Received: 26 February 2016 | Accepted: 7 June 2016
DOI: 10.1111/ina.12314

ORIGINAL ARTICLE

WILEY

Short-range airborne transmission of expiratory droplets between two people

L. Liu[1,2] | Y. Li[1] | P. V. Nielsen[2] | J. Wei[1] | R. L. Jensen[2]

[1]Department of Mechanical Engineering, The University of Hong Kong, Hong Kong SAR, China

[2]Department of Civil Engineering, Aalborg University, Aalborg SV, Denmark

Correspondence
Yuguo Li, Department of Mechanical Engineering, The University of Hong Kong, Hong Kong SAR, China.
Email: liyg@hku.hk

Abstract

The occurrence of close proximity infection for many respiratory diseases is often cited as evidence of large droplet and/or close contact transmission. We explored interpersonal exposure of exhaled droplets and droplet nuclei of two standing thermal manikins as affected by distance, humidity, ventilation, and breathing mode. Under the specific set of conditions studied, we found a substantial increase in airborne exposure to droplet nuclei exhaled by the source manikin when a susceptible manikin is within about 1.5 m of the source manikin, referred to as the proximity effect. The threshold distance of about 1.5 m distinguishes the two basic transmission processes of droplets and droplet nuclei, that is, short-range modes and the long-range airborne route. The short-range modes include both the conventional large droplet route and the newly defined short-range airborne transmission. We thus reveal that transmission occurring in close proximity to the source patient includes both droplet-borne (large droplet) and short-range airborne routes, in addition to the direct deposition of large droplets on other body surfaces. The mechanisms of the droplet-borne and short-range airborne routes are different; their effective control methods also differ. Neither the current droplet precautions nor dilution ventilation prevents short-range airborne transmission, so new control methods are needed.

KEYWORDS
building ventilation, interpersonal exposure, large droplet transmission, respiratory infection, short-range airborne route

1 | INTRODUCTION

Considerable uncertainty exists regarding the relative importance of airborne, large droplet, and contact transmission of respiratory viruses. This probably explains why some leading authorities have made contradictory recommendations about intervention methods for influenza, SARS, and other respiratory diseases. For example, during the 2009 H1N1 influenza epidemics, WHO[1] recommended the use of low-filtration efficiency surgical masks by healthcare workers, but the Institute of Medicine (IOM)[2] recommended the use of high-filtration efficiency N95 respirators.

There is also significant disagreement between theory and empirical experiences in the medical community with regard to transmission routes for some respiratory infections such as influenza. The generally accepted definition of airborne infection is the passage of microorganisms from a source patient to a susceptible individual through fine droplets or droplet nuclei (<5 μm in diameter), resulting in infection and consequent disease. Droplet infection occurs via large droplets (≥5 μm), which are propelled and directly deposited on the nasal or oral mucosa of the susceptible. Respiratory infection is observed to occur mostly in close proximity to the source patient (Fig. 1a), which is often cited as evidence for large droplet and close contact transmission.[3] Observed transmission of disease between people separated by more than 2 m is often used as evidence for airborne transmission.[4,5] On the other hand, a modeling study by Atkinson and Wein[6] suggested transmission by fine droplets or droplet nuclei (<5 μm diameter) was

the dominant mode for influenza, while Nicas and Jones[7] found that that it is as important as hand contact and close contact. Such disagreement has yet to be addressed in a convincing manner.

Our quantification of the proximity effect in this article may challenge the traditional association between the large droplet route and close proximity infection, and associated intervention methods. The concept of droplet spray infection originates from the findings of Flugge[8] that expiratory droplets contained bacteria and could not travel more than 1–2 m (Fig. 1b); this was further postulated by Chapin[9] and Wells.[10] Simple theoretical analysis[5] confirms that large droplets generally travel up to 1.5 m. Therefore, large droplet transmission, if it exists, would mostly occur within the first 1.5 m. The large droplet precaution would be effective because surgical masks are effective in filtering out large droplets. Although large droplet transmission is widely accepted and the large droplet precaution widely practiced, there has not been any detailed study of the amount of droplets that can be deposited on the mucous membranes of a susceptible individual within 1.5 m of the source patient, which is to be explored here. The proximity effect of airborne exposure refers to the substantial increase in airborne exposure when a susceptible individual is within 1.5 m of the source patient (Fig. 1c). Our interpretation is that this proximity effect suggests the short-range airborne transmission can potentially exist in any observed close proximity infection, in addition to large droplet transmission. Nicas and Jones[7] also argued that close contact permits droplet spray exposure and maximizes inhalation exposure to droplet nuclei and inspirable droplets.

Practical Implications

- Our short-range airborne route findings could potentially be used to improve understanding of the mechanisms of disease transmission. If the existence of the short-range airborne route can be confirmed further, the existing droplet precautions alone for close contact transmission are no longer valid for some diseases such as influenza, and there is a need to develop efficient short-range airborne disease transmission control methods in hospitals and in the community at large.

We thus hypothesized that infection occurring in close proximity to the source patient includes both large droplet-borne and short-range airborne routes. To explore such a hypothesis, we propose studying the interpersonal transport of expiratory droplets and droplet nuclei.

1.1 | Expiratory droplets and droplet nuclei

Human expiratory droplets are produced by the atomization of human secretions along the airway.[11] Droplets can contain elements such as sodium, potassium, and chloride in solutes and DNA, lipids, glycoproteins, and proteins in the suspended insoluble solids.[12–14] Xie et al.[15] measured and summarized the number and size distribution

