Additional Methods

NCRAS Rare Autoimmune Rheumatic Disease Cohort selection for invitation to the MELODY study

Inclusion criteria:

Patients aged ≥18 years on Nov 15, 2021 and resident in England who had a probable diagnosis of either anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis or lupus or myositis or scleroderma or giant cell arteritis and were identified by the National Disease Registration Service (NDRS) using the following algorithms applied to Hospital Episode Statistics data. National data opt outs and NDRS opt outs were applied.

At least two ordinary or day case admissions in Hospital Episode Statistics (HES) between Apr 1, 2017 and Aug 31, 2021with diagnostic codes indicating one of the above diagnoses (see ICD-10 codes in table 1) AND EITHER

1. An admission between Apr 1, 2019 and Aug 31, 2021 indicating the administration of either rituximab or belimumab (OPCS code X921 or X951)

OR

2. At least one renal, respiratory or rheumatology outpatient clinic appointment (treatment function codes Rheumatology: 410, Respiratory: 340, Renal: 361) between Apr 1, 2019 and Aug 31, 2021.

Table 1 ICD-10 codes and description[1]

Condition	**ICD-10 code**	**Description**
AAV	M301	Polyarteritis with lung involvement [Churg-Strauss]
AAV	M313	Wegener granulomatosis
AAV	M317	Microscopic polyangiitis
Lupus	M321	Systemic lupus erythematosus with organ or system involvement
Lupus	M328	Other forms of systemic lupus erythematosus
Lupus	M329	Systemic lupus erythematosus, unspecified
Myositis	M332	Polymyositis
Myositis	M609	Myositis, unspecified
Myositis	M608	Other myositis
Myositis	M331	Other dermatomyositis
Myositis	M339	Dermatopolymyositis, unspecified
Myositis	M360	Dermato(poly)myositis in neoplastic disease
Scleroderma	M340	Progressive systemic sclerosis
Scleroderma	M341	CR(E)ST syndrome
Scleroderma	M348	Other forms of systemic sclerosis
Scleroderma	M349	Systemic sclerosis, unspecified
Giant Cell Arteritis	M315	Giant cell arteritis with polymyalgia rheumatica
Giant Cell Arteritis	M316	Other giant cell arteritis

References:

1. Peach E, Rutter M, Lanyon P, Grainge MJ, Hubbard R, Aston J, et al. Risk of death among

people with rare autoimmune diseases compared with the general population in England during the 2020 COVID-19 pandemic. Rheumatol. 2021;60(4):1902–9.

NCRAS Blood Cancer Cohort selection for invitation to the MELODY study

Inclusion criteria:

Patients aged ≥18 years and resident in England at the time of diagnosis who were registered in the National Cancer Registration Dataset [1] in 2019 or in the Rapid Cancer Registration Dataset [2] in 2020 or 2021 with a diagnosis of lymphoma or multiple myeloma (see definition below).

Table 1 ICD-O-3 codes and description [3]

ICD-O code	Description
9665/3	Hodgkin lymphoma, nodular sclerosis, grade 1
9667/3	Hodgkin lymphoma, nodular sclerosis, grade 2
9652/3	Hodgkin lymphoma, mixed cellularity, NOS
9650/3	Hodgkin lymphoma, NOS
9695/3	Follicular lymphoma, grade 1
9691/3	Follicular lymphoma, grade 2
9698/3	Follicular lymphoma, grade 3
9690/3	Follicular lymphoma, NOS
9699/3	Marginal zone B-cell lymphoma, NOS
9671/3	Malignant lymphoma, lymphoplasmacytic
9761/3	Waldenstrom macroglobulinaemia
9673/3	Mantle cell lymphoma
9689/3	Splenic marginal zone B-cell lymphoma (C42.2)
9679/3	Mediastinal large B-cell lymphoma (C38.3)
9680/3	Malignant lymphoma, large B-cell, diffuse, NOS
9823/3	B-cell chronic lymphocytic leukaemia/small lymphocytic lymphoma
9732/3	Multiple myeloma C42.1

Data fields extracted

- NHSNUMBER
- BIRTHDATEBEST (Date of birth)
- FORENAME
- SURNAME
- TUMOURID
- ICD03_REV2011 (ICD-O-3 morphology codes [3])

References:

