

# THE LANCET

## Rheumatology

### Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Risk M, Hayek SS, Schioppa E, et al. COVID-19 vaccine effectiveness against omicron (B.1.1.529) variant infection and hospitalisation in patients taking immunosuppressive medications: a retrospective cohort study. *Lancet Rheumatol* 2022; published online Aug 16. [https://doi.org/10.1016/S2665-9913\(22\)00216-8](https://doi.org/10.1016/S2665-9913(22)00216-8).

# Supplement

## TABLE OF CONTENTS

Identification of Outcomes .....	2
Table S1. Medication List .....	3
Table S2. Medication Frequency Table by Type .....	4
Table S3. Results from Cox Regression for Vaccine Efficacy against Infection, Immunocompetent Individuals .....	5
Table S4. Results from Cox Regression for Vaccine Efficacy against Infection, Immunosuppressed Individuals .....	6
Table S5. Results from Cox Regression for Vaccine Efficacy against Hospitalisation, Immunocompetent Individuals .....	7
Table S6. Results from Cox Regression for Vaccine Efficacy against Hospitalisation, Immunosuppressed Individuals .....	8
Table S7. Results from Cox Regression for Medication Type and Infection Risk .....	9
Table S8. Results from Cox Regression for Medication Type and Hospitalisation Risk .....	10
Table S9. Results from Cox Regression for Vaccine Efficacy against ICU Admission, All Patients .....	11
Table S10. Characteristics of Infected Patients .....	12
Table S11. Characteristics of Hospitalized Patients .....	13
Figure S1. Unweighted Balance for all Covariates .....	14
Figure S2. Weighted Balance for all Covariates .....	15

## **IDENTIFICATION OF OUTCOMES**

### **ICD-10 Code Descriptions**

- U07.1 - COVID-19, Virus identified

### **Infection Criteria**

A patient was identified as having a SARS-CoV-2 infection after full vaccination if they had a positive SAR-CoV-2 PCR laboratory test result or U07.1 ICD-10 code. Where a patient had a positive SARS-CoV-2 PCR laboratory test, the collection date was used as the date of infection. For a reinfection to occur, the collection date or U07.1 code date was required to be:

1. At least 90 days from any previously identified infection
2. At least 14 days from any previous U07.1 code or positive SAR-CoV-2 PCR laboratory test result

The first criterion was used in accordance with CDC guidelines that states that covid-positive individuals should not test for 90 days after initial diagnosis, as many individuals continue to test positive for a long period of time after recovery from COVID-19. The second criterion was used as U07.1 was sometimes incorrectly used on an ongoing basis for patients who were hospitalised with COVID-19 for a substantial period of time.

### **Hospitalization Criteria**

Hospitalisation was determined based on chart reviewed data, only including hospitalisation where COVID-19 was the primary reason for hospitalisation.

**Table S1. Medication List**

<b>Immunosuppressive DMARDs</b>	<b>Immunomodulatory DMARDs</b>	<b>Glucocorticoids</b>
Daclizumab	Imatinib mesylate	Dexamethasone
Ocrelizumab	Nintedanib	Hydrocortisone
Satralizumab	Pirfenidone	Methylprednisolone
Efalizumab	Bosutinib	Prednisolone
Abatacept	Dasatinib	Prednisone
Anifrolumab	Nilotinib	Prednisone delayed-release
Basiliximab	Apremilast	
Belatacept	Sulfasalazine	
Adalimumab	Mesalazine	
Belatacept	Mesalamine	
Belimumab	Olsalazine	
Bimekizumab	Balsalazide	
Brodalumab	5-ASA	
Certolizumab pegol	5-aminosalicylic acid	
Dupilumab	Pomalidomide	
Etanercept	Chloroquine	
Golimumab	Dapsone	
Guselkumab	Hydroxychloroquine	
Infliximab	Lenalidomide	
Ixekizumab	Thalidomide	
Natalizumab		
Risankizumab		
Rituximab		
Sarilumab		
Secukinumab		
Tildrakizumab		
Tocilizumab		
Ustekinumab		
Vedolizumab		
Alemtuzumab		
Ofatumumab		
Belantamab mafodotin		
Daratumumab		
Elotuzumab		
Idecabtagene vicleucel		
Isatuximab		
Mepolizumab		
Anakinra		
Canakinumab		
Avacopan		
Apremilast		
Baricitinib		
Tofacitinib		
Upadacitinib		
Ponatinib		
Penicillamine		
Sodium aurothiomalate		
Azathioprine		
6-mercaptopurine		
Voclosporin		
Carfilzomib		
Bortezomib		
Sirolimus		
Everolimus		
Mycophenolate Mofetil		
Mycophenolic acid		
Tacrolimus		
Cyclophosphamide		
Cyclosporine		
Leflunomide		
Methotrexate		
Doxorubicin		
Melphalan flufenamide		
Panobinostat		
Selinexor		
Melphalan		
Carmustine		

