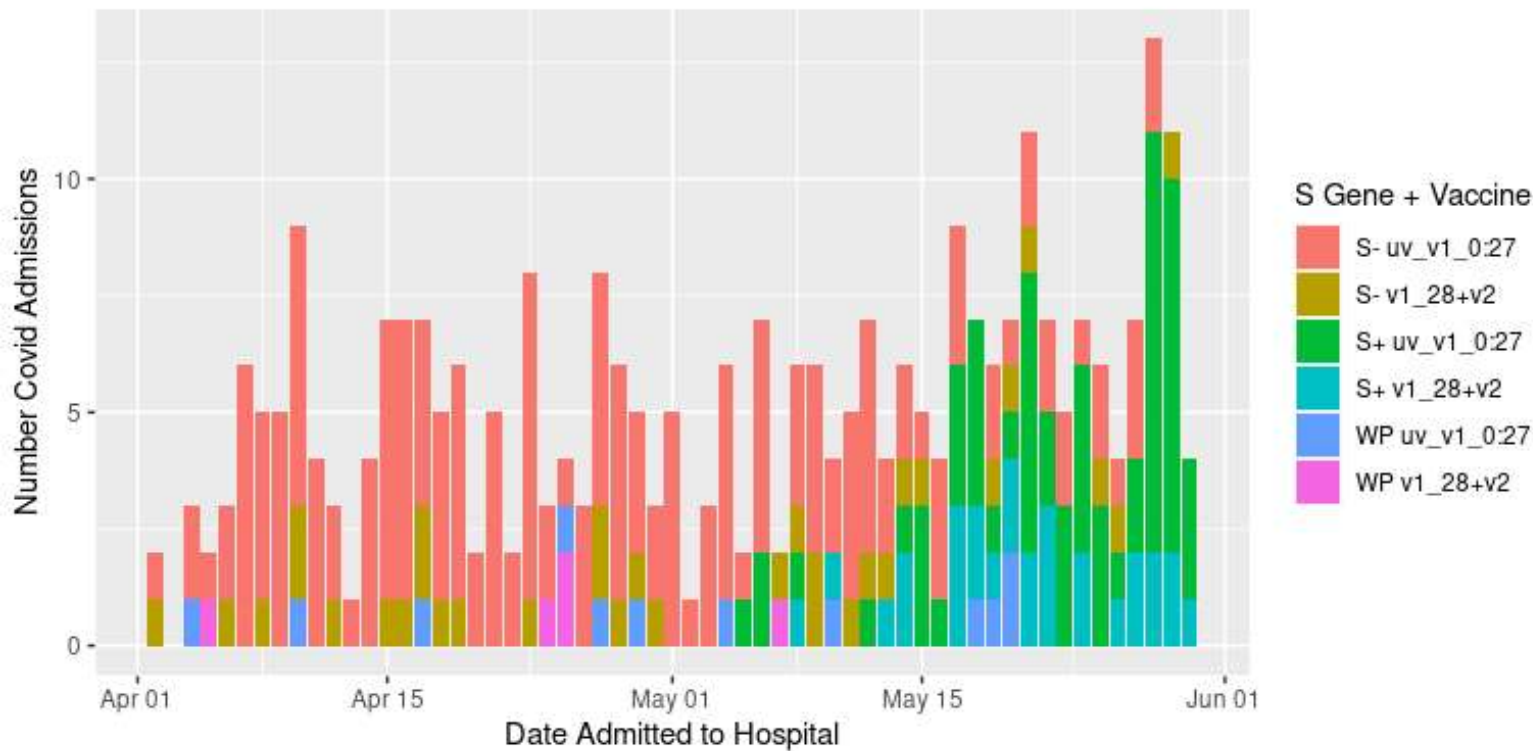
Hospital Admission – Vaccine and S Gene

Few individuals with week positive results are admitted to hospital

The age distribution of those admitted to hospital with S+ and S- is similar. Most patients are aged 25-55 and most are unvaccinated

Hospital Admission – Vaccine and S Gene

Hospital Admissions (known S Gene status linked to EAVE-II cohort)

Up until May 15th most admissions following community testing were S- and unvaccinated.

