

REVIEW ARTICLE

Effects of indoor environmental parameters related to building heating, ventilation, and air conditioning systems on patients' medical outcomes: A review of scientific research on hospital buildings

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Abstract

The indoor environment of a mechanically ventilated hospital building controls infection rates as well as influences patients' healing processes and overall medical outcomes. This review covers the scientific research that has assessed patients' medical outcomes concerning at least one indoor environmental parameter related to building heating, ventilation, and air conditioning (HVAC) systems, such as indoor air temperature, relative humidity, and indoor air ventilation parameters. Research related to the naturally ventilated hospital buildings was outside the scope of this review article. After 1998, a total of 899 papers were identified that fit the inclusion criteria of this study. Of these, 176 papers have been included in this review to understand the relationship between the health outcomes of a patient and the indoor environment of a mechanically ventilated hospital building. The purpose of this literature review was to summarize how indoor environmental parameters related to mechanical ventilation systems of a hospital building are impacting patients. This review suggests that there is a need for future interdisciplinary collaborative research to quantify the optimum range for HVAC parameters considering airborne exposures and patients' positive medical outcomes.

KEYWORDS

ambient temperature, indoor air quality, indoor environment of hospital buildings, mechanical ventilation, patient outcomes, relative humidity

1 | INTRODUCTION

Surgical site infections (SSIs) are infections that occur after surgery,¹ and they are the most common nosocomial infections.^{2,3} According to a Centers for Disease Control (CDC) and Prevention report, 31% of hospitalized patients get infected by SSIs among all other health care-associated infections (HAI).³ This nosocomial infection can cause morbidity and even contribute to mortality.^{4,5} SSI incidence is dependent on surgical sterilization procedures, mechanical ventilation systems, high-efficiency particulate absorbing (HEPA) filters, ultraviolet radiation, air renewal, humidity control, temperature,

differential air pressure, particle count, surface colony count, and antibiotic prophylaxis.⁶⁻⁹

The importance of the indoor environment on patients' healing processes was initially mentioned by Florence Nightingale¹⁰ and is one of the major issues to which healthcare professionals, environmental psychologists, consultants, and architects are giving priority.¹¹⁻¹⁹ The indoor environment controls infection rates and influences the overall patient outcome.¹⁹⁻³⁴ Appropriately designed building heating, ventilation, and air conditioning (HVAC) systems can enhance patients' recovery process,³⁵ can reduce the length of hospital stay,^{15,18,25,36,37} can lessen medical errors and infection

rates,^{20,23,38} and can improve the indoor air quality (IAQ) and minimize HAI.³⁹ An improved indoor environment of a hospital building can reduce costs associated with airborne illnesses by 9%-20%.⁴⁰

To establish the relationship between health outcomes and the physical environment, Rubin et al³⁰ identified 85 relevant studies where parameters including room size, room privacy, interior design of a room, patient control of his/her environment, music, lighting, exposure to sunlight, window view of nature, ventilation system contaminants, humidity, and temperature have been reviewed. Among these studies on the effect of healthcare environment on patient outcomes, seven were on humidity; four on air filtration system; four on ventilation system; two on temperature; one on (increase outside air changes, improve filter efficiency, maintain constant temperature and humidity, increase positive pressure of operating room air). They³⁰ concluded that there is convincing evidence linking patients' clinical outcomes and built environment parameters. Zimring et al³² identified a connection between the hospital indoor environment and patient and staff outcomes with respect to four sectors: staff stress and fatigue reduction and increased effectiveness in delivering care; patient safety improvement; stress reduction and improvement in patient outcomes; and overall healthcare quality improvement. Dijkstra et al²³ summarized literature on environmental stimuli (eg, furniture, art, color, nature, plants, gardens, carpeting, room size, spatial layout, private rooms, noise, music, odor, television/video, light, windows, and view from a window) and their impact on patients' psychological outcomes rather than on direct physiological outcomes. Huisman et al²⁵ reviewed hospital interior layouts and their relationship with medical staff error, patient falls, infection rates, indoor quality, comfort, building materials, visual comfort, acoustics, view, and privacy. They covered the indoor environment (eg, ambient temperature, humidity, ventilation strategies, and air quality) under the subtopic of safety and security, not patients' medical outcomes.²⁵

Previous studies related to the hospital building's indoor environment discretely focused on patients' thermal comfort,^{35,41-45} acoustic comfort,⁴⁶ visual comfort, and IAQ.⁴⁷⁻⁵⁰ The impacts of single or multiple indoor environmental parameters related to the mechanical ventilation system on overall patient outcomes have not been summarized yet. Hence, this review covers the findings from the published scientific literature on the associations of temperature, relative humidity, ventilation rate, air filter, differential pressure, and ventilation strategy, with patient outcomes. This literature review considered articles published after 1998 and was restricted to codes, guidelines, and standards published by professional societies, licensing agencies, and regulatory organizations. Studies related to natural ventilation for infection control are outside of the scope of this review. Additionally, parameters related to building design, architecture, interior design, noise, aroma, and lighting are being excluded from the scope of this literature review, since this review exclusively focuses on parameters related to the HVAC systems.

This review will help researchers, policymakers, healthcare, and building design professionals to understand the importance of indoor environmental parameters and provide information for enhancing standards related to the HVAC systems in attaining positive

Practical Implications

- The indoor environment of a mechanically ventilated hospital building controls infectious disease transmission and influences patients' outcomes.
- A summary of the recommended optimum ranges of temperature, relative humidity, ventilation rates, air filtration, differential pressure control, and ventilation strategies will be beneficial for the patients' wellbeing.
- These findings from the published scientific literature will be helpful for researchers, policy-makers, healthcare and building design professionals in enhancing standards related to the HVAC systems considering patients' outcomes.
- Future interdisciplinary collaborative research has been identified and can lead to specific optimum ranges for indoor environmental parameters in different spaces for hospital buildings.

medical outcomes for patients. The review also identified avenues for future interdisciplinary collaborative research to quantify the optimum range for indoor environmental parameters considering patients' positive medical outcomes.

