COVID-19 INCIDENCE AND EXCESS MORTALITY IN LOMBARDY, ITALY: AN ECOLOGICAL STUDY WITH FOCUS ON THE ROLE OF SOCIOECONOMIC AND ENVIRONMENTAL FACTORS

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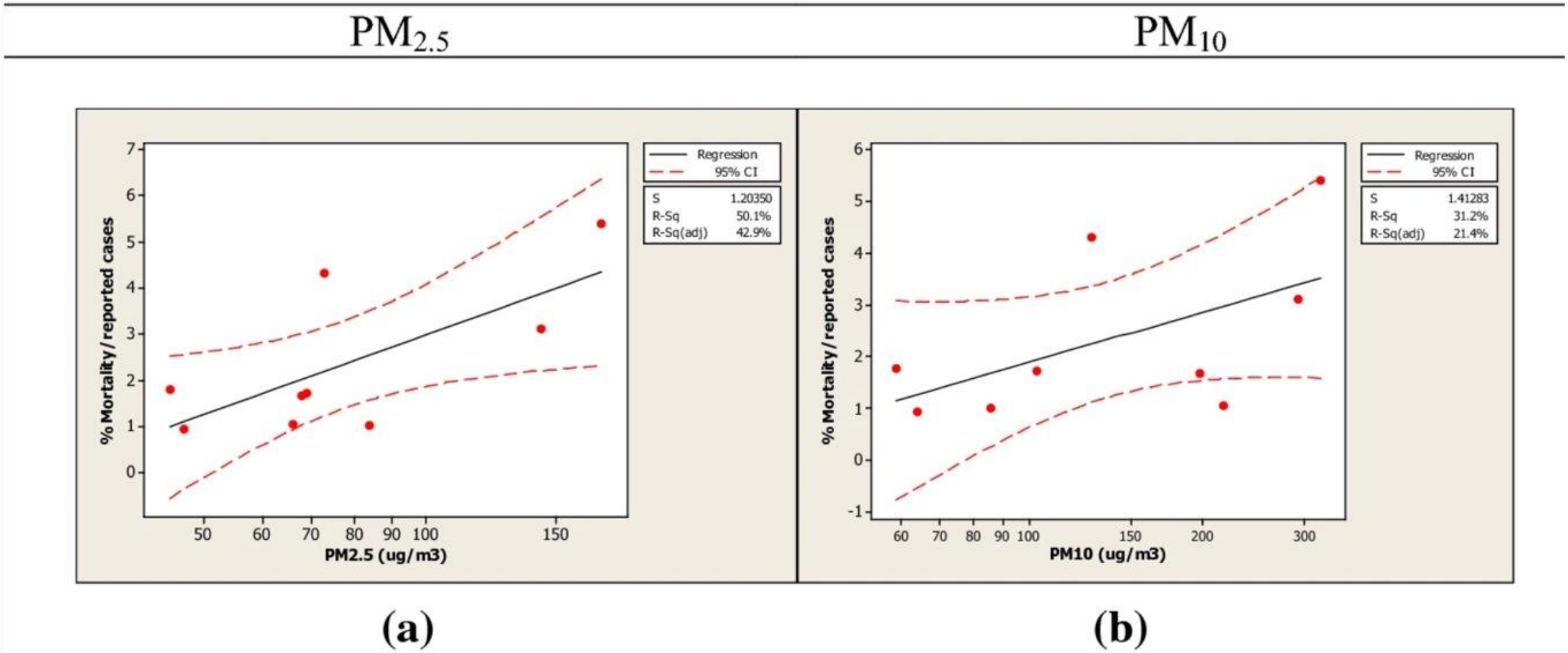
Environmental exposure to PM2.5 and PM10

Increasing literature shows that airborne particles may facilitate the virus diffusion and increase the risk for COVID-19 disease severity, progression and mortality

