

Supplementary Appendix

Early Omicron infection is associated with increased reinfection risk in older adults in long-term care and retirement facilities

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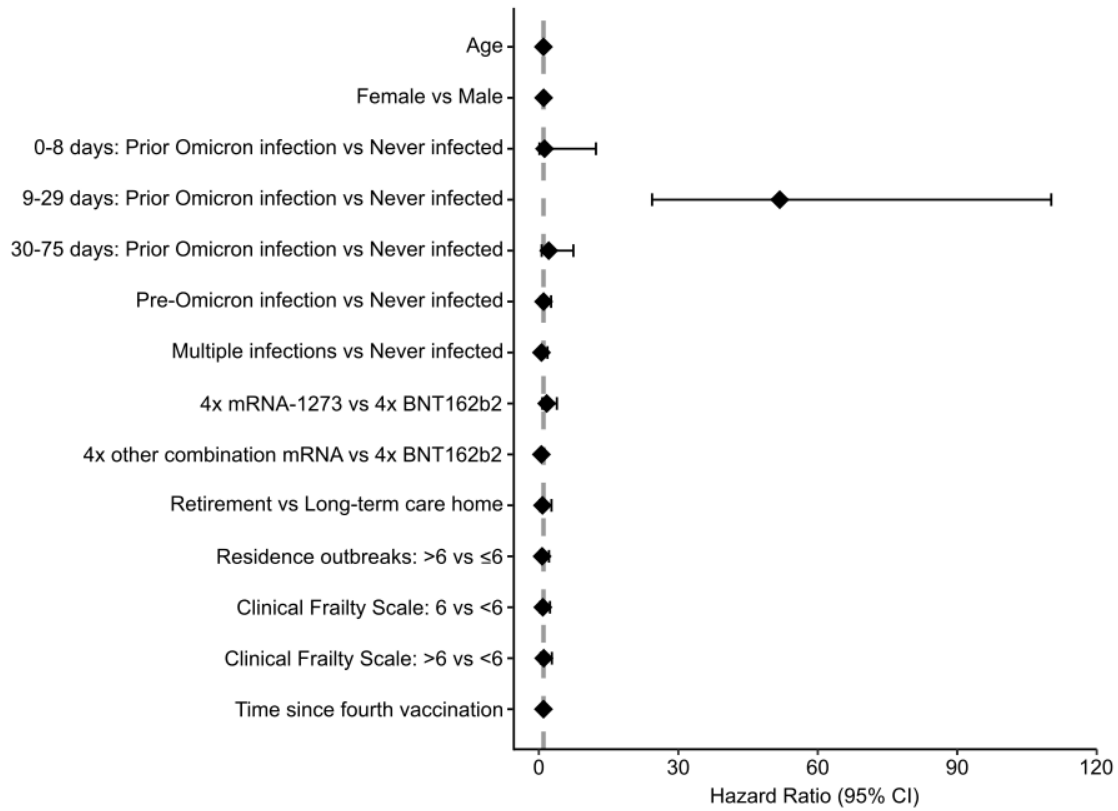
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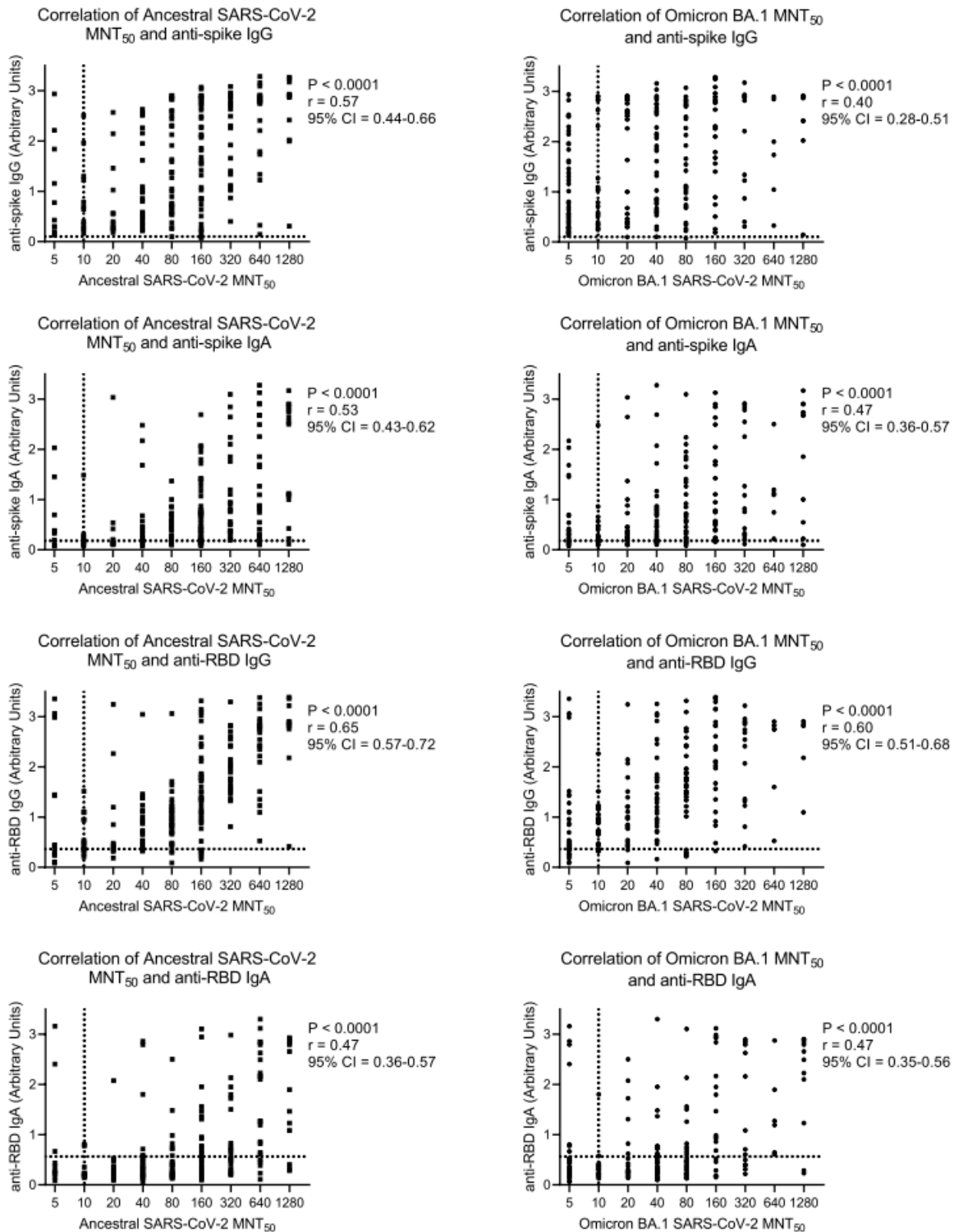
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Figure S1. Cox proportional hazards regression analysis – complete frailty dataset



