**Causal relationship between dietary macronutrient composition and anthropometric measures: a bidirectional two-sample Mendelian randomization analysis**

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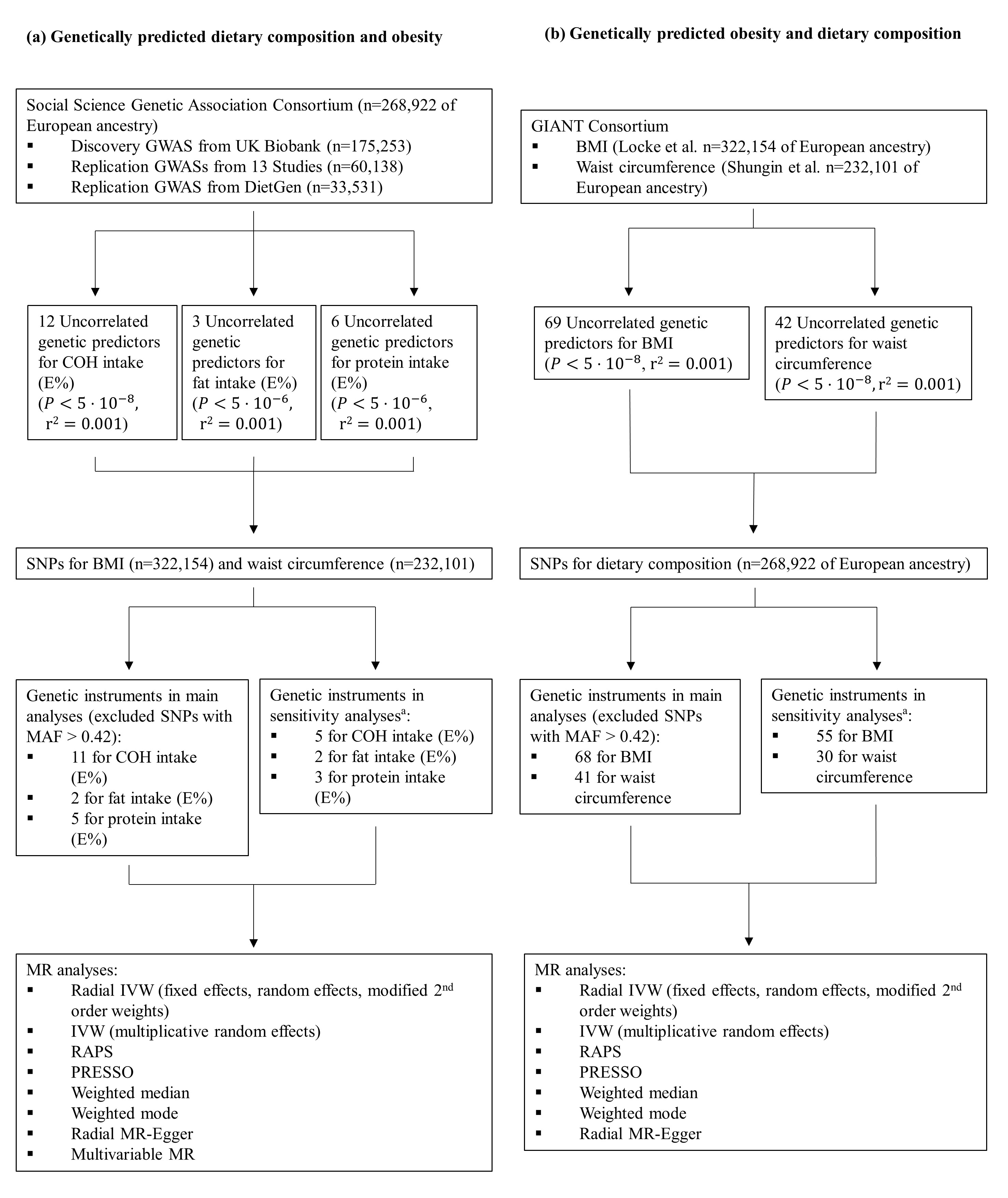
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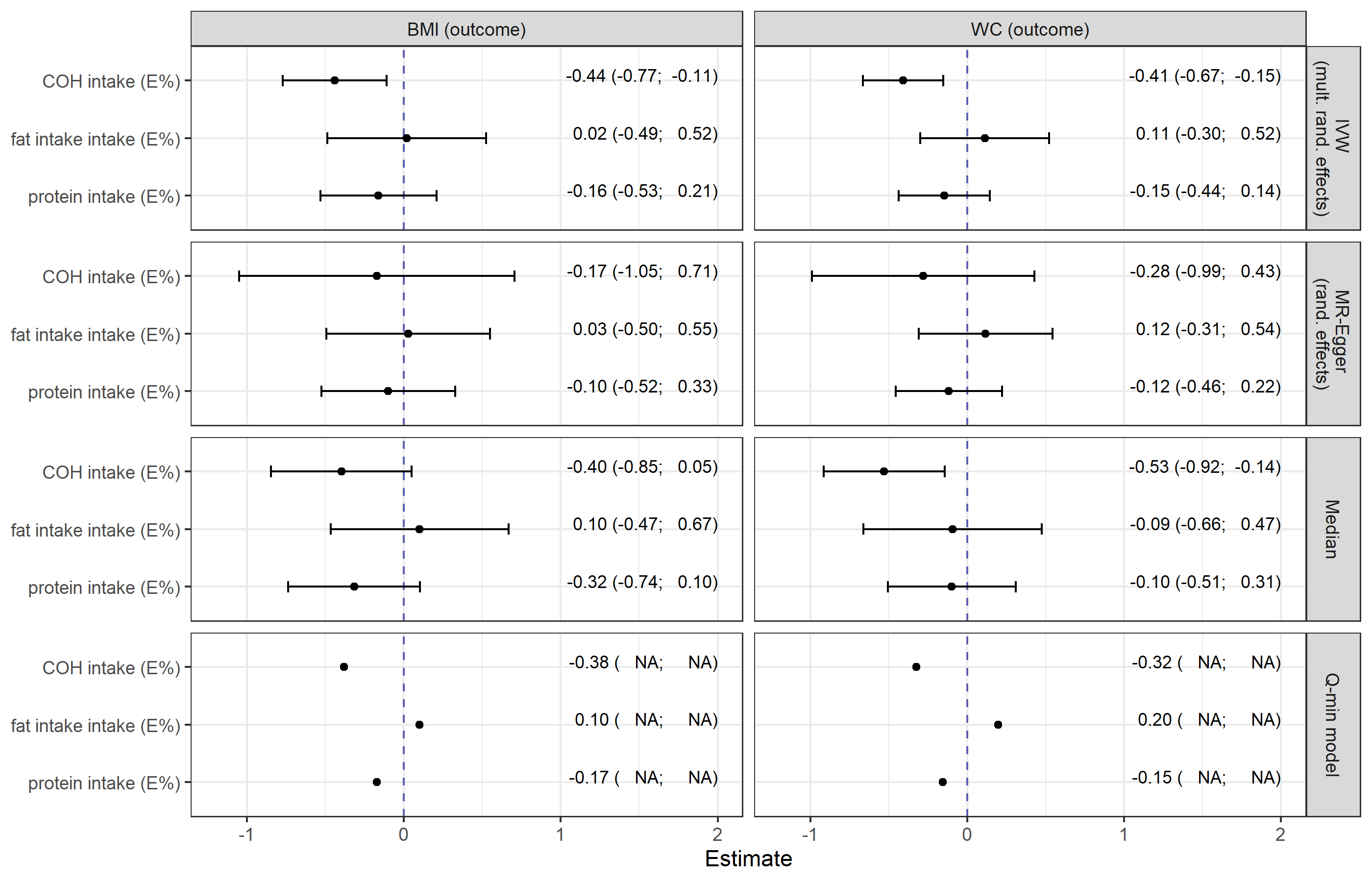
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**Supplementary Figure 1** Participant and analysis flow chart of the bidirectional Mendelian randomization study investigating causal relationship between dietary macronutrient composition (in % of total energy intake (E%)) and anthropometric measures.

Abbrevations: GWAS, genome-wide association study; BMI, body mass index; COH, carbohydrate; SNP, single nucleotide polymorphism; MR, Mendelian randomization; IVW, inverse-variance weighted; RAPS, Robust Adjusted Profile Score; PRESSO, Pleiotropy RESidual Sum and Outlier.

a Excluded genetic variants associated with possible confounders of the exposure-outcome association.



**Supplementary Figure 2** Mutually adjusted causal estimates (standard deviation (SD) change in each outcome per one SD change in the appropriate exposure) from multivariable Mendelian randomization sensitivity analyses of genetically predicted relative dietary intake of carbohydrates, fat, and proteins (in % of total energy intake (E%)) on the anthropometric measures body mass index (BMI) and waist circumference (WC).

**Supplementary Table 1** Determination of macronutrient intake per cohort for individuals included in the genome-wide association study of Meddens et al.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Study | Survey Instrument | Number of food items | Number of measurements | Sample size |
| ALSPAC-32wks | FFQ | 70 | 1 | 1,396 |
| DietGen | FFQ | mix | 1 | 33,531 |
| EPIC-Interact1 | mix | mix | 1 | 4,818 |
| Fenland | FFQ | 130 | 1 | 7,869 |
| FHS | FFQ | 145 | ≤4 | 6,331 |
| HRS | FFQ | 163 | 1 | 2,628 |
| LL | FFQ | 110 | 1 | 6,411 |
| RSI | FFQ | 170 | 1 | 4,816 |
| RSII | FFQ | 170 | 1 | 1,311 |
| RSIII | FFQ | 389 | 1 | 2,209 |
| UKB | 24HDR | ± 200 | ≤ 5 | 175,253 |
| WHI-GARNET | FFQ | 122 | ≤ 2 | 2,674 |

Abbrevations: FFQ, Food Frequency Questionaire; 24HDR, 24-hour dietary recall; mix, mix of survey instruments (FFQ, 24-hour dietary recall, other)

See <https://www.nature.com/articles/s41380-020-0697-5> for details

**Supplementary Table 2** Sample overlaps of genome-wide association studies for macronutrient composition with the genome-wide association studies for anthropometric measures body mass index (BMI) and waist circumference (WC), respectively.

|  |  |  |  |
| --- | --- | --- | --- |
| **Study** | **Samlesize macronutrients** | **Samplesize BMI** | **Samplesize WC** |
| Fenland | 7,869 | 1,402 | 1402 |
| HRS | 2,628 | 8,164 | 0 |
| LL | 6,411 | 8,118 | 8,117 |
| RSI | 4,816 | 5,744 | 5373 |
| RSII | 1,311 | 0 | 1911 |
| RSIII | 2,209 | 2,006 | 2006 |
| All studies | 268,922 | 322,154 | 232,101 |
|  |  |  |  |
|  | **Maximum total overlap** | | |
|  | **macronutrients BMI; WC** | **BMI macronutrients** | **WC macronutrients** |
| Overlap (abs) | 17263; 9649 | 17,263 | 9,649 |
| Overlap (rela) | 0.064; 0.059 | 0.054 | 0.042 |

Abbrevations: BMI, body mass index; WC, waist circumference; abs, absolute; rel, relative.

a overlap as proportion of the appropriate total sample.

**Supplementary Table 3** Power analysis for causal point estimates and confidence intervals limits, and estimation of expected bias due to sample overlaps in the Mendelian randomization analyses.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Exposure** | **Outcome** | **Power for** | **Power for CI** | **Bias** |
| Carbohydrate intake (E%) | Body mass index | 1.00 | (1.00, 1.00) | 3.85E-04 |
| Carbohydrate intake (E%) | Waist circumference | 1.00 | (1.00, 1.00) | 4.93E-04 |
| Fat intake (E%) | Body mass index | 1.00 | (0.18, 1.00) | 5.28E-04 |
| Fat intake (E%) | Waist circumference | 1.00 | (0.19, 1.00) | 6.76E-04 |
| Protein intake (E%) | Body mass index | 0.98 | (0.07, 1.00) | 4.75E-04 |
| Protein intake (E%) | Waist circumference | 1.00 | (0.37, 1.00) | 6.08E-04 |
| Body mass index | Carbohydrate intake (E%) | 0.13 | (0.84, 0.25) | 3.24E-04 |
| Body mass index | Fat intake (E%) | 0.64 | (0.08, 0.99) | 3.24E-04 |
| Body mass index | Protein intake (E%) | 1.00 | (1.00, 1.00) | 3.24E-04 |
| Waist circumference | Carbohydrate intake (E%) | 0.12 | (0.88, 0.34) | 2.14E-04 |
| Waist circumference | Fat intake (E%) | 0.90 | (0.17, 1.00) | 2.14E-04 |
| Waist circumference | Protein intake (E%) | 0.97 | (0.41, 1.00) | 2.14E-04 |

Abbrevations: CI, confidence interval.

Calculations of the statistical power based on results from the radial inverse-variance weighted approach using modified second order weights and a conservative hypothetical observational estimate of 0.3.

**Supplementary Table 4** Characteristics of independent Single Nucleotide Polymorphisms (SNPs) extracted as instrumental variables in the two-sample Mendelian randomization analyses.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **BMI** | **WC** | **Fat intake (E%)** | **Protein intake (E%)** | **Carbohydrate intake (E%)** |
| Sample size | 322,154 | 232,101 | 268,922 | 268,922 | 268,922 |
| Genome-wide significance threshold |  |  |  |  |  |
| Extracted SNPs (not in LD) | 69 | 42 | 3 | 6 | 12 |
| Instruments (in sensitivity analysis) | 68 (56) | 41 (32) | 2 (2) | 5 (3) | 11 (5) |
| Explained variance by instruments | 1.25 % | 0.89 % | 0.06 % | 0.12 % | 0.17 % |
| F-statistic, mean (min; max) | 57.52 (29.02; 238.53) | 49.8 (29.34; 144) | 72.53 (31.60; 113.47) | 57.99 (32.04; 111.75) | 39.73 (30.32; 71.36) |

Abbrevations: BMI, body mass index; LD, Linkage Disequilibrium; WC, waist circumference, (E%), % of total energy intake.

Extraction of SNPs based on LD cut-off . Within sensitivity analyses, SNPs associated with potential confounding factors of the exposure-outcome association were excluded.