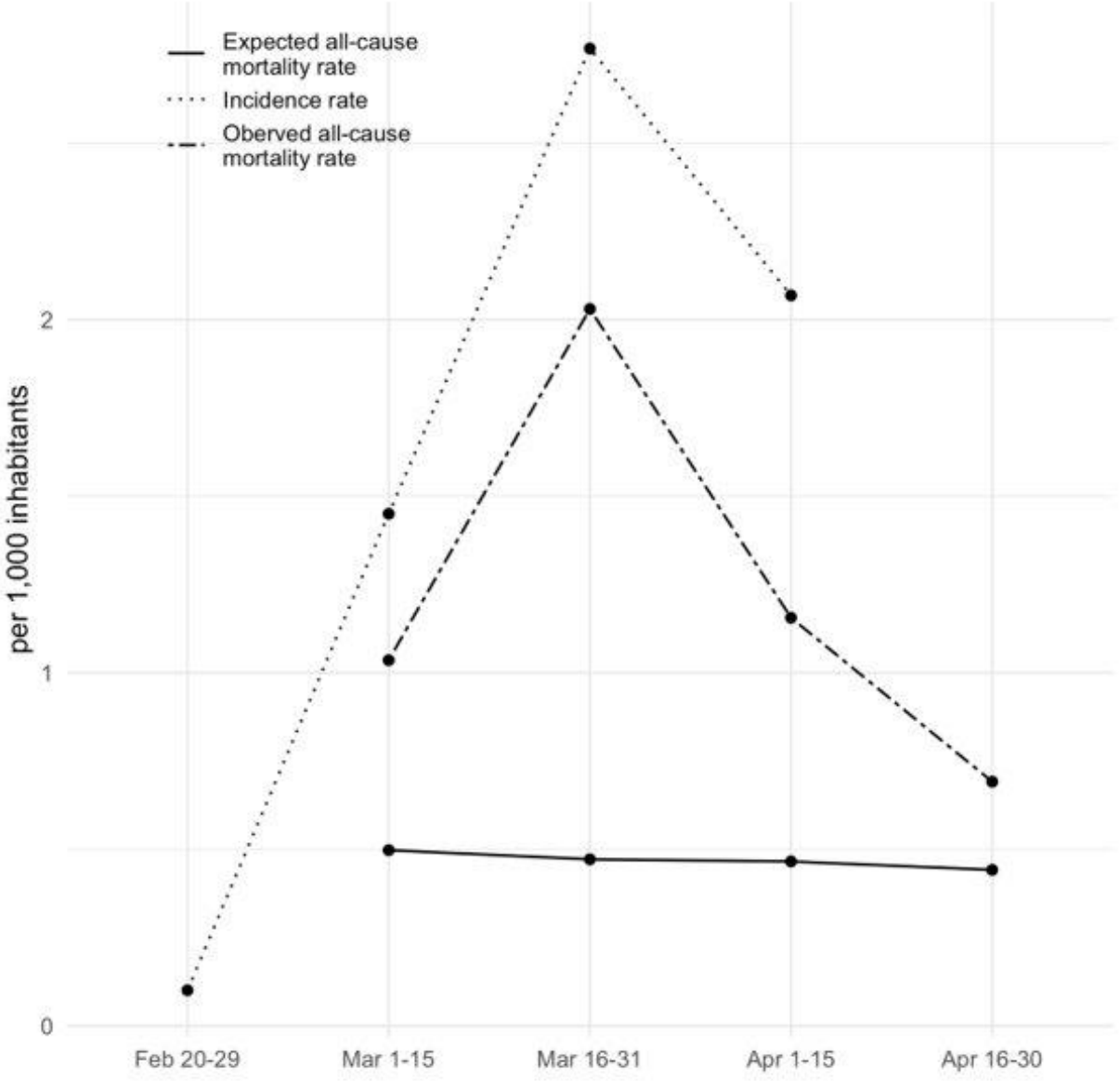
- Domingo et al., Influence of airborne transmission of SARS-CoV-2 on COVID-19 pandemic. A review. Environmental Research, Volume 188, September 2020,

- Wu, X et al. 2020. Air pollution and COVID-19 mortality in the United States: Strengths and limitations of an ecological regression analysis. *Science advances*, *6*, p.eabd4049