2 | METHODOLOGY OF THE REVIEW PROCESS

A multidisciplinary reviewing process was adopted to find out both quantitative and qualitative academic research evidence on indoor environmental parameters and their impact on patients' medical outcomes. PubMed [Medline], JSTOR, ScienceDirect, Scopus bibliographic databases, Google Scholar, and Texas A&M University Library databases were searched for 58 keywords. Combination keywords, such as "ambient temperature AND patient outcomes," "mechanical ventilation system AND patient outcomes," "indoor air quality AND patient outcomes," "airflow AND patient," "mechanical ventilation AND infection," "physical environment AND patient outcomes," and others were used as well to confine the search area. Scientific publications in the fields of both hospital buildings and parameters related to the HVAC system of a mechanically ventilated building were reviewed. Also, the citations in each study found during the main search were reviewed for potential relevance. This paper includes relevant articles that were published after the review done by Rubin et al.³⁰

Through a systematic review process, a total of 1871 abstracts were screened, with a total of 899 papers being identified as relevant to the scope of this study. These articles went through a full-text review process and were excluded if the patient outcomes were not biological and physiological, or if the built environment parameters are not related to the building HVAC system, variables such as

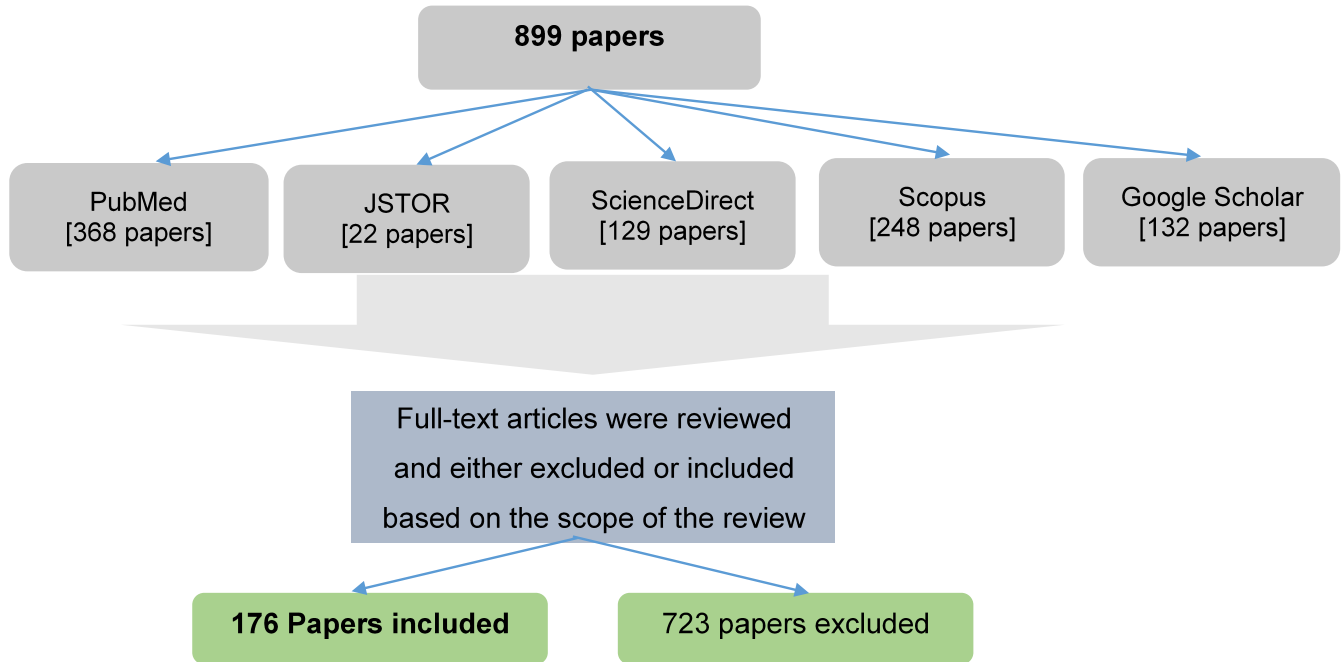


FIGURE 1 Diagram showing the methodology of the review process

noise, aroma, light, and other building layouts and interior design. Additionally, research on naturally ventilated hospital buildings was excluded as well since this review article solely focuses on the parameters related to the mechanical ventilation system of a hospital building. As a result, 176 articles have been included in this review paper. However, articles that partially fulfilled the objective of this review were included. For example, papers concentrating on both patient and staff outcomes were evaluated, though only patients' outcomes related study were included in this review paper. Among 176 papers in this review, 133 investigated patients' outcomes as a function of at least one indoor environmental parameter related to building HVAC systems.

The article selection process is shown in Figure 1. All the references of these articles were verified and crosschecked.

3 | INDOOR ENVIRONMENTAL PARAMETERS IMPACTING PATIENT OUTCOMES

Patient outcomes are dependent on the indoor environment of a hospital building.^{19,33,51-53} Previous research on evidence-based design for healthcare facilities has established that hospital-acquired infection rates are directly related to IAQ.^{17,25,45,54-57} Patients' psychological health is affected by poor indoor environment.^{58,59} Studies have demonstrated an association between environmental variables and "Sick building syndrome" (SBS).⁶⁰⁻⁶² Patients and elderly in hospitals and nursing homes are sensitive to these specific building-related illness caused by SBS; they are hypersensitivity pneumonitis; building-related asthma; and legionellosis.⁶¹ Environmental parameters can be modified to

improve the physical environment and promote patients' positive health outcomes.^{15,16,32,33}

Kameel and Khalil⁶³ have mentioned that HVAC supply air temperature and RH can inhibit the growth of bacteria and activate or deactivate viruses. Lutz et al⁶⁴ identified a positive correlation between infection rates and parameters related to the indoor environment (eg, type of air filter, the direction of airflow and air pressure, air changes per hour (ACH) in a room, humidity, and ventilation system cleaning and maintenance). Codinhoto et al²² summarized the built environment parameters relating to health outcomes of both patient and healthcare professionals by proposing a framework and grouped these environmental parameters to "ergonomics," "fabric and ambient," "art and esthetics," and "services." To propose a framework based on a cause-effect relationship, they categorized patient health outcomes under three sections: psychological, physical, and physiological.²² They concluded that the indoor environment of a healthcare facility has a considerable impact on patients' health outcomes.²² Rashid and Zimring⁶⁵ have developed a framework relating indoor environment with patient stress as an outcome. Ulrich et al⁶⁶ analyzed nine built environment parameters (eg, audio environment, visual environment, safety enhancement, way-finding system, sustainability, patient room, family support spaces, staff support spaces, and physician support spaces) with respect to patient recovery.

