Supplementary Materials

Detailed definition of covariates

For KNHANES, participants income was classified into four categories by quartiles; Education levels were divided into three categories: college or above, high school or equivalent, and below high school; smoking status was defined by the questionnaires: participants who never smoke was defined as never smoke, and participants smoke less than 5/more than 5 pack of cigarettes was defined as current smoker (current smoker and never); Alcohol drinking status was based on the question that whether the participant ever drink any type of alcoholic beverage, and participants who responded affirmatively were classified as alcohol drinkers (current drinker and never); and the history of diabetes/hypertension was also defined by the questionnaires about ever diagnosis by doctor (yes and no); Physical activity was categorized by whether moderate-intensity physical activity exceeds 2 hours and 30 minutes per week, or vigorous-intensity physical activity exceeds 1 hour and 15 minutes per week, or a combination of moderate and vigorous activities meets the equivalent time requirement for each (yes and no); The nutrient supplement use was also categorized by the answer of participants whether they used nutrient supplement (yes and no).

For UK Biobank, potential confounders, encompassed a range of demographic, socioeconomic, and health-related variables, including age, sex (male and female), education levels (college or above, high school or equivalent, below high school), race and ethnicity (White and others), Townsend deprivation index (TDI, which derived from the postcode of residence using aggregated data on unemployment, ownership of car and house, and household overcrowding), household income (< 18,000, 18,000 - < 30,999, 31,000- < 51,999, 52,000 - < 100,000, and ≥ 100,000), alcohol drinking status (current drinker, previous drinker, and never), smoking status (current smoker, previous smoker, and never), history of hypertension (yes and no), vitamin supplement use (non-user, vitamin D user, and multivitamin user), time spend outdoors in summer (hours per day), time spend outdoors in winter (hours per day), skin color (very fair, fair, light olive, dark olive, brown, black), ease of skin tanning (very tanned, moderately tanned, mildly/occasionally tanned, never tan/only burn), use of sun screen/UV protection (never/rarely, sometimes, most of times, always, and do not go out in sunshine), solarium/sunlamp use (times per year), consumption of oily fish (never/ less than once a week, and at least once a week), processed meat (never/ less than once a week, and at least once a week), and physical activity was computed as metabolic equivalent (MET) hours per week.

Supplementary Table 1. Complete list of baseline characteristics of the study population in UK Biobank

Characteristic	UK Biobank			
	Total (N = 229260)	With AD (N = 1647)	Without AD (N = 227613)	*P* value
Age (y), mean ± SD	56.3 ± 8.2	56.7 ± 8.1	56.3 ± 8.2	0.025
25(OH)D (n/mol), mean ± SD	50.0 ± 21.1	50.0 ± 21.1	48.3 ± 20.8	0.001
BMI (kg/m²,)	27.2 ± 4.6	27.2 ± 4.6	27.6 ± 4.8	0.004
WC (cm), mean ± SD	90.4 ± 13.3	90.4 ± 13.3	90.9 ± 13.5	0.103
TDI, mean ± SD	-1.5 ± 3.0	-1.5 ± 3.0	-1.5 ± 2.9	0.389
Time spent outdoors in summer (hours per day), mean ± SD	4.1 ± 2.3	4.1 ± 2.3	4.1 ± 2.4	0.816
Time spent outdoors in winter (hours per day), mean ± SD	2.2 ± 1.8	2.2 ± 1.8	2.1 ± 1.7	0.166
Solarium/sunlamp use (times per year), mean ± SD	0.6 ± 5.0	0.6 ± 4.9	0.7 ± 9.3	0.190
Physical activity (MET, minutes per week), mean ± SD	2868.2 ± 2726.7	2870.0 ± 2727.8	2628.9 ± 2554.7	<0.001
Gender, N (%)				0.120
Male	119630 (52.2)	118802 (52.2)	828 (50.3)	
Female	109630 (47.8)	108811 (47.8)	819 (49.7)	
Race and ethnicity, N (%)				0.356
White	220379 (96.1)	218803 (96.1)	1576 (95.7)	
Others [a]	8881 (3.9)	8810 (3.9)	71 (4.3)	
BMI, N (%)				0.158
≥ 25	77191 (33.7)	76672 (33.7)	519 (31.5)	
25 - <30	100092 (43.7)	99357 (43.7)	735 (44.6)	
≥ 30	51977 (22.7)	51584 (22.7)	393 (23.9)	
Educational level, N (%)				0.777
≥ College or above	82025 (35.8)	81436 (35.8)	589 (35.8)	
High school / equivalent	116803 (50.9)	115973 (51.0)	830 (50.4)	
< High school	30432 (13.3)	30204 (13.3)	228 (13.8)	
Household income, N (%)				0.070
Less than 18000	47488 (20.7)	47114 (20.7)	374 (22.7)	
18000 to 30999	58309 (25.4)	57875 (25.4)	434 (26.4)	
31000 to 51999	61662 (26.9)	61224 (26.9)	438 (26.6)	
52000 to 100000	48695 (21.2)	48372 (21.3)	323 (19.6)	
Greater than 100000	13106 (5.7)	13028 (5.7)	78 (4.7)	
Smoking status, N (%)				<0.001
Current	23143 (10.1)	22955 (10.1)	188 (11.4)	
Previous	82753 (36.1)	82096 (36.1)	657 (39.9)	
Never	123364 (53.8)	122562 (53.8)	802 (48.7)	
Alcohol drinking, N (%)				0.916
Current	214877 (93.7)	213337 (93.7)	1540 (93.5)	
Previous	7266 (3.2)	7211 (3.2)	55 (3.3)	
Never	7117 (3.1)	7065 (3.1)	52 (3.2)	

