## Supplementary Table 1. Incidence rates and hazard ratios for cardiovascular and mortality outcomes in participants with type 2 diabetes and incident OSA compared to participants with type 2 diabetes without OSA

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Outcome** | **Exposed** | **Unexposed** | **Outcome** | **Exposed** | **Unexposed** |
| **Composite Cardiovascular disease**, n | 2478 | 8014 | **Stroke/TIA**, n | 3360 | 9785 |
| Outcome events, n (%) | 250 (10.09) | 564 (7.04) | Outcome events, n (%) | 134 (3.99) | 261 (2.67) |
| Person-years | 9,386 | 32,411 | Person-years | 13,116 | 40,596 |
| Crude incidence rate/1000 person-years | 26.64 | 17.40 | Crude incidence rate/1000 person-years | 10.22 | 6.43 |
| Follow-up years, median (IQR) | 3.08 (1.58, 5.48) | 3.46 (1.70, 5.88) | Follow-up years, median (IQR) | 3.22 (1.63, 5.67) | 3.58 (1.74, 6.04) |
| Unadjusted hazard ratio (95% CI) | 1.54 (1.32, 1.78), p<0.001 | | Unadjusted hazard ratio (95% CI) | 1.60 (1.30, 1.97), p<0.001 | |
| Adjusted hazard ratio (95% CI)\* | 1.54 (1.32, 1.79), p<0.001 | | Adjusted hazard ratio (95% CI)\* | 1.57 (1.27, 1.94), p<0.001 | |
| Sensitivity analysis 1 aHR (95% CI)\* | 1.52 (1.30, 1.79), p<0.001 | | Sensitivity analysis 1 aHR (95% CI)\* | 1.66 (1.34, 2.07), p<0.001 | |
| Sensitivity analysis 2 aHR (95% CI)\* | 1.54 (1.32, 1.79), p<0.001 | | Sensitivity analysis 2 aHR (95% CI)\* | 1.57 (1.27, 1.94), p<0.001 | |
| **Ischaemic Heart Disease**, n | 2800 | 8614 | **Peripheral Vascular Disease**, n | 3060 | 9261 |
| Outcome events, n (%) | 144 (5.14) | 304 (3.53) | Outcome events, n (%) | 165 (5.39) | 434 (4.68) |
| Person-years | 10,723 | 35,367 | Person-years | 11,599 | 37,266 |
| Crude incidence rate/1000 person-years | 13.43 | 8.60 | Crude incidence rate/1000 person-years | 14.23 | 11.65 |
| Follow-up years, median (IQR) | 3.10 (1.61, 5.56) | 3.54 (1.74, 5.94) | Follow-up years, median (IQR) | 3.07 (1.58, 5.52) | 3.46 (1.66, 5.86) |
| Unadjusted hazard ratio (95% CI) | 1.57 (1.28, 1.91), p<0.001 | | Unadjusted hazard ratio (95% CI) | 1.21 (1.01, 1.44), p=0.040 | |
| Adjusted hazard ratio (95% CI)\* | 1.55 (1.26, 1.90), p<0.001 | | Adjusted hazard ratio (95% CI)\* | 1.10 (0.91, 1.32), p=0.319 | |
| Sensitivity analysis 1 aHR (95% CI)\* | 1.48 (1.19, 1.84), p<0.001 | | Sensitivity analysis 1 aHR (95% CI)\* | 1.01 (0.83, 1.23), p=0.906 | |
| Sensitivity analysis 2 aHR (95% CI)\* | 1.55 (1.26, 1.90), p<0.001 | | Sensitivity analysis 2 aHR (95% CI)\* | 1.10 (0.91, 1.32), p=0.319 | |
| **Heart Failure**, n | 3331 | 10073 | **Atrial Fibrillation**, n | 3292 | 9827 |
| Outcome events, n (%) | 141 (4.23) | 248 (2.46) | Outcome events, n (%) | 184 (5.59) | 382 (3.88) |
| Person-years | 13,086 | 41,791 | Person-years | 12,790 | 40,772 |
| Crude incidence rate/1000 person-years | 10.77 | 5.93 | Crude incidence rate/1000 person-years | 14.39 | 9.37 |
| Follow-up years, median (IQR) | 3.22 (1.65, 5.73) | 3.59 (1.74, 6.07) | Follow-up years, median (IQR) | 3.20 (1.61, 5.66) | 3.59 (1.74, 6.05) |
| Unadjusted hazard ratio (95% CI) | 1.83 (1.49, 2.25), p<0.001 | | Unadjusted hazard ratio (95% CI) | 1.55 (1.30, 1.85), p<0.001 | |
| Adjusted hazard ratio (95% CI)\* | 1.67 (1.35, 2.06), p<0.001 | | Adjusted hazard ratio (95% CI)\* | 1.53 (1.28, 1.83), p<0.001 | |
| Sensitivity analysis 1 aHR (95% CI)\* | 1.59 (1.27, 2.00), p<0.001 | | Sensitivity analysis 1 aHR (95% CI)\* | 1.51 (1.25, 1.83), p<0.001 | |
| Sensitivity analysis 2 aHR (95% CI)\* | 1.67 (1.35, 2.06), p<0.001 | | Sensitivity analysis 2 aHR (95% CI)\* | 1.53 (1.28, 1.83), p<0.001 | |
| **All-cause mortality**, n | 3667 | 10450 |  |  |  |
| Outcome events, n (%) | 434 (11.84) | 887 (8.49) |  |  |  |
| Person-years | 14,513 | 43,803 |  |  |  |
| Crude incidence rate/1000 person-years | 29.90 | 20.34 |  |  |  |
| Follow-up years, median (IQR) | 3.25 (1.66, 5.80) | 3.64 (1.78, 6.13) |  |  |  |
| Unadjusted hazard ratio (95% CI) | 1.49 (1.32, 1.67), p<0.001 | |  |  |  |
| Adjusted hazard ratio (95% CI)‡ | 1.24 (1.10, 1.40), p<0.001 | |  |  |  |
| Sensitivity analysis 1 aHR (95% CI)‡ | 1.13 (1.00, 1.29), p=0.058 | |  |  |  |
| Sensitivity analysis 2 aHR (95% CI)‡ | 1.24 (1.10, 1.40), p<0.001 | |  |  |  |

