

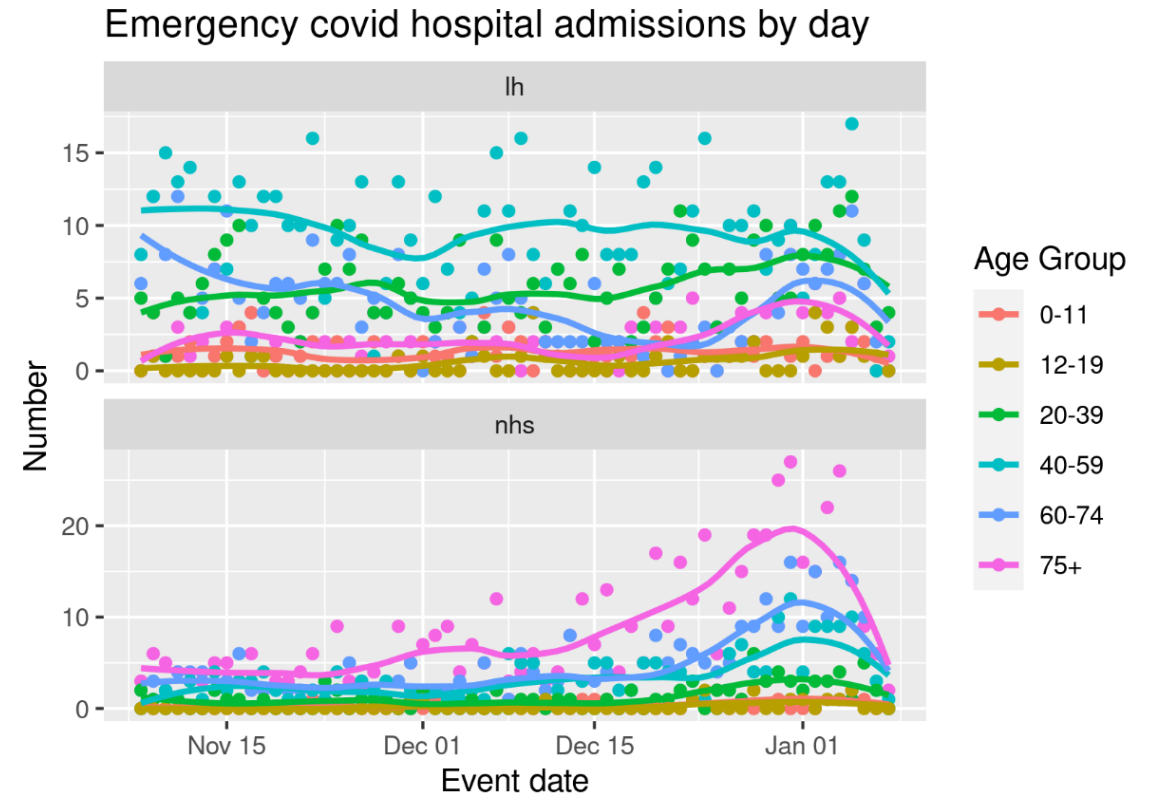
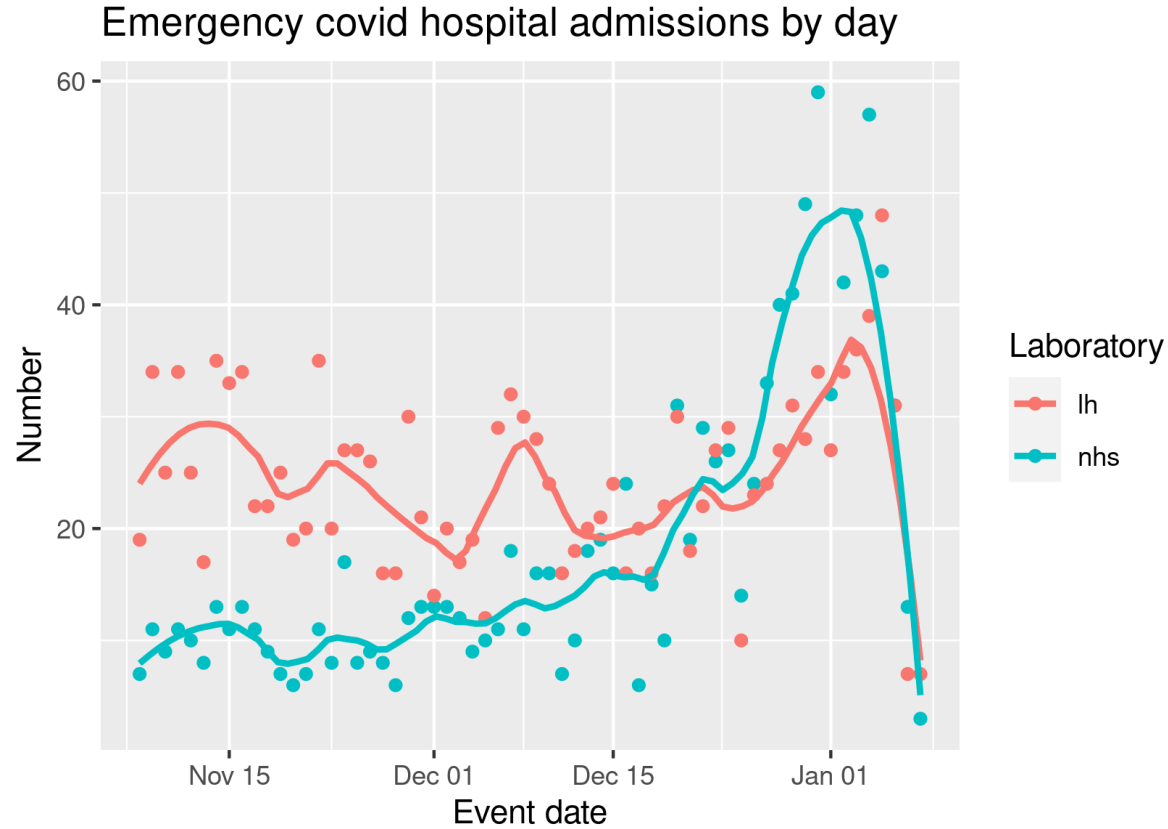
SARS-CoV-2 Vaccine Protection in Scotland: Omicron