Hypertension, N (%)				0.281
No	168808 (73.6)	216615 (95.2)	1558 (94.6)	
Yes	60452 (26.4)	10998 (4.8)	89 (5.4)	
Diabetes, N (%)				0.005
No	218173 (95.2)	167645 (73.7)	1163 (70.6)	
Yes	11087 (4.8)	59968 (26.3)	484 (29.4)	
Vitamin supplement use, N (%)				0.244
Non-user	172987 (75.5)	171764 (75.5)	1223 (74.3)	
Vitamin D user	8886 (3.9)	8810 (3.9)	76 (4.6)	
Multivitamin user	47387 (20.7)	47039 (20.7)	348 (21.1)	
Skin color, N (%)				0.061
Very fair	17098 (7.5)	16946 (7.4)	152 (9.2)	
Fair	156522 (68.3)	155416 (68.3)	1106 (67.2)	
Light olive	45085 (19.7)	44783 (19.7)	302 (18.3)	
Dark olive	4573 (2.0)	4534 (2.0)	39 (2.4)	
Brown	5060 (2.2)	5019 (2.2)	41 (2.5)	
Black	922 (0.4)	915 (0.4)	7 (0.4)	
Ease of skin tanning, N (%)				0.005
Very tanned	52084 (22.7)	51693 (22.7)	391 (23.7)	
Moderately tanned	93599 (40.8)	92976 (40.8)	623 (37.8)	
Mildly/occasionally tanned	47028 (20.5)	46703 (20.5)	325 (19.7)	
Never tan, only burn	36549 (15.9)	36241 (15.9)	308 (18.7)	
Use of sun screen/UV protection, N (%)				<0.001
Never/rarely	21606 (9.4)	21443 (9.4)	163 (9.9)	
Sometimes	77407 (33.8)	76896 (33.8)	511 (31.0)	
Most of times	82745 (36.1)	82172 (36.1)	573 (34.8)	
Always	46675 (20.4)	46288 (20.3)	387 (23.5)	
Do not go out in sunshine	827 (0.4)	814 (0.4)	13 (0.8)	
Consumption of oily fish, N (%)				
Never/ less than once a week	97268 (42.4)	96565 (42.4)	703 (42.7)	0.832
At least once a week	131992 (57.6)	131048 (57.6)	944 (57.3)	
Consumption of processed meat, N (%)				0.299
Never/ less than once a week	89714 (39.1)	89049 (39.1)	665 (40.4)	
At least once a week	139546 (60.9)	138564 (60.9)	982 (59.6)	