The Cox proportional-hazards regression model was used to estimate hazard ratios of Omicron infection between July 1 and September 13, 2022, with the baseline hazard on July 1, 2022. Variables (age, sex, previous infection, mRNA vaccine combination, residence type, number of outbreaks, clinical frailty scale, time since fourth vaccination) reflect characteristics at baseline, with adjustment for study site. The hazard ratios are presented with 95% confidence intervals based on robust standard errors.

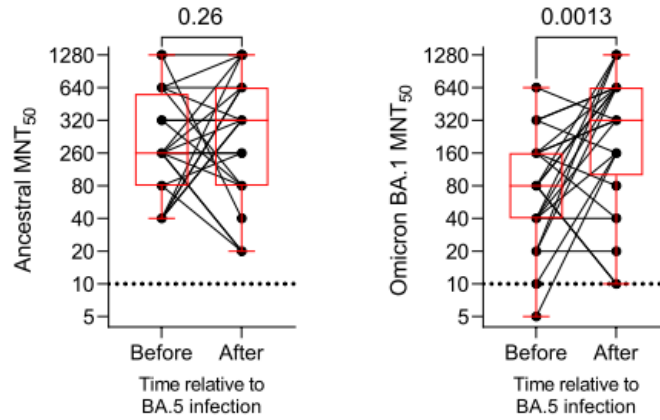
Figure S2. Correlations of serum antibody measurements



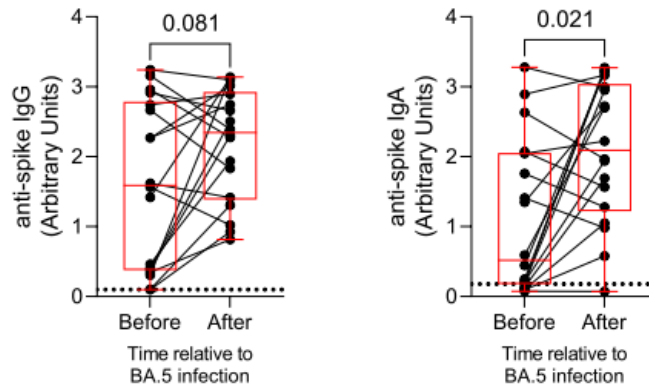
In serum samples collected within three months prior to the start of the observation period (i.e., collected between April 1 and June 30 before the July 1 to September 13, 2022 observation period), ancestral anti-spike and anti-RBD (receptor binding domain) IgG and IgA antibody levels were measured by ELISA, and microneutralization titres (MNT₅₀) of ancestral and Omicron BA.1 anti-SARS-CoV-2 antibodies were assessed. Data for microneutralization titres are presented on a log₂ scale. Each data point indicates an individual participant. Dotted lines indicate cutoff thresholds. Statistical significance was assessed by Spearman's rank correlation.

Figure S3. Paired analysis of serum antibody measurements in participants with Omicron reinfections

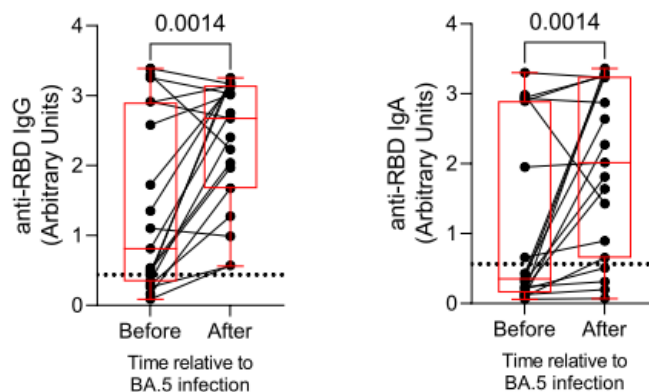
A. Omicron BA.1 neutralization increases after Omicron reinfection



B. Serum anti-spike IgA antibodies increase after Omicron reinfection



C. Serum anti-RBD IgG and IgA antibodies increase after Omicron reinfection



Panel A shows microneutralization titres (MNT₅₀) of serum antibodies against ancestral and Omicron BA.1 SARS-CoV-2. Serum anti-spike (Panel B) and anti-RBD (receptor binding domain; Panel C) IgG and IgA antibodies were assessed by ELISA. Data are presented as box and whisker plots, minimum to maximum, with the center line at the median. Each data point indicates an individual participant, with lines joining data before and after Omicron BA.5 infection (i.e., Omicron reinfection). Data in Panel A are presented on a log₂ scale. Dotted lines indicate cutoff thresholds. Statistical significance was assessed by Wilcoxon matched-pairs signed rank test. All P-values are shown.