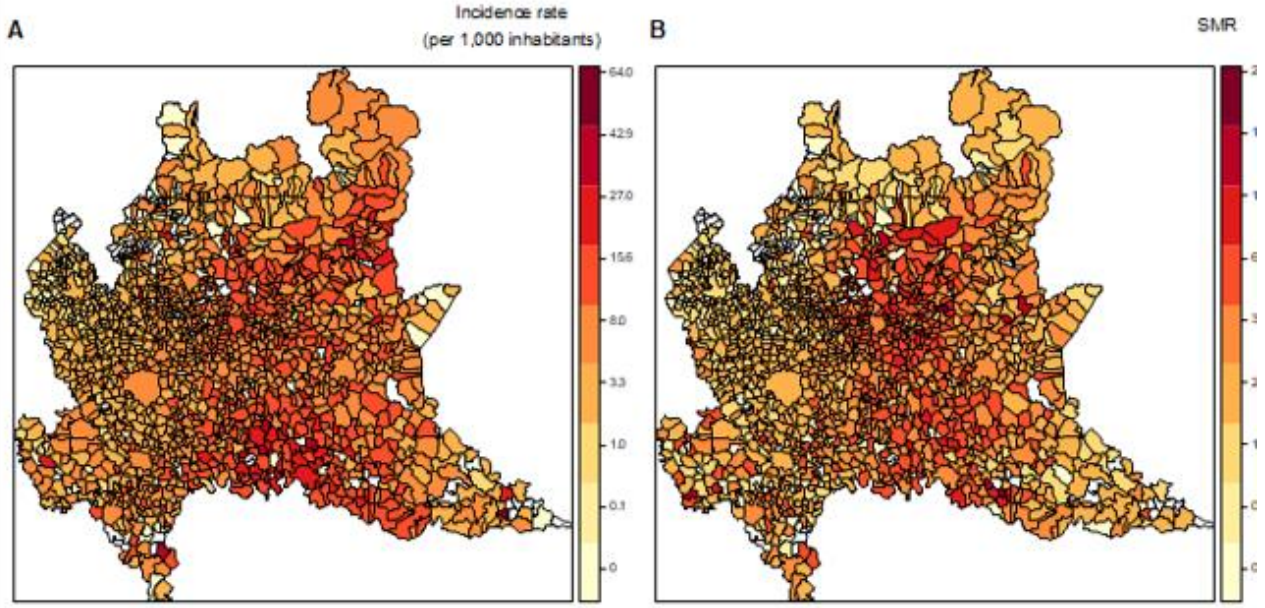
Linear regression fitted line plots for **a** $PM_{2.5}$ and **b** PM_{10}

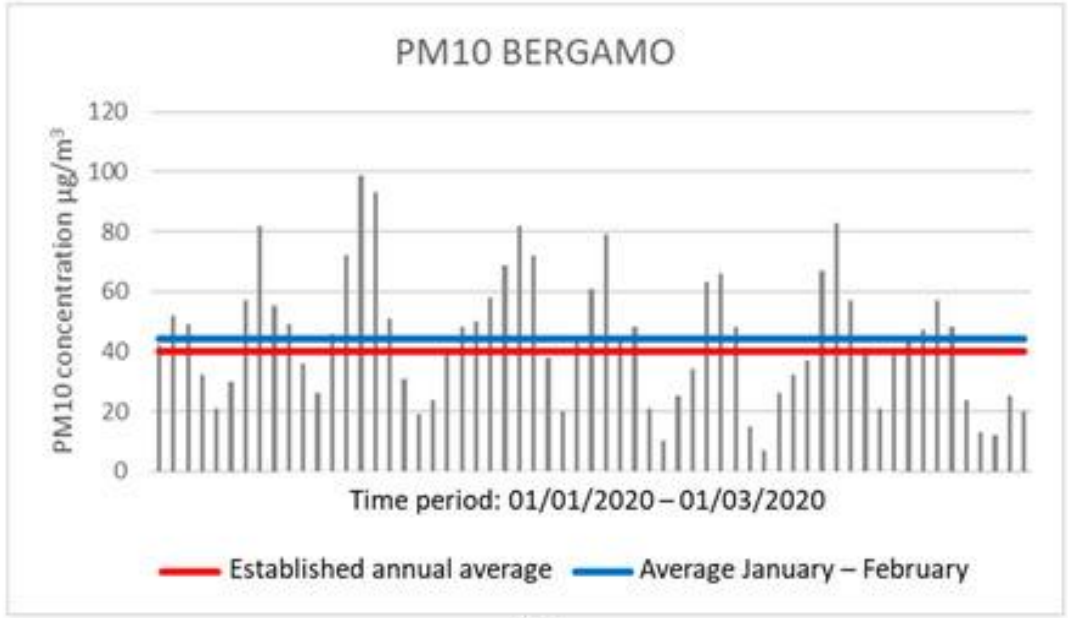
Gupta et al. **Air pollution aggravating COVID-19 lethality? Exploration in Asian cities using statistical models**. *Environment, Development and Sustainability* (2020)



