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Indoor Aerosol Science Aspects of SARS-CoV-2 Transmission

William W Nazaroff
Department of Civil and Environmental Engineering
University of California
Berkeley, California USA 94720-1710

Abstract
The state of knowledge about person-to-person transmission of SARS-CoV-2 is reviewed, emphasizing three components: emission of virus-containing particles and drops from infectious persons; transport and fate of such emissions indoors; and inhalation of viral particles by susceptible persons. Emissions are usefully clustered into three groups: small particles (diameter 0.1-5 μm), large particles (5-100 μm), and ballistic drops (> 100 μm). Speaking generates particles and drops across the size spectrum. Room-scale exposures have contributions from small and large particles. Small particles can be removed from air at room scale by ventilation and filtration. Large particles mainly deposit onto indoor surfaces. Proximate exposure enhancements are mainly associated with large particles with possible contributions from ballistic drops. Masking and social distancing can be effective to mitigate transmission from proximate exposures. Important information gaps prevent a quantitative reconciliation of the high overall global spread of Covid-19 with known transmission pathways. Available information supports several findings with moderate to high confidence: transmission occurs predominantly indoors; inhalation of airborne particles (up to 100 μm in diameter) contributes to viral spread; transmission occurs at room scale and in near proximity; speaking is a major source of airborne SARS-CoV-2 virus; and emissions occur without strong illness symptoms.

Running Title: Indoor Transmission of SARS-CoV-2
Keywords: Airborne, Covid-19, Infectious disease, Intake fraction, Particle, Virus

Practical Implications
• Virus-containing emissions from the respiratory tract are usefully grouped into three size ranges based on diameter: small particles (0.1-5 μm), large particles (5-100 μm), and ballistic drops (> 100 μm).
• Speaking (and other vocalization activities) by an infectious person when indoors appears to be especially important as a source of airborne virus-containing particles and consequently an important contributor to viral transmission of SARS-CoV-2.
• Indoor transmission at room scale is most likely to be a consequence of inhaling airborne particles, in either the small or large size range; ventilation, filtration, mask wearing, and limiting occupancy density and duration can all contribute to attenuating the transmission risk.
• Proximity-scale transmission probably involves inhaling large particles; the transmission risk can be attenuated by mask wearing and social distancing.
• Available evidence isn't sufficient to confirm that other transmission pathways are unimportant, including some that have not received much attention, such as those involving respiratory particle deposition onto and subsequent release from clothing fabrics.

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Introduction

The Covid-19 pandemic has revealed inadequacies in our collective understanding of the transmission of respiratory viral diseases. As an illustration of this point, consider the conflicting views of prominent scholars about the role of aerosols in the transmission of SARS-CoV-2, the causative agent of Covid-19. Heneghan et al.[1] wrote that "the lack of recoverable viral culture samples of SARS-CoV-2 prevents firm conclusions over airborne transmission." Greenhalgh et al.[2] responded: "there is consistent, strong evidence that SARS-CoV-2 spreads by airborne transmission."

Disagreements such as this are much more important than a purely academic concern. As of June 2021, about 1.5 years into the Covid-19 pandemic, the reported diagnosed cases total 180 million globally with 3.9 million deaths. The diagnosed case rate represents 2.3% of the world's population. The case fatality rate (ratio of deaths to diagnosed cases) is also high, at 2.2%. These disease outcomes have occurred notwithstanding vigorous efforts to manage the spread of the pandemic that have been broadly and deeply disruptive. Knowledge about modes of transmission and their relative importance is central to the design of effective public health interventions.

In historical context, Covid-19 is only one of several important respiratory viral diseases. Others of note include measles, SARS, the common cold, and influenza. Knowledge about the transmission of these diseases, albeit incomplete, contributes to our understanding of how SARS-CoV-2 transmission occurs and how nonpharmaceutical interventions may contribute toward limiting the spread. Conversely, scientific and public health efforts motivated to control the Covid-19 pandemic might improve our ability to control the incidence of other respiratory viral infections in the future.

The inadequate state of understanding regarding the transmission of SARS-CoV-2 is substantially attributable to the multidisciplinary complexity of the salient processes. Important scientific and technological disciplines that would study these processes include virology, immunology, respiratory physiology, aerosol dynamics, environmental fluid mechanics, building ventilation systems, and human behavior. It is highly probable that a sufficient future understanding will require the synthesis of contributions from multiple fields of knowledge that don't have an adequate shared history of collaboration or even cross-disciplinary communication.

Available evidence suggests that a large majority of the transmission of SARS-CoV-2 occurs indoors.[3,4] Evidence also strongly supports a view that virions emitted along with respiratory fluid from infectious persons is a major component in the chain of transmission. Such emissions are transported, diluted, and transformed during the time of travel between source and receptor. The transfer of viral materials to a susceptible person's sensitive tissues is pivotal in the initiation of new infections.

This article aims to contribute to an improved state of understanding about SARS-CoV-2 transmission by highlighting key elements from the disciplinary perspective of indoor aerosol science and technology. Key elements that are pertinent to the airborne transmission of SARS-CoV-2 are reviewed, including emissions from the respiratory tract, environmental transport and fate, and uptake by a susceptible person.

Key Concepts and Terms

It is apparent that an important challenge in making progress toward understanding transmission of respiratory infections is clear communication. With contributions needed from multiple disciplines that have developed independently there is considerable risk of misunderstanding because of differences in the denotation and connotation of terms. Such difficulties are highlighted nicely in a table in Tang et al.[5] that describes the different understandings of terms such as "airborne," "aerosol," and "particle" by clinicians, aerosol scientists, and the public. The purpose of this section is to define the language used for essential elements of this paper.

Along with exhaled air, a person with a viral respiratory tract infection can emit finely divided aqueous particles, droplets, or drops that contain virus. The suspended aqueous materials are a combination of mucus originating from the lining of the respiratory tract airways and saliva from the oral cavity. The site of origin of particles, droplets, or drops in the respiratory tract can vary according to the generating activity and associated particle-production mechanism.

It is convenient to divide the respiratory tract into three regions. The passages in the head can be referred to collectively as the naso-oro-pharyngo-laryngeal (NOPL) region. The "head region" of the respiratory tract will also be used to refer to this zone. Beginning with the trachea and proceeding through many generations of bifurcation are the conducting airways known collectively as the tracheobronchial (TB) region. Gas exchange occurs in the most distal portions of the lung known as the pulmonary (P) or alveolar region.

Aqueous particles emitted from the respiratory tract span a vast range of sizes, with diameters varying from less than 1 μm to more than 1 mm. Even this three-order-of-magnitude range of diameters corresponds to a factor of 1 billion (10^9) difference in volume or mass. Dynamic behavior varies markedly for airborne particles across this size range. At the smaller end, particles can remain airborne for long periods (hours) and, except when very close to surfaces, their movement is mainly associated with the prevailing motion of the air in which they are suspended. At the upper end of the size range, the drops behave ballistically, with motion dominated by their initial momentum and attenuated by air resistance. Milton[6] describes four particle size categories, incorporating information about respiratory tract deposition into the classification. The respirable particles are smaller than 5 μm in diameter. They can reach the pulmonary region of the respiratory tract and deposit there. At the other extreme are ballistic drops, larger than about 100 μm in diameter, which are not substantially inhaled. The intermediate size categories are termed thoracic (≤ 10-15 μm, capable of entering the TB region and depositing there), and inhalable (≤ 100 μm).

Pöhlker et al.[7] have also provided a very carefully described set of terms for the condensed phase emissions from the respiratory tract relevant to infectious disease transmission. For this paper, I'll use language that reflects a hybrid of the terms from Pöhlker et al. and from Milton. *Small particles* will refer to those with diameters less than 5 μm. *Large particles* will be those with diameters in the range 5-100 μm (or 5-50 μm in some cases). Small particles are respirable; large particles are inhalable. *Ballistic drops* (or simply *drops*) are emissions larger than 100 μm in diameter.

All manner of activities can influence the airborne emissions of respiratory particles and ballistic drops. For SARS-CoV-2, much of the transmission occurs from individuals who are asymptomatic.[8] Consequently, even the quotidian activities of quiet breathing and talking by people who are not evidently ill should be considered as having the potential to initiate transmission. Historically, much attention has focused on emissions resulting from the respiratory symptoms of illness, such as coughing or sneezing. That focus would be misdirected for understanding the bulk of community transmission of SARS-CoV-2.

Several articles discuss the mechanisms of particle and drop production in different regions of the respiratory tract.[7,9,10] These mechanisms include the bursting of bronchiolar fluid films during quiescent breathing, closing and opening of folds in the vocal cords during talking and other vocalization activities, and shear-induced instability of airway lining fluid in the tracheobronchial region and the mouth.

An important feature of respiratory emissions is that the aqueous particles undergo evaporation, losing water, and consequently shrinking. The speed of evaporation is rapid for small particles and for the smaller portion of the large particle mode.[11] The extent of shrinkage depends on the ambient humidity and on the proportion of nonvolatile solutes in the emitted particles. Evidence suggests that the diameter of equilibrated particles after shrinkage is in the range 25% to 50% of the emitted particle diameter.[7,11,12] For larger large particles and for ballistic drops, the evaporation rate can be sufficiently slow to not strongly influence airborne behavior prior to deposition.[13]

In the classical view, there are three potential modes for the transmission of respiratory viral infectious agents.[14] One mode is *droplet spray and direct contact*, which occur at close range and either involves direct physical contact between infectious and susceptible persons or the direct transfer via ballistic drops of viral material. A second mode is *fomite* mediated, in which a surface becomes contaminated with virus-containing emissions, a susceptible person acquires the virus by hand contact with the surface, and then transfers the virus to susceptible tissues in the eyes, mouth, or nose. The third mode is termed *airborne* or *aerosol* transmission; it critically entails inhalation of the infectious agent contained in suspended particles. One source of confusion in the literature concerns the role of exposure via inhalation when the infectious and susceptible persons are in proximity. Some have conflated transmission in proximity with the predominance of the droplet spray and direct contact route. However, others have clarified: exposures are elevated when in proximity not only via droplet spray but also by aerosol inhalation. Consequently, the identification of proximity as a factor in disease

transmission does not reliably confer understanding about the transmission mode. Aiming to improve clarity, Li[15] has separated the transmission scale from the transmission mode, indicating that, when in proximity, transmission can occur by any of the three modes of spray, inhalation, and touch, whereas at a distance (room scale), only inhalation and touch (via fomites) can occur.

For indoor transmission of a respiratory virus, the scale of transmission can vary in a manner that can be key to understanding and mitigating risk. The finest dimension is termed *short-range*,[10] *near field*,[7] *close contact*,[15] or *source proximate*.[16] The relevant separation scale, although not precisely defined, would typically be less than 2 m. Interpersonal distances for comfortable indoor conversation or seating separation at a meal would be examples of the short-range scale. A key feature of the short-range scale is both the potential for droplet spray transmission and for aerosol transmission at high efficiency in an exhaled plume.

A second indoor transmission scale applies to a room or to all the rooms that are well connected through open doorways or recirculating air-handling systems in a small building. For convenience, we will term transmission in these circumstances to be at *room scale*. Bond et al.[16] termed the processes operating on this scale as *confinement effects*. Other authors have termed this scale *long range*[10] or *distant*.[15] Those latter terms are avoided here because there is a potential concern about transmission over scales much larger than a room, and these would be more properly termed as long range.

This third indoor transmission scale applies when transport occurs over larger dimensions within a single building or even from one building to another. This larger scale has not been prominently evident in SARS-CoV-2 transmission, although there are examples of transmission seeming to have occurred between different dwelling units in an apartment building.[17] Transmission from one dwelling to another via open windows was investigated in Hong Kong apartment buildings for SARS.[18]

Indoor air motion and ventilation or air-change rates can influence the risk of transmission. Air motion is characterized by the velocity field, the time-dependent pattern of spatially varying air speeds and directions. Information on indoor velocity fields is limited, especially for circumstances that might be important for community spread of respiratory viruses. Available evidence about indoor air speeds indicates that a median speed of ~ 10 cm/s might be typical with some common conditions producing speeds as low as 1 cm/s or as high as 1 m/s.[19-21] *Ventilation rate* as used here will represent the supply of outdoor air to an indoor space. A common unit of measure for highly occupied spaces is volume flow rate per time per occupant, such as liters per second per person (L/s per person). Typical values specified in guidelines and standards are in the range 5-10 L/s per person. A poorly ventilated space might have a ventilation rate of < 3 L/s per person whereas a highly ventilated space might have a ventilation rate > 25 L/s per person. An indicator of ventilation rate is the increment of CO_2 indoors above the outdoor concentration. Persily and de Jonge[22] reviewed the evidence regarding carbon dioxide generation rates for building occupants, reporting central tendency values in the range 0.0025 L/s per person (18 g/h per person) for a child's bedroom to 0.0055 L/s per person (39

g/h per person) for a lobby. Using 21 g/h per person (0.0030 L/s per person) for a classroom of pupils in the age range 5-8 years, outdoor air ventilation rates of 3, 10, and 25 L/s per occupant would correspond to steady-state increments in indoor CO_2 level of 1070, 320, and 130 ppm, respectively (assuming P = 1 atm, T = 293 K). For residences, outdoor air ventilation is commonly reported in terms of the *air-change rate*, which is the outdoor air ventilation rate normalized by the indoor volume. A typical value for residential air-change rates is 0.5 h^{-1}. Residential air-change rates commonly vary across about two orders of magnitude, 0.05-4 h^{-1}.[23]

In mechanistic investigations of infectious disease transmission, it would be useful to know the quantity of virus needed to initiate a new infection. That information is generally not accessible, however. Some clues may be available from laboratory studies such as the tissue culture infective dose, or the dose needed to initiate a reaction in a laboratory animal. Quantitative modeling of disease transmission often utilizes the concept of *infectious quanta*. The probability of infection is related to the number of infectious quanta inhaled according to the expression $P = 1\text{-}e^{-q}$, so that if one quantum is inhaled, the likelihood of a new infection is $1\text{-}e^{-1} = 63\%$. Examples are available for applying this concept to the case of SARS-CoV-2.[24,25]

When considering potential pathways of infection, it is important to recognize that the infectious dose may be related to the receptor target. In other words, the quantity of virus necessary to initiate infection might be different if the virus deposits in the pulmonary region of the respiratory tract versus on the mucus membranes of the nose or mouth. To address such ideas conceptually, Milton[26] introduced the concept of disease isotropy. An isotropic infection is one that would be "transmitted with equal effectiveness and virulence by all routes, whether aerosol, large droplet, or direct contact …." Milton identified smallpox as an anisotropic infection, "most effectively and virulently transmitted by fine particle aerosols." Influenza is also classified as anisotropic, "with aerosolized virus infectious at lower doses and more likely to result in 'typical influenza-like disease' (fever plus cough) than intranasal inoculation."[27] Whether Covid-19 is similarly anisotropic isn't yet known.

A substantial proportion of SARS-CoV-2 transmission is believed to occur in superspreading events.[28-30] In such events, a sizeable number of new infections occurs, commonly from a single source. The circumstances of a gathering can certainly contribute to superspreading events, as has been documented in the case of a choir practice.[25] Other evidence points to "supershedding" as a possible factor contributing to superspreading. For example, Bueno de Mesquita et al.[31] reported considerable variability among individuals in the rate of shedding of the influenza virus. Asadi et al.[32] found that some individuals were particularly high emitters of respiratory particles during speech. The concept of superspreaders is well established in the case of other respiratory viral infections, including the common cold caused by coxsackievirus A21,[33] measles,[34] SARS,[35] and influenza.[36]

Outbreak Investigation Results

Case reports from outbreaks of Covid-19 provide important clues about how SARS-CoV-2 is transmitted. The most extensive such study assessed 318 outbreaks in China with three or more cases each.[4] The authors found that "all identified outbreaks of three or more cases

occurred in indoor environments." The authors also reported that "among our 7324 identified cases in China with sufficient descriptions, only one outdoor outbreak involving two cases occurred." All these cases occurred during the first winter of the pandemic, January-February 2020. Among the 318 outbreaks, only three involved 10 or more cases. Homes and transport environments were the dominant location category. The study relied on municipal case report investigations, which varied in quality, and which tended to lack some of the important information needed to fully understand transmission pathways.

More detailed investigations have been conducted of several specific outbreaks, including in a call center,[37] in fitness centers,[38] at a restaurant,[39] and at an apartment building[17] in South Korea; in a nursing home in the Netherlands;[40] in a choir rehearsal in USA;[25] in a restaurant in China;[41] on board the Diamond Princess cruise ship;[42] and in a courtroom in Switzerland.[43]

Madewell et al.[44] conducted a systematic literature review and meta-analysis of publications reporting household transmission of SARS-CoV-2. They identified 54 relevant studies aggregately reporting almost 78,000 household secondary transmissions. The estimated overall household attack rate was 17%, was higher among spouses (38%) than other family contacts (18%) and was higher for adult contacts (28%) than for child contacts (17%). The authors identify as potentially relevant factors that households are "closed spaces, where family members may crowd and be in close contact with conversation. There may be reduced use of personal protective equipment relative to other settings." Potentially important information such as the degree of crowding and the ventilation conditions of the dwellings was not available.

Bulfone et al.[3] reviewed the published evidence available through 12 August 2020 regarding outdoor transmission of SARS-CoV-2. They concluded that "existing evidence supports the wide-held belief that the risk of SARS-CoV-2 transmission is lower outdoors but there are significant gaps in our understanding of specific pathways."

In aggregate, these studies support a view that indoor environments are important in the transmission of SARS-CoV-2. However, they do not provide clear evidence about the relative importance of the different modes of transmission.

It is also important to recognize that the outbreak investigations cumulatively represent a very small fraction of SARS-CoV-2 infections. The proportion is almost certainly less than 10^{-3} (< 0.1%). The conditions that allow outbreaks to be assessed are not necessarily statistically representative of all conditions in which transmission occurs. The metaphor of the tip of the iceberg comes to mind, but in the case of an iceberg, the visible portion above water is about 10% of the total. The other relevant metaphor is lamppost science, with the caution that we should not only be looking where the light is good.[45] The main points are to accept what clues can be gleaned from this evidence but to recognize the limitations and to resist the temptation to generalize from that which may be particular.