Table S1. Cohort comorbidities at baseline by observation period outcome^a

	No Infection	Omicron Infection	Total
Participants (N)	558	129	657
Missing (N)	59	4	63
0	3 (0.5%)	0 (0.0%)	3 (0.4%)
1	18 (3.2%)	4 (3.1%)	22 (3.2%)
2	63 (11.3%)	14 (10.9%)	77 (11.2%)
3	85 (15.2%)	20 (15.5%)	105 (15.3%)
4	115 (20.6%)	30 (23.3%)	145 (21.1%)
5	105 (18.8%)	19 (14.7%)	124 (18.1%)
6	066 (11.8%)	17 (13.2%)	83 (12.1%)
7+	103 (18.5%)	25 (19.4%)	128 (18.6%)

^aData as of baseline on July 1, 2022

^bComorbidities: Alzheimer's disease/dementia, angina, back problems, bowel disorder, cancer, cataracts, diabetes, emphysema, glaucoma, heart disease, hypertension, kidney disease, macular degeneration, memory problems, osteoarthritis, osteoporosis, Parkinson's disease, peripheral vascular disease, rheumatoid arthritis, stomach ulcers, stroke, thyroidism, and transient ischemic attack.

Table S2. List of immunosuppressive medications^a

Class	Generic Name(s)	Brand Name(s)
Steroids	prednisone	
	dexamethasone	Decadron
	methylprednisolone	DepoMedrol, SoluMedrol, Medrol
Antimetabolites	cyclophosphamide	Procytox
	leflunomide	Arava
	methotrexate	Trexall, Metoject, Otrexup, Rasuvo, Rheumatrex
	azathioprine	Imuran
	6-mercaptopurine (6-MP)	Purinethol
	mycophenolic acid	Myfortic
	mycophenolate mofetil	Cellcept
Calcineurin inhibitors / mTOR kinase inhibitor	tacrolimus	Prograf, Advagraf, Envarsus PA
	cyclosporine	Neoral, Gengraf, Sandimmune
	sirolimus	Rapamune
JAK (Janus kinase) inhibitors	baricitinib	Olumiant
	tofacitinib	Xeljanz
	upadacitinib	Rinvoq
anti-TNF (tumor necrosis factor)	adalimumab	Humira, Amgevita, Hadlima, Hulio, Hyrimoz, Idacio
	golimumab	Simponi
	certolizumab pegol	Cimzia
	etanercept	Enbrel, Brenzys, Erelzi
	infliximab	Remicade, Avsola, Inflectra, Remsima, Renflexis
Anti-inflammatory	sulfasalazine	Salazopyrin, Azulfidine
	5-Aminosalicylic Acid (ASA) / mesalamine	Pentasa
Anti-CD20	rituximab	Rituxan, Ruxience, Riximyo, Truxima, Riabni
	ocrelizumab	Ocrevus
IL-1 RA (interleukin-1 receptor antagonist)	anakinra	Kineret
	canakinumab	Ilaris
Anti-IL6	tocilizumab	Actemra
	sarilumab	Kevzara
Anti-IL12/IL23	ustekinumab	Stelara
Anti-IL17	secukinumab	Cosentyx
	ixekizumab	Taltz
Anti-IL17R	brodalumab	Siliq
Anti-BLyS	belimumab	Benlysta
Anti-IL23	guselkumab	Tremfya
	risankizumab	Skyrizi
Selective T-cell costimulation blocker	abatacept	Orencia
S1PR (sphingosine 1-phosphate receptor) agonist	fingolimod	Gilenya
	siponimod	Mayzent
	ozanimod	Zeposia
Phosphodiesterase inhibitors	apremilast	Otezla
Anti-integrin	vedolizumab	Entyvio

^aImmunosuppressive medications likely to affect SARS-CoV-2 vaccination responses were identified from guidelines of the Ontario Ministry of Health: <https://www.phsd.ca/wp-content/uploads/2021/10/Guide-to-Verifying-Immunosuppressant-Prescriptions-for-Third-Doses-2021-10-15-FINAL.pdf>.

Table S3. Summary of participants taking immunosuppressive medications

Class	Generic Name(s)	Number of Participants^a
Steroids	prednisone	9
	methylprednisolone	7
	dexamethasone	3
Antimetabolites	methotrexate	5
	mycophenolate mofetil	1
	leflunomide	3
Calcineurin inhibitors / mTOR kinase inhibitor	tacrolimus	2
Anti-IL23	guselkumab	1
JAK (Janus kinase) inhibitors	tofacitinib	1
Anti-inflammatory	5-Aminosalicylic Acid (ASA) / mesalamine	1

^aFour participants were taking more than one immunosuppressive medication.

Table S4. Analysis of maximum likelihood estimates of risk of SARS-CoV-2 Omicron infection between July 1 and September 13, 2022

Parameter	Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
Age (years)	-0.004	0.009	0.183	0.67	1.00	0.98	1.01
Female vs Male	-0.005	0.190	0.001	0.98	1.00	0.69	1.44
(0-8 days) Prior Omicron infection vs Never Infected	0.778	0.888	0.768	0.38	2.18	0.38	12.42
(9-29 days) Prior Omicron Infection vs Never Infected	3.864	0.356	117.860	<0.0001	47.67	23.73	95.76
(30-75 days) Prior Omicron Infection vs Never Infected	0.512	0.626	0.667	0.41	1.67	0.49	5.69
Pre-Omicron Infection vs Never Infected	0.341	0.390	0.765	0.38	1.41	0.66	3.02
Multiple Pre-Omicron Infections vs Never Infected	-0.644	0.605	1.133	0.29	0.53	0.16	1.72
mRNA-1273 x4 vs BNT162b2 x4	0.382	0.395	0.933	0.33	1.47	0.68	3.18
Other mRNA combination x4 vs BNT162b2 x4	-0.725	0.318	5.196	0.023	0.49	0.26	0.90
Retirement Home vs Long-Term Care Home	-0.525	0.534	0.967	0.33	0.59	0.21	1.69
Number of Residence Outbreaks prior to July 1 2022 (>6 vs ≤6)	-0.055	0.476	0.013	0.91	0.95	0.37	2.41
Clinical Frailty Scale: 6 vs <6 ^a	0.003	0.511	0.00004	0.99	1.00	0.37	2.73
Clinical Frailty Scale: >6 vs <6 ^a	0.241	0.487	0.245	0.62	1.27	0.49	3.31
Clinical Frailty Scale: Missing vs <6 ^a	0.100	0.580	0.030	0.86	1.11	0.36	3.44
Time since fourth vaccination (days)	0.001	0.003	0.181	0.67	1.00	1.00	1.01

