**Supplementary Material**

Long-term exposure to air pollution and mortality in a Danish nationwide administrative cohort study: beyond mortality from cardiopulmonary disease and lung cancer

**Table of contents**

**Tables**

[Table S1. The Comparison of the baseline (2000) characteristics for 3,323,612 subjects from the Danish administrative cohort by the status: Being excluded or included in the final analysis. 1](#_Toc97553232)

[Table S2. The number of natural death by quantile of each air pollutants. 1](#_Toc97553233)

[Table S3. Hazard ratios for all-natural cause and cause-specific mortality associated with interquartile range increase in long-term exposure to air pollutants (2.0 µg/m3 for PM2.5, 10.3 µg/m3 for NO2, 0.5×10-5/m for BC) in the Danish administrative cohort (N=3,083,227). 4](#_Toc97553234)

[Table S4. Hazard ratios for all-natural cause and cause-specific mortality associated with long-term exposure to air pollutants (per 5 µg/m3, 10 µg/m3, 0.5 10-5/m, and 10 µg/m3 increase in PM2.5, NO2, BC, and O3, respectively) in main and subset analyses of the Danish administrative cohort study (N=3,083,227). 13](#_Toc97553235)

[Table S5. Effect modification of the association of long-termexposure to air pollutants (per 5 µg/m3, 10 µg/m3, 0.5 10-5/m, and 10 µg/m3 increase in PM2.5, NO2, BC, and O3, respectively) with all-natural cause mortality by cohort baseline characteristics in the Danish administrative cohort study (N=3,083,227). 20](#_Toc97553236)

[Table S6. The comparison of hazard ratios for the associations for all-natural cause and cause-specific mortality associated with long-term exposure to air pollutants (per 5 µg/m3, 10 µg/m3, 0.5 10-5/m, and 10 µg/m3 increase in PM2.5, NO2, BC, and O3, respectively): before and after the further adjustments for age-standardized municipality-level of mortality rate from lung cancer, chronic obstructive pulmonary disease, and diabetes as alternative approaches to adjust for missing lifestyle factors in the Danish administrative cohort (N=3,083,227). 22](#_Toc97553237)

[Table S7. The comparison of hazard ratios for all-natural cause and cause-specific mortality associated with long-term exposure to air pollutants (per 5 µg/m3, 10 µg/m3, 0.5 10-5/m, and 10 µg/m3 increase in PM2.5, NO2, BC, and O3, respectively): before and after applying the indirect adjustment for smoking status and body mass index in the Danish administrative cohort (N=3,083,227). 25](#_Toc97553238)

[Table S8. The risk estimates (log hazard ratio) for lifestyle risk factors (smoking status and body mass index) on mortality outcomes), used for the indirect adjustmenta, in the ELAPSE pooled cohorts. 28](#_Toc97553239)

[Table S9. Relationship between air pollutants and lifestyle risk factors (smoking status and body mass index), used for the indirect adjustmenta, in the Danish Health Survey dataset (N=139,183). 31](#_Toc97553240)

[Table S10. The comparison of hazard ratios for all-natural cause and cause-specific mortality associated with long-term exposure to air pollutants (per 5 µg/m3, 10 µg/m3, 0.5 10-5/m, and 10 µg/m3 increase in PM2.5, NO2, BC, and O3, respectively): between models with exposure estimate in 2010 and models with exposure estimate back-extrapolated to the cohort baseline (2000) in the Danish administrative cohort (N=3,083,227). 33](#_Toc97553241)

[Table S11. The comparison of hazard ratiosfor all-natural cause and cause-specific mortality associated with long-term exposure to air pollutants (per 5 µg/m3, 10 µg/m3, 0.5 10-5/m, and 10 µg/m3 increase in PM2.5, NO2, BC, and O3, respectively): between models with exposure estimate in 2010 and models back-extrapolated time-varying exposure in the Danish administrative cohort (N=3,068,510). 36](#_Toc97553242)

[Table S12. The Control of the false positive rate of 52 statistical tests for the association between 13 mortality outcomes and four exposures. 44](#_Toc97553243)

[Table S13. The Control of the false positive rate of 96 statistical tests for two-pollutant models for the association between 13 mortality outcomes and four exposures. 47](#_Toc97553244)

[Table S14. The comparison of the hazard ratio of association between long-term exposure to air pollution and natural mortality before and after applying inverse probability (IPW) weighting. 52](#_Toc97553245)

[Table S15. The comparison of the hazard ratio of association between long-term exposure to air pollution and natural mortality: The fully adjusted models (the main models) and the models with covariates selected from the DAG. 54](#_Toc97553246)

[Table S16. Comparison of descriptive statistics for demographic characteristics and air pollution exposures between the Danish nationwide administrative cohort and Danish health survey. 55](#_Toc97553247)

**Figures**

[Figure S1. Hazard ratios of all-natural cause and cause-specific mortality associated with interquartile range increase long-term exposure to air pollutants (2.0 µg/m3 for PM2.5, 10.3 µg/m3 for NO2, 0.5 10-5/m for BC) in the Danish administrative cohort (N=3,083,227). 2](#_Toc97553248)

[Figure S2. Exposure-response curve for the associationbetween long-term exposure to NO2 and mortality from (A) all-natural causes, (B) cardiovascular disease, (C) respiratory disease, (D) lung cancer, (E) diabetes, (F) chronic kidney disease, (G) dementia, and (H) psychiatric disorders in the Danish administrative cohort (N=3,083,227) 7](#_Toc97553249)

[Figure S3. Exposure-response curve for the association between long-term exposure to BC and mortality from (A) all-natural causes, (B) cardiovascular disease, (C) respiratory disease, (D) lung cancer, (E) diabetes, (F) chronic kidney disease, (G) dementia, and (H) psychiatric disorders in the Danish administrative cohort (N=3,083,227) 9](#_Toc97553250)

[Figure S4. Exposure-response curve for the association between long-term exposure to O3 and mortality from (A) all-natural causes, (B) cardiovascular disease, (C) respiratory disease, (D) lung cancer, (E) diabetes, (F) chronic kidney disease, (G) dementia, and (H) psychiatric disorders in the Danish administrative cohort (N=3,083,227) 11](#_Toc97553251)

[Figure S5. Unadjusted Directed Acyclic Graph of the association between long-term exposure to air pollution and mortality in the Danish nationwide administrative cohort. 39](#_Toc97553252)

[Figure S6. Forest plot for a visual comparison between recent studies on the association with long-term exposure to PM2.5 and (A) all natural-cause, (B) cardiovascular disease, (C) respiratory disease, and (D) lung cancer mortality and our main result 40](#_Toc97553253)

[Figure S7. Forest plot for a visual comparison between recent studies on the association with long-term exposure to NO2 and (A) all natural-cause, (B) cardiovascular disease, (C) respiratory disease, and (D) lung cancer mortality and our main result. 42](#_Toc97553254)

Table S1. The Comparison of the baseline (2000) characteristics for 3,323,612 subjects from the Danish administrative cohort by the status: Being excluded or included in the final analysis.

| **Characteristics** | **Total**  **N = 3,323,612** | **Excluded**  **N = 240,385** | **Included**  **N = 3,083,227** |
| --- | --- | --- | --- |
| Dead (at the end of follow-upa) | 912,400 (27.5) | 108,519 (45.1) | 803,881 (26.1) |
| Age at baseline (years), mean ± SD | 53.3 ± 15.5 | 58.1 ± 18.5 | 53.0 ± 15.2 |
| Sex, n (%) |  |  |  |
| Man | 1,609,299 (48.4) | 120,348 (50.1) | 1,488,951 (48.3) |
| Woman | 1,714,313 (51.6) | 120,037 (49.9) | 1,594,276 (51.7) |
| Household income, mean ± SD | 160,350.17 ± 166,624.55 | 135,210.9 ± 153,073.31 | 162,308.38 ± 167,475.82 |
| Household income in decile, n (%) |  |  |  |
| 1st (≤90,138 DKK) | 332,355 (10) | 54,348 (22.6) | 278,007 (9) |
| 2nd (90,138 - 103,683.1 DKK) | 332,324 (10) | 34,264 (14.3) | 298,060 (9.7) |
| 3rd (103,683.1 – 118,296.3 DKK) | 332,339 (10) | 31,045 (12.9) | 301,294 (9.8) |
| 4th (118,296.3 – 132789.9 DKK) | 332,338 (10) | 25,166 (10.5) | 307,172 (10) |
| 5th (132,789.9 – 146,860.3 DKK) | 332,339 (10) | 21,002 (8.7) | 311,337 (10.1) |
| 6th (146,860.3 – 161567.7 DKK) | 332,342 (10) | 17,722 (7.4) | 314,620 (10.2) |
| 7th (161,567.7 – 178,556.8 DKK) | 332,339 (10) | 15,884 (6.6) | 316,455 (10.3) |
| 8th (178,556.8 – 200,841.4 DKK) | 332,339 (10) | 14,254 (5.9) | 318,085 (10.3) |
| 9th (200,841.4 – 237,928.2 DKK) | 332,339 (10) | 12,827 (5.3) | 319,512 (10.4) |
| 10th (>237,928.2 DKK) | 332,340 (10) | 13,655 (5.7) | 318,685 (10.3) |
| Occupational status, n (%) |  |  |  |
| Unemployed | 86,028 (2.6) | 7,104 (3.0) | 78,924 (2.6) |
| Sick/cash support/ pension/student/others | 1,298,645 (39.1) | 136,186 (56.7) | 1,162,459 (37.7) |
| Employed | 1,938,894 (58.3) | 97,050 (40.4) | 1,841,844 (59.7) |
| Immigrant status |  |  |  |
| Danish origin | 3,133,505 (94.3) | 226,228 (94.1) | 2,907,277 (94.3) |
| Immigrants/descendants from western country of origin | 85,119 (2.6) | 7,069 (2.9) | 78,050 (2.5) |
| Immigrants/descendants from non-western country of origin | 104,964 (3.2) | 7,064 (2.9) | 97,900 (3.2) |
| Marital status |  |  |  |
| Unmarried | 579,299 (17.4) | 57,737 (24.0) | 521,562 (16.9) |
| Divorced | 371,446 (11.2) | 33,726 (14.0) | 337,720 (11) |
| Widowed | 346,690 (10.4) | 43,949 (18.3) | 302,741 (9.8) |
| Married/Partner | 2,025,959 (61.0) | 104,755 (43.6) | 1,921,204 (62.3) |
| Highest complete education level |  |  |  |
| Primary | 1,388,320 (41.8) | 134,692 (56.0) | 1,253,628 (40.7) |
| Upper secondary | 112,706 (3.4) | 7,305 (3.0) | 105,401 (3.4) |
| Vocation/qualifying | 1,137,187 (34.2) | 63,706 (26.5) | 1,073,481 (34.8) |
| Vocation bachelors/ short cycle higher education | 501,983 (15.1) | 24,803 (10.3) | 477,180 (15.5) |
| More than college level | 183,416 (5.5) | 9,879 (4.1) | 173,537 (5.6) |
| Parish level mean income in 2001, mean ± SD | 164,677.09 ± 27,161.64 | 159,746.7 ±  27,864.17 | 165,011.18 ± 27,080.93 |
| Parish level percentage of unemployment, mean ± SD | 1.94 ± 0.68 | 2.01 ± 0.74 | 1.94 ± 0.68 |

Abbreviations: SD – standard deviation; DKK – Danish Krone.

**a** All-cause natural death (A00-R99 based on International Classification of Disease 10th revision)

Table S2. The number of natural death by quantile of each air pollutants.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| PM2.5, µg/m3 | N | NO2, µg/m3 | N | BC,  10-5/m | N | O3,  µg/m3 | N |
| <11.3 | 177,879 | <14.6 | 173,720 | <0.7 | 179,757 | <78.6 | 226,859 |
| 11.3-12.3 | 195,060 | 14.6-18.7 | 198,959 | 0.7-0.9 | 192,959 | 78.6-81.2 | 207,649 |
| 12.3-13.3 | 212,209 | 18.7-24.9 | 211,348 | 0.9-1.2 | 204,493 | 81.2-82.8 | 186,463 |
| >13.3 | 218,733 | >24.9 | 219,854 | >3.7 | 226,672 | >82.8 | 182,910 |

Abbreviations: PM2.5 – Particulate matter aerodynamic diameter < 2.5 µm; NO2 – Nitrogen dioxide; BC – Black carbon, O3 – ozone, warm-season (April-September).

Figure S1. Hazard ratios of all-natural cause and cause-specific mortality associated with interquartile range increase long-term exposure to air pollutants (2.0 µg/m3 for PM2.5, 10.3 µg/m3 for NO2, 0.5 10-5/m for BC) in the Danish administrative cohort (N=3,083,227).

