

## Title

Severity of COVID-19 among hospitalized patients: Omicron remains a severe threat for immunocompromised hosts

## Authors:

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## Supplemental Table & Figures

**Supplemental Table S1.** Clinical summary of newly hospitalized adult patients (≥18 years old) with positive SARS-CoV-2 screening result.

		All patients N = 1291	COVID-19 outcomes		
			Moderate/severe/ critical/fatal COVID-19 N = 538 (41.7%)	ICU admission due to COVID-19 N = 129 (10.0%)	In-hospital mortality related to COVID-19 N = 99 (7.7%)
Patient characteristics					
	Age (years); median (IQR)	69 (50-83)	70 (59-82)	63 (53-72)	78 (68-86)
	Male; n (%)	619 (47.9%)	310 (57.6%)	83 (64.3%)	63 (63.6%)
	Immunocompromised; n (%)	286 (22.2%)	157 (29.2%)	51 (39.5%)	39 (39.4%)
SARS-CoV-2 screening					
	Omicron variant, n (%)	905 (70.1%)	323 (60.0%)	68 (52.7%)	58 (58.6%)
	Omicron BA.1 variant, n (%)	538 (41.7%)	294 (54.6%)	43 (33.3%)	31 (31.3%)
	Omicron BA.2 variant, n (%)	34 (2.6%)	14 (2.6%)	0 (0.0%)	1 (1.0%)
	Delta variant, n (%)	166 (12.9%)	126 (23.4%)	44 (34.1%)	31 (31.3%)
	Untyped, n (%)	220 (17.0%)	89 (16.5%)	17 (13.2%)	10 (10.1%)
Serology data at admission					
	IgG anti-N available, n (%)	117 (9.1%)	62 (11.5%)	20 (15.5%)	15 (15.2%)
	Positive IgG anti-N; n (%)	15/117 (12.8%)	9/62 (28.1%)	2/20 (10.0%)	3/15 (20.0%)
	IgG anti-S available, n (%)	194 (15.3%)	100 (18.6%)	36 (27.9%)	24 (24.2%)
	Positive IgG anti-S; n (%)	142/194 (73.2%)	61/100 (61.0%)	19/36 (52.8%)	17/24 (70.8%)
Hospitalization data					
	Hospital length-of-stay non-deceased patients (days); median (IQR)	8 (3-18)	8 (5-18)	22 (12-51)	
	Hospital length-of-stay deceased patients (days); median (IQR)	20 (7-27)	13 (6-25)	19 (12-32)	13 (6-25)
	ICU admission; n (%)	178 (13.8%)			
	Deceased in hospital; n (%)	139 (10.8%)			
Vaccination status					
	Vaccination status unknown; n (%)	120 (9.3%)	52 (9.7%)	6 (4.7%)	30 (30.3%)
	Unvaccinated; n (%)	221 (17.2%)	112 (22.7%)	34 (26.4%)	14 (14.1%)
	½ basic vaccination; n (%)	15 (1.2%)	6 (1.2%)	0 (0.0%)	1 (0.1%)
	Basic vaccination; n (%)	263 (20.4%)	104 (19.3%)	34 (26.4%)	14 (14.1%)
	Boosted; n (%)	672 (52.1%)	264 (49.1%)	55 (42.6%)	40 (40.4%)
	Type of vaccines available; n (%)	892 (69.1%)	351 (80.1%)	82 (63.6%)	40 (40.4%)
	Viral vector vaccinated; n (%)	262/892 (29.4%)	119/351 (33.9%)	32/82 (39.0%)	14/40 (35.0%)
	Time since last vaccination available; n [%]	870 (67.4%)	337 (62.6%)	73 (56.6%)	31 (31.3%)
	Vaccinated <2 months before admission; n [%]	215/870 (24.7%)	62/337 (18.4%)	13/73 (17.8%)	5/31 (16.1%)
	Vaccinated <4 months before admission; n [%]	486/870 (55.9%)	218/337 (64.7%)	43/73 (58.9%)	23/31 (74.2%)
	Vaccinated <6 months before admission; n [%]	739/870 (84.9%)	283/337 (84.0%)	61/73 (83.6%)	27/31 (87.1%)
SARS-CoV-2 reinfection					
	Documented previous infection; n [IQR]	17 (1.3%)	4 (0.7%)	1 (0.8%)	1 (1.0%)

**Supplemental Table S2.** Clinical summary of newly hospitalized children (<18 years old) with positive SARS-CoV-2 screening result.

