# Prevention of contaminated aerosol and the transmission during nebulized therapy in hospital settings: a systematic review

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## Abstract

Inhalation nebulization therapy is important for administering medications to patients in aerosolized form. However, there are persistent apprehensions in healthcare settings regarding aerosol contamination because of the significant infection risk. Despite rigorous adherence to established hospital protocols, concerns about potential contamination and transmission persist, raising considerable apprehension about nosocomial pneumonia. This condition shows the urgent need for implementing highly effective strategies to ensure patient safety during nebulization therapy. Therefore, this study aimed to review current investigations, focusing on interventions to mitigate aerosol contamination and minimize the transmission of contaminated aerosols. Adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, this systematic review included an exhaustive analysis of randomized and non-randomized clinical trials as well as, simulated experimental and in vitro studies published in English in the past decade. A meticulous search was conducted across four major databases, namely ScienceDirect, Cumulative Index to Nursing & Allied Health (CINAHL), PubMed, and Scopus. A total of 37 pertinent studies were identified and subjected to rigorous analysis. The preventive measures include a range of strategies, such as the use of masks by therapists, thorough disinfection of nebulizers, integration of filters, and regular environmental cleaning in the vicinity of the patient. In conclusion, these multifaceted interventions are significant in preventing the administration of contaminated aerosols and curbing the proliferation of infectious agents in the hospital environment.

## Introduction

Inhaled therapy through nebulization is a significant method for administering essential medications to patients, particularly those with respiratory conditions, such as chronic obstructive pulmonary disease (COPD), asthma, or cystic fibrosis.[1,2] This method ensures targeted delivery, with aerosolized drugs directly reaching the respiratory tract, including the lungs, optimizing therapeutic outcomes.[3] However, a growing concern in healthcare facilities is the potential for aerosol contamination during this process. Contaminated aerosols harbor various pathogens, such as bacteria, viruses, and fungi, thereby presenting a considerable risk for infection transmission.[4–6] Both patients and healthcare professionals are at risk, showing the critical need to maintain cleanliness and safety standards.[7,8]

Despite meticulous compliance with established protocols and guidelines in hospital settings, a persistent presence of aerosol contamination suggests potential limitations in current preventive measures.[6–9] The continuous existence of contaminated aerosols raises significant concern about the adequacy of existing protocols, necessitating a thorough evaluation of preventive strategies to bolster patient safety and infection control.[10,11] A nurse plays a crucial role in preventing and controlling infection in the hospital. This responsibility is significant in safeguarding the well-being and safety of patients.[12]

A primary concern in the contamination of aerosol is the high susceptibility to hospital-acquired infections, particularly pneumonia, specifically among medically compromised patient cohorts.[13,14] Hospital-acquired pneumonia (HAI) significantly impacts patient recovery, prolongs hospitalization, and increases healthcare expenditures.[14,15] Therefore, addressing and mitigating aerosol contamination represents a critical aspect of preventing and controlling infection in healthcare settings.

Due to the crucial need to ensure patient safety and mitigate the risk of nosocomial infections, this study conducts a rigorous systematic review of previous investigations. The main aim is to comprehensively assess and synthesize current studies, with a particular focus on preventive strategies to mitigate aerosol contamination during nebulized therapy. Through a synthesis of the available evidence, this study aimed to provide invaluable insights and evidence-based recommendations. The result will inform the refinement of protocols and strategies, thereby advancing patient care, safety, and infection control.

## Materials and Methods

This study adopted the updated Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[16] The method used was Population, Intervention, Comparison, and Outcome (PICO),[17] as follows: i) Population or problem (P): Patients experiencing nebulized therapy or simulation of nebulizing therapy; ii) Intervention or exposure (I): Implementation of

**Significance for public health**

*This study addresses critical concerns regarding aerosol contamination in inhalation nebulization therapy, showing the urgent need for comprehensive strategies to ensure patient safety and minimize infection risks. Adhering to PRISMA guidelines, this study analyzed 37 pertinent studies from the past decade, showing preventive measures, such as therapist masks, nebulizer disinfection, filter integration, and environmental cleaning. These multifaceted interventions are crucial in curbing aerosol contamination and enhancing patient safety in hospital environments, significantly impacting public health.*

strategies and measures to mitigate contaminated aerosol and the potential transmission during nebulized therapy; iii) Comparison (C): No comparison or regular intervention based on guidelines; iv) Outcome (O): Evaluating the efficiency of implemented prevention strategies in minimizing contaminated aerosols and transmission.