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on behalf of EAVE II and PHS

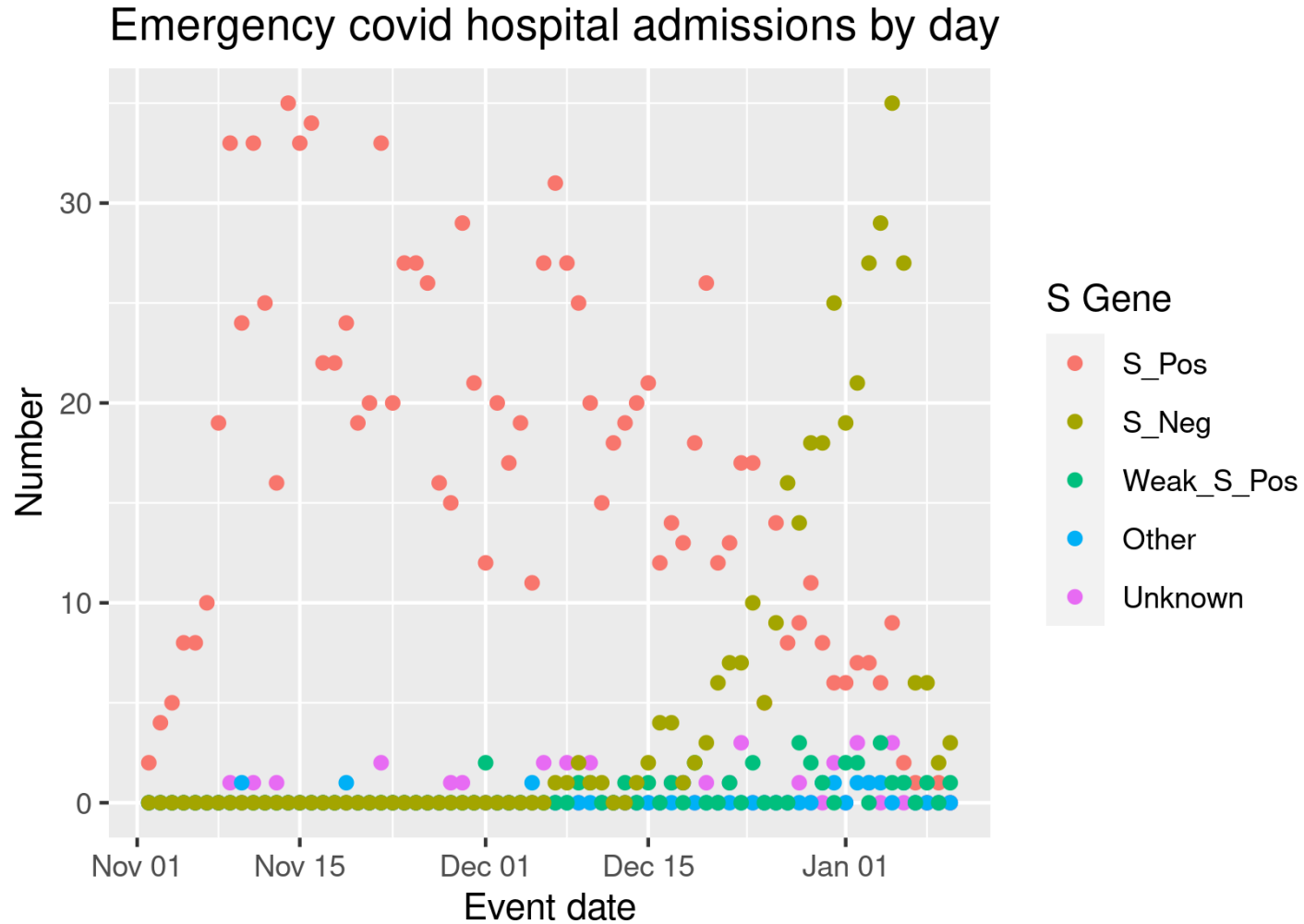
11 January 2022

Trends in hospital admissions within 14 days of a positive test by S gene status 8 November to 07 January in Scotland