		All patients N = 210	COVID-19 outcomes		
			Moderate/severe/ critical/MIS-C COVID-19 N = 50 (23.8%)	ICU admission due to COVID-19 N = 8	In-hospital mortality related to COVID-19 N = 0 (0.0%)
Patient characteristics					
	Age (years); median (IQR)	1 (1-6)	1 (1-5)	1 (1-1)	
	Male; n (%)	128 (60.1%)	18 (36.0%)	6 (75.0%)	
	Immunocompromised; n (%)	23 (10.1%)	4 (8.0%)	1 (12.5%)	
SARS-CoV-2 screening					
	Omicron variant, n (%)	125 (59.5%)	22 (44.0%)	3 (37.5%)	
	Omicron BA.1 variant, n (%)	83 (39.5%)	22 (44.0%)	2 (25.0%)	
	Omicron BA.2 variant, n (%)	6 (2.9%)	0 (0.0%)	0 (0.0%)	
	Delta variant, n (%)	21 (10.0%)	2 (4.0%)	1 (12.5%)	
	Untyped, n (%)	58 (27.6%)	26 (52.0%)	4 (50.0%)	
Serology data at admission					
	IgG anti-N available, n (%)	6 (2.9%)	2 (4.0%)	0 (0.0%)	
	Positive IgG anti-N; n (%)	3/6 (50.0%)	2/2 (100.0%)		
	IgG anti-S available, n (%)	4 (1.9%)	1 (2.0%)	0 (0.0%)	
	Positive IgG anti-S; n (%)	4/4 (100.0%)	1/1 (100.0%)		
Hospitalization data					
	Hospital length-of-stay non-deceased patients (days); median (IQR)	3 (2-5)	4.5 (2-7)	21 (10-35)	
	ICU admission; n (%)	20 (9.5%)			
	Deceased in hospital; n (%)	0 (0.0%)			
Vaccination status					
	Vaccination status unknown; n (%)	12 (5.7%)	7 (14.0%)	3 (37.5%)	
	Unvaccinated; n (%)	186 (88.6%)	43 (86.0%)	5 (62.5%)	
	½ basic vaccination; n (%)	3 (1.4%)	0 (0.0%)		
	Basic vaccination; n (%)	6 (2.9%)	0 (0.0%)		
	Boosted; n (%)	3 (1.4%)	0 (0.0%)		
	Type of vaccines available; n (%)	12 (5.7%)			
	Viral vector vaccinated; n (%)	0/12 (0.0%)			
	Time since last vaccination available; n [%]	12 (5.7%)			
	Vaccinated <2 months before admission; n [%]	3/12 (25.0%)			
SARS-CoV-2 reinfection					
	Documented previous infection; n [IQR]	0 (0.0%)			

**Supplemental Table S3. Mixed-model logistic regression analysis in adult patients infected with Delta (n=166).**

Covariates: 1. odds increase per year; 2. versus female; 3. versus non-immunocompromised; 4. versus any vaccination; 5. versus unvaccinated or (1/2) basic vaccination; 6. versus vaccinated with mRNA solely. 7. versus unvaccinated or vaccinated >2/>4/>6 months before admission. Abbreviations: OR, odds ratio; CI; confidence interval.

	Crude OR	95% CI	p value	Adjusted OR	95% CI	p value
<b>Outcome 1 – disease severity: odds of moderate/severe/critical/fatal COVID-19 (n=126/166, 75.9%)</b>						
Age at admission <sup>1</sup>	1.02	1.00-1.04	0.10	1.01	0.99-1.04	0.16
Male <sup>2</sup>	1.63	0.80-3.37	0.18	1.50	0.72-3.14	0.28
Immunocompromised <sup>3</sup>	1.12	0.52-2.51	0.77	1.01	0.45-2.32	0.97
Unvaccinated <sup>4</sup>	1.36	0.62-3.13	0.46	-	-	-
Boosted <sup>5</sup>	0.84	0.38-1.91	0.67	-	-	-
Viral vector vaccination <sup>6</sup>	1.93	0.67-6.43	0.25	-	-	-
Vaccinated <2 months before admission <sup>7</sup>	1.17	0.32-5.64	0.82	-	-	-
Vaccinated <4 months before admission <sup>7</sup>	0.48	0.16-1.34	0.18	-	-	-
Vaccinated <6 months before admission <sup>7</sup>	0.40	0.09-1.37	0.18	-	-	-
<b>Outcome 2 – ICU admission: odds of admission or transferred to ICU due to COVID-19 (n=44/166, 26.5%)</b>						
Age at admission <sup>1</sup>	0.99	0.98-1.01	0.59	0.99	0.97-1.10	0.36
Male <sup>2</sup>	2.23	1.09-4.78	<b>0.03</b>	2.37	1.14-5.16	<b>0.02</b>
Immunocompromised <sup>3</sup>	0.99	0.47-2.06	0.99	1.05	0.42-2.31	0.91
Unvaccinated <sup>4</sup>	1.44	0.69-2.97	0.32	-	-	-
Boosted <sup>5</sup>	0.61	0.26-1.33	0.23	-	-	-
Viral vector vaccination <sup>6</sup>	2.53	0.91-7.02	0.07	-	-	-
Vaccinated <2 months before admission <sup>7</sup>	0.27	0.01-1.55	0.23	-	-	-
Vaccinated <4 months before admission <sup>7</sup>	0.44	0.15-1.25	0.12	-	-	-
Vaccinated <6 months before admission <sup>7</sup>	0.80	0.26-2.80	0.71	-	-	-
<b>Outcome 3 – mortality: odds of in-hospital mortality related to COVID-19 (n=31/166, 18.7%)</b>						
Age at admission <sup>1</sup>	1.04	1.02-1.08	<b>0.002</b>	1.04	1.01-1.08	<b>0.005</b>
Male <sup>2</sup>	1.47	0.66-3.44	0.35	1.34	0.59-3.15	0.49
Immunocompromised <sup>3</sup>	2.46	1.08-5.78	<b>0.03</b>	2.12	0.92-4.87	0.07
Unvaccinated <sup>4</sup>	0.95	0.36-2.36	0.92	-	-	-
Boosted <sup>5</sup>	2.44	0.97-6.07	<b>0.05</b>	-	-	-
Viral vector vaccination <sup>6</sup>	1.53	0.36-5.85	0.54	-	-	-
Vaccinated <2 months before admission <sup>7</sup>	2.47	0.33-13.16	0.31	-	-	-
Vaccinated <4 months before admission <sup>7</sup>	4.30	0.69-83.33	0.19	-	-	-
Vaccinated <6 months before admission <sup>7</sup>	NA	NA	0.99	-	-	-

