
36th Annual Conference of the International Society for Environmental Epidemiology
August 25-28, 2024
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Interactive effects of long-term exposure to PM_{10}, NO_2 and O_3 on SARS-CoV-2 infection and severity: a population-based cohort study

Giovanni Veronesi, Sara De Matteis, Walter Ageno, Emanuele M Giusti, Camillo Silibello, Marco M Ferrario

Research Center in Epidemiology and Preventive Medicine, Department of Medicine and Surgery, University of Insubria,Varese, Italy
Web: https://epimed.uninsubria.eu
@: giovanni.veronesi@uninsubria.it

COI: none.

Background – prospective studies w/individual-level data investigating long-term (LT) exposure to air pollutants and COVID-19 pandemic

Year	Country	Study setting	Mean±SD $PM_{2.5}$ exposure ($\mu g/m^3$)	Infectivity			Severity		
				$PM_{2.5}$	NO_2	O_3	PM_2	NO_2	O_3
2023	Denmark	Nation-wide	7.4±0.5	**+**	**+**	**-**	**+**	**+**	**-**
2022	UK	Cohort study	9.99±1.05	**+**	**+**	NI	+	+	NI
2024	Netherlands	Nation-wide	11.07±1.35	**+**	**+**	NI	**+**	**+**	NI
2022	Italy (Varese)	Urban	12.5±1.3	**+**	**+**	**-**	not indagated (NI)		
2023	Spain (Catalonia)	Region-wide	13.9±2.2	not indagated (NI)			**+**	**+**	**-**
2022	Italy (Rome)	Urban	14.6	+	+	NI	**+**	**+**	NI
2021	Spain (Catalonia)	Cohort study	16.3±1.5	+	+	-	not indagated (NI)		

+: positive association; -: negative association; **bold**=statistical significance. Results from single-pollutant models.
NI=Not Indagated

Previous study by our research team, one city only (Varese)

Open questions

Interactive effects between pollutants not being investigated yet
- recently reported for PM & O_3 on mortality [Liu et al, *BMJ* 2023]
- may explain heterogeneity in estimates at different exposure levels

Study aims

To investigate the **presence of interactions** in the effect of each pollutant with SARS-CoV-2 infectivity and COVID-19 severity

- **in urban and non-urban areas**
- **across levels of co-pollutant** exposure

Study population & methods

709,864 adult (18+ y.o.) residents in the Province of Varese with individual data on:

a. SARS-CoV-2 cases, COVID-19 hospitalization and COVID-19 mortality from the pandemic outbreak up to December 2020
b. Pre-pandemic (2019) annual mean levels of PM_{10}, NO_2, O_3 from chemical-transport & random forest models – 1 Kmq spatial resolution, link through geo-coding of residential address
c. Demographic characteristics, comorbidities & treatment

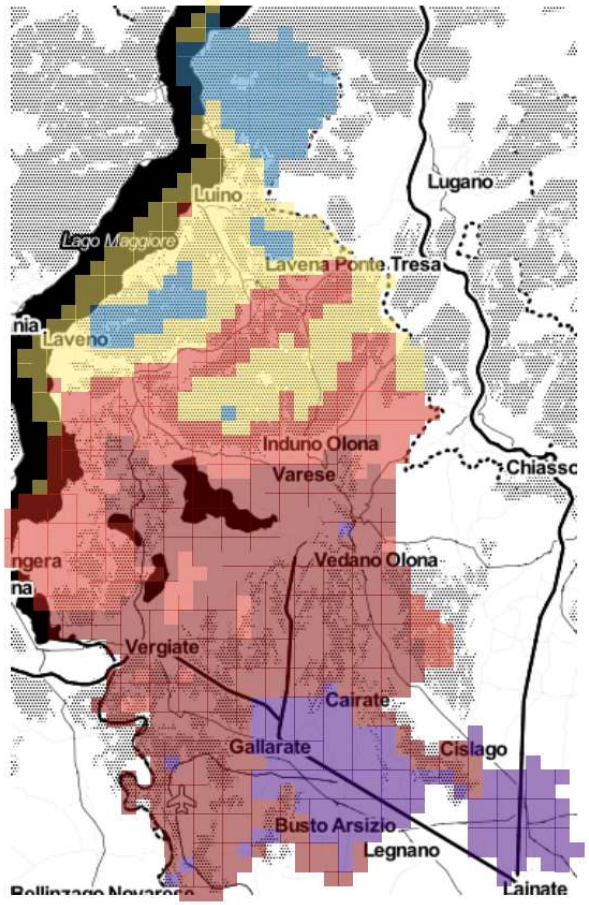
Deprivation index (Italian National Institute for Statistics) and degree of urbanization (EUROSTAT classification) available at an aggregated level

