The relationship between SARS-CoV-2 ORF8 knockout and clinical severity in Washington State

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Introduction

In this analysis, I explore the relationship between ORF8 knockout and clinical severity in COVID-19 cases in Washington State. Clinical data was graciously provided by the WA DOH. ORF8KO was defined as greater than 100 N's or 7+ gaps in ORF8. Or a translated protein length of less than 100 amino acids, which in WT virus is a 121 amino acid protein.

Regression

I'm using a multivariable logistic regression to compare the impact of ORF8KO on two different clinical outcomes. First, I look at probability of hospitalization. Second, I look at the probability of death.

The general logistic regression I'm performing takes the form:

$$log(\frac{\pi_i}{1-\pi_i}) = \beta_0 + \beta_1 Orf8KO_i + \beta_2 AgeGroup_i + \beta_3 SexAtBirth_i + \beta_4 Vaccination_i$$

Hospitalization

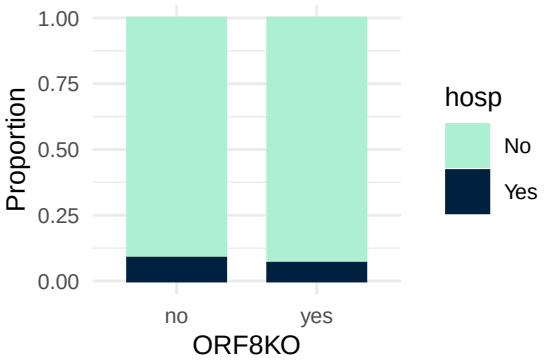

Table 1: Odds Ratio of Hospitalization

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	0.8307217	0.7354457	0.9360806	0.0025738
age_group	2.8742479	2.7609416	2.9932192	0.0000000
sex_at_birthMale	1.3566281	1.2497955	1.4729170	0.0000000
sex_at_birthOther	4.6164646	1.0778183	13.6272458	0.0144172
vaccinatedyes	0.4444734	0.4050192	0.4873974	0.0000000

Death

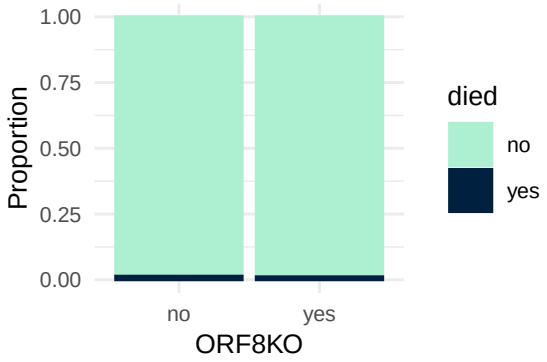

Table 2: Odds Ratio of Death

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	0.9866215	0.8086187	1.1938658	0.8921248
age_group	4.4731580	4.2369280	4.7255158	0.0000000
sex_at_birthMale	1.7681427	1.5768116	1.9843786	0.0000000
sex_at_birthOther	0.0000705	0.0000000	0.0051942	0.9414800
vaccinatedyes	0.5117940	0.4553164	0.5749462	0.0000000

Decomposed by variant

ORF8KO is not evenly distributed across variants. Therefore, it's possible that variant is a confounder for the correlation between ORF8KO and reduced risk of hospitalization. To address this: I'll run the same analyses for each variant with at least 30 samples with an ORF8KO.

20A

Hospitalization:

Table 3: Samples with hospitalization data in 20A .

orf8ko	n_samples
no	404
yes	50

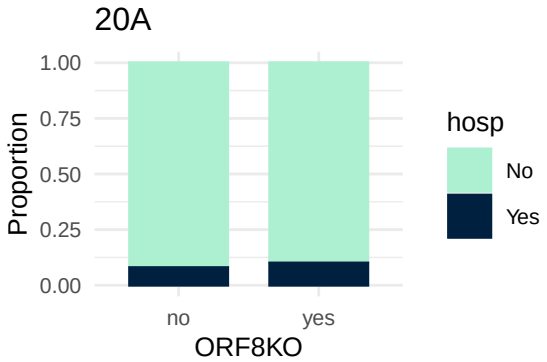

Table 4: Odds Ratio of Hospitalization for 20A .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	1.314852	0.3693812	3.865654	0.6421544
age_group	3.210178	2.2256741	4.779462	0.0000000
sex_at_birthMale	2.518855	1.1638376	5.748138	0.0222405
vaccinatedyes	9.475011	1.9035518	47.497933	0.0054005
NA	NA	NA	NA	NA

