Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Recommendations for ventilation of remodeled negative-pressure isolation wards for COVID-19 patients: A comparison of international guidelines

Chung-Yen Chen a,b,c, Ping-Hui Chen b,c,d, Jia-Kun Chen c,* Ta-Chen Su b,c

Abstract This mini-review provides the practice guideline recommendations for ventilation of remodeled negative-pressure isolation wards for COVID-19 Patients. Remodeled "quasi-negative-pressure" isolation wards had been proved a feasible, inexpensive, safe, and effective measure to contain nosocomial outbreaks. We should first determine the minimum required ventilation volume of an isolation ward based on the severity of COVID-19 patients. Mechanical ventilation remains the mainstay for achieving the requirement, while the assistance of recirculation is also helpful. Beyond adequate ventilation volume, the "clean to less-clean" directional airflow remains the golden rule for the solution of indoor ventilation. The virus-laden exhaust should be treated with HEPA/UV device or be kept away from living organisms, buildings, and air inlets.

Received 16 August 2021; accepted 20 November 2022

KEYWORD
COVID-19; Negative-pressure isolation ward; Mechanical ventilation; Directional airflow

* Corresponding author. No. 17, Xu-Zhou Road, Taipei 10055, Taiwan. Fax: +886 2 3366-8114.
E-mail address: jkchen29@ntu.edu.tw (J.-K. Chen).

https://doi.org/10.1016/j.jfma.2022.11.013
0929-6646/© 2022, Formosan Medical Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Backgrounds

Under the current epidemic, emergency and critical care resources in Taiwan and many other countries are tense and in shortage. When endless confirmed or suspected COVID-19 cases flow into medical facilities and the existing negative-pressure isolation wards overload, we will have to remodel general wards into “quasi-negative-pressure” isolation wards or establish temporary/ portable isolation wards. To convert normal-pressure wards into negative-pressure wards with industrial exhaust fans had been proved as a feasible option and a widespread measure during the peak of the SARS epidemic.1-2

In contrast, multiple nosocomial outbreaks of COVID-19 and other infectious diseases via aerosol transmission had been documented. For instance, a cluster infection of 138 probable SARS cases, including healthcare workers, medical students, patients, and visitors, occurred at the Prince of Wales Hospital in Hong Kong in March 2003. The spatial distribution pattern of the infection chain was in agreement with the computational fluid dynamic (CFD) simulation and thus proven to be related to bio-aerosol dispersion due to undesirable ventilation design.3-5 For SARS-CoV-2, positive results of sampling and identification of the viruses in the filters, supply air dampers, and air outlet fans were found in hospitals in Singapore and Oregon. These findings indirectly suggested that the risks of nosocomial airborne transmission through heating, ventilation, and air conditioning (HVAC) systems should not be excluded.6-7 We should first put away all preconceived impressions upon seeing the exhaust fan and focus on the correct implementation and evaluation of the ventilation system.

The current guidance summarizes two guidelines by the World Health Organization (WHO) relevant to the COVID-19 context.6,9 Guidelines for isolation wards by the Center for Disease Control and Prevention (US-CDC), American Society of Heating, Refrigerating, and Air-Condition Engineers (ASHRAE), and American Institute of Architects (AIA) are also included in the review and compared.10-12 We aim to provide the medical facilities a scoping view on modifying the ventilation system of the COVID-19 isolation ward. However, the guidance is for reference only in general. We recommend that the readers consult experienced experts in HVAC systems for specific scenarios and conditions first.

Recommended practice guidelines

Determine the required ventilation rate of an isolation ward based on the severity of COVID-19 patients

In the face of COVID-19 cases with different severity, medical facilities provide different treatment levels, with or without aerosol-generating procedures (AGPs), and the ventilation system requirements of the wards also vary accordingly. For the wards for mild cases, the WHO guidelines recommend that the minimum air changes per hour (ACH) is six times, or the minimum required ventilation rate is 60 L/s per patient, i.e., 3.6 m³/min (CMH). A minimum ACH of 12 times or a minimum ventilation rate of 160 L/s per patient (i.e., 9.6 CMH) is required for critical wards or intensive care units (ICU).8,9

Example 1.

- If there are three mild COVID-19 cases in the ward, the minimum required ventilation rate is 180 L/s (i.e., 10.8 CMH).
- If two critical COVID-19 cases are in the ICU, the minimum required ventilation rate is 320 L/s (i.e., 19.2 CMH).