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Abbreviations: IQR – Interquartile range; PM2.5 – Particulate matter aerodynamic diameter < 2.5 µm; NO2 – Nitrogen dioxide; BC – Black carbon: O3 – ozone, warm-season (April-September); COPD – Chronic obstructive pulmonary disease; ALRI – Acute Lower respiratory infection.

The solid circles and bars show the estimated hazard ratios and 95% confidence intervals.

Hazard ratios were obtained from models adjusting for age (underlying time scale), sex (strata), and parish level (cluster term), household income in decile, occupational status, immigrant status, marital status, and highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

Table S3. Hazard ratios for all-natural cause and cause-specific mortality associated with interquartile range increase in long-term exposure to air pollutants (2.0 µg/m3 for PM2.5, 10.3 µg/m3 for NO2, 0.5×10-5/m for BC) in the Danish administrative cohort (N=3,083,227).

|  |  |
| --- | --- |
| **Air pollutant** | **Hazard ratio (95% confidence interval)** |
| All-natural cause |  |
| PM2.5 | 1.04 (1.03, 1.05) |
| NO2 | 1.06 (1.05, 1.07) |
| BC | 1.05 (1.04, 1.06) |
| All cardiovascular diseases |  |
| PM2.5 | 1.04 (1.03, 1.05) |
| NO2 | 1.04 (1.03, 1.05) |
| BC | 1.03 (1.02, 1.04) |
| Ischemic heart disease |  |
| PM2.5 | 1.03 (1.02, 1.05) |
| NO2 | 1.05 (1.03, 1.06) |
| BC | 1.03 (1.01, 1.04) |
| Stroke |  |
| PM2.5 | 1.02 (1.01, 1.04) |
| NO2 | 1.02 (1.00, 1.04) |
| BC | 1.01 (1.00, 1.03) |
| All respiratory diseases |  |
| PM2.5 | 1.04 (1.03, 1.06) |
| NO2 | 1.09 (1.07, 1.10) |
| BC | 1.06 (1.05, 1.08) |
| Chronic obstructive pulmonary disease |  |
| PM2.5 | 1.03 (1.01, 1.05) |
| NO2 | 1.09 (1.07, 1.12) |
| BC | 1.06 (1.04, 1.08) |
| Asthma |  |
| PM2.5 | 1.05 (0.98, 1.13) |
| NO2 | 1.13 (1.04, 1.23) |
| BC | 1.09 (1.01, 1.19) |
| Acute lower respiratory infection |  |
| PM2.5 | 1.05 (1.03, 1.07) |
| NO2 | 1.06 (1.03, 1.09) |
| BC | 1.05 (1.02, 1.07) |
| Lung cancer |  |
| PM2.5 | 1.07 (1.06, 1.09) |
| NO2 | 1.13 (1.11, 1.15) |
| BC | 1.10 (1.08, 1.12) |
| Diabetes |  |
| PM2.5 | 1.04 (1.01, 1.06) |
| NO2 | 1.02 (1.00, 1.05) |
| BC | 1.00 (0.97, 1.03) |
| Chronic kidney disease |  |
| PM2.5 | 0.98 (0.94, 1.03) |
| NO2 | 1.06 (1.00, 1.12) |
| BC | 1.02 (0.96, 1.08) |
| Dementia |  |
| PM2.5 | 1.02 (1.00, 1.04) |
| NO2 | 1.05 (1.03, 1.07) |
| BC | 1.03 (1.01, 1.05) |
| Psychiatric disorders |  |
| PM2.5 | 1.13 (1.10, 1.17) |
| NO2 | 1.24 (1.20, 1.28) |
| BC | 1.21 (1.17, 1.25) |

Abbreviations: PM2.5 – Particulate matter aerodynamic diameter < 2.5 µm; NO2 – Nitrogen dioxide; BC – Black carbon.

Hazard ratios and confidence intervals were obtained from models adjusting for age (underlying time scale), sex (strata), and parish level (cluster term), household income in decile, occupational status, immigrant status, marital status, and highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

Figure S2. Exposure-response curve for the associationbetween long-term exposure to NO2 and mortality from (A) all-natural causes, (B) cardiovascular disease, (C) respiratory disease, (D) lung cancer, (E) diabetes, (F) chronic kidney disease, (G) dementia, and (H) psychiatric disorders in the Danish administrative cohort (N=3,083,227)

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Abbreviations: NO2 – Nitrogen dioxide.

Red vertical dashed lines show values used for subset analyses: 40 (the EU standard), 30, and 20 μg/m3.

The upper limit of the x-axis was truncated at 99.5 percentile of the distribution of NO2.

Associations were obtained from models adjusting for age (underlying time scale), sex (strata), household income in decile, occupational status, immigrant status, marital status, and highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

Figure S3. Exposure-response curve for the association between long-term exposure to BC and mortality from (A) all-natural causes, (B) cardiovascular disease, (C) respiratory disease, (D) lung cancer, (E) diabetes, (F) chronic kidney disease, (G) dementia, and (H) psychiatric disorders in the Danish administrative cohort (N=3,083,227)

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Abbreviations: BC – Black carbon.

Red vertical dashed lines show values used for subset analyses: 2, 1.5, 1.0×10-5/m.

The upper limit of the x-axis was truncated at the 99.5 percentile of the distribution of BC.

Associations were obtained from models adjusting for age (underlying time scale), sex (strata), household income in decile, occupational status, immigrant status, marital status, and highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

Figure S4. Exposure-response curve for the association between long-term exposure to O3 and mortality from (A) all-natural causes, (B) cardiovascular disease, (C) respiratory disease, (D) lung cancer, (E) diabetes, (F) chronic kidney disease, (G) dementia, and (H) psychiatric disorders in the Danish administrative cohort (N=3,083,227)

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Abbreviations: O3 – ozone, warm-season (April-September).

Red vertical dashed lines show values used for subset analyses: 80 μg/m3.

The upper limit of the x-axis was truncated at 99.5 percentile of the distribution of O3.

Associations were obtained from models adjusting for age (underlying time scale), sex (strata), household income in decile, occupational status, immigrant status, marital status, and highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

Table S4. Hazard ratios for all-natural cause and cause-specific mortality associated with long-term exposure to air pollutants (per 5 µg/m3, 10 µg/m3, 0.5 10-5/m, and 10 µg/m3 increase in PM2.5, NO2, BC, and O3, respectively) in main and subset analyses of the Danish administrative cohort study (N=3,083,227).

