

Supplement

Appendix S1

We enrolled 2767 COVID-19 patients in ARBs CORONA I. The following patients were excluded from the current analysis.

- Acute COVID-19 readmissions (n=83)
- Emergency Room admissions without hospitalization (n=149)
- Patients admitted to hospital but not due to acute COVID-19 (n=362; see file below)



Appendix_S1_admission_reasons.xlsx

- Patients with unknown discharge outcome or currently still hospitalized (n=19)
- Patients from sites which only enrolled ICU patients (Alberta; n=353)

Alberta site was different from the other participating sites in that it only enrolled patients who were admitted to ICU. Because the percentage of data from Alberta in ARBs CORONA I varied across waves (13%, 28%, 16% and 0% in waves 1, 2, 3 and Omicron respectively), the inclusion of Alberta site would thus confound and skew the crude results (for example, with the inclusion of Alberta data, ICU admission rate became 47%, 55%, 44% and 28% in waves 1, 2, 3 and Omicron respectively).

Pre-existing use of angiotensin receptor blockers and angiotensin-converting enzyme inhibitors prior to admission in patients included in the current study were 284/1794 (15.8%) and 332/1794 (18.5%) respectively.

Appendix S2 – ARBs CORONA I CRF



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CapCRF_V7.0_22Mar

Table E1 – Number of patients by province and site

Variable	Wave			
	1st (n=520)	2nd (n=575)	3rd (n=265)	Omicron (n=441)
Province, n (%)				
BC	136 (26.2)	361 (62.8)	200 (75.5)	226 (51.2)
ON	24 (4.6)	203 (35.3)	65 (24.5)	184 (41.7)
QC	360 (69.2)	11 (1.9)	0 (0.0)	31 (7.0)
Site, n (%)				
St. Paul's Hospital, Vancouver, BC	66 (12.7)	92 (16.0)	55 (20.8)	131 (29.7)
Vancouver General Hospital, Vancouver, BC	55 (10.6)	157 (27.3)	109 (41.1)	0 (0.0)
Surrey Memorial Hospital, Surrey, BC	15 (2.9)	112 (19.5)	36 (13.6)	95 (21.5)
Humber River Hospital, North York, ON	0 (0.0)	45 (7.8)	6 (2.3)	0 (0.0)
Kingston General Hospital, Kingston, ON	4 (0.8)	13 (2.3)	1 (0.4)	0 (0.0)
Mount Sinai Hospital, Toronto, ON	20 (3.8)	82 (14.3)	42 (15.8)	31 (7.0)
Sunnybrook Hospital, Toronto, ON	0 (0.0)	63 (11.0)	16 (6.0)	153 (34.7)
McGill University Health Centre, Montreal, QC	258 (49.6)	0 (0.0)	0 (0.0)	0 (0.0)
Centre hospitalier universitaire de Sherbrooke, QC	102 (19.6)	11 (1.9)	0 (0.0)	31 (7.0)

Table E2 – Co-morbidities of Omicron wave patients admitted with acute COVID-19 by vaccination status

Variable	Vaccination status		P
	Unvaccinated (n=130)	≥2 doses (n=242)	
Co-morbidities, n (%)			
Any of the four below	82/130 (63.1)	205/242 (84.7)	<0.001
Chronic cardiac disease	39/130 (30.0)	112/241 (46.5)	0.002
Chronic kidney disease	14/130 (10.8)	71/240 (29.6)	<0.001
Hypertension	63/130 (48.5)	159/242 (65.7)	0.001
Diabetes	39/130 (30.0)	90/242 (37.2)	0.165
Chronic pulmonary disease	23/130 (17.7)	54/241 (22.4)	0.285
Liver disease	2/130 (1.5)	14/239 (5.9)	0.052
Chronic neurological disorder	19/130 (14.6)	45/238 (18.9)	0.299
Malignant neoplasm	11/130 (8.5)	48/240 (20.0)	0.004
Chronic hematologic disease	7/130 (5.4)	51/241 (21.2)	<0.001
AIDS / HIV	2/127 (1.6)	1/238 (0.4)	0.278
Rheumatologic disorder	15/130 (11.5)	32/240 (13.3)	0.621
Dementia	3/130 (2.3)	24/241 (10.0)	0.007
Malnutrition	1/129 (0.8)	2/241 (0.8)	1.000
Obesity	10/130 (7.7)	16/229 (7.0)	0.804

P value was based on Chi-square test or Fisher's exact test as appropriate.

