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# Unanswered questions on the airborne transmission of COVID-19

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## Abstract

Policies and measures to control pandemics are often failing. While biological factors controlling transmission are usually well explored, little is known about the environmental drivers of transmission and infection. For instance, respiratory droplets and aerosol particles are crucial vectors for the airborne transmission of the severe acute respiratory syndrome coronavirus 2, the causation agent of the coronavirus 2019 pandemic (COVID-19). Once exhaled, respiratory droplets interact with atmospheric particulates that influence the viability and transmission of the novel coronavirus, yet there is little knowledge on this process or its consequences on virus transmission and infection. Here we review the effects of atmospheric particulate properties, vortex zones, and air pollution on virus survivability and transmission. We found that particle size, chemical constituents, electrostatic charges, and the moisture content of airborne particles can have notable effects on virus transmission, with higher survival generally associated with larger particles, yet some viruses are better preserved on small particles. Some chemical constituents and surface-adsorbed chemical species may damage peptide bonds in viral proteins and impair virus stability. Electrostatic charges and water content of atmospheric particulates may affect the adherence of virion particles and possibly their viability. In addition, vortex zones and human thermal plumes are major environmental factors altering the aerodynamics of buoyant particles in air, which can strongly influence the transport of airborne particles and the transmission of associated viruses. Insights into these factors may provide explanations for the widely observed positive correlations between COVID-19 infection and mortality with air pollution, of which particulate matter is a common constituent that may have a central role in the airborne transmission of the novel coronavirus.

**Keywords** Coronavirus · Viability · Particulate matter · Chemical constituents · Surface charge · Vortex

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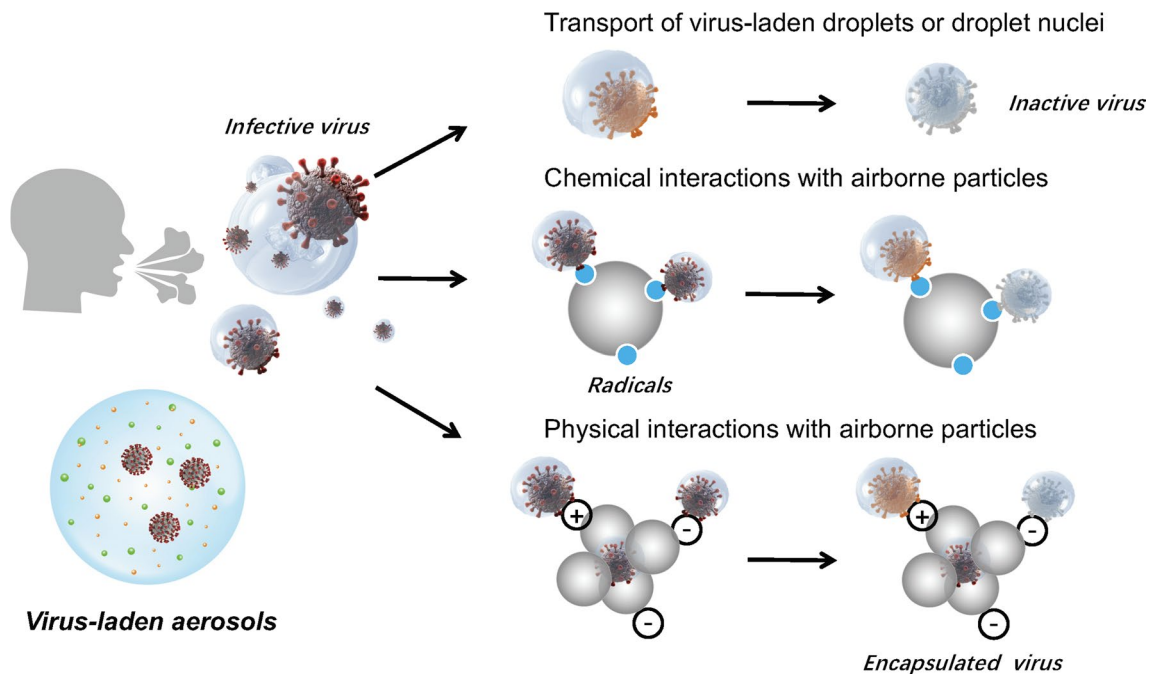
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## Introduction

Airborne transmission of diseases is a well-known phenomenon, yet the precise environmental mechanisms controlling transmission and further infection are poorly known. As a consequence, measures and policies to control pandemics, suggested by scientists and enforced by authorities, are not fully efficient, as observed during the coronavirus 2019 pandemic (COVID-19). While biological factors controlling disease transmission have been well studied, environmental factors have not been explored in depth (Sharma et al. 2020). COVID-19 can spread via respiratory droplets through inhalation or contact with fomites (CDC 2021; WHO 2020). At least one meter or six feet of social distancing is recommended for mitigating the transmission of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, CDC 2022; WHO 2022). However, cases of human-to-human infection at longer distances make these guidelines questionable (Li et al. 2021; Morawska and Cao 2020; Morawska and Milton 2020; Wang and Han 2022; Wang et al. 2021a). Moreover, when virus-laden aerosols remain buoyant in

air, these aerosols can travel far beyond the recommended safe social distances.

Most respiratory droplets from human respiratory activities are small enough to evaporate into droplet nuclei, of less than 5  $\mu\text{m}$ , within a few seconds (Johnson et al. 2009; Morawska 2006; Nicas et al. 2005; Vejerano et al. 2018). Both droplets and nuclei carrying coronaviruses could interact with airborne particulate matter that is often abundantly present in the ambient air. Airborne fine particulate matter contains complex, partly unknown mixtures of organo-mineral matter with varying physicochemical properties (Daelenbach et al. 2020; Guo et al. 2014). These could influence the aerodynamics, deposition, and possibly the viability of the viruses, yet little is known about the underlying mechanisms. The physicochemical properties of virus-laden aerosols include size, viral load, infectivity, and other chemical components such as electrolytes, proteins, surfactants, pH value, electrical charge, and properties on the air/liquid interfaces (Fig. 1). The questions remain on that (i) whether the association with airborne particulates would alter the aerodynamics of the viral particles (the answer is most definitely yes due to a change of size and density in the substrate of the viral particle, e.g., from droplet nuclei to airborne particulates, and perhaps their surface charges and



**Fig. 1** The fate of human respiratory viruses after being expectorated from the respiratory tract. Top: virus-laden droplets or droplet nuclei remain buoyant in air and progressively lose their infectivity. Middle: chemical interactions between droplets or droplet nuclei and chemical species e.g., radicals on the surface of buoyant fine particulates in air, which may affect the viability of the viruses. Bottom: physical interactions e.g., electrostatic interactions between droplets or droplet nuclei and buoyant fine particulates in air, which affect the transport,

deposition, and possibly the viability of viruses. Physicochemical properties of virus-laden aerosols include size, viral load and infectivity, other chemical components such as electrolytes, proteins, and surfactants, pH value, electrical charge, and properties on the air/liquid interfaces (Klein et al. 2022; Wang et al. 2021a, b, c). The enlarged illustration of the virus-laden aerosol is adapted from Wang et al. (2021a, b, c)

moisture contents as well, and (ii) whether the association with airborne particulates would affect the persistence of the viruses. Even though there are plenty of discussions and speculations on the latter (Ahlawat et al. 2020, 2022; Bozic and Kanduc 2021; Drossinos et al. 2022; Huynh et al. 2022; Lin et al. 2020; Luo et al. 2022; Niazi et al. 2021), the question remains unanswered in the present scientific literature.

The viability and infectivity of the virus associated with aerosols have recently attracted attention following the growing risk of COVID-19 airborne transmission (Hu et al. 2020; Morawska and Cao 2020; Morawska et al. 2021). For instance, SARS-CoV-2 remained experimentally viable for three hours in aerosols at room temperature, with a reduction in infectious titer from  $10^{3.5}$  to  $10^{2.7}$  in 50% tissue culture infectious dose per liter of air (van Doremalen et al. 2020). Likewise, laboratory experiments showed that SARS-CoV-2 maintained infectivity for 16 h in aerosol particles within an inhalable size range (Fears et al. 2020). There is, however, limited evidence on whether the size of aerosol particles has major effects on the viability and infectivity of SARS-CoV-2 (Chen et al. 2021; Sun et al. 2021). Further, the chemical constituents of airborne particulates, including airborne pollutants and radicals adsorbed or generated on particle surfaces, are likely to affect the viability of transported viruses. Moreover, how particle electrostatic charges, which are abundant on airborne particles, influence viral viability is largely unknown. Here we review the recent research on the role of airborne particulates in the viability and airborne transmission of COVID-19, with a focus on the physical and chemical properties of particulate matter such as particle size, chemical constituents, and electrostatic charges. We also discuss the influence of environmental factors such as localized flow fields e.g., vortex zones, human body thermal plumes, and the cofounding effects of air pollutants on COVID-19 infection.