This review focuses on summarizing published literature that investigates the impact of each or multiple indoor environmental parameters on patient outcomes. The following section will categorize studies related to patient medical outcomes under indoor air temperature, relative humidity, indoor air ventilation rate, air filtration system, differential pressure control, and mechanical ventilation strategies.

3.1 | Indoor air temperature

3.1.1 | Indoor air temperature and nosocomial pathogens

Potential airborne pathogens such as bacteria, viruses, and fungi can pose severe health effects.⁶⁷ The susceptibility of patients to nosocomial pathogens depends on the pathogen's survivability on various surfaces.^{68,69} Temperature is one of the major factors that influence the transmission and survivability of these microorganisms.⁷⁰⁻⁷²

Low ambient temperature increases *influenza* virus transmission since the survivability of infectious agents rises.^{73,74} The optimum temperature to control the survival of airborne *influenza* viruses is as high as 30°C (86°F) at 50% relative humidity,⁷⁵ which will create an uncomfortable indoor environment as per ASHRAE^a Standard 55.⁷⁶ Through an experimental study, Lowen et al^{73,77} concluded that at 20°C (68°F) *influenza* virus transmission is dependent on humidity, but at the higher temperature (30°C; 86°F), the transmission was eliminated regardless of relative humidity. Low temperature is associated with longer persistence of most viruses, such as the *astrovirus*,⁷⁸ *adenovirus*, *poliovirus*, *herpes simplex virus*, and *hepatitis A virus*.^{68,69} Most bacteria, fungi, and viruses are more stable and persist longer at low temperatures, such as 4°C (39.2°F) or 6°C (42.8°F).⁶⁹ Tang⁷⁵ focusing on the disease-oriented evidence reviewed the survival of airborne infectious bacteria in relation to indoor air temperature. He concluded that temperatures above about 24°C decrease the survival of gram-negative, gram-positive, and intracellular bacteria.⁷⁵ Clinically relevant airborne fungi, potentially life-threatening for immunocompromised patients are *Aspergillus* species (*Aspergillus flavus* and *Aspergillus fumigatus*)^{75,79}; *Blastomyces*; *Coccidioides*; *Cryptococcus*; and *Histoplasma* species.⁸⁰ Unlike the laboratory-based testing for viruses and bacteria, air sampling testing to identify the presence or absence of fungi and their spores in natural settings revealed higher spore counts at a higher temperature,^{75,81,82} although, based on the literature review, Kramer et al^{69,71} concluded opposite findings.

3.1.2 | Indoor air temperature and thermal comfort perception

Indoor air temperature is important for patients' thermal comfort perception.⁸³ Thermal comfort has an impact on patients' healing processes,^{35,84} satisfaction with surgical care,⁸⁵ well-being, and safety.^{35,86-88} Due to medication and drug use, a patient's thermoregulatory system affects the overall perception of thermal comfort.⁸⁹ Uncomfortable environments have negative effects on patients, such as sleeplessness and restlessness,⁸⁶ and can cause shivering, inattentiveness, and muscular and joint tension.^{63,85,90-94} Maintaining thermal comfort in an operating room (OR) is a challenge since the situation varies with the surgery types, various patient requirements, various activity levels of hospital staff, different interior settings of lights and equipment, and the total number of occupied people at a certain time.^{43,95} It is recommended to modulate the OR temperature according to the need of each surgery type for optimum comfort level.^{19,35,43}

3.1.3 | Optimum temperature and patient's thermal risks

In hospitals, researchers recommended separate thermal zones to address the different needs of patients, and their separate thermal preferences^{43,45,96-98} summarize the recommended optimum temperatures to prevent the thermal risk of patients (Table 1). Patients' thermal status^{99,100} and a low ambient OR temperature¹⁰¹⁻¹⁰⁵ are the main reasons that cause patients' intraoperative hypothermia. Studies have identified the correlation between low ambient room temperature and hypothermia among patients during the perianesthesia or perioperative period.^{101,106-108} Since high ambient temperature (>23°C or 73.4°F) is required to avoid perioperative hypothermia, it may be found uncomfortable for the OR personnel.^{109,110}

Surgical site infection is one of the leading effects of even mild hypothermia, where a 1.9°C (3.42°F) reduction in core body temperature increases the chance of SSI three times in a patient after

Spaces in a hospital building	Optimum temperature set point	References
Operating room	>26°C (78.8°F)	De Witte and Sessler ²³⁵
	24-26°C (74.2-78.8°F)	Balaras et al, ¹²⁸ Sadrizadeh, and Loomans ¹³⁷
	≥21°C (69.8°F)	Melhado et al, ⁴³ Khodakarami, and Nasrollahi ³⁵
Postoperative care area/room	≥24°C (75°F)	Hooper et al ²³⁶
Intraoperative area/room	20-25°C (68-77°F)	Hooper et al, ²³⁶ Association of Perioperative Registered Nurses, ²³⁷ Morris, ¹⁰⁴ Morris and Wilkey, ¹⁰⁵ Wang et al ²³⁸
Delivery room	≥26°C (78.8°F)	Knobel et al, ²³⁹ Knobel and Holditch ²⁴⁰
Nursery (for infants)	Around 28°C (82.4°F)	Lyon and Freer ¹²⁵

TABLE 1 Recommended optimum temperature for different spaces in a hospital building

colorectal surgery.⁹⁰ Mild perioperative core hypothermia may increase the risk of wound infection,^{90,111} increase the length of hospital stay,^{90,112,113} increase blood loss,¹¹⁴ cause cardiac complications,¹¹² and cause a prolonged post-anesthetic recovery.¹¹³ Perioperative hypothermia poses a relative risk of severe complications, such as cardiac events,¹¹⁵⁻¹¹⁸ blood loss,¹¹⁴ impaired wound healing,¹¹⁵⁻¹¹⁷ wound infections,¹¹⁹ an increased rate of morbidity and mortality,^{114,115,120,121} length of hospital stay, and the cost of treatment.¹¹⁵⁻¹¹⁷

