

## ELECTRONIC SUPPLEMENTARY MATERIAL

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## ELECTRONIC SUPPLEMENTARY TABLES

**ESM Table 1.** Number of relationships between pairs of phenotyped individuals

Kinship coefficient ( $\Phi$ ; range)	Relationship	Number of pairs
0.25 ( $0.20 \leq \Phi < 0.30$ )	First-degree relatives (PO, FS)	8,908
0.125 ( $0.10 \leq \Phi < 0.20$ )	Second-degree relatives (HS, AV, GG, D1C)	5,794
0.0625 ( $0.05 \leq \Phi < 0.10$ )	Third-degree relatives (1C, GAV, GGG)	29,706
0.03125 ( $0.02 \leq \Phi < 0.05$ )	Fourth-degree relatives (1.5C, D2C)	45,939
0.01563 ( $0.01 \leq \Phi < 0.02$ )	Fifth-degree relative (2C)	131,122
0.00781 ( $0.005 \leq \Phi < 0.01$ )	Sixth-degree relative (2.5C)	335,519
$0 \leq \Phi < 0.005$	Others	37,640,640

PO, parent–offspring; FS, full sibling; HS, half sibling; AV, avuncular; GG, grandparent–grandchild; D1C, double first cousins; 1C, first cousins; GAV, grand-avuncular; GGG, great grandparent-great grandchild; 1.5C, first cousin once removed; D2C, double second cousin; 2C, second cousin; 2.5C, second cousin once removed.

**ESM Table 2.** Principal component analysis of macronutrient intake

Macronutrients intake	Factor loading
Carbohydrate	-0.92
Protein	-0.10
Total fat	0.97
Saturated fat	0.80
MUFA	0.93
PUFA	0.57
Essential fatty acids	0.48
Fibre	-0.66
Eigenvalue	4.3
Percent of total variance	53.8%

MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids. Essential fatty acids: omega-3 and omega-6 fatty acids.

**ESM Table 3.** Variance components parameters estimates for genotype-age interactions on 11 cardiometabolic traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_e$	$\gamma_e$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
Weight, kg	16,296	-0.7763	-0.0055	0.0242	-0.6414	0.0146	0.35	<b><math>2 \times 10^{-6}</math>*</b>
BMI, kg/m <sup>2</sup>	16,281	-0.8220	0.0012	0.0145	-0.6011	0.0219	0.85	<b><math>3 \times 10^{-3}</math></b>
Waist circumference, cm	1,905	-0.7502	-0.0198	0	-0.6645	0.0221	0.59	0.50
TC, mmol/l	14,366	-0.8409	0.0036	0.0177	-0.5873	0.0131	0.66	<b><math>3 \times 10^{-3}</math></b>
HDL-C, mmol/l	3,266	-0.7780	-0.0027	0.0252	-0.6254	0.0094	0.79	0.06
LDL-C, mmol/l	3,169	-0.5760	0.0079	0.0393	-0.8441	0.0144	0.39	<b><math>1 \times 10^{-2}</math></b>
TG, mmol/l	11,681	-1.0485	0.0075	0	-0.4405	0.0047	0.33	0.50
Fasting glucose, mmol/l	14,507	-1.3952	0.0593	0	-0.3294	0.0063	<b><math>1 \times 10^{-2}</math></b>	0.50
2 h glucose, mmol/l	13,603	-1.2873	-0.0255	0.0207	-0.3827	0.0404	<b><math>3 \times 10^{-2}</math></b>	<b><math>3 \times 10^{-2}</math></b>
SBP, mmHg	16,097	-1.0200	0.0518	0.0253	-0.5231	0.0334	<b><math>&lt;1 \times 10^{-9}</math>*</b>	<b><math>1 \times 10^{-3}</math></b>
DBP, mmHg	16,092	-1.0881	0.0189	0.0188	-0.4225	0.0138	<b><math>9 \times 10^{-3}</math></b>	<b><math>1 \times 10^{-2}</math></b>

Significant estimates are marked in bold. \* Withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_e$  and  $\gamma_e$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

**ESM Table 4.** Variance components parameters estimates ( $\pm$ s.e.) for genotype-sex interactions on 11 cardiometabolic traits

Phenotypes	$N$	$\sigma_G$ Females	$\sigma_G$ Males	$\sigma_E$ Females	$\sigma_E$ Males	$\sigma$ $p$ -value	$\rho_G$	$\rho_G$ $p$ -value
Weight, kg	16,296	0.63 $\pm$ 0.03	0.60 $\pm$ 0.03	0.76 $\pm$ 0.02	0.80 $\pm$ 0.02	0.37	0.86 $\pm$ 0.08	<b>5<math>\times</math>10<sup>-2</sup></b>
BMI, kg/m <sup>2</sup>	16,281	0.72 $\pm$ 0.03	0.53 $\pm$ 0.03	0.81 $\pm$ 0.02	0.72 $\pm$ 0.02	<b>4<math>\times</math>10<sup>-6</sup>*</b>	0.89 $\pm$ 0.08	0.08
Waist circumference, cm	1,905	0.83 $\pm$ 0.20	0.60 $\pm$ 0.18	0.72 $\pm$ 0.23	0.68 $\pm$ 0.16	0.40	0.85 $\pm$ 0.50	0.39
TC, mmol/l	14,366	0.66 $\pm$ 0.03	0.61 $\pm$ 0.03	0.74 $\pm$ 0.02	0.79 $\pm$ 0.02	0.24	0.79 $\pm$ 0.08	<b>8<math>\times</math>10<sup>-3</sup></b>
HDL-C, mmol/l	3,266	0.61 $\pm$ 0.11	0.67 $\pm$ 0.08	0.86 $\pm$ 0.08	0.66 $\pm$ 0.08	0.65	0.80 $\pm$ 0.26	0.22
LDL-C, mmol/l	3,169	0.81 $\pm$ 0.08	0.48 $\pm$ 0.09	0.56 $\pm$ 0.10	0.89 $\pm$ 0.05	<b>2<math>\times</math>10<sup>-2</sup></b>	1	-
TG, mmol/l	11,681	0.54 $\pm$ 0.03	0.82 $\pm$ 0.04	0.61 $\pm$ 0.02	0.83 $\pm$ 0.04	<b>4<math>\times</math>10<sup>-7</sup>*</b>	0.55 $\pm$ 0.07	<b>2<math>\times</math>10<sup>-10</sup>*</b>
Fasting glucose, mmol/l	14,507	0.53 $\pm$ 0.03	0.51 $\pm$ 0.04	0.81 $\pm$ 0.02	0.89 $\pm$ 0.02	0.67	0.73 $\pm$ 0.13	<b>3<math>\times</math>10<sup>-2</sup></b>
2 h glucose, mmol/l	13,603	0.54 $\pm$ 0.04	0.53 $\pm$ 0.04	0.80 $\pm$ 0.03	0.89 $\pm$ 0.03	0.93	0.77 $\pm$ 0.14	0.06
SBP, mmHg	16,097	0.67 $\pm$ 0.03	0.52 $\pm$ 0.03	0.77 $\pm$ 0.03	0.82 $\pm$ 0.02	<b>2<math>\times</math>10<sup>-3</sup></b>	0.84 $\pm$ 0.08	<b>3<math>\times</math>10<sup>-2</sup></b>
DBP, mmHg	16,092	0.61 $\pm$ 0.03	0.51 $\pm$ 0.04	0.78 $\pm$ 0.02	0.87 $\pm$ 0.02	<b>4<math>\times</math>10<sup>-2</sup></b>	0.92 $\pm$ 0.10	0.21