Table E3 – COVID-19 therapies during the hospital course of Omicron wave patients admitted with acute COVID-19 by vaccination status

Variable	Vaccination status		P
	Unvaccinated (n=130)	≥2 doses (n=242)	
Co-intervention while hospitalized, n (%)			
Antiviral agent	34/129 (26.4)	81/241 (33.6)	0.151
Remdesivir	27/129 (20.9)	58/241 (24.1)	0.494
Antibiotic	92/130 (70.8)	163/242 (67.4)	0.499
Corticosteroid	109/130 (83.8)	182/242 (75.2)	0.054
Dexamethasone	99/130 (76.2)	159/242 (65.7)	0.037
Antifungal agent	10/129 (7.8)	14/241 (5.8)	0.470

P value was based on Chi-square test or Fisher's exact test as appropriate.

Table E4– Baseline characteristics of Omicron COVID-19 wave versus prior wave patients admitted to hospital for acute COVID-19.

Variable	Wave				p ¹	p ²	p ³
	1st (n=520)	2nd (n=575)	3rd (n=265)	Omicron (n=441)			
ARBs/ACEi prior to admission					0.376	0.102	0.178
Unknown	7	0	1	0			
None	1178 (65.7)	344 (66.2)	364 (63.4)	186 (70.2)			
ARBs	284 (15.8)	82 (15.8)	105 (18.3)	38 (14.3)			
ACEi	332 (18.5)	94 (18.1)	105 (18.3)	41 (15.5)			
Sex, n (%)					0.371	0.578	0.706
Unknown	1	0	0	1			
Male	293 (56.5)	351 (61.0)	161 (60.8)	261 (59.3)			
Female	226 (43.5)	224 (39.0)	104 (39.2)	179 (40.7)			
Age, mean (SD)	70.2 (16.3)	65.8 (17.3)	63.0 (17.1)	70.1 (15.2)	0.893	<0.001	<0.001
Received any COVID-19 vaccine prior to admission, n (%)	0/520 (0.0)	3/574 (0.5)	21/256 (8.2)	261/391 (66.8)	<0.001	<0.001	<0.001
Received at least 2 doses of COVID-19 vaccine prior to admission, n (%)	0/520 (0.0)	0/574 (0.0)	0/256 (0.0)	242/390 (62.1)	<0.001	<0.001	<0.001
Admitted to ICU on hospital admission day, n (%)	104 (20.0)	83 (14.4)	35 (13.3)	64 (14.5)	0.027	0.960	0.648
Organ support on admission day							
Invasive mechanical ventilation, n (%)	55/520 (10.6)	34/575 (5.9)	16/265 (6.0)	20/441 (4.5)	<0.001	0.332	0.380
RRT or dialysis, n (%)	8/511 (1.6)	7/570 (1.2)	4/262 (1.5)	8/439 (1.8)	0.759	0.439	0.770
Vasopressors, n (%)	35/520 (6.7)	33/575 (5.7)	14/265 (5.3)	18/440 (4.1)	0.074	0.234	0.461
Temperature (°C) - mean (SD)	37.5 (0.9)	37.4 (0.9)	37.4 (0.9)	37.1 (0.9)	<0.001	<0.001	<0.001
Missing, n	19	9	3	16			
Heart rate (beats per minute) - mean (SD)	91.4 (20.6)	95.5 (20.3)	96.7 (19.2)	92.6 (21.5)	0.382	0.031	0.010
Missing, n	6	4	3	2			
Respiratory rate (breaths per minute) - mean (SD)	22.9 (6.4)	24.9 (7.9)	24.1 (7.5)	23.2 (7.7)	0.413	0.001	0.144
Missing, n	15	6	4	12			
sBP - mean (SD)	128.8 (22.9)	130.5 (23.5)	126.9 (20.6)	131.2 (26.9)	0.132	0.648	0.027
Missing, n	2	5	2	7			
dBp - mean (SD)	73.7 (11.9)	74.3 (13.2)	72.4 (12.3)	73.9 (31.3)	0.060	0.013	0.760
Missing, n	3	14	9	9			
Oxygen saturation (SaO ₂ ; %) - mean (SD)	93.5 (4.2)	90.8 (8.5)	91.1 (7.8)	93.1 (6.7)	0.359	<0.001	<0.001
Missing, n	13	3	2	5			
Required oxygen therapy, n (%)	186/516 (36.0)	174/544 (32.0)	87/253 (34.4)	147/426 (34.5)	0.623	0.407	0.975
WBC count (x10 ³ /μL) - Median (IQR)	6.5 (4.9, 8.6)	6.9 (5.1, 9.2)	6.3 (4.7, 8.8)	7.3 (5.1, 9.9)	0.006	0.265	0.014
Missing, n	17	6	4	3			