**Supplementary Table 5** Extracted Single Nucleotide Polymorphisms (SNPs) for the exposure relative dietary carbohydrate intake (in % of total energy intake (E%)) based on the genome-wide significance threshold of .

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SNP** | **Chr** | **Pos(hg37)** | **EA** | **OA** | **EAF** |  | **SE** | **P-value** | **(%)** | **F-stat** |
| rs10206338 | 2 | 60209981 | A | G | 0.572 | -0.016 | 0.003 | 1.52E-08 | 0.012 | 31.949 |
| rs10433500 | 3 | 85546798 | A | G | 0.630 | 0.016 | 0.003 | 1.96E-08 | 0.012 | 31.611 |
| rs10510554 | 3 | 25099776 | T | C | 0.436 | 0.019 | 0.003 | 2.94E-12 | 0.018 | 48.798 |
| rs10962121 | 9 | 15702704 | T | G | 0.479 | -0.015 | 0.003 | 3.4E-08 | 0.012 | 30.510 |
| rs1104608 | 16 | 73912588 | C | G | 0.418 | 0.018 | 0.003 | 1.74E-10 | 0.017 | 40.845 |
| rs2472297 | 15 | 75027880 | T | C | 0.206 | -0.018 | 0.003 | 3.73E-08 | 0.012 | 30.317 |
| rs36123991 | 17 | 44359663 | T | G | 0.186 | 0.021 | 0.004 | 8.24E-09 | 0.015 | 33.320 |
| rs4420638 | 19 | 45422946 | A | G | 0.822 | -0.024 | 0.004 | 8.85E-11 | 0.018 | 42.145 |
| rs7012637 | 8 | 9173209 | A | G | 0.492 | 0.017 | 0.003 | 4.68E-10 | 0.015 | 38.905 |
| rs7190396 | 16 | 53822502 | T | G | 0.599 | 0.018 | 0.003 | 2.39E-10 | 0.015 | 40.171 |
| rs8097672 | 18 | 1839601 | A | T | 0.847 | 0.023 | 0.004 | 1.95E-09 | 0.014 | 36.000 |
| rs838144 | 19 | 49250239 | T | C | 0.534 | -0.023 | 0.003 | 3.26E-17 | 0.027 | 71.356 |

Abbrevations: , standard deviation change; Chr, chromosome; Pos(hg37), position at human build 37; EA, effect allele; EAF, effect allele frequency; F-stat, F-statistic OA, other allele; (%), explained variance given in percent; SE, standard error.

**Supplementary Table 6** Extracted Single Nucleotide Polymorphisms (SNPs) for the exposure relative dietary fat intake (in % of total energy intake (E%)) based on the genome-wide significance threshold of .

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SNP** | **Chr** | **Pos(hg37)** | **EA** | **OA** | **EAF** |  | **SE** | **P-value** | **(%)** | **F-stat** |
| rs10206338 | 2 | 60209981 | A | G | 0.572 | 0.013 | 0.003 | 3.61E-06 | 0.008 | 21.411 |
| rs10468280 | 16 | 53827479 | A | G | 0.611 | -0.019 | 0.003 | 7.02E-12 | 0.018 | 47.125 |
| rs10789340 | 1 | 72940273 | A | G | 0.354 | 0.015 | 0.003 | 2.47E-07 | 0.010 | 26.640 |
| rs113971372 | 9 | 97346136 | A | G | 0.022 | -0.048 | 0.010 | 2.59E-06 | 0.010 | 22.097 |
| rs11549609 | 19 | 3121247 | T | C | 0.007 | 0.089 | 0.019 | 4.43E-06 | 0.012 | 21.081 |
| rs11576925 | 1 | 96934086 | C | G | 0.793 | -0.017 | 0.004 | 4.94E-06 | 0.010 | 20.877 |
| rs11697842 | 20 | 16983598 | A | G | 0.311 | 0.014 | 0.003 | 2.68E-06 | 0.009 | 22.105 |
| rs1229984 | 4 | 100239319 | T | C | 0.048 | 0.098 | 0.009 | 2.64E-28 | 0.054 | 121.77 |
| rs12516875 | 5 | 32978655 | A | G | 0.343 | -0.014 | 0.003 | 2.46E-06 | 0.008 | 22.229 |
| rs143458040 | 13 | 72513342 | T | G | 0.007 | -0.097 | 0.020 | 1.68E-06 | 0.013 | 22.924 |
| rs1603891 | 3 | 2955478 | A | G | 0.483 | -0.014 | 0.003 | 1.17E-06 | 0.009 | 23.538 |
| rs2005737 | 7 | 1,44E+08 | A | G | 0.314 | -0.015 | 0.003 | 2.19E-06 | 0.009 | 22.350 |
| rs272678 | 7 | 24137455 | T | G | 0.455 | 0.015 | 0.003 | 1.36E-07 | 0.011 | 27.829 |
| rs33988101 | 19 | 49218111 | T | G | 0.499 | -0.029 | 0.003 | 1.66E-26 | 0.043 | 113.47 |
| rs35789556 | 11 | 8530406 | A | G | 0.744 | 0.016 | 0.003 | 1.32E-06 | 0.009 | 23.331 |
| rs4277294 | 15 | 61827850 | A | T | 0.075 | -0.028 | 0.005 | 1.57E-07 | 0.010 | 27.552 |
| rs4580876 | 6 | 98322872 | A | G | 0.463 | -0.013 | 0.003 | 1.82E-06 | 0.009 | 22.831 |
| rs4683902 | 3 | 1,01E+08 | A | C | 0.016 | 0.058 | 0.013 | 3.91E-06 | 0.011 | 21.312 |
| rs4886343 | 13 | 62173030 | A | G | 0.869 | -0.019 | 0.004 | 1.48E-06 | 0.009 | 23.226 |
| rs4891017 | 18 | 74097959 | A | G | 0.376 | -0.014 | 0.003 | 4.17E-06 | 0.009 | 21.141 |
| rs57193069 | 7 | 1862417 | A | G | 0.553 | -0.016 | 0.003 | 1.8E-08 | 0.012 | 31.600 |
| rs5755961 | 22 | 36236718 | T | G | 0.868 | 0.019 | 0.004 | 2.66E-06 | 0.008 | 22.094 |
| rs6131331 | 20 | 12378852 | A | C | 0.172 | 0.017 | 0.004 | 1.1E-06 | 0.009 | 23.803 |
| rs62466318 | 7 | 73042085 | T | C | 0.194 | -0.017 | 0.003 | 8.88E-07 | 0.009 | 24.117 |
| rs7012814 | 8 | 9173358 | A | G | 0.492 | -0.019 | 0.003 | 1.12E-11 | 0.018 | 46.220 |
| rs7218313 | 17 | 69831308 | A | C | 0.476 | -0.013 | 0.003 | 1.59E-06 | 0.009 | 23.110 |
| rs72881195 | 2 | 1,64E+08 | A | G | 0.038 | 0.033 | 0.007 | 4.48E-06 | 0.012 | 21.025 |
| rs729833 | 1 | 75601145 | T | C | 0.225 | -0.015 | 0.003 | 3.94E-06 | 0.008 | 21.240 |
| rs752208 | 2 | 25455389 | A | G | 0.212 | -0.019 | 0.004 | 3.16E-07 | 0.012 | 26.102 |
| rs75971153 | 2 | 24689143 | T | C | 0.811 | -0.018 | 0.004 | 4.6E-07 | 0.010 | 25.473 |
| rs7619139 | 3 | 25110415 | A | T | 0.587 | 0.015 | 0.003 | 1.01E-07 | 0.011 | 28.355 |
| rs8106503 | 19 | 11196886 | T | C | 0.878 | -0.020 | 0.004 | 2.44E-06 | 0.009 | 22.240 |
| rs873756 | 11 | 28480410 | C | G | 0.489 | -0.015 | 0.003 | 1.16E-06 | 0.012 | 23.614 |
| rs9315498 | 13 | 38099921 | A | C | 0.497 | 0.013 | 0.003 | 2.43E-06 | 0.008 | 22.313 |
| rs986527 | 11 | 31636481 | A | G | 0.379 | -0.013 | 0.003 | 3.9E-06 | 0.008 | 21.271 |
| rs9969531 | 8 | 28222586 | C | G | 0.408 | -0.014 | 0.003 | 1.44E-06 | 0.009 | 23.168 |

Abbrevations: , standard deviation change; Chr, chromosome; Pos(hg37), position at human build 37; EA, effect allele; EAF, effect allele frequency; F-stat, F-statistic OA, other allele; (%), explained variance given in percent; SE, standard error.

**Supplementary Table 7** Extracted Single Nucleotide Polymorphisms (SNPs) for the exposure relative dietary protein intake (in % of total energy intake (E%)) based on the genome-wide significance threshold of .

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SNP** | **Chr** | **Pos(hg37)** | **EA** | **OA** | **EAF** |  | **SE** | **P-value** | **(%)** | **F-stat** |
| rs10734012 | 10 | 34216806 | T | C | 0.530 | -0.014 | 0.003 | 7.22E-07 | 0.010 | 24.538 |
| rs10745508 | 12 | 89930626 | T | C | 0.518 | -0.013 | 0.003 | 1.47E-06 | 0.009 | 23.250 |
| rs10759212 | 9 | 109932877 | A | G | 0.525 | 0.013 | 0.003 | 3.69E-06 | 0.008 | 21.340 |
| rs10828186 | 10 | 21383516 | A | C | 0.127 | 0.019 | 0.004 | 2.9E-06 | 0.008 | 21.840 |
| rs11073752 | 15 | 88423051 | T | C | 0.655 | 0.016 | 0.003 | 1.27E-07 | 0.011 | 27.964 |
| rs1229984 | 4 | 100239319 | T | C | 0.048 | 0.044 | 0.009 | 8.99E-07 | 0.011 | 24.149 |
| rs13146907 | 4 | 39425248 | A | G | 0.625 | -0.022 | 0.003 | 1.24E-14 | 0.023 | 59.463 |
| rs1368285 | 5 | 146656123 | T | G | 0.182 | -0.017 | 0.004 | 4.05E-06 | 0.008 | 21.241 |
| rs138187954 | 6 | 23124702 | T | C | 0.022 | 0.044 | 0.010 | 4.24E-06 | 0.009 | 21.167 |
| rs139975395 | 4 | 121662495 | T | C | 0.014 | -0.077 | 0.016 | 1.05E-06 | 0.012 | 23.81 |
| rs141013224 | 2 | 8872953 | A | G | 0.019 | -0.050 | 0.011 | 3.56E-06 | 0.011 | 21.488 |
| rs141331590 | 8 | 39954405 | A | G | 0.015 | -0.059 | 0.012 | 1.16E-06 | 0.011 | 23.635 |
| rs1461729 | 8 | 9187242 | A | G | 0.098 | 0.032 | 0.005 | 4.09E-12 | 0.018 | 48.089 |
| rs1470690 | 3 | 22476200 | T | G | 0.602 | 0.013 | 0.003 | 2.79E-06 | 0.008 | 21.921 |
| rs1532769 | 3 | 147090343 | T | C | 0.468 | 0.016 | 0.003 | 5.05E-08 | 0.012 | 29.616 |
| rs1603978 | 3 | 25108236 | A | C | 0.694 | 0.019 | 0.003 | 1.35E-10 | 0.016 | 41.105 |
| rs17455688 | 13 | 66677935 | T | C | 0.944 | 0.028 | 0.006 | 8.55E-07 | 0.009 | 24.210 |
| rs1891210 | 9 | 15900348 | T | G | 0.570 | -0.014 | 0.003 | 9.75E-07 | 0.009 | 23.999 |
| rs192935283 | 1 | 39382448 | A | C | 0.007 | 0.090 | 0.019 | 2.82E-06 | 0.013 | 21.941 |
| rs228751 | 17 | 42120078 | A | G | 0.514 | -0.013 | 0.003 | 4.32E-06 | 0.008 | 21.173 |
| rs2582908 | 11 | 28522535 | C | G | 0.489 | -0.013 | 0.003 | 1.11E-06 | 0.009 | 23.779 |
| rs2624495 | 5 | 116727172 | A | G | 0.490 | -0.013 | 0.003 | 4.34E-06 | 0.008 | 21.073 |
| rs2953517 | 8 | 87332013 | T | C | 0.283 | 0.014 | 0.003 | 3.65E-06 | 0.008 | 21.458 |
| rs357537 | 9 | 98153936 | A | G | 0.096 | -0.023 | 0.005 | 1.08E-06 | 0.009 | 23.781 |
| rs445551 | 2 | 79697982 | A | G | 0.317 | 0.019 | 0.003 | 1.49E-08 | 0.016 | 32.044 |
| rs4708061 | 6 | 69095976 | A | G | 0.549 | -0.013 | 0.003 | 1.4E-06 | 0.009 | 23.355 |
| rs4775698 | 15 | 47873477 | T | G | 0.719 | -0.015 | 0.003 | 5.02E-07 | 0.010 | 25.266 |
| rs55872725 | 16 | 53809123 | T | C | 0.400 | 0.018 | 0.003 | 2.09E-10 | 0.015 | 40.368 |
| rs6024454 | 20 | 54393433 | T | C | 0.214 | -0.017 | 0.003 | 1.14E-06 | 0.009 | 23.688 |
| rs6041160 | 20 | 12169905 | T | C | 0.801 | 0.016 | 0.003 | 3.99E-06 | 0.008 | 21.250 |
| rs61882542 | 11 | 46054619 | T | C | 0.901 | -0.023 | 0.005 | 4.42E-07 | 0.010 | 25.482 |
| rs61928280 | 12 | 50650041 | A | C | 0.786 | 0.015 | 0.003 | 4.4E-06 | 0.008 | 21.061 |
| rs72835501 | 17 | 47451139 | C | G | 0.959 | 0.037 | 0.008 | 2.82E-06 | 0.012 | 21.906 |
| rs75248627 | 3 | 120061080 | C | G | 0.019 | 0.054 | 0.011 | 1.04E-06 | 0.011 | 23.830 |
| rs76900572 | 5 | 74332949 | T | G | 0.023 | 0.058 | 0.013 | 4.18E-06 | 0.012 | 21.163 |
| rs77656144 | 19 | 17146887 | C | G | 0.923 | -0.026 | 0.005 | 3.18E-06 | 0.010 | 21.676 |
| rs77975053 | 1 | 181151080 | C | G | 0.079 | -0.028 | 0.006 | 3.79E-06 | 0.012 | 21.346 |
| rs780094 | 2 | 27741237 | T | C | 0.398 | 0.018 | 0.003 | 5.58E-10 | 0.015 | 38.598 |
| rs79813431 | 11 | 41156223 | C | G | 0.971 | -0.040 | 0.009 | 3.3E-06 | 0.009 | 21.624 |
| rs838133 | 19 | 49259529 | A | G | 0.425 | -0.032 | 0.003 | 4.52E-26 | 0.050 | 111.75 |

Abbrevations: , standard deviation change; Chr, chromosome; Pos(hg37), position at human build 37; EA, effect allele; EAF, effect allele frequency; F-stat, F-statistic; OA, other allele; (%), explained variance given in percent; SE, standard error;.