| **Mortality outcome** | **Pollutant** | **Subset** | **N** | **case** | **HR (95% CI)** |
| --- | --- | --- | --- | --- | --- |
| All-natural causes | PM2.5 | Full dataset | 3,083,227 | 803,881 | 1.11 (1.09, 1.13) |
| <15 µg/m3 | 2,862,881 | 742,062 | 1.15 (1.13, 1.17) |
| <12 µg/m3 | 1,276,038 | 302,215 | 1.26 (1.21, 1.30) |
| NO2 | Full dataset | 3,083,227 | 803,881 | 1.06 (1.05, 1.07) |
| <40 µg/m3 | 3,053,801 | 795,060 | 1.07 (1.06, 1.07) |
| <30 µg/m3 | 2,637,650 | 673,606 | 1.11 (1.10, 1.12) |
| <20 µg/m3 | 1,756,452 | 431,267 | 1.19 (1.18, 1.21) |
| BC | Full dataset | 3,083,227 | 803,881 | 1.05 (1.04, 1.06) |
| <2×10-5/m | 3,064,493 | 797,801 | 1.05 (1.04, 1.06) |
| <1.5×10-5/m | 2,705,594 | 692,740 | 1.09 (1.08, 1.10) |
| <1×10-5/m | 1,754,873 | 427670 | 1.20 (1.18, 1.23) |
| O3 | Full dataset | 3,083,227 | 803,881 | 0.96 (0.95, 0.97) |
| <80 µg/m3 | 1,111,366 | 321,586 | 1.02 (1.00, 1.04) |
| All cardiovascular diseases | PM2.5 | Full dataset | 3,083,227 | 223,553 | 1.09 (1.07, 1.12) |
| <15 µg/m3 | 2,862,881 | 206,390 | 1.14 (1.11, 1.17) |
| <12 µg/m3 | 1,276,038 | 83,626 | 1.27 (1.20, 1.35) |
| NO2 | Full dataset | 3,083,227 | 223,553 | 1.04 (1.03, 1.05) |
| <40 µg/m3 | 3,053,801 | 221,124 | 1.05 (1.04, 1.06) |
| <30 µg/m3 | 2,637,650 | 186,868 | 1.07 (1.06, 1.09) |
| <20 µg/m3 | 1,756,452 | 121,335 | 1.17 (1.15, 1.20) |
| BC | Full dataset | 3,083,227 | 223,553 | 1.03 (1.02, 1.04) |
| <2×10-5/m | 3,064,493 | 221,856 | 1.04 (1.03, 1.05) |
| <1.5×10-5/m | 2,705,594 | 192,265 | 1.07 (1.05, 1.08) |
| <1×10-5/m | 1,754,873 | 120,043 | 1.19 (1.15, 1.23) |
| O3 | Full dataset | 3,083,227 | 223,553 | 0.98 (0.96, 0.99) |
| <80 µg/m3 | 1,111,366 | 90,230 | 1.02 (0.99, 1.05) |
| Ischemic heart disease | PM2.5 | Full dataset | 3,083,227 | 89,914 | 1.08 (1.05, 1.12) |
| <15 µg/m3 | 2,862,881 | 83,642 | 1.14 (1.09, 1.19) |
| <12 µg/m3 | 1,276,038 | 34,788 | 1.32 (1.20, 1.45) |
| NO2 | Full dataset | 3,083,227 | 89,914 | 1.04 (1.03, 1.06) |
| <40 µg/m3 | 3053801 | 89,061 | 1.05 (1.04, 1.07) |
| <30 µg/m3 | 2637650 | 76,871 | 1.09 (1.07, 1.11) |
| <20 µg/m3 | 1756452 | 50,955 | 1.21 (1.17, 1.25) |
| BC | Full dataset | 3,083,227 | 89,914 | 1.03 (1.01, 1.05) |
| <2×10-5/m | 3,064,493 | 89,306 | 1.03 (1.02, 1.05) |
| <1.5×10-5/m | 2,705,594 | 78,671 | 1.07 (1.05, 1.09) |
| <1×10-5/m | 1,754,873 | 50,308 | 1.22 (1.15, 1.28) |
| O3 | Full dataset | 3,083,227 | 89,914 | 0.98 (0.96, 1.01) |
| <80 µg/m3 | 1,111,366 | 35,482 | 1.01 (0.98, 1.05) |
| Stroke | PM2.5 | Full dataset | 3,083,227 | 63,492 | 1.06 (1.02, 1.10) |
| <15 µg/m3 | 2,862,881 | 58,696 | 1.10 (1.06, 1.15) |
| <12 µg/m3 | 1,276,038 | 23,800 | 1.35 (1.22, 1.49) |
| NO2 | Full dataset | 3,083,227 | 63,492 | 1.02 (1.00, 1.04) |
| <40 µg/m3 | 3053801 | 62,834 | 1.03 (1.01, 1.04) |
| <30 µg/m3 | 2637650 | 53,190 | 1.07 (1.05, 1.10) |
| <20 µg/m3 | 1756452 | 34,123 | 1.19 (1.15, 1.23) |
| BC | Full dataset | 3,083,227 | 63,492 | 1.01 (1.00, 1.03) |
| <2×10-5/m | 3,064,493 | 63,021 | 1.01 (1.00, 1.03) |
| <1.5×10-5/m | 2,705,594 | 54,727 | 1.06 (1.04, 1.08) |
| <1×10-5/m | 1,754,873 | 33,888 | 1.21 (1.15, 1.27) |
| O3 | Full dataset | 3,083,227 | 63,492 | 1.01 (0.99, 1.04) |
| <80 µg/m3 | 1,111,366 | 25,387 | 1.05 (1.01, 1.11) |
| All respiratory diseases | PM2.5 | Full dataset | 3,083,227 | 90,028 | 1.11 (1.07, 1.15) |
| <15 µg/m3 | 2,862,881 | 82,881 | 1.15 (1.10, 1.19) |
| <12 µg/m3 | 1,276,038 | 33,356 | 1.23 (1.13, 1.33) |
| NO2 | Full dataset | 3,083,227 | 90,028 | 1.08 (1.07, 1.10) |
| <40 µg/m3 | 3,053,801 | 89,016 | 1.09 (1.07, 1.11) |
| <30 µg/m3 | 2,637,650 | 74,882 | 1.14 (1.12, 1.17) |
| <20 µg/m3 | 1,756,452 | 47,568 | 1.25 (1.21, 1.29) |
| BC | Full dataset | 3,083,227 | 90,028 | 1.06 (1.05, 1.08) |
| <2×10-5/m | 3,064,493 | 89,324 | 1.06 (1.05, 1.08) |
| <1.5×10-5/m | 2,705,594 | 77,153 | 1.12 (1.10, 1.14) |
| <1×10-5/m | 1,754,873 | 47,024 | 1.21 (1.16, 1.26) |
| O3 | Full dataset | 3,083,227 | 90,028 | 0.94 (0.92, 0.96) |
| <80 µg/m3 | 1,111,366 | 37,196 | 1.07 (1.03, 1.11) |
| Chronic obstructive pulmonary disease | PM2.5 | Full dataset | 3,083,227 | 53,068 | 1.08 (1.04, 1.12) |
| <15 µg/m3 | 2,862,881 | 49,079 | 1.10 (1.05, 1.16) |
| <12 µg/m3 | 1,276,038 | 20,264 | 1.24 (1.12, 1.38) |
| NO2 | Full dataset | 3,083,227 | 53,068 | 1.09 (1.07, 1.11) |
| <40 µg/m3 | 3053801 | 52,494 | 1.09 (1.07, 1.11) |
| <30 µg/m3 | 2637650 | 44,760 | 1.16 (1.13, 1.18) |
| <20 µg/m3 | 1756452 | 28,831 | 1.28 (1.23, 1.33) |
| BC | Full dataset | 3,083,227 | 53,068 | 1.06 (1.04, 1.08) |
| <2×10-5/m | 3,064,493 | 52,676 | 1.06 (1.04, 1.09) |
| <1.5×10-5/m | 2,705,594 | 46,036 | 1.12 (1.10, 1.15) |
| <1×10-5/m | 1,754,873 | 28,343 | 1.20 (1.14, 1.27) |
| O3 | Full dataset | 3,083,227 | 53,068 | 0.93 (0.91, 0.96) |
| <80 µg/m3 | 1,111,366 | 21,642 | 1.12 (1.07, 1.18) |
| Asthma | PM2.5 | Full dataset | 3,083,227 | 1,506 | 1.13 (0.94, 1.36) |
| <15 µg/m3 | 2,862,881 | 1,360 | 1.24 (0.99, 1.55) |
| <12 µg/m3 | 1,276,038 | 531 | 1.62 (0.84, 3.14) |
| NO2 | Full dataset | 3,083,227 | 1,506 | 1.13 (1.04, 1.23) |
| <40 µg/m3 | 3053801 | 1,489 | 1.14 (1.04, 1.25) |
| <30 µg/m3 | 2637650 | 1,197 | 1.19 (1.06, 1.34) |
| <20 µg/m3 | 1,756,452 | 730 | 1.28 (1.01, 1.62) |
| BC | Full dataset | 3,083,227 | 1,506 | 1.10 (1.01, 1.20) |
| <2×10-5/m | 3,064,493 | 1,494 | 1.11 (1.01, 1.21) |
| <1.5×10-5/m | 2,705,594 | 1,236 | 1.15 (1.02, 1.29) |
| <1×10-5/m | 1,754,873 | 721 | 1.06 (0.80, 1.41) |
| O3 | Full dataset | 3,083,227 | 1,506 | 0.84 (0.75, 0.94) |
| <80 µg/m3 | 1,111,366 | 678 | 0.85 (0.68, 1.06) |
| Acute lower respiratory infection | PM2.5 | Full dataset | 3,083,227 | 27,772 | 1.14 (1.09, 1.20) |
| <15 µg/m3 | 2,862,881 | 25,366 | 1.17 (1.10, 1.25) |
| <12 µg/m3 | 1,276,038 | 9,809 | 1.18 (1.03, 1.37) |
| NO2 | Full dataset | 3,083,227 | 27,772 | 1.06 (1.03, 1.08) |
| <40 µg/m3 | 3053801 | 27,441 | 1.07 (1.04, 1.09) |
| <30 µg/m3 | 2637650 | 22,699 | 1.11 (1.08, 1.15) |
| <20 µg/m3 | 1756452 | 14,193 | 1.19 (1.12, 1.26) |
| BC | Full dataset | 3,083,227 | 27,772 | 1.05 (1.02, 1.07) |
| <2×10-5/m | 3,064,493 | 27,540 | 1.05 (1.02, 1.08) |
| <1.5×10-5/m | 2,705,594 | 23,402 | 1.09 (1.06, 1.13) |
| <1×10-5/m | 1,754,873 | 14,104 | 1.20 (1.11, 1.29) |
| O3 | Full dataset | 3,083,227 | 27,772 | 0.98 (0.95, 1.01) |
| <80 µg/m3 | 1,111,366 | 11,722 | 1.01 (0.95, 1.07) |
| Lung cancer | PM2.5 | Full dataset | 3,083,227 | 58,435 | 1.19 (1.15, 1.24) |
| <15 µg/m3 | 2,862,881 | 54,171 | 1.22 (1.17, 1.27) |
| <12 µg/m3 | 1,276,038 | 22,841 | 1.29 (1.17, 1.43) |
| NO2 | Full dataset | 3,083,227 | 58,435 | 1.13 (1.11, 1.15) |
| <40 µg/m3 | 3053801 | 57,803 | 1.13 (1.11, 1.15) |
| <30 µg/m3 | 2637650 | 49,992 | 1.18 (1.15, 1.20) |
| <20 µg/m3 | 1756452 | 32,520 | 1.27 (1.22, 1.32) |
| BC | Full dataset | 3,083,227 | 58,435 | 1.10 (1.09, 1.12) |
| <2×10-5/m | 3,064,493 | 58,001 | 1.10 (1.08, 1.12) |
| <1.5×10-5/m | 2,705,594 | 51,234 | 1.15 (1.12, 1.17) |
| <1×10-5/m | 1,754,873 | 32,306 | 1.29 (1.23, 1.36) |
| O3 | Full dataset | 3,083,227 | 58,435 | 0.89 (0.87, 0.92) |
| <80 µg/m3 | 1,111,366 | 22,227 | 0.96 (0.93, 1.00) |
| Diabetes | PM2.5 | Full dataset | 3,083,227 | 20,691 | 1.10 (1.04, 1.16) |
| <15 µg/m3 | 2,862,881 | 19,051 | 1.19 (1.11, 1.27) |
| <12 µg/m3 | 1,276,038 | 7,546 | 1.46 (1.23, 1.72) |
| NO2 | Full dataset | 3,083,227 | 20,691 | 1.02 (1.00, 1.05) |
| <40 µg/m3 | 3053801 | 20,469 | 1.03 (1.01, 1.06) |
| <30 µg/m3 | 2637650 | 17,413 | 1.12 (1.09, 1.16) |
| <20 µg/m3 | 1756452 | 11,072 | 1.25 (1.18, 1.33) |
| BC | Full dataset | 3,083,227 | 20,691 | 1.00 (0.97, 1.03) |
| <2×10-5/m | 3,064,493 | 20,531 | 1.01 (0.98, 1.03) |
| <1.5×10-5/m | 2,705,594 | 17,846 | 1.06 (1.02, 1.10) |
| <1×10-5/m | 1,754,873 | 10,941 | 1.21 (1.11, 1.31) |
| O3 | Full dataset | 3,083,227 | 20,691 | 1.03 (0.99, 1.07) |
| <80 µg/m3 | 1,111,366 | 8,254 | 1.06 (0.99, 1.13) |
| Dementia | PM2.5 | Full dataset | 3,083,227 | 41,141 | 1.05 (1.00, 1.10) |
| <15 µg/m3 | 2,862,881 | 38,236 | 1.13 (1.07, 1.19) |
| <12 µg/m3 | 1,276,038 | 14,558 | 1.29 (1.13, 1.48) |
| NO2 | Full dataset | 3,083,227 | 41,141 | 1.05 (1.03, 1.07) |
| <40 µg/m3 | 3053801 | 40,719 | 1.06 (1.03, 1.08) |
| <30 µg/m3 | 2637650 | 34,626 | 1.12 (1.09, 1.15) |
| <20 µg/m3 | 1756452 | 21,607 | 1.24 (1.18, 1.30) |
| BC | Full dataset | 3,083,227 | 41,141 | 1.03 (1.01, 1.05) |
| <2×10-5/m | 3,064,493 | 40,828 | 1.03 (1.01, 1.05) |
| <1.5×10-5/m | 2,705,594 | 35,561 | 1.10 (1.07, 1.13) |
| <1×10-5/m | 1,754,873 | 21,247 | 1.24 (1.17, 1.32) |
| O3 | Full dataset | 3,083,227 | 41,141 | 0.99 (0.95, 1.02) |
| <80 µg/m3 | 1,111,366 | 17,297 | 1.11 (1.04, 1.17) |
| Psychiatric disorders | PM2.5 | Full dataset | 3,083,227 | 12,801 | 1.38 (1.27, 1.50) |
| <15 µg/m3 | 2,862,881 | 11,398 | 1.60 (1.45, 1.77) |
| <12 µg/m3 | 1,276,038 | 4,035 | 2.17 (1.66, 2.83) |
| NO2 | Full dataset | 3,083,227 | 12,801 | 1.23 (1.19, 1.28) |
| <40 µg/m3 | 3053801 | 12,601 | 1.26 (1.22, 1.31) |
| <30 µg/m3 | 2637650 | 10,222 | 1.48 (1.41, 1.55) |
| <20 µg/m3 | 1756452 | 5,716 | 1.81 (1.67, 1.97) |
| BC | Full dataset | 3,083,227 | 12,801 | 1.22 (1.17, 1.26) |
| <2×10-5/m | 3,064,493 | 12,668 | 1.24 (1.19, 1.29) |
| <1.5×10-5/m | 2,705,594 | 10,613 | 1.42 (1.36, 1.49) |
| <1×10-5/m | 1,754,873 | 5,559 | 2.03 (1.81, 2.27) |
| O3 | Full dataset | 3,083,227 | 12,801 | 0.87 (0.83, 0.91) |
| <80 µg/m3 | 1,111,366 | 6,077 | 1.07 (0.99, 1.16) |

Abbreviations: HR – Hazard ratio; CI – Confidence interval; PM2.5 – Particulate matter aerodynamic diameter < 2.5 µm; NO2 – Nitrogen dioxide; BC – Black carbon, O3 – ozone, warm-season (April-September).

Hazard ratios and confidence intervals were obtained from models adjusting for age (underlying time scale), sex (strata), and parish level (cluster term), household income in decile, occupational status, immigrant status, marital status, and highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

Table S5. Effect modification of the association of long-termexposure to air pollutants (per 5 µg/m3, 10 µg/m3, 0.5 10-5/m, and 10 µg/m3 increase in PM2.5, NO2, BC, and O3, respectively) with all-natural cause mortality by cohort baseline characteristics in the Danish administrative cohort study (N=3,083,227).