1. Henson KE, Elliss-Brookes L, Coupland VH, et al. Data Resource Profile: National Cancer Registration Dataset in England. Int J Epidemiol. 2020; 49(1):16-16h.
2. http://www.ncin.org.uk/collecting_and_using_data/rcrd#:~:text=Rapid%20Cancer%20Registration%20Dataset%20The%20Rapid%20Cancer%20Registration,the%20most%20recently%20available%20data%20on%20cancer%20diagnoses.
3. World Health Organization. International Classification of Diseases for Oncology (ICD-O), First Revision. 3rd edn. Geneva: World Health Organization

Questionnaire response data processing

The raw LM and RAD self-report data was pre-processed prior to the analysis. This involved three main cleaning steps: mapping free-text responses, grouping categories and applying hierarchy to treatment and diagnoses.

Multiple free-text fields were present in the questionnaire allowing respondents to describe 'other' vaccine types, treatments and diagnoses outside of the available options. Many of these included synonyms, descriptive text and misspellings of options that should have been specifically indicated. Additionally, many free-text entries contained immaterial information that allowed the response to be transferred from the other to 'none' group. These entries were mapped to the appropriate response following a free-text review by clinical specialists.

To reduce the total number of diagnoses and treatments levels for analysis and to incorporate those with low prevalence (N<50), a clinically informed grouping was applied. Following this, a hierarchy was used to assign those within multiple groups to a primary group for analysis (RAD: 5% within multiple diagnoses groups, 8% within multiple treatment groups. LM: 3% within multiple diagnoses groups, 3% multiple treatment groups). An exception was made here for multiple blood cancer diagnoses when the most recent diagnosis was chosen as the primary.

Diagnosis grouping and multiple diagnoses hierarchy in rare autoimmune rheumatic disease cohort.

Group	Hierarchy rank	Condition
Small vessel vasculitis (SVV)	1	Primary CNS (Brain) vasculitis Behcet's disease Polyarteritis nodosa Churg Strauss (or EGPA, eosinophilic granulomatosis with polyangiitis) MPA (or microscopic polyangiitis) GPA (or granulomatosis with polyangiitis / Wegener's) ANCA vasculitis
Large vessel vasculitis (LVV)	2	Takayasu arteritis Giant cell arteritis (temporal arteritis)
SLE	3	Systemic lupus erythematosus
Scleroderma	4	Scleroderma
Myositis	5	Polymyositis Dermatomyositis
Other diagnoses	6	Other
None	7	None of these

Treatment grouping and multiple treatment hierarchy in rare autoimmune rheumatic disease cohort.

Group	Hierarchy rank	Treatment
Anti-CD20 (12 months)	1	Rituximab Ofatumumab Obinutuzumab Ocreluzimab
Cyclophosphamide (12 months)	2	Cyclophosphamide Alemtuzumab
Mycophenolate	3	MMF (Mycophenolate Mofetil, Mycophenolate Acid, Cellcept, Myfenax, Ceptava, Myfortic)
Azathioprine	4	Azathioprine (Imuran)
Methotrexate	5	Methotrexate Oral (Maxtrex, Jylamvo) Methotrexate Injection/Infusion (Nordimet, Zlatal, Methofill, Metoject)
Other	6	Other

Diagnosis grouping and multiple diagnoses hierarchy in lymphoid malignancies cohort.

Group	Hierarchy rank	Condition
Aggressive B-NHL	1 (Most recent)	Diffuse Large B cell lymphoma Burkitt lymphoma
Indolent B-NHL	1 (Most recent)	Follicular lymphoma Mantle cell lymphoma Marginal zone lymphoma Chronic lymphocytic lymphoma (CLL)
Plasma cell malignancies	1 (Most recent)	Multiple myeloma Plasmacytoma
Hodgkin Lymphoma	1 (Most recent)	Hodgkin Lymphoma
Other diagnoses	2	Other lymphoma or leukaemia
None	3	None of these

Treatment grouping and multiple treatment hierarchy in lymphoid malignancies cohort.

Group	Hierarchy rank	Treatment
Anti-CD20 (12 months)	1	Rituximab (Rituxan) Obinutuzumab (Gazyva)
Ibrutinib / Acalabrutinib (3 months)	2	Ibrutinib (Imbruvica) Acalabrutinib (Calquence)
Chemotherapy (3 months)	3	Chemotherapy Methotrexate (Within 4 weeks)
Lenalidomide (3 months)	4	Lenalidomide (Revlimid)
Radiotherapy (3 months)	5	Radiotherapy
Autologous SCT (12 months)	6	Autologous stem cell transplant
Other Treatment	7	Other

For the SOT group, a hierarchy was applied to the immunosuppression recorded with those receiving belatacept considered in the belatacept based group regardless of other immunosuppression drugs indicated. Those on antiproliferative or calcineurin were then considered by whether they had these in combination with each other. The ‘other’ group are those who selected a drug but did not select belatacept, antiproliferative, nor calcineurin. The ‘none’ group are those who selected ‘none of these’ on the survey.

