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The Impact of Hospital-Ward Ventilation on Airborne-Pathogen Exposure

To the Editor:

The coronavirus disease (COVID-19) pandemic has brought into sharp focus the importance of protecting patients and healthcare workers (HCW) from nosocomial infection (1). Hospital-associated infection can occur through contact with contaminated surfaces, either by droplets generated by coughing or sneezing settling on exposed mucous membranes or through direct inhalation of aerosols. Although the contribution of each route differs according to the setting and type of infection, the ventilation within hospitals is a key determinant of infection risk from airborne pathogens (2, 3), with low ventilation rates associated with increased risks of transmission of, for example, tuberculosis and Middle East respiratory syndrome (4, 5). For patients with cystic fibrosis (CF), acquisition of multidrug-resistant pathogens from other patients represents one of the greatest threats to health (6), with both experimental data (7) and room sampling (8) highlighting the risk of cross-infection through long-lived infectious aerosols.

As a direct response to these challenges, Royal Papworth Hospital installed a bespoke ventilation system during its relocation from a 100-year-old facility to a new state-of-the-art cardiothoracic hospital in Cambridge, United Kingdom. Whereas the old CF center relied on passive, natural ventilation, with airflow created by opening doors and windows, the mechanical ventilation in the new hospital provides 15 air changes per hour (ACH) in the CF center (both patient rooms and corridors), and 6 ACH in other clinical areas.

We examined the impact of high-frequency air changes within patient rooms by monitoring the dispersal, mixing, and ventilation of an injected tracer gas (CO_2) using eight CozIR-A sensors (Gas Sensing Solutions) in the new and old hospitals, just before occupation and just after vacation respectively, while the heating and ventilation systems were operational. Although CO_2 persisted in passively ventilated rooms for over 58 minutes, rooms actively ventilated at 6 or 15 ACH experienced exponential decay of tracer concentrations to 10% of peak concentration within 26.7 and 11.7 minutes, respectively (Figure 1A).

The type of ventilation determines the fraction of airborne droplets that settle in the patient's room before being removed. Because the fall speeds of droplets vary with particle size, the impact of changes in ventilation between old and new hospitals is particularly marked for particles in the respirable size range produced by coughing (9) (1–10 μm in diameter) (Figure 1B), indicating that high-frequency air changes may reduce transmission risks from aerosols.

We next explored air mixing and dispersal along hospital-ward corridors, again using a CO_2 tracer with sensors deployed 1.7–14.7 m from the CO_2 source (Figure 1C). With passive ventilation at the Old Papworth site, CO_2 spread rapidly along the corridor and persisted for 30 minutes. At the new site, active ventilation (at 6 ACH) limited dispersal distances and improved clearance rates (although detectible amounts of CO_2 remained after 30 min), whereas high ventilation with 15 ACH initially caused faster dispersal than conventional ventilation but led to clearance of CO_2 to below 10% of peak concentration by 13.3 minutes.

To examine the impact of ventilation on patient exposure to airborne pathogens, we deployed static NIOSH BC 251 two-stage cyclone aerosol samplers (9), positioned at 90 cm and 180 cm from the floor, to sample the air in unoccupied patient rooms and ward corridors in both the old and new CF centers during periods of similar ward–bed occupancy (92% ± 3.5% new ward vs. 94% ± 7.9% old ward; mean ± SD, $P = 0.43$). The amounts of total bacteria (quantified by *16S* quantitative PCR) were reduced in rooms and corridors with high-frequency air changes compared with those with passive ventilation (Figure 1D), suggesting reduced patient and HCW exposure to nosocomial airborne infections.

We also considered how people walking might influence air mixing and residence times in corridors. Given the high Reynolds number (*Re*) associated with a person walking ($Re = \rho u L/\mu \approx 0.5 \times 10^5$; based on a speed [$u$] of 1 m/s, size [$L$] of 0.5 m, air viscosity [μ] of 10^{-5} Pa·s, and density [ρ] of 1 kg/m^3), we expect the resultant wake to drive highly turbulent mixing. When measured in hospital corridors with high ventilation, a person walking along the corridor every 30 seconds considerably increased the residence time of CO_2 after a pulse release (Figure 1E), lengthening the half-life from 1.3 minutes to 6.7 minutes (Figure 1E).