**Supplemental Table S4. Mixed-model logistic regression analysis adult patients infected with Omicron (n=905).**

Covariates: 1. odds increase per year; 2. versus female; 3. versus non-immunocompromised; 4. versus any vaccination; 5. versus unvaccinated or (1/2) basic vaccination; 6. versus vaccinated with mRNA solely. 7. versus unvaccinated or vaccinated >2/>4/>6 months before admission. Abbreviations: OR, odds ratio; CI; confidence interval.

	Crude OR	95% CI	p value	Adjusted OR	95% CI	p value
<b>Outcome 1 – disease severity: odds of moderate/severe/critical/fatal COVID-19 (n = 323/905, 36%)</b>						
Age at admission <sup>1</sup>	1.02	1.1-1.03	<b>&lt;0.001</b>	1.02	1.01-1.03	<b>&lt;0.001</b>
Male <sup>2</sup>	2.20	1.65-2.94	<b>&lt;0.001</b>	2.02	1.51-2.73	<b>&lt;0.001</b>
Immunocompromised <sup>3</sup>	2.18	1.55-3.07	<b>&lt;0.001</b>	2.36	1.65-3.38	<b>&lt;0.001</b>
Unvaccinated <sup>4</sup>	1.00	0.65-1.53	0.99	-	-	-
Boosted <sup>5</sup>	1.25	0.92-1.70	0.16	-	-	-
Viral vector vaccination <sup>6</sup>	1.30	0.93-1.83	0.12	-	-	-
Vaccinated <2 months before admission <sup>7</sup>	0.57	0.38-0.82	<b>0.003</b>	-	-	-
Vaccinated <4 months before admission <sup>7</sup>	1.01	0.71-1.42	0.98	-	-	-
Vaccinated <6 months before admission <sup>7</sup>	1.18	0.74-1.90	0.50	-	-	-
<b>Outcome 2 – ICU admission: odds of admission or transferred to ICU due to COVID-19 (n = 68/905, 7.5%)</b>						
Age at admission <sup>1</sup>	0.99	0.98-1.00	0.08	0.99	0.98-1.00	0.07
Male <sup>2</sup>	1.76	1.07-2.95	<b>0.03</b>	1.72	1.03-2.92	<b>0.04</b>
Immunocompromised <sup>3</sup>	3.65	2.19-6.05	<b>&lt;0.001</b>	3.41	2.04-5.68	<b>&lt;0.001</b>
Unvaccinated <sup>4</sup>	0.99	0.42-2.03	0.98	-	-	-
Boosted <sup>5</sup>	0.94	0.56-1.64	0.83	-	-	-
Viral vector vaccination <sup>6</sup>	1.18	0.63-2.12	0.59	-	-	-
Vaccinated <2 months before admission <sup>7</sup>	0.97	0.48-1.86	0.94	-	-	-
Vaccinated <4 months before admission <sup>7</sup>	0.86	0.47-1.64	0.63	-	-	-
Vaccinated <6 months before admission <sup>7</sup>	0.93	0.43-2.32	0.86	-	-	-
<b>Outcome 3 –mortality: odds of in-hospital mortality related to COVID-19 (n= 58/905, 6.4%)</b>						
Age at admission <sup>1</sup>	1.04	1.02-1.06	<b>&lt;0.001</b>	1.05	1.03-1.07	<b>&lt;0.001</b>
Male <sup>2</sup>	2.24	1.29-3.98	<b>0.005</b>	2.08	1.19-3.75	<b>0.01</b>
Immunocompromised <sup>3</sup>	2.56	1.46-4.42	<b>&lt;0.001</b>	3.47	1.90-6.30	<b>&lt;0.001</b>
Unvaccinated <sup>4</sup>	0.58	0.14-1.66	0.38	-	-	-
Boosted <sup>5</sup>	1.08	0.55-2.25	0.83	-	-	-
Viral vector vaccination <sup>6</sup>	1.47	0.64-3.22	0.34	-	-	-
Vaccinated <2 months before admission <sup>7</sup>	0.30	0.05-1.05	0.11	-	-	-
Vaccinated <4 months before admission <sup>7</sup>	1.09	0.44-3.08	0.87	-	-	-
Vaccinated <6 months before admission <sup>7</sup>	0.96	0.32-4.13	0.94	-	-	-

**Supplemental Table S5. Mixed-model logistic regression analysis adult patients infected with Omicron comparing adult patients infected with Omicron and moderate/severe/critical/fatal COVID-19 (n=323) (i.e., excluding asymptomatic patients or patients with mild COVID-19 symptoms).** Covariates: 1. odds increase per year; 2. versus female; 3. versus non-immunocompromised; 4. versus any vaccination; 5. versus unvaccinated or (1/2) basic vaccination; 6. versus vaccinated with mRNA solely. 7. versus unvaccinated or vaccinated >2/>4/>6 months before admission. Abbreviations: OR, odds ratio; CI, confidence interval.

