**Legends of Supplemental Figures**

**Supplemental Figure S1.** Flow chart of study population

**Supplemental Figure S2.** Kaplan-Meier curves for incidence probabilities of myocardial infarction (MI), stroke, and all-cause mortality with respect to quartiles of variability independent of the mean for body weight. The incidence probabilities significantly increased in the higher quartile groups (all log rank P <0.001).

**Supplemental Table S1. HRs (95% CIs) of study outcomes with respect to quartiles of indices for body weight variability among patients with type 2 diabetes**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | n | Event | Person-years | IR\* | HR (95% CI) |  |  |
|  |  |  |  |  | Model 1† | Model 2‡ | Model 3§ |
| Standard deviation |  | |  |  |  |  |  |
| Myocardial infarction |  | |  |  |  |  |  |
| Q1 | 155,056 | 3725 | 1,194,646 | 3.12 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 157,613 | 3839 | 1,221,030 | 3.14 | 1.06 (1.02–1.11) | 1.05 (1.00–1.10) | 1.05 (1.00–1.10) |
| Q3 | 158,322 | 4114 | 1,215,316 | 3.39 | 1.14 (1.09–1.19) | 1.10 (1.05–1.15) | 1.10 (1.05–1.15) |
| Q4 | 153,246 | 4154 | 1,161,766 | 3.58 | 1.24 (1.19–1.30) | 1.15 (1.10–1.20) | 1.15 (1.10–1.21) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| Stroke |  | |  |  |  |  |  |
| Q1 | 155,056 | 5909 | 1,187,587 | 4.98 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 157,613 | 5979 | 1,213,351 | 4.93 | 1.07 (1.03–1.11) | 1.06 (1.02–1.10) | 1.06 (1.02–1.10) |
| Q3 | 158,322 | 6369 | 1,207,839 | 5.27 | 1.12 (1.08–1.16) | 1.09 (1.05–1.13) | 1.09 (1.05–1.13) |
| Q4 | 153,246 | 6781 | 1,152,938 | 5.88 | 1.29 (1.24–1.33) | 1.21 (1.17–1.25) | 1.21 (1.17–1.26) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| All-cause mortality |  | |  |  |  |  |  |
| Q1 | 155,056 | 9518 | 1,206,293 | 7.89 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 157,613 | 9800 | 1,232,921 | 7.95 | 1.09 (1.06–1.13) | 1.08 (1.05–1.11) | 1.08 (1.05–1.11) |
| Q3 | 158,322 | 11,414 | 1,228,044 | 9.29 | 1.24 (1.21–1.28) | 1.21 (1.18–1.24) | 1.21 (1.18–1.25) |
| Q4 | 153,246 | 13,984 | 1,173,993 | 11.91 | 1.63 (1.59–1.67) | 1.53 (1.49–1.57) | 1.53 (1.49–1.57) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| Coefficient of variation |  |  |  |  |  |  |  |
| Myocardial infarction |  |  |  |  |  |  |  |
| Q1 | 156,124 | 3633 | 1,206,047 | 3.01 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 156,197 | 3745 | 1,209,923 | 3.10 | 1.06 (1.01–1.11) | 1.04 (1.00–1.09) | 1.04 (1.00–1.09) |
| Q3 | 155,848 | 3969 | 1,200,133 | 3.31 | 1.13 (1.08–1.18) | 1.09 (1.04–1.14) | 1.09 (1.04–1.14) |
| Q4 | 156,068 | 4485 | 1,176,655 | 3.81 | 1.24 (1.19–1.30) | 1.16 (1.11–1.21) | 1.16 (1.11–1.21) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| Stroke |  |  |  |  |  |  |  |
| Q1 | 156,124 | 5588 | 1,199,824 | 4.66 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 156,197 | 5723 | 1,202,844 | 4.76 | 1.06 (1.02–1.10) | 1.05 (1.01–1.08) | 1.04 (1.01–1.08) |
| Q3 | 155,848 | 6197 | 1,192,488 | 5.20 | 1.14 (1.10–1.18) | 1.11 (1.07–1.15) | 1.09 (1.07–1.15) |
| Q4 | 156,068 | 7530 | 1,166,559 | 6.45 | 1.30 (1.26–1.35) | 1.23 (1.19–1.28) | 1.22 (1.18–1.27) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| All-cause mortality |  |  |  |  |  |  |  |
| Q1 | 156,124 | 8719 | 1,217,736 | 7.16 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 156,197 | 9382 | 1,221,466 | 7.68 | 1.13 (1.10–1.16) | 1.11 (1.08–1.15) | 1.09 (1.06–1.12) |
| Q3 | 155,848 | 10,595 | 1,212,331 | 8.74 | 1.28 (1.24–1.31) | 1.23 (1.20–1.27) | 1.20 (1.17–1.23) |
| Q4 | 156,068 | 16,020 | 1,189,718 | 13.47 | 1.81 (1.76–1.85) | 1.68 (1.64–1.72) | 1.57 (1.53–1.62) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| Average real variability |  |  |  |  |  |  |  |
| Myocardial infarction |  |  |  |  |  |  |  |
| Q1 | 160,355 | 3820 | 1,237,724 | 3.09 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 125,527 | 2976 | 976,514 | 3.05 | 1.06 (1.01–1.12) | 1.05 (1.00–1.11) | 1.05 (1.00–1.11) |
| Q3 | 166,230 | 4203 | 1,277,919 | 3.29 | 1.10 (1.06–1.15) | 1.08 (1.03–1.12) | 1.08 (1.03–1.12) |
| Q4 | 172,125 | 4833 | 1,300,601 | 3.72 | 1.24 (1.19–1.29) | 1.16 (1.11–1.21) | 1.16 (1.11–1.21) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| Stroke |  |  |  |  |  |  |  |
| Q1 | 160,355 | 6153 | 1,229,859 | 5.00 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 125,527 | 4493 | 971,312 | 4.63 | 1.03 (0.99–1.07) | 1.02 (0.98–1.06) | 1.02 (0.98–1.06) |
| Q3 | 166,230 | 6551 | 1,269,999 | 5.16 | 1.08 (1.04–1.11) | 1.05 (1.02–1.09) | 1.05 (1.02–1.09) |
| Q4 | 172,125 | 7841 | 1,290,545 | 6.08 | 1.23 (1.19–1.27) | 1.16 (1.12–1.20) | 1.17 (1.13–1.21) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| All-cause mortality |  |  |  |  |  |  |  |
| Q1 | 160,355 | 9735 | 1,249,726 | 7.79 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 125,527 | 7506 | 985,780 | 7.61 | 1.10 (1.07–1.13) | 1.09 (1.05–1.12) | 1.08 (1.05–1.12) |
| Q3 | 166,230 | 11,562 | 1,290,836 | 8.96 | 1.20 (1.17–1.23) | 1.17 (1.14–1.20) | 1.18 (1.14–1.21) |
| Q4 | 172,125 | 15,913 | 1,314,910 | 12.10 | 1.55 (1.51–1.59) | 1.46 (1.42–1.50) | 1.47 (1.44–1.51) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |

