

SUPPLEMENTARY MATERIALS

DEATH AND ICU ADMISSION ASSOCIATED WITH SARS-CoV-2 VARIANTS IN IMMUNOCOMPROMISED HOSPITALISED INDIVIDUALS: AN NATIONAL OBSERVATIONAL STUDY

Short title: *SARS-CoV-2 variants mortality in immunocompromised individuals*

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Supplement 1. Definition of immunocompromised

- *Immunocompromised individuals are defined as at least one of the following:*
 - Primary immunodeficiency (ICD-10 codes: D80.x, D81.x, D82.x, D83.x, D84.x, D89.x, D71; and SNOMED codes)
 - Secondary immunodeficiency (OPCS codes: X89.1 – X89.5, X89.8, X89.9; and Dictionary of medicines and devices (dm+d) codes for immunosuppressive medications)
 - High-dose, long-term moderate dose corticosteroids treatment (dm+d codes for corticosteroids)
 - End-stage kidney disease or dialysis (ICD-10 codes: N18.5, Z99.2, Y84.1, Z49.1, Z49.2; OPCS codes: X40.x; and SNOMED codes)
 - Organ transplants in the last five years (ICD-10 codes: Z94.0, Z94.1, Z94.2, Z94.3, Z94.4, Z94.5, Z94.6, Z94.9, T86.x and OPC and SNOMED codes)
 - Stem cell transplants (ICD-10 code: T86.0; OPC codes: X33.6, W34.x, W99.x, X33.4, X33.5; and SNOMED codes)
 - Solid tumours in the last five years (ICD-10 codes: C00 – C26, C30-C34, C37-C41, C43, C45-C80; SNOMED codes)
 - Hematological malignancies in the last five years (ICD-10 codes: C81-C86; C88, C90-C97, D45; and SNOMED codes)
 - HIV/AIDS (ICD-10 codes: B20.x, B21.x, B22.x, B23.x, B24.x; and SNOMED codes)

Supplement 2, Supplementary Table S1.

Proportion of hospital mortality due to COVID in population who are IC	Sample size of COVID hospitalization in population who are IC			
	n = 6 000		n = 7 000	
	CI	Precision	CI	Precision
15.0%	[14.1 – 15.9]	1.8%	[14.2 - 15.9]	1.7%
17.0%	[16.1 – 18.0]	1.9%	[16.1 - 17.9]	1.8%
19.0%	[18.0 – 20.0]	2.0%	[18.1 - 19.9]	1.9%
21.0%	[20.0 – 22.1]	2.1%	[20.1 - 22.0]	1.9%
23.0%	[21.9 – 24.1]	2.1%	[22.0 - 24.0]	2.0%

IC, immunocompromised; CI, confidence interval

Supplement 3, Supplementary Table S2.

Table S2. Clinical and epidemiological characteristics of male and female patients according to immunocompromised status