Variable	Wave				P ¹	P ²	P ³
	1st (n=520)	2nd (n=575)	3rd (n=265)	Omicron (n=441)			
Haemoglobin (g/L) - Median (IQR)	130.0 (118.0, 145.0)	132.0 (117.0, 145.0)	134.0 (119.0, 146.0)	127.0 (111.0, 141.0)	0.002	<0.001	<0.001
Missing, n	15	7	4	3			
Creatinine (µmol/L) - Median (IQR)	84.0 (68.0, 114.0)	87.0 (70.0, 120.5)	82.0 (66.0, 106.0)	95.0 (70.0, 136.0)	0.001	0.057	<0.001
Missing, n	10	11	7	4			
ALT (U/L) - Median (IQR)	29.0 (17.0, 50.5)	35.0 (22.0, 57.0)	38.5 (23.0, 63.0)	23.0 (16.0, 38.0)	0.003	<0.001	<0.001
Missing, n (%)	156	91	39	122			
AST (U/L) - Median (IQR)	45.0 (26.0, 77.0)	46.0 (32.0, 77.0)	47.0 (38.0, 74.0)	38.5 (23.0, 59.0)	0.082	0.002	<0.001
Missing, n (%)	430	271	106	343			
D-Dimer (ng/mL)- Median (IQR)	970.0 (580.0, 1860.0)	912.5 (597.0, 1905.0)	876.0 (636.5, 1423.5)	1117.0 (578.0, 1892.0)	0.622	0.801	0.355
Missing, n (%)	343	325	105	346			

P value was based on Chi-square test or Fisher's exact test as appropriate.

1. Comparison between wave 1 and Omicron
2. Comparison between wave 2 and Omicron
3. Comparison between wave 3 and Omicron

Table E5. COVID-19 therapies during the hospital course of Omicron COVID-19 wave versus prior wave patients admitted to hospital for acute COVID-19.

Variable	Wave				p ¹	p ²	p ³
	1st (n=520)	2nd (n=575)	3rd (n=265)	Omicron (n=441)			
Co-intervention while hospitalized, n (%)							
Antiviral agent	72/516 (14.0)	107/572 (18.7)	42/265 (15.8)	134/439 (30.5)	<0.001	<0.001	<0.001
Remdesivir	8/516 (1.6)	96/572 (16.8)	27/265 (10.2)	99/439 (22.6)	<0.001	0.021	<0.001
Antibiotic	434/520 (83.5)	488/575 (84.9)	210/265 (79.2)	306/441 (69.4)	<0.001	<0.001	0.004
Corticosteroid	160/520 (30.8)	501/575 (87.1)	241/265 (90.9)	340/441 (77.1)	<0.001	<0.001	<0.001
Dexamethasone	56/520 (10.8)	484/575 (84.2)	235/265 (88.7)	296/441 (67.1)	<0.001	<0.001	<0.001
Antifungal agent	34/520 (6.5)	24/575 (4.2)	22/265 (8.3)	29/439 (6.6)	0.966	0.085	0.400

