

Table 1. Baseline characteristics of 382,035 participants in the UK Biobank study

Characteristic	Overall	Incident Ankylosing Spondylitis		P value
		No	Yes	
N	382035	381341	694	
Demographic factors				
Age (mean (SD))	56.77 (8.00)	56.76 (8.00)	58.45 (7.57)	<0.001
Sex (%)				
Female	198263 (51.9)	197998 (51.9)	265 (38.2)	<0.001
Male	183772 (48.1)	183343 (48.1)	429 (61.8)	
Education (%)				
College or university degree	129467 (33.9)	129272 (33.9)	195 (28.1)	<0.001
Other degree	190029 (49.7)	189694 (49.7)	335 (48.3)	
None	62539 (16.4)	62375 (16.4)	164 (23.6)	
Household income (%)				
Less than 18,000	80002 (20.9)	79792 (20.9)	210 (30.3)	<0.001
18,000 to 30,999	96963 (25.4)	96776 (25.4)	187 (26.9)	
31,000 to 51,999	101168 (26.5)	101012 (26.5)	156 (22.5)	
52,000 to 100,000	81511 (21.3)	81398 (21.3)	113 (16.3)	
Greater than 100.000	22391 (5.9)	22363 (5.9)	28 (4.0)	
Healthy lifestyle factors				
Body mass index, n (%)				
Unhealth	260835 (68.3)	260318 (68.3)	517 (74.5)	<0.001
Health	121200 (31.7)	121023 (31.7)	177 (25.5)	
Smoking status, n (%)				
Smokier	38535 (10.1)	38439 (10.1)	96 (13.8)	0.001
Non-smoker	343500 (89.9)	342902 (89.9)	598 (86.2)	
Alcohol consumption, n (%)				
Excessive	168258 (44.0)	167940 (44.0)	318 (45.8)	0.365
Never/moderate	213777 (56.0)	213401 (56.0)	376 (54.2)	
Diet, n (%)				
Unhealth	212386 (55.6)	211980 (55.6)	406 (58.5)	0.132
Health	169649 (44.4)	169361 (44.4)	288 (41.5)	
Sleep duration, n (%)				
Ideal	48184 (12.6)	48054 (12.6)	130 (18.7)	<0.001
Poor	333851 (87.4)	333287 (87.4)	564 (81.3)	
Physical activity, n (%)				
Inactive	78890 (20.6)	78709 (20.6)	181 (26.1)	<0.001
Active	303145 (79.4)	302632 (79.4)	513 (73.9)	
No. of healthy lifestyle factors (%)				
0	692 (0.2)	689 (0.2)	3 (0.4)	<0.001
1	7249 (1.9)	7228 (1.9)	21 (3.0)	
2	34833 (9.1)	34732 (9.1)	101 (14.6)	
3	93502 (24.5)	93313 (24.5)	189 (27.2)	

4	128042 (33.5)	127835 (33.5)	207 (29.8)	
5	90769 (23.8)	90629 (23.8)	140 (20.2)	
6	26948 (7.1)	26915 (7.1)	33 (4.8)	
Diabetes (%)				
No	367980 (96.3)	367323 (96.3)	657 (94.7)	0.027
Yes	14055 (3.7)	14018 (3.7)	37 (5.3)	
Hypertension (%)				
No	188263 (49.3)	187974 (49.3)	289 (41.6)	<0.001
Yes	193772 (50.7)	193367 (50.7)	405 (58.4)	
Cardiovascular disease (%)				
No	361230 (94.6)	360598 (94.6)	632 (91.1)	<0.001
Yes	20805 (5.4)	20743 (5.4)	62 (8.9)	
Genetic risk ^a				
Low	131253 (34.4)	131051 (34.4)	202 (29.1)	0.005
Middle	127929 (33.5)	127693 (33.5)	236 (34.0)	
High	122853 (32.2)	122597 (32.1)	256 (36.9)	

a Genetic risk category defined according to the polygenic risk score as low (tertile 1), medium (tertile 2), and high (tertile 3) genetic risk.

