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

Supplementary Material

Veronesi G, *et al. Occup Environ Med* 2022; 79:192–199. doi: 10.1136/oemed-2021-107833

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			
No link with air pollution data (imprecise geocoding of residential address)	2081	141	6.8
Death or transferred outside Varese as of 31/12/2019	6944	270	3.9
Living in a residential care home outside Varese as of 31/12/2019	227	109	48.0
Age < 18 years	9443	445	4.7
Study sample	**62848**	**4408**	**7.0**

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Table S2: Distribution of the available air pollutants in the city of Varese and their correlations. Annual mean values and summer O_3, year 2018.

	Unit	Min	Max	Mean	SD	Median	P25	P75	Pearson correlation coefficients					
									$PM_{2.5}$	PM_{10}	NO_2	NO	O_3	$O_{3\ summer}$
$PM_{2.5}$	$\mu g/m^3$	7.0	14.6	12.5	1.33	12.7	11.8	13.6	1					
PM_{10}	$\mu g/m^3$	7.6	16.4	14.1	1.62	13.2	13.0	15.5	0.998	1				
NO_2	$\mu g/m^3$	6.6	24.3	20.1	2.99	20.7	18.2	22.8	0.989	0.994	1			
NO	$\mu g/m^3$	0.6	5.9	4.2	1.11	4.1	3.5	5.0	0.904	0.927	0.930	1		
O_3	$\mu g/m^3$	58.9	76.2	62.9	3.03	61.5	60.8	64.5	-0.974	-0.968	-0.964	-0.843	1	
$O_{3\ summer}$	$\mu g/m^3$	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 (m^2)

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:
S1: Number of foreign residents per 1000 Italian residents
A12: Average housing space per person (m^2)
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 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:

S1: Number of foreign residents per 1000 Italian residents
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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 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 I^2, 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/m3)	Single-pollutant model			Bi-pollutant model		
	RR	95%CI		RR	95%CI	
$PM_{2.5}$	1.051	1.027	1.075			
Adjusted for NO_2				1.347	1.163	1.561
Adjusted for NO				1.105	1.051	1.161
Adjusted for O_3				1.107	1.003	1.222
PM_{10}	1.040	1.020	1.060			
Adjusted for NO_2				1.330	1.133	1.561
Adjusted for NO				1.095	1.045	1.148
Adjusted for O_3				1.047	0.974	1.125
NO_2	1.020	1.009	1.030			
Adjusted for $PM_{2.5}$				0.894	0.837	0.955
Adjusted for PM_{10}				0.874	0.800	0.953
Adjusted for O_3				0.998	0.962	1.035
NO	1.040	1.013	1.068			
Adjusted for $PM_{2.5}$				0.936	0.882	0.993
Adjusted for PM_{10}				0.922	0.862	0.986
Adjusted for O_3				0.983	0.937	1.031
O_3	0.980	0.970	0.990			
Adjusted for $PM_{2.5}$				1.024	0.980	1.070
Adjusted for PM_{10}				1.004	0.966	1.044
Adjusted for NO_2				0.978	0.943	1.014
Adjusted for NO				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 $\mu g/m^3$ 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 $\mu g/m^3$ increase in the pollutant above its mean value, estimated at the mean values of the confounders