^aClinical Frailty Scale was not available for all participants, so a 'missing' variable was integrated into the regression analysis. This analysis was also repeated in a subset of participants with complete CFS information, with similar observations, shown in Supplementary Table S5 and Supplementary Figure S1.

Table S5. Analysis of maximum likelihood estimates of risk of SARS-CoV-2 Omicron infection between July 1 and September 13, 2022 – complete frailty dataset

Parameter	Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
Age (years)	-0.012	0.010	1.578	0.21	0.99	0.97	1.01
Female vs Male	0.032	0.200	0.026	0.87	1.03	0.70	1.53
(0-8 days) Prior Omicron infection vs Never Infected	0.207	1.174	0.031	0.86	1.23	0.12	12.28
(9-29 days) Prior Omicron Infection vs Never Infected	3.948	0.385	105.066	<0.0001	51.81	24.36	110.22
(30-75 days) Prior Omicron Infection vs Never Infected	0.755	0.638	1.401	0.237	2.13	0.61	7.43
Pre-Omicron Infection vs Never Infected	0.020	0.483	0.002	0.967	1.02	0.40	2.63
Multiple Pre-Omicron Infections vs Never Infected	-0.573	0.609	0.884	0.347	0.56	0.17	1.86
mRNA-1273 x4 vs BNT162b2 x4	0.525	0.424	1.535	0.215	1.69	0.74	3.88
Other mRNA combination x4 vs BNT162b2 x4	-0.604	0.337	3.215	0.073	0.55	0.28	1.06
Retirement Home vs Long-Term Care Home	-0.244	0.635	0.148	0.700	0.78	0.23	2.72
Number of Residence Outbreaks prior to July 1 2022 (>6 vs ≤6)	-0.348	0.576	0.364	0.546	0.71	0.23	2.19
Clinical Frailty Scale: 6 vs <6	-0.156	0.525	0.089	0.766	0.86	0.31	2.39
Clinical Frailty Scale: >6 vs <6	0.051	0.500	0.010	0.919	1.05	0.40	2.80
Time since fourth vaccination (days)	-0.001	0.003	0.062	0.804	1.00	0.99	1.01

Table S6. Immune analysis cohort demographics by early Omicron SARS-CoV-2 infection history^a

Pre-July 1, 2022 Infection Status	No Prior Infection	Early Omicron Infection	P ^b
N	255	63	
Time since early Omicron infection to blood draw (days)			
Mean (SD)	..	92 (45)	..
Median (IQR)	..	101 (55 – 127)	..
Time from blood draw to observation period (days)			
Mean (SD)	50 (25)	46 (27)	..
Median (IQR)	51 (31 – 74)	52 (22 – 59)	0.54
Observation Period Infection Outcome – N (%)			
No Omicron Infection	227 (89.0%)	26 (41.3%)	<0.0001
Omicron Infection	28 (11.0%)	37 (58.7%)	
Age (years)			
Mean (SD)	84.2 (9.9)	84.5 (8.7)	..
Median (IQR)	86.8 (80.0 – 91.0)	86.2 (80.3 – 91.8)	0.86
Sex – N (%)			
Female	176 (69.0%)	40 (63.5%)	0.40
Male	79 (31.0%)	23 (36.5%)	
Four-dose mRNA vaccine combination – N (%)			
mRNA1273 x4	83 (32.5%)	5 (7.9%)	<0.0001
BNT162b2 x4	126 (49.4%)	27 (42.9%)	
Other mRNA x4	46 (18.0%)	31 (49.2%)	
Time since fourth vaccination to July 1, 2022 baseline (days)^c			
Mean (SD)	147 (23)	119 (47)	..
Median (IQR)	155 (141 – 158)	127 (50 – 161)	0.0009
Time since last vaccination to blood draw (days)^c			
Mean (SD)	98.6 (25.2)	137.0 (67.3)	..
Median (IQR)	97.0 (79.0 – 113.0)	111.0 (84.0 – 244.0)	0.0008
Residence type – N (%)			
Long-term care residence	130 (51.0%)	42 (66.7%)	0.025
Retirement residence	125 (49.0%)	21 (33.3%)	
Residence outbreaks – N			
Mean (SD)	6.6 (2.0)	6.4 (1.9)	..
Median (IQR)	6.0 (5.0 – 7.0)	6.0 (5.0 – 7.0)	0.34
Participants in residences with outbreaks - N (%)			
≤ 6 (N)	170 (66.7%)	43 (68.3%)	0.81
> 6 (N)	85 (33.3%)	20 (31.7%)	
Clinical Frailty Scale^d			
Missing (N)	49	4	..
Mean (SD)	6.3 (1.3)	6.4 (1.1)	..
Median (IQR)	7.0 (6.0 – 7.0)	7.0 (6.0 – 7.0)	0.83
Clinical Frailty Scale – number of participants – N (%)^d			
CFS <6 (N)	40 (19.4%)	10 (16.9%)	0.85
CFS 6 (N)	45 (21.8%)	12 (20.3%)	
CFS >6 (N)	121 (58.7%)	37 (62.7%)	
Comorbidities – N^e			
Missing (N)	17	1	..
Mean (SD)	4.4 (2.2)	5.0 (2.3)	..
Median (IQR)	4.0 (3.0 – 6.0)	5.0 (3.0 – 7.0)	0.086
Immunosuppressive medication use – N (%)^f			
Missing (N)	47	8	..
No	193 (92.8%)	52 (94.6%)	0.65
Yes	15 (7.2%)	3 (5.5%)	

^aAs of baseline on July 1, 2022, with the exception of age and time since vaccination to blood draw, which were calculated as of blood collection date, between April 1 and June 30, 2022. Residence outbreaks and Clinical Frailty Scale are reported as absolute values and groups of participants.