Comparison of invited versus analysed participants

To assess how the sampled cohorts represent the whole population, a comparison between the baseline demographics of the invited and analysed cohorts were performed.

a. Transplant cohort

	Invited cohort* N (%)	Analysis cohort N (%)	p-value
Total	47684 (100)	9927 (100)	
Gender			
Male	29064 (61.0)	5426 (54.7)	<0.0001
Female	18592 (39.0)	4494 (45.3)	
Not reported	28	7	
Ethnicity			
White	35876 (79.3)	9268 (93.8)	<0.0001
Asian	5817 (12.9)	351 (3.6)	
Black	2639 (5.8)	134 (1.4)	
Other	892 (2.0)	133 (1.4)	
Not reported	2460	41	
Transplant type			<0.0001
Kidney only	34229 (71.8)	6591 (66.4)	
Liver only	8000 (16.8)	1981 (20.0)	
SPK/ Panc/ Islet/ SIK	2048 (4.3)	350 (3.5)	
Heart only	1942 (4.1)	596 (6.0)	
Lung (incl heart-lung)	1171 (2.5)	333 (3.4)	
Other	294 (0.6)	76 (0.8)	
Graft number			
First graft	41572 (87.2)	8696 (87.6)	0.26
Re-graft	6112 (12.8)	1231 (12.4)	
Age (median, IQR)	57 (46-66)	60 (50-67)	<0.0001

* People on the NHS BT register and ≥18 years and resident in England and Wales at the start of invitations (prior to exclusion due to National opt-out application)

b. Rare autoimmune rheumatic disease group

	Invited cohort* N (%)	Analysis cohort N (%)	p-value
Total	32587 (100)	6516 (100)	
Gender			
Male	7267 (22.4)	1439 (22.8)	0.91
Female	25163 (77.6)	5070 (77.8)	
Not reported	157	37	
Ethnicity			
White	26447 (81.7)	5992 (92.3)	<0.0001
Asian	2950 (9.1)	231 (3.6)	

Black	2032 (6.3)	130 (2.0)	
Other	945 (2.9)	142 (2.2)	
Not reported	213	21	
Diagnosis			
Small vessel vasculitis	4812 (14.8)	1364 (20.9)	<0.0001
Large vessel vasculitis	8127 (24.9)	574 (8.8)	
SLE	13237 (40.6)	2412 (37.0)	
Scleroderma	3926 (12)	869 (13.3)	
Myositis	2485 (7.6)	440 (6.8)	
Age (median, IQR)	66 (52.0 - 77.0)	65 (54.0 - 73.0)	<0.0001

*Data extracted from hospital records with some discrepancies to self-report data. *Those eligible to be invited at the start of invitations (31/01/22).

c. Lymphoid Malignancy Cohort

	Invited cohort* N (%)	**Analysis cohort N (%)**	**p-value**
Total	28748 (100)	6593 (100)	
Gender			
Male	16142 (56.8)	3620 (54.9)	0.0028
Female	12256 (43.2)	2971 (45.1)	
Not reported	350	2	
Ethnicity			
White	23913 (89.0)	6401 (97.3)	<0.0001
Asian	1291 (4.8)	73 (1.1)	
Black	760 (2.8)	38 (0.6)	
Other	902 (3.4)	64 (1.0)	
Not reported	1882	17	
Diagnosis			<0.0001
Aggressive B-NHL	5929 (20.6)	1017 (15.4)	
Indolent B-NHL	13655 (47.5)	2706 (41.0)	
Plasma cell malignancies	7223 (25.1)	1327 (20.1)	
Hodgkin Lymphoma	1941 (6.8)	499 (7.6)	
Age (median, IQR)	71 (60.0 - 78.0)	69 (61.0 - 75.0)	<0.0001

*Data extracted from hospital records with some discrepancies to self-report data. *Those eligible to be invited at the start of invitations (31/01/22).