aHR: adjusted hazard ratio. ACR: albumin-creatinine ratio.

Sensitivity analysis 1: excluding exposed patients with no available matched controls. Sensitivity analysis 2: using multiple imputation to replace missing values of BMI, HbA1c, eGFR and ACR.

\*Adjusted for age category, sex, BMI category, smoking catgeory, Townsend deprivation quintile, baseline hypertension, baseline prescription of lipid-lowering drugs, antihypertensives, antiplatelets and insulin within 60 days of index date, ethnicity, diabetes duration, HbA1c category, eGFR category, albumin-creatinine ratio category.

‡Adjusted for age category, sex, BMI category, smoking category, Townsend quintile, baseline prescription of lipid-lowering drugs, antihypertensives, antiplatelets, and insulin within 60 days of index date, ethnicity, diabetes duration, HbA1c category, Charlson comorbidity index.

## Supplementary Table 2. Incidence rates and hazard ratios for microvascular outcomes in participants with type 2 diabetes and incident OSA compared to participants with type 2 diabetes without OSA

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Outcome** | **Exposed** | **Unexposed** | **Outcome** | **Exposed** | **Unexposed** |
| **Peripheral neuropathy**, n | 2746 | 8453 | **Micro/macroalbuminuria: ACR > 3 mg/mmol**, n | 2276 | 7241 |
| Outcome events, n (%) | 288 (10.49) | 697 (8.24) | Outcome events, n (%) | 614 (26.98) | 1797 (24.80) |
| Person-years | 9,894 | 33,282 | Person-years | 7,565 | 25,954 |
| Crude incidence rate/1000 person-years | 29.11 | 20.94 | Crude incidence rate/1000 person-years | 81.17 | 69.24 |
| Follow-up years, median (IQR) | 2.89 (1.45, 5.22) | 3.31 (1.59, 5.74) | Follow-up years, median (IQR) | 2.67 (1.31, 4.74) | 2.89 (1.38, 5.25) |
| Unadjusted hazard ratio (95% CI) | 1.37 (1.19, 1.57), p<0.001 | | Unadjusted hazard ratio (95% CI) | 1.17 (1.06, 1.28), p<0.001 | |
| Adjusted hazard ratio (95% CI)\* | 1.32 (1.14, 1.51), p<0.001 | | Adjusted hazard ratio (95% CI)† | 1.11 (1.01, 1.22), p=0.035 | |
| Sensitivity analysis 1 aHR (95% CI)\* | 1.27 (1.10, 1.48), p=0.001 | | Sensitivity analysis 1 aHR (95% CI)† | 1.09 (0.99, 1.20), p=0.088 | |
| Sensitivity analysis 2 aHR (95% CI)\* | 1.31 (1.14, 1.51), p<0.001 | | Sensitivity analysis 2 aHR (95% CI)† | 1.11 (1.01, 1.21), p=0.035 | |
| **Diabetes-related foot disease (foot ulcer/ amputation/gangrene)**, n | 3420 | 10023 | **Macroalbuminuria: ACR > 30 mg/mmol**, n | 3320 | 9895 |
| Outcome events, n (%) | 161 (4.71) | 289 (2.88) | Outcome events, n (%) | 241 (7.26) | 502 (5.07) |
| Person-years | 13,288 | 41,575 | Person-years | 12,731 | 40,445 |
| Crude incidence rate/1000 person-years | 12.12 | 6.95 | Crude incidence rate/1000 person-years | 18.93 | 12.41 |
| Follow-up years, median (IQR) | 3.19 (1.61, 5.71) | 3.59 (1.75, 6.03) | Follow-up years, median (IQR) | 3.13 (1.59, 5.61) | 3.51 (1.70, 5.94) |
| Unadjusted hazard ratio (95% CI) | 1.76 (1.45, 2.13), p<0.001 | | Unadjusted hazard ratio (95% CI) | 1.52 (1.31, 1.78), p<0.001 | |
