Online Supplemental material

Supplement to: Yoriko Heianza, Tao Zhou, Dianjianyi Sun, Frank B. Hu, Lu Qi.

Healthful Plant-Based Dietary Patterns, Genetic Risk of Obesity, and Cardiovascular Risk in the UK Biobank Study

Online-Supplemental Methods

Dietary Assessment

The Oxford WebQ asked about consumption of >200 types of foods and >30 types of drinks during the previous 24 hours using standard categories to indicate the amount consumed. As compared with an interviewer-administrated dietary assessment, the Oxford WebQ captures similar food items and estimates similar nutrient intakes with moderate-to-strong correlations for the majority of nutrients (Spearman's correlation coefficients ranges of 0.5–0.9).[1] Study participants also answered the following question: "Would you say that what you ate and drank yesterday was fairly typical for you? (yes/no)"; we recognized that 81% (n=99014/121799) of the participants answered "yes" to the question. A previous study reported stable levels of food intakes over 4 years after a baseline assessment in this cohort[2]; we also confirmed that there was a strong correlation (Pearson correlation coefficient=0.88; *P* <0.0001) between a “hPDI assessed at baseline” and an “averaged hPDI” based on repeated measurements during 2009-2012 (maximum: five times, n of participants=121799). Therefore, the present study used the earliest data on dietary intake to maximize a follow-up time if participants had completed the dietary assessment more than once.

Covariates

Participants completed a touch screen questionnaire which asked to report income (less than £18,000, £18,000 to £30,999, £31,000 to £51,999, £52,000 to £100,000, or greater than £100,000), education, smoking habit (never, former, current), lifestyle habits (such as hours of TV watching and sleeping), the number of days and minutes per day spent walking, performing a moderate activity and vigorous activity at least 10 minutes at a time. According to the Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ),[3] we calculated minutes performing moderate or vigorous physical activity per week. The Townsend Social Deprivation Index was created by the UK Biobank group[4], a composite measure of deprivation based on unemployment, non-car ownership, non-home ownership, and household overcrowding. A negative value of the Townsend Social Deprivation Index represents high socio-economic status. The multivariate-adjusted model 1 included covariates of age, sex, top 5 principal components of ancestry; model 2 included additional variables of multivitamin supplement use, college education, smoking habit (never, former, current), energy intake (quintiles), alcohol intake (0, 0-<5, 5-<15, or ≥15 g/d), TV watching hours (0-<1, 1-3, ≥3 hours/d), physical activity (quintiles), sleeping hours (<7, 7-9, ≥9 hours/d), and the Townsend Social Deprivation Index (quintiles). We used missing indicators if there were missing data on the covariates.

References

1. Liu B, Young H, Crowe FL *et al.* Development and evaluation of the Oxford WebQ, a low-cost, web-based method for assessment of previous 24 h dietary intakes in large-scale prospective studies. *Public Health Nutr* 2011; **14**: 1998-2005.
2. Bradbury KE, Young HJ, Guo W, Key TJ. Dietary assessment in UK Biobank: an evaluation of the performance of the touchscreen dietary questionnaire. *J Nutr Sci* 2018; **7**: e6.
3. Guidelines for data processing and analysis of the International Physical Activity Questionnaire (IPAQ).2005. URL: <http://www.IPAQ.ki.se.
4. Adams J, Ryan V, White M. How accurate are Townsend Deprivation Scores as predictors of self-reported health? A comparison with individual level data. *J Public Health (Oxf)* 2005; **27**: 101-6.

STable 1: Overall characteristics of participants who were excluded (n=89,210) or included (n=121,799) in the present study

