

COVID-19 Scientific Advisory Group Rapid Response Report

Key Research Question:

- 1. What is the risk for COVID-19 transmission associated with oxygen therapy (conventional and humidified high flow (HHFO)) and when is oxygen therapy considered an AGMP?**
- 2. When is it appropriate to use conventional oxygen delivery vs humidified high flow oxygen therapy in the healthcare setting?**

Context

- Questions have arisen from the respiratory and emergency department health care professional community regarding the use of conventional oxygen therapy, high flow nasal oxygen therapy (HFNO), and humidified high flow oxygen therapy (HHFO) in patients with COVID-19 and the potential risk to health care workers (HCWs). HHFO can refer to heated humidified oxygen delivery systems (such as Optiflow™/AIRVO™) or cold nebulization via facemask.
- Media reports suggest that NIV and HHFO are being used extensively in the COVID-19 patient group⁶
- The rapid review excludes mask oxygen delivery including non-rebreather and Venturi mask.
- The rapid review was based upon limited literature and existing published guideline documents
- This review does not address the use of oxygen therapy in the home setting
- The information in this rapid review is meant to be used in addition to clinical judgment and to inform clinical decision making

Glossary of Terms:

AGMP: Aerosol generating medical procedure

Conventional oxygen therapy: nasal prongs, high flow nasal prongs

HHFO: Heated, humidified, high flow oxygen (any system that adds humidity to the delivered oxygen, such as the heated high flow oxygen delivery systems- AIRVO™ and Optiflow™)

HFNO: High flow nasal oxygen

HCW: Health care worker

Key Messages from the Evidence Summary

- Oxygen delivery by nasal prongs (from 1-5LPM) is not associated with an increased risk of COVID-19 transmission beyond droplet and contact risk. HHHFO is generally considered to be an AGMP and thus PPE with the use of N95 and a contained environment (ie private room) is required.
- Oxygen therapy is considered to be an AGMP when it is humidified
- The use of HHHFO during the COVID-19 pandemic is controversial. There is some indication that it may offer value to individuals' with early hypoxemia using appropriate PPE with inclusion of N95 mask, but is a very limited resource and creates the need for AGMP precautions where they would not otherwise be required.
- HHHFO may also be used in the event that ventilator care is not available, or delayed, so guidelines may need to be adjusted for future resource limitations.

Recommendations regarding question 1:

- Oxygen delivery by nasal prongs (from 1-5LPM) is not associated with an increased risk of COVID-19 transmission beyond droplet and contact risk
- There is no strong evidence to support that high flow oxygen by nasal prongs (ie 6 LPM to 15 LPM) is an AGMP
- HHHFO (via Optiflow™ or Airvo™) is AGMP and requires PPE plus N95 and private room.

Recommendations regarding question 2:

- When oxygen requirements exceed oxygen delivery by simple nasal prongs (ie >5 LPM), clinical judgement must be used, but first line therapy should continue to be conventional oxygen with high flow nasal prongs up to 15 LPM rather than heated, humidified oxygen delivery.
- HHHFO is an AGMP and thus requires increased resources (N95 and isolation rooms) compared to non-humidified oxygen delivery, and both Optiflow and Airvo are extremely limited resources in the current AHS environment. In a patient whose goals of care include possible intubation, involvement of critical care in decision making when oxygen requirements exceed 6 LPM or if there is rapid clinical deterioration is advised.

Committee discussion:

There was consensus among the committee about these recommendations. One reviewer noted that there is controversy about whether oxygen delivery at 6-15 LPM could pose a risk of aerosolization.

Summary of Evidence

Credible information sources were identified through a rapid online search. One reference is original research (RCT), four papers were published correspondence, and there were four review articles. Thirteen published guidelines or consensus documents were included, which use a range of research sources and likely expertise consensus within these organizations. One paper provided the clinical experience of those working China during the pandemic, and one Health Technology Assessment.

Key limitations of this review:

- Rapid turnaround time resulted in a limited time to conduct a thorough search of the research and grey literature.
- Given the rapidly changing information and literature related to COVID-19, the literature available is limited primarily to reviews, guideline documents, published letters, and descriptive papers.

