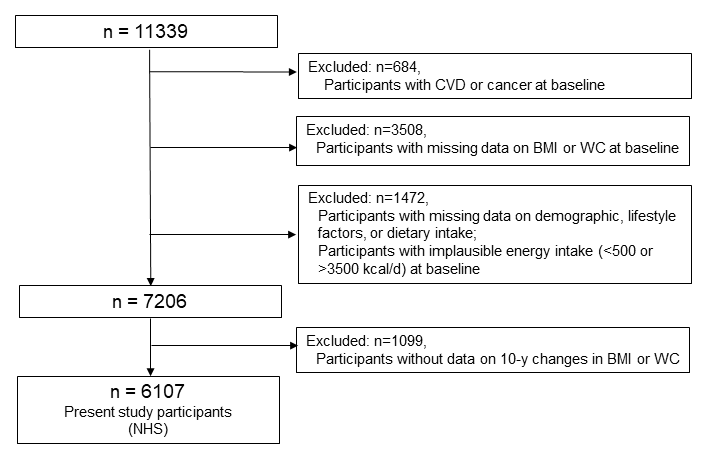
**Online Appendix**

**Supplement to:** Yoriko Heianza, Tao Zhou, Yuhang Chen, Tao Huang, Walter C Willett, Frank B. Hu, George A. Bray, Frank M Sacks, and Lu Qi.

Starch Digestion-Related Amylase Genetic Variants, Diet, and Changes in Adiposity: Analyses in Prospective Cohort Studies and a Randomized Dietary Intervention

**SFigure 1:** Selection of study participants in the Nurses' Health Study (NHS).



Abbreviation: CVD, cardiovascular disease; BMI, body mass index; WC, waist circumference.

**SFigure 2:** Selection of study participants in the Health Professionals Follow-Up Study (HPFS)



Abbreviation: CVD, cardiovascular disease; BMI, body mass index; WC, waist circumference.

**SFigure 3**: Selection of study participants in the Atherosclerosis Risk in Communities (ARIC) Study



Abbreviation: CVD, cardiovascular disease; BMI, body mass index; WC, waist circumference.

**SFigure 4:** Selection of study participants in the UK Biobank

A screenshot of a cell phone

Description automatically generated

Abbreviation: CVD, cardiovascular disease; BMI, body mass index; WC, waist circumference.

**SFigure 5:** Distribution of AMY1-GRS in four prospective cohort studies



Abbreviations: NHS, the Nurses' Health Study; HPFS, the Health Professionals Follow-Up Study; ARIC, the Atherosclerosis Risk in Communities Study; GRS, genetic risk score.

**SFigure 6:** Meta-analyzed associations of AMY1*-*GRS with changes in body mass index (BMI) (panel A) or changes in waist circumference (WC) (panel B)



Abbreviations: NHS, the Nurses' Health Study; HPFS, the Health Professionals Follow-Up Study; ARIC, the Atherosclerosis Risk in Communities Study; GRS, genetic risk score.

The ES (95% CI) indicates effect of AMY1-GRS for changes in BMI (panel A) or changes in WC (in panel B) after adjusting for the same covariates listed in main Table 1.

**SFigure 7:** Meta-analyzed associations of copy number increasing allele of *AMY1* SNPs for BMI changes



Abbreviations: NHS, the Nurses' Health Study; HPFS, the Health Professionals Follow-Up Study; ARIC, the Atherosclerosis Risk in Communities Study.

The ES (95% CI) indicates effect for changes in BMI per copy number increasing allele of each *AMY1* SNP after adjusting for the same covariates listed in main Table 1.

**SFigure 8:** Meta-analyzed associations of copy number increasing allele of *AMY1* SNPs for waist circumference (WC) changes



Abbreviations: NHS, the Nurses' Health Study; HPFS, the Health Professionals Follow-Up Study; ARIC, the Atherosclerosis Risk in Communities Study.

The ES (95% CI) indicates effect for changes in WC per copy number increasing allele of each *AMY1* SNP after adjusting for the same covariates listed in main Table 1.