**Supplementary Table 8** Extracted Single Nucleotide Polymorphisms (SNPs) for the exposure body mass index based on the genome-wide significance threshold of .

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SNP** | **Chr** | **Pos(hg37)** | **EA** | **OA** | **EAF** |  | **SE** | **P-value** | **(%)** | **F-stat** |
| rs1000940 | 17 | 5283252 | G | A | 0.225 | 0.019 | 0.003 | 1.28E-08 | 0.010 | 31.889 |
| rs10132280 | 14 | 25928179 | A | C | 0.333 | -0.023 | 0.003 | 1.14E-11 | 0.014 | 45.761 |
| rs1016287 | 2 | 59305625 | C | T | 0.675 | -0.023 | 0.003 | 2.25E-11 | 0.014 | 45.364 |
| rs10182181 | 2 | 25150296 | G | A | 0.500 | 0.031 | 0.003 | 8.78E-24 | 0.030 | 98.073 |
| rs10733682 | 9 | 129460914 | G | A | 0.575 | -0.017 | 0.003 | 1.83E-08 | 0.010 | 31.504 |
| rs10938397 | 4 | 45182527 | G | A | 0.433 | 0.040 | 0.003 | 3.2E-38 | 0.052 | 168.16 |
| rs10968576 | 9 | 28414339 | G | A | 0.292 | 0.025 | 0.003 | 6.61E-14 | 0.018 | 56.934 |
| rs11030104 | 11 | 27684517 | G | A | 0.200 | -0.041 | 0.004 | 5.56E-28 | 0.037 | 118.69 |
| rs11057405 | 12 | 122781897 | A | G | 0.092 | -0.031 | 0.006 | 2.02E-08 | 0.010 | 31.156 |
| rs11165643 | 1 | 96924097 | T | C | 0.575 | 0.022 | 0.003 | 2.07E-12 | 0.015 | 49.452 |
| rs1167827 | 7 | 75163169 | G | A | 0.542 | 0.020 | 0.003 | 6.33E-10 | 0.012 | 37.469 |
| rs11727676 | 4 | 145659064 | C | T | 0.075 | -0.036 | 0.006 | 2.55E-08 | 0.011 | 31.290 |
| rs12286929 | 11 | 115022404 | G | A | 0.433 | 0.022 | 0.003 | 1.31E-12 | 0.015 | 49.000 |
| rs12429545 | 13 | 54102206 | A | G | 0.100 | 0.033 | 0.005 | 1.09E-12 | 0.016 | 50.500 |
| rs12940622 | 17 | 78615571 | A | G | 0.458 | -0.018 | 0.003 | 2.49E-09 | 0.011 | 34.468 |
| rs12986742 | 2 | 58975143 | C | T | 0.500 | 0.021 | 0.004 | 1.01E-08 | 0.014 | 32.830 |
| rs13021737 | 2 | 632348 | G | A | 0.875 | 0.060 | 0.004 | 1.11E-50 | 0.071 | 225.75 |
| rs13078960 | 3 | 85807590 | G | T | 0.183 | 0.030 | 0.004 | 1.74E-14 | 0.018 | 57.994 |
| rs13107325 | 4 | 103188709 | T | C | 0.117 | 0.048 | 0.007 | 1.83E-12 | 0.015 | 49.206 |
| rs13191362 | 6 | 163033350 | G | A | 0.200 | -0.028 | 0.005 | 7.34E-09 | 0.010 | 33.302 |
| rs1516725 | 3 | 185824004 | C | T | 0.908 | 0.045 | 0.005 | 1.89E-22 | 0.030 | 96.125 |
| rs1528435 | 2 | 181550962 | T | C | 0.583 | 0.018 | 0.003 | 1.2E-08 | 0.010 | 32.970 |
| rs1558902 | 16 | 53803574 | A | T | 0.450 | 0.082 | 0.003 | 7.5E-153 | 0.194 | 447.02 |
| rs16851483 | 3 | 141275436 | T | G | 0.092 | 0.048 | 0.008 | 3.55E-10 | 0.017 | 39.347 |
| rs16951275 | 15 | 68077168 | C | T | 0.225 | -0.031 | 0.004 | 1.91E-17 | 0.022 | 70.650 |
| rs17001654 | 4 | 77129568 | G | C | 0.158 | 0.031 | 0.005 | 7.76E-09 | 0.014 | 33.334 |
| rs17024393 | 1 | 110154688 | C | T | 0.042 | 0.066 | 0.009 | 7.03E-14 | 0.019 | 55.909 |
| rs17066856 | 18 | 58049656 | C | T | 0.133 | -0.040 | 0.006 | 6.22E-13 | 0.016 | 51.578 |
| rs17094222 | 10 | 102395440 | C | T | 0.208 | 0.025 | 0.004 | 5.94E-11 | 0.013 | 42.937 |
| rs17405819 | 8 | 76806584 | C | T | 0.367 | -0.022 | 0.003 | 2.07E-11 | 0.014 | 46.075 |
| rs17724992 | 19 | 18454825 | G | A | 0.308 | -0.019 | 0.004 | 3.41E-08 | 0.010 | 30.723 |
| rs1808579 | 18 | 21104888 | T | C | 0.475 | -0.017 | 0.003 | 4.17E-08 | 0.009 | 29.021 |
| rs1928295 | 9 | 120378483 | C | T | 0.425 | -0.019 | 0.003 | 7.91E-10 | 0.011 | 36.778 |
| rs2033529 | 6 | 40348653 | G | A | 0.258 | 0.019 | 0.003 | 1.39E-08 | 0.010 | 33.149 |
| rs2033732 | 8 | 85079709 | C | T | 0.758 | 0.019 | 0.004 | 4.89E-08 | 0.009 | 30.093 |
| rs205262 | 6 | 34563164 | G | A | 0.267 | 0.022 | 0.004 | 1.75E-10 | 0.013 | 39.870 |
| rs2112347 | 5 | 75015242 | G | T | 0.375 | -0.026 | 0.003 | 6.19E-17 | 0.022 | 70.885 |
| rs2121279 | 2 | 143043285 | T | C | 0.117 | 0.025 | 0.004 | 2.31E-08 | 0.010 | 31.004 |
| rs2176598 | 11 | 43864278 | C | T | 0.800 | -0.020 | 0.004 | 2.97E-08 | 0.010 | 30.250 |
| rs2207139 | 6 | 50845490 | G | A | 0.100 | 0.045 | 0.004 | 4.13E-29 | 0.039 | 124.88 |
| rs2245368 | 7 | 76608143 | T | C | 0.758 | -0.032 | 0.006 | 3.19E-08 | 0.015 | 30.929 |
| rs2287019 | 19 | 46202172 | T | C | 0.150 | -0.036 | 0.004 | 4.58E-18 | 0.024 | 73.469 |
| rs2365389 | 3 | 61236462 | T | C | 0.342 | -0.020 | 0.003 | 1.63E-10 | 0.013 | 41.623 |
| rs2820292 | 1 | 201784287 | C | A | 0.508 | 0.020 | 0.003 | 1.83E-10 | 0.012 | 39.568 |
| rs29941 | 19 | 34309532 | G | A | 0.667 | 0.018 | 0.003 | 2.41E-08 | 0.009 | 30.417 |
| rs3101336 | 1 | 72751185 | C | T | 0.649 | 0.033 | 0.003 | 2.66E-26 | 0.037 | 116.08 |
| rs3736485 | 15 | 51748610 | G | A | 0.575 | -0.018 | 0.003 | 7.41E-09 | 0.010 | 32.233 |
| rs3817334 | 11 | 47650993 | T | C | 0.450 | 0.026 | 0.003 | 5.15E-17 | 0.022 | 71.429 |
| rs3849570 | 3 | 81792112 | A | C | 0.367 | 0.019 | 0.003 | 2.6E-08 | 0.011 | 30.574 |
| rs3888190 | 16 | 28889486 | A | C | 0.358 | 0.031 | 0.003 | 3.14E-23 | 0.031 | 99.355 |
| rs4256980 | 11 | 8673939 | G | C | 0.725 | 0.021 | 0.003 | 2.9E-11 | 0.014 | 45.453 |
| rs4740619 | 9 | 15634326 | C | T | 0.467 | -0.018 | 0.003 | 4.56E-09 | 0.010 | 33.341 |
| rs4889606 | 16 | 31011183 | G | A | 0.358 | -0.018 | 0.003 | 4.86E-09 | 0.011 | 34.848 |
| rs543874 | 1 | 177889480 | G | A | 0.267 | 0.048 | 0.004 | 2.62E-35 | 0.047 | 152.74 |
| rs6477694 | 9 | 111932342 | T | C | 0.642 | -0.017 | 0.003 | 2.67E-08 | 0.010 | 31.504 |
| rs6567160 | 18 | 57829135 | C | T | 0.283 | 0.056 | 0.004 | 3.93E-53 | 0.074 | 238.53 |
| rs657452 | 1 | 49589847 | G | A | 0.583 | -0.023 | 0.003 | 5.48E-13 | 0.017 | 53.620 |
| rs6656785 | 1 | 75005776 | G | A | 0.383 | 0.022 | 0.003 | 3.83E-12 | 0.015 | 49.000 |
| rs6804842 | 3 | 25106437 | G | A | 0.575 | 0.019 | 0.003 | 2.48E-09 | 0.011 | 35.614 |
| rs7138803 | 12 | 50247468 | A | G | 0.442 | 0.032 | 0.003 | 8.15E-24 | 0.032 | 103.25 |
| rs7141420 | 14 | 79899454 | T | C | 0.617 | 0.024 | 0.003 | 1.23E-14 | 0.018 | 57.466 |
| rs758747 | 16 | 3627358 | T | C | 0.267 | 0.023 | 0.004 | 7.47E-10 | 0.012 | 36.979 |
| rs7599312 | 2 | 213413231 | A | G | 0.292 | -0.022 | 0.003 | 1.17E-10 | 0.013 | 41.868 |
| rs7899106 | 10 | 87410904 | G | A | 0.050 | 0.040 | 0.007 | 2.96E-08 | 0.010 | 30.951 |
| rs7903146 | 10 | 114758349 | T | C | 0.250 | -0.023 | 0.003 | 1.11E-11 | 0.015 | 47.366 |
| rs879620 | 16 | 4015729 | T | C | 0.592 | 0.024 | 0.004 | 1.06E-09 | 0.016 | 37.210 |
| rs9400239 | 6 | 108977663 | C | T | 0.700 | 0.019 | 0.003 | 1.61E-08 | 0.010 | 32.455 |
| rs9579083 | 13 | 28017270 | C | G | 0.233 | 0.030 | 0.005 | 3.46E-10 | 0.017 | 39.395 |
| rs9926784 | 16 | 19941968 | C | T | 0.208 | -0.027 | 0.004 | 1.85E-10 | 0.013 | 39.810 |

Abbrevations: , standard deviation change; Chr, chromosome; Pos(hg37), position at human build 37; EA, effect allele; EAF, effect allele frequency; F-stat, F-statistic; OA, other allele; (%), explained variance given in percent; SE, standard error.

**Supplementary Table 9** Extracted Single Nucleotide Polymorphisms (SNPs) for the exposure waist circumference based on the genome-wide significance threshold of .