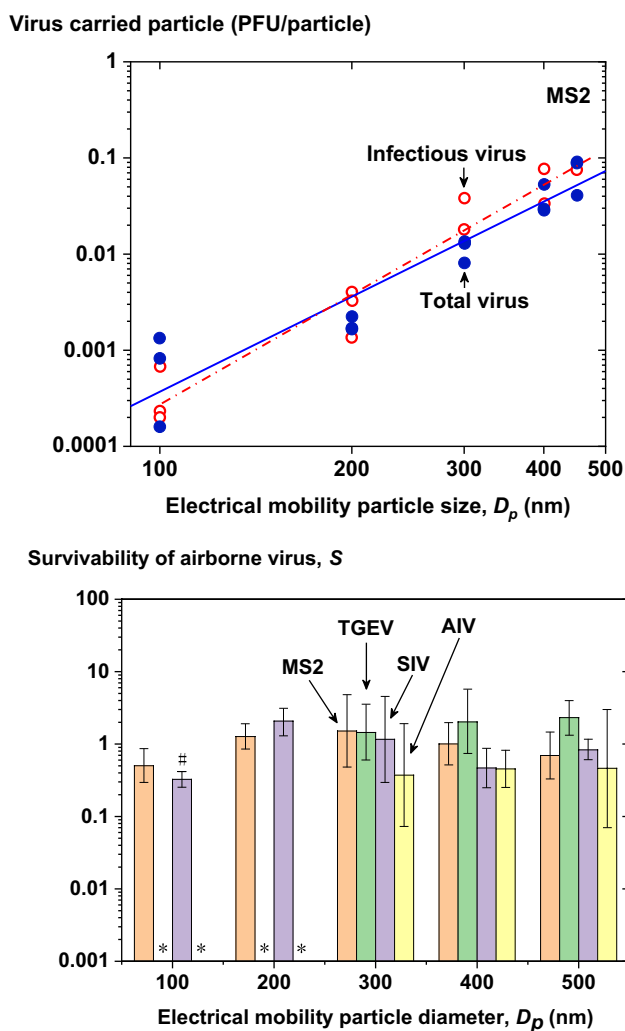
## Particle size

Particle size highly influences the airborne transmission of viral diseases (Gralton et al. 2011). In general, particles with larger sizes often settle in a shorter time, whereas small-sized particles remain buoyant in air for longer time periods. Therefore, small-sized particles potentially allow the transmission to hosts located at long distances from the source (Xie et al. 2007). For example, Lindsley et al. (2010) reported that spherical particles with small sizes of 1  $\mu\text{m}$ , took eight hours to settle one meter in still air, compared with larger particles, of 4  $\mu\text{m}$ , which took only 33 min. Particle size is also a predominant factor affecting the vertical distribution of particles in calm air. Simulations on vertical concentration gradients of influenza viruses in re-suspended air dust showed that viral

concentration at one meter above the ground was up to 40% higher than those measured at two meters and above, due to the higher settling velocities of particles with sizes larger than 20  $\mu\text{m}$  (Khare and Marr 2015).

Particle size also influences the persistence of viruses associated with particles (Appert et al. 2012; Stilianakis and Drossinos 2010). For instance, virus infectivity and survivability depend on the size of their particle carriers (Zuo et al. 2013). Results showed that the capacity of a particle to carry viruses generally increased with particle size, while the survivability depends both on virus type and particle size (Fig. 2). With the exception of the MS2 bacteriophage, the survivability of three animal viruses, the transmissible gastroenteritis virus, the swine influenza virus, and the avian influenza virus, was lower on particles with sizes comparable to virions, of 100–200 nm, compared with viruses carried on larger-size particles of 300–450 nm. The authors explained this observation by the shielding effects by larger particles. This physical protection is supported by the slower transformation of organic compounds that are encapsulated in complex organo-mineral media such as soils (Lichtfouse et al. 1998; Lichtfouse 1999, 2012). The protective effect of organo-mineral media is also demonstrated by the persistence of the plague bacterium *Yersinia Pestis* in soils under natural conditions, yet the underlying mechanisms are unknown (Eisen et al. 2008). Another indirect evidence for organo-mineral protection is the decrease in microplastic toxicity when microplastics are covered by soil particles (Liu et al. 2022a). By contrast, viruses should be more easily impaired on smaller size particles owing to the larger specific surface energies of particles, resulting in reduced virus survivability (Weber and Stilianakis 2008).

A study of viral survivability of three pig viruses of various transmission routes, the influenza A virus, the porcine reproductive and respiratory syndrome virus, and the porcine epidemic diarrhea virus, showed that viral viability was generally higher in larger-size particles (Alonso et al. 2015). Other reports revealed that particle size influences viral survivability and varies greatly with the type of virus. For instance, rhinovirus survived longer on coarse particles larger than 9  $\mu\text{m}$  than on smaller particles of 0–4  $\mu\text{m}$  (Tyrrell 1967). By contrast, the infectivity of adenovirus was better preserved on smaller, 0.5–1.9  $\mu\text{m}$  particles, compared with larger, 1.9–10  $\mu\text{m}$  particles (Appert et al. 2012). Noteworthy, a similar effect is observed in soils where organic compounds are older, and thus better preserved, in small, clay-like particles (Cayet and Lichtfouse 2001). Overall, particle size has notable effects on viral infectivity and transmission, with higher survival associated with larger particles in general, yet some viruses are better preserved on small particles.



**Fig. 2** Top: infectious virus and total virus carried per particle as a function of particle size for airborne bacteriophage MS2, a model virus used in the study. Equations and  $R^2$ -values of the curve fitting and the 95% confidence intervals of the slopes, where  $x$  represents particle size and  $y$  represents the amount of infectious virus or total virus carried per particle. Bottom: survivability of airborne viruses. Each bars represent standard deviations from geometric means. PFU, plaque forming unit; MS2, bacteriophage MS2, the model virus; TGEV, transmissible gastroenteritis virus; SIV, swine influenza virus; AIV, avian influenza virus. Asterisk (\*) denotes cases where no infectious virus could be recovered. The pound sign (#) denotes that infectious virus was recovered in only one of the three samples. Modified after Zuo et al (2013). Equations: red dashed fitting (top graph):  $y = (7.77 \times 10^{-12}) * x^{3.77}$ ,  $R^2 = 0.95$ ; C.I. (confidence intervals): 3.2–4.3; blue solid fitting (top graph):  $y = (9.97 \times 10^{-11}) * x^{3.23}$ ,  $R^2 = 0.89$ ; C.I.: 2.6–4.0. Discrepancies exist between graph reading values and the calculated results of the second equation (blue solid fitting)

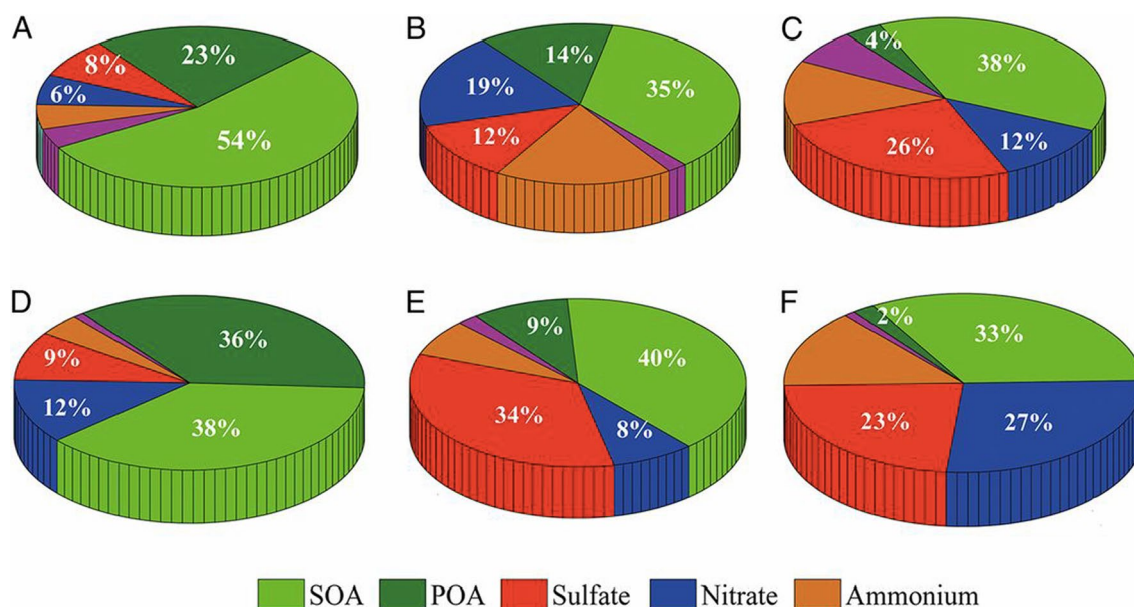
## Chemical constituents

Airborne particulate matter consists of a complex mixture of constituents from various sources (Almeida et al. 2005; Daellenbach et al. 2020). The composition of airborne

