The following information resources have been selected by the National Health Library and Knowledge Service Evidence Virtual Team in response to your question. The resources are listed in our estimated order of relevance to practicing healthcare professionals confronted with this scenario in an Irish context. In respect of the evolving global situation and rapidly changing evidence base, it is advised to use hyperlinked sources in this document to ensure that the information you are disseminating to the public or applying in clinical practice is the most current, valid and accurate.

# YOUR QUESTION

Is there an increased risk of transmission of COVID-19 [to health service personnel] associated with the use of nebulizers? Do nebulizers aerosolize COVID-19 particles?

## What does the World Health Organization say?

### Health Workers Exposure Risk Assessment and Management in the Context of COVID-19 Virus[1]

Nebulizer treatment is listed as one of the aerosol-generating procedures performed on COVID-19 patients. Q6 of the risk assessment also attempts to measure the risk involved by asking the health worker to "quantify the frequency you wore PPE … always, as recommended □; most of the time □; occasionally □; never □."

## What is the experience from China?

### Zhejiang University School of Medicine. Handbook of COVID-19 Prevention and Treatment[2]

Interferon nebulization is recommended in protocols for diagnosis and treatment of COVID-19. We recommend that it should be performed in negative pressure wards rather than general wards due to the possibility of aerosol transmission.

## What does the international literature say?

### Respiratory Care Committee of Chinese Thoracic Society. Expert consensus on preventing nosocomial transmission during respiratory care for critically ill patients infected by 2019 novel coronavirus pneumonia[3]

Definite evidence has shown that the novel coronavirus (COVID-19) could be transmitted from person to person. So far more than 1,700 bedside clinicians have been infected. A lot of respiratory treatments for critically ill patients are deemed as high-risk factors for nosocomial transmission due to the high possibility to cause or worsen the spread of the virus. We developed consensus recommendations on all those high-risk treatments based on the current evidence as well as the resource limitations in some areas with the aim to reduce the nosocomial transmission and optimize the treatment for the COVID-19 pneumonia patients. Those recommendations include: 1. Standard prevention and protection, and patient isolation; 2. Patient wearing mask during HFNC treatment; 3. Using dual limb ventilator with filters placed at the ventilator outlets, or using heat-moisture exchanger (HME) instead of heated humidification in single limb ventilator with HME placed between exhalation port and mask; avoid using mask with exhalation port on the mask; 4. Placing filter between resuscitator and mask or artificial airway; 5. For spontaneous breathing patients, placing mask for patients during bronchoscopy examination; for patients receiving noninvasive

[1] World Health Organization. https://apps.who.int/iris/bitstream/handle/10665/331340/WHO-2019-nCov-HCW_risk_assessment-2020.1-eng.pdf. [Accessed 24 March 2020].
[2] Handbook of COVID-19 Prevention and Treatment. https://www.alibabacloud.com/universal-service/pdf_reader?spm=a3c0i.14138300.8102420620.dreadnow.6df3647faryPkm&cdnorigin=video-intl&pdf=Read%20Online-Handbook%20of%20COVID-19%20Prevention%20and%20Treatment.pdf. [Accessed 24 March 2020].
[3] Respiratory Care Committee of the Chinese Thoracic Society. https://www.ncbi.nlm.nih.gov/pubmed/32077661. [Accessed 24 March 2020].

ventilation, using the special mask with bronchoscopy port to perform bronchoscopy; 6. Using sedation and paralytics during intubation, cuff pressure should be maintained between 25-30 cmH(2)O; 7. In-line suction catheter is recommended and it can be used for one week; 8. Dual-limb heated wire circuits are recommended and only changed with visible soiled; 9. For patients who need breathing support during transportation, placing an HME between ventilator and patient; 10. PSV is recommended for implementing spontaneous breathing trial (SBT), avoid using T-piece to do SBT. When tracheotomy patients are weaned from ventilator, HME should be used, avoid using T-piece or tracheostomy mask; 11. Avoid unnecessary bronchial hygiene therapy; 12. For patients who need aerosol therapy, dry powder inhaler metered dose inhaler with spacer is recommended for spontaneous breathing patients; while vibrating mesh nebulizer is recommended for ventilated patients and additional filter is recommended to be placed at the expiratory port of ventilation during nebulization.

