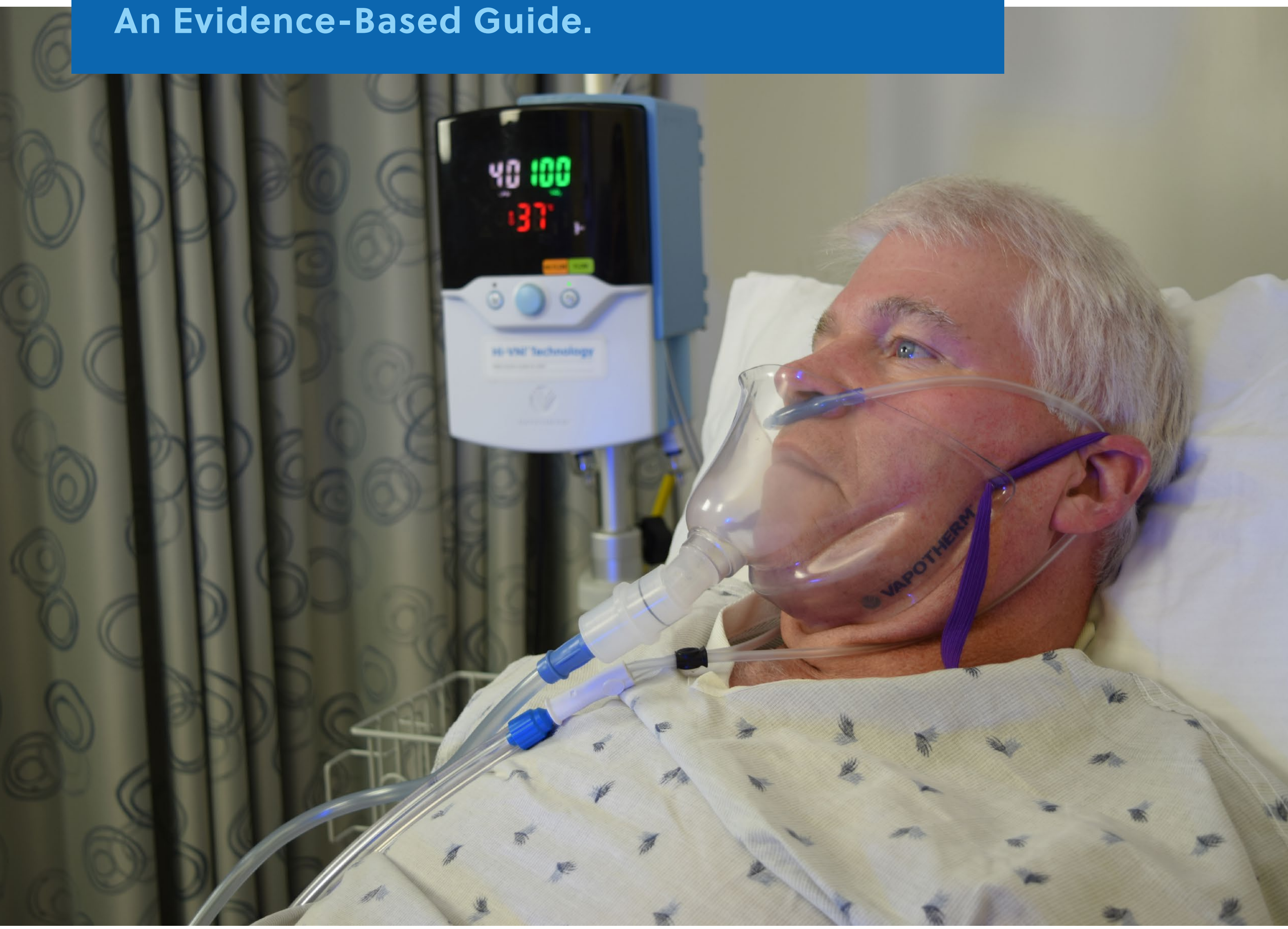
VAPOTHERM®

Vapotherm® High Velocity Therapy on COVID-19 Patients

An Evidence-Based Guide.



