

Figure S1. Subgroup analysis of association of substance abuse with the risk of psoriasis.

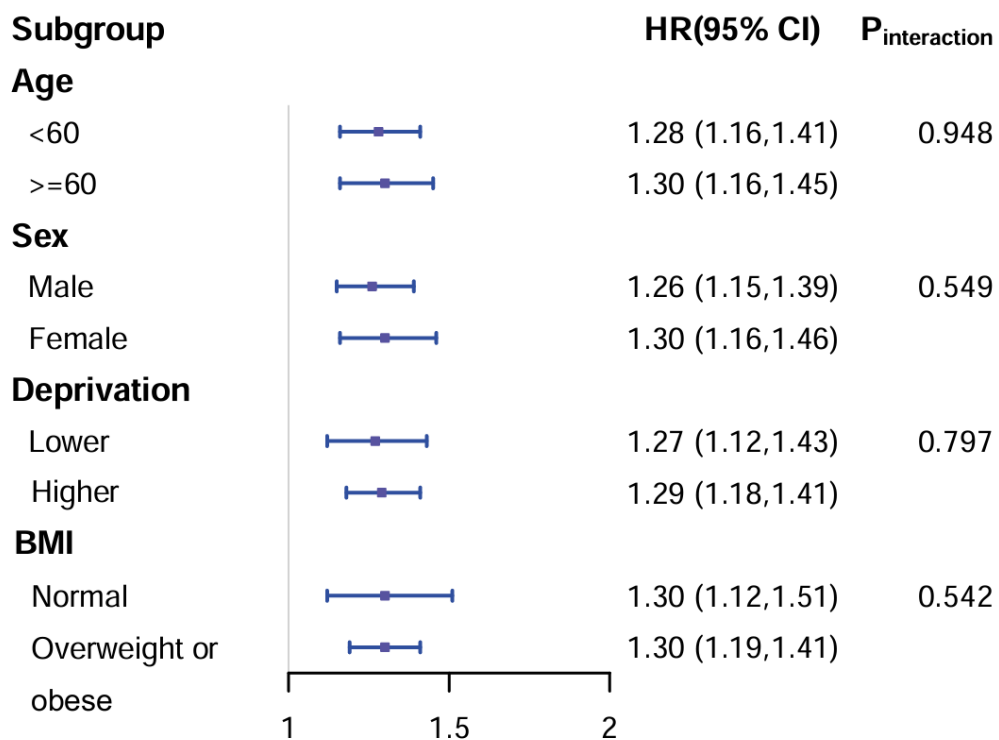


Figure S2. Subgroup analysis of association of psoriasis with the risk of incident substance abuse.

Table S1 Baseline characteristic of the study participants by substance abuse in Cohort 2.

