**Supplement table 1**

Tests for linearity. P-values for likelihood ratio tests comparing fully adjusted model linear model with model including also a quadratic term of the pollutant (A) and a categorical model with twenty equal sized categories of exposure (defined among controls) (B). Air pollution averaged over all addresses 10 years prior to index.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **BC** | **PM2.5** | **NO2** | **NOx** | **O3** |
| ***A: Including 2nd degree polynomial*** | | | | | |
| Intracranial CNS tumors | 0.40 | 0.16 | 0.55 | 0.33 | 0.32 |
| Malignant | 0.05 | 0.48 | 0.46 | 0.53 | 0.56 |
| Non-malignant | 0.51 | 0.50 | 0.86 | 0.13 | 0.78 |
| Glioma | 0.15 | 0.30 | 0.12 | 0.51 | 0.10 |
| Meningioma | 0.92 | 1.00 | 0.99 | 0.91 | 0.77 |
| Cranial nerves | 0.35 | 0.12 | 0.64 | 0.15 | 0.91 |
| Malignant non-glioma of the brain | 0.24 | 0.57 | 0.65 | 0.05 | 0.59 |
| Non-malignant non-glioma of the brain | 0.93 | 0.99 | 0.70 | 0.89 | 0.45 |
| ***B: 20 equal sized categories*** | | | | | |
| Intracranial CNS tumors | 0.83 | 0.01 | 0.89 | 0.70 | 0.24 |
| Malignant | 0.24 | 0.41 | 0.45 | 0.67 | 0.04 |
| Non-malignant | 0.93 | 0.09 | 0.91 | 0.81 | 0.74 |
| Glioma | 0.75 | 0.45 | 0.51 | 0.64 | 0.27 |
| Meningioma | 0.51 | 0.97 | 0.84 | 0.91 | 0.19 |
| Cranial nerves | 0.72 | 0.06 | 0.98 | 0.76 | 0.80 |
| Malignant non-glioma of the brain | 0.52 | 0.99 | 0.25 | 0.40 | 0.16 |
| Non-malignant non-glioma of the brain | 0.80 | 0.84 | 0.42 | 0.46 | 0.85 |

**Supplement table 2**: Linear associations between time-weighted average air pollution over 1, 5 and 10-year periods and risk of intracranial CNS tumors, Denmark 1989-2014

