AMERICAN UNIVERSITY OF BEIRUT

INDOOR AIR QUALITY IN HOSPITALS: PM AND AIRBORNE VIRUSES

by
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AN ABSTRACT OF THE THESIS OF

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In this study, we characterize particulate matter concentrations and airborne viruses at a health care facility and explore correlations with indoor parameters such as the air exchange rate, relative humidity and temperature. We also examine the transmission, decay, and suspension of virus shedding by patients. For this purpose, $PM_{2.5}$, PM_{10}, and airborne viruses (influenza A, influenza B, respiratory syncytial virus (RSV)) were monitored in patient rooms with confirmed infections. The indoor measurements showed that patients were exposed to elevated $PM_{2.5}$ levels, ranging between 7 and 53 $\mu g/m^3$ with a mean of 24.5 $\mu g/m^3$, and to PM_{10} concentrations that reached 89 $\mu g/m^3$. Overall, 91% of the monitored patient rooms exceeded the $PM_{2.5}$ daily exposure level of 10 mg/m^3, while 70% of the rooms exceeded the PM_{10} daily exposure level of 20 mg/m^3. Influenza A was detected in 42% of the monitored rooms, with concentrations ranging between 222 and 5,760 copies/m^3, with a mean of 820 copies/m^3. The results showed that while viral concentrations (RNA copies/m^3) tended to decrease significantly with distance away from the patient, traces were still detectable at 1 m and even at 1.5 m. Statistical and numerical analyses clearly showed that the viral removal efficiency was affected by changes in the relative humidity more than changes in room temperature. Moreover, the results from a calibrated Gaussian puff model showed that dispersion was the dominant pathways for viral removal. Based on the results of this study, a set of mitigation measures are proposed within a management framework to reduce exposure of staff, visitors and patients to particulate matter and airborne viruses in hospitals.

CONTENTS

LIST OF ILLUSTRATIONS

Figure Page

LIST OF TABLES

Table Page

LIST OF ABBREVATIONS

ACH	Air Change per hour
AER	Air Exchange Rate
ASHRAE	American Society of Heating, Refrigetating and Air-Conditoining Engineers
CDC	Centers for Disease Control and Prevention
CFD	Computational Fluid Dynamics
HCP	Healthcare Practitioners
NAAQS	National Ambient Air Quality Standards
PM	Particulate Matter
RH	Relative Humidity
RNA	Ribonucleic acid
RSV	Respiratory Syncitial Virus
T	Temperature
WHO	World Health Organization

CHAPTER I
INTRODUCTION

Air pollution constitutes a global concern that has been subject to extensive research because of its direct association with increased morbidity and mortality. It is currently ranked as the fourth leading cause of death worldwide (WHO, 2010). While people spend most of their time indoors, most research has targeted characterizing and assessing outdoor exposures (Zhang et al., 2011, Baik et al., 2012, Vahlsing and Smith, 2012, Sava and Carlsten, 2012). As air pollutants were progressively linked to various health effects, assessing the indoor air quality (IAQ) has gained momentum (Jeong and Lee, 2016, Harb et al., 2018, Gao et al., 2016, Katsoyiannis and Cincinelli, 2019, Blaszczyk et al., 2017, Al-Khateeb et al., 2017, Elbayoumi et al., 2013).

While IAQ is of importance in all confined spaces, some areas such as hospitals are more critical than others, particularly given the presence of vulnerable patients and unique sources of air pollutants. Besides staff and visitors, the exposure of highly vulnerable patients could negate the purpose of their hospital visit due to increased potential health risks associated with air pollutants. Several studies have examined IAQ in healthcare facilities, often limiting their analysis to the qualitative and quantitative characterization of the physical and chemical air pollutants, with more recent efforts targeting bioaerosols, especially viruses (Blachere et al., 2009, Lindsley et al., 2010, Kim et al., 2016, Leung et al., 2016, Baures et al., 2018, Fu Shaw et al., 2018, Asif et al., 2018). In fact, hospitals can be a hub for a variety

of bacteria and viruses even though their environments are often highly controlled. As such, managing their indoor environment presents a challenge towards maintaining good IAQ.

The most common viruses that have been previously assessed in hospital environments include influenza, respiratory syncytial virus (RSV), and the corona virus. In this context, Baures et al. (2018) measured the concentrations of adenovirus, influenza virus, and RSV in two French hospitals. They were only able to find traces of these viruses, possibly because their monitoring program occurred outside of the flu season. Likewise, Leung et al. (2016) quantified the RNA of the influenza virus in aerosols collected in patient rooms using cyclonic sampling in the presence of at least one patient with confirmed influenza A infection. Viruses were detected both at 1 and 1.5 m away from the bed. The highest recorded concentration was 383 copies/m^3 air and it occurred 1.0 m away from the bed. Meanwhile, the lowest positive sample had 94 copies/m^3 and occurred 1.5 m away from the bed. The study also reported that 80% of the viruses were found alongside particles with diameters > 4µm, 20% with particles with a diameter between 1-4 µm, and no virus RNA was found in particles below 1 µm. In a similar study, Blachere et al. (2009) measured the airborne influenza virus in a hospital emergency department using a 2-stage cyclonic sampling. They found that 53% of the detectable influenza virus particles were within the respirable aerosol fraction. Moreover, the study by Lindsley et al. (2010) showed that the influenza and RSV concentrations were not uniformly distributed in the hospital, with the examination rooms showing higher levels as compared to the waiting areas. The spatial variability in concentration was attributed to the time spent by the patients in each room, the size of the rooms, the ventilation rate, and the configuration of the HVAC system (Lindsley et al., 2010).

Seasonal viruses, such as influenza A, influenza B and respiratory syncytial virus (RSV), are a major concern in hospital environments as they are mainly transmitted via inhalation. Over the past few years, there has been an increase in hospital acquired influenza. According to the New Zealand's *District Health Board*, more than 132 patients were estimated to have caught influenza from visitors, other patients, or hospital staff in 2019 alone (Gibson, 2019). Recently, the Cambridge University Hospital restricted the visits by patients' families in an effort to reduce transmission risk as a result of a flu outbreak at the hospital, where one third of the hospital's wards contained patients with flu or other respiratory viruses (CUH, 2020). Also, in a study investigating the clinical characteristics of the novel coronavirus (2019-ncov), 41% of the 138 hospitalized patients caught the virus in a human-to-human hospital associated transmission (Dawei Wang et al., 2020).

There are two basic transmission routes for airborne viruses. These include transmission through droplets that are expelled through coughing and sneezing or through aerosols (<5μm). Transmission by droplets is highly effective over short distances (<1m or 3ft), while dispersal by aerosols has been shown to cover long distances (> 1m) (Kutter et al., 2018). Variations in temperature and relative humidity have been shown to play an important role in the activation or deactivation of viruses, which can potentially exacerbate health risks (Kameel and Khalil, 2003, Murphy, 2006). Similarly, changes to the adopted ventilation rates affect the transport and distribution of air contaminants, which influences the exposure levels of the occupants. These rates are in turn dependent on the ventilation system (natural, mechanical and mixed) that affect the removal of air contaminants (Jung et al., 2015). In this context, hospitals are subject to certain design criteria that aim to ensure

appropriate T, RH, pressure, filtration rate for the supplied air, an allowable air recirculation fraction, and a certain effectiveness for the air handling units (ASHRAE, 2017). Yet, much work remains to be desired in this regards, given that these parameters have a direct bearing on the survival of airborne viruses (CDC, 2018, WHO, 2018). This lack of clarity is a major source of concern to many hospitals since the aerosolization, transmission and survival of emitted viruses are well known to be a function of thermal comfort parameters such as temperature (T) and relative humidity (RH) (Khodakarami and Nasrollahi, 2012, Murphy, 2006) as well as the adopted ventilation rate (Jung et al., 2015). In this study, we examine the viral and physical air quality in patient rooms and identify statistically significant correlations between the measured virus concentration and physical parameters (AER, T, RH, $PM_{2.5}$ and PM_{10}) in patient rooms. Moreover, we model virus emission and transport in order to estimate the spatial variation in virus concentrations and examine the removal mechanisms affecting virus transmission routes.