Table S1. Antibody responses for all participants with 3 or more vaccines by IgM and IgG status

Antibody response	Transplant cohort		Rare autoimmune disease cohort		Lymphoid malignancy cohort	
	N	%	N	%	N	%
Negative	1950	20	710	11	1142	17
Negative – IgM only	360	4	212	3	224	3
Positive – IgG only	5624	57	4191	64	3888	59
Positive IgM + IgG	1993	20	1403	22	1339	20
TOTAL	**9927**	**100**	**6516**	**100**	**6593**	**100**

Table S2. i. Logistic regression for antibody positivity[1] in transplant recipients who had 3 or more vaccines (significant factors only)

	N	Odds ratio (95% CI)	p-value
Age (10-year increase)	9233	0.70 (0.66-0.73)	<0.0001
Vaccines at test			<0.0001
3	2472	1.00	
4	5649	1.91 (1.70-2.15)	
5+	1112	2.76 (2.28-3.35)	
Immunosuppression			<0.0001
Antiproliferative and Calcineurin	3080	1.00	
Antiproliferative only	181	1.71 (1.11-2.64)	
Calcineurin only	1349	2.02 (1.66-2.45)	
Other[2]	252	1.90 (1.31-2.75)	
Antiproliferative and Calcineurin and Steroid	2639	0.61 (0.53-0.70)	
Antiproliferative and Steroid	402	1.18 (0.90-1.54)	
Calcineurin and Steroid	1330	1.12 (0.94-1.32)	
Transplant type			<0.0001
Kidney only	6165	1.00	
Liver only	1814	1.27 (1.09-1.49)	
SPK/ Panc/ Islet/ SIK	323	0.69 (0.53-0.92)	
Heart only	545	0.94 (0.75-1.17)	
Lung (including heart-lung)	314	0.59 (0.46-0.77)	
Other	72	0.80 (0.46-1.38)	
Previous COVID-19 infection			<0.0001
No	5283	1.00	
Yes	3372	4.16 (3.65-4.75)	
Unknown	578	1.34 (1.09-1.66)	
Rejection			0.0002
No	9048	1.00	
Yes	185	0.51 (0.36-0.71)	
Gender			0.026
Male	5103	1.00	
Female	4130	0.89 (0.80-0.99)	
Vaccine type			0.0063
mRNA + mRNA	4077	1.00	
AZ + mRNA	5156	0.86 (0.78-0.96)	
Graft number			0.022
First graft	8088	1.00	
Re-do	1145	0.83 (0.71-0.97)	

[1] Positive antibody result = IgG only or IgG + IgM
[2] Other includes belatacept based and none. Those on other treatments and steroids are included in this group.

Table S2 ii. Logistic regression for antibody positivity[1] in transplant recipients who had 3 or more vaccines (all factors considered)

	N	Odds ratio (95% CI)	p-value
Age (10 year increase)	9233	0.70 (0.67-0.73)	<0.0001
Vaccines at test			<0.0001
3	2472	1.00	
4	5649	1.93 (1.71-2.17)	
5+	1112	2.79 (2.27-3.43)	
Vaccine type			0.0075
mRNA + mRNA	4077	1.00	
AZ + mRNA	5156	0.87 (0.80-0.96)	
Gender			0.036
Male	5103	1.00	
Female	4130	0.89 (0.80-0.99)	
Ethnicity			0.21
White	8668	1.00	
Asian	322	1.24 (0.91-1.69)	
Black	122	0.74 (0.47-1.14)	
Other	121	0.84 (0.53-1.32)	
Immunosuppression			<0.0001
Antiproliferative and Calcineurin	3080	1.00	
Antiproliferative only	181	1.74 (1.12-2.68)	
Calcineurin only	1349	2.02 (1.67-2.45)	
Other[2]	252	1.92 (1.33-2.79)	
Antiproliferative and Calcineurin and Steroid	2639	0.61 (0.53-0.70)	
Antiproliferative and Steroid	402	1.18 (0.90-1.55)	
Calcineurin and Steroid	1330	1.13 (0.95-1.34)	
Time from transplant to most recent vaccine			0.32
Pre-transplant or <90 days post-transplant	66	1.00	
90-364 days post-transplant	395	0.82 (0.44-1.54)	
>=365 days post-transplant	8772	0.71 (0.40-1.28)	
Transplant type			<0.0001
Kidney only	6165	1.00	
Liver only	1814	1.26 (1.08-1.47)	
SPK/ Panc/ Islet/ SIK	323	0.70 (0.53-0.92)	
Heart only	545	0.93 (0.75-1.16)	
Lung (incl heart-lung)	314	0.60 (0.46-0.78)	
Other	72	0.80 (0.46-1.39)	
Rejection			<0.0001

