

Supplementary Table 1 Baseline characteristics according to cardiovascular risk score, mean \pm SD/*n* (%)

	0 (<i>n</i> = 1125969)	1 (<i>n</i> = 775642)	2 (<i>n</i> = 451302)	\geq 3 (<i>n</i> = 173715)	<i>P</i> value
Sex (Male)	426,624 (37.89)	522,624 (67.38)	325,451 (72.11)	138,611 (79.79)	< 0.001
Age (year)	40.27 \pm 11.00	47.60 \pm 13.68	54.07 \pm 12.61	57.27 \pm 10.20	< 0.001
Smoking status					< 0.001
Non	868,864 (77.17)	365,831 (47.16)	181,775 (40.28)	48,764 (28.07)	
Past smoker	160,011 (14.21)	123,495 (15.92)	70,145 (15.54)	23,081 (13.29)	
Current smoker	97,094 (8.62)	286,316 (36.91)	199,382 (44.18)	101,870 (58.64)	
Alcohol intake					< 0.001
Non	595,366 (52.88)	360,773 (46.51)	218,505 (48.42)	81,376 (46.84)	
Moderate	464,754 (41.28)	337,495 (43.51)	186,093 (41.23)	72,481 (41.72)	
Heavy ^a	65,849 (5.85)	77,374 (9.98)	46,704 (10.35)	19,858 (11.43)	
Regular exercise ^b	185,583 (16.48)	142,431 (18.36)	88,687 (19.65)	35,814 (20.62)	< 0.001
BMI (kg/m ²)	22.92 \pm 3.17	24.15 \pm 3.14	24.66 \pm 3.09	25.01 \pm 3.00	< 0.001
Systolic BP (mm Hg)	118.40 \pm 13.95	123.86 \pm 14.52	126.86 \pm 15.24	128.31 \pm 15.37	< 0.001
Diastolic BP (mm Hg)	74.23 \pm 9.64	77.33 \pm 9.79	78.72 \pm 10.00	79.4 \pm 10.12	< 0.001
Hypertension	104,152 (9.25)	179,794 (23.18)	212,801 (47.15)	122,465 (70.50)	< 0.001
Dyslipidemia	138,014 (12.26)	136,180 (17.56)	106,122 (23.51)	49,100 (28.26)	< 0.001
Diabetes mellitus	37,996 (3.37)	65,939 (8.50)	70,838 (15.70)	40,697 (23.43)	< 0.001

PHx of PCI or CABG	737 (0.07)	2,523 (0.33)	5,211 (1.15)	4,676 (2.69)	< 0.001
PHx of MI	1,856 (0.16)	3,321 (0.43)	4,716 (1.04)	3,635 (2.09)	< 0.001
PHx of stroke	1,536 (0.14)	3,694 (0.48)	5,434 (1.20)	3,807 (2.19)	< 0.001
PHx of AAA	315 (0.03)	632 (0.08)	754 (0.17)	558 (0.32)	< 0.001
Statin use	30,180 (2.68)	54,443 (7.02)	62,701 (13.89)	35,557 (20.47)	< 0.0001
Fasting glucose (mg/dL)	93.08 ± 18.15	98.03 ± 23.94	102.83 ± 28.72	107.25 ± 32.49	< 0.001
Total cholesterol (mg/dL)	194.25 ± 35.57	196.44 ± 36.85	195.25 ± 37.32	190.56 ± 38.16	< 0.001
HDL-C (mg/dL)	64.47 ± 38.94	52.87 ± 27.22	47.02 ± 17.02	41.06 ± 9.78	< 0.001
LDL-C (mg/dL)	112.24 ± 41.23	116.12 ± 37.76	115.12 ± 38.73	111.19 ± 39.42	< 0.001
Triglycerides (mg/dL)	87 (62-126)	121 (84-176)	140 (98-204)	161 (113-234)	< 0.001

^aHeavy drinker is defined as average alcohol intake ≥ 30 g/day.

^bRegular exercise is defined as moderate exercise ≥ 5 days or vigorous exercise ≥ 3 days in a week.