^bData were assessed by non-parametric Mann-Whitney U-test for two-group comparisons of continuous variables including CFS and by Chi-square test for categorical variables.

^cAll participants had four mRNA vaccine vaccinations at the start of the observation window on July 1, 2022. Some participants received their fourth dose between the blood collection date and the start of the observation window.

^dThe Clinical Frailty Scale is a 9-point scale from 1 (very fit) to 9 (terminally ill). Data are reported as the CFS and by grouping participants with a CFS <6 (very fit to living with mild frailty), 6 (living with moderate frailty), and >6 (living with severe frailty to terminally ill).

^eIncidence of comorbidities is also summarized in Supplementary Table S7. List of comorbidities: Alzheimer's disease/dementia, angina, back problems, bowel disorder, cancer, cataracts, diabetes, emphysema, glaucoma, heart disease, hypertension, kidney disease, macular degeneration, memory problems, osteoarthritis, osteoporosis, Parkinson's disease, peripheral vascular disease, rheumatoid arthritis, stomach ulcers, stroke, thyroidism, and transient ischemic attack.

^fNumber of participants prescribed immunosuppressive medications; a list of medications is provided in Supplementary Table S2.

Table S7. Immune analysis cohort comorbidities by early Omicron SARS-CoV-2 infection history and observation period outcome^a

Infection outcome	No Prior Infection			Prior Omicron Infection		
	No Infection	Omicron Infection	Total	No Infection	Omicron Infection	Total
Participants (N)	212	26	238	25	37	62
Missing (N)	15	2	17	1	0	1
Number of Comorbidities – N (%)						
0	1 (0.05%)	0 (0.0%)	1 (0.004%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1	13 (6.1%)	1 (3.8%)	14 (5.9%)	3 (12.0%)	1 (2.7%)	4 (6.5%)
2	30 (14.2%)	4 (15.4%)	34 (14.3%)	0 (0.0%)	2 (5.4%)	2 (3.2%)
3	33 (15.6%)	5 (19.2%)	38 (16.0%)	5 (20.0%)	7 (18.9%)	12 (19.4%)
4	40 (18.9%)	8 (30.7%)	48 (20.2%)	5 (20.0%)	7 (18.9%)	12 (19.4%)
5	40 (18.9%)	2 (7.7%)	42 (17.6%)	4 (16.0%)	6 (16.2%)	10 (16.1%)
6	21 (9.9%)	2 (7.7%)	23 (9.7%)	0 (0.0%)	6 (16.2%)	6 (9.7%)
7+	34 (16.0%)	4 (15.4%)	38 (16.0%)	8 (32.0%)	8 (21.6%)	16 (25.8%)

^aComorbidities: Alzheimer's disease/dementia, angina, back problems, bowel disorder, cancer, cataracts, diabetes, emphysema, glaucoma, heart disease, hypertension, kidney disease, macular degeneration, memory problems, osteoarthritis, osteoporosis, Parkinson's disease, peripheral vascular disease, rheumatoid arthritis, stomach ulcers, stroke, thyroidism, and transient ischemic attack.

Table S8. Immune analysis cohort demographics by early Omicron SARS-CoV-2 infection history and observation period outcome^a