A comprehensive literature review was conducted across four databases, namely PubMed, ScienceDirect, Scopus, and Cumulative Index of Nursing and Allied Health (CINAHL). SECERLA terminologies were collected using synonyms and Medical Subject Headings (MESH) (Supplementary Materials, Table 1). The keywords used were Nebulizer, semi-critical devices, medical devices, and bacterial contamination, as well as Nebulization or aerosol therapy. Other keywords include aerosol generating procedure, medical aerosol, bioaerosol, aerosol transmission, and infection protection, as well as infection, contamination, nosocomial, and transmission prevention. Considered studies were in English, published in the last decade, and included randomized and non-randomized experimental design, simulation, in vitro, and non-experimental studies with data. The exclusion criteria are reviews, case reports, editorials, books, commentaries, and studies articles discussing interventions for preventing aerosol contamination without trial data.

Irrelevant titles, abstracts, and full-text studies were screened, followed by meticulous independent evaluation to assess the appropriateness of the retrieved studies. Any discrepancies were resolved through discussions, and data extraction elements were adjusted in agreement with the entire review team. Figure 1 shows a summary of the results and reasons for excluding studies during the full-text review. The studies meeting the inclusion criteria were subjected to descriptive analysis, presenting insights into feasible interventions and respective effectiveness. To reduce the risk of bias in the incorporated studies, two reviewers independently used the updated Cochrane risk of bias tool for randomized trials (RoB 2). However, non-randomized studies were assessed for bias using the Risk of Bias for Non-randomized Intervention Studies (ROBINS-I) tool.

## Results and Discussion

A total of 8,406 studies were initially identified through an extensive electronic search across four databases. After removing duplicates, comments, reviews, letters, and irrelevant titles, the corpus was narrowed down to 102 studies for a thorough full-text assessment. A total of 65 did not meet the inclusion criteria, resulting in a final selection of 37 studies for narrative synthesis. Only 2 out of the 37 selected studies were based on randomized experimental designs and 35 were non-randomized or simulation experiments.

### Using appropriate masks for mitigating aerosol contamination

The result shows the effectiveness of both face masks and respirators in mitigating bacterial colonization and co-infections in the upper respiratory tract among healthcare workers.[18] Surgical masks and unvented KN95 respirators were shown to significantly reduce outward particle emissions during speaking and coughing, without requiring fit-testing, suggesting the potential to curtail the dispersion of particles.[19] Furthermore, medical face masks is an important protective gear, effectively shielding the wearer from aerosol exposure and reducing the risk of respiratory infections. The medical face masks maintained bacterial filtration efficiency and breathability, ensuring practicality and comfort for prolonged use.[20-22] The use of a full-face mask had a highly protective measure against respiratory infections, showing the potential as a reliable preventive strategy.[23] Furthermore, various masks significantly reduced virus droplets in the air and minimized spread. The result also showed the potential of melt-blown layer and structure in enhancing filtration efficiency, stressing the need for a well-designed composition to increase mask effectiveness, specifically for different particle sizes.[24]

### Ensuring optimal nebulizer hygiene procedures

This study showed the efficiency of various nebulizer disinfection methods. Baby bottle steam sterilizers were proven to be highly effective in reducing bacterial pathogens and maintaining a sterile nebulizer environment.[25-27] Ultrasound and specific disinfectants significantly reduced contamination levels by 4-5 log10, showing the potential to enhance nebulizer cleanliness.[28] Previous studies showed that proper drying is crucial in eradicating bacterial residues, specifically in reducing *Pseudomonas aeruginosa*, a significant pathogen.[29,30] However, the eradication remains a challenge, necessitating specialized disinfection strategies. This study also showed the difficulty in completely removing biofilms accumulated in flexible endoscope channels using standard detergents or high-level disinfectants. This result suggests the need for innovative approaches to target and eliminate resilient biofilms effectively. Both *Methicillin-Sensitive Staphylococcus aureus* (MSSA) and *Methicillin-Resistant Staphylococcus aureus* (MRSA) were found to be vulnerable to drying, showing the potential in maintaining nebulizer hygiene, particularly for individuals with cystic fibrosis.[31,32]

