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Experimental measurement of bioaerosol concentrations and containment in long-term care environments

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ABSTRACT

Although many long-term care (LTC) facilities have implemented measures to isolate infectious residents from the general population, most are not designed for airborne infection control, and guidance for retrofitting existing LTC spaces for airborne isolation is limited. The purpose of this study was to evaluate the effect of ventilation, negative pressure, airflow barriers, and other retrofit measures on bioaerosol concentration and movement within long-term care LTC environments. To that end, a series of bioaerosol measurements was performed in an LTC facility under various pressurization and airflow configurations. We arranged active air sampling of DNA-tagged solutions release in the LTC environment, followed by quantitative polymerase chain reaction (qPCR) techniques to measure the released DNA in various spatial locations. Results from aerosol testing in an actual LTC facility suggest that increasing both total and outside ventilation rate had a modest and disproportional effect on the containment of bioaerosols, yet it significantly reduced the time necessary to remove 99% of aerosols from 3 h to approximately 40 min. Significant reductions in aerosol mobility between resident rooms, corridors, and common spaces were also observed with respect to negative room pressurization and anterooms.

1. Introduction

Of the 1.5 million people living in 16,000 U S. nursing homes, 90% are over 65 years of age, and half are 85 years of age or older [1]. For decades, this vulnerable population has shared air, food, and healthcare in overcrowded settings ideal for the spread of infection [2]. Each year, 2-3 million nursing home infections occur in the United States, resulting in 150,000 hospitalizations, 388,000 deaths, and up to \$2 billion in additional healthcare costs [3]. This issue is highlighted by the prevalence of respiratory disease, the limited efficacy of vaccines and, the estimated 5.3 million people who will require long-term care (LTC) in the U.S. by 2030 [4]. In 2020, LTC residents accounted for less than 0.5% of the U.S. population but almost 30% of its COVID-19 deaths. Prior to COVID-19, comparable numbers of nursing home residents died each year from seasonal influenza [5], respiratory syncytial virus [6], and pneumonia; despite vaccination rates exceeding 80%. Only since COVID-19 have the inadequacies of infection control in nursing homes and other skilled nursing, assisted living, and LTC facilities been brought to the forefront of the public conscious.

Transmission of COVID-19 can occur through direct or indirect contact with infected people or contaminated surfaces, through saliva and respiratory secretions [7]. Growing evidence suggests COVID-19 may also be transmitted through the air in poorly ventilated spaces by aerosolized droplets <5 µm in diameter [7]. Airborne transmission of COVID-19 has been implicated in several super-spreading events where social distancing, masking, surface disinfection, and other infection control procedures were observed, suggesting the virus may remain airborne and infectious for several hours and over distances well exceeding 2 m (6 ft) [8]. Given that transmission of COVID-19 through the air is sufficiently likely, airborne exposure to the virus should be controlled [9]. Furthermore, as hospitals reach acute care capacity, nursing homes retain greater COVID-19-infected residents longer [10]. A review of 9395 nursing homes in 30 states found nearly one-third (31.4%) had experienced a COVID-19 outbreak, with an average of 19.8 cases. Larger facilities in urban settings were significantly more likely to have a COVID-19 outbreak (p < 0.05). COVID-19 outbreaks,

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however, were not correlated to nursing home quality of care as determined by the Centers for Medicare & Medicaid Services five-star quality rating system [11]. In fact, several peer-reviewed case studies by the American Geriatrics Society document very rapid and widely disseminated outbreaks despite visitor exclusion, cessation of communal dining and group activities, regular resident and staff screenings, universal masking, and aggressive social distancing policies [12]. In nearly every case, more than 30% of residents tested positive for COVID-19 within two to three weeks of the first positive test result [13,14] despite early adoption of infection prevention and control measures. Of those, nearly one-third ultimately died.