Supplementary Table 2. Exclusion table of participants in KNHANES

Characteristic	Participants			
	Overall (N = 11145)	Included (N = 6340)	Excluded (N = 4805)	*P* value
Age (y), mean ± SD	53.9 ± 16.7	55.9 ± 10.3	51.3 ± 22.2	<0.001
Gender, N (%)				0.009
Male	4844 (43.5)	2688 (42.4)	2156 (44.9)	
Female	6301 (56.5)	3652 (57.6)	2649 (55.1)	
Educational level, N (%)				<0.001
≥ College or above	4408 (40.9)	2571 (40.6)	1837 (41.5)	
High school / equivalent	3509 (32.6)	2210 (34.9)	1299 (29.3)	
< High school	2852 (26.5)	1559 (24.6)	1293 (29.2)	

Abbreviations: SD: standard deviation.

Supplementary Table 3. Exclusion table of participants in UK Biobank

Characteristic	Participants			
	Overall (N = 501961)	Included (N = 229260)	Excluded (N = 272701)	*P* value
Age (y), mean ± SD	56.5 ± 8.1	56.3 ± 8.2	57.3 ± 8.0	<0.001
TDI, mean ± SD	-1.3 ± 3.1	-1.5 ± 3.0	-1.1 ± 3.2	<0.001
Gender, N (%)				<0.001
Male	228910 (45.6)	119630 (52.2)	109280 (40.1)	
Female	273051 (54.4)	109630 (47.8)	163421 (59.9)	
Race and ethnicity[a], N (%)				<0.001
White	471630 (94.0)	220379 (96.1)	251251 (92.1)	
Others [a]	30331 (6.0)	8881 (3.9)	21450 (7.9)	
Educational level, N (%)				<0.001
≥ College or above	160938 (32.1)	82025 (35.8)	78913 (28.9)	
High school / equivalent	255801 (51.0)	116803 (50.9)	138998 (51.0)	
< High school	85222 (17.0)	30432 (13.3)	54790 (20.1)	

Abbreviations: SD: standard deviation, TDI, Townsend deprivation index.
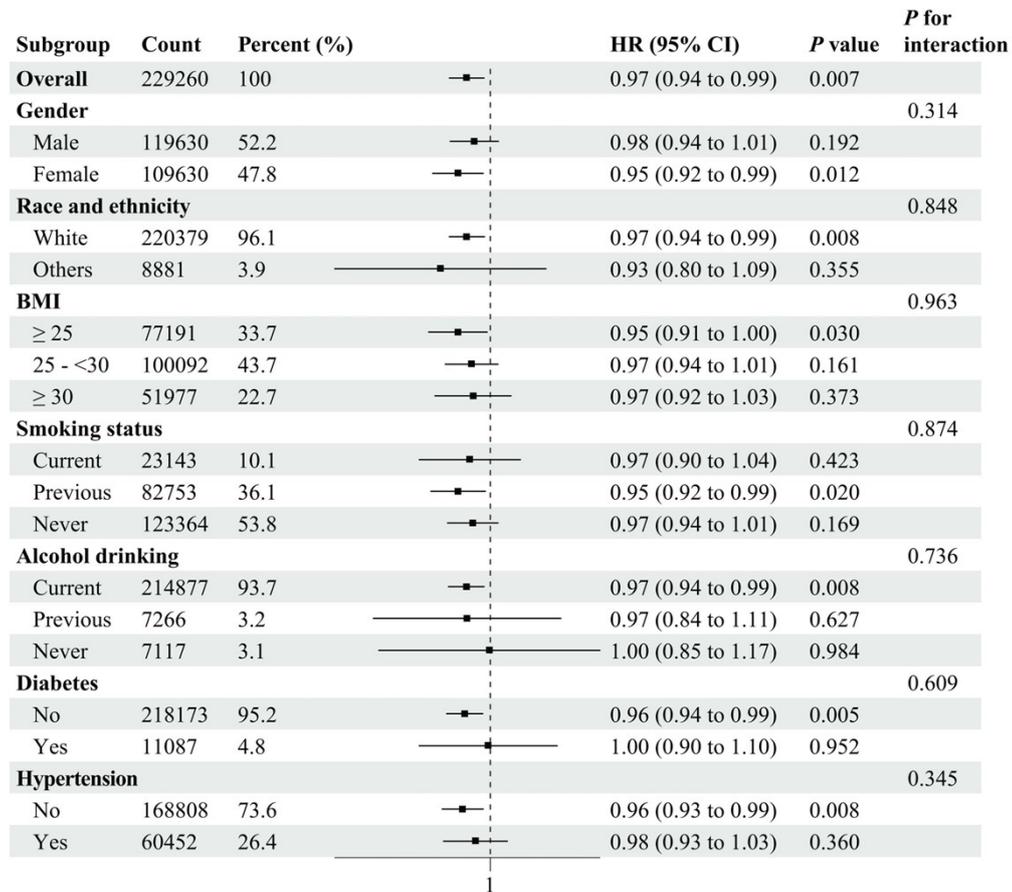
[a] In the UK Biobank, other included Asian or Asian British (including Bangladeshi, Indian, Pakistani, and any other Asian background), Black or Black British (including African, Caribbean, and any other Black background), Chinese, mixed race (including Black and White African, Black and White Caribbean, Asian and White, any other mixed background), or other ethnic group.