Here, mild cases are defined as uncomplicated upper respiratory tract viral infection or mild pneumonia not meeting the definition of severe pneumonia. Therefore, the wards for mild cases’ ventilation measures also apply to collective quarantine stations that isolate asymptomatic or mild cases. The definition of critical cases includes severe pneumonia, acute respiratory distress syndrome (ARDS), sepsis, and septic shock. Severe pneumonia is defined as Table 1.

Besides the WHO guidelines, recommendations to isolation wards by US-CDC, ASHRAE, and AIA fall within the range between 6 and 12 ACH.10-12 The ASHRAE guidelines had increased the minimum required ACH from 6 in the 1999 edition to 12 in the 2007 edition.14 According to estimation by US-CDC, under ideal conditions, if it is assumed that the source of infectious particles no longer exists indoors, when ACH = 6, it takes 46 min to reach 99% removal efficiency and 69 min to achieve 99.5% removal efficiency. When ACH = 12, it takes 23 min to reach 99% removal efficiency and 35 min to achieve 99.5% removal efficiency. In isolated wards with a relatively high ventilation rate, it usually requires threefold of time for complete removal. It may take longer in areas where the indoor air is stagnant or unable to be mixed evenly. The US-CDC generally recommends waiting until 99% of infectious particles are removed before entering the room.10

Requirements in ACH and ventilation rate are similar in spirit. The only difference is that the former is considered from the perspective of the entire wardroom, while the latter takes the number of patients into account. Therefore, the two indicators will not differ too much as long as the space allocated to each patient is reasonable (not too extremely crowded or spacious). If there is a single wardroom for a mild case with ACH = 6 and the ventilation rate is 3.6 CMH = 216 CMH, the volume of this ward is 36 m³. If there is a single ICU room with ACH = 12 and a ventilation rate of 9.6 CMH = 576 CMH, the volume of this ward is 48 m³. If the height of the ward is 2.4 m, the area for the first room is 15 m², and the second room is 20 m². Both are standard and common sizes.

In principle, the greater the ventilation rate, the lower the contaminant concentration ratio (CCR, i.e., the ratio of the virus concentration in the room to the patient’s exhaled virus concentration) in the isolation room; the larger the ACH, the shorter the time required for the CCR to reach 99% steady-state (T99%).15 However, an extreme high ventilation volume usually cannot be achieved without obtaining a
more powerful exhaust fan, consuming more energy, and making a tremendous noise. Therefore, it is a more comprehensive approach to ensure that the minimum standards of international consensus are followed.

Method to achieve adequate ventilation rate

The WHO guidelines primarily recommend the use of mechanical ventilation to achieve adequate ventilation.8,9 Options for mechanical ventilation include:

1. Installation of mechanical exhaust fans directly on the wall or window or connection by an air duct.
2. Installation of portable HEPA filters that can exhaust outward.

For these two mechanical ventilation methods, please refer to the rated ventilation volume provided by the manufacturer. Nevertheless, be aware of the gap between the rated exhaust volume and the actual performance due to pipeline resistance. In addition, the exhaust volume may be reduced because the grille and the air duct may accumulate dust, and the seal of the air duct joint may also leak. Therefore, the literature suggests a 10% reserve of the isolation ward’s exhaust volume and a 50% increase of the air duct’s size in advance to compensate for the subsequent airflow loss caused by the decline in performance.11

The following technical requirements for mechanical ventilation should be followed8,9:

- Adequate intake air volume (air supply) corresponding to the exhaust volume is required: According to the US-CDC guidelines, the exhaust volume should be 1.1 times the intake air volume or at least 50 CFM (1.4 CMM) more than the intake air volume, preferably 100 CFM (2.8 CMM)10,11.
- It is recommended to install the exhaust fan on the wall about 20 cm above the ground to avoid pollution or damage caused by splashing when cleaning the floor;
- It is recommended that the noise be controlled below 38 dBA at a distance of 3 m;
- The negative-pressure exhaust device should be marked (especially at the switch, with the phone numbers of the staff in charge of infection control attached).11 The setting should be prevented from being arbitrarily adjusted by the patient or other staff. It is recommended to connect to an uninterruptible power system (UPS);
- Minimize the obstruction of the exhaust port, and consider installing a backdraught shutter to prevent strong winds from blowing into the room.

