

Table S1. Definition of lifestyle factors.

Factors	Unhealthy level	Healthy level
Alcohol consumption	Never or Excessive consumption: women: >14g/day men: >28g/day	Moderate consumption: women: 0 and ≤14g/day men: 0 and ≤28g/day
BMI	Range of <20.0 kg/m ² or ≥ 25.0 kg/m ²	Range of 20.0-< 25.0 kg/m ²
Sleep duration	Defined as <6 or > 8 hours every day	Defined as 6 to 8 hours every day
Smoking status	Current smoker	Never smoker or former smoker
Physical activity	0-149 min/week of moderate activity OR 0-74 min/week of vigorous activity OR 0-149 min/week of moderate and vigorous activity	≥150 min/week of moderate activity OR ≥75 min/week of vigorous activity OR ≥150 min/week of moderate and vigorous activity
Diet	Intake of 0-3 healthy dietary components: 1. Fruits: ≥ 3 servings/day 2. Vegetables: ≥ 3 servings/day 3. Fish: ≥2 servings/week 4. Processed meats: ≤ 1 serving/week 5.Unprocessed red meats: ≤1.5 servings/week 6. Whole grains: ≥ 3servings/day 7. Refined grains: ≤1.5 servings/day	Intake of ≥ 4 dietary healthy dietary components: 1. Fruits: ≥ 3 servings/day 2. Vegetables: ≥ 3 servings/day 3. Fish: ≥2 servings/week 4. Processed meats: ≤ 1 serving/week 5.Unprocessed red meats: ≤1.5 servings/week 6. Whole grains: ≥ 3servings/day 7. Refined grains: ≤1.5 servings/day

Table S2. Single nucleotide polymorphisms (SNPs) used to build the polygenetic risk score for AS.

SNP	Chr	Position	Nearby gene(s)	Risk/non-risk allele	RAF (case/control)	OR	P value
rs6600247	1p36	25177701	<i>RUNX3</i>	C/T	0.540/0.501	1.16	1.30E-14
rs11209026	1p31	67478546	<i>IL23R</i>	G/A	0.959/0.934	1.65	6.00E-28
rs41299637	1q32	1.99E+08	<i>GPR25-KIF21B</i>	T/G	0.757/0.715	1.2	3.60E-41
rs6759298	2p15	62421949	Intergenic	C/G	0.447/0.378	1.31	5.40E-06
rs30187	5q15	96150086	<i>ERAP1</i>	T/C	0.405/0.338	1.32	1.30E-41
rs6871626	5q33	1.59E+08	<i>IL12B</i>	A/C	0.360/0.337	1.12	6.00E-08
rs1128905	9q34	1.38E+08	<i>CARD9</i>	C/T	0.529/0.503	1.12	1.60E-09
rs1860545	12p13	6317038	<i>LTBR-TNFRSF1A</i>	C/T	0.634/0.605	1.13	8.30E-10
rs9901869	17q21	42930205	<i>NPEPPS-TBKBPI-TBX21</i>	A/G	0.548/0.516	1.15	2.30E-12
rs2836883	21q22	39388614	Intergenic	G/A	0.768/0.734	1.19	1.8E -14
rs4129267	1q21	1.53E+08	<i>IL6R</i>	C/T	0.635/0.592	1.18	2.1E -15
rs1801274	1q23	1.6E+08	<i>FCGR2A</i>	T/C	0.487/0.476	1.12	9.9E -10
rs12615545	2q31	1.82E+08	<i>UBE2E3</i>	C/T	0.451/0.421	1.11	2.30E-07
rs4676410	2q37	2.41E+08	<i>GPR35</i>	T/C	0.232/0.209	1.13	2.10E-07
rs17765610	6q15	90722494	<i>BACH2</i>	G/A	0.131/0.118	1.17	3.30E-08
rs1250550	10q22	80730323	<i>ZMIZ1</i>	G/T	0.678/0.652	1.11	5.80E-07
rs11190133	10q24	1.01E+08	<i>NKX2-3</i>	C/T	0.737/0.707	1.18	1.70E-14
rs11065898	12q24	1.1E+08	<i>SH2B3</i>	T/C	0.237/0.216	1.13	1.70E-07
rs11624293	14q31	87558574	<i>GPR65</i>	C/T	0.106/0.087	1.23	1.80E-10
imm_16_28525386	16p11	28525386	<i>IL27-SULT1A1</i>	A/G	0.421/0.393	1.11	1.40E-07
rs2531875	17q11	23172294	<i>NOS2</i>	G/T	0.396/0.367	1.12	1.30E-08
rs35164067	19p13	10386181	<i>TYK2</i>	G/A	0.819/0.796	1.16	6.50E-09
rs7282490	21q22	44440169	<i>ICOSLG</i>	G/A	0.411/0.390	1.1	1.40E-06

Abbreviations: AS, ankylosing spondylitis; RAF, risk allele frequency; OR: odds ratio

Table S3. HRs (95% CIs) of AS according to individual healthy lifestyle factor.