Finally, we explored the potential for movement of infectious aerosols between corridors and rooms. We found that CO_2 released in the corridor rapidly penetrated into patient rooms with open doors (Figure 1F), despite the fact that both corridor and rooms had their own balanced system of inflow and outflow ducts and were at the same pressure. We saw a steep relationship between the duration of door opening and the resulting CO_2 concentrations in the room (Figure 1G), suggesting that limiting door opening could greatly reduce corridor-to-room pathogen spread.

We also noticed that movement of CO_2 into rooms increases with temperature contrasts. Airflow speeds across a doorway based on video recordings of tracer smoke show air flowed out of the room near the top (with mean speeds of 15–16 cm/s); whereas at lower heights, air flowed into the room at 16–18 cm/s ($P = 0.002$) (Figure 1H). The associated exchange flow driven by a 3°C temperature difference between the room and corridor (0.16 m^3/s) is comparable

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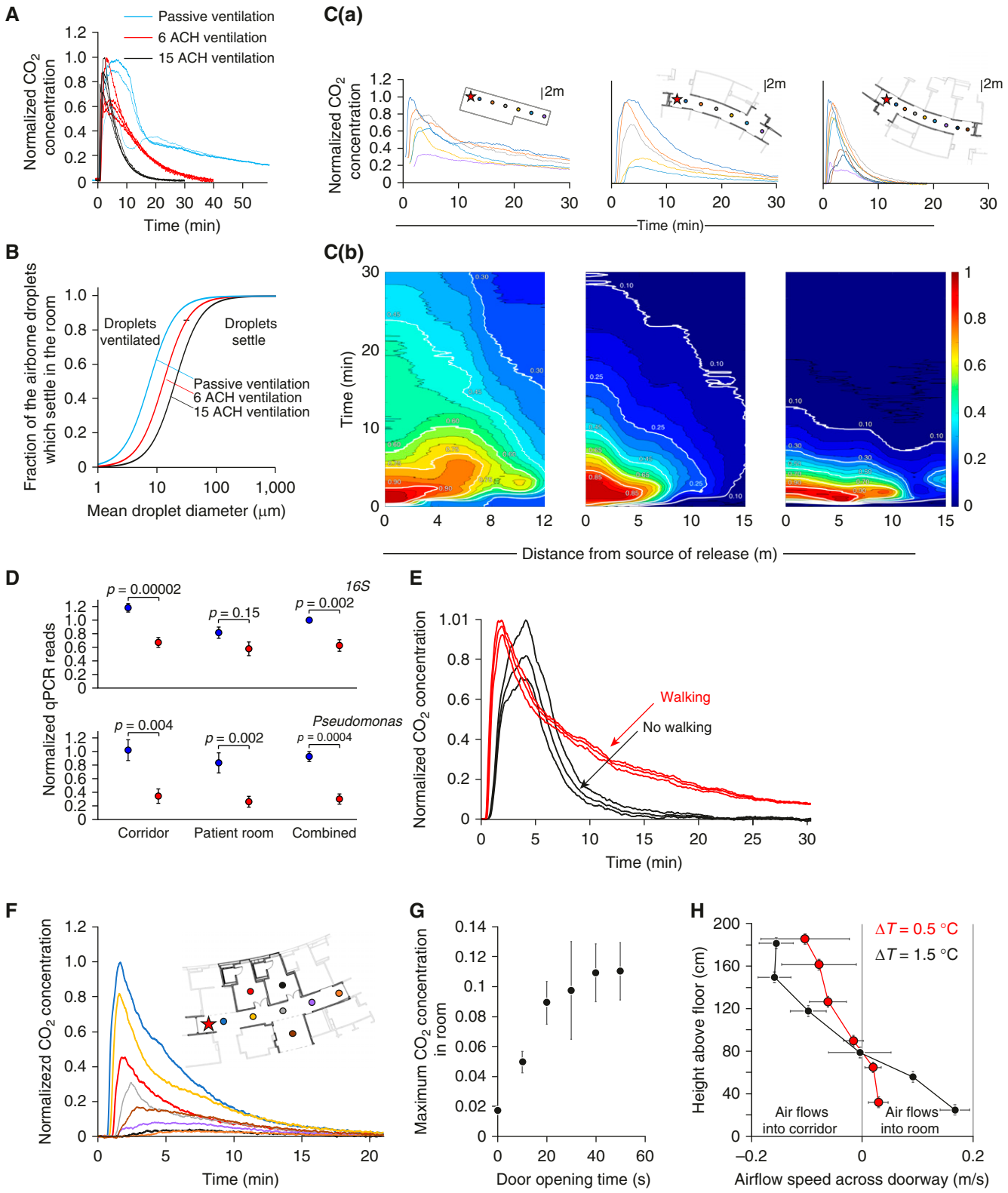