	Excluded (n=89,210)		Included (n=121,799)					
	Total		Total		Women		Men	
Characteristics	N	Data	N	Data	N	Data	N	Data
Age, y	89210	57.4 (7.8)	121799	55.1 (7.9)	69909	54.8 (7.8)	51890	55.5 (8.1)
Male sex	89210	48.1%	121799	42.6%	-	-	-	-
Current smoking, yes	88870	8.0%	121573	7.8%	69909	6.7%	51890	9.2%
Townsend deprivation index	88945	–1.2 (3)	121799	–1.8 (2.7)	69909	–1.8 (2.7)	51890	–1.8 (2.7)
College or university degree, yes	89210	40.9%	121799	43.7%	69909	41.7%	51890	46.50%
Physical activity, MET-hours/wk	84252	38.7 (39.6)	116268	40.2 (39.4)	66091	38.9 (37.4)	50177	41.9 (41.9)
Hours of TV-watching, hours per day	88621	2.7 (1.6)	121448	2.4 (1.5)	69670	2.4 (1.4)	51778	2.4 (1.5)
Healthful plant-based diet index	83381	56 (7)	121799	56 (7)	69909	57 (7)	51890	55 (7)
Genetic risk score of body mass index (BMI)	84710	70.8 (5.7)	121799	70.9 (5.6)	69909	70.9 (5.7)	51890	70.9 (5.6)
BMI, kg/m^2	88543	28 (5)	121799	26.2 (4.1)	69909	25.8 (4.4)	51890	26.7 (3.6)
Systolic blood pressure, mmHg	84579	141 (19)	121799	133 (17)	69909	131 (17)	51890	137 (16)
Diastolic blood pressure, mmHg	84584	84 (10)	121799	80 (10)	69909	79 (9)	51890	82 (9)
Mean arterial blood pressure, mmHg	84579	102 (12)	121799	98 (11)	69909	96 (11)	51890	100 (11)
Triglycerides, mmol/L	83001	1.78 (1.03)	115996	1.62 (0.94)	66565	1.41 (0.76)	49431	1.89 (1.09)
Total cholesterol, mmol/L	83064	5.50 (1.17)	116068	5.85 (1.06)	66600	5.94 (1.08)	49468	5.74 (1.03)
HDL cholesterol, mmol/L	75963	1.42 (0.38)	105951	1.51 (0.38)	60316	1.65 (0.37)	45635	1.33 (0.3)
LDL cholesterol, mmol/L	82921	3.42 (0.88)	115845	3.66 (0.82)	66479	3.65 (0.84)	49366	3.67 (0.79)
Glucose, mmol/L	75905	5.30 (1.48)	105869	4.96 (0.75)	60275	4.95 (0.68)	45594	4.98 (0.82)
HbA1c-IFCC, mmol/mol	81764	37 (8)	115869	35 (4)	66496	35 (4)	49373	35 (4)

N, number of participants with available data. Data are mean (SD) or %.

STable 2: Example of food items in the 17 food groups

Food groups	Food items	Scoring
Whole grains	Porridge, muesli, oat crunch, bran cereal, cereal bar, non-white bread (flour types, brown, wholemeal, other type), seeded or other bread, crispbread, whole-wheat cereal, other cereal, whole meal pasta, brown rice, couscous, other cooked grains (such as bulgur).	Positive
Fruits	Mixed fruit, apple, banana, berries, cherries, grapefruit, grapes, mango ,melon, orange, orange-like small fruits, peach/nectarine, pear, pineapple, plum, other fruits, stewed/cooked fruit, prunes, other dried fruit	Positive
Vegetables	Mixed vegetables, vegetable pieces, coleslaw, side salad, beetroot, broccoli, butternut squash, cabbage/kale, carrots, cauliflower, celery, courgette, cucumber, garlic, leeks, lettuce, mushrooms, onion, parsnip, sweet peppers, spinach, sprouts, sweetcorn, sweet potato, fresh tomatoes, cooked or tinned tomatoes, turnip/swede, watercress, other vegetable intake	Positive
Nuts	Salted peanuts, unsalted peanuts, salted nuts, unsalted nuts, seeds	Positive
Legumes, Vegetarian protein alternatives	Beans (baked beans), other beans or lentils, broad beans, green beans, peas, soy or vegetable milk, vegetarian sausages/burgers, tofu, quorn, other vegetarian alternative	Positive
Tea and coffee	Instant coffee, filtered coffee, cappuccino, latte, espresso, other coffee drinks, standard tea, rooibos tea, green tea, herbal tea, other tea	Positive
Refined grains	Sweetened cereal, plain cereal, white bread, naan bread, garlic bread, white pasta, white rice, pancake, scotch pancake, croissant, scone, savoury or cheesy biscuits, other savoury snack, snackpot	Reverse
Potatoes	Fried potatoes, boiled/baked potatoes, mashed potatoes, crisps (e.g., potato chips)	Reverse
Sugary drinks	Low calorie or diet drinks (e.g. fizzy, squash), carbonated (fizzy) drinks, squash or cordial	Reverse
Fruit juices	Orange juice, grapefruit juice, other fruit/vegetable juice, fruit smoothie	Reverse
Sweets and desserts	Double crust pie, single crust pie/flan, crumble topping, Yorkshire pudding, Danish pastry, fruitcake, cake, doughnuts, sponge pudding, other dessert, chocolate bar, white chocolate, milk chocolate, dark chocolate, chocolate-covered raisin, chocolate sweet, diet sweets, chocolate-covered biscuits, chocolate biscuits, sweet biscuits, other sweets	Reverse
Animal fat	Butter on bread/crackers (spreadable, low fat, normal fat, or unknown type), dairy spread on bread/crackers (very low fat, low fat, normal fat, unknown type)	Reverse
Dairy	Milk, dairy smoothie, flavored milk, yogurt, ice-cream, low fat hard cheese, hard cheese, soft cheese, blue cheese, low fat cheese spread, cheese spread, cottage cheese, feta cheese, mozzarella cheese, goat's cheese, other cheese, cheesecake, milk-based pudding, other milk-based pudding	Reverse
Eggs	Whole eggs, omelettes or scrambled egg, eggs in sandwiches, scotch egg, other egg dishes	Reverse
Fish or seafood	Tinned tuna, oily fish, breaded fish, battered fish, white fish, prawns, lobster/crab, shellfish, other fish intake	Reverse
Meat	Sausage, beef, pork, lamb, crumbed or deep-fried poultry, poultry, bacon, ham, liver, other meat intake	Reverse
Miscellaneous animal-based foods	Pizza, Indian snacks	Reverse