Death:

Table 5: Samples with death data in 20A .

orf8ko	n_samples
no	728
yes	102

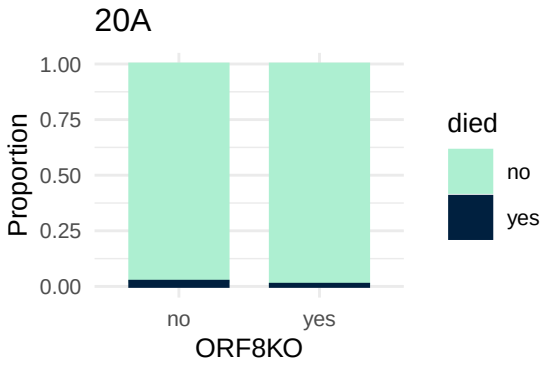

Table 6: Odds Ratio of dying for 20A .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	0.3821519	0.0195990	2.189331	0.3809494
age_group	3.9458705	2.4356035	6.712361	0.0000001
sex_at_birthMale	1.2492262	0.4410854	3.617398	0.6736341
vaccinatedyes	9.2551163	1.5610868	43.457313	0.0073133
NA	NA	NA	NA	NA

20B

Hospitalization:

Table 7: Samples with hospitalization data in 20B .

orf8ko	n_samples
no	526
yes	34

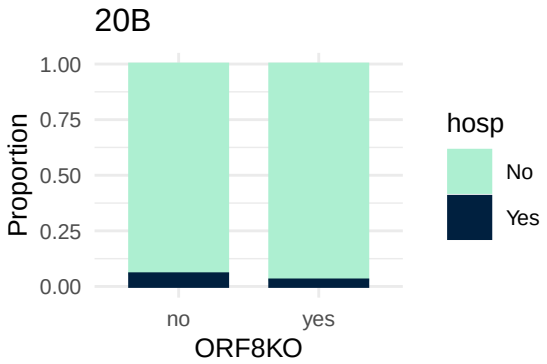

Table 8: Odds Ratio of Hospitalization for 20B .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	0.3296266	0.0174234	1.776944e+00	0.3010835
age_group	2.9459702	1.9502565	4.543336e+00	0.0000005
sex_at_birthMale	1.2819783	0.5984152	2.848303e+00	0.5287504
sex_at_birthOther	0.0000128	NA	1.603928e+73	0.9898198
vaccinatedyes	0.1691511	0.0085763	1.025061e+00	0.1108187

Death:

Table 9: Samples with death data in 20B .

orf8ko	n_samples
no	1033
yes	54

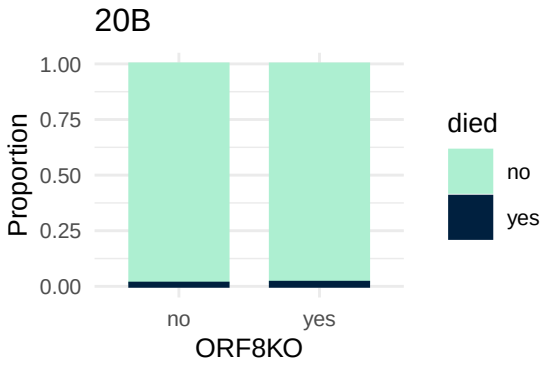

Table 10: Odds Ratio of dying for 20B .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	1.2208123	0.0652442	6.599608e+00	0.8515471
age_group	3.1246357	1.8462453	5.302732e+00	0.0000194
sex_at_birthMale	1.9939965	0.6974671	6.585603e+00	0.2182404
sex_at_birthOther	0.0000332	NA	1.457204e+124	0.9943455
vaccinatedyes	1.1060714	0.1525582	4.880263e+00	0.9054826

20C

Hospitalization:

Table 11: Samples with hospitalization data in 20C .

orf8ko	n_samples
no	353
yes	13

Death:

Table 12: Samples with death data in 20C .