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Introduction

The COVID-19 pandemic has swept the globe infecting millions and leaving hundreds of thousands dead. It is presenting the healthcare community with a host of novel challenges as clinicians, scientists, and researchers grapple to understand SARS-CoV-2 and the disease it causes. During this trying time, the international healthcare community, researchers, and scientists have stepped up in producing and publishing research and sharing experiences with the common goal of stemming the extent of this pandemic. Medical journals have been publishing information seemingly at lightning speed. While welcome and necessary, this influx of information can also become overwhelming.

We reached out to clinicians with a survey and asked what their greatest need was in feeling more prepared to face the next COVID-19 surge. Personal protective equipment and medical equipment in general rose to the top of the list, but not far behind was a resounding request for clear education and evidence-based information. (You can read the full survey results at the end of this book.)

We've heard you. In the spirit of collaboration and the open exchange of information, we've compiled this guide to help you make the most informed decisions about your patients and your safety when using Vapotherm high velocity therapy.

Stay healthy and keep doing the amazing work on the frontlines. We are by your side.

Section 1: What We Know So Far—Transmission, Symptoms, Mortality

Transmission

According to the World Health Organization (WHO), the chief driver of COVID-19 transmission is infectious droplets.1 With droplet spread, a disease can be transmitted either through close contact with a contagious person or potentially indirectly via fomites from contaminated surfaces. WHO also reports that fecal-oral spread is possible, but that it doesn't appear to be a driver. Additionally, no airborne spread has been reported outside of medical settings in which aerosol generating procedures (AGPs) are performed.

- Droplet transmission
- No airborne spread reported to date
- Fecal-oral spread possible, but doesn't appear to be driver

The latter conclusion generated some pushback from the general public which prompted WHO to revisit the literature. The organization reasserted that no airborne spread has been reported to date.[2] They clarified that in AGP settings, aerosolization of viable virus does occur and with it, airborne spread is possible. However, absent AGPs, there is no data yet showing that airborne transmission is a driver of the spread. Importantly, data shows that healthcare workers taking appropriate droplet and contact precautions outside of AGP settings exhibited no nosocomial transmission.

As for the infectiousness of this virus, its R0 is estimated to be 2.2 (95% CI 1.4 to 3.9).[3] In other words, without mitigation, each infected individual could infect approximately 2.2 others—an alarming ratio responsible for the rapid spread of cases worldwide.

Symptoms

The mean timeframe for development of symptoms is 5-6 days, though it can range between 1 -14 days.1 The breakdown of symptom severity is shown in Table 1, with the majority of people who develop symptoms experiencing mild to moderate ones. The severity can be impacted by underlying health conditions and comorbidities.

Table 1: COVID-19 Symptom Severity[1]

PERCENTAGE OF POPULATION EXPERIENCING SYMPTOMS

Mild to Moderate	80%
Severe	14%
Critical	6%

1. WHO. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). 2020.
2. WHO. Transmission of SARS-CoV-2: implications for infection prevention precautions. Scientific Brief. July 9, 2020.
3. Li, et al., Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-infected Pneumonia. NEJM 2020;382:1199-1207.

Section 1: What We Know So Far—Transmission, Symptoms, Mortality

The most frequent symptoms include[1]:

- Fever
- Cough
- Fatigue

And less common ones are[1]:

- Dyspnea
- Sputum production
- Sore throat
- Myalgia
- Nausea or vomiting
- Chills
- Nasal congestion
- Diarrhea

"As the pandemic has progressed, the reported mortality rates have reduced from above 50% in March 2020 to close to 40% at the end of May 2020."—Armstrong et al.