**SFigure 9:** Associations of carbohydrate food intake withbody mass index (BMI) changes (panel A) or waist circumference (WC) changes (panel B) in 4 prospective cohorts

****

Abbreviations: NHS, the Nurses' Health Study; HPFS, the Health Professionals Follow-Up Study; ARIC, the Atherosclerosis Risk in Communities Study.

The ES (95% CI) indicates effect for changes in BMI (panel A) or changes in WC (in panel B) per 1 SD of carbohydrate food intake after adjusting for the same covariates listed in main Table 1.

P value for the overall effect: P=0.13 in panel A; P=0.16 in panel B.

**SFigure 10:** Associations of starch intake with body mass index (BMI) changes (panel A) or waist circumference (WC) changes (panel B) in 4 prospective cohorts

****

Abbreviations: NHS, the Nurses' Health Study; HPFS, the Health Professionals Follow-Up Study; ARIC, the Atherosclerosis Risk in Communities Study.

The ES (95% CI) indicates effect for changes in BMI (panel A) or changes in WC (in panel B) per 1 SD of starch intake after adjusting for the same covariates listed in main Table 1.

*P* value for the overall effect: P=0.11 in panel A; P=0.12 in panel B.

**.**

**SFigure 11:** Meta-analyzed interaction effect between AMY1-GRS and dietary intake of carbohydrate foods for body mass index (BMI) changes (panel A) or waist circumference (WC) changes (panel B) among total participants from 4 prospective cohorts



Abbreviations: NHS, the Nurses' Health Study; HPFS, the Health Professionals Follow-Up Study; ARIC, the Atherosclerosis Risk in Communities Study; GRS, genetic risk score.

The ES (95% CI) indicates effect of interactions between GRS (per 1 unit) and carbohydrate food intake (per 1 SD) for changes in BMI (panel A) or changes in WC (in panel B) after adjusting for the same covariates listed in Table 1.

Test of overall ES (95% CI): summary *Pinteraction* = 0.001 in panel A; summary *Pinteraction* <0.001 in panel B.

**SFigure 12:** Meta-analyzedinteraction effect between *AMY1-*GRS and dietary starch intake for changes in body mass index (BMI) (panel A) or changes in waist circumference (WC) (panel B)



Abbreviations: NHS, the Nurses' Health Study; HPFS, the Health Professionals Follow-Up Study; ARIC, the Atherosclerosis Risk in Communities Study; GRS, genetic risk score.

The ES (95% CI) indicates effect of interactions between GRS (per 1 unit) and starch intake (per 1 SD) for changes in BMI (panel A) or changes in WC (in panel B) after adjusting for the same covariates listed in Table 1. Test of overall ES (95% CI): summary *Pinteraction* = 0.031 in panel A; summary *Pinteraction* <0.001 in panel B.

**SFigure 13:** Sex-differences in interactions between *AMY1-*GRS (per 1 unit) and dietary carbohydrate food intake (per 1 SD unit) for changes in BMI using the random-effect model

****

Test of overall ES (95% CI): summary *Pinteraction*= 0.002 in women; summary *Pinteraction*=0.95 in men.

**SFigure 14:** Changes in weight per 5-point increment in AMY1-GRS according to tertile (T) categories of carbohydrate food intake in female and male cohorts.



Data after adjusting for the same covariates listed in Table 1 (except for sex). Abbreviations: NHS, the Nurses' Health Study; HPFS, the Health Professionals Follow-Up Study; ARIC, the Atherosclerosis Risk in Communities Study.

**SFigure 15:** Changes in body mass index (BMI) and changes in waist circumference (WC) per SD increment in carbohydrate food intake according to tertile (T) categories of AMY1-GRS

****

Data after adjusting for the same covariates listed in Table 1 (except for sex). Abbreviations: NHS, the Nurses' Health Study; HPFS, the Health Professionals Follow-Up Study; ARIC, the Atherosclerosis Risk in Communities Study.

**SFigure 16:** Interaction between *AMY1-*GRS (per 1 unit) and individual carbohydrate food groups (per 1 SD) for WC changes in women

****

Significance tests of interactions: *p* = 0.046 for Grains; p = 0.021 for Potatoes; p = 0.017 for Sugar-sweetened beverages, SSB; p = 0.009for Sweets, p <0.001 for Overall.