Variable	Total	Non-Psoriasis	Psoriasis	<i>P</i>
N	451547	442217	9330	
Sex, n (%)				<0.001
Male	203605 (45.1)	198871(45.0)	4734(50.7)	
Female	247942 (54.9)	243346 (55.0)	4596(49.3)	
Age (y), mean (SD)	56.48 (8.09)	56.48 (8.09)	56.79 (7.99)	<0.001
TDI, mean (SD)	-1.42 (3.02)	-1.43 (3.02)	-1.30 (3.05)	<0.001
Ethnicity, n (%)				<0.001
White	429048 (95.0)	419980 (95.0)	9068 (97.2)	
Mixed	2597 (0.6)	2550 (0.6)	47 (0.5)	
Asian	7905 (1.8)	7775 (1.8)	130 (1.4)	
Black	6842 (1.5)	6817 (1.5)	25 (0.3)	
Chinese	1373 (0.3)	1364 (0.3)	9 (0.1)	
Other	3782 (0.8)	3731 (0.8)	51 (0.5)	
Education, n (%)				<0.001
College degree	153019 (33.9)	149952 (33.9)	3067 (32.9)	
A-levels	51881 (11.5)	50855 (11.5)	1026 (11.0)	
O-levels	97395 (21.6)	95396 (21.6)	1999 (21.4)	
CSEs	24151 (5.3)	23636 (5.3)	515 (5.5)	
NVQ/HND/HNC	29390 (6.5)	28721 (6.5)	669 (7.2)	
Other	23744 (5.3)	23299 (5.3)	445 (4.8)	
None of the above	71967 (15.9)	70358 (15.9)	1609 (17.2)	
Smoking, n (%)				<0.001
Never	257923 (57.1)	253399 (57.3)	4524 (48.5)	
Previous	156092 (34.6)	152233 (34.4)	3859 (41.4)	
Current	37532 (8.3)	36585 (8.3)	947 (10.2)	
Alcohol, n (%)				<0.001
Never	19101 (4.2)	18759 (4.2)	342 (3.7)	
Previous	14717 (3.3)	14352 (3.2)	365 (3.9)	
Current	417729 (92.5)	409106 (92.5)	8623 (92.4)	
BMI (kg/m ²), n (%)				<0.001
Underweight	2265 (0.5)	2230 (0.5)	35 (0.4)	
Normal weight	149084 (33.0)	146561 (33.1)	2523 (27.0)	
Overweight	192439 (42.6)	188439 (42.6)	4000 (42.9)	
Obese	107759 (23.9)	104987 (23.7)	2772 (29.7)	
Regular exercise, n (%)	176667 (39.1)	173135 (39.2)	3532 (37.9)	0.012
Substance abuse, n (%)	25176 (5.6)	24423 (5.5)	753 (8.1)	<0.001
Alcohol abuse	6977 (1.5)	6747 (1.5)	230 (2.5)	<0.001
Tobacco abuse	19452 (4.3)	18884 (4.3)	568 (6.1)	<0.001
Other substance abuse	483 (0.1)	467 (0.1)	16 (0.2)	0.077

Table S2 Mediation effect of symptoms of variables

Mediation variables	Proportion mediated (95% CI)	<i>P</i> value
Depression symptoms	0.017 (0.007, 0.030)	<0.001
Anxiety symptoms	0.034 (0.026, 0.060)	<0.001
Poor sleep quality	0.018 (0.011, 0.030)	<0.001

Table S3 Association of substance abuse with the risk of psoriasis (Excluding substance abuse cases that occurred within the first two years in Cohort 1).

Exposures	Cases/person-years	Cases/100 person-years ^a	Unadjusted Model		Adjusted Model 1 ^b		Adjusted Model 2 ^c		
			HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	
Substance abuse									
No	3011 of 5631845	0.5	Ref		Ref		Ref		
Yes	342 of 277125	1.2	2.29 (2.05, 2.56)	<0.001	2.15 (1.92, 2.41)	<0.001	2.15 (1.92, 2.41)	<0.001	
Types of substance abuse									
Alcohol									
No	3297 of 5868202	0.6	Ref		Ref		Ref		
Yes	56 of 40768	1.4	2.44 (1.88, 3.18)	<0.001	2.13 (1.63, 2.78)	<0.001	2.13 (1.63, 2.78)	<0.001	
Tobacco									
No	3054 of 5669635	0.7	Ref		Ref		Ref		
Yes	299 of 239335	1.6	2.30 (2.04, 2.59)	<0.001	2.16 (1.91, 2.43)	<0.001	2.17 (1.93, 2.45)	<0.001	
Other									
No	3347 of 5902367	0.6	Ref		Ref		Ref		
Yes	6 of 6604	0.9	1.60 (0.72, 3.56)	0.251	1.54 (0.69, 3.43)	0.168	1.53 (0.69, 3.41)	0.299	

CI, confidence interval; HR, hazard ratio.

^aPresented as events per 1000 person-years.

^bAdjusted for sex, age, ethnicity, Townsend deprivation score, educational level, physical activity, and body mass index.

^cAdditionally adjusted for polygenic risk scores.