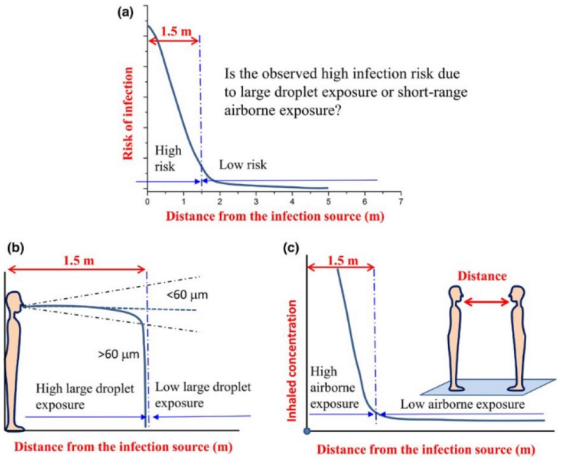

FIGURE 1 (a) Illustration of the qualitative relationship between infection risk and distance from the infection source based on data from Lidwell and Williams,[45] Kowalski and Bahnfleth,[44] and Wong et al.[56] (b) Illustration of the trajectory of respiratory droplets in an exhalation jet.[5] (c) Illustration of the inhaled tracer gas concentration of the receiving manikin as a function of distance from the exhaled manikin based on data from Nielsen et al.[33] and this study

of exhaled droplets using the measured data of Duguid[16,17] Louden and Roberts,[18] and Papineni and Rosenthal[19] and found substantial inconsistencies. Breathing, coughing, and sneezing can release thousands of droplets per respiration, with a wide size spectrum from submicrons to millimeters. Once exhaled, droplets evaporate and become droplet nuclei.[10] The size of the droplet nuclei was found to depend on droplet composition and humidity.[20,21] Hence, we consider the formation of droplet nuclei in our computer modeling study below.

1.2 | Exposure of exhaled substances between people

Some studies exist, but studies considering distance as a parameter are limited. Exposure between two face-to-face breathing thermal manikins was first measured by Bjørn and Nielsen[22] in a room with displacement ventilation. Qian et al.[23] extended this study to two recumbent patients in a ward. Computational fluid dynamics (CFD) simulations have also been carried out in a number of studies, for example, Gao and Niu[24] for two seated persons. The dispersion of expiratory droplets in an aircraft cabin was presented by Sze To et al.,[25] Wan et al.,[26] and Gupta et al.[27]; dispersion was also studied in a high-speed rail cabin by Zhang et al.[28]; in hospital rooms by Chao et al.[29]; and in office rooms by Zhu et al.,[30] Chen and Zhao,[31] and Licina et al.,[32] among others. Nielsen et al.[33] measured the interpersonal exposure with distances up to 1.2 m, and the maximum distance is 1.1 m in the studies by Olmedo et al.[34,35] This study is to extend the distance to 3.0 m and to investigate the exposure to both large and small droplets.

2 | METHODOLOGY

The physical process for droplet exposure includes release by the source patient, transport and evaporation in air, and finally capture by the susceptible individual. Interpersonal transport of droplets involves at least three length scales: dispersion and evaporation of droplets at 1–100 μm, exhalation flows and human body plumes at 0.1–1 m, and the indoor environment at 1–10 m. We explore the droplet exposure between two people using both full-scale laboratory experiments and computer simulations.

2.1 | Full-scale laboratory experiment setup

Our experiments were carried out in a full-scale environmental test room of 4.2 m (length) × 3.2 m (width) × 2.7 m (height) (Fig. 2). The room was ventilated by displacement or mixing at a rate of 5.6 air changes per hour. A 600 W radiator was used to enhance the thermal stratification. Two breathing thermal manikins stood face-to-face symmetrically with varying distances (Fig. 2a). The manikin in red represented the source patient, and the other in gray represented the susceptible individual. Both manikins were used in our earlier studies[22,23,36]; they are 1.7 m tall and represent an average-sized woman. The total surface area of each manikin without clothes is 1.44 m^2. An artificial lung was used in each of the manikins to generate periodical breathing. The breathing frequency was 15 times/min for both, with a pulmonary ventilation rate of 10 L/min for the susceptible manikin and about 11 L/min for the source manikin. During each breathing period, both manikins exhaled for 2 s and then inhaled for 2 s. The two nose airflow jets were positioned 30° apart and were tilted toward the chest at an angle of 45°. The mouth outflow was roughly horizontal. The areas of the nose and mouth openings were 100 mm^2 each. The body temperature of the two manikins was between 29.0 to 32.0°C and controlled by a computer. The total heat power of each manikin is 102 W.

N_2O was used as a tracer gas to represent the exhaled fine droplet nuclei (<5 μm). The N_2O volume fraction of the exhaled air by the source manikin was around 4%, which is approximately the CO_2 concentration in exhaled air from a human.[37] The concentration distribution was measured by two INNOVA Multi-gas Samplers 1303 (6×2=12 channels) and one INNOVA Multi-gas Monitor 1412 [±10%,

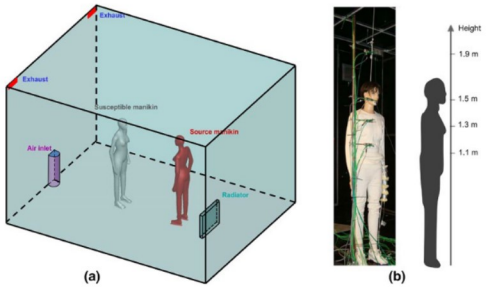

FIGURE 2 (a) Breathing thermal manikins standing face-to-face in the test room with a radiator, an air inlet and two exhausts. When the room is used for mixing ventilation, the supply and exhaust openings are swapped. (b) The locations of concentration samplers (2, 3, 4, and 5 in Fig. S1) along the susceptible manikin are at 1.1, 1.3, 1.5, and 1.9 m

LumaSense Technologies, Ballerup, Denmark]. A number of existing studies demonstrate the validity of using tracer gas as a surrogate for fine droplet nuclei (<5 μm).[38] The transport of tracer gas cannot reveal the dispersion of large droplets. The transport of large droplets and droplet nuclei was investigated by CFD simulations.

Other details of the measurement including locations are provided in Supporting Information and Fig. S1.

Twenty-eight (28) tests were conducted to investigate the effects of breathing mode, relative manikin height, thermal plume, separation distance, and exhalation synchronization on the interpersonal transport of expiratory fine droplet nuclei. The parameters of each test are listed in Table 1.

2.2 | CFD simulations

The airflows as well as the dispersion and evaporation of exhaled droplets in the same test room were also simulated by CFD. Two computer manikins were constructed to represent the source and the susceptible individuals, as shown in Fig. 3a. Other details of the CFD methods are presented in Supporting Information.