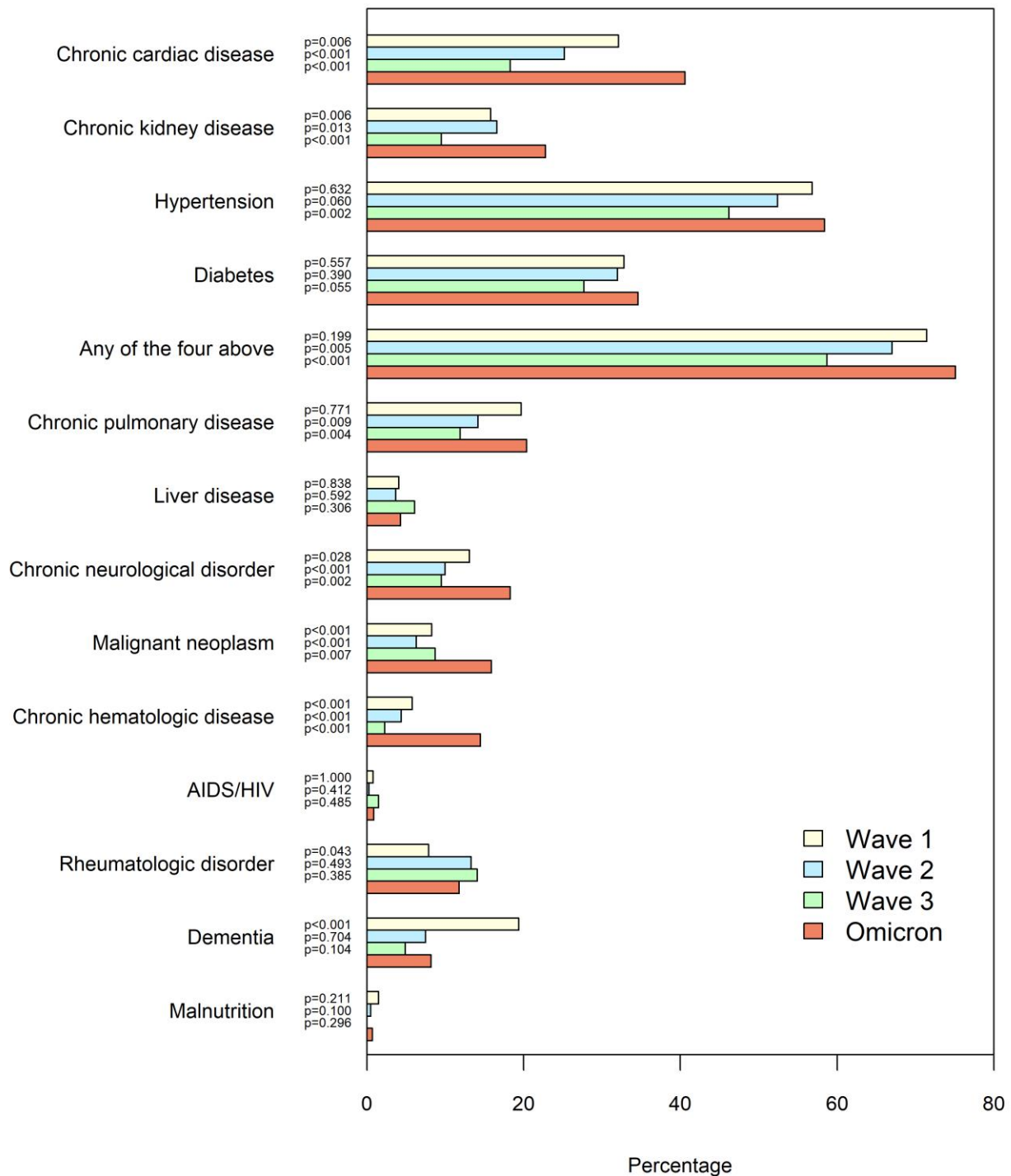
P value was based on Chi-square test or Fisher's exact test as appropriate.