Significant estimates are marked in bold. \* Withstand the Bonferroni corrected  $P$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\sigma_G$ : Genetic standard deviation;  $\sigma_E$ : Environmental standard deviation;  $\sigma$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\rho_G$ : genetic correlation;  $\rho_G$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

**ESM Table 5.** Variance components parameters estimates ( $\pm$ s.e.) for genotype-physical activity interactions on 11 cardiometabolic traits

Phenotypes	$N$	$\sigma_G$ Active	$\sigma_G$ Inactive	$\sigma_E$ Active	$\sigma_E$ Inactive	$\sigma$ $p$ -value	$\rho_G$	$\rho_G$ $p$ -value
Weight, kg	14,350	0.60 $\pm$ 0.05	0.70 $\pm$ 0.02	0.71 $\pm$ 0.04	0.75 $\pm$ 0.02	0.06	0.99 $\pm$ 0.10	0.45
BMI, kg/m <sup>2</sup>	14,341	0.61 $\pm$ 0.05	0.68 $\pm$ 0.03	0.69 $\pm$ 0.04	0.77 $\pm$ 0.02	0.17	0.92 $\pm$ 0.10	0.21
Waist circumference, cm	1,846	0.37 $\pm$ 0.20	0.79 $\pm$ 0.12	0.84 $\pm$ 0.09	0.66 $\pm$ 0.14	0.08	1	-
TC, mmol/l	12,828	0.71 $\pm$ 0.05	0.62 $\pm$ 0.03	0.70 $\pm$ 0.04	0.78 $\pm$ 0.02	0.14	1	-
HDL-C, mmol/l	2,296	0.55 $\pm$ 0.21	0.68 $\pm$ 0.13	0.82 $\pm$ 0.14	0.74 $\pm$ 0.11	0.63	1	-
LDL-C, mmol/l	2,271	0.78 $\pm$ 0.20	0.57 $\pm$ 0.12	0.59 $\pm$ 0.26	0.83 $\pm$ 0.09	0.44	1	-
TG, mmol/l	10,446	0.62 $\pm$ 0.06	0.63 $\pm$ 0.03	0.61 $\pm$ 0.05	0.83 $\pm$ 0.02	0.91	0.77 $\pm$ 0.11	<b>3<math>\times</math>10<sup>-2</sup></b>
Fasting glucose, mmol/l	12,831	0.50 $\pm$ 0.06	0.49 $\pm$ 0.03	0.86 $\pm$ 0.03	0.87 $\pm$ 0.02	0.97	1	-
2 h glucose, mmol/l	12,133	0.38 $\pm$ 0.06	0.54 $\pm$ 0.04	0.87 $\pm$ 0.03	0.86 $\pm$ 0.02	<b>4<math>\times</math>10<sup>-2</sup></b>	1	-
SBP, mmHg	14,153	0.51 $\pm$ 0.06	0.63 $\pm$ 0.03	0.79 $\pm$ 0.04	0.81 $\pm$ 0.02	0.07	0.86 $\pm$ 0.14	0.17
DBP, mmHg	14,148	0.43 $\pm$ 0.08	0.61 $\pm$ 0.03	0.85 $\pm$ 0.04	0.82 $\pm$ 0.02	<b>2<math>\times</math>10<sup>-2</sup></b>	0.95 $\pm$ 0.21	0.40

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol. Physical activity variable was categorized on two categories (inactive and active).

$\sigma_G$ : Genetic standard deviation;  $\sigma_E$ : Environmental standard deviation;  $\sigma$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\rho_G$ : genetic correlation;  $\rho_G$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

**ESM Table 6.** Variance components parameters estimates ( $\pm$ s.e.) for genotype-smoking status interactions on 11 cardiometabolic traits

Phenotypes	$N$	$\sigma_G$ Non-smokers	$\sigma_G$ Smokers	$\sigma_E$ Non-smokers	$\sigma_E$ Smokers	$\sigma$ $p$ -value	$\rho_G$	$\rho_G$ $p$ -value
Weight, kg	10,677	0.69 $\pm$ 0.03	0.69 $\pm$ 0.05	0.72 $\pm$ 0.03	0.71 $\pm$ 0.05	0.90	0.79 $\pm$ 0.11	<b>4<math>\times</math>10<sup>-2</sup></b>
BMI, kg/m <sup>2</sup>	10,668	0.67 $\pm$ 0.03	0.65 $\pm$ 0.05	0.74 $\pm$ 0.03	0.75 $\pm$ 0.05	0.67	0.84 $\pm$ 0.12	0.09
Waist circumference, cm	1,143	0.01 $\pm$ 0.33	0.95 $\pm$ 0.26	0.98 $\pm$ 0.03	0.38 $\pm$ 0.65	0.17	1	-
TC, mmol/l	9,423	0.63 $\pm$ 0.03	0.65 $\pm$ 0.05	0.75 $\pm$ 0.02	0.79 $\pm$ 0.04	0.70	1	-
HDL-C, mmol/l	1,974	0.59 $\pm$ 0.12	0.60 $\pm$ 0.27	0.81 $\pm$ 0.08	0.78 $\pm$ 0.20	0.98	1	-
LDL-C, mmol/l	1,914	0.69 $\pm$ 0.11	0.64 $\pm$ 0.19	0.69 $\pm$ 0.10	0.81 $\pm$ 0.15	0.82	1	-
TG, mmol/l	7,683	0.57 $\pm$ 0.04	0.60 $\pm$ 0.08	0.74 $\pm$ 0.03	0.93 $\pm$ 0.05	0.76	1	-
Fasting glucose, mmol/l	9,510	0.57 $\pm$ 0.04	0.48 $\pm$ 0.09	0.81 $\pm$ 0.03	0.89 $\pm$ 0.05	0.25	0.68 $\pm$ 0.24	0.12
2 h glucose, mmol/l	8,934	0.52 $\pm$ 0.04	0.54 $\pm$ 0.08	0.84 $\pm$ 0.03	0.86 $\pm$ 0.05	0.78	0.97 $\pm$ 0.24	0.46
SBP, mmHg	10,522	0.64 $\pm$ 0.03	0.57 $\pm$ 0.05	0.78 $\pm$ 0.03	0.80 $\pm$ 0.04	0.31	1	-
DBP, mmHg	10,519	0.56 $\pm$ 0.04	0.56 $\pm$ 0.06	0.82 $\pm$ 0.02	0.84 $\pm$ 0.04	0.98	1	-

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol. Smoking status variable was categorized in two categories (smokers and non-smokers).

$\sigma_G$ : Genetic standard deviation;  $\sigma_E$ : Environmental standard deviation;  $\sigma$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\rho_G$ : genetic correlation;  $\rho_G$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

**ESM Table 7.** Variance components parameters estimates for genotype-alcohol intake interactions on 11 cardiometabolic traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
Weight, kg	12,640	-0.3658	0.0501	0.1692	-1.4583	-0.4680	<b><math>1 \times 10^{-5}</math>*</b>	<b><math>7 \times 10^{-7}</math>*</b>
BMI, kg/m <sup>2</sup>	12,632	-0.5156	0.0432	0.1353	-1.1108	-0.3938	<b><math>3 \times 10^{-4}</math></b>	<b><math>5 \times 10^{-3}</math></b>
Waist circumference, cm	1,773	-2.1234	-0.7836	0	-0.3446	0.0303	1	0.50
TC, mmol/l	11,300	-0.8384	-0.0981	0	-0.5819	0.0285	0.10	0.50
HDL-C, mmol/l	2,141	-0.4385	0.0617	0.1640	-1.0869	-0.0831	0.30	0.11
LDL-C, mmol/l	2,120	-0.7464	-0.0175	0.0073	-0.6546	-0.0142	0.78	0.47
TG, mmol/l	9,797	-0.9303	0.0151	0.0543	-0.5132	0.0423	0.69	0.17
Fasting glucose, mmol/l	11,298	-1.4051	-0.1374	0	-0.2970	0.0224	0.23	0.50
2 h glucose, mmol/l	10,675	-1.5793	-0.3111	0	-0.2770	0.0568	<b><math>4 \times 10^{-3}</math></b>	0.50
SBP, mmHg	12,464	-0.9552	-0.1070	0.0964	-0.5009	0.0255	0.12	0.07
DBP, mmHg	12,459	-1.0945	-0.0555	0.0755	-0.4143	0.0325	0.36	0.14

Significant estimates are marked in bold. \* Withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_e$  and  $\gamma_e$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.



