

Long term exposure to air pollution and COVID-19 incidence: a prospective study of residents in the city of Varese, northern Italy.

Supplementary Material

Table S1: Sample selection criteria, number of excluded individuals, and number of COVID-19 cases

| | N | COVID-19 cases | |
|---|--------------|----------------|------------|
| | | n | % (on N) |
| Residents in Varese city as of 31/12/2017, to be linked to air pollution data (average 2018 annual value) | 81543 | 5373 | 6.6 |
| Exclusions | | | |
| <i>No link with air pollution data (imprecise geocoding of residential address)</i> | 2081 | 141 | 6.8 |
| <i>Death or transferred outside Varese as of 31/12/2019</i> | 6944 | 270 | 3.9 |
| <i>Living in a residential care home outside Varese as of 31/12/2019</i> | 227 | 109 | 48.0 |
| <i>Age < 18 years</i> | 9443 | 445 | 4.7 |
| Study sample | 62848 | 4408 | 7.0 |

Table S2: Distribution of the available air pollutants in the city of Varese and their correlations. Annual mean values and summer O₃, year 2018.

| | Unit | Min | Max | Mean | SD | Median | P25 | P75 | Pearson correlation coefficients | | | | | | |
|-----------------------|-------------------|-------|-------|-------|------|--------|-------|-------|----------------------------------|------------------|-----------------|--------|----------------|-----------------------|--|
| | | | | | | | | | PM _{2.5} | PM ₁₀ | NO ₂ | NO | O ₃ | O ₃ summer | |
| PM _{2.5} | µg/m ³ | 7.0 | 14.6 | 12.5 | 1.33 | 12.7 | 11.8 | 13.6 | 1 | | | | | | |
| PM ₁₀ | µg/m ³ | 7.6 | 16.4 | 14.1 | 1.62 | 13.2 | 13.0 | 15.5 | 0.998 | 1 | | | | | |
| NO ₂ | µg/m ³ | 6.6 | 24.3 | 20.1 | 2.99 | 20.7 | 18.2 | 22.8 | 0.989 | 0.994 | 1 | | | | |
| NO | µg/m ³ | 0.6 | 5.9 | 4.2 | 1.11 | 4.1 | 3.5 | 5.0 | 0.904 | 0.927 | 0.930 | 1 | | | |
| O ₃ | µg/m ³ | 58.9 | 76.2 | 62.9 | 3.03 | 61.5 | 60.8 | 64.5 | -0.974 | -0.968 | -0.964 | -0.843 | 1 | | |
| O ₃ summer | µg/m ³ | 100.5 | 110.1 | 104.4 | 2.27 | 102.8 | 102.5 | 104.6 | -0.909 | -0.903 | -0.882 | -0.790 | 0.964 | 1 | |

Abbreviation: SD = Standard Deviation; P25 = 25th percentile; P75 = 75th percentile

Table S3: Census indicators of socio-economic condition and mobility propensity by census areas, and summary statistics (mean and coefficient of variation).

| | Census area | | | | | | Summary statistics | |
|-------------------------------------|-------------|--------|--------|--------|--------|--------|--------------------|------|
| | Area 0 | Area 1 | Area 2 | Area 3 | Area 4 | Area 5 | Mean | CV |
| No of. Residents at the last census | 2942 | 14682 | 15417 | 17007 | 15854 | 13891 | - | - |
| Socio-economic condition | | | | | | | | |
| S1 | 52.7 | 149.9 | 92.2 | 81.0 | 139.6 | 81.2 | 105.3 | 29.4 |
| A12 | 45.8 | 46.5 | 41.4 | 47.1 | 39.8 | 50.0 | 45.0 | 8.2 |
| I6 | 57.7 | 71.9 | 62.7 | 70.9 | 53.0 | 73.9 | 66.0 | 11.8 |
| L21 | 11.3 | 12.6 | 13.8 | 9.8 | 19.3 | 10.2 | 13.0 | 26.2 |
| V6 | 1.2 | 1.4 | 0.8 | 1.1 | 1.7 | 1.0 | 1.2 | 25.1 |
| Mobility propensity | | | | | | | | |
| M2 | 25.8 | 22.8 | 22.7 | 23.1 | 23.0 | 24.7 | 23.4 | 3.7 |
| M5 | 74.5 | 50.2 | 61.9 | 71.5 | 65.7 | 68.8 | 64.5 | 11.6 |
| M6 | 14.8 | 16.7 | 19.3 | 16.2 | 18.3 | 15.9 | 17.2 | 8.0 |

Indicators are available for 6 census areas within the city of Varese. They are produced by the National Institute of Statistics (ISTAT) and referred to the year 2011 (last available census). Individuals in the study have been uniquely attributed to one census area based on the address of residency.