Since mid May there has been an increase in the numbers admitted who are S+ and who are S+ and vaccinated

S Gene + Vaccine
- S- uv_v1_0:27
- S- v1_28+v2
- S+ uv_v1_0:27
- S+ v1_28+v2
- WP uv_v1_0:27
- WP v1_28+v2

Vaccine Status and Vaccine Type among those admitted to hospital

Vaccine	Dose_1	Dose_2	
AZ	983856	928192	
Mo	18608	<5	
PB	233282	779435	
Unvaccinated	2432511	0	
Vaccine Status	AZ	PB	uv
uv			206
v1_0:27	28	5	
v1_28+	40	8	
v2_0:13	7	0	
v2_14+	8	<5	

Roughly the same number have had 2 doses of Pfizer and AZ; Hospitalisations after PB are lower but age distributions and risk group status of PB recipients are not the same as for AZ so the raw numbers cannot be interpreted as a comparison of the vaccines

Roughly the same number have had 2 doses of AZ as 1 dose of AZ; Hospitalisations after dose 2 are lower but age distributions and risk group status of dose 2 recipients are not the same as for dose 1 only (they will be younger). Consequently the raw numbers cannot be interpreted as a comparison of 2 doses compared to 1 dose
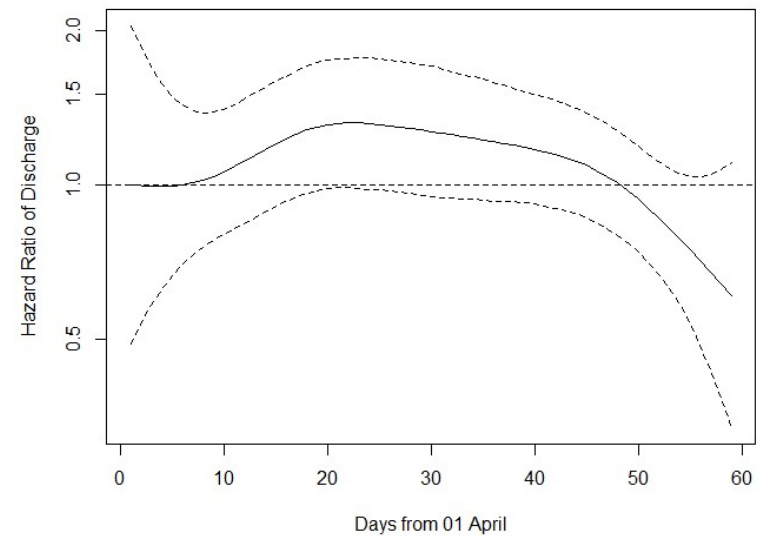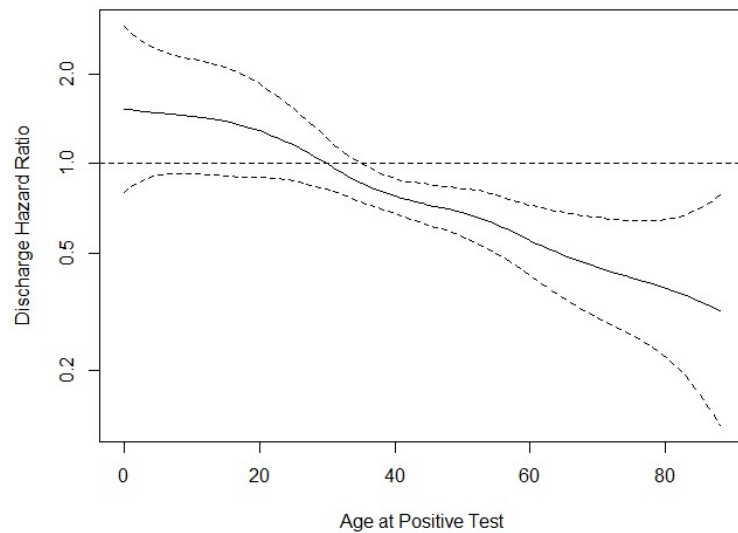
Length of Stay
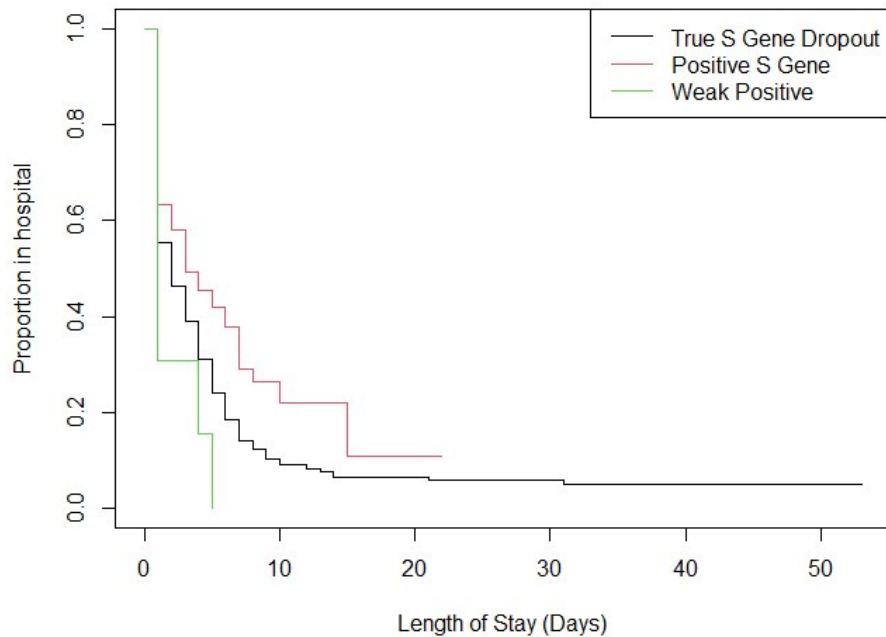
	Length of Stay				
	Admitted	Discharged	median	0.95LCL	0.95UCL
True S Gene Dropout	179	164	2	1	3
Positive S Gene	90	55	3	2	7
Weak Positive	13	13	1	1	NA