Lighthouse lab is pillar 2 – S Gene status available
NHS lab is Pillar 1 – S Gene status unknown

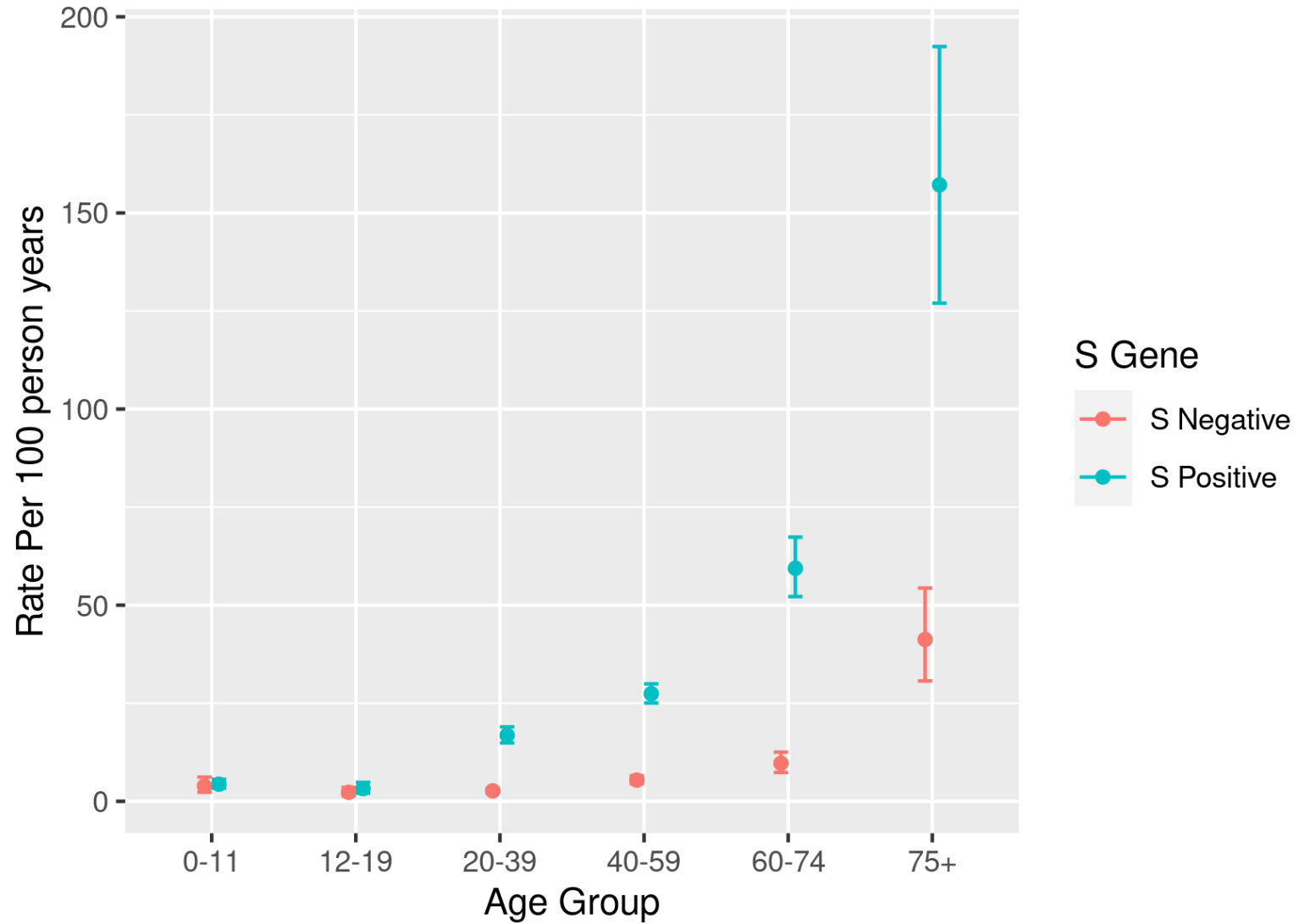
Trends in hospital admissions within 14 days of a positive test by S gene status 1 November to January 10 in Scotland