1. Comparison between wave 1 and Omicron
2. Comparison between wave 2 and Omicron
3. Comparison between wave 3 and Omicron

Table E6– Outcomes of Omicron COVID-19 wave versus prior wave patients admitted to hospital for acute COVID-19.

Variable	Wave			
	1st (n=520)	2nd (n=575)	3rd (n=265)	Omicron (n=441)
28-day mortality, n (%)	95/520 (18.3)	93/575 (16.2)	19/264 (7.2)	42/433 (9.7)
In-hospital death, n (%)	111/520 (21.3)	103/575 (17.9)	25/265 (9.4)	63/441 (14.3)
Admitted to ICU, n (%)	201/520 (38.7)	217/575 (37.7)	89/264 (33.7)	121/441 (27.4)
Septic shock, n (%)	50/510 (9.8)	44/547 (8.0)	15/255 (5.9)	39/430 (9.1)
Acute respiratory distress syndrome, n (%)	107/490 (21.8)	100/540 (18.5)	34/256 (13.3)	66/437 (15.1)
Acute kidney injury, n (%)	131/513 (25.5)	132/538 (24.5)	34/246 (13.8)	119/429 (27.7)
Acute cardiac injury, n (%)	40/495 (8.1)	47/547 (8.6)	17/252 (6.7)	18/418 (4.3)
Organ support while hospitalized, n (%)				
Invasive mechanical ventilation	130/520 (25.0)	118/575 (20.5)	42/265 (15.8)	61/441 (13.8)
RRT or dialysis	33/511 (6.5)	30/570 (5.3)	7/262 (2.7)	30/439 (6.8)
Vasopressors	120/520 (23.1)	125/575 (21.7)	49/265 (18.5)	70/440 (15.9)
Organ support during first 14 days, n (%)				
Invasive mechanical ventilation	127/520 (24.4)	116/575 (20.2)	40/265 (15.1)	53/439 (12.1)
RRT or dialysis	26/508 (5.1)	24/568 (4.2)	6/262 (2.3)	23/436 (5.3)
Vasopressors	116/520 (22.3)	122/574 (21.3)	47/264 (17.8)	62/437 (14.2)
DAF invasive mechanical ventilation - first 14 days				
Mean (SD)	10.0 (5.9)	11.0 (5.3)	12.1 (4.4)	12.5 (4.0)
Unknown, n	2	2	3	18
DAF RRT- first 14 days				
Mean (SD)	11.8 (5.0)	12.3 (4.5)	13.1 (3.3)	13.1 (3.2)
Unknown, n	11	5	2	23
DAF Vasopressors - first 14 days				
Mean (SD)	10.7 (5.5)	11.3 (5.0)	12.4 (3.9)	12.6 (3.8)
Unknown, n	2	2	2	20
Hospital length of stay- decedents				
n	111	103	24	48
Median (IQR)	11.0 (6.0, 21.0)	11.0 (7.0, 20.0)	12.0 (9.5, 24.0)	16.5 (9.5, 35.5)
Range	(0.0, 63.0)	(1.0, 44.0)	(2.0, 62.0)	(2.0, 246.0)
Hospital length of stay- survivors				
n	409	471	240	378
Median (IQR)	15.0 (7.0, 26.0)	9.0 (5.0, 17.0)	9.0 (5.0, 17.0)	8.0 (4.0, 16.0)
Range	(2.0, 151.0)	(2.0, 313.0)	(2.0, 114.0)	(1.0, 143.0)
ICU length of stay - decedents				
n	51	57	12	37
Median (IQR)	15.0 (5.0, 26.0)	12.0 (7.0, 21.0)	21.5 (10.0, 45.5)	15.0 (10.0, 29.0)
Range	(0.0, 61.0)	(0.0, 38.0)	(3.0, 57.0)	(0.0, 246.0)
ICU length of stay - survivors				
n	149	159	73	77
Median (IQR)	10.0 (4.0, 17.0)	7.0 (4.0, 12.0)	9.0 (3.0, 16.0)	6.0 (3.0, 12.0)
Range	(0.0, 92.0)	(0.0, 113.0)	(1.0, 75.0)	(0.0, 85.0)