Description of the Therapy

Heated and humidified oxygen may have a number of benefits compared to conventional oxygen therapy, however this needs to be weighed against the fact that heated HHHFO is a very limited resource and its use is an AGMP thus increasing use of other limited resources (N95 and private rooms). Standard oxygen therapy delivered through a nasal cannula or another device, delivers cold and dry gas. This cold, dry gas may lead to airway inflammation, increase airway resistance, and impair mucociliary function, possibly impairing secretion clearance.¹⁴ Also, a significant amount of energy is expended by individuals to both warm and humidify gas during normal breathing.¹⁰ Thus, heated and humidified oxygen may improve secretion clearance, decrease airway inflammation, and also decrease energy expenditure, particularly in the setting of acute respiratory failure.^{10,14} A 2019 meta-analysis by Huang et al.¹⁰ assessed the use of high-flow nasal cannula therapy compared to conventional oxygen therapy or non-invasive ventilation for treatment of acute respiratory failure in emergency department.¹⁰ They found that compared to conventional oxygen therapy, those that received HFNO therapy had a reduced need for treatment escalation, reduced dyspnea scores, and improved comfort. However, the interventions across the studies varied, making studies difficult to compare. In addition, there was an increasing trend in intubation rate associated with the use of HFNO therapy, although this result was not significant.¹⁰

A previous meta-analysis of RCTs from Ou et al. in 2017, found HFNO had lower intubation rates than conventional oxygen therapy and similar rate to non-invasive ventilation in critical care patients with acute hypoxemic respiratory failure.²⁰ It is congruent with the results from a 2019 systematic review that found HFNO may decrease tracheal intubation without impacting mortality when used to treat patient with acute hypoxemic respiratory failure.⁷ The applicability of these studies is limited, as the primary outcome was the need for intubation.

Research Question 1

What is the risk for COVID-19 transmission associated with oxygen therapy (conventional and HHHFO)?

SARS-CoV-2, the causative agent of COVID-19, can be transmitted by large respiratory droplets or aerosol via inhalation or mucosal surfaces; feces; and contaminated objects (fomites). The World Health organization (WHO) suggests that all respiratory care poses a potential risk to health care workers (HCW) during the COVID-19 pandemic.²⁷ HCW should strictly adhere to hand hygiene protocol and ensure they use optimal donning and doffing technique of all PPE to reduce risk.

Conventional Oxygen Therapy

Conventional Oxygen Therapy is not considered an AGMP

A systematic review in 2012 by Tran et al. evaluated the transmission of acute respiratory infections to HCWs, and determined conventional oxygen therapy is not significantly associated with a risk of transmission to HCWs.²⁴

Only 10 studies were identified and all evaluated transmission of SARS virus to HCWs (2002-2003). All studies were graded very low quality. Manipulation of the oxygen mask was based on 2 cohort studies with a pooled estimate of OR 4.6 (95% CI 0.6 to 32.5), and was not a significant risk of transmission. Simonds and colleagues (2010) evaluated characteristics of droplets and aerosol generating in an observational study of 44 patients (normal controls, those with symptomatic viral infection and those with chronic lung disease). They determined that providing O₂ via mask at 24% and 60% was neither aerosol nor droplet generating.

As per the previously described review by Tran et al. one cohort study evaluated the risk of SARS transmission with the use of high-flow oxygen (non-humidified). This study found no statistically significant risk of viral transmission (OR 0.4, 95%CI 0.1-1.7). Leung and colleagues (2018) found HHNO use in patients with Gram negative bacteria pneumonia did not increase airborne and surface contamination when compared with an oxygen mask.

Heated humidified high flow oxygen (HHHFO)

HHHFO is considered a risk for AGMP and thus requires the use of PPE for contact and droplet plus the use of N95 and private room.

HHHFO studies suggest that aerosol generation with HHHFO at 60L/min is minimal, and less than that caused by typical coughing and sneezing when the equipment is used appropriately and fits well.⁶ Additionally, the risk of exposure to aerosolization to a HCW from HHHFO depends upon the duration of use, flow rate, patient coughing and cooperation, fit of the patient apparatus, and the quality and fit of HCW's personal protective equipment (PPE).^{6,17}

However, in contrast, Cheung et al. did not recommend HHHFO for COVID-19 patients, as current published research demonstrating minimal dispersion of exhaled air was conducted in simulation with optimally fitting equipment, which would imply reduced exposure. They also elaborated that variability of models and modes of delivery differ across jurisdictions and also the potential/theoretical risk of transmission is uncertain. In addition, a consensus statement from the Safe Airway Society of Australia and New Zealand published March 16th, 2020 cautions that there is little evidence for HFNC's utility in viral pandemics, although anecdotal information indicates it being used internationally during COVID-19 pandemic.⁶

When is oxygen therapy considered an aerosol generating medical procedure (AGMP)?