Twenty-one (21) tests were conducted to investigate the impact of droplet initial size, ambient humidity, ventilation conditions, distance, and synchronization of exhalation airflows on the interpersonal transport of expiratory droplets and droplet nuclei. The test conditions are listed in Table 2. We denote each scenario as Case # [droplet size/gas, ventilation mode, ACH, RH, distance, phase difference]. For example, Scenario 5 is referred to as Case 5 [1 μm, mixing, 5.6 ACH, 35%, 0.8 m, 0]. Our CFD simulations considered only breathing (not coughing or sneezing) for both the source and susceptible (see Fig. S2). We first conducted tests of four cases (scenarios 1–4 in Table 2) with a tracer gas in exhalation to compare with the experimental data. The air change rate was 5.6 air changes per hour. The inlet air temperature was 16.0°C.

Simulations for scenarios 5–21 were also repeated in the same large room (6 m×6.7 m×2.7 m) as in Qian and Li,[38] which is more suitable for investigating a distance of 3 m. A large test room can minimize the

TABLE 1 Test lists of exposure measurements. Full set of distance = [0.5, 0.8, 1.0, 1.5, 2.0, 2.5, 3.0 m]

Test no.	Source breathing mode	Susceptible breathing mode	Susceptible heating	Manikin heights	Distance (m)
1–7	Mouth inhalation/exhalation	Mouth inhalation/exhalation	Yes	Same	Full set
8–14	Nose inhalation/exhalation	Mouth inhalation/exhalation	Yes	Same	Full set
15–21	Coughing	Mouth inhalation/exhalation	Yes	Same	Full set
22	Mouth inhalation/exhalation	Mouth inhalation/exhalation	No	Same	0.8
23	Mouth inhalation/exhalation	Mouth inhalation/exhalation	Yes	Source 0.15 m taller	0.8
24	Mouth inhalation/exhalation	Mouth inhalation/exhalation	Yes	Susceptible 0.15 m taller	0.8
25	Mouth inhalation/exhalation	Mouth inhalation only, no exhalation	Yes	Same	0.8
26	Nose inhalation/exhalation	Mouth inhalation only, no exhalation	Yes	Same	0.8
27	Coughing	Mouth inhalation only, no exhalation	Yes	Same	0.8
28	Mouth inhalation/exhalation	Mouth inhalation/exhalation Phase difference = π	Yes	Same	0.8

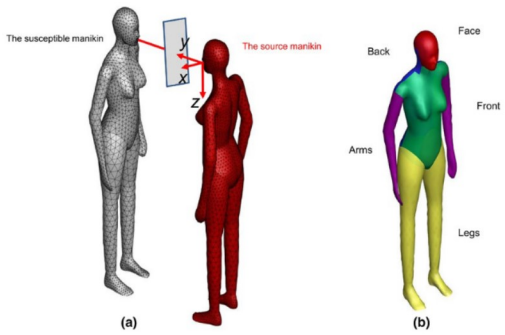

FIGURE 3 (a) Two life-sized 3D manikins used in our CFD analyses. (b) Body parts of the susceptible manikin. A Cartesian coordinate with source manikin's mouth as the origin is also shown for studying the dispersion of droplets

TABLE 2 List of CFD simulation scenarios

Scenario no.	Droplet size (μm) or gas	Ventilation mode	Ventilation rate (ACH)	RH (%)	Distance (m)	Phase difference
1	N_2O	Displacement	5.6	35	0.5	0
2	N_2O	Displacement	5.6	35	1.0	0
3	N_2O	Displacement	5.6	35	1.5	0
4	N_2O	Displacement	5.6	35	2.0	0
5	1	Mixing	5.6	35	0.8	0
6	25	Mixing	5.6	35	0.8	0
7	50	Mixing	5.6	35	0.8	0
8	100	Mixing	5.6	35	0.8	0
9	100	Mixing	5.6	95	0.8	0
10	100	Mixing	3.0	35	0.8	0
11	100	Displacement	5.6	35	0.8	0
12	100	Displacement	5.6	35	0.5	0
13	100	Displacement	5.6	35	1.0	0
14	100	Displacement	5.6	35	1.5	0
15	100	Displacement	5.6	35	3.0	0
16	1	Mixing	5.6	35	0.8	π/2
17	25	Mixing	5.6	35	0.8	π/2
18	50	Mixing	5.6	35	0.8	π/2
19	100	Mixing	5.6	35	0.8	π/2
20	100	Mixing	5.6	35	0.8	π
21	100	Mixing	5.6	35	0.8	3π/2

impact of the test room geometry. The room setup is similar to Fig. 2a, with the air inlet at the bottom of the wall behind the source "patient," and three exhausts at the top wall behind the susceptible individual.

2.3 | Susceptible exposure index

Following Qian and Li,[38] we define an exposure index for the susceptible individual to quantify the relative intake of droplet nuclei, exhaled by the source patient.[39] The susceptible exposure index is defined as $\varepsilon_i = ((C_i - C_s)/(C_r - C_s))$, where C_r, C_i, and C_s are concentrations at the exhaust (return), in the inhaled air of the susceptible individual (i.e., receiving individual) and at supply, respectively. The average concentration of four breathing cycles (16 s) is used. The tracer gas (N_2O) concentration of the supply air was zero (0) in our experiments or simulations, thus $\varepsilon_i = (C_i/C_r)$. Note that the susceptible exposure index is a reciprocal of the commonly used "local ventilation index"; see Qian et al.[23] and Mundt et al.[40] A high susceptible exposure index also means a high exposure by the susceptible individual to the airborne substances exhaled by the source patient. If the susceptible exposure index is unity (1), the air in the room was fully mixed. In this study, the susceptible exposure index is also extended to the general exposure index $\varepsilon = ((C - C_s)/(C_r - C_s))$, where the concentration C can be the concentration at any point in the room.

Computer simulations allow us to count how many droplets or droplet nuclei deposit on any surface. We divide the surface of the susceptible manikin into five parts, that is, the face, front, arms, legs, and back (Fig. 3b). In each simulation, the number of droplets/droplet nuclei inhaled or deposit on these body parts was observed to vary in each test due to turbulence. Hence, we performed three simulations for each scenario, and the average values from three repeated simulations are presented here.