Figure 1. The impact of ventilation on air-handling in hospitals. (*A*) Concentrations of tracer gas (CO_2) monitored over time after a pulse release in three patient rooms with 15 air changes per hour (ACH) (black line) within New Papworth Cystic Fibrosis Centre, 6 ACH (red line) within New Papworth Hospital, or passive ventilation (blue line) from Old Papworth Hospital. The concentrations normalized to the maximum recorded value. (*B*) Model prediction of the fraction of airborne droplets that sediment to the floor or are ventilated in a patient room as a function of mean droplet diameter, shown for rooms passively ventilated (blue) or with 6 (red) or 15 (black) ACH. (*C*) Variations in normalized CO_2 concentration after tracer release (at the point marked by a star)

in magnitude to the high-frequency ventilation (about 0.20 m^3/s) and may contribute to pathogen transmission between room and corridor.

In summary, our results indicate that high-frequency ventilation can reduce residence times of infectious aerosols, despite residual impacts of people walking in corridors and temperature-dependent exchange flow across doorways. We believe that this strategy has the potential to improve safety for CF patients and other vulnerable individuals in the hospital and impede cross-infection between HCW and patients. Airborne transmission has been implicated in the spread of several nosocomial infections (3, 6), most recently severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1), which remains viable in aerosols for over 3 hours (10) and is likely to be transmitted by both large and small airborne droplets (3). Enhanced hospital ventilation, coupled with limiting door opening times, equilibration of temperature, minimizing corridor traffic, and wearing facemasks could play a critical role in the response to this current pandemic. ■

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Figure 1. (*Continued*). measured by sensors located along ward corridors (as shown in floor plans) in Old Papworth Hospital under passive ventilation (left) and in New Papworth Hospital in areas with ventilation with 6 ACH (middle) or ventilation with 15 ACH (right). (*Ca*) Normalized CO_2 concentrations detected over time by each sensor. (*Cb*) Normalized CO_2 concentrations as a distance–time plot. (*D*) Comparison of the relative amounts of total bacteria (*16S*) (quantified by qPCR) detected in air samples from ward corridors and unoccupied rooms in Old Papworth Hospital (blue) under passive ventilation, compared with equivalent areas in New Papworth Hospital receiving ventilation with 15 ACH (red) during periods of similar ward-bed occupancy levels. (*E*) CO_2 concentrations over time after tracer release in a corridor with ventilation with 15 ACH, in the presence (red) or absence (black) of people walking along it. (*F*) CO_2 concentrations over time after tracer released in the corridor (red star) measured by sensors deployed along the corridor and inpatient rooms. (*G*) Peak CO_2 concentrations detected in rooms (expressed as a fraction of maximum corridor concentration) as a function of the time the doorway is kept open. (*H*) Variation of the airflow speed across a doorway as a function of height above the floor (quantified from a video of smoke released from an Artic Hayes pen) when the room is 0.5°C (red) or 1.5°C (black) hotter than the corridor. ΔT = change in temperature; qPCR = quantitative PCR.