Figure E1. Comorbidities of patients in Omicron wave versus prior wave patients admitted to hospital for acute COVID-19.

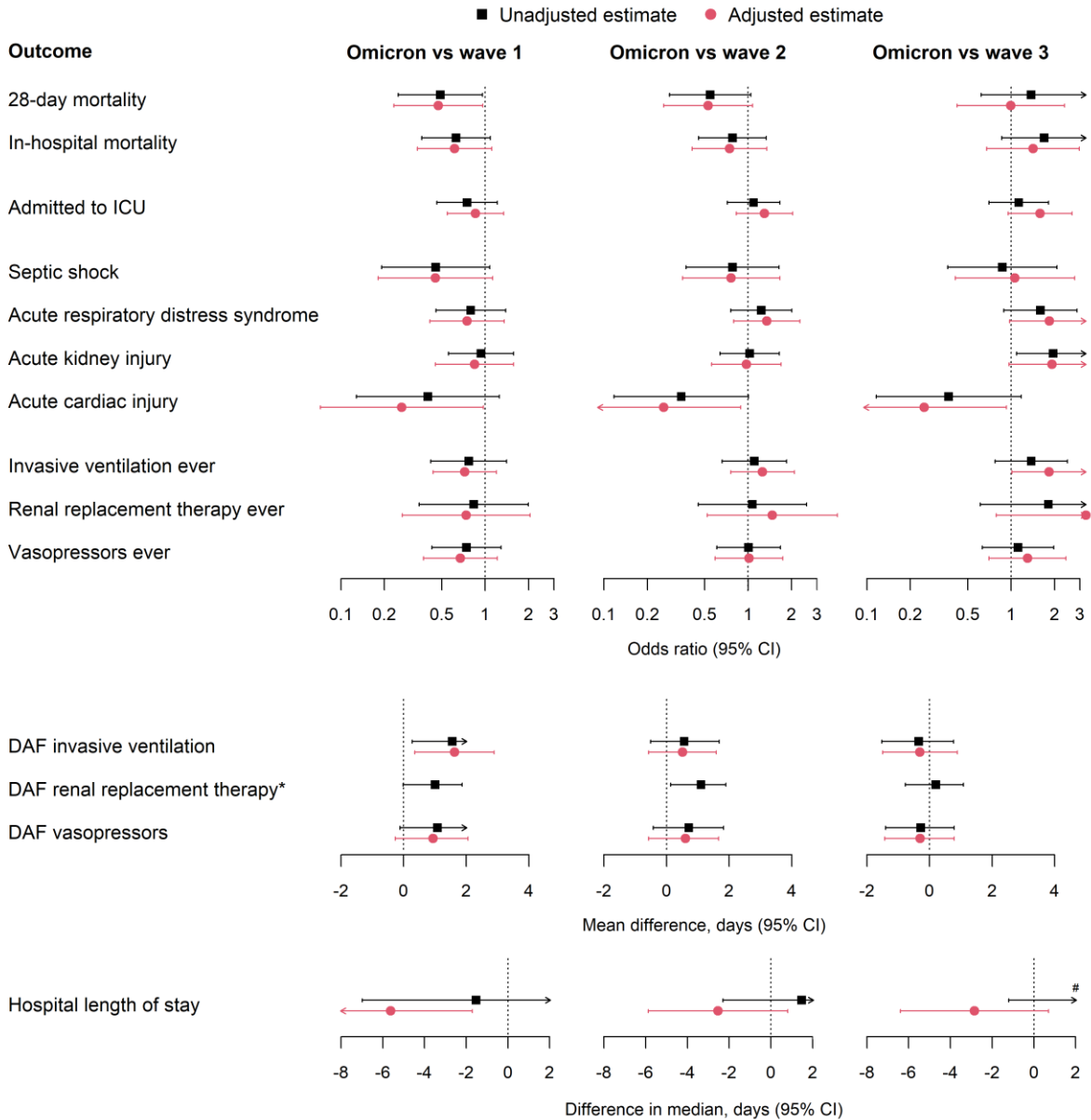


P value was based on Chi-square test or Fisher's exact test as appropriate and was for the comparison between Omicron wave and waves 1,2 and 3.

Variable	Wave				p ¹	p ²	p ³
	1st (n=520)	2nd (n=575)	3rd (n=265)	Omicron (n=441)			
Co-morbidities, n (%)							
Any of the four below	370/518 (71.4)	383/572 (67.0)	155/264 (58.7)	331/441 (75.1)	0.207	0.005	<0.001
Chronic cardiac disease	166/517 (32.1)	143/568 (25.2)	48/262 (18.3)	179/440 (40.7)	0.006	<0.001	<0.001
Chronic kidney disease	82/519 (15.8)	95/573 (16.6)	25/263 (9.5)	100/438 (22.8)	0.006	0.013	<0.001
Hypertension	295/519 (56.8)	300/572 (52.4)	121/262 (46.2)	257/441 (58.3)	0.654	0.064	0.002
Diabetes	170/518 (32.8)	183/571 (32.0)	73/264 (27.7)	152/441 (34.5)	0.590	0.418	0.060
Chronic pulmonary disease	102/519 (19.7)	81/570 (14.2)	31/261 (11.9)	90/440 (20.5)	0.757	0.009	0.004
Liver disease	21/517 (4.1)	21/573 (3.7)	16/264 (6.1)	19/438 (4.3)	0.832	0.586	0.310
Chronic neurological disorder	68/519 (13.1)	57/572 (10.0)	25/262 (9.5)	80/437 (18.3)	0.027	<0.001	0.002
Malignant neoplasm	43/517 (8.3)	36/567 (6.3)	23/263 (8.7)	70/439 (15.9)	<0.001	<0.001	0.006
