

Supplementary materials

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33 **Supplementary Table S 1.** Single-nucleotide polymorphisms used to construct the genetic risk scores for

34 COPD

SNPs	Chromosome	Position	Effect Allele	Weight	<i>P</i>
rs9435731	1	17306029	A	0.058	6.60E-10
rs76841360	1	40060025	A	0.077	5.00E-10
rs4660861	1	45946636	G	0.058	4.40E-08
rs72673419	1	60913143	T	0.131	4.00E-09
rs629619	1	111738108	T	0.077	2.90E-10
rs3009947	1	218689155	C	0.058	4.00E-09
rs11118406	1	219924894	T	0.077	4.10E-11
rs11579382	1	239901006	C	0.058	6.50E-09
rs955277	2	9290357	T	0.068	1.90E-10
rs10929386	2	15906179	C	0.058	9.10E-09
rs12466981	2	42433247	C	0.058	4.90E-08
rs72902175	2	157013035	T	0.086	1.60E-08
rs2571445	2	218683154	A	0.068	3.40E-12
rs16825267	2	229569919	C	0.174	1.80E-20
rs62191105	2	239872704	C	0.086	2.60E-12
rs2442776	3	11640601	G	0.086	2.00E-10
rs1529672	3	25520582	C	0.086	2.50E-11
rs13073544	3	29472412	C	0.058	2.00E-08
rs17759204	3	55158224	G	0.068	8.80E-11
rs62259026	3	57746515	C	0.068	2.40E-08
rs4093840	3	123077042	A	0.058	3.90E-10
rs2955083	3	127961178	A	0.122	3.50E-15
rs7650602	3	141147414	C	0.058	4.90E-08
rs7642001	3	168746145	A	0.077	1. 10E-14
rs4585380	4	75673363	G	0.068	3.40E-09
rs7671261	4	89883818	A	0.086	1.40E-18
rs34712979	4	106819053	A	0.166	3.00E-46
rs13140176	4	145489098	A	0.166	4.10E-59
rs1551943	5	52195033	A	0.077	5.80E-10
rs34651	5	72144005	C	0.104	3.00E-08
rs153916	5	95036700	T	0.058	6.30E-10
rs62375246	5	132439010	A	0.058	2.20E-08
rs10037493	5	147854970	C	0.122	2.60E-33
rs979453	5	150595073	G	0.058	1.40E-08
rs10866659	5	156937043	G	0.086	1.20E-16

rs12519165	5	170901586	A	0.068	1.10E-09
rs1334576	6	7211818	A	0.058	1.20E-08
rs9350191	6	19842661	T	0.113	5.10E-14
rs13198656	6	22004909	T	0.058	1.20E-09
rs2284174	6	30713580	C	0.113	2.10E-21
rs2070600	6	32151443	C	0.191	1.10E-17
rs2806356	6	109266255	C	0.095	2.90E-15
rs674621	6	117257018	C	0.058	7.60E-09
rs646695	6	140280398	C	0.077	4.60E-11
rs9399401	6	142668901	T	0.148	1.60E-40
rs798565	7	2752152	G	0.068	3.90E-09
rs2040732	7	20418134	C	0.058	6.90E-09
rs2897075	7	99630342	C	0.068	7.30E-10
rs9329170	8	8697658	C	0.095	3.60E-10
rs10114763	9	4143749	T	0.068	8.70E-13
rs7866939	9	85126163	C	0.058	1.70E-08
rs10760580	9	101661650	G	0.068	1.20E-10
rs803923	9	119401650	A	0.058	2.70E-08
rs7068966	10	12277992	C	0.095	6.20E-23
rs2579762	10	78318879	C	0.058	2.60E-10
rs721917	10	81706324	G	0.058	2.20E-08
rs1570221	10	105656874	A	0.058	2.20E-08
rs4757118	11	13171236	T	0.058	3.80E-09
rs117261012	11	86444761	G	0.086	6.90E-10
rs11049386	12	28320536	T	0.058	2.70E-08
rs7307510	12	96237570	C	0.077	2.60E-09
rs7958945	12	115947901	G	0.058	1.000E-09
rs9525927	13	44842503	G	0.077	2.80E-09
rs72699855	14	93105953	G	0.077	4.80E-09
rs72731149	15	49984710	G	0.113	8.30E-09
rs1441358	15	71612514	G	0.122	7.40E-33
rs55676755	15	78898932	G	0.104	2.70E-26
rs10152300	15	84392907	G	0.077	4.20E-12
rs56134392	16	10709013	C	0.058	4.50E-08
rs8044657	16	58022625	G	0.104	1.10E-08
rs4888379	16	75340231	T	0.095	5.90E-21
rs8080772	17	28413129	T	0.058	1.40E-08
rs34727469	17	36835079	T	0.086	1.10E-08
rs62065216	17	38218773	A	0.058	8.10E-09
rs12373142	17	43924200	G	0.077	9.90E-10
rs11655567	17	69216687	C	0.058	1.90E-09
rs647097	18	8808464	C	0.077	1.000E-11
rs72626215	19	46294136	G	0.068	1.70E-09
rs2096468	21	35661745	A	0.058	4.00E-08