**Table S2. Medication Frequency Table by Type\***

<b>Immunosuppressive DMARDs [No. (%)]</b>	<b>Immunomodulatory DMARDs [No. (%)]</b>	<b>Glucocorticoids [No. (%)]</b>
Methotrexate [753 (19·6)]	Hydroxychloroquine [850 (51·9)]	Prednisone [4428 (72·8)]
Mycophenolate Mofetil [527 (13·7)]	Mesalamine [414 (25·3)]	Dexamethasone [726 (11·9)]
Tacrolimus [412 (10·7)]	Sulfasalazine [222 (13·6)]	Methyl Prednisolone [721 (11·8)]
Azathioprine [379 (9·9)]	Balsalazide [52 (3·2)]	Hydrocortisone [194 (3·2)]
Infliximab [291 (7·6)]	Nintedanib [40 (2·4)]	All Others [16 (0·3)]
Etanercept [178 (4·6)]	Imatinib Mesylate [24 (1·4)]	
Adalimumab [168 (4·4)]	All Others [35 (2·0)]	
Ustekinumab [155 (4·0)]		
Leflunomide [136 (3·5)]		
Vedolizumab [102 (2·7)]		
Rituximab [100 (2·6)]		
Dupilimab [94 (2·5)]		
Tocilizumab [77 (2·0)]		
Cyclosporine [69 (1·8)]		
Tofacitinib [65 (1·7)]		
Ocrelizumab [61 (1·6)]		
Abatacept [48 (1·2)]		
All Others [219 (5·7)]		

\*Medications comprising at least 1% of prescriptions within a given type listed. If a patient had multiple prescriptions for a single medication, only one was counted.

**Table S3. Results from Cox Regression for Vaccine Efficacy against Infection, Immunocompetent Individuals\***

Variable	HR (95% CI)	P-Value	No. Events
Vaccine (Reference Group: Unvaccinated)			(Ref <sup>§</sup> : 908)
- 3 doses mRNA-1273	0.43 (0.38-0.49)	<0.0001	369
- 3 doses BNT162b2	0.65 (0.59-0.71)	<0.0001	1051
- 2 doses mRNA-1273	0.84 (0.74-0.95)	0.0043	367
- 2 doses BNT162b2	1.06 (0.96-1.16)	0.24	1039
Age Range (Reference Group: <31)			(Ref: 820)
- 31-50	1.12 (1.03-1.22)	0.0076	1461
- 51-64	0.81 (0.73-0.89)	<0.0001	823
- 65+	0.61 (1.03-1.23)	<0.0001	630
Race (Reference: White)			(Ref: 2792)
- African-American/Black	1.14 (1.03-1.26)	0.0092	474
- Other	0.88 (0.80-0.98)	0.015	468
Weighted Comorbidity Index (Reference: 0)			(Ref: 3015)
- 1-2	1.03 (0.94-1.14)	0.50	518
- 3-4	1.20 (1.00-1.44)	0.056	130
- 5+	1.03 (0.80-1.31)	0.82	71
Sex=Male (Reference: Female)	0.87 (0.81-0.93)	<0.0001	1309 (Ref: 2425)
Prior Infection=1 (Reference: No Prior Infection)	0.97 (0.86-1.09)	0.57	296 (Ref: 3438)
Prior Visits (Reference: 0)			(Ref: 158)
- 1	1.56 (1.26-1.93)	<0.0001	183
- 2-5	2.26 (1.90-2.69)	<0.0001	845
- 6-10	3.44 (2.88-4.11)	<0.0001	853
- 11+	4.11 (3.42-4.93)	<0.0001	1695
Prior Negative Tests (Reference: 0)			(Ref: 1680)
- 1	1.51 (1.38-1.64)	<0.0001	928
- 2-4	2.12 (1.93-2.32)	<0.0001	890
- 5+	3.57 (3.96-4.15)	<0.0001	236
Transplantation Status=1 (Reference: No Transplant)	1.71 (1.15-2.54)	0.0086	25 (Ref: 3709)

