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Air pollution* - related effects:
a) impaired airways permeability**
b) development of diseases known as COVID-19 comorbidities

Lung diseases 

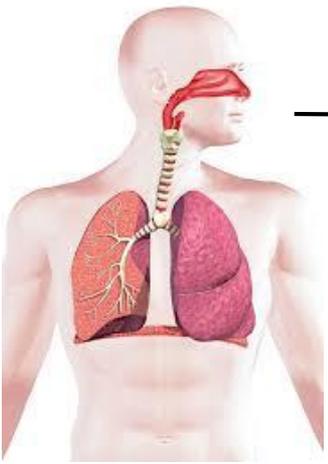
 Cardiovascular diseases

Kidney diseases 

 Neural diseases

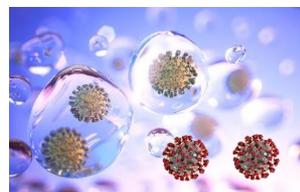
Cancer

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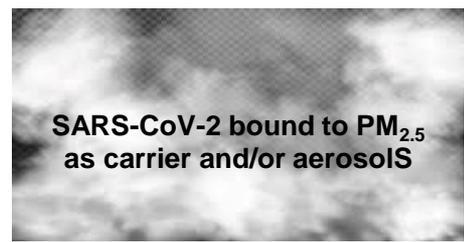


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Increased risk of exposure to SARS-CoV-2 suspended in the air in polluted zones



SARS-CoV-2 droplet or airborne (droplet nuclei) transmission



SARS-CoV-2 bound to PM_{2.5} as carrier and/or aerosols

Increased risk of COVID-19

*: O₃, NO₂, PM

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

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

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

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5 3 frequency and severity of COVID-19 infection. Consequently, researchers have rightly
6 4 recognized the importance of considering the role of air pollution in the COVID-19 pandemic.
7 5 Here, we discuss the pros and cons of air pollution as a contributing factor to COVID-19,
8 6 according to existing research questions (Table 1).

9
10 7 *What data exist on the relation of air pollution to SARS-CoV-2 or COVID-19?*

11 8 At the general population level, COVID-19 hospitalizations and deaths rates have skyrocketed
12 9 in countries (e.g., Iran, China, South Korea, regions (Lombardy), and towns (e.g., New York,
13 10 Madrid) most of which characterized by high levels of air pollution (e.g., Lombardy, Iran, China,
14 11 South Korea, New York, Madrid). Early in the pandemic, an Italian study positively related the
15 12 proportion of daily exceedances of concentrations of particulate matter (PM) with 10 μm of
16 13 diameter or less (PM₁₀) with the number of COVID-19 admissions reported within the following
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19 16 study that calculated the extent to which air pollution could be blamed for COVID-19 deaths
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22 19 which has some of the highest levels of harmful pollution on the planet, it found that 27% of
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34 28 *How can this be explained?*

35 29 Two patterns seem possible² (Figure 1). On the one hand, air pollution may render people
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40 34 decrease the ability of macrophages to phagocytize the virus as well as prevent an effective
41 35 immune response against the infection. Additionally, long-term endemic exposure to air
42 36 pollution is responsible through oxidative stress for chronic systemic inflammation at the origin
43 37 of the comorbidities, such as cardiovascular and respiratory diseases, metabolic diseases, etc.
44 38 that put COVID-19 patients at higher risk of severe events and death. Specifically, the
45 39 Angiotensin-converting enzyme 2 (ACE-2) receptor on lung cell surfaces, which is known to
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50 43 On the other hand, there is now growing evidence that SARS-CoV-2 is exhaled as a result of
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52 45 the air, the virus can either be carried by fine particles or mix with secondary ultrafine aerosols².
53 46 Experimentally, it has been observed that SARS-CoV-2 remains viable in aerosols for up to 3
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58 50 The viability and long range transport of respiratory viruses in open air, and thus their potential
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both indoors⁴ and outdoors². A recent study observed that the overburdening of the health services and hospitals, as well as the high over-mortality due to COVID-19 observed in various regions of Europe in the Spring of 2020 may be linked to peaks of PM_{2.5} and likely particular weather situations that have favored the spread and enhanced the virulence of the virus⁶. Ergo, air pollution may be an important factor in viral disease transmission and further investigations into the interaction of SARS-Cov-2 and air pollution are warranted. Interestingly, recent data showed the ability of pollen to suppress innate antiviral immunity, independent of allergy⁷.

In which matters should we be cautious?