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | N | Case (%) | PM2.5, Mean | NO2, Mean | BC, Mean | PM2.5  HR (95% CI) | NO2  HR (95% CI) | BC  HR (95% CI) | p-value for interaction |
| Age (years) |  |  |  |  |  |  |  |  | PM2.5:<.0001; NO2:<.0001;  BC: :<.0001 |
| < 65 | 2,385,070 | 281,922 (11.8) | 12.4 | 20.1 | 1.0 | 1.21  (1.19 ,1.22) | 1.11  (1.10 ,1.12) | 1.11  (1.10 ,1.11) |
| ≥ 65 | 698,157 | 521,959 (74.8) | 12.5 | 20.9 | 1.0 | 1.06  (1.05 ,1.07) | 1.04  (1.03 ,1.04) | 1.02  (1.02 ,1.03) |
| Sex |  |  |  |  |  |  |  |  | PM2.5:<.0001; NO2:<.0001;  BC: :<.0001 |
| Men | 1,488,951 | 390,752 (26.2) | 12.4 | 20.1 | 1.0 | 1.18  (1.17 ,1.19) | 1.09  (1.09 ,1.10) | 1.09  (1.08 ,1.09) |
| Women | 1,594,276 | 413,129 (25.9) | 12.4 | 20.5 | 1.0 | 1.04  (1.03 ,1.05) | 1.03  (1.03 ,1.03) | 1.02  (1.01 ,1.02) |
| Household income in quintile |  |  |  |  |  |  |  |  | PM2.5:<.0001; NO2:<.0001;  BC: :<.0001 |
| 1st  (<103,683.1 DKK) | 576,067 | 282,030 (49.0) | 12.5 | 20.9 | 1.1 | 1.10  (1.08 ,1.11) | 1.04  (1.04 ,1.05) | 1.03  (1.03 ,1.04) |
| 2nd  (103,683.1 – 132,789.9 DKK) | 608,466 | 208,313 (34.2) | 12.4 | 20.0 | 1.0 | 1.14  (1.12 ,1.16) | 1.08  (1.07 ,1.08) | 1.06  (1.06 ,1.07) |
| 3rd  (132,789.9 – 161,567.7 DKK) | 625,957 | 124,065 (19.8) | 12.3 | 19.6 | 1.0 | 1.12  (1.10 ,1.14) | 1.07  (1.07 ,1.08) | 1.07  (1.06 ,1.07) |
| 4th  (161,567.7 – 200,841.4 DKK) | 634,540 | 97,466 (15.4) | 12.4 | 20.0 | 1.0 | 1.10  (1.08 ,1.12) | 1.07  (1.06 ,1.08) | 1.06  (1.05 ,1.07) |
| 5th  (>200,841.4 DKK) | 638,197 | 92,007 (14.4) | 12.4 | 21.0 | 1.0 | 1.06  (1.04 ,1.09) | 1.06  (1.05 ,1.07) | 1.05  (1.04 ,1.06) |
| Immigrant status |  |  |  |  |  |  |  |  | PM2.5:<.0001; NO2:<.0001;  BC: :<.0001 |
| Danish | 2,907,277 | 777,888 (26.8) | 12.4 | 20.0 | 1.0 | 1.11  (1.10 ,1.12) | 1.06  (1.06 ,1.07) | 1.05  (1.05 ,1.06) |
| Immigrants/descendants  from western countries | 78,050 | 17,736 (22.7) | 12.8 | 23.3 | 1.1 | 0.98  (0.94 ,1.03) | 1.01  (0.99 ,1.02) | 1.00  (0.98 ,1.02) |
| Immigrants/descendants from non-western countries | 97,900 | 8,257  (8.4) | 13.1 | 25.8 | 1.3 | 0.88  (0.82 ,0.94) | 0.93  (0.90 ,0.96) | 0.90  (0.88 ,0.93) |
| Highest completed education level |  |  |  |  |  |  |  |  | PM2.5:<.0001; NO2:<.0001;  BC: :<.0001 |
| Primary | 1,253,628 | 520,970 (41.6) | 12.4 | 19.8 | 1.0 | 1.11  (1.1 ,1.12) | 1.06  (1.05 ,1.06) | 1.05  (1.04 ,1.05) |
| Upper secondary | 105,401 | 9,497  (9.0) | 12.7 | 23.3 | 1.1 | 1.00  (0.95 ,1.06) | 1.03  (1.01 ,1.06) | 1.02  (1.00 ,1.05) |
| Vocation/qualifying | 1,073,481 | 195,331 (18.2) | 12.3 | 19.8 | 1.0 | 1.13  (1.12 ,1.15) | 1.08  (1.07 ,1.09) | 1.07  (1.06 ,1.08) |
| Vocation bachelors/ short cycle higher education | 477,180 | 58,448 (12.2) | 12.4 | 20.6 | 1.0 | 1.09  (1.06 ,1.12) | 1.05  (1.04 ,1.06) | 1.04  (1.03 ,1.05) |
| More than college level | 173,537 | 19,635 (11.3) | 12.7 | 24.1 | 1.2 | 1.00  (0.96 ,1.04) | 1.02  (1.00 ,1.03) | 1.01  (0.99 ,1.03) |
| Occupational status |  |  |  |  |  |  |  |  | PM2.5:<.0001; NO2:<.0001;  BC: :<.0001 |
| Unemployed | 1,841,844 | 157,803 (8.6) | 12.6 | 21.2 | 1.1 | 1.18  (1.16 ,1.20) | 1.10  (1.09 ,1.11) | 1.10  (1.09 ,1.11) |
| Sick/cash support/ pension/student/others | 78,924 | 10,999 (13.9) | 12.5 | 20.9 | 1.0 | 1.12  (1.06 ,1.18) | 1.07  (1.05 ,1.09) | 1.06  (1.04 ,1.09) |
| Employed | 1,162,459 | 635,079 (54.6) | 12.3 | 19.9 | 1.0 | 1.09  (1.08 ,1.1) | 1.05  (1.05 ,1.06) | 1.04  (1.04 ,1.04) |

Abbreviations: HR – hazard ratio; CI – Confidence interval; PM2.5 – Particulate matter aerodynamic diameter < 2.5 µm; NO2 – Nitrogen dioxide; BC – Black carbon.

Associations were obtained from models adjusting for age (underlying time scale), sex (strata), household income in decile, occupational status, immigrant status, marital status, and highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

Table S6. The comparison of hazard ratios for the associations for all-natural cause and cause-specific mortality associated with long-term exposure to air pollutants (per 5 µg/m3, 10 µg/m3, 0.5 10-5/m, and 10 µg/m3 increase in PM2.5, NO2, BC, and O3, respectively): before and after the further adjustments for age-standardized municipality-level of mortality rate from lung cancer, chronic obstructive pulmonary disease, and diabetes as alternative approaches to adjust for missing lifestyle factors in the Danish administrative cohort (N=3,083,227).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Mortality outcome** | **Model** | **Hazard ratio (95% confidence interval)** | | | |
| **PM2.5** | **NO2** | **BC** | **O3** |
| All-natural causes | Main modela | 1.11 (1.09, 1.13) | 1.06 (1.05, 1.07) | 1.05 (1.04, 1.06) | 0.96 (0.95, 0.97) |
| Further adjustment | 1.11 (1.09 ,1.13) | 1.06 (1.05 ,1.07) | 1.05 (1.04 ,1.06) | 0.96 (0.95 ,0.97) |
| All cardiovascular diseases | Main modela | 1.09 (1.07, 1.12) | 1.04 (1.03, 1.05) | 1.03 (1.02, 1.04) | 0.98 (0.96, 0.99) |
| Further adjustment | 1.09 (1.07 ,1.12) | 1.04 (1.03, 1.05) | 1.03 (1.02, 1.04) | 0.98 (0.96, 0.99) |
| Ischemic heart disease | Main modela | 1.08 (1.05, 1.12) | 1.04 (1.03, 1.06) | 1.03 (1.01, 1.05) | 0.98 (0.96, 1.01) |
| Further adjustment | 1.08 (1.05, 1.12) | 1.04 (1.03, 1.06) | 1.03 (1.01, 1.05) | 0.98 (0.96, 1.01) |
| Stroke | Main modela | 1.06 (1.02, 1.10) | 1.02 (1.00, 1.04) | 1.01 (1.00, 1.03) | 1.01 (0.99, 1.04) |
| Further adjustment | 1.06 (1.02 ,1.10) | 1.02 (1.00 ,1.04) | 1.01 (1.00 ,1.03) | 1.01 (0.99 ,1.04) |
| All respiratory diseases | Main modela | 1.11 (1.07, 1.15) | 1.08 (1.07, 1.10) | 1.06 (1.05, 1.08) | 0.94 (0.92, 0.96) |
| Further adjustment | 1.11 (1.06 ,1.15) | 1.08 (1.07 ,1.10) | 1.06 (1.05 ,1.08) | 0.94 (0.93 ,0.96) |
| Chronic obstructive pulmonary disease | Main modela | 1.08 (1.04, 1.12) | 1.09 (1.07, 1.11) | 1.06 (1.04, 1.08) | 0.93 (0.91, 0.96) |
| Further adjustment | 1.08 (1.03 ,1.11) | 1.08 (1.06 ,1.11) | 1.06 (1.04 ,1.08) | 0.93 (0.91 ,0.96) |
| Asthma | Main modela | 1.13 (0.94, 1.36) | 1.13 (1.04, 1.23) | 1.10 (1.01, 1.20) | 0.84 (0.75, 0.94) |
| Further adjustment | 1.12 (0.93 ,1.35) | 1.12 (1.04 ,1.22) | 1.10 (1.01 ,1.19) | 0.84 (0.75 ,0.94) |
| Acute lower respiratory infection | Main modela | 1.14 (1.09, 1.20) | 1.06 (1.03, 1.08) | 1.05 (1.02, 1.07) | 0.98 (0.95, 1.01) |
| Further adjustment | 1.14 (1.09 ,1.20) | 1.06 (1.03 ,1.08) | 1.05 (1.02 ,1.07) | 0.98 (0.96 ,1.01) |
| Lung cancer | Main modela | 1.19 (1.15, 1.24) | 1.13 (1.11, 1.15) | 1.10 (1.09, 1.12) | 0.89 (0.87, 0.92) |
| Further adjustment | 1.17 (1.13 ,1.22) | 1.13 (1.11 ,1.15) | 1.09 (1.09 ,1.11) | 0.90 (0.88 ,0.93) |
| Diabetes | Main modela | 1.10 (1.04, 1.16) | 1.02 (1.00, 1.05) | 1.00 (0.97, 1.03) | 1.03 (0.99, 1.07) |
| Further adjustment | 1.10 (1.04 ,1.16) | 1.02 (1.00 ,1.05) | 1.00 (0.97 ,1.03) | 1.03 (0.99 ,1.07) |
| Chronic kidney disease | Main modela | 0.95 (0.84, 1.07) | 1.05 (1.00, 1.11) | 1.02 (0.96, 1.08) | 0.90 (0.83, 0.98) |
| Further adjustment | 0.94 (0.83 ,1.06) | 1.05 (1.00 ,1.11) | 1.01 (0.96 ,1.08) | 0.91 (0.84 ,0.98) |
| Dementia | Main modela | 1.05 (1.00, 1.10) | 1.05 (1.03, 1.07) | 1.03 (1.01, 1.05) | 0.99 (0.95, 1.02) |
| Further adjustment | 1.05 (1.00 ,1.10) | 1.05 (1.03 ,1.07) | 1.03 (1.01 ,1.05) | 0.99 (0.95 ,1.02) |
| Psychiatric disorders | Main modela | 1.38 (1.27, 1.50) | 1.23 (1.19, 1.28) | 1.22 (1.17, 1.26) | 0.87 (0.83, 0.91) |
| Further adjustment | 1.39 (1.29 ,1.51) | 1.23 (1.19 ,1.29) | 1.22 (1.17 ,1.26) | 0.86 (0.82 ,0.90) |

Abbreviations: PM2.5 – Particulate matter aerodynamic diameter < 2.5 µm; NO2 – Nitrogen dioxide; BC – Black carbon; O3 – ozone, warm-season (April-September).

a Adjusting for age (underlying time scale), sex (strata), parish level (cluster term), household income in decile, occupational status, immigrant status, marital status, and highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