**ESM Table 8.** Variance components parameters estimates for genotype-diet pattern interactions on 11 cardiometabolic traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
Weight, kg	12,640	-0.5710	0.0496	0.0446	-0.8483	-0.0155	0.33	<b><math>3 \times 10^{-2}</math></b>
BMI, kg/m <sup>2</sup>	12,632	-0.6104	0.0085	0.0700	-0.7873	-0.0305	0.87	<b><math>1 \times 10^{-2}</math></b>
Waist circumference, cm	1,773	-0.2747	0.0437	0.2306	-1.6262	-0.2328	0.30	0.05
TC, mmol/l	11,300	-0.8216	-0.0568	0	-0.5870	0.0187	0.18	0.50
HDL-C, mmol/l	2,141	-0.6773	0.0195	0	-0.7263	-0.0408	0.78	0.50
LDL-C, mmol/l	2,120	-0.8408	-0.1349	0	-0.6227	0.0730	0.17	0.50
TG, mmol/l	9,797	-1.0116	0.0687	0	-0.4752	0.0619	0.27	0.50
Fasting glucose, mmol/l	11,298	-1.0490	-0.0890	0.1542	-0.4487	0.0429	0.13	<b><math>6 \times 10^{-3}</math></b>
2 h glucose, mmol/l	10,675	-1.1781	0.0806	0.0993	-0.3771	-0.0232	0.18	<b><math>5 \times 10^{-2}</math></b>
SBP, mmHg	12,464	-1.0752	-0.1182	0.0004	-0.4354	0.0225	<b><math>2 \times 10^{-2}</math></b>	0.50
DBP, mmHg	12,459	-1.2013	-0.0669	0	-0.3659	0.0326	0.38	0.50

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

**ESM Table 9.** Variance components parameters estimates for genotype-carbohydrate intake interactions on 11 cardiometabolic traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
Weight, kg	12,640	-0.5892	-0.0050	0.0111	-0.8187	-0.0074	0.78	0.08
BMI, kg/m <sup>2</sup>	12,632	-0.6357	0.0130	0.0184	-0.7614	-0.0119	0.46	<b>2</b> $\times 10^{-2}$
Waist circumference, cm	1,773	-0.2298	-0.0054	0.1029	-1.6915	0.0462	0.66	<b>2</b> $\times 10^{-2}$
TC, mmol/l	11,300	-0.8269	0.0220	0	-0.5848	-0.0053	0.06	0.50
HDL-C, mmol/l	2,141	-0.5920	-0.0030	0.0055	-0.8209	0.0088	0.88	0.45
LDL-C, mmol/l	2,120	-0.8437	0.0530	0	-0.6435	-0.0280	<b>4</b> $\times 10^{-2}$	0.50
TG, mmol/l	9,797	-1.0175	-0.0117	0	-0.4746	-0.0270	0.56	0.50
Fasting glucose, mmol/l	11,298	-1.0650	0.0185	0.0490	-0.4352	-0.0150	0.38	<b>9</b> $\times 10^{-3}$
2 h glucose, mmol/l	10,675	-1.2305	-0.0257	0.0254	-0.3532	0.0052	0.39	0.09
SBP, mmHg	12,464	-1.0757	0.0385	0	-0.4364	-0.0116	<b>1</b> $\times 10^{-2}$	0.50
DBP, mmHg	12,459	-1.2057	0.0300	0	-0.3694	-0.0145	0.13	0.50

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

**ESM Table 10.** Variance components parameters estimates for genotype-protein intake interactions on 11 cardiometabolic traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
Weight, kg	12,640	-0.5469	0.0633	0.0541	-0.8847	-0.0163	0.48	<b><math>1 \times 10^{-2}</math></b>
BMI, kg/m <sup>2</sup>	12,632	-0.6410	0.0790	0.0607	-0.7697	0.0369	0.07	<b><math>2 \times 10^{-2}</math></b>
Waist circumference, cm	1,773	-0.8454	0.0371	0.0206	-0.5888	0.0589	0.59	0.45
TC, mmol/l	11,300	-0.7721	-0.0590	0.0242	-0.6307	0.0326	0.20	0.22
HDL-C, mmol/l	2,141	-0.1986	-0.0029	0.2265	-1.7454	-0.0090	0.95	0.06
LDL-C, mmol/l	2,120	-0.8343	0.0546	0	-0.6071	-0.0875	0.28	0.50
TG, mmol/l	9,797	-1.0054	0.1508	0	-0.4986	-0.0129	<b><math>1 \times 10^{-2}</math></b>	0.50
Fasting glucose, mmol/l	11,298	-1.2205	0.1154	0.0633	-0.3687	-0.0082	0.33	0.18
2 h glucose, mmol/l	10,675	-1.2601	-0.1374	0.0752	-0.3600	0.0584	<b><math>3 \times 10^{-2}</math></b>	0.11
SBP, mmHg	12,464	-1.0134	0.0565	0.0228	-0.4570	0.0060	0.36	0.27
DBP, mmHg	12,459	-1.1653	0.0476	0.0153	-0.3787	-0.0176	0.55	0.36

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

**ESM Table 11.** Variance components parameters estimates for genotype-fibre intake interactions on 11 cardiometabolic traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
Weight, kg	12,640	-0.6622	-0.0884	0	-0.7362	0.1194	0.50	0.50
BMI, kg/m <sup>2</sup>	12,632	-0.7489	0.1351	0.0065	-0.6484	0.1310	0.40	0.47
Waist circumference, cm	1,773	-0.4229	0.0385	0.4968	-1.1072	0.2548	0.83	0.14
TC, mmol/l	11,300	-0.7805	0.0545	0.0429	-0.6149	0.0420	0.71	0.34
HDL-C, mmol/l	2,141	-0.5287	0.0802	0.2652	-0.9063	0.0274	0.64	0.32
LDL-C, mmol/l	2,120	-0.7305	-0.0638	0	-0.6740	0.1548	0.82	0.50
TG, mmol/l	9,797	-0.9766	0.1316	0.0827	-0.5140	-0.4016	0.26	0.25
Fasting glucose, mmol/l	11,298	-1.3461	0.2015	0.0192	-0.3134	0.0984	0.41	0.45
2 h glucose, mmol/l	10,675	-1.2774	-0.2798	0.1916	-0.3360	0.1006	0.37	0.23
SBP, mmHg	12,464	-1.0820	0.4028	0	-0.4338	-0.0353	<b><math>2 \times 10^{-3}</math></b>	0.50
DBP, mmHg	12,459	-1.2068	0.2737	0	-0.3677	-0.1398	0.08	0.50