Chronic hematologic disease	30/518 (5.8)	25/572 (4.4)	6/263 (2.3)	64/440 (14.5)	<0.001	<0.001	<0.001
AIDS / HIV	4/491 (0.8)	2/573 (0.3)	4/264 (1.5)	4/433 (0.9)	1.000	0.411	0.486
Rheumatologic disorder	41/517 (7.9)	76/573 (13.3)	37/263 (14.1)	52/439 (11.8)	0.042	0.501	0.391
Dementia	100/516 (19.4)	43/572 (7.5)	13/263 (4.9)	36/440 (8.2)	<0.001	0.696	0.103
Malnutrition	8/517 (1.5)	3/573 (0.5)	0/264 (0.0)	3/439 (0.7)	0.212	1.000	0.295

Variable	Wave				p ¹	p ²	p ³
	1st (n=520)	2nd (n=575)	3rd (n=265)	Omicron (n=441)			
Obesity	53/482 (11.0)	53/571 (9.3)	25/244 (10.2)	31/426 (7.3)	0.054	0.260	0.182

Figure E2. Comparison of outcomes between COVID-19 Omicron and prior waves by regression analysis – among unvaccinated patients.



The following factors were accounted for in the adjusted analysis: age, sex, co-morbidities (chronic heart disease, hypertension, chronic kidney disease, diabetes, chronic pulmonary disease, chronic neurological disorder, cancer and chronic hematologic disease), baseline systolic blood pressure, heart rate, SaO₂ and serum creatinine.

*Adjusted regression analysis was not feasible numerically as too few patients received renal replacement therapy during the first 14 days

Estimated difference from unadjusted regression analysis was 2.46 days.