orf8ko	n_samples
no	637
yes	33

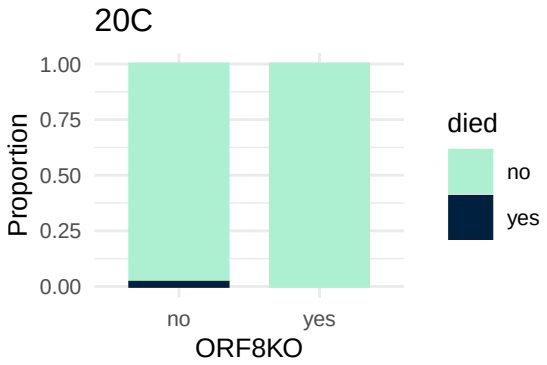

Table 13: Odds Ratio of dying for 20C .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	0.0000002	NA	1.992491e+48	0.9927959
age_group	5.4575402	2.9725612	1.112801e+01	0.0000003
sex_at_birthMale	1.0187152	0.2707341	3.766443e+00	0.9774498
vaccinatedyes	0.3453697	0.0176801	2.074884e+00	0.3365492
NA	NA	NA	NA	NA

20G

Hospitalization:

Table 14: Samples with hospitalization data in 20G .

orf8ko	n_samples
no	1160
yes	86

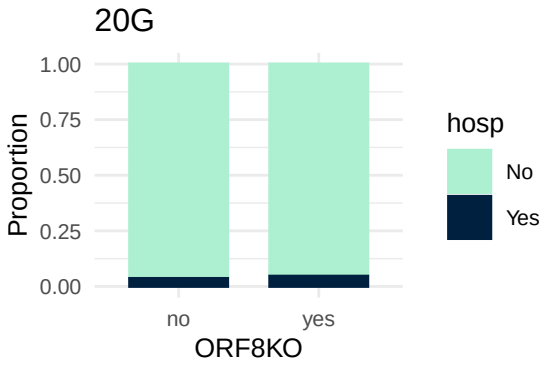

Table 15: Odds Ratio of Hospitalization for 20G .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	1.8585165	0.5125629	5.258632	0.2854611
age_group	3.8570949	2.8293183	5.353992	0.0000000
sex_at_birthMale	0.9853553	0.5171852	1.886507	0.9641472
vaccinatedyes	0.8445757	0.2834267	2.265316	0.7481638
NA	NA	NA	NA	NA

Death:

Table 16: Samples with death data in 20G .

orf8ko	n_samples
no	2074
yes	139

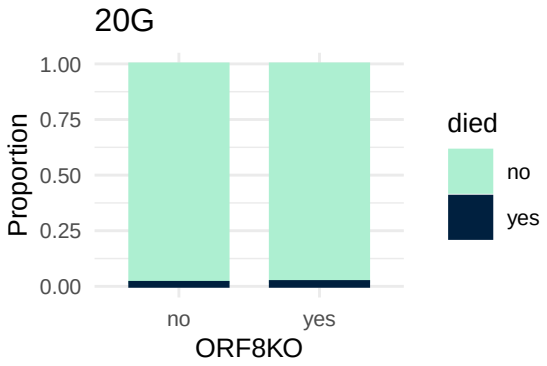

Table 17: Odds Ratio of dying for 20G .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	2.0449126	0.4373722	6.925758e+00	0.2955296
age_group	6.6176328	4.4465312	1.030845e+01	0.0000000
sex_at_birthMale	2.6028393	1.1946163	5.993928e+00	0.0192876
sex_at_birthOther	0.0001232	NA	2.309811e+65	0.9929746
vaccinatedyes	5.3466824	2.1606885	1.301327e+01	0.0002390

20J (Gamma, V3)

Hospitalization:

Table 18: Samples with hospitalization data in 20J (Gamma, V3) .

orf8ko	n_samples
no	1095
yes	118

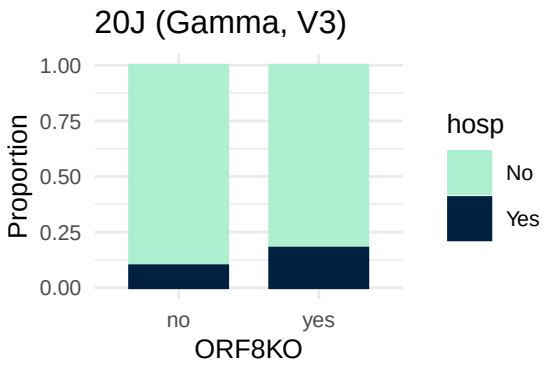

Table 19: Odds Ratio of Hospitalization for 20J (Gamma, V3) .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	2.2443965	1.2553402	3.881729e+00	0.0048175
age_group	2.9962849	2.4274887	3.733957e+00	0.0000000
sex_at_birthMale	1.6447897	1.1047305	2.468902e+00	0.0150733
sex_at_birthOther	0.0000719	NA	1.722262e+43	0.9857828
vaccinatedyes	0.4413514	0.2401308	7.797115e-01	0.0063759