Particle and Drop Dynamic Behavior

The SARS-CoV-2 virion is approximately 0.1 μm in diameter. In the environment it doesn't tend to exist as a free entity. Rather, when emitted from the respiratory tract, it is associated with the aqueous suspensions of mucus and saliva from the respiratory tract. The evaporation of water causes the emitted particles to shrink to some extent, with the ultimate degree of shrinkage limited by the nonvolatile substances in the emitted particles.

The particles and drops emitted from the respiratory tract span a diameter range of more than three orders of magnitude, from less than 1 μm to more than 1 mm. It is worth repeating that a 1 mm drop contains a billion times more material than a 1 μm particle. However, there are orders of magnitude more small particles emitted than ballistic drops, so the contribution of small particles to total emitted material can be substantial.

The size of particles and drops containing potentially infectious virions is of central importance to the disease transmission process. Size also is related to where in the respiratory tract the emissions originate and that, in turn, is associated with the viral load. In general, emissions that originate from deep in the respiratory tract tend to be small particles, whereas large particles and especially ballistic drops are generated in the NOPL region. The environmental transport, dynamic behavior, and fate of airborne particles and drops is strongly influenced by size. Whether and where virion-containing particles and ballistic drops deposit on the exterior surface of or in the respiratory tract of a susceptible person is also highly dependent on size.

The literature on respiratory viral disease transmission is permeated with an error regarding particle size that has profound significance. As one illustrative example, Seto[46] wrote, "it is apparent now that only small particles of < 5 μm … will result in airborne transmission potentially over longer distances because these particles can remain suspended in the air for prolonged periods. Most lung infections result in droplet transmission whereby the larger particles from the cough are transmitted for < 1 m and do not remain suspended in the air." This statement contains some truth, in that large (ballistic) drops do not travel far. But it is seriously wrong in suggesting that the particles larger than 5 μm cannot travel beyond 1 m distance. In describing the history of this widespread misunderstanding, Randall et al.[47] emphasize that the pattern of deposition in the respiratory tract became inappropriately conflated with the airborne travel distance. The facts are these. First, 5 μm is an appropriate estimate of the upper bound size for particles that penetrate to and deposit in the pulmonary region of the respiratory tract.[48] Second, the minimum diameter of a ballistic drop that is likely to travel no further than 1 m from the source is about 100 μm.[5]

It is difficult to overstate the importance of this error. Particles in the size range 5-100 μm do not fall to the floor within a meter of the emission source, but rather can travel room-scale distances. Furthermore, these particles can be inhaled and deposit in the respiratory tract. Because emissions in approximate diameter range of 5-100 μm can be substantial, there is a great risk of error in understanding the potential for inhalation exposure to respiratory viruses by mistakenly believing that all particles larger than 5 μm fall within 1 m of the source.

To elaborate, consider the information presented in Figure 1. The data points and connecting line segments display the settling velocity of water drops and particles when the two main forces — gravity and drag — are balanced.[49] The three horizontal lines, marked at 1, 10, and 100 cm/s respectively, represent lower bound, central tendency, and upper bound estimates for indoor air speed. The vertical lines divide the particle or drop size into zones, as follows. For particles smaller than about 20 µm in diameter, motion indoors is more strongly controlled by indoor air flow than by gravitational settling under all common indoor conditions. Conversely, for drops larger than about 300 µm in diameter, gravitational settling dominates, independent of the prevailing indoor air motion. In the intermediate region, the movement of particles and drops reflects a balance between the influence of indoor air currents carrying suspended particles and the influence of gravity pulling the particles downward. For indoor air speeds that are relatively still, 1-10 cm/s, particles in the range of 20-60 µm diameter can experience motion that is about equally balanced between the effects of air currents and gravitational settling. For indoor air speeds that are moderately high, 10-100 cm/s, the corresponding size range for these balanced flow conditions is approximately 60-300 µm.

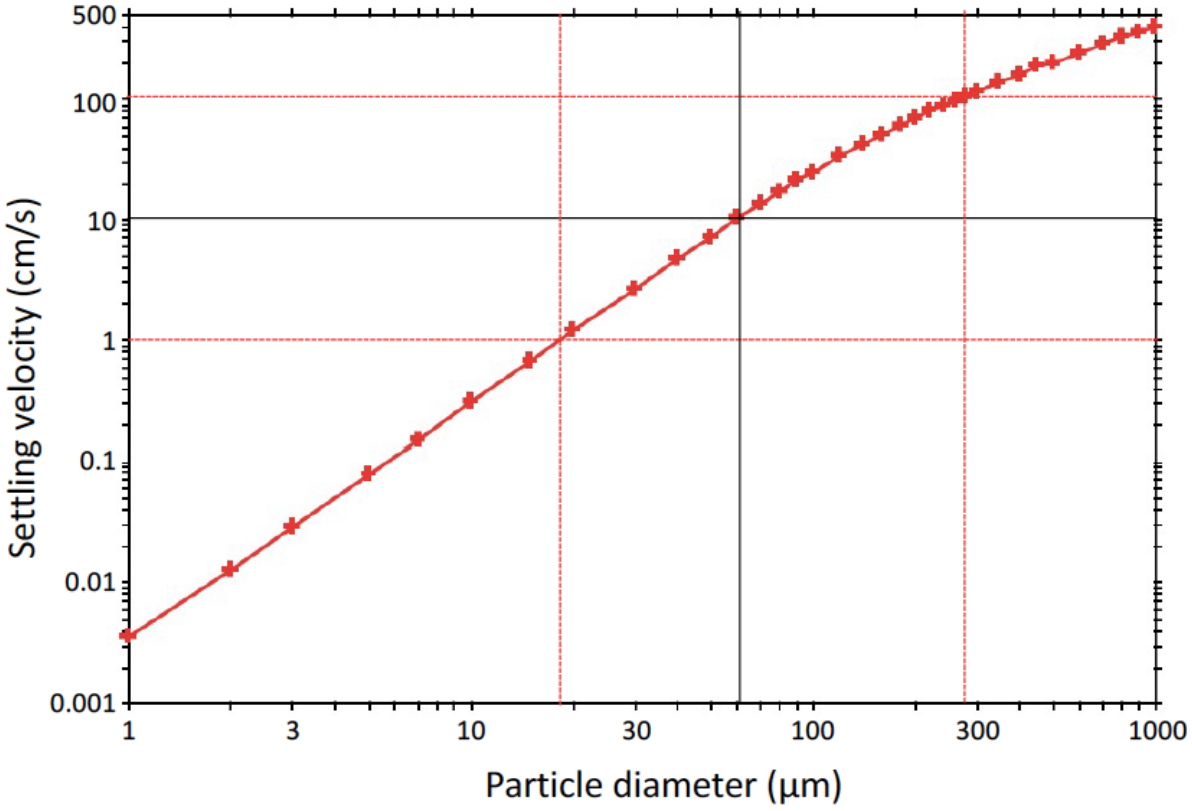

Figure 1. The data points and upward sloping line represent the terminal settling velocities of water droplets as a function of particle and drop diameter.[49] The three horizontal lines indicate approximately the minimum, central tendency, and maximum indoor airspeeds commonly encountered in occupied spaces.

A common distance for a drop to settle from the mouth or nose of an infectious person to an upward surface is on the order of 1 m. That distance might be as high as about 1.5 m from a standing person to the floor. It might be less than about 0.5 m from a seated person to a table. In a magnitude sense, the noteworthy comparison would be the competition for an airborne particle between settling 1 m versus being transported by air currents a horizontal distance of 1 m. The assessment is a magnitude comparison in part because the relevant fall distance is variable, as noted above, and because of variability in both the speed and direction of motion of indoor air currents.

Regarding the range of expired drops and particles, the evidence presented in Figure 1 can be summarized as follows. Drops larger than about 300 µm will fall within 1 m of the source largely independent of the indoor air flow conditions. If the indoor air motion is moderately strong (i.e., with speeds of 10-100 cm/s), then some portion of the particles in the size range 60-300 µm will also fall to an upward surface within 1 m of the source, with the proportion being progressively smaller as particle size decreases. Particles smaller than 60 µm will remain suspended beyond 1 m from the source to a substantial extent under these conditions. For weak indoor airflow conditions (speeds of 1-10 cm/s), large particles can fall substantially to upward surfaces, with the possibility that the proportion that settles is greater than the proportion that travels beyond 1 m down to particle diameters of approximately 20 µm. However, under any airflow conditions, most of the emitted particles that are smaller than 20 µm in diameter will remain suspended for enough time to travel well beyond 1 m from the emission source.

In addition to background air motion and gravitational settling, the motion of respiratory drops can be strongly influenced by the impetus provided with their emission. Bourouiba investigated the fluid mechanics of exhalations, sneezes, and coughs.[50] She reported that "given various combinations of an individual patient's physiology and environmental conditions, such as humidity and temperature, the gas cloud and its payload of pathogen bearing droplets of all sizes can travel 23 to 27 feet (7-8 m)." Xie et al. likewise reported that "expelled large droplets are carried more than 6 m away by exhaled air at a velocity of 50 m/s (sneezing), more than 2 m away at a velocity of 10 m/s (coughing) and less than 1 m away at a velocity of 1 m/s (breathing)." [13] The travel distance of emissions is substantially reduced if the mouth and nose are covered.[51-53]

A noteworthy feature of respiratory emissions is that the particles and drops can shrink owing to evaporative loss of water. Upon leaving the respiratory tract, aqueous particles emitted indoors encounter an environment with lower temperature and lower water vapor content. Since water is the dominant component of the emitted particles, its evaporation can be sufficient to cause particle size to shrink. The shrinkage phenomenon has several complex aspects, including heat and mass transfer kinetics and the influence of dissolved solutes and suspended mucins. In brief, the key elements are these: (a) small particles evaporate so rapidly that they reach their equilibrium state essentially instantaneously; (b) large drops may fall to the floor before much evaporation occurs; and (c) the nonvolatile impurities are sufficient in abundance so that shrinkage is limited to a diameter decrease typically in the range of about 2-

4×. This last point means that what was classically referred to as droplet nuclei,[54] i.e., the persistent, airborne dried residue of emitted droplets with a maximum size of about 5 µm, would have been emitted with a diameter of less than 20 µm. Conversely, drops emitted at 100 µm diameter or larger would not shrink to become droplet nuclei as classically understood. Indeed, these larger drops will deposit by settling more rapidly than they can reach their equilibrium size by means of evaporation. Being limited to less than about a factor of 4 effect on diameter, the role of evaporation is much less important for airborne particle dynamics than the variability in the sizes of emitted particles and drops, whose diameters can span a factor of 1000 or more.

The state of knowledge about the chemical composition of emitted respiratory particles and drops is surprisingly incomplete. Nicas et al.[11] modeled the emissions as a combination of normal saline with glycoproteins and estimated that a fully desiccated particle would decrease in diameter to 44% of the aqueous emission. Liu et al.[55] assumed a model solution of 150 mM of NaCl in predicting a dried droplet nuclei size of 32% of the original diameter. Walker et al.[56] concluded that an emitted drop of 100 µm would shrink to an equilibrium size at 50% relative humidity of 28 µm for artificial saliva and 30.4 µm for artificial deep lung fluid, respectively. Investigating the seasonality of influenza infections, Marr et al.[57] proposed a novel physicochemical interpretation in which the evaporation of respiratory emissions influenced droplet physics and chemistry in such a way as to modulate virus survival and transmission. Recent investigations of the evaporation of respiratory droplets include a detailed modeling study[58] and single-particle levitation experiments.[59]

A final primary consideration for the airborne behavior of respiratory emissions is inertial drift. Airborne particles tend to follow accelerating, decelerating or bending streamlines to the extent that the drag exerted on them by air is sufficient to overcome their momentum's tendency to continue moving at a constant speed in a straight line. Inertia is relatively weak for ordinary indoor airflows and small particles; however, for large particles and especially for ballistic drops inertia becomes increasingly important. A characteristic measure of the strength of inertia is the *stopping distance*, a calculated result indicating how far a particle would travel before coming to rest if injected into stagnant air at an initial velocity U_o. In this calculation, the only force opposing particle motion is drag. For the purposes of illustration here, we will assume that drag is described by Stokes law, for which it is necessary that the particle Reynolds number is much smaller than 1. (For ballistic drops moving at high speeds, this assumption doesn't hold. The actual drag would be higher and the stopping distance smaller than predicted by equation 1.)

Equation (1) presents the stopping distance, S, for a particle of diameter, d_p, and density, ρ_p, injected with initial velocity, U_o, into stagnant air of viscosity, μ. Table 1 summarizes the stopping distance for water droplets across a range of particle diameters and initial velocities.

$$S = \frac{\rho_p \, d_p^2 \, U_o}{18 \, \mu} \qquad (1)$$

Several important qualitative features are evident in Table 1. First, inertial drift is not important for transport of small particles. Second, inertial drift is generally a short-range phenomenon, operating on scales of a few cm or less for inhalable particles at ordinary indoor air speeds. Third, inertial drift can be meaningful for transport close to surfaces for large particles (or, by inference, for ballistic drops), especially at higher air speeds.

Table 1. Stopping distances (*S*) for particles and drops of different sizes as a function of initial velocity. [a]

	d_p = 1 µm	d_p = 10 µm	d_p = 100 µm
U_o = 1 cm/s	3×10^{-6} cm	3×10^{-4} cm	0.03 cm
U_o = 10 cm/s	3×10^{-5} cm	0.003 cm	0.31 cm
U_o = 1 m/s	3×10^{-4} cm	0.03 cm	3 cm [b]

[a] Computed using equation (1) in which the drag force is assumed to follow Stokes law. Air viscosity is $\mu = 1.8 \times 10^{-4}$ g cm^{-1} s^{-1}. Particle density is $\rho_p = 1.0$ g cm^{-3}. The application of equation (1) in the presented form assumes that no slip correction is required for drag predicted by Stokes law. In turn, that necessitates that the particle diameter be much larger than the mean-free-path of gas molecules, which is 0.066 µm at T = 293 K, P = 1 atm.
[b] At diameter d_p = 100 µm and initial speed U_o = 1 m/s, the particle Reynolds number is 6.7. The drag is greater than predicted by Stokes law and consequently the stopping distance would be somewhat less than 3 cm.

Respiratory Emissions

Respiratory particle emissions have been investigated for different types of respiratory activities: breathing, talking (and other vocalization activities), coughing and sneezing. This research has generally been concerned with application to infectious disease transmission, including not only viral diseases but also bacterial diseases such as tuberculosis[60] and whooping cough.[61] Earlier studies characterizing emissions emphasized coughing and sneezing. More recent investigations have emphasized breathing and vocalization.

For each type of important respiratory activity, one would like to know the pattern of emissions in terms of the time-rate of emission of size-resolved numbers of particles and drops. One would like to have this information in relation to influencing variables, such as the pattern of breathing or the intensity of speech. One would especially want to know how the infectious agents are distributed among the respiratory emissions. And one would ideally have such information not only across populations of individuals but also longitudinally over time as the period of infectiousness progresses. The pattern of how an infectious agent is distributed across the size of respiratory emissions almost certainly varies from one infectious agent to another. And, depending on how the infectious agent reproduces in and is shed from different regions of the respiratory tract, that distribution may even vary with circumstances (e.g., with the time course of infectiousness) for a given illness. In combination, these circumstances are scientifically and technologically challenging. Available evidence provides important clues; however, a complete picture is not yet accessible of the aspects of respiratory emissions that are pertinent for understanding respiratory disease transmission.

Several cautions should be recognized when considering the available evidence. First, many published studies only report a portion of the emitted size range of particles and drops. The

older literature tends to rely on manual sampling and analysis technologies that were effective in capturing the larger emissions but not so reliable in determining size segregated smaller particles. Conversely, many recent studies rely on automated instruments for measuring airborne particle size distributions that are unable to characterize ballistic drops.

Second, a large majority of empirical studies have characterized the emissions without regard to their viral (or bacterial) content. A common approach used to estimate size-resolved virion emissions combines size resolved particle and drop emissions with information about the viral load of respiratory tract fluids. This approach is vulnerable to large errors if the portion of the respiratory tract from which particles are generated has a different abundance of virions than the sampled respiratory fluids. This point will be addressed in more detail below.

Pöhlker et al.[7] recently provided a thorough review and assessment of particle and drop emissions from the respiratory tract in the context of infectious disease transmission. Two major concerns about emission patterns are effectively addressed in that report. First, the authors consider a full range of particle and drop sizes, from less than 0.1 µm diameter (smaller than the SARS-CoV-2 virion) to drops much larger than 100 µm. Second, they interpret the available evidence in a way that associates the emitted particles and drops with sites of origin in the respiratory tract. This latter point is missed in much of the literature and is pivotal for ultimately associating respiratory emissions with infectivity.

Pöhlker et al.[7] highlight three primary mechanisms leading to particle generation in four regions of the respiratory tract. One mechanism is bronchiolar fluid film bursting, which is believed to be the primary means of particle generation in the pulmonary region.[62] A similar process may occur in the folds of the vocal cords as they move with vocalization activities. A second mechanism is associated with high-speed airflows that cause strong interfacial shear and can produce particles and drops through fragmentation of stretched mucus or saliva. This second mechanism could occur in the trachea and in the upper respiratory tract (oral and nasal cavities), and would be especially pronounced for vigorous expiratory actions, such as coughing or sneezing. A third mechanism involves the motion of mouth, lips, and tongue through which drops are formed mechanically from saliva. The four associated regions for particle generation are the small bronchioles in the distal airways, the trachea and main bronchi, the larynx and associated vocal cords, and the oral cavity.

Consolidating and distilling the available empirical evidence, Pöhlker et al.[7] present parameters of lognormal distributions that are intended to represent the central tendency of particle and drop emission for three regions of the respiratory tract and for three different respiratory activities. The three regions are the bronchiolar (B), larynx and trachea (LT), and the oral cavity (O). The respiratory activities characterized are breathing, speaking, and coughing.

Table 2 presents a further quantitative interpretation of the work of Pöhlker et al., in which their reported lognormal representations are integrated over size sections that correspond to small particles (0.1-5 µm), large particles (5-100 µm), and ballistic drops (100 µm – 1 mm).

