**Supplementary Table 1** Baseline characteristics of participants in HPHS and HDNNCDS by type 2 diabetes

|  |  |  |  |
| --- | --- | --- | --- |
|  | HDNNCDS | HPHS |  |
| Variable | Without diabetes (N=3639) | Diabetes (N=385) | *P*-value | Total(N=4024) | Without diabetes(N=1601) | Diabetes(N=148) | *P*-value | Total(N=1749) | *P*-value \* |
| Age (years) | 49.3(9.7) | 52.0(9.1) | <0.001 | 49.6(9.6) | 45.6 (10.4) | 49.4(10.7) | <0.001 | 45.9(10.4) | <0.001 |
| Male [n, (%)] | 1183 (29.4) | 157(40.8) | 0.001 | 1340(33.3) | 487 (30.4) | 56(37.8) | <0.001 | 544(31.1) | 0.099 |
| Alcohol consumption [n, (%)] | 1277(35.1) | 136(35.3) | 0.955 | 1413(35.1) | 459 (28.7) | 43 (29.1) | 0.924 | 503(28.7) | <0.001 |
| Current smoking [n, (%)] | 559(15.4) | 63 (16.4) | 0.817 | 622(15.5) | 232 (14.5) | 26 (17.6) | 0.135 | 258(14.7) | 0.773 |
| Regular exercise habits [n, (%)] | 1968 (54.1) | 176 (45.7) | <0.001 | 2144 (53.2) | 900 (56.2) | 91 (61.5) | 0.226 | 991(56.7) | 0.018 |
| Family history of diabetes [n (%)] | 529 (14.5) | 71(18.4) | 0.050 | 600(14.9) | 163 (10.2) | 28 (18.9) | 0.618 | 191(10.9) | 0.001 |
| Over senior middle school [n (%)] | 2639 (72.5) | 260 (67.5) | 0.042 | 2899 (72.0) | 1023 (64.5) | 80 (54.1) | 0.013 | 1103 (63.0) | <0.001 |
| BMI (kg/m2) | 24.7(3.4) | 26.0(3.4) | <0.001 | 24.9(3.5) | 25.0 (3.4) | 26.6 (4.1) | <0.001 | 25.2(3.5) | <0.001 |
| Total calorie intake (kcal/d) | 2377(887) | 2399(914) | 0.914 | 2380(890) | 2211 (880) | 2258 (843) | 0.518 | 2253(847) | <0.001 |
| Protein (g/day) | 72.4(36.9) | 73.3(35.4) | 0.800 | 72.5(36.8) | 68.3 (33.7) | 65.3 (30.8) | 0.264 | 68.0(33.4) | <0.001 |
| Fiber (g/day) | 14.1(6.9) | 13.7(7.3) | 0.231 | 14.0(7.0) | 14.3 (7.3) | 13.6 (6.8) | 0.180 | 14.2(7.2) | 0.112 |
| Saturated fatty acid (g/day) | 16.2(8.4) | 16.6(7.9) | 0.246 | 16.2(8.3) | 14.1 (6.7) | 15.1 (7.1) | 0.105 | 14.9(6.7) | <0.001 |
| Fasting glucose (mmol/L) | 4.43(0.59) | 5.36(0.95) | <0.001 | 4.52(0.69) | 4.67 (0.67) | 5.09 (0.87) | <0.001 | 4.71(0.70) | <0.001 |
| 2-hour glucose (mmol/L) | 5.63(1.47) | 6.57(2.21) | <0.001 | 5.80(1.64) | 5.60 (1.57) | 6.76 (2.25) | <0.001 | 5.68(1.67) | 0.790 |
| Fasting insulin (µU/mL) | 8.1(6.4) | 12.2(21.1) | <0.001 | 8.5(6.1) | 8.2 (7.8) | 10.5(14.9) | 0.022 | 8.5(9.1) | 0.744 |
| TG (mmol/L) | 1.64(1.57) | 2.03(1.93) | <0.001 | 1.69(1.61) | 1.69 (1.26) | 2.08 (1.73) | 0.026 | 1.73(1.31) | 0.146 |
| TCHO (mmol/L) | 5.10(1.00) | 5.31(1.03) | 0.003 | 5.12(1.01) | 4.90 (0.94) | 5.10 (0.81) | 0.131 | 4.91(0.93) | <0.001 |
| HDL-C (mmol/L) | 1.27(0.32) | 1.18(0.31) | <0.001 | 1.26(0.32) | 1.29 (0.33) | 1.28 (0.35) | 0.750 | 1.28(0.33) | 0.041 |
| LDL-C (mmol/L) | 2.99(0.85) | 3.11(0.87) | 0.088 | 3.00(0.85) | 2.87(0.97) | 2.94 (0.90) | 0.573 | 2.87(0.97) | 0.006 |

Mean ± Standard Deviation was used for continuous variables.