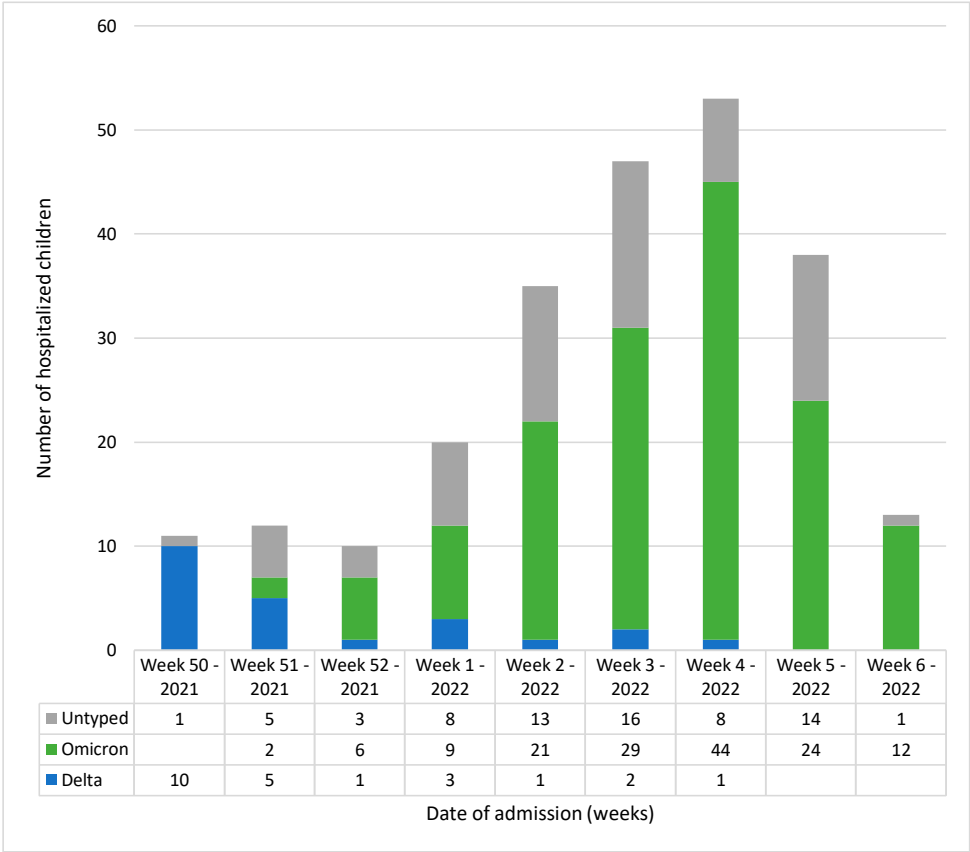
	Crude OR	95% CI	p value	Adjusted OR	95% CI	p value
<b>Outcome 1 – disease severity: odds of critical/fatal COVID-19 (n=92/323, 28.5%)</b>						
Age at admission <sup>1</sup>	1.01	0.99-1.02	0.32	1.02	1.00-1.03	0.06
Male <sup>2</sup>	1.60	0.96-2.68	0.07	1.63	0.98-2.76	0.06
Immunocompromised <sup>3</sup>	2.12	1.24-3.58	<b>0.005</b>	2.42	1.39-4.22	<b>0.002</b>
Unvaccinated <sup>4</sup>	0.69	0.27-1.55	0.40	-	-	-
Boosted <sup>5</sup>	0.89	0.50-1.59	0.68	-	-	-
Viral vector vaccination <sup>6</sup>	0.85	0.44-1.60	0.62	-	-	-
Vaccinated <2 months before admission <sup>7</sup>	0.80	0.32-1.78	0.60	-	-	-
Vaccinated <4 months before admission <sup>7</sup>	0.80	0.41-1.58	0.51	-	-	-
Vaccinated <6 months before admission <sup>7</sup>	0.84	0.35-2.25	0.72	-	-	-
<b>Outcome 2 – ICU admission: odds of admission or transferred to ICU due to COVID-19 (n=68/323, 21.1%)</b>						
Age at admission <sup>1</sup>	0.96	0.95-0.98	<b>&lt;0.001</b>	0.97	0.95-0.98	<b>&lt;0.001</b>
Male <sup>2</sup>	1.06	0.61-1.86	0.84	0.97	0.54-1.75	0.93
Immunocompromised <sup>3</sup>	1.79	0.95-3.35	0.07	1.96	1.06-3.57	<b>0.03</b>
Unvaccinated <sup>4</sup>	0.99	0.40-2.19	0.97	-	-	-
Boosted <sup>5</sup>	0.77	0.43-1.41	0.39	-	-	-
Viral vector vaccination <sup>6</sup>	0.97	0.50-1.85	0.94	-	-	-
Vaccinated <2 months before admission <sup>7</sup>	1.65	0.75-3.45	0.20	-	-	-
Vaccinated <4 months before admission <sup>7</sup>	0.83	0.43-1.67	0.59	-	-	-
Vaccinated <6 months before admission <sup>7</sup>	0.80	0.33-2.13	0.62	-	-	-
<b>Outcome 3 – mortality: odds of in-hospital mortality related to COVID-19 (n=58/323, 18.0%)</b>						
Age at admission <sup>1</sup>	1.04	1.02-1.06	<b>0.001</b>	1.06	1.03-1.09	<b>&lt;0.001</b>
Male <sup>2</sup>	1.42	0.78-2.63	0.25	1.63	0.87-3.13	0.13
Immunocompromised <sup>3</sup>	1.79	0.95-3.35	0.07	3.13	1.52-6.62	<b>0.002</b>
Unvaccinated <sup>4</sup>	0.56	0.13-1.66	0.35	-	-	-
Boosted <sup>5</sup>	0.92	0.44-1.98	0.82	-	-	-
Viral vector vaccination <sup>6</sup>	1.25	0.53-2.83	0.60	-	-	-
Vaccinated <2 months before admission <sup>7</sup>	0.44	0.07-1.59	0.28	-	-	-
Vaccinated <4 months before admission <sup>7</sup>	1.09	0.42-3.17	0.87	-	-	-
Vaccinated <6 months before admission <sup>7</sup>	0.84	0.26-3.77	0.80	-	-	-