Higher ambient temperature is recommended during anesthetic induction and surgical skin preparation; conversely, a lower ambient temperature is recommended before surgical incision.¹⁹ However, this method has limited effectiveness among adult patients because of the time interval for warming the room is relatively brief and requires wide swings in temperature to have a significant clinical effect.¹²² A study on critically ill trauma patients confirmed that there is no correlation between the decrease of ambient OR temperature and patient core body temperature with effective use of active warming strategies on patients.^{123,124} Controlling indoor air temperature is crucial for other severely ill patients (eg, burn victims) where the application of active warming strategy is difficult.^{19,86} Thermal stability is important for preterm infants to reduce harmful side effects, such as delayed adaptation to extrauterine life, hypoglycemia, respiratory distress, hypoxia, metabolic acidosis, coagulation

defects, acute renal failure, necrotizing enterocolitis, and failure to gain weight or weight loss and morbidity.¹²⁵⁻¹²⁷

3.2 | Relative humidity (RH)

3.2.1 | Influence of relative humidity on infectious disease transmission

In hospital buildings, evidence has confirmed that RH affects infection control because it is related to the growth and transfer of airborne bacteria,¹²⁸ some strains of viruses, and fungi.^{35,83,129} A strong correlation has been found between the transmission of viruses and absolute humidity,⁷⁴ and viruses outbreak when the vapor content of the air decrease.¹³⁰ Several controlled studies concluded that both RH and humidity ratio values influence the survival of viruses and bacteria.^{69,74,131-134}

An RH level higher than 45%-50% promotes fungal growth indoors^{75,83,135,136} and affects the concentrations of allergens, bacteria,^{98,137} and increase the settling rate of aerosols.¹³⁶ Most fungal species cannot grow when RH is below 60%.⁶⁹ High humidity levels support microbial growth due to moisture absorption by building materials.¹³⁶ Pathogenic microorganisms can adhere quickly to moist and slick or damaged walls and ceilings¹³⁸ which can affect patient and staff well-being.¹³⁹⁻¹⁴²

TABLE 2 Favorable relative humidity (RH) ranges for the survivability of nosocomial pathogens and microorganisms

	Example	Relative humidity (RH)	References
Virus			
Viruses (with lipid envelopes)	Respiratory viruses (<i>Influenza virus</i> , <i>Para-Influenza virus</i> , <i>Corona virus</i> , <i>Respiratory syncytial virus</i> , <i>Herpes simplex virus</i> , <i>Measles virus</i> , <i>Rubella virus</i> , and <i>Varicella zoster virus</i>)	Lower RH (20%-30% RH)	Tang, ⁷⁵ Kramer et al ⁶⁹
	<i>Influenza</i> , <i>Lassa fever virus</i> , and <i>Human coronavirus (hCV)</i>	Lower RH (<50% RH)	Tang et al, ¹³⁴ Noti et al ¹³¹
	<i>Influenza</i>	20%-35% RH	Lowen et al ⁷³
	<i>Influenza</i>	23%-43% RH	Noti et al ¹³¹
Viruses (non-lipid enveloped)	<i>Adenovirus</i> , <i>Enterovirus</i> , and <i>Rhinoviruses</i>	Higher RH (70%-90% RH)	Tang, ⁷⁵ Kramer et al ⁶⁹
	<i>Poliovirus</i>	Higher RH (>50% RH)	Tang et al ¹³⁴
Bacteria			
Gram-negative bacteria	<i>Pseudomonas</i> spp., <i>Enterobacter</i> spp., <i>Klebsiella</i> spp., <i>Salmonella seftenberg</i> , <i>Pseudomonas aeruginosa</i> , <i>Chlamydia trachomatis</i>	Higher RH	Tang, ⁷⁵ Tang et al ¹³⁴
	<i>Serratia marcescens</i> , <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> , and <i>Proteus vulgaris</i>	Lower RH (<50% RH)	Tang, ⁷⁵ Kramer et al, ⁶⁹ Tang et al, ¹³⁴ Cox ¹⁴⁴
Airborne gram-positive bacteria	<i>Staphylococcus epidermidis</i> , <i>Streptococcus haemolyticus</i> , <i>Bacillus subtilis</i> , and <i>Streptococcus pneumoniae</i>	Lower RH (<50% RH)	Tang, ⁷⁵ Tang et al ¹³⁴
	<i>Enterococcus faecalis</i>	Lower RH	Robine et al ²⁴¹
	<i>Listeria monocytogenes</i>	Higher RH	Kramer et al, ⁶⁹ Tang et al ¹³⁴

Relative humidity has an impact on the viability of both airborne and droplet transmission of viruses.^{75,143} However, this relationship is quite complex. Both lipid-enveloped and non-lipid-enveloped viruses are less stable at relative humidities between 40% and 70%,¹⁴³ while an ideal range for the airborne *influenza* survival is 23%-81%.⁷³ A study¹³¹ found that at 23% RH, the infectivity of *influenza* virus is as high as 71% to 77%, whereas at higher RH level (43% RH) the infectivity found 16% to 22%. Based on an experimental study, Lowen et al⁷³ concluded that airborne transmission of *influenza* virus was maximum at 20%-35% RH, and poor at 50% RH. Tang et al¹³⁴ summarized that higher RH (>50%) is favorable to viruses without a lipid envelope, for example, poliovirus.¹⁴⁴ However, lipid-enveloped viruses, for example, *influenza*,^{73,74} Lassa fever virus, and human coronavirus survive longer in low RH (<50%) and their persistence eliminate at RH >80%.¹³⁴ Findings on the effects of RH on the survival of airborne bacteria appear to be more complicated than with viruses.^{75,143,144} A literature review⁶⁹ on the persistence of nosocomial pathogens on any intimate surfaces concluded that at higher humidity most types of bacteria persist longer and spore concentrations of most fungi were higher. However, conflicting results were found on the on the persistence of clinically relevant pathogens. Table 2 summarizes research findings on favorable RH ranges for the growth and survivability of various nosocomial pathogens and microorganisms.

