Transmission risk of respiratory viruses in natural and mechanical ventilation environments: implications for SARS-CoV-2 transmission in Africa

ABSTRACT
Respiratory viruses can be transmitted through contact, droplet and airborne routes. Viruses that are not naturally airborne may be aerosolised during medical procedures and transmitted to healthcare workers. Most resource-limited healthcare settings lack complex air handling systems to filter air and create pressure gradients that are necessary for minimising viral transmission. This review explores the association between ventilation and the transmission of respiratory viruses like SARS-CoV-2. When used appropriately, both natural and mechanical ventilation can decrease the concentration of viral aerosols, thereby reducing transmission. Although mechanical ventilation systems are more efficient, installation and maintenance costs limit their use in resource-limited settings, whereas the prevailing climate conditions make natural ventilation less desirable. Cost-effective hybrid systems of natural and mechanical ventilation may overcome these limitations.

INTRODUCTION
In December 2019, an outbreak of unexplained pneumonia occurred in Wuhan, Hubei Province, China.¹ By 7 January 2020, the aetiological agent was identified as a novel coronavirus, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and its manifestations termed coronavirus disease-2019 (COVID-19). As of 16 June 2020, over 8.1 million people worldwide have been infected with SARS-CoV-2, with more than 441,407 deaths.² In Africa, over 252,544 cases have been reported with more than 6779 deaths. In the absence of a therapeutic cure or a preventive vaccine, countries have put in place mitigating measures such as physical distancing, large scale land and air travel cancellations, hand hygiene protocols and community wearing of face coverings to reduce person-to-person viral transmission. Despite these measures, the infection continues to disproportionately affect people living in low socioeconomic conditions,² who tend to live in more densely populated areas with poor ventilation. Interestingly, little is known about the contribution of environmental factors such as natural or mechanical ventilation in the transmission of SARS-CoV-2.

TRANSMISSION OF RESPIRATORY VIRUSES
Respiratory viruses are transmitted through contact, droplet and airborne routes. Viruses that are not naturally airborne may be aerosolised during medical procedures and transmitted to healthcare workers. Most resource-limited healthcare settings lack complex air handling systems to filter air and create pressure gradients that are necessary for minimising viral transmission. This review explores the association between ventilation and the transmission of respiratory viruses like SARS-CoV-2. When used appropriately, both natural and mechanical ventilation can decrease the concentration of viral aerosols, thereby reducing transmission. Although mechanical ventilation systems are more efficient, installation and maintenance costs limit their use in resource-limited settings, whereas the prevailing climate conditions make natural ventilation less desirable. Cost-effective hybrid systems of natural and mechanical ventilation may overcome these limitations.

Summary box
- Viruses like SARS-CoV-2 that are normally transmitted via droplet can become aerosolised during medical procedures and malfunctioning air conditioners.
- Lack of proper air circulation in a building has been shown to promote the spread of airborne viral infections.
- Most resource-limited healthcare settings lack air handling systems to filter infectious contaminants in the air.
- A hybrid approach of using natural ventilation coupled with affordable mechanical ventilation devices could prove useful in controlling infection transmission in low-income and middle-income countries.

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viable viral particles from an infected person. Once an individual is infected with a respiratory virus, he/she can emit virus-laden droplets when coughing, sneezing, breathing or speaking, which can then be deposited on surfaces.

Droplets are relatively large (measuring ≥5 µm in diameter) and, therefore, do not remain suspended in the air for long periods, but fall rapidly to the ground or other surfaces within <1 m radius on release. Recently, it was observed that ‘violent respiratory events’ such as coughing and sneezing can create a turbulent gas cloud that can be propelled as far as 7 to 8 m (23–26 feet) in 6 s.

Airborne transmission occurs by the dispersion of small droplets or droplet nuclei (<5 µm in diameter) of evaporated droplets containing microorganisms that can remain suspended in the air and viable for long periods (hours). In the early 1900s, Wells first introduced the concept of ‘droplet nuclei’ and their role in the transmission of respiratory viruses. As they are lighter than droplets, they travel farther distances and could exist for longer periods around an infected individual and in rooms that the individual has visited. A recent study reported that SARS-CoV-2, like severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1), can remain viable in aerosols (or droplet nuclei) for at least 3 hours, thus, aerosol-generating procedures in healthcare facilities may put health workers at risk via this route.