The role of airborne SARS-CoV-2 transmission due to small respiratory droplets of diameter < 5 µm emitted by symptomatic as well as asymptomatic, but infected, individuals at the origin of droplet nuclei remaining suspended in the air is, however, still challenged by a lack of studies. A major drawback in this respect is that the minimum infectious dose, as expressed in viral RNA copies necessary to promote the infection, is not yet defined. In addition, very few studies so far have assessed RNA copies in outdoor air and they are not conclusive. In a Chinese study, the observed RNA concentrations were above the detection limits only in crowded areas⁸. In Italy, a study also observed detectable SARS-Cov-2 RNA in congested zones, but not in less polluted zones (below 10 µg/m³ in mean)⁹. A previous Italian study had similarly found traces of SARS-Cov-2 RNA in 23% of the sampled PM₁₀ in a polluted zone but without assessing RNA copies¹⁰. However, sampling the virulence of the sampled virus has proved challenging so far.

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

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

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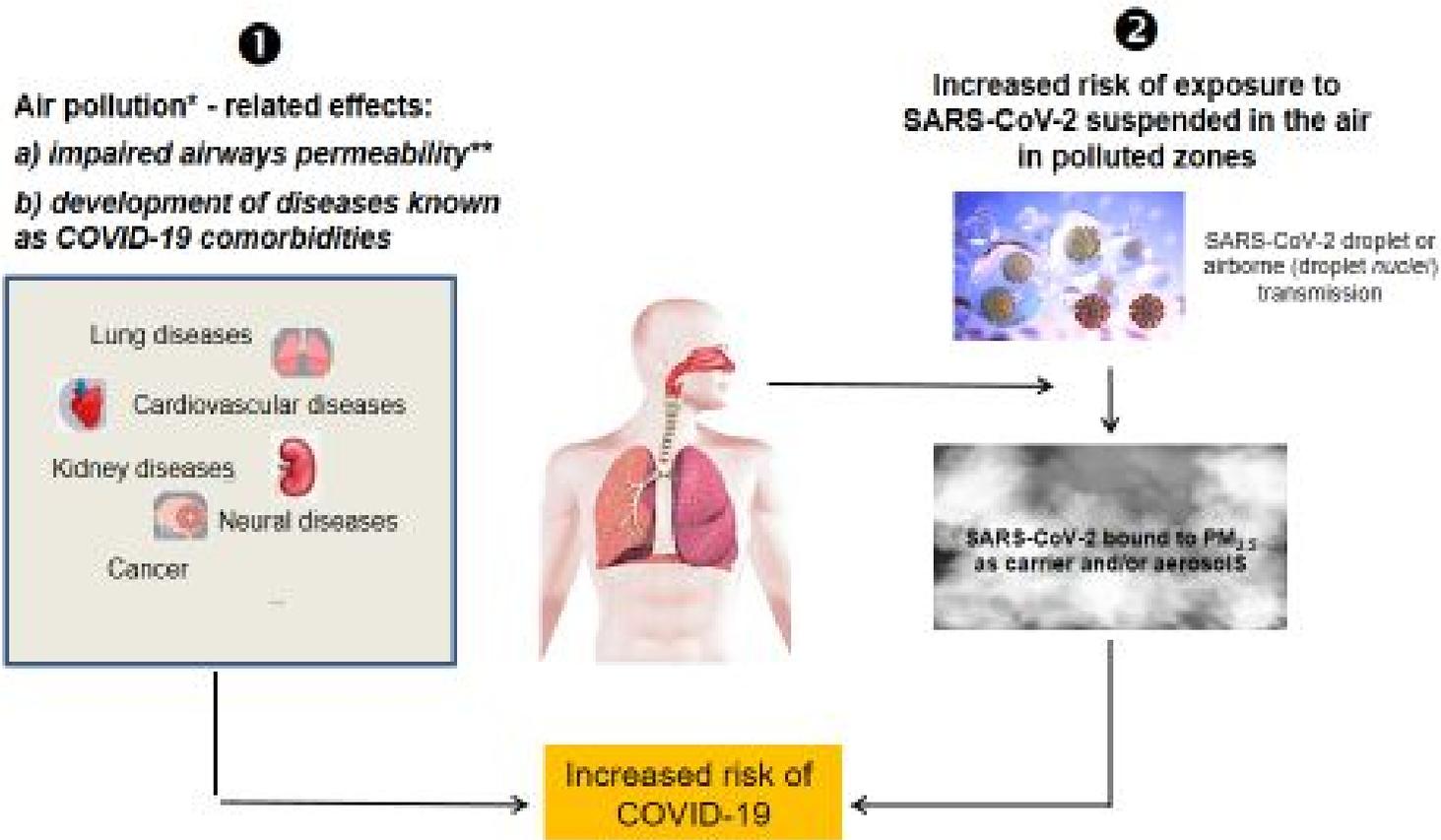
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34 **Table 1:** Research questions on air pollution as a contributing factor to COVID 19 infection

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.