Lifestyle factors	No. of cases /person-years	Model 1		Model 2	
		HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value
Body mass index					
Unhealth	517/3443290	Ref		Ref	
Health	177/1614884	0.82 (0.69, 0.98)	0.025	0.87 (0.73, 1.04)	0.124
Smoking status					
Smokier	96/496353	Ref		Ref	
Non-smoker	598/4561821	0.66 (0.53, 0.82)	1.91E-04	0.72 (0.58, 0.90)	3.53E-03
Alcohol consumption					
Excessive	318/2234795	Ref		Ref	
Never/moderate	376/2823379	0.91 (0.78, 1.05)	0.203	0.92 (0.79, 1.06)	0.255
Diet					
Unhealth	406/2802405	Ref		Ref	
Health	288/2255770	0.93 (0.80, 1.09)	0.378	0.97 (0.83, 1.13)	0.673
Sleep duration					
Ideal	130/625578	Ref		Ref	
Poor	564/4432596	0.63 (0.52, 0.76)	2.67E-06	0.70 (0.57, 0.85)	2.80E-04
Physical activity					
Inactive	181/1034363	Ref		Ref	
Active	513/4023811	0.72 (0.60, 0.85)	1.27E-04	0.74 (0.62, 0.88)	5.84E-04

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 S4. HRs (95% CIs) of AS according to genetic risk

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
Low (N=131253)	202/1738351	Ref		Ref	
Intermediate (N=127929)	236/1694557	1.20 (1.00, 1.45)	5.58E-02	1.20 (1.00, 1.45)	5.59E-02
High (N=122853)	256/1625266	1.36 (1.13, 1.63)	1.16E-03	1.36 (1.13, 1.63)	1.25E-03
<i>P</i> for trend	-	-	1.16E-03	-	1.25E-03

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

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.

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

Table S5. Multivariable-adjusted linear regression models for the association between the healthy lifestyle score and systemic inflammation markers.

Inflammation markers	β	Lower 95% CI	Upper 95% CI	<i>P</i> value
NLR	-0.0192	-0.0227	-0.0156	<0.0001
SII	-12.2405	-13.3035	-11.1774	<0.0001
PLR	2.1809	1.9801	2.3817	<0.0001
LMR	-0.0222	-0.0342	-0.0103	0.0003
MHR	-0.0182	-0.0189	-0.0176	<0.0001
NHR	-0.1830	-0.1871	-0.1789	<0.0001
CAR	-0.0105	-0.0108	-0.0102	<0.0001
CLR	-0.2193	-0.2286	-0.2100	<0.0001
CRP	-0.4576	-0.4698	-0.4455	<0.0001

Model was adjusted for age (continuous), sex, education, household income, diabetes, hypertension and cardiovascular disease.

Abbreviations: CRP: C-reactive protein; CAR: CRP-to-albumin Ratio; CLR: CRP-to-lymphocyte Ratio; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; MHR: monocyte-to-HDL ratio; NHR: neutrophil-to-HDL-c ratio; SII: systemic immune-inflammation index CI, confidence interval

Table S6. Risk estimates of AS associated with the systemic inflammation markers.

Inflammation markers	HR	Lower 95% CI	Upper 95% CI	<i>P</i> value
NLR	1.0531	1.0419	1.0645	<0.0001
SII	1.0002	1.0001	1.0002	<0.0001
PLR	1.0003	1.0002	1.0004	<0.0001
LMR	0.9877	0.9545	1.0220	0.4776
MHR	1.1717	1.0221	1.3431	0.0230
NHR	1.1418	1.1041	1.1807	<0.0001
CAR	8.3521	6.1873	11.2745	<0.0001
CLR	1.0268	1.0229	1.0307	<0.0001
CRP	1.0532	1.0463	1.0602	<0.0001

Model was adjusted for age (continuous), sex, education, household income, diabetes, hypertension, cardiovascular disease and lifestyle score (continuous).