CHAPTER II
MATERIALS AND METHODS

A. Study Design

Air sampling was conducted during the influenza season from January to March 2019 at a major tertiary care hospital, namely the American University of Beirut Medical Center (AUBMC). Air samples were collected from patient rooms that were selected after receiving laboratory-confirmation that the patient had influenza or RSV infections. The Coriolis µ Biological Air Sampler (Bertin Instruments, FRANCE) was used to collect the air samples at two locations within each of the patient rooms. In each room, one sample was taken at 0.5 m away from the patient head, while the other was taken 1 m away (Figure 1). In one of the rooms, samples were collected at 1 m and 1.5 m to check whether RNA copies would be detected at these distances. The choice of the two distances was based on the critical droplet transmission distance. In order to maintain unbiased and accurate sampling, the patient was instructed to look in the direction of the air sampler to capture the largest amount of expelled viruses during sampling. The air samples collection using the Coriolis instrument was challenging as a result of the high suction capacity of the sampler. The impact areas of the samplers could overlap if used concomitantly in a small area such as the patient rooms. As such, samples at 0.5 m and 1 m were not collected simultaneously to ensure accurate and unbiased sampling. As a result, consistency of the results could be affected due to different number of coughs counted during each sample collection. This was mitigated for in the data analysis by normalizing the resulting viral concentrations by the number of cough (dividing

the concentrations by the reported number of coughs during each sample collection). All samples were collected at the breathing zone level of 1.5 meters and at least 1 meter away from walls. Furthermore, windows and doors were kept closed during the sampling process. The air collected from patient rooms was aspirated for 10 minutes at a flow rate of 300 L/min and drawn into a collection tube containing 15 ml of sterile viral transport media (VTM). The air sampler was decontaminated with concentrated ethanol and air dried after each sample run to prevent potential carry-over contamination. The temperature and relative humidity inside the patients' rooms were also monitored and recorded over a period of 20 minutes using a portable Langan analyzer (model L76n), with a log interval of 10 seconds. Similarly, $PM_{2.5}$ and PM_{10} levels were monitored using a portable TSI DustTrak II aerosol monitor (model 8532) with a log interval of 1 minute. During the monitoring period, occupancy levels and the number of coughs were recorded.

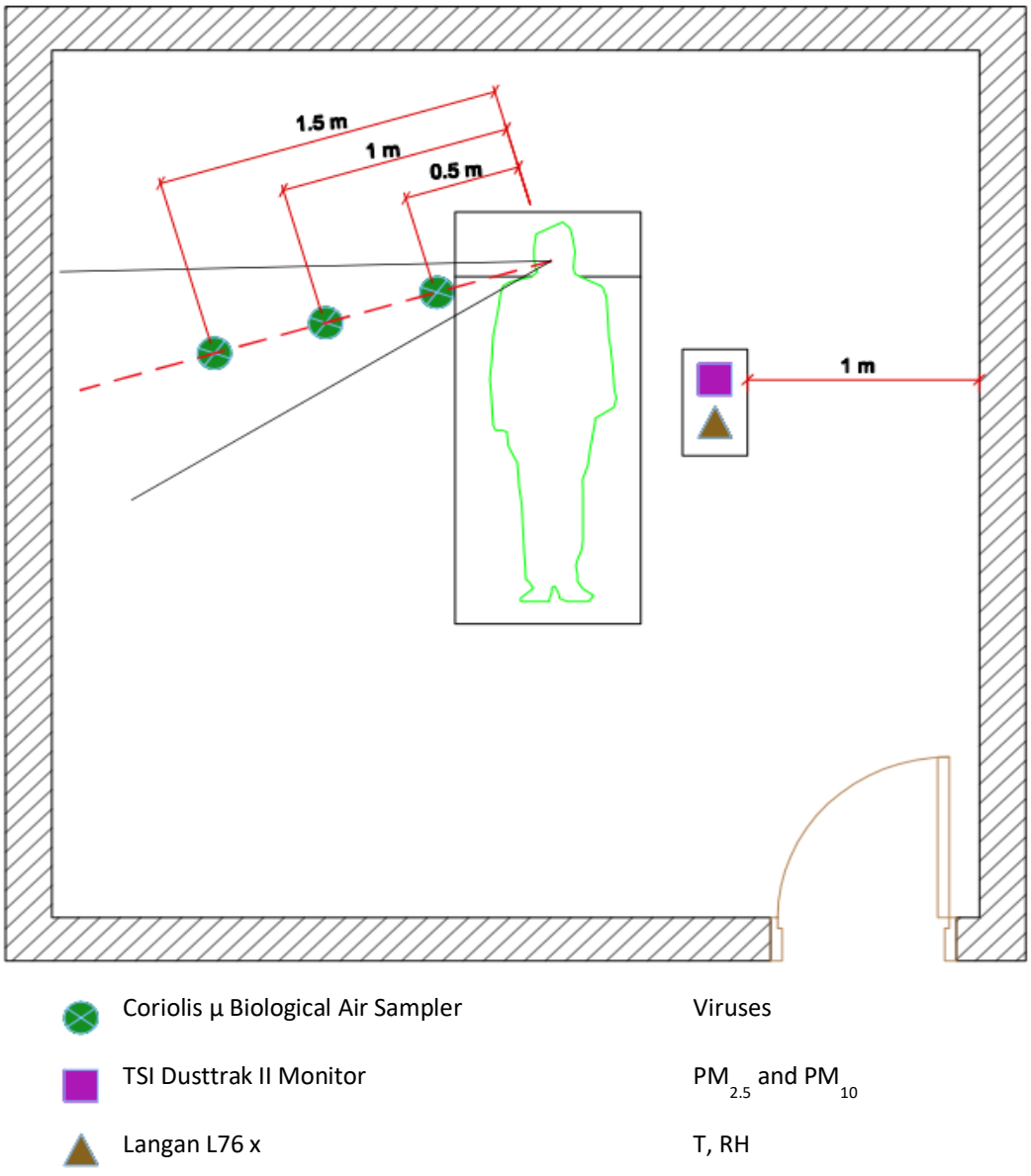

Figure 1 Patient room layout and positioning of sampling equipment

B. Laboratory Analysis

Following virus collection through the Coriolis µ Biological Air Sampler (Bertin Instruments, FRANCE), the samples were transported to the Center for Infectious Disease

Research (CIDR) at the American University of Beirut, where two 500 µl aliquots were taken from the sample and the rest were poured in a 50 ml falcon tube and stored at -80°C. RNA extraction was performed on 250 µl from one of the aliquots using the Purelink viral RNA/DNA Mini Kit (ThermoFisher Scientific) and eluted in 40 µl nuclease free water. Following extraction, 2 µl of the RNA extract was screened for influenza A virus (IAV) by probe based quantitative reverse-transcription polymerase chain reaction (rt-qPCR) targeting the matrix gene (M gene) of influenza A (Scoizec et al., 2018). Positive samples had their copy numbers of the M gene estimated from the cycle threshold obtained from the rt-qPCR run, according to a standard curve correlating the logarithmic dilution on a complete purified genome of known copy numbers (Vircell) to its Ct value. The standard curve was done in duplicates. For each sample, the number of IAV M gene copies per m^3 air was calculated using Equation 1.

$$\text{M gene copies}/m^3 = \text{Copies}/\mu l \times V_e \times V_m/V_r \div (U \times T) \quad (1)$$

Where Vm is the volume of total media left after collection, Vr is the volume of specimen used for extraction, V_e is the eluted volume from the extraction, U is the collection flow rate in m^3/min, and T is the collection time in min.