Modelling of interactive effects

Single-pollutant Cox (relative scale) or Poisson (additive scale) regression models, adjusted for covariates, with interaction term(s) between the pollutant and:

a. Degree of urbanization (urban vs. non-urban)
b. Quartiles of another pollutant as co-exposure – particulate matter w/ gaseous pollutants
    - PM_{10} & NO_2
    - PM_{10} & O_3

Results

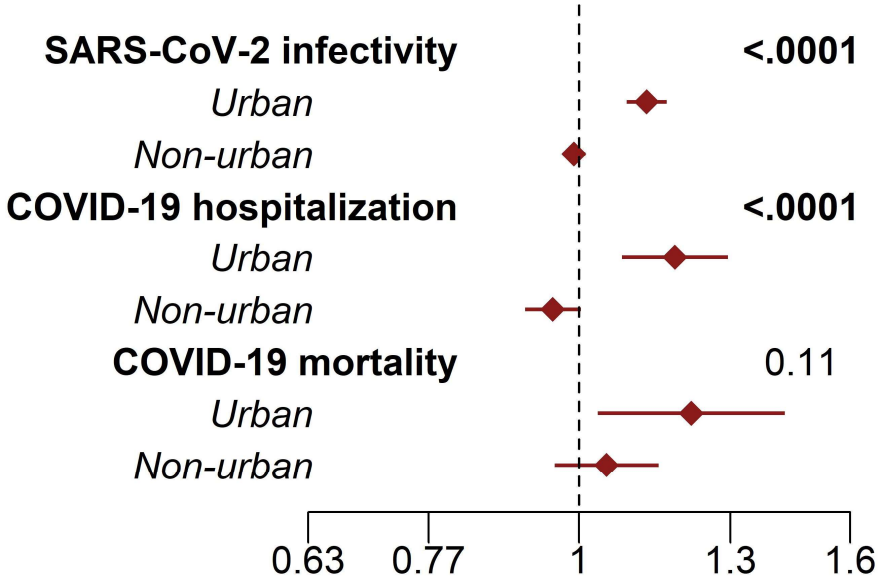


PM_{10}

Values (µg/m3)
- (10,15.5]
- (15.5,18.5]
- (18.5,23]
- (23,26]
- (26,31]

	PM_{10} [µg/m3]	NO_2 [µg/m3]	O_3 [µg/m3]
2019 annual mean (±SD)	24.3±3.0	26.1±5.4	52.1±5.8
By degree of urbanization			
Urban	**26.2±1.6**	**30.2±3.5**	**48.2±4.2**
Non-urban	22.5±2.9	22.4±4.0	55.7±4.7

Endpoint	No. of cases	Rate (per 100,000 py)	HR (95%CI) per 3.5 µg/m³ increase in PM_{10}
SARS-CoV-2 infectivity	41065	6424	**1.02 (1.01; 1.03)**
COVID-19 Hospitalization	5203	747	1.00 (0.96; 1.05)
COVID-19 mortality	1543	220	**1.09 (1.01; 1.17)**



Additional cases (per 100,000 py) in urban settings **due to interaction**:

854 (600-1107)

174 (86-261)