**Supplemental Table S6. Differences in total hospital length-of-stay (days) in adult patients infected with Omicron and moderate/severe/critical/fatal COVID-19 (n=323), dependent on COVID-19 symptoms and immune status or vaccination status at admission.**

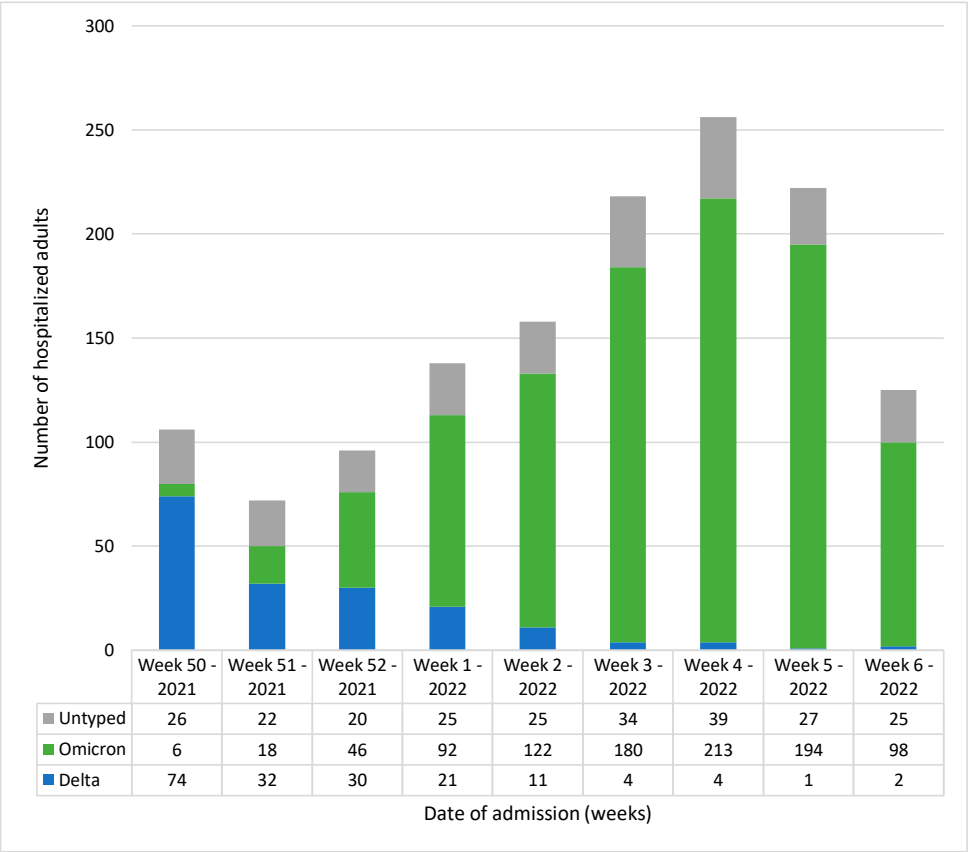
	Hospital length-of-stay (days)				
	Worst COVID-19 symptoms during admission				All symptomatic patients N = 323
	Moderate N = 89	Severe N = 142	Critical N = 34	Fatal N = 58	
Immune status					
Immunocompromised	5 (4-7) N = 29	8 (6-17) N = 30	42 (18-67) N = 16	18 (6-36) N = 23	9 (5-25) N = 184
Non-immunocompromised	10 (5-19) N = 60	8 (5-15) N = 112	17 (12-38) N = 18	11 (5-17) N = 35	10 (5-18) N = 657
<i>p-value</i>	<b>0.005</b>	0.96	0.18	0.09	0.75
Vaccination status					
Unvaccinated	7 (3-34) N= 11	8 (4-18) N = 19	39 (24-56) N = 4	7 (6-12) N = 3	8 (4-28) N = 37
Vaccinated	7 (4-14) N = 74	8 (6-16) N = 117	21 (12-59) N = 30	12 (5-26) N = 35	9 (5-18) N = 256
<i>p-value</i>	0.57	0.76	0.72	0.63	0.82
Unboosted	4 (2-17) N = 26	7 (4-15) N = 39	29 (8-63) N = 11	10 (5-14) N = 12	8 (4-17) N = 88
Boosted	8 (5-14) N = 59	8 (5-12) N = 97	22 (14-59) N = 23	13 (5-26) N = 26	10 (6-19) N = 205
<i>p-value</i>	0.08	0.08	0.77	0.71	<b>0.03</b>
Viral vector	8 (6-18) N = 22	9 (6-16) N = 40	35 (12-57) N = 7	16 (11-39) N = 10	10 (6-19) N = 79
mRNA	6 (4-13) N = 51	8 (6-14) N = 73	27 (21-77) N = 23	9 (3-27) N = 17	8 (4-17) N = 164
<i>p-value</i>	0.25	0.39	0.29	0.42	0.12

Supplemental Figure S1. Number of newly hospitalized patients with positive SARS-CoV-2 screening, divided by age, date of admission and VOC. A. Children (<18 years old); B. Adults (≥18 years old).