Available area-based census indicators:

S1: Number of foreign residents per 1000 Italian residents

A12: Average housing space per person (m²)

I6: Percentage of residents 25-64 years old with high high-school degree or higher

L21: Percentage of un-skilled manual workers, on the working population

V6: Percentage of families on potential economic disadvantage, defined as family with kids without at least one member employed or retired

M2: Percentage of individuals moving daily outside the city boundaries for study or work, on the population up to 64 years

M5: Percentage of individuals using private car/motorbike, on the number of individuals moving daily outside the city boundaries for study or work

M6: Percentage of individuals using public transportation, on the number of individuals moving daily outside the city boundaries for study or work

Table S4: Pearson's correlation coefficients between census indicators and air pollutants.

| | | Socio-economic condition | | | | | Mobility propensity | | |
|--------------------------|-------------------|--------------------------|----------|----------|----------|----------|---------------------|----------|----------|
| | | S1 | A12 | I6 | L21 | V6 | M2 | M5 | M6 |
| Socio-economic condition | S1 | 1 | | | | | | | |
| | A12 | -0.43 | 1 | | | | | | |
| | I6 | -0.30 | 0.91 | 1 | | | | | |
| | L21 | 0.66 | -0.88 | -0.89 | 1 | | | | |
| | V6 | 0.75 | -0.37 | -0.51 | 0.68 | 1 | | | |
| Mobility propensity | M2 | -0.56 | 0.59 | 0.24 | -0.40 | -0.21 | 1 | | |
| | M5 | -0.76 | 0.16 | -0.10 | -0.22 | -0.19 | 0.51 | 1 | |
| | M6 | 0.34 | -0.87 | -0.62 | 0.68 | 0.01 | -0.68 | -0.30 | 1 |
| Air pollutant | PM _{2.5} | 0.34 | -0.29 | -0.17 | 0.35 | -0.06 | -0.14 | -0.51 | 0.48 |
| | PM ₁₀ | 0.36 | -0.27 | -0.15 | 0.34 | -0.04 | -0.15 | -0.53 | 0.46 |
| | NO ₂ | 0.33 | -0.21 | -0.08 | 0.28 | -0.07 | -0.13 | -0.52 | 0.41 |
| | NO | 0.50 | -0.22 | -0.08 | 0.32 | 0.11 | -0.25 | -0.61 | 0.37 |
| | O ₃ | -0.29 | 0.25 | 0.17 | -0.34 | 0.04 | 0.04 | 0.43 | -0.41 |

Available area-based census indicators:

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V6: Percentage of families on potential economic disadvantage, defined as family with kids without at least one member employed or retired

M2: Percentage of individuals moving daily outside the city boundaries for study or work, on the population up to 64 years

M5: Percentage of individuals using private car/motorbike, on the number of individuals moving daily outside the city boundaries for study or work

M6: Percentage of individuals using public transportation, on the number of individuals moving daily outside the city boundaries for study or work

Table S5: Univariate association between census indicators and COVID-19 incidence rate, from Poisson regression models.

| | | Estimate | SE | Z | p |
|---------------------------------|-----|-----------------|-----------|----------|----------|
| Socio-economic condition | S1 | 0.0011 | 0.0005 | 2.37 | 0.0179 |
| | A12 | -0.0201 | 0.004 | -4.98 | <.0001 |
| | I6 | -0.0074 | 0.002 | -3.99 | <.0001 |
| | L21 | 0.0193 | 0.004 | 4.70 | <.0001 |
| | V6 | 0.0000 | 0.051 | 0.00 | 0.99 |
| Mobility propensity | M2 | -0.0464 | 0.018 | -2.62 | 0.009 |
| | M5 | -0.0049 | 0.00 | -2.58 | 0.010 |
| | M6 | 0.0635 | 0.01 | 5.95 | <0.0001 |

Available area-based census indicators:

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Table S6: Sensitivity analyses of the association between annual mean levels of air pollutants and COVID-19 incidence rate: area-based indicators of socio-economic condition and mobility propensity, and E-value for the point estimate and for the confidence interval.