Results are presented separately for the three sites of origin (B, LT, and O) and for the three reported respiratory actions.

Table 2. Particle and drop emission rates from the respiratory tract during breathing, talking, and coughing. [a]

	Breathing		**Speaking**		**Coughing**	
	E_N (h^{-1})	E_V ($\mu m^3\ h^{-1}$)	E_N (h^{-1})	E_V ($\mu m^3\ h^{-1}$)	E_N ($cough^{-1}$)	E_V (μm^3/cough)
B modes						
Small PM (0.1-5 μm)	8.2×10^5	3.1×10^4	2.0×10^6	6.4×10^4	1.2×10^5	3.6×10^3
Large PM (5-100 μm)	1.4	190	3.5	360	< 1	21
LT mode						
Small PM (0.1-5 μm)	—	—	8.2×10^5	2.0×10^6	4.5×10^3	1.2×10^4
Large PM (5-100 μm)	—	—	4.8×10^3	7.2×10^5	46	8.3×10^3
O modes						
Small PM (0.1-5 μm)	—	—	2.5×10^3	7.7×10^4	190	6.0×10^3
Large PM (5-100 μm)	—	—	6.0×10^4	8.0×10^9	1.6×10^3	4.9×10^7
Drops (100 μm – 1 mm)	—	—	4.2×10^4	3.0×10^{11}	370	4.7×10^9

[a] Based on Pöhlker et al.[7] PM = particulate matter (particles); B modes are bronchiolar; LT mode is larynx-trachea; O modes are oral. Volume flow rates and exhaled volume are taken as 360 L/h for breathing, 700 L/h for speaking, and 1.5 L for a cough, respectively. Lognormal parameters of particle and drop size distributions, as reported in Table VI of Pöhlker et al., have been integrated over the indicated size ranges of small and large particles and drops to obtain the results reported here. The lognormal parameter values are reproduced here for completeness and transparency. For breathing, there are two B modes (B1, B2) with respective values of A_i = 7.7 and 1.1 cm^{-3}, D_i = 0.07 and 0.30 μm, and σ_i = 0.90 and 0.90. For speaking, there are two B modes (B1, B2), one LT mode, and two O modes (O1, O2). The respective parameters for these modes are as follows: A_i = 9.8, 1.4, 1.7, 0.03, 0.17 cm^{-3}; D_i = 0.07, 0.3, 1, 10, 96 μm; and σ_I = 0.90, 0.90, 0.90, 0.98, 0.97. Likewise, for coughing, there are the same five modes with parameter values as follows: A_i = 262, 37, 4, 1.4, 0.5 cm^{-3}; D_i = 0.07, 0.3, 1, 11, 128 μm; and σ_I = 0.90, 0.90, 0.98, 0.95, 1.0. See Pöhlker et al.[7] for definitions of the parameters A_i, D_i, and σ_i.

A few details of the analysis supporting Table 2 should be highlighted. The minimum particle size in the calculation was selected as 0.1 μm because that is the approximate size of the SARS-CoV-2 virion. A smaller particle could not contain the virus. The results are reported in emission rates or as emission factors, both in terms of count (number or particles or drops per time, for example) and in terms of volume of the condensed-phase respiratory emissions. The primary reporting by Pöhlker et al. is in terms of concentration in undiluted exhalations; I have used exhaled volumes as reported by Pöhlker et al. for breathing (360 L/h), speaking (700 L/h), and for a single cough (1.5 L) to obtain the emission rates and emission factors reported in Table 2. The assumed flow rate associated with breathing corresponds to a sedentary or passive condition. The speaking air flow is based on an estimated rate of 120 words per minute. The frequency of coughing is so highly variable that it seems most appropriate to express emissions on a per-cough basis, rather than per time.

Sneezing is another type of respiratory emission event that can contribute to infectious disease transmission. Particle and drop emissions from sneezing have been characterized experimentally by Duguid[63] and Han et al.[64] In their review, Pöhlker et al. reported that the Han et al. data were presented in such a way that "no mode-specific particle number and volume concentrations could be retrieved for the further steps of our analysis."

Some important qualitative features emerge from Table 2. This discussion will emphasize particle and drop volume emissions, as viral content seems more likely to vary with that indicator rather than with emissions by number. Emissions from the deep lung (B modes) are primarily in the small particle size range. The estimate for speaking is of similar magnitude but somewhat higher than for quiescent breathing, mainly because the exhalation flow rate for speaking is assumed to be higher (by about 2×). Considering all small-particle emissions for speaking, the LT mode is the largest, more than an order of magnitude bigger than the B and O modes. Large particle emissions from the oral mode appear potentially important. Particles in the diameter range 5-100 µm are emitted with speaking at a volumetric rate that is several orders of magnitude higher than are small-particle emissions. This evidence reinforces the importance of the common error in the literature, assuming that particles larger than 5 µm all deposit within a few meters of the emission source. These facts are all potentially important aspects for transmission of respiratory diseases: that these emissions are so high during speech, that the particles can travel room-scale distances, and that they can be inhaled and deposit within the (upper portion) of the respiratory tract. The emitted volume associated with ballistic drops is even larger, but these emissions generally do not travel more than a few m from the source and also tend not to be inhaled, so additional steps in the source-to-receptor transfer process would be needed to complete the chain of transmission.

Evidence from the spread of Covid-19 suggests that a considerable proportion of the transmission occurs without symptoms, i.e., without illness induced sneezing or coughing.[8,65] Even for influenza, Lindsley et al.[66] suggested that emissions from illness symptoms may not dominate. “Because individuals breathe much more often than they cough, … breathing may generate more airborne infectious material than coughing over time.”

Efforts to model the transmission of SARS-CoV-2 using bottom-up approaches have combined emission information of the type reported in Table 2 with viral load data.[67] Viral load data reporting the number of viral RNA copies per volume of respiratory fluid have been reported for sputum samples,[68,69] for “posterior oropharyngeal saliva,”[70] and from swabbing, reported as “throat samples.”[69] Reviewing such evidence, Buonanno et al.[67] concluded that “the concentrations of viral load in the mouth can reach values of 10^9 RNA copies mL^{-1} and occasionally up to 10^{11} RNA copies mL^{-1} during the course of the [Covid-19] disease.” If one assumes that 10^9 RNA copies mL^{-1} (= 10^{-3} RNA copies μm^{-3}) applies to fluid throughout the respiratory tract, and if one also assumes that the particle and drop emissions rates in Table 2 apply, then the emissions rate from speaking would be 2100 RNA copies per hour in the small particle size range (< 5 µm), 8 million RNA copies per hour in the large particle size range (5-100 µm), and 300 million RNA copies per hour in the drop mode (100 µm – 1 mm). The significance of these numbers regarding the transmission of a SARS-CoV-2 infection would need to consider the fate of the particles and drops after emission, the consequential exposures, and the resulting doses and susceptibility of specific sites for a receptor.

Information available about the spatial distribution of viral load in the respiratory tract is sparse. Sputum samples might reasonably represent the fluids lining the trachea and therefore correspond reasonably well to particles emitted in the LT mode. It is an open question to what extent that swabs sampling from the upper respiratory tract reflect the particles and drops emitted from the mouth during speaking or coughing. For the pulmonary region, sampling technologies are available to collect samples via bronchoalveolar lavage.[71] However, this is a highly invasive procedure that would not be applied without medical necessity. That restriction would likely make inaccessible the direct determination of viral load in the respiratory fluid of the pulmonary tract for asymptomatic SARS-CoV-2 infections.

A focus on viral shedding from the upper respiratory tract may be appropriate. Gandhi et al.[8] remarked on the "high level of SARS-CoV-2 shedding in the upper respiratory tract," noting that "live coronavirus clearly sheds at high concentrations from the nasal cavity even before symptom development." Hou et al.[72] reported "a striking gradient of SARS-CoV-2 infection in proximal (high) versus distal (low) pulmonary epithelial cultures. … These findings highlight the nasal susceptibility to SARS-CoV-2 with likely subsequent aspiration-mediated virus seeding to the lung in SARS-CoV-2 pathogenesis."

An important feature of the emissions evidence is the large variability. Regarding respiratory particles and drops, the information in Table 2 is intended to reflect average conditions. Emissions from speech increase strongly with loudness. "Furthermore, a small fraction of individuals behaves as 'speech superemitters,' consistently releasing an order of magnitude more particles than their peers."[32] Viral load data indicate even greater variability, both across the population of subjects sampled and with time for any individual.[68-70] He et al.[65] studied the time course of viral shedding in 94 patients with Covid-19. They "inferred that infectiousness started from 12.3 days … before symptom onset and peaked at symptom onset." The large variability in viral load and in respiratory emissions would contribute greatly to an uneven pattern of transmission risk.

Particle Deposition in the Respiratory Tract

Among the various factors influencing airborne transmission of respiratory diseases, deposition of inhaled particles in the respiratory tract may be the best understood. This topic has broad relevance and has been studied in many contexts, including radiological protection, air pollution toxicology, industrial hygiene, and drug delivery. The phenomenon is affected by a combination of the morphometry of the respiratory tract, the physiology of respiration, the fluid mechanics of breathing airflow, and the physics of airborne particle motion.

For ordinary breathing conditions, it is entirely reasonable to assume that an inhaled particle will deposit if it strikes the lining of the respiratory tract. For particles in the size range of concern, from 0.1 μm to 100 μm in diameter, the primary means of airborne motion are advective flow, gravitational sedimentation, and inertial drift. The smallest particles in this size range are also influenced by Brownian motion (diffusion).

In industrial hygiene, particles are broadly classified by size as *inhalable* (< 100 µm), *thoracic* (< ~ 10 µm), and *respirable* (< ~ 4 µm). See Figure 2. Inhalable particles can be brought into the respiratory tract during normal inhalation. Thoracic particles can penetrate past the head into the tracheobronchial tree. Respirable particles can penetrate to the alveolar or pulmonary region of the lung.

With respect to airborne disease transmission, three key conceptual points can be inferred from Figure 2. First, particles up to 100 µm in diameter can be brought into the respiratory tract through inhalation. Second, particles smaller than about 5 µm are respirable and therefore can penetrate to the alveolar region. Third, the different size categories are not sharply divided at their respective boundaries.

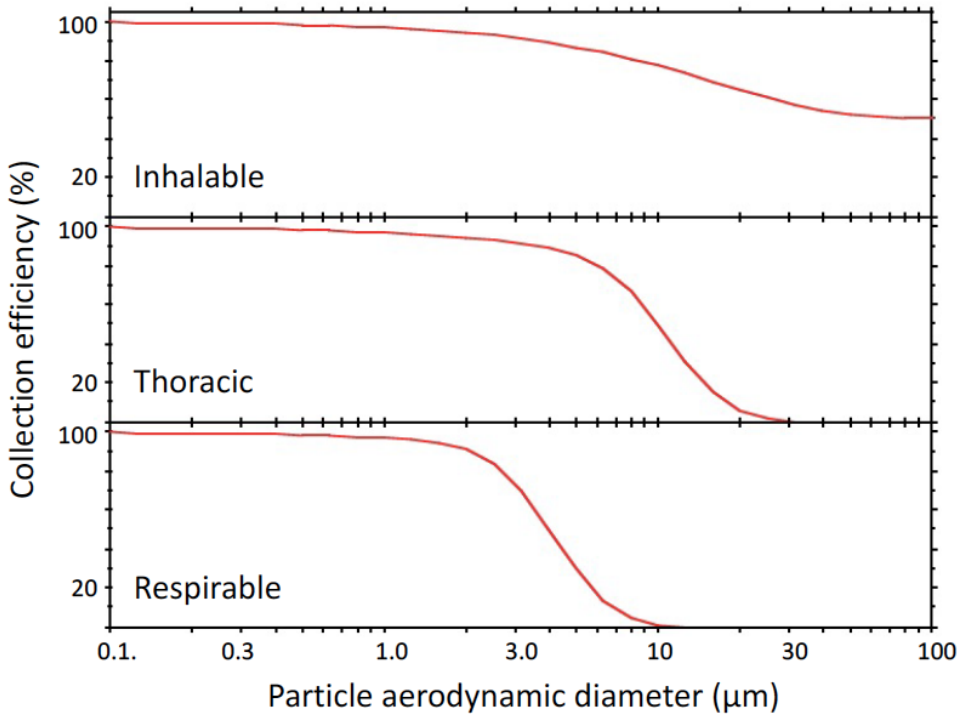

Figure 2. Collection efficiency of particle samplers as a function of diameter specified for instruments that capture inhalable (upper), thoracic (middle), and respirable (lower) size fractions of airborne particulate matter, as defined by the American Conference of Governmental Industrial Hygienists.[73]

For particles in the diameter range 0.1-10 µm, Figure 3 displays modeled overall deposition efficiency in the respiratory tract along with subdivided efficiencies for three different respiratory-tract zones: in the head or upper respiratory tract, in the tracheobronchial tree, and in the alveolar or pulmonary region. Overall deposition efficiency exhibits a minimum of about 13% for diameters in the range 0.3-0.5 µm. Smaller particles deposit more efficiently because of their stronger tendency to diffuse. Larger particles deposit more efficiently because they are more strongly influenced by inertial drift through the bending flow paths in the respiratory

tract, and because of the influence of gravitational settling if they reach the deep lung. Where virus-containing particles deposit in the respiratory tract is important in relation to the susceptibility of these different regions to the initiation of an infection.

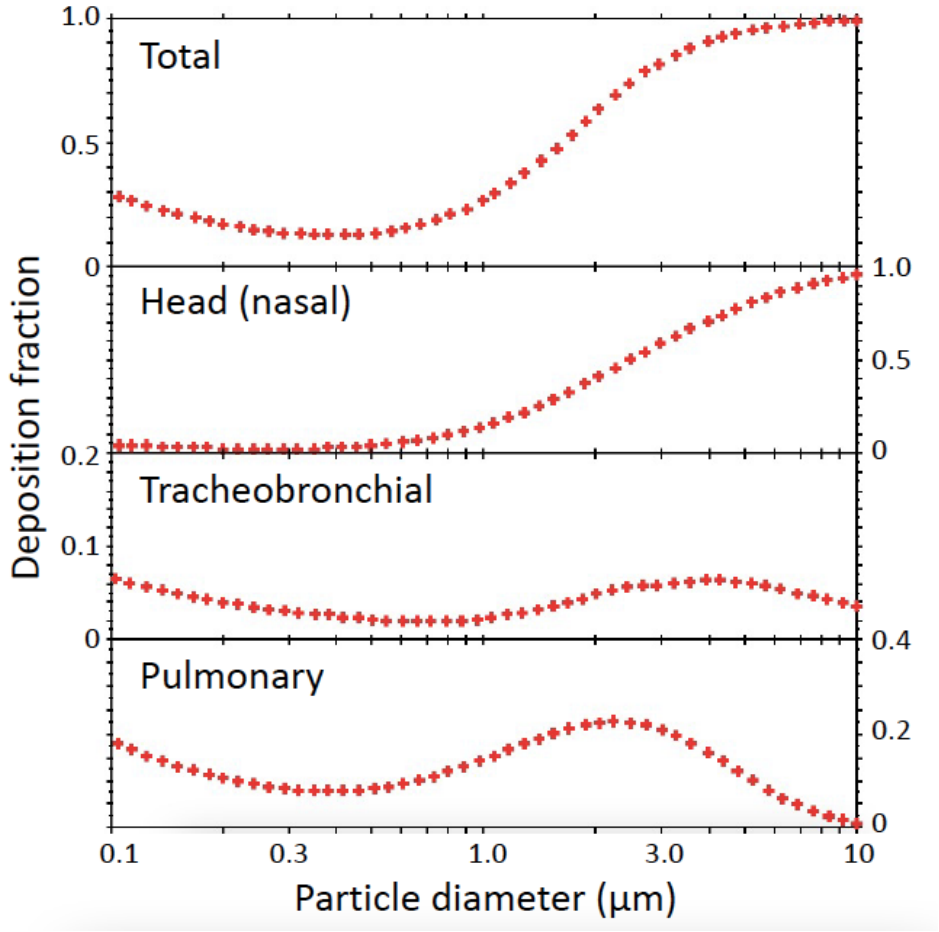

Figure 3. Deposition fraction as a function of particle size in the overall respiratory tract (upper), and in three different regions: in the head (2nd frame), in the tracheobronchial tree (3rd frame), and in the pulmonary region (bottom). For each frame, the normalization is based on the abundance of particles in air as it enters the respiratory tract. So, for example, for 10 µm particles, the low deposition in the pulmonary region occurs because such particles are deposited with high efficiency as air passes through the upper portion of the respiratory tract (the head) before reaching the pulmonary region. These results reflect predictions for a seated adult breathing through the nose, using a semiempirical model of the International Commission on Radiological Protection (ICRP) as reported by Hofmann.[48] Note that the vertical axes should be read from the left-hand scale labels for the top and 3rd frames, and from the right-hand scale labels for the 2nd and bottom frames.

There is a noteworthy complementarity between regional emissions and regional deposition of particles in the respiratory tract. Large particles primarily emitted from the head will mainly be

deposited in the head if inhaled. Small particles emitted from the pulmonary region have the potential to penetrate and deposit deep within the lungs of those subsequently exposed. If a viral infection is established regionally, with subsequent viral shedding from that region, the associated particles emitted from the infectious person can preferentially deposit in the same region of the respiratory tract of a susceptible individual. A part of this process is governed by size dependent penetration and deposition patterns in the respiratory tract. Specifically, any large particles that might be generated in the lower respiratory tract have a low probability of escaping because inertial drift and gravitational settling will tend to cause them to deposit as they traverse from the distal airways to the mouth or nose.[74]

The total rate at which airborne particles are deposited in the respiratory tract can be estimated as the product of three terms: the airborne concentration, the volumetric breathing rate (also known as the minute volume), and the deposition fraction. Because concentrations and deposition fractions are size dependent, accurate analysis requires that this product be computed for each (typically narrow) particle size interval separately and then summed to determine the total. Handbook values from exposure studies can be applied for the volumetric breathing rate. For example, the USEPA's Exposure Factors Handbook[75] recommends a mean inhalation rate of about 16 m^3 d^{-1} for adults, which corresponds to an average of 11 L/min. Values of about 5 L/min apply for sleep and sedentary/passive conditions, rising to about 12 L/min for light intensity activity and 25-30 L/min for moderate intensity. These values are somewhat age dependent and reflect average conditions for men and women combined.