\*Patient population is immunocompetent individuals (N = 162 805). § Ref is used to indicate the reference group.

**Table S4. Results from Cox Regression for Vaccine Efficacy against Infection, Immunosuppressed Individuals**

Variable	HR (95% CI)	P-Value	No. Events
Vaccine (Reference Group: Unvaccinated)			(Ref: 72)
- 3 doses mRNA-1273	0.40 (0.27-0.58)	<0.0001	49
- 3 doses BNT162b2	0.50 (0.36-0.69)	<0.0001	96
- 2 doses mRNA-1273	0.43 (0.26-0.71)	0.0011	19
- 2 doses BNT162b2	0.87 (0.61-1.23)	0.43	57
Age Range (Reference Group: <31)			(Ref: 33)
- 31-50	1.24 (0.83-1.83)	0.29	106
- 51-64	0.88 (0.51-1.18)	0.23	76
- 65+	0.75 (0.48-1.15)	0.19	68
Race (Reference: White)			(Ref: 217)
- African-American/Black	1.19 (0.87-1.63)	0.29	51
- Other	0.96 (0.63-1.45)	0.83	25
Weighted Comorbidity Index (Reference: 0)			(Ref: 118)
- 1-2	1.02 (0.76-1.36)	0.90	103
- 3-4	1.24 (0.83-1.87)	0.29	40
- 5+	1.22 (0.78-1.91)	0.38	32
Sex=Male (Reference: Female)	0.99 (0.78-1.27)	0.94	109 (Ref: 184)
Prior Infection=1 (Reference: No Prior Infection)	1.01 (0.73-1.40)	0.96	46 (Ref: 247)
Prior Visits (Reference: 6-10)*			(Ref: 28)
- 0	1.54 (0.46-5.15)	0.48	3
- 1	0.36 (0.05-2.65)	0.32	1
- 2-5	0.95 (0.52-1.75)	0.88	17
- 11+	1.32 (0.86-2.01)	0.20	244
Prior Negative Tests (Reference: 0)			(Ref: 76)
- 1	1.19 (0.83-1.72)	0.34	53
- 2-4	1.86 (1.34-2.59)	0.00024	102
- 5+	2.55 (1.72-3.78)	<0.0001	62
Transplantation Status=1 (Reference: No Transplant)	1.80 (1.31-2.48)	0.00027	57 (Ref: 236)

\*6-10 coded as reference as very few immunosuppressed individuals had 0 prior visits so interpretation of hazard ratio relative to this group was too uncertain to be meaningful. Patient population is immunosuppressed individuals (N = 5609).