Adjusting for Age, Sex, temporal trend there is no difference in length of stay since April 01 among the 3 S gene categories, p=0.24

This slides shows the survival curves for the length of time in hospital for patients who are admitted with covid. The analysis is based upon the RAPID data set in Scotland. This is an episode of stay based system and may not accurately reflect complex stays. As a consequence the absolute lengths of stay may be biased towards shorter stays but the comparison of median lengths of stay over groups should be valid as they are all subject to the same bias.

Length of Stay

No evidence of a trend in length of stay since April as the curve and its confidence intervals span 1,
There are longer durations for older patients as the hazard of a discharge decreases with increasing age.

Vaccine Effect – Test Negative Design

30-May-21		S Gene Positive					S Gene Negative				
Vaccine	Vaccine Status	N	R	VE	LCL	UCL	N	R	VE	LCL	UCL
	Unvaccinated	67143	1813	0.00	0.00	0.00	68688	3358	0.00	0.00	0.00
Pfizer	V1_0-28	4752	147	20.81	5.05	33.95	4745	140	33.58	20.71	44.36
Biontech	V1_28+	6994	59	37.90	18.79	52.50	7044	109	48.40	36.56	58.03
	V2_0-7	1886	8	39.45	-22.92	70.18	1899	21	56.02	31.34	71.83
	V2_8+	41592	90	84.32	80.24	87.56	41576	74	92.55	90.51	94.14
	Unvaccinated	65892	1811	0.00	0.00	0.00	67482	3401	0.00	0.00	0.00
Oxford	V1_0-28	6215	117	18.98	0.08	34.30	6326	228	13.07	-0.66	24.93
AstraZeneca	V1_28+	35741	456	26.24	16.11	35.15	35970	685	40.71	34.54	46.30
	V2_0-7	4669	53	40.14	20.27	55.05	4650	34	67.20	53.62	76.80
	V2_8+	28534	144	52.51	41.69	61.32	28488	98	72.05	64.73	77.85

A test negative case control design was used to estimate the odds of vaccination in all PCR confirmed cases irrespective of symptom reports compared to those testing negative. Vaccine Effect (VE) = 1-OR.
Analysis by generalised additive logistic regression with spline terms for age, day the swab sample was taken and number of PCR tests prior to vaccination. Further adjustment was made for gender and deprivation.

Vaccine effect is lower in the S Gene positive cases compared to the S Gene negative for 8+ days post dose 2 for both AZ and Pfizer.

Conclusions

- S Gene positive cases have slight demographic differences to S Gene dropout (less deprived, slightly more in 25-39 age group) but similar risk group and vaccination profile

- **Hospital -** Few but increasing S Gene positive cases in hospital with covid 19. There is now evidence of a higher risk of hospitalisation in S-gene positive cases but that in this cohort, vaccine reduces the risk of hospitalisation

- **Hospital** – Two doses of a vaccine are associated with a reduced risk of hospitalisation for both S gene negative and S gene positive cases, possible with lower vaccine effect for s gene positive

- **Hospital** – Adjusting for age there is no evidence that hospital stays are getting shorter, length of stay is not strongly associated with S gene status

- **Whole population –**
  - 2 doses
    - **PF – Excellent vaccine effect for 2 doses** for both S Gene positive and S Gene negative cases for PF/Biontec vaccine (though vaccine effect is lower for S-Gene positive by an 8% difference).
    - **AZO – Lower but still moderate/high vaccine effect -** lower and non-overlapping confidence intervals for AZO for both S-gene positive and S-gene negative (20% lower in S-gene positive than S-gene negative)
  - 1 dose
    - Lower/Moderate vaccine effect for both vaccines