| Air pollutant | Individual-level covariates | | | Individual + area-based covariates* | | | E-value [^] | |
|-------------------|-----------------------------|-------|-------|-------------------------------------|-------|-------|----------------------|------|
| | RR | 95%CI | | RR | 95%CI | | Estimate | CI |
| PM _{2.5} | 1.051 | 1.027 | 1.075 | 1.036 | 1.009 | 1.064 | 1.23 | 1.11 |
| PM ₁₀ | 1.040 | 1.020 | 1.060 | 1.027 | 1.006 | 1.049 | 1.20 | 1.08 |
| NO ₂ | 1.020 | 1.009 | 1.030 | 1.013 | 1.002 | 1.025 | 1.13 | 1.05 |
| NO | 1.040 | 1.013 | 1.068 | 1.021 | 0.992 | 1.051 | 1.17 | 1.00 |
| O ₃ | 0.980 | 0.970 | 0.990 | 0.987 | 0.976 | 0.998 | 1.13 | 1.05 |

RR = Rate Ratios estimated from single pollutant Poisson regression models, per 1 µg/m³ increase in the annual average exposure to each pollutant

Individual-level covariates: Model 2 in the main text (age, sex, residential care home living, positive history of stroke, treatment for diabetes, anti-hypertensive treatment, and treatment for obstructive airway diseases)

*: Area-based covariates: census-based indicators L21 (proportion of un-skilled manual workers) and M6 (use of public transportation for daily mobility). These have been chosen according to: variability across the census areas (CV in Table S3); weaker correlation between indices, and stronger correlation with the exposure (Table S4); stronger correlation with the outcome (Table S5).

[^]: for the model with individual and area-based covariates

Table S7: Summary statistics and rate ratios (with 95%CI) for the association between seasonal mean levels of air pollutants and COVID-19 incidence rate.

| Air pollutant | Season | Mean | SD | RR (1SD increase) | 95%CI | Het I ² | Q test statistic | Q p-value |
|------------------|--------|-------|-----|----------------------|-------------|--------------------|------------------|-----------|
| PM ₂₅ | Spring | 7.8 | 1.0 | 1.072 | 1.041 1.105 | 0.00% | 0.19 | 0.98 |
| | Summer | 5.3 | 0.5 | 1.073 | 1.042 1.105 | | | |
| | Autumn | 14.0 | 2.5 | 1.067 | 1.035 1.101 | | | |
| | Winter | 17.2 | 5.0 | 1.065 | 1.032 1.098 | | | |
| PM ₁₀ | Spring | 8.7 | 1.3 | 1.068 | 1.037 1.101 | 0.00% | 0.08 | 0.99 |
| | Summer | 6.0 | 0.7 | 1.068 | 1.037 1.100 | | | |
| | Autumn | 15.4 | 2.9 | 1.064 | 1.032 1.097 | | | |
| | Winter | 18.7 | 5.5 | 1.063 | 1.031 1.096 | | | |
| NO ₂ | Spring | 11.7 | 3.7 | 1.060 | 1.029 1.093 | 0.00% | 0.24 | 0.97 |
| | Summer | 6.9 | 2.4 | 1.052 | 1.022 1.084 | | | |
| | Autumn | 19.6 | 6.1 | 1.056 | 1.024 1.089 | | | |
| | Winter | 26.1 | 8.6 | 1.063 | 1.030 1.097 | | | |
| NO | Spring | 2.8 | 1.3 | 1.038 | 1.008 1.068 | 0.00% | 0.58 | 0.90 |
| | Summer | 0.4 | 0.1 | 1.031 | 1.002 1.061 | | | |
| | Autumn | 4.2 | 1.1 | 1.041 | 1.011 1.072 | | | |
| | Winter | 6.2 | 3.6 | 1.047 | 1.017 1.079 | | | |
| O ₃ | Spring | 73.4 | 4.0 | 0.938 | 0.910 0.968 | 0.00% | 0.04 | 0.99 |
| | Summer | 104.4 | 2.3 | 0.945 | 0.917 0.975 | | | |
| | Autumn | 56.9 | 6.3 | 0.943 | 0.914 0.973 | | | |
| | Winter | 28.0 | 8.0 | 0.941 | 0.912 0.972 | | | |

Abbreviation: SD = Standard Deviation

RR: Rate Ratios estimated from Poisson regression model, adjusting for age, sex, residential care home living, positive history of stroke, treatment for diabetes, anti-hypertensive treatment, and treatment for obstructive airway