**Table S5. Results from Cox Regression for Vaccine Efficacy against Hospitalisation, Immunocompetent Individuals\***

Variable	HR (95% CI)	P-Value	No. Events
Vaccine (Reference Group: Unvaccinated)			(Ref: 71)
- 3 doses	0.08 (0.05-0.13)	<0.0001	29
- 2 doses	0.32 (0.22-0.47)	<0.0001	44
Age Range (Reference Group: <31)			(Ref: 19)
- 31-50	0.85 (0.47-1.56)	0.62	25
- 51-64	1.49 (0.83-2.69)	0.18	32
- 65+	2.90 (1.64-5.11)	0.00024	68
Race (Reference: White)			(Ref: 96)
- African-American/Black	1.77 (1.14-2.73)	0.011	27
- Other	1.66 (1.03-2.68)	0.038	21
Weighted Comorbidity Index (Reference: 0)			(Ref: 70)
- 1-2	2.10 (1.32-3.32)	0.0016	34
- 3-4	5.22 (3.04-8.95)	<0.0001	26
- 5+	4.22 (2.18-8.17)	<0.0001	14
Sex=Male (Reference: Female)	1.02 (0.73-1.43)	0.91	61 (Ref: 83)
Prior Infection=1 (Reference: No Prior Infection)	0.82 (0.47-1.42)	0.47	15 (Ref: 129)
Prior Visits (Reference: 0)			(Ref: 14)
- 1	0.36 (0.10-1.26)	0.11	3
- 2-5	0.50 (0.23-1.10)	0.086	12
- 6-10	1.07 (0.51-2.27)	0.86	18
- 11+	2.17 (1.06-4.48)	0.035	97
Prior Negative Tests (Reference: 0)			(Ref: 55)
- 1	1.35 (0.82-2.21)	0.24	30
- 2-4	1.63 (0.98-2.70)	0.059	35
- 5+	3.97 (2.20-7.16)	<0.0001	24
Transplantation Status=1 (Reference: No Transplant)	4.77 (2.05-11.07)	0.00028	6 (Ref: 138)

\*Patient population is immunocompetent individuals (N = 162 805).



**Table S6. Results from Cox Regression for Vaccine Efficacy against Hospitalisation, Immunosuppressed Individuals\***

Variable	HR (95% CI)	P-Value	No. Events
Vaccine (Reference Group: Unvaccinated)			(Ref: 21)
- 3 doses	0.13 (0.07-0.26)	<0.0001	19
- 2 doses	0.15 (0.06-0.38)	<0.0001	6
Age >= 65 (Reference Group: <65)	2.51 (1.33-4.74)	0.0044	21 (Ref: 25)
Race=African-American/Black (Reference: All Others)	2.35 (1.23-4.50)	0.010	14 (Ref: 32)
Prior Visits >= 15 (Reference: <15)	3.23 (1.20-8.70)	0.021	41 (Ref: 5)
PriorTest >= 1 (Reference: 0)	3.45 (1.29-9.19)	0.013	41 (Ref: 5)
Transplantation Status=1 (Reference: No Transplant)	3.82 (2.08-7.02)	<0.0001	17 (Ref: 29)
Sex=Male (Reference: Female)	0.93 (0.51-1.71)	0.83	19 (Ref: 27)

\*Covariate categories simplified due to difficulties with estimation given lower sample size (number of events). Patient population is immunosuppressed individuals (N = 5609).

**Table S7. Results from Cox Regression for Medication Type and Infection Risk**

Variable	HR (95% CI)	P-Value	No. Events
Medication (Reference Group: No Medication)			(Ref: 3734)
- Glucocorticoid	1.48 (1.21-1.80)	0.00013	104
- Immunosuppressive DMARD	1.39 (1.13-1.72)	0.0022	97
- Immunomodulatory DMARD	1.04 (0.72-1.49)	0.85	29
- Combination	1.58 (1.21-2.06)	0.00077	63
Vaccine (Reference Group: Unvaccinated)			(Ref: 980)
- 3 doses mRNA-1273	0.43 (0.39-0.49)	<0.0001	418
- 3 doses BNT162b2	0.64 (0.58-0.70)	<0.0001	1147
- 2 doses mRNA-1273	0.80 (0.71-0.90)	0.00026	386
- 2 doses BNT162b2	1.04 (0.96-1.14)	0.34	1096
Age Range (Reference Group: <31)			(Ref: 853)
- 31-50	1.13 (1.04-1.23)	0.0043	1567
- 51-64	0.80 (0.73-0.88)	<0.0001	899
- 65+	0.62 (0.55-0.69)	<0.0001	708
Race (Reference: White)			(Ref: 3009)
- African-American/Black	1.14 (1.04-1.25)	0.0067	525
- Other	0.89 (0.81-0.98)	0.015	493
Weighted Comorbidity Index (Reference: 0)			(Ref: 3133)
- 1-2	1.03 (0.93-1.13)	0.59	621
- 3-4	1.20 (1.01-1.41)	0.035	170
- 5+	1.06 (0.86-1.30)	0.61	103
Sex=Male (Reference: Female)	0.88 (0.82-0.94)	0.00013	1418 (Ref: 2609)
Prior Infection=1 (Reference: No Prior Infection)	0.97 (0.86-1.08)	0.56	342 (Ref: 3685)
Prior Visits (Reference: 0)			(Ref: 161)
- 1	1.54 (1.24-1.90)	<0.0001	184
- 2-5	2.26 (1.90-2.68)	<0.0001	862
- 6-10	3.42 (2.87-4.08)	<0.0001	881
- 11+	4.10 (3.43-4.90)	<0.0001	1939
Prior Negative Tests (Reference: 0)			(Ref: 1756)
- 1	1.49 (1.37-1.62)	<0.0001	981
- 2-4	2.11 (1.92-2.31)	<0.0001	992
- 5+	3.40 (2.95-3.91)	<0.0001	298
Transplantation Status=1 (Reference: No Transplant)	1.70 (1.33-2.18)	<0.0001	82 (Ref: 3945)