Observation Period Infection Outcome	No Prior Infection N=255			Prior Omicron Infection N=63		
	No Infection	Omicron Infection	P	No Infection	Omicron Infection	P ^b
N	227	28	..	26	37	..
Time since blood draw to July 1, 2022 baseline (days)						
Mean (SD)	50 (25)	53 (23)	..	41 (29)	50 (26)	..
Median (IQR)	50 (31 – 74)	58 (37 – 75)	0.41	43 (22 – 56)	57 (33 – 59)	0.095
Time since early Omicron infection to blood draw (days)						
Mean (SD)	99 (50)	87 (42)	..
Median (IQR)	105 (49 – 139)	101 (65 – 108)	0.34
Time from blood draw to Omicron infection (days)						
Mean (SD)	..	96 (23)	67 (27)	..
Median (IQR)	..	96 (89 – 107)	72 (48 – 79)	..
Age (years)						
Mean (SD)	84.6 (9.5)	81.5 (12.7)	..	84.1 (8.1)	84.8 (9.2)	..
Median (IQR)	87.1 (80.5 – 91.1)	86.3 (73.1 – 90.8)	0.43	83.9 (79.1 – 91.2)	86.6 (80.5 – 92.2)	0.61
Sex – N (%)						
Female	156 (68.7%)	20 (71.4%)	0.77	18 (69.2%)	22 (59.5%)	0.43
Male	71 (31.3%)	8 (28.6%)		8 (30.8%)	15 (40.5%)	
Four-dose mRNA vaccine combination – N (%)						
mRNA1273 x4	63 (27.8%)	20 (71.4%)	<0.0001	1 (3.8%)	4 (10.8%)	0.0099
BNT162b2 x4	122 (53.7%)	4 (14.3%)		17 (65.4%)	10 (27.0%)	
Other mRNA combination x4	42 (18.5%)	4 (14.3%)		8 (30.8%)	23 (62.2%)	
Time since fourth vaccination to baseline (days)^c						
Mean (SD)	147 (24)	149 (10)	..	138 (27)	106 (53)	..
Median (IQR)	155 (140 – 159)	148 (145 – 157)	0.33	150 (117 – 157)	113 (50 – 163)	0.10
Time since last vaccination to blood draw (days)^c						
Mean (SD)	99 (25)	96 (24)	..	97 (27)	165 (73)	..
Median (IQR)	97 (79 – 113)	89 (83 – 120)	0.71	87 (77 – 108)	126 (96 – 244)	0.0001
Residence type – N (%)						
Long-term care	107 (47.2%)	23 (82.1%)	0.0005	10 (38.5%)	32 (86.5%)	<0.0001
Retirement	120 (52.9%)	5 (17.9%)		15 (57.7%)	5 (13.5%)	
Residence outbreaks – N						
Mean (SD)	6.6 (2.0)	6.5 (2.0)	..	7.3 (2.4)	5.7 (1.1)	..
Median (IQR)	6.0 (6.0 – 7.0)	6.0 (5.0 – 7.0)	0.59	6.0 (6.0 – 9.5)	6.0 (5.0 – 6.0)	0.0016
Participants in residences with outbreaks - N (%)						
≤ 6 outbreaks	152 (67.0%)	18 (64.3%)	0.78	11 (42.3%)	32 (86.5%)	0.0002
> 6 outbreaks	75 (33.0%)	10 (35.7%)		15 (57.6%)	5 (13.5%)	
Clinical Frailty Scale^d						
Missing (N)	45	4	..	3	1	..
Mean (SD)	6.3 (1.3)	6.7 (0.8)	..	6.0 (1.2)	6.6 (0.8)	..
Median (IQR)	7.0 (6.0 – 7.0)	7.0 (6.0 – 7.0)	0.14	6.0 (5.0 – 7.0)	7.0 (7.0 – 7.0)	0.0062
Clinical Frailty Scale – number of participants – N (%)^d						
CFS < 6 (N)	38 (20.9%)	2 (8.3%)	0.30	7 (30.4%)	3 (8.3%)	0.0097
CFS = 6 (N)	40 (22.0%)	5 (10.8%)		7 (30.4%)	5 (13.9%)	
CFS > 6 (N)	104 (57.1%)	17 (70.8%)		9 (39.1%)	28 (77.8%)	
Comorbidities - N^e						
Missing (N)	15	2	..	1	0	..
Mean (SD)	4.4 (2.1)	4.3 (2.4)	..	5.0 (2.8)	4.9 (2.0)	..
Median (IQR)	4.0 (3.0 – 6.0)	4.0 (3.0 – 5.3)	0.59	4.0 (3.0 – 7.0)	5.0 (3.0 – 6.0)	0.91
Immunosuppressive medication use – N (%)^f						
Missing	45	2	..	6	2	..
No	167 (91.8%)	26 (100.0%)	..	17 (85.0%)	35 (100.0%)	..
Yes	15 (8.2%)	0 (0.0%)		3 (15.0%)	0 (0.0%)	

^aAs of baseline on July 1, 2022, with the exception of age and time since vaccination to blood draw, which were calculated as of blood collection date, between April 1 and June 30, 2022.

Residence outbreaks and Clinical Frailty Scale are reported as absolute values and groups of participants.

^bData were assessed by non-parametric Mann-Whitney U-test for two-group comparisons of continuous variables including CFS and by Chi-square test for categorical variables.

^cAll participants had four mRNA vaccine vaccinations at the start of the observation window on July 1, 2022. Some participants received their fourth dose between the blood collection date and the start of the observation window.

^dThe Clinical Frailty Scale is a 9-point scale from 1 (very fit) to 9 (terminally ill). Data are reported as the CFS and by grouping participants with a CFS <6 (very fit to living with mild frailty), 6 (living with moderate frailty), and >6 (living with severe frailty to terminally ill).

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^fNumber of participants prescribed immunosuppressive medications; a list of medications is provided in Supplementary Table S2.

Table S9. Humoral and cellular assessments by SARS-CoV-2 Omicron infection history before the observation period^a