C. Statistical and numerical analysis

Initially, the indoor $PM_{2.5}$ and PM_{10} levels in each room were averaged over the sampling period and compared with the relevant IAQ guidelines (EPA, 2014, WHO, 2010). Additionally, the correlation (Pearson's) between the measured response variables ($PM_{2.5}$,

PM_{10}, and RNA copies) and several potential predictors, such as temperature, relative humidity, occupancy rate, and number of coughs, were calculated. Note that several virus-related IAQ studies have relied on statistical analysis to assess the variability observed in the aerosols distribution and exposure risks within the monitored hospital environments (Baures et al., 2018; Blachere et al., 2009; Kim et al., 2016; Leung et al., 2016; Lindsley et al., 2010a; Marchand et al., 2016). Baures et al. (2018) attempted to statistically conduct a risk assessment and to characterize the spatial variability in virus concentrations in two French hospitals. On the other hand, Lindsley et al. (2016) measured influenza levels in patient rooms and concluded that exhalation was potentially a source of the influenza viruses found in the room. However, their results did not find a statistically significant correlation between exhalation, as a source, and the measured influenza A levels. Yet, their study showed that more virus positive samples were collected when patients were actively coughing. Similarly, Blachere et al. (2009) collected size fractioned influenza A from positively infected patients and found that 53% of the detectable influenza A were within the respirable aerosol fraction. While all these studies highlight important findings, no work has been conducted to establish clear statistical relationships between the influenza virus concentrations in patient rooms and the different physical parameters such as the location of the patient in the room, T, RH (Relative Humidity), and AER (Air exchange rate).

Limited work has been reported to simulate the transport of viruses from a patient into a room. Of the few studies conducted, most made use of computational fluid dynamics (CFD) (ANSYS) or assumed a well-mixed volume (CONTAM). Myatt et al. (2010) used CONTAM to assess the impact of humidification on the survival of airborne influenza;

however, their developed model remained theoretical and was never calibrated with field-based measurements. Moreover, the model did not account for the effects of temperature and relative humidity on the transmission routes. Yu et al. (2016) adopted a non-uniform concentration assumption under a Eulerian framework to define an optimal ventilation rate towards reducing infection risks. Yet, their model assumed a steady-state airflow field and that patients were shedding the virus at a constant frequency, time, and rate. It also did not consider the effects of temperature and humidity on the dispersion and transport of airborne viruses. Similarly, Cheong and Lee (2018) simulated the dispersion of airborne pathogens using CFDs to assess the effects of changing the location of the ventilation diffusers, the addition of partitions between beds, and increasing ventilation rates. In this study, we adopted a steady-state Gaussian puff model (Holzbecher, 2012) to assess viral levels as a function of distance, air exchange rate, shedding rate and frequency, RH and T. The adopted model was used to simulate the spatial trajectory of particles that move by advection, dispersion and settling with a transformation mechanism at the beginning of the trajectory (Equations 2-5).

$$c(x,y,z) = \frac{M}{(2\pi)^{\frac{3}{2}}} \sum_{k=1}^{N} \frac{1}{\sigma_{xk}\sigma_{yk}\sigma_{zk}} \exp\left(-\frac{(x_k-x)^2}{2\sigma_{xk}^2} - \frac{(y_k-y)^2}{2\sigma_{yk}^2} - \frac{(z_k-z)^2}{2\sigma_{zk}^2} - \lambda t\right) \quad (2)$$

$$RH = \exp\left(\frac{4\,\sigma M_w}{\rho R T D_{eq}} - \frac{M_w}{\rho_w\left(\left(D_{eq}-D_{m,s}\right)^3-1\right)} \sum \frac{v_y \theta_y \rho_y x_{s,y}}{M_y}\right) \quad (3)$$

$$S_i = \frac{2\rho g D_{eq}^2}{9\eta} \quad (4)$$

$$\lambda_{Settling} = -\frac{S_i}{H} \quad (5)$$

$$AER = \frac{AI \times 60}{V} \quad (6)$$

Where $c(x, y, z)$ is the virus concentration (RNA copies/m^3); M is the exhausted viral mass (number of RNA copies) relative to each particle diameter; N is the number of coughs and sneezes; x, y and z are the coordinates of the particles (m)[1]; $\sigma_{x,k}$, $\sigma_{y,k}$, and $\sigma_{z,k}$ (m) are the x-directional, y-directional and z-directional deviation of the Gaussian distribution inside the k^{th} puff, respectively where $\sigma_i = \frac{x \times u_i}{u_x}$ (Holzbecher, 2012);[2] λ is the decay term due to settling and air exchange rate (1/minute) (Yang and Marr, 2011); (x_k, y_k, z_k) is the spatial position of the k^{th} cough[3]; σ is the surface tension of the droplet = 0.072 Nm^{-1} (Mikhailov et al., 2004); M_w is the molar mass of water = 18 g mol^{-1}; M_y is the molar mass of component y (M_{NaCl} = 58.4 g mol^{-1}, M_{TP} = 66.5 x 10^3 g mol^{-1}) (Yang and Marr, 2011); ρ is the density of the entire droplet; ρ_y is the density of the component (NaCl = 2165Kg.m^{-3}, TP = 1362Kg.m^{-3}) (Yang and Marr, 2011); R is the ideal gas constant; T is the temperature (Zhang et al.); D_{eq} is the equilibrium diameter (µm); ρ_w is the density of water; $D_{m,s}$ (µm) is the mass equivalent diameter of a particle consisting of dry solutes; V_y is the stoichiometric dissociation number of component y (v_{NaCl} = 2, v_{TP} = 1) (Mikhailov et al., 2004); $X_{s,y}$ is the mass fraction of component y (x_{NaCl} = 0.104, x_{TP} = 0.896) (Yang and Marr, 2011, Nicas et al., 2005); θ_y is the practical osmotic coefficient (TP = 3.75; NaCl = 0.95) (Yang and Marr, 2011, Nicas et al., 2005); S_i is the settling velocity (m/second); H is the settling height estimated in the model as the patient breathing level (H=1.5 m); η is the viscosity of the particle (g/m.s); AER is the air exchange rate (in 1/hour); AI is the air intake in (m^3/min); V is the room volume (m^3).

[1] x is the distance from the patient (0.5 m, 1 m, or 1.5 m); y = z = 0 since the model is calibrated based on collected samples at the level of the patient and with 0 offsets.

[2] Lateral deviations of the Puff model vary with the velocity u_x, which varies from one patient to another. σ_y and σ_z were estimated for every patient within a stepwise Monte-Carlo analysis aiming to minimize to the mean square error

According to Nicas et al. (2005), after coughing the emitted particles directly shrink from their original diameter to an equilibrium diameter D_{eq}. This is a function of the ambient relative humidity and temperature. At low RH levels, droplets are likely to lose more water than at higher levels. In this context, Mikhailov et al. (2004), developed a relationship to estimate the D_{eq} as a function of relative humidity, temperature, as well as the physiochemical properties of the droplets and the Kelvin effect (Equation 3). In this study, the change in diameter was assumed to occur immediately after a cough (y=0) and the physiochemical properties of the emitted respiratory fluid was considered to include 8.8 g/L NaCl (inorganic components) and 76 g/L total proteins (organic components) (Nicas et al., 2005, Yang and Marr, 2011). The size of the droplet in turn affected the estimated settling rate and removal efficiency (Equation 4). In this study, it was assumed that all patients have the same coughed droplets diameter distribution as reported by Xie et al. (Xie et al., 2009). The RNA copies remaining airborne over distance were calculated for each droplet diameter size before the total virus concentration was estimated. The particles were assumed to move at a constant velocity equal to that of the cough. Coughs were considered to occur at equal time intervals Δt. Moreover, the viruses were assumed to be equally distributed across cough particles. While virus transmission can occur through droplets expelled through coughing and sneezing or via aerosols, this model only accounts for the short-range transmission due to the lack of sufficient data on deposition, resuspension and fractionation of infected aerosols, which can introduce significant bias to the model. It should also be noted that due to lack of data on the viability of the collected viruses, the biological decay of the shed viruses was unaccounted for in the model. Instead, the model was calibrated by varying the cough velocity (Baures et

al.) and the shedding rate for each of the monitored patient rooms that reported a positive influenza RNA at 0.5 m and 1 m (Figure 2).

