

Table S1. Codes Used in the UK Biobank Study to Identify Pemphigus and Pemphigoid Case

Disease	ICD-10
Pemphigus	L10.0, L10.2, L10.4, L10.5, L10.8, L10.9
Pemphigoid	L12.0, L12.1, L12.3, L12.8, L12.9

Table SII. List of Single Nucleotide Polymorphisms (SNPs) Included in the Polygenic Risk Score (PRS) for Autoimmune Bullous Skin Diseases.

SNP	Chr	Effect allele	Other allele	Eaf
rs138282808	1	A	G	0.006978
rs6673787	1	T	C	0.014471
rs76054997	1	C	T	0.023955
rs6675856	1	G	A	0.027051
rs148279538	2	A	G	0.044228
rs75865342	2	T	A	0.022293
rs1465833	2	T	C	0.054286
rs116166168	3	G	A	0.007172
rs141177109	3	T	A	0.010585
rs116135711	3	C	T	0.036356
rs3774496	3	G	A	0.075326
rs183578353	3	A	T	0.004107
rs143760470	3	T	G	0.03471
rs115835118	4	T	A	0.01468
rs74648426	4	T	A	0.022816
rs183772245	4	C	T	0.011975
rs11934951	4	A	G	0.033952
rs186115056	4	C	T	0.008816
rs34762325	5	C	T	0.008268
rs250742	5	C	T	0.381995
rs190867351	5	T	A	0.051854
rs7730640	5	T	C	0.019054
rs3778541	6	C	T	0.966265
rs72819952	6	G	A	0.013995
rs1130375	6	G	C	0.182569
rs12111077	6	A	G	0.018628
rs117295883	7	A	G	0.026441
rs2083147	7	A	G	0.367684
rs10225185	7	C	A	0.140705
rs327729	7	A	G	0.853773
rs75735645	7	C	T	0.017469
rs16894170	8	A	G	0.026279
rs1374100	8	A	C	0.000251
rs16893023	8	A	C	0.202887
rs151026437	8	G	C	0.029244
rs117791977	9	C	T	0.015484
rs983370	9	C	T	0.045879
rs62573123	9	T	C	0.088172
rs12004030	9	C	G	0.167762
rs10905975	10	A	G	0.015277
rs12354419	10	C	T	0.029859
rs10748885	10	G	A	0.634366
rs183294719	12	A	T	0.01192
rs73099993	12	A	G	0.010486
rs7972368	12	G	A	0.255135

rs1921534	12	A	G	0.013436
rs17515619	13	A	G	0.026984
rs7316958	13	G	T	0.021052
rs112244057	13	T	C	0.074231
rs150431832	14	G	A	0.016285
rs35527453	15	A	G	0.651406
rs140814229	15	G	A	0.00703
rs149144671	16	T	C	0.008726
rs2190721	17	T	C	0.311138
rs117947296	17	T	C	0.010525
rs66513369	18	G	C	0.233967
rs78167688	18	A	T	0.063792
rs3892355	19	A	G	0.325974
rs73256196	20	A	T	0.080881
rs113076011	20	A	G	0.016115
rs151238913	21	A	G	0.012641
rs144638310	22	G	A	0.010904

Table SIII. Definition of Risk Factor Variables From the UK Biobank Study

Variable	UK Biobank variable name	How it was used in the analyses
Age	21022	Dummy variable: 0=Lowest tertile 1=Middle tertile 2=Highest tertile
Sex	31	Dummy variable: 0=female 1=male
Ethnic Background	21000	Dummy variable: 0=the white race 1=the other ethnic groups
BMI	21001	Dummy variable: 0=No overweight (BMI < 25) 1=Overweight (BMI 25-30) 2=Obesity (BMI ≥30)
Level of education	6138	Dummy variable: 0=Other 1=College/University degree/other professional degree
Socio-economic status	189	Make quintiles and use as dummy variables: 0=Least deprived (lowest quintile) 1=Intermediate deprivation (quintile 2-4) 2=Most deprived (highest quintile)
Alcohol use	1558, 20117, 1558, 1568, 1578, 1588, 1598, 1608, 5364, 4407, 4418, 4429, 4440, 4451, 4462	Dummy variable: 0=abstainers 1=Moderate alcohol consumption (women: 0 – 14 g/d, men: 0 – 28 g/d) 2=Heavy alcohol consumption (women: > 14 g/d, men: >28 g/d)
Smoking	20116	Dummy variable:

0=never

1=previous

2=current

Diet

1309, 1319, 1289,
1299, 1329, 1339,
1349, 1369, 1379,
1389, 1438, 1448,
1458, 1468

Dummy variable:

Fruits: ≥ 3 servings/day

Vegetables: ≥ 3 servings/day

Fish: ≥ 2 servings/week

Processed meats: ≤ 1 serving/week

Unprocessed red meats: ≤ 1.5 servings/week

Whole grains: ≥ 3 servings/day

Refined grains: ≤ 1.5 servings/day

Dummy variable:

0=less than 4 of the above

1=4 or more of the above

Physical activity

884, 894, 904, 914

Dummy variables:

Step 1: >6 days per week moderate activity/ <6 days per week moderate activity

Duration of moderate activity >150 minutes/ <150 minutes

>1 days per week vigorous activity/ <1 days per week vigorous activity

Duration of vigorous activity >75 minutes/ <75 minutes

Step 2: combine above variables to 1 dummy variable
yes/no

0=inactive (no)

1=active (yes)

Table SIV. Sensitivity Analysis Results**A. Sensitivity Analyses for the Association Between Physical Activity and AIBD Risk**

Analysis	HR (95% CI)	P-value
Excluding first 2 years of follow-up	0.69 (0.53-0.89)	0.005
Excluding first 5 years of follow-up	0.66 (0.50-0.88)	0.004
Censoring follow-up at 10 years	0.55 (0.40-0.75)	<0.001
Excluding individuals with extreme BMI (<18.5 or ≥40)	0.73 (0.57-0.94)	0.015
Additionally adjusting for assessment center	0.69 (0.54-0.89)	0.004

B. Sensitivity Analyses for the Association Between Physical Activity and Pemphigus and pemphigoid Risk

Analysis	Pemphigus		Pemphigoid	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Excluding first 2 years of follow-up	0.52 (0.30-0.91)	0.021	0.73 (0.55-0.97)	0.028
Excluding first 5 years of follow-up	0.50 (0.26-0.95)	0.035	0.68 (0.50-0.93)	0.015
Censoring follow-up at 10 years	0.50 (0.28-0.89)	0.018	0.57 (0.40-0.83)	0.003
Excluding individuals with extreme BMI (<18.5 or ≥40)	0.51 (0.30-0.87)	0.013	0.78 (0.59-1.04)	0.091
Additionally adjusting for assessment center	0.53 (0.32-0.90)	0.018	0.72 (0.55-0.95)	0.021

Note: All models were adjusted for age, sex, ethnic background, socio-economic status, level of education, smoking status, alcohol use, diet, and BMI in categories. All missing values in categorical covariates were included as a separate 'Unknown' category.

Table SV. Stratified Analysis Results**a. Stratified Analyses for the Association Between Physical Activity and Pemphigus Risk.**

Subgroup	HR (95% CI)	P for Interaction
Sex		
Female	0.61 (0.28-1.33)	0.423
Male	0.43 (0.21-0.88)	
Age		
Lowest tertile	0.48 (0.20-1.16)	0.472
Middle tertile	0.81 (0.24-2.68)	
Highest tertile	0.45 (0.20-0.98)	
Ethnic background		
White	0.59 (0.34-1.04)	0.258
Not White	0.21 (0.04-1.01)	
BMI		
No overweight	0.16 (0.03-0.75)	0.082
Overweight	0.76 (0.37-1.56)	
Obesity	0.45 (0.17-1.18)	
Level of education		
Lower degree	0.62 (0.31-1.24)	0.391
Academic or other professional degree	0.39 (0.17-0.88)	
Social economic status		
Least deprived	0.30 (0.06-1.54)	0.490
Intermediate	0.62 (0.32-1.18)	
Most deprived	0.40 (0.14-1.19)	
Alcohol use		
Abstainers	0.82 (0.31-2.14)	0.074

Subgroup	HR (95% CI)	P for Interaction
Moderate	0.54 (0.26-1.09)	
Heavy	0.18 (0.04-0.84)	
Smoking status		
Never	0.52 (0.25-1.10)	0.760
Previous	0.46 (0.20-1.05)	
Current	0.69 (0.11-4.21)	
Diet		0.956
Not healthy diet	0.51 (0.27-0.99)	
Healthy diet	0.51 (0.21-1.22)	

b. Stratified Analyses for the Association Between Physical Activity and Pemphigoid Risk.