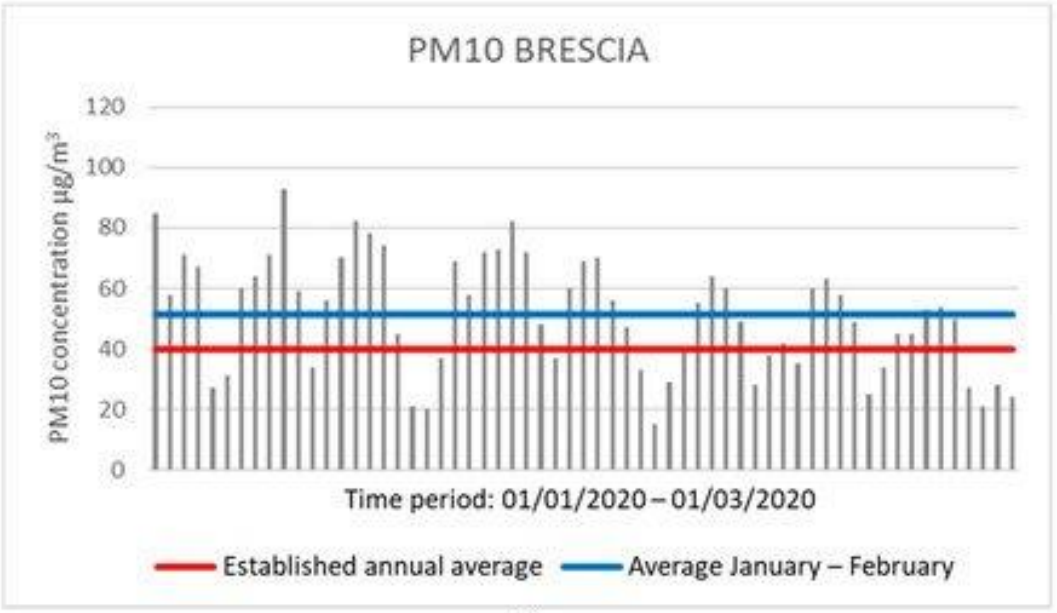
Data presented here have been submitted for publication as:

De Angelis E and Renzetti S, Volta M, Donato F, Calza S, Placidi D, Lucchini RG, Rota M. **COVID-19 incidence and excess mortality in Lombardy, Italy: an ecological study with focus on the role of socioeconomic and environmental factors**