These statistics suggest new infection control strategies must be considered to contain infectious respiratory outbreaks in U.S. nursing homes, including measures to provide temporary airborne isolation capacity in existing facilities. In addition to engineering controls targeting airborne transmission, nursing homes should consider procedural measures as part of infectious isolation or quarantine planning [15]. Such measures may include limits to avoid overcrowding, dedicated isolation staff, restricted access, and limits on resident transport and movement. Additional measures may include dedicated resident bathrooms and confining aerosol-generating procedures to resident rooms, preferably negative pressure rooms if possible [16].

According to ASHRAE Standard 170, airborne infectious isolation requires dedicated heating, ventilation, and air-conditioning (HVAC) systems that provide 12 room air changes per hour (ACH) to dilute and remove airborne contaminants [17]. Airborne isolation also requires airflow from spaces outside of the isolation zone inward, toward spaces within the isolation zone to contain airborne contaminants. Nursing homes, however, are not designed for airborne infection control, and isolation is difficult to achieve [18]. Common limitations in existing facilities are the inability to maintain thermal comfort while providing added ventilation air, directional airflow, increased air filtration, and sufficient isolation space to physically separate infectious residents and attending staff from the general population. HVAC systems in most nursing homes do not maintain directional airflow, have significantly fewer room air changes and minimal air filtration, and recirculate air between resident rooms and communal areas. Nursing homes and other LTC facilities may, however, have reserve HVAC capacity to increase air filtration and outdoor air ventilation, especially during milder weather. Nursing homes may further consider the use of room air cleaners with upper-room ultraviolet (UV) disinfection [19] or high-efficiency particulate air (HEPA) filters [20,21]. HEPA filters may also be used to clean recirculated air or air that cannot be exhausted directly to the outdoors, although the use of high-efficiency filters can diminish the amount of air supplied to the room and cause more air to bypass the filter [22].

The existing literature reveals that the indoor built environment plays (at least) a non-negligible role in the spread of SARS-CoV-2 and environmental parameters such as air flowrate, filtration, distribution, temperature, and relative humidity must be studied and possibly controlled [23–25]. Of this list of environmental parameters and in the context of the recent pandemic, temperature [26-28], relative humidity [27,29,30], and filtration [31] have been studied in greater detail. Hence, this paper aims to explore the overall spread of contamination within LTC facilities and evaluate the effectiveness of ventilation rate, outside air ratio, and space pressurization on the containment and removal of contaminants from the space. To that end, a residential wing of an actual LTC facility was converted into an experimental isolation test space, and a series of air sampling tests were conducted under various airflow rates and pressurization scenarios. A DNA-coded tracer aerosol was used to simulate the contaminant load from infectious residents and staff. Contaminant concentrations and movement within the experimental test space and to adjacent spaces were then collected and analyzed.

2. Methods

2.1. Design of experiments

A test plan was developed to evaluate the effect of ventilation rate, directional airflow (e.g., air pressure relationships), and airflow barriers on bioaerosol spread within a long-term care (LTC) facility. According to this test plan, a total of four major experimental setups were designed to allow for variation of the three independent variables, namely pressurization (negative vs. neutral), airflow rate (i.e., total and outside air change rates), and outside air (Fig. 1). As the natural state of the HVAC system in LTC is to provide a pressure balance in the space, we called the neutral pressure the Control case, agains the Experiment cases establishing negative pressurization. Furthermore, those cases that supplied full outside air were labled as 100%, in contrast with those that allowed for recirculation (labeled as 30%). Although full factorial design for three variables demanded eight sets of experiments, the proposed fractional design provided sufficient variation in each independent variable by offering six distinct cases pair-wise comparisons. The dependent variable of experiments was level of contamination as measured via releasing a tracer aerosol within an LTC environment (e.g., resident rooms, corridors, HVAC systems, etc.) to simulate the respiratory release of COVID-19 from infectious residents and staff. The aerosol used to simulate airborne respiratory droplets consisted of a water-soluble blend of DNA-coded particles sized and formulated to have a mean aerodynamic diameter of 5 µm. Aerosol was released into the LTC environment, collected by air sampling equipment, and analyzed by polymerase chain reaction (PCR) technology. PCR log₁₀ reduction values ranging from 1 to 5 were then calculated for each sample with a value of '1' corresponding to 100,000 particles per liter (p/L) of indoor air, '2' 10,000 p/L, '3' 1000 p/L, '4' 100 p/L and '5' corresponding to 10 p/L.