Table S7. The comparison of hazard ratios for all-natural cause and cause-specific mortality associated with long-term exposure to air pollutants (per 5 µg/m3, 10 µg/m3, 0.5 10-5/m, and 10 µg/m3 increase in PM2.5, NO2, BC, and O3, respectively): before and after applying the indirect adjustment for smoking status and body mass index in the Danish administrative cohort (N=3,083,227).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Mortality outcomes** | **Model** | **Hazard ratio (95% confidence interval )** | | | |
| **PM2.5** | **NO2** | **BC** | **O3** |
| All-natural causes | Main modela | 1.11 (1.09, 1.13) | 1.06 (1.05, 1.07) | 1.05 (1.04, 1.06) | 0.96 (0.95, 0.97) |
| Main modela + indirect adjustmentb | 1.09 (1.08, 1.11) | 1.05 (1.05, 1.06) | 1.05 (1.04, 1.06) | 0.96 (0.95, 0.97) |
| All cardiovascular diseases | Main modela | 1.09 (1.07, 1.12) | 1.04 (1.03, 1.05) | 1.03 (1.02, 1.04) | 0.98 (0.96, 0.99) |
| Main modela + indirect adjustmentb | 1.09 (1.07, 1.12) | 1.04 (1.03, 1.05) | 1.03 (1.02, 1.05) | 0.97 (0.95, 0.98) |
| Ischemic heart disease | Main modela | 1.08 (1.05, 1.12) | 1.04 (1.03, 1.06) | 1.03 (1.01, 1.05) | 0.98 (0.96, 1.01) |
| Main modela + indirect adjustmentb | 1.08 (1.04, 1.12) | 1.04 (1.03, 1.06) | 1.03 (1.02, 1.05) | 0.97 (0.95, 1.00) |
| Stroke | Main modela | 1.06 (1.02, 1.10) | 1.02 (1.00, 1.04) | 1.01 (1.00, 1.03) | 1.01 (0.99, 1.04) |
| Main modela + indirect adjustmentb | 1.05 (1.01, 1.09) | 1.02 (1.00, 1.03) | 1.01 (0.99, 1.03) | 1.01 (0.99, 1.04) |
| All Respiratory diseases | Main modela | 1.11 (1.07, 1.15) | 1.08 (1.07, 1.10) | 1.06 (1.05, 1.08) | 0.94 (0.92, 0.96) |
| Main modela + indirect adjustmentb | 1.06 (1.02, 1.09) | 1.05 (1.03, 1.07) | 1.04 (1.02, 1.06) | 0.97 (0.95, 1.00) |
| Chronic obstructive pulmonary disease | Main modela | 1.08 (1.04, 1.12) | 1.09 (1.07, 1.11) | 1.06 (1.04, 1.08) | 0.93 (0.91, 0.96) |
| Main modela + indirect adjustmentb | 1.00 (0.96, 1.05) | 1.04 (1.02, 1.06) | 1.03 (1.01, 1.05) | 0.98 (0.95, 1.01) |
| Asthma | Main modela | 1.13 (0.94, 1.36) | 1.13 (1.04, 1.23) | 1.10 (1.01, 1.20) | 0.84 (0.75, 0.94) |
| Main modela + indirect adjustmentb | 1.07 (0.89, 1.29) | 1.09 (1.00, 1.18) | 1.06 (0.98, 1.16) | 0.88 (0.78, 0.99) |
| Acute lower respiratory infection | Main modela | 1.14 (1.09, 1.20) | 1.06 (1.03, 1.08) | 1.05 (1.02, 1.07) | 0.98 (0.95, 1.01) |
| Main modela + indirect adjustmentb | 1.12 (1.07, 1.18) | 1.04 (1.02, 1.07) | 1.04 (1.01, 1.06) | 0.99 (0.95, 1.02) |
| Lung cancer | Main modela | 1.19 (1.15, 1.24) | 1.13 (1.11, 1.15) | 1.10 (1.09, 1.12) | 0.89 (0.87, 0.92) |
| Main modela + indirect adjustmentb | 1.12 (1.08, 1.16) | 1.08 (1.07, 1.10) | 1.07 (1.06, 1.09) | 0.93 (0.91, 0.96) |
| Diabetes | Main modela | 1.10 (1.04, 1.16) | 1.02 (1.00, 1.05) | 1.00 (0.97, 1.03) | 1.03 (0.99, 1.07) |
| Main modela + indirect adjustmentb | 1.12 (1.06, 1.18) | 1.04 (1.01, 1.06) | 1.02 (0.99, 1.05) | 0.99 (0.95, 1.02) |
| Chronic kidney disease | Main modela | 0.95 (0.84, 1.07) | 1.05 (1.00, 1.11) | 1.02 (0.96, 1.08) | 0.90 (0.83, 0.98) |
| Main modela + indirect adjustmentb | 0.95 (0.24, 3.75) | 1.08 (0.01, 80.96) | 1.05 (0.03, 33.48) | 0.86 (0, 251.92) |
| Dementia | Main modela | 1.05 (1.00, 1.10) | 1.05 (1.03, 1.07) | 1.03 (1.01, 1.05) | 0.99 (0.95, 1.02) |
| Main modela + indirect adjustmentb | 1.04 (0.99, 1.09) | 1.04 (1.02, 1.07) | 1.02 (1.00, 1.05) | 0.99 (0.96, 1.03) |
| Psychiatric disorders | Main modela | 1.38 (1.27, 1.50) | 1.23 (1.19, 1.28) | 1.22 (1.17, 1.26) | 0.87 (0.83, 0.91) |
| Main modela + indirect adjustmentb | 1.33 (1.23, 1.44) | 1.20 (1.16, 1.25) | 1.19 (1.15, 1.24) | 0.90 (0.85, 0.94) |

Abbreviations: PM2.5 – Particulate matter aerodynamic diameter < 2.5 µm; NO2 – Nitrogen dioxide; BC – Black carbon; O3 – ozone, warm-season (April-September).

aAdjusting for age (underlying time scale), sex (strata), parish level (cluster term), household income in decile, occupational status, immigrant status, marital status, and highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

b The information for applying the indirect adjustment was obtained from the Danish Health Survey.

Table S8. The risk estimates (log hazard ratio) for lifestyle risk factors (smoking status and body mass index) on mortality outcomes), used for the indirect adjustmenta, in the ELAPSE pooled cohorts.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Mortality outcome** | **Previous smoker** | **Current smoker** | **Underweight (BMI<18.5)** | **Overweight (BMI: 25-30)** | **Obese  (BMI>30)** |
| All-natural causes | 0.1480  (0.1206, 0.1755) | 0.7577  (0.7345, 0.7809) | 0.5379  (0.473, 0.6028) | 0.0771  (0.0564, 0.0977) | 0.3646  (0.3376, 0.3916) |
| Cardiovascular diseases | 0.1075  (0.0574, 0.1576) | 0.5895  (0.5454, 0.6335) | 0.4974  (0.3708, 0.6241) | 0.1856  (0.1493, 0.2219) | 0.5012  (0.4549, 0.5475) |
| Ischemic heart disease | 0.1582  (0.0853, 0.231) | 0.6937  (0.6314, 0.7559) | 0.3847  (0.1785, 0.5909) | 0.2339  (0.181, 0.2868) | 0.5834  (0.5168, 0.6501) |
| Stroke | 0.0646  (-0.0358, 0.165) | 0.4581  (0.3678, 0.5484) | 0.5939  (0.3674, 0.8204) | 0.0578  (-0.0142, 0.1297) | 0.1513  (0.0515, 0.251) |
| Respiratory disease | 0.5533  (0.4354, 0.6713) | 1.5921  (1.4969, 1.6873) | 1.3542  (1.1857, 1.5227) | -0.2586  (-0.3435, -0.1736) | -0.0425  (-0.1611, 0.0761) |
| Chronic obstructive pulmonary disease | 0.8349  (0.6664, 1.0034) | 2.1476  (2.0161, 2.279) | 1.4904  (1.2912, 1.6896) | -0.4172  (-0.5285, -0.3058) | -0.2325  (-0.3933, -0.0718) |
| Asthma | 0.8806  (0.2456, 1.5155) | 1.2952  (0.7585, 1.8319) | 1.193  (0.2498, 2.1362) | -0.2889  (-0.754, 0.1762) | -0.5717  (-1.3326, 0.1891) |
| Acute lower respiratory infection | 0.2207  (0.0063, 0.435) | 0.8078  (0.6098, 1.0057) | 1.0404  (0.6483, 1.4324) | -0.0833  (-0.2523, 0.0857) | 0.2624  (0.04, 0.4848) |
| Lung cancer | 0.7341  (0.6171, 0.8512) | 2.192  (2.1035, 2.2805) | 0.7017  (0.5077, 0.8957) | -0.1076  (-0.1789, -0.0363) | -0.1374  (-0.2468, -0.028) |
| Diabetes | 0.1869  (-0.0067, 0.3805) | 0.7194  (0.5541, 0.8847) | 0.3884  (-0.2796, 1.0563) | 0.6251  (0.4641, 0.7861) | 1.5781  (1.4107, 1.7454) |
| Chronic kidney disease | 0.0638  (-0.401, 0.5287) | 0.999  (0.6253, 1.3727) | -14.9129  (-2707.2, 2677.4) | 0.3267  (-0.0008, 0.6542) | 0.7594  (0.3602, 1.1587) |
| Dementia | 0.0133  (-0.1664, 0.1931) | -0.0546  (-0.2717, 0.1624) | 0.3951  (0.0028, 0.7875) | -0.1391  (-0.2873, 0.0091) | -0.1934  (-0.4247, 0.0378) |
| Psychiatric disorders | -0.0111  (-0.4836, 0.4613) | 1.2242  (0.9403, 1.5081) | 0.7024  (0.077, 1.3278) | -0.4494  (-0.7545, -0.1442) | -0.2798  (-0.7479, 0.1883) |

Abbreviations: BMI – body mass index; PM2.5 – Particulate matter aerodynamic diameter < 2.5 µm; NO2 – Nitrogen dioxide; BC – Black carbon, O3 – ozone, warm-season (April-September).

The risk estimates were adjusted for age (underlying time scale), sex (strata), sub-cohort (strata), smoking status, body mass index, marital status, neighborhood-level mean income in 2001.

a The method proposed by Shin et al.

Table S9. Relationship between air pollutants and lifestyle risk factors (smoking status and body mass index), used for the indirect adjustmenta, in the Danish Health Survey dataset (N=139,183).

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Lifestyle factor** | **PM2.5** | | | **NO2** | | | **BC** | | | **O3** | | |
| **Beta** | **SE** | **p-value** | **Beta** | **SE** | **p-value** | **Beta** | **SE** | **p-value** | **Beta** | **SE** | **p-value** |
| Smoking |  |  |  |  |  |  |  |  |  |  |  |  |
| Previous smoker | 0.0035 | 0.0009 | 0.0001 | 0.0012 | 0.0002 | <.0001 | 0.0172 | 0.0045 | 0.0002 | -0.0017 | 0.0003 | <.0001 |
| Current smoker | 0.0043 | 0.0008 | <.0001 | 0.0012 | 0.0002 | <.0001 | 0.0155 | 0.0042 | 0.0002 | -0.0010 | 0.0003 | 0.0007 |
| Body mass index (BMI) |  |  |  |  |  |  |  |  |  |  |  |  |
| Underweight (BMI<18.5) | 0.0001 | 0.0002 | 0.6795 | 0.0002 | 0.0001 | 0.0111 | 0.0026 | 0.0013 | 0.0419 | -0.0002 | 0.0001 | 0.0194 |
| Overweight (BMI: 25-30) | -0.0022 | 0.0009 | 0.0139 | -0.0012 | 0.0002 | <.0001 | -0.0236 | 0.0047 | <.0001 | 0.0018 | 0.0003 | <.0001 |
| Obese  (BMI>30) | -0.0039 | 0.0007 | <.0001 | -0.0011 | 0.0002 | <.0001 | -0.0263 | 0.0035 | <.0001 | 0.0025 | 0.0003 | <.0001 |

Abbreviations: SE – standard error; PM2.5 – Particulate matter aerodynamic diameter < 2.5 µm; NO2 – Nitrogen dioxide; BC – Black carbon, O3 – ozone, warm-season (April-September).

Associations were adjusted for age, sex, household income in decile, occupational status, immigrant status, marital status, highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

a The method proposed by Shin et al.

