

## **Supplemental Material**

Supplemental Table 1. Community prevalence of variants and available inpatient treatments by time period.

Supplemental Table 2. Association of second-dose vaccination with severe Covid-19 outcomes in subgroups with SARS-CoV-2 infection.

Supplemental Table 3. Association of second-dose vaccination with severe Covid-19 outcomes in sensitivity analyses.

Supplemental Table 4. Characteristics of subgroup patients (N=1253) stratified by SARS-CoV-2 PCR status.

**Supplemental Table 1.** Community prevalence of variants and available inpatient treatments by time period.

Time period	Variant prevalence (%)			Treatments available for hospitalised patients		
	Alpha	Delta	Other	Dexamethasone	Remdesivir	Tocilizumab
1 (Dec 2020) <sup>a</sup>	-	-	-	✓		
2 (Jan 2021) <sup>b</sup>	5	20	75	✓		
3 (Feb-Mar 2021)	69	13	18	✓		✓
4 (Apr-July 2021)	28	57	15	✓	✓	✓
5 (Aug 2021)	0	96	4	✓	✓	✓
6 (Sept 2021)	0	60	40	✓	✓	✓

<sup>a</sup>Data unavailable for December 2020

<sup>b</sup>Data based on small sample for January 2021

**Supplemental Table 2.** Association of second-dose vaccination with severe Covid-19 outcomes in subgroups with SARS-CoV-2 infection.

Subgroup	N <sup>a</sup>	Odds ratio (95%CI) for severe Covid-19 outcomes								
		Admission <sup>c</sup>		Oxygen <sup>d</sup>		Ventilation <sup>d</sup>		Death <sup>d</sup>		
Age group	65-95 years	88	<b>0.05</b>	(0.02-0.16)	<b>0.06</b>	(0.02-0.22)	<b>0.06</b>	(0.02-0.21)	<b>0.04</b>	(0.01-0.17)
	18-64 years	102	0.57	(0.27-1.17)	<b>0.34</b>	(0.15-0.78)	0.71	(0.26-1.96)	0.53	(0.16-1.80)
Vaccine type	BNT162b2	79	<b>0.26</b>	(0.13-0.53)	<b>0.17</b>	(0.08-0.39)	<b>0.18</b>	(0.07-0.49)	<b>0.15</b>	(0.06-0.43)
	AZD1222	107	<b>0.23</b>	(0.12-0.45)	<b>0.19</b>	(0.09-0.40)	<b>0.26</b>	(0.11-0.62)	<b>0.10</b>	(0.03-0.30)
Time since <sup>b</sup>	0-4 months	87	<b>0.29</b>	(0.15-0.58)	<b>0.25</b>	(0.11-0.53)	<b>0.29</b>	(0.11-0.74)	<b>0.15</b>	(0.05-0.52)
	4-8 months	103	<b>0.21</b>	(0.10-0.42)	<b>0.13</b>	(0.06-0.29)	<b>0.18</b>	(0.07-0.44)	<b>0.11</b>	(0.04-0.30)

Odds ratio (95% CI), including variables in Table 2, within subgroup comparing second-dose with no vaccination

Clinical outcomes are 'all cause', not specifically due to Covid-19

<sup>a</sup>Number of infections >10 days after second dose within subgroup

<sup>b</sup>Time since second dose

<sup>c</sup>Within 14 days of positive PCR

<sup>d</sup>Within 28 days of positive PCR

**Supplemental Table 3.** Association of second-dose vaccination with severe Covid-19 outcomes in sensitivity analyses.

Condition	N <sup>a</sup>	Odds ratio (95%CI) for severe Covid-19 outcomes							
		Admission <sup>b</sup>		Oxygen <sup>c</sup>		Ventilation <sup>c</sup>		Death <sup>c</sup>	
Prior SARS-CoV-2 excluded	178 / 1018	<b>0.24</b>	(0.13-0.44)	<b>0.17</b>	(0.09-0.34)	<b>0.20</b>	(0.09-0.43)	<b>0.12</b>	(0.05-0.29)
Period 4 only (1 Apr - 31 July)	62 / 29	<b>0.21</b>	(0.06-0.79)	0.25	(0.06-1.04)	0.12	(0.01-1.26)	<b>0.00</b>	(0.00-0.35)
Period 5 only (1 - 31 Aug)	71 / 17	<b>0.11</b>	(0.03-0.45)	<b>0.04</b>	(0.01-0.22)	0.16	(0.03-1.04)	<b>0.13</b>	(0.02-0.93)
Period 6 only (1 - 26 Sept)	55 / 19	<b>0.28</b>	(0.08-0.99)	<b>0.23</b>	(0.06-0.89)	0.28	(0.07-1.15)	<b>0.22</b>	(0.05-0.95)

Odds ratio (95% CI), including variables in Table 2, comparing second-dose with no vaccination, under condition specified

Clinical outcomes are 'all cause', not specifically due to Covid-19

<sup>a</sup>Number of infections >10 days after second dose / number of infections in unvaccinated

<sup>b</sup>Within 14 days of positive PCR

<sup>c</sup>Within 28 days of positive PCR

**Supplemental Table 4.** Characteristics of subgroup patients (N=1253) stratified by SARS-CoV-2 PCR status.

	PCR positive	PCR negative
N	272	981
Age, median(IQR)	65 (56-74)	65 (55-75)
Gender		
Male	162 (60)	588 (60)
Ethnicity		
Asian/other	132 (49)	436 (44)
Black	67 (25)	261 (27)
White	73 (27)	284 (29)
Diabetes	117 (43)	419 (43)
Prior SARS-CoV-2	11 (4)	236 (24)
Vaccine <sup>a</sup>		
unvaccinated	214 (79)	86 (9)
>10d post 1 <sup>st</sup> dose	25 (9)	30 (3)
>10d post 2 <sup>nd</sup> dose	33 (12)	865 (88)

Except where stated data are N (%)

<sup>a</sup>Status at positive PCR, or end of observation in those with negative PCR