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#### REFERENCES

1620

- Planas D, Saunders N, Maes P, et al. Considerable escape of SARS-CoV-2 Omicron to antibody neutralization. *Nature*. 2022;602(7898):671-675. doi: 10.1038/s41586-021-04389-z
- Wang L, Cheng G. Sequence analysis of the emerging SARS-CoV-2 variant Omicron in South Africa. J Med Virol. 2021;94(4):1728-1733. doi:10.1002/jmv.27516
- Gattinger P, Niespodziana K, Stiasny K, et al. Neutralization of SARS-CoV-2 requires antibodies against conformational receptorbinding domain epitopes. *Allergy*. 2022;77(1):230-242. doi:10.1111/ all.15066
- Blain H, Tuaillon E, Gamon L, et al. Receptor binding domain-IgG levels correlate with protection in residents facing SARS-CoV-2 B.1.1.7 outbreaks. Allergy. 2022. doi:10.1111/all.15142
- Gattinger P, Borochova K, Dorofeeva Y, et al. Antibodies in serum of convalescent patients following mild COVID-19 do not always prevent virus-receptor binding. *Allergy*. 2021;76(3):878-883. doi:10.1111/all.14523

- Rössler A, Riepler L, Bante D, et al. SARS-CoV-2 Omicron variant neutralization in serum from vaccinated and convalescent Persons. N Engl J Med. 2022;386(7):698-700. doi:10.1056/NEJMc2119236
- Vogel M, Augusto G, Chang X, et al. Molecular definition of severe acute respiratory syndrome coronavirus 2 receptor-binding domain mutations: Receptor affinity versus neutralization of receptor interaction. *Allergy*. 2022;77(1):143-149. doi:10.1111/all.15002
- Li D, Edwards RJ, Manne K, et al. In vitro and in vivo functions of SARS-CoV-2 infection-enhancing and neutralizing antibodies. *Cell*. 2021;184(16):4203-4219.e32. doi:10.1016/j.cell.2021.06.021
- Sievers BL, Chakraborty S, Xue Y, et al. Antibodies elicited by SARS-CoV-2 infection or mRNA vaccines have reduced neutralizing activity against Beta and Omicron pseudoviruses. *Sci Transl Med.* 2022:eabn7842. doi: 10.1126/scitranslmed.abn7842

# SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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# Has the Spring 2020 lockdown modified the relationship between air pollution and COVID-19 mortality in Europe?

To the Editor,

Studies conducted in countries around the world have reported significant associations between air pollution and COVID-19 severity and death.<sup>1,2</sup> Experimental studies have shown that air pollution impairs airways permeability (by diminishing in the airways ciliated cell functioning, macrophage phagocytosis and immune response), thus facilitating the penetration of bacteria and viruses, including the SARS-CoV-2 virus responsible for COVID-19. Air pollution also contributes to the development of chronic illnesses, including cardiovascular, metabolic and neurodegenerative diseases, all known to increase the risk of suffering from severe forms of COVID-19 leading to death.<sup>1</sup> This observation has led to the hypothesis that air pollution diminution during lockdowns may have engendered a reduction in COVID-19 severity and mortality.

Regrettably, available data show that results on air pollution diminution and related benefit during lockdown were contradictory. Using national monitoring station assessments, the European Environmental Agency showed that lockdown measures in 2020 have resulted in air pollution modifications in air pollutants concentrations, though with notable differences among air pollutants, cities and countries and sometimes not significantly.<sup>3</sup> Similarly, differences were observed in the rest of the world. Among other examples, gaseous and particulate matter (PM) concentrations diminished during the 2020 spring lockdown in forty-four cities in northern China due to reduced human activity and travel restrictions.<sup>4</sup> However, during the same period in the UK, after an initial abrupt reduction, nitrogen dioxide (NO<sub>2</sub>) increased gradually, suggesting that the early return of vehicles to the road during the lockdown had already offset much of the temporary air-quality improvement.<sup>5</sup> Regarding health impact, the risk of COVID-19 mortality during lockdown diminished alongside major air pollutants in Delhi, India,<sup>6</sup> but not in Mexico City, Mexico, where an inverse relationship was found in the case of fine particulate matter.<sup>7</sup> Furthermore, no reduction in COVID-19 deaths was associated with lockdowns as defined by social isolation (staying at home) in 87 regions and countries in the world.<sup>8</sup>

We used the Spring 2020 lockdown as a natural experiment to understand what happened to the COVID-19 syndemic in terms of mortality when air pollution due to the lockdown restriction in terms of circulation and mobility was abruptly lowered in the European region, providing a distinct look at short-term health impacts of lockdown to compare against the long-term health impacts observed in previous studies relating air pollution exposure to COVID-19 events in highly polluted zones.<sup>1</sup> COVID-19 provides a choice criterion for such a comparison because it is a specific disease, which was the same in each country at the start of the epidemics.