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*: O₃, NO₂, PM

** : ↓ 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

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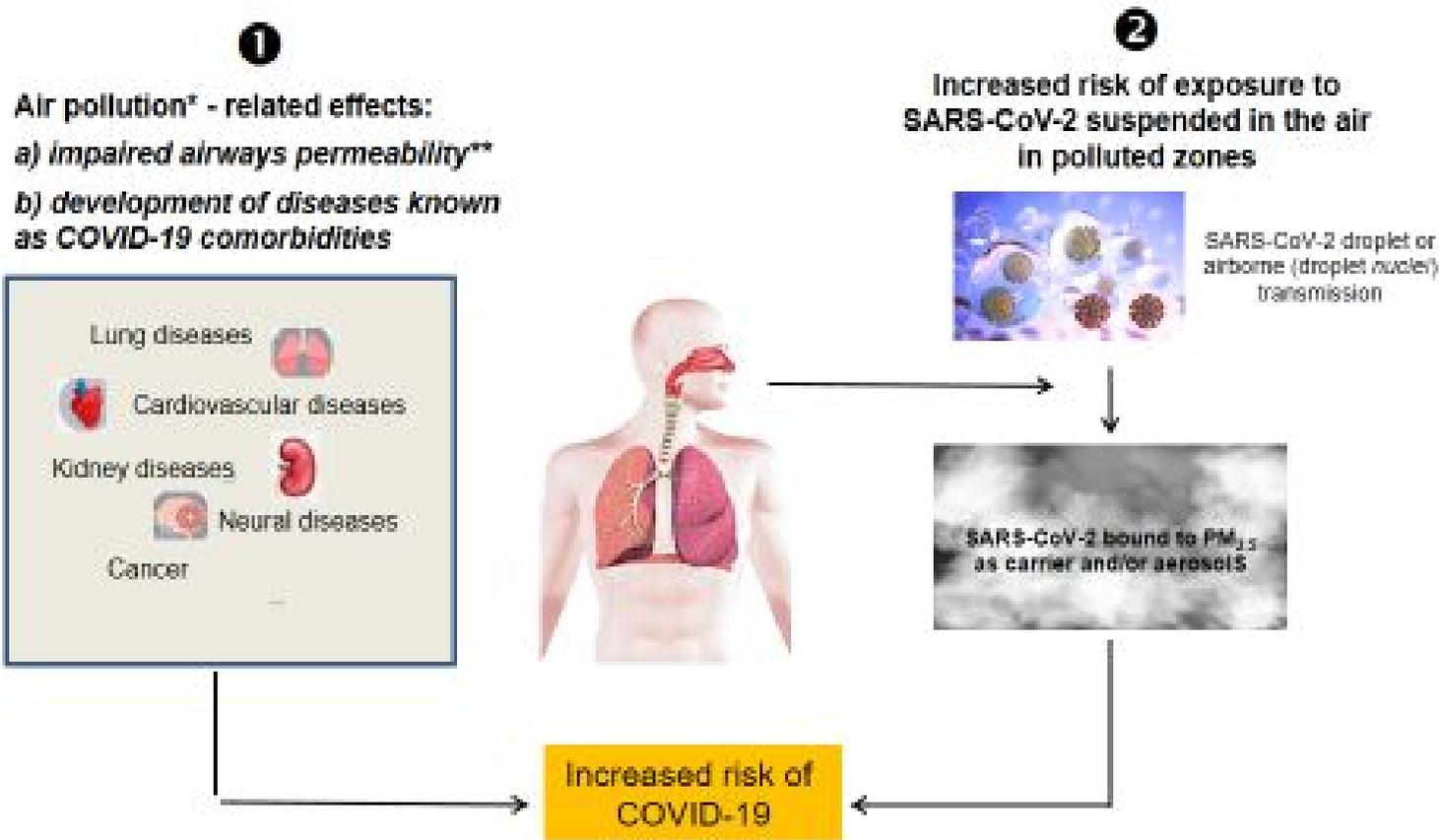
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32 30 Epidemiological Studies of Air Pollution and the SARS and COVID-19 Coronavirus
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34 32 Epub 2020 Sep 9. PMID: 32902328; PMCID: PMC7480171.

