Table S1. Basic characteristics of participants included and excluded.

|  |  |  |  |
| --- | --- | --- | --- |
| Cohort A |  |  |  |
| Variables, N (%) | Excluded (N=2313) | Included (N=6039) | p |
| Age (y) | 58.02±9.30 | 60.37±8.87 | <.0001 |
| Gender, Male (%) | 845 (36.5) | 2456 (40.7) | <.0001 |
| SBP (mmHg) | 126.71±20.17 | 122.39±17.05 | <.0001 |
| DBP (mmHg) | 79.33±12.45 | 78.32±10.31 | 0.001 |
| BMI (kg/m2) | 24.40±3.53 | 23.87±3.76 | <.0001 |
| WC (cm) | 84.12±8.81 | 83.73±8.71 | 0.073 |
| Fasting glucose (mg/dL) | 98.68±22.84 | 100.75±28.74 | 0.001 |
| TC (mg/dL) | 199.25±37.71 | 199.38±37.93 | 0.886 |
| TG (mg/dL) | 147.56±92.70 | 149.53±103.63 | 0.399 |
| HDL (mg/dL) | 45.51±11.26 | 45.48±11.14 | 0.893 |
| Current smoker, n((%) | 266 (11.5) | 1026 (17.0) | <.0001 |
| Alcohol , n (%) | 989 (42.8) | 2540 (42.1) | 0.239 |
| Exercise, n (%) | 797 (34.5) | 1524 (25.2) | <.0001 |

|  |  |  |  |
| --- | --- | --- | --- |
| Cohort B |  |  |  |
| Variables, N (%) | Excluded (N=2506) | Included (N=7524 | p |
| Age (y) | 52.28±8.95 | 52.29±8.92 | 0.984 |
| Gender, Male (%) | 1210 (48.3) | 3548 (47.2) | 0.169 |
| SBP (mmHg) | 122.00±18.26 | 122.34±18.93 | 0.430 |
| DBP (mmHg) | 80.78±11.56 | 80.65±11.77 | 0.628 |
| BMI (kg/m2) | 18.26±11.01 | 19.52±10.32 | <.0001 |
| WC (cm) | 82.61±9.53 | 82.61±9.01 | 0.992 |
| Fasting glucose (mg/dL) | 88.90±24.46 | 89.93±28.24 | 0.100 |
| TC (mg/dL) | 197.47±36.77 | 198.84±36.95 | 0.109 |
| TG (mg/dL) | 154.06±113.05 | 153.03±108.82 | 0.683 |
| HDL (mg/dL) | 49.61±11.82 | 49.47±11.89 | 0.623 |
| Current smoker, n((%) | 582 (23.25) | 1673 (22.2) | <.0001 |
| Alcohol , n (%) | 1210 (48.3) | 3481 (46.3) | 0.239 |
| Exercise, n (%) | 1698 (67.7) | 5184 (68.8) | 0.311 |

Table S2. Non-significant association of genetic polymorphisms of *HTR2A* gene and risk of hypertension