STable 3: Nutrient intake according to quartile (Q) categories of healthful plant-based diet index (hPDI)

	Q1	Q2	Q3	Q4
N	30550	32123	26255	32871
Healthful plant-based diet index	47 (3)	54 (1)	58 (1)	65 (3)
Food intake, servings/day				
Whole grains	1.9 (2.2)	2.6 (2.3)	3.1 (2.4)	3.6 (2.5)
Fruits	1.4 (1.5)	2 (1.7)	2.4 (1.8)	3.2 (2)
Vegetables	1.7 (1.9)	2.3 (2.3)	2.7 (2.4)	3.6 (2.8)
Nuts	0.1 (0.3)	0.1 (0.4)	0.2 (0.4)	0.3 (0.6)
Legumes	0.2 (0.5)	0.3 (0.6)	0.4 (0.7)	0.7 (0.8)
Tea and coffee	3.9 (1.9)	4.4 (1.8)	4.7 (1.8)	5.1 (1.8)
Fruit juices	0.6 (0.7)	0.5 (0.7)	0.4 (0.6)	0.3 (0.6)
Refined grains	1.9 (1.6)	1.2 (1.4)	0.8 (1.1)	0.5 (0.9)
Potatoes	0.9 (0.8)	0.8 (0.7)	0.7 (0.7)	0.5 (0.6)
Sugar sweetened beverages	0.9 (1.2)	0.5 (1)	0.3 (0.8)	0.2 (0.6)
Sweets and desserts	2.8 (2.2)	2.3 (2)	1.9 (1.8)	1.4 (1.6)
Animal fat	1.2 (1.5)	0.8 (1.3)	0.6 (1.2)	0.3 (1)
Dairy	1.2 (1)	1.1 (1)	1 (1)	1 (1)
Egg	0.4 (0.7)	0.3 (0.6)	0.2 (0.5)	0.1 (0.5)
Fish or seafood	0.4 (0.6)	0.3 (0.6)	0.3 (0.6)	0.3 (0.5)
Meat	1.5 (1.3)	1.2 (1.1)	1 (1)	0.8 (0.9)
Miscellaneous animal-based foods	0.2 (0.7)	0.1 (0.5)	0.1 (0.4)	0 (0.3)
Daily nutrient intake				
Total energy (E) intake, kcal/d	2293 (623)	2097 (596)	1997 (582)	1923 (565)
Total protein, %E	15.4 (4)	15.9 (4.1)	16.2 (4.2)	16.3 (4.2)
Total fat, %E	34.8 (7.2)	33 (7.6)	32 (7.8)	30.9 (8.2)
Total carbohydrate, %E	46.8 (8.8)	48 (9.2)	49 (9.4)	50.5 (9.7)
Total sugar, g	124 (52)	119 (51)	117 (49)	118 (48)
Polyunsaturated fatty acids, %E	6 (2.6)	5.9 (2.6)	5.9 (2.7)	6.2 (2.9)
Dietary fiber, g	13.6 (5.8)	15.4 (6.5)	16.8 (6.8)	19.8 (7.5)
Beta Carotene, ug	2299 (2338)	2817 (2707)	3258 (2980)	4135 (3485)
Folate, ug	293 (115)	297 (119)	302 (121)	322 (127)
Vitamin C, mg	144 (110)	147 (114)	152 (117)	166 (120)
Vitamin E, mg	8.8 (4.3)	8.8 (4.5)	9 (4.6)	10 (5)

Data are mean (SD).

STable 4: Single nucleotide polymorphisms (SNPs) included in a genetic risk score of BMI