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

**ESM Table 12.** Variance components parameters estimates for genotype-total fat intake interactions on 11 cardiometabolic traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
Weight, kg	12,640	-0.5691	0.0194	0.0152	-0.8546	-0.0103	0.14	<b><math>2 \times 10^{-2}</math></b>
BMI, kg/m <sup>2</sup>	12,632	-0.5984	0.0088	0.0261	-0.8079	-0.0183	0.52	<b><math>3 \times 10^{-3}</math></b>
Waist circumference, cm	1,773	-0.3612	0.0163	0.0562	-1.3263	-0.0618	0.27	0.1
TC, mmol/l	11,300	-0.8185	-0.0140	0	-0.5867	0.0048	0.27	0.50
HDL-C, mmol/l	2,141	-0.6748	0.0012	0	-0.7288	-0.0157	0.95	0.50
LDL-C, mmol/l	2,120	-0.8026	-0.0347	0	-0.6344	0.0191	0.39	0.50
TG, mmol/l	9,797	-1.0060	0.0191	0	-0.4737	0.0189	0.16	0.50
Fasting glucose, mmol/l	11,298	-1.0811	-0.0272	0.0453	-0.4315	0.0174	0.22	<b><math>1 \times 10^{-2}</math></b>
2 h glucose, mmol/l	10,675	-1.1759	0.0295	0.0343	-0.3788	-0.0054	0.10	<b><math>4 \times 10^{-2}</math></b>
SBP, mmHg	12,464	-1.0707	-0.0346	0	-0.4340	0.0081	0.07	0.50
DBP, mmHg	12,459	-1.1845	-0.0155	0.0018	-0.3698	0.0072	0.65	0.45

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

**ESM Table 13.** Variance components parameters estimates for genotype-saturated fat intake interactions on 11 cardiometabolic traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
Weight, kg	12,640	-0.5273	0.0255	0.0411	-0.9139	-0.0401	0.14	<b><math>3 \times 10^{-3}</math></b>
BMI, kg/m <sup>2</sup>	12,632	-0.5786	0.0192	0.0569	-0.8502	-0.0663	0.23	<b><math>4 \times 10^{-4}</math></b>
Waist circumference, cm	1,773	-0.6582	0.0243	0.0260	-0.7769	-0.0633	0.43	0.36
TC, mmol/l	11,300	-0.8111	-0.0063	0	-0.5893	-0.0030	0.82	0.50
HDL-C, mmol/l	2,141	-0.6645	-0.0105	0	-0.7376	-0.0193	0.78	0.50
LDL-C, mmol/l	2,120	-0.7685	-0.0434	0	-0.6445	0.0114	0.60	0.50
TG, mmol/l	9,797	-0.9924	0.0063	0	-0.4696	0.0080	0.77	0.50
Fasting glucose, mmol/l	11,298	-1.1116	0.0670	0.0774	-0.4234	-0.0354	<b><math>2 \times 10^{-2}</math></b>	<b><math>2 \times 10^{-2}</math></b>
2 h glucose, mmol/l	10,675	-1.2858	0.0465	0.0309	-0.3306	-0.0105	0.19	0.17
SBP, mmHg	12,464	-1.0633	-0.0647	0.0026	-0.4376	0.0130	0.10	0.46
DBP, mmHg	12,459	-1.1070	-0.0231	0.0256	-0.4047	0.0080	0.63	0.19

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

**ESM Table 14.** Variance components parameters estimates for genotype-essential fatty acids intake interactions on 11 cardiometabolic traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
Weight, kg	12,640	-0.6282	0.0307	0.0229	-0.7730	0.0405	0.58	0.27
BMI, kg/m <sup>2</sup>	12,632	-0.7026	0.0458	0.0359	-0.6871	-0.0072	0.37	0.17
Waist circumference, cm	1,773	-0.0672	0.0138	0.7816	-3.5709	-0.8476	0.66	0.12
TC, mmol/l	11,300	-0.8251	-0.0918	0	-0.5865	0.0346	0.16	0.50
HDL-C, mmol/l	2,141	-0.7081	0.0487	0	-0.6958	-0.0243	0.72	0.50
LDL-C, mmol/l	2,120	-0.8031	-0.0629	0	-0.6103	0.0315	0.54	0.50
TG, mmol/l	9,797	-1.0157	0.0940	0	-0.4696	0.0591	<b>4×10<sup>-2</sup></b>	0.50
Fasting glucose, mmol/l	11,298	-1.1138	-0.1005	0.1934	-0.4090	0.0369	0.20	<b>3×10<sup>-2</sup></b>
2 h glucose, mmol/l	10,675	-1.3978	0.0720	0	-0.2886	-0.0226	0.37	0.50
SBP, mmHg	12,464	-1.0518	0.0931	0.0073	-0.4422	-0.0644	0.06	0.42
DBP, mmHg	12,459	-1.1939	0.1056	0.0048	-0.3725	-0.0466	<b>4×10<sup>-2</sup></b>	0.46

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

**ESM Table 15.** Variance components parameters estimates for genotype-polyunsaturated fat intake interactions on 11 cardiometabolic traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
Weight, kg	12,640	-0.6181	0.0338	0.0311	-0.7869	0.0529	0.37	0.18
BMI, kg/m <sup>2</sup>	12,632	-0.6920	0.0372	0.0473	-0.6973	0.0163	0.32	0.11
Waist circumference, cm	1,773	-0.6584	0.0539	0.1357	-0.7597	-0.0626	0.58	0.35
TC, mmol/l	11,300	-0.8240	-0.0796	0	-0.5863	0.0372	0.19	0.50
HDL-C, mmol/l	2,141	-0.7137	0.0537	0	-0.6918	-0.0256	0.57	0.50
LDL-C, mmol/l	2,120	-0.8003	-0.0723	0	-0.6161	0.0478	0.48	0.50
TG, mmol/l	9,797	-1.0194	0.1066	0	-0.4689	0.0495	<b>3×10<sup>-2</sup></b>	0.50
Fasting glucose, mmol/l	11,298	-1.0603	-0.0895	0.2241	-0.4365	0.0417	0.17	<b>1×10<sup>-2</sup></b>
2 h glucose, mmol/l	10,675	-1.4079	0.0828	0	-0.2863	-0.0241	0.29	0.50
SBP, mmHg	12,464	-1.0301	0.0894	0.0214	-0.4548	-0.0686	0.05	0.30
DBP, mmHg	12,459	-1.2055	0.1083	0	-0.3682	-0.0482	<b>4×10<sup>-2</sup></b>	0.50

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.



**ESM Table 16.** Variance components parameters estimates for genotype-monounsaturated fat intake interactions on 11 cardiometabolic traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
Weight, kg	12,640	-0.5788	0.0322	0.0366	-0.8356	0.0245	0.33	<b><math>4 \times 10^{-2}</math></b>
BMI, kg/m <sup>2</sup>	12,632	-0.6489	0.0014	0.0475	-0.7412	0.0120	0.96	<b><math>3 \times 10^{-2}</math></b>
Waist circumference, cm	1,773	-0.2592	0.0650	0.2758	-1.7000	-0.2205	0.09	<b><math>3 \times 10^{-2}</math></b>
TC, mmol/l	11,300	-0.8221	-0.0464	0	-0.5857	0.0175	0.15	0.50
HDL-C, mmol/l	2,141	-0.7020	0.0300	0	-0.7037	-0.0387	0.63	0.50
LDL-C, mmol/l	2,120	-0.5298	-0.0649	0.1001	-0.9257	0.0515	0.79	0.25
TG, mmol/l	9,797	-1.0165	0.0956	0	-0.4742	0.0319	0.32	0.50
Fasting glucose, mmol/l	11,298	-1.1380	-0.0848	0.0961	-0.4022	0.0343	0.11	<b><math>4 \times 10^{-2}</math></b>
2 h glucose, mmol/l	10,675	-1.0631	0.0575	0.1415	-0.4321	-0.0292	0.21	<b><math>6 \times 10^{-3}</math></b>
SBP, mmHg	12,464	-0.9912	-0.0686	0.0340	-0.4727	-0.0064	0.08	0.21
DBP, mmHg	12,459	-1.1823	-0.0393	0.0066	-0.3700	0.0125	0.47	0.44