## Hui et al. Severe acute respiratory syndrome (SARS): lessons learnt in Hong Kong[4]

Many healthcare workers were infected while looking after the SARS patients on the medical wards in 2003. The high infectivity of the SARS coronavirus with peak viral load on day 10 of illness when patients were ill, overcrowding of the old medical wards with low air changes/hr (ACH), and aerosol-generating procedures while resuscitating the patients were the major factors. Procedures reported to present an increased risk of SARS transmission include tracheal intubation, non-invasive ventilation, tracheotomy and manual ventilation before intubation whereas oxygen therapy and bed distance <1 m were also implicated. Studies based on laser visualization technique with smoke particles as smokers in the human patient simulator has shown that oxygen therapy via Hudson mask and nasal cannula could disperse exhaled air of patients to 0.4 and 1 m respectively whereas jet nebulizer could disperse exhaled air >0.8 m from the patient. Bigger isolation rooms with 16 ACH are more effective than smaller isolation rooms with 12 ACH in removing exhaled air and preventing room contamination but at the expense of more noise and electricity consumption. Non-invasive ventilation via face masks and single circuit can disperse exhaled air from 0.4 to 1 m. Both higher inspiratory pressures and use of whisper swivel device (to facilitate carbon dioxide removal) could increase the exhaled air leakage and isolation room contamination during on-invasive ventilation. Addition of a viral-bacterial filter during manual ventilation by bagging may reduce the exhaled air leakage forward and yet increase the sideway leakage. N95 mask was more effective than surgical mask in preventing expelled air leakage during patient's coughing but there was still significant sideway leakage to 15 cm. Clinicians should be aware of air leakage from the various face masks and adopt strict infection control measures during resuscitation of patients with severe respiratory infections. Carefully designed clinical trials are required to determine the optimal timing and dosage of any antiviral agents, convalescent plasma, and immuno-modulating agents in the treatment of the possibly immune-mediated lung injury in SARS and newly emerged infection such as the Middle East Respiratory Syndrome.

## Tran et al. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review[5]

Aerosol generating procedures (AGPs) may expose health care workers (HCWs) to pathogens causing acute respiratory infections (ARIs), but the risk of transmission of ARIs from AGPs is not fully known. We sought to determine the clinical evidence for the risk of transmission of ARIs to HCWs caring for patients undergoing AGPs compared with the risk of transmission to HCWs caring for patients not undergoing AGPs. We searched PubMed, EMBASE, MEDLINE, CINAHL, the Cochrane Library, University of York CRD databases, EuroScan, LILACS, Indian Medlars, Index Medicus for SE Asia, international health technology agencies and the Internet in all languages for articles from 01/01/1990 to 22/10/2010. Independent reviewers screened abstracts using pre-defined criteria, obtained full-text articles, selected relevant studies, and abstracted data. Disagreements were resolved by consensus. The outcome of interest was risk of ARI transmission. The quality of evidence was rated using the GRADE system. We identified 5 case-control and 5 retrospective cohort studies which evaluated transmission of SARS to HCWs.

[4] Hui et al. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3747521/. [Accessed 24 March 2020].
[5] Tran et al. https://www.ncbi.nlm.nih.gov/pubmed/22563403. [Accessed 24 March 2020].

Procedures reported to present an increased risk of transmission included [n; pooled OR(95%CI)] tracheal intubation [n=4 cohort; 6.6 (2.3, 18.9), and n=4 case-control; 6.6 (4.1, 10.6)], non-invasive ventilation [n=2 cohort; OR 3.1(1.4, 6.8)], tracheotomy [n=1 case-control; 4.2 (1.5, 11.5)] and manual ventilation before intubation [n=1 cohort; OR 2.8 (1.3, 6.4)]. Other intubation associated procedures, endotracheal aspiration, suction of body fluids, bronchoscopy, nebulizer treatment, administration of O2, high flow O2, manipulation of O2 mask or BiPAP mask, defibrillation, chest compressions, insertion of nasogastric tube, and collection of sputum were not significant. Our findings suggest that some procedures potentially capable of generating aerosols have been associated with increased risk of SARS transmission to HCWs or were a risk factor for transmission, with the most consistent association across multiple studies identified with tracheal intubation.