Abbreviations: HR, hazard ratio; Q, quartile.

\* Incidence per 1000 person-years

† Model 1 was adjusted for age and sex.

‡ Model 2 was adjusted for age, sex, smoking status, alcohol consumption, physical activity, income, hypertension, dyslipidemia, chronic kidney disease, insulin use, and number of oral antidiabetic agents used.

§ Model 3 was adjusted for age, sex, smoking status, alcohol consumption, physical activity, income, hypertension, dyslipidemia, chronic kidney disease, insulin use, number of oral antidiabetic agents used, and baseline BMI.

**Supplemental Table S2. HRs (95% CIs) of study outcomes with 3-year of lag time with respect to quartiles of VIM for body weight among patients with type 2 diabetes**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | n | Event | Person-years | IR\* | HR (95% CI) |  |  |
|  |  |  |  |  | Model 1† | Model 2‡ | Model 3§ |
| **Myocardial infarction** |  | |  |  |  |  |  |
| Q1 | 151,209 | 2413 | 733,204 | 3.29 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 150,961 | 2497 | 736,368 | 3.39 | 1.06 (1.00–1.12) | 1.05 (0.99–1.11) | 1.05 (0.99–1.11) |
| Q3 | 150,720 | 2620 | 731,141 | 3.58 | 1.12 (1.06–1.19) | 1.09 (1.03–1.15) | 1.09 (1.03–1.15) |
| Q4 | 148,266 | 2847 | 707,018 | 4.03 | 1.23 (1.16–1.30) | 1.15 (1.09–1.22) | 1.15 (1.09–1.22) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| **Stroke** |  | |  |  |  |  |  |
| Q1 | 151,209 | 3686 | 730,379 | 5.05 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 150,961 | 3683 | 733,532 | 5.02 | 1.03 (0.98–1.08) | 1.02 (0.97–1.06) | 1.02 (0.97–1.06) |
| Q3 | 150,720 | 3977 | 727,889 | 5.46 | 1.12 (1.07–1.17) | 1.09 (1.05–1.14) | 1.09 (1.04–1.14) |
| Q4 | 148,266 | 4605 | 703,093 | 6.55 | 1.26 (1.21–1.32) | 1.20 (1.15–1.26) | 1.20 (1.15–1.25) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| **All-cause mortality** |  | |  |  |  |  |  |
| Q1 | 151,209 | 6343 | 738,084 | 8.59 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 150,961 | 6789 | 741,129 | 9.16 | 1.12 (1.08–1.16) | 1.10 (1.07–1.14) | 1.09 (1.05–1.12) |
| Q3 | 150,720 | 7525 | 736,193 | 10.22 | 1.25 (1.21–1.30) | 1.22 (1.18–1.26) | 1.19 (1.15–1.23) |
| Q4 | 148,266 | 10,577 | 712,297 | 14.85 | 1.69 (1.64–1.74) | 1.59 (1.54–1.64) | 1.52 (1.47–1.57) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |

Abbreviations: HR, hazard ratio; VIM, variability independent of the mean; Q, quartile.