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SNP** | **Chr** | **Pos(hg37)** | **EA** | **OA** | **EAF** |  | **SE** | **P-value** | **(%)** | **F-stat** |
| rs10132280 | 14 | 25928179 | A | C | 0.333 | -0.022 | 0.004 | 2.2E-09 | 0.015 | 35.354 |
| rs10767658 | 11 | 27672252 | G | C | 0.642 | -0.031 | 0.004 | 3.3E-17 | 0.031 | 70.197 |
| rs10840100 | 11 | 8669437 | G | A | 0.725 | 0.020 | 0.004 | 5.4E-09 | 0.014 | 32.653 |
| rs10938397 | 4 | 45182527 | G | A | 0.433 | 0.032 | 0.004 | 6.1E-20 | 0.036 | 83.591 |
| rs10968576 | 9 | 28414339 | G | A | 0.292 | 0.025 | 0.004 | 1.2E-11 | 0.021 | 48.225 |
| rs11165623 | 1 | 96893000 | A | G | 0.483 | 0.020 | 0.003 | 5.2E-09 | 0.015 | 34.602 |
| rs12429545 | 13 | 54102206 | A | G | 0.100 | 0.031 | 0.005 | 2.5E-09 | 0.016 | 35.540 |
| rs1516725 | 3 | 185824004 | C | T | 0.908 | 0.031 | 0.005 | 1.7E-09 | 0.016 | 36.947 |
| rs1558902 | 16 | 53803574 | A | T | 0.450 | 0.074 | 0.004 | 3.7E-101 | 0.217 | 696.28 |
| rs16894959 | 6 | 34825662 | C | T | 0.100 | 0.026 | 0.005 | 3.4E-08 | 0.013 | 29.340 |
| rs16996700 | 20 | 50981945 | C | T | 0.300 | -0.023 | 0.004 | 1.5E-09 | 0.017 | 38.641 |
| rs17066856 | 18 | 58049656 | C | T | 0.133 | -0.037 | 0.006 | 9E-10 | 0.017 | 38.027 |
| rs17381664 | 1 | 78048331 | C | T | 0.425 | 0.022 | 0.004 | 4.2E-10 | 0.017 | 39.510 |
| rs2033529 | 6 | 40348653 | G | A | 0.258 | 0.021 | 0.004 | 1.7E-08 | 0.014 | 32.213 |
| rs2112347 | 5 | 75015242 | G | T | 0.375 | -0.025 | 0.004 | 3.2E-13 | 0.022 | 51.020 |
| rs2287019 | 19 | 46202172 | T | C | 0.150 | -0.035 | 0.005 | 1.7E-14 | 0.027 | 57.892 |
| rs2293576 | 11 | 47434986 | A | G | 0.367 | -0.022 | 0.004 | 9.4E-10 | 0.017 | 37.345 |
| rs2325036 | 3 | 85819412 | C | A | 0.408 | -0.023 | 0.004 | 2.1E-11 | 0.019 | 43.183 |
| rs2489623 | 6 | 127455821 | C | A | 0.558 | 0.019 | 0.003 | 3.4E-08 | 0.013 | 31.228 |
| rs2531992 | 16 | 4021734 | G | A | 0.833 | 0.028 | 0.005 | 3E-09 | 0.015 | 34.027 |
| rs2820292 | 1 | 201784287 | C | A | 0.508 | 0.019 | 0.003 | 2.4E-08 | 0.013 | 31.228 |
| rs3127553 | 1 | 49438005 | A | G | 0.633 | -0.023 | 0.004 | 1.6E-10 | 0.019 | 43.183 |
| rs3849570 | 3 | 81792112 | A | C | 0.367 | 0.021 | 0.004 | 2.2E-08 | 0.016 | 30.540 |
| rs4776970 | 15 | 68080886 | T | A | 0.342 | -0.020 | 0.004 | 2.3E-08 | 0.014 | 32.653 |
| rs6163 | 10 | 104596924 | A | C | 0.392 | 0.019 | 0.004 | 3.7E-08 | 0.013 | 29.469 |
| rs633715 | 1 | 177852580 | C | T | 0.267 | 0.043 | 0.004 | 3.3E-23 | 0.046 | 99.999 |
| rs6440003 | 3 | 141094209 | A | G | 0.483 | 0.021 | 0.003 | 2.9E-10 | 0.016 | 38.148 |
| rs6545714 | 2 | 59307725 | A | G | 0.625 | -0.022 | 0.004 | 1.9E-10 | 0.017 | 39.510 |
| rs6567160 | 18 | 57829135 | C | T | 0.283 | 0.048 | 0.004 | 2.6E-33 | 0.062 | 144.00 |
| rs6755502 | 2 | 635721 | C | T | 0.875 | 0.051 | 0.005 | 2E-30 | 0.055 | 128.44 |
| rs7138803 | 12 | 50247468 | A | G | 0.442 | 0.028 | 0.004 | 1.6E-15 | 0.028 | 63.999 |
| rs7144011 | 14 | 79940383 | T | G | 0.275 | 0.033 | 0.004 | 9.4E-16 | 0.028 | 64.782 |
| rs7239883 | 18 | 40147671 | A | G | 0.683 | -0.021 | 0.004 | 2.3E-09 | 0.016 | 36.000 |
| rs749671 | 16 | 31088347 | A | G | 0.375 | -0.019 | 0.004 | 3.2E-08 | 0.013 | 29.469 |
| rs7498665 | 16 | 28883241 | G | A | 0.358 | 0.034 | 0.004 | 1.4E-22 | 0.041 | 94.367 |
| rs7531118 | 1 | 72837239 | C | T | 0.608 | 0.027 | 0.004 | 1.5E-14 | 0.026 | 59.510 |
| rs7550711 | 1 | 110082886 | T | C | 0.034 | 0.058 | 0.010 | 3.4E-09 | 0.017 | 35.027 |
| rs7903146 | 10 | 114758349 | T | C | 0.250 | -0.022 | 0.004 | 3.9E-09 | 0.015 | 35.354 |
| rs806794 | 6 | 26200677 | G | A | 0.275 | -0.022 | 0.004 | 2.1E-09 | 0.016 | 35.354 |
| rs929641 | 2 | 58792377 | G | A | 0.383 | -0.021 | 0.003 | 1.2E-09 | 0.016 | 38.148 |
| rs9400239 | 6 | 108977663 | C | T | 0.700 | 0.024 | 0.004 | 1.9E-11 | 0.019 | 44.444 |
| rs943005 | 6 | 50865820 | T | C | 0.100 | 0.039 | 0.004 | 7.2E-19 | 0.034 | 78.563 |

Abbrevations: , standard deviation change; Chr, chromosome; Pos(hg37), position at human build 37; EA, effect allele; EAF, effect allele frequency; F-stat, F-statistic; OA, other allele; (%), explained variance given in percent; SE, standard error.

**Supplementary Table 10** Single Nucleotide Polymorphisms (SNPs) associated with potential confounders of exposure-outcome associations based on from the PhenoScanner database and therefore excluded within sensitivity analyses.

|  |  |  |
| --- | --- | --- |
| **Excluded SNP** | **Exposure** | **Trait** |
| rs10433500 | COH intake | Alcohol intake frequency, Ever smoked, Past tobacco smoking, Smoking status: previous, Types of physical activity in last 4 weeks: other exercises |
| rs1104608 | COH intake | Alcohol intake frequency |
| rs36123991 | COH intake | Alcohol intake frequency |
| rs7190396 | COH intake | Alcohol intake frequency, Average weekly beer plus cider intake, Average weekly red wine intake, Usual walking pace |
| rs838144 | COH intake | Alcohol intake frequency |
| rs34444368 | COH intake | Years of educational attainment |
| rs10468280 | Fat intake | Alcohol intake frequency, Average weekly beer plus cider intake, Average weekly red wine intake, Usual walking pace |
| rs4580876 | Fat intake | Alcohol intake frequency, Average weekly red wine intake, Years of educational attainment |
| rs10789340 | Fat intake | Depressive symptoms multi trait analysis |
| rs780094 | Protein intake | Alcohol consumption, Alcohol consumption in current drinkers, Alcohol intake frequency, Alcohol intake versus 10 years previously |
| rs13146907 | Protein intake | Alcohol intake frequency, Reason for reducing amount of alcohol drunk: health precaution |
| rs55872725 | Protein intake | Alcohol intake frequency, Usual walking pace |
| rs13107325 | BMI | Alcohol intake frequency, Qualifications: college or university degree, Types of physical activity in last 4 weeks: strenuous sports, Usual walking pace |
| rs1808579 | BMI | Alcohol intake frequency, Average weekly red wine intake, Usual walking pace, Years of educational attainment |
| rs3817334 | BMI | Alcohol intake frequency, Usual walking pace |
| rs3888190 | BMI | Alcohol intake frequency, Qualifications: college or university degree, Qualifications: none, Types of physical activity in last 4 weeks: light diy, Years of educational attainment |
| rs4889606 | BMI | Alcohol intake frequency |
| rs6567160 | BMI | Alcohol intake frequency |
| rs13078960 | BMI | Ever smoked, Past tobacco smoking |
| rs11030104 | BMI | Past tobacco smoking |
| rs3101336 | BMI | Qualifications: college or university degree |
| rs9400239 | BMI | Qualifications: college or university degree |
| rs205262 | BMI | Usual walking pace |
| rs6567160 | WC | Alcohol intake frequency |
| rs749671 | WC | Alcohol intake frequency, Usual walking pace |
| rs7498665 | WC | Alcohol intake frequency, Intelligence, Types of physical activity in last 4 weeks: light diy, Years of educational attainment |
| rs2325036 | WC | Ever smoked, Past tobacco smoking |
| rs6163 | WC | Ever smoked, Past tobacco smoking |
| rs9400239 | WC | Intelligence |
| rs806794 | WC | Pack years of smoking preview only |

Abbrevations: COH, carbohydrate; BMI, body mass index; WC, waist circumference.

**Supplementary Table 11** Associations of Single Nucleotide Polymorphisms (SNPs) used as instruments (based on the genome-wide significance threshold of ) for relative dietary carbohydrate intake (in % of total energy intake (E%)) with anthropometric measures (outcomes).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **Body Mass Index (BMI)** | | | | | | | **Waist Circumference (WC)** | | | | | | |
| **SNP** | **Chr** | **Pos(hg37)** |  | **EA** | **OA** | **EAF** |  | **SE** | **P-value** |  | **EA** | **OA** | **EAF** |  | **SE** | **P-value** | |
| rs10206338 | 2 | 60209981 | 233923 | A | G | 0.592 | 0.002 | 0.004 | 0.599 | 153885 | A | G | 0.592 | 0.003 | 0.004 | 0.440 | |
| rs10433500 | 3 | 85549020 | 234018 | A | G | 0.567 | -0.013 | 0.004 | 0.001 | 153947 | A | G | 0.567 | -0.012 | 0.004 | 0.005 | |
| rs10510554a | 3 | 25099776 | 321404 | T | C | 0.433 | -0.018 | 0.003 | 4.2E-09 | 231893 | T | C | 0.433 | -0.014 | 0.003 | 2.4E-05 | |
| rs10962121 | 9 | 15702704 | 227722 | T | G | 0.433 | 0.016 | 0.004 | 1.2E-04 | 150860 | T | G | 0.433 | 0.009 | 0.005 | 0.056 | |
| rs1104608 | 16 | 73912588 | 206083 | C | G | 0.392 | -0.004 | 0.005 | 0.350 | 131506 | C | G | 0.392 | -0.006 | 0.005 | 0.250 | |
| rs2472297 | 15 | 75027880 | 314662 | T | C | 0.208 | 0.005 | 0.004 | 0.168 | 230721 | T | C | 0.208 | 0.005 | 0.004 | 0.200 | |
| rs36123991 | 17 | 44364829 | 233760 | T | G | 0.192 | 0.003 | 0.005 | 0.496 | 153882 | T | G | 0.192 | 0.004 | 0.005 | 0.440 | |
| rs4420638 | 19 | 45422946 | 210960 | A | G | 0.817 | 0.020 | 0.006 | 0.001 | 133531 | A | G | 0.817 | 0.024 | 0.007 | 4.5E-04 | |
| rs7190396a | 16 | 53828066 | 321602 | T | G | 0.558 | -0.078 | 0.003 | 8E-139 | 231723 | T | G | 0.558 | -0.071 | 0.004 | 8.9E-94 | |
| rs8097672 | 18 | 1839601 | 233947 | A | T | 0.867 | -0.018 | 0.005 | 0.001 | 153924 | A | T | 0.867 | -0.010 | 0.006 | 0.090 | |
| rs838144 | 19 | 49250239 | 233232 | T | C | 0.475 | 0.009 | 0.004 | 0.015 | 153147 | T | C | 0.475 | 0.009 | 0.004 | 0.043 | |

Abbrevations: , standard deviation change; Chr, chromosome; Pos(hg37), position at human build 37; EA, effect allele; EAF, effect allele frequency; OA, other allele; SE, standard error; SNP, Single Nucleotide Polymorphism.

Instruments listed before outlier-correction by IVW and MR-Egger Qj-statistics. Estimates are given per one standard deviation.

a SNP was removed from the analysis with BMI due to a strong association with the appropriate outcome at the genome-wide significance threshold of .

**Supplementary Table 12** Associations of Single Nucleotide Polymorphisms (SNPs) used as instruments (based on the genome-wide significance threshold of ) for relative dietary fat intake (in % of total energy intake (E%)) with anthropometric measures (outcomes).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **Body Mass Index (BMI)** | | | | | | | **Waist Circumference (WC)** | | | | | | |
| **SNP** | **Chr** | **Pos(hg37)** |  | **EA** | **OA** | **EAF** |  | **SE** | **P-value** |  | **EA** | **OA** | **EAF** |  | **SE** | **P-value** | |
| rs10206338 | 2 | 60209981 | 233923 | A | G | 0.592 | 0.002 | 0.004 | 0.599 | 153885 | A | G | 0.592 | 0.003 | 0.004 | 0.440 | |
| rs10468280a | 16 | 53828066 | 321602 | A | G | 0.558 | -0.078 | 0.003 | 7.8E-139 | 231723 | A | G | 0.558 | -0.071 | 0.004 | 8.9E-94 | |
| rs10789340a | 1 | 72940273 | 321615 | A | G | 0.317 | -0.030 | 0.003 | 5.9E-20 | 231957 | A | G | 0.317 | -0.025 | 0.004 | 2.7E-12 | |
| rs11576925 | 1 | 96934086 | 233666 | C | G | 0.768 | -0.004 | 0.005 | 0.447 | 153843 | C | G | 0.768 | -0.015 | 0.005 | 0.005 | |
| rs11697842 | 20 | 16983598 | 231797 | A | G | 0.350 | 0.001 | 0.004 | 0.886 | 152996 | A | G | 0.350 | 0.003 | 0.005 | 0.580 | |
| rs12516875 | 5 | 32978655 | 220861 | A | G | 0.300 | -0.003 | 0.005 | 0.528 | 141730 | A | G | 0.300 | -0.003 | 0.005 | 0.530 | |
| rs272678 | 7 | 24137455 | 233452 | T | G | 0.408 | -0.001 | 0.004 | 0.752 | 153775 | T | G | 0.408 | 0.002 | 0.004 | 0.690 | |
| rs33988101 | 19 | 49241976 | 221526 | T | G | 0.525 | -0.009 | 0.004 | 0.019 | 141381 | T | G | 0.525 | -0.007 | 0.004 | 0.140 | |
| rs35789556 | 11 | 8564778 | 322006 | A | G | 0.800 | 0.017 | 0.004 | 5.4E-06 | 232007 | A | G | 0.800 | 0.016 | 0.004 | 9.5E-05 | |
| rs4277294 | 15 | 61827850 | 220864 | A | T | 0.100 | 0.000 | 0.007 | 1.000 | 141148 | A | T | 0.100 | 0.002 | 0.008 | 0.780 | |
| rs4580876 | 6 | 98326012 | 234011 | A | G | 0.533 | -0.009 | 0.004 | 0.013 | 153945 | A | G | 0.533 | -0.008 | 0.004 | 0.070 | |
| rs4683902 | 3 | 101134976 | 197836 | A | C | 0.008 | -0.004 | 0.018 | 0.806 | 120114 | A | C | 0.008 | -0.028 | 0.022 | 0.210 | |
| rs4886343 | 13 | 62173030 | 234018 | A | G | 0.867 | 0.003 | 0.006 | 0.544 | 153949 | A | G | 0.867 | 0.003 | 0.006 | 0.670 | |
| rs4891017 | 18 | 74097959 | 153541 | A | G | 0.375 | -0.002 | 0.005 | 0.744 | 94152 | A | G | 0.375 | -4E-04 | 0.006 | 0.950 | |
| rs57193069 | 7 | 1864444 | 229246 | A | G | 0.525 | -0.004 | 0.004 | 0.236 | 151474 | A | G | 0.525 | -0.004 | 0.004 | 0.340 | |
| rs5755961 | 22 | 36236718 | 179679 | T | G | 0.905 | -0.001 | 0.006 | 0.864 | 112487 | T | G | 0.905 | -5E-04 | 0.007 | 0.950 | |
| rs6131331 | 20 | 12378852 | 233877 | A | C | 0.158 | -0.004 | 0.005 | 0.441 | 153711 | A | C | 0.158 | -0.012 | 0.005 | 0.028 | |
| rs7218313 | 17 | 69831308 | 233942 | A | C | 0.508 | -0.006 | 0.004 | 0.123 | 153898 | A | C | 0.508 | 0.002 | 0.004 | 0.630 | |
| rs729833 | 1 | 75601145 | 178638 | T | C | 0.259 | 0.010 | 0.005 | 0.045 | 112416 | T | C | 0.259 | 0.009 | 0.006 | 0.130 | |
| rs7619139 | 3 | 25110415 | 233281 | A | T | 0.600 | 0.019 | 0.004 | 3.3E-06 | 153765 | A | T | 0.600 | 0.013 | 0.004 | 0.003 | |
| rs8106503 | 19 | 11198187 | 90251 | T | C |  | -0.015 | 0.009 | 0.075 | 80261 | T | C |  | -0.022 | 0.009 | 0.010 | |
| rs9315498 | 13 | 38099921 | 233368 | A | C | 0.467 | -0.001 | 0.004 | 0.732 | 153787 | A | C | 0.467 | -0.001 | 0.004 | 0.870 | |
| rs986527 | 11 | 31636481 | 233954 | A | G | 0.308 | -0.007 | 0.004 | 0.069 | 153931 | A | G | 0.308 | -0.004 | 0.004 | 0.330 | |
| rs9969531 | 8 | 28222586 | 233841 | C | G | 0.375 | -0.007 | 0.004 | 0.068 | 153899 | C | G | 0.375 | -0.010 | 0.004 | 0.023 | |

