**Table S5**. **Outcome characteristics of included individuals for the total population of interest and by obstructive sleep apnea presence and severity**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Outcomes** | **TOTAL** | **Normal** | **Mild OSA** | **Moderate OSA** | **Severe OSA** |
|  | N=33,711 | N=10,670 | N=8,964 | N=6,483 | N=7,594 |
| **Primary Outcome** |  |  |  |  |  |
| **First Cancer** | **2,498 (7.4)** | **654 (6.1)** | **618 (6.9)** | **507 (7.8)** | **719 (9.5)** |
| **Follow Up Time**, Years, Median (IQR) | **7 (3-10)** | **6 (3-10)** | **7 (3-10)** | **7 (3-10)** | **7 (4-10)** |
|  |  |  |  |  |  |
| **Secondary Outcomes** |  |  |  |  |  |
|  |  |  |  |  |  |
| **Site-specific** |  |  |  |  |  |
| Prostate | 460 (1.4) | 93 (0.9) | 119 (1.3) | 102 (1.6) | 146 (1.9) |
| Breast | 315 (0.9) | 132 (1.2) | 85 (0.9) | 50 (0.8) | 48 (0.6) |
| Lung | 241 (0.7) | 56 (0.5) | 48 (0.5) | 53 (0.8) | 84 (1.1) |
| Kidney | 108 (0.3) | 32 (0.3) | 19 (0.2) | 20 (0.3) | 37 (0.5) |
| Urinary | 86 (0.3) | 19 (0.2) | 20 (0.2) | 11 (0.2) | 36 (0.5) |
| Melanoma | 131 (0.4) | 25 (0.2) | 38 (0.4) | 31 (0.5) | 37 (0.5) |
| Colorectal | 268 (0.8) | 58 (0.5) | 63 (0.7) | 62 (1.0) | 85 (1.1) |
|  |  |  |  |  |  |
| **Etiology-specific** |  |  |  |  |  |
| Smoking-related | 585 (1.7) | 147 (1.4) | 132 (1.5) | 115 (1.8) | 191 (2.5) |
| Immune-related | 311 (0.9) | 84 (0.8) | 79 (0.9) | 61 (0.9) | 87 (1.1) |
| Alcohol-related | 125 (0.4) | 33 (0.3) | 35 (0.4) | 23 (0.4) | 34 (0.4) |
| Hormone-related | 900 (2.7) | 256 (2.4) | 239 (2.7) | 180 (2.8) | 225 (3.0) |
|  |  |  |  |  |  |
| Detectable by Screening  | 1,057 (3.1) | 290 (2.7) | 269 (3.0) | 216 (3.3) | 282 (3.7) |
|  |  |  |  |  |  |
| **Competing event: death** | 2,832 (8.4) | 667 (6.3) | 629 (7.0) | 506 (7.8) | 1,030 (13.6) |

Data are presented as No (%) unless otherwise indicated.