2.2. Space geometry

Test spaces included one residential wing designated as the control test space and another identical wing designated as the experimental test space (Fig. 2). Test spaces consisted of an entry foyer, corridor, and six resident rooms, one of which was used as a staff room. As demonstrated in Fig. 2, These two wings are identical, with identical naming schemes, in their layout design; only one is the 90° rotation of the other. Note that the negative experiments, by definition, were conducted in the Experiment Wing; whereas the neutral experiment were conducted in the Control Wing. Each resident room was approximately 175SF, and the test spaces, including resident rooms, corridor and foyer were approximately 1500 SF. Testing in the control space was performed under normal operating conditions according to ASHRAE Standard-170 guidelines [32]. Testing in the experimental space was performed

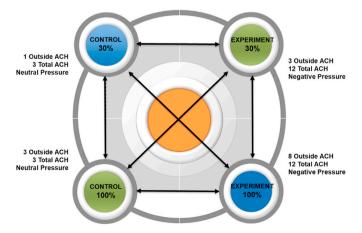


Fig. 1. Overall experimental design strategy.

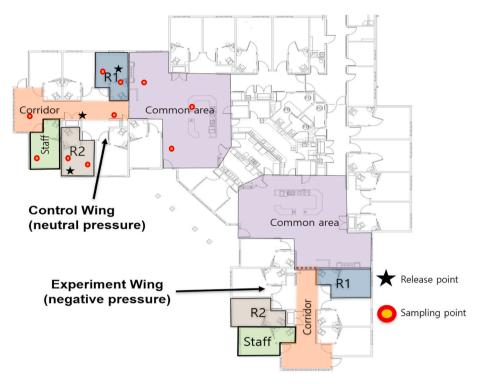


Fig. 2. Architectural layout of the control and the experiment wings.

under modified temporary isolation conditions to include physical separation of the resident wing from the facility, anterooms at the entrance to each resident space, higher ventilation rates and negative (inward) airflow.

Resident rooms in the control test space were conditioned with $+75 \mathrm{cfm}$ of supply air with $-10 \mathrm{cfm}$ of return air and $-65 \mathrm{cfm}$ of bathroom exhaust, producing 3 total air changes per hour (TACH) and a neutral air pressure relationship with the corridor. Modified resident rooms in the experimental test space were conditioned with $+220 \mathrm{cfm}$ of supply air with $-240 \mathrm{cfm}$ of return air and $-80 \mathrm{cfm}$ of bathroom exhaust, producing 12 TACH and a negative air pressure relationship with the corridor (Fig. 3). It is worth mentioning that these TACH values are commensurate with the ASHRAE Standard 170 recommendation for a general patient room (4 ACH) and Airborne Infection Isolation Room (12 ACH).

2.3. Bioaerosol generation and sampling

The release and tracing were performed using the veriDART DNA-labeled solutions by SafeTraces, using a SafeTraces Pneumatic nebulizer, CA, USA [33]. The active sampling of air was performed by using a 7 lpm air pump to pass air through microfiber filer media (pore size = $1.0~\mu m$). Filter samples contained were then transferred to 2 mL DNA LoBind Eppendorf Tubes. Samples were transferred into the lab in $-20~\rm ^{\circ}C$ freezers. Next, 0.5 mL of elution buffer was added into the 2 mL tube containing the filter samples, vortexed and centrifuged via a standard protocol. The samples were inserted on a 96 well non-skirted polymerase chain reaction (PCR) plate and upon standard processing, they were loaded into a QuantStudio 5 qPCR instrument for annealing/extension. The measured input DNA concentration values were then used to estimate the number of DNA copies in the reaction well. Similar methodology and instrument has been used in the literature [34].