To this extent, we compared the impact of lockdown restrictions, namely isolation instituted as a security measure, taken for people on air quality during the first lockdown and the first phase of unlocking with respect to COVID-19 mortality in 33 countries of the European region. The analysis timespan for each country ranged from the date of the first day of lockdown until 20 July 2020 (the cutoff date for the analysis). Daily COVID-19 mortality data (deaths per million people) were obtained from the Johns Hopkins Coronavirus Resource Centre (https://coronavirus.jhu.edu/data/ mortality). Air temperature, humidity, particulate matter of 10  $\mu$ m of diameter (PM<sub>10</sub>), and NO<sub>2</sub> were assessed through the CHIMERE chemistry-transport model provided by INERIS<sup>9</sup> at various resolutions, with a broader spatial coverage than the monitoring station assessments. Lockdown periods were found in the web sites of the Health Authorities in the considered countries.

The relationship between each air pollutant and mortality rates per million inhabitants on a daily basis was analyzed by a generalized additive model (GAM) using a distributed nonlinear lag model (DNLM) framework, which assumes a quasi-Poisson distribution of the mortality rates. The covariates adjusted for were daily average temperature and daily average relative humidity; a 3-day moving average was applied to each of these meteorological variables, with natural (cubic) smoothing splines of 6 and 3 degrees of freedom in the GAM. The associations were expressed as risk ratios (RR) with 95% confidence intervals. Only the maximum RRs were retained.

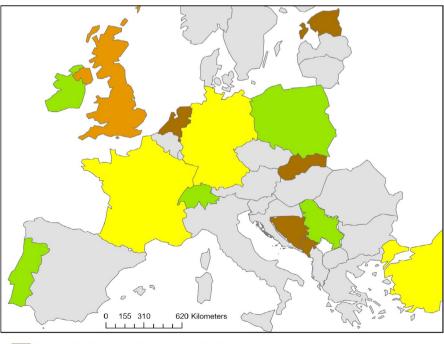
Averaged air pollutants levels as obtained through the dispersion model were lower during the lockdown than during the unlocking only in 8 (Algeria, Armenia, Greece, Israel, Lebanon, Lithuania, Morocco, and Tunisia) for  $NO_2$  and in 7 countries (Bulgaria, Israel, Lebanon, Lithuania, Morocco, Spain, and Turkey) for  $NO_2$  and  $PM_{10}$ , respectively. No decreases were seen elsewhere.

Overall, the relationship between air pollution levels and death rates during and after the lockdown varied from one country to another (Figure 1). In Ireland, Poland, Portugal, Serbia, and Switzerland, NO<sub>2</sub>, PM<sub>10</sub>, or both levels were significantly associated with COVID-19 mortality in the post-lockdown period but not during

the lockdown, thus suggesting that air pollution diminution during the lockdown might be protective. In France and Germany,  $PM_{10}$ , levels were significantly related to a higher risk of COVID-19 death both during and after the lockdown. The association was significant with NO<sub>2</sub> during and after the lockdown in Turkey. Conversely, in the UK, a significant relationship was seen for both  $PM_{10}$  and  $NO_2$ during the lockdown, but not after. Lastly, in five countries (Bosnia and Herzegovina, Estonia, Macedonia, The Netherlands, and Slovakia) that did not adopt lockdown restrictions at the beginning of epidemic and for which the entire timespan was considered, the COVID-19 mortality risk was significantly higher only for  $PM_{10}$  for all the countries, except Estonia where a significantly increased COVID-19 mortality risk was seen only for NO<sub>2</sub>. No significant relationship was observed in the other countries whether or not they adopted a lockdown.

Altogether, our national observations are not conclusive on whether the first lockdown modified the relationship between air pollution and COVID-19 mortality in Europe throughout the COVID-19 pandemic. Only the results obtained in five countries sustain the beneficial effect of the lockdown, but this is small at the country level. In three additional countries, air pollution was related to a higher COVID-19 death risk both during and after the lockdown. Overall, and this is the main message of this work, in some countries short-term measures seemed useless or at least insufficient to exert a significant positive effect on air pollution COVID-19-related mortality.