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **1-yr time weighted average exposure** | |  | **5-yr time weighted average exposure** | |  | **10-yr time weighted average exposure** | |
| **Air pollutant** | | **IQR (µg/m3)** | **OR pr IQRa** | **95% CI** |  | **OR pr IQRa** | **95% CI** |  | **OR pr IQRa** | **95% CI** |
| **Intracranial CNS tumors** | | | | | | | | | | |
|  | NOx | 18.86 | 1.002 | (0.984-1.020) |  | 1.007 | (0.988-1.026) |  | 1.011 | (0.992-1.030) |
|  | NO2 | 10.78 | 1.019 | (0.985-1.054) |  | 1.027 | (0.993-1.062) |  | 1.031 | (0.997-1.066) |
|  | BC | 0.39 | 1.011 | (0.991-1.031) |  | 1.015 | (0.995-1.035) |  | 1.016 | (0.996-1.037) |
|  | PM2.5 | 5.39 | 1.017 | (0.956-1.082) |  | 1.000 | (0.937-1.066) |  | 1.010 | (0.944-1.080) |
|  | O3 | 9.72 | 0.971 | (0.936-1.006) |  | 0.970 | (0.936-1.005) |  | 0.967 | (0.934-1.002) |
| **Malignant** | |  |  |  |  |  |  |  |  |  |
|  | NOx | 18.86 | 1.012 | (0.985-1.039) |  | 1.017 | (0.989-1.045) |  | 1.026 | (0.998-1.056) |
|  | NO2 | 10.78 | 1.026 | (0.977-1.079) |  | 1.031 | (0.981-1.084) |  | 1.042 | (0.992-1.095) |
|  | BC | 0.39 | 1.023 | (0.994-1.053) |  | 1.026 | (0.997-1.056) |  | 1.034 | (1.005-1.065) |
|  | PM2.5 | 5.39 | 0.998 | (0.911-1.092) |  | 0.988 | (0.900-1.085) |  | 1.021 | (0.926-1.126) |
|  | O3 | 9.72 | 0.973 | (0.924-1.025) |  | 0.972 | (0.923-1.023) |  | 0.962 | (0.913-1.012) |
| **Non-malignant** | | |  |  |  |  |  |  |  |  |
|  | NOx | 18.86 | 0.994 | (0.969-1.019) |  | 0.999 | (0.973-1.026) |  | 0.998 | (0.972-1.025) |
|  | NO2 | 10.78 | 1.015 | (0.969-1.063) |  | 1.025 | (0.978-1.073) |  | 1.022 | (0.976-1.070) |
|  | BC | 0.39 | 1.000 | (0.973-1.028) |  | 1.005 | (0.978-1.033) |  | 1.000 | (0.972-1.028) |
|  | PM2.5 | 5.39 | 1.036 | (0.951-1.128) |  | 1.010 | (0.924-1.104) |  | 1.000 | (0.912-1.096) |
|  | O3 | 9.72 | 0.966 | (0.919-1.016) |  | 0.967 | (0.921-1.016) |  | 0.972 | (0.926-1.021) |
| **Glioma** | |  |  |  |  |  |  |  |  |  |
|  | NOx | 18.86 | 1.008 | (0.977-1.041) |  | 1.010 | (0.977-1.044) |  | 1.017 | (0.983-1.052) |
|  | NO2 | 10.78 | 1.016 | (0.959-1.077) |  | 1.018 | (0.960-1.079) |  | 1.026 | (0.969-1.087) |
|  | BC | 0.39 | 1.024 | (0.990-1.059) |  | 1.025 | (0.991-1.060) |  | 1.028 | (0.993-1.063) |