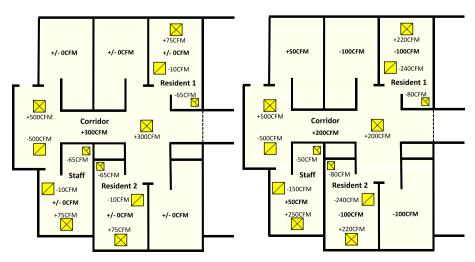


Fig. 3. Control (left) and Experimental (right, rotated 90° clockwise) test space airflow configurations.

2.4. Experimental setup

As mentioned, a total of 4 tests were conducted, two each in the control and experimental (e.g., isolation) test spaces. Each test in each space consisted of one test at 30% outside air and one at 100% outside air. For each test, approximately 10-12 mL of tracer aerosol was released from four locations, including three resident rooms and the central corridor. Air filter samples (~9 Lpm) were collected at a total of 12 locations, including eight locations within the test space, two in adjacent spaces outside of the test space, and one each in the supply and return air duct. The duration of each test from aerosol release to cessation of sampling was approximately 40 min. These tests were repeated in two different resident rooms, one staff room, and one in the common corridor. Tracer aerosol was released at the head of the resident room bed toward the opposite corner of the room at the height of 0.8 m (30in) above the floor. During tests, doors between resident rooms and corridors remained closed while bathroom doors inside resident rooms remained open. Two additional tests were also conducted to evaluate the effect of outdoor air ventilation rates on room recovery or, the reduction in concentration of DNA-coded aerosols over time in communal spaces such as exercise rooms and dining areas. One test was conducted at 1 ACH (100cfm) and another was conducted at 6 ACH (650cfm) in a 750sf commons space. The duration of each test was 40 min and utilized two tracer aerosol release points and, two air sampling locations. Each sampling location consisted of four air samplers, each operating for 10 min to record the degradation in DNA-coded aerosol concentration at 10-min intervals over the 40-min test sequence. From this data, the research team evaluated seven environmental transmission scenarios, as detailed in Table 1.

3. Results and discussions

3.1. Resident room release

To evaluate the effect of ventilation on contaminant load within resident rooms, DNA-coded tracer aerosol was released inside resident rooms 1 and 2 and sampled under four different air change rates. Following PCR analyses of resident room samples, moderate aerosol (e. g., 'contaminant load') reductions were associated with increasing ventilation rates. Specifically, increasing ventilation rates from 1 to 3 outdoor ACH reduced the airborne contaminant load by approximately 17% from 70,795 (1.15 \log_{10} reduction) particles per liter (p/L) of indoor air, to 58,884 p/L (1.23 \log_{10} reduction). Increasing ventilation rates from 3 to 8 outdoor ACH further reduced contaminant load by another 33% from 58,884 p/L to 39,811 p/L (Fig. 4). Overall, increasing air change rates from 1 to 8 outdoor ACH reduced the contaminant load

Table 1Environmental Transmission Scenarios under Study (see Fig. 2, and S1 through S7 for details).

Testing Scenario	Release location(s) [OP]	Sampling location(s) [SP]	Test schematic
Resident room contaminant load	R1 and R2	R1 and R2	Fig. S1
Transmission for resident room to corridor	R1 and R2	Corridor	Fig. S2
Transmission from corridor to resident room	Corridor	R1 and R2	Fig. S3
Transmission from resident room to staff room	R1 and R2	Staff	Fig. S4
Transmission from isolation zone to common area	R1 and R2	Common area	Fig. S5
Transmission in HVAC system	R1 and R2	HVAC	Fig. S6
Contaminant decay in exercise room	Recovery	Recovery	Fig. S7