Table 2. Risk of incident AS according to lifestyle categories

Healthy lifestyle categories	No. of cases/ person-years	Model 1		Model 2	
		HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value
Unfavorable lifestyle	125/553485	Ref		Ref	
Intermediate lifestyle	396/2934646	0.60 (0.49, 0.74)	1.05E-06	0.65 (0.53, 0.80)	3.47E-05
Favorable lifestyle	173/1570043	0.52 (0.41, 0.66)	4.22E-08	0.59 (0.46, 0.74)	1.16E-05
Per one-point increment	-	0.83 (0.78, 0.89)	3.24E-08	0.86 (0.81, 0.92)	9.27E-06
<i>P</i> for trend	-	-	< 0.001	-	< 0.001

Model 1: Cox regression model adjusted for adjusted for age (continuous) and sex.

Model 2: Cox regression model adjusted for adjusted for age (continuous), sex, education, household income, diabetes, hypertension, and cardiovascular disease.

Abbreviations: HR, hazard ratio; CI, confidence interval; AS, ankylosing spondylitis

Table 3. Risk of incident AS according to genetic and healthy lifestyle risk

Subgroup	No. of cases/ person-years	Model 1		Model 2	
		HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value
Low genetic risk					
Favorable lifestyle	59/542055	Ref		Ref	
Intermediate lifestyle	109/1007218	0.95 (0.69, 1.30)	0.729	0.90 (0.65, 1.24)	0.529
Unfavorable lifestyle	34/189077	1.57 (1.03, 2.39)	0.038	1.38 (0.90, 2.12)	0.124
Intermediate genetic risk					
Favorable lifestyle	52/525361	0.91 (0.63, 1.33)	0.635	0.92 (0.63, 1.33)	0.645
Intermediate lifestyle	139/984010	1.24 (0.91, 1.68)	0.174	1.17 (0.87, 1.60)	0.288
Unfavorable lifestyle	45/185186	2.13 (1.44, 3.14)	1.58E-04	1.86 (1.26, 2.76)	1.61E-03
High genetic risk					
Favorable lifestyle	62/943417	1.14 (0.80, 1.62)	0.484	1.13 (0.79, 1.62)	0.487
Intermediate lifestyle	148/943417	1.38 (1.02, 1.86)	0.039	1.31 (0.97, 1.77)	0.078
Unfavorable lifestyle	46/179222	2.23 (1.52, 3.29)	5.13E-05	1.95 (1.32, 2.89)	6.61E-04

Model 1: Cox regression model adjusted for adjusted for age (continuous), sex and the first five genetic principal components (continuous).

Model 2: Cox regression model adjusted for adjusted for age (continuous), sex, education, household income, diabetes, hypertension, cardiovascular disease and the first five genetic principal components (continuous).

Abbreviations: HR, hazard ratio; CI, confidence interval; AS, ankylosing spondylitis

Table 4. Additive and multiplicative interaction between lifestyle categories and PRS on risk of incident AS

	Addictive scale		Multiplicative scale	
	RERI (95% CI)	AP (95% CI)	HR (95% CI)	<i>P</i> value
Medium genetic risk				
Unfavorable lifestyle	0.57 (-0.20, 1.34)	0.30 (-0.07, 0.68)	1.48 (0.83, 2.64)	0.189
Intermediate lifestyle	0.36 (-0.04, 0.75)	0.31 (-0.05, 0.66)	1.43 (0.91, 2.23)	0.122
High genetic risk				
Unfavorable lifestyle	0.42 (-0.36, 1.19)	0.22 (-0.16, 0.61)	1.25 (0.71, 2.20)	0.450
Intermediate lifestyle	0.27 (-0.16, 0.71)	0.21 (-0.14, 0.55)	1.28 (0.83, 1.98)	0.265

Cox regression model adjusted for age (continuous), sex, education, household income, diabetes, hypertension, cardiovascular disease and the first five genetic principal components (continuous).

Abbreviations: RERI, relative excess risk due to interaction; AP, attributable proportion. Dur to interaction; HR, hazard ratio; CI, confidence interval; AS, ankylosing spondylitis, PRS, polygenic risk score.