Supplemental Table 1. Baseline characteristics of the study subjects.

|  |  |  |  |
| --- | --- | --- | --- |
| Variables | Inclusion (n=8,443,351) | Exclusion (n=6,724,670) | Total (n=15,168,021) |
| Age (years) | 55.84±10.89 | 52.69±10.18 | 54.79±10.76 |
| Sex (Male, n) | 4182836 (49.54) | 3063760 (45.56) | 7312503 (48.21) |
| Height (cm) | 161.36±8.93 | 161.66±8.58 | 161.46±8.82 |
| Weight (kg) | 63.07±10.70 | 61.97±10.59 | 62.70±10.68 |
| BMI (kg/m2) | 24.15±3.08 | 23.64±2.98 | 23.98±3.06 |
| WC (cm) | 81.78±8.64 | 79.95±8.58 | 81.17±8.66 |
| SBP (mmHg) | 125.09±15.62 | 122.3±15.12 | 124.16±15.51 |
| DBP (mmHg) | 77.47±10.12 | 76.17±10.20 | 77.04±10.16 |
| Fasting glucose level (mg/dL) | 101.84±26.66 | 96.59±20.12 | 100.09±24.79 |
| Total cholesterol level (mg/dL) | 198.17±37.27 | 200.59±36.82 | 198.98±37.14 |
| Rural area (n, %) | 4718145 (55.88) | 3499518 (52.04) | 8281739 (54.60) |
| Current Smoker (n, %) | 1647298 (19.51) | 1387299 (20.63) | 3015403 (19.88) |
| Heavy drinker (n, %) | 515889 (6.11) | 412895 (6.14) | 928283 (6.12) |
| Regular exercise (n, %) | 4141464 (49.05) | 3370405 (50.12) | 7493002 (49.40) |
| Obesity (n, %) | 3086889 (36.56) | 2021436 (30.06) | 5216282 (34.39) |
| Dyslipidemia (n, %) | 2256908 (26.73) | 1246081 (18.53) | 3638808 (23.99) |
| Chronic kidney disease (n, %) | 710086 (8.41) | 435759 (6.48) | 1178555 (7.77) |
| Cardiovascular disease (n, %) | 348710 (4.13) | 335561 (4.99) | 630990 (4.16) |
| Cerebrovascular disease (n, %) | 163801(1.94) | 163409 (2.43) | 297293 (1.96) |

IFG, impaired fasting glucose; DM, diabetes mellitus; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Supplemental Table 2. Mortality of the study subjects

|  |  |  |  |
| --- | --- | --- | --- |
| Group | Person-years | Events (n) | Incidence per 1,000 PY |
|
| Non-DM vs. DM |  |  |  |
| Non-DM | 41773272.48 | 252817 | 6.05 |
| DM | 7302876.27 | 109743 | 15.03 |
| All subgroups |  |  |  |
| Non-DM | 29331717.53 | 165588 | 5.65 |
| IFG | 12276937.07 | 87229 | 7.11 |
| DM <5 yrs | 4345219.48 | 52570 | 12.09 |
| DM ≥5 yrs | 3122274.66 | 57173 | 18.31 |

PY, person-years; DM, diabetes mellitus; IFG, impaired fasting glucose.

Supplemental Table 3. Comparison of the incidence of Parkinson’s disease according to the subjects’ baseline diabetes status and changes during the observational period.

|  |  |  |  |
| --- | --- | --- | --- |
| Group | HR (95% CI) | | |
| Model 1\* | Model 2\*\* | Model 3\*\*\* |
| Non-DM vs. DM |  |  |  |
| Non-DM | 1.000 (ref.) | 1.000 (ref.) | 1.000 (ref.) |
| DM | 1.813 (1.780–1.847) | 1.267 (1.243–1.291) | 1.245 (1.222–1.269) |
| All subgroups |  |  |  |
| Non-DM | 1.000 (ref.) | 1.000 (ref.) | 1.000 (ref.) |
| IFG | 1.229 (1.205–1.254) | 1.088 (1.066–1.110) | 1.074 (1.053–1.096) |
| DM <5 yrs | 1.788 (1.743–1.834) | 1.204 (1.174–1.235) | 1.174 (1.144–1.204) |
| DM ≥5 yrs | 2.905 (2.820–2.993) | 1.632 (1.584–1.682) | 1.597 (1.550–1.646) |

\* Model 1: non-adjusted; \*\*Model 2: adjusted for age and sex; \*\*\*Model 3: adjusted for factors in Model 2 and body mass index, smoking, drinking, and physical activity.

