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Pros and cons for the role of air pollution on COVID-19 development

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As SARS-CoV-2 has spread across the globe, it has been difficult to ignore patterns suggesting that regions with poor air quality are witnessing disproportionate impacts in terms of the frequency and severity of COVID-19 infection. Consequently, researchers have rightly recognized the importance of considering the role of air pollution in the COVID-19 pandemic. Here, we discuss the pros and cons of air pollution as a contributing factor to COVID-19, according to existing research questions (Table 1).

What data exist on the relation of air pollution to SARS-CoV-2 or COVID-19?

At the general population level, COVID-19 hospitalizations and deaths rates have skyrocketed in countries (e.g., Iran, China, South Korea, regions (Lombardy), and towns (e.g., New York, Madrid) most of which characterized by high levels of air pollution (e.g., Lombardy, Iran, China, South Korea, New York, Madrid). Early in the pandemic, an Italian study positively related the proportion of daily exceedances of concentrations of particulate matter (PM) with 10 μm of diameter or less (PM_{10}) with the number of COVID-19 admissions reported within the following 14 days¹. Since then, various studies have confirmed the existence of a significant association between air pollution exposure and SARS-CoV-2 infection or COVID-19 mortality². A recent study that calculated the extent to which air pollution could be blamed for COVID-19 deaths worldwide clearly showed that when both long-term exposure to air pollution and infection with the COVID-19 virus come together there is a significant adverse effect on health³. In East Asia, which has some of the highest levels of harmful pollution on the planet, it found that 27% of COVID-19 deaths could be attributed to the health effects of poor air quality. The proportion was 19% in Europe, and 17% in North America. Not surprisingly, previous research has already shown the significant impact of air pollution on other respiratory viruses, such as SARS, influenza, syncytial virus and measles, also transmissible via the respiratory route². However, no significant impact of air pollution on COVID-19 was found in other zones also highly polluted (e.g. Athens, London, Qatar). This may depend on the fact that SARS-CoV-2 infection is multifactorial.

How can this be explained?

Two patterns seem possible² (Figure 1). On the one hand, air pollution may render people more susceptible to infection by SARS-CoV-2. It is well established that gases such as nitrogen dioxide (NO_2) or ozone (O_3) and respirable PM may modify airways permeability. In particular, exposure to either fine or ultrafine particles including black carbon may significantly damage lung epithelial cilia, the first line of defence against respiratory viruses including SARS-CoV-2, decrease the ability of macrophages to phagocytize the virus as well as prevent an effective immune response against the infection. Additionally, long-term

1 endemic exposure to air pollution is responsible through oxidative stress for chronic systemic
2 inflammation at the origin of the comorbidities, such as cardiovascular and respiratory
3 diseases, metabolic diseases, etc. that put COVID-19 patients at higher risk of severe events
4 and death. Specifically, the Angiotensin-converting enzyme 2 (ACE-2) receptor on lung cell
5 surfaces, which is known to be involved in the way COVID-19 infects patients² is over-
6 expressed under chronic exposure to air pollution. This has been described as a double hit:
7 air pollution damages the lungs and increases the activity of ACE-2, which in turn leads to
8 enhanced uptake of the virus.

9 On the other hand, there is now growing evidence that SARS-CoV-2 is exhaled as a result of
10 regular breathing of an individual, becoming airborne and hence inhalable by others⁴. Once
11 in the air, the virus can either be carried by fine particles or mix with secondary ultrafine
12 aerosols². Experimentally, it has been observed that SARS-CoV-2 remains viable in aerosols
13 for up to 3 hours, with rate of decrease of SARS-CoV2 infectious titer comparable to that
14 found for SARS-CoV-1, which supports another possible route of infection transmission other
15 than respiratory droplets and contact via contaminated surfaces⁵.