Table S10. The comparison of hazard ratios for all-natural cause and cause-specific mortality associated with long-term exposure to air pollutants (per 5 µg/m3, 10 µg/m3, 0.5 10-5/m, and 10 µg/m3 increase in PM2.5, NO2, BC, and O3, respectively): between models with exposure estimate in 2010 and models with exposure estimate back-extrapolated to the cohort baseline (2000) in the Danish administrative cohort (N=3,083,227).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Mortality outcome** | **Exposure estimation type** | **PM2.5** | **NO2** | **BC** | **O3** |
| All-natural causes | Exposure in 2010 (main) | 1.11 (1.09, 1.13) | 1.06 (1.05, 1.07) | 1.05 (1.04, 1.06) | 0.96 (0.95, 0.97) |
| Exposure at the baseline (2000) | 1.07 (1.06 ,1.09) | 1.05 (1.04 ,1.05) | 1.05 (1.04 ,1.06) | 0.96 (0.95 ,0.97) |
| All cardiovascular diseases | Exposure in 2010 (main) | 1.09 (1.07, 1.12) | 1.04 (1.03, 1.05) | 1.03 (1.02, 1.05) | 0.98 (0.96, 0.99) |
| Exposure at the baseline (2000) | 1.06 (1.05 ,1.08) | 1.02 (1.03 ,1.04) | 1.03 (1.03 ,1.05) | 0.98 (0.96 ,0.99) |
| Ischemic heart disease | Exposure in 2010 (main) | 1.08 (1.05, 1.12) | 1.04 (1.03, 1.06) | 1.03 (1.01, 1.05) | 0.98 (0.96, 1.01) |
| Exposure at the baseline (2000) | 1.05 (1.04 ,1.08) | 1.03 (1.03 ,1.04) | 1.04 (1.01 ,1.05) | 0.98 (0.96 ,1.01) |
| Stroke | Exposure in 2010 (main) | 1.06 (1.02, 1.10) | 1.02 (1.00, 1.04) | 1.01 (1.00, 1.03) | 1.01 (0.98, 1.04) |
| Exposure at the baseline (2000) | 1.04 (1.02 ,1.07) | 1.02 (1.00 ,1.03) | 1.01 (1.00 ,1.03) | 1.01 (0.98 ,1.04) |
| All respiratory diseases | Exposure in 2010 (main) | 1.11 (1.07, 1.15) | 1.08 (1.07, 1.10) | 1.06 (1.05, 1.08) | 0.94 (0.92, 0.96) |
| Exposure at the baseline (2000) | 1.08 (1.05 ,1.11) | 1.06 (1.06 ,1.07) | 1.06 (1.05 ,1.08) | 0.94 (0.92 ,0.96) |
| Chronic obstructive pulmonary disease | Exposure in 2010 (main) | 1.08 (1.04, 1.12) | 1.09 (1.07, 1.11) | 1.06 (1.04, 1.08) | 0.93 (0.91, 0.96) |
| Exposure at the baseline (2000) | 1.06 (1.03 ,1.08) | 1.07 (1.05 ,1.08) | 1.06 (1.04 ,1.09) | 0.93 (0.91 ,0.96) |
| Asthma | Exposure in 2010 (main) | 1.13 (0.94, 1.36) | 1.13 (1.04, 1.23) | 1.10 (1.01, 1.20) | 0.84 (0.75, 0.94) |
| Exposure at the baseline (2000) | 1.09 (0.96 ,1.24) | 1.10 (1.03 ,1.17) | 1.11 (1.00 ,1.20) | 0.84 (0.76 ,0.94) |
| Acute lower respiratory infection | Exposure in 2010 (main) | 1.14 (1.09, 1.20) | 1.06 (1.03, 1.08) | 1.05 (1.02, 1.07) | 0.98 (0.95, 1.01) |
| Exposure at the baseline (2000) | 1.10 (1.06 ,1.14) | 1.04 (1.03 ,1.06) | 1.05 (1.02 ,1.08) | 0.98 (0.95 ,1.01) |
| Lung cancer | Exposure in 2010 (main) | 1.19 (1.15, 1.24) | 1.13 (1.11, 1.15) | 1.10 (1.09, 1.12) | 0.89 (0.87, 0.92) |
| Exposure at the baseline (2000) | 1.13 (1.10 ,1.16) | 1.10 (1.09 ,1.12) | 1.10 (1.10 ,1.12) | 0.89 (0.87 ,0.92) |
| Diabetes | Exposure in 2010 (main) | 1.10 (1.04, 1.16) | 1.02 (1.00, 1.05) | 1.00 (0.97, 1.03) | 1.03 (0.99, 1.07) |
| Exposure at the baseline (2000) | 1.07 (1.03 ,1.10) | 1.01 (1.00 ,1.04) | 1.00 (0.97 ,1.03) | 1.03 (0.99 ,1.07) |
| Chronic kidney disease | Exposure in 2010 (main) | 0.95 (0.84, 1.07) | 1.05 (1.00, 1.11) | 1.02 (0.96, 1.08) | 0.90 (0.83, 0.98) |
| Exposure at the baseline (2000) | 0.96 (0.89 ,1.05) | 1.04 (0.99 ,1.09) | 1.02 (0.96 ,1.08) | 0.90 (0.84 ,0.98) |
| Dementia | Exposure in 2010 (main) | 1.05 (1.00, 1.10) | 1.05 (1.03, 1.07) | 1.03 (1.01, 1.05) | 0.99 (0.95, 1.02) |
| Exposure at the baseline (2000) | 1.03 (1.00 ,1.07) | 1.04 (1.02 ,1.06) | 1.03 (1.01 ,1.05) | 0.99 (0.95 ,1.02) |
| Psychiatric disorders | Exposure in 2010 (main) | 1.38 (1.27, 1.50) | 1.23 (1.19, 1.28) | 1.22 (1.17, 1.26) | 0.87 (0.83, 0.91) |
| Exposure at the baseline (2000) | 1.24 (1.18 ,1.32) | 1.17 (1.14 ,1.21) | 1.23 (1.18 ,1.27) | 0.87 (0.83 ,0.91) |

Abbreviations: PM2.5 – Particulate matter aerodynamic diameter < 2.5 µm; NO2 – Nitrogen dioxide; BC – Black carbon, O3 – ozone, warm-season (April-September).

Hazard ratios and confidence intervals were adjusted for age (underlying time scale), sex (strata), parish level (cluster term), household income in decile, occupational status, immigrant status, marital status, and highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

Table S11. The comparison of hazard ratiosfor all-natural cause and cause-specific mortality associated with long-term exposure to air pollutants (per 5 µg/m3, 10 µg/m3, 0.5 10-5/m, and 10 µg/m3 increase in PM2.5, NO2, BC, and O3, respectively): between models with exposure estimate in 2010 and models back-extrapolated time-varying exposure in the Danish administrative cohort (N=3,068,510).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Mortality outcome** | **Exposure assessment type** | **Hazard ratio (95% confidence interval)** | | | |
| **PM2.5** | **NO2** | **BC** | **O3** |
| All-natural cause | Exposure in 2010 (main) | 1.11 (1.09, 1.13) | 1.06 (1.05, 1.07) | 1.05 (1.04, 1.06) | 0.96 (0.95, 0.97) |
| Time-varying exposure | 1.08 (1.07, 1.09) | 1.04 (1.04, 1.05) | 1.05 (1.04, 1.05) | 1.00 (1.00, 1.00) |
| All cardiovascular diseases | Exposure in 2010 (main) | 1.09 (1.07, 1.12) | 1.04 (1.03, 1.05) | 1.03 (1.02, 1.04) | 0.98 (0.96, 0.99) |
| Time-varying exposure | 1.03 (1.03, 1.04) | 1.01 (1.00, 1.02) | 1.01 (1.00, 1.01) | 1.00 (1.00, 1.00) |
| Ischemic heart disease | Exposure in 2010 (main) | 1.08 (1.05, 1.12) | 1.04 (1.03, 1.06) | 1.03 (1.01, 1.05) | 0.98 (0.96, 1.01) |
| Time-varying exposure | 1.01 (0.99, 1.03) | 0.99 (0.98, 1.00) | 0.98 (0.97, 1.00) | 1.00 (1.00, 1.00) |
| Stroke | Exposure in 2010 (main) | 1.06 (1.02, 1.10) | 1.02 (1.00, 1.04) | 1.01 (1.00, 1.03) | 1.01 (0.98, 1.04) |
| Time-varying exposure | 1.02 (0.99 ,1.04) | 0.99 (0.98 , 1.00) | 0.99 (0.97 , 1.00) | 1.00 (1.00 ,1.00) |
| All respiratory diseases | Exposure in 2010 (main) | 1.11 (1.07, 1.15) | 1.08 (1.07, 1.10) | 1.06 (1.05, 1.08) | 0.94 (0.92, 0.96) |
| Time-varying exposure | 1.11 (1.08 ,1.13) | 1.08 (1.07 ,1.09) | 1.07 (1.06 ,1.08) | 1.00 (1.00 ,1.00) |
| Chronic obstructive pulmonary disease | Exposure in 2010 (main) | 1.08 (1.04, 1.12) | 1.09 (1.07, 1.11) | 1.06 (1.04, 1.08) | 0.93 (0.91, 0.96) |
| Time-varying exposure | 1.09 (1.06 ,1.11) | 1.08 (1.07 ,1.10) | 1.07 (1.05 ,1.09) | 1.00 (1.00 ,1.00) |
| Asthma | Exposure in 2010 (main) | 1.13 (0.94, 1.36) | 1.13 (1.04, 1.23) | 1.10 (1.01, 1.19) | 0.84 (0.75, 0.94) |
| Time-varying exposure | 1.08 (0.93 ,1.25) | 1.11 (1.03 ,1.20) | 1.12 (1.02 ,1.22) | 0.99 (0.99 ,1.00) |
| Acute lower respiratory infection | Exposure in 2010 (main) | 1.14 (1.09, 1.20) | 1.06 (1.03, 1.08) | 1.05 (1.02, 1.07) | 0.98 (0.94, 1.01) |
| Time-varying exposure | 1.12 (1.08 ,1.16) | 1.04 (1.02 ,1.07) | 1.05 (1.02 ,1.07) | 1.00 (1.00 ,1.00) |
| Lung cancer | Exposure in 2010 (main) | 1.19 (1.15, 1.24) | 1.13 (1.11, 1.15) | 1.10 (1.09, 1.12) | 0.89 (0.87, 0.92) |
| Time-varying exposure | 1.16 (1.13 ,1.19) | 1.13 (1.11 ,1.14) | 1.12 (1.11 ,1.14) | 0.98 (0.98 ,1.00) |
| Diabetes | Exposure in 2010 (main) | 1.10 (1.04, 1.16) | 1.02 (1.00, 1.05) | 1.00 (0.97, 1.03) | 1.03 (0.99, 1.07) |
| Time-varying exposure | 1.09 (1.05 ,1.13) | 1.01 (1.00 ,1.04) | 1.00 (0.96 ,1.03) | 1.01 (1.00 ,1.01) |
| Chronic kidney disease | Exposure in 2010 (main) | 0.95 (0.84, 1.07) | 1.05 (1.00, 1.11) | 1.02 (0.96, 1.08) | 0.90 (0.83, 0.98) |
| Time-varying exposure | 1.03 (0.93 ,1.15) | 1.09 (1.03 ,1.16) | 1.06 (0.99 ,1.14) | 0.99 (0.99 ,1.00) |
| Dementia | Exposure in 2010 (main) | 1.05 (1.00, 1.10) | 1.05 (1.03, 1.07) | 1.03 (1.01, 1.05) | 0.99 (0.95, 1.02) |
| Time-varying exposure | 1.00 (0.97 ,1.03) | 0.99 (0.98 ,1.01) | 1.00 (0.98 ,1.02) | 1.00 (1.00 ,1.00) |
| Psychiatric disorders | Exposure in 2010 (main) | 1.38 (1.27, 1.50) | 1.23 (1.19, 1.28) | 1.22 (1.17, 1.26) | 0.87 (0.83, 0.91) |
| Time-varying exposure | 1.41 (1.33 ,1.48) | 1.27 (1.23 ,1.31) | 1.32 (1.26 ,1.35) | 0.99 (0.99 ,0.99) |

Abbreviations: PM2.5 – Particulate matter aerodynamic diameter < 2.5 µm; NO2 – Nitrogen dioxide; BC – Black carbon; COPD – Chronic obstructive pulmonary disease; ALRI – Acute lower respiratory infection.

Hazard ratiosand confidence intervals were adjusted for age (underlying time scale), sex (strata), household income in decile, occupational status, immigrant status, marital status, and highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