Mortality

Mortality data from COVID-19 differs significantly from country to country. For example, the US, Brazil, Spain, and the UK are reporting triple digit mortality numbers per 1 million of residents while China is reporting single digits as of end of July 2020.[4] Certainly a variety of factors could be impacting these numbers, anywhere from data accuracy, mean population age, access to healthcare, population density, as well as measures each country has taken to combat the spread of the virus, among others. Nevertheless, a meta-analysis by Armstrong et al. suggests that overall ICU mortality rates have been trending downward across the globe.[5]

The analysis included 24 observational studies, amounting to over 10,000 patients combined. The authors state that by comparison to other viral pneumonias, ICU mortality rates from COVID-19 are high. But according to their research, the rate dropped since the start of the pandemic from more than 50% to about 42%. This decline is consistent across continents. The authors attribute it to better treatment and resources as more becomes known about the course of the disease.

4. COVID-19 Coronavirus Pandemic. Worldometer. https://www.worldometers.info/coronavirus/#countries. Last accessed July 30, 2020.

5. Armstrong RA, Kane AD, Cook TM. "Outcomes from intensive care in patients with COVID- 19: a systematic review and meta- analysis of observational studies." Anasthesia. June 2020. Anaesthesia 2020 doi:10.1111/anae.15201

Section 2: Guidance for Respiratory Symptom Management

Guidances From Around the World

Quickly following on the heels of the pandemic onset, several medical organizations released guidance for healthcare workers. Below are highlights from a variety of organizations in regard to management of acute respiratory failure (ARF) associated with COVID-19.

World Health Organization (WHO)[6]

The guidelines (revised on March 13, 2020) call for high velocity therapy/HFNC or NiPPV to be used only in selected patients with hypoxemic respiratory failure.

- MERS Limited data suggest that patients treated with NiPPV for other viral infections have a high risk of treatment failure.
- Patients treated with HVNI/HFNC or NiPPV should be closely monitored for clinical deterioration. In the case of HVNI/HFNC the guidelines call for a one-hour trial on the therapy to determine whether it needs to be discontinued.
- The use of HVNI/HFNC can proceed with caution. The modality is reported to reduce the need for intubation compared to standard oxygen therapy.

Centers for Disease Control and Prevention (CDC)

At this time, the CDC hasn't released specific guidance, but is sharing the recommendations of the National Institutes of Health (NIH) below.

National Institutes of Health (NIH)

At the time of this writing, in regard to respiratory distress management, the NIH urges clinicians to follow the guidelines released by the Society of Critical Care Medicine (SCCM) below.

6. World Health Organization. Clinical management of severe acute respiratory infection when Novel coronavirus (2019-nCoV) infection is suspected: Interim Guidance. WHO reference number: WHO/nCoV/Clinical/2020.3 13 March 2020.

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Society of Critical Care Medicine (SCCM)[7]

The journal for SCCM (Critical Care Medicine), has posted guidelines jointly with the Intensive Care Medicine journal, including an infographic algorithm.

- Suggests use of high velocity therapy/HFNC in management of Acute Hypoxemic Respiratory Failure when conventional oxygen therapy fails.
- Use of HVNI/HFNC suggested over the use of noninvasive positive pressure ventilation (NiPPV) for these patients.
- Trial of NiPPV suggested with close monitoring and short-interval assessments if HVNI/HFNC not available and the patient didn't need urgent intubation.
- Close monitoring recommended on any modality in case of worsening condition requiring intubation.

Italian Thoracic Society/Associazione Italiana Pneumologi Ospedalieri (AIPO)[8]

- Calls for high velocity therapy/HFNC equipment setup on all critical patients.
- Recommend FiO_2 of up to 0.9-1.0 to maintain saturation.
- HVNI/HFNC can be used either as a 'ceiling option' or a precursor to CPAP/NiPPV. They urge caution due to possible droplet formation.
- When using CPAP/NiPPV, first choice is helmet interface without humidification, up to 15-20 cmH2 CPAP with a mask is second choice and NiPPV with a mask/filter is third choice.
- Click here to read the AIPO's full recommendations.

The Respiratory Care Committee of the Chinese Thoracic Society[9]

Provides an expert consensus paper on preventing nosocomial transmission during respiratory care for critically ill patients with COVID-19. They acknowledge that respiratory treatment of the patients includes high-risk factors for nosocomial transmission (at writing, 1700 bedside clinicians

7. Alhazzani W, Moller MH, Arabi YM, et al. Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19). Critical care medicine. 2020;PREPUBLICATION.