Room-Scale Airborne Transmission

In outbreak investigations, evidence clearly points to indoor environments being much more important than outdoor settings for the transmission of SARS-CoV-2 infections. Among the classic pathways of exposure, a consensus also has emerged that fomites are not of primary importance. However, other key issues are not yet resolved. The relative importance of airborne transmission via inhalation versus droplet or contact-mediated transmission continues to be vigorously debated. Some part of the debate can be attributed to the misunderstanding regarding large particles (diameter range 5-100 µm), which are incorrectly believed by some to consistently deposit within a few m of the emission source. Even accounting for this misunderstanding, there remain important questions. How important is large particle inhalation compared with small particle inhalation? How important is inhalation near a source (within a few m) compared with room-scale transmission? Does the deposition of ballistic drops make a meaningful contribution to the spread of SARS-CoV-2 infections? These questions are important because the answers help guide the nonpharmaceutical public health interventions that are key to limiting the adverse consequences of the pandemic but also disruptive to normal life. This section explores what indoor aerosol science can contribute about understanding airborne transmission of SARS-CoV-2 at the room or small building scale. In the following section, issues related to transmission in proximity will be explored.

To frame the discussion, a few additional points should be made. First, some factors that affect transmission are highly variable. For these, the dominant portions of transmission may occur under conditions that are more favorable for spread, rather than under average conditions. So,

for example, in assessing SARS-CoV-2 transmission risk, one might reasonably emphasize circumstances in which ventilation rates are within common ranges, but lower than average. Second, community spread of an airborne viral infection would commonly be associated with spaces where people congregate and socially interact. The evidence summarized in Table 2 illustrates that emission rates are much higher during speaking than from quiet tidal breathing. Emissions increase with speech loudness.[32] Consequently, circumstances in which many people gather unmasked in crowded indoor environments and engage vigorously in speaking or other vocalization would be of particularly strong interest and concern.

Two key limitations in the state of knowledge regarding indoor aerosol science should also be acknowledged. First, most aerosol science research has been focused on particles smaller than 10 µm in diameter. And, with public health and public policy emphasizing fine particles, there has been even greater attention devoted to the particles smaller than 2.5 µm in diameter. The state of understanding regarding the dynamic behavior of coarse particles (2.5-10 µm diameter) is less developed than for fine particles (< 2.5 µm). The state of knowledge about large particles (5-100 µm) is even weaker. Second, quantitative assessments of room-scale transmission rely on the indoor air being relatively well mixed, so that the airborne concentrations are close to uniform spatially, at least when assessed on a time-averaged basis. The state of knowledge about air mixing in indoor environments is substantially incomplete, another fact that contributes to uncertainty in any assessment.

One widely used approach for modeling spread of airborne infection at the room or small-building scale is based on the Wells-Riley model[34] for assessing infection risk associated with inhaling droplet nuclei (diameter < 5 µm). In this model framework, emissions are parameterized in units of infectious quanta, with inhalation of one quantum yielding a 63% (= 1 – 1/e) chance of initiating an infection. Airborne concentrations of quanta are determined from a material-balance model that typically assumes that the indoor air is well mixed. In the original model formulation, the material balance was based on assumed steady-state conditions and removal of droplet nuclei from indoor air occurred by means of ventilation potentially augmented by particle filtration. Subsequent applications that have built on the Wells-Riley approach have allowed for time-varying indoor concentrations[76] and have incorporated loss of droplet nuclei from indoor air by mechanisms other that ventilation and filtration, such as deposition and airborne inactivation of the infectious agent.[24,25] One of the substantial challenges in applying this approach is to determine quanta emission rates. Efforts in the case of SARS-CoV-2 include bottom-up calculations that combine respiratory particle emission data with viral load information[67] and retrospective assessments of outbreaks.[24,25]

The Wells-Riley modeling approach was devised and has mainly been applied for assessing transmission risk involving the inhalation of small particles (droplet nuclei). It is not well suited for evaluating infection risk associated with the inhalation of large particles. In common applications, well-mixed indoor conditions also have been assumed. That approach has not been used to address proximate exposure conditions.

An alternative approach to assessing the transmission of infectious agents emphasizes transfer efficiency for respiratory emissions between infectious and susceptible persons. Broadly, such an approach is built around answering this question: what proportion of the material emitted from the respiratory tract of someone who is infectious is subsequently inhaled by a susceptible person? That proportion, combined with information on emission rate, would yield an estimate of the quantity inhaled. If combined with information about fractional deposition in the respiratory tract (as in Figure 3), then the quantity of infectious particles deposited in the respiratory tract can be computed, considering regional deposition efficiency.

This transfer-efficiency approach has been applied to infectious disease transmission and to other indoor air quality concerns. One quantitative metric is the *intake fraction*, which in this context would represent the fraction of an emission that is inhaled by all exposed persons.[77] Rudnick and Milton[78] explored exposure to metabolic CO_2 as a means of quantifying the *rebreathed fraction*, i.e., the proportion of air inhaled that would have come from the exhalations of other building occupants. Melikov et al.[79] used the intake fraction concept to quantify the benefits of intermittent occupancy for reducing the risk of airborne transmission. Bond et al.[16] introduced the related idea of the *effective rebreathed volume* as an indicator of infection risk and explored how that could specifically address the differential influence of particle size.

Table 3 presents parameters for three example categories of indoor spaces that are commonly occupied and have either long occupant duration (residences) or high occupant density (classroom and restaurant). For each category, data are presented for a base-case condition and for a higher-risk condition. These parameter values will be used in the assessments to follow as illustrations of the influence especially of occupant density and ventilation rate on transmission risk. The emissions considered will emphasize the asymptomatic activities of breathing and speaking, as described in Table 2.

Table 3. Indoor environmental parameters influencing airborne disease transmission risk. [a]

Environment (Condition)	Occupants	Air-change rate (h^{-1})	Vent. rate (L/s $pers^{-1}$)
Residence (Base case)	4	0.5	8.7
Residence (High exposure)	12	0.2	1.2
Classroom (Base case)	25	2.5	6.7
Classroom (High exposure)	25	1	2.8
Restaurant (Base case)	60	4.3	5.0
Restaurant (High exposure)	60	1	1.2

[a] For each indoor environment, the floor area is assumed to be 100 m^2 and the volume is 250 m^3.

Before proceeding, it is necessary to consider the deposition of airborne particles to room surfaces, which commonly dominates the rate of loss for large particles indoors. Across the size range of particles emitted from the respiratory tract, the influence of deposition to room surfaces as a removal mechanism is both highly variable and potentially very important. For particle diameters larger than about 10 µm, this loss process has not been well studied.

One relevant experimental investigation was reported by Thatcher et al.[80] In a (small) room-sized experimental chamber (V = 14 m^3), the size-resolved particle deposition rate was determined following pulsed injection of polydisperse particles spanning the approximate diameter range 0.5-10 µm. The experiments were conducted for three distinct furnishing levels (empty, carpet only, and fully furnished) and for four airflow rate conditions (fans off, and mean air speed induced by fan of 5, 14, or 19 cm/s). Results were reported in terms of size-resolved deposition rates for the different conditions of indoor airflow and furnishing level. Considering that densely occupied spaces would tend to have high surface areas and high air movement, the fully furnished condition with the highest airspeed is selected for analysis here.

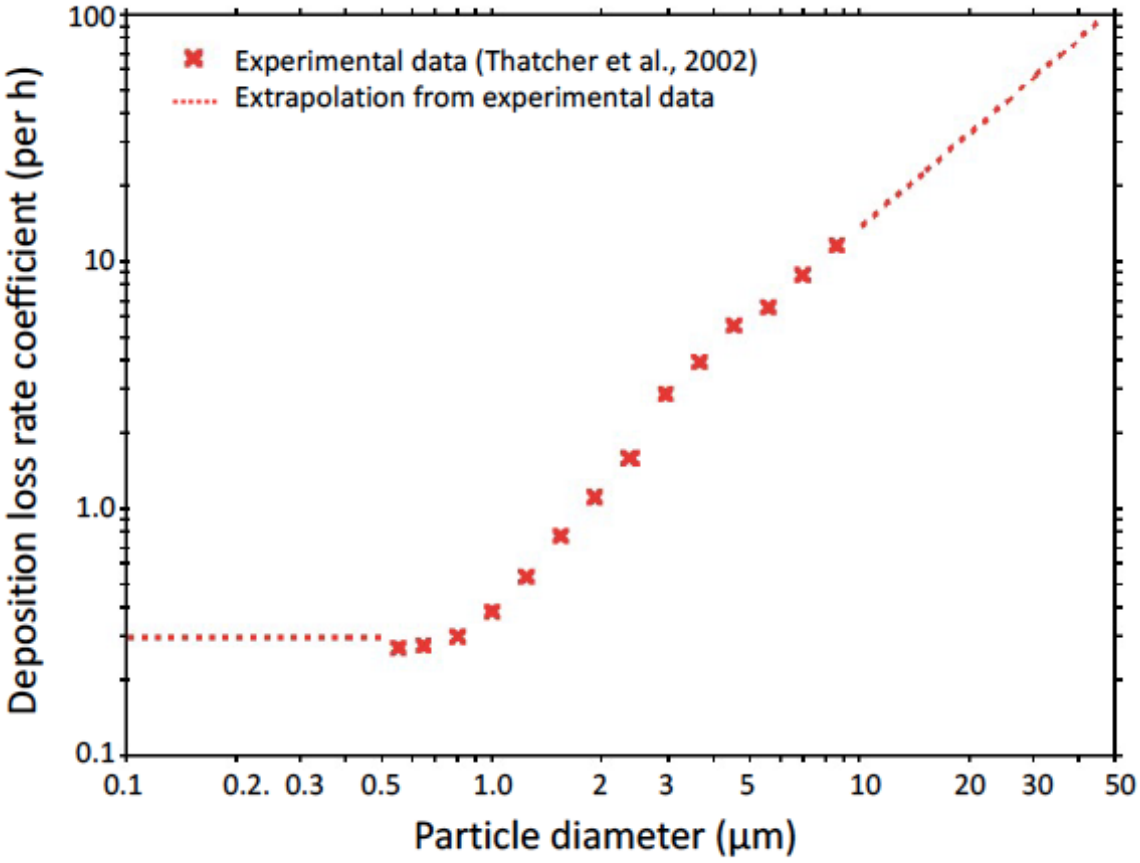

Figure 4. Deposition loss rate to room surfaces as a function of particle diameter. The experimental data are for a small furnished room with an average air speed of 19 cm/s, as measured by Thatcher et al.[80] The dashed lines represent extrapolations, with an estimated deposition loss rate of 0.3 per h for particle diameters of 0.1-0.5 µm. The large-particle extrapolation is based on a linear regression of log(loss rate [h^{-1}]) against log(diameter [µm]) using the six measurements with largest diameters. The slope and intercept of the regression line are 1.27 and -0.125, respectively.

Figure 4 displays the experimental measurement results for deposition loss rate from Thatcher et al.[80] for the 19 cm/s average airspeed in a fully furnished room. The experimental data only

span the range of 0.5-9 µm, so extrapolations are presented to extend the ranges downward to 0.1 µm and upward to 50 µm diameter. For particles larger than 1 µm, Thatcher et al. found that the effect of higher interior air motion was substantial, with an average deposition loss rate 2× as high for an airspeed of 19 cm/s compared with fan off conditions (with airspeed < 2 cm/s) in the fully furnished chamber. The effect of furnishing level was smaller, with the average loss rate for the fully furnished case being 23% higher than for carpet only (in both cases with an average airspeed of 19 cm/s).

For well-mixed indoor environments, with either sustained occupancy or under steady-state conditions, the aggregate intake fraction, *iF*, satisfies the following expression[81]

$$iF = \frac{(N-1) \times Q_{\mathrm{b}}}{\lambda_{tot} \times V} \qquad (2)$$

Here, *N* is the number of occupants of the indoor space. It is assumed that one person is infectious and that the others are susceptible, so $N - 1$ represents the number of susceptible persons. The parameter Q_{b} is the average volumetric breathing rate of each exposed person, λ_{tot} is the total pollutant removal rate constant, and *V* is the interior mixed volume. The total removal rate constant would reflect the sum of contributions from ventilation, deposition, filtration, and any inactivation of the airborne virus. For the purposes of evaluating *iF*, the possibility of resuspension following deposition isn't considered. For the explorations considered here, no contributions from filtration or inactivation are included in the analysis; the total loss rate coefficient is taken to be the sum of the air-change rate plus the deposition loss rate coefficient. The per-person average volumetric breathing rate is assumed to be Q_{b} = 10 L/min. The air-change rates are those values reported for the six cases in Table 3. The deposition loss rate coefficients are as presented in Figure 4. The analysis is not extended beyond 50 µm because of the high degree of uncertainty about deposition and mixing for large particles in the diameter range 50-100 µm.

Figure 5 displays the estimated intake fractions for the six cases. The strong particle size dependence for large particles (diameter ≥ ~ 5 µm) is attributable to the high deposition loss-rate coefficient for the bigger inhalable particles. Focusing on particles in the submicron mode, the intake fractions vary over an order of magnitude across exposure conditions, from about 9 per thousand (0.9%) for the base-case conditions in a residential setting to about 110 per thousand (11%) for the high-exposure case in a restaurant.

To obtain an estimated quantity that is closer to infection risk, the intake fraction results can be combined with emission factors to yield total intake rates. Table 4 presents a summary of such estimates, in which the intake fractions as displayed in Figure 5 are combined with emissions data from Table 2. Two emission cases are considered, one with the infectious person only breathing and the second case with the infectious person speaking. The time scale of an hour is selected to represent, in magnitude, duration of a gathering in a home (the high exposure case for a residence), the duration of a university lecture, or the time spent at a meal in a restaurant.

Several features of the results merit discussion. First, although not displayed in Table 4, it is important to note the emission modes associated with the small and large particles. As seen in Table 2, only the B modes contribute to emissions from quiet breathing. These modes represent particles originating in the distal airways from bronchiolar fluid film bursting. Even on a volume basis, these modes are dominated by small particles. For speaking, most particles in the small size range originate from the LT mode, representing the larynx and tracheal region, with most of the remainder associated with the B modes. Almost all the large particles from speaking are associated with the O modes, originating in the oral cavity. For speaking, there are substantial contributions to inhalation intake in both the small particle and large particle size ranges, and the intake rate in both cases is very much larger than when emissions only originate from quiet breathing.

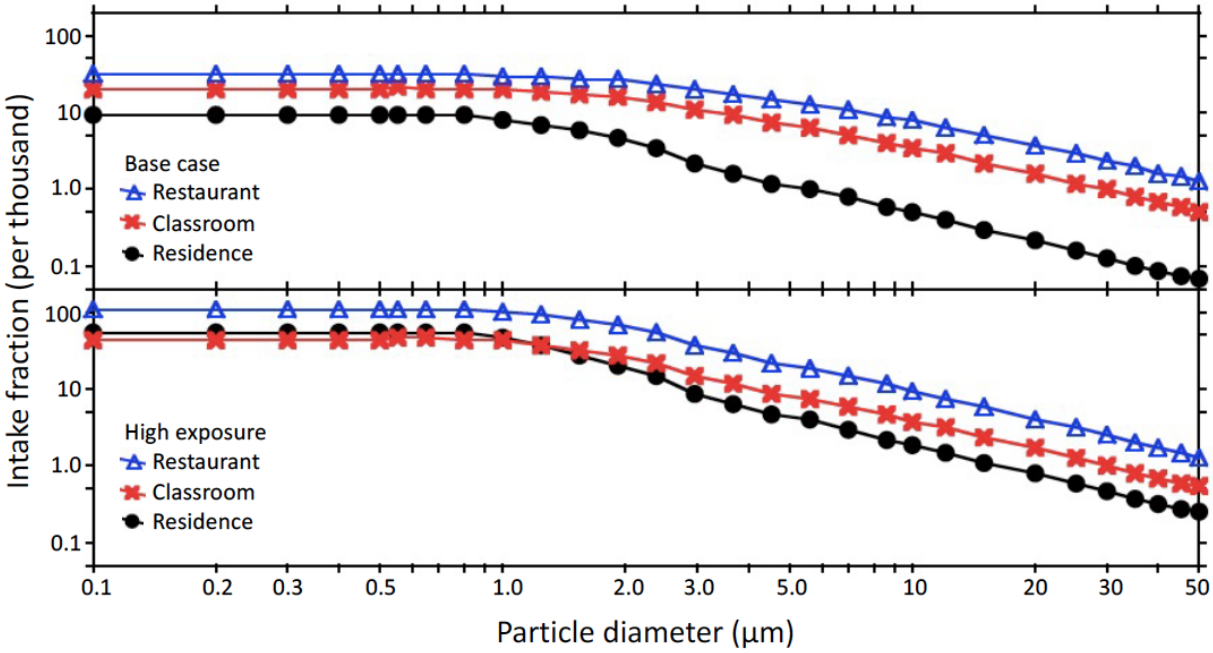

Figure 5. Aggregate intake fraction as a function of particle diameter for emissions of respiratory particles in three different settings (restaurant, classroom, and residence) and for two different exposure conditions (base case and high exposure). The vertical axis in each case represents the estimated proportion of the emitted particles that are cumulatively inhaled by the susceptible occupants, with a value of 10 (per thousand) indicating that 1% of the particles emitted would be inhaled. See Table 3 for assumed parameter values. The steep decrease in intake fraction with increasing particle diameter is attributable to the much higher deposition rate of the larger particles, as displayed in Figure 4.

A second important feature is revealed in pairwise comparisons of the high exposure versus base-case conditions. For small particles, the high exposure circumstances produce substantially higher aggregate exposures for all pairs, with high:base ratios ranging from 1.6× (small particles from speaking in a classroom) to 5.5× (small particles from breathing in a

residence). By contrast, for the large-particle exposures, there is little difference between high and base case conditions for the classroom and for the restaurant. The dominant removal mechanism for large particles is deposition, which is assumed to be consistent across indoor environments (although strongly dependent on particle size). The influence of ventilation rate on large-particle concentrations is consequently small and with no change in assumed occupancy, the inhalation intake of large particles isn't strongly influenced by the high versus base-case assumptions. A difference is seen in the modeled residential case; here, that difference is attributable to the higher assumed occupancy for the high exposure case.