**Table S8. Results from Cox Regression for Medication Type and Hospitalisation Risk**

Variable	HR (95% CI)	P-Value	No. Events
Medication (Reference Group: No Medication)			(Ref: 144)
- Glucocorticoid	2.93 (1.77-4.86)	<0.0001	19
- Immunosuppressive DMARD	2.32 (1.23-4.38)	0.0097	14
- Immunomodulatory DMARD	2.02 (0.64-6.37)	0.23	3
- Combination	1.90 (0.90-4.01)	0.09	10
Vaccine (Reference Group: Unvaccinated)			(Ref: 92)
- 3 doses mRNA-1273	0.08 (0.04-0.14)	<0.0001	15
- 3 doses BNT162b2	0.11 (0.07-0.16)	<0.0001	33
- 2 doses mRNA-1273	0.21 (0.12-0.37)	<0.0001	14
- 2 doses BNT162b2	0.33 (0.22-0.49)	<0.0001	36
Age Range (Reference Group: <31)			(Ref: 21)
- 31-50	1.05 (0.61-1.81)	0.86	36
- 51-64	1.63 (0.95-2.80)	0.077	44
- 65+	3.23 (1.91-5.47)	<0.0001	89
Race (Reference: White)			(Ref: 125)
- African-American/Black	1.84 (1.28-2.65)	0.0010	41
- Other	1.51 (0.97-2.35)	0.067	24
Weighted Comorbidity Index (Reference: 0)			(Ref: 82)
- 1-2	1.86 (1.24-2.79)	0.0027	49
- 3-4	4.05 (2.52-6.51)	<0.0001	39
- 5+	2.90 (1.63-5.17)	0.0010	20
Sex=Male (Reference: Female)	1.01 (0.75-1.35)	0.96	80 (Ref: 110)
Prior Infection=1 (Reference: No Prior Infection)	0.89 (0.57-1.39)	0.62	24 (Ref: 166)
Prior Visits (Reference: 0)			(Ref: 14)
- 1	0.48 (0.16-1.46)	0.19	4
- 2-5	0.48 (0.22-1.05)	0.068	12
- 6-10	1.11 (0.54-2.28)	0.78	21
- 11+	2.10 (1.05-4.21)	0.036	139
Prior Negative Tests (Reference: 0)			(Ref: 60)
- 1	1.50 (0.95-2.37)	0.079	37
- 2-4	1.91 (1.21-3.01)	0.0051	49
- 5+	4.78 (2.90-7.90)	<0.0001	44
Transplantation Status=1 (Reference: No Transplant)	3.52 (2.01-6.16)	<0.0001	23 (Ref: 167)

**Table S9. Results from Cox Regression for Vaccine Efficacy against ICU Admission, All Patients\***

Variable	HR (95% CI)	P-Value	No. Events
Vaccine (Reference Group: Unvaccinated)			(Ref: 16)
- 3 doses	0.09 (0.03-0.25)	<0.0001	6
- 2 doses	0.08 (0.02-0.34)	0.00065	2
Age >= 65 (Reference Group: <65)	3.82 (1.58-9.19)	0.00028	12 (Ref: 12)
Comorbidity Index >= 1 (Reference: 0)	3.99 (1.66-9.60)	0.00020	10 (Ref: 14)

\*Covariate categories simplified due to difficulties with estimation given lower sample size (number of events).