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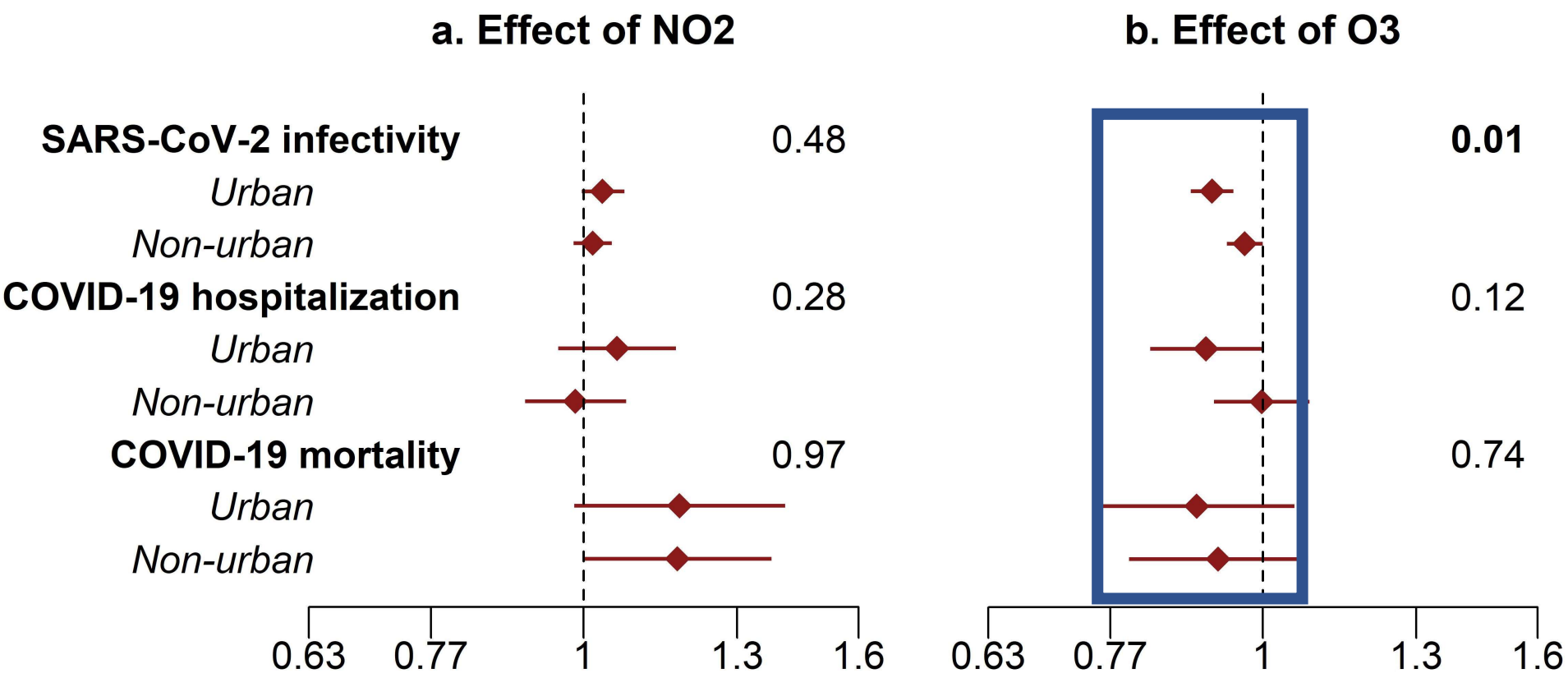