PY, person-years; CI, confidence interval; DM, diabetes mellitus; IFG, impaired fasting glucose

Supplemental Table 4. Comparison of the incidence of Parkinson’s disease according to the subjects’ diabetes status. The results were analyzed using only the outcomes that occurred after 3 years in the baseline to identify the lagged effects.

|  |  |  |  |
| --- | --- | --- | --- |
| Group | HR (95% CI) | | |
| Model 1\* | Model 2\*\* | Model 3\*\*\* |
| Non-DM vs. DM |  |  |  |
| Non-DM | 1.000 (ref.) | 1.000 (ref.) | 1.000 (ref.) |
| DM | 2.000 (1.942–2.060) | 1.371 (1.331–1.412) | 1.352 (1.312–1.393) |
| All subgroups |  |  |  |
| Non-DM | 1.000 (ref.) | 1.000 (ref.) | 1.000 (ref.) |
| IFG | 1.212 (1.174–1.251) | 1.047 (1.014–1.081) | 1.034 (1.002–1.068) |
| DM <5 yrs | 1.562 (1.474–1.654) | 1.153 (1.087–1.223) | 1.135 (1.069–1.204) |
| DM ≥5 yrs | 2.861 (2.753–2.974) | 1.616 (1.555–1.680) | 1.586 (1.525–1.649) |

\* Model 1: non-adjusted; \*\*Model 2: adjusted for age and sex; \*\*\*Model 3: adjusted for factors in Model 2 and body mass index, smoking, drinking, and physical activity.

PY, person-years; CI, confidence interval; DM, diabetes mellitus; IFG, impaired fasting glucose

Supplemental Table 5. Comparison of Parkinson’s disease incidence during the observation period based on comorbidity and diabetes mellitus status of subjects.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Comorbidity | Status | DM | Subjects (n) | Person-years | Events (n) | Incidence per 1,000 PY | HR (95% CI) | | |
| Model 1\*\* | Model 2\*\*\* | Model 3\*\*\*\* |
| Cardiovascular disease | No | No | 6896863 | 40234558.12 | 21228 | 0.52761 | 1.000 (ref.) | 1.000 (ref.) | 1.000 (ref.) |
| Yes | 267790 | 1538714.36 | 2071 | 1.34593 | 2.548 (2.435–2.665) | 1.380 (1.318–1.444) | 1.356 (1.296–1.419) |
| Yes | No | 1197661 | 6852492.54 | 7434 | 1.08486 | 2.059 (2.005–2.114) | 1.403 (1.366–1.440) | 1.388 (1.351–1.425) |
| Yes | 81037 | 450383.73 | 844 | 1.87396 | 3.570 (3.333–3.825) | 1.670 (1.559–1.790) | 1.622 (1.514–1.738) |
| Cerebrovascular disease | No | No | 7035646 | 41033759.51 | 22277 | 0.54289 | 1.000 (ref.) | 1.000 (ref.) | 1.000 (ref.) |
| Yes | 129007 | 739512.97 | 1022 | 1.38199 | 2.540 (2.385–2.704) | 1.589 (1.492–1.692) | 1.565 (1.470–1.667) |
| Yes | No | 1243830 | 7112942.19 | 7889 | 1.10911 | 2.046 (1.994–2.099) | 1.397 (1.361–1.433) | 1.380 (1.345–1.416) |
| Yes | 34868 | 189934.07 | 389 | 2.04808 | 3.802 (3.439–4.202) | 1.873 (1.694–2.071) | 1.816 (1.643–2.008) |
| Chronic kidney disease\* | ≥90 | No | 2391780 | 13954681.82 | 5247 | 0.376 | 1.000 (ref.) | 1.000 (ref.) | 1.000 (ref.) |
| Yes | 4235237 | 24725398.35 | 14404 | 0.58256 | 1.548 (1.500–1.598) | 1.127 (1.092–1.164) | 1.115 (1.080–1.151) |
| 90-60 | No | 389062 | 2233007.1 | 2960 | 1.32557 | 3.520 (3.365–3.682) | 1.283 (1.225–1.344) | 1.260 (1.203–1.320) |
| Yes | 148574 | 860185.21 | 688 | 0.79983 | 2.118 (1.956–2.293) | 1.237 (1.142–1.340) | 1.218 (1.124–1.319) |
| 60-45 | No | 401177 | 2311577.14 | 1555 | 0.6727 | 1.790 (1.692–1.895) | 1.341 (1.267–1.419) | 1.334 (1.260–1.411) |
| Yes | 705094 | 4043405.47 | 4736 | 1.17129 | 3.116 (2.996–3.241) | 1.545 (1.485–1.608) | 1.512 (1.453–1.574) |
| <45 | No | 128434 | 714711.24 | 1495 | 2.09175 | 5.582 (5.270–5.912) | 1.756 (1.656–1.862) | 1.704 (1.607–1.808) |
| Yes | 43993 | 233182.42 | 492 | 2.10994 | 5.667 (5.167–6.215) | 2.004 (1.826–2.199) | 1.934 (1.762–2.123) |