Table 4. Estimated inhalation intake rates ($\mu m^3\ h^{-1}$) of respiratory particles from an infectious emitter for several illustrative indoor environmental conditions.[a]

Exposure conditions	Susceptible persons ($N-1$)	Particles from breath		Particles from speaking	
		Small	Large	Small	Large
Residence (base)	3	220	0.2	6.6×10^3	4.5×10^4
Residence (high)	11	1220	0.6	3.0×10^4	1.6×10^5
Classroom (base)	24	570	1.0	2.5×10^4	3.5×10^5
Classroom (high)	24	1150	1.2	4.1×10^4	3.5×10^5
Restaurant (base)	59	890	2.1	4.4×10^4	8.3×10^5
Restaurant (high)	59	2830	2.9	10.0×10^4	8.6×10^5

[a] The estimated volumetric particle inhalation rate is the total summed over all susceptible persons. The small particle diameter range is 0.1-5 μm; the large particle diameter range is 5-50 μm. Emission profiles are as reported in Table 2, assuming a single infectious person for each condition. Indoor environmental parameters for the model predictions are as reported in Table 3 and deposition loss rates are as displayed in Figure 4. The exposed (susceptible) persons are assumed to be breathing at a volumetric rate of 10 L/min each.

Another important point to stress regarding the risk of transmission is not fully evident from Table 4. Occupancy levels can have a second-order or quadratic influence on the risk of airborne transmission. The Table 4 data illustrates one factor: the volume of air inhaled by susceptible persons scales linearly with the number of occupants. A second factor not displayed in the Table 4 data is that the likelihood of an infectious person being present would also tend to scale linearly with the number of occupants. Consequently, by reducing occupancy levels by 50%, the risk of transmission would tend to be reduced by 4×, for conditions in which the well-mixed indoor air model apply.

The evidence in Table 4 suggests that, depending on circumstances, the cumulative inhalation rate of respiratory particles that are emitted from one occupant can be in the approximate range 10^3-10^6 $\mu m^3\ h^{-1}$. Is this rate high enough to make a meaningful contribution to the transmission of SARS-CoV-2? Recall that in their bottom-up modeling calculations, Buonanno et al.[67] found that "the concentrations of viral load in the mouth can reach values of 10^9 RNA copies mL^{-1}." A unit conversion shows that 10^9 RNA copies mL^{-1} corresponds to 10^{-3} RNA copies μm^{-3}. Combining the results, emissions from breathing only might yield a cumulative inhalation intake of ~ 1 RNA copy per hour for the exposure conditions represented in Table 4, whereas speaking could produce cumulative intakes in the approximate range 10-1000 RNA copies per hour. Buonanno et al.[67] cited evidence from studies of SARS-CoV to suggest that inhalation of

10-100 RNA copies might be required to constitute an infectious quantum. The exploration summarized in Table 4 indicates that speaking could meaningfully contribute to the risk of infectious spread of SARS-CoV-2 indoors, whereas quiet breathing would generally not.

An important caution must be stressed. The finding of higher intake rates for large particles compared to small particles for emissions from speaking does not automatically imply that the large particles dominate the risk of infection. Large particles originate mainly in the mouth and will deposit predominantly in the head when inhaled. Small particles originate from throughout the respiratory tract and can also deposit throughout, including in the pulmonary region. The source location can influence the viral load in respiratory fluids and therefore the abundance of virus in emitted particles. Although not known, SARS-CoV-2 might exhibit infection isotropy such that the risk of infection for a given amount of deposited viral RNA varies with location in the respiratory tract.

Airborne Transmission in Close Proximity

A key unresolved topic regarding airborne transmission of SARS-CoV-2 is the importance of proximity. How much does it matter whether a susceptible person is within conversational distance (< 1-2 m) of an infectious person? A classical view of airborne transmission involving aerosol inhalation assumes that it occurs over room scale, incorrectly conflating near-field transmission with droplet or contact transmission mechanisms.[5] Part of the misunderstanding arises from misclassifying the size that divides inhalable airborne particles from ballistic drops, as has already been discussed. Exposure to ballistic drops, i.e., those larger than about 100 µm in diameter, would occur predominantly near the source. Those ballistic drops mostly don't travel very far before depositing on surfaces because of their high inertia and high settling velocities. One should also expect some near-field enhancement of small (0.1-5 µm) and large (5-100 µm) particles, simply because of the time required for advective and turbulent transport to distribute the emissions throughout the indoor space. But evidence isn't sufficient to fully discern the extent of concentration enhancements for inhalable particles when a susceptible person is close to an infectious source.

Chu et al.[82] conducted a systematic review and meta-analysis of the evidence regarding physical distancing and the risk of viral transmission. They concluded that "transmission of viruses was lower with physical distancing of 1 m or more, compared with a distance of less than 1 m …; protection was increased as distance was lengthened …." Two aspects of their assessment should be highlighted. First, the scope of their investigation included studies of SARS-CoV and MERS-CoV in addition to SARS-CoV-2. Second, most of the studies reviewed were from health-care settings rather than reflecting community spread. The authors did indicate that "the association was seen irrespective of causative virus … [and also irrespective of] health-care setting versus non-health-care setting."

In this section, relevant mechanistic evidence about the influence of proximity in airborne viral transmission will be assessed. Evidence regarding person-to-person transmission from experiments and from numerical modeling is presented and critically evaluated. This section also considers the fluid mechanics of airflow from exhalations, the buoyant thermal plume of

building occupants, and general indoor air motion. The role of proximity influencing risk from ballistic drops is undisputed: such drops pose their primary impact when a susceptible person is within 2 m of an infectious source. However, the cumulative evidence isn't conclusive regarding transmission via large or small particles. The evidence suggests that near-field exposure via inhalation of large particles can make a meaningful contribution to the overall transmission risk. On the other hand, the evidence does not point toward a strong excess contribution of proximity for the transmission risk associated with small particle inhalation.

Direct experimental investigations of tracer-gas flows from person to person can provide valuable insight into the potential for airborne transmission. Olmedo et al.[83] reported one such investigation, employing two breathing thermal manikins in a 35-m^3 chamber operated at an air-change rate of 5.6 h^{-1}, which corresponds to a per-manikin ventilation rate of 27 L/s, i.e., a well-ventilated condition. Air motion in the room was also influenced by natural convection: a 488 W heat load was provided by a combination of a radiator (300 W) plus the two manikins (94 W each). The mean room air temperature was 22 °C and the air supply temperature was 16 °C. One experimental configuration used a common mixing ventilation design, with a supply register at the ceiling and two return registers at the top of one wall. With the supply of cool air and high heat dissipation rate in the room, mixing would occur rapidly. Indeed, the concentration of tracer gas in the breathing zone of the receptor manikin was only slightly higher than the concentration in room exhaust air (difference of < 5%) for a case with the manikins standing face to face and separated by distances in the range 0.35-1.1 m. The receptor manikin was breathing at a rate of about 10 L/min. Given the spatially uniform concentrations, the intake fraction for a nonreactive tracer would be the ratio of the inhalation flow rate to the ventilation exhaust flow rate, or 10 L/min/(54 L/s $\times$ 60 s/min) = 3.0 per thousand (0.3%). This value is considerably lower than the modeled small-particle intake fractions displayed in Figure 5 primarily because of the high per-person ventilation rate in the experiments of Olmedo et al.

When considering exposure in proximity, an important feature is that, at least for direct transmission, the transport time scale from source to receptor is very much shorter than the time scale for loss by deposition. For the Olmedo et al. experiments, in which the near-field enhancement was small, the overall age distribution for exhaled air might be similar at the receptor manikin as at the exhaust. However, it is worthwhile to make an upper bound estimate of intake considering the possibility that deposition losses between source and receptor might be negligible when the two persons are in proximity.

Table 5 compares intake rates of inhalable particles for two conditions based on the Olmedo et al. experiments with mixing ventilation. In the upper bound case, it is assumed that there are no depositional losses. In the lower bound case, the well-mixed model representation is assumed with deposition losses incorporated as in the previous section. Note that the difference between the two bounds is very big for the large-particle case (15$\times$) whereas it is only moderate for intake of small particles (40%).

Another noteworthy feature of the findings of Olmedo et al.[83] is their sensitivity to specific experimental conditions. As one example, in addition to measuring exhaled tracer gas in the breathing zone of the exposed manikin, they also measured concentrations at the chest and in the thermal plume 10 cm above the head (termed "C_{10}"). The concentrations at chest level were similar to those in the breathing zone, as were C_{10} values when the spacing between manikins was ≥ 0.8 m. However, for closer spacing, the C_{10} value rose substantially, reaching 35% above that in the breathing zone with 0.35 m spacing between manikins.

Table 5. Bounding estimates of the inhalation intake rate ($\mu m^3\ h^{-1}$) of respiratory emitted particles for mixing ventilation configuration investigated by Olmedo et al.[83,a]

	Particles from speaking	
Exposure conditions	**Small**	**Large**
Upper bound (no deposition)	6300	1.51×10^6
Lower bound (well-mixed)	4400	9.8×10^4

[a] Two breathing, thermal manikins (source and receptor) occupy a 35-m^3 chamber, which is operated at an air-change rate of 5.6 h^{-1}. The receptor manikin breathed at a volumetric rate of 10 L/min. The small particle diameter range is 0.1-5 µm; the large particle diameter range is 5-50 µm. Respiratory particle emission profiles are as reported in Table 2.

Much larger effects were seen when a displacement ventilation configuration was used instead of mixing ventilation. In this case, cool ventilation supply air was provided at the floor and, as before, the air was exhausted from the ceiling. Strong thermal stratification was established, with buoyant warm air aloft and dense cooler air below. Such stratification impedes vertical mixing and so the exhaled air from the source manikin could be effectively trapped in a horizontal band of air close to the emitted height. Under these conditions, for some source-receptor placements, the breathing zone concentration of tracer gas at the receptor manikin was as much as an order of magnitude higher than the concentration in the room exhaust air. Substantial spatial gradients with enhanced breathing-zone levels were also observed in a test with ventilation only through an open doorway (no mechanical system operating). The enhancements were substantial when the manikins were spaced at 0.35 or 0.5 m distance, but not when the spacing was 0.8 or 1.1 m.

Chen et al.[84] reviewed the work of Olmedo et al.[83] along with similar experimental studies of exposure to exhaled contaminants in mechanically ventilated rooms. That assessment specifically aimed to differentiate what they termed as "direct exposure" from "indirect exposure." Direct exposure occurred when the "exhaled jet from the infected person directly enters the breathing zone of the target person." Their review identified 191 experimental cases cumulatively reported in 10 research papers of which 133 (70%) used mixing ventilation conditions and 58 used displacement ventilation. As in Olmedo et al.,[83] the results were quantified in terms of a concentration ratio of tracer, dividing the breathing zone level (C_{exp}) by the concentration in the room exhaust (C_R). Chen et al.[84] defined a threshold concentration ratio of $C_{exp}/C_R \geq 1.2$ as indicating a significant contribution from direct exposure. Note that at the lower bound this condition represents only a 20% increment in exposure above well-mixed conditions. Using this threshold, they reported that 28/133 (21%) of cases with mixing

ventilation had significant direct exposure as did 30/58 (52%) of the cases with displacement ventilation. In the reviewed studies, the distance between source and receptor varied in the range 0.3-3 m. Air-change rates tended to be high, mostly in the range of 4-12 h^{-1}. Per-person ventilation rates were consistently high across all the reviewed studies, in the range 20-110 L/s per person. At the 1.0 m scale, a clear effect of interpersonal spacing was reported: "When the inter-person distance was greater than or equal to 1.0 m, the normalized exposure for most of the cases was lower than 1.1." Conversely, "when the inter-person distance was less than 1.0 m, there were many cases with a normalized exposure significantly larger than 1.0 (as high as 13.0)."

Although substantial, the cumulative body of experimental work is insufficient to characterize the importance of proximity influencing inhalation exposure to respiratory particle emissions. The experimental configurations all featured high ventilation rates and high air-change rates that are typical for well-designed health-care environments but are less representative of community conditions where people congregate and socialize. The experiments were conducted typically with just two breathing thermal manikins to represent occupants. The manikins were stationary. The fluid mechanics of emission events were represented by breathing only (except for several experiments simulating coughing in Liu et al.[85]), most commonly with exhalation through the mouth rather than the nose. Some of the investigations specifically targeted health-care environments, such as assessing the transmission risk between patients in a two-bed ward.[86,87] None of these studies can be taken as specifically representative of conditions that would prevail for people sharing a meal at a table in a restaurant, or while socializing in a crowded nightclub. The high degree of variability in the results suggests a need for caution in extrapolating beyond the specific conditions studied.

A caution also must be expressed about interpreting a concentration ratio, such as C_{exp}/C_R, as a performance figure for assessing exposure risk. In investigations with high ventilation rates, the denominator in the ratio becomes small, leading to a perceived enhancement of risk in proximity. However, these chamber experiments also show that high ventilation rates produce relatively small concentrations except under some conditions at quite close proximity. The highest C_{exp}/C_R ratios, roughly 10 for some cases with proximity at a scale of ~ 0.5 m, indicate that the very near field exposure is 10× the value that would prevail in a well-mixed room. However, with a high per-person ventilation rate as in these experiments, the well-mixed room condition might be as much as 10× lower than in a poorly ventilated space. Consequently, another interpretation of the proximity effect from these experiments could be this: being very close to an infectious person in a well-ventilated space has comparable risk to sharing occupancy in a poorly ventilated room, even when separated by 2 m or more.

The first detailed study of person-to-person transfer using breathing thermal manikins was reported by Bjørn and Nielsen.[88] Their application was especially focused on assessing displacement ventilation systems, which were being implemented with the idea of improving the overall efficiency of pollutant removal in occupied spaces and thereby improving the energy efficiency of ventilation systems. That study contains interesting and important qualitative

insights. For example, the authors note that "exhalation does not necessarily follow the boundary layer flow close to the body but is able to 'break free' and penetrate the breathing zone of other persons." This effect would be enhanced in the presence of thermal stratification associated with displacement ventilation. However, Bjørn and Nielsen[88] go on to say that "this is probably not a problem for most practical ventilation applications. People rarely stand 0.4 m apart, breathing through the mouth directly into each other's faces. … The most common breathing mode is through the nose, while sitting apart at some distance, perhaps facing each other's backs, e.g., in an auditorium or concert hall, in public transportation, etc. The experiments show that these situations are not critical. At mutual distances larger than 1 m, the phenomenon is losing its importance…."

All experiments reviewed by Chen et al.[84] used a tracer gas (N_2O) to mark the exhaled breath from the source manikin. In a complementary effort, Liu et al.[85] used a numerical modeling approach to assess the behavior of particles up to 100 µm in diameter. A limitation is that the assessment still applied only for the fluid mechanics of emissions by breathing. (Recall, as summarized in Table 2, one expects particles of 100 µm diameter and larger to be emitted from the mouth during speech, but not from quiet breathing.) In each simulation, the positions of each of 1600 particles were numerically tracked after simulated release from the source. For the 100-µm particles, at manikin spacings of 0.5 m, 1.0 m, and 1.5 m, respectively, the total number depositing anywhere on the receptor manikin surface were 99 (6.2%), 91 (5.7%), and 13 (0.8%). The proportion of those depositing that landed on the face was in the range 1-10% and none specifically deposited on exposed mucosae. The mean ± standard error of numbers of particles inhaled at the three distances were, respectively, 3.0 ± 0.5, 9.0 ± 2.8, and 0.3 ± 0.3. This evidence supports the idea that a proximity effect enhances exposure when the spacing between source and receptor is about 1 m or less. Note that the inferred intake fraction by inhalation for the three spacings would be approximately 0.2%, 0.6%, and 0.02%, respectively. For comparison, assuming well-mixed conditions and no proximity effect, Nazaroff reported,[81] "that a typical inhalation intake fraction associated with release of a nonreactive contaminant into a US residence would be ~4000 per million [0.4%]." Note that 100-µm particles settle very rapidly and that loss mechanism attenuates the contribution to exposure of this particle size in a well-mixed room. In sum, these simulations by Liu et al.[85] suggest that proximity might contribute materially to an increase in inhalation exposure to large particles when source-receptor separation distances are less than about 1 m.

The potential influence of proximity on exposure depends crucially on fluid flow conditions. There are at least three interacting aspects that merit attention: the fluid flow induced by the expiratory event from the infectious source; the airflow in the vicinity of the susceptible person; and the background airflow conditions in the indoor environment. Details of such flows exhibit complexity that is well beyond the scope of this article. So, the emphasis will be to highlight some major features with pointers to the literature as a starting point for the reader interested in deeper study.

The detailed investigation of fluid flows associated with exhalation and other expiratory events is a recent development, with most of the relevant studies having been published in the last

few decades. Murakami[89] provided an early review of the application of computational fluid dynamics to the study of "the microclimate surrounding the human body." His analysis documented the asymmetry of airflows induced by breathing. Exhalation produces a cone-shaped jet that can travel tens of cm with airspeeds attenuating as more air is entrained. Inhalation produces a more nearly uniform hemispherical converging inflow field with smaller extension from the face. Such asymmetry is also discussed by Abkarian et al.[90]

Schlieren and shadowgraph techniques have been applied for qualitative investigation of airflow fields induced by emissions from the respiratory tract, including coughing, sneezing, breathing, whistling, laughing, and talking[51,52,91] These investigations were motivated by interest in the spread of respiratory infectious diseases. Based on their imaging work, Tang et al.[52] remarked that "typical conversation at distance on the order of 1 m apart appears to be safe for much of the time, but … individuals talk in very different ways with a large variety of airflow patterns, even when speaking the same words." Xu et al.[92] extended these imaging techniques to generate quantitative assessments of "turbulent exhaled airflow from 18 healthy human subjects whilst standing and lying." They reported peak velocities during exhalation that were measured at 3 cm from the nose or mouth. Individual values (depending on subject, whether mouth or nose breathing, and whether standing or lying) spanned about an order of magnitude, from 0.3-3 m/s. Mean values across subjects for the different modes of breathing and body positions spanned about a factor of 2, from 0.8 to 1.8 m/s. The authors also reported that the exhaled centerline airspeed diminished to below 0.1 m/s at a distance of ~ 0.4 m from the subject. At this speed, background room air motion would commonly begin to dominate.