SARS-CoV-2 is currently thought to be primarily spread through large droplets that fall to the ground or surfaces in the vicinity of an infected individual. However, we should also remain open to the possibility of the airborne transmission of COVID-19. This risk has been identified with other similar viruses. During the Middle East respiratory syndrome coronavirus (MERS-CoV) epidemic in South Korea, researchers detected the virus in air samples collected from a healthcare setting housing infected patients. Furthermore, several studies reported the airborne transmission of SARS-CoV-1 in 2003. A recent study used real-time PCR to confirm the presence of SARS-CoV-2 in air samples collected in an isolation treatment facility. These studies raise the possibility of the airborne transmission of SARS-CoV-2 but have not tested the viability and/or infectivity of SARS-CoV-2 nucleic acid obtained from such environmental sources. In the absence of a complete explanation for the high infectivity and spread of SARS-CoV-2 and the evidence of the airborne transmission of viruses in the same family, there is still the possibility of airborne transmission of SARS-CoV-2. Moreover, it has been shown that aerosol-generating procedures (chest compressions, tracheal intubation and extubation, bronchoscopy and so on) increase the risk of infection in healthcare workers (HCWs). If SARS-CoV-2 is being transmitted through the airborne route, then special attention to ventilation and air handling is needed especially in healthcare settings.

**PRINCIPLES OF AIR VENTILATION: NATURAL VERSUS MECHANICAL**

Air circulation in space is largely driven by wind and thermal energy; as hot air rises, cool air sinks to replace the vacuum created. This process can be influenced by either natural or mechanical ventilation.

**Natural ventilation**

During natural ventilation, the air in a room is replaced with air from the outdoors, through appropriately positioned openings such as windows and doors. This effectively controls indoor temperature, humidity and can dilute indoor pollutants, most relevantly, virus-laden droplets and droplet nuclei. The American Society of Heating, Refrigerating and Air-Conditioning Engineers published a document in 2010 that highlights the minimum requirements in spaces intended to be naturally ventilated. However, it is important to note that their recommendations for ventilation in healthcare settings are centred around the use of mechanical air handling systems, not natural ventilation.

When there was a rampant transmission of tuberculosis in healthcare settings in the USA (in the late 1990s), the Centers for Disease Control and Prevention (CDC) published guidelines (with a revision in 2005) recommending that rooms in healthcare centres should be equipped to conduct between 6 and 12 air exchanges per hour for proper infection prevention and control (IPC). A study of HCWs (n=1289) in Canada showed a 3.4 adjusted hazard ratio of tuberculin skin test conversion in those who worked in non-isolation patient rooms with fewer than two air exchanges per hour on average. Similarly, a study conducted during the SARS-CoV-1 epidemic found that isolating infected patients in wards with good natural or mechanical ventilation resulted in decreased viral burden in the ward and could be useful in preventing transmission among HCWs. Subsequently, several models have outlined the potential of increasing ventilation rates as an effective strategy for controlling airborne diseases.

In low-income and middle-income countries (LMICs), the WHO guidelines on the prevention of infection and control of the spread of pandemic promote natural ventilation as not only a suitable and affordable way to effectively control infection but one that may be as effective as the more-expensive alternative—mechanical ventilation. A systematic review of papers published between 1965 and 2005 showed that there was strong and sufficient evidence to support an association between ventilation rates and airflow patterns (both natural and mechanical) and the transmission and spread of diseases such as measles, tuberculosis, chickenpox, anthrax, influenza, smallpox and SARS-CoV-1.

However, the air-purifying benefit of natural ventilation is only as good as the quality of outdoor air. This is particularly significant in highly industrialised cities with significant air pollution. A prospective trial conducted among 1325 students noted that environments with an increased load of the particulate matter about 10µm in
size were associated with an increased incidence of respiratory infections. This has also been observed with the particulate matter under 2.5 \( \mu m \) size, which falls within the size range of droplet nuclei. These pollutants or particulate matter may cause inflammation of the airway providing an enabling environment for the successful transmission of viral infection. Thus, location-specific air quality may influence the infection prevention quality of natural ventilation.

Mechanical ventilation
Mechanical ventilation involves the use of machines to facilitate air exchange with the external environment as well as airflow within a room. There are several forms of mechanical ventilation including portable units, like fans, and standalone air conditioners or combined systems involving heating, ventilation and air conditioning (HVAC) systems.

Fans are useful appliances that regulate the temperature, humidity and airflow in a room. When used in residential and commercial settings, they can serve as affordable alternatives to some standalone air conditioners and HVAC systems. As such, they remain a popular fixture in residential spaces in LMICs. Despite these benefits, their use could be detrimental when the air contains aerosolised infectious particles or droplet nuclei as they can facilitate the circulation of these particles. A study showed that fans were able to nebulise a liquid suspension of soil contaminated with \textit{Staphylococcus aureus} such that sterile Petri dishes placed in the vicinity of the fan grew \textit{S. aureus}. This study confirms that air currents created by fans can circulate droplet nuclei containing viable microorganisms.