Abbrevations: , standard deviation change; Chr, chromosome; Pos(hg37), position at human build 37; EA, effect allele; EAF, effect allele frequency; OA, other allele; SE, standard error; SNP, Single Nucleotide Polymorphism.

Instruments listed before outlier-correction by IVW and MR-Egger Qj-statistics. Estimates are given per one standard deviation.

a SNP was removed from the analysis with BMI due to a strong association with the appropriate outcome at the genome-wide significance threshold of .

**Supplementary Table 13** Associations of Single Nucleotide Polymorphisms (SNPs) used as instruments (based on the genome-wide significance threshold of ) for relative dietary protein intake (in % of total energy intake (E%)) with anthropometric measures (outcomes).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **Body Mass Index (BMI)** | | | | | | | **Waist Circumference (WC)** | | | | | | |
| **SNP** | **Chr** | **Pos(hg37)** |  | **EA** | **OA** | **EAF** |  | **SE** | **P-value** |  | **EA** | **OA** | **EAF** |  | **SE** | **P-value** |
| rs10734012 | 10 | 34216806 | 233339 | T | C | 0.508 | -3E-04 | 0.004 | 0.937 | 153750 | T | C | 0.508 | -2E-04 | 0.004 | 0.960 |
| rs10759212 | 9 | 109932877 | 233828 | A | G | 0.517 | 0.004 | 0.004 | 0.292 | 153783 | A | G | 0.517 | 0.004 | 0.004 | 0.320 |
| rs10828186 | 10 | 21391665 | 230015 | A | C | 0.100 | 0.003 | 0.006 | 0.599 | 150184 | A | C | 0.100 | 0.008 | 0.007 | 0.240 |
| rs11073752 | 15 | 88423051 | 179163 | T | C | 0.681 | 0.002 | 0.005 | 0.640 | 112535 | T | C | 0.681 | 0.006 | 0.005 | 0.260 |
| rs13146907 | 4 | 39425248 | 233177 | A | G | 0.650 | -1E-04 | 0.004 | 0.980 | 153112 | A | G | 0.650 | 0.001 | 0.004 | 0.790 |
| rs1368285 | 5 | 146656123 | 233956 | T | G | 0.233 | 0.004 | 0.005 | 0.462 | 153937 | T | G | 0.233 | 1E-04 | 0.006 | 0.990 |
| rs1461729 | 8 | 9187242 | 233922 | A | G | 0.092 | -0.001 | 0.006 | 0.885 | 153860 | A | G | 0.092 | 0.008 | 0.007 | 0.280 |
| rs1532769 | 3 | 147090343 | 233931 | T | C | 0.425 | 0.006 | 0.004 | 0.108 | 153933 | T | C | 0.425 | 0.005 | 0.004 | 0.240 |
| rs17455688 | 13 | 66677935 | 226158 | T | C | 0.942 | -2E-04 | 0.007 | 0.979 | 146800 | T | C | 0.942 | -0.001 | 0.009 | 0.940 |
| rs1891210 | 9 | 15900348 | 308993 | T | G | 0.558 | -0.016 | 0.003 | 3.0E-07 | 222120 | T | G | 0.558 | -0.018 | 0.004 | 1.8E-07 |
| rs228751 | 17 | 42154011 | 233882 | A | G | 0.475 | -0.008 | 0.004 | 0.027 | 153913 | A | G | 0.475 | -0.006 | 0.004 | 0.150 |
| rs2624495 | 5 | 116727172 | 233985 | A | G | 0.475 | 0.001 | 0.004 | 0.746 | 153941 | A | G | 0.475 | 2E-04 | 0.004 | 0.960 |
| rs2953517 | 8 | 87332013 | 233611 | T | C | 0.325 | 0.004 | 0.004 | 0.283 | 153858 | T | C | 0.325 | -5E-04 | 0.005 | 0.920 |
| rs357537 | 9 | 98154815 | 307638 | A | G | 0.117 | -0.013 | 0.006 | 0.030 | 219479 | A | G | 0.117 | -0.002 | 0.006 | 0.740 |
| rs445551 | 2 | 79697982 | 233572 | A | G | 0.250 | -0.003 | 0.004 | 0.479 | 153821 | A | G | 0.250 | -0.004 | 0.005 | 0.370 |
| rs4708061 | 6 | 69100302 | 229711 | A | G | 0.500 | -0.004 | 0.004 | 0.368 | 150375 | A | G | 0.500 | 0.001 | 0.005 | 0.840 |
| rs4775698 | 15 | 47873477 | 233831 | T | G | 0.700 | 0.004 | 0.004 | 0.306 | 153883 | T | G | 0.700 | 0.013 | 0.005 | 0.006 |
| rs55872725a | 16 | 53816838 | 321909 | T | C | 0.450 | 0.078 | 0.003 | 6E-144 | 231882 | T | C | 0.450 | 0.071 | 0.003 | 3.5E-95 |
| rs6024454 | 20 | 54393433 | 233955 | T | C | 0.250 | -0.016 | 0.005 | 0.001 | 153789 | T | C | 0.250 | -0.012 | 0.005 | 0.027 |
| rs6041160 | 20 | 12169905 | 72856 | T | C |  | 0.009 | 0.008 | 0.294 | 53049 | T | C |  | 0.010 | 0.009 | 0.270 |
| rs61928280 | 12 | 50824232 | 232642 | A | C | 0.808 | 0.001 | 0.005 | 0.811 | 153436 | A | C | 0.808 | -0.001 | 0.005 | 0.910 |
| rs780094 | 2 | 27741237 | 322044 | T | C | 0.383 | -0.012 | 0.003 | 2.0E-04 | 232032 | T | C | 0.383 | -0.009 | 0.004 | 0.015 |
| rs79813431 | 11 | 41173522 | 232441 | C | G | 0.958 | 0.011 | 0.011 | 0.317 | 153047 | C | G | 0.958 | 0.004 | 0.013 | 0.780 |
| rs838133 | 19 | 49259529 | 223372 | A | G | 0.492 | -0.010 | 0.004 | 0.022 | 143054 | A | G | 0.492 | -0.012 | 0.005 | 0.010 |

Abbrevations: , standard deviation change; Chr, chromosome; Pos(hg37), position at human build 37; EA, effect allele; EAF, effect allele frequency; OA, other allele; SE, standard error; SNP, Single Nucleotide Polymorphism.

Instruments listed before outlier-correction by IVW and MR-Egger Qj-statistics. Estimates are given per one standard deviation.

a SNP was removed from the analysis with BMI due to a strong association with the appropriate outcome at the genome-wide significance threshold of .