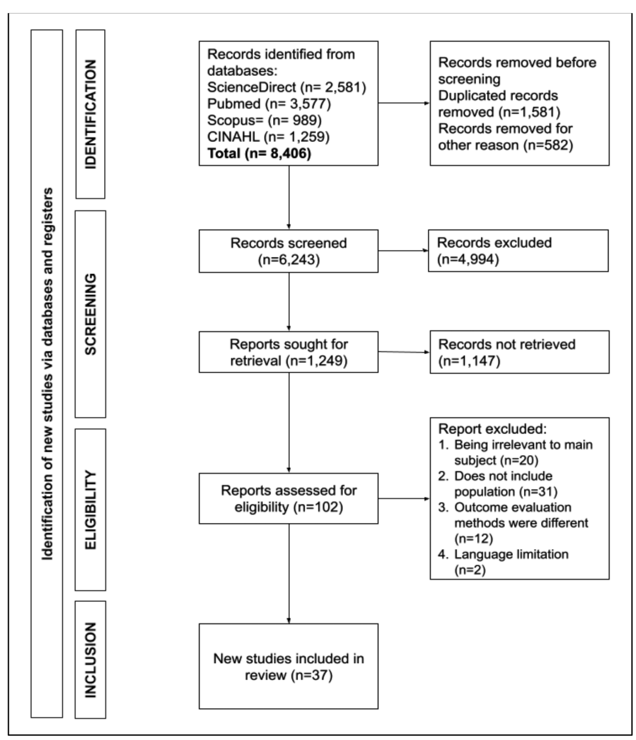


**Figure 1.** The literature search conducted across four databases adhered to the guidelines by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Innovative methods, such as UV-C light and ozone, were effective in combatting bacterial biofilms. UV-C light effectively eliminated all tested bacteria, including *M. abscessus* complex. Similarly, the ozone showed bactericidal effects on various bacterial biofilms, showing the potential for advanced nebulizer disinfection.[33–36] In general, this study provided crucial insights into designed disinfection processes, the significance of appropriate drying methods, and the promise of developing technologies in mitigating bacterial contamination, ensuring the safety and effectiveness of nebulizer use.

## Integration of bacterial filters and negative pressure for effective aerosol contamination reduction

This study showed crucial results regarding aerosolization and the implications for mechanical ventilation and aerosol therapy. Regular monitoring of bacterial filters was essential to mitigate contamination. Caution should be exercised with 10% Acetylcysteine Aerosolization during mechanical ventilation because it can increase bacterial filter pressure.[37] The result showed that the addition of a bacterial filter to aerosol delivery systems significantly reduced aerosol release, confirming the effectiveness in minimizing environmental contamination during aerosol therapy.[38] Additionally, this study evaluated specific nebulizer models, particularly the BAN™ Nebulizer with a filter kit, which removed all aerosol losses, in contrast to minor emissions from other nebulizers.[39] The implementation of negative pressure (HEPA) also proved highly beneficial in minimizing contaminated aerosols. An analysis using fluorescein particles effectively showed the impact of negative pressure in diminishing particle deposition. The result showed the critical role of suitable ventilation measures in mitigating exposure risks among healthcare workers,[40] as well as contributing valuable insights for optimizing aerosol administration protocols and ensuring enhanced safety.

## Enhancing patient environmental cleanliness

This study presents various highly effective approaches for the deactivation of bioaerosol and decontamination of surface. The ozone-based decontamination device showed exceptional efficiency, achieving a substantial reduction (>4 log10) of surrogate organisms across diverse surfaces and positions.[41] Furthermore, on-site disinfection tests using chlorine dioxide gas effectively removed *Escherichia coli*.[42] This study also investigated the potent neutralization of exhaled bioaerosols using far-UVC light at 222 nm, showing the efficiency and safe usage.[43] According to a previous study, rotating UVC proved more effective than stationary UVC, showing the potential for enhancing disinfection efficiency.[44] The use of far-UVC (222-nm) radiation effectively deactivated bioaerosols, providing promising results for independent or combined usage. Additionally, the result showed different levels of resistance on the decay rates and susceptibility constants of different bacteria to 222-nm far-UVC.[45] A combination of UV-C air treatment and ozone treatment exhibited a substantial reduction of pathogens in daily operations, showing the effectiveness of integrated methods in pathogen control, with an exception for certain pathogens, such as *Clostridioides spp*.[46-47] In general, the results provide valuable insights into advanced methods for bioaerosol control and surface disinfection, ensuring significant advancements in ensuring a safer and cleaner environment.