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

**ESM Table 17.** Sensitivity analyses for glycaemic and lipid traits excluding non-fasted individuals

a) Heritability estimates ( $h^2$ ) of glycaemic and lipid traits

Phenotypes	<i>N</i>	$h^2$	S.E.	<i>p</i> -value
TC, mmol/l	11,916	0.41	0.03	$2 \times 10^{-64}$
HDL-C, mmol/l	2,278	0.42	0.12	$4 \times 10^{-4}$
LDL-C, mmol/l	2,256	0.44	0.12	$8 \times 10^{-5}$
TG, mmol/l	10,392	0.36	0.03	$8 \times 10^{-42}$
Fasting glucose, mmol/l	12,043	0.27	0.03	$2 \times 10^{-36}$
2 h glucose, mmol/l	11,360	0.27	0.03	$2 \times 10^{-26}$

TC, total cholesterol; TG, triacylglycerol.

b) Variance components parameters estimates for genotype-age interactions on glycaemic and lipid traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
TC, mmol/l	11,916	-0.8155	0.0031	0.0118	-0.5961	0.0126	0.73	0.08
HDL-C, mmol/l	2,278	-0.9072	-0.0292	0.0005	-0.543	0.0043	0.3	0.49
LDL-C, mmol/l	2,256	-0.8234	0.0065	0	-0.589	0.0006	0.76	0.5
TG, mmol/l	10,392	-1.034	0.006	0	-0.4513	0.0034	0.43	0.5
Fasting glucose, mmol/l	12,043	-1.2952	0.0232	0	-0.3501	0.0223	0.35	0.5
2 h glucose, mmol/l	11,360	-1.1764	0.0297	0.0217	-0.3945	0.0224	0.08	0.07

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

c) Variance components parameters estimates ( $\pm$ s.e.) for genotype-sex interactions on glycaemic and lipid traits

Phenotypes	$N$	$\sigma_G$ Females	$\sigma_G$ Males	$\sigma_E$ Females	$\sigma_E$ Males	$\sigma$ $p$ -value	$\rho_G$	$\rho_G$ $p$ -value
TC, mmol/l	11,916	0.66 $\pm$ 0.04	0.67 $\pm$ 0.04	0.74 $\pm$ 0.03	0.74 $\pm$ 0.03	0.78	0.82 $\pm$ 0.09	<b>3<math>\times</math>10<sup>-2</sup></b>
HDL-C, mmol/l	2,278	0.77 $\pm$ 0.17	0.77 $\pm$ 0.12	0.72 $\pm$ 0.18	0.53 $\pm$ 0.16	0.99	0.36 $\pm$ 0.32	<b>5<math>\times</math>10<sup>-2</sup></b>
LDL-C, mmol/l	2,256	0.68 $\pm$ 0.13	0.64 $\pm$ 0.15	0.71 $\pm$ 0.13	0.79 $\pm$ 0.12	0.85	1	-
TG, mmol/l	10,392	0.57 $\pm$ 0.03	0.85 $\pm$ 0.05	0.57 $\pm$ 0.03	0.82 $\pm$ 0.04	<b>2<math>\times</math>10<sup>-6</sup>*</b>	0.48 $\pm$ 0.08	<b>5E<sup>-11</sup>*</b>
Fasting glucose, mmol/l	12,043	0.57 $\pm$ 0.04	0.53 $\pm$ 0.05	0.79 $\pm$ 0.03	0.87 $\pm$ 0.03	0.42	0.78 $\pm$ 0.14	0.07
2 h glucose, mmol/l	11,360	0.55 $\pm$ 0.04	0.55 $\pm$ 0.05	0.78 $\pm$ 0.03	0.89 $\pm$ 0.03	0.94	0.77 $\pm$ 0.15	0.08

Significant estimates are marked in bold. \* Withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\sigma_G$ : Genetic standard deviation;  $\sigma_E$ : Environmental standard deviation;  $\sigma$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\rho_G$ : genetic correlation;  $\rho_G$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

d) Variance components parameters estimates ( $\pm$ s.e.) for genotype-physical activity interactions on glycaemic and lipid traits

Phenotypes	$N$	$\sigma_G$ Active	$\sigma_G$ Inactive	$\sigma_E$ Active	$\sigma_E$ Inactive	$\sigma$ $p$ -value	$\rho_G$	$\rho_G$ $p$ -value
TC, mmol/l	11,434	0.69 $\pm$ 0.05	0.64 $\pm$ 0.03	0.71 $\pm$ 0.05	0.77 $\pm$ 0.02	0.37	1	-
HDL-C, mmol/l	2,166	0.58 $\pm$ 0.23	0.62 $\pm$ 0.14	0.80 $\pm$ 0.16	0.78 $\pm$ 0.11	0.9	1	-
LDL-C, mmol/l	2,144	0.72 $\pm$ 0.22	0.58 $\pm$ 0.13	0.65 $\pm$ 0.24	0.83 $\pm$ 0.09	0.61	1	-
TG, mmol/l	9,967	0.61 $\pm$ 0.06	0.63 $\pm$ 0.03	0.61 $\pm$ 0.05	0.83 $\pm$ 0.03	0.73	0.77 $\pm$ 0.11	<b>3<math>\times</math>10<sup>-2</sup></b>
Fasting glucose, mmol/l	11,434	0.56 $\pm$ 0.08	0.52 $\pm$ 0.03	0.82 $\pm$ 0.05	0.86 $\pm$ 0.02	0.6	0.93 $\pm$ 0.18	0.35
2 h glucose, mmol/l	10,810	0.37 $\pm$ 0.07	0.57 $\pm$ 0.04	0.87 $\pm$ 0.03	0.85 $\pm$ 0.02	<b>1<math>\times</math>10<sup>-2</sup></b>	1	-

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol. Physical activity variable was categorized on two categories (inactive and active).

$\sigma_G$ : Genetic standard deviation;  $\sigma_E$ : Environmental standard deviation;  $\sigma$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\rho_G$ : genetic correlation;  $\rho_G$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

e) Variance components parameters estimates ( $\pm$ s.e.) for genotype-smoking status interactions on glycaemic and lipid traits

Phenotypes	$N$	$\sigma_G$ Non-smokers	$\sigma_G$ Smokers	$\sigma_E$ Non-smokers	$\sigma_E$ Smokers	$\sigma$ $p$ -value	$\rho_G$	$\rho_G$ $p$ -value
TC, mmol/l	7,941	0.65 $\pm$ 0.04	0.66 $\pm$ 0.06	0.73 $\pm$ 0.03	0.79 $\pm$ 0.05	0.98	1	-
HDL-C, mmol/l	1,456	0.65 $\pm$ 0.18	0.98 $\pm$ 0.03	0.76 $\pm$ 0.15	0	0.21	-0.13 $\pm$ 0.56	0.07
LDL-C, mmol/l	1,444	0.69 $\pm$ 0.17	0.53 $\pm$ 0.27	0.68 $\pm$ 0.17	0.90 $\pm$ 0.16	0.59	1	-
TG, mmol/l	6,955	0.60 $\pm$ 0.04	0.60 $\pm$ 0.08	0.71 $\pm$ 0.03	0.94 $\pm$ 0.05	0.97	1	-
Fasting glucose, mmol/l	8,018	0.61 $\pm$ 0.04	0.43 $\pm$ 0.10	0.79 $\pm$ 0.03	0.90 $\pm$ 0.05	0.08	0.97 $\pm$ 0.33	0.46
2 h glucose, mmol/l	7,559	0.52 $\pm$ 0.05	0.53 $\pm$ 0.08	0.83 $\pm$ 0.03	0.88 $\pm$ 0.05	0.95	1	-

TC, total cholesterol; TG, triacylglycerol. Smoking status variable was categorized in two categories (smokers and non-smokers).