**SFigure 17:** Interactions between *AMY1-*GRS and intake of foods high in resistant starch for changes in body mass index (BMI) (panel A) or changes in waist circumference (WC) (panel B) in total participants

****

Abbreviations: NHS, the Nurses' Health Study; HPFS, the Health Professionals Follow-Up Study; ARIC, the Atherosclerosis Risk in Communities Study; GRS, genetic risk score.

The ES (95% CI) indicates effect of interactions between AMY1-GRS (per 1 unit) and intake of foods high in resistant starch (per 1 SD) for changes in BMI (panel A) or changes in WC (in panel B) after adjusting for the same covariates listed in Table 1.

Test of overall ES (95% CI): summary *Pinteraction* = 0.042 in panel A; summary *Pinteraction* =0.006 in panel B.

**SFigure 18:** Interactions between *AMY1-*GRS and intake of foods high in resistant starch for changes in waist circumference (WC) in women and men.

****

Summary *Pinteraction* =0.006 in women; Summary *Pinteraction* = 0.2 in men.

**SFigure 19:** Interactions between individual *AMY1* SNPsand carbohydrate food intake (per 1 SD) for WC changes in women



Significance tests of interactions: SNP rs4244372, *p* < 0.001; SNP rs11577390, *p* = 0.029; SNP rs1566154, *p* = 0.36; SNP rs1930212, p = 0.097; SNP rs2132957, *p* = 0.184; SNP rs11185098, *p* = 0.003; SNP rs1999478, *p* = 0.012; SNP rs1330403, *p* = 0.792; SNP rs6696797, *p* = 0.398; Overall, *p* <0.001.

**SFigure 20:** Changes in weight (panel A) and waist circumference (WC) in response to diets with different carbohydrate intake in participants with low or high AMY1-GRS scores

****

**STable 1:** Summary of food groups across studies

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Food group** | Nurses' Health Study (NHS) | Health Professionals Follow-Up Study (HPFS) | Atherosclerosis Risk in Communities Study (ARIC) | UK Biobank |
| **Grains** | Whole grain breakfast cereal, Other cooked breakfast cereal, Cooked Oatmeal, Dark Bread, Brown Rice, Other grains, Bran added to food, Wheat Germ, Popcorn, Refined grain breakfast cereal, White Bread, including pita bread, English Muffins, Bagels, Rolls, Muffins/Biscuits, White Rice, Pancakes/Waffles, Crackers, and Pasta | Whole grain breakfast cereal, Other cooked breakfast cereal, Cooked Oatmeal, Dark Bread, Brown Rice, Other grains, Bran added to food, Wheat Germ, Popcorn, Refined grain breakfast cereal, White Bread, including pita bread, English Muffins, Bagels, Rolls, Muffins/Biscuits, White Rice, Pancakes/Waffles, Crackers, and Pasta | White bread, Dark or whole grain bread, Cold breakfast cereal, Cooked cereals such as oatmeal, grits, cream of wheat, Rice, and Spaghetti, noodles or other pasta. | Sweetened cereal, Plain cereal, Sliced bread, Sandwich baguette, Large sandwich bap, Bread roll, Naan bread, Garlic bread, Crispbread, Other bread, White pasta, White rice, Snackpot, Pancake, Scotch pancake, Croissant, Scone, Savory biscuits, Cheesy biscuits, Other savory snack, Porridge, Muesli, Oat crunch, Bran cereal, Whole-wheat cereal, Other cereal, Whole meal pasta, Brown rice ,Couscous, Other grain, Cereal bar, Oatcakes. |
| **Potatoes** | Baked/Boiled/Mashed potatoes, French fried potatoes, Potato/corn chips, and Yams/Sweet potatoes | Baked/Boiled/Mashed potatoes, French dried potatoes, Potato/corn chips, and Yams/Sweet potatoes | French fried potatoes, Potatoes, mashed or baked, Potato/corn chips, and Sweet potatoes. | Boiled/baked potatoes, Mashed potato, Fried potatoes, Crisp, Sweet potatoes |
| **Sugar-sweetened beverages** | Soda with sugar, Punch, lemonade, or other non-carbonated fruit drinks with sugar | Coke, Pepsi, or other colas with sugar, Caffeine Free Coke, Pepsi or other cola with sugar, Other carbonated beverages with sugar, Punch, lemonade, or other non-carb fruit drinks with sugar | Regular soft drinks, Fruit-flavored punch or non-carbonated beverages, such as lemonade, Kool-Aid or Hawaiian Punch; not diet | Fizzy drink, Squash |
| **Sweets/**  **desserts** | Chocolate bars or pieces, Candy bars, Candy without chocolate, Cookies, home-baked, Cookies, ready-made, Brownies, Doughnuts, Cake, home-baked, Cake, ready-made, Pie, home-baked, Pie, ready-made, Jams, jellies, preserves, syrup, or honey, and Sweet roll, coffee cake or other pastry | Chocolate bars or pieces, Candy bars, Candy without chocolate, Cookies, home-baked, Cookies, ready-made, Brownies, Doughnuts, Cake, home-baked, Cake, ready-made, Pie, home-baked, Pie, ready-made, Jams, jellies, preserves, syrup, or honey, and Sweet roll, coffee cake or other pastry | Chocolate bars or pieces, Candy without chocolate, Cookies, Cake or brownie, Pie, homemade from scratch, Pie, ready-made or from a mix, Donut, Biscuits or cornbread, and Danish pastry, sweet roll, coffee cake, croissant. | Chocolate bar, White chocolate, Milk chocolate, Dark chocolate, Chocolate-covered raisin, Chocolate sweet, Chocolate-covered biscuits, Sweets, Chocolate biscuits, Sweet biscuits, Other sweets, Double crust pastry, Single crust pastry, Crumble, Danish pastry, Fruitcake, Cake, Doughnut, and Other dessert. |