3.2.2 | Impact on indoor comfort

In a hospital building, RH levels are related to patients' indoor thermal comfort and hygiene of spaces.^{35,128} Low humidity levels can affect patients' indoor comfort perception^{145,146} and can cause irritations,^{63,146} dry skin and nose,^{35,63} and throat irritation.^{35,63,145,146} Dryness can promote blood coagulation, which is undesirable for patients during surgery.^{35,128,137} Research confirmed that for pre-term infants, higher humidity levels along with a warm temperature are recommended to control evaporative heat loss.^{147,148} A study confirmed that if the humidity of the incubator decreased below 60%, then the infant body temperature decreased by as much as 1°C (33.8°F) within 5 minutes.¹⁴⁸ To reduce evaporative heat loss among newborns, increasing the humidity level is the most effective option.¹²⁵ Balaras et al¹²⁸ suggested the recommended RH range for a hospital building should be 30% to 60%.

3.3 | Indoor air ventilation

Pathogens and other respiratory viruses, such as *influenza*,^{134,149-151} SARS-associated coronavirus (SARS-CoV),^{134,152,153} tuberculosis,^{134,152,154} Q-fever, and measles¹⁵² can be transmitted through an airborne route. There is sufficient evidence to support that indoor air ventilation can contribute to the spread of airborne infectious disease in hospitals.^{152,155-162} Several literature reviews covering both naturally and mechanically ventilated buildings have examined the impact of ventilation on health outcomes.^{152,159,163-166} Some of these covered other building types along with hospitals.^{152,163-165}

The following subsections summarize suggested ventilation requirements considering airborne pathogen transmission. Primarily, based on previous research findings, this will review the optimum range of ventilation rates or flow rates for positive patient outcomes. Additionally, ventilation strategies, air filtration systems, and desirable room pressurization with respect to the adjacent areas in a hospital building will be reviewed. This review excluded all published standards and guidelines (eg, ANSI/ASHRAE/ASHE Standard 170,¹⁶⁷ FGI,¹⁶⁸ AIA,¹⁶⁹ ASHRAE Handbook,¹⁷⁰ 2013 ASHRAE HVAC Design Manual for Hospitals and Clinics¹⁷¹), that specify mandatory or recommended requirements including ventilation rates, filtration, and pressure relationships. Additionally, studies on naturally ventilated hospital buildings are being excluded since this review exclusively focuses on parameters related to the mechanical ventilation systems.

3.3.1 | Ventilation rate

Ventilation rates are measured as ACH, that is, how many times the air in a defined space is replaced per hour. Several comprehensive literature reviews on ACH and infectious disease transmission concluded that there is insufficient evidence to specify the minimum and maximum ventilation requirements in hospitals based on infection control risk to patients.^{152,164,172,173} English¹⁶⁶ reviewed the ventilation guidelines of US hospitals and concluded that the effect of ventilation requirements on general infection rates is still unidentified except in ORs¹⁷⁴ and airborne isolation rooms.¹⁷⁵ English¹⁶⁶ showed a chronological summary of air change rates in hospitals, where establishing the relationship with patient outcomes was outside of his scope.

Although many studies observed that lower ventilation rates could increase the risk of airborne cross-infection,^{154,160,174-176} increasing the ACH only may not always be advantageous for the patients' well-being from the infection risk perspective.^{164,173,177-182} Using numerical modeling through computational fluid dynamics (CFD) analysis, Memarzadeh and Xu¹⁷⁷ suggested that in an enclosed mechanically ventilated room (eg, an isolation room) increasing the airflow rate (ie, ACH) may not be the major contributing factor to control infections transmission. Instead, the ventilation system design and the distance from the contaminant source are important factors than flow rate.¹⁷⁷ They¹⁷⁷ suggested uninterrupted path between the contaminant source and the exhaust to control contaminants. Grosskopf and Mousavi¹⁸³ had a similar conclusion for general patient and isolation patient test room studies. Results from another study conducted in the field environmental chamber concluded that increasing supply ACH might escalate the airborne infection risk transmission under certain circumstances (eg, position of the source and the susceptible person in relation to the supply and return air grills).¹⁷⁹ A study in a simulated two-bed hospital isolation room with mixing air distribution system showed that the elevated ventilation rates might increase the risk of airborne cross-infection.¹⁷³ The exposure level depended on the positioning and distance from the source, and posture of the infected patients.¹⁷³ The recommended

12 ACH in the present standards and guidelines resulted in draft discomfort within the occupied zone due to higher air velocities.¹⁷³

Conversely, across-sectional observational study by Menzies et al¹⁵⁴ showed a higher tuberculosis infection risk for healthcare workers in non-isolation rooms (eg, general patient rooms) with ventilation rates of less than 2 ACH. Another study⁸⁷ of ventilation performance in patient rooms showed that a ventilation rate of 4 ACH with supplemental heating and cooling would be favorable in terms of thermal comfort, uniformity, and ventilation effectiveness. Results also suggested that six ACH is optimum, and similar conclusions have been found for hospital isolation rooms.⁸⁷ Through a CFD study, Memarzadeh and Jiang¹⁷⁵ suggested that total ventilation rates over 10 ACH will not be effective for Airborne Infection Isolation Rooms (AIIR) since this flow rate did not decrease the exposure to infectious disease transmission. Based on the review on aerosol-transmitted infections in the isolation room, Tang et al¹³⁴ recommended minimum 12 ACH, so that the air moves from healthcare workers to a patient. They¹³⁴ also suggested that placing patients close to the exhaust vent will reduce the cross-contamination risks. A study following airflow modeling and particle tracking methodologies concluded that an OR with ceiling heights between 2.74 m (9 ft) and 3.66 m (12 ft) should maintain 20-25 ACH for contamination control.¹⁸⁴ A study on 4-bed patient rooms showed a minor reduction in infectious disease transmission through hand colonization when ventilation rates change from four ACH to six ACH.¹⁸⁵ The results of a CFD simulation in the general wards of Hong Kong hospitals showed that a flow rate of nine ACH effectively minimized infection risk of three respiratory viruses.¹⁸⁶ Table 3 below summarizes the recommended minimum total ACH of the supply air and outside air comparison between Ninomura and Bartley¹⁸⁷ and English.¹⁶⁶

Based on results discussed above, it is evident that the current air distribution methods practiced today are insufficient in order to control the spread of infectious disease within a hospital environment. Along with ACH, the contamination risk depends on the (a)

TABLE 3 Comparison of total ACH of the supply air and outside air recommendation in different hospital building spaces