Gene	**Chr.**	Published SNP	**Effect allele**	**Other allele**	**ß**	**SE**
SEC16B	1	rs543874	G	A	0.048	0.004
NEGR1	1	rs3101336	C	T	0.033	0.003
FPGT-TNNI3K	1	rs12566985	G	A	0.024	0.003
PTBP2	1	rs11165643	T	C	0.022	0.003
FUBP1	1	rs12401738	A	G	0.021	0.003
NAV1	1	rs2820292	C	A	0.020	0.003
AGBL4	1	rs657452	A	G	0.023	0.003
ELAVL4	1	rs11583200	C	T	0.018	0.003
TMEM18	2	rs13021737	G	A	0.060	0.004
ADCY3	2	rs10182181	G	A	0.031	0.003
LINC01122	2	rs1016287	T	C	0.023	0.003
EHBP1	2	rs11688816	G	A	0.017	0.003
ERBB4	2	rs7599312	G	A	0.022	0.003
UBE2E3	2	rs1528435	T	C	0.018	0.003
LRP1B	2	rs2121279	T	C	0.025	0.004
KCNK3	2	rs11126666	A	G	0.021	0.003
ETV5	3	rs1516725	C	T	0.045	0.005
RASA2	3	rs16851483	T	G	0.048	0.008
CADM2	3	rs13078960	G	T	0.030	0.004
FHIT	3	rs2365389	C	T	0.020	0.003
RARB	3	rs6804842	G	A	0.019	0.003
GBE1	3	rs3849570	A	C	0.019	0.003
GNPDA2	4	rs10938397	G	A	0.040	0.003
SCARB2	4	rs17001654	G	C	0.031	0.005
SLC39A8	4	rs13107325	T	C	0.048	0.007
HHIP	4	rs11727676	T	C	0.036	0.006
POC5	5	rs2112347	T	G	0.026	0.003
TFAP2B	6	rs2207139	G	A	0.045	0.004
PARK2	6	rs13191362	A	G	0.028	0.005
C6orf106	6	rs205262	G	A	0.022	0.004
TDRG1	6	rs2033529	G	A	0.019	0.003
FOXO3	6	rs9400239	C	T	0.019	0.003
PMS2L11	7	rs2245368	C	T	0.032	0.006
HIP1	7	rs1167827	G	A	0.020	0.003
HNF4G	8	rs17405819	T	C	0.022	0.003
RALYL	8	rs2033732	C	T	0.019	0.004
LINGO2	9	rs10968576	G	A	0.025	0.003
LMX1B	9	rs10733682	A	G	0.017	0.003
TLR4	9	rs1928295	T	C	0.019	0.003
EPB41L4B	9	rs6477694	C	T	0.017	0.003
C9orf93	9	rs4740619	T	C	0.018	0.003
HIF1AN	10	rs17094222	C	T	0.025	0.004
GRID1	10	rs7899106	G	A	0.040	0.007
NT5C2	10	rs11191560	C	T	0.031	0.005

TCF7L2	10	rs7903146	C	T	0.023	0.003
BDNF	11	rs11030104	A	G	0.041	0.004
MTCH2	11	rs3817334	T	C	0.026	0.003
TRIM66	11	rs4256980	G	C	0.021	0.003
CADM1	11	rs12286929	G	A	0.022	0.003
HSD17B12	11	rs2176598	T	C	0.020	0.004
BCDIN3D	12	rs7138803	A	G	0.032	0.003
CLIP1	12	rs11057405	G	A	0.031	0.006
MTIF3	13	rs12016871	T	C	0.030	0.005
OLFM4	13	rs12429545	A	G	0.033	0.005
NRXN3	14	rs7141420	T	C	0.024	0.003
PRKD1	14	rs12885454	C	A	0.021	0.003
STXBP6	14	rs10132280	C	A	0.023	0.003
MAP2K5	15	rs16951275	T	C	0.031	0.004
DMXL2	15	rs3736485	A	G	0.018	0.003
FTO	16	rs1558902	A	T	0.082	0.003
GPRC5B	16	rs12446632	G	A	0.040	0.005
ATP2A1	16	rs3888190	A	C	0.031	0.003
SBK1	16	rs2650492	A	G	0.021	0.004
KAT8	16	rs9925964	A	G	0.019	0.003
NLRC3	16	rs758747	T	C	0.023	0.004
RPTOR	17	rs12940622	G	A	0.018	0.003
RABEP1	17	rs1000940	G	A	0.019	0.003
MC4R	18	rs6567160	C	T	0.056	0.004
C18orf8	18	rs1808579	C	T	0.017	0.003
GRP	18	rs7243357	T	G	0.022	0.004
ZC3H4	19	rs3810291	A	G	0.028	0.004
QPCTL	19	rs2287019	C	T	0.036	0.004
KCTD15	19	rs29941	G	A	0.018	0.003
PGPEP1	19	rs17724992	A	G	0.019	0.004
TOMM40	19	rs2075650	A	G	0.026	0.005

Single nucleotide polymorphisms (SNPs) that showed genome-wide significant associations (P <5×10^{-8}) for BMI in a study by Locke AE, Kahali B, Berndt SI *et al.* Genetic studies of body mass index yield new insights for obesity biology. *Nature* 2015; **518**: 197-206.