The HEPA filter has a collection efficiency of more than 99.97% for particles at 0.3 μm, and its efficiency in capturing SARS-CoV-2 with a 0.1 μm diameter should be higher in theory. Recirculation cannot wholly replace mechanical ventilation, but it is better than taking no measures at all.17 Therefore, instead of stand-alone use, it is

the unstable ventilation volume subject to weather changes.

Recirculation is a practical approach that assists in diluting the pollutant concentration and making up the gap to the required ventilation volume, and feasible options include8,9:

- 1. Portable HEPA filter.
- 2. Ceiling-mounted HEPA-UV air filter.

Example 2:

- In a 3-bed wardroom for mild cases, the minimum requirement for ventilation volume is 10.8 CMM. If the room is not equipped with an exhaust fan, the ventilation volume of the stand-alone portable HEPA filter should be at least 10.8 CMM.
- In a 2-bed ICU room, the minimum requirement for ventilation volume is 19.2 CMM. If the room is already equipped with an 11 CMM exhaust fan, the ventilation volume of the portable HEPA filter combination in use should be at least 8.2 CMM.
still most recommended that the combined use of HEPA filter with outward exhaustion if feasible. However, if the mechanical ventilation does not meet the minimum required ventilation rate, the HEPA filter recirculation device can also make up the gap, as exemplified in Example 2.

The following technical requirements for recirculation should also be followed:

1. The recirculation system without HEPA filtration or UV disinfection will significantly increase the risk of infection and should be banned from use.18,19
2. The HEPA filter should be placed as close as possible to the pollution source (patient breathing zone) to increase the collection efficiency. It should also be placed as far away from the door as possible, and the door should be kept closed to maximize the effect of diluting the pollution.
3. The HEPA filter device must operate continuously. After a patient leaves the ward, the device must remain in operation for 30 min before a new patient entering the ward. The staff who enter the wardroom during this period should wear personal protective equipment properly.
4. The filtration material should be replaced regularly and should be deemed contaminated during replacement. The personnel responsible for replacement should wear appropriate personal protective equipment, and the replaced material should be sealed in a plastic bag before discarding.

The principle for directional airflow

Beyond the minimum required ACH or ventilation volume, another two critical factors to ventilation of isolation wards are8,9:

1. Air distribution: The outdoor air is delivered effectively and efficiently to every corner of the room, and the polluted air in every corner of the room is removed efficiently and effectively.
2. Directional airflow: The airflow flows from the clean area to the polluted or less clean area.

The directional airflow concept had already been mentioned, although not underscored, in a footnote of the AIA guideline, no later than the 2001 edition. The requirement of continuous monitoring of the airflow direction is first added in this edition.13 It was also described at least since the 1999 edition of the ASHRAE guideline, although the specific term was not referred to14. We also found that the 1996 edition of the US-CDC guidelines regarding isolation precautions took no account of the principle, in contrast to the 2007 edition.20,21 The 2007 edition of the WHO guideline also instructed on the prevention of unfavored airflow direction. A paradigm shift that emphasized directional flow as much as ACH had occurred, but the former was often neglected in practice in Taiwan and other countries, probably due to the relative simplicity of the latter. We specified the principle as follows8,9:

1. In terms of wards: flow from the work area (nurses’ station) to the intermediary area (corridor of the ward) and then to the contaminated area (wardrooms). Use plastic curtains in the wardroom to enclose an anteroom to strengthen the isolation between the intermediary and the contaminated areas.
2. In terms of wardrooms: follow the principle of flowing from high to low and from outside to inside. The airflow goes from the inlet at the height and around the door to the pollution source (around the bed and the patient’s breathing zone) and then to the exhaust outlet at a lower spot and around the window.
3. Within the tolerable range of noise, the exhaust fan should be installed as close as possible to the pollution source (patient breathing zone) to increase the collection efficiency. The collection efficiency declines as the distance increases.
4. Use a smoke generator to check whether the airflow direction is as expected.

Here we provide a real-world example from a tertiary medical center in Taiwan to explain the design of directional airflow from clean to less clean area.

Example 3.

In addition to adequate air exchange rate or ventilation volume, a more efficient flow design in the indoor environment is essential for establishing or accommodating an isolation ward.

As shown in Fig. 1, we designed a directional airflow based on the “clean to less-clean” principle and converted the normal-pressure general ward into a negative-pressure isolation ward for COVID-19 patients at a university hospital in late May 2021, during the peak of the epidemic in Taiwan.