| Adjusted hazard ratio (95% CI)\* | 1.42 (1.16, 1.74), p<0.001 | | Adjusted hazard ratio (95% CI)† | 1.33 (1.13, 1.55), p<0.001 | |
| Sensitivity analysis 1 aHR (95% CI)\* | 1.35 (1.08, 1.67), p=0.007 | | Sensitivity analysis 1 aHR (95% CI)† | 1.27 (1.07, 1.50), p=0.006 | |
| Sensitivity analysis 2 aHR (95% CI)\* | 1.42 (1.16, 1.74), p=0.001 | | Sensitivity analysis 2 aHR (95% CI)† | 1.33 (1.13, 1.55), p=0.001 | |
| **Referable retinopathy**, n | 3347 | 9751 | **Severe macroalbuminuria: ACR > 300**, n **mg/mmol** | 3641 | 10417 |
| Outcome events, n (%) | 156 (4.66) | 395 (4.05) | Outcome events, n (%) | 49 (1.35) | 82 (0.79) |
| Person-years | 12,901 | 39,800 | Person-years | 14,308 | 43,479 |
| Crude incidence rate/1000 person-years | 12.09 | 9.92 | Crude incidence rate/1000 person-years | 3.42 | 1.89 |
| Follow-up years, median (IQR) | 3.15 (1.59, 5.63) | 3.51 (1.71, 5.94) | Follow-up years, median (IQR) | 3.22 (1.63, 5.76) | 3.61 (1.75, 6.10) |
| Unadjusted hazard ratio (95% CI) | 1.22 (1.01, 1.47), p=0.036 | | Unadjusted hazard ratio (95% CI) | 1.82 (1.28, 2.59), p<0.001 | |
| Adjusted hazard ratio (95% CI)\* | 0.99 (0.82, 1.21), p=0.952 | | Adjusted hazard ratio (95% CI)† | 1.33 (0.92, 1.93), p=0.129 | |
| Sensitivity analysis 1 aHR (95% CI)\* | 0.99 (0.80, 1.22), p=0.914 | | Sensitivity analysis 1 aHR (95% CI)† | 1.23 (0.83, 1.83), p=0.309 | |
| Sensitivity analysis 2 aHR (95% CI)\* | 0.99 (0.82, 1.21), p=0.952 | | Sensitivity analysis 2 aHR (95% CI)† | 1.33 (0.92, 1.93), p, 0.129 | |
| **CKD stage 3-5**, n | 2839 | 8594 |  |  |  |
| Outcome events, n (%) | 276 (9.72) | 740 (8.61) |  |  |  |
| Person-years | 10,588 | 34,101 |  |  |  |
| Crude incidence rate/1000 person-years | 26.07 | 21.70 |  |  |  |
| Follow-up years, median (IQR) | 3.00 (1.51, 5.46) | 3.39 (1.65, 5.77) |  |  |  |
| Unadjusted hazard ratio (95% CI) | 1.20 (1.05, 1.38), p=0.009 | |  |  |  |
| Adjusted hazard ratio (95% CI)† | 1.18 (1.02, 1.36), p=0.023 | |  |  |  |
| Sensitivity analysis 1 aHR (95% CI)† | 1.16 (1.00, 1.34), p=0.055 | |  |  |  |
| Sensitivity analysis 2 aHR (95% CI)† | 1.18 (1.02, 1.36), p=0.023 | |  |  |  |

aHR: adjusted hazard ratio. ACR: albumin-creatinine ratio.

Sensitivity analysis 1: excluding exposed patients with no available matched controls. Sensitivity analysis 2: using multiple imputation to replace missing values of BMI, HbA1c, eGFR and ACR.

\*Adjusted for age category, sex, BMI category, smoking catgeory, Townsend deprivation quintile, baseline hypertension, baseline prescription of lipid-lowering drugs, antihypertensives, antiplatelets and insulin within 60 days of index date, ethnicity, diabetes duration, HbA1c category, eGFR category, albumin-creatinine ratio category.

†Adjusted for age category, sex, BMI category, smoking category, Townsend deprivation quintile, baseline hypertension, baseline cardiovascular disease (ischaemic heart disease, heart failure, stroke/transient ischaemic attack), baseline prescription of lipid-lowering drugs, antihypertensives, antiplatelets and insulin within 60 days from index date, ethnicity, diabetes duration, HbA1c category.