Figure 2 Model Calibration and Analysis Process

Several variables were predefined in the model. These included temperature, relative humidity, number of coughs, and air exchange rate. Temperature and relative humidity were averaged over the monitoring period. The air exchange rate (AER) was calculated using equation (6) and was estimated to be 7.2 ach. The formula variables were obtained and validated by the AUBMC physical plant. The number of coughs was based on the actual counts in each room. The parametrization of the remaining variables that included the shedding rate, air flow velocities, lateral air velocities, and cough velocity was done through assigning statistical distributions to each based on literature reported values. The uniform distribution was adopted for most the parameters, as it represents vague prior information on the parameter of interest. As such, the shedding rate was assumed to follow a normal distribution of mean 15.8 and standard deviation of 29.3 copies/cough (Lindsley et al., 2010). Similarly, lateral air velocities (u_y and u_z) were assigned a uniform distribution with a minimum of 0.125 and maximum of 0.25 m/s (Chamseddine, 2018). Note that these values were based on CFD simulations that were conducted for the same patient rooms measured in this study. All patient rooms were assumed to have similar volumes, geometry and

ventilation. As for the cough velocity (Baures et al.), it was assumed to follow a uniform distribution with a minimum of 2.2 and a maximum of 22 m/s (Tang et al., 2012a, Kwon et al., 2012, Gupta et al., 2009). Since samples were collected independently at different times, the reported number of coughs varied between the two samples. As such, normalized concentrations were used to calibrate the puff model. Moreover, the model was calibrated for each room that had two positive samples independently. This allowed us to account for the unique shedding characteristics of each patient (shedding rate and coughing speed).

A probabilistic Monte-Carlo (MC) simulation was then used to calibrate the model. One million randomly generated combinations of shedding rates, air flow velocities, lateral air velocities, and coughing speeds were sampled independently and used to estimate the virus concentration at 0.5 m and 1 m. The combination of parameters that resulted in the minimal mean square error between the predicted and measured virus concentrations at 0.5 and 1 m away from the patient bed were selected and used to predict the virus concentrations at source (x=0.1 m) is estimated. Finally, the calibrated model was used to predict the concentration near the patient's mouth (0.10 m away) and to assess how varying T, RH and AER would affect viral transmission.

CHAPTER III
RESULTS AND DISCUSSION

A. Patient characteritics and virus detection

Thirty-three subjects/patients who were admitted to the sampled hospital and screened for RSV and influenza virus volunteered to undergo the study. All patients that have been isolated with droplet precaution and tested positive for influenza A, influenza B or RSV were approached to volunteer in the sampling program. A total of 33 met enrollment criteria and 65 air samples were collected. All patients were on anti-viral medical treatment. Twenty-eight patients tested positive for influenza A virus, 5 patients tested positive for influenza B, and none had RSV (Figure 3). Air samples were collected at 0.5 m and 1 m from the patient. Patients were defined as emitters if they were influenza virus-positive subjects based on the PCR analysis and had at least one virus positive air sample collected in their room. Fourteen out of the 33 recruited patients were found to be emitters (Figure 3).

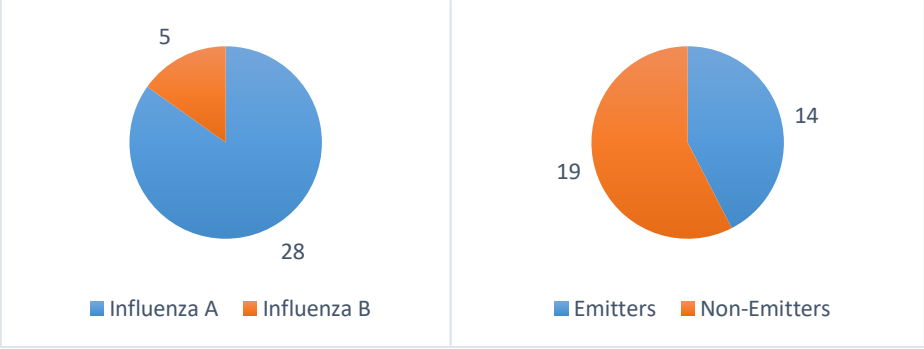

Figure 3 Admitted patients' characteristics

Moreover, only air samples collected from influenza A patients yielded positive virus results. In total, 19 of the 65 air samples had detectable viral RNA; of which 6 (32%) were collected at a 0.5 m distance away from the patient, 12 samples (63%) at 1m, and 1 sample at 1.5 m (5 %) (Figure 4). Positive viral RNA concentrations across patient rooms ranged between 222 copies/m^3 and 5760 copies/m^3 with a mean of 820 copies/m^3 (Table 1).

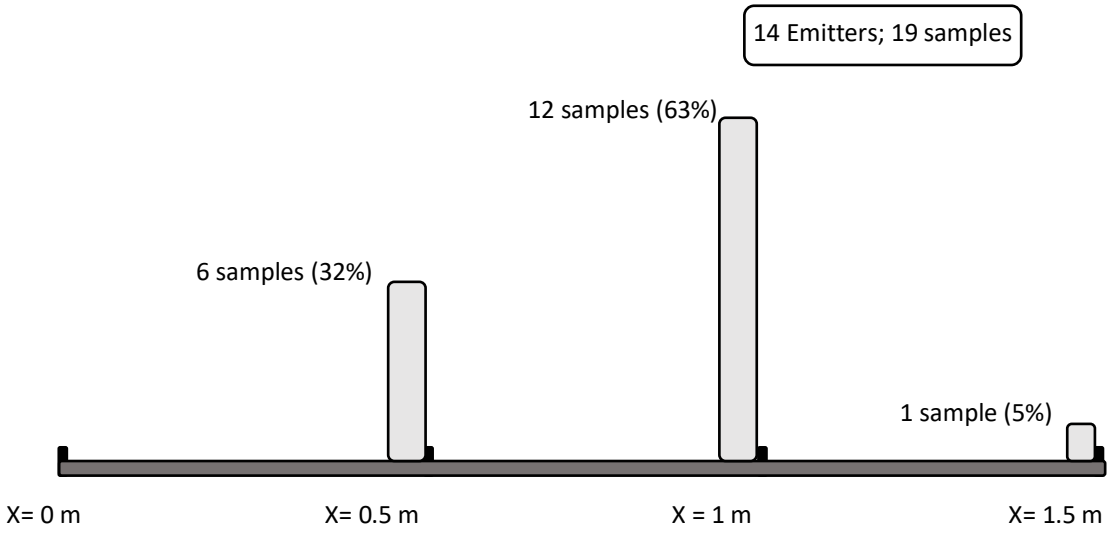

Figure 4 Positive samples distribution

Given that our results showed that 68% of the positive samples were detected at 1 m or beyond, there is strong evidence to show that a significant fraction of the detected virus is present on very fine particles in suspension and thus can travel away from the patient and present a risk of airborne transmission. This raises concerns that the current WHO and CDC safe distance recommendations (i.e. spacing of 1 m) may not be adequate to ensure the protection of visitors and HCPs (Healthcare practitioners) during routine care operations in hospitals and similar healthcare facilities. Our results concur with several previous studies that have reported that influenza transmission may occur through large droplets traveling up

to 1 m from the source (Redrow et al., 2011, Lindsley et al., 2010, Killingley and Nguyen-Van-Tam, 2013, Fabian et al., 2008, La Rosa et al., 2013).