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Cohort A | |  | | | | | |
| SNP |  | Crude | *p* | Model 1 | *p* | Model 2 | *p* |
| rs1360020 | GG | 1.000 | | 1.000 | | 1.000 | |
|  | GA | 0.946 (0.755-1.186) | 0.667 | 0.951 (0.757-1.195) | 0.667 | 1.011 (0.757-1.349) | 0.943 |
|  | AA | 1.229 (0.929-1.626) | 0.137 | 1.239 (0.934-1.643) | 0.137 | 1.294 (0.908-1.843)) | 0.154 |
|  |  |  | |  | |  | |
| rs4941573 | CC | 1.000 | | 1.000 |  | 1.000 |  |
|  | CT | 0.900 (0.714-1.134) | 0.371 | 0.893 (0.707-1.129) | 0.345 | 0.956 (0.711-1.286) | 0.766 |
|  | TT | 1.233 (0.930-1.634 | 0.146 | 1.239 (0.932-1.647 | 0.140 | 1.218 (0.853-1.740) | 0.277 |
|  |  |  | |  | |  | |
| rs6313 | AA | 1.000 | | 1.000 | | 1.000 | |
|  | AG | 0.924 (0.730-1.168) | 0.507 | 0.919 (0.725-1.165) | 0.483 | 0.960 (0.711-1.297) | 0.791 |
|  | GG | 1.193 (0.902-1.579) | 0.217 | 1.195 (0.900-1.586) | 0.217 | 1.233 (0.865-1.758) | 0.247 |
|  |  |  | |  | |  | |
| rs970 | AA | 1.000 | | 1.000 | | 1.000 | |
|  | AC | 0.906 (0.685-1.198) | 0.488 | 0.923 (0.696-1.223) | 0.577 | 0.867 (0.600-1.254) | 0.449 |
|  | CC | 0.573 (0.036-9.181) | 0.694 | 0.656 (0.041-10.526) | 0.766 | 1.390 (0.035-55.901) | 0.861 |
|  |  |  | |  | |  | |
| rs184 | GG | 1.000 | | 1.000 | | 1.000 | |
|  | AG | 1.017 (0.833-1.241) | 0.869 | 1.029 (0.842-1.258) | 0.781 | 1.114 (0.864-1.438) | 0.405 |
|  | AA | 1.262 (0.836-1.905) | 0.268 | 1.228 (0.811-1.860) | 0.331 | 1.113 (0.666-1.860) | 0.682 |
|  |  |  |  |  |  |  |  |
| rs186 | GG | 1.000 |  | 1.000 |  | 1.000 |  |
|  | GT | 1.033 (0.847-1.261) | 0.747 | 1.048 (0.858-1.281) | 0.645 | 1.157 (0.897-1.492) | 0.262 |
|  | TT | 1.367 (0.905-2.067) | 0.137 | 1.328 (0.876-2.013) | 0.182 | 1.179 (0.701-1.980) | 0.535 |
|  |  |  |  |  |  |  |  |
| rs886 | AA | 1.000 |  | 1.000 |  | 1.000 |  |
|  | GA | 1.000 (0.807-1.240) | 0.999 | 1.011 (0.814-1.255) | 0.924 | 1.037 (0.787-1.366) | 0.797 |
|  | GG | 1.185 (0.886-1.585) | 0.252 | 1.198 (0.893-1.607 | 0.228 | 1.148 (0.794-1.659) | 0.464 |
|  |  |  |  |  |  |  |  |
| rs991 | TT | 1.000 |  | 1.000 |  | 1.000 |  |
|  | TC | 0.867 (0.636-1.183) | 0.368 | 1.126 (0.916-1.384) | 0.261 | 1.179 (0.907-1.533) | 0.219 |
|  | CC | 0.966 (0.711-1.311) | 0.822 | 1.152 (0.842-1.576) | 0.377 | 1.083 (0.731-1.605) | 0.692 |

Model 1 was adjusted for age, gender, smoking status, alcohol consumption, and regular exercise. Model 2 was adjusted for Model 1, and additionally adjusted for systolic blood pressure, total cholesterol and baseline body mass index.

Table S3. Non-significant association of genetic polymorphisms of *HTR2A* gene and risk of hypertension

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Cohort B | |  | | | | | |
| SNP |  | Crude | *p* | Model 1 | *p* | Model 2 | *p* |
| rs977003 | AA | 1.000 | | 1.000 | | 1.000 | |
|  | AC | 1.023 (0.932-1.123) | 0.627 | 1.011 (0.918-1.115) | 0.820 | 1.032 (0.912-1.169) | 0.615 |
|  | CC | 1.065 (0.879-1.290) | 0.523 | 1.065 (0.871-1.301) | 0.539 | 1.120 (0.871-1.440) | 0.379 |
|  |  |  | |  | |  | |
| rs9316232 | TT | 1.000 | | 1.000 | | 1.000 | |
|  | TC | 0.944 (0.850-1.049) | 0.288 | 0.936 (0.838-1.045) | 0.238 | 0.967 (0.840-1.114) | 0.644 |
|  | CC | 1.005 (0.888-1.138) | 0.933 | 1.008 (0.886-1.147) | 0.906 | 1.035 (0.878-1.221) | 0.680 |
|  |  |  | |  | |  | |
| rs582854 | GG | 1.000 | | 1.000 | | 1.000 | |
|  | GT | 0.961 (0.876-1.054) | 0.397 | 0.970 (0.880-1.068) | 0.530 | 0.931 (0.808-1.072) | 0.321 |
|  | TT | 0.991 (0.835-1.176) | 0.919 | 0.974 (0.815-1.165) | 0.773 | 0.832 (0.638-1.084) | 0.174 |
|  |  |  | |  | |  | |
| rs1360020 | AA | 1.000 | | 1.000 | | 1.000 | |
|  | AC | 1.080 (0.973-1.199) | 0.150 | 1.097 (0.984-1.224) | 0.096 | 1.141 (0.973-1.339) | 0.105 |
|  | CC | 0.947 (0.835-1.074) | 0.397 | 0.955 (0.838-1.089) | 0.489 | 0.855 (0.706-1.036) | 0.109 |
|  |  |  | |  | |  | |
| rs2183057 | AA | 1.000 | | 1.000 | | 1.000 | |
|  | AG | 1.088 (0.988-1.199) | 0.087 | 1.094 (0.989-1.211) | 0.081 | 1.121 (0.967-1.300) | 0.131 |
|  | GG | 0.993 (0.871-1.133) | 0.918 | 0.989 (0.862-1.134) | 0.872 | 0.881 (0.719-1.079) | 0.220 |
|  |  |  |  |  |  |  |  |
| rs9590999 | CC | 1.000 |  | 1.000 |  | 1.000 |  |
|  | CT | 1.076 (0.971-1.193) | 0.163 | 1.082 (0.971-1.205) | 0.152 | 1.130 (0.983-1.299) | 0.805 |
|  | TT | 1.000 (0.882-1.133) | 1.011 | 1.011(0.887-1.152) | 0.871 | 1.046 (0.884-1.239) | 0.599 |