rs9617650	22	18488883	G	0.077	4.40E-10
rs73158393	22	33335386	C	0.068	7.70E-09

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39 **Supplementary Table S 2.** Definition of each component of a healthy diet score

Characteristics	Goal (1 point)	One serving equals to
Fruits	≥4 servings/day	1 heaped tablespoons of fresh fruit/dried fruit
Vegetables	≥3 servings/day	1 pieces of cooked vegetable/salad/raw vegetable
Fish	≥2 servings/week	Once/week (including oily fish, nonoily fish)
Unprocessed meat	≤2 servings/week	Once/week
Processed meat	≤2 servings/week	Once/week (including beef, lambmutton, pork)

40 **Note:** Data on food consumption were derived from the baseline questionnaire. If participants
41 achieved the intake goal of each diet component, they were considered to have an adequate intake
42 and get one point. The points were then accumulated to calculate the final healthy diet score. A
43 higher score indicated a healthier diet pattern.

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Characteristics	Questionnaire	Healthy Answer (1 point)
chronotype	Do you consider yourself to be?	Definitely a "morning" person; More a "morning" than "evening" person
Duration	About how many hours sleep do you get in every 24 hours? (please include naps)	sleep 7–8 hour/day
Insomnia	Do you have trouble falling asleep at night or do you wake up in the middle of the night?	never or rarely
Snoring	Does your partner or a close relative or friend complain about your snoring?	no
Daytime sleepiness	How likely are you to doze off or fall asleep during the daytime when you don't mean to? (e.g. when working, reading or driving)	Never or rarely

49 **Note:** Each healthy dietary behavior scored 1 point, resulting in a healthy diet score ranging from
50 0 (unhealthiest) to 5 (healthiest).

52 **Supplementary Table S 4.** Detailed information on missing covariates

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Covariates	Number of missing	Missing rate (%)
Age	0	0
Sex	0	0
BMI	1350	0.35
Race	1137	0.30
TDI	481	0.13
Smoking status	1039	0.27
Drinking status	279	0.07
Sleep scores	58678	15.27
Diet scores	7429	1.93

54 **Note:** BMI, body mass index; TDI, townsend deprivation index.

55 **Supplementary Table S 5.** Multivariable-adjusted *HRs* (95% *CI*s) for incident COPD when stratifying by age

Subgroup	≤45		(45-55]		(55-65]		>65	
	<i>HR</i>	<i>P</i> value	<i>HR</i>	<i>P</i> value	<i>HR</i>	<i>P</i> value	<i>HR</i>	<i>P</i> value
Low genetic risk								
Low PA	1.000(reference)	-	1.000(reference)	-	1.000(reference)	-	1.000(reference)	-
Moderate PA	0.650(0.332-1.270)	0.420	0.635(0.451-0.894)	<0.05	0.964(0.804-1.160)	0.737	0.778(0.608-0.995)	0.093
High PA	0.939(0.494-1.780)	0.896	0.632(0.450-0.888)	<0.05	0.909(0.754-1.100)	0.379	0.782(0.609-1.0000)	0.098
Intermediate genetic risk								
Low PA	1.000(reference)	-	1.000(reference)	-	1.000(reference)	-	1.000(reference)	-
Moderate PA	0.670(0.401-1.120)	0.310	0.738(0.591-0.923)	<0.05	0.919(0.814-1.040)	0.202	0.747(0.630-0.885)	<0.01
High PA	0.855(0.522-1.400)	0.686	0.826(0.662-1.030)	0.176	0.890(0.786-1.010)	0.090	0.786(0.662-0.933)	<0.05
High genetic risk								
Low PA	1.000(reference)	-	1.000(reference)	-	1.000(reference)	-	1.000(reference)	-
Moderate PA	0.977(0.596-1.600)	0.926	0.720(0.591-0.879)	<0.01	0.842(0.753-0.941)	<0.01	0.775(0.663-0.905)	<0.01
High PA	0.927(0.566-1.520)	0.853	0.884(0.729-1.070)	0.256	0.846(0.764-0.959)	<0.01	0.727(0.620-0.853)	<0.01