Generally speaking, when we open the door, the indoor and outdoor air will be exchanged. To avoid this situation, we use a plastic curtain to create a buffer zone behind the door and leave a 1-cm gap under the plastic curtain as a slot suction inlet. According to existing literature, the proper capture velocity (Vc) at the slot suction inlet to prevent contaminant from dispersion should occur between 0.5 and 1 m/s.22

Besides, the exhaust port is close to the patient’s breathing zone to suck away the aerosol particles produced by the patient right away. The exhaust port is connected to the exhaust fan installed on the window through a pipe.
HEPA is installed in front of the exhaust fan to filter the air and exhaust it outward. Results of the on-site measurement of the ventilation system’s performance and effectiveness are shown in Fig. 2. The velocity of the slot suction inlet \( V_s = 1.0 \sim 1.14 \) m/s with the door of the ward opened, and the center velocity of the suction inlet at the window can reach 7.0 m/s.

**Exhaust treatment**

If the mechanical ventilation system can operate smoothly, then the next thing to worry about is whether the discharge of infectious particles causes a public hazard. The recommended exhaust treatment methods are as follows:

1. Place the HEPA filter in front of the exhaust fan or the upstream exhaust air duct.
2. Connect the portable HEPA filter to exhaust outward.

However, it is necessary to measure the extent to which the resistance of the filter medium reduces the ventilation volume to ensure that the minimum required ventilation volume can still be met.

In addition, ultraviolet germicidal irradiation (UVGI) that emits UVC with a 254 nm wavelength can also further...
enhance (though not replace) the ventilation system and the HEPA filter device. However, it is necessary to consider the flow velocity and irradiation volume to ensure that the irradiation dose disinfects effectively.\textsuperscript{19,23–25}

If neither the HEPA filter/UV disinfection device is available, there is no choice for the ventilation system but to exhaust outward. Nevertheless, the location of the exhaust outlet must be carefully selected, such as preferably on the roof or at least 7–10 feet (i.e., 2.13–3.05 m) high, discharge vertically upward at a speed of 2000 FPM (10.16 m/s), and the discharge position should be at least 25 feet (7.62 m) away from the public area or building opening.\textsuperscript{1} The WHO guidelines refer to the European Union Energy Performance of Buildings Directive EN 16798-4 and recommend that the exhaust outlet be at least 4 m away from humans or animals (use fences to keep the distance). It is also recommended to keep the outlet from the inlet below it for a minimum of 4 m (2 m for the inlet above it).\textsuperscript{9,19}

**Conclusion**

Remodeled "quasi-negative-pressure" isolation wards had been proved a feasible, inexpensive, safe, and effective measure to contain nosocomial outbreaks. The essential elements of a well-functioned ventilation system in isolation wards as required or suggested in the guidelines are summarized in Table 2.

In conclusion, we should first determine the minimum required ventilation volume of an isolation ward based on the severity of COVID-19 patients. Mechanical ventilation remains the mainstay for achieving the requirement, while the assistance of recirculation is also helpful. Beyond adequate ventilation volume, the "clean to less-clean" directional airflow remains the golden rule for the solution of indoor ventilation. The virus-laden exhaust should be treated with HEPA/UV device or be kept away from living organisms, buildings, and air inlets.

**Conflicts of interest**

We declare no potential financial and nonfinancial conflicts of interest.