particulates generally includes soil crusts, minerals and salts, and metal species (Daellenbach et al. 2020; Mikrut et al. 2018). Using an aerosol mass spectrometer, Guo et al. (2014) measured the mass fractions of organics, nitrates, and sulfates in fine particulate matter that have a diameter of less than  $2.5 \mu\text{m}$  ( $\text{PM}_{2.5}$ ) in Beijing, China. The authors found that particle compositions in Beijing exhibited similarities to those commonly measured in many areas around the globe, consistent with the chemical constituents dominated by secondary aerosol formation (Fig. 3). In addition, airborne particulates often contain abundant inorganic and organic contaminants adsorbed from the surrounding environment or natively associated with their sources of emission (Daellenbach et al. 2020; Huang et al. 2014). These pollutants are often related to emissions from anthropogenic sources (Huang et al. 2014). Organic pollutants and metal species generally dominate the surface reactivity, acidity or alkalinity, and redox potential of airborne particulates, which in turn may affect the viability of viruses associated with these particulates.

Combination with airborne dust and particulate matter has been postulated to improve virus stability and even facilitate the long-range transport of COVID-19 (Qu et al. 2020; Wathore et al. 2020), although no definitive evidence has been reported to date to support these hypotheses or elucidate their underlying mechanism (Chen et al. 2021). By contrast, earlier reports suggested that some common properties of airborne particulates may, in fact, decrease virus stability. For instance, surface-adsorbed organic substances may undergo photochemical reactions to generate oxidizing radicals, which in turn could damage peptide bonds in viral proteins and impair virus viability (Fig. 1; Gehling and Dellinger 2013; Ram et al. 2021). Groulx et al. (2018) reported a 44% reduction in infectivity of bacteriophage  $\Phi 6$ , a virus similar to COVID-19, by contact with airborne particles collected near a major high-traffic street in Toronto, Canada, compared to the virus in purified air.

Radicals may also impair virus survival. For instance, secondary organic aerosols or organic precursors adsorbed on particles often contain persistent free radicals and reactive oxidant species such as hydroxyl radicals, semiquinone radicals, and peroxides, which can potentially oxidize or inactivate viruses (Djellabi et al. 2021; Yoo 2018). Redox-active transition metals and irradiated conditions in open environments can further increase the concentrations of reactive oxidant species on airborne particulates (Gehling and Dellinger 2013; Mokrzynski et al. 2021; Tong et al. 2018). Reactive oxidant species can react with saturated lipids and then impair the integrity of virions by lipid peroxidation and the alteration of surrounding proteins and nucleic acids such as guanine (Imani et al. 2020). Therefore, common chemical contaminants in airborne particulates are likely to reduce the survival of associated virions.



**Fig. 3** Particle chemical compositions during the clean, transition, and polluted periods for the 25–29 September and 2–7 October episodes. SOA, secondary organic aerosol; POA, primary organic aerosols. (A–C) Chemical compositions for 80-nm (A), 100-nm (B), and 240-nm (C) particles were measured by the aerosol mass spectrometer at 1500 h on 25 September, 1200 h on 27 September, and 1800 h on 28 September, respectively. The three particle sizes (i.e., close to the mean size) are selected to represent the dominant features in the chemical composition during the clean, transition, and polluted peri-

ods. The numbers for the colors denote the mass concentrations of the aerosol constituents, i.e., light green for secondary organics, dark green for primary organics, blue for nitrate, red for sulfate, yellow for ammonium, and purple for chloride. The ammonium (yellow) mass fractions are 5% (A), 18% (B), 13% (C), 4% (D), 7% (E), and 14% (F), and the chloride (purple) mass fractions are 4% (A), 2% (B), 7% (C), 1% (D), 2% (E), and 1% (F). Reprinted with permission of the National Academy of Sciences from Guo et al. (2014)

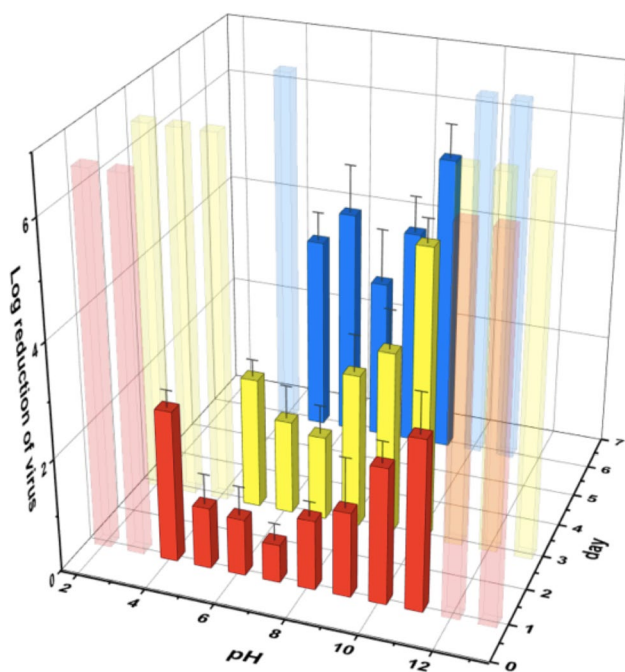
Chemical constituents can also affect the acidity of particulate matter (Zhang et al. 2012). Depending on their sources of emission, airborne particulates may be acidic, e.g., pH 3–5, due to the presence of sulfate compounds (Gao et al. 2020; Shi et al. 2017; Weber et al. 2016). Geographic location, local climate, and anthropogenic activities also strongly influence the acidity of airborne particulate matter. For instance, Karydis et al. (2021) investigated the acidity of global aerosols from 1970 to 2020. They found that the acidity of aerosol particles generally decreased in Europe and North America in the past few decades. Nonetheless, aerosols collected in the eastern part of the United States and Europe, and in Southeast Asia still show strong acidity with a pH lower than 4 in 2011–2020.

Figure 4 shows that the survivability of SARS-CoV-2 decreases under high acidity. For example, SARS-CoV-2 can be detected at pH 5–10 for several days, whereas the virus loses infectivity within one day at pH 2–3. As a consequence, adherence to highly acidic aerosols may result in rapid virus inactivation for SARS-CoV-2. Furthermore, low pH also facilitates the formation of secondary aerosols and increases the presence of soluble transition metals in particulates—the latter could catalyze viral inactivation by forming reactive oxygen species (Charrier and Anastasio 2015; Chen et al. 2019; Ingall et al. 2018; Tong et al. 2018). The

chemical constituents of airborne particulate matter need to be better considered when probing the survival of SARS-CoV-2 on aerosol particles in laboratory studies (Fears et al. 2020; van Doremalen et al. 2020). Some airborne particulates emitted from common anthropogenic sources show distinct physical and chemical properties, which affect their surface reactivity, acidity, charges, or redox potential, and these could have a major influence on the survival of their associated virions (Chen et al. 2021; He and Han 2021).