**Supplementary Table 14** Associations of Single Nucleotide Polymorphisms (SNPs) used as instruments (based on the genome-wide significance threshold of ) for body mass index with dietary composition (in % of total energy intake (E%)) (outcomes).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  | **Relative Carbohydrate Intake** | | | | | | **Relative Fat Intake** | | | | | | **Relative Protein Intake** | | | | | |
| **SNP** | **Chr** | **Pos(hg37)** | **n** | **EA** | **OA** | **EAF** |  | **SE** | **P-value** | **EA** | **OA** | **EAF** |  | **SE** | **P-value** | **EA** | **OA** | **EAF** |  | **SE** | **P-value** |
| rs1000940 | 17 | 5283252 | 264000 | G | A | 0.318 | -0.009 | 0.003 | 0.002 | G | A | 0.318 | 0.006 | 0.003 | 0.034 | G | A | 0.318 | 0.002 | 0.003 | 0.493 |
| rs10132280 | 14 | 25928179 | 264000 | A | C | 0.312 | -0.006 | 0.003 | 0.045 | A | C | 0.312 | 0.006 | 0.003 | 0.051 | A | C | 0.312 | -0.001 | 0.003 | 0.833 |
| rs1016287 | 2 | 59305625 | 205000 | C | T | 0.709 | -0.009 | 0.003 | 0.010 | C | T | 0.709 | 0.001 | 0.003 | 0.728 | C | T | 0.709 | 0.003 | 0.003 | 0.454 |
| rs10182181 | 2 | 25150296 | 264000 | G | A | 0.477 | 0.004 | 0.003 | 0.124 | G | A | 0.477 | -0.010 | 0.003 | 4.7E-07 | G | A | 0.477 | 0.003 | 0.003 | 0.329 |
| rs10733682 | 9 | 129460914 | 248000 | G | A | 0.519 | 0.004 | 0.003 | 0.120 | G | A | 0.519 | -0.003 | 0.003 | 0.322 | G | A | 0.519 | -0.007 | 0.003 | 0.018 |
| rs10938397 | 4 | 45182527 | 264000 | G | A | 0.426 | 0.003 | 0.003 | 0.360 | G | A | 0.426 | 0.004 | 0.003 | 0.195 | G | A | 0.426 | 0.009 | 0.003 | 0.002 |
| rs10968576 | 9 | 28414339 | 264000 | G | A | 0.288 | 0.001 | 0.003 | 0.730 | G | A | 0.288 | 0.003 | 0.003 | 0.298 | G | A | 0.288 | 0.008 | 0.003 | 0.009 |
| rs11030104 | 11 | 27684517 | 264000 | G | A | 0.220 | 0.010 | 0.003 | 0.002 | G | A | 0.220 | 0.001 | 0.003 | 0.874 | G | A | 0.220 | -0.002 | 0.003 | 0.597 |
| rs11057405 | 12 | 122781897 | 258000 | A | G | 0.079 | 0.012 | 0.005 | 0.010 | A | G | 0.079 | -0.005 | 0.005 | 0.302 | A | G | 0.079 | -0.011 | 0.005 | 0.017 |
| rs11165643 | 1 | 96924097 | 264000 | T | C | 0.570 | -0.008 | 0.003 | 0.006 | T | C | 0.570 | 0.006 | 0.003 | 0.024 | T | C | 0.570 | 0.009 | 0.003 | 0.001 |
| rs1167827 | 7 | 75163169 | 258000 | G | A | 0.552 | -0.003 | 0.003 | 0.232 | G | A | 0.552 | 0.000 | 0.003 | 0.969 | G | A | 0.552 | 0.006 | 0.003 | 0.021 |
| rs11727676 | 4 | 145659064 | 229000 | C | T | 0.082 | -0.002 | 0.005 | 0.697 | C | T | 0.082 | -0.004 | 0.005 | 0.373 | C | T | 0.082 | -0.001 | 0.005 | 0.842 |
| rs12286929 | 11 | 115022404 | 264000 | G | A | 0.514 | -0.003 | 0.003 | 0.252 | G | A | 0.514 | 0.005 | 0.003 | 0.073 | G | A | 0.514 | 0.001 | 0.003 | 0.643 |
| rs12429545 | 13 | 54102206 | 258000 | A | G | 0.131 | 0.000 | 0.004 | 0.962 | A | G | 0.131 | 0.004 | 0.004 | 0.378 | A | G | 0.131 | -0.001 | 0.004 | 0.767 |
| rs12940622 | 17 | 78615571 | 264000 | A | G | 0.432 | -0.001 | 0.003 | 0.684 | A | G | 0.432 | 0.001 | 0.003 | 0.598 | A | G | 0.432 | -0.006 | 0.003 | 0.026 |
| rs12986742 | 2 | 58975143 | 264000 | C | T | 0.475 | -0.001 | 0.003 | 0.661 | C | T | 0.475 | 0.003 | 0.003 | 0.348 | C | T | 0.475 | 0.004 | 0.003 | 0.158 |
| rs13021737 | 2 | 632348 | 264000 | G | A | 0.830 | 0.005 | 0.004 | 0.141 | G | A | 0.830 | -0.010 | 0.004 | 0.005 | G | A | 0.830 | 0.004 | 0.004 | 0.337 |
| rs13078960 | 3 | 85807590 | 264000 | G | T | 0.198 | -0.007 | 0.003 | 0.039 | G | T | 0.198 | 0.005 | 0.003 | 0.111 | G | T | 0.198 | -0.003 | 0.003 | 0.319 |
| rs13107325 | 4 | 103188709 | 258000 | T | C | 0.065 | 0.018 | 0.005 | 0.001 | T | C | 0.065 | -0.005 | 0.005 | 0.336 | T | C | 0.065 | 0.022 | 0.005 | 3.6E-05 |
| rs13191362 | 6 | 163033350 | 264000 | G | A | 0.117 | 0.003 | 0.004 | 0.500 | G | A | 0.117 | -0.003 | 0.004 | 0.426 | G | A | 0.117 | 0.000 | 0.004 | 0.938 |
| rs1516725 | 3 | 185824004 | 264000 | C | T | 0.878 | -0.004 | 0.004 | 0.265 | C | T | 0.878 | 0.008 | 0.004 | 0.039 | C | T | 0.878 | 0.006 | 0.004 | 0.148 |
| rs1528435 | 2 | 181550962 | 264000 | T | C | 0.634 | -0.002 | 0.003 | 0.521 | T | C | 0.634 | -0.002 | 0.003 | 0.594 | T | C | 0.634 | 0.000 | 0.003 | 0.908 |
| rs16851483 | 3 | 141275436 | 264000 | T | G | 0.061 | 0.002 | 0.006 | 0.778 | T | G | 0.061 | 0.009 | 0.006 | 0.105 | T | G | 0.061 | 0.010 | 0.006 | 0.077 |
| rs16951275 | 15 | 68077168 | 264000 | C | T | 0.230 | 0.008 | 0.003 | 0.018 | C | T | 0.230 | -0.002 | 0.003 | 0.518 | C | T | 0.230 | -0.007 | 0.003 | 0.032 |
| rs17001654 | 4 | 77129568 | 264000 | G | C | 0.152 | -0.003 | 0.004 | 0.390 | G | C | 0.152 | 0.005 | 0.004 | 0.233 | G | C | 0.152 | 0.000 | 0.004 | 0.972 |
| rs17024393 | 1 | 110154688 | 231000 | C | T | 0.029 | 0.000 | 0.009 | 0.969 | C | T | 0.029 | -0.003 | 0.009 | 0.758 | C | T | 0.029 | -0.004 | 0.009 | 0.649 |
| rs17066856 | 18 | 58049656 | 264000 | C | T | 0.104 | -0.003 | 0.005 | 0.492 | C | T | 0.104 | 0.001 | 0.005 | 0.777 | C | T | 0.104 | -0.002 | 0.005 | 0.619 |
| rs17094222 | 10 | 102395440 | 256000 | C | T | 0.209 | -0.002 | 0.003 | 0.508 | C | T | 0.209 | 0.004 | 0.003 | 0.198 | C | T | 0.209 | -0.001 | 0.003 | 0.771 |
| rs17405819 | 8 | 76806584 | 264000 | C | T | 0.291 | 0.001 | 0.003 | 0.760 | C | T | 0.291 | 0.000 | 0.003 | 0.997 | C | T | 0.291 | -0.001 | 0.003 | 0.672 |
| rs17724992 | 19 | 18454825 | 264000 | G | A | 0.254 | 0.005 | 0.003 | 0.083 | G | A | 0.254 | -0.003 | 0.003 | 0.348 | G | A | 0.254 | -0.006 | 0.003 | 0.069 |
| rs1808579 | 18 | 21104888 | 264000 | T | C | 0.461 | 0.000 | 0.003 | 0.884 | T | C | 0.461 | 0.001 | 0.003 | 0.656 | T | C | 0.461 | -0.005 | 0.003 | 0.088 |
| rs1928295 | 9 | 120378483 | 264000 | C | T | 0.434 | -0.001 | 0.003 | 0.816 | C | T | 0.434 | 0.002 | 0.003 | 0.522 | C | T | 0.434 | -0.006 | 0.003 | 0.027 |
| rs2033529 | 6 | 40348653 | 205000 | G | A | 0.278 | -0.004 | 0.003 | 0.285 | G | A | 0.278 | -0.002 | 0.003 | 0.470 | G | A | 0.278 | 0.006 | 0.003 | 0.081 |
| rs2033732 | 8 | 85079709 | 264000 | C | T | 0.753 | 0.002 | 0.003 | 0.497 | C | T | 0.753 | -0.001 | 0.003 | 0.728 | C | T | 0.753 | 0.002 | 0.003 | 0.450 |
| rs205262 | 6 | 34563164 | 264000 | G | A | 0.286 | -0.005 | 0.003 | 0.110 | G | A | 0.286 | -0.001 | 0.003 | 0.742 | G | A | 0.286 | -0.002 | 0.003 | 0.585 |
| rs2112347 | 5 | 75015242 | 264000 | G | T | 0.375 | 0.002 | 0.003 | 0.584 | G | T | 0.375 | -0.007 | 0.003 | 0.011 | G | T | 0.375 | 0.000 | 0.003 | 0.876 |
| rs2121279 | 2 | 143043285 | 264000 | T | C | 0.130 | -0.001 | 0.004 | 0.787 | T | C | 0.130 | 0.004 | 0.004 | 0.388 | T | C | 0.130 | 0.010 | 0.004 | 0.014 |
| rs2176598 | 11 | 43864278 | 264000 | C | T | 0.739 | 0.001 | 0.003 | 0.677 | C | T | 0.739 | 0.003 | 0.003 | 0.312 | C | T | 0.739 | -0.007 | 0.003 | 0.026 |
| rs2207139 | 6 | 50845490 | 264000 | G | A | 0.162 | -0.004 | 0.004 | 0.241 | G | A | 0.162 | 0.002 | 0.004 | 0.514 | G | A | 0.162 | -0.001 | 0.004 | 0.798 |
| rs2245368 | 7 | 76608143 | 216000 | T | C | 0.807 | 0.005 | 0.004 | 0.217 | T | C | 0.807 | 0.004 | 0.004 | 0.340 | T | C | 0.807 | -0.009 | 0.004 | 0.028 |
| rs2287019 | 19 | 46202172 | 264000 | T | C | 0.189 | 0.013 | 0.004 | 2.9E-04 | T | C | 0.189 | -0.015 | 0.004 | 1.5E-05 | T | C | 0.189 | 0.005 | 0.004 | 0.144 |
| rs2365389 | 3 | 61236462 | 264000 | T | C | 0.426 | 0.000 | 0.003 | 0.890 | T | C | 0.426 | 0.000 | 0.003 | 0.908 | T | C | 0.426 | -0.005 | 0.003 | 0.073 |
| rs2820292 | 1 | 201784287 | 264000 | C | A | 0.541 | 0.003 | 0.003 | 0.259 | C | A | 0.541 | -0.003 | 0.003 | 0.294 | C | A | 0.541 | 0.003 | 0.003 | 0.280 |
| rs29941 | 19 | 34309532 | 264000 | G | A | 0.660 | -0.001 | 0.003 | 0.752 | G | A | 0.660 | 0.001 | 0.003 | 0.636 | G | A | 0.660 | 0.002 | 0.003 | 0.471 |
| rs3101336 | 1 | 72751185 | 264000 | C | T | 0.628 | 0.010 | 0.003 | 2.9E-04 | C | T | 0.628 | -0.012 | 0.003 | 1.8E-05 | C | T | 0.628 | 0.001 | 0.003 | 0.815 |
| rs3736485 | 15 | 51748610 | 264000 | G | A | 0.521 | 0.001 | 0.003 | 0.601 | G | A | 0.521 | -0.001 | 0.003 | 0.822 | G | A | 0.521 | -0.005 | 0.003 | 0.099 |
| rs3817334 | 11 | 47650993 | 264000 | T | C | 0.396 | 0.010 | 0.003 | 4.7E-04 | T | C | 0.396 | -0.001 | 0.003 | 0.642 | T | C | 0.396 | 0.011 | 0.003 | 4.3E-05 |
| rs3849570 | 3 | 81792112 | 264000 | A | C | 0.348 | -0.006 | 0.003 | 0.054 | A | C | 0.348 | 0.004 | 0.003 | 0.164 | A | C | 0.348 | 0.006 | 0.003 | 0.034 |
| rs3888190 | 16 | 28889486 | 258000 | A | C | 0.381 | 0.005 | 0.003 | 0.080 | A | C | 0.381 | -0.001 | 0.003 | 0.832 | A | C | 0.381 | 0.006 | 0.003 | 0.036 |
| rs4256980 | 11 | 8673939 | 264000 | G | C | 0.621 | -0.001 | 0.003 | 0.613 | G | C | 0.621 | 0.008 | 0.003 | 0.008 | G | C | 0.621 | 0.006 | 0.003 | 0.041 |
| rs4740619 | 9 | 15634326 | 264000 | C | T | 0.473 | 0.014 | 0.003 | 4.7E-07 | C | T | 0.473 | -0.006 | 0.003 | 0.039 | C | T | 0.473 | -0.011 | 0.003 | 6.4E-05 |
| rs4889606 | 16 | 31011183 | 264000 | G | A | 0.403 | -0.002 | 0.003 | 0.415 | G | A | 0.403 | 0.000 | 0.003 | 0.990 | G | A | 0.403 | 0.001 | 0.003 | 0.765 |
| rs543874 | 1 | 177889480 | 264000 | G | A | 0.179 | 0.001 | 0.003 | 0.797 | G | A | 0.179 | -0.002 | 0.003 | 0.519 | G | A | 0.179 | 0.005 | 0.003 | 0.141 |
| rs6477694 | 9 | 111932342 | 264000 | T | C | 0.646 | -0.003 | 0.003 | 0.363 | T | C | 0.646 | 0.000 | 0.003 | 0.861 | T | C | 0.646 | -0.001 | 0.003 | 0.782 |
| rs6567160 | 18 | 57829135 | 264000 | C | T | 0.225 | 0.001 | 0.003 | 0.830 | C | T | 0.225 | 0.001 | 0.003 | 0.681 | C | T | 0.225 | 0.008 | 0.003 | 0.015 |
| rs657452 | 1 | 49589847 | 264000 | G | A | 0.597 | -0.001 | 0.003 | 0.667 | G | A | 0.597 | 0.000 | 0.003 | 0.919 | G | A | 0.597 | -0.001 | 0.003 | 0.669 |
| rs6656785 | 1 | 75005776 | 264000 | G | A | 0.381 | 0.000 | 0.003 | 0.922 | G | A | 0.381 | -0.001 | 0.003 | 0.832 | G | A | 0.381 | -0.001 | 0.003 | 0.763 |
| rs6804842a | 3 | 25106437 | 264000 | G | A | 0.570 | -0.019 | 0.003 | 5.4E-12 | G | A | 0.570 | 0.015 | 0.003 | 1.7E-07 | G | A | 0.570 | 0.017 | 0.003 | 9.4E-10 |
| rs7138803 | 12 | 50247468 | 264000 | A | G | 0.360 | 0.009 | 0.003 | 0.002 | A | G | 0.360 | -0.003 | 0.003 | 0.287 | A | G | 0.360 | 0.001 | 0.003 | 0.756 |
| rs7141420 | 14 | 79899454 | 264000 | T | C | 0.530 | 0.006 | 0.003 | 0.019 | T | C | 0.530 | 0.001 | 0.003 | 0.796 | T | C | 0.530 | -0.003 | 0.003 | 0.259 |
| rs758747 | 16 | 3627358 | 252000 | T | C | 0.282 | 0.000 | 0.003 | 0.894 | T | C | 0.282 | -0.002 | 0.003 | 0.564 | T | C | 0.282 | 0.003 | 0.003 | 0.389 |
| rs7599312 | 2 | 213413231 | 256000 | A | G | 0.262 | 0.001 | 0.003 | 0.738 | A | G | 0.262 | -0.001 | 0.003 | 0.871 | A | G | 0.262 | -0.003 | 0.003 | 0.380 |
| rs7899106 | 10 | 87410904 | 231000 | G | A | 0.051 | -0.009 | 0.007 | 0.167 | G | A | 0.051 | -0.007 | 0.007 | 0.326 | G | A | 0.051 | 0.013 | 0.007 | 0.047 |
| rs7903146 | 10 | 114758349 | 264000 | T | C | 0.294 | -0.003 | 0.003 | 0.363 | T | C | 0.294 | -0.003 | 0.003 | 0.365 | T | C | 0.294 | 0.000 | 0.003 | 0.978 |
| rs879620 | 16 | 4015729 | 250000 | T | C | 0.585 | -0.006 | 0.003 | 0.040 | T | C | 0.585 | 0.000 | 0.003 | 0.995 | T | C | 0.585 | 0.007 | 0.003 | 0.012 |
| rs9400239 | 6 | 108977663 | 264000 | C | T | 0.663 | -0.006 | 0.003 | 0.059 | C | T | 0.663 | 0.002 | 0.003 | 0.556 | C | T | 0.663 | -0.001 | 0.003 | 0.834 |
| rs9579083 | 13 | 28017270 | 205000 | C | G | 0.178 | 0.009 | 0.004 | 0.031 | C | G | 0.178 | -0.004 | 0.004 | 0.307 | C | G | 0.178 | -0.001 | 0.004 | 0.776 |
| rs9926784 | 16 | 19941968 | 264000 | C | T | 0.200 | -0.001 | 0.004 | 0.783 | C | T | 0.200 | 0.002 | 0.004 | 0.513 | C | T | 0.200 | -0.001 | 0.004 | 0.751 |

Abbrevations: , standard deviation change; Chr, chromosome; Pos(hg37), position at human build 37; EA, effect allele; EAF, effect allele frequency; OA, other allele; SE, standard error; SNP, Single Nucleotide Polymorphism.

Instruments listed before outlier-correction by IVW and MR-Egger Qj-statistics. Estimates are given per one standard deviation.

a SNP was removed from the analysis with BMI due to a strong association with the appropriate outcome at the genome-wide significance threshold of .