Abbreviations: CRP: C-reactive protein; CAR: CRP-to-albumin Ratio; CLR: CRP-to-lymphocyte Ratio; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; MHR: monocyte-to-HDL ratio; NHR: neutrophil-to-HDL-c ratio; SII: systemic immune-inflammation index; HR, hazard ratio; CI, confidence interval; AS, ankylosing spondylitis

Table S7. Risk of incident AS according to lifestyle categories based on the weighted healthy lifestyle score.

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	49/182829	Ref		Ref	
Intermediate lifestyle	236/1349503	0.65 (0.48, 0.89)	6.94E-03	0.71 (0.52, 0.97)	3.34E-02
Favorable lifestyle	409/3525842	0.44 (0.33, 0.59)	6.62E-08	0.51 (0.38, 0.69)	1.38E-05
Per one-point increment	-	0.80 (0.76, 0.85)	1.17E-12	0.86 (0.81, 0.92)	7.91E-06
P for trend	-	-	< 0.001	-	< 0.001

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

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.

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

Table S8. Risk of incident AS according to lifestyle categories based on the lifestyle score excluding non-significant factors.

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	77/312680	Ref		Ref	
Intermediate lifestyle	346/1505526	0.66 (0.51, 0.85)	1.50E-03	0.72 (0.55, 0.93)	1.10E-02
Favorable lifestyle	371/3239967	0.46 (0.36, 0.59)	6.97E-10	0.52 (0.41, 0.67)	4.47E-07
Per one-point increment	-	0.70 (0.63, 0.77)	1.13E-11	0.74 (0.66, 0.82)	2.19E-08
<i>P</i> for trend	-	-	< 0.001	-	< 0.001

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

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.

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

Table S9. Risk of incident AS according to lifestyle categories after excluding participants diagnosed with AS within the first 2 years of follow-up.

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	105/553465	Ref		Ref	
Intermediate lifestyle	352/2934593	0.63 (0.51, 0.79)	4.20E-05	0.68 (0.55, 0.85)	5.81E-04
Favorable lifestyle	147/1570017	0.52 (0.40, 0.67)	3.41E-07	0.58 (0.45, 0.75)	3.62E-05
Per one-point increment	-	0.84 (0.78, 0.90)	4.34E-07	0.86 (0.80, 0.93)	4.66E-05
<i>P</i> for trend	-	-	< 0.001	-	< 0.001

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

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.

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

Table S10. Risk of incident AS according to lifestyle categories after excluding participants with missing covariates.

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	118/478646	Ref		Ref	
Intermediate lifestyle	342/2561862	0.55 (0.44, 0.67)	1.53E-08	0.59 (0.48, 0.73)	1.31E-06
Favorable lifestyle	150/1370223	0.47 (0.37, 0.60)	1.19E-09	0.54 (0.42, 0.69)	1.23E-06
Per one-point increment	-	0.81 (0.76, 0.87)	1.86E-09	0.84 (0.79, 0.90)	1.65E-06
<i>P</i> for trend	-	-	< 0.001	-	< 0.001

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

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.