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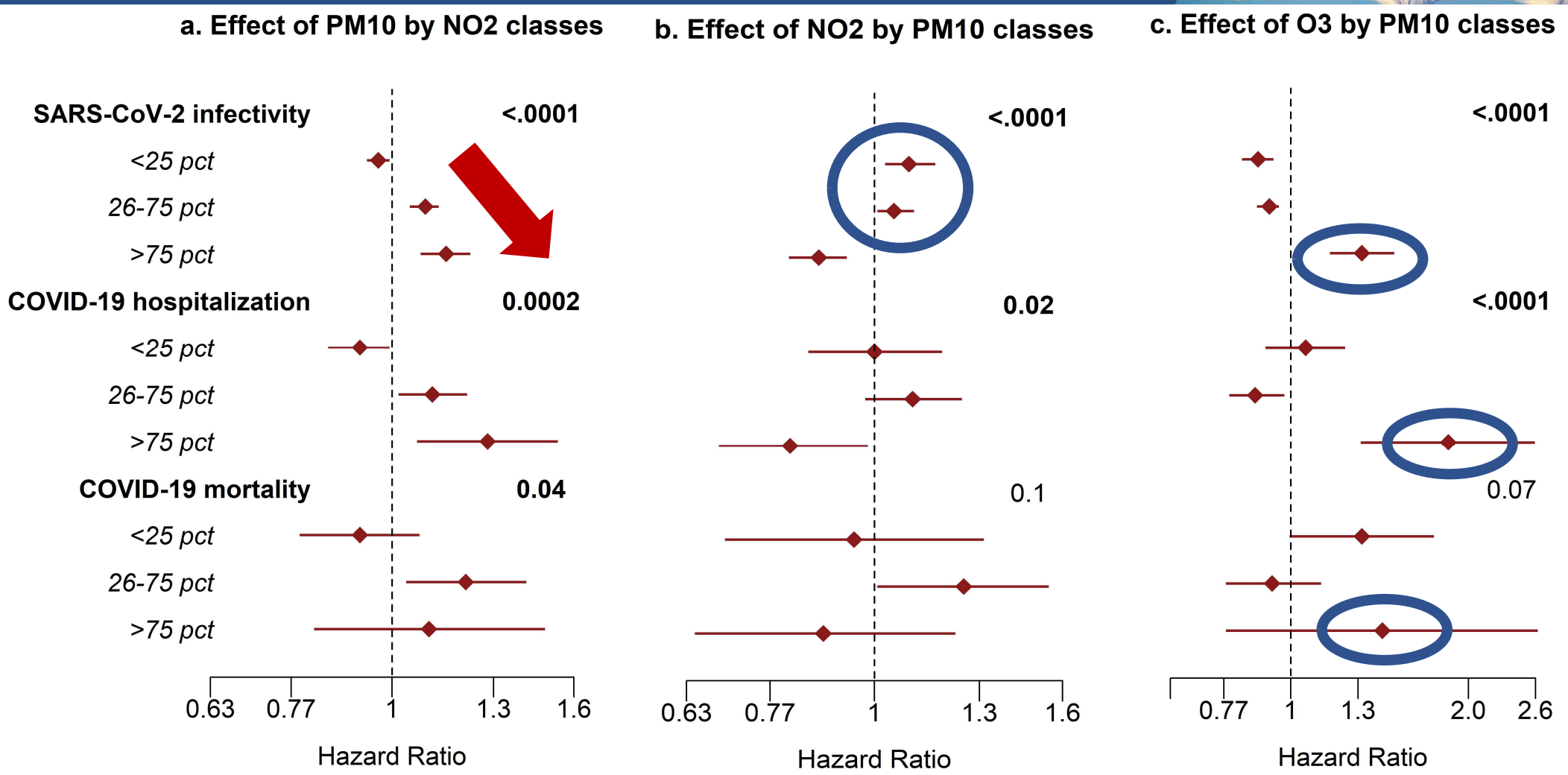

Discussion & take-home messages

Evidence of interactive effects for long-term exposure to PM with NO_2 **on infectious diseases risks**

The most detrimental mixture in highly-conglomerated urban settings exacerbated the pandemic risk for residents in these areas

At high PM_{10} co-exposure levels the detrimental effects of **ozone** through inflammation/oxidative stress pathways **may overcome** the advantages due to virus inactivation mechanisms

Thanks to the working team!

Giovanni Veronesi[1], Sara De Matteis[2], Walter Ageno[1], Emanuele M Giusti[1], Camillo Silibello[3], Marco M Ferrario[1]

1. Research Center in Epidemiology and Preventive Medicine, Department of Medicine and Surgery, University of Insubria,Varese, Italy
2. Department of Health Sciences, University of Milan, Milan, Italy
3. Arianet, Milan, Italy

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Epidemiology

Interactive effects of long-term exposure to PM10, NO2 and O3 on SARS-CoV-2 infection and severity: a population-based cohort study in northern Italy

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