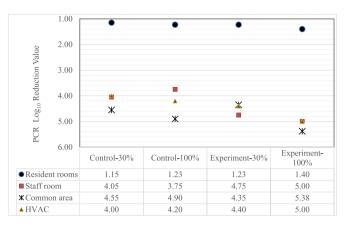


Fig. 4. \log_{10} reduction of DNA-aerosol in various sampling locations and testing configurations.

and potential exposure risk to healthcare workers by roughly half. Results suggest that resident room contaminant loads did not correspond proportionately to air change rates. It can be further seen that increasing the total ACH had very little effect on indoor contaminant load as changing the TACH from 3 to 8, practically did not change aerosol concentrations. To assess exposure risks to healthcare workers and residents outside of the isolation zone, DNA tracer aerosol was released inside resident rooms 1 and 2 and sampled in a nearby resident room, living room, and kitchen area. Following PCR analyses of common area samples, reductions in tracer aerosol movement from resident rooms in the isolation zone to common areas outside of the isolation zone were not associated with directional airflow and only weakly associated with air change rates ($r^2 > 0.44$). With positive air pressure in the corridor and neutral airflow in resident rooms, the average DNA tracer reduction log₁₀ value in the areas outside of the isolation zone ranged between 4.55 and 4.90, corresponding to a contaminant load of approximately 13-28 p/L (Fig. 4). With positive air pressure in the corridor and negative airflow in resident rooms, the average DNA tracer reduction log₁₀ value in areas outside of the isolation zone ranged between 4.35 and 5.38, corresponding to a contaminant load of approximately 4-45 p/L (see Fig. 5).

With positive air pressure in the corridor and neutral air pressure in the staff room and resident rooms, the average DNA tracer reduction log₁₀ value in the staff room ranged between 3.75 and 4.05, corresponding to a contaminant load of approximately 89-178 p/L. With positive air pressure in the staff room and corridor and negative air pressure in the resident rooms, the average DNA tracer reduction log₁₀ value in the staff room ranged between 4.75 and 5.45, corresponding to a contaminant load of approximately 4-18 p/L. Overall, tracer aerosol movement from resident rooms to the staff room was correlated to directional airflow ($r^2 > 0.93$). In contrast, outdoor air change rates and subsequent contaminant loads in resident rooms were weakly correlated to contaminant loads in the staff room ($r^2 < 0.51$). For tracer aerosol released in the corridor, however, aerosol movement from the corridor to the staff room was significantly greater in the neutral airflow mode compared to the negative airflow mode ($r^2 > 0.99$). With the staff room and resident rooms in the neutral airflow mode, the average DNA tracer reduction \log_{10} value in the staff room ranged between 1.70 and 2.0, corresponding to a contaminant load of approximately 10,000 to 19,953 p/L. With the staff room positive and resident rooms negative, the average DNA tracer reduction log₁₀ value in the staff room ranged between 4.30 and 4.40, corresponding to a contaminant load of approxi-

Though the experiments were not specifically designed to capture the impact of barriers such as doors and walls, some general inferences can be made. For instance, results showed the \log_{10} removal rate dropped two to three levels (i.e., from 1 to 3–4) between inside the room

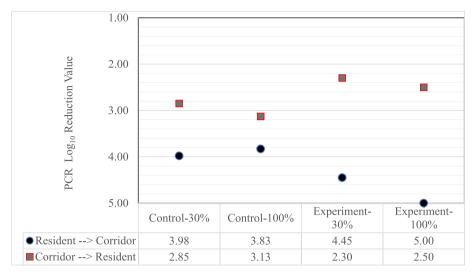


Fig. 5. Log₁₀ reduction of DNA aerosol between the resident rooms and the corridor.

and immediately outside in the corridor (Figs. S9–15). This change could also be attribute to distance from the release point. However, in one experimental case where the release location was at the corridor, the sampling station in the corridor (nearly 40 ft away from the release point) had a \log_{10} value of 1.8 compared to 0.8 at the release source (Fig. S15). Assuming that up to 40 ft distance between sample and source associates with one \log_{10} reduction, one could infer that the physical barriers brought about another 2–3 \log_{10} reduction of the contaminant levels.