Standalone air conditioning involves maintaining temperature, humidity, and, in some cases, the purity of an enclosed space with an isolated air conditioning unit as opposed to a centralised system that can serve an entire building. Most standalone air conditioners are designed with some air-filtering capacity. However, these air conditioners can usually only filter micro dust, mould and microorganisms that are \( \geq 5 \mu m \). For large spaces to be properly filtered, they need enough suctioning of the contaminated air, which can then be passed through filters. However, this is difficult without the ventilation duct that is found in HVAC systems. Another important prerequisite to proper air filtration by standalone air conditioners is the availability of regular maintenance services. Failure to replace filters can lead to the accumulation of particulate pollutants that, on build-up, can be reintroduced to the indoor environment. For example, PCR testing showed the presence of SARS-CoV-2 on two out of three air outlet fans in the room of symptomatic patients suggesting that small droplets may be displaced by air currents and deposited in ventilation equipment like fans and air conditioners. Thus, air conditioning filters need to be changed regularly per manufacturer’s specifications. This is a significant challenge in LMICs due to cost and lack of trained maintenance personnel.

HVAC systems are designed to combine temperature and humidity regulation with air quality control in indoor spaces. These systems are used in healthcare settings, residential, commercial and industrial buildings. In healthcare settings, HVAC systems are further equipped with pressure gradient-generating capabilities and can create negative pressure that is especially useful for isolating individuals with highly contagious airborne infections or positive pressure such as in nurseries, operating rooms and so on. Several filters can be installed in buildings equipped with HVAC systems. They range from affordable and recyclable options like fibreglass and washable filters to the more specialised alternatives like high-efficiency particulate aerosol (HEPA) and ultraviolet (UV) filters that can filter particles \( \geq 0.3 \mu m \) and kill microorganisms, respectively. Given that majority of SARS-CoV-2 aerosols range from 0.25 to 4 \( \mu m \), HEPA filters are suitable for trapping viral particles. Although no studies have tested the efficacy of UV germicidal units on SARS-CoV-2, a study of murine hepatitis virus coronavirus showed a survival rate of 12\% after 10 min of exposure to 254 nm UV light. However, HEPA and UV filters are not only costly, but they also require frequent maintenance by highly skilled technicians.

AIR CIRCULATION AND RISK OF INFECTION

The concept of droplet nuclei having the potential to move from one place to another either via natural or mechanical airflow systems and causing infections is not new. This has been reported in both animals and humans. In the 1980s, a study found that guinea pigs exposed to air vented from a tuberculosis ward became infected. Similarly, in humans, studies have shown that the dispersion of droplet nuclei containing viral and bacterial particles can lead to infection in susceptible individuals as illustrated in table 1.

A study on tuberculosis, with human subjects, compared a well mechanically ventilated hospital ward to one that had an air conditioning system that lacked appropriate filtering. They showed that approximately 44\% of infections were due to the circulation of bacilli-laden droplet nuclei, as a result of ventilatory systems that lacked appropriate filters. Similarly, during the 2003 SARS-CoV-1 epidemic, a WHO investigative team deployed to examine the conditions around the Amoy Gardens housing estate outbreak in Hong Kong observed that aerosols generated from contaminated sewage were drawn into the building by an exhaust fan and dispersed to the rest of the apartment as a result of the interconnected ventilation system of the building.

Computational fluid dynamics and multizone modelling of this housing settlement revealed that apartment units on upper floors were at higher probabilities of contamination due to the buoyancy of warm air. In addition, Lu et al. reported an outbreak of COVID-19 in an air-conditioned restaurant in Guangzhou, China, involving three family clusters. These customers had dined in three
### Table 1  
**Studies in support of airborne transmission of respiratory pathogens**