3 | RESULTS

3.1 | The proximity effect—a substantial increase in airborne exposure at 1.5 m proximity to the source patient

Figure 4 summarizes the measured exposure of the susceptible manikin as a function of the distance to the source manikin. The data of Nielsen et al.[33] are also included in Fig. 4. The trend agrees well with our new data; however, their distance was limited to 1.2 m. In theory, the susceptible exposure index is unity (1) at a remote distance to the source manikin, if the room air is fully mixed. In some tests, a displacement flow pattern was created; hence, the susceptible exposure index can be smaller than unity (1) at a remote distance. On the other hand, the susceptible exposure index can be as high as seven times of that at the remote distance when the source manikin exhales by mouth. When the source and susceptible manikins are of the same height, stand face-to-face, and both breathe by mouth, we observed the highest interpersonal exposure at close proximity. Interestingly,

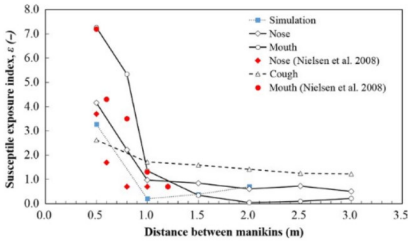

FIGURE 4 Exposure index as a function of distance between two manikins. Test cases 1–21 (see Table 1) and simulation scenarios 1–5 (see Table 2, corresponding to test cases 1, 3, 4, and 5 in Table 1) are presented. The average value during a sampling interval of 4 minutes is presented. Under displacement ventilation, the exposure index could drop below unit. The mouth or nose in the legend refers to the breathing mode of the source manikin

the mouth-breathing situation leads to a rapid decay of exposure as the distance increases. The situation of coughing deserves special attention. We experienced difficulties in obtaining a steady-state condition when the source manikin coughs. The tracer gas concentration at the exhaust fluctuates. Coughing is shown to lead to further penetration of the exhaled air stream and hence can extend the range of the proximity distance. For coughing, the susceptible exposure index remains higher than unity, even at a distance of 3 m. This is quite different from the results by Pantelic et al.[41] that exposure to cough drops dramatically with the distance. Reasons for the mild decrease in exposure risk in our study are probably that the tracer gas is used instead of particles and that there is the trapping phenomenon under the displacement ventilation.

Figure 4 shows that the exposure is very high at a close distance (within the first meter), and decreases rapidly to the room average data when the distance increases to 1 m. Direct exposure took place in most situations within 1 m. We refer to this as the short-range airborne exposure. At the closest distance that we studied (0.5 m), exhaled droplets and droplet nuclei (tracer gas as the surrogate in our study) penetrate both the exhalation jet and the thermal plume of the susceptible manikin. The susceptible manikin is directly exposed to the droplets and droplet nuclei exhaled by the index patient. At 0.8 m, droplets and droplet nuclei travel upwards across the susceptible individual. The exposure of the susceptible individual is lower than when the distance is 0.5 m.

Four simulated cases with breathing by mouth are also included in Fig. 4 for comparison. The simulation data reveal the same pattern of airborne exposure being high when two manikins stand close together and decrease as they stand further apart. Note that the exposure predicted by CFD simulations was lower than that measured in the full-scale test room at a separation distance of 0.5 and 1.0 m. There is a high risk of direct exposure when the distance between two manikins is <1 m. Within 1 m, exposure decreases dramatically with increasing distance between the two manikins. It appears that the transition from close contact transmission to long-range airborne occurs from 1 to 1.5 m between two manikins. Beyond 1.5 m, the exposure index drops below unit, so 1.5 m is defined as the threshold value in our study. Breathing through the mouth or nose generates different exposures at a close distance.

Obviously, the number of people, respiratory, and room airflow parameters has an impact on interpersonal exposure. The use of manikins allowed us to carry out a number of experimental tests to study the impact of human thermal plume, human height, the distance between the index patient and the susceptible individual and the exhalation modes, for example, breathing by mouth, breathing through the nose, coughing.

Measured susceptible exposure indexes for a standard distance of 0.8 m are summarized in Table 3. Comparisons are made with the two reference cases of using mouth and nose breathing to illustrate the impact of an individual parameter. Three observations can be made as follows:

First, it came as a surprise that coughing did not introduce a high susceptible airborne exposure index. This is attributed to the fact that the coughing airflow reaches the susceptible manikin quickly, so there is only a short time (<0.5 s) for the susceptible manikin to inhale directly from the coughing jet. Furthermore, the entrainment of the surrounding cleaner air is also greater for an exhalation flow, which dilutes the concentration of droplets in the coughing jet.

Second, exposure is expected to be influenced by the interaction between the breathing jet from the source manikin and the inhalation region of the susceptible manikin. The thermal plume plays a protective role for the susceptible manikin at a close distance, for example, 0.8 m. Without a thermal plume above the susceptible manikin's body, exposure was found to increase during nasal breathing under the investigated conditions (Table 3). The thermal plume prevents the penetration of the exhalation flow from the source manikin and dilutes it before it reaches the breathing zone of the susceptible manikin.

Third, as shown by the smoke visualization (Fig. S3), the difference in heights of two manikins at a close distance may directly influence

TABLE 3 The measured normalized exposure by the susceptible manikin under different manikin parameters when the distance between the source manikin and the susceptible manikin is 0.8 m

	Susceptible exposure index $\varepsilon_i = (C_i/C_r)$	
Parameter changed	from mouth of source manikin	from nose of source manikin
The source manikin breathing	5.34	2.22
The source manikin coughing	1.76	
The susceptible manikin without thermal plume	6.42	4.89
The susceptible manikin is 0.15 m taller	6.97	2.42
The susceptible manikin is 0.15 m shorter	0.31	4.11

the exposure. When the susceptible manikin was 0.15 m taller than the source manikin, the buoyant breathing jet from the mouth of the source manikin travelled directly to the inhalation region of the susceptible manikin and led to a greater exposure (see Table 3). For nasal breathing, the exposure was almost equal to that when the two manikins were at the same height. This may be due to similar concentrations of the substances that travel with the body thermal boundary in the breathing zone for people with a height of 1.7 and 1.85 m. When the source manikin was 0.15 m taller, the air from the mouth-breathing jet travelled over the susceptible manikin, and the resultant exposure was quite low, for example, 0.31. On the other hand, the breathing jet from the nose of the source manikin could reach the inhalation region of the susceptible manikin and generate a larger exposure value of 4.11.