Generally, oxygen is delivered dry, at a low flow rate, however, high gas flows (up to 60 L/min) may cause aerosolization of infectious particles and spread of infection¹³, creating concern for the HCW during the COVID-19 pandemic.

HHHFO is considered an AGMP

Recent guidelines indicate that HHFO is considered an AGMP.^{2,4-6,12,15,16, 21,25,27,28} However, there is no evidence that conventional oxygen delivery by nasal prongs, even using high flow nasal prongs up to 15 LPM are a AGMP²⁴ In a clinical practice guideline by Restrepo et al. they describe some of the hazards associated with the use of humidification devices and describe that when it is disconnected from the patient, some ventilators generate a high flow through the patient circuit that may aerosolize contaminated condensate, putting the patient and HCW at risk.²²

As the clinical benefit of HHHFO is controversial and not standard of care as a first line treatment for severe hypoxemia, consideration should be given to use of conventional oxygen delivery via nasal prongs as initial therapy. If a patient is deteriorating and oxygen demands increasing, clinical judgement needs to be used with consideration of involvement of critical care if intubation is within the goals of care of the patient. HHHFO is a limited resource within the hospital that requires the use of PPE plus N95 in a closed environment, thus the use of this modality during a COVID pandemic needs to be balanced with the increased system demands.

Therefore, as HHHFO is considered an AGMP, **any patient** treated with HHHFO require PPE with N95 respirator, and a single room with 4 walls and a closed door

Research Question 2

When is it appropriate to use high flow vs humidified high flow oxygen therapy in the healthcare setting?

Conventional Oxygen Therapy

The WHO recommends preparing to provide advanced respiratory support to all COVID-19 patients. The guidelines endorse giving supplemental oxygen therapy (oxygen by nasal prongs) immediately to patients with severe acute respiratory illness and respiratory distress, hypoxaemia or shock with the target of $SpO_2 > 94\%$.

HHHFO

According to the World Health Organization, there are no evidence-based guidelines on HHHFO and literature specific to coronavirus-infected patients is limited. The American Association of Respiratory Care in their guideline document suggest HHHFO may be useful in patients with early hypoxemia. Experience from China has suggested HHHFO may be used for mild-to-moderate hypoxemia ($100 \text{ mmHg} \leq PaO_2/FiO_2 < 300 \text{ mmHg}$); no indications for intubation; and generally stable vital signs.²⁶ Their response should be closely monitored over one to two hours. Similarly, Matthay suggest HHHFO may delay or prevent intubation for patients with moderately severe hypoxaemia.¹⁸ Corley and colleagues (2017) conducted a review of HHHFO use in ICU compared to other oxygen delivery. A total of 11 studies and 1972 patients were included and they found no evidence that HHHFO reduced the rate of treatment failure or risk of death compared with low-flow oxygen devices, no advantage in adverse event rates, ICU length of stay, or duration of respiratory support. They observed no differences in participants' lab values, and small differences in breathing rates (not considered clinically meaningful). There were no

differences in patient-rated measures of comfort. Only one study found evidence of less dry mouth when HHHFO was used.

Given that HHHFO is a very limited resource and is an AGMP which will contribute to the demand for private rooms and N95 masks with little evidence of clinical benefit, the use of HHHFO over conventional oxygen delivery is not recommended in routine practice. Application of clinical judgement in the context of resource availability and patient goals of care will remain essential.

HHHFO should be avoided in patients with severe respiratory failure hemodynamic instability, multiple organ failure, disorders of consciousness, or when intubation is likely.^{6,26}

HHHFO

The CADTH review in 2019 summarized the literature on the clinical effectiveness of heated humidified high flow oxygen in hospital and during transfers as well as the cost-effectiveness of heated humidified high flow oxygen compared with other respiratory support. Eight systematic reviews, 8 RCTs, and 1 cost-effectiveness analysis were included. Their key findings indicate that the evidence supports that HHHFO may help to avoid intubation compared to conventional oxygen therapy or non-invasive ventilation, though the findings were not consistent. The evidence does not suggest that the length of stay or oxygenation outcomes are improved with HHHFO compared to conventional oxygen therapy or non-invasive ventilation.

One possible additional indication of HHHFO is in the event that mechanical ventilators are unavailable, HHHFO may be required.⁶ However, further details regarding its use under these circumstances would need to be explored more fully.

Evolving Evidence

We acknowledge that the evidence regarding the care and management of individuals that are suspect or confirmed COVID-19 is rapidly evolving. Therefore significant changes in clinical guidelines may occur and impact this rapid review.

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Authorship & Committee Members

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