One-way ANOVA was used for continuous variables; Chi-square tests were used for categorical variables.

BMI, body mass index; TG, triglyceride; TCHO, total cholesterol; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; HbA1c, glycosylated hemoglobin; HPHS, Harbin People health Study; HDNNCDS, the Harbin Cohort Study on Diet, Nutrition and Chronic Noncommunicable Disease

Supplementary Table 2 Associations between serum AAs influenced by AACI and incidence of type 2 diabetes in HPHS and HDNNCDS

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Serum AAs | Case/N | Model 1 | Model 2 | Model 3 |
| HDNNCDS |  |  |  |  |
| Valine |  |  |  |  |
| <87.1 | 77/1010 | 1 | 1 | 1 |
| 87.1-98.1 | 64/1006 | 0.81(0.57-1.15) | 0.82(0.58-1.16) | 0.81(0.57-1.15) |
| 98.1-108.7 | 78/1005 | 1.08(0.77-1.52) | 1.07(0.76-1.50) | 1.07 (0.76-1.50) |
| >108.7 | 166/1003 | 2.52(1.86-3.41) | 2.47(1.82-3.35) | 2.36 (1.73-3.21) |
| P for trend |  | <0.001 | <0.001 | <0.001 |
| Isoleucine |  |  |  |  |
| <17.3 | 80/1015 | 1 | 1 | 1 |
| 17.3-21.7 | 94/999 | 1.24(0.91-1.71) | 1.26(0.92-1.74) | 1.29(0.94-1.78) |
| 21.7-27.1 | 87/1017 | 1.11(0.80-1.54) | 1.13(0.81-1.56) | 1.12(0.81-1.56) |
| >27.1 | 124/993 | 1.60(1.17-2.19) | 1.62(1.18-2.22) | 1.43(1.03-1.97) |
| P for trend |  | 0.016 | 0.014 | 0.069 |
| Glycine |  |  |  |  |
| <259.5 | 122/1006 | 1 | 1 | 1 |
| 259.5-286.8 | 106/1006 | 0.84(0.63-1.11) | 0.84(0.63-1.12) | 0.89(0.66-1.18) |
| 286.8-309.2 | 78/1006 | 0.57(0.41-0.78) | 0.57(0.41-0.78) | 0.59(0.43-0.81) |
| >309.2 | 79/1006 | 0.54(0.39-0.74) | 0.54(0.39-0.75) | 0.56(0.40-0.78) |
| P for trend |  | <0.001 | <0.001 | 0.001 |
| Glutamic acid |  |  |  |  |
| <45.6 | 72/1007 | 1 | 1 | 1 |
| 45.6-51.2 | 56/1024 | 0.84(0.58-1.22) | 0.83(0.58-1.20) | 0.81(0.56-1.17) |
| 51.2-56.0 | 111/996 | 1.41(1.03-1.93) | 1.40(1.02-1.92) | 1.35(0.98-1.86) |
| >56.0 | 146/997 | 1.78(1.29-2.44) | 1.77(1.28-2.43) | 1.75(1.26-2.41) |
| P for trend |  | <0.001 | <0.001 | 0.003 |
| Phenylalanine |  |  |  |  |
| <45.6 | 88/1006 | 1 | 1 | 1 |
| 45.6-51.2 | 72/1013 | 0.80(0.58-1.12) | 0.81(0.58-1.12) | 0.83(0.60-1.16) |
| 51.2-56.0 | 94/1000 | 1.22(0.89-1.66) | 1.21(0.88-1.65) | 1.24(0.90-1.70) |
| >56.0 | 131/1005 | 1.64(1.22-2.20) | 1.62(1.21-2.19) | 1.54(1.14-2.08) |
| P for trend |  | <0.001 | <0.001 | 0.001 |
| histidine |  |  |  |  |
| <45.6 | 132/1006 | 1 | 1 | 1 |
| 45.6-51.2 | 70/1007 | 0.78 (0.53-1.03) | 0.81 (0.61-1.09) | 0.85(0.61-1.19) |
| 51.2-56.0 | 108/1006 | 0.58 (0.26-0.92) | 0.62 (0.35-1.01) | 0.63(0.42-1.04) |