The four vertical concentration samplers (Fig. 2b) close to the susceptible manikin allow us to examine the physics of susceptible exposure index. When the distance is within the first 1.5 m, the penetration of the exhaled jet of the source manikin to the proximity of the susceptible manikin is clearly shown in Fig. 5. At a distance of 0.5 m, the general exposure index is at a similar level to the corresponding susceptible exposure index. When the distance between two manikins is >2 m, the concentrations along the susceptible manikin at heights of 1.1, 1.3, 1.5, and 1.9 m are rather uniform and almost the same as the concentration inhaled by the susceptible manikin. This indicates that the substances inhaled by the susceptible manikin contain a considerable contribution from those entrained by its thermal boundary layer.

3.2 | Inhalation and face deposition of droplet nuclei as a function of distance

In our experiments, only trace gas was used for studying short-range airborne exposure. To explore more realistic situations, we performed CFD simulations by releasing 1600 droplets between 4 and 6 s as shown in Fig. S2. While airborne exposure is easy to quantify, droplet transmission exposure is not straightforward. In general, large droplet transmission considers first the deposition of large droplets/droplet nuclei on mucous membranes (mucosae) of the eyelids, nostrils, and lips. In theory, our approach should be able to quantify the amount of droplets directly deposited on these sites, but we failed to detect any in our simulations. So we consider the deposition of droplets on the entire face as an indicator for large droplet deposition here.

Figure 6 summarizes the number of droplet nuclei inhaled by the susceptible manikin and deposited on different parts of her body at six instants (20, 30, 40, 50, 100, and 200 s). It reveals that the large droplet (direct spray), short-range airborne, and indirect contact routes are all possible transport mechanisms at a distance of <1 m. At a distance of 0.5, 1, 1.5 and 3 m, the total number of droplet nuclei deposited on the susceptible manikin over the entire period (200 s) was found to be 99, 91, 13, and 6, respectively. These numbers represent only 6.2%, 5.7%, 0.8%, and 0.4% of the 1600 droplets exhaled by the source manikin, and the majority was deposited on the front, back, and legs of the susceptible manikin's body, which will probably result into indirect contact transmission. Other droplets either deposit on the floor or are removed by ventilation. Large droplet transmission is only effective at close proximity.

The inhaled number of droplet nuclei at 200 s was 3.0±0.47, 9.0±2.82, 0.3±0.27, and 0 for a distance of 0.5, 1, 1.5, and 3 m, respectively. These numbers are the average and standard error of three CFD runs, and each run results in a different result due to the effects of turbulence. The maximum ratio of the standard deviation of three runs to the mean value in our simulations is 1.41 (0.3 droplet nuclei inhaled from 1,5 m). The number of droplets deposited on the face was 1.0±0.47, 7.7±0.27, 0.3±0.27, and 0 for the four distances, respectively. The trend is generally similar to the results for gaseous exposure shown in Fig. 4. The close proximity exposure is high. No droplets deposit on manikin's face or are re-inhaled beyond the distance of 1.5 m, indicating insignificant number of droplet nuclei enter

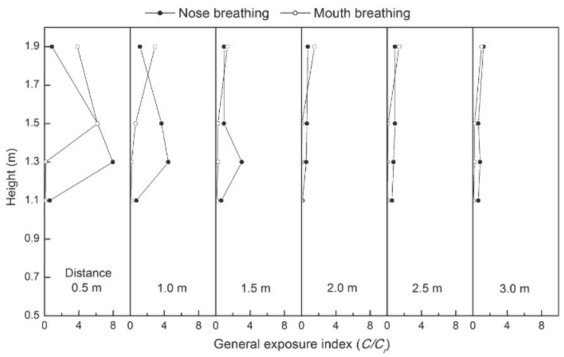

FIGURE 5 The dimensionless measured concentration of tracer gas at different heights along the body of the susceptible manikin. Two breathing modes of the source manikin are included, including nose and mouth breathing

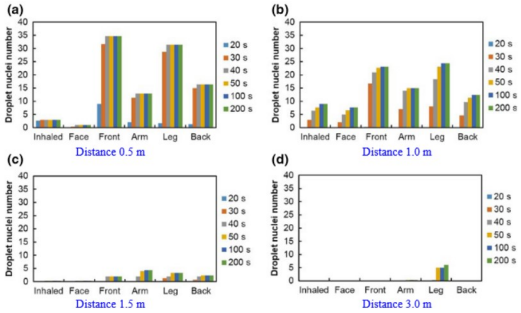

FIGURE 6 Number of droplet nuclei inhaled by the susceptible manikin and deposited on her body. Large droplets (100 μm) were released; the distance between the susceptible manikin and the source manikin is (a) 0.5 m; Case 12 [100, displacement, 5.6ACH, 35%, 0.5 m, 0], (b) 1.0 m; Case 13 [100, displacement, 5.6ACH, 35%, 1.0 m, 0], (c) 1.5 m; Case 14 [100, displacement, 5.6ACH, 35%, 1.5 m, 0], and (d) 3.0 m; Case 15 [100, displacement, 5.6ACH, 35%, 3.0 m, 0]

the breathing zone at a separation distance of 1.5 m, which also agrees with the data in Fig. 4.

Deposition of droplets on the manikin body is shown in Fig. 6. Droplets that already deposited on walls and the floor are not shown here. The remaining droplet nuclei either deposited on surfaces, or were inhaled by the susceptible manikin or ventilated out of the room. Figure 6 shows that major deposition on the body surface of the susceptible manikin occurred between 20 and 30 s, and the deposition mostly ceased after 40 s. This agrees with Figs S7 and S8 which shows that most droplet nuclei travelled over the susceptible manikin at 50 s after exhalation for a distance up to 2.5 m.