Seasons: spring: March to May; summer: June to August; autumn: September to November; winter: December to February

Het I², Q test statistics and Q p-value (3 df) estimated from random effect meta-analysis

Table S8: Association between annual mean levels of air pollutants and COVID-19 incidence rate, in single- and bi-pollutant models.

| Air pollutant (per 1 µg/m ³) | Single-pollutant model | | | Bi-pollutant model | | |
|--|------------------------|-------|-------|--------------------|-------|-------|
| | RR | 95%CI | | RR | 95%CI | |
| PM _{2.5} | 1.051 | 1.027 | 1.075 | | | |
| <i>Adjusted for NO₂</i> | | | | 1.347 | 1.163 | 1.561 |
| <i>Adjusted for NO</i> | | | | 1.105 | 1.051 | 1.161 |
| <i>Adjusted for O₃</i> | | | | 1.107 | 1.003 | 1.222 |
| PM ₁₀ | 1.040 | 1.020 | 1.060 | | | |
| <i>Adjusted for NO₂</i> | | | | 1.330 | 1.133 | 1.561 |
| <i>Adjusted for NO</i> | | | | 1.095 | 1.045 | 1.148 |
| <i>Adjusted for O₃</i> | | | | 1.047 | 0.974 | 1.125 |
| NO ₂ | 1.020 | 1.009 | 1.030 | | | |
| <i>Adjusted for PM_{2.5}</i> | | | | 0.894 | 0.837 | 0.955 |
| <i>Adjusted for PM₁₀</i> | | | | 0.874 | 0.800 | 0.953 |
| <i>Adjusted for O₃</i> | | | | 0.998 | 0.962 | 1.035 |
| NO | 1.040 | 1.013 | 1.068 | | | |
| <i>Adjusted for PM_{2.5}</i> | | | | 0.936 | 0.882 | 0.993 |
| <i>Adjusted for PM₁₀</i> | | | | 0.922 | 0.862 | 0.986 |
| <i>Adjusted for O₃</i> | | | | 0.983 | 0.937 | 1.031 |
| O ₃ | 0.980 | 0.970 | 0.990 | | | |
| <i>Adjusted for PM_{2.5}</i> | | | | 1.024 | 0.980 | 1.070 |
| <i>Adjusted for PM₁₀</i> | | | | 1.004 | 0.966 | 1.044 |
| <i>Adjusted for NO₂</i> | | | | 0.978 | 0.943 | 1.014 |
| <i>Adjusted for NO</i> | | | | 0.975 | 0.957 | 0.993 |

RR: Rate Ratios estimated from Poisson regression model, adjusting for age, sex, residential care home living, positive history of stroke, treatment for diabetes, anti-hypertensive treatment, and treatment for obstructive airway

Table S9: Association between annual mean levels of air pollutants and COVID-19 incidence rate, and estimated number of additional COVID-19 cases due to air pollution, after having excluded subjects living in residential care homes (n=407).

| Air pollutant | Model 1 | | | Model 2 | | | | | |
|-------------------|---------|-------|-------|---------|-------|-------|--------------------|--------|-------|
| | RR | 95%CI | | RR | 95%CI | | Cases [^] | 95%CI | |
| PM _{2.5} | 1.046 | 1.022 | 1.070 | 1.045 | 1.021 | 1.070 | 261.4 | 120.1 | 402.7 |
| PM ₁₀ | 1.036 | 1.016 | 1.055 | 1.035 | 1.016 | 1.055 | 204.0 | 88.8 | 319.2 |
| NO ₂ | 1.017 | 1.007 | 1.028 | 1.017 | 1.007 | 1.028 | 100.1 | 38.6 | 161.5 |
| NO | 1.037 | 1.010 | 1.064 | 1.036 | 1.009 | 1.064 | 211.0 | 45.9 | 376.0 |
| O ₃ | 0.982 | 0.972 | 0.992 | 0.982 | 0.972 | 0.992 | -103.0 | -162.0 | -44.0 |

RR = Rate Ratios estimated from Poisson regression model, per 1 µg/m³ increase in the annual average exposure to each pollutant

Model 1: single pollutants, adjusting for age and sex

Model 2: Model 1 + positive history of stroke, treatment for diabetes, anti-hypertensive treatment, and treatment for obstructive airway diseases

[^]: Number of cases per 100.000 p-y due to 1 µg/m³ increase in the pollutant above its mean value, estimated at the mean values of the confounders