## Supplementary Table 3. Baseline characteristics of study participants in the sensitivity analysis excluding participants with no matched controls

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Participant characteristic** | **Incident OSA** | | **Prevalent OSA** | |
|  | **Exposed** | **Unexposed** | **Exposed** | **Unexposed** |
| **Population, n** | 3,071 | 10,450 | 4,445 | 15,589 |
| **Age (years), mean (SD)†** | 60.62 (9.58) | 60.99 (9.08) | 57.29 (10.93) | 57.60 (10.89) |
| **Age at diagnosis of T2DM (years), mean (SD)** | 54.25 (9.24) | 54.95 (8.71) | 57.29 (10.93) | 57.60 (10.89) |
| **Age at diagnosis of OSA (years), mean (SD)** | 60.62 (9.58) | - | 51.65 (10.99) | - |
| **T2DM to OSA development time (years), mean (SD)** | 6.37 (5.39) | - | - | - |
| **OSA to T2DM development time (years), mean (SD)** | - | - | 5.64 (4.79) | - |
| **Sex, n (%)†** |  |  |  |  |
| Male | 2279 (74.21) | 7914 (75.73) | 3468 (78.02) | 12062 (77.38) |
| Female | 792 (25.79) | 2536 (24.27) | 977 (21.98) | 3527 (22.62) |
| **BMI (kg/m2), mean (SD)†** | 36.37 (6.62) | 35.70 (6.00) | 37.80 (7.37) | 36.89 (6.95) |
| **BMI categories, n (%)** |  |  |  |  |
| Underweight (< 25 kg/m2) | 47 (1.53) | 183 (1.75) | 59 (1.33) | 243 (1.56) |
| Overweight (25 - 30 kg/m2) | 342 (11.14) | 1431 (13.69) | 494 (11.11) | 2050 (13.15) |
| Obese (> 30 kg/m2) | 2675 (87.11) | 8828 (84.48) | 3781 (85.06) | 12871 (82.56) |
| Missing | 7 (0.23) | 8 (0.08) | 111 (2.50) | 425 (2.73) |
| **Smoking status, n (%)** |  |  |  |  |
| Non-smoker | 1213 (39.50) | 4548 (43.52) | 1766 (39.73) | 6846 (43.92) |
| Ex-smoker | 1353 (44.06) | 4284 (41.00) | 1794 (40.36) | 5690 (36.50) |
| Smoker | 504 (16.41) | 1608 (15.39) | 874 (19.66) | 2988 (19.17) |
| Missing | 1 (0.03) | 10 (0.10) | 11 (0.25) | 65 (0.42) |
| **Ethnicity, n (%)** |  |  |  |  |
| White | 1487 (48.42) | 4939 (47.26) | 2157 (48.53) | 7473 (47.94) |
| Black Afro-Caribbean | 35 (1.14) | 154 (1.47) | 58 (1.30) | 213 (1.37) |
| Chinese | 9 (0.29) | 25 (0.24) | 8 (0.18) | 29 (0.19) |
| South Asian | 89 (2.90) | 230 (2.20) | 89 (2.00) | 344 (2.21) |
| Mixed race | 13 (0.42) | 42 (0.40) | 30 (0.67) | 82 (0.53) |
| Missing | 1438 (46.83) | 5060 (48.42) | 2103 (47.31) | 7448 (47.78) |
| **Townsend deprivation quintile, n (%)** |  |  |  |  |
| 1 (least deprived) | 543 (17.68) | 1868 (17.88) | 754 (16.96) | 2651 (17.01) |
| 2 | 510 (16.61) | 1854 (17.74) | 804 (18.09) | 2698 (17.31) |
| 3 | 588 (19.15) | 2003 (19.17) | 868 (19.53) | 2987 (19.16) |
| 4 | 571 (18.59) | 1857 (17.77) | 791 (17.80) | 2823 (18.11) |
| 5 (most deprived) | 446 (14.52) | 1452 (13.89) | 614 (13.81) | 2265 (14.53) |
| Missing | 413 (13.45) | 1416 (13.55) | 614 (13.81) | 2165 (13.89) |
| **HbA1c (mmol/mol), mean (SD)** | 59.35 (16.84) | 58.37 (16.78) | 62.43 (21.23) | 63.98 (21.76) |
| **HbA1c category, n (%)** |  |  |  |  |
| ≤ 47.5 mmol/mol | 609 (19.83) | 2169 (20.76) | 387 (8.71) | 1303 (8.36) |
| 47.5 - 58.5 mmol/mol | 943 (30.71) | 3321 (31.78) | 1236 (27.81) | 3744 (24.02) |
| 58.5 - 69.4 mmol/mol | 492 (16.02) | 1462 (13.99) | 352 (7.92) | 1235 (7.92) |