Model 1 was adjusted for age, gender, smoking status, alcohol consumption, and regular exercise. Model 2 was adjusted for Model 1, and additionally adjusted for systolic blood pressure, total cholesterol and baseline body mass index.

Table S4. Distribution of *HTR2A* genetic variations according to development of hypertension

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Cohort A (N=6039) | | | | |  |
| SNP | Genotype | No  Hypertension  (N=4621), N (%) | Hypertension  (N=1418), N (%) | *p*-value | adjusted *p*-value\* |
| rs7330636 | GG | 555 (85.9) | 989 (89.2) | 0.092 | 0.107 |
|  | GA | 89 (13.8) | 115 (10.4) |  |  |
|  | AA | 2 (0.3) | 5 (0.5) |  |  |
| rs9590999 | CC | 167 (25.1) | 335 (29.2) | 0.056 | 0.087 |
|  | CT | 354 (53.2) | 545 (47.6) |  |  |
|  | TT | 144 (21.7) | 266 (23.2) |  |  |
| rs2183057 | AA | 253 (38.0) | 401 (34.9) | 0.026 | 0.087 |
|  | AG | 331 (49.7) | 553 (48.1) |  |  |
|  | GG | 82 (12.3) | 195 (17.0) |  |  |
| rs4942595 | TT | 168 (25.2) | 339 (29.5) | 0.041 | 0.087 |
|  | TC | 354 (53.1) | 541 (47.1) |  |  |
|  | CC | 145 (21.7) | 269 (23.4) |  |  |
| rs4531630 | AA | 168 (25.3) | 338 (29.6) | 0.062 | 0.087 |
|  | AG | 344 (51.7) | 584 (51.1) |  |  |
|  | GG | 153 (23.0) | 221 (12.2) |  |  |
| rs17069883 | AA | 197 (29.5) | 287 (25.0) | 0.041 | 0.087 |
|  | AC | 341 (51.1) | 594 (51.7) |  |  |
|  | CC | 129 (19.3) | 268 (23.3) |  |  |
| rs4942578 | CC | 258 (38.7) | 431 (37.5) | 0.225 | 0.225 |
|  | CA | 320 (48.0) | 530 (46.1) |  |  |
|  | AA | 89 (13.3) | 188 (16.4) |  |  |

Cohort B (N=7524) (N=4999) (N=2525)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| rs4942578 | CC | 1834 (39.2) | 949 (40.2) | 0.605 | 0.605 |
|  | CA | 2171 (46.5) | 1089 (46.2) |  |  |
|  | AA | 668 (14.3) | 320 (13.6) |  |  |
| rs985933 | AA | 1526 (32.8) | 781 (33.2) | 0.496 | 0.595 |
|  | AG | 2257 (48.5) | 1154 (49.1) |  |  |
|  | GG | 875 (18.8) | 414 (17.6) |  |  |
| rs4941573 | TT | 1184 (25.4) | 565 (24.0) | 0.196 | 0.389 |
|  | TC | 2314 (49.6) | 1221 (51.8) |  |  |
|  | CC | 1172 (25.1) | 571 (24.2) |  |  |
| rs6313 | GG | 1229 (26.3) | 584 (24.8) | 0.153 | 0.389 |
|  | GA | 2301 (49.2) | 1218 (51.7) |  |  |
|  | AA | 1143 (24.5) | 556 (23.6) |  |  |
| rs1328685 | TT | 4031 (86.3) | 2054 (87.1) | 0.259 | 0.389 |
|  | TC | 611 (13.1) | 295 (12.5) |  |  |
|  | CC | 31 (0.7) | 9 (0.4) |  |  |
| rs2567675 | TT | 2823 (60.4) | 1483 (62.9) | 0.124 | 0.389 |
|  | TC | 1616 (34.6) | 762 (32.3) |  |  |
|  | CC | 234 (5.0) | 112 (4.8) |  |  |