3.3 | The effect of relative humidity

Relative humidity affects the evaporation of droplets. When the ambient relative humidity was 35%, the dispersion of droplets and droplet nuclei was totally distinct from the dispersion at a relative humidity of 95%, as shown in Fig. 7. As shown in Fig. S6, the average trajectories for droplets with an initial size of 1, 25, and 50 μm were almost the same. For droplets with an initial size of 100 μm, the droplet nucleus size at a relative humidity of 95% was 1.5 times that at a relative humidity of 35%. It takes more than 100 s for a droplet with an initial diameter of 100 μm to evaporate at a relative humidity of 95%, while <2 s at 35%. Hence, the droplet composition as well as ambient humidity must be noted before defining the threshold size for "large droplets."

Droplet exposure is also found to be affected by ventilation rates and air distribution systems. Stronger mixing in a room with a larger air change rate would induce more mixing of droplet nuclei in a room. At the same time, in a room ventilated by displacement ventilation, the vertical temperature gradient can result in a lockup phenomenon, as first revealed by Qian and Li.[38]

4 | DISCUSSION

4.1 | Distinction of short-range airborne and large droplet transmission

We regard the size of exhaled droplets just released from the mouth or nose as the droplet initial size. The droplet nuclei size varies both temporally and spatially depending on the evaporation and dispersion process as a function of relative humidity. In dry air, the size of the droplet nuclei is about one-third of the droplet initial size.[20] A 30 μm exhaled droplet becomes droplet nuclei of about 10 μm in <1 s, during which it can travel about 1 m due to the exhalation flow from the source patient. The droplet nuclei can be inhaled and deposited in the respiratory tract and may result into infection if they contains viable pathogens.

In our study, we explored two routes of exposure for droplets and droplet nuclei—direct inhalation by nose or mouth of the susceptible individual (i.e., airborne transmission) and deposition on her face (i.e., leading to droplet transmission). The airborne route is particularly important, because the majority of respiratory droplets are in the submicron size[19,42] and the study by Lindsley et al.[43] indicated 65% of exhaled influenza virus is contained in droplets smaller than 4 μm during coughing. We divided the airborne infection into short-range airborne infection (direct inhalation due to close contact) and long-range airborne infection (sharing the same indoor environment). The most significant conclusion here is that the short-range airborne route is potentially much more important than the long-range airborne route. As summarized in the introduction, epidemiological evidence shows that respiratory infection often occurs in close proximity (within the first 1.5 m). Infection risk with distance from a source patient is shown in Fig. 1a for an exposure of 8 hours per day over 1–5 days. Infection risk decreased sharply from 0 to 1.3 m,[44,45] which conforms well to our predicted and measured results.

A large number of respiratory diseases are considered to be transmitted by large droplet route.[46] For the transmission of influenza,

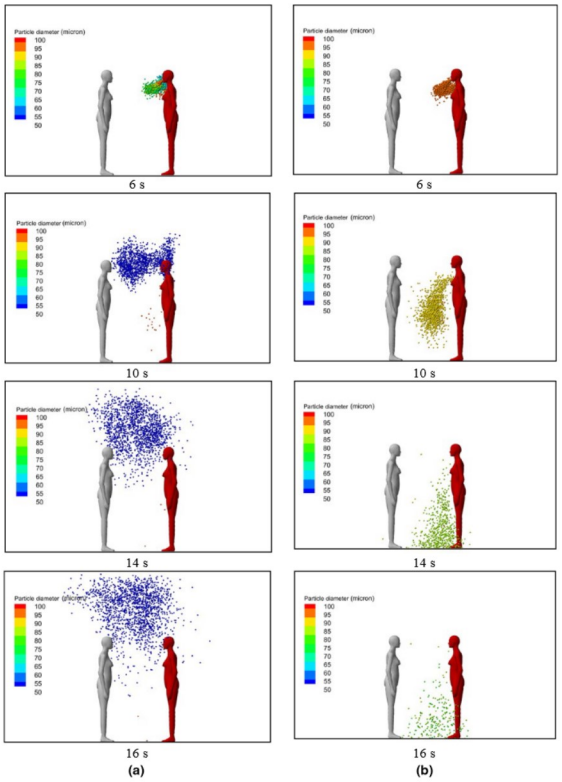

FIGURE 7 Computer simulated dispersion of large expiratory droplets (initial size, 100 μm in diameter) due to normal breathing in a mixing ventilated room with a low (35% 0 and a high (95%) RH (a) Case 8 [100, mixing, 5.6 ACH, 35%, 0.8 m, 0] (b) Case 9 [100, mixing, 5.6 ACH, 95%, 0.8 m, 0] at 6 instances (6, 10, 14, and 16 s)

Brankston et al.[47] and Tellier[48] came to different conclusions, with the former for the large droplet route and the latter for the possible existence of the airborne transmission route. It is probable that short-range airborne infection has been incorrectly grouped in the category of droplet infection since Wells.[10]

4.2 | Control mechanisms for short-range airborne and large droplet transmission are different

The findings related to short-range airborne exposure have significant implications for intervention. One of the reasons that the droplet precaution does not work effectively in some situations[3] might be that the short-range airborne route was neglected. The mechanisms of the droplet-borne and the short-range airborne routes are different; hence, their effective control methods also differ.

Dilution ventilation is recommended for controlling airborne diseases. For example, in negative pressure isolation rooms for airborne diseases, very high ventilation of 12 ACH has been recommended. However, the short-range airborne route is mainly due to direct exposure to the exhaled air stream of the source when two people are in close proximity. An air speed of 2–20 m/s is involved in the exhalation or cough jets, while the typical air speed in a room due to dilution ventilation is only around 0.2–0.3 m/s. Therefore, general dilution ventilation is ineffective for the short-range airborne route.