|  | PM2.5 | 5.39 | 0.932 | (0.838-1.037) |  | 0.916 | (0.821-1.024) |  | 0.938 | (0.836-1.053) |
|  | O3 | 9.72 | 0.982 | (0.925-1.044) |  | 0.981 | (0.924-1.042) |  | 0.973 | (0.916-1.033) |
| **Meningioma** | | | | | | | |  |  |  |
|  | NOx | 18.86 | 1.000 | (0.965-1.036) |  | 1.006 | (0.970-1.044) |  | 1.009 | (0.972-1.047) |
|  | NO2 | 10.78 | 1.067 | (1.000-1.139) |  | 1.084 | (1.016-1.157) |  | 1.083 | (1.016-1.154) |
|  | BC | 0.39 | 1.016 | (0.977-1.057) |  | 1.015 | (0.976-1.056) |  | 1.016 | (0.977-1.057) |
|  | PM2.5 | 5.39 | 1.129 | (1.000-1.275) |  | 1.101 | (0.971-1.248) |  | 1.088 | (0.955-1.239) |
|  | O3 | 9.72 | 0.924 | (0.861-0.992) |  | 0.921 | (0.859-0.987) |  | 0.923 | (0.862-0.988) |
| **Cranial Nerves** | | | | | | | | | | |
|  | NOx | 18.86 | 0.996 | (0.937-1.057) |  | 0.991 | (0.928-1.057) |  | 0.970 | (0.908-1.036) |
|  | NO2 | 10.78 | 0.984 | (0.886-1.093) |  | 0.983 | (0.883-1.094) |  | 0.952 | (0.858-1.058) |
|  | BC | 0.39 | 0.989 | (0.926-1.057) |  | 0.969 | (0.904-1.039) |  | 0.943 | (0.879-1.011) |
|  | PM2.5 | 5.39 | 1.080 | (0.889-1.311) |  | 1.012 | (0.823-1.245) |  | 0.963 | (0.776-1.194) |
|  | O3 | 9.72 | 0.987 | (0.882-1.105) |  | 1.006 | (0.899-1.126) |  | 1.046 | (0.936-1.169) |
| **Malignant Non-glioma tumors of the brain** | | | | |  |  |  |  |  |  |
|  | NOx | 18.86 | 1.017 | (0.966-1.071) |  | 1.035 | (0.982-1.090) |  | 1.049 | (0.996-1.106) |
|  | NO2 | 10.78 | 1.039 | (0.942-1.147) |  | 1.065 | (0.965-1.175) |  | 1.084 | (0.983-1.194) |
|  | BC | 0.39 | 1.019 | (0.964-1.077) |  | 1.032 | (0.978-1.089) |  | 1.051 | (0.996-1.110) |
|  | PM2.5 | 5.39 | 1.214 | (1.018-1.449) |  | 1.220 | (1.020-1.459) |  | 1.267 | (1.053-1.524) |
|  | O3 | 9.72 | 0.975 | (0.878-1.082) |  | 0.955 | (0.861-1.058) |  | 0.937 | (0.846-1.037) |
| **Non-Malignant Non-glioma tumors of the brain** | | | | | | | | | | |
|  | NOx | 18.86 | 0.988 | (0941-1.037) |  | 0.991 | (0.946-1.039) |  | 0.995 | (0.950-1.042) |
|  | NO2 | 10.78 | 0.962 | (0.883-1.048) |  | 0.958 | (0.879-1.044) |  | 0.969 | (0.890-1.054) |
|  | BC | 0.39 | 0.985 | (0.965-1.038) |  | 1.006 | (0.961-1.053) |  | 1.003 | (0.956-1.053) |
|  | PM2.5 | 5.39 | 0.866 | (0.727-1.031) |  | 0.869 | (0.732-1.033) |  | 0.897 | (0.759-1.060) |
|  | O3 | 9.72 | 1.005 | (0.918-1.101) |  | 1.018 | (0.929-1.117) |  | 0.994 | (0.920-1.073) |