| > 69.4 mmol/mol | 547 (17.81) | 1681 (16.09) | 642 (14.44) | 2498 (16.02) |
| Missing | 480 (15.63) | 1817 (17.39) | 1828 (41.12) | 6809 (43.68) |
| **eGFR (ml/min per 1.73 m2), mean (SD)** | 79.23 (21.45) | 81.42 (19.10) | 85.18 (18.18) | 85.03 (18.18) |
| **eGFR category, n (%)** |  |  |  |  |
| > 60 ml/min per 1.73 m2 (stage 2 and below) | 2474 (80.56) | 8808 (84.29) | 3887 (87.45) | 13393 (85.91) |
| 30-59 ml/min per 1.73 m2 (stage 3) | 456 (14.85) | 1223 (11.70) | 345 (7.76) | 1175 (7.54) |
| < 30 ml/min per 1.73 m2 (stage 4-5) | 69 (2.25) | 101 (0.97) | 12 (0.27) | 57 (0.37) |
| Missing | 72 (2.34) | 318 (3.04) | 201 (4.52) | 964 (6.18) |
| **Albumin creatinine ratio (mg/mmol), mean (SD)** | 9.95 (34.10) | 6.16 (26.04) | 7.05 (20.42) | 7.47 (29.75) |
| **Albumin creatinine ratio category, n (%)** |  |  |  |  |
| < 3 mg/mmol | 1282 (41.75) | 4791 (45.85) | 379 (8.53) | 1366 (8.76) |
| 3.0 - 30.0 mg/mmol | 461 (15.01) | 1293 (12.37) | 169 (3.80) | 507 (3.25) |
| > 30 mg/mmol | 130 (4.23) | 243 (2.33) | 32 (0.72) | 87 (0.56) |
| Missing | 1198 (39.01) | 4123 (39.45) | 3865 (86.95) | 13629 (87.43) |
| **Baseline cardiovascular conditions, n (%)** |  |  |  |  |
| Heart failure | 254 (8.27) | 377 (3.61) | 219 (4.93) | 437 (2.80) |
| Ischaemic heart disease | 731 (23.80) | 1836 (17.57) | 751 (16.90) | 2037 (13.07) |
| Stroke/TIA | 268 (8.73) | 665 (6.36) | 253 (5.69) | 729 (4.68) |
| Peripheral vascular disease | 477 (15.53) | 1189 (11.38) | 105 (2.36) | 366 (2.35) |
| Atrial fibrillation | 305 (9.93) | 623 (5.96) | 325 (7.31) | 780 (5.00) |
| Hypertension | 2054 (66.88) | 6615 (63.30) | 2317 (52.13) | 7699 (49.39) |
| **Baseline microvascular conditions, n (%)** |  |  |  |  |
| Peripheral neuropathy | 742 (24.16) | 1997 (19.11) | 79 (1.78) | 161 (1.03) |
| Diabetes-related foot disease | 170 (5.54) | 427 (4.09) | 134 (3.01) | 349 (2.24) |
| Referable retinopathy | 243 (7.91) | 699 (6.69) | 91 (2.05) | 194 (1.24) |
| CKD stage 3-5 | 657 (21.39) | 1856 (17.76) | 541 (12.17) | 1645 (10.55) |
| Micro-macroalbuminuria | 1128 (36.73) | 3209 (30.71) | 292 (6.57) | 823 (5.28) |
| Macroalbuminuria | 270 (8.79) | 555 (5.31) | 66 (1.48) | 148 (0.95) |
| Sever macroalbuminuria | 18 (0.59) | 33 (0.32) | 5 (0.11) | 17 (0.11) |
| **Baseline drug use (within 60 days of index), n (%)** |  |  |  |  |
| Lipid-lowering drugs | 2239 (72.91) | 7267 (69.54) | 1924 (43.28) | 6381 (40.93) |
| Antihypertensives | 2435 (79.29) | 7600 (72.73) | 2735 (61.53) | 8941 (57.35) |
| Antiplatelets | 1239 (40.35) | 3616 (34.60) | 1019 (22.92) | 2953 (18.94) |
| Insulin | 520 (16.93) | 930 (8.90) | 16 (0.36) | 42 (0.27) |
| **Charlson comorbidity index, n (%)** |  |  |  |  |
| 1 | 1018 (33.15) | 4511 (43.17) | 2147 (48.30) | 9234 (59.23) |
| 2 | 987 (32.14) | 3330 (31.87) | 1404 (31.59) | 4004 (25.68) |
| 3 | 556 (18.10) | 1481 (14.17) | 534 (12.01) | 1463 (9.38) |
| ≥4 | 510 (16.61) | 1128 (10.79) | 360 (8.10) | 888 (5.70) |

†Matching parameters. T2DM = type 2 diabetes; BMI = body mass index; eGFR = estimated glomerular filtration rate.