There are two basic categories of engineering- and/or personal protection-related approaches. The first is source control. The source patient could wear a surgical mask, which can filter our most large droplets, and also extinguish the exhalation jet. However, it cannot filter out all fine droplets; they can only reduce the infection risk.[49,50] Personalized exhaust method is also proved to extinguish the exhalation jet or remove droplets efficiently; it is useful for sitting gestures that people stay still.[51] The second method is susceptible control. Personalized ventilation (PV) system[52] or wearable PV[53] provides the susceptible protection with a clean air stream. A unidirectional airflow from the susceptible individual to the source patient can prevent the exhalation jet from moving from the source to the susceptible individual.[54] The susceptible individual could also use various personal protection devices, such as a N95 respirator, which is more effective than surgical masks.[55]

4.3 | Limitations of this study

We only estimated exposure, which constitutes the prerequisite of the pathogen transmission, and therefore infection transmission. We considered perhaps the worst situation in terms of exposure risks—two people standing face-to-face with similar heights; close proximity arrangement of two people also includes sitting, sleeping, working, etc. The 1.5 m threshold is a reference value; apparently, it does not account for the cough scenario, in which the jet has much greater momentum and a more large droplets is produced. The two manikins were set in the middle of the room in our experimental study, and different values would be expected under different test conditions, for example, if the manikins were closer to the supply diffuser, and during such situations, the room airflow would affect the short-range exposure. In addition, we were unable to repeat our experiments, although a relatively large number of conditions were tested. In addition, our study does not include the fomite mediated or the surface contact route.

5 | CONCLUSIONS

The interpersonal exposure of exhaled droplets and droplet nuclei between two standing people was investigated using both full-scale laboratory tests and CFD simulations. Such exposure is shown to be affected by distance, humidity, and ventilation and breathing mode. The proximity effect was identified, that is, there exists a substantial increase in exposure to droplet nuclei exhaled by the source patient when a susceptible individual is close to the source patient within 1–1.5 m under the specific set of conditions studied. This agrees with the field observation that infection of influenza and other respiratory diseases often occurs at proximity. The hypothesized short-range airborne route of respiratory infection is a possible explanation for close proximity infection. The traditional explanation for the observed close proximity infection is due to large droplet transmission.

The threshold distance of about 1–1.5 m distinguishes the two basic transmission processes, that is, the short-range modes and the long-range airborne route. The short-range modes include both the conventional large droplet mode and the new short-range airborne transmission. Droplet dispersion also varies with humidity, thus the impact on interpersonal transmission. With the same initial size, droplets could form droplet nuclei sufficiently fine enough to be suspended in air for a substantial length of time in relatively dry air (e.g., relative humidity 35% and 23°C as studied here), while droplets could also evaporate 10 times slower and settle rapidly in humid air (e.g., at relative humidity 95% and 23°C).

The distinction between the short-range airborne route and that of large droplets for close proximity infection implies that different control methods are needed. Neither the existing droplet precaution nor dilution ventilation effectively prevents short-range airborne transmission; new control methods are needed.

ACKNOWLEDGEMENT

We are grateful to the financial support by RGC (HKU7142/12) and NSFC (Grant number 51278440 and 51378415).

REFERENCES

1. WHO. Infection prevention and control in health care for confirmed or suspected cases of pandemic (H1N1) 2009 and influenza-like illnesses. Geneva, Switzerland: WHO; 2009.
2. Institute of Medicine (IOM). *Respiratory protection for healthcare workers in the workplace against novel H1N1 influenza A: a letter report*, Washington, D.C.: The National Academies Press; 2009.
3. Han K, Zhu X, He F, et al. Lack of airborne transmission during outbreak of pandemic (H1N1) 2009 among tour group members, China, June 2009. *Emerg Infect Dis*. 2009;15:1578–1581.
4. Wei J, Li Y. Enhanced spread of expiratory droplets by turbulence in a cough jet. *Build Environ*. 2015;93:86–96.
5. Xie X, Li Y, Chwang AT, Ho PL, Seto WH. How far droplets can move in indoor environments – revising the Wells evaporation-falling curve. *Indoor Air*. 2007;17:211–225.
6. Atkinson MP, Wein LM. Quantifying the routes of transmission for pandemic influenza. *Bull Math Biol*. 2008;70:820–867.
7. Nicas M, Jones RM. Relative contributions of four exposure pathways to influenza infection risk. *Risk Anal*. 2009;29:1292–1303.
8. Flugge C. Uber luftinfection. *Z Hyg Infektionskr*. 1897;25:179–224.
9. Chapin CV. *Sources and Modes of Infection*. New York, NY: John Wiley and Sons; 1910.
10. Wells WF. On air-borne infection. Study II. Droplets and droplet nuclei. *Am J Hyg*. 1934;20:611–618.
11. Hare R. The transmission of respiratory infections. *Proc Roy Soc Med*. 1964;57:221–230.
12. Dodds MW, Johnson DA, Mobley CC, Hattaway KM. Parotid saliva protein profiles in caries-free and caries active adults. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1997;83:244–251.
13. Effros RM, Wahlen K, Bosbous M, et al. Dilution of respiratory solutes in exhaled condensates. *Am J Resp Crit Care Med*. 2002;165:663–669.
14. Potter JL, Matthews LW, Lemm J, Spector S. Human pulmonary secretions in health and disease. *Am Rev Respir Dis*. 1963;96:83–87.
15. Xie X, Li Y, Sun HQ, Liu L. Expiratory droplets due to talking and coughing. *J R Soc Interface*. 2009;6:703–714.
16. Duguid JF. The numbers and the sites of origin of the droplets expelled during expiratory activities. *Edinburg Med J*. 1945;52:335–340.
17. Duguid JF. The size and duration of air-carriage of respiratory droplets and droplet-nuclei. *J Hyg*. 1946;4:471–480.