**Supplementary Table 15** Associations of Single Nucleotide Polymorphisms (SNPs) used as instruments (based on the genome-wide significance threshold of ) for waist circumference with dietary composition (in % of total energy intake (E%)) (outcomes).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  | **Relative Carbohydrate Intake** | | | | | | **Relative Fat Intake** | | | | | | **Relative Protein Intake** | | | | | |
| **SNP** | **Chr** | **Pos(hg37)** | **n** | **EA** | **OA** | **EAF** |  | **SE** | **P-value** | **EA** | **OA** | **EAF** |  | **SE** | **P-value** | **EA** | **OA** | **EAF** |  | **SE** | **P-value** |
| rs10132280 | 14 | 25928179 | 264000 | A | C | 0.312 | -0.006 | 0.003 | 0.045 | A | C | 0.312 | 0.006 | 0.003 | 0.051 | A | C | 0.312 | -0.001 | 0.003 | 0.833 |
| rs10767658 | 11 | 27672252 | 264000 | G | C | 0.714 | 0.004 | 0.003 | 0.229 | G | C | 0.714 | -0.004 | 0.003 | 0.160 | G | C | 0.714 | 0.001 | 0.003 | 0.714 |
| rs10840100 | 11 | 8669437 | 264000 | G | A | 0.623 | -0.001 | 0.003 | 0.635 | G | A | 0.623 | 0.008 | 0.003 | 0.008 | G | A | 0.623 | 0.006 | 0.003 | 0.035 |
| rs10938397 | 4 | 45182527 | 264000 | G | A | 0.426 | 0.003 | 0.003 | 0.360 | G | A | 0.426 | 0.004 | 0.003 | 0.195 | G | A | 0.426 | 0.009 | 0.003 | 0.002 |
| rs10968576 | 9 | 28414339 | 264000 | G | A | 0.288 | 0.001 | 0.003 | 0.730 | G | A | 0.288 | 0.003 | 0.003 | 0.298 | G | A | 0.288 | 0.008 | 0.003 | 0.009 |
| rs11165623 | 1 | 96893000 | 264000 | A | G | 0.488 | -0.005 | 0.003 | 0.085 | A | G | 0.488 | 0.006 | 0.003 | 0.027 | A | G | 0.488 | 0.006 | 0.003 | 0.019 |
| rs12429545 | 13 | 54102206 | 258000 | A | G | 0.131 | 0.000 | 0.004 | 0.962 | A | G | 0.131 | 0.004 | 0.004 | 0.378 | A | G | 0.131 | -0.001 | 0.004 | 0.767 |
| rs1516725 | 3 | 185824004 | 264000 | C | T | 0.878 | -0.004 | 0.004 | 0.265 | C | T | 0.878 | 0.008 | 0.004 | 0.039 | C | T | 0.878 | 0.006 | 0.004 | 0.148 |
| rs16894959 | 6 | 34825662 | 264000 | C | T | 0.151 | -0.003 | 0.004 | 0.466 | C | T | 0.151 | -0.005 | 0.004 | 0.243 | C | T | 0.151 | -0.003 | 0.004 | 0.486 |
| rs16996700 | 20 | 50981945 | 264000 | C | T | 0.276 | 0.004 | 0.003 | 0.160 | C | T | 0.276 | -0.005 | 0.003 | 0.074 | C | T | 0.276 | 0.003 | 0.003 | 0.308 |
| rs17066856 | 18 | 58049656 | 264000 | C | T | 0.104 | -0.003 | 0.005 | 0.492 | C | T | 0.104 | 0.001 | 0.005 | 0.777 | C | T | 0.104 | -0.002 | 0.005 | 0.619 |
| rs17381664 | 1 | 78048331 | 264000 | C | T | 0.347 | 0.001 | 0.003 | 0.619 | C | T | 0.347 | -0.004 | 0.003 | 0.204 | C | T | 0.347 | 0.000 | 0.003 | 0.991 |
| rs2033529 | 6 | 40348653 | 205000 | G | A | 0.278 | -0.004 | 0.003 | 0.285 | G | A | 0.278 | -0.002 | 0.003 | 0.470 | G | A | 0.278 | 0.006 | 0.003 | 0.081 |
| rs2112347 | 5 | 75015242 | 264000 | G | T | 0.375 | 0.002 | 0.003 | 0.584 | G | T | 0.375 | -0.007 | 0.003 | 0.011 | G | T | 0.375 | 0.000 | 0.003 | 0.876 |
| rs2287019 | 19 | 46202172 | 264000 | T | C | 0.189 | 0.013 | 0.004 | 2.9E-04 | T | C | 0.189 | -0.015 | 0.004 | 1.5E-05 | T | C | 0.189 | 0.005 | 0.004 | 0.144 |
| rs2293576 | 11 | 47434986 | 264000 | A | G | 0.332 | -0.003 | 0.003 | 0.375 | A | G | 0.332 | -0.006 | 0.003 | 0.051 | A | G | 0.332 | -0.004 | 0.003 | 0.135 |
| rs2325036 | 3 | 85819412 | 264000 | C | A | 0.390 | 0.005 | 0.003 | 0.078 | C | A | 0.390 | -0.004 | 0.003 | 0.170 | C | A | 0.390 | 0.004 | 0.003 | 0.176 |
| rs2489623 | 6 | 127455821 | 264000 | C | A | 0.523 | 0.003 | 0.003 | 0.218 | C | A | 0.523 | 0.000 | 0.003 | 0.921 | C | A | 0.523 | -0.002 | 0.003 | 0.399 |
| rs2531992 | 16 | 4021734 | 264000 | G | A | 0.845 | -0.008 | 0.004 | 0.033 | G | A | 0.845 | 0.004 | 0.004 | 0.249 | G | A | 0.845 | 0.008 | 0.004 | 0.029 |
| rs2820292 | 1 | 201784287 | 264000 | C | A | 0.541 | 0.003 | 0.003 | 0.259 | C | A | 0.541 | -0.003 | 0.003 | 0.294 | C | A | 0.541 | 0.003 | 0.003 | 0.280 |
| rs3127553 | 1 | 49438005 | 264000 | A | G | 0.630 | -0.002 | 0.003 | 0.423 | A | G | 0.630 | 0.001 | 0.003 | 0.792 | A | G | 0.630 | -0.002 | 0.003 | 0.405 |
| rs3849570 | 3 | 81792112 | 264000 | A | C | 0.348 | -0.006 | 0.003 | 0.054 | A | C | 0.348 | 0.004 | 0.003 | 0.164 | A | C | 0.348 | 0.006 | 0.003 | 0.034 |
| rs4776970 | 15 | 68080886 | 264000 | T | A | 0.371 | 0.006 | 0.003 | 0.054 | T | A | 0.371 | -0.003 | 0.003 | 0.284 | T | A | 0.371 | -0.004 | 0.003 | 0.117 |
| rs6163 | 10 | 104596924 | 264000 | A | C | 0.384 | -0.007 | 0.003 | 0.019 | A | C | 0.384 | 0.006 | 0.003 | 0.025 | A | C | 0.384 | -0.002 | 0.003 | 0.533 |
| rs633715 | 1 | 177852580 | 264000 | C | T | 0.184 | 0.000 | 0.003 | 0.895 | C | T | 0.184 | -0.001 | 0.003 | 0.716 | C | T | 0.184 | 0.006 | 0.003 | 0.085 |
| rs6440003 | 3 | 141094209 | 264000 | A | G | 0.433 | 0.003 | 0.003 | 0.361 | A | G | 0.433 | -0.001 | 0.003 | 0.745 | A | G | 0.433 | -0.001 | 0.003 | 0.622 |
| rs6545714 | 2 | 59307725 | 264000 | A | G | 0.608 | -0.002 | 0.003 | 0.547 | A | G | 0.608 | -0.002 | 0.003 | 0.552 | A | G | 0.608 | -0.004 | 0.003 | 0.133 |
| rs6567160 | 18 | 57829135 | 264000 | C | T | 0.225 | 0.001 | 0.003 | 0.830 | C | T | 0.225 | 0.001 | 0.003 | 0.681 | C | T | 0.225 | 0.008 | 0.003 | 0.015 |
| rs6755502 | 2 | 635721 | 264000 | C | T | 0.830 | 0.005 | 0.004 | 0.142 | C | T | 0.830 | -0.010 | 0.004 | 0.005 | C | T | 0.830 | 0.003 | 0.004 | 0.359 |
| rs7138803 | 12 | 50247468 | 264000 | A | G | 0.360 | 0.009 | 0.003 | 0.002 | A | G | 0.360 | -0.003 | 0.003 | 0.287 | A | G | 0.360 | 0.001 | 0.003 | 0.756 |
| rs7144011 | 14 | 79940383 | 264000 | T | G | 0.201 | 0.008 | 0.003 | 0.012 | T | G | 0.201 | -0.001 | 0.003 | 0.692 | T | G | 0.201 | 0.002 | 0.003 | 0.567 |
| rs7239883 | 18 | 40147671 | 264000 | A | G | 0.607 | 0.000 | 0.003 | 0.984 | A | G | 0.607 | 0.001 | 0.003 | 0.707 | A | G | 0.607 | -0.005 | 0.003 | 0.053 |
| rs749671 | 16 | 31088347 | 264000 | A | G | 0.396 | -0.002 | 0.003 | 0.421 | A | G | 0.396 | 0.000 | 0.003 | 0.880 | A | G | 0.396 | 0.003 | 0.003 | 0.366 |
| rs7498665 | 16 | 28883241 | 258000 | G | A | 0.381 | 0.005 | 0.003 | 0.080 | G | A | 0.381 | 0.000 | 0.003 | 0.869 | G | A | 0.381 | 0.006 | 0.003 | 0.027 |
| rs7531118 | 1 | 72837239 | 244000 | C | T | 0.525 | 0.011 | 0.003 | 2.5E-04 | C | T | 0.525 | -0.014 | 0.003 | 9.3E-07 | C | T | 0.525 | 0.001 | 0.003 | 0.788 |
| rs7550711 | 1 | 110082886 | 231000 | T | C | 0.027 | -0.001 | 0.009 | 0.927 | T | C | 0.027 | -0.003 | 0.009 | 0.758 | T | C | 0.027 | -0.004 | 0.009 | 0.683 |
| rs7903146 | 10 | 114758349 | 264000 | T | C | 0.294 | -0.003 | 0.003 | 0.363 | T | C | 0.294 | -0.003 | 0.003 | 0.365 | T | C | 0.294 | 0.000 | 0.003 | 0.978 |
| rs806794 | 6 | 26200677 | 264000 | G | A | 0.321 | 0.005 | 0.003 | 0.089 | G | A | 0.321 | -0.006 | 0.003 | 0.055 | G | A | 0.321 | 0.000 | 0.003 | 0.871 |
| rs929641 | 2 | 58792377 | 264000 | G | A | 0.427 | 0.001 | 0.003 | 0.597 | G | A | 0.427 | -0.004 | 0.003 | 0.194 | G | A | 0.427 | 0.003 | 0.003 | 0.302 |
| rs9400239 | 6 | 108977663 | 264000 | C | T | 0.663 | -0.006 | 0.003 | 0.059 | C | T | 0.663 | 0.002 | 0.003 | 0.556 | C | T | 0.663 | -0.001 | 0.003 | 0.834 |
| rs943005 | 6 | 50865820 | 264000 | T | C | 0.162 | -0.004 | 0.004 | 0.242 | T | C | 0.162 | 0.002 | 0.004 | 0.505 | T | C | 0.162 | -0.001 | 0.004 | 0.815 |

Abbrevations: , standard deviation change; Chr, chromosome; Pos(hg37), position at human build 37; EA, effect allele; EAF, effect allele frequency; OA, other allele; SE, standard error; SNP, Single Nucleotide Polymorphism;.

Instruments listed before outlier-correction by IVW and MR-Egger Qj-statistics. Estimates are given per one standard deviation.

**Supplementary Table 16** Characteristics of independent Single Nucleotide Polymorphisms (SNPs) extracted as instrumental variables for the intake of fat and protein in % of total energy intake (E%) in the two-sample Mendelian randomization sensitivity analyses with the relaxed threshold of .

|  |  |  |
| --- | --- | --- |
|  | **Fat intake (E%)** | **Protein intake (E%)** |
| Sample size | 268,922 | 268,922 |
| Genome-wide significance threshold |  |  |
| Extracted SNPs (not in LD) | 36 | 40 |
| Instruments (in sensitivity analysis) | 24 (21) | 24 (21) |
| Explained variance by instruments | 0.27 % | 0.30 % |
| F-statistic, mean (min; max) | 28.34 (20.88; 113.47) | 31.2 (21.06; 111.75) |

Abbrevations: LD, Linkage Disequilibrium, (E%), % of total energy intake.

Extraction of SNPs based on LD cut-off . Within sensitivity analyses, SNPs associated with potential confounding factors of the exposure-outcome association were excluded.

**Supplementary Table 17** Results of the MR-PRESSO global and Egger-intercept tests for detecting horizontal and directional pleiotropy as well as between SNP-heterogeneity based on final models of the iterative radial regression framework investigating associations between macronutrient composition (in % of total energy intake) and anthropometric measures.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Exposure** | **Outcome** | **MR-PRESSO RSSobs** | **PPRESSO** | **Radial MR-Egger-intercept** | **SE** | **PEgger** | **Cochran's Q** | **df** | **PQ** | **Rücker's Q'** | **PQ'** | **Q-Q'** | **PQ-Q'** | **Q'/Q** | **Suggested method** |
| COH intake | BMI | 24.933 | 0.041 | 0.167 | 2.852 | 0.955 | 15.710 | 8 | 0.047 | 14.711 | 0.065 | 1.000 | 0.317 | 0.936 | IVW (RE) |
| COH intake | WC | 19.203 | 0.120 | 0.689 | 2.307 | 0.773 | 14.094 | 9 | 0.119 | 12.899 | 0.167 | 1.195 | 0.274 | 0.915 |  |
| Fat intake | BMI | 18.475 | 0.513 | 1.167 | 1.992 | 0.566 | 16.248 | 17 | 0.506 | 15.910 | 0.530 | 0.338 | 0.561 | 0.979 |  |
| Fat intake | WC | 33.167 | 0.048 | -2.357 | 2.545 | 0.367 | 29.203 | 18 | 0.046 | 19.340 | 0.371 | 9.863 | 0.002 | 0.662 | MR-Egger (FE) |
| Protein intake | BMI | 22.844 | 0.377 | -0.073 | 0.861 | 0.933 | 20.065 | 19 | 0.391 | 20.006 | 0.394 | 0.059 | 0.809 | 0.997 |  |
| Protein intake | WC | 17.105 | 0.714 | -0.158 | 0.727 | 0.830 | 14.689 | 19 | 0.742 | 14.555 | 0.750 | 0.133 | 0.715 | 0.991 |  |
| BMI | COH intake | 80.087 | 0.033 | -1.129 | 0.505 | 0.029 | 77.079 | 56 | 0.032 | 69.457 | 0.107 | 7.622 | 0.006 | 0.901 | MR-Egger (FE) |
| BMI | Fat intake | 67.304 | 0.376 | 0.069 | 0.486 | 0.888 | 65.087 | 62 | 0.370 | 65.114 | 0.369 | -0.026 | 1.000 | 1.000 |  |
| BMI | Protein intake | 82.374 | 0.075 | 0.680 | 0.484 | 0.165 | 78.622 | 62 | 0.076 | 77.275 | 0.091 | 1.347 | 0.246 | 0.983 |  |
| WC | COH intake | 58.841 | 0.017 | -1.524 | 0.790 | 0.062 | 55.716 | 36 | 0.019 | 48.497 | 0.080 | 7.219 | 0.007 | 0.870 | MR-Egger (FE) |
| WC | Fat intake | 55.528 | 0.047 | 0.886 | 0.867 | 0.313 | 52.591 | 37 | 0.046 | 51.323 | 0.059 | 1.268 | 0.260 | 0.976 | IVW (RE) |
| WC | Protein intake | 62.639 | 0.025 | -0.717 | 0.798 | 0.374 | 59.026 | 40 | 0.027 | 56.178 | 0.046 | 2.848 | 0.091 | 0.952 | IVW (RE) |

Abbrevations: COH, carbohydrate; BMI, Body Mass Index; df, degrees of freedom; MR-PRESSO RSSobs, observed Residual Sum of Squares of the Mendelian Randomization Pleiotropy RESidual Sum and Outlier method; SE, standard error; WC, Waist Circumference.