BMI, body mass index; PHx, previous history; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; MI, myocardial infarction, AAA, aneurysm of abdominal aorta; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Supplementary Table 2 Comparison of clinical characteristics and cardiovascular risk factors by gender

	Male (n = 1413310)	Female (n = 1113318)	P value
Age (year)	44.67 ± 12.90	48.04 ± 14.03	< 0.0001
Smoking status			< 0.0001
Non	413485 (29.26)	1051749 (94.47)	
Past smoker	354543 (25.09)	22189 (1.99)	
Current smoker	645282 (45.66)	39380 (3.54)	
Alcohol intake			< 0.0001
Non	435079 (30.78)	820941 (73.74)	
Moderate	781415 (55.29)	279408 (25.10)	
Heavy ^a	196816 (13.93)	12969 (1.16)	
Regular exercise ^b	278962 (19.74)	173553 (15.59)	< 0.0001
BMI (kg/m ²)	24.17 ± 3.06	23.22 ± 3.36	< 0.0001
Systolic BP (mm Hg)	124.42 ± 13.94	119.54 ± 15.68	< 0.0001
Diastolic BP (mm Hg)	78.04 ± 9.61	74.19 ± 10.03	< 0.0001
Hypertension	354935 (25.11)	264277 (23.74)	< 0.0001
Dyslipidemia	220963 (15.63)	208453 (18.72)	< 0.0001
Diabetes mellitus	133965 (9.48)	81505 (7.32)	< 0.0001
PHx of PCI or CABG	9445 (0.67)	3702 (0.33)	< 0.0001
PHx of MI	8899 (0.63)	4629 (0.42)	< 0.0001
PHx of stroke	8103 (0.57)	6368 (0.57)	0.8876

PHx of AAA	1323 (0.09)	936 (0.08)	0.0118
Statin use	88,282 (6.25)	94,599 (8.50)	< 0.0001
Fasting glucose (mg/dL)	99.04 ± 25.52	95.13 ± 21.03	< 0.0001
Total cholesterol (mg/dL)	194.34 ± 35.94	195.49 ± 37.17	< 0.0001
HDL-C (mg/dL)	53.01 ± 28.32	60.21 ± 35.80	< 0.0001
LDL-C (mg/dL)	112.50 ± 39.83	115.61 ± 39.40	< 0.0001
Triglycerides (mg/dL)	126 (86-188)	92 (64-134)	< 0.0001
Risk score			< 0.0001
0	426,624 (30.19)	699,345 (62.82)	
1	522,624 (36.98)	253,018 (22.73)	
2	325,451 (23.03)	125,851 (11.30)	
≥ 3	138,611 (9.81)	35,104 (3.16)	
Risk 1 (M ≥ 45yrs, F ≥ 55yrs)	651,235 (46.08)	346,674 (31.14)	< 0.0001
Risk 2 (FHx of CAD)	167,939 (11.88)	144,746 (13.00)	< 0.0001
Risk 3 (Hypertension)	202,400 (14.32)	191,015 (17.16)	< 0.0001
Risk 4 (Current smoker)	645,282 (45.66)	39,380 (3.54)	< 0.0001
Risk 5 (HDL < 40)	206,015 (14.58)	72,599 (6.52)	< 0.0001
Risk 6 (HDL ≥ 60)	334,868 (23.69)	471,473 (42.35)	< 0.0001

^aHeavy drinker is defined as average alcohol intake ≥ 30 g/day.

^bRegular exercise is defined as moderate exercise ≥ 5 days or vigorous exercise ≥ 3 days in a week.

BMI, body mass index; PHx, previous history; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; MI, myocardial infarction, AAA, aneurysm of abdominal aorta; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Supplementary Table 3 Risk of colorectal cancer according to cardiovascular risk score, stratified by diabetes mellitus status

Gender	DM	Risk score	<i>n</i>	Events	Person years	IR ^a	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)	Model 4 HR (95%CI)
Total	DM (-)	0	1,087,973	7,379	11,161,407	0.66	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
		1	709,703	8,276	7,206,847	1.15	1.737 (1.683, 1.792)	0.940 (0.909, 0.972)	0.931 (0.900, 0.963)	0.933 (0.902, 0.965)
		2	380,464	6,739	3,810,646	1.77	2.675 (2.588, 2.765)	1.033 (0.996, 1.072)	1.017 (0.980, 1.056)	1.023 (0.985, 1.062)
		≥ 3	133,018	3,093	1,313,088	2.36	3.568 (3.421, 3.720)	1.177 (1.124, 1.233)	1.156 (1.103, 1.211)	1.164 (1.111, 1.220)
		<i>P</i> for trend					< 0.001	< 0.001	< 0.001	< 0.001