The increase in admissions at the beginning of the time period for individuals with S Positive infections reflects the selection criterion of testing positive from November 1st and the time to hospital admission from testing positive.

Individuals can be admitted any day following the positive test but most are admitted within 5 to 10 days following testing positive.

Covid Hospitalisations among those who tested positive in the community – rates by age group



Vaccine effects of any combination of 1, 2, and 3 doses in Scotland November 1st 2021 to 04 January 2022

Hazard ratios of being admitted to hospital within 14 days of a positive community test are estimated from a cox model.

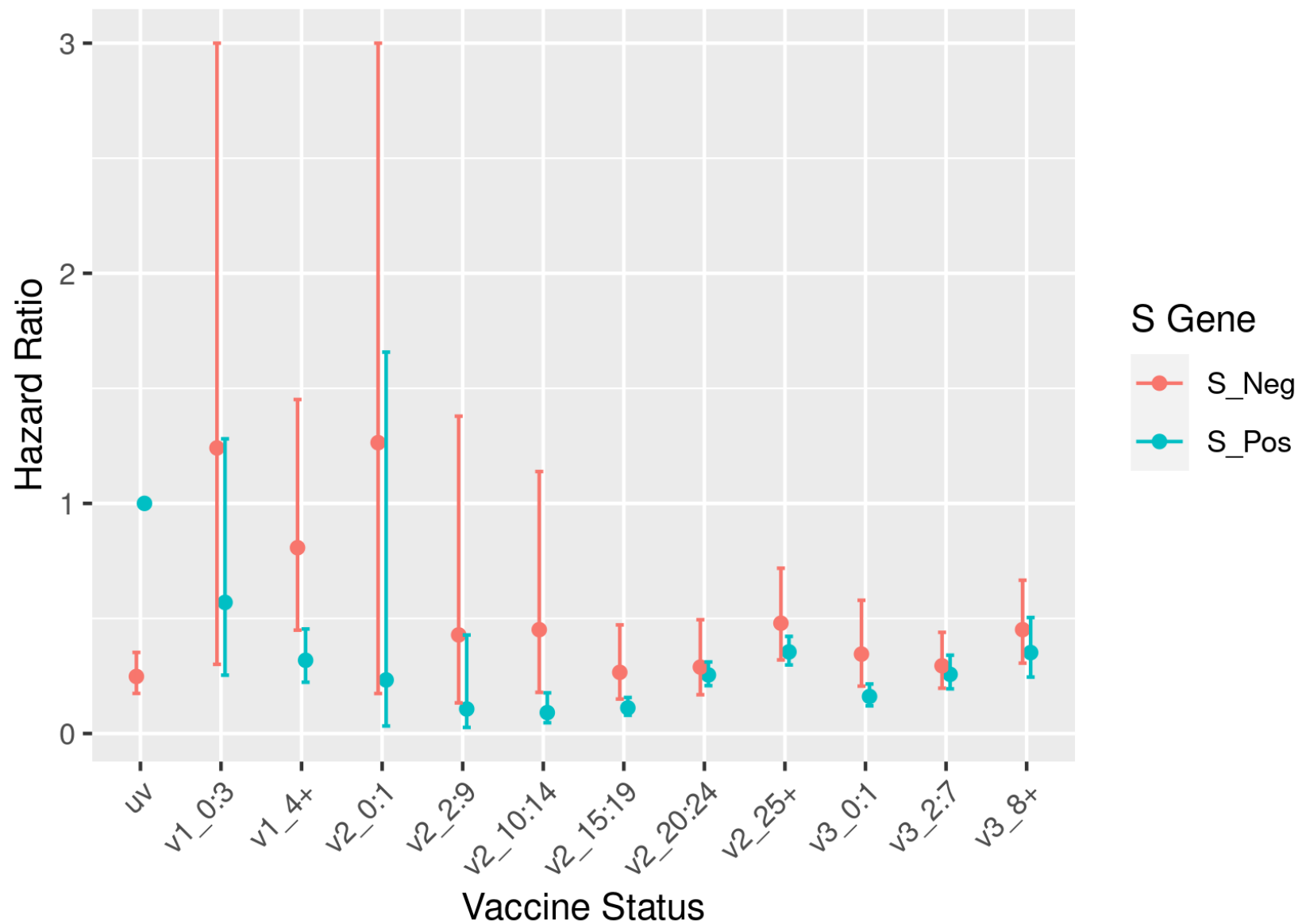
The analysis is based upon individuals testing positive in the community and who are not in hospital at the time of test and who also link into the EAVE-II cohort.