## Electrostatic charges

The role of surface charges on airborne particles in SARS-CoV-2 infectivity has been overlooked. Indeed, electrostatic charge is a major property of airborne particulate matter. For instance, electrostatic charges strongly influence particle coagulation and interactions with other airborne matter (Pushpawela et al. 2018; Wei and Gu 2015; Zhang et al. 2016). The effects of surface charges between solids and viruses have been extensively studied in some environmental media such as water, sediments, and soils (Bitton 1975; Gerba 1984; Michen and Graule 2010; Redman et al. 1997; Shields and Farrah 1983). Reports on airborne particles have focused on the effect of surface charges on the adsorption of



**Fig. 4** Survival of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) under different pH conditions. Include untreated virus stock solution as the viral load for the positive control median tissue culture infectious dose/mL =  $6.50 \pm 0.61$ . Column colors: red, day 1; yellow, day 3; blue, day 6. Faded colors denote negative culture (i.e.,  $\log_{10}$  reduction = 6.50). All tests were neutralized before testing and performed in triplicate. Modified after Chan et al. (2020). Original data are provided in a tabulated format in the Supplementary Information (Table S1)

virions on particles. For instance, many viruses have protein polypeptide coats containing amino acids with weakly acidic and basic groups, which, upon ionization, give the viral capsid an electrical charge (Gerba 1984). Like other solid matter, viral surface charges show strong pH dependence, which also varies with the type or strain of the virus (Burge and Enkiri 1978; Gerba 1984). Michen and Graule (2010) reviewed the isoelectric point measurements of viruses that replicate in hosts of kingdom plantae, bacteria, and animalia. They found that the isoelectric points of viruses were found in the pH range of 1.9–8.4 and most frequently, their isoelectric points were measured to be within the range of 3.5–7.0, although the data appeared to be scattered widely within single virus species (Michen and Graule 2010).

Some researchers reported that solids with high isoelectric points were generally better adsorbents for viruses (Gerba 1984; Murray and Parks 1980), although this needs to be assessed for different virus-particle systems. Zerda et al. (1985) studied the adsorption of five viruses, namely, the bacteriophage MS-2 (*Emesvirus zinderi*), enterobacteria phage T2, and reovirus type 1, all with isoelectric points near pH 4.0, and poliovirus strains LSc and Brunhilde which had isoelectric points of 6.6 and 7.1, to surface-modified silica

particles under different pH. The study showed that when pH conditions were favorable to a positive surface charge on the virions, all viruses were adsorbed exclusively on negatively charged silica, whereas all of them were adsorbed to positively charged silica when the pH increased above their isoelectric points.

Similar effects of electric charges are likely to occur between SARS-CoV-2 and the associated particulate matter. For example, the pH of airborne particulates typically lies in the acidic to a neutral range (Karydis et al. 2021). As a consequence, particles with low isoelectric points and negatively charged surfaces are more likely to adsorb SARS-CoV-2 virions, which have isoelectric points in the neutral to alkaline range. Indeed, isoelectric points of 8.24–9.32 for the SARS-CoV-2 receptor-binding domain with Fc-tag protein, 7.36–9.88 for its receptor-binding domain with His-tag protein, and 7.30–8.37 for the S1 subunit with His-tag protein, have been observed in commercially available SARS-CoV-2 proteins (Krebs et al. 2021).

Since the surface charges of virion particles vary with pH, the control of electrostatic interactions between viral particles and environmental surfaces may be a viable strategy to alter their deposition and persistence in the environment (Gerba 1984; Vasickova et al. 2010). Whether surface charges could impair the proteins of viruses carried on particulates and affect their infectivity when deposited into new hosts is a further question for future investigations. In this vein, modeling results suggest that charge-laden particulates could reach deeper regions of the human respiratory tract compared with non-charged counterparts of equivalent sizes (Koullapis et al. 2016). Overall, the association between virions and particles via electrostatic charges depends on both their isoelectric points and the pH conditions, which vary in different virion-particle systems and particle charges may affect the viability of associated virions and the deposition of particles in human airways.

## Moisture

The humidity of the ambient environment is a common factor potentially affecting the survival and transmission of airborne pathogens (Lin and Marr 2020; Prussin et al. 2018; Yang et al. 2012). Some researchers proposed that the incidence of respiratory tract infections can be reduced by controlling relative humidity at a level that is not conducive to the survival and spread of viruses in the environment (Gelperin 1973; Reiman et al. 2018; Sale 1972). Moce-Llivina et al. (2006) reported that viruses with higher lipid contents tend to be more persistent at low relative humidity. Vasickova et al. (2010) showed that enveloped viruses were generally more stable under low relative humidity. These early findings received considerable interest during the COVID-19

pandemic as indoor humidity can be easily regulated and monitored by home appliances.

Statistical analyses on meteorological factors and COVID-19 incidence revealed that COVID-19 transmission decreases with rising humidity (Qi et al. 2020; Wu et al. 2020a). Indeed, the water contents in airborne particulates may deter the adhesion of the coronavirus, given the fact that the spike protein has an N-terminal peptide that is strongly hydrophobic (Baron 2021; Robson 2020). Particles with high moisture contents could, in theory, deter viral adherence, which could be the reason for the apparent resistance to the first wave of COVID-19 dominated by viral Clade D in coastal cities (Baron 2021). This may not be the case in the second wave of COVID-19 which was dominated by Clade G of SARS-CoV-2. The different orientations of spike protein peptides may have influenced their hydrophobicity and adherence to airborne particulates (Baron 2021). Overall, there is a need to validate earlier hypotheses on the correlations between particle moisture content and virus adherence or viability and the correlation between virus persistence and relative humidity, given that SARS-CoV-2 originates from respiratory droplets and that humidity is a ubiquitous environmental factor.

## Localized flow fields

COVID-19 is rapidly inactivated when exposed to simulated sunlight (Ratnesar-Shumate et al. 2020; Wondrak et al. 2021). Localized flow fields, such as thermophoresis and vortex zones, are common in ambient airflows which can have dominant effects on the aerodynamics of buoyant particulates in air, especially in indoor environments. In general, expiratory aerosols are transmitted in two stages, namely, the expiratory flow and the secondary stage of dispersion through airflows, which can result in short-range and long-range airborne transmission of respiratory pathogens, respectively (Wei and Li 2016). There are two main sources of flow fields in the indoor atmospheric environment, namely, natural or forced air ventilation and human thermal plumes (Mittal et al. 2020). Many studies adopted computational fluid dynamics models to simulate the indoor transport of respiratory pathogens in various settings such as hospitals (Zorzi et al. 2022), flight cabins (Zhang et al. 2021a, b), subway trains (Armand and Tâche 2022), elevators (Nouri et al. 2021), and offices (Srivastava et al. 2021). Particularly, localized flow fields generated by differences in temperature, pressure, and movements may prolong the buoyance and travel distance of aerosol particles in air (Zhao et al. 2022). In addition, the human body constantly generates upward thermal plumes which bring buoyant particulates from the lower atmosphere to the breathing zone (Sun et al. 2021). Thermal plumes are created by the constant exchange of

heat between the human body and the surrounding environment, where the human body generally has higher temperatures than that of the air it is surrounded by. When the air approaches a heat source, it rises along the surface of the source, forming a constant plume that carries buoyant aerosol particles in air. Liu et al. (2022b) found that the upward airflow caused by the thermal plume disrupted the indoor unidirectional airflow and result in the diffusion of indoor pollutants in the operating room microenvironment. Thermal body plumes create re-circulatory motions in the room and as a result, aerosol clouds generated from coughing and talking move upwards with their concentrations reduced along their movements (Hossain et al. 2022). While the impact of indoor ventilation systems on COVID-19 transmission has been extensively discussed, vortex flows received less attention (Biryukov et al. 2021; Han et al. 2021; Sharma et al. 2020; Valsamatzi-Panagiotou and Penchovsky 2022; Wang et al. 2021b). In reality, both outdoor and indoor environments have time-varying and spatially distributed localized flow fields, including vortex zones (Ma et al. 2021). The vortex zone is strongly associated with the concentration of bioaerosol particles in air (Liu et al. 2020). The vortex, which weakens the carrying capacity for buoyant particles by airflows, can result in the shedding of bioaerosol particles, forming high-concentration localized areas (Wang et al. 2022). Airborne particles tend to accumulate in vortex zones where elevated loadings of virus-laden particles can increase the risk of airborne transmission of respiratory pathogens (Khmelev et al. 2021; Lin and Marr 2020; Prussin et al. 2018; Yang et al. 2012). Overall, localized indoor flow fields can significantly influence the transport of airborne particles and the respiratory viruses associated with those particles.