56 **Note:** Multivariable model was adjusted for sex, BMI, race, TDI, smoking status, drinking status, sleep scores, diet scores, genetic risk categories and low physical activity
57 level. All statistical tests were two-sided, with significance set at FDR-adjusted *p* value< 0.05 (Benjamini-Hochberg method).
58 HR, hazard ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; PA, physical activity; BMI, body mass index; TDI, townsend deprivation index.

Supplementary Table S 6. Multivariable-adjusted HRs (95% CIs) for incident COPD when stratifying bysex

Subgroup	Male		Female	
	HR	P value	HR	P value
Low genetic risk				
Low PA	1.000(reference)	-	1.000(reference)	-
Moderate PA	0.934(0.782-1.12)	0.479	0.756(0.622-0.919)	<0.05
High PA	0.898(0.750-1.08)	0.272	0.749(0.613-0.915)	<0.05
Intermediate genetic risk				
Low PA	1.000(reference)	-	1.000(reference)	-
Moderate PA	0.790(0.700-0.891)	<0.01	0.874(0.766-0.997)	0.067
High PA	0.903(0.803-1.01)	0.111	0.750(0.652-0.862)	<0.01
High genetic risk				
Low PA	1.000(reference)	-	1.000(reference)	-
Moderate PA	0.874(0.783-0.974)	<0.05	0.736(0.652-0.831)	<0.01
High PA	0.864(0.775-0.964)	<0.05	0.763 (0.673-0.865)	<0.01

Note: Multivariable model was adjusted for age, BMI, race, TDI, smoking status, drinking status, sleep scores, diet scores, genetic risk categories and low physical activity level. All statistical tests were two-sided, with significance set at FDR-adjusted p value< 0.05 (Benjamini-Hochberg method). HR, hazard ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; PA, physical activity; BMI, body mass index; TDI, townsend deprivation index.

Supplementary Table S 7. Multivariable-adjusted HRs (95% CIs) for incident COPD after excluding participants with missing data for covariates

Subgroup	Cases/N	HR	P value
Low genetic risk			
Low PA	348/11461	1.000(reference)	-
Moderate PA	634/26036	0.852(0.747-0.973)	<0.05
High PA	608/25975	0.832(0.727-0.951)	<0.05
Intermediate genetic risk			
Low PA	778/23138	1.000(reference)	-
Moderate PA	1348/51635	0.827(0.757-0.904)	<0.001
High PA	1330/51889	0.837(0.765-0.916)	<0.001
High genetic risk			
Low PA	934/23341	1.000(reference)	-
Moderate PA	1589/52062	0.818(0.754-0.888)	<0.001
High PA	1565/51202	0.825(0.760-0.896)	<0.001

Note: Multivariable model was adjusted for age, sex, BMI, race, TDI, smoking status, drinking status, sleep scores, diet scores, genetic risk categories and low physical activity level. All statistical tests were two-sided. P < 0.05 was considered significant.

HR, hazard ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; PA, physical activity; BMI, body mass index; TDI, townsend deprivation index.

80 **Supplementary Table S 8.** Multivariable-adjusted HRs (95% CIs) for Incident COPD after
81 excluding participants with COPD within the first two years of follow-up

Subgroup	Cases/N	HR	P value
Low genetic risk			
Low PA	347/11479	1.000(reference)	-
Moderate PA	620/26117	0.839(0.735-0.958)	<0.05
High PA	595/26037	0.820(0.716-0.939)	<0.05
Intermediate genetic risk			
Low PA	761/23323	1.000(reference)	-
Moderate PA	1321/51777	0.833(0.761-0.911)	<0.001
High PA	1296/52028	0.838(0.765-0.918)	<0.001
High genetic risk			
Low PA	912/23495	1.000(reference)	-
Moderate PA	1547/52218	0.818(0.753-0.888)	<0.001
High PA	1526/51327	0.827(0.760-0.899)	<0.001