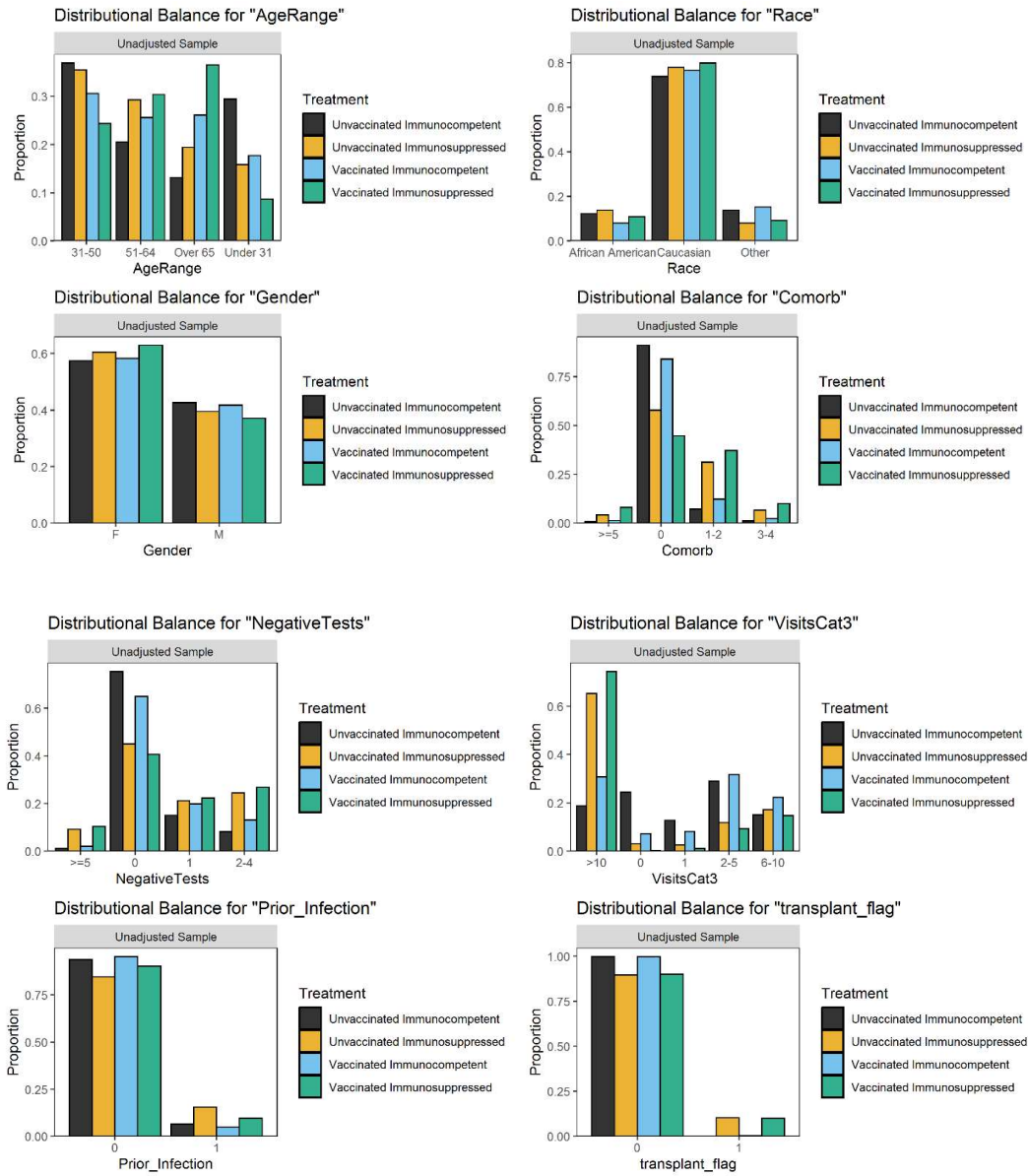
**Table S10. Characteristics of Infected Patients**