$\sigma_G$ : Genetic standard deviation;  $\sigma_E$ : Environmental standard deviation;  $\sigma$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\rho_G$ : genetic correlation;  $\rho_G$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

f) Variance components parameters estimates for genotype-alcohol intake interactions on glycaemic and lipid traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
TC, mmol/l	10,650	-0.8058	-0.0738	0.0275	-0.6031	0.0207	0.5	0.26
HDL-C, mmol/l	2,038	-0.5625	0.0686	0.143	-0.8898	-0.0779	0.29	0.19
LDL-C, mmol/l	2,018	-0.8182	-0.0147	0	-0.5945	-0.0165	0.83	0.5
TG, mmol/l	9,432	-0.8951	0.0289	0.0727	-0.5379	0.0396	0.44	0.1
Fasting glucose, mmol/l	10,649	-1.3892	-0.1557	0	-0.3059	0.0257	0.22	0.5
2 h glucose, mmol/l	10,072	-1.5676	-0.313	0	-0.2822	0.0582	<b><math>4 \times 10^{-3}</math></b>	0.5

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

g) Variance components parameters estimates for genotype-diet pattern interactions on glycaemic and lipid traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
TC, mmol/l	10,650	-0.834	-0.032	0	-0.574	-0.0033	0.45	0.5
HDL-C, mmol/l	2,038	-0.7844	0.0204	0	-0.6247	-0.0348	0.81	0.5
LDL-C, mmol/l	2,018	-0.9097	-0.1352	0	-0.5644	0.0554	0.29	0.5
TG, mmol/l	9,432	-1.0102	0.0822	0	-0.4796	0.063	0.17	0.5
Fasting glucose, mmol/l	10,649	-1.0001	-0.0811	0.1635	-0.4752	0.041	0.17	<b><math>4 \times 10^{-3}</math></b>
2 h glucose, mmol/l	10,072	-1.1269	0.0792	0.1123	-0.4013	-0.0254	0.17	<b><math>4 \times 10^{-2}</math></b>

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.



h) Variance components parameters estimates for genotype-carbohydrate intake interactions on glycaemic and lipid traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
TC, mmol/l	10,650	-0.8374	0.0156	0	-0.5734	0.0003	0.18	0.5
HDL-C, mmol/l	2,038	-0.7388	-0.0043	0	-0.663	0.0075	0.86	0.5
LDL-C, mmol/l	2,018	-0.9024	0.0518	0	-0.5877	-0.0222	0.09	0.5
TG, mmol/l	9,432	-1.0112	-0.021	0	-0.4784	-0.0236	0.29	0.5
Fasting glucose, mmol/l	10,649	-1.0409	0.0131	0.0469	-0.4448	-0.0118	0.59	<b><math>1 \times 10^{-2}</math></b>
2 h glucose, mmol/l	10,072	-1.2073	-0.0225	0.0251	-0.3617	0.0043	0.41	0.1

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

i) Variance components parameters estimates for genotype-protein intake interactions on glycaemic and lipid traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
TC, mmol/l	10,650	-0.7785	-0.053	0.0279	-0.6249	0.0299	0.25	0.19
HDL-C, mmol/l	2,038	-0.0779	-0.004	0.3458	-2.6808	-0.0478	0.9	<b><math>1 \times 10^{-2}</math></b>
LDL-C, mmol/l	2,018	-0.3889	0.0271	0.2744	-1.1926	-0.1129	0.54	0.18
TG, mmol/l	9,432	-1.0005	0.1421	0	-0.497	-0.007	<b><math>2 \times 10^{-2}</math></b>	0.5
Fasting glucose, mmol/l	10,649	-1.2692	0.12	0.0292	-0.349	-0.0062	0.18	0.29
2 h glucose, mmol/l	10,072	-1.2752	-0.1338	0.0628	-0.3528	0.0572	0.05	0.15

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

j) Variance components parameters estimates for genotype-fibre intake interactions on glycaemic and lipid traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
TC, mmol/l	10,650	-0.7714	-0.0117	0.0816	-0.6252	0.1016	0.94	0.25
HDL-C, mmol/l	2,038	-0.4597	0.0755	0.6086	-1.0178	0.0388	0.67	0.2
LDL-C, mmol/l	2,018	-0.8051	-0.0656	0	-0.6095	0.1483	0.86	0.5
TG, mmol/l	9,432	-0.9578	0.1013	0.1037	-0.5247	-0.3979	0.4	0.2
Fasting glucose, mmol/l	10,649	-1.2939	0.2016	0.0585	-0.3332	0.1018	0.34	0.36
2 h glucose, mmol/l	10,072	-1.2271	-0.3054	0.2491	-0.3585	0.116	0.28	0.18

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

k) Variance components parameters estimates for genotype-total fat intake interactions on glycaemic and lipid traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
TC, mmol/l	10,650	-0.8324	-0.0079	0	-0.5745	-0.001	0.51	0.5
HDL-C, mmol/l	2,038	-0.7808	0.003	0	-0.628	-0.014	0.91	0.5
LDL-C, mmol/l	2,018	-0.8695	-0.0358	0	-0.5791	0.0145	0.51	0.5
TG, mmol/l	9,432	-1.0032	0.022	0	-0.4785	0.0205	0.1	0.5
Fasting glucose, mmol/l	10,649	-1.0195	-0.0244	0.0507	-0.4636	0.0166	0.27	<b><math>5 \times 10^{-3}</math></b>
2 h glucose, mmol/l	10,072	-1.1278	0.0285	0.0383	-0.4013	-0.0062	0.1	<b><math>3 \times 10^{-2}</math></b>

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

l) Variance components parameters estimates for genotype-saturated fat intake interactions on glycaemic and lipid traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
TC, mmol/l	10,650	-0.8265	0.0055	0	-0.5792	-0.0131	0.83	0.5
HDL-C, mmol/l	2,038	-0.7699	-0.0044	0	-0.6351	-0.0167	0.92	0.5
LDL-C, mmol/l	2,018	-0.8296	-0.036	0	-0.5905	-0.0009	0.72	0.5
TG, mmol/l	9,432	-0.9766	0.0061	0.0009	-0.4792	0.0087	0.77	0.49
Fasting glucose, mmol/l	10,649	-1.042	0.0605	0.0889	-0.4599	-0.0388	<b><math>4 \times 10^{-2}</math></b>	<b><math>9 \times 10^{-3}</math></b>
2 h glucose, mmol/l	10,072	-1.2132	0.0448	0.0454	-0.3607	-0.0148	0.15	0.1

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

m) Variance components parameters estimates for genotype-essential fatty acids intake interactions on glycaemic and lipid traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
TC, mmol/l	10,650	-0.8404	-0.0922	0	-0.5756	0.0323	0.19	0.5
HDL-C, mmol/l	2,038	-0.8114	0.0045	0	-0.5993	0.0089	0.96	0.5
LDL-C, mmol/l	2,018	-0.1718	-0.0154	0.9188	-1.8899	0.0025	0.67	0.24
TG, mmol/l	9,432	-1.012	0.1054	0	-0.4749	0.0619	<b><math>2 \times 10^{-2}</math></b>	0.5
Fasting glucose, mmol/l	10,649	-1.101	-0.0984	0.1827	-0.416	0.0423	0.18	<b><math>4 \times 10^{-2}</math></b>
2 h glucose, mmol/l	10,072	-1.3765	0.0558	0	-0.2944	-0.0117	0.55	0.5