\* Incidence per 1000 person-years

† Model 1 was adjusted for age and sex.

‡ Model 2 was adjusted for age, sex, smoking status, alcohol consumption, physical activity, income, hypertension, dyslipidemia, chronic kidney disease, insulin use, and number of oral antidiabetic agents used.

§ Model 3 was adjusted for age, sex, smoking status, alcohol consumption, physical activity, income, hypertension, dyslipidemia, chronic kidney disease, insulin use, number of oral antidiabetic agents used, and baseline BMI.

**Supplemental Table S3. HRs (95% CIs) of study outcomes by quartiles of VIM for body weight according to insulin use among patients with type 2 diabetes**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | n | Event | Person-years | IR\* | HR (95% CI) |  |  |
|  |  |  |  |  | Model 1† | Model 2‡ | Model 3§ |
| **Myocardial infarction** |  | |  |  |  |  |  |
| Insulin use (-) |  |  |  |  |  |  |  |
| Q1 | 147,250 | 3181 | 1,140,766 | 2.79 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 146,679 | 3288 | 1,139,597 | 2.89 | 1.06 (1.01–1.12) | 1.05 (1.00–1.11) | 1.05 (1.00–1.11) |
| Q3 | 145,507 | 3442 | 1,124,697 | 3.06 | 1.13 (1.08–1.19) | 1.11 (1.06–1.17) | 1.11 (1.06–1.17) |
| Q4 | 140,826 | 3604 | 1,069,976 | 3.37 | 1.21 (1.15–1.27) | 1.17 (1.11–1.22) | 1.17 (1.11–1.23) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| Insulin use (+) |  |  |  |  |  |  |  |
| Q1 | 8653 | 468 | 63,442 | 7.38 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 9328 | 456 | 68,459 | 6.66 | 0.91 (0.80–1.03) | 0.91 (0.80–1.04) | 0.91 (0.80–1.03) |
| Q3 | 10,760 | 556 | 78,528 | 7.08 | 0.99 (0.87–1.12) | 0.99 (0.87–1.12) | 0.98 (0.87–1.11) |
| Q4 | 15,234 | 837 | 107,292 | 7.80 | 1.07 (0.96–1.20) | 1.06 (0.94–1.18) | 1.04 (0.93–1.17) |
| P for trend |  |  |  |  | 0.062 | 0.199 | 0.434 |
| P for interaction |  |  |  |  | 0.127 | 0.158 | 0.158 |
| **Stroke** |  |  |  |  |  |  |  |
| Insulin use (-) |  |  |  |  |  |  |  |
| Q1 | 147,250 | 4957 | 1,135,185 | 4.37 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 146,679 | 5064 | 1,133,429 | 4.47 | 1.06 (1.02–1.10) | 1.05 (1.01–1.09) | 1.05 (1.01–1.09) |
| Q3 | 145,507 | 5367 | 1,118,168 | 4.80 | 1.13 (1.09–1.18) | 1.11 (1.07–1.16) | 1.11 (1.07–1.15) |
| Q4 | 140,826 | 6119 | 1,061,603 | 5.76 | 1.27 (1.22–1.32) | 1.23 (1.19–1.28) | 1.23 (1.18–1.27) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| Insulin use (+) |  |  |  |  |  |  |  |
| Q1 | 8653 | 668 | 62,699 | 10.65 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 9328 | 706 | 67,442 | 10.47 | 0.99 (0.89–1.10) | 0.99 (0.89–1.10) | 0.98 (0.88–1.09) |
| Q3 | 10,760 | 834 | 77,514 | 10.76 | 1.04 (0.94–1.15) | 1.04 (0.94–1.15) | 1.03 (0.93–1.14) |
| Q4 | 15,234 | 1323 | 105,675 | 12.52 | 1.18 (1.08–1.30) | 1.17 (1.06–1.28) | 1.15 (1.05–1.27) |
| P for trend |  |  |  |  | <0.001 | <0.001 | 0.003 |
| P for interaction |  |  |  |  | 0.499 | 0.580 | 0.577 |
| **All-cause mortality** |  |  |  |  |  |  |  |
| Insulin use (-) |  |  |  |  |  |  |  |
| Q1 | 147,250 | 7630 | 1,150,879 | 6.63 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 146,679 | 8168 | 1,149,647 | 7.10 | 1.13 (1.09–1.16) | 1.12 (1.08–1.15) | 1.10 (1.06–1.13) |
| Q3 | 145,507 | 9051 | 1,135,193 | 7.97 | 1.27 (1.23–1.31) | 1.24 (1.20–1.28) | 1.21 (1.17–1.24) |
| Q4 | 140,826 | 12,806 | 1,080,266 | 11.85 | 1.74 (1.69–1.79) | 1.68 (1.63–1.72) | 1.59 (1.54-1.63) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| Insulin use (+) |  |  |  |  |  |  |  |
| Q1 | 8653 | 1137 | 65,025 | 17.49 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 9328 | 1317 | 69,978 | 18.82 | 1.10 (1.01–1.19) | 1.09 (1.00–1.18) | 1.06 (0.98–1.15) |
| Q3 | 10,760 | 1601 | 80,339 | 19.93 | 1.20 (1.12–1.30) | 1.19 (1.10–1.28) | 1.16 (1.07–1.25) |
| Q4 | 15,234 | 3006 | 109,923 | 27.35 | 1.64 (1.53–1.75) | 1.59 (1.49–1.71) | 1.49 (1.39–1.60) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| P for interaction |  |  |  |  | 0.341 | 0.461 | 0.371 |