	Immunocompetent (N=3930)		Immunosuppressed (N=315)	
	Unvaccinated (N=872)	Vaccinated (N=3058)	Unvaccinated (N=73)	Vaccinated (N=242)
Age Median (IQR)	42 (30-57)	45 (32-59)	51 (36-59)	53 (40-67)
Sex No. (%)				
- Male	295 (34)	1069 (35)	29 (40)	87 (36)
- Female	577 (66)	1989 (65)	44 (60)	155 (64)
Race No. (%)				
- Caucasian	640 (73)	2327 (76)	47 (64)	188 (78)
- African American	173 (20)	340 (11)	20 (27)	35 (14)
- Asian	21 (2)	243 (8)	3 (4)	7 (3)
- American Indian or Alaska Native	0 (0)	13 (0.4)	0 (0)	0 (0)
- Native Hawaiian and Other Pacific Islander	2 (0.2)	2 (0.1)	0 (0)	0 (0)
- Other	36 (4)	133 (4)	3 (4)	12 (5)
Weighted Comorbidity Index				
- 0	739 (85)	2432 (80)	42 (58)	84 (35)
- 1-2	102 (12)	448 (15)	20 (27)	94 (39)
- 3-4	23 (3)	114 (4)	9 (12)	34 (14)
- ≥5	8 (1)	64 (2)	2 (3)	30 (12)
Medication Type No. (%)				
- None	872 (100)	3058 (100)	NA	NA
- Glucocorticoid	NA	NA	34 (47)	80 (33)
- Immunosuppressive DMARD	NA	NA	19 (26)	83 (34)
- Immunomodulatory DMARD	NA	NA	4 (5)	26 (11)
- Multiple Types	NA	NA	16 (22)	53 (22)
Transplantation Patients No. (%)	4 (0.5)	21 (0.6)	13 (18.0)	48 (20.0)

**Table S11. Characteristics of Hospitalised Patients**

	Immunocompetent (N=156)		Immunosuppressed (N=47)	
	Unvaccinated (N=62)	Vaccinated (N=94)	Unvaccinated (N=20)	Vaccinated (N=27)
Age Median (IQR)	53 (33-68)	69 (53-79)	54 (46-65)	68 (54-74)
Sex No. (%)				
- Male	20 (32)	43 (46)	8 (40)	11 (41)
- Female	42 (68)	51 (54)	12 (60)	16 (59)
Race No. (%)				
- Caucasian	40 (65)	67 (71)	8 (40)	21 (78)
- African American	14 (23)	16 (17)	10 (50)	5 (19)
- Asian	2 (3)	3 (3)	2 (10)	1 (4)
- American Indian or Alaska Native	0 (0)	1 (1)	0 (0)	0 (0)
- Native Hawaiian and Other Pacific Islander	0 (0)	0 (0)	0 (0)	0 (0)
- Other	6 (10)	7 (7)	0 (0)	0 (0)
Weighted Comorbidity Index				
- 0	42 (68)	31 (33)	8 (40)	4 (15)
- 1-2	14 (23)	25 (27)	6 (30)	10 (37)
- 3-4	6 (10)	24 (26)	5 (25)	8 (30)
- ≥5	0 (0)	14 (15)	1 (5)	5 (19)
Medication Type No. (%)				
- None	62 (100)	94 (100)	NA	NA
- Glucocorticoid	NA	NA	10 (50)	10 (37)
- Immunosuppressive DMARD	NA	NA	3 (15)	11 (41)
- Immunomodulatory DMARD	NA	NA	1 (5)	2 (7)
- Multiple Types	NA	NA	6 (30)	4 (15)
Transplantation Patients No. (%)	2 (3.2)	4 (4.3)	7 (35.0)	10 (37.0)

**Figure S1. Unweighted Balance for all Covariates**



**Figure S2. Weighted Balance for all Covariates**