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

n) Variance components parameters estimates for genotype-polyunsaturated fat intake interactions on glycaemic and lipid traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
TC, mmol/l	10,650	-0.838	-0.0751	0	-0.5753	0.0311	0.27	0.5
HDL-C, mmol/l	2,038	-0.8149	0.0193	0	-0.5972	-0.001	0.84	0.5
LDL-C, mmol/l	2,018	-0.438	-0.0337	0.3454	-1.0587	0.0381	0.64	0.35
TG, mmol/l	9,432	-1.0173	0.1161	0	-0.4731	0.0527	<b><math>2 \times 10^{-2}</math></b>	0.5
Fasting glucose, mmol/l	10,649	-1.0258	-0.0793	0.2299	-0.4552	0.0461	0.19	<b><math>1 \times 10^{-2}</math></b>
2 h glucose, mmol/l	10,072	-1.3859	0.0737	0	-0.2926	-0.0154	0.38	0.5

Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG, triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.

o) Variance components parameters estimates for genotype-monounsaturated fat intake interactions on glycaemic and lipid traits

Phenotypes	$N$	$\alpha_G$	$\gamma_G$	$\lambda$	$\alpha_E$	$\gamma_E$	$\gamma_G$ $p$ -value	$\lambda$ $p$ -value
TC, mmol/l	10,650	-0.8353	-0.0323	0	-0.5734	0.0019	0.31	0.5
HDL-C, mmol/l	2,038	-0.8074	0.0377	0	-0.6094	-0.0351	0.63	0.5
LDL-C, mmol/l	2,018	-0.4531	-0.067	0.1656	-1.0576	0.0587	1	0.17
TG, mmol/l	9,432	-1.0125	0.089	0	-0.477	0.042	0.22	0.5
Fasting glucose, mmol/l	10,649	-1.0964	-0.0704	0.1	-0.4196	0.0304	0.22	<b><math>3 \times 10^{-2}</math></b>
2 h glucose, mmol/l	10,072	-0.9906	0.0577	0.1652	-0.4737	-0.0323	0.19	<b><math>3 \times 10^{-3}</math></b>

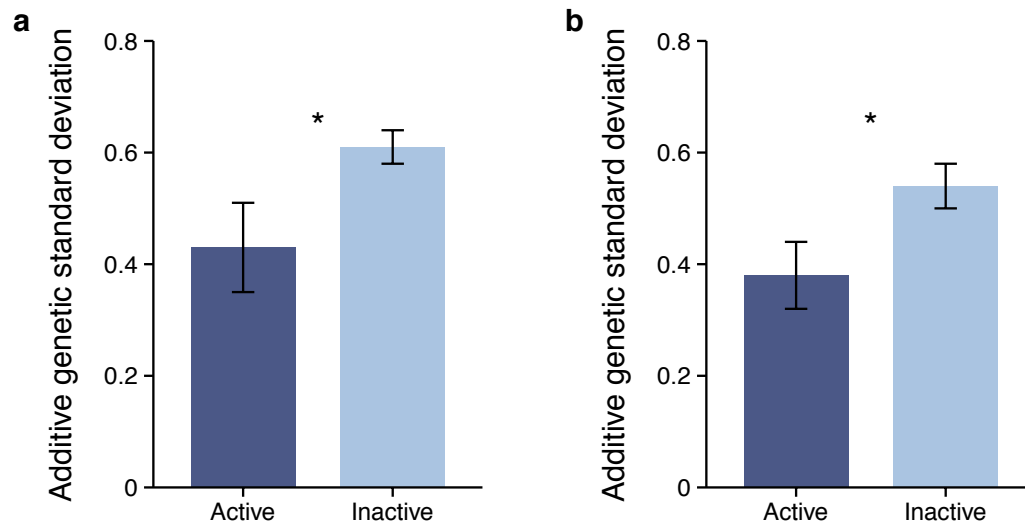
Significant estimates are marked in bold. None of the results withstand the Bonferroni corrected  $p$ -value of 0.00019.

TC, total cholesterol; TG: triacylglycerol.

$\alpha_G$ ,  $\gamma_G$ ,  $\lambda$ ,  $\alpha_E$  and  $\gamma_E$  are parameters estimated in the genotype-environment interaction model for continuous environmental exposures (see Eq. 4 and 5).  $\gamma_G$   $p$ -value:  $p$ -value of the variance homogeneity null hypothesis;  $\lambda$   $p$ -value:  $p$ -value of the genetic correlation equal to 1 null hypothesis.



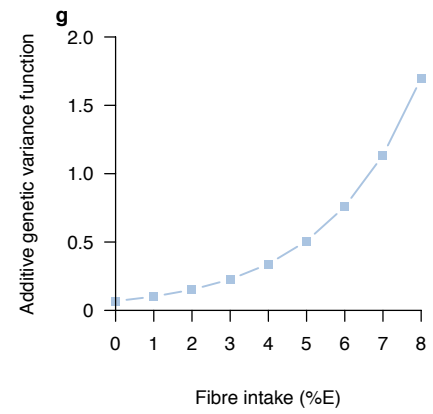
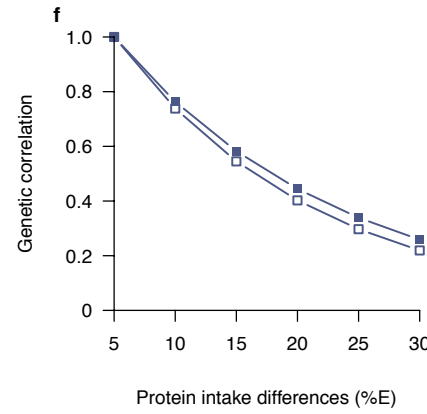
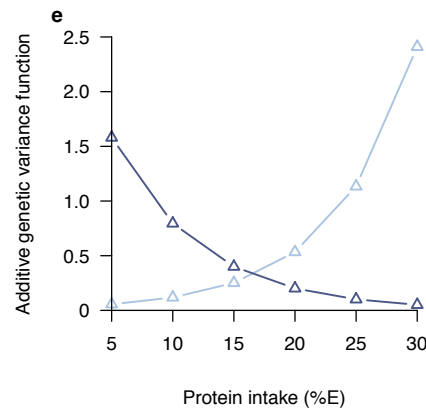
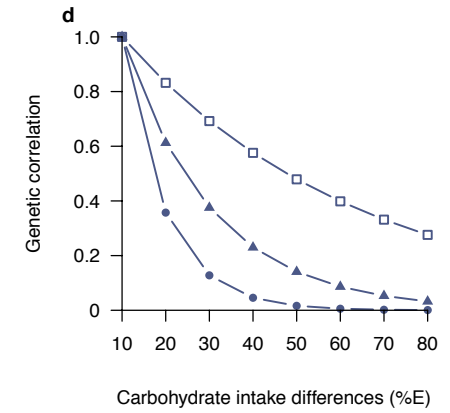
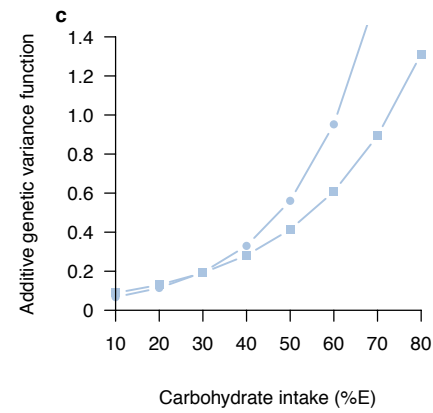
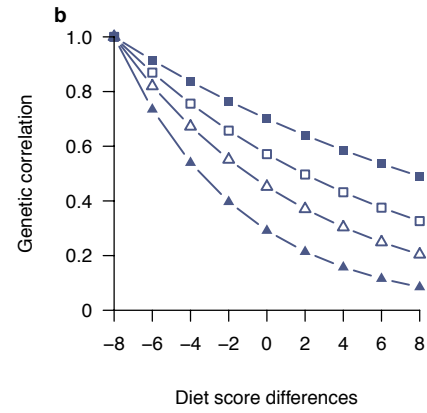
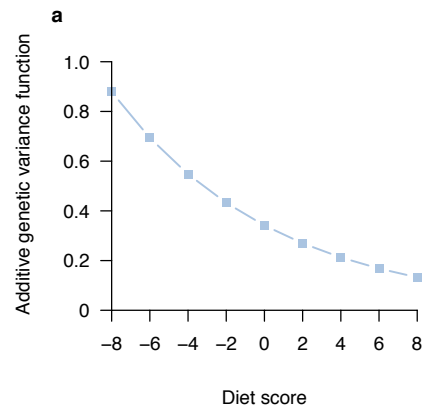
## ELECTRONIC SUPPLEMENTARY FIGURES



**ESM Figure 1. *Class 1* genotype-physical activity interactions for a) DBP and b) 2 h glucose**

Only significant traits are represented in the figure; \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ .

All interactions were nominally significant ( $p < 0.05$ ).

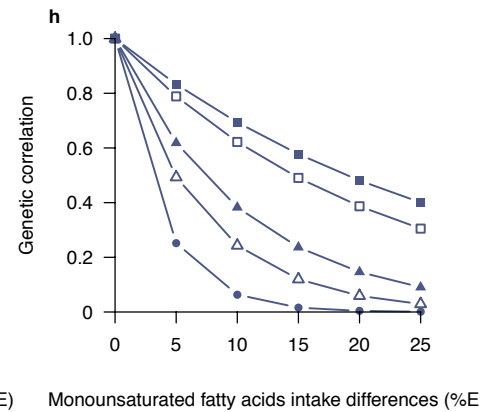
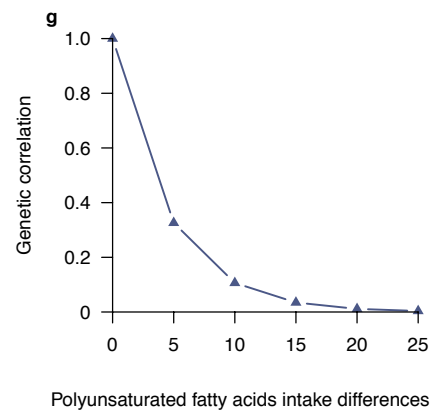
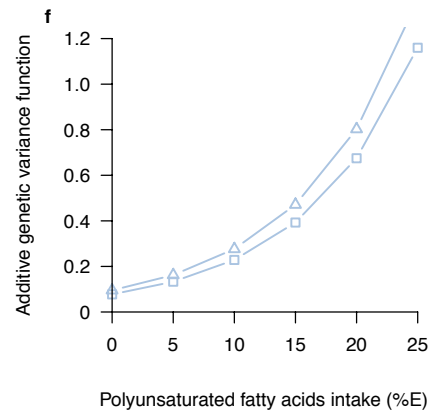
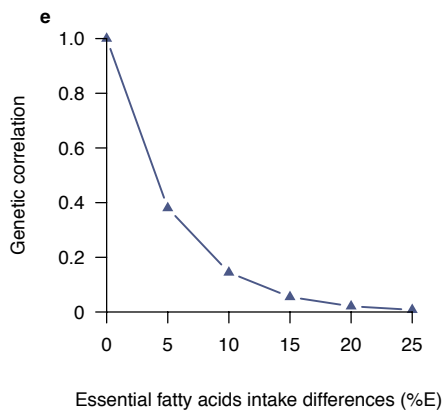
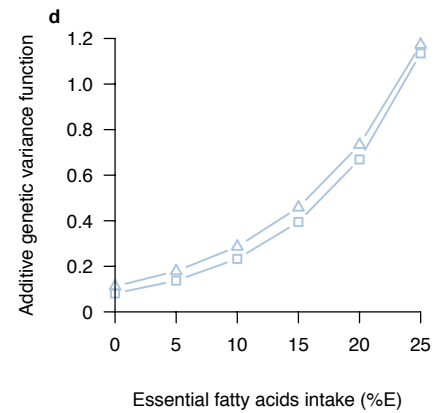
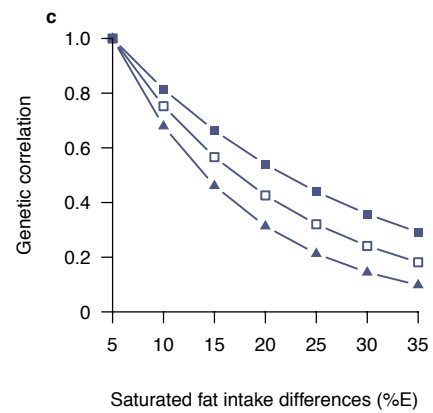
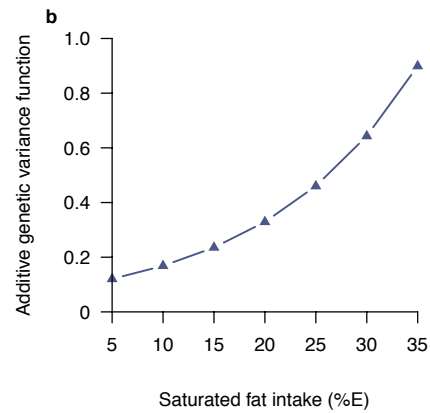
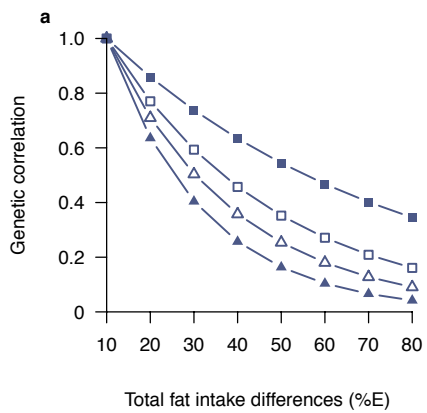


**ESM Figure 2. Genotype-diet components interactions**

a) *class 1* genotype-diet score interactions, b) *class 2* genotype-diet score interactions, c) *class 1* genotype-carbohydrate intake interactions, d) *class 2* genotype-carbohydrate intake interactions, e) *class 1* genotype-protein intake interactions, f) *class 2* genotype-protein intake interactions, g) *class 1* genotype-fibre intake interactions.

Dark blue full square, weight; dark blue empty square, BMI; dark blue full circle, waist circumference; dark blue full triangle, fasting glucose; dark blue empty triangle, 2 h glucose; light blue full square, SBP; light blue empty triangle, triacylglycerol; light blue full circle, LDL-C.

Only significant traits are represented in the Figure. All interactions were nominally significant ( $p < 0.05$ ).



### ESM Figure 3. Genotype-fat intake interactions

a) *class 2* genotype-total fat intake interactions, b) *class 1* genotype-saturated fat intake interactions, c) *class 2* genotype-saturated fat intake interactions, d) *class 1* genotype-essential fatty acid intake interactions, e) *class 2* genotype-essential fatty acid intake interactions, f) *class 1* genotype-polyunsaturated fatty acids intake interactions, g) *class 2* genotype-polyunsaturated fatty acids intake interactions, e) *class 2* genotype-monounsaturated fatty acids intake interactions.

Dark blue full square, weight; dark blue empty square, BMI; dark blue full circle, waist circumference; dark blue full triangle, fasting glucose; dark blue empty triangle, 2 h glucose; light blue empty square, DBP; light blue empty triangle, triacylglycerol.

Only significant traits are represented in the Figure. All interactions were nominally significant ( $p < 0.05$ ).