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Urban–Rural Disparities in Deaths from Chronic Lower Respiratory Disease in the United States

To the Editor:

Chronic lower respiratory disease (CLRD), including asthma and chronic obstructive pulmonary disease, is the fourth leading cause of death in the United States (1). CLRD is more prevalent in rural areas, where access to pulmonologists is limited and many rural hospitals have closed (2, 3). Recent analyses have demonstrated that rural, compared with urban, areas in the United States have higher mortality from chronic diseases such as cardiovascular disease and a slower decline in cardiovascular disease–associated mortality over the past two decades (4). However, rural–urban disparities in CLRD-associated mortality and trends have not been similarly explored. The objective of this study was to examine trends in mortality due to CLRD and to investigate disparities in deaths due to CLRD between rural and urban areas across the United States.

Methods

We analyzed adjudicated death certificate data between 1999 and 2018 from the national Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research (CDC WONDER) database. We identified CLRD as the cause of death using J40–J47 codes from the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision*. We calculated age-adjusted mortality rates (AAMRs) as previously described and expressed AAMRs as per 100,000 population per year using the population for year 2000 (4). We divided the cohort into three county designations as large metro (≥1 million), medium/small metro (50,000–999,999), and rural (<50,000) using the National Center for Health Statistics Urban-Rural Classification Scheme and the 2013 U.S. Census classification (5). We stratified results by age (<25, 25–64, and ≥65 yr), sex, race, and ethnicity. We estimated annual percentage change (APC) in AAMR using Poisson regression with log link and robust SEs. In an additional model, an interaction term was included to assess differences in trends over time. We performed all analyses using Stata version 16 (StataCorp) and considered a two-tailed $P < 0.05$ as statistically significant. Our analysis did not require institutional review board approval as the data were publicly available and deidentified.

Results

We analyzed data from 2,754,413 CLRD-attributable deaths between 1999 and 2018. Of these, 44.8% of decedents were from large metros, 33.3% from medium/small metros, and 21.9% from rural areas (Table 1 and Figure 1). In all areas, older adults ≥65 years, males, and non-Hispanic white individuals had the highest AAMR. From 1999 to 2018, CLRD AAMR decreased from 42.6 to 33.2 in large metros (APC, −1.1%; 95% confidence interval [CI], −1.2% to −1.0%) and from 47.7 to 43.2 in medium/small metros (APC, −0.4%; 95% CI, −0.5% to −0.2%). In contrast, CLRD AAMR increased from 49.5 to 53.6 in rural areas (APC, +0.6%; 95% CI, 0.5% to 0.8%). Rural area subgroups with the greatest increase in AAMR were adults aged 25–64 years (1.7%; 95% CI, 1.5% to 2.0%), females (1.5%; 95% CI, 1.4% to 1.7%)], and non-Hispanic white individuals (0.8%; 95% CI, 0.6% to 0.9%). Trends over time were significantly different between regions ($P < 0.001$). The absolute rural–urban difference in CLRD AAMR in the United States more than tripled from 6.9 (95% CI, 6.2 to 7.6) to 20.4 (95% CI, 19.7 to 21.1) over the past 20 years.

Discussion

In this study, we found that rural areas in the United States have higher CLRD AAMRs than urban areas. Although CLRD-associated mortality declined in urban areas over the past two decades, deaths attributable to CLRD increased in rural areas. The most notable increases in CLRD-associated mortality in rural America occurred in middle-aged adults, females, and non-Hispanic white individuals.

Our finding of higher CLRD AAMRs in rural compared with urban areas was similar to recent data in cardiovascular disease (4). However, CLRD mortality in our study increased in rural areas, in contrast to the declining cardiovascular-associated mortality in both rural and urban areas. These rural–urban disparities in CLRD mortality may be driven by higher rates of smoking in rural areas, limited access to pulmonologists, and rural hospital closures that have impacted access to acute care (1, 3, 6).

The widening rural–urban gap in CLRD mortality in the United States has several urgent policy implications. Ways to improve primary and secondary prevention of CLRD in rural areas may include more resources devoted to

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