**STable 2:** Summary of food groups that are major sources of dietary resistant starch

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Food group** | Nurses' Health Study (NHS) | Health Professionals Follow-Up Study (HPFS) | Atherosclerosis Risk in Communities Study (ARIC) | UK Biobank |
| **Bread** | White Bread, including pita bread; English Muffins, Bagels, Rolls; Dark Bread | White Bread, including pita bread; English Muffins, Bagels, Rolls; Dark Bread | White bread; Dark or whole grain bread; Danish pastry, croissant, etc. | Bread (all types); Danish pastry; Croissant |
| **Cooked cereals/Rice/Pasta** | Cooked Oatmeal; White Rice, Brown Rice; Pasta (e.g. spaghetti, noodles etc.) | Cooked Oatmeal; White Rice, Brown Rice; Pasta (e.g. spaghetti, noodles etc.) | Cooked cereals such as oatmeal, grits, cream of wheat; Rice; Spaghetti, noodles, or other pasta | Porridge; White rice; Brown rice; White pasta; Whole meal pasta |
| **Starchy vegetables (other than legumes)** | Baked/Boiled/Mashed potatoes; French fried potatoes; Yams/Sweet potatoes; Corn, Peas, or lima beans | Baked/Boiled/Mashed potatoes; French fried potatoes; Yams/Sweet potatoes; Corn; Peas, or lima beans | Mashed or baked Potatoes; French fried potatoes; Sweet potatoes; Corn; Peas or lima beans | Boiled/baked potatoes; Mashed potato; Fried potatoes; Sweet potato; Sweetcorn; Pea; Broad bean |
| **Banana** | Banana | Banana | Banana | Banana |

**STable 3:** A total of 9 single nucleotide polymorphisms (SNPs) associated with *AMY1* copy number included in a genetic risk score