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83 **Note:** Multivariable model was adjusted for age, sex, BMI, race, TDI, smoking status, drinking status,
84 sleep scores, diet scores, genetic risk categories and low physical activity level. All statistical tests were
85 two-sided. P < 0.05 was considered significant.
86 HR, hazard ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; PA, physical
87 activity; BMI, body mass index; TDI, townsend deprivation index.
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Characteristic	Before Propensity Scores Matching			After Propensity Scores Matching		
	Low physical activity (n=58370)	Moderate-high physical activity (n=259715)	P value	Low physical activity (n=58370)	Moderate-high physical activity (n=116740)	P value
Age			<0.001			1.0000
<60	36645(62.8%)	149509(57.6%)		36645(62.8%)	73290(62.8%)	
≥60	21725(37.2%)	110206(42.4%)		21725(37.2%)	43450(37.2%)	
Sex			<0.001			1.0000
Male	27768(47.6%)	121182(46.7%)		27768(47.6%)	55536(47.6%)	
Female	30602(52.4%)	138533(53.3%)		30602(52.4%)	61204(52.4%)	
Race			<0.001			1.0000
White	55052(94.3%)	248153(95.5%)		55052(94.3%)	110104(94.3%)	
Non-White	3318(5.68%)	11562(4.45%)		3318(5.68%)	6636(5.68%)	
BMI			<0.001			<0.001
Normal/underweight(<25kg/m ²)	15450(26.5%)	92580(35.6%)		15450(26.5%)	41681(35.7%)	
Overweight(25-30kg/m ²)	24067(41.2%)	112727(43.4%)		24067(41.2%)	50404(43.2%)	
Obese(≥30kg/m ²)	18853(32.3%)	54408(20.9%)		18853(32.3%)	24655(21.1%)	
TDI,mean(SD)			<0.05			<0.001
Quartile1	14874(25.5%)	64653(24.9%)		14874(25.5%)	28670(24.6%)	
Quartile2	14615(25.0%)	64905(25.0%)		14615(25.0%)	29111(24.9%)	
Quartile3	14316(24.5%)	65204(25.1%)		14316(24.5%)	29176(25.0%)	
Quartile4	14565(25.0%)	64953(25.0%)		14565(25.0%)	29783(25.5%)	
Smoking status			<0.001			<0.001
Current	6605(11.3%)	24234(9.33%)		6605(11.3%)	11101(9.51%)	

Former	19901(34.1%)	91597(35.3%)		19901(34.1%)	40475(34.7%)	
Never	31864(54.6%)	143884(55.4%)		31864(54.6%)	65164(55.8%)	
Drinking status			<0.001			<0.001
Current	53590(91.8%)	242415(93.3%)		53590(91.8%)	108792(93.2%)	
Former	2133(3.65%)	7994(3.08%)		2133(3.65%)	3695(3.17%)	
Never	2647(4.53%)	9306(3.58%)		2647(4.53%)	4253(3.64%)	
Diet scores			<0.001			<0.001
0	1297(2.22%)	3874(1.49%)		1297(2.22%)	1785(1.53%)	
1	8358(14.3%)	25861(9.96%)		8358(14.3%)	11915(10.2%)	
2	17821(30.5%)	64291(24.8%)		17821(30.5%)	29100(24.9%)	
3	19189(32.9%)	88214(34.0%)		19189(32.9%)	39537(33.9%)	
4	9378(16.1%)	58611(22.6%)		9378(16.1%)	26022(22.3%)	
5	2327(3.99%)	18864(7.26%)		2327(3.99%)	8381(7.18%)	
Sleep scores			<0.001			<0.001
Poor	7161(12.3%)	20937(8.06%)		7161(12.3%)	9425(8.07%)	
Intermediate	35524(60.9%)	150090(57.8%)		35524(60.9%)	67430(57.8%)	
Healthy	15685(26.9%)	88688(34.1%)		15685(26.9%)	39885(34.2%)	
PRS			<0.05			0.175
Low	11485(19.7%)	52193(20.1%)		11485(19.7%)	23364(20.0%)	
Intermediate	23349(40.0%)	103881(40.0%)		23349(40.0%)	46724(40.0%)	
High	23536(40.3%)	103641(39.9%)		23536(40.3%)	46652(40.0%)	

Note: All statistical tests were two-sided. P < 0.05 was considered significant. BMI:body mass index; TDI:townsend deprivation index; PA:physical activity level;
PRS:polygenic risk scores.