## Supplementary Table 4. Incidence rates and hazard ratios for cardiovascular and mortality outcomes in participants with type 2 diabetes and prevalent OSA compared to participants with type 2 diabetes without OSA

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Outcome** | **Exposed** | **Unexposed** | **Outcome** | **Exposed** | **Unexposed** |
| **Composite Cardiovascular disease**, n | 3525 | 12832 | **Stroke/TIA**, n | 4307 | 14860 |
| Outcome events, n (%) | 223 (6.33) | 702 (5.47) | Outcome events, n (%) | 90 (2.09) | 280 (1.88) |
| Person-years | 13,058 | 49,975 | Person-years | 16,364 | 59,302 |
| Crude incidence rate/1000 person-years | 17.08 | 14.05 | Crude incidence rate/1000 person-years | 5.50 | 4.72 |
| Follow-up years, median (IQR) | 2.97 (1.34, 5.46) | 3.18 (1.45, 5.72) | Follow-up years, median (IQR) | 3.10 (1.40, 5.63) | 3.28 (1.52, 5.86) |
| Unadjusted hazard ratio (95% CI) | 1.21 (1.04, 1.41), p=0.011 | | Unadjusted hazard ratio (95% CI) | 1.17 (0.92, 1.48), p=0.204 | |
| Adjusted hazard ratio (95% CI)\* | 1.23 (1.05, 1.43), p=0.008 | | Adjusted hazard ratio (95% CI)\* | 1.20 (0.94, 1.52), p=0.142 | |
| Sensitivity analysis 1 aHR (95% CI)\* | 1.21 (1.04, 1.41), p=0.013 | | Sensitivity analysis 1 aHR (95% CI)\* | 1.20 (0.95, 1.53), p=0.133 | |
| Sensitivity analysis 2 aHR (95% CI)\* | 1.23 (1.05, 1.43), p=0.008 | | Sensitivity analysis 2 aHR (95% CI)\* | 1.20 (0.94, 1.52), p=0.142 | |
| **Ischaemic Heart Disease**, n | 3799 | 13552 | **Peripheral Vascular Disease**, n | 4458 | 15223 |
| Outcome events, n (%) | 140 (3.69) | 453 (3.34) | Outcome events, n (%) | 266 (5.97) | 752 (4.94) |
| Person-years | 14,265 | 53,237 | Person-years | 16,034 | 58,148 |
| Crude incidence rate/1000 person-years | 9.81 | 8.51 | Crude incidence rate/1000 person-years | 16.59 | 12.93 |
| Follow-up years, median (IQR) | 3.04 (1.36, 5.57) | 3.21 (1.47, 5.79) | Follow-up years, median (IQR) | 2.83 (1.26, 5.30) | 3.07 (1.38, 5.65) |
| Unadjusted hazard ratio (95% CI) | 1.15 (0.95, 1.39), p=0.148 | | Unadjusted hazard ratio (95% CI) | 1.26 (1.09, 1.45), p=0.001 | |
| Adjusted hazard ratio (95% CI)\* | 1.14 (0.95, 1.38), p=0.165 | | Adjusted hazard ratio (95% CI)\* | 1.27 (1.11, 1.47), p<0.001 | |
| Sensitivity analysis 1 aHR (95% CI)\* | 1.13 (0.94, 1.37), p=0.201 | | Sensitivity analysis 1 aHR (95% CI)\* | 1.25 (1.08, 1.44), p=0.002 | |
| Sensitivity analysis 2 aHR (95% CI)\* | 1.14 (0.95, 1.39), p=0.165 | | Sensitivity analysis 2 aHR (95% CI)\* | 1.27 (1.11, 1.47), p=0.001 | |
| **Heart Failure**, n | 4338 | 15152 | **Atrial Fibrillation**, n | 4225 | 14809 |
| Outcome events, n (%) | 81 (1.87) | 236 (1.56) | Outcome events, n (%) | 136 (3.22) | 457 (3.09) |
| Person-years | 16,501 | 60,781 | Person-years | 15,966 | 58,900 |
| Crude incidence rate/1000 person-years | 4.91 | 3.88 | Crude incidence rate/1000 person-years | 8.52 | 7.76 |
| Follow-up years, median (IQR) | 3.09 (1.39, 5.63) | 3.31 (1.53, 5.89) | Follow-up years, median (IQR) | 3.05 (1.39, 5.61) | 3.27 (1.51, 5.86) |
| Unadjusted hazard ratio (95% CI) | 1.27 (0.99, 1.64), p=0.061 | | Unadjusted hazard ratio (95% CI) | 1.11 (0.91, 1.34), p=0.300 | |
| Adjusted hazard ratio (95% CI)\* | 1.26 (0.98, 1.63), p=0.072 | | Adjusted hazard ratio (95% CI)\* | 1.11 (0.91, 1.34), p=0.301 | |
| Sensitivity analysis 1 aHR (95% CI)\* | 1.25 (0.96, 1.61), p=0.093 | | Sensitivity analysis 1 aHR (95% CI)\* | 1.10 (0.90, 1.34), p=0.344 | |
| Sensitivity analysis 2 aHR (95% CI)\* | 1.26 (0.98, 1.63), p=0.072 | | Sensitivity analysis 2 aHR (95% CI)\* | 1.11 (0.91, 1.34), p=0.301 | |
| **All-cause mortality**, n | 4564 | 15589 |  |  |  |
| Outcome events, n (%) | 292 (6.40) | 1000 (6.41) |  |  |  |
| Person-years | 17,494 | 62,829 |  |  |  |
| Crude incidence rate/1000 person-years | 16.69 | 15.92 |  |  |  |
| Follow-up years, median (IQR) | 3.13 (1.41, 5.66) | 3.32 (1.54, 5.91) |  |  |  |
| Unadjusted hazard ratio (95% CI) | 1.06 (0.93, 1.20), p=0.414 | |  |  |  |
| Adjusted hazard ratio (95% CI)‡ | 1.00 (0.88, 1.14), p=0.968 | |  |  |  |
| Sensitivity analysis 1 aHR (95% CI)‡ | 0.99 (0.86, 1.13), p=0.847 | |  |  |  |
| Sensitivity analysis 2 aHR (95% CI)‡ | 1.00 (0.88, 1.14), p=0.968 | |  |  |  |