The observed differences could possibly be explained by the variation in the duration and the type of lockdown and by a large proportion of countries not having adopted the lockdown among the



Significant relationship both during and after the lockdown
 Significant relationship in the post-lockdown only
 Significant relationship during the lockdown but not after
 Significant relationship without lockdown
 No significant relationship

FIGURE 1 Relationship of air pollution to COVID-19 mortality during and after the lockdown in the Spring and Summer 2020 in Europe countries. Lockdown restrictions ranged from strict stay-at-home to curfew during some hours of the day and included different limitations of activities and working procedures. The heterogeneity of air pollution exposure could also help to understand the results as we considered national data through a high-resolution dispersion model. Moreover, indoor air pollution might have increased during the lockdown, as people spent more time indoors and burnt more fuel for cooking and heating. However, the heterogeneity of the observed results could be due to other risk factors that vary according to the countries such as individual susceptibility, lifestyle, food habits, obesity, gender, age group, ethnicity, complex social, economic, cultural, and even historical factors. In this context, it is important to underline the burden paid by people from low social classes that are highly exposed to both indoor and outdoor air pollution and that have reduced access to health care.

Our mixed results suggest that sharp, but short-term effects, of air pollution reduction may not be as important in mitigating immediate health impacts as the longer-term effects. Indeed, it is the longterm, sustained impacts of air pollution that contribute most to the risk of COVID-19 severity and mortality.<sup>1,2</sup> The strongest links our study found between air pollution concentrations and COVID-19 outcomes during and after the lockdown were observed in countries where air-quality impacts are severe and prolonged.

To sum up, only in 5 countries out of 33 considered there was no significant relationship between air pollution and COVID-19 mortality during the lockdown whereas there was a link after, which supports the hypothesis that diminishing air pollution emissions may be beneficial for the severe forms of COVID-19. Our findings, however, must be interpreted cautiously as we adopted an ecological approach at the country level. Individual-level data with exposure and contagion outcomes information are needed to adequately address whether the reduction of air pollution emissions during the lockdown did or did not contribute to a diminution of COVID-19 mortality.

## CONFLICTS OF INTEREST

All the authors declare no conflicts of interest related to the contents of this work.

#### AUTHOR CONTRIBUTIONS

IAM involved in conceptualization. SB and AC involved in methodology. SB and BD involved in data management and software. SB involved in formal analysis. BD involved in data curation. IAM and CM involved in writing—original draft preparation. JP and BD involved in visualization. All authors involved in validation and writing—review & editing, and have read and agreed to the published version of the manuscript. Isabella Annesi-Maesano<sup>1</sup> Cara Nichole Maesano<sup>1</sup> Boris Dessimond<sup>1</sup> Julie Prud'homme<sup>1</sup> Augustin Colette<sup>2</sup> Soutrik Banerjee<sup>1</sup>

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#### REFERENCES

- Bourdrel T, Annesi-Maesano I, Alahmad B, Maesano CN, Bind MA. The impact of outdoor air pollution on COVID-19: a review of evidence from *in vitro*, animal, and human studies. *Eur Respir Rev*. 2021;30:200242.
- Mein SA, Annesi-Maesano I, Rice MB. COVID-19 pandemic: a wake-up call for clean air. Ann Am Thorac Soc. 2021;18(9):1450-1455.
- 3. Air Quality in Europe 2020 Report. Report. European Environment Agency (EEA); 2020.
- Bao R, Zhang A. Does lockdown reduce air pollution? Evidence from 44 cities in northern China. *Sci Total Environ*. 2020;20(731):139052.
- Ropkins K, Tate JE. Early observations on the impact of the COVID-19 lockdown on air quality trends across the UK. *Sci Total Environ.* 2021;1(754):142374.
- Maji KJ, Namdeo A, Bell M, et al. Unprecedented reduction in air pollution and corresponding short-term premature mortality associated with COVID-19 lockdown in Delhi, India. J Air Waste Manag Assoc. 2021;15:1-17.
- Kutralam-Muniasamy G, Pérez-Guevara F, Roy PD, Elizalde-Martínez I, Shruti VC. Impacts of the COVID-19 lockdown on air quality and its association with human mortality trends in megapolis Mexico City. Air Qual Atmos Health. 2020;28:1-10.
- Savaris RF, Pumi G, Dalzochio J, Kunst R. Stay-at-home policy is a case of exception fallacy: an internet-based ecological study. *Sci Rep.* 2021;11(1):5313.
- Marécal V, Peuch V-H, Andersson C, et al. A regional air quality forecasting system over Europe: the MACC-II daily ensemble production. *Geosci Model Dev.* 8, 2777-2813.