3.2. Transmission to and from corridor

Following PCR analyses of corridor samples, reductions in tracer aerosol movement from resident rooms to the corridor were associated with directional airflow. With positive air pressure in the corridor and neutral air pressure in the resident rooms, a contaminant load of approximately 105–148 p/L was observed in the corridor. With positive air pressure in the corridor and negative air pressure in the resident rooms a contaminant load of approximately 10–35 p/L was observed in the corridor, indicating the effectiveness of positive pressurization in the corridor and closed resident room doors. In contrast, with positive air pressure in the corridor and negative air pressure in resident rooms, the average DNA tracer reduction \log_{10} value in the resident rooms ranged

between 2.30 and 2.50, corresponding to a contaminant load of approximately 3162 to 5012 p/L. Overall, tracer aerosol movement from the corridor to the resident rooms was correlated to directional airflow (${\bf r}^2>0.82$). In contrast, air change rates in resident rooms were not correlated to contaminant movement from the corridor to the resident rooms (${\bf r}^2<0.09$). Working against directional airflow, room doors had less effect on the containment of airborne contaminants moving from the corridor to resident rooms. With resident room and anteroom doors closed, tracer aerosol movement from the corridor to the resident rooms was significantly greater in the negative airflow mode compared to the neutral airflow mode.

3.3. Room recovery and decay rates

Two additional tests were conducted to evaluate the effect of ventilation rates on room recovery or, the reduction in contaminant load over time. One test was conducted at 1 outdoor ACH and another was conducted at 6 outdoor ACH in a 70 $\rm m^2$ (750 SF) exercise room located outside of the isolation zone. The duration of each test was 40 min and utilized two (2) DNA-coded tracer aerosol release points and, two (2) air sampling locations (Fig. 6). Each sampling location consisted of four air samplers to record the decay of tracer aerosol at 10-min intervals over the 40-min test sequence. Following PCR analyses of exercise room

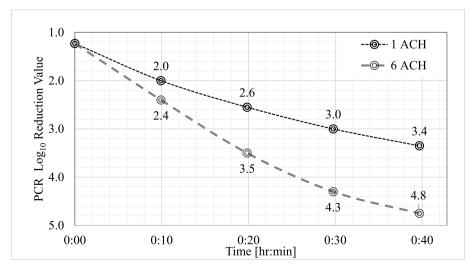


Fig. 6. Contaminate load (p/L) vs. ACH indicating the 'decay' in contaminant level over time.

samples, significant contaminant load reductions were associated with increasing ventilation rates. Specifically, increasing ventilation rates from 1 to 6 outdoor ACH, a contaminant load reduction from 10,000 p/L to 3981 p/L was observed after 10 min (Fig. 6). Increasing ventilation rates from 1 to 6 outdoor ACH further reduced contaminant loads from 447 p/L to 18 p/L after 40 min. At 1 outdoor ACH, a 99.0% contaminant load reduction would have required more than 3 h. At 6 outdoor ACH, a 99.0% contaminant load reduction was achieved after 40 min.

Under the assumption of a well-mixed space, it can be shown that contaminants decay exponentially in time [35]. In spaces with recirculated air (e.g., <100% outside air), the contaminant concentrations can be expressed as a function of the air change rate,

$$C(t) = C_0 e^{ACH \times [(1-\alpha) \times (1-\eta) - 1] \times t}$$

where, C_0 is the initial contaminant concentration, C(t) is the contaminant concentration as a function of time, α is the outside air percentage, η is the filtration efficiency. In spaces with 100% outside air (or 100% filter efficiency), the decay rate can be simplified as,