Furthermore, only individuals who are either S Positive or S Negative are included.

The fitted model includes a direct term for S gene status, with S Negative (Omicron) compared to S Positive (Delta) , and a nested effect of vaccine status within each S gene level.

Other factors included are age group, gender, deprivation, number of Q Covid clinical risk groups, previous positive test, time period (week from Nov 1)

Vaccine effects relative to unvaccinated in the same S gene group



Previously positive more than 90 days prior to positive test has a hazard ratio of 0.53 (95% CI 0.33, 0.85)

S Gene	Vaccine Status	Person Years	N	Hospital Admissions	HR	LCL	UCL
S_Pos	uv	2041.0	50715	355	1.00	1.00	1.00
S_Neg	uv	1023.1	35812	45	0.25	0.17	0.35
S_Pos	v1_0:3	42.3	1045	6	0.57	0.25	1.28
S_Neg	v1_0:3	32.4	1034	2	1.24	0.30	5.12
S_Pos	v1_4+	409.8	10192	34	0.32	0.22	0.45
S_Neg	v1_4+	445.6	15404	15	0.81	0.45	1.45
S_Pos	v2_0:1	14.0	344	1	0.23	0.03	1.66
S_Neg	v2_0:1	18.5	477	1	1.26	0.17	9.19
S_Pos	v2_2:9	38.9	968	2	0.11	0.03	0.43
S_Neg	v2_2:9	118.6	4063	3	0.43	0.13	1.38
S_Pos	v2_10:14	214.7	5261	9	0.09	0.05	0.18
S_Neg	v2_10:14	197.9	6248	5	0.45	0.18	1.14
S_Pos	v2_15:19	596.4	14647	38	0.11	0.08	0.16
S_Neg	v2_15:19	995.7	30572	16	0.27	0.15	0.47
S_Pos	v2_20:24	795.7	19684	164	0.25	0.21	0.31
S_Neg	v2_20:24	772.2	26138	19	0.29	0.17	0.49
S_Pos	v2_25+	769.2	19217	300	0.35	0.30	0.42
S_Neg	v2_25+	939.7	31774	51	0.48	0.32	0.72
S_Pos	v3_0:1	296.4	7290	60	0.16	0.12	0.22
S_Neg	v3_0:1	575.0	15051	22	0.35	0.21	0.58
S_Pos	v3_2:7	171.7	4431	72	0.26	0.19	0.34
S_Neg	v3_2:7	1049.0	39128	58	0.29	0.20	0.44
S_Pos	v3_8+	80.1	2115	39	0.35	0.25	0.50
S_Neg	v3_8+	650.5	24099	79	0.45	0.31	0.67

Among the unvaccinated being S Negative as opposed to S Positive is associated with a 75% (95% CI 65%, 83%) reduction in the hazard of admission to Hospital.