STable 5: Effect of 10-unit increment of genetic risk score (GRS) for differences in body mass index and mean arterial blood pressure according to quartile (Q) categories of healthful plant-based diet index

	Healthful plant-based diet index				$P_{interaction}$
Outcomes	Q1	Q2	Q3	Q4	
Body mass index					
Model 1	1.07 (0.04)	0.92 (0.04)	0.89 (0.04)	0.69 (0.04)	<0.0001
Model 2	1.05 (0.04)	0.89 (0.04)	0.86 (0.04)	0.65 (0.04)	<0.0001
Mean arterial blood pressure					
Model 1	0.48 (0.11)	0.31 (0.11)	0.28 (0.12)	0.15 (0.1)	0.033
Model 2	0.47 (0.11)	0.27 (0.11)	0.27 (0.12)	0.12 (0.1)	0.021

Data are β (SE) per 10-unit increment of GRS for the outcomes. Model 1: age, sex, and the top five principal components of ancestry

Model 2: model 1 + college education history, the Townsend deprivation index, smoking habit, total energy intake, multivitamin supplement use, alcohol intake, physical activity, sleep duration, and TV watching hours.

STable 6: Effect of 10-unit increment of a genetic risk score (GRS) for differences in lipid markers according to quartile (Q) categories of healthful plant-based diet index

Participants	N	Healthful plant-based diet index				*P* interaction
Outcomes		Q1	Q2	Q3	Q4	
Total participants						
Log-transformed triglycerides	115996	0.023 (0.005)	0.011 (0.005)	0.013 (0.005)	0.002 (0.005)	0.002
HDL cholesterol	105951	–0.019 (0.003)	–0.021 (0.003)	–0.014 (0.004)	–0.006 (0.004)	0.012
Participants without a history of known dyslipidemia						
Log-transformed triglycerides	108939	0.024 (0.005)	0.013 (0.005)	0.014 (0.005)	0.003 (0.005)	0.006
HDL cholesterol	99434	–0.019 (0.004)	–0.021 (0.004)	–0.016 (0.004)	–0.008 (0.004)	0.037

N, number of participants with available data on each outcome measurement.

Data β (SE) per 10-unit increment of GRS after adjusted for age, sex, and the top 5 principal components of ancestry, college education history, smoking habit, total energy intake, multivitamin supplement use, alcohol intake, physical activity, sleeping hours, TV-watching hours per day, and the Townsend deprivation index, and a history of known dyslipidemia (i.e., self-reported history of dyslipidemia or cholesterol-lowering medication use, if the analysis was performed in total participants).

STable 7: Effect of 10-unit increment of a genetic risk score for differences in body mass index and mean arterial blood pressure according to quartile (Q) categories of healthful plant-based diet index in the subpopulation*

	Healthful plant-based diet index				*P* interaction
Outcomes	Q1	Q2	Q3	Q4	
Body mass index					
Model 1	1.10 (0.05)	0.93 (0.05)	0.90 (0.05)	0.68 (0.04)	<.0001
Model 2	1.07 (0.05)	0.91 (0.04)	0.87 (0.05)	0.64 (0.04)	<.0001
Mean arterial blood pressure					
Model 1	0.61 (0.13)	0.33 (0.12)	0.18 (0.13)	0.14 (0.11)	0.006
Model 2	0.60 (0.12)	0.31 (0.12)	0.17 (0.13)	0.11 (0.11)	0.004

Model 1: age, sex, and the top 5 principal components of ancestry

Model 2: model 1 + multivitamin supplement use, college education history, smoking habit, total energy intake, alcohol intake, physical activity, sleeping hours, TV watching hours, and the Townsend deprivation index.

*In the subpopulation of participants after excluding those who reported their dietary intake yesterday was not a typical intake.

STable 8: Odds ratio (OR) for untreated high blood pressure per 10-unit increment in healthful plant-based diet index (hPDI) stratified by quartiles of genetic risk score (GRS) in the subpopulation*

Stratification	OR (95% CI) per 10 unit of hPDI	P interaction
Quartiles of GRS		
Q1	0.96 (0.92, 1.00)	
Q2	0.92 (0.88, 0.96)	0.0002
Q3	0.91 (0.87, 0.95)	
Q4	0.87 (0.84, 0.91)	

Solid lines are estimates; dotted lines are 95% CIs. Data and 95% CIs after adjusted for covariates of Figure 1. *In the subpopulation of participants after excluding those who reported their dietary intake yesterday was not a typical intake.