\*, adjusted p-value was calculated with the Benjamini-Hochberg method

Table S5. Association of genetic polymorphisms of *HTR2A* gene and risk of hypertension

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Cohort A | | Crude | | Model 1 | | Model 2 | |
| SNP |  | OR (adj. 95% CI)*§* | *p (adj. p)§* | OR (adj. 95% CI)\* | *p (adj. p)* | OR (adj. 95% CI)# | *p (adj. p)* |
| rs7330636 | GG | 1.000 | | 1.000 | | 1.000 | |
|  | GA | 0.725 (0.467-1.128) | 0.033 (0.077) | 0.725 (0.463-1.134) | 0.034 (0.079) | 0.644 (0.330-1.255) | 0.026 (0.098) |
|  | AA | 1.403 (0.638-3.087) | 0.686 (0.800) | 1.520 (0.226-10.240) | 0.619 (0.667) | 1.415 (0.451-4.439) | 0.724 (0.724) |
| rs9590999 | CC | 1.000 | | 1.000 |  | 1.000 |  |
|  | CT | 0.767 (0.545-1.080) | 0.023 (0.064) | 0.757 (0.542-1.056) | 0.018 (0.050) | 0.738 (0.465-1.170) | 0.042 (0.098) |
|  | TT | 0.921 (0.829-1.024) | 0.921 (0.936) | 0.914 (0.552-1.512) | 0.522 (0.637) | 0.880 (0.289-2.674) | 0.463 (0.589) |
| rs2183057 | AA | 1.000 | | 1.000 | | 1.000 | |
|  | AG | 1.054 (0.927-1.200) | 0.620 (0.789) | 1.067 (0.742-1.535) | 0.546 (0.637) | 1.131 (0.003-370.600) | 0.369 (0.517) |
|  | GG | 1.500 (0.889-2.534) | 0.009 (0.064) | 1.500 (0.924-2.432) | 0.009 (0.050) | 1.448 (0.797-2.628) | 0.056 (0.112) |
| rs4942595 | TT | 1.000 | | 1.000 | | 1.000 | |
|  | TC | 0.757 (0.529-1.084) | 0.017 (0.064) | 0.748 (0.528-1.058) | 0.013 (0.050) | 0.739 (0.467-1.169) | 0.042 (0.098) |
|  | CC | 0.919 (0.733-1.153) | 0.547 (0.766) | 0.911 (0.542-1.533) | 0.510 (0.637) | 0.907 (0.585-1.404) | 0.574 (0.670) |
| rs4531630 | AA | 1.000 | | 1.000 | | 1.000 | |
|  | AG | 0.844 (0.544-1.309) | 0.144 (0.224) | 0.834 (0.557-1.250) | 0.122 (0.190) | 0.792 (0.459-1.367) | 0.115 (0.201) |
|  | GG | 0.718 (0.469-1.101) | 0.019 (0.064) | 0.705 (0.465-1.070) | 0.015 (0.050) | 0.658 (0.349-1.241) | 0.021 (0.098) |
| rs17069883 | AA | 1.000 |  | 1.000 |  | 1.000 |  |
|  | AC | 1.196 (0.774-1.848) | 0.119 (0.210) | 1.197 (0.801-1.789) | 0.121 (0.190) | 1.197 (0.486-2.944) | 0.224 (0.348) |
|  | CC | 1.426 (0.902-2.255) | 0.012 (0.064) | 1.449 (0.930-2.257) | 0.009 (0.050) | 1.447 (0.827-2.530) | 0.040 (0.098) |
| rs4942578 | CC | 1.000 |  | 1.000 |  | 1.000 |  |
|  | CA | 0.991 (0.980-1.002) | 0.935 (0.936) | 1.007 (0.999-1.015) | 0.950 (0.950) | 1.054 (0.885-1.256) | 0.696 (0.724) |
|  | AA | 1.264 (0.715-2.239) | 0.120 (0.210) | 1.288 (0.732-2.264) | 0.096 (0.190) | 1.562 (0.794-3.071) | 0.020 (0.098) |

OR, odds ratio; 95% CI, 95% confidential interval.