34 **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 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?	<u>Yes</u> Potentially <u>yes</u> , but <u>lacking sufficient additional ad hoc</u> -data <u>are needed</u> . In addition, the mechanisms are not understood.



*: O₃, NO₂, PM

** : ↓ 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

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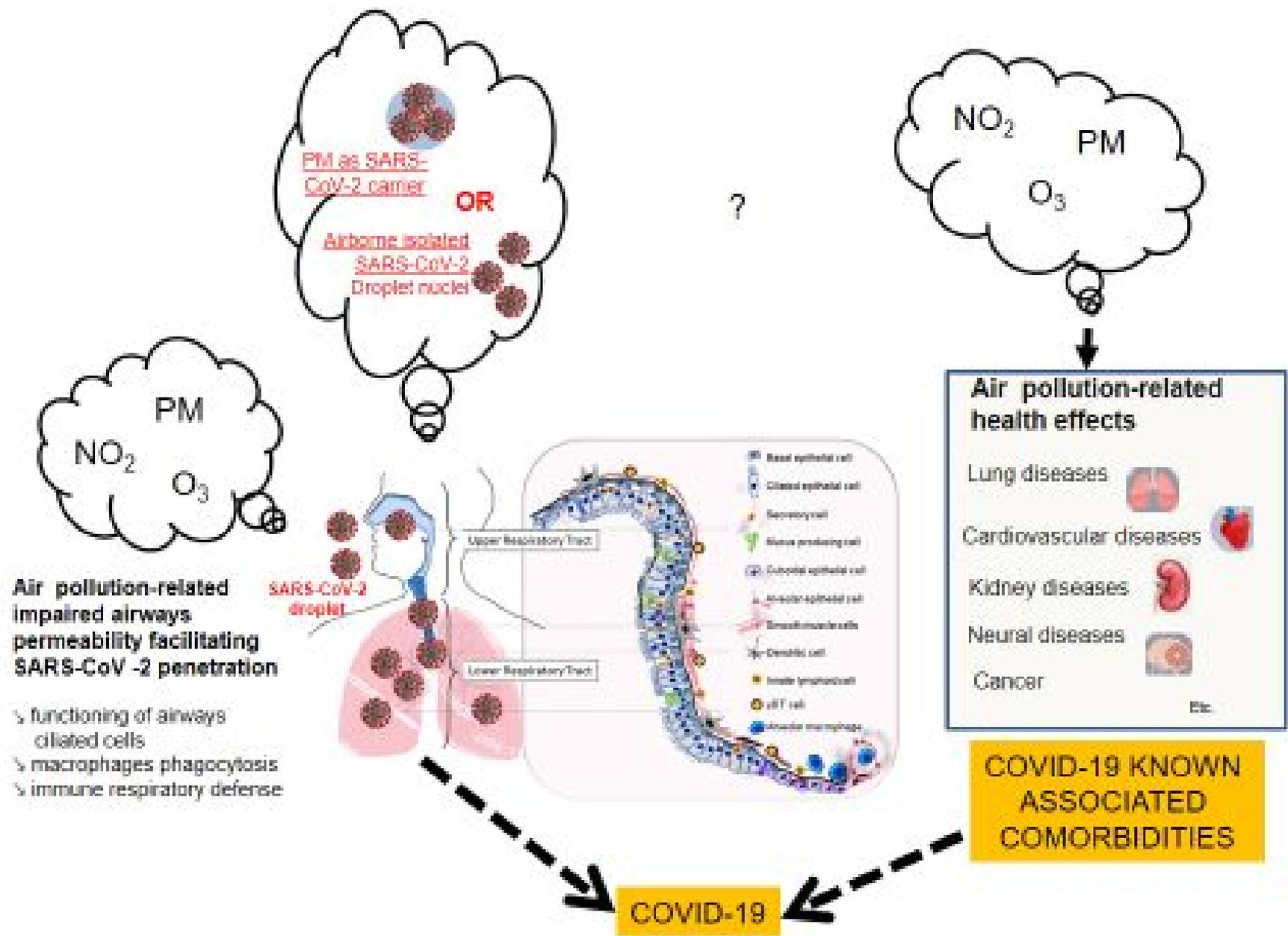


Fig 1: Patterns of air pollutants/SARS-CoV-2 interaction

Two patterns seem possible. Air pollution may contribute to COVID-19 pandemic by 1) rendering people more susceptible to infection by SARS-CoV-2 through impaired mucosal permeability or increasing individual susceptibility to develop chronic diseases putting COVID-19 patients at higher risk of severe 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

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