Death:

Table 20: Samples with death data in 20J (Gamma, V3) .

orf8ko	n_samples
no	1731
yes	192

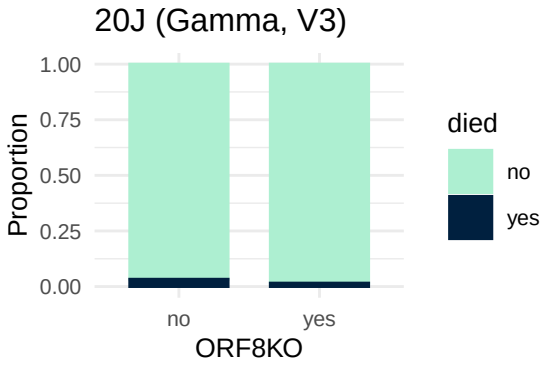

Table 21: Odds Ratio of dying for 20J (Gamma, V3) .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	0.5735709	0.1295417	1.760828e+00	0.3892238
age_group	5.5796114	4.0982368	7.807311e+00	0.0000000
sex_at_birthMale	2.4861337	1.3453164	4.734637e+00	0.0043903
sex_at_birthOther	0.0005981	NA	6.728756e+74	0.9932918
vaccinatedyes	0.6709056	0.3258128	1.334659e+00	0.2661466

21A (Delta)

Hospitalization:

Table 22: Samples with hospitalization data in 21A (Delta) .

orf8ko	n_samples
no	682
yes	83

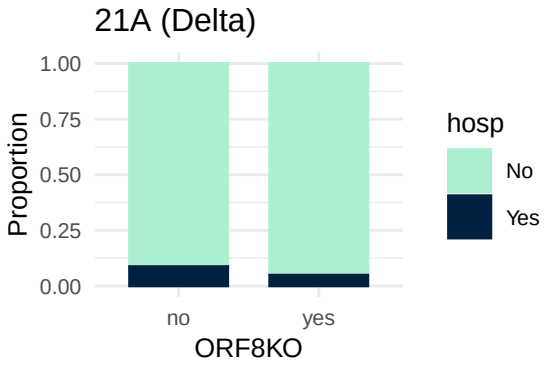

Table 23: Odds Ratio of Hospitalization for 21A (Delta) .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	0.4002578	0.1141732	1.0689149	0.1004738
age_group	3.2247337	2.4451080	4.3309130	0.0000000
sex_at_birthMale	1.5948267	0.9070155	2.8552901	0.1090455
vaccinatedyes	0.4337538	0.2235246	0.8071713	0.0104751
NA	NA	NA	NA	NA

Death:

Table 24: Samples with death data in 21A (Delta) .

orf8ko	n_samples
no	1250
yes	172

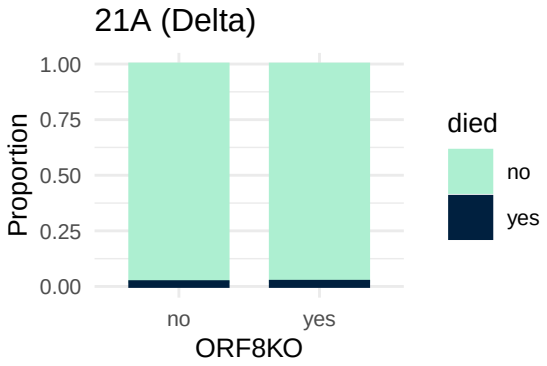

Table 25: Odds Ratio of dying for 21A (Delta) .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	0.9649963	0.2680008	2.715811e+00	0.9507502
age_group	4.8448017	3.2821635	7.430573e+00	0.0000000
sex_at_birthMale	4.3406226	1.8019634	1.220274e+01	0.0022329
sex_at_birthOther	0.0009942	NA	9.249832e+74	0.9937511
vaccinatedyes	0.4857986	0.2006493	1.114543e+00	0.0966177

21J (Delta)

Hospitalization:

Table 26: Samples with hospitalization data in 21J (Delta) .