A



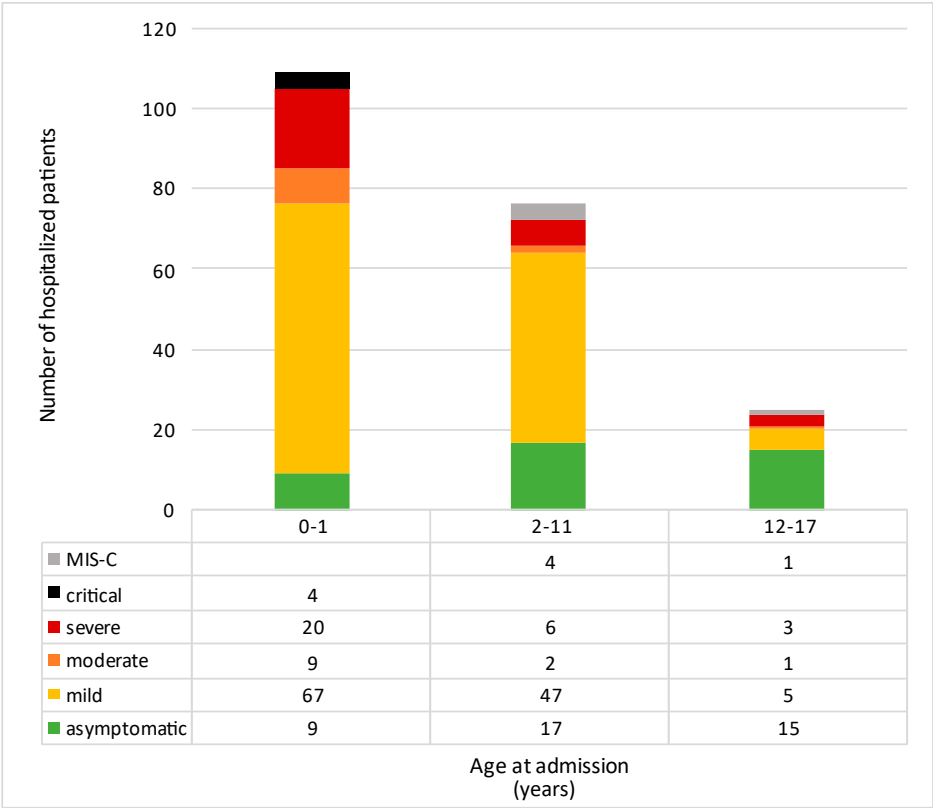
B



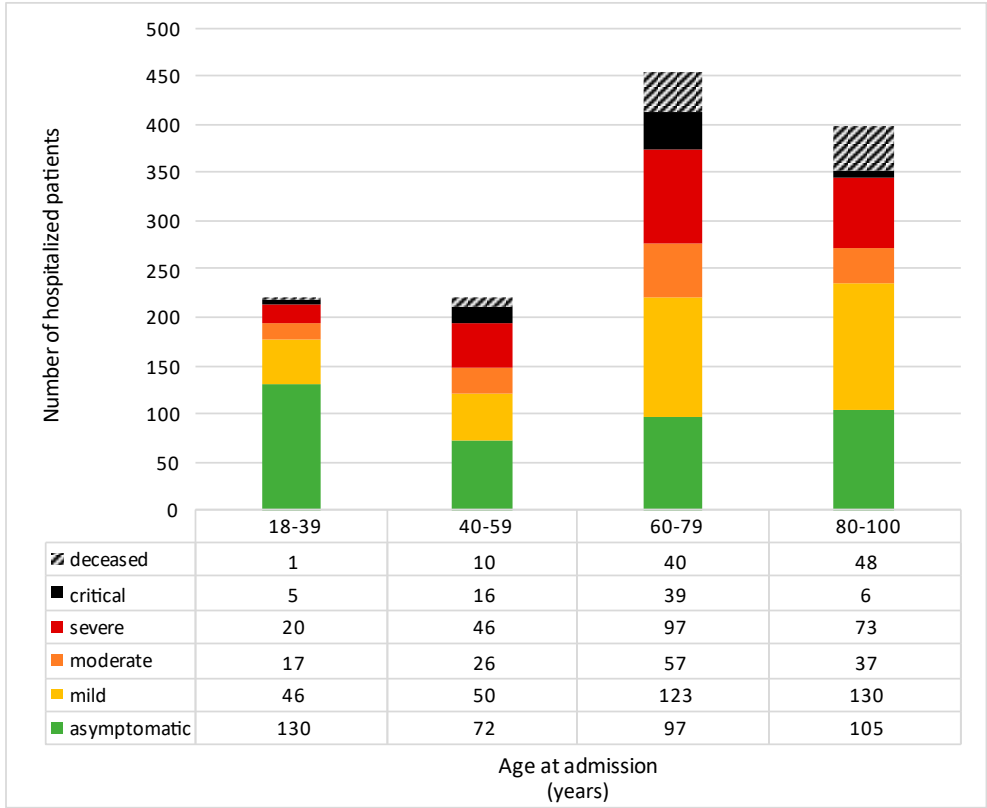


Supplemental Figure S2. Number of newly hospitalized patients with positive SARS-CoV-2 screening, divided by age and classification during hospitalization. A. Children (<18 years old); B. Adults (≥18 years old).