Abbreviations: HR, hazard ratio; VIM, variability independent of the mean; Q, quartile.

\* Incidence per 1000 person-years

† Model 1 was adjusted for age and sex.

‡ Model 2 was adjusted for age, sex, smoking status, alcohol consumption, physical activity, income, hypertension, dyslipidemia, chronic kidney disease, and number of oral antidiabetic agents used.

§ Model 3 was adjusted for age, sex, smoking status, alcohol consumption, physical activity, income, hypertension, dyslipidemia, chronic kidney disease, number of oral antidiabetic agents used, and baseline BMI.

**Supplemental Table S4. HRs (95% CIs) of study outcomes by quartiles of VIM for body weight according to duration between the date of first diabetes claim and index date among patients with type 2 diabetes**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | n | Event | Person-years | IR\* | HR (95% CI) |  |  |
|  |  |  |  | Model 1† | Model 2‡ | Model 3§ |
| **Myocardial infarction** |  | |  |  |  |  |  |
| ≤5 years |  |  |  |  |  |  |  |
| Q1 | 103,059 | 1946 | 802,454 | 2.43 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 103,706 | 2074 | 809,460 | 2.56 | 1.09 (1.03–1.16) | 1.08 (1.02–1.15) | 1.08 (1.02–1.15) |
| Q3 | 103,273 | 2122 | 802,928 | 2.64 | 1.14 (1.07–1.21) | 1.11 (1.04–1.18) | 1.11 (1.04–1.18) |
| Q4 | 102,272 | 2256 | 781,576 | 2.89 | 1.21 (1.14–1.29) | 1.15 (1.08–1.22) | 1.16 (1.09–1.23) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| >5 years |  |  |  |  |  |  |  |
| Q1 | 52,844 | 1703 | 401,755 | 4.24 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 52,301 | 1670 | 398,596 | 4.19 | 1.00 (0.94–1.07) | 0.98 (0.92–1.05) | 0.98 (0.92–1.05) |
| Q3 | 52,994 | 1876 | 400,297 | 4.69 | 1.12 (1.05–1.19) | 1.08 (1.01–1.15) | 1.08 (1.01–1.15) |
| Q4 | 53,788 | 2185 | 395,692 | 5.52 | 1.27 (1.19–1.35) | 1.16 (1.09–1.24) | 1.16 (1.08–1.23) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| P for interaction |  |  |  |  | 0.031 | 0.080 | 0.080 |
| **Stroke** |  |  |  |  |  |  |  |
| ≤5 years |  |  |  |  |  |  |  |
| Q1 | 103,059 | 2926 | 799,377 | 3.66 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 103,706 | 3015 | 806,137 | 3.74 | 1.06 (1.01–1.12) | 1.05 (1.00–1.11) | 1.05 (1.00–1.11) |
| Q3 | 103,273 | 3215 | 799,153 | 4.02 | 1.15 (1.09–1.20) | 1.12 (1.07–1.18) | 1.12 (1.07–1.18) |
| Q4 | 102,272 | 3649 | 777,119 | 4.70 | 1.25 (1.19–1.31) | 1.20 (1.14–1.26) | 1.19 (1.14–1.25) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| >5 years |  |  |  |  |  |  |  |
| Q1 | 52,844 | 2699 | 398,506 | 6.77 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 52,301 | 2755 | 394,735 | 6.98 | 1.05 (0.99–1.10) | 1.03 (0.98–1.09) | 1.03 (0.98–1.09) |
| Q3 | 52,994 | 2986 | 396,528 | 7.53 | 1.12 (1.06–1.18) | 1.09 (1.04–1.15) | 1.09 (1.03–1.15) |
| Q4 | 53,788 | 3793 | 390,159 | 9.72 | 1.36 (1.30–1.43) | 1.28 (1.21–1.34) | 1.27 (1.21–1.34) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| P for interaction |  |  |  |  | 0.032 | 0.104 | 0.101 |
| **All-cause mortality** |  |  |  |  |  |  |  |
| ≤5 years |  |  |  |  |  |  |  |
| Q1 | 103,059 | 4697 | 808,839 | 5.81 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 103,706 | 5206 | 816,054 | 6.38 | 1.16 (1.12–1.21) | 1.14 (1.10–1.19) | 1.12 (1.08–1.17) |
| Q3 | 103,273 | 5670 | 809,723 | 7.00 | 1.28 (1.23–1.33) | 1.24 (1.19–1.29) | 1.21 (1.16–1.26) |
| Q4 | 102,272 | 8314 | 788,421 | 10.55 | 1.79 (1.73–1.86) | 1.69 (1.63–1.75) | 1.59 (1.53–1.65) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| >5 years |  |  |  |  |  |  |  |
| Q1 | 52,844 | 4070 | 407,066 | 10.00 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 52,301 | 4279 | 403,571 | 10.60 | 1.10 (1.05–1.14) | 1.07 (1.03–1.12) | 1.05 (1.01–1.10) |
| Q3 | 52,994 | 4982 | 405,810 | 12.28 | 1.27 (1.22–1.32) | 1.22 (1.17–1.27) | 1.19 (1.14–1.24) |
| Q4 | 53,788 | 7498 | 401,768 | 18.66 | 1.79 (1.72–1.86) | 1.65 (1.58–1.71) | 1.56 (1.50–1.62) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| P for interaction |  |  |  |  | 0.070 | 0.202 | 0.164 |