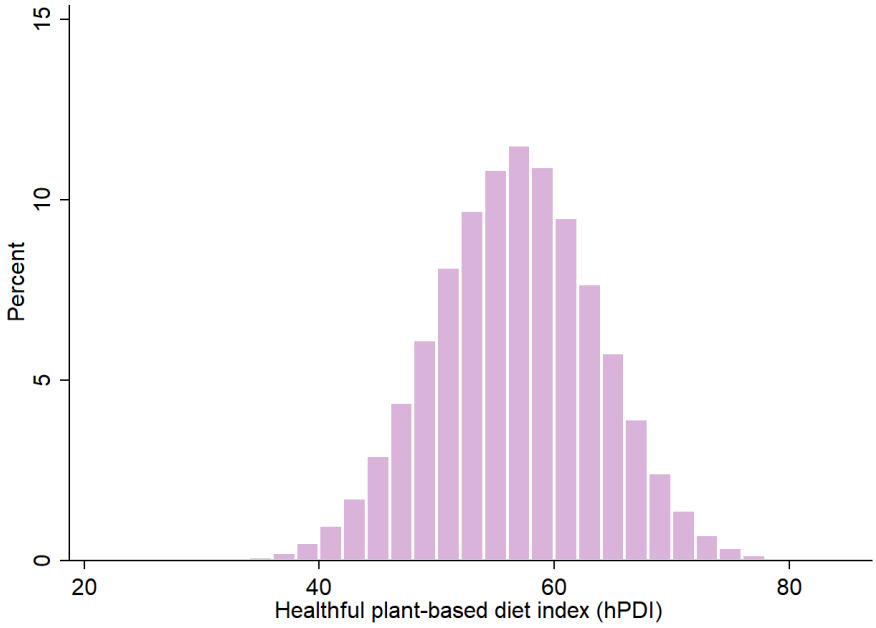
STable 9: Hazard ratios (HRs) for CVD or MI according to 10-unit increment of the healthful plant-based diet index among individuals with high genetic risk score (GRS) or low GRS in the subpopulation*

Outcomes	High-GRS group		Low-GRS group
CVD			
HR (95% CI)	0.78 (0.67, 0.90)		0.96 (0.84, 1.11)
P interaction		0.045	
MI			
HR (95% CI)	0.69 (0.57, 0.84)		0.95 (0.79, 1.13)
P interaction		0.011	

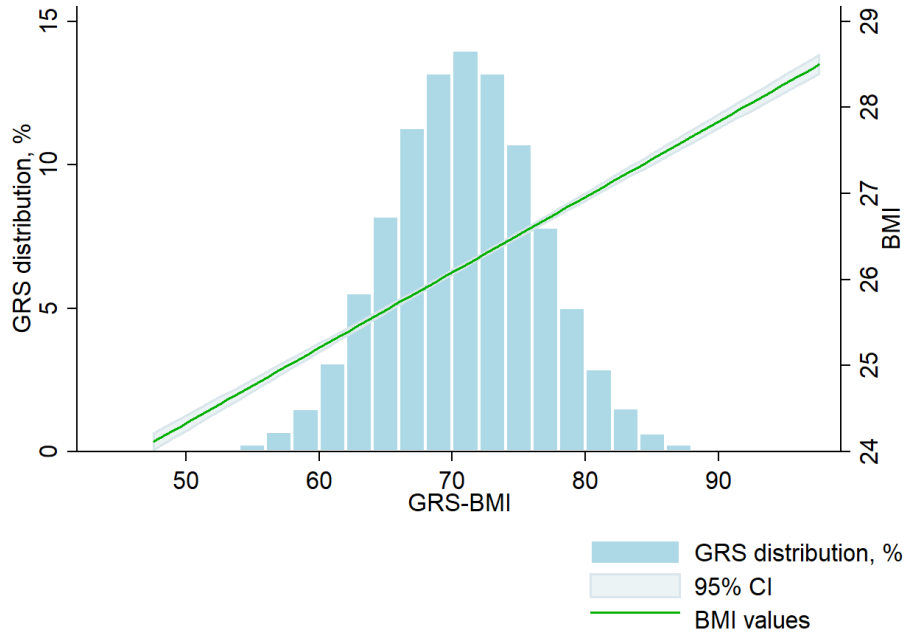
Data and 95% CIs after adjusted for covariates in Figure 1.

*In the subpopulation of participants after excluding those who reported their dietary intake yesterday was not a typical intake.

SFigure 1: Distribution of the healthful plant-based diet index (hPDI)