No	9048	1.00	
Yes	185	0.50 (0.35-0.70)	
Cancer diagnosis since transplant			0.49
No	8019	1.00	
Yes	1214	1.06 (0.90-1.24)	
Graft number			0.028
First graft	8088	1.00	
Re-do	1145	0.84 (0.72-0.98)	
Previous COVID-19 infection			<0.0001
No	5283	1.00	
Yes	3372	4.17 (3.65-4.76)	
Unknown	578	1.34 (1.09-1.66)	
Days from latest vaccine to test	9233	1.00 (1.00-1.00)	0.96
BMI (kg/m^2)	9233	1.01 (1.00-1.02)	0.27
Comorbidities	9233	0.97 (0.93-1.01)	0.11

[1] Positive antibody result = IgG only or IgG + IgM
[2] Other includes belatacept based and none. Those on other treatments and steroids are included in this group.

Table S3. i. Logistic regression for antibody positivity[1] in participants with rare autoimmune rheumatic disease who had 3 or more vaccines (significant factors only)

	N	Odds ratio (95% CI)	p-value
Age (10-year increase)	4866	0.90 (0.83 - 0.97)	0.004
Vaccines at test			<0.0001
3	1861	1.00	
4	2710	1.62 (1.33 - 1.99)	
5+	295	3.28 (2.03 – 5.30)	
Immunosuppression			<0.0001
None[2]	1347	1.00	
Anti-CD20 (1 year)	708	0.07 (0.05 – 0.10)	
Cyclophosphamide (1 year)	92	0.49 (0.24 – 0.98)	
Mycophenolate (current)	806	0.39 (0.28 – 0.55)	
Azathioprine (current)	447	0.68 (0.44 – 1.06)	
Methotrexate (current)	580	0.79 (0.53 – 1.18)	
Other	886	0.65 (0.46 – 0.91)	
Steroid for immunosuppression			<0.0001
No	2773	1.00	
Yes	2093	0.66 (0.55 - 0.80)	
Diagnosis			0.0006
Systemic lupus erythematosus	2011	1.00	
Large vessel vasculitis	520	1.31 (0.87 – 1.97)	
Small vessel vasculitis	1194	0.69 (0.55 - 0.87)	
Scleroderma	730	1.17 (0.84 - 1.61)	
Myositis	396	1.18 (0.84 - 1.67)	
Other diagnosis	15	0.51 (0.13 – 2.04)	
Previous COVID-19 infection			<0.0001
No	2747	1.00	
Yes	1756	2.32 (1.87 - 2.87)	
Unknown	363	1.59 (1.10 - 2.30)	

[1] positive antibody result = IgG only or IgG + IgM
[2] includes hydroxychloroquine

Table S3 ii. Logistic regression for antibody positivity[1] in participants with rare autoimmune rheumatic disease who had 3 or more vaccines – all factors considered

	N	Odds ratio (95% CI)	p-value
Age (10-year increase)	4866	0.90 (0.84 - 0.98)	0.011
Vaccines at test			<0.0001
3	1861	1.00	
4	2710	1.56 (1.21 – 2.00)	
5+	295	3.084 (1.82– 5.22)	
Immunosuppression			<0.0001
None[2]	1347	1.00	
Anti-CD20 (1 year)	708	0.07 (0.05 – 0.09)	
Cyclophosphamide (1 year)	92	0.49 (0.24 – 0.99)	
Mycophenolate (current)	806	0.39 (0.28 – 0.55)	
Azathioprine (current)	447	0.67 (0.43 – 1.05)	
Methotrexate (current)	580	0.78 (0.52 – 1.17)	
Other	886	0.65 (0.46 – 0.91)	
Steroid for immunosuppression			<0.0001
No	2773	1.00	
Yes	2093	0.66 (0.55 - 0.80)	
Diagnosis			0.0013
Systemic lupus erythematosus	2011	1.00	
Large vessel vasculitis	520	1.34 (0.86 – 2.08)	
Small vessel vasculitis	1194	0.70 (0.55 - 0.91)	
Scleroderma	730	1.18 (0.85 - 1.64)	
Myositis	396	1.20 (0.83 - 1.71)	
Other diagnosis	15	0.51 (0.13 – 1.99)	
Previous COVID-19 infection			<0.0001
No	2747	1.00	
Yes	1756	2.33 (1.88 - 2.88)	
Unknown	363	1.60 (1.10 - 2.31)	
Vaccine type			0.77
mRNA + mRNA	2223	1.00	
AZ + mRNA	2643	1.03 (0.86 – 1.23)	
Ethnicity			0.76
White	4463	1.00	
Asian	187	1.17 (0.72 – 1.90)	
Black	102	0.88 (0.48 – 1.64)	
Other	114	0.79 (0.44 – 1.42)	