	No prior Omicron infection	Prior Omicron infection	Total	P Value
Anti-spike IgG (AU)				
N	176	50	226	..
Mean (SD)	1.58 (1.06)	1.88 (0.97)	1.64 (1.04)	..
Median (IQR)	1.38 (0.55 – 2.75)	2.13 (1.09 – 2.80)	1.65 (0.58 – 2.75)	0.061
Anti-spike IgA (AU)				
N	176	50	226	..
Mean (SD)	0.61 (0.71)	1.33 (1.07)	0.77 (0.85)	..
Median (IQR)	0.32 (0.16 – 0.75)	1.03 (0.31 – 2.31)	0.38 (0.18 – 1.00)	<0.0001
Anti-RBD IgG (AU)				
N	176	50	226	..
Mean (SD)	1.29 (0.85)	2.02 (1.10)	1.45 (0.96)	..
Median (IQR)	1.11 (0.51 – 1.79)	2.41 (0.98 – 2.93)	1.22 (0.53 – 2.23)	<0.0001
Anti-RBD IgA (AU)				
N	176	50	226	..
Mean (SD)	0.60 (0.71)	1.38 (1.11)	0.77 (0.87)	..
Median (IQR)	0.31 (0.21 – 0.61)	1.28 (0.30 – 2.53)	0.37 (0.22 – 0.82)	<0.0001
Ancestral SARS-CoV-2 neutralization (MNT50)				
N	253	63	316	..
Mean (SD)	203 (303)	368 (388)	236 (328)	..
Median (IQR)	80 (40 – 160)	160 (80 – 640)	80 (40 – 320)	<0.0001
Omicron BA.1 SARS-CoV-2 neutralization (MNT50)				
N	253	63	316	..
Mean (SD)	95 (207)	274 (408)	131 (269)	..
Median (IQR)	20 (10 – 80)	80 (40 – 320)	40 (10 – 80)	<0.0001
Ancestral SARS-CoV-2 complete spike memory AIM⁺CD4⁺ T cells (%CD4⁺ T cells)				
N	199	48	247	..
Mean (SD)	3.90 (2.87)	3.47 (2.13)	3.82 (2.74)	..
Median (IQR)	3.34 (1.83-5.18)	3.24 (1.97-4.40)	3.34 (1.83-5.05)	0.65
Ancestral SARS-CoV-2 immunodominant spike memory AIM⁺CD4⁺ T cells (%CD4⁺ T cells)				
N	199	48	247	..
Mean (SD)	3.44 (2.80)	3.21 (2.13)	3.40 (2.68)	..
Median (IQR)	2.50 (1.59 – 4.49)	3.13 (1.48 – 4.39)	2.59 (1.54 – 4.49)	0.89
Omicron BA.1 SARS-CoV-2 complete spike memory AIM⁺CD4⁺ T cells (%CD4⁺ T cells)				
N	167	41	208	..
Mean (SD)	2.78 (2.20)	2.77 (1.76)	2.78 (2.12)	..
Median (IQR)	2.29 (1.29-3.69)	2.35 (1.48-3.51)	2.30 (1.34-3.65)	0.72
Ancestral SARS-CoV-2 complete spike memory AIM⁺CD8⁺ T cells (%CD8⁺ T cells)				
N	192	46	238	..
Mean (SD)	1.08 (1.61)	1.39 (1.71)	1.14 (1.63)	..
Median (IQR)	0.49 (0.18-1.27)	0.64 (0.22-1.85)	0.50 (0.19-1.41)	0.24
Ancestral SARS-CoV-2 immunodominant spike memory AIM⁺CD8⁺ T cells (%CD8⁺ T cells)				
N	192	46	238	..
Mean (SD)	0.48 (1.09)	0.35 (0.56)	0.46 (1.01)	..
Median (IQR)	0.14 (0.00 – 0.40)	0.10 (0.01 – 0.52)	0.13 (0.00 – 0.41)	0.84
Omicron BA.1 SARS-CoV-2 complete spike memory AIM⁺CD8⁺ T cells (%CD8⁺ T cells)				
N	160	39	199	..
Mean (SD)	0.46 (1.14)	0.26 (0.36)	0.42 (1.04)	..
Median (IQR)	0.14 (0.029-0.52)	0.11 (0.014-0.40)	0.14 (0.020-0.48)	0.40

^aImmunological assessments were performed on blood collected between within three months before the start of the observation period.

Table S10. Humoral and cellular assessments in individuals with no prior SARS-CoV-2 Omicron infection by Omicron infection outcome during the observation period^a

	Not infected with Omicron	Infected with Omicron	Total	P Value
Anti-spike IgG (AU)				
N	156	20	176	..
Mean (SD)	1.54 (1.05)	1.87 (1.06)	1.58 (1.06)	..
Median (IQR)	1.34 (0.54 – 2.74)	2.33 (0.73 – 2.82)	1.38 (0.55 – 2.75)	0.19
Anti-spike IgA (AU)				
N	156	20	176	..
Mean (SD)	0.61 (0.70)	0.66 (0.84)	0.61 (0.71)	..
Median (IQR)	0.34 (0.16 – 0.75)	0.28 (0.16 – 0.76)	0.32 (0.16 – 0.75)	0.97
Anti-RBD IgG (AU)				
N	156	20	176	..
Mean (SD)	1.26 (0.84)	1.51 (0.95)	1.29 (0.85)	..
Median (IQR)	1.10 (0.50 – 1.78)	1.30 (0.80 – 2.42)	1.11 (0.51 – 1.79)	0.26
Anti-RBD IgA (AU)				
N	156	20	176	..
Mean (SD)	0.59 (0.70)	0.66 (0.81)	(0.60 – 0.71)	..
Median (IQR)	0.31 (0.22 – 0.60)	0.33 (0.19 – 0.77)	0.31 (0.21 – 0.61)	0.91
Ancestral SARS-CoV-2 neutralization (MNT50)				
N	225	28	253	..
Mean (SD)	199 (297)	231 (354)	203 (303)	..
Median (IQR)	80 (40 – 160)	80 (20 – 240)	80 (40 – 160)	0.73
Omicron BA.1 SARS-CoV-2 neutralization (MNT50)				
N	225	28	253	..
Mean (SD)	99 (217)	58 (86)	95 (207)	..
Median (IQR)	20 (10 – 80)	20 (5 – 80)	20 (10 – 80)	0.44
Ancestral SARS-CoV-2 complete spike memory AIM⁺CD4⁺ T cells (%CD4⁺ T cells)				
N	177	22	199	..
Mean (SD)	3.92 (2.89)	3.73 (2.76)	3.90 (2.87)	..
Median (IQR)	3.43 (1.85-5.23)	3.16 (1.64-4.85)	3.34 (1.83-5.18)	0.75
Ancestral SARS-CoV-2 immunodominant spike memory AIM⁺CD4⁺ T cells (%CD4⁺ T cells)				
N	177	22	199	..
Mean (SD)	3.47 (2.83)	3.24 (2.53)	3.44 (2.80)	..
Median (IQR)	2.47 (1.60 – 4.52)	2.68 (1.55 – 4.08)	2.50 (1.59 – 4.49)	0.85
Omicron BA.1 SARS-CoV-2 complete spike memory AIM⁺CD4⁺ T cells (%CD4⁺ T cells)				
N	150	17	157	..
Mean (SD)	2.82 (2.21)	2.48 (2.16)	2.78 (2.20)	..
Median (IQR)	2.33 (2.40-2.85)	1.89 (0.99-3.61)	2.29 (1.29-3.69)	0.35
Ancestral SARS-CoV-2 complete spike memory AIM⁺CD8⁺ T cells (%CD8⁺ T cells)				
N	171	21	192	..
Mean (SD)	1.07 (1.59)	1.15 (1.81)	1.08 (1.61)	..
Median (IQR)	0.64 (0.22-1.85)	0.28 (0.18-1.56)	0.49 (0.18-1.27)	0.69
Ancestral SARS-CoV-2 immunodominant spike memory AIM⁺CD8⁺ T cells (%CD8⁺ T cells)				
N	171	21	192	..
Mean (SD)	0.48 (1.12)	0.44 (0.72)	0.48 (1.09)	..
Median (IQR)	0.14 (0.00 – 0.38)	0.25 (0.01 – 0.44)	0.14 (0.00 – 0.40)	0.45
Omicron BA.1 SARS-CoV-2 complete spike memory AIM⁺CD8⁺ T cells (%CD8⁺ T cells)				
N	144	16	160	..
Mean (SD)	0.48 (1.19)	0.34 (0.505)	0.46 (1.14)	..
Median (IQR)	0.15 (0.029-0.55)	0.11 (0.01-0.44)	0.14 (0.029-0.52)	0.63