Nevertheless, the results of this study also highlighted the importance of increasing the separation distance between the patient and visitors and HCPs. When the RNA concentrations were normalized by the number of coughs, we found that the virus concentrations showed a statistically significant drop with increasing distances (Wilcoxon signed rank test, $p=0.03125$), with the normalized concentrations at 1 m being on average half of those measured at 0.5 m in the same room. In one of the rooms, where samples were collected at 1 and 1.5 meters, concentrations at 1.5 m were 8 times lower than those measured at 1 m.

Table 1 Relative humidity, ambient temperature, PM, and viral concentrations measured in patient rooms with at least one positive sasmple

Room Number	RH (%)	T	PM_{10} (mg/m^3)	$PM_{2.5}$ (mg/m^3)	Distance (m)	Number of coughs	Concentration (RNA copies/m^3)
617	51.69	22.51	0.035	0.018	1	18	1804.8
					0.5	1	339.4
912	38.74	24.95	0.046	0.039	1	1	393.1
					0.5	0	0
905	47.86	21.79	0.009	0.007	1	7	290.6
					0.5	4	0
1041	42.76	22.58	0.021	0.013	1	8	0
					0.5	6	730.6
527	40.84	24.04	0.019	0.015	1	5	0
					0.5	4	370
526	44.05	24.98	0.026	0.017	1	12	298.8
					0.5	6	337.2
915	45.49	22.5	0.019	0.009	1	1	221.9
					0.5	1	264.7
1009	48.71	22.66	0.059	0.047	1	9	308.2
					0.5	8	0
1012	44.99	21.06	0.059	0.045	1	30	224.8
					0.5	26	302.5
1001	59.26	20.6	0.043	0.026	1	11	724.2
					0.5	4	0
1007	50.97	23.42	0.02	0.014	1	7	290.5
					0.5	28	0
1014	48.68	25.41	0.012	0.01	1	1	5760
					0.5	0	0
924	42.73	21.68	0.078	0.042	1	3	575.4
					0.5	3	0
1030	62.6	23.53	0.089	0.036	1	9	3225.6
					1.5	10	437.5

RH: Relative humidity; T: Temperature; PM: Particulate matter; RNA: Ribonucleic acid

In this study, coughing was assumed to be the major virus emission factor. This was reinforced by the sampling results that showed that patients who were more actively coughing were associated with a higher positive rate of virus detection in the collected air samples (t-test; p-value=0.049). Note that the discrepancy in the coughing rate explained to a large extent the instances when the concentrations measured at 1 m were found to be higher than those measured at 0.5 m. Nevertheless, two positive viral RNA copies were recorded in the absence of any cough. This highlights the potential of the virus to remain suspended for

extended periods in the air or to be transmitted by normal breathing and talking (Killingley and Nguyen-Van-Tam, 2013, Cowling et al., 2013, Nikitin et al., 2014, La Rosa et al., 2013). The influenza A virus has been suspected to be transmitted by other mechanisms such as talking or simply breathing, which in turn expels fine infected aerosols (Lindsley et al., 2016). For instance and based on an observational study, Fabian et al. (2008) reported that the virus might be contained in fine particles generated during tidal breathing. Similarly, Stelzer-Braid et al. (2009) stated that the virus can be emitted during talking.

With regards to the association of the viral concentrations with the physical environment in the patient rooms, the normalized viral RNA copies were found to be positively correlated with temperature ($r = 0.43$, p-value = 0.1). No significant correlations were found between virus concentrations and the measured PM_{10} or $PM_{2.5}$ levels in the rooms. Similarly, there was no statistically significant correlation between the measured virus concentrations and the relative humidity ($r=-0.29$, p-value = 0.2). Yet, the percent drop in virus concentrations between 0.5 m and 1 m (ranged between 16.18% and 87.79%) was found to have a strong positive correlation with RH ($r = 0.803$; p-value = 0.0358).

B. PM and thermal comfort parameters

Temperature (T) and relative humidity (RH) in patient rooms ranged from 20.6 to 25.4 ^{o}C and 38.7 to 62.6%, with a mean of 23 ^{o}C and 48.4% and a standard deviation of 1.25 ^{o}C and 5.8%, respectively (Table 2). Particulate matter was monitored concomitantly with viruses. The time-averaged PM_{10} levels across patient rooms ranged between 9 and 89 $\mu g/m^3$, with a mean of 34 $\mu g/m^3$. As for $PM_{2.5}$ it ranged between 7 and 53 $\mu g/m^3$, with a mean of

24.5 µg/m^3. Similar ranges were reported in the literature (Ostro et al., 2009, Slezakova et al., 2012). The measured concentrations in several patient rooms exceeded international guidelines (Figure 5).

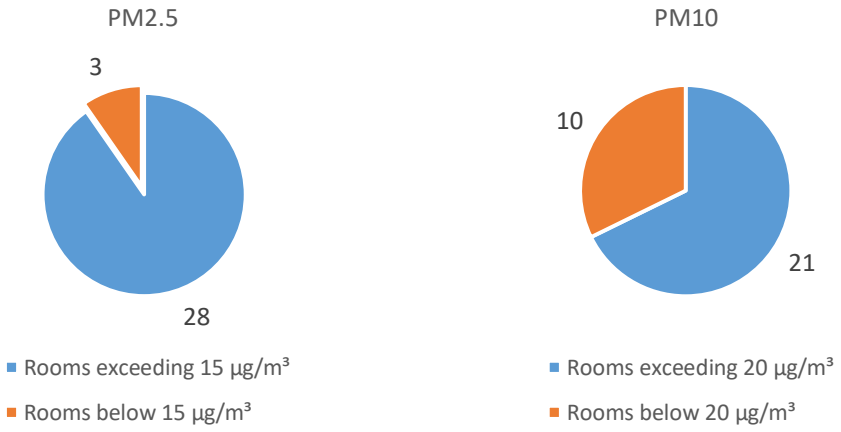

Figure 5 PM levels in patient rooms in comparison to WHO guidelines

This could be attributed to the resuspension of settled PM due to frequent visits or to the infiltration of outdoor PM_{10} and $PM_{2.5}$ due to high indoor-outdoor PM interaction in the tested patient rooms (Chamseddine and El-Fadel, 2015). Interestingly, no statistically significant correlation was detected between PM levels and occupancy rates.

Table 2 Thermal comfort parameters

Parameter	Mean	Minimum	Median	Maximum	Standard Deviation
Temperature	23	21	23	25	1.25
Relative Humidity (%)	48	39	48	63	5.80