Gupta et al.[93] conducted experimental measurements to characterize the basic flow properties of coughs. Their study subjects were 25 healthy volunteers (12 female, 13 male). The researchers found considerable variability across the subjects and concluded that "cough flow characteristics from a subject cannot be used to represent the whole population." Ranges of reported values are reproduced here, separately for male (M) and female (F) subjects: cough peak flow rate (3-8.5 L/s M; 1.6-6 L/s F) and cough expired volume (0.4-1.6 L M; 0.25-1.25 L F). A subsequent study used similar methods to assess airflows from breathing and talking.[94] For a subject reading a passage, over the course of a two-minute period, the volume inhaled and exhaled was about 27 L (13.5 L/min), only modestly higher than the average flow rate from breathing quietly (12 L/min for that subject). Significantly, while speaking, although 86% of the volume inhaled was through the nose, 85% of the exhaled air passed through the mouth. Even for habitual nose breathers, much of the exhaled air when speaking would be from the mouth, which would produce different nearfield airflow characteristics. The evidence from this study also demonstrates that speech produces highly irregular exhalation flows, with short term rates up to 1-2 L/s.

Bourouiba et al.[95] evaluated the flow fields induced by uncovered coughs and sneezes. Their study included evaluations of the dynamic behavior of suspended aqueous particles, as influenced by momentum, drag, and evaporation. Chen et al.[53] studied the fluid flow aspects of coughing with the mouth covered. They reported that "covering a cough with a tissue, a cupped

hand, or an elbow can significantly reduce the horizontal velocity and cause the exhaled particles to move upward with the thermal plumes generated by human bodies."

The complexity of airflow fields induced by breathing was studied by Xu et al.[96] For exhalation through the mouth, the peak velocity averaged across many subjects, measured at 3 cm distance, varied between about 0.6 and 1.0 m/s. The influence of exhaled air on the CO_2 concentration could be observed out to a horizontal distance of about 35 cm from the mouth. Similarly, the influence of exhalation on airspeed was discernable out to a range of about 30-40 cm from the mouth. A later study[92] included nose breathing, which generated somewhat higher average peak airspeeds (at 3 cm distance), varying between 1.1 and 1.8 m/s.

Abkarian et al.[90] recently reported on detailed airflow investigations associated with breathing and speaking, referring to this subject as "linguistic aerodynamics" or "aerophonetics." Their work highlights the importance of sequential plosives in conversational speech. They find that "exhaled materials reach 0.5 to 1 m in 1 s during normal breathing and speaking." Furthermore, "airflow speeds at 1- to 2-m distances from a speaker are typically tens of centimeters per second." They caution, however, that their work does not account for "movement of the head or trunk of the speaker and the influence of background motions of the air due to ventilation."

In considering the risk of airborne transmission of a respiratory virus when source and receptor are in proximity, airflow conditions around the susceptible person are also important. A major feature of indoor air flow near people is the convective boundary layer, which is established because of metabolic heat generation combined with the buoyancy of warm air.

A standard heat generation measure is the metabolic unit, or met, with 1 met = 58 W/m^2 corresponding to the condition of being seated and relaxed. With a typical body surface area for an adult of 1.8 m^2, the at-rest metabolic energy production would be 104 W. That energy is dissipated through a combination of radiant heat transfer, evaporation of water, and convective heat transfer. Worth noting is that a 2000 (kilo)calorie per day diet corresponds to an average power dissipation rate of 8.4 MJ/d = 97 W.

Substantial air flow is associated with the personal convective boundary layer. Licina et al.[97] cited previous work to suggest that as much as 60 L/s of volumetric flow was entrained into the plume above a standing person. Interpreting the airspeed profile as reported by Gena et al. above a thermal manikin suggests a similar value.[98] Craven and Settles[99] reported thermal plume flow rates above a human to be in range 20-35 L/s for a linearly stratified room environment. The peak air speed above the head can be as high as 23-25 cm/s.[89,98] Note that the volumetric flow rate in the convective boundary layer is higher than typical outdoor air ventilation rates (generally on the order of 10 L/s per person). It is very much higher than the volumetric flow rate associated with breathing. In near-field exposure conditions, emissions from the respiratory tract of an infectious person will be diluted both by entrainment of airflow in the exhaled jet and by the movement of air in the convective boundary layer of the susceptible person. Sun et al.[100] reviewed the personal convective boundary layer (which they term the "human thermal plume"), in the context of airborne transmission of SARS-CoV-2. The

interaction of the personal convective boundary layer with room air flows induced by ventilation systems has been explored experimentally[101] and numerically.[102]

Although substantial research efforts have aimed to understand indoor airflow conditions, these studies have tended to stress idealized circumstances, for example, evaluating ventilation system concepts or modeling system performance in small rooms with simple boundary conditions and low occupancy levels. As observed in a recent review,[103] "air flow patterns within a space are crucial for determining the distribution, transport and fate of any airborne contaminants. Predicting these flow patterns is extremely challenging since they depend critically on both the boundary conditions … and on the internal dynamics of the fluid, particularly buoyancy forces associated with temperature differences." Bhagat et al.[103] address the influence of people on indoor air motion in relation to the transmission of airborne infectious diseases. Themes discussed include the exhaled jet, the thermally buoyancy plume, and the wake flow behind a moving person. To this latter point, the authors note that "wake velocity is approximately 80% of the person speed, implying [that] flows behind a person [are] of the order of 0.8 m s^{-1} [and] are possibly the largest in a space." With walking, the body sheds its thermal plume, so that forced convection replaces natural convection in removing the metabolically generated heat. In their summary, Bhagat et al.[103] write that, "room flows are 'turbulent' in the sense that spatiotemporal variations of the flow are larger than the mean flow. They take place in complex geometries where the placement and sizes of inlets and outlets determine overall flow patterns, superimposed on which are significant perturbations associated with often transient events such as the movement of occupants, the opening and closing of doors and … variations in the external conditions." In the context of airborne infectious disease transmission, the complexity of airflow conditions, from the source, near the receptor, and throughout the indoor environment represents only one axis in a system with multidimensional complexity.

Masks and Face Coverings

The wearing of masks and face coverings in public, already common in some countries, became a worldwide phenomenon during the Covid-19 pandemic. The preexisting scientific foundation justifying their use to protect against community transmission of infectious diseases was surprisingly meager, and so many articles have been published recently reporting on new evaluations. The degree to which masking is effective can provide some clues about the aerosol science aspects of SARS-CoV-2 transmission. This section presents some highlights on the current state of knowledge.

In an editorial published a decade ago, Li outlined several fundamentally important points about masking, and he also described some important limitations to our understanding.[104] That editorial was inspired by the experience in Hong Kong and elsewhere with the 2003 SARS epidemic and the 2009 H1N1 influenza pandemic. That editorial is remarkably prescient for issues relevant to the Covid-19 pandemic.

There are at least three important dimensions to understanding the efficacy of masking for the spread of respiratory infectious agents such as SARS-CoV-2. First and second, masks remove

particles from airstreams, reducing their release from infectious persons in exhaled air and reducing their intake along with air inhaled by susceptible persons. A key feature in the control benefit on both the source and receptor side is that filter efficiency is a strong function both of particle size and of mask quality. This aspect interacts with the important and inadequately understood element regarding the sizes of particles that are responsible for airborne transmission. The third key aspect, as described by Li,[104] is that the mask "stops the exhalation puff of the wearer from being directly injected into air, instead redirecting it into the body's thermal plume." This third aspect would not matter much for room-scale airborne transmission but could be important for protecting against transmission when the infectious and susceptible persons are proximate. This third point is demonstrated nicely by studies that use visualization techniques to display the influence of masking on exhaled airflows.[51,52,105]

Three tiers of face coverings and masks have been in common use in community settings during the SARS-CoV-2 pandemic. The most highly protective are N95 respirators or their close relatives (such as KN95). The second tier is the surgical mask. The third tier is a face covering in which one or more layers of fabric (or other porous or permeable materials) are adapted in such a way as to provide covering of the mouth and nose of the wearer. Prior to the SARS-CoV-2 pandemic, published research on the performance of masks focused on N95 respirators and surgical masks and emphasized particle sizes smaller than 5 μm diameter. From this earlier work, good examples of the laboratory evaluation of mask efficacy have been published.[106,107] Cowling et al.[108] reported on a systematic review of the efficacy of mask wearing to limit influenza transmission in the wake of the H1N1 pandemic. They concluded that, "further studies in controlled settings and studies of natural infections in healthcare and community settings are required to better define the effectiveness of face masks and respirators in preventing influenza virus transmission." Face coverings are also used for protection against particulate air pollution. Shakya et al.[109] assessed the efficiency of several types of cloth masks and a surgical mask against particles in the size range 0.03-2.5 μm.

Leung et al.[110] tested the effectiveness of surgical face masks on the emission of viral particles from subjects with acute respiratory illness. Respiratory emissions were collected for 30-minute sampling periods during quiet breathing; natural coughing was allowed and recorded. The sampling was size segregated into small (< 5 μm) and large particles, without a clearly specified upper bound for the large particles. For subjects without a mask and infected with a coronavirus (but not SARS-CoV-2), viral RNA was identified in large particles for 3 of 10 (30%) subjects and in small particles for 4 out of 10 (40%) subjects. The researchers "did not detect any virus [in either large or small particles] from participants wearing face masks." The effect of masking in reducing emissions was smaller for subjects infected with influenza virus and no significant differences were observed with masking for emissions from those with rhinovirus infections. An important experimental design detail should be noted in the context of community transmission of SARS-CoV-2: these tests did not involve the subjects speaking.

Three contemporary studies motivated by the Covid-19 pandemic demonstrate progress but also illustrate challenging aspects in advancing knowledge about the efficacy of masks and face coverings. Asadi et al.[111] used human subjects to measure outward emission of respiratory

particles with and without masks during speaking and coughing. They tested N95 and KN95 respirators, surgical masks, and several cloth face coverings. They measured size-distributed emissions in the approximate diameter range 0.3-20 µm. Their primary reporting was in terms of the change in particle *number* concentration sampled, summed across the entire size range measured. That choice might be associated with lower performance than would a *volume-weighted* effectiveness measure. The sampling approach collected only a subset of the emitted particles, those projected forward into a sampling cone. A higher proportion of emitted particles may have escaped detection during experiments with masks because of the altered flow field. This study also revealed the interesting finding that movement of the jaw against mask material could generate particles. The authors attributed this observation to "friable cellulosic fibers in homemade cotton-fabric masks." Earlier literature, as reviewed by Licina et al.,[112] has shown that the movement of fabric against skin can liberate skin flake particles into the air.

Konda et al.[113] used a two-chamber laboratory apparatus to measure size-resolved particle penetration through various fabrics, alone or in combination. The test sample had an area of 59 cm^2 and two constant flow rates were tested, 35 L/min and 90 L/min. These flow rates are substantially higher than the at-rest volumetric breathing rates that would apply in common social settings. The particle diameters measured in this study spanned a range from 10 nm to 6 µm. The lowest order of magnitude in size is not directly relevant to assessing the transmission risk for viruses that are ~ 100 nm in diameter alone and are emitted in association with the nonvolatile components of respiratory fluids.

Pan et al.[114] used a test chamber outfitted with two manikin heads to assess the performance of various masks and face-covering fabrics both for control of exhaled particles and for protection on inhalation. They used four different particle generators to produce polydisperse particles spanning an overall diameter range of 0.04 µm to >100 µm. Airborne particles were measured with an aerodynamic particle sizer (range 0.3-20 µm). Glass slides were mounted on the face of the receiver manikin to optically measure the deposition of larger particles. Among the key findings was that "the fit of the mask was important." For high quality protection, the authors recommended "a three-layer mask consisting of outer layers of a flexible, tightly woven fabric and an inner layer consisting of a material designed to filter out particles. This combination should produce an overall efficiency of >70% at the most penetrating particle size and >90% for particles 1 µm and larger if the mask fits well."

The Covid-19 pandemic has also inspired several synthesis studies that assemble and interpret the literature on mask wearing and its effectiveness. Chu et al.[82] undertook a systematic review and meta-analysis on the effect of mask wearing on the transmission of respiratory viral infections. They concluded, albeit with low certainty, that "medical or surgical face masks might result in a large reduction in virus infection." Altogether, they identified 39 relevant studies for their analysis; however, only five of these were undertaken outside of health-care settings. The review by Howard et al.[115] effectively highlights an important point that is underappreciated: conditions in healthcare environments are considerably different than in the broader community. Transmission risks and mitigation measures can be rationally differentiated

between these circumstances. Specifically, with regards to wearing masks, Howard et al.[115] recommends an "increasing focus on a previously overlooked aspect of mask usage: mask wearing by infectious people ('source control') with benefits at the population level, rather than only mask wearing by susceptible people, such as health care workers, with focus on individual outcomes."

Synthesis

This article has addressed the airborne transmission of SARS-CoV-2 in indoor environments in community settings. It has been structured around the three key steps in direct airborne transmission: emission of virus-containing particles from an infectious person, transport in the indoor environment between source and receptor, and inhalation intake and deposition in the respiratory tract of a susceptible person. This section provides a summary of important aspects of the current state of knowledge. However, before proceeding with the synthesis, three major challenges are highlighted.

First, this system is remarkably complex across several dimensions. These include where in the respiratory tract the virus replicates and sheds, differences in how and where particle emissions occur in the respiratory tract according to the type of activity (breathing, speaking, coughing, etc.), the broad range of inhalable particle sizes that are emitted, the widely varying dynamic behavior of airborne particles indoors according to particle size, the substantial influence of indoor environmental factors such as ventilation and filtration rates, the wide variability with particle size of deposition location within the respiratory tract, and the relative importance of source-receptor proximity as a key factor affecting airborne transmission risk.

A second broad concern is the pervasive error in the literature regarding respiratory infectious diseases about the size that differentiates airborne particles from ballistic drops. Starting from an incorrect assumption that particles larger than 5 μm won't travel more than 2 m from the emission source produces downstream errors in interpreting the evidence. Such errors have clouded understanding and impeded progress.

A third feature is the novelty and virulence of SARS-CoV-2. Covid-19 is the most severe pandemic in the past century. Although caused by nominally similar viral agents, the transmission characteristics of SARS-CoV-2 are remarkably different from those of SARS-CoV, the coronavirus responsible for the 2003 SARS epidemic. An appropriate response to these circumstances demands a fresh look at the evidence.

A useful organizing principle for thinking about airborne transmission of SARS-CoV-2 is in terms of an array with 3×3 elements. One axis represents size, clustered into small particles (0.1-5 μm diameter), large particles (5-100 μm), and ballistic drops (> 100 μm). The other axis is the stage in the transmission process: emissions from the infectious source, transport in the indoor environment, and uptake by the susceptible person. As the elements in this array are described below, one should be mindful that the boundaries among categories are not sharply defined, especially with regards to particle size. The top end of the small particle size range can exhibit

similar behavior as the lower end of the large particle range. Similarly, the smallest of the ballistic drops can exhibit behavior like the biggest of the large particles. Despite the fuzziness of the boundaries, clustering is useful because the bulk of each grouping has distinct features.

Ballistic drops are emitted from the nose and mouth. Although considerable attention historically emphasized symptomatic events, such as coughing and sneezing, it is also apparent that talking (and other vocalization activities such as laughing and singing) can be a substantial source of ballistic drops. Although the number of ballistic drops emitted is relatively small, these drops contain a substantial proportion of the volume of emitted respiratory liquids. To the extent that virus is generated and shed in the upper throat, mouth, and/or nasal passages, these ballistic drops could be a significant contributor to total transmission risk. Once emitted, the ballistic drops remain airborne for only a short time and generally travel only a short distance from the source. (Exceptions to the travel distance can occur for events such as uncovered sneezes,[95] but events such as an uncovered sneeze would be unusual outliers, rather than predominant features of total emissions.) During the short period that they are airborne, ballistic drops don't evaporate much, so that their size when deposited is close to the size as emitted. Indoor environmental conditions normally would have relatively little influence on the fate of ballistic drops. Indoor airflow speeds are generally small enough (typically well below 1 m/s) to not strongly affect the trajectory of ballistic drops. The deposition of ballistic drops on the body envelope of a susceptible receptor could occur by a combination of inertial impaction and gravitational settling if the receptor is situated proximate to the source. If sufficient viral deposition occurs directly on exposed mucus membranes, then a new infection could be initiated. Deposition of ballistic drops onto other surfaces could contribute to exposure via fomites. That is typically thought of in terms of transfer from a virus-contaminated surface to the mucus membranes of a susceptible person via hand contact. So, if sufficient virus containing ballistic drops deposit on the clothing of a susceptible person through a substantial period of exposure near an infectious person, e.g., in conversation, then it is conceivable for an infection to be initiated because of hand-mediated transfer of the virus from the clothing surface to the mucus membranes of the susceptible person. The same process could apply with the initial deposition onto an inanimate surface, such as a table, during a shared meal.

Large particles are generated in the upper respiratory tract. Emission sites can include the larynx and mouth during speech as well as the trachea, oral, and nasal cavities during coughing and sneezing. Two prominent features of their behavior distinguish large particles from the two other size modes. First, as compared with small particles, large particles settle rapidly and therefore have relatively short indoor air residence times. The short residence time has several important consequences. (a) The fraction of emitted large particles that is inhaled is attenuated by the rapid deposition-associated removal. (b) The opportunity to control exposure through improved filtration and ventilation is diminished for large particles. (c) To the extent that indoor air lifetimes are on the same scale or shorter than mixing time scales, the proximity effect becomes especially pronounced for large particles. To elaborate on point (c), because of the high rate of removal by deposition of large particles to indoor surfaces, there would be a tendency for the near-source concentration to be more substantially enhanced for large particles than would be expected for small particles. Second, as compared with ballistic drops,

large particles can be inhaled, which is a more efficient mode of transfer to mucus membranes than impaction restricted to the small areas of open eyes, nostrils, or mouth. When inhaled, large particles would tend to be deposited primarily in the head and secondarily in the tracheobronchial tree; they are unlikely to penetrate to the pulmonary region of the respiratory tract.