Abbreviations: HR, hazard ratio; VIM, variability independent of the mean; Q, quartile.

\* Incidence per 1000 person-years

† Model 1 was adjusted for age and sex.

‡ Model 2 was adjusted for age, sex, smoking status, alcohol consumption, physical activity, income, hypertension, dyslipidemia, chronic kidney disease, insulin use, and number of oral antidiabetic agents used.

§ Model 3 was adjusted for age, sex, smoking status, alcohol consumption, physical activity, income, hypertension, dyslipidemia, chronic kidney disease, insulin use, number of oral antidiabetic agents used, and baseline BMI.

**Supplemental Table S5. HRs (95% CIs) of study outcomes with excluding cancer patients with respect to quartiles of VIM for body weight among patients with type 2 diabetes**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | n | Event | Person-years | IR\* | HR (95% CI) |  |  |
|  |  |  |  |  | Model 1† | Model 2‡ | Model 3§ |
| **Myocardial infarction** |  | |  |  |  |  |  |
| Q1 | 152,581 | 3550 | 1,180,071 | 3.01 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 152,640 | 3650 | 1,183,533 | 3.08 | 1.05 (1.01–1.10) | 1.04 (0.99–1.09) | 1.04 (0.99–1.09) |
| Q3 | 152,606 | 3864 | 1,177,147 | 3.28 | 1.12 (1.07–1.18) | 1.09 (1.04–1.14) | 1.09 (1.04–1.14) |
| Q4 | 150,691 | 4285 | 1,140,700 | 3.76 | 1.25 (1.19–1.30) | 1.16 (1.11–1.21) | 1.16 (1.11–1.21) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| **Stroke** |  | |  |  |  |  |  |
| Q1 | 152,581 | 5466 | 1,173,878 | 4.66 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 152,640 | 5629 | 1,176,520 | 4.78 | 1.06 (1.02–1.10) | 1.05 (1.01–1.09) | 1.04 (1.01–1.08) |
| Q3 | 152,606 | 6016 | 1,169,751 | 5.14 | 1.14 (1.09–1.18) | 1.11 (1.07–1.15) | 1.10 (1.06–1.14) |
| Q4 | 150,691 | 7141 | 1,131,092 | 6.31 | 1.30 (1.26–1.35) | 1.23 (1.19–1.27) | 1.22 (1.18–1.27) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| **All-cause mortality** |  | |  |  |  |  |  |
| Q1 | 152,581 | 8257 | 1,191,476 | 6.93 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 152,640 | 8953 | 1,194,850 | 7.49 | 1.14 (1.10–1.17) | 1.12 (1.08–1.15) | 1.10 (1.06–1.13) |
| Q3 | 152,606 | 9995 | 1,189,094 | 8.41 | 1.27 (1.24–1.31) | 1.23 (1.20–1.27) | 1.20 (1.17–1.24) |
| Q4 | 150,691 | 14,482 | 1,153,237 | 12.56 | 1.77 (1.72–1.82) | 1.65 (1.61–1.70) | 1.56 (1.52–1.61) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |

Abbreviations: HR, hazard ratio; VIM, variability independent of the mean; Q, quartile.