Different spaces in a hospital building	Minimum total ACH/outside ACH	
	Ninomura and Bartley ¹⁸⁷	English ¹⁶⁶
Patient room	6-4 ACH/2 ACH	4 ACH/2 ACH
Labor/Delivery/Recovery/Postpartum	6-4 ACH/2 ACH	6 ACH/2 ACH
AIIR	12 ACH/2 ACH	-
Emergency rooms and radiology—waiting and triage rooms	12 ACH/2 ACH	-
Procedure rooms/operating rooms	15 ACH/3 ACH	6 ACH/2 ACH
Nursery	-	6 ACH/2 ACH
Anesthetic storage	-	8 ACH/-
Patient corridor	-	2 ACH/-

positioning and distance of the susceptible person (eg, caregiver; patient) from the infected source; (b) position of both susceptible person and infected source in relation to the supply and return air grills; (c) posture of the infected source; (d) air velocities; and (e) air distribution pattern.

3.3.2 | Ventilation strategies

The ventilation strategy and air distribution pattern in a hospital building are correlated with the airborne transmission of infectious agents.^{152,158,188-190} This section will evaluate the role of various ventilation strategies in removing airborne pathogens from different spaces in hospitals.

CFD analysis found that in patient rooms, displacement ventilation made larger bioaerosols (>10 μm) suspend in the air for longer periods, whereas smaller particles were able to escape the space.¹⁹¹ Another experimental study concluded that in multiple bed patient rooms, the spacing between beds should be farther apart with the displacement ventilation strategy compared with mixing the air.¹⁹² Qian et al¹⁹² also concluded that the exhaled nuclei droplet from infected patients penetrates long distances during displacement ventilation, and takes longer to dissipate than mixing ventilation strategies.

A comparative experimental study for hospital wards showed that the displacement ventilation system would have higher contaminant concentration than a mixing ventilation system if the auxiliary exhaust is located to the lower part of the wall.¹⁹³ However, when the exhaust was relocated at the upper part of the wall, the displacement ventilation at 4 ACH showed lower contaminant concentration than traditional mixing ventilation at six ACH.¹⁹³ Another study with a similar conclusion added that, for better performance, supply air diffusers should be unobstructed and located at a lower level and toilet transfer grilles at a high level.¹⁹⁴ Compared with pure mixing ventilation, the displacement ventilation increases the cross-infection risk 12 times when two persons (source and target) are at face-to-face and face-to-side position at 0.35 m distance.¹⁸¹ The contaminant concentration profile showed that the displacement ventilation showed higher risk of transmission close to the contaminant source and exhaust, compared with a mixing ventilation system.¹⁹³⁻¹⁹⁵ Guity et al¹⁹⁴ also concluded that the displacement ventilation delivers much lower contaminant concentration in areas further away from the patient.

Conversely, a study on two floor-supply-type ventilation flow patterns showed that unidirectional-upward system was more efficient in removing the smallest droplet nuclei (<1.5 μm), but the single-side-floor system was effective at removing large droplets and droplet nuclei.¹⁸⁸ Another study on supply air inlet locations showed that the underfloor air distribution system performs better in reducing bioaerosol concentration than the ceiling type and side wall supply systems.¹⁹⁶

Experimental test chamber results and Eulerian-Lagrangian computations revealed that the mixing ventilation system has a positive influence on bioaerosol dispersion.¹⁷⁶ A simulation of the hospital

ward with a ceiling-mixing type ventilation system showed that the dispersions of airborne contaminants were significantly affected by the location of the exhaust air vents.¹⁹⁷ They also concluded that the decay rate of contaminant concentration is exponential with a complete mixing ventilation system.¹⁹⁷ Using an engineering computational technique for the isolation room, researchers have found that the parallel-directional airflow pattern and staggered air-supply and exhaust vents positioning can efficiently control infectious disease contamination.¹⁹⁸ This study also concluded that the ceiling to floor level ventilation airflow resulted in poor infection control.¹⁹⁸ An analytical CFD study in hospital ward showed that when the air was supplied and extracted through the ceiling, it was more effective in removing airborne pathogens compared with other strategies.¹⁸⁹

After reviewing 20 ORs, Balaras et al¹²⁸ summarized that for quicker dissipation of contaminated air, laminar downward airflow was found to be effective with air changes ranging from 3.2 to 58 ACH. Another simulated study showed that positioning the ventilation grills at the ceiling removes the aerosol more quickly than the wall ventilation system.¹⁸⁹ For downward air movement, Khalil¹⁹⁹ recommended the supply air outlets need to be located at the ceiling and the exhaust inlets on the opposite walls. The optimum location of supply outlets is crucial to reduce the residence time of pollutants efficiently.⁹⁵ In ORs, laminar airflow can limit surgical-site infections by lessening the bacterial air contamination.^{65,200-202} Based on routine surveillance data on hospital ORs, Brandt et al⁸ concluded that ventilation with vertical laminar airflow was associated with a higher risk for severe SSIs. To control the contamination through microbiological organisms, a laminar airflow system promotes high ACH at low supply air speed.²⁰⁰

Based on above discussion, while designing ventilation strategy in any spaces within a hospital building, the posture and distance between two persons (source and target), the location of diffusers (inlet and outlet vents), and air change rates are important factors in reducing contaminant concentration. It is worth to mention that these test results are either simulation-based or an outcome from the experimental test chamber, which are usually done in a static environment without considering real-world scenarios (eg, provider traffic).

3.3.3 | Air filtration system

A high-efficiency particulate air (HEPA) filtration system can reduce the load of bacteria, which is the most common cause of hospital-associated infections²⁰³ and other infectious particles.²⁰⁴⁻²¹¹ HEPA filters were found to be effective for patients having environmental fungal contamination, such as invasive fungal infections (IFIs) caused by construction near hospitals.^{207,211-216} This filtration system can decrease the airborne concentrations of aerosolized pathogens and viruses.^{217,218} Full outside air ventilation along with return air through HEPA filtration is capable of reducing the concentration of droplet nuclei with 30%-90% effectiveness.²¹⁹ However, HEPA filter within ducts can become a breeding ground of microorganisms which may significantly contaminate the filtered air.^{64,220-222} Lutz et al⁶⁴ found

that the insulation and filter materials are vulnerable to fungal degradation under high humidity. Due to the ineffectiveness of HEPA filters in reducing environmental fungal spore counts,²²³ researcher emphasized the importance of terminal filtrations system,⁶⁴ photocatalytic oxidation application,²²¹ and portable HEPA filtration units²²³ in areas with vulnerable immunocompromised patients.