Gender			0.73
Male	1065	1.00	
Female	3801	1.04 (0.83 – 1.30)	
Latest vaccine to test (days)	4866	1.00 (1.00 – 1.00)	0.53
BMI	4866	1.00 (0.99 – 1.02)	0.32
Comorbidities	4866	0.98 (0.91 – 1.06)	0.63
Diagnosis to latest vaccine (years)	4866	1.00 (0.99 – 1.01)	0.71

[1] positive antibody result = IgG only or IgG + IgM
[2] includes hydroxychloroquine

Table S4 i. Logistic regression for antibody positivity[1] in participants with lymphoid malignancies who had 3 or more vaccines (significant factors only)

	N	Odds ratio (95% CI)	p-value
Age (10 year increase)	5737	0.76 (0.71 - 0.82)	<0.0001
Vaccines at test			<0.0001
3	1073	1	
4	4101	1.37 (1.14 - 1.66)	
5+	563	1.96 (1.42 - 2.71)	
Immunosuppression			<0.0001
None	3071	1	
Chemotherapy (3 months) [2]	482	0.12 (0.09 - 0.16)	
Anti-CD20	370	0.05 (0.04 - 0.06)	
Radiotherapy (3 months)	50	0.21 (0.12 - 0.39)	
BTKi (3 months)	180	0.16 (0.12 - 0.23)	
Thalidomide analogue (3 months)	358	0.34 (0.21 - 0.57)	
ASCT (12 months)	94	0.29 (0.14 - 0.58)	
Other	1132	0.19 (0.16 - 0.23)	
Diagnosis			<0.0001
Hodgkin Lymphoma	463	1	
Indolent B-NHL	2539	0.58 (0.43 - 0.77)	
Aggressive B-NHL	944	0.50 (0.37 - 0.69)	
Plasma cell malignancies	1194	3.19 (2.20 - 4.62)	
Other NHL	524	0.67 (0.47 - 0.96)	
Other diagnosis	73	0.84 (0.41 - 1.71)	
Previous COVID-19 infection			<0.0001
No	3548	1	
Yes	1769	1.93 (1.63 - 2.29)	
Unknown	420	1.53 (1.13 - 2.08)	

[1] positive antibody result = IgG only or IgG + IgM

Table S4. ii. Logistic regression for antibody positivity[1] in participants with lymphoid malignancies who had 3 or more vaccines – all factors considered

	N	Odds ratio (95% CI)	p-value
Age (10 year increase)	5737	0.77 (0.71 - 0.83)	<0.0001
Vaccines at test			0.011
3	1073	1	
4	4101	1.27 (1.01 - 1.58)	
5+	563	1.75 (1.21 - 2.55)	
Immunosuppression			<0.0001
None	3071	1	
Chemotherapy (3 months) [2]	482	0.12 (0.09 - 0.15)	
Anti-CD20	370	0.05 (0.04 - 0.06)	
Radiotherapy (3 months)	50	0.20 (0.11 - 0.38)	
BTKi (3 months)	180	0.17 (0.12 - 0.24)	
Thalidomide analogue (3 months)	358	0.33 (0.20 - 0.55)	
ASCT (12 months)	94	0.28 (0.13 - 0.56)	
Other	1132	0.19 (0.16 - 0.23)	
Diagnosis			<0.0001
Hodgkin Lymphoma	463	1	
Indolent B-NHL	2539	0.58 (0.44 - 0.78)	
Aggressive B-NHL	944	0.52 (0.38 - 0.72)	
Plasma cell malignancies	1194	3.39 (2.32 - 4.96)	
Other NHL	524	0.68 (0.48 - 0.97)	
Other diagnosis	73	0.88 (0.43 - 1.81)	
Previous COVID-19 infection			<0.0001
No	3548	1	
Yes	1769	1.94 (1.63 - 2.31)	
Unknown	420	1.53 (1.13 - 2.08)	
Steroid for immunosuppression			0.32
No	5542	1	
Yes	195	1.21 (0.83 – 1.75)	
Vaccine type			0.84
mRNA + mRNA	2632	1	
AZ + mRNA	3105	0.98 (0.85 – 1.14)	
Ethnicity			0.40
White	5600	1	
Asian	57	1.87 (0.74 – 4.72)	
Black	26	1.17 (0.32 – 4.31)	
Other	54	0.70 (0.35 – 1.42)	