aHR: adjusted hazard ratio. ACR: albumin-creatinine ratio.

Sensitivity analysis 1: excluding exposed patients with no available matched controls. Sensitivity analysis 2: using multiple imputation to replace missing values of BMI, HbA1c, eGFR and ACR.

\*Adjusted for age category, sex, BMI category, smoking catgeory, Townsend deprivation quintile, baseline hypertension, baseline prescription of lipid-lowering drugs, antihypertensives, antiplatelets and insulin within 60 days of index date, ethnicity, HbA1c category, eGFR category, albumin-creatinine ratio category.

‡Adjusted for age category, sex, BMI category, smoking category, Townsend quintile, baseline prescription of lipid-lowering drugs, antihypertensives, antiplatelets, and insulin within 60 days of index date, ethnicity, HbA1c category, Charlson comorbidity index.

## Supplementary Table 5. Incidence rates and hazard ratios for microvascular outcomes in participants with type 2 diabetes and prevalent OSA compared to participants with type 2 diabetes without OSA

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Outcome** | **Exposed** | **Unexposed** | **Outcome** | **Exposed** | **Unexposed** |
| **Peripheral neuropathy**, n | 4483 | 15428 | **Micro/macroalbuminuria: ACR > 3 mg/mmol** | 4268 | 41766 |
| Outcome events, n (%) | 576 (12.85) | 1721 (11.16) | Outcome events, n (%) | 1249 (29.26) | 3961 (26.83) |
| Person-years | 14,941 | 55,083 | Person-years | 12,035 | 45,722 |
| Crude incidence rate/1000 person-years | 38.55 | 31.24 | Crude incidence rate/1000 person-years | 103.78 | 86.63 |
| Follow-up years, median (IQR) | 2.55 (1.10, 4.93) | 2.83 (1.23, 5.26) | Follow-up years, median (IQR) | 2.03 (0.74, 4.21) | 2.29 (0.90, 4.65) |
| Unadjusted hazard ratio (95% CI) | 1.21 (1.10, 1.33), p<0.001 | | Unadjusted hazard ratio (95% CI) | 1.17 (1.09, 1.24), p<0.001 | |
| Adjusted hazard ratio (95% CI)\* | 1.22 (1.11, 1.34), p<0.001 | | Adjusted hazard ratio (95% CI)† | 1.16 (1.09, 1.24), p<0.001 | |
| Sensitivity analysis 1 aHR (95% CI)\* | 1.23 (1.11, 1.35), p<0.001 | | Sensitivity analysis 1 aHR (95% CI)† | 1.15 (1.08, 1.22), p<0.001 | |
| Sensitivity analysis 2 aHR (95% CI)\* | 1.22 (1.11, 1.34), p<0.001 | | Sensitivity analysis 2 aHR (95% CI)† | 1.16 (1.09, 1.24), p<0.001 | |
| **Diabetes-related foot disease (foot ulcer/ amputation/gangrene)** | 4417 | 15240 | **Macroalbuminuria: ACR > 30 mg/mmol** | 4498 | 15441 |
| Outcome events, n (%) | 100 (2.26) | 274 (1.80) | Outcome events, n (%) | 226 (5.02) | 656 (4.25) |
| Person-years | 16,713 | 60,801 | Person-years | 16,592 | 60,283 |
| Crude incidence rate/1000 person-years | 5.98 | 4.51 | Crude incidence rate/1000 person-years | 13.62 | 10.88 |
| Follow-up years, median (IQR) | 3.06 (1.37, 5.65) | 3.28 (1.51, 5.86) | Follow-up years, median (IQR) | 2.93 (1.31, 5.45) | 3.18 (1.44, 5.75) |
| Unadjusted hazard ratio (95% CI) | 1.33 (1.06, 1.67), p=0.015 | | Unadjusted hazard ratio (95% CI) | 1.24 (1.07, 1.44), p=0.005 | |