HEPA filters can add pressure losses, which results in higher fan power, greater water quality control (for legionella), and moisture control due to the impact of moisture content on the survival of pathogens.^{83,167} Memarzadeh⁷⁰ suggested that for effective patient outcomes, these filtration systems should be paired with higher ACH.

3.3.4 | Differential pressure control

Differential pressure is important to control the contamination of airborne infectious agents through airflows between the protective and less protective spaces of a hospital building.^{157,224-226} In a hospital building, pressurization or depressurization relative to its surroundings needs to be maintained in the microbiology laboratories, the anteroom to AIIRs, AIIRs, autopsy suites, bronchoscopy rooms, emergency department and radiology waiting rooms, and ORs or surgical rooms.²²⁶ AIIRs need to be maintained at negative differential air pressure ("negative" means that the air pressure of the area is lower than the adjacent spaces) to avoid contamination from patients with highly infectious diseases (ASHRAE 170-2008 as cited in Aliabadi et al¹⁶¹). Sterilizing spaces and service zones, such as laundry and bathrooms, should be negatively pressurized.¹⁶¹ In contrast, surgery rooms should continuously maintain positive differential air pressure to avoid particle infiltration.^{161,227} Protective environment rooms for immunocompromised patients (eg, AIDS) need to be kept at positive differential air pressure.^{161,168,224} To control the IAQ, Ninomura and Bartley¹⁸⁷ summarized that the critical care; AIIRs; bronchoscopy rooms; and endoscopy rooms should be negatively pressurized with respect to its adjacent areas, whereas, diagnostic and treatment area; ORs; pharmacy; sterile storage; and clean linen storage should be positively pressurized.¹⁸⁷

After reviewing international standards, Kao and Yang¹⁹⁸ mentioned that the minimum pressure differential requirements between the isolation and non-isolation zone varied from 2.5 to 30 Pa. US guidelines recommend the minimum pressure difference for the AIIR should be 2.5 Pa (0.01 in. of H₂O).^{157,169,224,225,228} The Curry International Tuberculosis Center²²⁹ mentioned that a small negative pressure might not be adequately maintained due to external factors, such as fluctuating air currents caused by elevators, doors, or windows to the outside. They suggested a minimum of 7.5 Pa (0.03 in. of H₂O) differential pressure between the isolation room and the anteroom following the recommendation from the California Division of Occupational Safety and Health (Cal/OSHA).²²⁹ Depending on the need and restrictions for surgery rooms and adjacent spaces, 5-15 Pa (0.02-0.06 in. of H₂O) differential pressure was recommended,²²⁷ while others suggested up to 20-25 Pa (0.08-0.1 in. of H₂O).²³⁰

Experimental tracer gas studies performed in a test chamber simulating an AIIR showed that the pressure differential -15.0 Pa (0.06 in. of H₂O) could effectively reduce the risk of infectious disease contamination.²³¹ According to Streifel,²²⁸ the minimum differential pressure for ORs and protective environment rooms should be 0.25 Pa (0.001 in. of H₂O). A multi-zone airflow simulation study concluded that the leakage in room pressure control could significantly affect contaminant transfer.²³² This emphasizes the importance of considering leakage in achieving design pressure differentials.²³² Results from the tracer containment testing of AIIR showed that due to people's movement, differential pressure 15 Pa (0.06 in. of H₂O) might not even effectively prevent the migration of air volume.²³³ Adams et al²³⁴ compared the containment efficiency in an anteroom-equipped hospital AIIR at varied differential pressure (2.5, 11, and 20 Pa) in the presence or absence of care provider movement. They concluded that the higher pressure differential (>2.5 Pa or 0.01 in. of H₂O) would control the contamination effectively with and without provider traffic.²³⁴

Based on the above discussion, it is important to note that in a hospital building critically important spaces need to be pressurized or depressurized with respect to its surroundings. To prevent contamination by infected patients, negative air pressure inside the room (eg, AIIR) relative to the surrounding areas should be maintained by mechanically removing (exhausting) more air than is supplied. Conversely, to protect patients (eg, immunocompromised patients in OR) from airborne infectious agents, the room needs to be positively pressurized. While designing and controlling this inlet and outlet airflows disequilibrium in a mechanically ventilated hospital building, the movement of people and leakages through doors, windows, or cracks need to be considered.

4 | CONCLUSION

4.1 | Summary of literature findings

In a hospital building, the built environment can have a beneficial impact on patients' healing processes.^{12,22,23,25,29,30,32,34,35,38,43} This review covered the published research that has assessed patients' medical outcomes with respect to at least one indoor environmental

parameter related to the mechanical ventilation system of a building including temperature, relative humidity, and overall IAQ. Scientific publications in the fields of both healthcare and building HVAC systems published after the review paper of Rubin et al³⁰ have been included in this review process. Studies related to the natural ventilation system, building design, architecture, interior design, noise, aroma, and lighting were outside of the scope of this review. This review summarized peer-reviewed papers on how indoor environmental parameters related to the mechanical ventilation systems of a hospital building impact patient outcomes.

Higher indoor air temperature is recommended to control the survivability and transmission of most bacteria,⁷⁵ fungi,^{69,71} and viruses.^{68,69,73-75,78} Low ambient OR temperatures are critical for patients, which lead researchers to recommend the optimum temperature to prevent thermal risk, with a minimum suggested temperature for ORs of 21°C (69.8°F),^{35,43} and a maximum of 26°C (78.8°F)^{128,137,235} or higher.²³⁵ Based on the existing literature, this recommended range varies depending on the types of surgery, patient demographics (eg, age, gender), and OR personnel.