orf8ko	n_samples
no	16326
yes	272

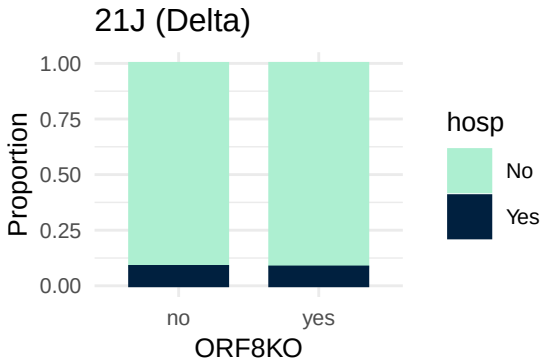

Table 27: Odds Ratio of Hospitalization for 21J (Delta) .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	1.0351251	0.6393483	1.6001559	0.8822517
age_group	3.1180092	2.9427856	3.3062298	0.0000000
sex_at_birthMale	1.3849462	1.2314310	1.5583146	0.0000001
sex_at_birthOther	2.0602448	0.1124591	10.6080682	0.4897049
vaccinatedyes	0.3442643	0.3013735	0.3925546	0.0000000

Death:

Table 28: Samples with death data in 21J (Delta) .

orf8ko	n_samples
no	33622
yes	546

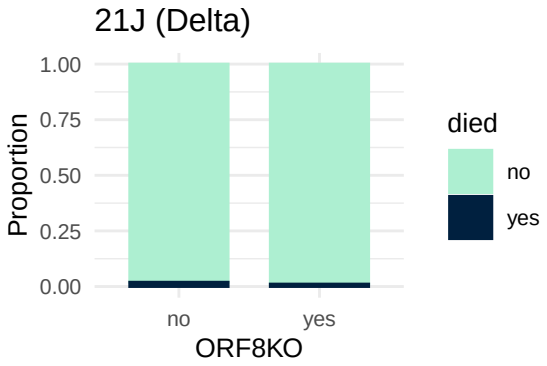

Table 29: Odds Ratio of dying for 21J (Delta) .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	0.5910078	0.2285257	1.2496743	0.2171728
age_group	4.4465742	4.1011858	4.8281051	0.0000000
sex_at_birthMale	1.6909253	1.4324105	1.9994048	0.0000000
sex_at_birthOther	0.0000767	0.0000000	0.5700519	0.9637162
vaccinatedyes	0.6085674	0.5121740	0.7219776	0.0000000

21K (Omicron)

Hospitalization:

Table 30: Samples with hospitalization data in 21K (Omicron) .

orf8ko	n_samples
no	3122
yes	314

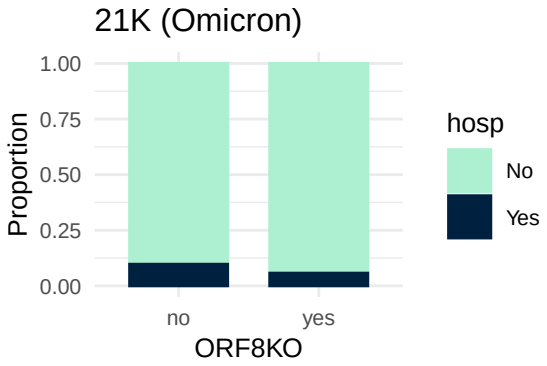

Table 31: Odds Ratio of Hospitalization for 21K (Omicron) .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	0.7018008	0.4090155	1.1348171	0.1712725
age_group	2.0894309	1.8884915	2.3162650	0.0000000
sex_at_birthMale	1.3899411	1.0898893	1.7759582	0.0081510
sex_at_birthOther	42.6539392	4.0213557	926.9579940	0.0023410
vaccinatedyes	0.3879870	0.3027586	0.4964938	0.0000000

Death:

Table 32: Samples with death data in 21K (Omicron) .

orf8ko	n_samples
no	20700
yes	1434

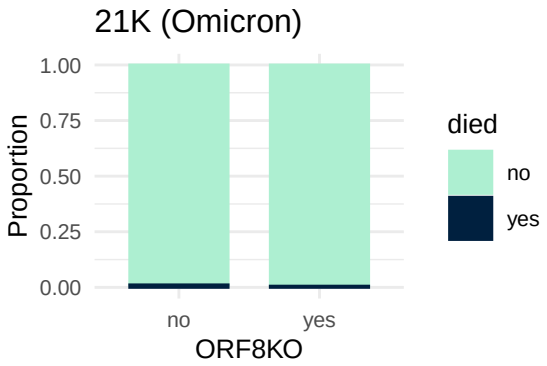

Table 33: Odds Ratio of dying for 21K (Omicron) .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	0.7421267	0.3313094	1.4314241	0.4183195
age_group	4.2163457	3.7430491	4.7624510	0.0000000
sex_at_birthMale	1.6658081	1.2781392	2.1796309	0.0001753
sex_at_birthOther	0.0001416	0.0000000	233.8500146	0.9742143
vaccinatedyes	0.5790801	0.4444411	0.7559796	0.0000543