16 The viability and long range transport of respiratory viruses in open air, and thus their
17 potential to infect individuals, have also been observed under real life conditions², and for
18 SARS-Cov-2 both indoors⁴ and outdoors². A recent study observed that the overburdening of
19 the health services and hospitals, as well as the high over-mortality due to COVID-19
20 observed in various regions of Europe in the Spring of 2020 may be linked to peaks of
21 PM_{2.5} and likely particular weather situations that have favored the spread and enhanced the
22 virulence of the virus⁶. Ergo, air pollution may be an important factor in viral disease
23 transmission and further investigations into the interaction of SARS-Cov-2 and air pollution
24 are warranted. Interestingly, recent data showed the ability of pollen to suppress innate
25 antiviral immunity, independent of allergy⁷.

26 *In which matters should we be cautious?*

27 The role of airborne SARS-CoV-2 transmission due to small respiratory droplets of diameter
28 < 5 µm emitted by symptomatic as well as asymptomatic, but infected, individuals at the origin
29 of droplet nuclei remaining suspended in the air is, however, still challenged by a lack of
30 studies. A major drawback in this respect is that the minimum infectious dose, as expressed
31 in viral RNA copies necessary to promote the infection, is not yet defined. In addition, very
32 few studies so far have assessed RNA copies in outdoor air and they are not conclusive. In a
33 Chinese study, the observed RNA concentrations were above the detection limits only in
34 crowded areas⁸. In Italy, a study also observed detectable SARS-Cov-2 RNA in congested
35 zones, but not in less polluted zones (below 10 µg/m³ in mean)⁹. A previous Italian study had

1 similarly found traces of SARS-Cov-2 RNA in 23% of the sampled PM₁₀ in a polluted zone
2 but without assessing RNA copies¹⁰. However, sampling the virulence of the sampled virus
3 has proved challenging so far.

4 Other major criticisms to the population-based data are methodological. Studies of air
5 pollution and SARS-Cov-2 or COVID-19 are cross-sectional or more rarely temporal series,
6 have relied mainly on ecological measures of exposures and outcomes, and are susceptible
7 to important sources of bias: selection bias, underreporting of health data, exposure
8 misclassification, no taking into account of the infection dynamics, and poor adjustment for
9 confounders¹¹. Most of the studies published so far have only considered the one factor
10 under study and usually without following strict methodological protocols for data
11 harmonization for epidemiological studies. Only in the UK biobank dataset, data on the
12 SARS-CoV2 infection and some characteristics for adjustment were available at the
13 individual². Additional co-factors that could interact with air pollution and/or viral infections
14 and that have to be taken into account in the models include among others air temperature
15 (negative effect), UV radiation (negative association), comorbidity². Furthermore, longitudinal
16 studies with individual-level data are needed to adequately address this topic. In addition,
17 careful peer review is necessary.

18 Though more studies are imperative, collectively the data existing so far suggest that air
19 pollution – regardless of origin – should be considered as a contributing factor to the dynamics
20 of COVID-19 epidemics in terms of both viral transmission as well as pre-existing
21 susceptibility to viral infection, and advocate the need to diminish air pollution emissions in
22 the interest of public health.

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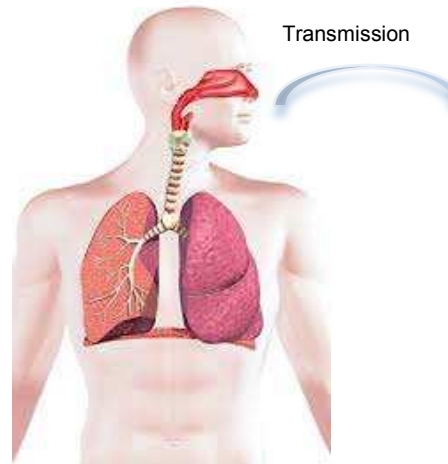
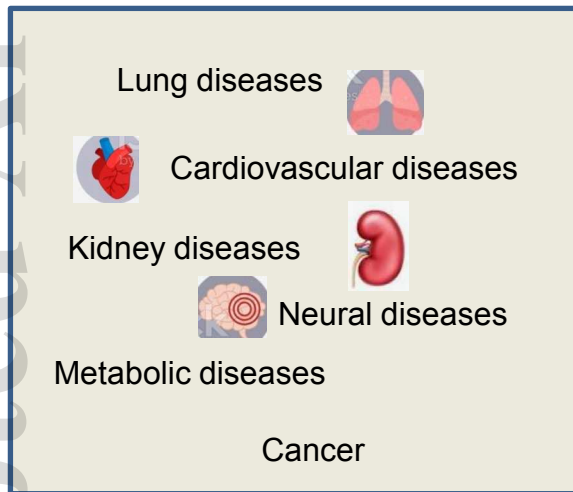
Table 1: Research questions on air pollution as a contributing factor to COVID 19 infection