Table S4 Association of psoriasis with the risk of incident substance abuse (Excluding substance abuse cases occurred within first two years in Cohort 2)

Outcomes	Cases/person-years	Cases per 1000 person-years ^a	Unadjusted Model		Adjusted Model ^b	
			HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
Substance abuse						
Non-psoriasis	21248 of 5615536	3.8	Ref		Ref	
psoriasis	613 of 115038	5.3	1.41 (1.30,1.52)	<0.001	1.21 (1.12,1.31)	<0.001
Types of substance abuse						
Alcohol						
Non-psoriasis	5787 of 5719055	1.0	Ref		Ref	
psoriasis	190 of 117923	1.6	1.59 (1.38,1.84)	<0.001	1.38 (1.19,1.59)	<0.001
Tobacco						
Non-psoriasis	16425 of 5642983	2.9	Ref		Ref	
psoriasis	455 of 115916	3.9	1.34 (1.23, 1.48)	<0.001	1.15 (1.05,1.26)	<0.001
Other						
Non-psoriasis	387 of 5748879	0.07	Ref		Ref	
psoriasis	13 of 118910	0.11	1.62 (0.93, 2.82)	0.086	1.39 (0.80, 2.42)	0.240

N=446366

CI, confidence interval; HR, hazard ratio.

^aPresented as events per 1000 person-years.^bAdjusted for sex, age, ethnicity, Townsend deprivation index, educational level, physical activity, smoking status, alcohol status, and body mass index.

Table S5 Association of substance abuse with the risk of psoriasis (Excluding non-white populations in Cohort 1).

Exposures	Cases/person-years	Cases/1000 person-years ^a	Unadjusted Model		Adjusted Model 1 ^b		Adjusted Model 2 ^c	
			HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
Substance abuse								
No	3520 of 5356213	0.7	Ref		Ref		Ref	
Yes	441 of 265795	1.7	2.49 (2.26, 2.75)	<0.001	2.32 (2.10, 2.56)	<0.001	2.33 (2.11, 2.58)	<0.001
Types of substance abuse								
Alcohol								
No	3887 of 5582425	0.7	Ref		Ref		Ref	
Yes	74 of 39581	1.9	2.64 (2.09, 3.32)	<0.001	2.28 (1.81, 2.88)	<0.001	2.28 (1.80, 2.87)	<0.001
Tobacco								
No	3576 of 5392795	0.7	Ref		Ref		Ref	
Yes	385 of 229212	1.7	2.50 (2.25, 2.78)	<0.001	2.34 (2.10, 2.60)	<0.001	2.35 (2.12, 2.62)	<0.001
Other								
No	3953 of 5615784	0.7	Ref		Ref		Ref	
Yes	8 of 6623	1.3	1.80 (0.90, 3.61)	0.096	1.69 (0.84, 3.38)	0.139	1.67 (0.83, 3.35)	0.146

N=431942

CI, confidence interval; HR, hazard ratio.

^aPresented as events per 1000 person-years.^bAdjusted for sex, age, ethnicity, Townsend deprivation score, educational level, physical activity, and body mass index.^cAdditionally adjusted for polygenic risk scores.

Table S6 Association of psoriasis with the risk of incident substance abuse (Excluding non-white populations in Cohort 2)

Outcomes	Cases/person-years	Cases per 1000 person-years ^a	Unadjusted Model		Adjusted Model ^b	
			HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
Substance abuse						
Non-psoriasis	23253 of 5339338	4.4	Ref		Ref	
psoriasis	731 of 111976	6.5	1.49 (1.39, 1.61)	<0.001	1.28 (1.19, 1.38)	<0.001
Types of substance abuse						
Alcohol						
Non-psoriasis	6553 of 5460845	1.2	Ref		Ref	
psoriasis	228 of 115898	2.0	1.64 (1.43, 1.87)	<0.001	1.42 (1.25, 1.62)	<0.001
Tobacco						
Non-psoriasis	17852 of 5374308	3.3	Ref		Ref	
psoriasis	547 of 113152	4.8	1.45 (1.33, 1.58)	<0.001	1.23 (1.13, 1.34)	<0.001
Other						
Non-psoriasis	425 of 5498995	0.08	Ref		Ref	
psoriasis	15 of 117226	0.13	1.65 (0.99, 2.76)	0.056	1.35 (0.81, 2.27)	0.250

N=429048

CI, confidence interval; HR, hazard ratio.

^aPresented as events per 1000 person-years.^bAdjusted for sex, age, ethnicity, Townsend deprivation index, educational level, physical activity, smoking status, alcohol status, and body mass index.