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  | EA frequency | | | | |
| RS Number | Position | Alleles (from Reference Report in Europeans, EUR)\* | | Effect Allele (EA) for increases in CNVs | Change in copy number/EA | NHS | HPFS | ARIC | UK Biobank | POUNDS Lost trial |
| rs4244372 | chr1:104040027 | T=0.664, | A=0.336 | T | 1.25 | 63.0 | 62.9 | 65.6 | 62.8 | 66.4 |
| rs11577390 | chr1:104360512 | C=0.917, | T=0.083 | T | 1.88 | 2.0 | 1.9 | 7.6 | 8.6 | 7.4 |
| rs1566154 | chr1:104329877 | A=0.841, | G=0.159 | G | 0.88 | 18.5 | 17.8 | 21.3 | 18.6 | 17.0 |
| rs1930212 | chr1:104324819 | A=0.811, | G=0.189 | A | 1.05 | 80.8 | 79.9 | 83.0 | 79.9 | 84.5 |
| rs2132957 | chr1:104895687 | A=0.968, | G=0.032 | A | 1.29 | 97.7 | 97.4 | 97.7 | 96.8 | 97.4 |
| rs11185098 | chr1:104321349 | G=0.738, | A=0.262 | A | 0.79 | 22.7 | 22.6 | 22.8 | 23.9 | 27.0 |
| rs1999478 | chr1:104311712 | C=0.803, | A=0.197 | C | 0.92 | 80.5 | 80.8 | 80.9 | 79.7 | 80.2 |
| rs1330403 | chr1:104580702 | A=0.867, | G=0.133 | G | 0.75 | 13.2 | 13.0 | 13.2 | 13.8 | 13.6 |
| rs6696797 | chr1:104017778 | G=0.353, | A=0.647 | A | 0.72 | 63.3 | 63.6 | 63.4 | 65.7 | 69.0 |

**\***Phase 3 (Version 5) of the 1000 Genomes Project (<https://ldlink.nci.nih.gov/>).

Abbreviations: NHS, the; HPFS, the Health Professionals Follow-Up Study; ARIC, the Atherosclerosis Risk in Communities Study.