## Simonds et al. Evaluation of droplet dispersion during non-invasive ventilation, oxygen therapy, nebuliser treatment and chest physiotherapy in clinical practice: implications for management of pandemic influenza and other airborne infections[6]

Background: Influenza viruses are thought to be spread by droplets, but the role of aerosol dissemination is unclear and has not been assessed by previous studies. Oxygen therapy, nebulised medication and ventilatory support are treatments used in clinical practice to treat influenzal infection are thought to generate droplets or aerosols.
Objectives: Evaluation of the characteristics of droplet/aerosol dispersion around delivery systems during non-invasive ventilation (NIV), oxygen therapy, nebuliser treatment and chest physiotherapy by measuring droplet size, geographical distribution of droplets, decay in droplets over time after the interventions were discontinued.
Methods: Three groups were studied: 1. normal controls, 2. subjects with coryzal symptoms and 3. adult patients with chronic lung disease who were admitted to hospital with an infective exacerbation. Each group received oxygen therapy, NIV using a vented mask system and a modified circuit with non-vented mask and exhalation filter, and nebulised saline. The patient group had a period of standardised chest physiotherapy treatment. Droplet counts in mean diameter size ranges from 0.3 to > 10 μm were measured with an counter placed adjacent to the face and at a 1-m distance from the subject/patient, at the height of the nose/mouth of an average health-care worker.
Results: NIV using a vented mask produced droplets in the large size range (> 10 μm) in patients ($p = 0.042$) and coryzal subjects ($p = 0.044$) compared with baseline values, but not in normal controls ($p = 0.379$), but this increase in large droplets was not seen using the NIV circuit modification. Chest physiotherapy produced droplets predominantly of > 10 μm ($p = 0.003$), which, as with NIV droplet count in the patients, had fallen significantly by 1 m. Oxygen therapy did not increase droplet count in any size range. Nebulised saline delivered droplets in the small- and medium-size aerosol/droplet range, but did not increase large-size droplet count.
Conclusions: NIV and chest physiotherapy are droplet (not aerosol)-generating procedures, producing droplets of > 10 μm in size. Due to their large mass, most fall out on to local surfaces within 1 m. The only device producing an aerosol was the nebuliser and the output profile is consistent with nebuliser characteristics rather than dissemination of large droplets from patients. These findings suggest that health-care workers providing NIV and chest physiotherapy, working within 1 m of an infected patient should have a higher level of respiratory protection, but that infection control measures designed to limit aerosol spread may have less relevance for these procedures. These results may have infection control implications for other airborne infections, such as severe acute respiratory syndrome and tuberculosis, as well as for pandemic influenza infection.

[6] Simonds et al. https://www.ncbi.nlm.nih.gov/pubmed/20923611. [Accessed 24 March 2020].

## Chan-Yeung et al. Severe acute respiratory syndrome (SARS) and healthcare workers[7]

The recent outbreak of severe acute respiratory syndrome (SARS) was spread by international air travel, a direct result of globalization. The disease is caused by a novel coronavirus, transmitted from human to human by droplets or by direct contact. Healthcare workers (HCWs) were at high risk and accounted for a fifth of all cases globally. Risk factors for infection in HCWs included lack of awareness and preparedness when the disease first struck, poor institutional infection control measures, lack of training in infection control procedures, poor compliance with the use of personal protection equipment (PPE), exposure to high-risk procedures such as intubation and nebulization, and exposure to unsuspected SARS patients. Measures to prevent nosocomial infection included establishing isolation wards for triage, SARS patients, and step-down; training and monitoring hospital staff in infection-control procedures; active and passive screening of HCWs; enforcement of droplet and contact precautions; and compliance with the use of PPE.