Supplementary Table 4. Assessment of multicollinearity of covariates using variance inflation factors (VIF).

Features	VIF
Age	1.3
Gender	1.7
Race/ethnicity	1.5
BMI	2.6
Education level	1.3
Household income	1.4
TDI	1.1
Physical activity	1.2
Smoking status	1.1
Alcohol drinking	1.1
Hypertension	1.2
Diabetes	1.1
WC	3.5
25(OH)D	1.2
Vitamin supplement use	1.0
Time spend outdoors in summer	1.9
Time spend outdoors in winter	1.9
Skin color	1.6
Ease of skin tanning	1.3
Use of sun screen/UV protection	1.2
Solarium/sunlamp use	1.0
Consumption of oily fish	1.0
Processed meat	1.1

Abbreviations: BMI: body mass index; SD: standard deviation, TDI, Townsend deprivation index; WC, waist circumference; 25(OH)D, 25-hydroxyvitamin D.

Supplementary Figure 1

Subgroup	Count	Percent (%)		HR (95% CI)	*P* value	*P* for interaction
Overall	229260	100		0.97 (0.94 to 0.99)	0.007	
Gender						0.314
Male	119630	52.2		0.98 (0.94 to 1.01)	0.192	
Female	109630	47.8		0.95 (0.92 to 0.99)	0.012	
Race and ethnicity						0.848
White	220379	96.1		0.97 (0.94 to 0.99)	0.008	
Others	8881	3.9		0.93 (0.80 to 1.09)	0.355	
BMI						0.963
≥ 25	77191	33.7		0.95 (0.91 to 1.00)	0.030	
25 - <30	100092	43.7		0.97 (0.94 to 1.01)	0.161	
≥ 30	51977	22.7		0.97 (0.92 to 1.03)	0.373	
Smoking status						0.874
Current	23143	10.1		0.97 (0.90 to 1.04)	0.423	
Previous	82753	36.1		0.95 (0.92 to 0.99)	0.020	
Never	123364	53.8		0.97 (0.94 to 1.01)	0.169	
Alcohol drinking						0.736
Current	214877	93.7		0.97 (0.94 to 0.99)	0.008	
Previous	7266	3.2		0.97 (0.84 to 1.11)	0.627	
Never	7117	3.1		1.00 (0.85 to 1.17)	0.984	
Diabetes						0.609
No	218173	95.2		0.96 (0.94 to 0.99)	0.005	
Yes	11087	4.8		1.00 (0.90 to 1.10)	0.952	
Hypertension						0.345
No	168808	73.6		0.96 (0.93 to 0.99)	0.008	
Yes	60452	26.4		0.98 (0.93 to 1.03)	0.360	

1

Supplementary Figure 1. Subgroup analysis

Each stratification was adjusted for all co-variables except the stratification factor itself.

Squares indicate the HRs, while the lines showing their 95% CIs.