Healthcare professionals need to emphasize the thorough use of personal protective equipment (PPE) to minimize the spread of contaminated aerosols during nebulization procedures. The use of PPE was endorsed during the 2019 Coronavirus Disease (COVID-19) pandemic, characterized by an increasing transmission rate.[48] The typical use of eye protection, gowns, and gloves was considered standard practice. However, in terms of guarding against respiratory transmission, PPE for healthcare workers is a topic of debate and different opinions.[49,50]

This study focused mainly on the discourse of using masks as a means to protect healthcare professionals, while also considering other PPE. The most important recommendation was the use of N95 masks to effectively reduce the transmission of contaminated aerosols during medical procedures. However, in instances of constrained N95 supply, surgical masks remain a reliable alternative for providing protection. The application of surgical masks as an integral component of PPE remains effective even in the context of administering nebulization procedures for non-COVID patients.[51] Considering the use of a full-face mask during aerosol-generating procedures could be a prudent choice under certain circumstances, such as in the event of a developing or unknown epidemic.[52] Full-face masks could be used in situations that demand a highly efficient filtration system. According to Weng *et al.*,[23] wearing the mask resulted in a minor discomfort over time, but it remained in an acceptable threshold. In the assessment, the clarity of vision was not altered and the mask successfully met the breathability criteria. Furthermore, the observation of meticulous nebulizer hygiene practices represents a crucial measure in reducing and controlling aerosol contamination. The prevalent consensus in multiple authoritative guidelines showed the importance of conducting cleaning procedures, using either water or a 70% alcohol solution.[53–55] The recent use of heat/boiling and chemical approaches, as well as UV or ozone for disinfection, had shown good potential. In selecting a particular approach, an individual needs to consider the accessibility of materials and tools necessary to support and maintain proper nebulizer hygiene practices.

Previous studies showed that the use of hot water for disinfection could modify the nebulizer output, necessitating careful consideration.[56-60] Conversely, ozone and ultraviolet-C (UV-C) show good potential by maintaining nebulizer output in simulations. Ozone acts as an oxidizing agent, neutralizing reactive oxygen species (ROS), activating cellular respiration and metabolism, and triggering protective responses in bacterial and fungal cells.[61] Furthermore, ozone directly interacts with surface proteins and membrane receptors in viruses, altering the structure and ability to infect by modifying essential viral binding receptors.[62]

UV-C with a wavelength between 200 and 280 nm, has a well-established reputation for antimicrobial and disinfectant properties. The mechanism of action includes the formation of pyrimidine dimers, resulting in DNA damage.[63] UV-C light and ozone have been combined in several studies to achieve a higher and more efficient reduction of microorganisms. These components were also used to enhance environmental cleanliness in the vicinity of patients. The strategy was implemented in response to the identification of pathogens in the nebulizer and the surrounding air, resulting in HAP, in patient's environment.[64-65]

Caution is important when using UV-C because the repercussions of prolonged exposure remain uncertain. UV radiation, imperceptible to the human eye, can harm tissues without immediate notice. Prolonged exposure intensifies the adverse effects, potentially causing tissue damage, skin changes, wrinkles, and cancers, such as melanoma and basal cell carcinoma.[66] Similarly, ozone, a potent oxidant, effectively targets bacteria, viruses, and fungi by interacting with organic substances, but also has risks to health and safety. Appropriate ozone use includes disinfecting unoccupied spaces and maintaining concentrations that eradicate viruses while minimizing material harm.[67]

Another intervention is incorporating filtration during nebulization to prevent contamination. Filtration is the deliberate separation of solid particles from a solid-fluid mixture to enhance purity. Primary filtration categories include solid-gas and solid-liquid separation. Furthermore, the key to effective filtration is the use of a specialized membrane or filter aimed at reducing undesirable particle concentrations. These particles are different in size, ranging from nano-scale, including viruses, micro-scale, such as bacteria (e.g., *Staphylococcus, Pseudomonas*), to larger particles.[68]

A crucial consideration in choosing infection prevention and control (IPC) strategies for implementation is the proper management of associated costs in the hospital. Several IPC initiatives and judicious financial allocation are needed due to the impact of Healthcare-Associated Infections (HAIs) on patient well-being and extended hospitalization.[69] Furthermore, assessing the efficiency of each program is important when determining the allocation of resources for IPC programs. Economic evaluations can ascertain the cost-effectiveness of various IPC strategies, ensuring a judicious use of resources that deliver optimal value for money.

## Conclusions

In conclusion, persistent concerns in healthcare facilities regarding potential aerosol contamination showed the need for proactive measures. The preventive measures included several array of strategies, such as the use of masks by therapists, thorough disinfection of nebulizers, integration of filters, and consistent environmental cleaning in patient's vicinity. These multifaceted interventions were important in preventing the administration of contaminated aerosols and reducing the spread of infectious agents. The implementation was crucial in enhancing patient safety during nebulization therapy, thereby contributing to more effective and secure healthcare practices. Further studies and advancements in preventive methods were essential to improve infection control efforts, ensuring a safe therapeutic environment for both patients and healthcare providers.

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