Table S12. The Control of the false positive rate of 52 statistical tests for the association between 13 mortality outcomes and four exposures.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Mortality outcomes | Pollutant | Beta1 | Se1 | z-statistics1 | p-value1 | q-value2 |
| Natural cause | PM2.5 | 0.0204 | 0.0018 | 11.4 | 0.0% | 0.0% |
| NO2 | 0.0059 | 0.0004 | 14.9 | 0.0% | 0.0% |
| BC | 0.0976 | 0.0080 | 12.2 | 0.0% | 0.0% |
| O3 | -0.0042 | 0.0006 | -6.6 | 0.0% | 0.0% |
| All cardiovascular diseases | PM2.5 | 0.0181 | 0.0025 | 7.3 | 0.0% | 0.0% |
| NO2 | 0.0040 | 0.0006 | 7.3 | 0.0% | 0.0% |
| BC | 0.0620 | 0.0106 | 5.8 | 0.0% | 0.0% |
| O3 | -0.0025 | 0.0009 | -2.9 | 0.4% | 0.6% |
| Ischemic heart disease | PM2.5 | 0.0159 | 0.0036 | 4.4 | 0.0% | 0.0% |
| NO2 | 0.0044 | 0.0008 | 5.2 | 0.0% | 0.0% |
| BC | 0.0561 | 0.0164 | 3.4 | 0.1% | 0.1% |
| O3 | -0.0020 | 0.0013 | -1.6 | 11.6% | 13.7% |
| Stroke | PM2.5 | 0.0112 | 0.0036 | 3.1 | 0.2% | 0.3% |
| NO2 | 0.0021 | 0.0009 | 2.4 | 1.5% | 2.1% |
| BC | 0.0281 | 0.0171 | 1.6 | 10.0% | 12.1% |
| O3 | 0.0011 | 0.0013 | 0.8 | 40.6% | 43.1% |
| All respiratory diseases | PM2.5 | 0.0207 | 0.0034 | 6.0 | 0.0% | 0.0% |
| NO2 | 0.0081 | 0.0008 | 10.0 | 0.0% | 0.0% |
| BC | 0.1228 | 0.0166 | 7.4 | 0.0% | 0.0% |
| O3 | -0.0060 | 0.0012 | -4.9 | 0.0% | 0.0% |
| Chronic obstructive pulmonary disease | PM2.5 | 0.0153 | 0.0042 | 3.6 | 0.0% | 0.0% |
| NO2 | 0.0087 | 0.0010 | 8.9 | 0.0% | 0.0% |
| BC | 0.1234 | 0.0202 | 6.1 | 0.0% | 0.0% |
| O3 | -0.0070 | 0.0015 | -4.7 | 0.0% | 0.0% |
| Asthma | PM2.5 | 0.0251 | 0.0188 | 1.3 | 18.2% | 20.6% |
| NO2 | 0.0121 | 0.0043 | 2.8 | 0.5% | 0.8% |
| BC | 0.1844 | 0.0877 | 2.1 | 3.6% | 4.7% |
| O3 | -0.0178 | 0.0057 | -3.1 | 0.2% | 0.3% |
| Acute lower respiratory infection | PM2.5 | 0.0266 | 0.0052 | 5.2 | 0.0% | 0.0% |
| NO2 | 0.0056 | 0.0012 | 4.7 | 0.0% | 0.0% |
| BC | 0.0904 | 0.0239 | 3.8 | 0.0% | 0.0% |
| O3 | -0.0022 | 0.0018 | -1.3 | 20.9% | 23.2% |
| Lung cancer | PM2.5 | 0.0355 | 0.0035 | 10.1 | 0.0% | 0.0% |
| NO2 | 0.0121 | 0.0008 | 14.3 | 0.0% | 0.0% |
| BC | 0.1967 | 0.0167 | 11.8 | 0.0% | 0.0% |
| O3 | -0.0111 | 0.0012 | -9.3 | 0.0% | 0.0% |
| Diabetes | PM2.5 | 0.0188 | 0.0058 | 3.2 | 0.1% | 0.2% |
| NO2 | 0.0022 | 0.0013 | 1.7 | 9.4% | 11.7% |
| BC | 0.0013 | 0.0281 | 0.0 | 96.4% | 96.4% |
| O3 | 0.0027 | 0.0018 | 1.5 | 13.9% | 16.0% |
| Chronic kidney disease | PM2.5 | -0.0100 | 0.0123 | -0.8 | 41.8% | 43.4% |
| NO2 | 0.0053 | 0.0029 | 1.8 | 6.9% | 8.7% |
| BC | 0.0403 | 0.0606 | 0.7 | 50.6% | 51.6% |
| O3 | -0.0108 | 0.0040 | -2.7 | 0.8% | 1.1% |
| Dementia | PM2.5 | 0.0094 | 0.0048 | 1.9 | 5.2% | 6.7% |
| NO2 | 0.0048 | 0.0011 | 4.3 | 0.0% | 0.0% |
| BC | 0.0556 | 0.0213 | 2.6 | 0.9% | 1.3% |
| O3 | -0.0014 | 0.0017 | -0.9 | 39.0% | 42.2% |
| Psychiatric disorders | PM2.5 | 0.0645 | 0.0082 | 7.8 | 0.0% | 0.0% |
| NO2 | 0.0210 | 0.0017 | 12.2 | 0.0% | 0.0% |
| BC | 0.3898 | 0.0365 | 10.7 | 0.0% | 0.0% |
| O3 | -0.0139 | 0.0024 | -5.8 | 0.0% | 0.0% |

1From model 3 adjusting for age (underlying time scale), sex (strata), household income in decile, occupational status, immigrant status, marital status, and highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

2If q-value=p-value×m/i <0.05 than reject null hypothesis. This procedure controls the false discovery rate at 0.05. (m: total number of testing simultaneously considered, i: rank of a statistical test among m statistical tests) (Benjamini and Hochberg 1995).

Table S13. The Control of the false positive rate of 96 statistical tests for two-pollutant models for the association between 13 mortality outcomes and four exposures.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Mortality outcomes | Pollutant | Further adjusted pollutant | Beta1 | Se1 | z-statistics1 | p-value1 | q-value2 |
| Natural cause | PM2.5 | adj. for NO2 | 0.0084 | 0.0024 | 3.6 | 0.0% | 0.1% |
| adj. for BC | 0.0127 | 0.0022 | 5.7 | 0.0% | 0.0% |
| adj. for O3 | 0.0189 | 0.0020 | 9.5 | 0.0% | 0.0% |
| NO2 | adj. for PM2.5 | 0.0047 | 0.0005 | 9.2 | 0.0% | 0.0% |
| adj. for BC | 0.0073 | 0.0008 | 9.0 | 0.0% | 0.0% |
| adj. for O3 | 0.0095 | 0.0008 | 12.6 | 0.0% | 0.0% |
| BC | adj. for PM2.5 | 0.0601 | 0.0097 | 6.2 | 0.0% | 0.0% |
| adj. for NO2 | -0.0324 | 0.0164 | -2.0 | 4.8% | 6.7% |
| adj. for O3 | 0.1165 | 0.0137 | 8.5 | 0.0% | 0.0% |
| O3 | adj. for PM2.5 | -0.0011 | 0.0007 | -1.6 | 12.0% | 14.6% |
| adj. for NO2 | 0.0064 | 0.0011 | 5.6 | 0.0% | 0.0% |
| adj. for BC | 0.0018 | 0.0010 | 1.8 | 6.9% | 9.0% |
| All cardiovascular diseases | PM2.5 | adj. for NO2 | 0.0125 | 0.0033 | 3.8 | 0.0% | 0.0% |
| adj. for BC | 0.0163 | 0.0031 | 5.2 | 0.0% | 0.0% |
| adj. for O3 | 0.0189 | 0.0030 | 6.4 | 0.0% | 0.0% |
| NO2 | adj. for PM2.5 | 0.0022 | 0.0007 | 3.0 | 0.3% | 0.5% |
| adj. for BC | 0.0059 | 0.0011 | 5.2 | 0.0% | 0.0% |
| adj. for O3 | 0.0070 | 0.0010 | 6.8 | 0.0% | 0.0% |
| BC | adj. for PM2.5 | 0.0144 | 0.0135 | 1.1 | 28.8% | 32.1% |
| adj. for NO2 | -0.0416 | 0.0223 | -1.9 | 6.2% | 8.3% |
| adj. for O3 | 0.0774 | 0.0176 | 4.4 | 0.0% | 0.0% |
| O3 | adj. for PM2.5 | 0.0006 | 0.0010 | 0.6 | 57.0% | 60.1% |
| adj. for NO2 | 0.0053 | 0.0016 | 3.3 | 0.1% | 0.2% |
| adj. for BC | 0.0015 | 0.0014 | 1.1 | 28.3% | 32.0% |
| All respiratory diseases | PM2.5 | adj. for NO2 | 0.0000 | 0.0044 | 0.0 | 99.5% | 99.5% |
| adj. for BC | 0.0080 | 0.0043 | 1.9 | 6.2% | 8.3% |
| adj. for O3 | 0.0159 | 0.0038 | 4.2 | 0.0% | 0.0% |
| NO2 | adj. for PM2.5 | 0.0081 | 0.0010 | 8.0 | 0.0% | 0.0% |
| adj. for BC | 0.0121 | 0.0016 | 7.7 | 0.0% | 0.0% |
| adj. for O3 | 0.0126 | 0.0013 | 10.0 | 0.0% | 0.0% |
| BC | adj. for PM2.5 | 0.0997 | 0.0204 | 4.9 | 0.0% | 0.0% |
| adj. for NO2 | -0.0898 | 0.0323 | -2.8 | 0.5% | 0.9% |
| adj. for O3 | 0.1308 | 0.0234 | 5.6 | 0.0% | 0.0% |
| O3 | adj. for PM2.5 | -0.0034 | 0.0013 | -2.6 | 1.1% | 1.7% |
| adj. for NO2 | 0.0080 | 0.0019 | 4.3 | 0.0% | 0.0% |
| adj. for BC | 0.0008 | 0.0017 | 0.5 | 64.1% | 66.2% |
| Lung cancer | PM2.5 | adj. for NO2 | 0.0069 | 0.0046 | 1.5 | 14.0% | 16.2% |
| adj. for BC | 0.0171 | 0.0046 | 3.7 | 0.0% | 0.0% |
| adj. for O3 | 0.0260 | 0.0041 | 6.3 | 0.0% | 0.0% |
| NO2 | adj. for PM2.5 | 0.0110 | 0.0011 | 10.0 | 0.0% | 0.0% |
| adj. for BC | 0.0161 | 0.0017 | 9.5 | 0.0% | 0.0% |
| adj. for O3 | 0.0157 | 0.0015 | 10.4 | 0.0% | 0.0% |
| BC | adj. for PM2.5 | 0.1451 | 0.0218 | 6.7 | 0.0% | 0.0% |
| adj. for NO2 | -0.0924 | 0.0341 | -2.7 | 0.7% | 1.1% |
| adj. for O3 | 0.1770 | 0.0267 | 6.6 | 0.0% | 0.0% |
| O3 | adj. for PM2.5 | -0.0067 | 0.0014 | -4.8 | 0.0% | 0.0% |
| adj. for NO2 | 0.0067 | 0.0021 | 3.2 | 0.1% | 0.2% |
| adj. for BC | -0.0019 | 0.0019 | -1.0 | 30.3% | 33.5% |
| Diabetes | PM2.5 | adj. for NO2 | 0.0210 | 0.0072 | 2.9 | 0.3% | 0.6% |
| adj. for BC | 0.0297 | 0.0071 | 4.2 | 0.0% | 0.0% |
| adj. for O3 | 0.0295 | 0.0065 | 4.6 | 0.0% | 0.0% |
| NO2 | adj. for PM2.5 | -0.0009 | 0.0016 | -0.5 | 59.6% | 62.2% |
| adj. for BC | 0.0101 | 0.0029 | 3.5 | 0.0% | 0.1% |
| adj. for O3 | 0.0100 | 0.0023 | 4.4 | 0.0% | 0.0% |
| BC | adj. for PM2.5 | -0.0869 | 0.0347 | -2.5 | 1.2% | 1.9% |
| adj. for NO2 | -0.1787 | 0.0604 | -3.0 | 0.3% | 0.6% |
| adj. for O3 | 0.0629 | 0.0412 | 1.5 | 12.7% | 15.3% |
| O3 | adj. for PM2.5 | 0.0075 | 0.0021 | 3.7 | 0.0% | 0.1% |
| adj. for NO2 | 0.0139 | 0.0031 | 4.5 | 0.0% | 0.0% |
| adj. for BC | 0.0059 | 0.0027 | 2.2 | 2.7% | 3.8% |
| Chronic kidney disease | PM2.5 | adj. for NO2 | -0.0383 | 0.0159 | -2.4 | 1.6% | 2.4% |
| adj. for BC | -0.0244 | 0.0155 | -1.6 | 11.6% | 14.3% |
| adj. for O3 | -0.0327 | 0.0138 | -2.4 | 1.7% | 2.6% |
| NO2 | adj. for PM2.5 | 0.0110 | 0.0037 | 2.9 | 0.3% | 0.6% |
| adj. for BC | 0.0162 | 0.0060 | 2.7 | 0.7% | 1.1% |
| adj. for O3 | -0.0018 | 0.0046 | -0.4 | 70.1% | 71.6% |
| BC | adj. for PM2.5 | 0.1129 | 0.0763 | 1.5 | 13.9% | 16.3% |
| adj. for NO2 | -0.2464 | 0.1252 | -2.0 | 4.9% | 6.7% |
| adj. for O3 | -0.1560 | 0.0851 | -1.8 | 6.7% | 8.8% |
| O3 | adj. for PM2.5 | -0.0162 | 0.0046 | -3.5 | 0.0% | 0.1% |
| adj. for NO2 | -0.0128 | 0.0064 | -2.0 | 4.7% | 6.6% |
| adj. for BC | -0.0189 | 0.0056 | -3.4 | 0.1% | 0.1% |
| Dementia | PM2.5 | adj. for NO2 | -0.0040 | 0.0063 | -0.6 | 52.5% | 56.6% |
| adj. for BC | 0.0036 | 0.0061 | 0.6 | 55.5% | 59.2% |
| adj. for O3 | 0.0096 | 0.0056 | 1.7 | 8.8% | 11.3% |
| NO2 | adj. for PM2.5 | 0.0053 | 0.0014 | 3.7 | 0.0% | 0.0% |
| adj. for BC | 0.0103 | 0.0024 | 4.3 | 0.0% | 0.0% |
| adj. for O3 | 0.0105 | 0.0019 | 5.6 | 0.0% | 0.0% |
| BC | adj. for PM2.5 | 0.0453 | 0.0267 | 1.7 | 9.0% | 11.3% |
| adj. for NO2 | -0.1228 | 0.0464 | -2.6 | 0.8% | 1.3% |
| adj. for O3 | 0.0879 | 0.0339 | 2.6 | 1.0% | 1.5% |
| O3 | adj. for PM2.5 | 0.0001 | 0.0019 | 0.1 | 95.2% | 96.2% |
| adj. for NO2 | 0.0102 | 0.0028 | 3.6 | 0.0% | 0.1% |
| adj. for BC | 0.0032 | 0.0026 | 1.2 | 22.6% | 25.8% |
| Psychiatric disorders | PM2.5 | adj. for NO2 | 0.0164 | 0.0109 | 1.5 | 13.3% | 15.8% |
| adj. for BC | 0.0249 | 0.0106 | 2.3 | 1.9% | 2.7% |
| adj. for O3 | 0.0574 | 0.0094 | 6.1 | 0.0% | 0.0% |
| NO2 | adj. for PM2.5 | 0.0186 | 0.0022 | 8.4 | 0.0% | 0.0% |
| adj. for BC | 0.0185 | 0.0040 | 4.6 | 0.0% | 0.0% |
| adj. for O3 | 0.0346 | 0.0031 | 11.0 | 0.0% | 0.0% |
| BC | adj. for PM2.5 | 0.3176 | 0.0463 | 6.9 | 0.0% | 0.0% |
| adj. for NO2 | 0.0585 | 0.0857 | 0.7 | 49.5% | 54.0% |
| adj. for O3 | 0.5003 | 0.0570 | 8.8 | 0.0% | 0.0% |
| O3 | adj. for PM2.5 | -0.0046 | 0.0028 | -1.7 | 9.6% | 11.9% |
| adj. for NO2 | 0.0232 | 0.0042 | 5.6 | 0.0% | 0.0% |
| adj. for BC | 0.0103 | 0.0036 | 2.9 | 0.4% | 0.7% |

1From two-pollutant models adjusting for age (underlying time scale), sex (strata), household income in decile, occupational status, immigrant status, marital status, and highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

2If q-value=p-value×m/i <0.05 than reject null hypothesis. This procedure controls the false discovery rate at 0.05. (m: total number of testing simultaneously considered, i: rank of a statistical test among m statistical tests) (Benjamini and Hochberg 1995).