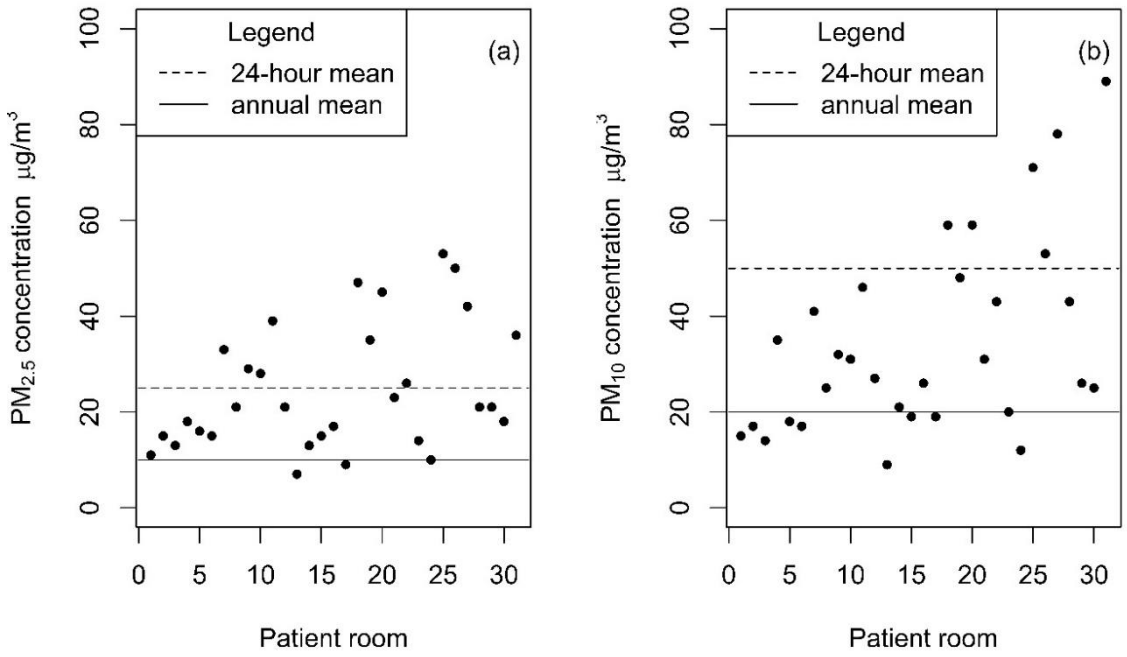

Figure 6 Patient room measurements and WHO guidelines: (a) PM2.5 and (b) PM10

C. Numerical model

Several studies have attempted to simulate the transmission of the influenza virus, often focusing on the physical dispersion of the cough and neglecting the impact of temperature and relative humidity on the influenza transmission route (Tang et al., 2012b, Tang et al., 2012a). Few studies highlighted the possible impact of humid and cold spaces on influenza survival (Noti et al., 2013, Zuk et al., 2009, Metz and Finn, 2015). This study attempted to combine both aspects to assess their potential impacts on the survival, aerosolization, and transmission of influenza. The steady-state Gaussian puff model was used to simulate the emission, dispersion and removal of emitted aerosols and was calibrated using the collected data. The model was used to predict the initial concentrations at the source for

each patient. Those were found to range between 405 and 20,029 RNA copies/m^3 across the 5 patient rooms. Note that previous studies have reported that the shedding rate vary significantly across patients and are a function of specific patient characteristics such as sex, influenza vaccination date, smoking habits, antiviral medication, BMI (Body Mass Index) and body temperature (Yan et al., 2018). Overall, the model was found to predict viral concentrations at 0.5 m much better than those at 1 m. Concentrations at 1 m tended to be over-predicted, while those at 0.5 m were predicted with a difference < 10% (Table 3).

Table 3 Predicted versus observed viral concentrations along with estimated shedding rates and viral concentrations 0.1 m from patient

Room Number	Distance (m)	Normalized Measured Concentration (RNA copies/m^3)	Predicted Normalized Concentration (RNA copies/m^3)	Percent Difference (%)	Estimated Shedding rate (RNA copies/cough)	Estimated Concentration at source (RNA copies/m^3)
617	0.5	339.36	346.32	2	38	12,447
	1	100.27	59.51	-40		
526	0.5	56.2	58.72	4.5	39	1,902.8
	1	24.9	10.09	-59		
915	0.5	264.72	294.19	11.1	5.84	9,533.6
	1	221.88	50.55	-76		
1012	0.5	11.64	12.5	7.4	9.8	405.08
	1	7.452	2.15	-71		
1030	1	358.4	349.03	2.6	24	20,029
	1.5	43.75	83.03	88		

The model was used to compare between the relative magnitude of the viral removal pathways. Three major mechanisms that affect the virus concentrations were considered, namely dispersion, settling, and ventilation (air exchange rate). Dispersion had the highest impact in reducing the concentration. The model predicted that dispersion alone was able to reduce the virus concentrations by 11.30% in the initial 0.5 m and then by an additional 73.45% by 1m, yielding a total reduction of 84.76%. Interestingly, the impact of dispersion was more pronounced in the second half meter as compared to the first half. This can be explained by the typical dispersion pattern of a cough (Tang et al., 2012a, Gupta et al., 2009, Bourouiba et al., 2014) (Figure 8). Settling, which is mainly affected by temperature and relative humidity, came second; it was responsible for a reduction of around 13.5 % over the first 1 m distance. Moreover, the role of AER on removal was found to be marginal with a reduction rate of 1 % (Figure 7).

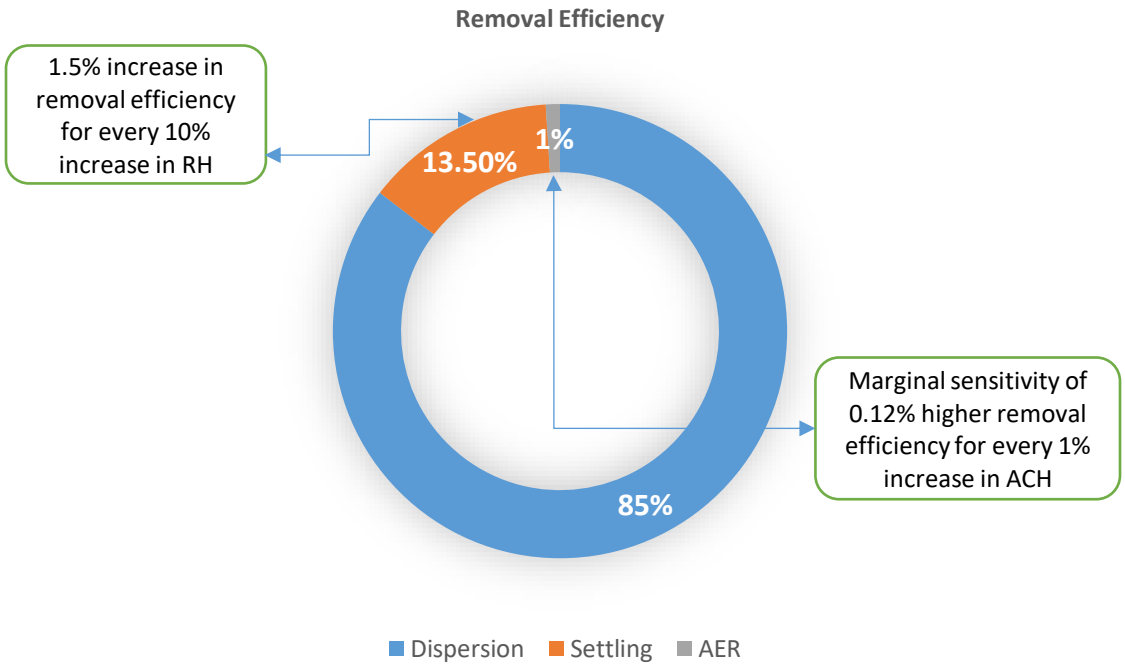

Figure 7 Major virus removal mechanisms

A one-at-a-time sensitivity analysis was conducted to assess the impact of changing ambient parameters (RH, T, AER) on virus removal efficiency. The model showed no sensitivity to variations in temperature over the tested range of [20.6 – 25.4 ^{o}C]. Conversely, increasing relative humidity (from 38 % to 62 %) was found to increase the settling efficacy. Note that the impact of RH on the removal rate is mainly due to the transformation of droplets, which takes place right after the shedding point. Depending on the RH of the room, the droplets moisture content decreases, affecting its size and as a result it's settling velocity. As such, at higher relative humidity levels the coughed droplets are able to retain their moisture content and as such are heavier and tend to settle better. Conversely, in less damp environments the droplets tend to lose their moisture content to the ambient environment, leading to smaller particles that higher probability to remain in suspension. Nevertheless, we found that the model's sensitivity to changes in relative humidity was low (+1.5 % change in removal rate for a 10 % increase in RH). With regards to AER, the model was found to be largely insensitive to changes in AER. The overall removal efficiency was found to have improved by 0.12 % for every 1 ACH increase. Note that while increasing the AER is expected to improve the removal rate as a result of improving air recirculation, it can at the same time result in accelerating dispersion in a patient room due to increased lateral air velocities.