Small particles can be generated in the deep lung through the bronchiolar fluid film bursting mechanism.[62] Vocalization including speech and singing also generates small particles, which may be produced at and near the vocal cords.[9] Small particle dynamic behavior has been extensively studied in indoor air and is relatively well understood.[116,117] Indoor air concentrations resulting from a given time-pattern of emissions are influenced mainly by ventilation and filtration rates and by deposition loss. The well-mixed model of an indoor environment commonly provides a reasonable approximation of reality. When inhaled, small particles can deposit throughout the respiratory tract, with the bigger of the small particles depositing significantly in the head. There is substantial probability of tracheobronchial and pulmonary deposition across the small particle size range.

Large and small particles shrink after emission through the evaporative loss of water. This process only causes a loss of volatile components. The residual nonvolatile components are sufficient in abundance so that the equilibrated particles have diameters that are approximately 30-40% of the emitted sizes. The kinetics of evaporation are rapid both for small particles and for the lower end of the large particle size range such that the equilibrium state can be assumed to be attained instantaneously. For the bigger of the large particles, mass and heat transfer limitations may cause the airborne dynamic behavior to depend on time-varying size.[13]

Not widely appreciated in the contemporary literature concerned with infectious disease transmission is the possibility that viral transfer from source to receptor could involve two successive airborne stages. To envision such a process for SARS-CoV-2, consider two important points. First, the virus can remain viable on surfaces for periods of hours to days.[118,119] Second, particles that deposit on surfaces can become resuspended. This latter point has been substantially investigated for abiotic particles.[120-122] Regarding microbes, Duguid and Wallace[123] highlighted the “bacterial contamination of air produced by liberation of dust from the skin and personal clothing during bodily movement.” They reported: “Experiments with nasal carriers of *Staphylococcus aureus* showed that the air was infected with this pathogenic organism more regularly and to a greater degree by the liberation of dust from clothing than by sneezing.” Licina et al.[112] have reviewed the role of clothing as an intermediary contributor to microbial exposures. Prior to onset of the Covid-19 pandemic, Stephens et al.[124] reviewed fomites more broadly, including infectious viral agents. Asadi et al.[125] recently demonstrated that viral particles shed from the body of a guinea pig could infect a susceptible partner in a separate cage through airborne transmission. This evidence points to the plausibility of SARS-CoV-2 transmission involving the deposition of ballistic drops or large particles on clothing followed by subsequent release from the clothing through ordinary movement, transport to the breathing zone assisted by the personal convective plume, inhalation intake and deposition in the upper

respiratory tract. If ballistic drops are involved in this process, one should recognize that the initial deposition and persistence on a clothing surface would allow for drying and shrinkage to full equilibration with local environmental conditions. Also plausible is that the movement of fabric fibers fragments the drop residue, producing inhalable particles from larger emissions. The process of respiratory drops becoming fractured and released from surfaces after depositing hasn't been specifically studied. However, at least at the level of "proof of principle" there may be parallels with the phenomenon of "thunderstorm asthma," which involves the environmental rupture of pollen grains to produce respirable allergenic fragments.[126]

Is it possible to assemble all the evidence and present a coherent picture of the primary modes of indoor airborne transmission of SARS-CoV-2? Perhaps. Key features of the evidence are these. In well less than two years since the onset of the pandemic, Covid-19 has spread to every community. Notwithstanding enormous social effort entailing widespread use of nonpharmaceutical interventions to stem the spread, more than 180 million diagnosed cases have occurred. The infections appear to be mainly spread indoors rather than outdoors. Much of the transmission originates from infectious persons who are not particularly symptomatic at the time. Superspreading events also are common and contribute to the overall rapid spread of the disease. Community spread is dominant. Social distancing and masking are at least moderately effective control measures. From a mechanistic perspective, emissions are considerably larger from speaking and other vocalization activities than from quiet breathing. Emissions from speaking span a broad range of sizes with substantial contributions to small particles, large particles, and ballistic drops. In combination with limited information on viral loads in respiratory fluids and on anticipated infectious doses, emissions from speaking are sufficient to initiate new infections in circumstances in which the transfer efficiencies from source to receptor are high. Such circumstances could occur when the infectious and susceptible persons are in proximity and engaged in unmasked conversation. They could also occur at the room scale, especially under poor ventilation conditions.

The importance of superspreading events points in the direction of important room-scale transmission mediated by small particles. The room-scale transmission provides the means for all occupants to share in the exposure. The emphasis on small particle contributions is indicated by such particles persisting sufficiently in indoor air to be present at high concentrations, especially if the removal rate isn't sufficient, i.e., because of low ventilation rates and nonexistent or weak filtration. Surgical masks and cloth face coverings would not eliminate the transmission risk associated with small particles. However, absent N95-level respiratory protection, a combination of these factors would contribute to effectively lowering risk: low occupant density, short occupancy intervals, sufficient outdoor air ventilation, effective room-air filtration, and face coverings.

Indications that masking and proximity are important factors that influence the transmission risk suggests that large particle inhalation and/or ballistic drop transmission would contribute. Ballistic drops can only make a large contribution to exposure in the near-field range (within a meter or two from the source). Large particles can travel farther, but because of their high rate of deposition, the probability of high exposure is enhanced through direct exposure to the

plume of emissions. For proximate exposures, masking is likely to be an effective mitigation measure because large particles can be effectively removed from airstreams on both the emissions and inhalation intake sides, even with surgical masks and cloth face coverings. Also, a mask on an infectious source who is speaking will attenuate the exhaled air plume from the mouth, limiting the efficiency of large particle transport across meter-scale distances.

The descriptions in the previous two paragraphs might seem contradictory. However, the available evidence does not even suggest that they are mutually exclusive. Instead of thinking about routes of exposure as "either/or," the high rates of community spread would strongly argue that "both/and" would apply.

The relative dominance of indoor versus outdoor environments as settings for disease transmission provides some additional clues about transmission mechanisms. First, transmission that is modulated by the indoor confinement of small particles indoors does not have a direct analog in outdoor air. That is, to the extent that small-particle, room-scale transmission is a dominant contributor to the overall spread, the concomitant dominance of indoor settings over outdoor venues is clearly consistent. Less clear is to reconcile that proximity is a major risk factor indoors, but not outdoors. On the one hand, it is plausible that proximity is a risk factor outdoors but that it doesn't emerge strongly from data such as outbreak investigations because sustained proximity cannot involve large numbers of susceptible persons within a meter or so of an infectious person. For example, a minimum of three new cases was one of the inclusion criteria for the outbreak investigations reported by Qian et al.[4] Outdoor transmission in proximity that may have infected one or two persons per event would not have been detected. It is also plausible that the altered airflow conditions between outdoor and indoor environments attenuates the near-field risk outdoors. To elaborate, indoors a typical airspeed is 0.1 m/s. Outdoors, routine monitoring data measured at 10 m height for meteorological and climatological purposes show that typical airspeeds are in the range 2-8 m/s (https://www.ncdc.noaa.gov/societal-impacts/wind/). Even when diminished to a fraction of this range when considering the breathing height of 1-2 m, outdoor air speeds would commonly be much higher than those indoors. The higher outdoor airspeeds would tend to reduce the near-field concentrations by speeding the rate of dilution. That effect would likely be more pronounced for small and large particles than for ballistic drops, whose motion is less affected by background air speeds. So, considering the indications that transmission risks in proximity are higher indoors than outdoors, this point of comparison might argue in favor of the close-proximity indoor transmission being dominated by large particles rather than ballistic drops. However, all this evidence about the indoor and outdoor transmission relationships is at best suggestive. Systematic investigations are needed of transmission and fate of large particles and ballistic drops in relation to source-receptor proximity under different airflow conditions.

Conclusion

In the legal system of the United States, different standards of proof apply, depending on the type of decision to be made.[127] For conviction in a criminal trial, the evidence presented must persuade the decision maker to a level that is *beyond a reasonable doubt*. In the case of a civil suit seeking financial damages, the decision must be supported by *a preponderance of the*

evidence, with "preponderance" indicating "more likely than not." An intermediate standard, *clear and convincing evidence*, applies in certain circumstances. In working toward an understanding of the modes of transmission of SARS-CoV-2, these qualitative descriptors about standards of proof can help clarify the strength of evidence and its consistency in supporting interpretations. Community transmission of infectious diseases in general, and of Covid-19 in particular, occurs through processes that are understood at a broad conceptual level but are sufficiently complex in detail to defy reliable quantitative assessment. Important public health and public policy decisions should be made using the best available scientific understanding, even if we cannot meet an empirical scientific standard of *statistically significant* based on randomized controlled trials. This concluding section summarizes key elements in the transmission of SARS-CoV-2 along with my qualitative judgements about the strength of the supporting evidence. There is clear precedent for providing such interpretations in the case of infectious disease transmission indoors, as illustrated in this quote from a multidisciplinary systematic review: "There is strong and sufficient evidence to demonstrate the association between ventilation, air movements in buildings and the transmission/spread of infectious diseases such as measles, tuberculosis, chickenpox, influenza, smallpox and SARS." [128]

Beyond a reasonable doubt, in terms of influence on global public health and well-being, Covid-19 is the most impactful pandemic of the past century. In about 18 months since the onset of the pandemic, the disease has spread globally and infected more than 2% of the human population. In the United States, which has seen the largest death total of any country, Covid-19 was the third leading cause of death in 2020, behind cardiovascular disease and cancer.

Beyond a reasonable doubt, SARS-CoV-2 transmission occurs primarily in community settings, both in households and in environments where people from different households gather. Predominantly, the transmission process is initiated by the emission of the SARS-CoV-2 virus from the respiratory tract of an infectious person, in particles and drops that are mainly comprised of respiratory fluids. Transmission occurs much more commonly indoors than outdoors. Many people are infectious without experiencing strong symptoms of illness.

The evidence is clear and convincing that superspreading events make major contributions to the overall community spread of Covid-19. Clear and convincing evidence also supports a view that several nonpharmaceutical interventions can contribute to reducing (but not eliminating) the risk of transmission in the community: mask wearing, maintaining social distance (≥ 1-2 m), adequate ventilation and/or air filtration.

A preponderance of the evidence suggests that speaking and other vocalizations are important means by which the virus is emitted. It also seems more likely than not that inhaling either or both small particles (0.1-5 μm diameter) and large particles (5-100 μm) containing the SARS-CoV-2 virus constitutes the dominant exposure mechanism for a susceptible person. A preponderance of the evidence supports a view that transmission can occur either at room scale or when the susceptible person is proximate to an infectious person. Mitigation of room-scale transmission would emphasize providing sufficient ventilation and/or filtration, limiting occupancy, and limiting event duration. Protecting against room-scale transmission also points

toward the importance of masks that are efficient in filtering small particles. Room-scale transmission is the more likely contributor when superspreading events occur. Mitigation of transmission in proximity would emphasize mask wearing and maintaining social distance. Proximity can amplify the source-to-receptor transmission efficiency of large particles especially. Face coverings can reduce the risk of transmission at the proximate scale not only by filtering particles but also by attenuating the range of the exhaled jet of air from the infectious source. At close range, ballistic drops may also contribute materially to exposure risk through deposition onto a susceptible person, not only directly onto sensitive mucus membranes, but also onto other surfaces such as exposed skin and clothing. The final portion of the source-to-receptor transmission chain for ballistic drops and large particles that deposit onto a susceptible person's skin and clothing has not been adequately studied. There is enough evidence to at least suggest a concern that the resuspension of viral particles from such surfaces followed by entrainment into the human convective boundary layer and inhalation could contribute to overall transmission risk. Mitigation strategies for transmission by ballistic drops overlap substantially with the mitigation of proximate-scale transmission by means of large particle inhalation. Mask wearing and maintaining social distances are key.

This article has been written from the perspective of one person, with expertise in aerosol science, indoor environmental quality, and environmental engineering science. These areas of expertise emphasize a fusion of empirical evidence with mechanistic, process-oriented descriptions, along with a particular focus on source-receptor relationships. Another orientation of these subject areas is the need for science to guide the development and application of technology for improving the human condition even when the state of knowledge is incomplete. An overarching goal in preparing this review is to contribute toward more complete awareness of what is known and what we don't yet know. I acknowledge that my perspective is limited by the scope of my experience and imagination, permitting only partial insight into important aspects of the complex process of indoor aerosol transmission of SARS-CoV-2.

A remarkable feature of the Covid-19 pandemic has been the collective involvement across humankind in rising to face a newly emergent challenge. Individually, and collectively, we are faced with decisions about our actions that matter substantially in ways that were not relevant two years ago. Loevinger's[127] essay about the foundations of proof in science and law closes with a statement that expresses an apt ambition for these circumstances: that application of the "disciplines of analysis, synthesis, and explication will result in sufficient agreement among a large enough segment of the population to get the world's work done in a tolerably satisfactory manner and to produce observable benefits from the process."

References

1. Heneghan CJ, Spencer EA, Brassey J, et al. SARS-CoV-2 and the role of airborne transmission: a systematic review. *F1000 Research*. 2021;10:232.
2. Greenhalgh T, Jimenez JL, Prather KA, Tufekci Z, Fisman D, Schooley R. Ten scientific reasons in support of airborne transmission of SARS-CoV-2. *BMJ*. 2021;397:1603-1605.

3. Bulfone TC, Malekinejad M, Rutherford GW, Razani N. Outdoor transmission of SARS-CoV-2 and other respiratory viruses: A systematic review. *The Journal of Infectious Diseases*. 2021;223:550-561.
4. Qian H, Miao T, Liu L, Zheng X, Luo D, Li Y. Indoor transmission of SARS-CoV-2. *Indoor Air*. 2021;31:639-645.
5. Tang JW, Bahnfleth WP, Bluyssen PM, et al. Dismantling myths on the airborne transmission of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). *Journal of Hospital Infection.* 2021;110:89-96.
6. Milton DK. A Rosetta Stone for understanding infectious drops and aerosols. *Journal of the Pediatric Infectious Diseases Society*. 2020;9:413-415.
7. Pöhlker ML, Krüger OO, Förster J-D, et al. Respiratory aerosols and droplets in the transmission of infectious diseases. *arXiv*. 2021:2103.01188v3.
8. Gandhi M, Yokoe DS, Havlir DV. Asymptomatic transmission, the Achilles' heel of current strategies to control Covid-19. *New England Journal of Medicine*. 2020;382:2158-2160.
9. Johnson GR, Morawska L, Ristovski ZD, et al. Modality of human expired aerosol size distributions. *Journal of Aerosol Science*. 2011;42:839-851.
10. Wei J, Li Y. Airborne spread of infectious agents in the indoor environment. *American Journal of Infection Control*. 2016;44:S102-S108.
11. Nicas M, Nazaroff WW, Hubbard A. Toward understanding the risk of secondary airborne infection: Emission of respirable pathogens. *Journal of Occupational and Environmental Hygiene*. 2005;2:143-154.
12. Vejerano EP, Marr LC. Physico-chemical characteristics of evaporating respiratory fluid droplets. *Journal of the Royal Society Interface*. 2018;15:20170939.
13. Xie X, Li Y, Chwang ATY, Ho PL, Seto WH. How far droplets can move in indoor environments — Revisiting the Wells evaporation-falling curve. *Indoor Air*. 2007;17:211-225.
14. Moriyama M, Hugentobler WJ, Iwasaki A. Seasonality of respiratory viral infections. *Annual Review of Virology*. 2020;7:2.1-2.19.
15. Li Y. Basic routes of transmission of respiratory pathogens — A new proposal for transmission categorization based on respiratory spray, inhalation, and touch. *Indoor Air*. 2021;31:3-6.
16. Bond TC, Bosco-Lauth A, Farmer DK, et al. Quantifying proximity, confinement, and interventions in disease outbreaks: A decision support framework for air-transported pathogens. *Environmental Science & Technology*. 2021;55:2890-2898.
17. Hwang SE, Chang JH, Oh B, Heo J. Possible aerosol transmission of COVID-19 associated with an outbreak in an apartment in Seoul, South Korea, 2020. *International Journal of Infectious Diseases*. 2021;104:73-76.
18. Mao J, Gao N. The airborne transmission of infection between flats in high-rise residential buildings: A review. *Building and Environment*. 2015;94:516-531.
19. Matthews TG, Thompson CV, Wilson DL, Hawthorne AR. Air velocities inside domestic environments: An important parameter in the study of indoor air quality and climate. *Environment International.* 1989;15:545-550.
20. Baldwin PEJ, Maynard AD. A survey of wind speeds in indoor workplaces. *Annals of Occupational Hygiene*. 1998;42:303-313.