| Study          | Country, Setting                  | Pathogen          | Type of ventilation                      | Infection identified by          | Main findings                                                                                                                                 |
|----------------|----------------------------------|-------------------|------------------------------------------|-----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------|
| Lu et al       | China, restaurant                | SARS-CoV-2        | Mechanical: standalone air conditioner (A/C) | Clinical diagnosis; unspecified   | Development of symptoms in 12% of diners in the vicinity of the index patient; viral droplets propagated by A/C airflow                              |
| Kulkarni et al | UK, hospital                     | RSV               | Mechanical: centralised, unspecified     | PCR diagnosis                     | Virus-laden aerosols from index patient were present within 10 m radius, remained for 2 hours after the patient was discharged and infected respiratory epithelial cells in vitro |
| Wong et al     | Hong Kong, hospital              | Influenza         | Mechanical: with HEPA filter close to index patient | RNA sequencing                   | Imbalanced airflow pattern facilitated infection transmission; identical viral strain in the index patient and contacts                                |
| Li et al       | Hong Kong, hospital              | SARS-CoV-1        | Mechanical: central air conditioning      | Unspecified                       | CFDS showed an association between the concentration decay from the index patient’s bed and the spatial SARS infection pattern involving 138 people    |
| Yu et al       | Hong Kong, multifloor apartment complexes | SARS-CoV-1       | Natural and mechanical: central circulation system | Unspecified                       | Experimental studies showed that aerosols were generated and drawn in by an exhaust fan from contaminated sewage leading to infections on multiple floors |
| Olsen et al    | Taiwan, aircraft                 | SARS-CoV-1        | Mechanical: aircraft ventilation         | RT-PCR and serology               | Proximity-dependent viral spread from a symptomatic host in aircraft                                                                          |
| Jiang et al    | China, hospital                  | SARS-CoV-1        | Natural and mechanical                   | Unspecified                       | Increased rate of HCW infection with a lower ratio of window size to room volume and laminar air flow mechanical ventilation but no (or closed) windows |
| Hoge et al     | USA, jail                        | Streptococcus pneumonia | Mechanical: HVAC                         | Culture and enzyme immunoassay    | Increased incidence of pneumococcal disease (identical strain) with overcrowding and decreased outside air delivery by the ventilation system       |
| Shigematsu and Minowa | Japan, building | Tuberculosis | Mechanical: central air conditioning | Unspecified                       | Indoor infection of tuberculosis attributed to interrupted ventilation leading to high carbon dioxide concentrations                      |
| Bloch et al    | USA, paediatric office           | Measles           | Mechanical: HVAC                         | Physician diagnoses               | Measles outbreak in an office with a high volume of recirculated air via the dispersion of droplet nuclei from the index patient                |
| Moser et al    | USA, aircraft                     | Influenza         | Mechanical: interrupted aircraft ventilation | Culture and serology               | Influenza outbreak-associated air travel with 3 hour interruption in aircraft ventilation; similar strain in 26% of contacts                   |
| Ehrenkranz and Kicklighter | USA, hospital | Tuberculosis | Mechanical: central air conditioning | Mantoux test                      | Tuberculosis outbreak associated with recirculation of air-containing droplet nuclei and lack of high-efficiency filters                      |
| Wehrle et al   | Germany, hospital                | Smallpox          | Natural ventilation                     | Physician diagnosis               | Outbreak of 17 cases of smallpox mediated by air currents and low relative humidity                                                             |

CFDS, computational fluid dynamic simulations; HCWs, healthcare workers; HVAC, heating ventilation and air conditioning system; MERS-CoV, Middle East respiratory syndrome-related coronavirus; RSV, respiratory syncytial virus; RT-PCR, real-time PCR; SARS-CoV-1, severe acute respiratory syndrome coronavirus 1; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
groups adjacent to one another (distance between each table was about 1 m) and were near an air conditioner with strong airflow. The researchers concluded that the mechanism of spread was droplet nuclei transmission promoted by directional air-conditioned ventilation (i.e., in the direction of air flow created by the air conditioner). Thus, air circulation and air conditioners likely play a role in the transmission of respiratory viruses such as SARS-CoV-2, at least, in the vicinity of the air conditioner if contaminated with droplets.

**IMPLICATIONS AND RECOMMENDATIONS FOR AFRICA**

Understanding the role of ventilation in the spread of SARS-CoV-2 is even more important in Africa where: (1) the high temperature and humidity conditions may make it uncomfortable for HCWs to comply with recommended and required personal protective equipment (PPE); (2) there is shortage of negative pressure rooms in healthcare settings where aerosol-generating procedures are performed; and (3) there is lack of strict enforcement of building design and town planning codes to support optimal natural ventilation. The combination of suboptimal building designs, temperature barriers to the use of PPE and habitual use of inconsistently maintained mechanical ventilation devices creates circumstances where the risk of the airborne transmission of SARS-CoV-2 could be increased in homes and healthcare facilities in Africa.