Subgroup	HR (95% CI)	P for Interaction
Sex		
Female	0.92 (0.62-1.38)	0.226
Male	0.63 (0.42-0.93)	
Age		
Lowest tertile	0.54 (0.22-1.32)	0.311
Middle tertile	0.83 (0.50-1.41)	
Highest tertile	0.76 (0.53-1.09)	
Ethnic background		
White	0.78 (0.59-1.04)	0.230
Not White	0.34 (0.09-1.34)	
BMI		
No overweight	0.68 (0.40-1.15)	0.296
Overweight	0.99 (0.62-1.59)	

Subgroup	HR (95% CI)	P for Interaction
Obesity	0.61 (0.38-0.99)	
Level of education		
Lower degree	0.73 (0.50-1.07)	0.955
Academic or other professional degree	0.78 (0.52-1.19)	
Social economic status		
Least deprived	0.93 (0.48-1.82)	0.371
Intermediate	0.59 (0.41-0.85)	
Most deprived	1.28 (0.69-2.38)	
Alcohol use		
Abstainers	0.95 (0.54-1.69)	0.382
Moderate	0.68 (0.46-1.01)	
Heavy	0.73 (0.42-1.26)	
Smoking status		
Never	0.76 (0.50-1.14)	0.308
Previous	0.82 (0.53-1.26)	
Current	0.49 (0.20-1.20)	
Diet		
Not healthy diet	0.72 (0.50-1.02)	0.709
Healthy diet	0.82 (0.52-1.29)	

The analysis was based on a complete-case cohort. From an initial 476,057 participants, 10,332 (2.2%) were excluded due to missing data in one or more variables required for the model. The final analysis included 465,725 participants.

Models were adjusted for all variables listed in the methods section (age, sex, socio-economic status, level of education, ethnic background, smoking status, alcohol use, diet, and BMI categories), except for the stratification variable itself.

Table SVI. Association between the Polygenic Risk Score and Risk of Autoimmune Bullous Disease.

Predictor Variable	Crude Model OR (95% CI)	Adjusted Model OR (95% CI)
Polygenic Risk Score (per 1-SD increase)	1.17 (1.13, 1.21)	1.18 (1.13, 1.23)
<i>P</i> -value	<0.001	<0.001

Adjusted Model: Adjusted for age, sex, ethnic background, socio-economic status, level of education, smoking status, alcohol use, diet, and Body Mass Index (BMI).

Abbreviations: CI, Confidence Interval; OR, Odds Ratio; PRS, Polygenic Risk Score; SD, Standard Deviation.

Table SVII. Stratified Analyses for the Associations Between Physical Activity and Risk of AIBD by Genetic Risk for AIBD (Median Split)

PRS for AIBD	Inactive	Active	P for interaction
Low PRS	1.00 (Reference)	0.68 (0.45, 1.01)	0.693
High PRS	1.00 (Reference)	0.73 (0.53, 1.01)	

Models were adjusted for age, sex, ethnic background, socio-economic status, level of education, smoking status, alcohol use, diet, and BMI categories.

Table SVIII. Association Between Physical Activity and AIBD Using a Stricter Case Definition

Outcome	Number of cases	HR (95% CI)	P-value
AIBD	63	0.58 (0.35-0.98)	0.040
Pemphigus	12	0.28 (0.08-1.05)	0.060
Pemphigoid	51	0.66 (0.38-1.15)	0.143

Note: Cases were defined as participants with at least two qualifying diagnostic records. Models were adjusted for age, sex, ethnic background, socio-economic status, level of education, smoking status, alcohol use, diet, and BMI categories.