93 **Supplementary Table S 10.** Multivariable-adjusted *HRs* (95% *CI*s) for incident COPD after propensity
 94 score matching with 1:1 matching

Subgroup	Cases/N	<i>HR</i>	<i>P</i> value
Low genetic risk			
Low PA	353/11485	1.000(reference)	-
Moderate PA	116/5866	0.726(0.587-0.897)	<0.01
High PA	134/5824	0.864(0.704-1.060)	0.161
Intermediate genetic risk			
Low PA	787/23349	1.000(reference)	-
Moderate PA	286/11631	0.830(0.724-0.952)	<0.01
High PA	290/11679	0.862(0.751-0.989)	<0.05
High genetic risk			
Low PA	953/23536	1.000(reference)	-
Moderate PA	344/11878	0.810(0.715-0.917)	<0.01
High PA	352/11492	0.876(0.773-0.992)	<0.05

95 **Note:** Multivariable model was adjusted for age, sex, BMI, race, TDI, smoking status, drinking status,
 96 sleep scores, diet scores, genetic risk categories and low physical activity level. All statistical tests were
 97 two-sided. *P* < 0.05 was considered significant.
 98 *HR*, hazard ratio; *CI*, confidence interval; COPD, chronic obstructive pulmonary disease; *PA*, physical
 99 activity; *BMI*, body mass index; *TDI*, townsend deprivation index.

Supplementary Table S 11. Multivariable-adjusted HRs (95%CI) for incident COPD after propensity score matching with 1:2 matching

Subgroup	Cases/N	HR	P value
Low genetic risk			
Low PA	353/11485	1.000(reference)	-
Moderate PA	242/11716	0.758(0.642-0.894)	<0.001
High PA	261/11648	0.814(0.691-0.959)	<0.05
Intermediate genetic risk			
Low PA	787/23349	1.000(reference)	-
Moderate PA	580/23343	0.835(0.750-0.931)	<0.05
High PA	570/23381	0.844(0.756-0.943)	<0.05
High genetic risk			
Low PA	953/23536	1.000(reference)	-
Moderate PA	660/23544	0.793(0.717-0.877)	<0.001
High PA	677/23108	0.838(0.757-0.927)	<0.001

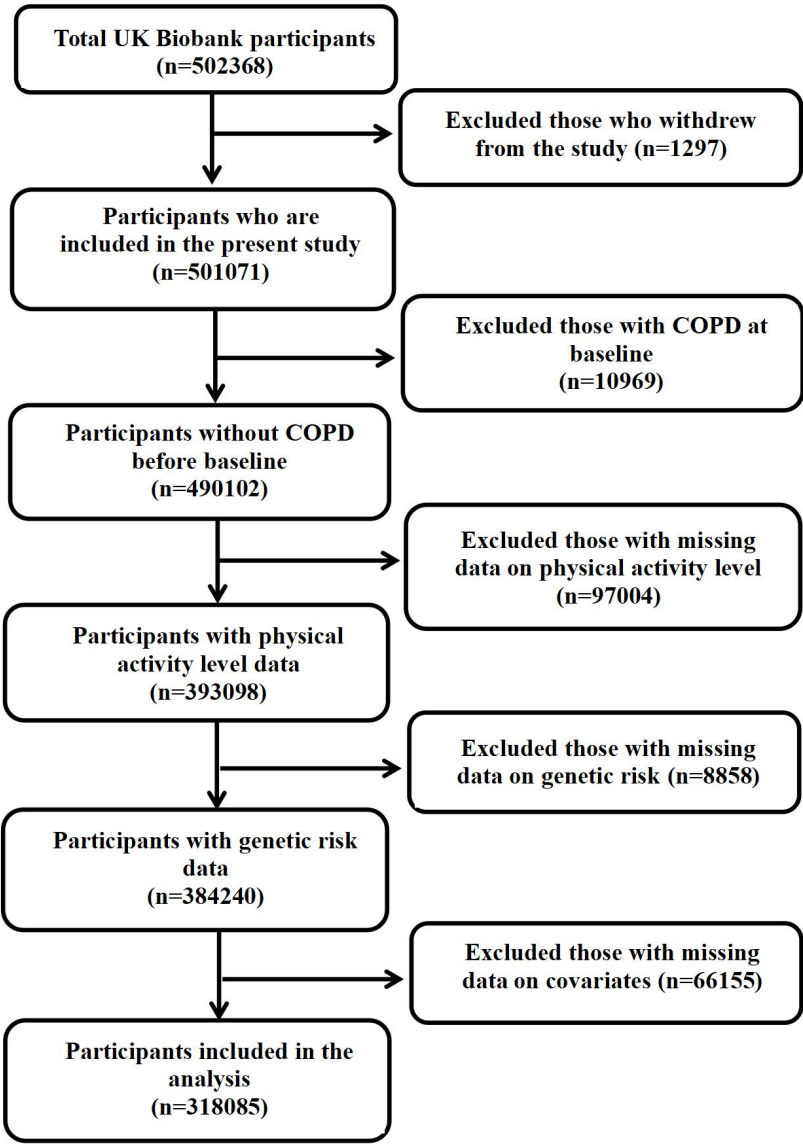
Note: Multivariable model was adjusted for age, sex, BMI, race, TDI, smoking status, drinking status, sleep scores, diet scores, genetic risk categories and low physical activity level. All statistical tests were two-sided. P < 0.05 was considered significant.
HR, hazard ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; PA, physical activity; BMI, body mass index; TDI, townsend deprivation index.