	Female non-IC (N=159698)	Male non-IC (N=194716)	Female IC (N=3611)	Male IC (N=3873)	Total (N=361898)
Death	56228 (35.2%)	70864 (36.4%)	1752 (48.5%)	2069 (53.4%)	130913 (36.2%)
ICU admission	59075 (37.0%)	77453 (39.8%)	1502 (41.6%)	1687 (43.6%)	139717 (38.6%)
Death or ICU admission	79146 (49.6%)	100367 (51.5%)	2191 (60.7%)	2473 (63.9%)	184177 (50.9%)
Age group, years					
<18	2435 (1.5%)	3012 (1.5%)	46 (1.3%)	49 (1.3%)	5542 (1.5%)
18-59	71928 (45.0%)	98943 (50.8%)	1691 (46.8%)	1721 (44.4%)	174283 (48.2%)
60-69	34197 (21.4%)	39255 (20.2%)	915 (25.3%)	926 (23.9%)	75293 (20.8%)
70-79	27633 (17.3%)	31494 (16.2%)	570 (15.8%)	749 (19.3%)	60446 (16.7%)
80+	23505 (14.7%)	22012 (11.3%)	389 (10.8%)	428 (11.1%)	46334 (12.8%)
LoS, days					
0	1670 (1.0%)	2030 (1.0%)	42 (1.2%)	49 (1.3%)	3791 (1.0%)
1-7	87540 (54.8%)	104251 (53.5%)	1660 (46.0%)	1679 (43.4%)	195130 (53.9%)
15-21	15323 (9.6%)	18931 (9.7%)	430 (11.9%)	528 (13.6%)	35212 (9.7%)
22-28	6485 (4.1%)	8127 (4.2%)	253 (7.0%)	257 (6.6%)	15122 (4.2%)
29+	5250 (3.3%)	6517 (3.3%)	190 (5.3%)	266 (6.9%)	12223 (3.4%)
8-14	43430 (27.2%)	54860 (28.2%)	1036 (28.7%)	1094 (28.2%)	100420 (27.7%)
Abdominal pain	9230 (5.8%)	9906 (5.1%)	271 (7.5%)	241 (6.2%)	19648 (5.4%)
Fatigue	39579 (24.8%)	47297 (24.3%)	1007 (27.9%)	1046 (27.0%)	88929 (24.6%)
Loss of smell	15043 (9.4%)	17074 (8.8%)	279 (7.7%)	248 (6.4%)	32644 (9.0%)
Loss of taste	15320 (9.6%)	17596 (9.0%)	268 (7.4%)	264 (6.8%)	33448 (9.2%)
Fever	81830 (51.2%)	111737 (57.4%)	1959 (54.3%)	2324 (60.0%)	197850 (54.7%)
Continuous cough	112120 (70.2%)	139409 (71.6%)	2452 (67.9%)	2617 (67.6%)	256598 (70.9%)
Dyspnea	123912 (77.6%)	152553 (78.3%)	2807 (77.7%)	3025 (78.1%)	282297 (78.0%)
Orthopnea	96705 (60.6%)	119248 (61.2%)	2162 (59.9%)	2281 (58.9%)	220396 (60.9%)
Low oxygen saturation	110508 (69.2%)	136797 (70.3%)	2607 (72.2%)	2750 (71.0%)	252662 (69.8%)
Postpartum	565 (0.4%)	0 (0.0%)	6 (0.2%)	0 (0.0%)	586 (0.2%)
Down Syndrome	503 (0.3%)	458 (0.2%)	25 (0.7%)	24 (0.6%)	1010 (0.3%)

Asthma	5108 (3.2%)	3258 (1.7%)	129 (3.6%)	82 (2.1%)	8577 (2.4%)
Diabetes	42768 (26.8%)	41083 (21.1%)	872 (24.1%)	930 (24.0%)	85653 (23.7%)
Obesity	19062 (11.9%)	16207 (8.3%)	368 (10.2%)	208 (5.4%)	35845 (9.9%)
Chronic heart disease	57246 (35.8%)	58586 (30.1%)	1274 (35.3%)	1313 (33.9%)	118419 (32.7%)
Chronic hematological disease	872 (0.5%)	815 (0.4%)	179 (5.0%)	198 (5.1%)	2064 (0.6%)
Chronic liver disease	860 (0.5%)	1497 (0.8%)	123 (3.4%)	190 (4.9%)	2670 (0.7%)
Chronic neurological disease	5741 (3.6%)	6070 (3.1%)	214 (5.9%)	245 (6.3%)	12270 (3.4%)
Chronic pneumopathic disease	5276 (3.3%)	6456 (3.3%)	279 (7.7%)	333 (8.6%)	12344 (3.4%)
Received two doses of the COVID-19 vaccine	19545 (12.2%)	20768 (10.7%)	661 (18.3%)	704 (18.2%)	41678 (11.5%)
Predominant SARS-CoV-2 variant, in Brazil					
B.1.1.28/33	28365 (17.8%)	34664 (17.8%)	693 (19.2%)	905 (23.4%)	64627 (17.9%)
Delta	34532 (21.6%)	44719 (23.0%)	665 (18.4%)	669 (17.3%)	80585 (22.3%)
Gamma	72876 (45.6%)	86573 (44.5%)	1214 (33.6%)	1234 (31.9%)	161897 (44.7%)
Omicron	12604 (7.9%)	13632 (7.0%)	611 (16.9%)	624 (16.1%)	27471 (7.6%)
Omicron XBB	610 (0.4%)	647 (0.3%)	46 (1.3%)	41 (1.1%)	1344 (0.4%)
Original WT	10711 (6.7%)	14481 (7.4%)	382 (10.6%)	400 (10.3%)	25974 (7.2%)
Year of admission to hospital					
2020	39076 (24.5%)	49145 (25.2%)	1075 (29.8%)	1305 (33.7%)	90601 (25.0%)
2021	107408 (67.3%)	131292 (67.4%)	1879 (52.0%)	1903 (49.1%)	242482 (67.0%)
2022	12604 (7.9%)	13632 (7.0%)	611 (16.9%)	624 (16.1%)	27471 (7.6%)
2023	610 (0.4%)	647 (0.3%)	46 (1.3%)	41 (1.1%)	1344 (0.4%)