21L (Omicron)

Hospitalization:

Table 34: Samples with hospitalization data in 21L (Omicron) .

orf8ko	n_samples
no	1668
yes	48

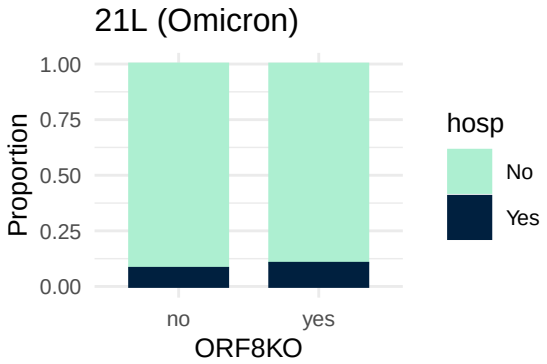

Table 35: Odds Ratio of Hospitalization for 21L (Omicron) .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	1.1137724	0.3716273	2.701528e+00	0.8280553
age_group	2.0358195	1.7242192	2.421660e+00	0.0000000
sex_at_birthMale	1.0723831	0.7522722	1.529366e+00	0.6989092
sex_at_birthOther	0.0000477	NA	1.137624e+43	0.9851726
vaccinatedyes	0.6205554	0.4185757	9.336646e-01	0.0194281

Death:

Table 36: Samples with death data in 21L (Omicron) .

orf8ko	n_samples
no	12470
yes	447

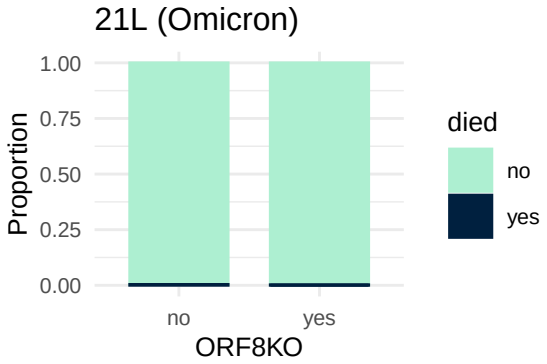

Table 37: Odds Ratio of dying for 21L (Omicron) .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	0.5767584	0.0323536	2.690319e+00	0.5885366
age_group	3.6151764	2.7857407	4.742448e+00	0.0000000
sex_at_birthMale	1.0691451	0.5968992	1.910699e+00	0.8206219
sex_at_birthOther	0.0000152	NA	8.561748e+19	0.9869503
vaccinatedyes	0.8566146	0.4470972	1.777363e+00	0.6569869

22C (Omicron)

Hospitalization:

Table 38: Samples with hospitalization data in 22C (Omicron) .

orf8ko	n_samples
no	578
yes	21

Death:

Table 39: Samples with death data in 22C (Omicron) .

orf8ko	n_samples
no	5625
yes	225

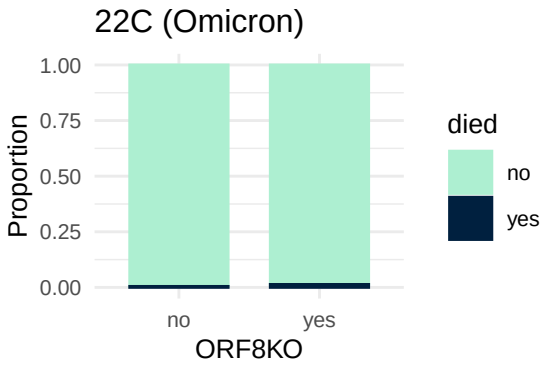

Table 40: Odds Ratio of dying for 22C (Omicron) .

Predictor	OR	2.5 %	97.5 %	p
orf8koyes	3.0522899	0.6980623	9.345761e+00	0.0811751
age_group	4.2807316	2.9644720	6.393272e+00	0.0000000
sex_at_birthMale	3.9571093	1.7282323	1.023817e+01	0.0020880
sex_at_birthOther	0.0057053	NA	5.079608e+75	0.9953303
vaccinatedyes	0.9415436	0.3962613	2.600238e+00	0.8983093

Conclusion

When broken down by variant, Orf8KO is not correlated with clinical severity in all but one variant. In Gamma, Orf8KO is correlated with an increased risk of hospitalization. There is not an increased risk of death.

Overall, Orf8KO does not seem to be associated with changes in clinical severity in Washington State.