Supplementary Table S 12. Multivariable-adjusted HRs (95%CI) for incident COPD after propensity score matching with 1:3 matching

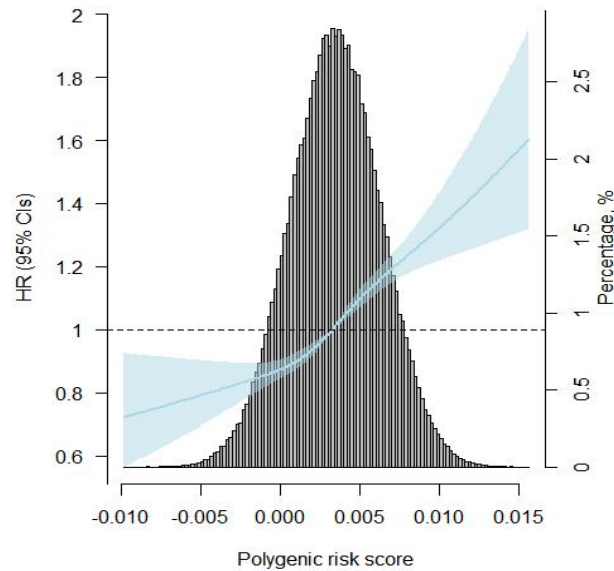
Subgroup	Cases/N	HR	P value
Low genetic risk			
Low PA	353/11485	1.000(reference)	-
Moderate PA	385/17616	0.800(0.691-0.925)	<0.01
High PA	401/17552	0.836(0.722-0.968)	<0.05
Intermediate genetic risk			
Low PA	787/23349	1.000(reference)	-
Moderate PA	856/34947	0.829(0.752-0.915)	<0.01
High PA	856/35131	0.848(0.768-0.936)	<0.01
High genetic risk			
Low PA	953/23536	1.000(reference)	-
Moderate PA	1016/35202	0.814(0.745-0.890)	<0.01
High PA	1006/34662	0.824(0.752-0.902)	<0.01

Note: Multivariable model was adjusted for age, sex, BMI, race, TDI, smoking status, drinking status, sleep scores, diet scores, genetic risk categories and low physical activity level. All statistical tests were two-sided. P < 0.05 was considered significant.
HR, hazard ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; PA, physical activity; BMI, body mass index; TDI, townsend deprivation index.

130 **Supplementary Figure S 1.** Flow chart of participants enrolment



Supplementary Figure S 2. The dose-response relationship and distribution plot of polygenic risk scores



Note: Adjusted for age, sex, BMI, race, TDI, smoking status, drinking status, sleep scores, diet scores, and physical activity level. All statistical tests were two-sided. $P < 0.05$ was considered significant. HR, hazard ratio; CI, confidence interval; BMI, body mass index; TDI, townsend deprivation index.