## Correlations between air pollution and COVID-19 spread

Since early in the pandemic, researchers have observed that COVID-19 hospitalization and mortality rates increased with air pollution levels (Magazzino et al. 2020; Meo et al. 2021; Yao et al. 2020a, 2020b; Zhang et al. 2021a, b; Zhu et al. 2020; Zoran et al. 2020). Recent data from Germany, Italy, and China showed that populations chronically breathing polluted air were at risk of having worsened effects from COVID-19 infection (Konduracka and Rostoff 2022; Li et al. 2022; Prinz and Richter 2022; Veronesi et al. 2022). On the contrary, lower mortality rates were reported in Italian forested areas (Roviello and Roviello 2021, 2022).

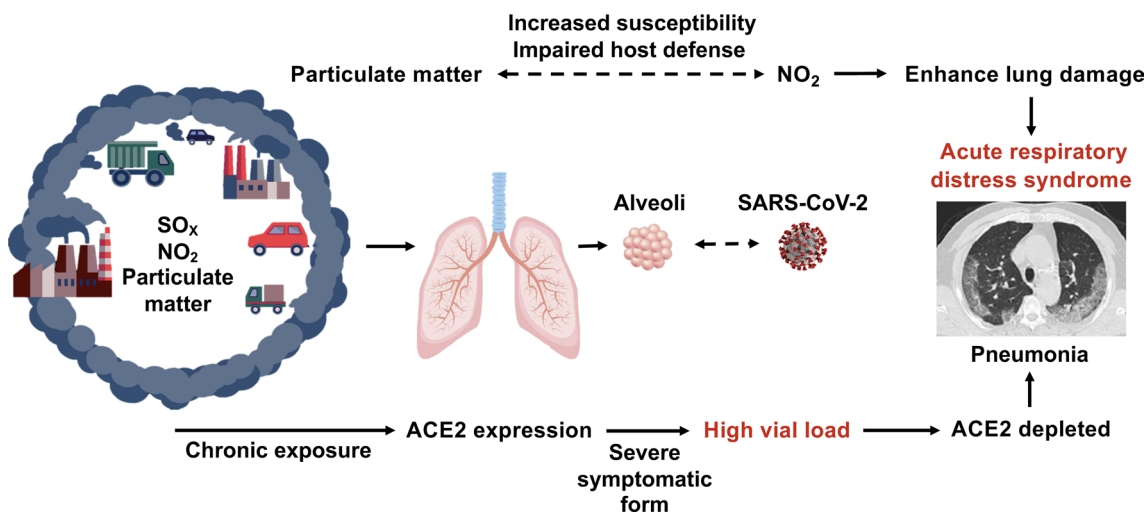
The Harvard T.H. Chan School of Public Health has compiled a list of studies on the association between air pollution and COVID-19 (Harvard Chan C-CHANGE 2021). In Europe, several studies reported that short-term air pollution exposure was positively associated with an increased



risk of COVID-19 infection in young adults ( $n=425$ ) in Sweden, and similar results were reported in England and Netherlands (Cole et al. 2020; Travaglio et al. 2021; Yu et al. 2022). The UK Office for National Statistics found that long-term exposure to fine particulate matter could increase the risk of contracting and dying from COVID-19 by up to 7% (ONS UK 2020). Higher death rates from COVID-19 infection were reported in areas with air pollution in Italy, Spain, France, and Germany (Conticini et al. 2020; Ogen et al. 2020). In China, it was also reported that  $\text{NO}_2$  concentration was positively associated with the transmission ability of COVID-19 and that air pollution was positively associated with fatality rates (Yao et al. 2020a, b, 2021; Zhu et al. 2020). Despite these widely observed correlations, the question remains as to *how* prior or concurrent exposure to air pollutants contributes to COVID-19 infection, severity, or mortality. While the underlying mechanisms are under debate (Ishmatov 2022; Sunyer et al. 2021), several hypotheses were put forward for these widely observed correlations. For instance, some researchers proposed that the airborne transmission of COVID-19 could be facilitated by airborne particulate matter (Ishmatov 2022; Qu et al. 2020). Others emphasized the fact that long-term prior exposure to air pollutants is known to compromise the human respiratory system, which could induce specific vulnerabilities to pathogenic infections (Kutter et al. 2021; Setti et al. 2020a, b; Srivastava 2021; Tian et al. 2021). Some researchers postulated that exposure to elevated levels of particulate matter smaller than  $2.5 \mu\text{m}$  ( $\text{PM}_{2.5}$ ) could cause the overexpression of alveolar angiotensin-converting enzyme 2 (ACE-2) receptors on the human airway epithelial cells, the major cell entry receptor for SARS-CoV-2, and the exhaustion of Th2

immune responses which facilitates viral penetration and increases host susceptibility to infections (Fig. 5; Frontera et al. 2020; Naidoo et al. 2021; Paital and Agrawal 2021; Wu et al. 2020b). In addition to the effects caused by inhaled fine particulates themselves, chemical pollutants, reactive oxidant species, and redox-active transition metals that are inhaled or carried by these airborne particulates can undergo biotransformation in vivo and elicit oxidative stress in the human respiratory tract. To conclude, positive correlations have been widely observed between COVID-19 infection and mortality and air pollution, of which airborne particulate matter is a major component and may have a central role in these cause-and-effect correlations.

The types of air pollutants investigated in those correlation analyses included particulate matter 2.5 ( $\text{PM}_{2.5}$ ), particulate matter 10 ( $\text{PM}_{10}$ ),  $\text{SO}_2$ , CO,  $\text{NO}_2$ , and  $\text{NO}_x$ , ozone, lead, and volatile organic compounds (VOCs), which showed positive correlations with the confirmed cases of COVID-19 infections in areas investigated by the researchers (Zhu et al. 2020; Fattorini et al., 2020; Coccia, 2020; Travaglio et al. 2021; Bashir et al. 2020; Zoran et al. 2020) or in other cases, the mortality and morbidity rates after COVID-19 infection (Wu et al. 2020a, b; Travaglio et al. 2021; Pozzer et al. 2020; Yao et al. 2020a, b). A tabulated summary of the relevant information reviewed is available in the Supplementary Information (Table S2). In the scenario of long-term exposure, individuals exposed to air pollution were prone to chronic respiratory diseases which in turn increased their susceptibility to viral infection by SARS-CoV-2 (Conticini et al. 2020). For instance, long exposure to  $\text{NO}_2$  was the suspected driving factor of the high mortality rates observed in 66 administrative regions in Italy, Spain,



**Fig. 5** Chronic exposure to fine particulate matter may cause overexpression of alveolar angiotensin-converting enzyme 2 (ACE2) receptors. This could increase viral loads in patients previously exposed to air pollutants and subsequently cause depletion of ACE2 recep-

tors and impairment of host defenses. Additionally, exposure to high concentrations of airborne nitrogen dioxide may cause more severe symptoms after infection by SARS-CoV-2 in the lungs. Modified after Frontera et al. (2020)

France, and Germany (Ogen 2020). In a recent review, Sun et al. (2022) analyzed the findings of 67 studies. The authors concluded that the majority of existing studies ( $n = 49$ , or 73%) reported positive correlations between PM<sub>2.5</sub> levels and the prevalence of COVID-19, while nine studies ( $n = 9$ ) observed negative correlations. The rest of the studies ( $n = 9$ ) reviewed by Sun et al. (2022) did not find a definitive correlation between PM<sub>2.5</sub> levels and COVID-19 infection. Also, a study in Switzerland found that the first wave of severe cases of COVID-19 infections was positively correlated with the exposure of individuals with prior exposure to particulate matter and nitrogen dioxide, while such trends were not evident in the second wave of COVID-19 infection (Belocconi and Vounatsou 2023). The different findings reported in those studies were confounded by the models, meteorological conditions, and socioeconomic developments in the areas or communities of interest (Moriyama et al. 2020). There is a need for a standardized, rigorous approach in correlation analyses to provide more robust, consistent, and even comparable results between different studies (Bourdrel et al. 2021; Cao et al. 2014; Chen et al. 2010; Chirizzi et al. 2021; de la Fuente et al. 2022; Hsiao et al. 2022; Kayalar et al. 2021; Sharma and Balyan 2020; Stern et al. 2021; Tao et al. 2022). Further, the fundamental insights into such correlations need to be gained to probe the underlying mechanisms of these statistical correlations and to validate the current hypotheses (Comunian et al. 2020; Frontera et al. 2020).