	DM	0	37,996	519	382,957	1.36	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	(+)									
		1	65,939	1,336	649,893	2.06	1.519	0.972	0.966	0.969
							(1.372,	(0.877,	(0.870,	(0.873,
							1.681)	1.078)	1.071)	1.075)
		2	70,838	1,824	682,267	2.67	1.977	1.039	1.032	1.037
							(1.794,	(0.938,	(0.931,	(0.936,
							2.180)	1.151)	1.144)	1.150)
		≥ 3	40,697	1,163	384,848	3.02	2.237	1.094	1.091	1.098
							(2.017,	(0.981,	(0.977,	(0.983,
							2.481)	1.220)	1.219)	1.227)
							<i>P</i> for trend	< 0.001	0.009	0.010
							<i>P</i> for interaction	< 0.001	0.212	0.528
Male	DM	0	410,113	2,273	4,199,077	0.54	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	(-)									
		1	482,825	5,080	4,898,821	1.04	1.915	1.128	1.112	1.113
							(1.823,	(1.072,	(1.057,	(1.058,
							2.012)	1.186)	1.170)	1.171)

	2	279,430	4,831	2,797,487	1.73	3.190 (3.034, 3.353)	1.267 (1.202, 1.334)	1.237 (1.174, 1.304)	1.242 (1.178, 1.309)
	≥ 3	106,977	2,506	1,054,807	2.38	4.391 (4.148, 4.647)	1.400 (1.319, 1.485)	1.359 (1.280, 1.443)	1.369 (1.289, 1.454)
	<i>P</i> for trend					< 0.001	< 0.001	< 0.001	< 0.001
DM	0	16,511	239	164,904	1.45	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
(+)	1	39,799	840	390,425	2.15	1.485 (1.287, 1.715)	1.031 (0.892, 1.192)	1.028 (0.889, 1.188)	1.031 (0.892, 1.191)
	2	46,021	1,262	441,383	2.86	1.976 (1.721, 2.269)	1.121 (0.973, 1.290)	1.118 (0.970, 1.288)	1.126 (0.977, 1.297)
	≥ 3	31,634	956	298,417	3.20	2.216 (1.923, 2.553)	1.192 (1.031, 1.377)	1.193 (1.031, 1.381)	1.206 (1.042, 1.396)
	<i>P</i> for trend					< 0.001	< 0.001	< 0.001	< 0.001
	<i>P</i> for interaction					< 0.001	0.002	0.028	0.026

Female	DM	0	677,860	5,106	6,962,330	0.73	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
		(-)								
		1	226,878	3,196	2,308,026	1.38	1.888	0.973	0.957	0.958
							(1.806, 1.973)	(0.925, 1.023)	(0.911, 1.007)	(0.911, 1.007)
		2	101,034	1,908	1,013,158	1.88	2.569	0.991	0.966	0.967
							(2.437, 2.707)	(0.932, 1.053)	(0.908, 1.027)	(0.909, 1.029)
		≥ 3	26,041	587	258,281	2.27	3.104	1.090	1.058	1.060
							(2.850, 3.381)	(0.994, 1.195)	(0.964, 1.160)	(0.966, 1.163)
		<i>P</i> for trend					< 0.001	0.362	0.977	0.936
	DM	0	21,485	280	218,054	1.28	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
		(+)								
		1	26,140	496	259,468	1.91	1.492	1.032	1.029	1.026
							(1.289, 1.727)	(0.884, 1.205)	(0.880, 1.203)	(0.878, 1.200)
		2	24,817	562	240,884	2.33	1.824	1.087	1.083	1.079
							(1.580, 2.105)	(0.927, 1.275)	(0.921, 1.273)	(0.917, 1.269)

≥ 3	9,063	207	86,431	2.39	1.874	1.072	1.071	1.067
					(1.566,	(0.883,	(0.879,	(0.876,
					2.243)	1.302)	1.305)	1.300)
	<i>P</i> for trend				< 0.001	0.323	0.343	0.365
	<i>P</i> for interaction				< 0.001	0.490	0.667	0.668

^aColorectal cancer incidence rate *per* 1000 person-years.

Model 1: Not adjusted; Model 2: Adjusted for sex and age; Model 3: Adjusted for sex, age, alcohol consumption, regular exercise, body mass index, diabetes mellitus, and previous history of percutaneous coronary intervention or coronary artery bypass graft, myocardial infarction, stroke, and aneurysm of abdominal aorta; Model 4: Adjusted for sex, age, alcohol consumption, regular exercise, body mass index, diabetes mellitus, previous history of percutaneous coronary intervention or coronary artery bypass graft, myocardial infarction, stroke, aneurysm of abdominal aorta, and statin use; IR: Incidence rate; HR: Hazard ratio; CI: Confidence interval.