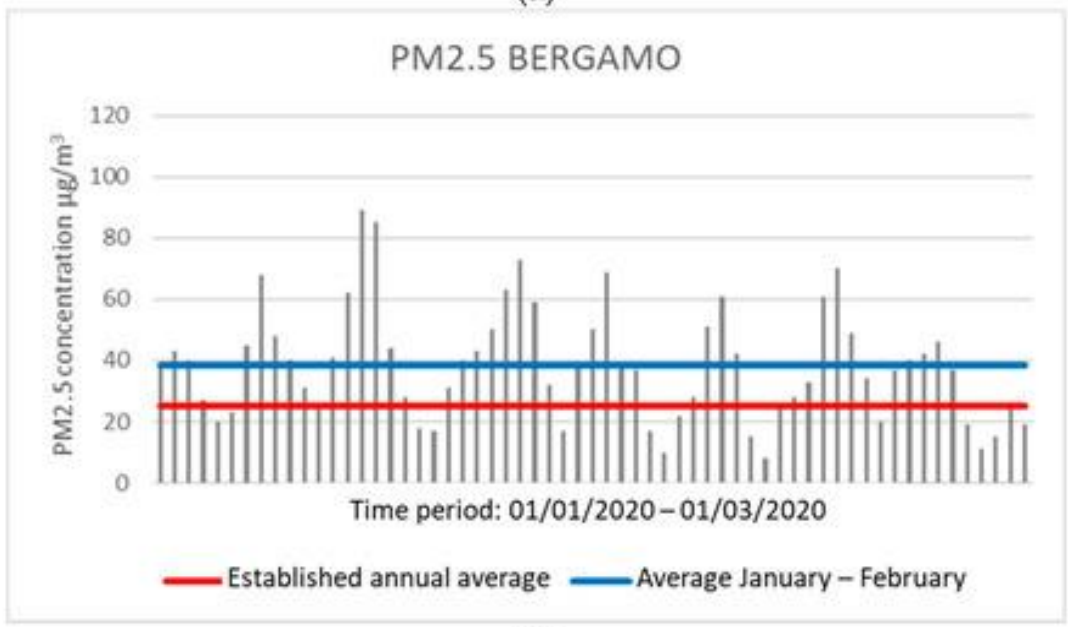


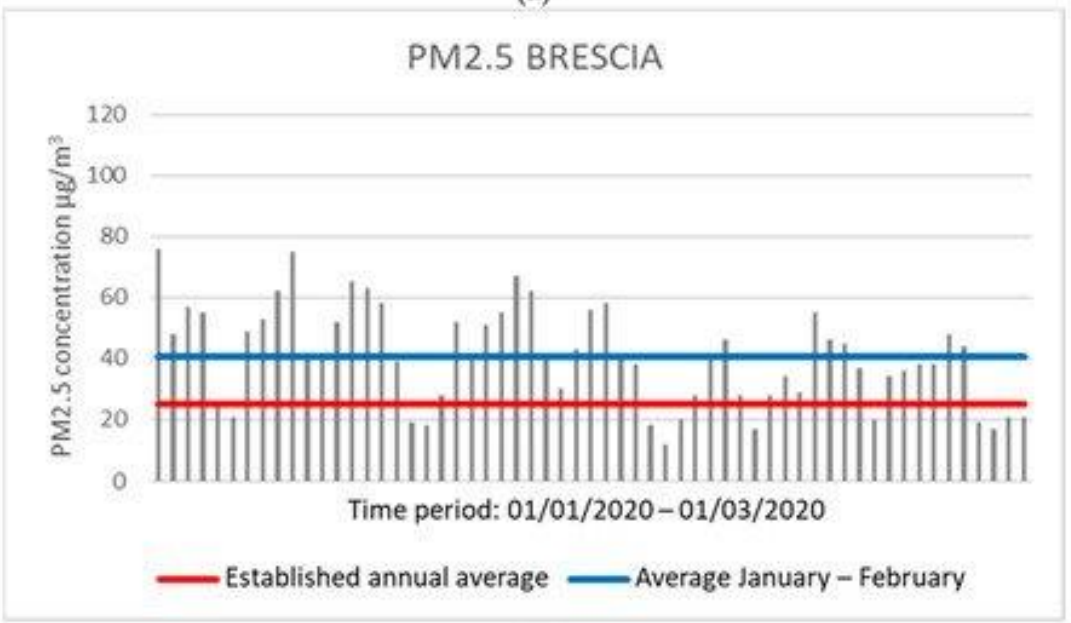


(a)



(a)





Comunian et al., **Air Pollution and COVID-19: The Role of Particulate Matter in the Spread and Increase of COVID-19's Morbidity and Mortality.** *Int. J. Environ. Res. Public Health* 2020, *17*(12), 4487; https://doi.org/10.3390/ijerph17124487