**STable 4:** Characteristics of participants across 4 prospective cohorts

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | NHS | HPFS | ARIC |  |  |  | UK Biobank |  |  |
| Variables | (n=6107) | (n=4621) | Total | Women | Men |  | Total | Women | Men |
|  |  | (n=6515) | (n=3465) | (n=3050) |  | (n=14811) | (n=7599) | (n=7212) |
| AMY1-GRSweighted | 8.6 (7.1, 9.9) | 8.5 (7.1, 9.9) | 8.6 (7.8, 10.2) | 8.6 (7.8, 10.2) | 8.7 (7.8, 10.2) |  | 8.6 (7.1, 10.2) | 8.6 (7.1, 10.2) | 8.6 (7.1, 10.2) |
| AMY1-GRSunweighted | 9 (7, 10) | 9 (7, 10) | 9 (8, 10) | 9 (8, 10) | 9 (8, 10) |  | 9 (7, 10) | 9 (7, 10) | 9 (7, 10) |
| Age, y | 54.3 (6.5) | 54.9 (8.6) | 54.1 (5.6) | 53.8 (5.6) | 54.4 (5.7) |  | 56.3 (7.4) | 55.5 (7.3) | 57.1 (7.4) |
| Smoking status |  |  |  |  |  |  |  |  |  |
| Never | 46.9 | 46.6 | 42.4 | 53 | 30.4 |  | 60.8 | 65.3 | 56 |
| Former | 36.7 | 45.6 | 35.8 | 24.9 | 48.3 |  | 33.6 | 30.2 | 37.3 |
| Current | 16.4 | 7.8 | 21.7 | 22.1 | 21.3 |  | 5.6 | 4.5 | 6.7 |
| College/university or higher degree | 30.3 | - | 42.2 | 36.5 | 48.8 |  | 47.3 | 46.3 | 48.3 |
| Physical activity, MET-hours/week | 14.8 (19.9) | 20.0 (26.5) | - | - | - |  | 38.5 (38) | 36.9 (36) | 40.2 (39.8) |
| Physical activity index | - | - | 2.5 (0.5) | 2.5 (0.5) | 2.4 (0.5) |  | - | - | - |
| Alcohol intake, g/d | 6.4 (10.7) | 12.3 (16.0) | 6.9 (13.6) | 3.6 (7.5) | 10.7 (17.5) |  | 16.6 (24) | 11.7 (17.7) | 21.9 (28.2) |
| Total energy intake, kcal/day | 1800 (511) | 2037 (603) | 1639 (595) | 1496 (516) | 1802 (636) |  | 2109 (608) | 1940 (531) | 2286 (633) |
| Starch, g/day | 67 (26) | 68 (29) | 54 (25) | 50 (22) | 60 (28) |  | 123 (50) | 111 (44) | 136 (53) |
| Carbohydrate, g/day | 218 (73) | 237 (82) | 197 (81.7) | 185 (74) | 212 (87) |  | 254 (83) | 238 (75) | 271 (87) |
| Carbohydrate food, servings/day | 4.8 (2.3) | 5.6 (2.9) | 4.9 (2.6) | 4.5 (2.3) | 5.5 (2.8) |  | 6.1 (2.8) | 5.5 (2.5) | 6.7 (3.0) |
| Grains | 2.9 (1.6) | 3.2 (1.9) | 2.5 (1.5) | 2.4 (1.4) | 2.7 (1.7) |  | 3.7 (2.0) | 3.3 (1.8) | 4.0 (2.1) |
| Potatoes | 0.5 (0.4) | 0.6 (0.5) | 0.7 (0.5) | 0.6 (0.5) | 0.7 (0.5) |  | 0.7 (0.7) | 0.7 (0.7) | 0.8 (0.8) |
| Sugar-sweetened beverages | 0.2 (0.5) | 0.3 (0.6) | 0.4 (0.8) | 0.3 (0.7) | 0.6 (0.9) |  | 0.3 (0.7) | 0.2 (0.6) | 0.3 (0.8) |
| Sweets and desserts | 1.2 (1.1) | 1.5 (1.5) | 1.3 (1.2) | 1.2 (1.2) | 1.5 (1.3) |  | 1.4 (1.5) | 1.2 (1.4) | 1.5 (1.7) |
| Food sources of resistant starch, servings/day | 2.8 (1.4) | 3.1 (1.7) | 3.3 (1.7) | 3.1 (1.5) | 3.5 (1.8) |  | 3.7 (1.8) | 3.3 (1.6) | 4.1 (1.9) |
| Breads | 1.4 (1.1) | 1.6 (1.3) | 1.7 (1.3) | 1.5 (1.2) | 1.9 (1.5) |  | 2.1 (1.6) | 1.7 (1.3) | 2.5 (1.7) |
| Cooked cereals/pastas | 0.4 (0.3) | 0.4 (0.4) | 0.4 (0.4) | 0.5 (0.4) | 0.4 (0.4) |  | 0.4 (0.6) | 0.4 (0.6) | 0.4 (0.6) |
| Starchy vegetables | 0.7 (0.4) | 0.8 (0.5) | 0.8 (0.5) | 0.7 (0.5) | 0.9 (0.5) |  | 0.7 (0.8) | 0.7 (0.8) | 0.7 (0.8) |
| Bananas | 0.3 (0.3) | 0.3 (0.4) | 0.3 (0.4) | 0.4 (0.4) | 0.3 (0.4) |  | 0.5 (0.6) | 0.5 (0.6) | 0.5 (0.6) |
| Body mass index (BMI), kg/m2 | 24.9 (4.4) | 25.6 (3.2) | 26.9 (4.7) | 26.5 (5.3) | 27.4 (3.8) |  | 26.6 (4.3) | 26.1 (4.6) | 27.1 (3.9) |
| Weight, kg | 67 (13) | 82 (12) | 77 (16) | 70 (14) | 85 (13) |  | 77 (15) | 70 (13) | 85 (13) |
| Waist circumference (WC), cm | 79 (11) | 96 (10) | 96 (13) | 93 (15) | 100 (10) |  | 88 (13) | 82 (11) | 95 (11) |
| Follow-up year for outcomes | 10 y | 10 y | 6 y | 6 y | 6 y |  | 5.5 y | 5.5 y | 5.5 y |
| Changes in BMI, kg/m2 | 0.9 (-0.3, 2.3) | 0.5 (-0.4, 1.4) | 0.9 (-0.1, 2.0) | 1.1 (0, 2.4) | 0.6 (-0.3, 1.6) |  | 0 (-0.9, 0.9) | 0 (-0.9, 1) | 0 (–0.8, 0.8) |
| Changes in weight, kg | 2 (-1, 6) | 2 (-1, 5) | 2 (-1, 5) | 3 (0, 6) | 1 (-1, 5) |  | 0 (-3, 2) | 0 (-3, 2) | -1 (-3, 2) |
| Changes in WC, cm | 8 (3, 13) | 3 (0, 6) | 4 (0, 7) | 5 (0, 9) | 3 (0, 6) |  | 0 (-4, 5) | 1 (-4, 5) | 0 (–4, 4) |

Data are median (25th, 75th), mean (SD), or % of total N. \*Carbohydrate food included grains, potatoes, sugar-sweetened beverages, and sweets and desserts.