Most bacteria, fungi, and viruses persist longer at higher humidity (eg, >70%) and infectivity lessens exposure in the RH range between 40% and 70%.⁶⁹ Higher RH (50% RH or higher) is recommended to control the transmission of lipid-enveloped viruses, for example, *influenza*.^{73,74,131} However, lower RH (50% RH or lower) is suggested for viruses without a lipid envelope.⁷⁵ For most gram-negative bacteria (eg, *Escherichia coli*; *Klebsiella pneumonia*), higher RH (50% RH or higher) is detrimental to their survival,^{69,75,134,144} except a few (eg, *Pseudomonas* spp., *Enterobacter* spp., *Klebsiella* spp., and *Salmonella* *Seftenberg*).^{75,134} Similarly, higher RH is recommended to control airborne gram-positive bacteria.^{75,134} Figure 2 summarizes the favorable RH ranges for the survivability of nosocomial pathogens and microorganisms. Higher RH is also suggested for hospitals to avoid thermal discomfort^{145,146} and other negative consequences due to dryness.^{35,63,128,145,146} It is evident from these findings that maintaining certain RH ranges may be detrimental for some microorganisms but favorable for others. Guidelines for humidity ranges in any hospital areas should consider both survival and infectivity of airborne-transmitted infectious disease control and thermal comfort.

Microorganisms	Favorable relative humidity (RH) ranges											References	
	0	10	20	30	40	50	60	70	80	90	100		
Viruses (with lipid envelopes)			■	■	■								Tang, ⁷⁵ Kramer et al ⁶⁹ Tang et al, ¹³⁶ Noti et al ¹³³ Lowen et al ⁷³ Noti et al ¹³³
Viruses (non-lipid enveloped)									■	■	■	■	Tang, ⁷⁵ Kramer et al ⁶⁹ Tang et al ¹³⁶
Gram-negative bacteria	■	■	■	■	■								Tang, ⁷⁵ Kramer et al, ⁶⁹ Tang et al, ¹³³ Cox ¹⁴⁴
Airborne gram-positive bacteria	■	■	■	■	■								Tang, ⁷⁵ Tang et al ¹³⁶
Fungi								■	■	■	■	■	Kramer et al ⁶⁹

FIGURE 2 Diagram of favorable RH ranges for different microorganisms

This review found that ventilation rates, ventilation strategies, air filtration, and differential pressure control can contribute to the spread of airborne infectious disease in hospitals, although specific recommendations are institution specific. The evidence indicates that higher ventilation rates may reduce the infection rate in several situations. However, the maximum required ventilation rates (above which there is no further reduction of infection risk) at different spaces in hospitals are yet unknown,¹⁶⁴ and it depends on other parameters, such as air distribution pattern; position and distance of the susceptible person from both source and air diffusers; and position and posture of infected source.^{134,173,177,179,183}

Results from both experimental and computational studies confirmed that for patient rooms, the mixing ventilation strategies showed better contamination control and lowered the infectious disease transmission risks.^{176,181,189,192-195} For multiple bed patient rooms, displacement ventilation strategies may not be suitable unless beds are placed apart; the exhaust is located at the upper part of the wall; and unobstructed supply air diffusers are located at a lower level of the wall. Additionally, the posture and distance between two persons (source and target) have impacts on the contaminant concentration profile. These results are highly dependent on a subject's position and distance from the source of the contaminant^{181,194}; location of the vents^{189,193,194,196-199}; and ventilation rates.^{128,176} Along with appropriate ventilation strategies, the HEPA filtration system can effectively reduce the contamination load.^{204-211,217-219} However, maintaining the differential air pressure with respect to the adjacent spaces is very critical since the HEPA filters within ducts may have limited control over airborne nosocomial infections due to contaminated air from adjacent spaces.²²⁰ In order to control airborne contamination through pressurization-depressurization in critical areas of a hospital building, important considerations are leakage in room pressure control²³² and provider traffic.^{233,234} The comprehensive ventilation guidelines for different zones within a hospital require patient-oriented evidence incorporating ACH along with the (a) positioning and distance of the susceptible person (eg, caregiver; patient) from the infected source; (b) position of both susceptible person and contaminated source in relation to the supply and return air grills; (c) posture of the infected source; (d) air velocities; (e) air distribution pattern; and (f) location of the air filtration system.

4.2 | Recommendations

Based on this literature review, temperature, humidity, and the indoor air ventilation system in hospital buildings affect various infectious organisms, which then have an effect on patient outcomes. Published results contain contradictory findings, which made the comparative assessment difficult due to inconsistency in experimental design, choice of variables, location and settings, demographics, diseases, patients, and the types of outcome measurements. Hence, it is impossible to make evidence-based decisions regarding the optimum ranges to improve patient-oriented outcomes such as symptoms, morbidity, quality of life, or mortality. These contradictory results of the current research suggest that all indoor environmental parameters related to the HVAC

system need to be measured or included in the comparative analysis of each study. Additionally, a common set of variables need to be defined for comparative analysis.

A few epidemiological studies have been undertaken specifically to investigate the suitable ranges of multiple indoor environmental parameters (eg, temperature, RH, ACH); there is little patient-oriented evidence to formulate guidelines for hospitals. While extensive simulation-based research has been performed, very little patient-oriented evidence has been produced. For validation, simulations and experiments need to correlate by physical measurements. Additional multidisciplinary studies including researchers, patients, building owners, facility managers, and maintenance staffs studies are needed, which would address evidence-based decisions regarding the optimum ranges to improve patient-oriented outcomes.

Studies that look at nosocomial infection rates, the spread of infection within hospitals, and associated costs are potential avenues of research. A multidisciplinary study combining available molecular biology testing, advanced computer modeling, experimental testing, and on-site experimental designs could provide evidence to identify optimum ranges for temperature, humidity, and ACH along with appropriate ventilation design strategies. It is also necessary to address these variables as a function of spaces within a hospital since each zone has unique occupants and different functionality. Additionally, the structural variation of infectious agents (ie, viruses, bacteria, and fungi) may need to be considered separately when investigating airborne survival since each will have differing conditions under which they may be optimally suppressed. Finally, the relationship between IEQ variables, thermal comfort perception of patients, and airborne contamination need to be investigated. The health effects of ventilation in locations with highly polluted outdoor air and other diverse outdoor conditions present an important area of future research.

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ENDNOTE

³ASHRAE was formed as the American Society of Heating, Refrigerating, and Air-Conditioning Engineers and from 2012, ASHRAE began doing business as "ASHRAE." <https://www.ashrae.org/about>.

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