| >56.0 | 75/1005 | 0.37(0.19-0.53) | 0.39 (0.22-0.75) | 0.43(0.28-0.65) |
| P for trend |  | <0.001 | <0.001 | <0.001 |
| HPHS |  |  |  |  |
| Valine |  |  |  |  |
| <69.2 | 26/439 | 1 | 1 | 1 |
| 69.2-85.5 | 29/436 | 1.76(0.82-3.82) | 1.70(0.78-3.68) | 1.71(0.79-3.71) |
| 85.5-109.3 | 43/437 | 2.46(1.18-5.15) | 2.28(1.09-4.79) | 2.28(1.08-4.79) |
| >109.3 | 43/438 | 2.76(1.34-5.69) | 2.57(1.24-5.32) | 2.55(1.23-5.28) |
| P for trend |  | 0.004 | 0.008 | 0.009 |
| Isoleucine |  |  |  |  |
| <25.2 | 21/438 | 1 |  |  |
| 25.2-33.9 | 31/437 | 1.45(0.80-2.61) | 1.44(0.80-2.61) | 1.37(0.76-2.49) |
| 33.9-39.4 | 40/437 | 1.98(1.12-3.50) | 1.91(1.08-3.38) | 1.82(1.02-3.24) |
| >39.4 | 49/438 | 2.63(1.50-4.60) | 2.42(1.38-4.24) | 2.22(1.26-3.93) |
| P for trend |  | 0.004 | 0.014 | 0.035 |
| Glycine |  |  |  |  |
| <252.8 | 36/437 |  |  |  |
| 252.8-285.6 | 43/437 | 1.24(0.77-1.99) | 1.26(0.78-2.03) | 1.25(0.77-2.02) |
| 285.6-317.9 | 32/437 | 0.84(0.50-1.40) | 0.84(0.51-1.41) | 0.84(0.50-1.40) |
| >317.9 | 30/439 | 0.75(0.44-1.26) | 0.77(0.46-1.31) | 0.76(0.45-1.29) |
| P for trend |  | 0.201 | 0.213 | 0.212 |
| Glutamic acid |  |  |  |  |
| <41.7 | 18/439 | 1 | 1 | 1 |
| 41.7-51.0 | 31/436 | 1.55(0.85-2.86) | 1.51(0.82-2.78) | 1.46(0.79-2.69) |
| 51.0-67.9 | 45/437 | 2.60(1.47-4.60) | 2.46(1.38-4.37) | 2.34(1.31-4.17) |
| >56.0 | 47/438 | 2.71(1.53-4.78) | 2.50(1.41-4.46) | 2.46(1.38-4.37) |
| P for trend |  | 0.001 | 0.003 | 0.005 |
| Phenylalanine |  |  |  |  |
| <45.6 | 36/439 | 1 | 1 | 1 |
| 45.6-51.2 | 30/436 | 0.76(0.45-1.26) | 0.76(0.46-1.28) | 0.76(0.46-1.28) |
| 51.2-56.0 | 39/438 | 1.01(0.62-1.64) | 1.02(0.63-1.66) | 1.02(0.63-1.66) |
| >56.0 | 43/437 | 1.25(0.78-2.01) | 1.21(0.75-1.94) | 1.12(0.69-1.82) |
| P for trend |  | 0.271 | 0.369 | 0.513 |
| histidine |  |  |  |  |
| <52.5 | 38/437 | 1 | 1 | 1 |
| 52.5-58.2 | 37/438 | 0.72(0.44-1.17) | 0.76(0.46-1.25) | 0.76(0.46-1.25) |
| 58.2-64.3 | 38/437 | 0.55(0.32-0.92) | 0.60(0.35-1.03) | 0.58(0.34-0.99) |
| >64.3 | 28/438 | 0.32(0.18-0.59) | 0.36(0.20-0.67) | 0.36(0.20-0.67) |
| P for trend |  | 0.003 | 0.012 | 0.012 |

Data are RRs (95%CI).

Model 1 was adjusted by demographic covariates including age, gender, BMI, education, alcohol consumption rate, smoking rate and regular exercise habits;

Model 2 was further adjusted by nutritional covariates including dietary energy intake, protein intake, fiber, saturated fatty acid, overall diet quality and AACI;

Model 3 was further adjusted by biochemical indices including total cholesterol, triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and HOMA2-IR;