**STable 5:** Differences in dietary starch or carbohydrate food intake per 1-point increment of AMY1-GRS

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | NHS |  |  | HPFS |  |  | ARIC |  |  | UK Biobank |  |
| Dietary intake | β (SE) | *P* |  | β (SE) | *P* |  | β (SE) | *P* |  | β (SE) | P |
| Starch, g/day | 0.03 (0.12) | 0.82 |  | 0.2 (0.17) | 0.25 |  | 0.14 (0.11) | 0.19 |  | 0.08 (0.14) | 0.57 |
| Carbohydrate food, servings/day | 0.02 (0.01) | 0.15 |  | –0.01 (0.02) | 0.54 |  | 0.01 (0.01) | 0.19 |  | 0 (0.01) | 0.6 |

Abbreviations: NHS, the; HPFS, the Health Professionals Follow-Up Study; ARIC, the Atherosclerosis Risk in Communities Study; GRS, genetic risk score.

β (SE) per 1 point increment of AMY1-GRS for differences in dietary intake after adjusting for age, sex (in ARIC and UK Biobank), and total energy intake.

**STable 6:** Main genetic effect of *AMY1*-GRS or individual SNPs for BMI changes

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | NHS |  |  | HPFS |  |  | ARIC |  |  | UK Biobank |  |
| Variables | Effect | β (SE) | *P* |  | β (SE) | *P* |  | β (SE) | *P* |  | β (SE) | *P* |
| *AMY1*-GRS | Per 1 unit | –0.01 (0.02) | 0.41 |  | 0.01 (0.01) | 0.58 |  | –0.02 (0.01) | 0.1 |  | 0 (0.01) | 0.56 |
| rs4244372 | T | –0.03 (0.04) | 0.57 |  | 0.02 (0.04) | 0.65 |  | –0.06 (0.04) | 0.12 |  | 0 (0.02) | 0.91 |
| rs11577390 | T | –0.06 (0.15) | 0.72 |  | 0.03 (0.14) | 0.83 |  | –0.08 (0.06) | 0.21 |  | 0 (0.04) | 0.92 |
| rs1566154 | G | 0.02 (0.06) | 0.71 |  | 0.1 (0.05) | 0.03 |  | –0.04 (0.04) | 0.34 |  | 0.01 (0.03) | 0.72 |
| rs1930212 | A | 0.01 (0.05) | 0.81 |  | 0 (0.04) | 0.96 |  | –0.01 (0.05) | 0.91 |  | –0.01 (0.03) | 0.7 |
| rs2132957 | A | –0.09 (0.14) | 0.54 |  | –0.09 (0.11) | 0.44 |  | –0.01 (0.11) | 0.94 |  | –0.06 (0.06) | 0.32 |
| rs11185098 | A | –0.07 (0.05) | 0.17 |  | 0.01 (0.04) | 0.74 |  | –0.03 (0.04) | 0.44 |  | –0.03 (0.02) | 0.18 |
| rs1999478 | C | –0.04 (0.05) | 0.4 |  | –0.01 (0.05) | 0.9 |  | –0.07 (0.04) | 0.13 |  | –0.02 (0.03) | 0.33 |
| rs1330403 | G | 0.06 (0.06) | 0.38 |  | –0.03 (0.05) | 0.55 |  | 0 (0.05) | 0.94 |  | 0.03 (0.03) | 0.35 |
| rs6696797 | A | –0.03 (0.04) | 0.44 |  | –0.01 (0.04) | 0.73 |  | 0.02 (0.04) | 0.61 |  | 0 (0.02) | 0.99 |

β (SE) for BMI changes after adjusting for age, sex (in ARIC and UK Biobank), five ancestry principal components (in UK Biobank), Townsend Social Deprivation Index (in UK Biobank), education, smoking habit (never, former, current), physical activity, total energy intake, total fat intake, alcohol consumption, baseline BMI.