	Mean (SD)	Median (Q1, Q3)
Number of observed deaths (Mar-Apr 2020)	27.3 (123.6)	11.0 (4.0, 25.0)
Number of expected deaths (Mar-Apr 2020)	11.0 (63.7)	4.4 (2.0, 9.8)
Standardized Mortality Ratio (SMR)	2.9 (2.2)	2.4 (1.5, 3.8)
Number of COVID-19 cases	41.5 (184.4)	16.0 (5.5, 40.0)
Demographic, socioeconomic and community variables		
Population size	6,495.7 (33826.1)	2,842.0 (1227.5, 6033.5)
Population density (inhabitants per Km2)	564.7 (787.9)	269.8 (101.0, 745.6)
Sex ratio	98.2 (5.4)	97.9 (95.0, 101.0)
Proportion of population over 75 years old	9.8 (3.3)	9.3 (7.7, 11.3)
Average family size	2.4 (0.2)	2.4 (2.3, 2.5)
House crowding index	0.4 (0.3)	0.3 (0.2, 0.5)
High to low education ratio	133.4 (48.8)	126.4 (100.8, 157.3)
Income per capita (€)	14,449.6 (2,770.6)	14,311.0 (12,824.2, 16,017.2)
Percentage of private mobility use	68.0 (7.3)	68.5 (63.6, 73.1)
Number of beds in nursing homes	43.0 (222.2)	0.0 (0.0, 60.0)
Distance to the closest hospital (meters)	5,976.6 (3856.1)	5,443.1 (3426.8, 8090.2)
# employees in bars, restaurants and catering per capita (per 1000 inhabitants)	16.9 (30.3)	11.2 (7.7, 16.9)
# employees in health and social assistance per capita (per 1000 inhabitants)	0.5 (0.6)	0.3 (0.0, 0.7)
# employees in sports, entertainment and recreational activities per capita (>0.9 vs ≤0.4 per 1000 inhabitants)	0.8 (0.0)	0.6 (0.0, 1.1)

	Mean (SD)	Median (Q1, Q3)
Meteorological factors		
Winter (Feb-Apr 2020) average temperature (°C)	7.6 (2.0)	8.3 (7.5, 8.7)
Winter (Feb-Apr 2020) average humidity (%)	68.7 (6.2)	68.7 (63.5, 75.1)
Estimates of recent and historical environmental PM concentrations		
Recent (Nov-Dec 2019) PM2.5 (µg/m3)†	18.9 (5.3)	19.4 (16.9, 21.8)
Recent (Nov-Dec 2019) PM10 (µg/m3)†	21.6 (6.3)	22.5 (18.6, 25.7)
Historical winter PM2.5 (µg/m3)§	27.3 (8.3)	28.7 (23.2, 32.9)
Historical yearly PM2.5 (µg/m3)	18.6 (4.8)	19.8 (15.6, 22.1)
Historical winter PM10 (µg/m3)§	31.1 (8.5)	32.6 (26.2, 37.2)
Historical yearly PM10 (µg/m3)	21.8 (5.4)	22.7 (18.2, 25.8)
Pre-lockdown estimates of environmental PM concentrations		
Pre-lockdown (Jan-Feb 2020) PM2.5 (µg/m3)‡	25.3 (8.8)	25.3 (19.7, 31.9)
Pre-lockdown (Jan-Feb 2020) PM10 (µg/m3)‡	33.0 (12.3)	33.6 (24.5, 42.5)

[univariate negative binomial mixed effect models]	Incidence Rate Ratio	95% CI	p-value
Recent and historical estimates of environmental PM concentrations			
Recent (Nov-Dec 2019) PM2.5 (μg/m^3)†	0.98	0.94 – 1.03	0.43
Recent (Nov-Dec 2019) PM10 (μg/m^3)†	1.08	1.03 – 1.13	<0.01
Historical winter PM2.5 (μg/m^3)§	1.01	0.97 – 1.06	0.59
Historical yearly PM2.5 (μg/m^3)	1.12	1.07 – 1.18	<0.01
Historical winter PM10 (μg/m^3)§	1.04	0.99 – 1.09	0.11
Historical yearly PM10 (μg/m^3)	1.11	1.06 – 1.17	<0.01
Pre-lockdown estimates of environmental PM concentrations			
Pre-lockdown (Jan-Feb 2020) PM2.5 (μg/m^3)‡	1.13	1.08 – 1.18	<0.01
Pre-lockdown (Jan-Feb 2020) PM10 (μg/m^3)‡	1.08	1.03 – 1.13	<0.01

[univariate negative binomial mixed effect models]	SMR	95% CI	p-value
Recent and historical estimates of environmental PM concentrations			
Recent (Nov-Dec 2019) PM2.5 (μg/m^3)†	1.02	0.98 – 1.06	0.27
Recent (Nov-Dec 2019) PM10 (μg/m^3)†	1.06	1.02 – 1.10	<0.01
Historical winter PM2.5 (μg/m^3)§	1.05	1.02 – 1.09	<0.01
Historical yearly PM2.5 (μg/m^3)	1.10	1.06 – 1.14	<0.01
Historical winter PM10 (μg/m^3)§	1.06	1.02 – 1.10	<0.01
Historical yearly PM10 (μg/m^3)	1.08	1.05 – 1.12	<0.01
Pre-lockdown estimates of environmental PM concentrations			
Pre-lockdown (Jan-Feb 2020) PM2.5 (μg/m^3)‡	1.09	1.05 – 1.13	<0.01
Pre-lockdown (Jan-Feb 2020) PM10 (μg/m^3)‡	1.03	1.00 – 1.07	0.09