Table S14. The comparison of the hazard ratio of association between long-term exposure to air pollution and natural mortality before and after applying inverse probability (IPW) weighting.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | PM2.5  HR (95%CI) | NO2  HR (95%CI) | BC  HR (95%CI) | O3  HR (95%CI) |
| The main model1 | 1.11 (1.09, 1.13) | 1.06 (1.05, 1.07) | 1.05 (1.04, 1.06) | 0.96 (0.95, 0.97) |
| The main model1+IPW2 | 1.11 (1.09, 1.13) | 1.06 (1.05, 1.07) | 1.05 (1.04, 1.06) | 0.96 (0.95, 0.97) |

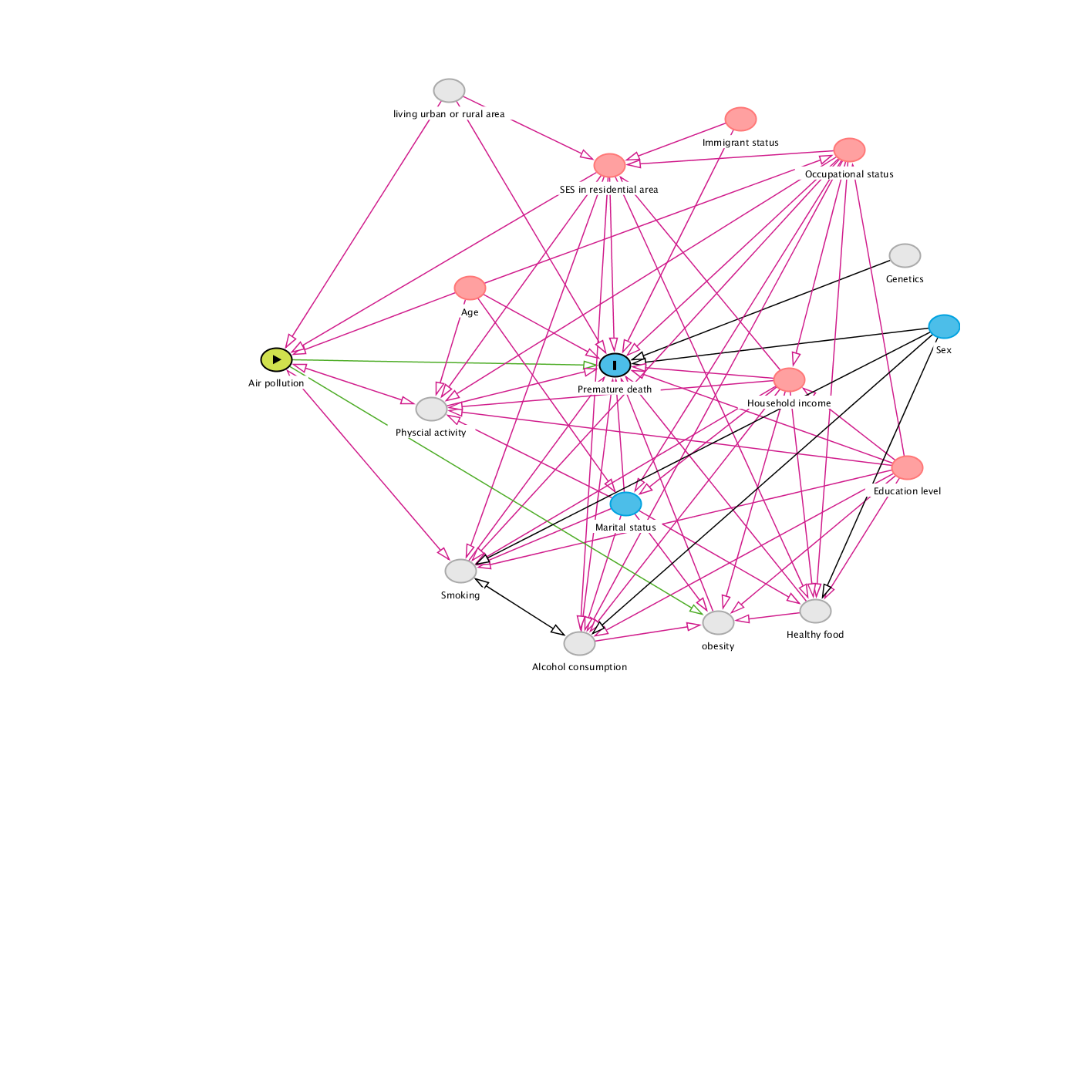
Abbreviations: PM2.5 – Particulate matter aerodynamic diameter < 2.5 µm; NO2 – Nitrogen dioxide; BC – Black carbon; O3 – ozone, warm-season (April-September).

Hazard ratios and confidence intervals were calculated per 5 µg/m3 for PM2.5, 10 µg/m3 for NO2, 0.5**×**10-5/m for BC, and 10 µg/m3 for O3.

1From two-pollutant models adjusting for age (underlying time scale), sex (strata), household income in decile, occupational status, immigrant status, marital status, and highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

2We estimated the probabilities of being included in the main analyses using the most available variables (age, sex, household income, occupational status, education level, immigrant status, marital status; only 244 subjects had missing these variables) as the predictors. We took the inverse of probability and used it as a weight in the cox model.

Figure S5. Unadjusted Directed Acyclic Graph of the association between long-term exposure to air pollution and mortality in the Danish nationwide administrative cohort.



Exposure: air pollution. Outcome: premature death. Green arrow: direct causal pathway.  
Pink arrows: biased paths. Pick factor: confounder of the association. Blue factor: a risk of premature death.  
Gray factor: unobserved variable

Table S15. The comparison of the hazard ratio of association between long-term exposure to air pollution and natural mortality: The fully adjusted models (the main models) and the models with covariates selected from the DAG.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | PM2.5  HR (95%CI) | NO2  HR (95%CI) | BC  HR (95%CI) | O3  HR (95%CI) |
| The main model1 | 1.11 (1.09, 1.13) | 1.06 (1.05, 1.07) | 1.05 (1.04, 1.06) | 0.96 (0.95, 0.97) |
| The DAG model2 | 1.14 (1.12, 1.16) | 1.09 (1.08, 1.09) | 1.07 (1.06, 1.08) | 0.93 (0.92, 0.94) |

Abbreviations: PM2.5 – Particulate matter aerodynamic diameter < 2.5 µm; NO2 – Nitrogen dioxide; BC – Black carbon; O3 – ozone, warm-season (April-September).

Hazard ratios and confidence intervals were calculated per 5 µg/m3 for PM2.5, 10 µg/m3 for NO2, 0.5**×**10-5/m for BC, and 10 µg/m3 for O3.

1 Adjusting for age (underlying time scale), sex (strata), household income in decile, occupational status, immigrant status, marital status, and highest completed education level, regional mean household income, regional percentage of unemployment, and the difference of mean household income and percentage of unemployment, between parish and region.

2 All variables in the main model excluding marital status (see Figure S7)

Figure S6. Forest plot for a visual comparison between recent studies on the association with long-term exposure to PM2.5 and (A) all natural-cause, (B) cardiovascular disease, (C) respiratory disease, and (D) lung cancer mortality and our main result 



Abbreviations: PM2.5 – Particulate matter aerodynamic diameter < 2.5 µm; HR – Hazard ratio; CI – Confidence interval.

Figure S7. Forest plot for a visual comparison between recent studies on the association with long-term exposure to NO2 and (A) all natural-cause, (B) cardiovascular disease, (C) respiratory disease, and (D) lung cancer mortality and our main result. ****

****

Abbreviations: NO2 – Nitrogen dioxide; HR – Hazard ratio; CI – Confidence interval.

Table S16. Comparison of descriptive statistics for demographic characteristics and air pollution exposures between the Danish nationwide administrative cohort and Danish health survey.

|  |  |  |
| --- | --- | --- |
| **Characteristics** | **Danish nationwide administrative cohort (%)** | **Danish Health Survey (%)** |
| **Age (years)** |  |  |
| 30-39 | 24.4 | 21.6 |
| 40-49 | 22.6 | 24.3 |
| 50-59 | 22.5 | 20.9 |
| 60-69 | 14.5 | 19.6 |
| 70-79 | 10.5 | 9.4 |
| 80-89 | 4.8 | 3.9 |
| ≥90 | 0.7 | 0.3 |
| **Sex** |  |  |
| Men | 48.3 | 49.4 |
| Women | 51.7 | 50.6 |
| **Household income** |  |  |
| 1st | 9 | 4.1 |
| 2nd | 9.7 | 2.8 |
| 3rd | 9.8 | 6.4 |
| 4th | 10 | 7.8 |
| 5th | 10.1 | 7.4 |
| 6th | 10.2 | 8.3 |
| 7th | 10.3 | 9.9 |
| 8th | 10.3 | 12.5 |
| 9th | 10.4 | 16.7 |
| 10th | 10.3 | 24.1 |
| **Occupational status** |  |  |
| Unemployed | 2.6 | 1.3 |
| Sick/cash support/ pension/student/others | 37.7 | 34.7 |
| Employed | 59.7 | 64.0 |
| **Immigrant status** |  |  |
| Danish origin | 94.3 | 91.6 |
| Immigrants/descendants from western country of origin | 2.5 | 4.1 |
| Immigrants/descendants from non-western country of origin | 3.2 | 4.2 |
| **Marital status** |  |  |
| Unmarried | 16.9 | 17.8 |
| Divorced | 11 | 11.4 |
| Widowed | 9.8 | 7.2 |
| Married/Partner | 62.3 | 63.6 |
| **Highest complete education level** |  |  |
| Primary | 40.7 | 24.7 |
| Upper secondary | 3.4 | 4.2 |
| Vocation/qualifying | 34.8 | 38.5 |
| Vocation bachelors/ short cycle higher education | 15.5 | 22.1 |
| More than college level | 5.6 | 10.4 |
| **Regional mean income / percentage of unemployment** |  |  |
| North Denmark : 155,994.2 / 2.55 | 10.6 | 10.5 |
| Central Denmark : 162,312.0 / 1.90 | 21.9 | 22.2 |
| South Denmark : 158,840.3 / 1.87 | 22.2 | 21.3 |
| Capital region : 175,561.2 / 1.90 | 29.9 | 29.9 |
| Zealand : 166,371.4 / 1.86 | 15.4 | 15.9 |
| **Parish level mean income in quintile** |  |  |
| 1st | 20 | 1.6 |
| 2nd | 20 | 2.6 |
| 3rd | 20 | 5.4 |
| 4th | 20 | 19.5 |
| 5th | 20 | 71.0 |
| **Parish level percentage of unemployment in quintile** |  |  |
| 1st | 20 | 49.2 |
| 2nd | 19.8 | 18.3 |
| 3rd | 20.1 | 15.4 |
| 4th | 20.1 | 9.8 |
| 5th | 20 | 7.3 |