**Table S6. Primary outcome and primary exposure separately per each sleep cohort. Results from multivariable Cox cause-specific regressions on the associations between incident cancer (primary outcome) and the presence and severity of obstructive sleep apnea as defined by the apnea-hypopnea index or the degree of nocturnal oxygen desaturation. Estimates are presented as adjusted hazard ratios and 95% confidence intervals.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Exposure description** | **TOH Surgical** | **London** | **St. Michael’s** | **Sunnybrook** | **TOH Sleep Clinic** |
| **OSA severity by apnea-hypopnea (AHI)** |
| Model 1 | Severe OSA: Yes vs. No | **1.21 (1.02-1.44)** | **1.52 (1.28-1.80)** | **1.53 (1.33-1.75)** | 1.21 (0.76-1.92) | **2.95 (1.51-5.77)** |
| Model 2 |  | 1.04 (0.87-1.24) | 1.15 (0.97-1.37) | **1.18 (1.02-1.35)** | 0.81 (0.50-1.30) | 1.74 (0.88-3.45) |
| Model 3 |  | 1.04 (0.87-1.25) | 1.13 (0.95-1.35) | 1.13 (0.98-1.31) | 0.73 (0.45-1.19) | 1.72 (0.86-3.46) |
| Model 4 |  | 1.08 (0.89-1.30) | 1.18 (0.98-1.43) | 1.14 (0.98-1.32) | 0.72 (0.43-1.20) | 1.64 (0.80-3.36) |
|  |  |  |  |  |  |  |
| Model 1 | Severe vs normal | **1.29 (1.07-1.56)** | **2.03 (1.61-2.56)** | **2.11 (1.74-2.56)** | 1.56 (0.94-2.59) | **4.70 (1.92-11.5)** |
|  | Moderate vs normal | 1.11 (0.89-1.37) | **1.74 (1.36-2.23)** | **1.71 (1.39-2.10)** | 1.53 (0.89-2.62) | **3.14 (1.30-7.59)** |
|  | Mild vs normal | 1.19 (0.98-1.44) | **1.38 (1.08-1.76)** | **1.45 (1.19-1.77)** | **1.85 (1.22-2.82)** | 1.34 (0.52-3.46) |
| Model 2 | Severe vs normal | 1.00 (0.83-1.22) | 1.26 (0.99-1.60) | **1.33 (1.08-1.63)** | 0.85 (0.50-1.44) | 1.99 (0.79-5.01) |
|  | Moderate vs normal | 0.87 (0.70-1.08) | 1.17 (0.91-1.51) | 1.17 (0.95-1.45) | 0.95 (0.55-1.65) | 1.59 (0.65-3.87) |
|  | Mild vs normal | 0.99 (0.81-1.19) | 1.09 (0.85-1.39) | 1.16 (0.95-1.42) | 1.17 (0.76-1.79) | 0.88 (0.34-2.29) |
| Model 3 | Severe vs normal | 1.00 (0.82-1.23) | 1.24 (0.98-1.58) | **1.26 (1.03-1.55)** | 0.74 (0.43-1.27) | 2.06 (0.81-5.25) |
|  | Moderate vs normal | 0.87 (0.70-1.08) | 1.18 (0.92-1.51) | 1.15 (0.93-1.42) | 0.87 (0.50-1.51) | 1.66 (0.68-4.05) |
|  | Mild vs normal | 0.98 (0.81-1.19) | 1.09 (0.86-1.39) | 1.14 (0.94-1.40) | 1.11 (0.72-1.71) | 0.94 (0.36-2.44) |
| Model 4 | Severe vs normal | 1.05 (0.85-1.29) | **1.34 (1.03-1.74)** | **1.27 (1.03-1.57)** | 0.71 (0.39-1.29) | 1.98 (0.74-5.28) |
|  | Moderate vs normal | 0.90 (0.72-1.12) | 1.23 (0.95-1.59) | 1.15 (0.93-1.43) | 0.84 (0.46-1.52) | 1.61 (0.64-4.05) |
|  | Mild vs normal | 1.00 (0.82-1.21) | 1.10 (0.86-1.41) | 1.14 (0.94-1.40) | 1.09 (0.70-1.71) | 0.93 (0.35-2.43) |
|  | **AHI Quartiles (Q)** |  |  |  |  |  |
| Model 1 | Q4 vs Q1  | — | **2.21 (1.72-2.86)** | **2.32 (1.88-2.87)** | 1.64 (0.99-2.71) | **5.87 (2.09-16.48)** |
|  | Q3 vs Q1  | — | **2.01 (1.55-2.6)** | **1.80 (1.45-2.25)** | **1.89 (1.19-3.01)** | **3.67 (1.33-10.10)** |
|  | Q2 vs Q1  | — | **1.46 (1.11-1.92)** | **1.59 (1.28-1.99)** | **1.64 (1.03-2.59)** | 1.93 (0.65-5.75) |
| Model 2 | Q4 vs Q1  | — | **1.32 (1.02-1.72)** | **1.42 (1.14-1.77)** | 0.87 (0.51-1.48) | 2.35 (0.81-6.76) |
|  | Q3 vs Q1  | — | **1.35 (1.04-1.75)** | **1.25 (1.00-1.56)** | 1.14 (0.71-1.84) | 1.88 (0.68-5.21) |