Abbreviations: IC, immunocompromised; non-IC, non-immunocompromised; ICU, Intensive Unit Care; LoS, Length of Stay; COPD was defined as ICD-10 codes J40–J44, particularly J44; asthma as J45–J46; autoimmune disease as selected ICD-10 codes including M32, M05, K50, and K51; cardiovascular disease as selected cardiovascular diagnoses including I20–I25, I42, and I50; stroke (I60–I69 broadly); chronic liver disease as K70–K77; chronic kidney disease as N18; obesity as body mass index ≥ 30 kg/m² and/or E66; diabetes mellitus as E10–E14; cancer as C00–C97; and COVID-19 infection as U07.1 or U07.2 recorded in the SARI database.. Low oxygen saturation was defined as SpO₂ <90% on room air.

Supplement 4, Supplementary Table S3 and Table S4.

Table S3: Logistic regression of immunocompromised hospitalized population associated with ICU admissions

Characteristic	Original WT			B.1.1.28/.33			Gamma			Delta			Omicron			Omicron XBB		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Immunocompromised status			0.002			0.002			<0.001			<0.001			0.34			0.12
<i>No</i>	—	—		—	—		—	—		—	—		—	—		—	—	
<i>Yes</i>	1.38	1.13 - 1.70		1.27	1.09 - 1.47		1.24	1.10 - 1.39		1.31	1.12 - 1.53		1.09	0.91 - 1.29		1.69	0.86 - 3.17	
Sex			<0.001			<0.001			<0.001			<0.001			<0.001			<0.001
<i>Female</i>	—	—		—	—		—	—		—	—		—	—		—	—	
<i>Male</i>	1.22	1.16 - 1.29		1.15	1.12 - 1.19		1.09	1.07 - 1.12		1.08	1.05 - 1.11		1.23	1.17 - 1.29		1.69	1.31 - 2.17	
Immunocompromised status Sex			0.13			0.88			0.64			0.97			0.66			0.46
<i>Male</i>	0.80	0.60 - 1.07		0.98	0.80 - 1.21		0.96	0.82 - 1.13		1.00	0.81 - 1.25		0.95	0.75 - 1.20		0.71	0.28 - 1.78	

Abbreviations: CI = Confidence Interval, OR = Odds Ratio

Table S4. Logistic regression of immunocompromised hospitalized population associated with mortality

Characteristic	Original WT			B.1.1.28/33			Gamma			Delta			Omicron			Omicron XBB		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Immunocompromised status			0.026			<0.001			<0.001			<0.001			<0.001			0.0094
<i>No</i>	—	—		—	—		—	—		—	—		—	—		—	—	
<i>Yes</i>	1.26	1.03 - 1.55		1.79	1.54 - 2.09		1.71	1.53 - 1.91		1.86	1.59 - 2.17		2.01	1.71 - 2.36		2.32	1.24 - 4.27	
Sex			<0.001			<0.001			0.24			0.96			<0.001			0.002
<i>Female</i>	—	—		—	—		—	—		—	—		—	—		—	—	
<i>Male</i>	1.19	1.13 - 1.25		1.12	1.09 - 1.16		1.01	0.99 - 1.03		1.00	0.97 - 1.03		1.19	1.13 - 1.25		1.46	1.14 - 1.88	
Immunocompromised individual Sex			0.63			0.19			0.004			0.006			0.09			0.80
<i>Male</i>	0.93	0.70 - 1.24		1.14	0.94 - 1.40		1.27	1.08 - 1.49		1.35	1.09 - 1.68		0.82	0.65 - 1.03		1.12	0.47 - 2.75	

Abbreviations: CI = Confidence Interval, OR = Odds Ratio