$$C(t) = C_0 e^{-ACH \times t}$$

It would be expected, therefore, that contaminant loads observed in resident rooms would correspond proportionately to air change rates and specifically, outdoor air change rates. Results suggest that resident room contaminant loads did not correspond proportionately to air change rates. Possible explanations include the likelihood that the resident rooms are not well mixed, suggesting that areas of the room between the supply air and the exhaust air may receive more air changes, whereas areas of the room obstructed by partitions or furnishings may receive fewer air changes. Other explanations may include the effects of air turbulence, particularly at higher air change rates. Air turbulence may impede other contaminant removal mechanisms such as surface deposition and gravitational settling. Vortices created by turbulence may further 'trap' and suspend contaminants in room air currents, preventing their effective removal. Moreover, door position, door motion, and healthcare worker movement have been implicated in the transmission of airborne disease in several epidemiological studies dating back more than 40 years [36–43]. Analysis of the door opening motion in these and other studies suggests that directional airflow relationships between isolation and adjacent healthcare spaces can be terminated and even reversed by door position, door motion, and healthcare worker movement. Overall, contaminant loads observed in spaces outside of resident rooms were on average 10^{-3} of contaminant loads observed inside of the resident rooms, suggesting the effectiveness of both physical airflow barriers and directional airflow to limit bioaerosol mobility. Under normal operational conditions however, with healthcare workers entering and exiting resident rooms, the effects of room pressurization and directional airflow would likely have been more evident.

4. Conclusions

Results suggest ventilation rates had a modest effect on contaminant loads and exposure risks within resident rooms. Increasing air change rates from 1 to 8 outdoor ACH for example, reduced the contaminant load and potential exposure risk to healthcare workers from an infectious occupant by roughly half (43.8%) from 7.1×103 p/L to 3.9×103 p/L. This finding was consistent with results from other similar studies that found air change rates were not effective in proportionately reducing aerosol concentrations within hospital patient rooms [44]. Similarly, outside ACH had a modest effect on contaminant loads in HVAC systems. Increasing air change rates from 1 to 8 OACH only reduced the contamination level by 50%. Moreover, for the control tests, increasing outside air ratio from 30% to 100% did not significantly change the \log_{10} reduction values (p-value of paired t-test = 0.223). In contrast, adding HEPA return air filtration reduced the contaminant

load in the return air from 100 to 10 p/L. Ventilation rates, however, were found to have a significant effect on contaminant decay in common areas. Increasing air change rates from 1 to 6 OACH reduced the time required to achieve "room recovery," or the removal of 99% of contaminants, from 3 h to less than 40 min once the infectious source was removed.

Directional airflow was found to have a profound effect on contaminant mobility from resident rooms to adjacent spaces. Contaminant movement from negative pressure resident rooms to the corridor was significantly less (10–35 p/L) than contaminant movement observed from neutral pressure rooms to the corridor (105–148 p/L). Similarly, contaminant movement from the negative pressure resident room to the staff room was significantly less (4–18 p/L) than contaminant movement observed from the neutral pressure resident room to the staff room (89–178 p/L).

Aerosol movement from the isolation test spaces to areas outside of the isolation zone and to HVAC return air systems was minimal regardless of air change rate, directional airflow or physical airflow barriers. With resident rooms in the 'control' or neutral airflow mode, the isolation zone overall was moderately positive (+300cfm) with respect to adjacent common areas, resulting in a contaminant load of approximately 79-200 p/L in these areas. With resident rooms in the 'experimental' or negative airflow mode, the isolation zone overall was slightly negative (-100cfm) with respect to adjacent common areas, resulting in a contaminant load of approximately 5-63 p/L in these areas. Based on these findings, best retrofit practices for healthcare facilities is to (a) create physical barrier around the isolation environments and (b) create a directional (negative) airflow between the isolation area and the adjacent spaces. Increasing ventilation rates seems to be the last resort as it contributes significantly to the building's energy consumption levels.

CRediT authorship contribution statement

Ehsan Mousavi: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. Kevin Grosskopf: Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization. Phil Arnold: Project administration, Methodology, Conceptualization. Roger Lautz: Writing – review & editing, Methodology, Investigation. Josephine Lau: Resources, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.buildenv.2022.109415.

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