^aImmunological assessments were performed on blood collected between within three months before the start of the observation period.

Table S11. Humoral and cellular assessments in individuals with prior Omicron infection by SARS-CoV-2 Omicron infection outcome during the observation period^a

	Not reinfected with Omicron	Reinfected with Omicron	Total	P Value
Anti-spike IgG (AU)				
N	22	28	50	..
Mean (SD)	2.04 (0.71)	1.75 (1.13)	1.88 (0.97)	..
Median (IQR)	2.13 (1.36 – 2.87)	1.96 (0.39 – 2.77)	2.13 (1.09 – 2.80)	0.62
Anti-spike IgA (AU)				
N	22	28	50	..
Mean (SD)	1.84 (0.92)	1.03 (1.12)	1.38 (1.11)	..
Median (IQR)	2.09 (0.98 – 2.69)	0.41 (0.18 – 1.86)	1.28 (0.30 – 2.53)	0.0072
Anti-RBD IgG (AU)				
N	22	28	50	..
Mean (SD)	2.65 (0.64)	1.52 (1.14)	2.02 (1.10)	..
Median (IQR)	2.85 (2.41 – 3.05)	1.25 (0.44 – 2.78)	2.41 (0.98 – 2.93)	0.0009
Anti-RBD IgA (AU)				
N	22	28	50	..
Mean (SD)	1.51 (1.04)	1.19 (1.09)	1.33 (1.07)	..
Median (IQR)	1.35 (0.57 – 2.70)	0.69 (0.20 – 2.09)	1.03 (0.31 – 2.31)	0.099
Ancestral SARS-CoV-2 neutralization (MNT50)				
N	26	37	63	..
Mean (SD)	489 (450)	283 (317)	368 (388)	..
Median (IQR)	320 (160 – 640)	160 (80 – 320)	160 (80 – 640)	0.079
Omicron BA.1 SARS-CoV-2 neutralization (MNT50)				
N	26	37	63	..
Mean (SD)	464 (523)	140 (230)	274 (408)	..
Median (IQR)	160 (80 – 1280)	80 (40 – 160)	80 (40 – 320)	0.0072
Ancestral SARS-CoV-2 complete spike memory AIM⁺CD4⁺ T cells (%CD4⁺ T cells)				
N	17	31	48	..
Mean (SD)	3.54 (2.40)	3.44 (2.01)	3.47 (2.13)	..
Median (IQR)	2.65 (1.96-4.22)	3.52 (1.91-4.71)	3.24 (1.97-4.40)	0.81
Ancestral SARS-CoV-2 immunodominant spike memory AIM⁺CD4⁺ T cells (%CD4⁺ T cells)				
N	17	31	48	..
Mean (SD)	3.13 (1.99)	3.35 (2.41)	3.21 (2.13)	..
Median (IQR)	3.13 (1.47 – 4.53)	3.13 (1.59 – 4.66)	3.13 (1.48 – 4.39)	0.93
Omicron BA.1 SARS-CoV-2 complete spike memory AIM⁺CD4⁺ T cells (%CD4⁺ T cells)				
N	15	26	41	..
Mean (SD)	2.71 (1.60)	2.80 (1.88)	2.77 (1.76)	..
Median (IQR)	2.10 (1.64-4.29)	2.63 (1.42-3.44)	2.35 (1.48-3.51)	0.90
Ancestral SARS-CoV-2 complete spike memory AIM⁺CD8⁺ T cells (%CD8⁺ T cells)				
N	15	31	46	..
Mean (SD)	0.79 (0.79)	1.67 (1.95)	1.39 (1.71)	..
Median (IQR)	0.49 (0.13-1.42)	0.81 (0.22-3.06)	0.64 (0.22-1.85)	0.24
Ancestral SARS-CoV-2 immunodominant spike memory AIM⁺CD8⁺ T cells (%CD8⁺ T cells)				
N	15	31	46	..
Mean (SD)	0.17 (0.31)	0.63 (0.44)	0.35 (0.56)	..
Median (IQR)	0.15 (0.05 – 0.64)	0.01 (0.00 – 0.21)	0.10 (0.01 – 0.52)	0.055
Omicron BA.1 SARS-CoV-2 complete spike memory AIM⁺CD8⁺ T cells (%CD8⁺ T cells)				
N	13	26	39	..
Mean (SD)	0.22 (0.22)	0.28 (0.41)	0.26 (0.36)	..
Median (IQR)	0.15 (0.015-0.44)	0.086 (0.013-0.39)	0.11 (0.014-0.40)	0.78

^aImmunological assessments were performed on blood collected between within three months before the start of the observation period.