| Adjusted hazard ratio (95% CI)\* | 1.36 (1.08, 1.71), p=0.009 | | Adjusted hazard ratio (95% CI)† | 1.21 (1.04, 1.41), p=0.012 | |
| Sensitivity analysis 1 aHR (95% CI)\* | 1.31 (1.04, 1.66), p=0.023 | | Sensitivity analysis 1 aHR (95% CI)† | 1.20 (1.03, 1.40), p=0.019 | |
| Sensitivity analysis 2 aHR (95% CI)\* | 1.36 (1.08, 1.71), p=0.009 | | Sensitivity analysis 2 aHR (95% CI)† | 1.21 (1.04, 1.41), p=0.012 | |
| **Referable retinopathy** | 4473 | 15395 | **Severe macroalbuminuria: ACR > 300 mg/mmol** | 4559 | 15572 |
| Outcome events, n (%) | 100 (2.24) | 399 (2.59) | Outcome events, n (%) | 17 (0.37) | 45 (0.29) |
| Person-years | 16,812 | 60,633 | Person-years | 17,432 | 62,646 |
| Crude incidence rate/1000 person-years | 5.95 | 6.58 | Crude incidence rate/1000 person-years | 0.98 | 0.72 |
| Follow-up years, median (IQR) | 3.04 (1.36, 5.59) | 3.23 (1.48, 5.78) | Follow-up years, median (IQR) | 3.11 (1.41, 5.65) | 3.31 (1.53, 5.91) |
| Unadjusted hazard ratio (95% CI) | 0.90 (0.72, 1.12), p=0.335 | | Unadjusted hazard ratio (95% CI) | 1.36 (0.78, 2.37), p=0.285 | |
| Adjusted hazard ratio (95% CI)\* | 0.93 (0.75, 1.16), p=0.513 | | Adjusted hazard ratio (95% CI)† | 1.37 (0.78, 2.41), p=0.272 | |
| Sensitivity analysis 1 aHR (95% CI)\* | 0.95 (0.76, 1.18), p=0.637 | | Sensitivity analysis 1 aHR (95% CI)† | 1.40 (0.80, 2.47), p=0.238 | |
| Sensitivity analysis 2 aHR (95% CI)\* | 0.93 (0.75, 1.16), p=0.513 | | Sensitivity analysis 2 aHR (95% CI)† | 1.37 (0.78, 2.41), p=0.272 | |
| **CKD stage 3-5** | 4013 | 13944 |  |  |  |
| Outcome events, n (%) | 323 (8.05) | 1161 (8.33) |  |  |  |
| Person-years | 14,693 | 52,781 |  |  |  |
| Crude incidence rate/1000 person-years | 21.98 | 22.00 |  |  |  |
| Follow-up years, median (IQR) | 2.96 (1.29, 5.36) | 3.06 (1.38, 5.56) |  |  |  |
| Unadjusted hazard ratio (95% CI) | 1.00 (0.88, 1.13), p=0.996 | |  |  |  |
| Adjusted hazard ratio (95% CI)† | 1.01 (0.89, 1.15), p=0.847 | |  |  |  |
| Sensitivity analysis 1 aHR (95% CI)† | 1.02 (0.90, 1.16), p=0.754 | |  |  |  |
| Sensitivity analysis 2 aHR (95% CI)† | 1.01 (0.89, 1.15), p=0.847 | |  |  |  |

aHR: adjusted hazard ratio. ACR: albumin-creatinine ratio.

Sensitivity analysis 1: excluding exposed patients with no available matched controls. Sensitivity analysis 2: using multiple imputation to replace missing values of BMI, HbA1c, eGFR and ACR.

\*Adjusted for age category, sex, BMI category, smoking catgeory, Townsend deprivation quintile, baseline hypertension, baseline prescription of lipid-lowering drugs, antihypertensives, antiplatelets and insulin within 60 days of index date, ethnicity, HbA1c category, eGFR category, albumin-creatinine ratio category.

†Adjusted for age category, sex, BMI category, smoking category, Townsend deprivation quintile, baseline hypertension, baseline cardiovascular disease (ischaemic heart disease, heart failure, stroke/transient ischaemic attack), baseline prescription of lipid-lowering drugs, antihypertensives, antiplatelets and insulin within 60 days from index date, ethnicity, HbA1c category.