## Conclusion

The novel coronavirus disease 2019 (COVID-19) is primarily transmitted by respiratory droplets. Despite the intensive research efforts in the past two and a half years, many questions remain unanswered to date. Of these, understanding how viruses in respiratory droplets and droplet nuclei interact with airborne particulates present in the ambient air is a priority, given the abundance of the latter in the airborne environment and their potential effects on virus viability and airborne transmission. In this domain, major knowledge gaps exist in understanding how the physiochemical attributes and electrostatic charges of airborne particulates could affect the viability of SARS-CoV-2 associated with them and further the transmission through ambient air. Here, environmental factors are also important to consider given the fact that after exhalation from respiratory airways, the viability of viruses carried on droplets or particulates is closely related to the environmental conditions to which they are exposed. Studies on animal viruses generally found higher virus survivability on larger-sized particles, which are more easily impaired on smaller size particles due to the high surface reactivity of the latter. Chemical constituents of fine particulate matter, including contaminants emitted from anthropogenic sources

and adsorbed on particles, could damage peptide bonds in viral proteins and impair virus viability by releasing radicals, increasing particle acidity and the solubility of metal species in particulates. In addition, many airborne particulates carry electrostatic charges, which influence their coagulation and association with virions. Surface charges of particles and virions are strongly influenced by pH conditions. Isoelectric point measurements on SARS-CoV-2 receptor-binding domains are generally in the neutral to alkaline range. Water contents in airborne particulates have been hypothesized to deter viral adherence, given the fact that the spike protein has an N-terminal peptide that is strongly hydrophobic. Two of the less studied factors, vortex zones and human thermal plumes, which are common in airborne environments, have a strong influence on the transport of airborne particles and the transmission of the viruses associated with these particles. The widely observed positive correlations between air pollution and COVID-19 infection and mortality necessitate studies on the role of airborne particulates, which represents a common and key component of air pollutants, in effectuating the transmission and symptom aggravation of COVID-19.

**Supplementary Information** is available below and at <https://doi.org/10.1007/s10311-022-01557-z>.

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## Declarations

**Conflict of interest** The authors declare that they have no conflict of interest.

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## Unanswered questions on the airborne transmission of COVID-19

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**Method S1.** The underlying idea of this article is to conduct a critical analysis of the existing evidence, consensus (including preliminary conclusions), and scholarly discussions (including debates) revolving around the airborne transmission of COVID-19—an important but previously under-appreciated route of transmission of COVID-19—and then, based on the authors' own research experience and expertise in relevant research domains, to articulate the questions and knowledge gaps that have *not* been addressed or adequately addressed in the current literature.

To achieve these goals, we first looked at current review articles and analyzed the compilation, syntheses, and critical assessments of the existing literature. We then expanded our searches to original articles, including publications that are categorized as articles (research articles), letters, case reports, data papers, thesis dissertation to analyze the frequencies of keywords that appeared in those publications as well as the inter-connections between those keywords. We then selected publications with the most prominent keywords and the highest degree of relevance to the topics discussed in our article and conducted a further analysis of these publications.

Below are the search keywords, databases, search results, inclusion criteria, and the strategies we used when analyzing evidence and scholarly discussions on the topics discussed in the article.

Databases: Clarivate Web of Science, all databases, including all of the following:

- Web of Science Core Collection
- BIOSIS Citation Index
- Chinese Science Citation Database
- Derwent Innovation Index
- Inspec®
- KCI-Korean Journal Database
- MEDLINE®
- SciELO Citation Index

Search keywords:

Topic: "Severe Acute Respiratory Syndrome" OR "SARS" OR "coronavirus" OR "CoV" OR covid OR "COVID-19" OR "Human Coronaviruses" OR "HCoV" OR "Severe Acute Respiratory Syndrome-Coronaviruses" OR "SARS-CoV" OR "Severe Acute Respiratory Syndrome- Coronaviruses-2" OR "SARS-CoV-2" OR "new coronavirus" OR "Novel Coronaviruses" OR "nCov" OR "2019 Novel Coronavirus" OR "2019-nCoV"

AND

Topic: Particle\* OR "Particulate Matter" OR "PM" OR "PM10" OR "PM2.5" OR "air pollut\*" OR "environmental factor\*"

AND

Topic: airborn\* OR transmit\* OR spread\*

Inclusion criteria:

- Year of publication: 2020 or 2021 or 2022 or 2023
- Article type: Review article

Search results:

- 669

Preliminary analysis:

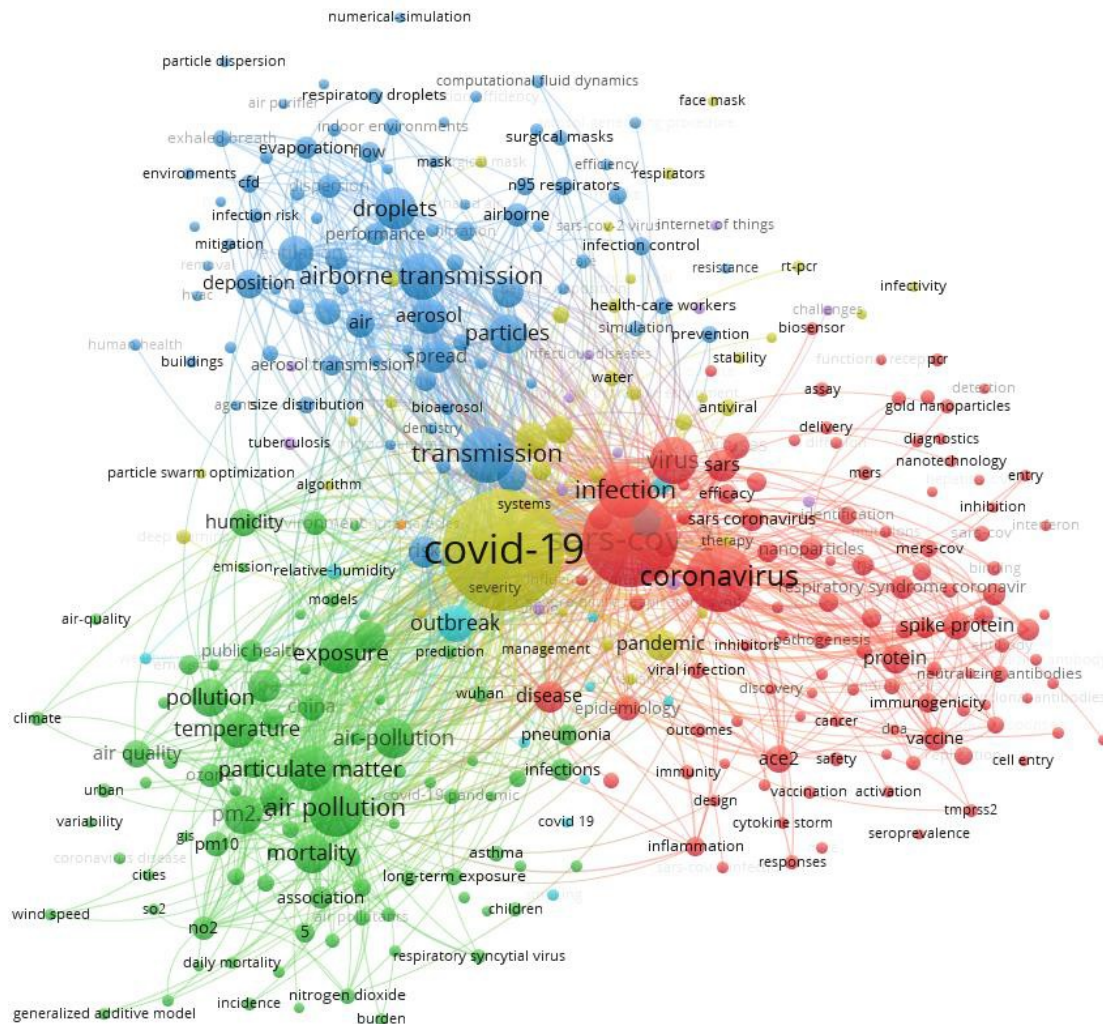
- We then analyzed the titles and abstracts of these articles.
- A total of 120 review articles were selected for detailed analysis, based on their relevance to the topics of discussion in our article.