\* Incidence per 1000 person-years

† Model 1 was adjusted for age and sex.

‡ Model 2 was adjusted for age, sex, smoking status, alcohol consumption, physical activity, income, hypertension, dyslipidemia, chronic kidney disease, insulin use, and number of oral antidiabetic agent used.

§ Model 3 was adjusted for age, sex, smoking status, alcohol consumption, physical activity, income, hypertension, dyslipidemia, chronic kidney disease, insulin use, number of oral antidiabetic agents used, and baseline BMI.

**Supplemental Table S6. HRs (95% CIs) of study outcomes by quartiles of VIM for blood pressure and total cholesterol levels among patients with type 2 diabetes**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | n | Event | Person-years | IR\* | HR (95% CI) |  |  |
|  |  |  |  |  | Model 1† | Model 2‡ | Model 3§ |
| **Myocardial infarction** |  | |  |  |  |  |  |
| VIM for systolic BP |  |  |  |  |  |  |  |
| Q1 | 156,053 | 3729 | 1,199,148 | 3.11 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 156,198 | 3600 | 1,208,199 | 2.98 | 0.99 (0.94–1.04) | 0.98 (0.94–1.03) | 0.98 (0.94–1.03) |
| Q3 | 155,915 | 3835 | 1,200,726 | 3.19 | 1.02 (0.97–1.07) | 1.00 (0.96–1.05) | 1.00 (0.96–1.05) |
| Q4 | 156,071 | 4668 | 1,184,684 | 3.94 | 1.14 (1.09–1.19) | 1.09 (1.04–1.14) | 1.09 (1.04–1.14) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| VIM for diastolic BP |  |  |  |  |  |  |  |
| Q1 | 156,214 | 3596 | 1,202,805 | 2.99 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 155,904 | 3845 | 1,199,788 | 3.20 | 1.04 (1.00–1.09) | 1.03 (0.98–1.08) | 1.03 (0.98–1.08) |
| Q3 | 156,121 | 3836 | 1,205,439 | 3.18 | 1.06 (1.01–1.11) | 1.04 (0.99–1.09) | 1.04 (0.99–1.09) |
| Q4 | 155,998 | 4555 | 1,184,726 | 3.84 | 1.14 (1.09–1.19) | 1.09 (1.04–1.14) | 1.09 (1.04–1.14) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| VIM for total cholesterol |  |  |  |  |  |  |  |
| Q1 | 156,059 | 3811 | 1,199,316 | 3.18 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 156,058 | 3769 | 1,206,100 | 3.12 | 1.01 (0.97–1.06) | 1.00 (0.95–1.04) | 1.00 (0.95–1.04) |
| Q3 | 156,061 | 3969 | 1,199,631 | 3.31 | 1.04 (1.00–1.09) | 1.00 (0.96–1.05) | 1.00 (0.96–1.05) |
| Q4 | 156,059 | 4283 | 1,187,711 | 3.61 | 1.07 (1.03–1.12) | 0.96 (0.92–1.00) | 0.96 (0.91–1.00) |
| P for trend |  |  |  |  | 0.001 | 0.076 | 0.071 |
| **Stroke** |  |  |  |  |  |  |  |
| VIM for systolic BP |  |  |  |  |  |  |  |
| Q1 | 156,053 | 5602 | 1,193,182 | 4.70 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 156,198 | 5458 | 1,201,591 | 4.54 | 1.02 (0.98–1.05) | 1.01 (0.97–1.05) | 1.01 (0.97–1.05) |
| Q3 | 155,915 | 6188 | 1,192,766 | 5.19 | 1.10 (1.06–1.14) | 1.08 (1.04–1.12) | 1.08 (1.04–1.11) |
| Q4 | 156,071 | 7790 | 1,174,175 | 6.63 | 1.22 (1.18–1.27) | 1.16 (1.12–1.21) | 1.16 (1.12–1.20) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| VIM for diastolic BP |  |  |  |  |  |  |  |
| Q1 | 156,214 | 5551 | 1,196,523 | 4.64 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 155,904 | 5995 | 1,191,941 | 5.03 | 1.04 (1.00–1.08) | 1.03 (0.99–1.06) | 1.02 (0.99–1.06) |
| Q3 | 156,121 | 5905 | 1,198,542 | 4.93 | 1.06 (1.02–1.10) | 1.04 (1.00–1.08) | 1.04 (1.00–1.08) |
| Q4 | 155,998 | 7587 | 1,174,708 | 6.46 | 1.17 (1.13–1.21) | 1.11 (1.08–1.15) | 1.11 (1.07–1.15) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| VIM for total cholesterol |  |  |  |  |  |  |  |
| Q1 | 156,059 | 6118 | 1,191,607 | 5.13 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 156,058 | 5901 | 1,198,707 | 4.92 | 1.00 (0.97–1.04) | 0.99 (0.96–1.03) | 0.99 (0.96–1.03) |
| Q3 | 156,061 | 6284 | 1,191,999 | 5.27 | 1.03 (1.00–1.07) | 1.01 (0.98–1.05) | 1.01 (0.97–1.05) |
| Q4 | 156,059 | 6735 | 1,179,401 | 5.71 | 1.03 (1.00–1.07) | 0.98 (0.95–1.02) | 0.98 (0.95–1.02) |
| P for trend |  |  |  |  | 0.029 | 0.494 | 0.424 |
| **All-cause mortality** |  | |  |  |  |  |  |
| VIM for systolic BP |  |  |  |  |  |  |  |
| Q1 | 156,053 | 9574 | 1,210,791 | 7.91 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 156,198 | 9749 | 1,219,156 | 8.00 | 1.07 (1.04–1.10) | 1.06 (1.03–1.09) | 1.06 (1.03–1.09) |
| Q3 | 155,915 | 10,841 | 1,212,599 | 8.94 | 1.13 (1.10–1.16) | 1.11 (1.08–1.14) | 1.10 (1.07–1.13) |
| Q4 | 156,071 | 14,552 | 1,198,705 | 12.14 | 1.31 (1.28–1.35) | 1.26 (1.23–1.29) | 1.23 (1.20–1.27) |
| P for trend |  | |  |  | <0.001 | <0.001 | <0.001 |
| VIM for diastolic BP |  |  |  |  |  |  |  |
| Q1 | 156,214 | 9365 | 1,214,207 | 7.71 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 155,904 | 10,726 | 1,211,463 | 8.85 | 1.09 (1.06–1.12) | 1.07 (1.04–1.10) | 1.06 (1.04–1.09) |
| Q3 | 156,121 | 10,285 | 1,217,264 | 8.45 | 1.09 (1.06–1.12) | 1.07 (1.04–1.10) | 1.06 (1.03–1.09) |
| Q4 | 155,998 | 14,340 | 1,198,318 | 11.97 | 1.26 (1.23–1.30) | 1.22 (1.19–1.25) | 1.20 (1.17–1.23) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |
| VIM for total cholesterol |  |  |  |  |  |  |  |
| Q1 | 156,059 | 10,446 | 1,211,151 | 8.62 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
| Q2 | 156,058 | 10,242 | 1,217,845 | 8.41 | 1.03 (1.00–1.06) | 1.03 (1.00–1.06) | 1.02 (0.99–1.05) |
| Q3 | 156,061 | 11,425 | 1,211,731 | 9.43 | 1.12 (1.09–1.15) | 1.12 (1.09–1.15) | 1.11 (1.08–1.14) |
| Q4 | 156,059 | 12,603 | 1,200,524 | 10.50 | 1.16 (1.13–1.19) | 1.19 (1.16–1.23) | 1.18 (1.15–1.21) |
| P for trend |  |  |  |  | <0.001 | <0.001 | <0.001 |