|  | Q2 vs Q1  | — | 1.16 (0.88-1.53) | **1.29 (1.04-1.62)** | 1.05 (0.66-1.68) | 1.29 (0.43-3.87) |
| Model 3 | Q4 vs Q1  | — | **1.31 (1.01-1.71)** | **1.35 (1.08-1.69)** | 0.75 (0.44-1.30) | 2.44 (0.84-7.11) |
|  | Q3 vs Q1  | — | **1.35 (1.04-1.76)** | 1.23 (0.98-1.54) | 1.05 (0.65-1.70) | 1.99 (0.71-5.52) |
|  | Q2 vs Q1  | — | 1.17 (0.88-1.53) | **1.28 (1.02-1.60)** | 0.99 (0.62-1.59) | 1.37 (0.45-4.11) |
| Model 4 | Q4 vs Q1  | — | **1.40 (1.06-1.86)** | **1.36 (1.08-1.71)** | 0.74 (0.41-1.36) | 2.34 (0.77-7.09) |
|  | Q3 vs Q1  | — | **1.39 (1.07-1.82)** | 1.23 (0.98-1.54) | 1.04 (0.62-1.75) | 1.93 (0.68-5.48) |
|  | Q2 vs Q1  | — | 1.17 (0.89-1.54) | **1.28 (1.02-1.60)** | 0.98 (0.61-1.59) | 1.36 (0.45-4.09) |
| **By the degree of nocturnal oxygen desaturation**  |
|  | **Mean SaO2 Quartiles (Q)** |  |  |  |  |  |
| Model 1 | Q3 vs Q4 | — | 4.14 (0.48-35.47) | **1.38 (1.12-1.70)** | 1.79 (0.89-3.62) | 1.73 (0.49-6.12) |
|  | Q2 vs Q4 | — | 2.69 (0.3-24.06) | **1.82 (1.51-2.21)** | 1.74 (0.78-3.87) | **3.63 (1.19-11.02)** |
|  | Q1 vs Q4 | — | 5.97 (0.75-47.77) | **2.51 (2.07-3.04)** | **2.89 (1.49-5.62)** | **6.75 (2.28-19.96)** |
| Model 2 | Q3 vs Q4 | — | 2.56 (0.29-22.25) | 1.10 (0.89-1.36) | 1.09 (0.53-2.24) | 1.02 (0.29-3.63) |
|  | Q2 vs Q4 | — | 1.12 (0.12-10.46) | **1.25 (1.02-1.52)** | 0.87 (0.38-1.96) | 1.44 (0.46-4.46) |
|  | Q1 vs Q4 | — | 2.18 (0.26-18.25) | **1.39 (1.14-1.70)** | 1.11 (0.55-2.24) | 1.78 (0.58-5.45) |
| Model 3 | Q3 vs Q4 | — | 2.41 (0.28-20.89) | 1.11 (0.90-1.37) | 1.07 (0.52-2.2) | 1.08 (0.30-3.86) |
|  | Q2 vs Q4 | — | 1.04 (0.11-9.83) | **1.21 (1.00-1.48)** | 0.81 (0.35-1.84) | 1.48 (0.48-4.60) |
|  | Q1 vs Q4 | — | 2.31 (0.27-19.42) | 1.29 (1.05-1.58) | 0.97 (0.47-1.98) | 1.86 (0.60-5.76) |
| Model 4 | Q3 vs Q4 | — | 2.30 (0.26-19.97) | 1.11 (0.90-1.37) | 1.07 (0.52-2.2) | 1.07 (0.30-3.82) |
|  | Q2 vs Q4 | — | 0.95 (0.10-9.08) | 1.21 (1.00-1.48) | 0.81 (0.36-1.85) | 1.45 (0.47-4.51) |
|  | Q1 vs Q4 | — | 2.04 (0.24-17.29) | **1.29 (1.05-1.58)** | 0.98 (0.47-2.03) | 1.77 (0.57-5.54) |
|  |  |  |  |  |  |  |
| Model 1 | >30% of TST spent with SaO2<90%: Yes vs. No |  | 2.12 (0.48-9.40) | **2.11 (1.72-2.59)** | **2.56 (1.47-4.46)** | 2.04 (0.28-14.82) |
| Model 2 |  | 2.08 (0.46-9.33) | **1.46 (1.19-1.79)** | 1.64 (0.94-2.89) | 1.31 (0.18-9.52) |
| Model 3 |  | 2.11 (0.42-10.58) | **1.32 (1.07-1.63)** | 1.43 (0.78-2.60) | 1.10 (0.15-8.18) |
| Model 4 |  | 2.04 (0.40-10.38) | **1.32 (1.07-1.63)** | 1.46 (0.79-2.69) | 1.05 (0.14-7.88) |

Statistically significant values in bold

AHI Quartiles: Q4 (AHI ≥28), Q3 (AHI 12-28), Q2 (AHI 4-12), Q1 (AHI<4)

Mean SaO2 Quartiles: Q4 (SaO2 ≥96%), Q3 (SaO2 94.9%-96%), Q2 (SaO2 93.4-94.9%), Q1 (SaO2 <93.4%)

Model 1: Exposure + year of study + sleep clinic site

Model 2: Model 1 + age +sex

Model 3: Model 2 + alcohol use disorder + prior CHF + COPD + hypertension + diabetes

Model 4: Model 3 + OSA treatment as time varying covariate

AHI, apnea-hypopnea index; CHF, chronic heart failure; COPD, chronic obstructive pulmonary disease; OSA, obstructive sleep apnea; SaO2, oxygen saturation; TOH, the Ottawa Hospital; TST, total sleep time; Q, quartile (1 to 4)