Detailed analysis:

- After conducting a detailed analysis, we found that the selected 120 review articles mainly revolved around five broad topics:
  - 42 articles: virus-laden aerosols, including their generation, spread in the air, and virus transmission, and the underlying mechanisms
  - 42 articles: influence of environmental factors including temperature, humidity, and sunlight on the survival of SARS-CoV-2
  - 19 articles: effects on human respiratory and immune systems by air pollutants including particulate matter, ozone, and nitrogen oxide
  - 13 articles: correlations between local air pollution and the numbers of confirmed cases of COVID-19 infection, mortality rates, and morbidity rates after infection
  - 3 articles: airborne particulates and aerosols as potential carriers of SARS-CoV-2 and the interactions between viruses and particle or aerosol substrates
- It is clear that most of the current syntheses of scholarly publications on the airborne transmission of COVID-19 have focused on the first two sub-topics and to a similar extent, the third and the fourth topics, i.e., the correlations between air pollution and COVID-19 infection or symptom aggravation. After analyzing the review articles on the last topic listed above, we found that currently there is only one review article that has compiled the existing evidence, theories, and opinions on airborne particulates and aerosols as potential carriers of SARS-CoV-2 and possible interactions between viruses and their associated particle or aerosol substrates. The authors, however, only presented a brief discussion on these topics in the article (Bourdrel et al. 2021). Below is an excerpt of the relevant texts in this reference.

- “When the air and virus mixture was previously filtered through a high-efficiency particulate absorbing filter, which removes a large fraction of fine particles, the activity of the viruses on the host bacteria was significantly modified: for some viruses, the presence of fine particles had a potentiating effect on viral infection, whereas for other viruses, fine particles significantly reduced viral replication [73]. This study illustrates the fact that the chemical and electrical characteristics of both particles and viruses play an important role in virus–particulate matter interactions.”
  - Ref.: Bourdrel et al. 2021. The impact of outdoor air pollution on COVID- 19: a review of evidence from in vitro, animal, and human studies. *European Respiratory Review* 30 (159) 200242.

Below is the visualized map of the keywords of non-review type publications in our phase-two literature analysis, using the search keywords and databases listed above. We then analyzed the significance and inter-relations of the keywords and hand-selected about 120 original articles that are most relevant to the topics discussed in the article. A majority of these articles are cited and discussed in our article and listed in the reference section.



**Method S2.** In mid-December 2022, the authors searched in the Clarivate Web of Science® database using keywords “air pollut\*” AND “covid OR sars-cov-2 OR “novel coronavirus\*”, and then ranked the search results by their total number of times cited by articles indexed in the database. The authors then manually screened the 150 top cited articles, of which nine articles identified positive correlations between the occurrence or magnitude of local air pollution and the rates of local infection as well as the mortality and morbidity rates of COVID-19.

The types of air pollutants investigated in those correlation analyses included particulate matter 2.5 (PM<sub>2.5</sub>), particulate matter 10 (PM<sub>10</sub>), SO<sub>2</sub>, CO, NO<sub>2</sub> and NO<sub>x</sub>, ozone, lead, and volatile organic compounds (VOCs), which showed positive correlations with the confirmed cases of COVID-19 infections in areas investigated by the researchers (Zhu et al., 2020; Fattorini et al., 2020; Coccia M, 2020; Travaglio et al., 2021; Bashir et al., 2020; Zoran et al., 2020) or in other cases, the mortality and morbidity rates after COVID-19 infection (Wu et al., 2020; Travaglio et al., 2021; Pozzer et al., 2020; Yao et al., 2020). A tabulated summary of the relevant information reviewed is available in the Supplementary Information (**Table S2**). In the scenario of long-term exposure, individuals exposed to air pollution were prone to chronic respiratory diseases which in turn increased their susceptibility to viral infection by SARS-CoV-2 (Conticini et al. 2020). For instance, long exposure to NO<sub>2</sub> was the suspected driving factor of the high mortality rates observed in 66 administrative regions in Italy, Spain, France, and Germany (Ogen 2020). In a recent review, Sun et al. (2022) analyzed the findings in 67 studies. The authors concluded that the majority of existing studies ( $n = 49$ , or 73%) reported positive correlations between PM<sub>2.5</sub> levels and the prevalence of COVID-19, while nine studies ( $n = 9$ ) observed negative correlations. The rest of those studies ( $n = 9$ ) reviewed by Sun et al. (2022) did not find a definitive correlation between PM<sub>2.5</sub> levels and COVID-19 infection. Also, a study in Switzerland found that the first wave of severe cases of COVID-19 infections was positively correlated to the exposure of the individuals with prior exposure to particulate matter and nitrogen dioxide, while such trends were not evident in the second wave of COVID-19 infection (Beloconi and Vounatsou 2022). The different findings reported in those studies were confounded by the models, meteorological conditions, and socioeconomic developments in the areas or communities of interest. There is a need for a standardized, rigorous approach in correlation analyses to provide more robust, consistent, even comparable results between different studies. Further, the fundamental insights into such correlations need to be gained to probe the underlying mechanisms of these statistical correlations and to validate the current hypotheses (Comunian et al. 2020; Frontera et al. 2020).

**Evidence analysis.** There are already over a handful of peer-reviewed studies showing that, in real environments and specifically for SARS-CoV-2, there were viruses associated with airborne particulates. These studies were conducted in different countries and real-life settings and reported by different groups of authors. Please see below for a list of references.

The first group of references below reported the detection of SARS-CoV-2 on airborne particulates. Overall, the results showed that viral loadings were generally low on particulates, and further studies are needed to measure their infectivity.

- Tao et al., 2022. SARS-CoV-2 and other airborne respiratory viruses in outdoor aerosols in three Swiss cities before and during the first wave of the COVID-19 pandemic. *Environment International* 164, 107266.  
“Therefore, in this study, we collected airborne particulate matter (PM) samples from November 2019 to April 2020 in Bern, Lugano, and Zurich. Among 14 detected viruses, influenza A, HCoV-NL63, HCoV-HKU1, and HCoV-229E were abundant in air. SARS-CoV-2 and enterovirus were moderately common, while the remaining viruses occurred only in low concentrations. **SARS-CoV-2 was detected in PM<sub>10</sub> (PM below 10 μm) samples of Bern and Zurich, and PM<sub>2.5</sub> (PM below 2.5 μm) samples of Bern which exhibited a concentration positively correlated with the local COVID-19 case number. The concentration was also correlated with the concentration of enterovirus which raised the concern of coinfection.**”
- Kayalar et al., 2021. Existence of SARS-CoV-2 RNA on ambient particulate matter samples: A nationwide study in Turkey. *Science of The Total Environment* 789, 147976.  
“A total of 203 daily samples (TSP,  $n = 80$ ; PM<sub>2.5</sub>,  $n = 33$ ; PM<sub>2.5-10</sub>,  $n = 23$ ; PM<sub>10μm</sub>,  $n = 19$ ; and 6 size segregated PM,  $n = 48$ ) were collected using various samplers. The N1 gene and RdRP gene expressions were analyzed for the presence of SARS-CoV-2, as suggested by the Centers for Disease Control and Prevention (CDC). According to real time (RT)-PCR and three-dimensional (3D) digital (d) PCR analysis, dual RdRP and N1 gene positivity were detected in 20 (9.8%) samples. **Ambient PM-bound SARS-CoV-2 was analyzed quantitatively and the air concentrations of the virus ranged from 0.1 copies/m<sup>3</sup> to 23 copies/m<sup>3</sup>.**”
- Stern et al., 2021. Levels and particle size distribution of airborne SARS-CoV-2 at a healthcare facility in Kuwait. *Science of The Total Environment* 782, 146799.  
“Providing the largest dataset of size-fractionated airborne SARS-CoV-2 RNA to date, we showed that **SARS-CoV-2 RNA is present with airborne particles ≤2.5 μm, 2.5–10 μm, and ≥10 μm.**”
- Chirizzi et al., 2021. SARS-CoV-2 concentrations and virus-laden aerosol size distributions in outdoor air in north and south of Italy. *Environment International* 146, 106255.  
“The results found indicate that outdoor atmospheric concentrations of SARS-CoV-2 were very small (<0.8

*copies m<sup>3</sup>) in both northern and southern Italy. The same applies for each size range investigated with the impactor, which gave virus-laden aerosol concentrations <0.4 copies m<sup>3</sup>.*”

- Sharma AK, Balyan P, 2020. Air pollution and COVID-19: Is the connect worth its weight? *Indian Journal of Public Health* 64, S132-S134.  
“**SARS-CoV-2 positive detection was only obtained from one fine fraction (PM2.5) sample, corresponding to one occupancy room, where a patient with positive PCR and cough was present.**”
- Setti et al., 2020. SARS-Cov-2 RNA found on particulate matter of Bergamo in Northern Italy: First evidence. *Environmental Research* 188, 109754.  
“**This is the first evidence that SARS-CoV-2 RNA can be present on outdoor particulate matter in defined conditions of atmospheric stability and high concentrations of PM10, thus suggesting a possible use of this test as indicator of epidemic recurrence.**”

The second group of references are two earlier studies which showed that respiratory pathogens could travel long distances in air along with airborne particulates they were associated with.