a: interquartile range (IQR) and percentiles calculated for the 10-year period among all controls.

Matched on age, sex and month of birth and adjusted for marital status, occupational status, personal income, region of origin and area level information on % of parish population with income in lowest quartile, unemployed, manual labor, retired, basic education, living in social housing, owning their own dwelling, single parent families, previously convicted, of Danish origin.

**Supplement table 3:** Linear associations between mean air pollution (10 years before diagNOsis) and incidence of intracranial CNS tumors with and without adjustment for drug use, Denmark 1996-2014

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **Model 3a** | |  | **Model 4b** | |
| **Air pollutant** | | **IQR (µg/m3)** | **OR pr IQR** | **95%CI** |  | **OR pr IQR** | **95%CI** |
| **Intracranial CNS tumors** *(Case: 16579 Controls: 29148)* | | | | | | | |
|  | BC | 0.39 | 1.017 | (0.992-1.042) |  | 1.017 | (0.992-1.042) |
|  | NOx | 18.88 | 1.010 | (0.986-1.034) |  | 1.010 | (0.986-1.034) |
|  | NO2 | 10.78 | 1.034 | (0.994-1.075) |  | 1.034 | (0.994-1.075) |
|  | O3 | 9.72 | 0.967 | (0.928-1.009) |  | 0.967 | (0.928-1.009) |
|  | PM2.5 | 5.40 | 1.013 | (0.931-1.103) |  | 1.013 | (0.931-1.102) |
| **Malignant** *(Case: 7431 Controls: 13087)* | | | | | | | |
|  | BC | 0.39 | 1.042 | (1.005-1.080) |  | 1.042 | (1.005-1.081) |
|  | NOx | 18.88 | 1.032 | (0.996-1.070) |  | 1.033 | (0.997-1.071) |
|  | NO2 | 10.78 | 1.054 | (0.993-1.118) |  | 1.055 | (0.995-1.119) |
|  | O3 | 9.72 | 0.955 | (0.898-1.016) |  | 0.954 | (0.896-1.015) |
|  | PM2.5 | 5.40 | 1.032 | (0.911-1.170) |  | 1.033 | (0.911-1.171) |
| **Non-malignant** *(Case: 9148 Controls: 16061)* | | | | | | | |
|  | BC | 0.39 | 0.994 | (0.960-1.029) |  | 0.992 | (0.958-1.027) |
|  | NOx | 18.88 | 0.992 | (0.960-1.024) |  | 0.990 | (0.959-1.023) |
|  | NO2 | 10.78 | 1.017 | (0.965-1.072) |  | 1.015 | (0.963-1.070) |
|  | O3 | 9.72 | 0.978 | (0.924-1.035) |  | 0.980 | (0.926-1.038) |
|  | PM2.5 | 5.40 | 0.993 | (0.885-1.114) |  | 0.989 | (0.881-1.110) |
| **Glioma** *(Case: 5701 Controls: 9904)* | | | | | | | |
|  | BC | 0.39 | 1.038 | (0.995-1.084) |  | 1.039 | (0.996-1.085) |
|  | NOx | 18.88 | 1.022 | (0.979-1.067) |  | 1.024 | (0.980-1.069) |
|  | NO2 | 10.78 | 1.040 | (0.971-1.114) |  | 1.042 | (0.973-1.116) |
|  | O3 | 9.72 | 0.964 | (0.897-1.036) |  | 0.962 | (0.895-1.034) |
|  | PM2.5 | 5.40 | 0.982 | (0.846-1.140) |  | 0.984 | (0.847-1.142) |
| **Meningioma** *(Case: 4665 Controls: 8261)* | | | | | | | |
|  | BC | 0.39 | 1.032 | (0.984-1.083) |  | 1.028 | (0.980-1.078) |
|  | NOx | 18.88 | 1.024 | (0.979-1.070) |  | 1.020 | (0.975-1.067) |
|  | NO2 | 10.78 | 1.107 | (1.029-1.190) |  | 1.101 | (1.023-1-185) |
|  | O3 | 9.72 | 0.906 | (0.837-0.980) |  | 0.911 | (0.842-0.986) |
|  | PM2.5 | 5.40 | 1.175 | (1.001-1.378) |  | 1.163 | (0.990-1.366) |
| **Cranial Nerves** *(Case: 2025 Controls: 3505)* | | | | | | | |
|  | BC | 0.39 | 0.904 | (0.830-0.985) |  | 0.902 | (0.827-0.982) |
|  | NOx | 18.88 | 0.940 | (0.868-1.018) |  | 0.938 | (0.866-1.017) |
|  | NO2 | 10.78 | 0.920 | (0.816-1.037) |  | 0.918 | (0.814-1.036) |
|  | O3 | 9.72 | 1.084 | (0.954-1.232) |  | 1.085 | (0.954-1.233) |
|  | PM2.5 | 5.40 | 0.96 | (0.739-1.248) |  | 0.964 | (0.741-1.253) |
| **Malignant Non-glioma tumors of brain proper**  *(Case: 1750 Controls: 3200)* | | | | | | | |
|  | BC | 0.39 | 1.043 | (0.975-1.116) |  | 1.043 | (0.975-1.116) |
|  | NOx | 18.88 | 1.051 | (0.984-1.122) |  | 1.051 | (0.984-1.122) |
|  | NO2 | 10.78 | 1.081 | (0.963-1.214) |  | 1.082 | (0.964-1.215) |
|  | O3 | 9.72 | 0.946 | (0.836-1.070) |  | 0.945 | (0.836-1.069) |
|  | PM2.5 | 5.40 | 1.111 | (0.879-1.405) |  | 1.112 | (0.879-1.406) |
| **Non-malignant Non-glioma tumors of the brain proper**  *(Case: 2438 Controls: 4278)* | | | | | | | |
|  | BC | 0.39 | 0.983 | (0.922-1.048) |  | 0.985 | (0.924-1.050) |
|  | NOx | 18.88 | 0.967 | (0.910-1.027) |  | 0.969 | (0.912-1.029) |
|  | NO2 | 10.78 | 0.932 | (0.841-1.032) |  | 0.935 | (0.844-1.036) |
|  | O3 | 9.72 | 1.048 | (0.939-1.169) |  | 1.044 | (0.936-1.165) |
|  | PM2.5 | 5.40 | 0.764 | (0.612-0.954) |  | 0.765 | (0.612-0.955) |

a: Matched on age, sex and month of birth and adjusted for individual marital status, occupational status, personal income, region of origin and area level information on % of parish population with income in lowest quartile, unemployed, manual labor, retired, basic education, living in social housing, owning their own dwelling, single parent families, previously convicted, of Danish origin

b: Model 3 with additional adjustment for forever redeeming 2 prescriptions within a year for Aspirin, Non-aspirin NSAID, HRT, Antidiabetic medication or anti allergic medication.