A



B



## Supplemental Materials & Methods

### A. Classification COVID-19 symptoms

To classify patients based on COVID-19 symptoms, NIH guidelines [1] were used as symptom definition:

- 1) asymptomatic [or presymptomatic] *i.e.*, no symptoms that are consistent with COVID-19
- 2) mild illness *i.e.*, any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging
- 3) moderate illness *i.e.*, evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO<sub>2</sub>)  $\geq 94\%$  on room air at sea level
- 4) severe illness *i.e.*, SpO<sub>2</sub>  $< 94\%$  on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO<sub>2</sub>/FiO<sub>2</sub>)  $< 300$  mm Hg, a respiratory rate  $> 30$  breaths/min, or lung infiltrates  $> 50\%$ . Remark: A patient can only be classified as "severe illness" if he/she also has clinical signs of lower respiratory tract infection (via clinical examination or via imaging = definition of "moderate illness"). So, individuals who have SpO<sub>2</sub>  $< 94\%$  on room air at sea level but no evidence of lower respiratory disease are NOT classified as "severe illness"
- 5) critical illness *i.e.*, respiratory failure, septic shock, and/or multiple organ dysfunction. Remark: a patient who is admitted with septic shock with no respiratory clinic and who is clearly NOT linked to the (accidentally found) positive SARS-CoV-2 screening is NOT classified as "critical illness"
- 6) MIS-C *i.e.*, multisystem inflammatory syndrome in children associated with COVID-19 (case definition: CDC [2]).
- 7) fatal: deceased due to COVID-19. Remark: a patient who dies where the (incidentally found) positive SARS-CoV-2 screening is clearly unrelated to the death is not classified as "deceased due to COVID-19. However, from the slightest suspicion that COVID-19 may have contributed to the death of the patient, the patient is classified as "deceased due to COVID-19"

## **B. Classification immune status**

To classify patients as immunocompromised, CDC criteria [3] for moderately or severely immunocompromised people are applied:

- 1) a patient receiving active cancer treatment for tumors or cancers of the blood
- 2) a patient who received an organ transplant and is taking medicine to suppress the immune system
- 3) a patient who received a stem cell transplant within the last 2 years or is taking medicine to suppress the immune system
- 4) a patient with moderate or severe primary immunodeficiency (such as DiGeorge syndrome, Wiskott-Aldrich syndrome – see categorization Inborn errors of immunity (primary immunodeficiencies), UpToDate 2022 [4])
- 5) a patient with advanced or untreated HIV infection
- 6) a patient with active treatment with high-dose corticosteroids (defined as a daily intake of  $\geq 15$ mg of prednisolone or its equivalent for  $>2$  weeks [5]) or other drugs that may suppress your immune response

[1] COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at <https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/>. Accessed January 10, 2022

[2] CDC Health Alert Network. MIS-C associated with COVID-19. Available via <https://emergency.cdc.gov/han/2020/han00432.asp>. Accessed February 10, 2022

[3] CDC. COVID-19 Vaccines for Moderately or Severely Immunocompromised People. Available via <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html>. Accessed February 9, 2022

[4] Sullivan KE, Jyonouchi SC. Inborn errors of immunity (primary immunodeficiencies): Classification (UpToDate, last updated December 15, 2021)). Available via <https://www.uptodate.com/contents/inborn-errors-of-immunity-primary-immunodeficiencies->

[5] Shroff A, Mertz D. Infectious Diseases Risk Whole in Chronic, High-Dose Corticosteroids. Canadian Journal of General Internal Medicine;2017;12(1):10-13

### C. Classification vaccination status

Vaccination status as registered at time of admission were registered, including date of last administrated vaccine. Abbreviations: Pfizer vaccine, BNT162b2 (COMIRNATY), Pfizer, Inc., and BioNTech [mRNA vaccine]; Moderna vaccine, mRNA-1273 (Spikevax), ModernaTX, Inc. [mRNA vaccine]; AstraZeneca vaccine, ChAdOx1-S [recombinant] (Vaxzevria), Oxford/AstraZeneca [viral vector vaccine]; J&J vaccine, JNJ-78436735, Janssen Pharmaceuticals Companies of Johnson & Johnson [viral vector vaccine]