**STable 7:** Main effect of *AMY1*-GRS or individual SNPs for waist circumference (WC) changes

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | NHS |  |  | HPFS |  |  | ARIC |  |  | UK Biobank |  |
| Variables | Effect | β (SE) | *P* |  | β (SE) | *P* |  | β (SE) | *P* |  | β (SE) | *P* |
| *AMY1*-GRS | Per 1 unit | 0.02 (0.07) | 0.75 |  | 0.01 (0.05) | 0.83 |  | –0.05 (0.04) | 0.16 |  | –0.02 (0.02) | 0.54 |
| rs4244372 | T | 0.1 (0.18) | 0.57 |  | 0.07 (0.13) | 0.61 |  | –0.19 (0.13) | 0.13 |  | –0.04 (0.08) | 0.58 |
| rs11577390 | T | 0.24 (0.63) | 0.7 |  | –0.5 (0.49) | 0.3 |  | –0.14 (0.21) | 0.51 |  | –0.07 (0.14) | 0.62 |
| rs1566154 | G | 0.22 (0.23) | 0.34 |  | 0.25 (0.17) | 0.15 |  | –0.12 (0.15) | 0.4 |  | 0.06 (0.1) | 0.52 |
| rs1930212 | A | –0.09 (0.23) | 0.7 |  | 0.05 (0.16) | 0.77 |  | 0.08 (0.15) | 0.61 |  | –0.09 (0.1) | 0.36 |
| rs2132957 | A | –0.4 (0.59) | 0.5 |  | 0.1 (0.41) | 0.8 |  | 0.02 (0.37) | 0.97 |  | –0.17 (0.22) | 0.43 |
| rs11185098 | A | 0 (0.21) | 0.99 |  | 0.09 (0.16) | 0.54 |  | –0.08 (0.14) | 0.54 |  | –0.08 (0.09) | 0.37 |
| rs1999478 | C | 0.05 (0.22) | 0.81 |  | –0.11 (0.16) | 0.51 |  | –0.28 (0.14) | 0.05 |  | 0.04 (0.09) | 0.7 |
| rs1330403 | G | –0.03 (0.26) | 0.92 |  | –0.32 (0.19) | 0.1 |  | –0.16 (0.16) | 0.33 |  | 0.07 (0.11) | 0.53 |
| rs6696797 | A | –0.04 (0.18) | 0.81 |  | 0.01 (0.13) | 0.93 |  | 0.1 (0.12) | 0.4 |  | –0.02 (0.08) | 0.85 |

β (SE) for WC changes after adjusting for age, sex (in ARIC and UK Biobank), five ancestry principal components (in UK Biobank), Townsend Social Deprivation Index (in UK Biobank), education, smoking habit (never, former, current), physical activity, total energy intake, total fat intake, alcohol consumption, baseline WC.

**STable 8:** Characteristics of the present study participants in the POUNDS Lost trial

|  |  |
| --- | --- |
| Age, years | 52.1 (8.9) |
| Females | 301 (59.5%) |
| White ethnicity, yes | 442 (87.4%) |
| AMY1-GRSweighted | 8.9 (2.1) |
| BMI at 6 months, kg/m2 | 30 (4.2) |
| Weight, at 6 months, kg | 85.8 (15.4) |
| Waist circumference (WC) at 6 months, cm | 96.4 (13.1) |
| Changes in BMI, kg/m2\* | 0.88 (–0.06, 1.95) |
| Changes in weight, kg\* | 2.5 (–0.2, 5.5) |
| Changes in WC, cm\* | 1.6 (–1.6, 4.6) |
| Carbohydrate intake target (% of total energy intake) |  |
| 35% | 134 (26.5%) |
| 45–55% | 244 (48.2%) |
| 65% | 128 (25.3%) |

Data are mean (SD), N (%), or median (25th, 75th). \*Changes from 6 months to 2 years after the intervention.