**Supplement table 4:** Summaries of results from our previous studies rescaled to the IQRs of the present study: PM2.5=5.39µg/m3, NOx=18.86 µg/m3, NO2=10.78 µg/m3.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **End point** |  | **N Cases** |  |  |  |
| Raaschou-nielsen et al 2011[1] - *Cohort. Population: Danish Diet Cancer and health cohort. Follow-up period 2000-2009. Covariates: Age and occupation in oil refineries* | | | | | | |
|  | Malignant neoplasm of brain and other parts of nervous system (ICD7: 193) | | 95 | NOx | IRR: | 1.17 (1.04-1.31) |
|  |  |  |  |  |  |  |
| Poulsen et al 2016[2] - *Case Control. Population: Danish population. Follow-up 2000-2009. Covariates: Sex, year of birth, years of living in highly urbanized municipalities.* | | | | | | |
|  | Tumors situated in the brain (ICD10: C71.0-C71.9. D33.0.-D33.2. D43.0-D43.2) | | 4183 | NOx | OR: | 1.02 (0.97-1.07) |
|  | Malignant (ICD10: C71.0-C71.9) | | 3220 | NOx | OR: | 1.02 (0.96-1.08) |
|  | Non-malignant (ICD10: D33.0.-D33.2. D43.0-D43.2) | | 963 | NOx | OR: | 1.03 (0.91-1.15) |
|  | Glioma (ICD-O-3 topography: C71.0–71.9 and morphology: 9380/3–9481/3) | | 2596 | NOx | OR: | 0.97 (0.90-1.04) |
|  | Non-glioma | | 1587 | NOx | OR: | 1.08 (1.00-1.17) |
|  |  | | | | | |
| Andersen et al[3] - *Escape study. pooled European cohort including Danish Diet Cancer and Health cohort. Covariates: age. sex. education. occupation in petrochemical industry. area-level SES* | | | | | | |
|  | Intracranial CNS tumors (ICD10: C70.0. C71.0-C71.9.C72.2-C72.5. D32.0. D33.0-D33.3.D42.0. D43.0-D43.3) | | 466 | PM2.5 | HR: | 1.14 (0.59-2.21) |
|  |  |  |  | NO2 | HR: | 1.04 (0.82-1.34) |
|  |  |  |  | NOx | HR: | 1.01 (0.85-1.21) |
|  | Malignant (ICD10: C70.0. C71.0-C71.9.C72.2-C72.5) | | 190 | PM2.5 | HR: | 0.98 (0.60-1.62) |
|  |  |  |  | NO2 | HR: | 1.04 (0.81-1.34) |
|  |  |  |  | NOx | HR: | 1.05 (0.87-1.26) |
|  | Non-malignant (ICD10: D32.0. D33.0-D33.3. D42.0.D43.0-D43.3) | | 176 | PM2.5 | HR: | 1.13 (0.43-2.95) |
|  |  |  |  | NO2 | HR: | 0.95 (0.70-1.29) |
|  |  |  |  | NOx | HR: | 0.97 (0.76-1.23) |
|  | Situated in brain (ICD10: C71.0-C71.9. D33.0-D33.2. D43.0-D43.2) | | 188 | PM2.5 | HR: | 0.87 (0.37-2.03) |
|  |  |  |  | NO2 | HR: | 1.24 (0.90-1.70) |
|  |  |  |  | NOx | HR: | 1.11 (0.89-1.39) |
|  | Meningioma (ICD10: C70.0. D32.0.D42.0) | | 115 | PM2.5 | HR: | 2.72 (0.86-8.66) |
|  |  |  |  | NO2 | HR: | 0.98 (0.60-1.62) |
|  |  |  |  | NOx | HR: | 0.99 (0.67-1.47) |

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