- 1) Unvaccinated
- 2) 1x Pfizer vaccine (1/2 basic vaccination, mRNA vaccination)
- 3) 2x Pfizer vaccine (basic vaccination, mRNA vaccination)
- 4) 3x Pfizer vaccine (boosted, mRNA vaccination)
- 5) 2x Pfizer vaccine + 1x Moderna vaccine (boosted, mRNA vaccination)
- 6) 1x Moderna vaccine (1/2 basic vaccination, mRNA vaccination)
- 7) 2x Moderna vaccine (basic vaccination, mRNA vaccination)
- 8) 3x Moderna vaccine (boosted, mRNA vaccination)
- 9) 2x Moderna vaccine + 1x Pfizer vaccine (boosted, mRNA vaccination)
- 10) 1x AstraZeneca vaccine (1/2 basic vaccination, viral vector vaccination)
- 11) 2x AstraZeneca vaccine (basic vaccination, viral vector vaccination)
- 12) 2x AstraZeneca vaccine + 1x Pfizer vaccine (boosted, counted as viral vector vaccination)
- 13) 2x AstraZeneca vaccine + 1x Moderna vaccine (boosted, counted as viral vector vaccination)
- 14) 1x J&J vaccine (basic vaccination, viral vector vaccination)
- 15) 1x J&J vaccine + 1x Pfizer vaccine (boosted, counted as viral vector vaccination)
- 16) 1x J&J vaccine + 1x Moderna vaccine (boosted, counted as viral vector vaccination)
- 17) ½ basic vaccination, vaccines unknown
- 18) Basic vaccination, vaccines unknown
- 19) Boosted, vaccines unknown
- 20) Vaccination status unknown

D. Used PCR, WGS and serology analyzers and assay in the participating centers. Abbreviations: N.A., not applicable

Laboratory	PCR analyses	WGS analyses	Marker PCR analyses	Serology analyses
University Hospitals Leuven	Analyzer: Panther (Hologic); KingFisher + Quantstudio 7 flex (ThermoFisher); Alinity m (Abbott); GeneXpert (Cepheid) Assay: MVP II nuclear extraction followed by TaqPath COVID-19 RT PCR (Thermo Fisher); Aptima SARS-CoV-2 (Hologic); Alinity m SARS-CoV-2 (Abbott molecular); Xpert SARS-CoV-2 (Cepheid)	Analyzer: GridION (Oxford Nanopore Technologies) Assay: COVID Midi kit (C19MIDI; Oxford Nanopore Technologies) / Artic nCoV-2019 last version	Analyzer: KingFisher + Quantstudio 5/7 flex (ThermoFisher) Assay: MVP II nuclear extraction followed by Taqman™ SARS-CoV-2 Mutation Panel Assay	Analyzer: Architect (Abbott) Assay: SARS-CoV-2 IgG II Quant (anti-S) & SARS-CoV-2 IgG assay (anti-N)
University Hospitals Brussel	Analyzer: AltoStar® (Altona Diagnostics); GeneXpert (Cepheid) Assay: Altostar® SARS-CoV-2 RT- kit 1.5 (Altona Diagnostics); Xpert SARS-CoV-2 (Cepheid)	Analyzer: GridION (Oxford Nanopore Technologies) Assay: 1200bp amplicon “midnight” primer set, using Nanopore Rapid Barcoding Kit	N.A.	N.A.
ZNA Antwerp	Analyzer: Cobas 6800 (Roche) Assay: RT-PCR	Analyzer: MiSeq (Illumina) Assay: AmpliSeq SARS-CoV-2	Analyzer: KingFisher + Quantstudio 5 (ThermoFisher) Assay: MVP II nuclear extraction followed by TaqPath COVID-19 RT PCR (Thermo Fisher)	N.A.
OLV Hospital Aalst	Analyzer: Starlet & Biorad Assay: In-house PCR (N1 & E-gene)	Analyzer: MinION (Oxford Nanopore Technologies)	Assay: In-house PCR assays (multiplex)	Analyzer: Cobas (Roche)
Laboratoire Hospitalier Universitaire de Bruxelles	Analyzer: Alinity m (Abbott); Abbott-M2000 (Abbott) Assay: Alinity m SARS-CoV-2; Abbott Real Time SARS-CoV-2	Analyzer: N.A. (Oxford Nanopore Technologies) Assay: Artic nCoV-2019 last version	N.A.	Analyzer: Liaison XL Assay: Liaison SARS-CoV-2 Trimerics IgG
AZ Sint-Jan Brugge-Oostende	Analyzer: GeneXpert (Cepheid); Cobas 6800 (Roche) Assay: Xpert SARS-CoV-2 (Cepheid); Cobas® SARS-CoV-2 (Roche)	Analyzer: MiSeq (Illumina) Assay: QIAseq® DIRECT SARS-CoV-2	Analyzer: ViiA7 Assay: Taqman™ SARS-CoV-2 Mutation Panel Assay	Analyzer: Architect (Abbott) Assay: SARS-CoV-2 IgG II Quant (anti-S) & SARS-CoV-2 IgG assay (anti-N)

Jessa Hospital Hasselt	Analyzers: Alinity M (Abbott), GeneXpert GX16 (Cepheid), Cobas LIAT System (Roche), Luminex Aries (Thermo Fisher), M2000 (Abbott)	Analyzer: MiSeq (Illumina) Assay: AmpliSeq SARS-CoV-2	N.A.	Analyzer: Alinity I (Abbott) Assay: SARS-CoV-2 IgG anti-S
University Hospitals Antwerp	Analyzer: BD MAX System (BD); GeneXpert (Cepheid) Assay: SARS-CoV-2 for BD MAX (BD); Xpert SARS-CoV-2 (Cepheid)	Analyzer: NextSeq (Illumina) Assay: COVIDSeq	Analyzer: KingFisher + Quantstudio 7 flex (ThermoFisher) Assay: MVP II nuclear extraction followed by TaqPath COVID-19 RT PCR (Thermo Fisher)	N.A.