Abbreviations: HR, hazard ratio; VIM, variability independent of the mean; Q, quartile.

\* Incidence per 1000 person-years

† Model 1 was adjusted for age and sex.

‡ Model 2 was adjusted for age, sex, smoking status, alcohol consumption, physical activity, income, hypertension, dyslipidemia, chronic kidney disease, insulin use, and number of oral antidiabetic agents used.

§ Model 3 was adjusted for age, sex, smoking status, alcohol consumption, physical activity, income, hypertension, dyslipidemia, chronic kidney disease, insulin use, number of oral antidiabetic agents used, and baseline BMI.

**Supplemental Table S7. Incidence rate of study outcomes by body weight change status among patients with type 2 diabetes**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Weight change status (%) | n | Event | Person-years | IR\* |
| **Myocardial infarction** |  | |  |  |
| ≤−5 | 120,706 | 3610 | 907,876 | 3.98 (3.85–4.11) |
| −5 to 5 | 420,271 | 10,319 | 3,242,240 | 3.18 (3.12–3.24) |
| ≥5 | 83,260 | 1903 | 642,641 | 2.96 (2.83–3.10) |
| P |  |  |  | <0.001 |
| **Stroke** |  | |  |  |
| ≤−5 | 120,706 | 5801 | 900,665 | 6.44 (6.28–6.61) |
| −5 to 5 | 420,271 | 15,980 | 3,223,116 | 4.96 (4.88–5.03) |
| ≥5 | 83,260 | 3257 | 637,934 | 5.11 (4.93–5.28) |
| P |  |  |  | <0.001 |
| **All-cause mortality** |  | |  |  |
| ≤−5 | 120,706 | 12,343 | 918,476 | 13.44 (13.20–13.70) |
| −5 to 5 | 420,271 | 26,582 | 3,274,299 | 8.12 (8.02–8.22) |
| ≥5 | 83,260 | 5791 | 648,477 | 8.93 (8.70–9.16) |
| P |  |  |  | <0.001 |

Abbreviations: IR, incidence rate.