- Cao et al., 2014. Inhalable Microorganisms in Beijing’s PM2.5 and PM10 Pollutants during a Severe Smog Event. *Environmental Science & Technology* 48(3) 1499–1507.  
“**Among the identified microbial species, several are known to cause human allergies and respiratory diseases, including *Streptococcus pneumoniae*, *Aspergillus fumigatus*, and human adenovirus C (with average genome coverage of 2.0%, 14.5%, and 6.5%, respectively) ...Its representation within the entire bacteria community (analyzed by MetaPhlAn) was 0.012% in PM2.5 samples and 0.017% in PM10 samples, and the normalized number of hit reads (hit abundance) appeared to have increased by ~2 fold from an average of 0.024% during the first 2 less polluted days to an average of 0.05 ± 0.02% in the 5 heavily polluted days in PM2.5 samples (Figure 4A) ... The hit abundance of adenovirus in our samples also appeared to have increased during the heavily polluted days, though with more daily variations than those of *S. pneumoniae* and *A. fumigatus* (SI Figure S5).**”
- Chen et al., 2010. Ambient Influenza and Avian Influenza Virus during Dust Storm Days and Background Days. *Environmental Health Perspectives* 118(9), 1211-1216.  
“**Previous virus survival studies report a relationship between particle association/attachment and enhanced survival, thus suggesting that the attachment of infectious viruses to dust particles moving across the ocean might enhance long-range host- to-host transport (Chung and Sobsey 1993; Cox 1995; Labelle and Gerba 1981; Rao et al. 1984). In the present study, we successfully quantified ambient influenza A virus during both ADS days and background days. Our data showed that ambient influenza virus concentration during ADS days was 21 and 31 times higher at the Wan-Li and Shin- Jhuang air monitoring stations, respectively, than that during background days.**”

**Table S1** Effects of different pH conditions on infectivity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)<sup>a</sup>. Reprinted from Chan et al. (2020).

<b>pH</b>	<b>Day 1</b> <i>(log<sub>10</sub> reduction ± SD)</i>	<b>Day 3</b> <i>(log<sub>10</sub> reduction ± SD)</i>	<b>Day 6</b> <i>(log<sub>10</sub> reduction ± SD)</i>
<b>2</b>	Negative (6.50±0.00)	Negative (6.50±0.00)	ND
<b>3</b>	Negative (6.50±0.00)	Negative (6.50±0.00)	ND
<b>4</b>	Positive (2.67±0.29)	Negative (6.50±0.00)	Negative (6.50±0.00)
<b>5</b>	Positive (1.08±0.52)	Positive (2.33±0.29)	Positive (3.50±0.50)
<b>6</b>	Positive (1.00±0.50)	Positive (1.67±0.58)	Positive (4.10±0.85)
<b>7</b>	Positive (0.67±0.29)	Positive (1.50±0.50)	Positive (2.90±0.96)
<b>8</b>	Positive (1.23±0.25)	Positive (2.73±0.64)	Positive (3.92±0.63)
<b>9</b>	Positive (1.50±0.87)	Positive (3.23±0.68)	Positive (5.33±0.58)
<b>10</b>	Positive (2.40±0.36)	Positive (5.13±0.40)	Negative (6.50±0.00)
<b>11</b>	Positive (3.00±0.70)	Negative (6.50±0.00)	Negative (6.50±0.00)
<b>12</b>	Negative (6.50±0.00)	Negative (6.50±0.00)	ND
<b>13</b>	Negative (6.50±0.00)	Negative (6.50±0.00)	ND

**Notes:** (a) Include untreated virus stock solution as the viral load for the positive control median tissue culture infectious dose/mL = 6.50 ± 0.61. All tests were neutralized before testing and performed in triplicate. Abbreviations used in the table: Positive, culture positive; negative, culture negative; ND, not done; SD, standard deviation.

**Table S2.** Summary of findings reported in nine relevant studies in the top 150 most cited peer-reviewed journal articles on correlation analyses between air pollution and COVID-19 as of mid-December 2022

<b>Countries and regions</b>	<b>Types of air pollutants</b>	<b>Result</b>	<b>Ref.</b>
120 cities were obtained from January 23, 2020 to February 29, 2020 in China	PM2.5, PM10, SO <sub>2</sub> , CO, NO <sub>2</sub> and O <sub>3</sub>	Significant positive associations of PM2.5, PM10, NO <sub>2</sub> and O <sub>3</sub> in the last two weeks with newly COVID-19 confirmed cases.	Zhu et al. 2020
in up to 71 Italian provinces during the last 4 years	NO <sub>2</sub> , O <sub>3</sub> , PM2.5 and PM10	Long-term air-quality data significantly correlated with cases of COVID-19	Fattorini et al. 2020
N = 55 Italian provincial capitals, considering variables in 2018–2019– 2020 to explain the relationships between diffusion of COVID-19, demographic, geographical and environmental variables.	PM10 or ozone	The acceleration of transmission dynamics of COVID-19 has a high association with air pollution of cities measured with days exceeding the limits set for PM10 or ozone.	Coccia 2020
in the United States averaged from 2000 to 2016) from an established exposure prediction model	PM2.5	Higher historical PM2.5 exposures are positively associated with higher county-level COVID-19 mortality rates after accounting for many area-level confounders.	Wu et al. 2020
England from 2018 to 2019	Nitrogen dioxide, nitrogen oxide and ozone, PM2.5 and PM10	PM2.5 was a major contributor to COVID-19 cases, a small increase in air pollution leads to a large increase in the COVID-19 infectivity and mortality rate in England	Travaglio et al. 2021
March 4, 2020, to April 24, 2020	Spearman and Kendall correlation tests to analyze the association of PM 2.5, PM 10, SO <sub>2</sub> , NO <sub>2</sub> , Pb, VOC, and CO with COVID-19 cases in California	Environmental pollutants such as PM10, PM2.5, SO <sub>2</sub> , NO <sub>2</sub> , and CO have a significant correlation with the COVID-19 epidemic in California	Bashir et al. 2020

<p>Milan metropolitan area, Lombardy region, Italy</p>	<p>Daily average concentrations of inhalable particulate matter (PM) in two size fractions PM<sub>2.5</sub>, PM<sub>10</sub> and maxima PM<sub>10</sub> ground level atmospheric pollutants together air quality and climate variables (daily average temperature, relative humidity, wind speed, atmospheric pressure field and Planetary Boundary Layer-PBL height) collected during 1 January–30 April 2020 were analyzed.</p>	<p>The strong influence of daily averaged ground levels of particulate matter concentrations, positively associated with average surface air temperature and inversely related to air relative humidity on COVID-19 cases outbreak in Milan.</p>	<p>Zoran et al. 2020</p>
<p>We applied a global atmospheric chemistry general circulation model (EMAC) which comprehensively simulates atmospheric chemical and meteorological processes and interactions with the oceans and the biosphere, in the same set-up as in recent studies on climate change, air pollution, and public health.</p>	<p>The annual atmospheric near-surface PM<sub>2.5</sub> concentrations were taken from model-integrated satellite data, for the year 2019</p>	<p>We estimate that particulate air pollution contributed ~15% (95% confidence interval 7–33%) to COVID-19 mortality worldwide, 27% (13 – 46%) in East Asia, 19% (8–41%) in Europe, and 17% (6–39%) in North America. Globally, ~50–60% of the attributable, anthropogenic fraction is related to fossil fuel use, up to 70–80% in Europe, West Asia, and North America.</p>	<p>Pozzer et al. 2020</p>
<p>Associations between particulate matter (PM) concentrations and the case fatality rate (CFR) of COVID-19 in 49 Chinese cities, including the epicenter of Wuhan.</p>	<p>PM<sub>2.5</sub> and PM<sub>10</sub>  Average PM concentrations from January 15, 2020 to February 29, 2020</p>	<p>Positive associations between PM pollution and COVID-19 CFR in cities both inside and outside Hubei Province. For every 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> and PM<sub>10</sub> concentrations, the COVID- 19 CFR increased by 0.24% (0.01%–0.48%) and 0.26% (0.00%–0.51%), respectively.</p>	<p>Yao et al. 2020</p>



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