**Supplementary Table 18** Influential Single Nucleotide Polymorphisms (SNPs) identified and excluded by an iterative approach calculating SNP-specific Qj-statistics in the radial inverse-variance weighted as well as MR-Egger methods for the impact of relative dietary carbohydrate intake (in % of total energy intake (E%)) on anthropometric measures.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **SNP** |  |  |  |  | **Iteration** |
| **Body Mass Index** | | | | | | |
| rs7190396 | 202.717 | 3.2E-45 | 35.001 | 8.3E-06 | 1 |
| rs10206338 | 7.780 | 0.005 |  |  | 1 |
| rs838144 | 7.920 | 0.005 |  |  | 1 |
| rs36123991 | 8.204 | 0.004 | 6.898 | 0.009 | 2 |
| **Waist Circumference** | | | | | | |
| rs7190396 | 160.804 | 7.6E-37 | 36.848 | 1.3E-09 | 1 |
| rs36123991 | 12.924 | 3.2E-04 |  |  | 1 |

Abbrevations: SNP, Single Nucleotide Polymorphisms.

**Supplementary Table 19** Influential Single Nucleotide Polymorphisms (SNPs) identified and excluded by an iterative approach calculating SNP-specific Qj-statistics in the radial inverse-variance weighted as well as MR-Egger methods for the impact of relative dietary fat intake (in % of total energy intake (E%)) on anthropometric measures.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **SNP** |  |  |  |  | **Iteration** |
| **Body Mass Index** | | | | | |
| rs10468280 | 385.039 | 10.0E-86 | 81.512 | 1.7E-19 | 1 |
| rs10789340 | 105.720 | 8.5E-25 | 25.554 | 4.3E-07 | 1 |
| rs33988101 |  |  | 10.415 | 0.001 | 1 |
| rs35789556 | 11.307 | 0.001 |  |  | 2 |
| rs729833 | 7.430 | 0.006 |  |  | 2 |
| rs7619139 | 13.044 | 3.0E-04 |  |  | 2 |
| **Waist Circumference** | | | | | |
| rs10468280 | 266.558 | 6.4E-60 | 67.267 | 2.4E-16 | 1 |
| rs10789340 | 68.938 | 1.0E-16 | 19.706 | 9.0E-06 | 1 |
| rs33988101 |  |  | 9.661 | 0.002 | 1 |
| rs729833 | 6.988 | 0.008 |  |  | 1 |
| rs35789556 | 8.060 | 0.005 |  |  | 2 |
| rs6131331 | 8.535 | 0.003 |  |  | 2 |

Abbrevations: SNP, Single Nucleotide Polymorphisms.

**Supplementary Table 20** Influential Single Nucleotide Polymorphisms (SNPs) identified and excluded by an iterative approach calculating SNP-specific Qj-statistics in the radial inverse-variance weighted as well as MR-Egger methods for the impact of relative dietary protein intake (in % of total energy intake (E%)) on anthropometric measures.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **SNP** |  |  |  |  | **Iteration** |
| **Body Mass Index** | | | | | |
| rs445551 | 7.001 | 0.008 |  |  | 1 |
| rs55872725 | 431.970 | 6.1E-96 | 220.400 | 7.4E-50 | 1 |
| rs780094 | 33.767 | 6.2E-09 | 19.107 | 1.2E-05 | 1 |
| rs1891210 | 17.216 | 3.3E-05 | 17.413 | 3.0E-05 | 2 |
| rs6024454 | 7.539 | 0.006 | 7.434 | 0.006 | 3 |
| **Waist Circumference** | | | | | |
| rs4775698 | 16.888 | 4.0E-05 | 7.614 | 0.006 | 1 |
| rs55872725 | 301.688 | 1.4E-67 | 135.188 | 3.0E-31 | 1 |
| rs780094 | 19.085 | 1.3E-05 | 10.387 | 0.001 | 1 |
| rs1891210 | 17.331 | 3.1E-05 | 16.800 | 4.2E-05 | 2 |

Abbrevations: SNP, Single Nucleotide Polymorphisms.

**Supplementary Table 21** Influential Single Nucleotide Polymorphisms (SNPs) identified and excluded by an iterative approach calculating SNP-specific Qj-statistics in the radial inverse-variance weighted as well as MR-Egger methods for the impact of body mass index on dietary composition (in % of total energy intake (E%)).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **SNP** |  |  |  |  | **Iteration** |
| **Relative Carbohydrate Intake** | | | | | |
| rs1016287 | 7.227 | 0.007 | 9.477 | 0.002 | 1 |
| rs11030104 | 7.818 | 0.005 | 11.394 | 0.001 | 1 |
| rs13107325 | 11.891 | 0.001 | 11.521 | 6.9E-04 | 1 |
| rs2287019 | 11.803 | 0.001 | 12.994 | 3.1E-04 | 1 |
| rs3101336 | 14.744 | 1.2E-04 | 10.233 | 0.001 | 1 |
| rs3817334 | 13.485 | 2.4E-04 | 12.375 | 4.4E-04 | 1 |
| rs4740619 | 24.067 | 9.3E-07 | 18.781 | 1.5E-05 | 1 |
| rs6804842 | 45.631 | 1.4E-11 | 38.223 | 6.3E-10 | 1 |
| rs7138803 | 10.608 | 0.001 | 7.736 | 0.005 | 1 |
| rs1000940 | 8.505 | 0.004 |  |  | 2 |
| rs11165643 | 6.720 | 0.010 |  |  | 3 |
| **Relative Fat Intake** | | | | | |
| rs10182181 | 14.055 | 1.7E-04 | 11.777 | 0.001 | 1 |
| rs2287019 | 16.859 | 4.0E-05 | 17.955 | 2.3E-05 | 1 |
| rs3101336 | 20.811 | 5.1E-06 | 17.187 | 3.4E-05 | 1 |
| rs6804842 | 25.886 | 3.6E-07 | 22.621 | 2.0E-06 | 1 |
| rs13021737 | 10.741 | 0.001 | 7.439 | 0.006 | 2 |
| **Relative Protein Intake** | | | | | |
| rs13107325 | 8.595 | 0.003 | 8.751 | 0.003 | 1 |
| rs2287019 | 7.663 | 0.006 | 6.994 | 0.008 | 1 |
| rs3817334 | 8.045 | 0.005 | 8.515 | 0.004 | 1 |
| rs4740619 | 9.686 | 0.002 | 8.047 | 0.005 | 1 |
| rs6804842 | 27.057 | 2.0E-07 | 24.722 | 6.6E-07 | 1 |

Abbrevations: SNP, Single Nucleotide Polymorphisms.

**Supplementary Table 22** Influential Single Nucleotide Polymorphisms (SNPs) identified by an iterative approach in the models waist circumference on dietary composition (in % of total energy intake (E%)).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **SNP** |  |  |  |  | **Iteration** |
| **Relative Carbohydrate Intake** | | | | | |
| rs2287019 | 13.401 | 2.5E-04 | 13.882 | 1.9E-04 | 1 |
| rs7138803 | 9.105 | 0.003 | 7.659 | 0.006 | 1 |
| rs7531118 | 13.189 | 2.8E-04 | 11.860 | 0.001 | 1 |
| rs7144011 | 6.695 | 0.010 |  |  | 2 |
| **Relative Fat Intake** | | | | | |
| rs2287019 | 15.226 | 9.5E-05 | 16.151 | 5.8E-05 | 1 |
| rs7531118 | 28.159 | 1.1E-07 | 26.561 | 2.6E-07 | 1 |
| rs6755502 | 12.112 | 0.001 |  |  | 2 |

Abbrevations: SNP, Single Nucleotide Polymorphisms.

In the models waist circumference on relative protein intake no influential SNPs were detected.

**Supplementary Table 23** Associations between Single Nucleotide Polymorphisms (SNPs) and dietary composition (in % of total energy intake (E%)) and anthropometric measures (outcomes) in the multivariable Mendelian randomization approach.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Carbohydrate intake (E%)** | | | **Fat intake (E%)** | | | **Protein intake (E%)** | | | **Body mass index** | | | **Waist circumference** | | |
| **SNP** |  | **SE** | **P-value** |  | **SE** | **P-value** |  | **SE** | **P-value** |  | **SE** | **P-value** |  | **SE** | **P-value** |
| rs10206338 | -0.016 | 0.003 | 1.52E-08 | 0.013 | 0.003 | 3.61E-06 | 0.002 | 0.003 | 0.387 | 0.002 | 0.004 | 0.599 | 0.003 | 0.004 | 0.440 |
| rs10433500 | 0.016 | 0.003 | 1.96E-08 | -0.002 | 0.003 | 0.559 | 0.001 | 0.003 | 0.813 | -0.013 | 0.004 | 0.001 | -0.012 | 0.004 | 0.005 |
| rs10510554a | 0.019 | 0.003 | 2.94E-12 | -0.014 | 0.003 | 5.43E-07 | -0.017 | 0.003 | 4.54E-10 |  |  | 4.18E-09 | -0.014 | 0.003 | 2.40E-05 |
| rs10962121 | -0.015 | 0.003 | 3.40E-08 | 0.007 | 0.003 | 0.009 | 0.012 | 0.003 | 2.21E-05 | 0.016 | 0.004 | 1.16E-04 | 0.009 | 0.005 | 0.056 |
| rs1104608 | 0.018 | 0.003 | 1.74E-10 | -0.011 | 0.003 | 8.26E-05 | 0.002 | 0.003 | 0.397 | -0.004 | 0.005 | 0.350 | -0.006 | 0.005 | 0.250 |
| rs13146907 | -0.010 | 0.003 | 4.08E-04 | -0.004 | 0.003 | 0.208 | -0.022 | 0.003 | 1.24E-14 | 0.000 | 0.004 | 0.980 | 0.001 | 0.005 | 0.790 |
| rs1461729 | -0.024 | 0.005 | 2.65E-07 | 0.019 | 0.005 | 3.69E-05 | 0.032 | 0.005 | 4.09E-12 | -0.001 | 0.006 | 0.885 | 0.008 | 0.007 | 0.280 |
| rs2472297 | -0.018 | 0.003 | 3.73E-08 | 0.007 | 0.003 | 0.028 | 0.008 | 0.003 | 0.013 | 0.005 | 0.004 | 0.168 | 0.005 | 0.004 | 0.200 |
| rs33988101 | 0.023 | 0.003 | 1.91E-16 | -0.029 | 0.003 | 1.66E-26 | -0.026 | 0.003 | 3.04E-21 | -0.009 | 0.004 | 0.019 | -0.007 | 0.005 | 0.140 |
| rs36123991 | 0.021 | 0.004 | 8.24E-09 | 0.006 | 0.004 | 0.083 | -0.011 | 0.004 | 0.003 | 0.003 | 0.005 | 0.496 | 0.004 | 0.005 | 0.440 |
| rs445551 | -0.007 | 0.003 | 0.036 | 0.004 | 0.003 | 0.295 | 0.019 | 0.003 | 1.49E-08 | -0.003 | 0.004 | 0.479 | -0.004 | 0.005 | 0.370 |
| rs57193069 | 0.008 | 0.003 | 0.003 | -0.016 | 0.003 | 1.80E-08 | -0.001 | 0.003 | 0.636 | -0.005 | 0.004 | 0.236 | -0.004 | 0.005 | 0.340 |
| rs780094 | 0.004 | 0.003 | 0.127 | 0.012 | 0.003 | 3.73E-05 | 0.018 | 0.003 | 5.58E-10 | -0.012 | 0.003 | 2.05E-04 | -0.009 | 0.004 | 0.015 |
| rs8097672 | 0.023 | 0.004 | 1.95E-09 | -0.010 | 0.004 | 0.008 | -0.015 | 0.004 | 1.56E-04 | -0.018 | 0.005 | 0.001 | -0.010 | 0.006 | 0.090 |

Abbrevations: , standard deviation change; SE, standard error; SNP, Single Nucleotide Polymorphism;.

a SNP was removed from the analysis with the outcome BMI due to a strong association at the genome-wide significance threshold of .

**Supplementary Table 24** Conditional F-statistics, Q-statistics, and Egger-intercept tests for multivariable Mendelian randomization models of genetically predicted relative dietary intake of carbohydrates (COH), fat, and proteins (in % of total energy intake (E%)) on the anthropometric measures body mass index (BMI) and waist circumference (WC).

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** |  |  |  |  |  | **Egger intercept** |  |
| BMI | 8.771 | 9.256 | 42.470 | 31.561 |  | -0.004 | 0.514 |
| WC | 8.136 | 8.560 | 40.691 | 16.827 | 0.113 | 0.002 | 0.703 |