\*,Model 1 was adjusted for gender, smoking status, alcohol consumption, regular exercise and age.

#,Model 2 was adjusted for Model 1 and systolic blood pressure, total cholesterol and baseline body mass index additionally.

*§*, adjusted p-value and 95% CI were corrected with Hochberg step-up method.

Table S6. Association of genetic polymorphisms of *HTR2A* gene and risk of hypertension

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Cohort B | | Crude | | | Model 1 | | | Model 2 | | |
| SNP |  | OR (adj. 95% CI)*§* | *P (adj. p)§* | OR (adj. 95% CI)\* | | *P (adj. p)* | OR (adj. 95% CI)# | |  | *P (adj. p)* |
| rs4942578 | CC | 1.000 | | 1.000 | | | 1.000 | | | |
|  | CA | 0.969 (0.889-1.057) | 0.569 (0.759) | 0.979 (0.927-1.034) | | 0.710 (0.775) | 0.894 (0.576-1.387) | | | 0.180 (0.309) |
|  | AA | 0.926 (0.636-1.348) | 0.328 (0.656) | 0.949 (0.826-1.088) | | 0.521 (0.775) | 0.735 (0.521-1.038) | | | 0.010 (0.040) |
| rs985933 | AA | 1.000 | | 1.000 | | | 1.000 | | | |
|  | AG | 0.999 (0.998-1.000) | 0.986 (0.986) | 1.013 (0.986-1.041) | | 0.824 (0.824) | 1.057 (0.559-2.000) | | | 0.521 (0.568) |
|  | GG | 0.924 (0.628-1.359) | 0.289 (0.656) | 0.922 (0.522-1.628) | | 0.293 (0.610) | 0.789 (0.572-1.088) | | | 0.037 (0.074) |
| rs4941573 | TT | 1.000 | | 1.000 | | | 1.000 | | | |
|  | TC | 1.106 (0.445-2.751) | 0.106 (0.414) | 1.137 (0.851-1.516) | | 0.048 (0.192) | 1.327 (1.019-1.729) | | | 0.003 (0.018) |
|  | CC | 1.021 (0.981-1.064) | 0.774 (0.844) | 1.033 (0.950-1.122) | | 0.670 (0.775) | 1.113 (0.493-2.513) | | | 0.332 (0.398) |
| rs6313 | GG | 1.000 | | 1.000 | | | 1.000 | | | |
|  | GA | 1.114 (0.421-2.951) | 0.079 (0.414) | 1.157 (0.890-1.505) | | 0.023 (0.138) | 1.365 (1.042-1.788) | | | 0.001 (0.012) |
|  | AA | 1.024 (0.979-1.070) | 0.745 (0.844) | 1.042 (0.937-1.159) | | 0.586 (0.775) | 1.130 (0.589-2.173) | | | 0.267 (0.356) |
| rs1328685 | TT | 1.000 | | 1.000 | | | 1.000 | | | |
|  | TC | 0.948 (0.788-1.139) | 0.478 (0.717) | 0.939 (0.769-1.146) | | 0.427 (0.732) | 0.982 (0.952-1.013) | | | 0.875 (0.875) |
|  | CC | 0.570 (0.004-91.460) | 0.138 (0.414) | 0.544 (0.018-16.396) | | 0.121 (0.363) | 0.292 (0.057-1.492) | | | 0.029 (0.070) |
| rs2567675 | TT | 1.000 |  | 1.000 | |  | 1.000 | | |  |
|  | TC | 0.898 (0.339-2.378) | 0.047 (0.414) | 0.868 (0.672-1.120) | | 0.012 (0.138) | 0.832 (0.653-1.061) | | | 0.027 (0.070) |
|  | CC | 0.911 (0.663-1.252) | 0.435 (0.717) | 0.880 (0.361-2.147) | | 0.305 (0.610) | 0.799 (0.311-2.055) | | | 0.214 (0.321) |

OR, odds ratio; 95% CI, 95% confidential interval.

\*,Model 1 was adjusted for gender, smoking status, alcohol consumption, regular exercise and age.

#,Model 2 was adjusted for Model 1 and systolic blood pressure, total cholesterol and baseline body mass index additionally.

*§*, adjusted p-value and 95% CI were corrected with Hochberg step-up method.