multivariable negative binomial mixed effect model	Incidence rate ratios	95% CI	p-value
Demographic, socioeconomic and community variables			
High to low education ratio	0.88	0.83 – 0.93	<0.01
Percentage of private mobility use	0.91	0.87 – 0.94	<0.01
Number of beds in nursing homes (> 80 vs 0)	1.50	1.34 – 1.68	<0.01
Distance to the closest hospital (meters)	0.91	0.87 – 0.95	<0.01
# employees in bars, restaurants and mobile catering activities per capita	1.13	1.03 – 1.24	<0.01
# employees in sports, entertainment and recreational activities per capita	1.13	1.03 – 1.24	<0.01
Meteorological factors			
Winter (Feb-Apr 2020) average temperature (°C)	0.89	0.85 – 0.94	<0.01
Winter (Feb-Apr 2020) average humidity (%)	1.73	1.65 – 1.82	<0.01
Estimates of recent and historical environmental PM concentrations			
Recent (Nov-Dec 2019) PM2.5 (µg/m3)	1.01	0.96 – 1.05	0.82
Recent (Nov-Dec 2019) PM10 (µg/m3)	1.06	1.00 – 1.11	0.04
Historical winter PM2.5 (µg/m3)	0.95	0.89 – 1.01	0.11
Historical yearly PM2.5 (µg/m3)	0.97	0.90 – 1.04	0.38
Historical winter PM10 (µg/m3)	0.97	0.91 – 1.04	0.39
Historical yearly PM10 (µg/m3)	0.98	0.92 – 1.05	0.63
Pre-lockdown estimates of environmental PM concentrations			
Pre-lockdown (Jan-Feb 2020) PM2.5 (µg/m3)	1.18	1.12 – 1.24	<0.01
Pre-lockdown (Jan-Feb 2020) PM10 (µg/m3)	1.06	0.96 – 1.07	0.68