There is no evidence on an interaction ($p=0.02$) so the vaccine effects are slightly different for S positive compared to S negative.

Relative to unvaccinated S Positive cases 3 doses and 2-7 weeks post booster is associated with a 74% (66%, 81%) reduction in the hazard of hospital admission

Relative to unvaccinated S Negative cases 3 doses and 2-7 weeks post booster is associated with a 71% (56%, 80%) reduction in the hazard of hospital admission

Lower reductions for 8+ weeks post booster

Symptomatic Infection – Test Negative Design - 1st November to 04 January – Individuals aged 16+

Vaccine Status	N	S Positive		S Positive			S Negative		
		Events	Events	RR	LCL	UCL	RR	LCL	UCL
uv	67582	9480	14625	1.68	1.60	1.77	0.77	0.74	0.80
v1_0:3	2841	285	431	1.30	1.08	1.57	0.48	0.41	0.56
v1_4+	33519	3516	6596	1.21	1.13	1.29	0.64	0.61	0.67
v2_0:1	2637	168	301	0.55	0.45	0.68	0.27	0.23	0.32
v2_10:14	40853	3590	4960	0.45	0.42	0.47	0.61	0.57	0.64
v2_15:19	113861	9929	24079	0.64	0.62	0.67	0.69	0.67	0.72
v2_2:9	21858	607	2885	0.27	0.24	0.30	0.42	0.39	0.44
v2_20:24	98911	13414	19032	0.89	0.86	0.93	0.75	0.72	0.78
v2_25+	105367	11283	21482	1.00	1.00	1.00	1.00	1.00	1.00
v3_0	34306	2983	6085	0.67	0.63	0.71	0.60	0.57	0.63
v3_1	41593	740	5537	0.21	0.19	0.23	0.34	0.33	0.36
v3_2:3	83290	798	10969	0.12	0.11	0.13	0.34	0.33	0.36
v3_4:5	56155	726	7853	0.14	0.12	0.15	0.41	0.39	0.42
v3_6:7	42673	627	6436	0.17	0.16	0.19	0.49	0.46	0.51
v3_8+	77129	924	13169	0.27	0.24	0.29	0.69	0.66	0.71

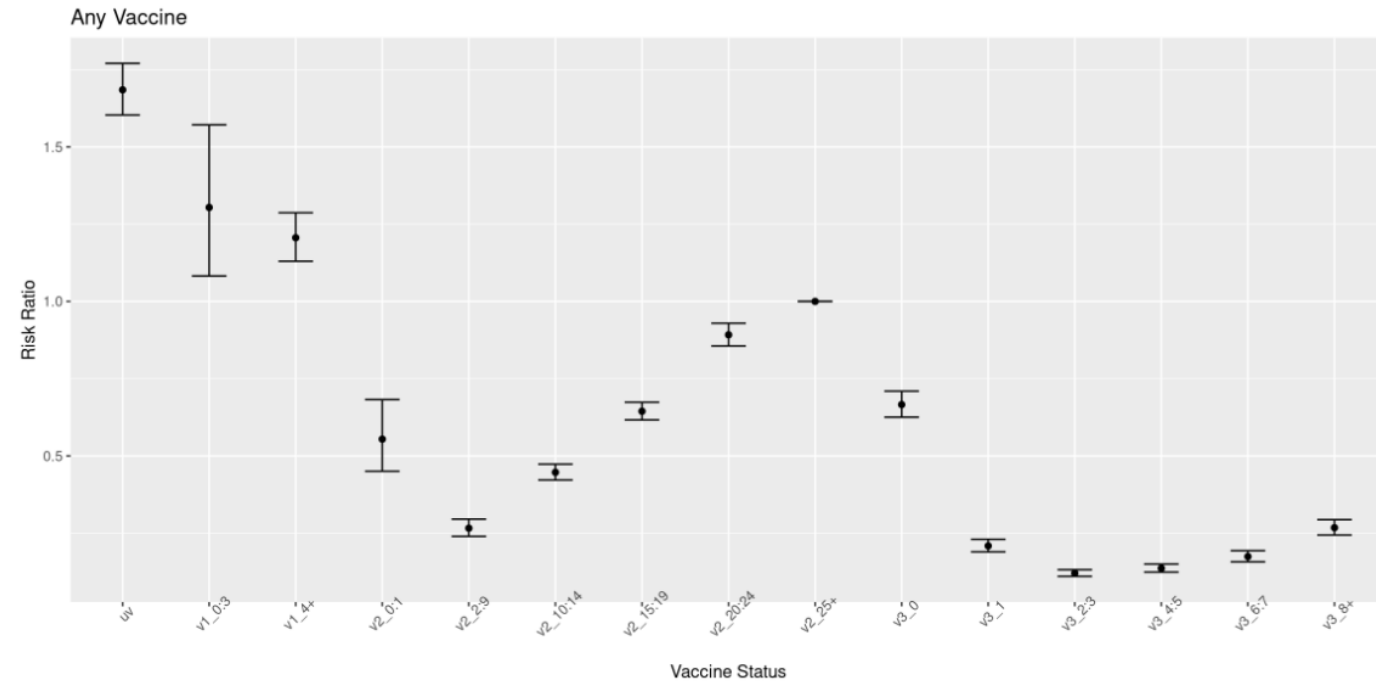
Each positive case is matched to three negative tests by date of symptom onset and local authority.