Finally, it is important to highlight that the adopted model has several simplifying assumptions and limitations. One of the main limitations of the model was the need to calibrate it using only two time integrated sampled collected in each patient room. This limits the confidence in the decay curve that was developed to track virus concentration development over distance. Furthermore, the model assumed that the AER and the lateral diffusivity terms were the same across all rooms. Similarly, the model assumed that the emitted droplet distribution didn't vary by

patient. Moreover, the model assumes homogeneity in the expelled viral load per cough through normalization. Future work should aim towards taking multiple measurements per patient room. In addition, future studies should attempt to collect patient specific information in order to better estimate shedding rates and coughing speeds. Finally, the model will benefit from incorporating biological decay and to model it as a function of temperature and RH. This could be incorporated in the model by adjusting the virus concentration, to only include the viable viruses.

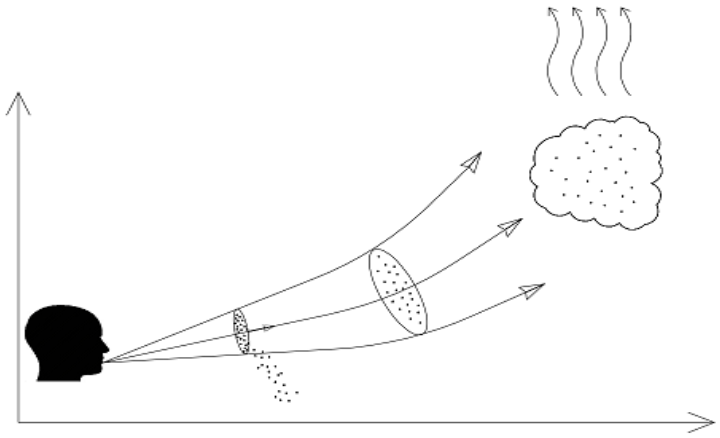

Figure 8 Horizontal physical representation of the evolution of a cough cloud

CHAPTER IV
CONCLUSION

According to CDC, an estimated 35.5 million people in the US have gotten the flu and 34.200 passed away from it (CDC, 2019). The results from this study reflect concerns about IAQ in healthcare facilities and potential exposure of healthcare staff and visitors to viruses caused by the shedding of infected patients. Moreover, it highlighted that elevated indoor PM levels caused by outdoor sources and/or re-suspension of settled particles by indoor activities were a concern. Comparing the measured PM levels with the WHO guidelines for indoor air quality, it was found that 91% of the monitored patient rooms exceeded the $PM_{2.5}$ daily exposure level of 10 mg/m^3, while 70% of the rooms exceeded the PM_{10} daily exposure level of 20 mg/m^3. In addition to the elevated PM levels, the results showed a real concern with virus exposure and the transmission in patient rooms. In this study out of the 33 patient rooms that were monitored, influenza A was detected in 14 rooms with 63% of the positive samples collected at 1 m away from the patient. In such case, virus transmission to staff, visitors or other patients is highly probable. The detection of viral RNA and at such elevated levels could be the result of inadequate ventilation, reduced relative humidity or high indoor temperatures.

In light of the findings of this study, potential mitigation measures that could prove to be effective in improving the IAQ in patient rooms, can be summarized as follows:

- Adjust placement of bed, to maximize the distance between the patient and the visitors and healthcare facility workers

– Create a buffer area inside the room via curtains at least 1.5 m away from the patient to separate the infected patient zone from the hospital ward. According to Ching et al. (2008), curtains could be effective to minimize influenza transmission.
– Adopt a set of measures to disinfect the patient room before taking in a new patient. These include setting the room under extreme temperature and RH conditions, increasing the air exchange rate and cleaning frequencies. This is vital, as viruses could remain suspended and travel inside the room.
– Adjust temperature and RH in order to enhance the removal of airborne viruses

Additional healthcare management practices are summarized in the below table (Table 4). As can be seen, the proper management of the indoor air quality of healthcare facilities does not only depend on the presence of an infection control team, but rather should be complemented with a well-trained facility management team that can implement an integrated approach that aims to control the different aspects of air quality and movement inside patient rooms.

Table 4 Specific factors and mitigation measures associated with hospitals indoor air quality

Factor	Mitigation measure
Indoor Sources (Bioaerosols, Particulate Matter)	- Clean patient rooms regularly while proper ventilation is ensured. - Avoid unnecessary visits to patient rooms to avoid re-suspension of settled particles. - Use hospital curtains to create an extra buffer zone between the patient and the hospital ward. - Use of UV and face masks to disrupt environmental transmission of influenza virus. - Keep door closed to disrupt influenza virus dispersal.
Ventilation	- Open windows occasionally to provide fresh air from the outside (in case outdoor air is clean). - Rely on decentralized mechanical ventilation for droplet isolation patient rooms with maximized ventilation rates. - Check and maintain mechanical ventilation system to preserve stable comfort parameters. - Change ventilation system filters regularly
Comfort Parameters	- Maintain temperature and maximum RH within specified thermal comfort range.

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APPENDIX A

Table 5: Model input parametrs and assumptions

Parameter	Unit	Definition	Value/range used	Justification / Reference
u_x	m/sec	Coughing speed	2.2 - 22	(Gupta et al., 2009, Kwon et al., 2012, Tang et al., 2012b)
u_y, u_z	m/sec	Lateral velocities	0.125 – 0.250	(Chamseddine, 2018)
M	RNA copies/cough	Shedding rate	p-norm (mean = 15.8; sd = 29.3)	(Lindsley et al., 2010)
σ	N.m-1	Surface Tension	0.072	(Mikhailov et al., 2004)
M_w	$g.mol^{-1}$	Molar mass of water	18	-
M_{NaCl}	$g.mol^{-1}$	Molar mass of NaCl	58.4	(Yang and Marr, 2011)
M_{TP}	$g.mol^{-1}$	Molar mass of total protein	66.5×10^3	(Yang and Marr, 2011)
ρ_{NaCl}	$g.m^{-3}$	Density of NaCl	0.997	(Yang and Marr, 2011)
ρ_{TP}	$g.m^{-3}$	Density of Total protein	2.165	(Yang and Marr, 2011)
ρ_w	$g.m^{-3}$	Density of water	1.362	-
R	J/k.mol	Ideal Gas constant	8.31	-
v_{NaCl}	-	Stoichiometric dissociation number of NaCl	2	(Mikhailov et al., 2004)
v_{TP}	-	Stoichiometric dissociation number of TP	1	(Mikhailov et al., 2004)
x_{NaCl}	%	NaCl mass fraction of droplet	0.104	(Nicas et al., 2005, Yang and Marr, 2011)
x_{TP}	%	TP mass fraction of droplet	0.896	(Nicas et al., 2005, Yang and Marr, 2011)
θ_{NaCl}	-	Practical osmotic coefficient of NaCl	3.75	(Yang and Marr, 2011)
θ_{TP}	-	Practical osmotic coefficient of TP	0.95	(Yang and Marr, 2011)
g	$m.sec^{-2}$	Gravitational acceleration	9.81	-
η	$g.m^{-1}.sec^{-1}$	Air viscosity	0.0185	-
H	m	Settling Height	1.5	H is assumed to be the distance from the source (mouth of the patient) to the ground
AI	$m^3.min^{-1}$	Air Intake	8.5	The air intake was obtained from the AUBMC physical plant
V	m^3	Patient room volume	70	The volume was obtained from the AUBMC physical plant and was assumed to be the same for all patient rooms