## Newhouse. Transmission of coronavirus by nebulizer: a serious unappreciated risk[8]

The current pandemic of COVID-19 cases demands greater infection control precautions. Nebulizers generate aerosol particles in the size of 1-5 μm that can carry bacteria and viruses into the deep lung. The risk of infection transmission via droplet nuclei and aerosols may increase during nebulizer treatments because of the potential to generate a high volume of respiratory aerosols that may be propelled over a longer distance than that involved in natural dispersion pattern. Furthermore, the larger particles may stimulate both patients and bystanders cough and thus increase the risk of spreading the disease. Nebulizer therapy in patients with pandemic COVID-19 infection has the potential to transmit potentially viable COVID-19 to susceptible bystander hosts.

In recent years there has been a welcome shift, in some centers, from the use of nebulizers to metered dose inhalers (pMDI) with Valved-Holding Chambers (VHCs). In Alberta Canada for example, any order for nebulizer is now restricted and nebulizer is only to be used in the following situations:

1. Severe, life-threatening respiratory disease (eg those with severe or impending respiratory arrest, those with hypoventilation or ventilation compromise, continuous nebulization, end-stage COPD, cystic fibrosis); OR
2. Patients who are uncooperative or are unable to follow the directions required for a metered-dose inhaler (MDI) with spacer use; OR
3. Patients with a history of poor response to MDI with spacer.

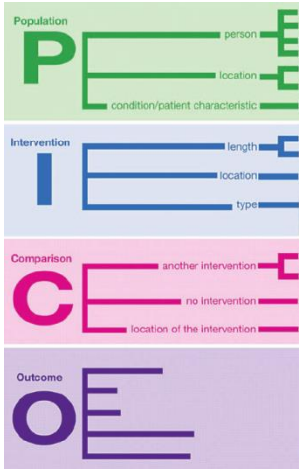
However, despite a large body of evidence suggesting their lack of superiority or inferiority, compared to MDI +VHC, the nebulizer is still widely used in many healthcare facilities (especially in the USA).

Given the current outbreak of COVID-19, Alberta Health Services (AHS) in Canada has now requested to reconsider any plan or order for a nebulizer therapy. To reduce the risk of transmission of all infectious respiratory illnesses in healthcare facilities we would encourage all caregivers in all other provinces to align with the above restrictions and seriously consider avoiding the use of nebulizers. Keeping our patients and staff safety should be our priority.

[7] Chan-Yeung et al. https://www.ncbi.nlm.nih.gov/pubmed/15702757. [Accessed 24 March 2020].
[8] Newhouse. https://www.cmaj.ca/content/re-transmission-corona-virus-nebulizer-serious-underappreciated-risk. [Accessed 24 March 2020].

Produced by the members of the National Health Library and Knowledge Service Evidence Team.† Current as at 24 March 2020.This evidence summary collates the best available evidence at the time of writing. Emerging literature or subsequent developments in respect of COVID-19 may require amendment to the information or sources listed in the document. Although all reasonable care has been taken in the compilation of content, the National Health Library and Knowledge Service Evidence Team makes no representations or warranties expressed or implied as to the accuracy or suitability of the information or sources listed in the document. This evidence summary is the property of the National Health Library and Knowledge Service and subsequent re-use or distribution in whole or in part should include acknowledgement of the service.

The following PICO(T) was used as a basis for the evidence summary:




COVID-19 patient requiring nebulization.

RISK OF TRANSMISSION OF INFECTION TO HEALTH WORKERS.

The following search strategy was used:

[ABBREVIATED] ((coronavirus OR COVID-19 OR (Wuhan ADJ3 virus) OR 2019-nCoV OR SARS-COV-2) AND (nebuliz$ OR nebulis$ OR "Aero Comfort" OR "Aero Mist" OR atomiz$ OR atomis$ OR eRapid OR nembuliz$ OR nembulis$))

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