Conditional logistic regression adjusted for age, sex, deprivation, number of risk groups, testing history, vaccine and positive before test

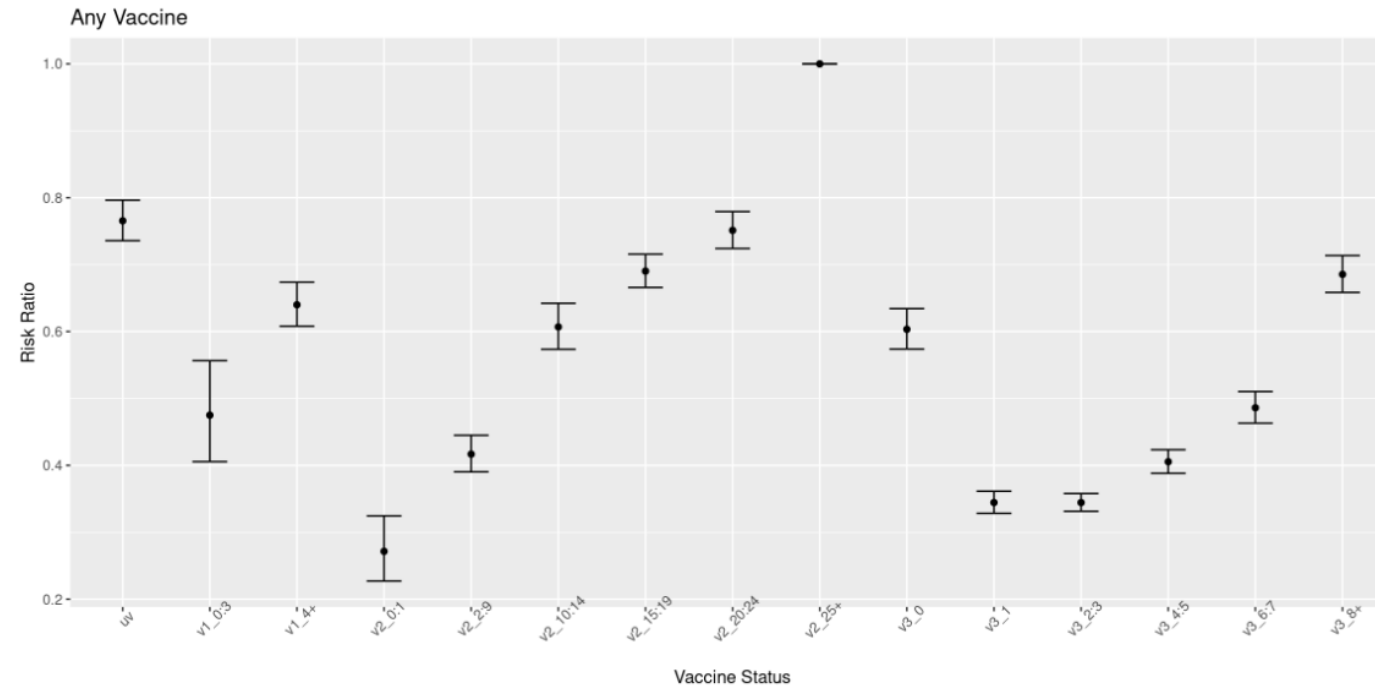
Relative to 2 doses 25+ weeks from second dose there is a 66% reduction in risk of an S- Infection with booster 2-3 weeks after compared to 88% reduction with S Positive.