\* Incidence per 1000 person-years

**Supplemental Table S8. Risk of study outcomes by combination of weight change status and body weight variability degrees**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Weight change status (%) | VIM for body weight | n | Event | Person-years | IR\* | HR (95% CI) |  |  |
|  |  |  |  | Model 1† | Model 2‡ | Model 3§ |
| **Myocardial infarction** |  |  | |  |  |  |  |  |
| ≤−5 | Q1-Q3 | 44,649 | 1227 | 341,917 | 3.59 | 1.14 (1.07–1.20) | 1.11 (1.05–1.18) | 1.11 (1.05–1.18) |
|  | Q4 | 76,057 | 2383 | 565,960 | 4.21 | 1.25 (1.19–1.31) | 1.18 (1.13–1.23) | 1.18 (1.13–1.24) |
| −5 to 5 | Q1-Q3 | 387,872 | 9371 | 2,995,904 | 3.13 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
|  | Q4 | 32,399 | 948 | 246,336 | 3.85 | 1.21 (1.13–1.29) | 1.14 (1.06–1.22) | 1.14 (1.06–1.22) |
| ≥5 | Q1-Q3 | 35,656 | 793 | 277,669 | 2.86 | 1.00 (0.93–1.08) | 1.00 (0.93–1.07) | 0.99 (0.93–1.07) |
|  | Q4 | 47,604 | 1110 | 364,972 | 3.04 | 1.05 (0.99–1.12) | 0.99 (0.93–1.06) | 0.99 (0.93–1.06) |
| **Stroke** |  |  | |  |  |  |  |  |
| ≤−5 | Q1-Q3 | 44,649 | 1881 | 339,748 | 5.54 | 1.12 (1.06–1.17) | 1.09 (1.04–1.15) | 1.09 (1.03–1.14) |
|  | Q4 | 76,057 | 3920 | 560,917 | 6.99 | 1.26 (1.21–1.30) | 1.20 (1.16–1.24) | 1.18 (1.14–1.23) |
| −5 to 5 | Q1-Q3 | 387,872 | 14,467 | 2,978,665 | 4.86 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
|  | Q4 | 32,399 | 1513 | 244,450 | 6.19 | 1.21 (1.15–1.28) | 1.16 (1.10–1.22) | 1.16 (1.10–1.22) |
| ≥5 | Q1-Q3 | 35,656 | 1248 | 276,023 | 4.52 | 1.05 (0.99–1.11) | 1.04 (0.98–1.10) | 1.05 (0.99–1.11) |
|  | Q4 | 47,604 | 2009 | 361,911 | 5.55 | 1.23 (1.18–1.29) | 1.18 (1.12–1.23) | 1.19 (1.13–1.24) |
| **All-cause mortality** |  |  | |  |  |  |  |  |
| ≤−5 | Q1-Q3 | 44,649 | 3336 | 345,697 | 9.65 | 1.24 (1.20–1.29) | 1.21 (1.17–1.25) | 1.14 (1.10–1.18) |
|  | Q4 | 76,057 | 9007 | 572,779 | 15.73 | 1.79 (1.75–1.84) | 1.68 (1.64–1.73) | 1.52 (1.48–1.56) |
| −5 to 5 | Q1-Q3 | 387,872 | 23,516 | 3,025,276 | 7.77 | 1 (ref.) | 1 (ref.) | 1 (ref.) |
|  | Q4 | 32,399 | 3066 | 249,022 | 12.31 | 1.50 (1.45–1.56) | 1.42 (1.36–1.47) | 1.39 (1.34–1.45) |
| ≥5 | Q1-Q3 | 35,656 | 2052 | 280,089 | 7.33 | 1.09 (1.04–1.14) | 1.06 (1.02–1.11) | 1.10 (1.05–1.15) |
|  | Q4 | 47,604 | 3739 | 368,388 | 10.15 | 1.42 (1.37–1.47) | 1.34 (1.30–1.39) | 1.40 (1.36–1.45) |

Abbreviations: VIM, variability independent of the mean; HR, hazard ratio; Q, quartile.

\* Incidence per 1000 person-years

† Model 1 was adjusted for age and sex.

‡ Model 2 was adjusted for age, sex, smoking status, alcohol consumption, physical activity, income, hypertension, dyslipidemia, chronic kidney disease, insulin use, and number of oral antidiabetic agents used.

§ Model 3 was adjusted for age, sex, smoking status, alcohol consumption, physical activity, income, hypertension, dyslipidemia, chronic kidney disease, insulin use, number of oral antidiabetic agents used, and baseline BMI.