18. Louden RG, Roberts RM. Relation between the airborne diameter of respiratory droplets and the diameter of the stains left after recovery. *Nature*. 1967;213:95–96.
19. Papineni RS, Rosenthal FS. The size distribution of droplets in the exhaled breath of healthy human subjects. *J Aerosol Med*. 1997;10:105–116.
20. Liu L, Wei J, Li Y, Andrew O. Evaporation and dispersion of respiratory droplets from coughing. *Indoor Air*. 2017;27:179–190.
21. Nicas M, Nazaroff WW, Hubbard A. Toward understanding the risk of secondary airborne infection: emission of respirable pathogen. *J Occup Environ Hyg*. 2005;2:143–154.
22. Bjørn E, Nielsen PV. Dispersal of exhaled air and personal exposure in displacement ventilated rooms. *Indoor Air*. 2002;12:147–164.
23. Qian H, Li Y, Nielsen PV, Hyldgaard CE, Wong TW, Chwang ATY. Dispersion of exhaled droplet nuclei in a two-bed hospital ward with three different ventilation systems. *Indoor Air*. 2006;16:111–128.
24. Gao N, Niu J. Modeling particle dispersion and deposition in indoor environments. *Atmos Environ*. 2007;41:3862–3876.
25. Sze To GN, Wan MP, Chao CYH, Fang L, Melikov AK. Experimental study of dispersion and deposition of expiratory aerosols in aircraft cabins and impact on infectious disease transmission. *Aerosol Sci Technol*. 2009;43:466–485.
26. Wan MP, Sze To GN, Chao CYH, Fang L, Melikov A. Modeling the fate of expiratory aerosols and the associated infection risk in an aircraft cabin environment. *Aerosol Sci Technol*. 2009;43:322–343.
27. Gupta J, Lin CH, Chen Q. Transport of expiratory droplets in an aircraft cabin. *Indoor Air*. 2010a;21:3–11.
28. Zhang L, Li Y. Dispersion of coughed droplets in a fully-occupied high-speed rail cabin. *Build Environ*. 2012;47:58–66.
29. Chao CYH, Wan MP, Sze To GN. Transport and removal of expiratory droplets in hospital ward environment. *Aerosol Sci Technol*. 2008;42:377–394.
30. Zhu S, Kato S, Yang JH. Study on transport characteristics of saliva droplets produced by coughing in a calm indoor environment. *Build Environ*. 2006;41:1691–1702.
31. Chen C, Zhao B. Some questions on dispersion of human exhaled droplets in ventilation room: answers from numerical investigation. *Indoor Air*. 2010;20:95–111.
32. Licina D, Melikov A, Pantelic J, Sekhar C, Tham KW. Human convection flow in spaces with and without ventilation: Personal exposure to floor released particles and cough released droplets. *Indoor Air*. 2015;25:672–682.
33. Nielsen PV, Winther FV, Buus M, Thilageswaran M. Contaminant flow in the microenvironment between people under different ventilation conditions. *ASHRAE Trans*. 2008;114:632–638.
34. Olmedo I, Nielsen PV, de Adana MR, Jensen RL. Distribution of exhaled contaminants and personal exposure in a room using three different air distribution strategies. *Indoor Air*. 2012;22:64–76.
35. Olmedo I, Nielsen PV, de Adana MR, Jensen RL. The risk of airborne cross-infection in a room with vertical low-velocity ventilation. *Indoor Air*. 2013;23:62–73.
36. Brohus H. Personal exposure to contaminant sources in ventilated rooms. Ph.D. Thesis, Aalborg University, Aalborg, Denmark, 1997.
37. Tsoukias NM, Tannous Z, Wilson AF, George SC. Single-exhalation profiles of NO and CO2 in humans: effect of dynamically changing flow rate. *J Appl Physiol*. 1998;85:642–652.
38. Qian H, Li Y. Removal of exhaled particles by ventilation and deposition in a multibed airborne infection isolation room. *Indoor Air*. 2010;20:284–297.
39. Nazaroff WW, Nicas M, Miller SL. Framework for evaluating measures to control nosocomial tuberculosis transmission. *Indoor Air*. 1998;8:205–218.
40. Mundt E, Mathisen HM, Nielsen PV, Moser A. *Ventilation effectiveness*. Brussels, Belgium: REHVA; 2004.
41. Pantelic J, Tham KW, Licina D. Effectiveness of a personalized ventilation system in reducing personal exposure against directly released simulated cough droplets. *Indoor Air*. 2015;25:683–693.
42. Yang S, Lee GWM, Chen CM, Wu CC, Yu KP. The size and concentration of droplets generated by coughing in human subjects. *J Aerosol Med*. 2007;20:484–494.
43. Lindsley WG, Blachere FM, Thewlis RE, et al. Measurements of airborne influenza virus in aerosol particles from human coughs. *PLoS One*. 2010:5:e15100.
44. Kowalski WJ, Bahnfleth W. Airborne respiratory diseases and mechanical systems for control of microbes. *Heat Piping Air Cond*. 1998;70:34–46, 48.
45. Lidwell OM, Williams REO. The epidemiology of the common cold I. *J Hyg*. 1961;59:309–319.
46. Tang JW, Li Y, Eames I, Chan PK, Ridgway GL. Factors involved in the aerosol transmission of infection and control of ventilation in healthcare premises. *J Hosp Infect*. 2006;64:100–114.
47. Brankston G, Gitterman L, Hirji Z, Lemieux C, Gardam M. Transmission of influenza A in human beings. *Lancet Infect Dis*. 2007;7:257–265.
48. Tellier R. Review of aerosol transmission of influenza A virus. *Emerg Infect Dis*. 2006;12:1657–1662.
49. Cowling BJ, Zhou Y, Ip DKM, Leung GM, Aiello AE. Face masks to prevent transmission of influenza virus: a systematic review. *Epidemiol Infect*. 2010;138:449–456.
50. 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. *J R Soc Interface*. 2009;6(Suppl. 6):S727–S736.
51. Yang J, Sekhar SC, Cheong KWD, Raphael B. Performance evaluation of a novel personalized ventilation–personalized exhaust system for airborne infection control. *Indoor Air*. 2015;25:176–187.
52. Bolashikov ZD, Melikov AK. Methods for air cleaning and protection of building occupants from airborne pathogens. *Build Environ*. 2009;44:1378–1385.
53. Bolashikov Z, Melikov A, Spilak M. Experimental investigation on reduced exposure to pollutants indoors by applying wearable personalized ventilation. *HVAC&R Res*. 2013;19:385–399.
54. Morimoto S, Hori S, Tanabe S, Tsutsumi H, Hiramatsu K. Push-pull airflow to prevent droplet nuclei leak. *Jpn J Infect Prevent Control*. 2011;26:74–78.
55. Qian Y, Willeke K, Grinshpun SA, Donnelly J, Coffey CC. Performance of N95 respirators: filtration efficiency for airborne microbial and inert particles. *Am Ind Hyg Assoc J*. 1998;59:128–132.
56. Wong TW, Lee CK, Tam W, et al. Cluster of SARS among medical students exposed to single patient, Hong Kong. *Emerg Infect Dis*. 2004;10:269–276.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.