Gender			0.35
Male	3125	1	
Female	2612	1.07 (0.93 – 1.24)	
Latest vaccine to test (days)	5737	1.00 (1.00 – 1.00)	0.16
BMI	5737	1.00 (0.99 – 1.02)	0.65
Comorbidities	5737	1.02 (0.95 – 1.10)	0.59
Diagnosis to latest vaccine (years)	5737	0.99 (0.96 – 1.03)	0.76

[1] positive antibody result = IgG only or IgG + IgM

Table S5. Mental health comorbidities by antibody positivity in the transplant cohort

	Antibody negative N (%)	Antibody positive N (%)	p-value
Total	2310 (23.3%)	7617 (76.7%)	
Depression			
No	2107 (23.0%)	7049 (77.0%)	0.041
Yes	203 (26.3%)	568 (73.7%)	
Anxiety			
No	2100 (23.3%)	6918 (76.7%)	0.93
Yes	210 (23.1%)	699 (76.9%)	
Psychiatric disorder			
No	2296 (23.3%)	7577 (76.7%)	0.76
Yes	14 (25.9%)	40 (74.1%)	
Any mental health comorbidity			
No	2011 (23.1%)	6681 (76.9%)	0.42
Yes	299 (24.2%)	936 (75.8%)	

Table S6. Mental health comorbidities by antibody positivity in the rare disease cohort

	Antibody negative N (%)	Antibody positive N % (%)	p-value
Total	922 (14.1%)	5594 (85.9%)	
Depression			
No	827 (14.5%)	4892 (85.4%)	0.061
Yes	95 (12.0%)	702 (88.0%)	
Anxiety			
No	832 (14.5%)	4894 (85.5%)	0.020
Yes	90 (11%)	700 (89%)	
Psychiatric disorder			
No	919 (14.2%)	5554 (85.8%)	0.257
Yes	3 (7.0%)	40 (93.0%)	
Any mental health comorbidity			
No	791 (14.7%)	4588 (85.3%)	0.006
Yes	131 (11.5%)	1006 (88.5%)	

Table S7. Mental health comorbidities by antibody positivity in the Lymphoid Malignancy Cohort

	Antibody negative	Antibody positive	p-value
	N (%)	N (%)	
Total	1366 (20.7%)	5227 (79.3%)	
Depression			
No	1306 (20.8%)	4979 (79.2%)	0.633
Yes	60 (19.5%)	248 (80.5%)	
Anxiety			
No	1296 (20.9%)	4915 (79.1%)	0.261
Yes	70 (18.3%)	312 (81.7%)	
Psychiatric disorder			
No	1364 (20.8%)	5207 (79.2%)	0.278
Yes	2 (9.1%)	20 (90.9%)	
Any mental health comorbidity			
No	1261 (20.9%)	4776 (79.1%)	0.289
Yes	105 (18.9%)	451 (81.1%)	

Table S8. Logistic regression results for impact of psychological distress on antibody positivity[1] by disease cohort

Cohort	Psychological Distress[2]	N (%)	Odds ratio (95% CI)
Transplant	No	6715 (87.6)	1
N=9233	Yes	951 (12.4)	0.64 (0.54-0.76)
	Not reported	1567	0.86 (0.74-0.99)
Rare autoimmune disease	No	3270 (83.1)	1
N=4866	Yes	664 (16.9)	1.17 (0.88 -1.55)
	Not reported	932	0.70 (0.56-0.88)
Lymphoid malignancy	No	4466 (92.6)	1
N=5737	Yes	356 (7.4)	0.87 (0.64 -1.17)
	Not reported	915	0.89 (0.73 -1.08)

[1] positive antibody result = IgG only or IgG + IgM. [2]Psychological distress was determined by a PHQ-ADS score of 20