**References**

1. Siow WT, Liew MF, Shrestha BR, Muchtar F, See KC. Managing COVID-19 in resource-limited settings: critical care considerations. Crit Care 2020;24:167. London, England.
2. Gomersall CD, Tai DYM, Loo S, Derrick JL, Goh MS, Buckley TA, et al. Expanding ICU facilities in an epidemic: recommendations based on experience from the SARS epidemic in Hong Kong and Singapore. Intensive Care Med 2006;32(7):1004–13. Jul.
3. Li Y, Leung GM, Tang JW, Yang X, Chao CYH, Lin JZ, et al. Role of ventilation in airborne transmission of infectious agents in the built environment - a multidisciplinary systematic review. Indoor Air 2007;17(1):2–18. Feb.
4. Li Y, Huang X, Yu ITS, Wong TW, Qian H. Role of air distribution in SARS transmission during the largest nosocomial outbreak in Hong Kong. Indoor Air 2005;15(2):83–95. Apr.
5. Yu ITS, Wong TW, Chiu YL, Ng N, Li Y. Temporal-spatial analysis of severe acute respiratory syndrome among hospital inpatients. Clin Infect Dis an Off Publ Infect Dis Soc Am 2005;40(9):1237–43. May.
6. Ong SWX, Tan YK, Chia PY, Lee TH, Ng OT, Wong MSY, et al. Air surface environmental, and personal protective equipment contamination by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from a symptomatic patient. JAMA 2020;323(16):1610–2. Apr.
7. Horve PF, Dietz LG, Fretz M, Constant DA, Wilkes A, Townes JM, et al. Identification of SARS-CoV-2 RNA in healthcare heating, ventilation, and air conditioning units. Indoor Air 2021;31(6):1826–32. Jun.
8. WHO. Roadmap to improve and ensure good indoor ventilation in the context of COVID-19. 2021. p. 38.
9. WHO. Severe acute respiratory infections treatment centre. Geneva: World Health Organization; 2020.
10. Jensen PA, Lambert LA, Iademarco MF, Ridzon R. Guidelines for preventing the transmission of Mycobacterium tuberculosis in health-care settings. 2005 MMWR Recomm Rep Morb Mortal Wkly Rep Recomm reports 2005;54(RR-17):1–141. Dec.

11. Francis J. Curry national tuberculosis center. Isolation rooms: design, assessment, and upgrade. Francis J. Curry National Tuberculosis Center, Institutional Consultation Services; 1999.

12. ASHRAE. Guidelines for design and construction of hospitals. American Society of Heating, Refrigerating, and Air-Condition Engineer; 2018.

13. AIA. Guidelines for design and construction of hospital and Health care facilities. Washington, DC: The American Institute of Architects; 2001.

14. ASHRAE. 1999 ASHRAE handbook. American Society of Heating, Refrigerating, and Air-Condition Engineer; 1999.

15. Silich BA. Method to reduce aerosolized contaminant concentration exposure to healthcare workers during the COVID-19 pandemic when temporary isolation systems are required. West J Emerg Med 2020;21(6):93–8. Oct.

16. WHO. Natural ventilation for infection control in health-care settings. Geneva: World Health Organization; 2009.

17. Qian H, Li Y, Sun H, Nielsen PV, Huang X, Zheng X. Particle removal efficiency of the portable HEPA air cleaner in a simulated hospital ward. Build Simulat 2010;3(3):215–24.

18. Mousavi ES, Kananizadeh N, Martinello RA, Sherman JD. COVID-19 outbreak and hospital air quality: a systematic review of evidence on air filtration and recirculation. Environ Sci Technol 2021;55(7):4134–47. Apr.

19. Morawska L, Tang JW, Bahnfleth W, Bluyssen PM, Boerstra A, Buonanno G, et al. How can airborne transmission of COVID-19 indoors be minimised? Environ Int 2020;142:105832.

20. Garner JS. Guideline for isolation precautions in hospitals. The hospital infection control practices advisory committee. Infect Control Hosp Epidemiol 1996;17(1):53–80. Jan.

21. Siegel JD, Rhinehart E, Jackson M, Chiarello L. 2007 guideline for isolation precautions: preventing transmission of infectious agents in health care settings. Am J Infect Control 2007;35(10 Suppl 2):S65–164. Dec.

22. Zhivov A, Skistad H, Mundt E, Posokhin V, Ratcliff M, Shilkrot E, et al. Chapter 7 - principles of air and contaminant movement inside and around buildings. In: Goodfellow HD, editor. Kosonen RBT-IVDG. Second E. Academic Press; 2020. p. 245–370.

23. Barnewall RE, Bischoff WE. Removal of SARS-CoV-2 bioaerosols using ultraviolet air filtration. Infect Control Hosp Epidemiol 2021:1–2. Mar.

24. Beggs CB, Avital EJ. Upper-room ultraviolet air disinfection might help to reduce COVID-19 transmission in buildings: a feasibility study. PeerJ 2020;8:e10196.

25. Kujundzic E, Zander DA, Hernandez M, Angenent LT, Henderson DE, Miller SL. Effects of ceiling-mounted HEPA-UV air filters on airborne bacteria concentrations in an indoor therapy pool building. J Air Waste Manag Assoc 2005;55(2):210–8. Feb.