Research question	Certainty vs. Uncertainty
Is SARS-Cov-2 exhaled?	Yes
Is SARS-Cov-2 airborne?	Yes: evidence has accumulated that the majority of transmissions occur as a result of infected people spewing large droplets and small particles called aerosols when they cough, talk, sing or breathe.
Is SARS-Cov-2 found in PM aerosols?	Potentially, as it can be carried by or mixed with secondary aerosols
Is SARS-Cov-2 viable once in suspension?	Yes, but needs to be confirmed
Is air pollution a co-factor of SARS-Cov-2 infection?	Yes, based on several mechanisms. A link has already been observed in the cases of SARS, influenza, syncytial virus and measles.
Is COVID-19 significantly related to air pollution?	Potentially yes, but additional <i>ad hoc</i> data are needed. In addition, the mechanisms are not understood.

1

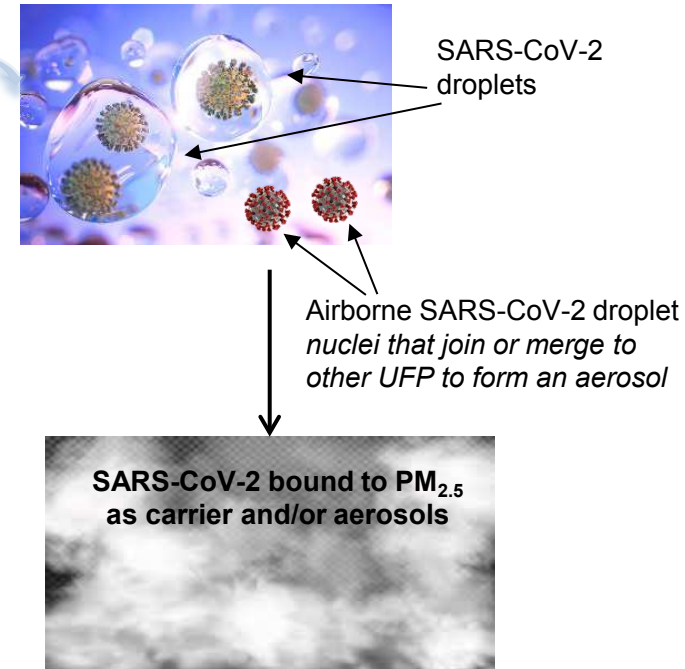
Air pollution* - related effects:

- a) impaired airways permeability****
b) development of diseases known as COVID-19 comorbidities



2

Increased risk of exposure to SARS-CoV-2 suspended in the air in polluted zones



Increased risk of COVID-19

*: O₃ (ozone), NO₂ (nitrogen dioxide), PM (particulate matter of various dimension), UFP (ultrafine particles)

** : ↓ functioning of airways ciliated cells, ↓ macrophages phagocytosis, ↓ immune respiratory defense

Fig 1: Patterns of air pollutants and SARS-CoV 2 interaction

Air pollution may contribute to COVID-19 pandemic by 1) rendering people more susceptible to SARS-CoV-2 infection through impaired mucosal permeability and/or in the long term increased individual susceptibility to develop chronic diseases putting COVID-19 patients at higher risk of severe COVID-19 events and death; 2) augmenting the risk of exposure to SARS-CoV-2. Once in the air, SARS-CoV-2 can either be carried by fine particles or mix with secondary ultrafine aerosols

O₃: Ozone; NO₂: Nitrogen dioxide; PM: Particulate matter;
↘ : diminution