Table 6: PM_{10} and $PM_{2.5}$ data

	PM_{10} (µg/m^3)			$PM_{2.5}$ (µg/m^3)				T	RH
Date	**Average**	**Minimum**	**Maximum**	**Average**	**Minimum**	**Maximum**	**Occupancy**	**(C)**	**(%)**
12/27/2018							2	22.8	49.9
12/27/2018	15	13	16	11	11	11	2	23.8	45.4
12/27/2018	17	16	18	15	13	19	3	24.2	44.9
12/27/2018	14	13	16	13	13	13	2	24.3	45
12/28/2018	35	29	68	18	17	20	5	22.5	51.7
12/31/2018	18	18	19	16	16	17	3	22.9	53.2
12/31/2018	17	15	21	15	13	16	3	23.9	51.7
1/2/2019	41	35	48	33	31	35	3	22.2	45.2
1/2/2019	25	23	26	21	20	23	3	23.8	40.6
1/2/2019	32	31	33	29	28	30	3	24.5	40.7
1/2/2019	31	29	33	28	27	30	2	24.5	44.2
1/2/2019	46	42	49	39	37	40	5	25	38.7
1/4/2019	27	25	29	21	20	22	3	22.5	49
1/7/2019	9	8	10	7	7	7	3	21.8	47.9
1/9/2019	21	18	24	13	12	15	3	22.6	42.8
1/9/2019	19	17	22	15	13	18	3	24	40.8
1/9/2019	26	19	45	17	13	21	3	25	44.1
1/14/2019							3	22.7	53.1
1/16/2019	19	16	22	9	8	12	3	22.5	45.5
1/21/2019	59	55	64	47	45	48	2	22.7	48.7
1/21/2019	48	42	55	35	31	38	3	23.7	44.2
1/23/2019	59	53	72	45	43	46	2	21.1	45
1/23/2019	31	28	36	23	21	24	4	23.1	50.1
1/29/2019	43	30	54	26	24	29	2	20.6	59.3
1/29/2019	20	17	23	14	13	15	2	23.4	51
1/29/2019	12	11	15	10	9	11	3	25.4	48.7
1/30/2019	71	65	77	53	48	56	2	21.2	56.8
2/4/2019	53	48	56	50	30	70	2	22	47.2
2/8/2019	78	70	90	42	39	46	2	21.7	42.7
2/11/2019	43	23	60	21	17	38	3	21	59.9
2/11/2019	26	24	28	21	20	22	3	23.2	54.5
2/13/2019	25	22	30	18	17	20	2	21	51.3
2/27/2019	89	57	131	36	31	49	3	23.5	62.6

Table 7: Virus data

Date	Number of Coughs	Distance	Flu Detection	Ct	Starting quantity /µL	Starting quantity /2 µL	Elution Volume (µL)	Extraction Volume (µL)	RNA Copies/m^3	Normalized RNA Copies /m^3
12/27/2018	0	1	Negative	0			40	500	0	0
	1	0.5	Negative	0			40	500	0	0
12/27/2018	6	1	Negative	0			40	500	0	0
	25	0.5	Negative	0			40	500	0	0
12/27/2018	23	1	Negative	0			40	500	0	0
	20	0.5	Negative	0			40	500	0	0
12/27/2018	8	1	Negative	0			40	500	0	0
		0.5								
12/28/2018	18	1	Positive	35	11.3	5.6	40	500	1805	100.3
	1	0.5	Positive	37	2.1	1.06	40	500	339.4	339.4
12/31/2018	7	1	Negative	0			40	500	0	0
	5	0.5	Negative	0			40	500	0	0
12/31/2018	4	1	Negative	0			40	500	0	0
	3	0.5	Negative	0			40	500	0	0
1/2/2019	0	1	Negative	0			40	500	0	0
	0	0.5	Negative	0			40	500	0	0
1/2/2019	15	1	Negative	0			40	500	0	0
	13	0.5	Negative	0			40	500	0	0
1/2/2019	5	1	Negative	0			40	500	0	0
	1	0.5	Negative	0			40	500	0	0
1/2/2019	0	1	Negative	0			40	500	0	0
	0	0.5	Negative	0			40	500	0	0
1/2/2019	1	1	Positive	37	2.5	1.2	40	500	393.1	393.1
	0	0.5	Negative	0			40	500	0	0
1/4/2019	1	1	Negative	0			40	500	0	0
	1	0.5	Negative	0			30	500	0	0
1/7/2019	7	1	Positive	37	2.4	1.2	30	500	290.6	41.5
	4	0.5	Negative	0			30	500	0	0
1/9/2019	8	1	Negative	0			30	500	0	0
	6	0.5	Positive	36	6.1	3	30	500	730.6	121.8
1/9/2019	5	1	Negative	0			30	500	0	0
	4	0.5	Positive	36	3.1	1.5	30	500	367	92.5
1/9/2019	12	1	Positive	37	2.5	1.25	30	500	298.8	24.9
	6	0.5	Positive	36	2.8	1.4	30	500	337.2	56.2
1/14/2019	0	1	Negative	0			30	500	0	0
	0	0.5	Negative	0			30	500	0	0
1/16/2019	1	1	Positive	37	1.85	0.93	30	500	221.9	221.9
	1	0.5	Positive	37	2.2	1.1	30	500	264.7	264.7
1/21/2019	9	1	Positive	37	2.6	1.3	30	500	308.2	34.2
	8	0.5	Negative	0			30	500	0	0
1/21/2019	8	1	Negative	0			30	500	0	0
	0	0.5	Negative	0			30	500	0	0
1/23/2019	30	1	Positive	37	1.9	0.94	30	500	224.8	7.5
	26	0.5	Positive	37	2.5	1.3	30	500	302.5	11.6
1/23/2019	4	1	Negative	0			30	500	0	0
	9	0.5	Negative	41	0.095	0.05	30	500	0	0
1/29/2019	11	1	Positive	36	6	3	30	500	724.2	65.8
	4	0.5	Negative	0			30	500	0	0
1/29/2019	7	1	Positive	37	2.4	1.2	30	500	290.5	41.5
	28	0.5	Negative	0			30	500	0	0
1/29/2019	1	1	Positive	33	48	24	30	500	5760	5760
	0	0.5	Negative	0			30	500	0	0
1/30/2019	13	1	Negative	0			30	500	0	0
	28	0.5	Negative	0			30	500	0	0
2/4/2019	0	1	Negative	0			30	500	0	0
	0	0.5	Negative	0			30	500	0	0
2/8/2019	3	1	Positive	36	4.8	2.4	30	500	575.4	191.8
	3	0.5	Negative	0			30	500	0	0
2/11/2019	8	1	Negative	0			30	500	0	0
	10	0.5	Negative	0			30	500	0	0
2/11/2019	2	1	Negative	0			30	500	0	0
	0	0.5	Negative	0			30	500	0	0
2/13/2019	0	1	Negative	0			30	500	0	0
	0	0.5	Negative	0			30	500	0	0
2/27/2019	9	1	Positive	34	26.9	13.4	30	500	3225.6	358.4
	10	0.5	Positive	36	3.7	1.8	30	500	437.52	43.752

Table 8 Droplets diameter ranges emitted during coughing

Average Diameter (µm)	Range (µm)	Droplet Percentage (%)
1.5	[1-2]	0
3	[2-4]	0
6	[4-8]	0
12	[8-16]	0
20	[16-24]	0.3
28	[24-32]	0
36	[32-40]	0.5
45	[40-50]	6.2
62.5	[50-75]	30.8
87.5	[75-100]	23.4
112.5	[100-125]	15.0
137.5	[125-150]	5.9
175	[150-200]	7.4
225	[200-250]	3.4
375	[250-500]	4.5
750	[500-1000]	2.4
1500	[1000-2000]	0.2