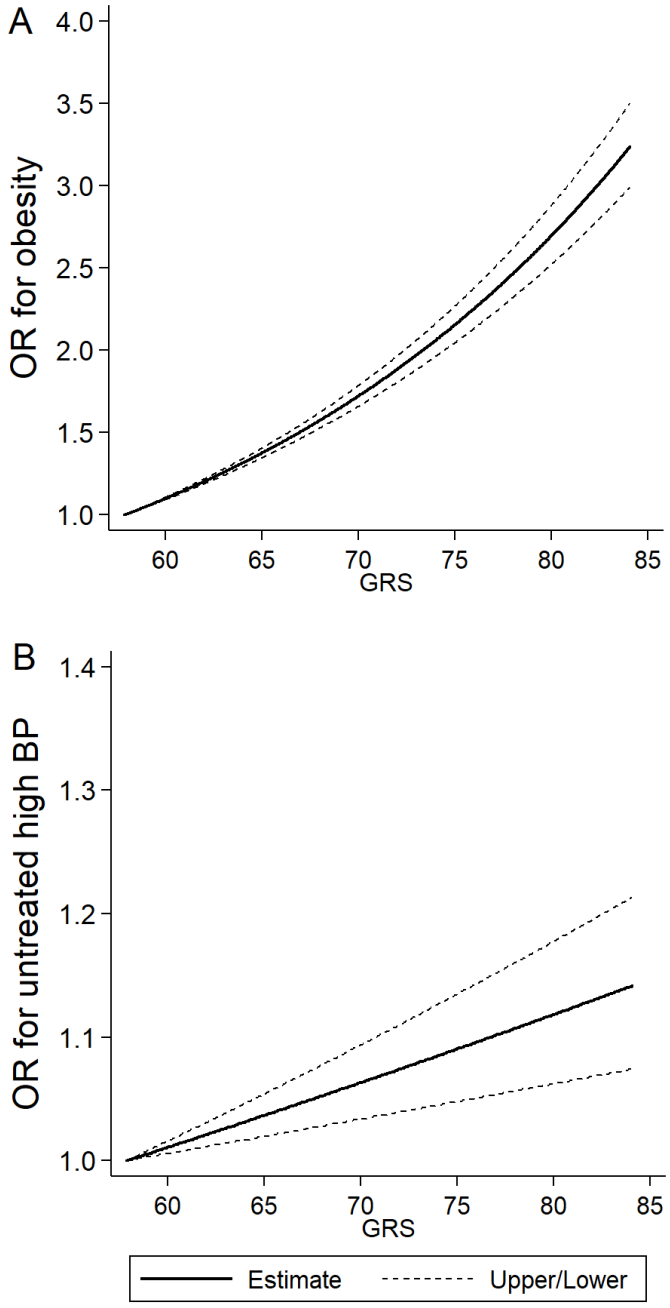


SFigure 2: Distribution of genetic risk score (GRS) of body mass index (BMI)



Dotted green lines are 95% CIs for BMI values.

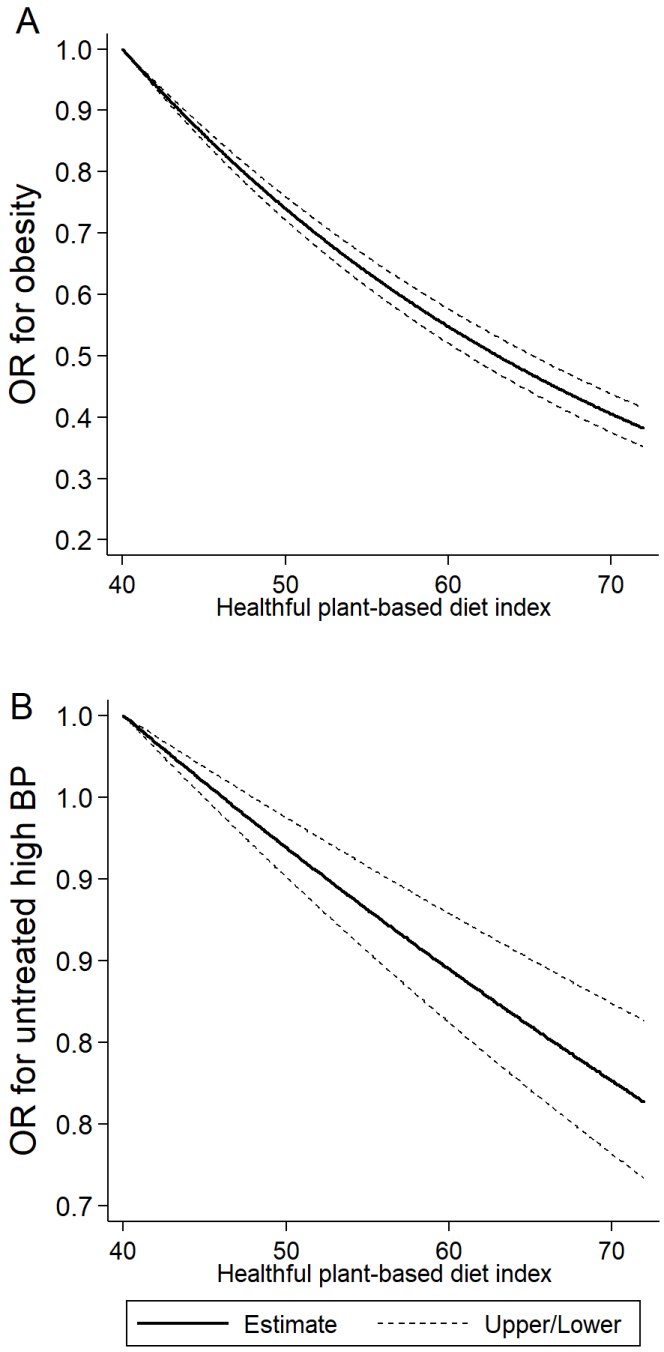
SFigure 3: Odds ratios (ORs) for obesity (panel A) and untreated high blood pressure (BP) (panel B) by genetic risk score (GRS) of BMI



Solid lines are estimates; dotted lines are 95% CIs.