21. Zhai Y, Zhang H, Zhang Y, Pasut W, Arens E, Meng Q. Comfort under personally controlled air movement in warm and humid environments. *Building and Environment*. 2013;65:109-117.
22. Persily A, de Jonge L. Carbon dioxide generation rates for building occupants. *Indoor Air*. 2017;27:868-879.
23. Nazaroff WW. Residential air-change rates: A critical review. *Indoor Air*. 2021;31:282-313.
24. Buonanno G, Morawska L, Stabile L. Quantitative assessment of the risk of airborne transmission of SARS-CoV-2 infection: Prospective and retrospective applications. *Environment International*. 2020;145:106112.
25. Miller SL, Nazaroff WW, Jimenez JL, et al. Transmission of SARS-CoV-2 by inhalation of respiratory aerosol in the Skagit Valley Chorale superspreading event. *Indoor Air*. 2021;31:314-323.
26. Milton DK. What was the primary mode of smallpox transmission? Implications for biodefense. *Frontiers in Cellular and Infection Microbiology*. 2012;2:150.
27. Nguyen-Van-Tam JS, Killingley B, Enstone J, et al. Minimal transmission in an influenza A (H3N2) human challenge-transmission model within a controlled exposure environment. *PLoS Pathogens.* 2020;16:e1008704.
28. Althouse BM, Wenger EA, Miller JC, et al. Superspreading events in the transmission dynamics of SARS-CoV-2: Opportunities for interventions and control. *PLoS Biology*. 2020;18:e3000897.
29. Lau MSY, Grenfell B, Thomas M, Bryan M, Nelson K, Lopman B. Characterizing superspreading events and age-specific infectiousness of SARS-CoV-2 transmission in Georgia, USA. *Proceedings of the National Academy of Sciences of the USA.* 2020;117:22430-22435.
30. Majra D, Benson J, Pitts J, Stebbing J. SARS-CoV-2 (COVID-19) superspreader events. *Journal of Infection*. 2021;82:36-40.
31. Bueno de Mesquita PJ, Noakes CJ, Milton DK. Quantitative aerobiologic analysis of an influenza human challenge-transmission trial. *Indoor Air*. 2020;30:1189-1198.
32. Asadi S, Wexler AS, Cappa CD, Barreda S, Bouvier NM, Ristenpart WD. Aerosol emission and superemission during human speech increase with voice loudness. *Scientific Reports*. 2019;9:2348.
33. Buckland FE, Bynoe ML, Tyrrell DAJ. Experiments on the spread of colds. II. Studies in volunteers with coxsackievirus A21. *Journal of Hygiene*. 1965;63:327-343.
34. Riley EC, Murphy G, Riley RL. Airborne spread of measles in a suburban elementary school. *American Journal of Epidemiology*. 1978;107:421-432.
35. Riley S, Fraser C, Donnelly CA, et al. Transmission dynamics of the etiological agent of SARS in Hong Kong: Impact of public health interventions. *Science*. 2003;300:1961-1966.
36. Glass LM, Glass, RJ. Social contact networks for the spread of pandemic influenza in children and teenagers. *BMC Public Health*. 2008;8:61.
37. Park SY, Kim Y-M, Yi S, et al. Coronavirus disease outbreak in call center, South Korea. *Emerging Infectious Diseases*. 2020;26:1666-1670.
38. Bae S, Kim H, Jung T-Y, et al. Epidemiological characteristics of COVID-19 outbreak at fitness centers in Cheonan, Korea. *Journal of Korean Medical Science*. 2020;35:e288.

39. Kwon K-S, Park J-I, Park YJ, Jung D-M, Ryu K-W, Lee J-H. Evidence of long-distance droplet transmission of SARS-CoV-2 by direct air flow in a restaurant in Korea. *Journal of Korean Medical Science*. 2020;35:e415.
40. de Man P, Paltansing S, Ong DSY, Vaessen N, van Nielen G, Koeleman JGM. Outbreak of coronavirus disease 2019 (COVID-2019) in a nursing home associated with aerosol transmission as a result of inadequate ventilation. *Clinical Infectious Diseases*. 2020;DOI:10.1093/cid/ciaa1270.
41. Li Y, Qian H, Hang J, et al. Probable airborne transmission of SARS-CoV-2 in a poorly ventilated restaurant. *Building and Environment*. 2021;196:107788.
42. Xu P, Jia W, Qian H, et al. Lack of cross-transmission of SARS-CoV-2 between passenger's cabins on the *Diamond Princess* cruise ship. *Building and Environment*. 2021;198:107839.
43. Vernez D, Schwarz S, Sauvain J-J, Petignat C, Suarez G. Probable aerosol transmission of SARS-CoV-2 in a poorly ventilated courtroom. *Indoor Air*. 2021;doi:10.1111/ina.12866.
44. Madewell ZJ, Yang Y, Longini Jr IM, Halloran ME, Dean NE. Household transmission of SARS-CoV-2: A systematic review and meta-analysis. *JAMA Network Open*. 2020;3:e2031756.
45. Collins FS. No longer just looking under the lamppost. *American Journal of Human Genetics*. 2006;79:421-426.
46. Seto WH. Airborne transmission and precautions: facts and myths. *Journal of Hospital Infection*. 2015;89:225-228.
47. Randall K, Ewing ET, Marr LC, Jimenez JL, Bourouiba L. How did we get here: What are droplets and aerosols and how far do they go? A historical perspective on the transmission of respiratory infectious diseases (April 15, 2021). SSRN:https://ssrn.com/abstract=3829873.
48. Hofmann W. Modelling inhaled particle deposition in the human lung — A review. *Journal of Aerosol Science*. 2011;42:693-724.
49. Beard KV. Terminal velocity and shape of cloud and precipitation drops aloft. *Journal of the Atmospheric Sciences*. 1976;33:851-864.
50. Bourouiba L. Turbulent gas clouds and respiratory pathogen emissions: Potential implications for reducing transmission of COVID-19. *JAMA*. 2020;323:1837-1838.
51. Tang JW, Liebner TJ, Craven BA, Settles GS. A schlieren optical study of the human cough with and without wearing masks for aerosol infection control. *Journal of the Royal Society Interface*. 2009;6:S727-S736.
52. Tang JW, Nicolle ADG, Pantelic J et al. Qualitative real-time schlieren and shadowgraph imaging of human exhaled airflows: An aid to aerosol infection control. *PLoS One*. 2011;6:e21392.
53. Chen C, Lin C-H, Jiang Z, Chen Q. Simplified models for exhaled airflow from a cough with the mouth covered. *Indoor Air*. 2014;24:580-591.
54. Wells WF. On air-borne infection. Study II. Droplets and droplet nuclei. *American Journal of Epidemiology*. 1934;20:611-618.
55. Liu L, Wei J, Li Y, Ooi A. Evaporation and dispersion of respiratory droplets from coughing. *Indoor Air*. 2017;27:179-190.
56. Walker JS, Archer J, Gregson FKA, Michel SES, Bzdek BR, Reid JP. Accurate representations of the microphysical processes occurring during the transport of exhaled aerosols and droplets. *ACS Central Science*. 2021;7:200-209.

57. Marr LC, Tang JW, Van Mullekom J, Lakdawala SS. Mechanistic insights into the effect of humidity on airborne influenza virus survival, transmission and incidence. *Journal of the Royal Society Interface*. 2019;16:20180298.
58. Netz RR. Mechanisms of airborne infection via evaporating and sedimenting droplets produced by speaking. *Journal of Physical Chemistry B*. 2020;124:7093-7101.
59. Lieber C, Melekidis S, Koch R, Bauer H-J. Insights into the evaporation characteristics of saliva droplets and aerosols: Levitation experiments and numerical modeling. *Journal of Aerosol Science*. 2021;154:105760.
60. Riley RL. Airborne infection. *American Journal of Medicine*. 1974;57:466-475.
61. Warfel JM, Beren J, Merkel TJ. Airborne transmission of *Bordetella pertussis*. *Journal of Infectious Diseases*. 2012;206:902-906.
62. Johnson GR, Morawska L. The mechanism of breath aerosol formation. *Journal of Aerosol Medicine and Pulmonary Drug Delivery*. 2009;22:229-237.
63. Duguid JP. The size and the duration of air-carriage of respiratory droplets and droplet nuclei. *Journal of Hygiene*. 1946;44:471-479.
64. Han ZY, Weng WG, Huang QY. Characterizations of particle size distribution of the droplets exhaled by sneeze. *Journal of the Royal Society Interface*. 2013;10:20130560.
65. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nature Medicine*. 2020;26:672-675.
66. Lindsley WG, Blachere FM, Beezhold DH, et al. Viable influenza A virus in airborne particles expelled during coughs versus exhalations. *Influenza and Other Respiratory Viruses*. 2016;10:404-413.
67. Buonanno G, Stabile L, Morawska L. Estimation of airborne viral emission: Quanta emission rate of SARS-CoV-2 for infection risk assessment. *Environment International*. 2020;141:105794.
68. Wölfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. *Nature*. 2020;581:465-469.
69. Pan Y, Zhang D, Yang P, Poon LLM, Wang Q. Viral load of SARS-CoV-2 in clinical samples. *Lancet Infectious Diseases*. 2020;20:411-412.
70. To KK-W, Tsang OT-Y, Leung W-S, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infectious Diseases*. 2020;20:565-574.
71. Baron A, Hachem M, Van Nhieu JT, et al. Bronchoalveolar lavage in patients with COVID-19 with invasive mechanical ventilation for acute respiratory distress syndrome. *Annals of the American Thoracic Society*. 2021;18:723-726.
72. Hou YJ, Okuda K, Edwards CE, et al. SARS-CoV-2 reverse genetics reveals a variable infection gradient in the respiratory tract. *Cell*. 2020;182:429-446.
73. Jensen PA, O'Brien D. Industrial Hygiene. In Willeke K, Baron PA, eds. *Aerosol Measurement: Principles, Techniques, and Applications.* New York: Van Nostrand Reinhold. 1993:537-559.
74. Guo Y, Wei J, Ou C, et al. Deposition of droplets from the trachea or bronchus in the respiratory tract during exhalation: A steady-state numerical investigation. *Aerosol Science and Technology*. 2020; 54:869-879.
75. USEPA. Inhalation rates. Chapter 6. In: *Exposure Factors Handbook*. United States Environmental Protection Agency; 2011.

76. Gammaitoni L, Nucci MC. Using a mathematical model to evaluate the efficacy of TB control measures. *Emerging Infectious Diseases*. 1997;3:335-342.
77. Bennett DH, McKone TE, Evans JS. Defining intake fraction. *Environmental Science & Technology*. 2002;36:206A-211A.
78. Rudnick SN, Milton DK. Risk of indoor airborne infection transmission estimated from carbon dioxide concentration. *Indoor Air*. 2003;13:237-245.
79. Melikov AK, Ai ZT, Markov DG. Intermittent occupancy combined with ventilation: An efficient strategy for the reduction of airborne transmission indoors. *Science of the Total Environment*. 2020;744:140908.
80. Thatcher TL, Lai ACK, Moreno-Jackson R, Sextro RG, Nazaroff WW. Effects of room furnishings and air speed on particle deposition rates indoors. *Atmospheric Environment*. 2002;36:1811-1819.
81. Nazaroff WW. Inhalation intake fraction of pollutants from episodic indoor emissions. *Building and Environment*. 2008;43:269-277.
82. Chu DK, Akl EA, Duda S, et al. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. *Lancet*. 2020;395:1973-1987.
83. Olmedo I, Nielsen PV, Ruiz de Adana M, Jensen RL, Grzelecki P. Distribution of exhaled contaminants and personal exposure in a room using three different air distribution strategies. *Indoor Air*. 2012;22:64-76.
84. Chen C, Zhao B, Lai D, Liu W. A simple method for differentiating direct and indirect exposure to exhaled contaminants in mechanically ventilated rooms. *Building Simulation*. 2018;11:1039-1051.
85. Liu L, Li Y, Nielsen PV, Wei J, Jensen RL. Short-range airborne transmission of expiratory droplets between two people. *Indoor Air*. 2017;27:452-462.
86. Qian H, Li Y, Nielsen PV, Hyldgaard CE. Dispersion of exhalation pollutants in a two-bed hospital ward with a downward ventilation system. *Building and Environment*. 2008;43:344-354.
87. Nielsen PV, Li Y, Buus M, Winther FV. Risk of cross-infection in a hospital ward with downward ventilation. *Building and Environment*. 2010;45:2008-2014.
88. Bjørn E, Nielsen PV. Dispersal of exhaled air and personal exposure in displacement ventilated rooms. *Indoor Air*. 2002;13:147-164.
89. Murakami S. Analysis and design of micro-climate around the human body with respiration by CFD. *Indoor Air*. 2004;14(Suppl 7):144-156.
90. Abkarian M, Mendez S, Xue N, Yang F, Stone HA. Speech can produce jet-like transport relevant to asymptomatic spreading of virus. *Proceedings of the National Academy of Sciences of the USA.* 2020;117:25237-25245.
91. Tang JW, Nicolle AD, Klettner CA, et al., Airflow dynamics of human jets: Sneezing and breathing – potential sources of infectious aerosols. *PLoS One*. 2013;8:e59970.
92. Xu C, Nielsen PV, Liu L, Jensen RL, Gong G. Human exhalation characterization with the aid of schlieren imaging technique. *Building and Environment*. 2017;112:190-199.
93. Gupta JK, Lin C-H, Chen Q. Flow dynamics and characterization of a cough. *Indoor Air*. 2009;19:517-525.

94. Gupta JK, Lin C-H, Chen Q. Characterizing exhaled airflow from breathing and talking. *Indoor Air*. 2010;20:31-39.
95. Bourouiba L, Dehandschoewercker E, Bush JWM. Violent expiratory events: on coughing and sneezing. *Journal of Fluid Mechanics*. 2014;745:537-563.
96. Xu C, Nielsen PV, Gong G, Liu L, Jensen RL. Measuring the exhaled breath of a manikin and human subjects. *Indoor Air*. 2015;25:188-197.
97. Licina D, Pantelic J, Melikov A, Sekhar C, Tham KW. Experimental investigation of the human convective boundary layer in a quiescent indoor environment. *Building and Environment*. 2014;75:79-91.
98. Gena AW, Voelker C, Settles GS. Qualitative and quantitative schlieren optical measurement of the human thermal plume. *Indoor Air*. 2020;30:757-766.
99. Craven BA, Settles GS. A computational and experimental investigation of the human thermal plume. *Journal of Fluids Engineering*. 2006;128:1251-1258.
100. Sun S, Li J, Han J. How human thermal plume influences near-human transport of respiratory droplets and airborne particles: a review. *Environmental Chemistry Letters*. 2021;19:1971-1982.
101. Licina D, Melikov A, Sekhar C, Tham KW. Human convective boundary layer and its interaction with room ventilation flow. *Indoor Air*. 2015;25:21-35.
102. Ma J, Qian H, Nielsen PV, Liu L, Li Y, Zheng X. What dominates personal exposure? Ambient airflow pattern or local human thermal plume. *Building and Environment*. 2021;196:107790.
103. Bhagat RK, Davies Wykes MS, Dalziel SB, Linden PF. Effects of ventilation on the indoor spread of COVID-19. *Journal of Fluid Mechanics*. 2020;903:F1. DOI:10.1017/jfm.2020.720.
104. Li Y. The secret behind the mask. *Indoor Air*. 2011;21:89-91.
105. Verma S, Dhanak M, Frankenfield J. Visualizing the effectiveness of face masks in obstructing respiratory jets. *Physics of Fluids*. 2020;32:061708.
106. Grinshpun SA, Haruta H, Eninger RM, Reponen T, McKay RT, Lee S-A. Performance of an N95 filtering facepiece particulate respirator and a surgical mask during human breathing: Two pathways for particle penetration. *Journal of Occupational and Environmental Hygiene.* 2009;6:593-603.
107. Lai ACK, Poon CKM, Cheung ACT. Effectiveness of facemasks to reduce exposure hazards for airborne infections among general populations. *Journal of the Royal Society Interface*. 2012;9:938-948.
108. Cowling BJ, Zhou Y, Ip DKM, Leung GM, Aiello AE. Face masks to prevent transmission of influenza virus: a systematic review. *Epidemiology and Infection*. 2010;138:449-456.
109. Shakya KM, Noyes A, Kallin R, Peltier RE. Evaluating the efficacy of cloth facemasks in reducing particulate matter exposure. *Journal of Exposure Science and Environmental Epidemiology*. 2017;27:352-357.
110. Leung NHL, Chu DKW, Shiu EYC, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nature Medicine*. 2020;26:676-680.
111. Asadi S, Cappa CD, Barreda S, Wexler AS, Bouvier NM, Ristenpart WD. Efficacy of masks and face coverings in controlling outward aerosol particle emission from expiratory activities. *Scientific Reports*. 2020;10:15665.
112. Licina D, Morrison GC, Bekö G, Weschler CJ, Nazaroff WW. Clothing-mediated exposures to chemicals and particles. *Environmental Science & Technology*. 2019;53:5559-5575.

113. Konda A, Prakash A, Moss GA, Schmoldt M, Grant GD, Guha S. Aerosol filtration efficiency of common fabrics used in respiratory cloth masks. *ACS Nano*. 2020;14:6339-6347.
114. Pan J, Harb C, Leng W, Marr LC. Inward and outward effectiveness of cloth masks, a surgical mask, and a face shield. *Aerosol Science and Technology*. 2021;55:718-733.
115. Howard J, Huang A, Li Z, et al. An evidence review of face masks against COVID-19. *Proceedings of the National Academy of Sciences of the USA*. 2021;118:e2014564118.
116. Nazaroff WW. Indoor particle dynamics. *Indoor Air*. 2004;14(Suppl 7):175-183.
117. Nazaroff WW. Indoor bioaerosol dynamics. *Indoor Air*. 2016;26:61-78.
118. Chin AWH, Chu JTS, Perera MRA, et al. Stability of SARS-CoV-2 in different environmental conditions. *Lancet Microbe*. 2020;1:e10.
119. Marquès M, Domingo JL. Contamination of inert surfaces by SARS-CoV-2: Persistence, stability and infectivity. A review. *Environmental Research*. 2021;193:110559.
120. Qian J, Peccia J, Ferro AR. Walking-induced particle resuspension in indoor environments. *Atmospheric Environment*. 2014;89:464-481.
121. Licina D, Tian Y, Nazaroff WW. Emission rates and the personal cloud effect associated with particle release from the perihuman environment. *Indoor Air*. 2017;27:791-802.
122. Licina D, Nazaroff WW. Clothing as a transport vector for airborne particles: Chamber study. *Indoor Air*. 2018;28:404-414.
123. Duguid JP, Wallace AT. Air infection with dust liberated from clothing. *Lancet*. 1948;252:845-849.
124. Stephens B, Azimi P, Thoemmes MS, Heidarinejad M, Allen JG, Gilbert JA. Microbial exchange via fomites and implications for human health. *Current Pollution Reports*. 2019;5:198-213.
125. Asadi S, Gaaloul ben Hnia N, Barre RS, Wexler AS, Ristenpart WD, Bouvier NM. Influenza A virus is transmissible via aerosolized fomites. *Nature Communications.* 2020;11:4062.
126. D'Amato G, Vitale C, D'Amato M, et al. Thunderstorm-related asthma: what happens and why. *Clinical & Experimental Allergy*. 2016;46:390-396.
127. Loevinger L. Standards of proof in science and law. *Jurimetrics*. 1992;32:323-344.
128. Li Y, Leung GM, Tang JW, et al. Role of ventilation in airborne transmission of infectious agents in the built environment — a multidisciplinary systematic review. *Indoor Air*. 2007;17:2-18.