\*Chronic kidney disease status was determined based on the eGFR (mL/min/1.73 m2)calculated using the MDRD Study equation.

\*\*Model 1: non-adjusted; \*\*\*Model 2: adjusted for age and sex; \*\*\*\*Model 3: adjusted for factors in Model 2 and body mass index, smoking, drinking, and physical activity.

PY, person-years; CI, confidence interval; DM, diabetes mellitus; IFG, impaired fasting glucose.

Supplemental Table 6. Comparison of Parkinson’s disease incidence by anti-diabetic medication in diabetes subjects.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Medication | Status | Subjects (n) | Person-years | Events (n) | Incidence per 1,000 PY | HR (95% CI) | | |
| Model 1\* | Model 2\*\* | Model 3\*\*\* |
| Insulin | No | 1186891 | 6799848.32 | 7243 | 1.06517 | 1.000 (ref.) | 1.000 (ref.) | 1.000 (ref.) |
| Yes | 121082 | 665955.66 | 1266 | 1.90103 | 1.790 (1.686–1.900) | 1.611 (1.518–1.710) | 1.599 (1.506–1.698) |
| Sulfonylurea | No | 597315 | 3396533.73 | 3102 | 0.91328 | 1.000 (ref.) | 1.000 (ref.) | 1.000 (ref.) |
| Yes | 710658 | 4069270.25 | 5407 | 1.32874 | 1.449 (1.387–1.515) | 1.194 (1.142–1.248) | 1.193 (1.141–1.247) |
| Metformin | No | 663052 | 3762134.52 | 3710 | 0.98614 | 1.000 (ref.) | 1.000 (ref.) | 1.000 (ref.) |
| Yes | 644921 | 3703669.47 | 4799 | 1.29574 | 1.309 (1.254–1.366) | 1.224 (1.173–1.278) | 1.221 (1.100–1.274) |
| Meglitinide | No | 1265165 | 7225212.18 | 8107 | 1.12204 | 1.000 (ref.) | 1.000 (ref.) | 1.000 (ref.) |
| Yes | 42808 | 240591.8 | 402 | 1.67088 | 1.490 (1.348–1.647) | 1.355 (1.226–1.497) | 1.347 (1.219–1.489) |
| Thiazolidinedione | No | 1186598 | 6768357.85 | 7658 | 1.13144 | 1.000 (ref.) | 1.000 (ref.) | 1.000 (ref.) |
| Yes | 121375 | 697446.13 | 851 | 1.22017 | 1.077 (1.003–1.156) | 1.159 (1.080–1.244) | 1.157 (1.078–1.242) |
| DPP4 inhibitor | No | 1227822 | 7003759.1 | 7956 | 1.13596 | 1.000 (ref.) | 1.000 (ref.) | 1.000 (ref.) |
| Yes | 80151 | 462044.88 | 553 | 1.19685 | 1.053 (0.966–1.148) | 1.210 (1.110–1.319) | 1.204 (1.104–1.312) |
| Alpha glucosidase inhibitor | No | 1103106 | 6304471.24 | 6711 | 1.06448 | 1.000 (ref.) | 1.000 (ref.) | 1.000 (ref.) |
| Yes | 204867 | 1161332.74 | 1798 | 1.54822 | 1.454 (1.380–1.532) | 1.262 (1.198–1.330) | 1.261 (1.197–1.329) |

\*Model 1: non-adjusted; \*\*Model 2: adjusted for age and sex; \*\*\*Model 3: adjusted for factors in Model 2 and body mass index, smoking, drinking, and physical activity.

PY, person-years; CI, confidence interval; DPP4, dipeptidyl peptidase 4.