There is evidence of waning post booster

S Positive – Risk reduction relative to 2 doses 25+ weeks



S Negative – Risk reduction relative to 2 doses 25+ weeks



Preliminary estimates of vaccine effectiveness against Omicron hospitalisations

	ve	lcl	ucl
uv	0.0	0.0	0.0
v1_0:3	-57.4	-554.8	62.1
v1_4+	5.1	-70.6	47.2
v2_0:1	27.4	-428.7	90.0
v2_2:9	65.8	-10.5	89.4
v2_10:14	55.2	-12.7	82.2
v2_15:19	63.1	34.6	79.2
v2_20:24	58.5	29.0	75.8
v2_25+	31.0	-3.7	54.0
v3_0	55.2	24.7	73.4
v3_1	85.9	76.2	91.7
v3_2:3	87.4	80.9	91.7
v3_4:5	85.8	78.5	90.7
v3_6:7	81.8	72.4	88.0
v3_8+	63.7	45.6	75.8

This is similar to the analysis by PHE/UKHSA, but involves an additional step as we cannot estimate VE against symptomatic omicron infection in Scotland – we can only reliably estimate VE for S Positive and the relative VE of Booster doses compared to dose 2 25+ weeks.

Take the VE for symptomatic S+ infection and use a multiplier derived from the vaccine predictors of S- infection among the positive cases to get an estimate of the VE for S-. Then apply the HR of hospitalisation given S- infection

Note that these estimates are based on 316 admissions from the community

Expected S Negative Covid Deaths among those who tested positive in the community

Person years, numbers and expected numbers of covid deaths by S Gene status

S Gene	N	Person Years	Deaths	Expected Admissions	Obs/Exp	LCL	UCL
S_Pos	133704	12351.7	88	88.1	1.00	0.81	1.22
S_Neg	148626	2608.6	2	5.6	0.36	0.07	1.15
Weak_S_Pos	10521	247.9	0	0.7	0.00	0.00	3.56
Other	5436	106.4	0	0.5	0.00	0.00	4.77
Unknown	2999	175.2	4	2.4	1.67	0.56	3.96

Individuals were not in hospital at the time of test. Deaths (81% definitely covid) within 28 days of a positive test.

The expected numbers of deaths were calculated by fitting a cox proportional hazards regression model to the time to hospital admissions among the S Positive cases only in the study period using predictors of age group, gender, deprivation, previous positive history, number of co-morbid Q Covid conditions, vaccine status including vaccine type, dose and duration. The expected number of cases is derived from the predictions of expected survival from the model in all cases. Hence the expected number of deaths in the S positive group will match the observed.

Summary

- Very Preliminary Results
- Evidence of vaccine protection against symptomatic S negative infection for dose 3/ booster compared to dose 2 25+ weeks - 66% (95% CI 64, 67)% reduction in odds of testing positive 2-3 weeks post booster
- But lower than for S Positive where the reduction is 88% (95% CI 87%, 89%)
- Evidence of waning protection after booster/dose 3
- The hazard of hospital admission following a positive S Negative (Omicron) test are lower in comparison to S Positive infections (Delta).
- 75% (95% CI 65%, 83%) reduction in the hazard of admission.
- Vaccine effects associated with the prevention of hospital admission among those with infections are similar for S Negative and S Positive infections – though there is a statistical interaction
- Estimates of overall VE against hospitalisation following symptomatic infection are 88% (95% CI 81%, 92%) at 2-3 weeks post booster and 64% (95% CI 46%, 76%) at 8+ weeks
- Similar reductions in Omicron Deaths over expected as seen with Hospitalisations but based on very small numbers