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

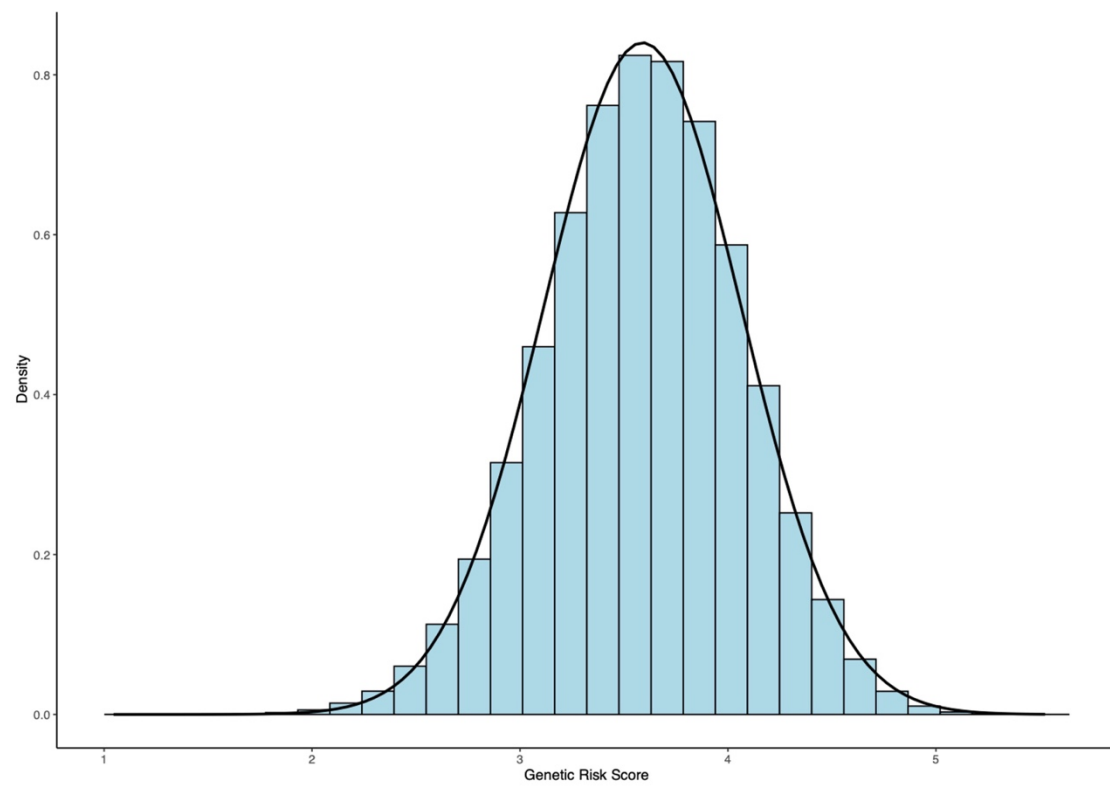


Figure S1. Distribution of the polygenic risk score (PRS) for AS using 24 SNPs

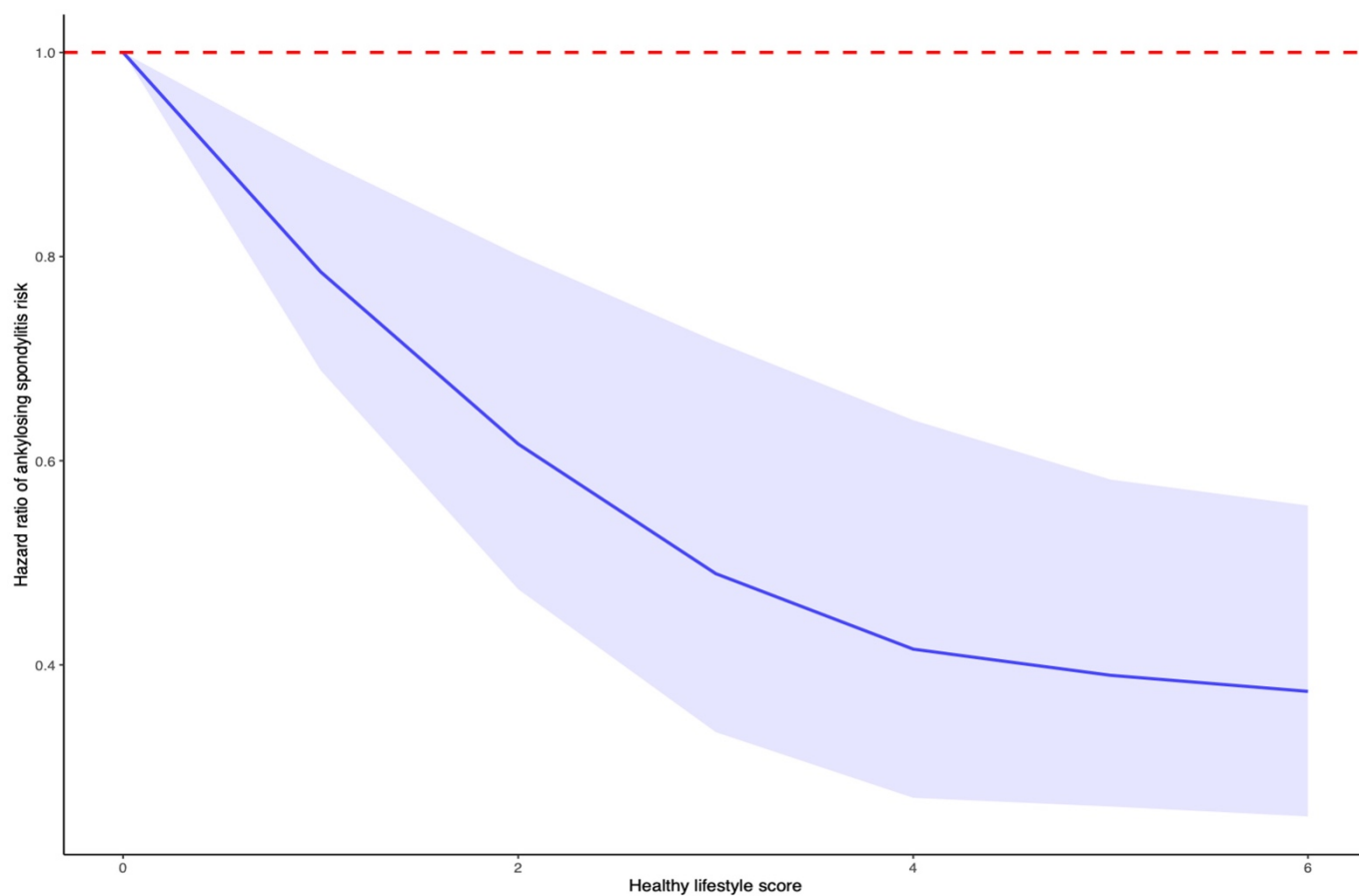


Figure S2. Dose-response relationship of healthy lifestyle score with risk of AS

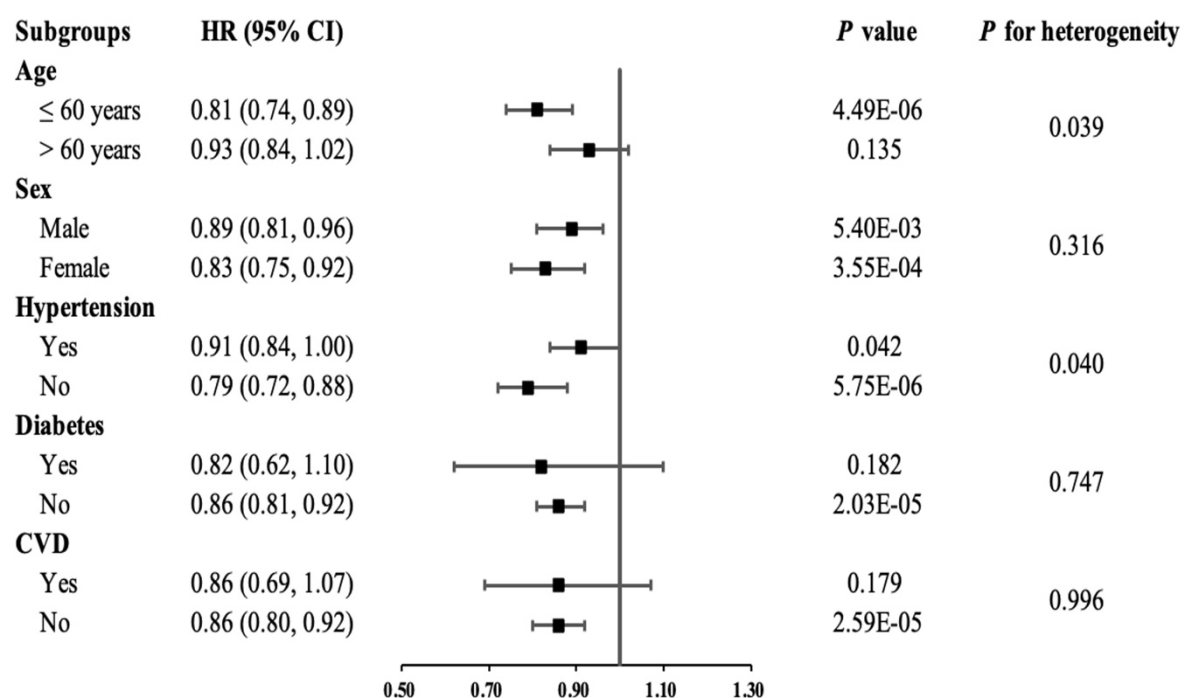


Figure S3. Stratified analyses of the associations of the healthy lifestyle score[†] with risks of AS

Models were adjusted for age (continuous), sex, education, household income, diabetes, hypertension and cardiovascular disease

[†]Per one-point increment of the healthy lifestyle score

Abbreviations: HR, hazard ratio; CI, confidence interval