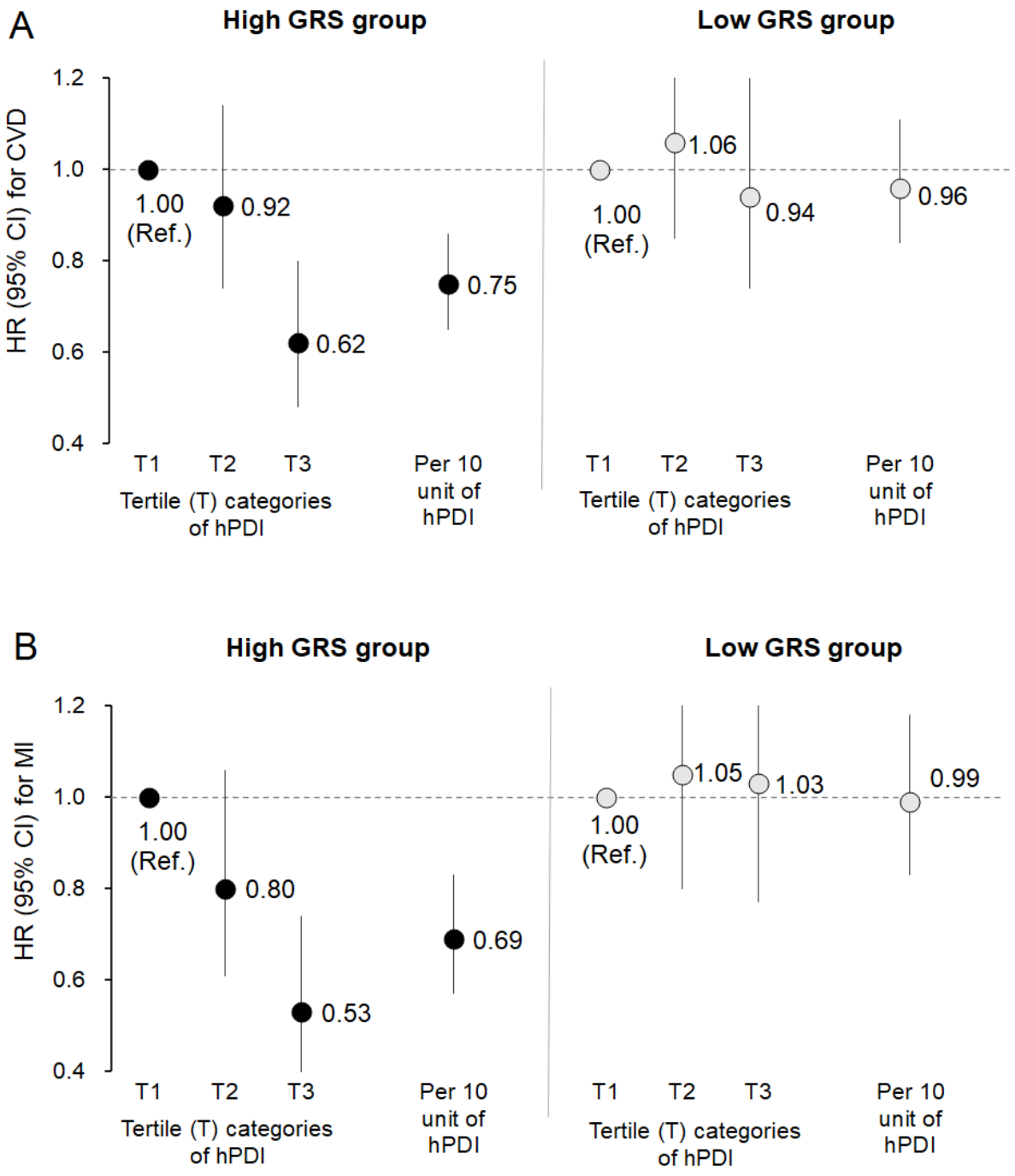
Data after adjusted for age, sex, and the top 5 principal components of ancestry.

SFigure 4: Odds ratios (ORs) for obesity (panel A) and untreated high blood pressure (BP) (panel B) by healthful plant-based diet index scores



Solid lines are estimates; dotted lines are 95% CIs. Data after adjusted for covariates of Figure 1.

SFigure 5: Hazard ratios (HRs) for CVD (A) or MI (B) according to high- or low-genetic risk score (GRS) and tertile (T) categories of the healthful plant-based diet index (hPDI) or per 10-unit increment in hPDI among participants with obesity or high blood pressure at baseline.



Data and 95% CIs after adjusted for covariates of Figure 1.