Ideally, both natural and mechanical ventilation can be used to decrease infection transmission. Natural ventilation in a well-designed house or building with optimal ambient climatic conditions is a way to control infection by effectively cleansing the air of viral contaminants, and is recommended by the WHO. However, healthcare facilities depending on natural ventilation must be designed properly with high ceilings and thick walls to maintain an ambient temperature and provide the recommended ventilation rate of up to 160 L/s/patient in airborne precaution rooms and 40–60 L/s/patient for other hospital spaces. The biggest advantage of a natural ventilation system is its cost-effectiveness. However, there are several drawbacks including its susceptibility to the extremes of temperature and humidity, the cost of erecting buildings that optimise air exchange, and space and design limitations in already existing buildings, leading to densely populated wards. These challenges compromise the efficacy of natural ventilation and lead to increased risk of the transmission of airborne pathogens.

In resource-rich settings, individuals are protected from exposure to airborne infections by isolating infected patients in special negative pressure rooms. These mechanically ventilated rooms are reliable, efficient and engineered to isolate and quickly remove pathogens, particulate matter, gases and odours, thus decreasing the transmission of infections. However, in resource-limited settings with unreliable power supply and variable compliance with manufacturer-recommended maintenance practices, mechanical ventilation systems may rather enhance the spread of infections. For instance, portable units such as fans and standalone air conditioners have become necessities due to the extreme climate conditions with high temperatures ranging from 45°C to 50°C (113–122°F) in places in Africa, coupled with extremes of humidity. However, in a crowded setting, a fan or standalone air conditioner unit without adequate maintenance could become a two-edged sword—providing comfort from the hot temperature, while setting the stage for the transmission of infection. Therefore, as the transmission of respiratory viruses could occur in both natural and poorly maintained mechanically ventilated areas, building codes by town and country planning departments and maintenance recommendations must be adhered to.

With the increasing number of patients with COVID-19, many countries including those in Africa resorted to converting repurposing existing buildings, erecting tents and building completely new isolations centres. Given the climatic conditions in Africa that is predominantly hot with many regions recording over 40°C issues of comfort have to be considered along with IPC requirements. The materials from which the tents are made are such that they are usually very hot and also do not lend themselves to good natural ventilation arrangements. Often these tents then need to be fitted with some sort of system that allows the space to be cool enough allowing people (patients and HCWs) to stay and work in these tents comfortably. Given these issues and IPC implications of air conditioning units discussed in this paper, decisions need to be taken on the utility of these tents and implications for IPC.

Given the importance of adequate temperature control for the comfort of both patients and HCWs as well as the need for proper ventilation and filtration as an infection control strategy, we recommend a hybrid approach of using mechanical ventilation devices that are equipped with air-filtering capabilities to augment natural ventilation. Several models of this approach have been proven effective in IPC including: (1) an ordinary fan or HEPA fan can be used to exhaust air outside through a window. (2) A HEPA fan can be used to discharge room air into a return air system. (3) Portable UV filtering or germicidal units could be combined with air conditioners to ensure proper air disinfection. (4) The use of devices to create negative pressure around a patient in a room. The National Institute for Occupational Safety and Health developed the Ventilated Headboard (figure 1) to create negative pressure in the immediate vicinity of an infected patient to protect other patients and healthcare personnel from airborne infections. In addition, natural ventilation should be optimised with proper design to prevent summer overheating from external (weather conditions) and internal (overcrowding and lighting) sources.

There are currently little empiric data on the role of substandard ventilation in the transmission of respiratory
viruses at homes and in the healthcare settings in LMICs. Moreover, HCWs in LMICs face other challenges that limit optimum infection control including shortage of good quality PPE, variable knowledge on the appropriate use and maintenance of PPE, rapidly evolving policies and lack of proper infrastructure. In the context of the global COVID-19 pandemic, it is essential to conduct further operational research to develop robust evidence to support decision-making and planning by healthcare managers, clinicians and the wider population. Several research questions that could inform policy-makers include: (1) What are the rates of infection transmission in settings with suboptimal versus optimal ventilation? (2) Is the adoption of the hybrid approach effective in reducing the transmission of infections in LMICs? (3) What can be done to maintain thermal comfort in hospital units and makeshift tents without increasing the risk of the transmission of infection? The design of these research projects would benefit from multidisciplinary teams including architects, surveyors, engineers, IPC practitioners and clinicians.

CONCLUSION
Both natural and mechanical ventilation, if designed properly and well maintained, can be integral parts of effective IPC programme. However, the infection prevention efficiency of the more cost-effective option, natural ventilation, could be compromised by high temperatures and humidity. Moreover, sophisticated mechanical ventilation systems are virtually impractical in resource-limited settings due to the high cost of establishing and maintaining them. Adopting a hybrid approach may be necessary but research is urgently needed to guide policy-makers and IPC specialists to support health workers and minimise the risk of the nosocomial transmission of SARS-CoV-2.

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