COVID-19 increased risk estimates

Lombardy study

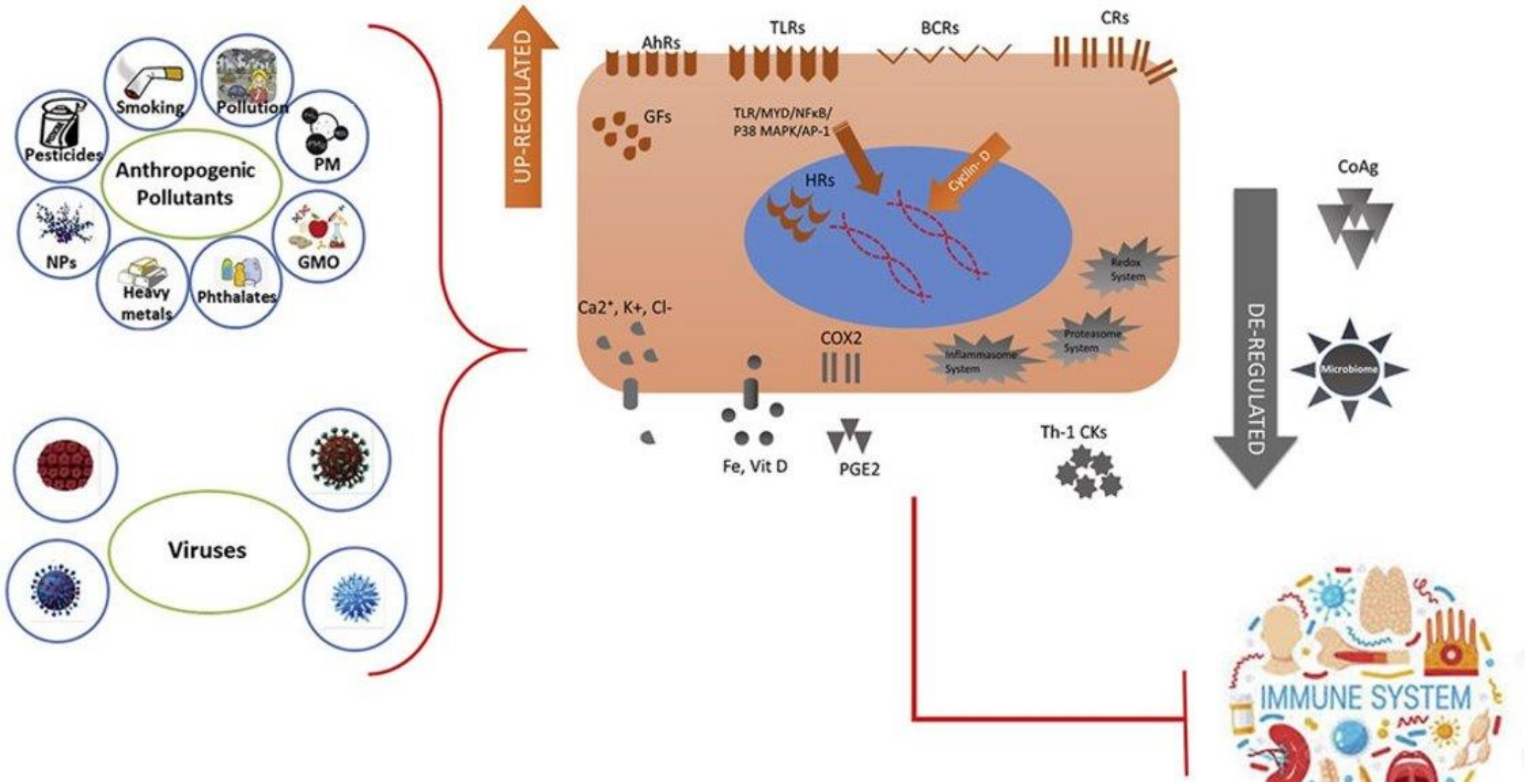
- increase of 1 $\mu g/m^3$ in pre-lockdown $PM_{2.5}$ associated with **18%** increase in the COVID-19 incidence rate (95% CI: 12%, 24%)
- increase of 1 $\mu g/m^3$ in $PM_{2.5}$ associated with **3%** increase in the COVID-19 death rate (95% CI: -1%, 8%)

USA study (Wu et al., 2020)

- increase of 1 $\mu g/m^3$ in $PM_{2.5}$ associated with **8%** increase in the COVID-19 death rate (95% CI: 2%, 15%)

Tsatsakis et al.COVID-19, an opportunity to reevaluate the correlation between long-term effects of anthropogenic pollutants on viral epidemic/pandemic events and prevalence Food and Chemical Toxicology, Volume 141, July 2020, 111418 https://doi.org/10.1016/j.fct.2020.111418

- Developmental and long-term low-dose exposure to chemical mixtures (fossil fuel derivatives, exposure to particle matters, metals, UV–B radiation, ionizing radiation) is linked to imunodeficiency
- Immunodeficiency contributes to chronic diseases and the current Covid-19 pandemics
- Environmental chemicals and microorganisms may share similar molecular pathomechanisms: Aryl hydrocarbon receptors (AhR) pathway


Smoking
Pollution
Pesticides
PM
Anthropogenic Pollutants
NPs
GMO
Heavy metals
Phthalates
Viruses
UP-REGULATED
AhRs
TLRs
BCRs
CRs
GFs
TLR/MYD/NFκB/
P38 MAPK/AP-1
HRs
Cyclin- D
Redox System
Ca2+, K+, Cl-
COX2
Proteasome System
Inflammasome System
Fe, Vit D
PGE2
Th-1 CKs
DE-REGULATED
CoAg
Microbiome
IMMUNE SYSTEM

CONCLUSION

- Significant contribution of pre-lockdown PM2.5 to the incidence of severe COVID19 disease in Lombardy, Northern Italy
- In the highly industrialized provinces of Brescia and Bergamo, where mining, steel and metallurgic operations are active since last century
- Small increases of PM2.5 contribute to COVID19 disease and mortality worldwide
- Limitation: ecological design, lack of data on occupational exposure
- Need for cohort studies to improve exposure metrics and address preexisting comorbidities
- Need to include occupational exposure and to investigate among workers with occupational lung disease