8. Harari SA, Vitacca M, Blasi F, Centanni S, Santus PA, Tarsia P. Managing the Respiratory care of patients with COVID-19. http://www.aiponet.it: Italian Thoracic Society – Associazione Italiana Pneumologi Ospedalieri – Societa Italiana Di Pneumologia;2020.

9. Respiratory care committee of Chinese Thoracic S. [Expert consensus on preventing nosocomial transmission during respiratory care for critically ill patients infected by 2019 novel coronavirus pneumonia]. Zhonghua jie he he hu xi za zhi = Zhonghua jiehe he huxi zazhi = Chinese journal of tuberculosis and respiratory diseases. 2020;17(0):E020.

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had been infected) and call for specific interventions to mitigate the risk.

- Use of Personal Protective Equipment (PPE), filters for ventilators and bag-valve-mask resuscitators, and masks for bronchoscopy.
- Specifically call for use of a simple surgical mask over the face of the patient, covering the mouth and nose with the high velocity therapy/HFNC cannula in place. Vapotherm's science team recently conducted modeling to test the effectiveness of this intervention with high velocity therapy. (see Section 4 in this book)
- Recommend securing HFNC system tubing if it has the capability to disengage at the nosepiece (Vapotherm high velocity therapy uses a fused single-piece cannula without the possibility to thus disengage).
- For technologies with heavy tubing sets, recommend securing the tubing so as not to disturb the surgical mask.

Guidelines from Germany[10]

The German Society for Internal Intensive Care Medicine and Emergency Medicine, the German Interdisciplinary Association for Intensive Care and Emergency Medicine, the German Society for Pulmonology and Breathing Medicine, the German Society for Anesthesiology and Intensive Care, and the ARDS Network of Germany issued guidelines on the intensive care therapies for patients with COVID-19.

- Recommend both NiPPV and high velocity therapy/HFNC to maintain $SpO_2 \geq 90\%$.
- Recognize that both modalities can lead to aerosol generation but cite research[11,12] supporting safe administration so long as the interface is properly applied in the case of NiPPV.
- Call for use of proper PPE and FFP2.
- Caution that for severe hypoxaemia ($PaO_2/FiO_2 \leq 200$ mmHg) intubation/mechanical ventilation may be preferable to avoid increased risk of aerosol exposure during emergency intubation.

10. Kluge S, Janssens U, Welte T, Weber-Carstens S, Marx G, Karagiannidis C. [Recommendations for critically ill patients with COVID-19]. Medizinische Klinik, Intensivmedizin und Notfallmedizin. 2020.

11. Hui DS, Chow BK, Lo T, et al. Exhaled air dispersion during noninvasive ventilation via helmets and a total facemask. Chest. 2015;147(5):1336-1343.

12. Hui DS, Chow BK, Lo T, et al. Exhaled air dispersion during high-flow nasal cannula therapy versus CPAP via different masks. The European respiratory

Section 2: Guidance for Respiratory Symptom Management

Guidelines from France[13]

A management paradigm was proposed by a French team.

- Priority placed on PPE and transmission control.
- Possible admissions to the ICU should be considered on a daily basis.
- Care to COVID-19 patients should not be limited, but procedures which are likely to pose a transmission risk (e.g., ECMO, BAL, transport) must be discussed.
- Note that ARDS is often associated with shock and multiple organ failure. HVNI/HFNC is specifically recommended in a treatment example, between standard oxygen cannula and mechanical ventilation.

The Australian and New Zealand Intensive Care Society (ANZICS)[14]

A COVID-19 working group of clinicians published the ANZICS guidelines in the context of caring for COVID-19 patients in the ICU.

- Recommend high velocity therapy/HFNC for routine use as long as staff uses PPE and practice infection control precautions. Note that the transmission risk with proper fit is low.
- Preferred use of negative pressure rooms when high velocity therapy/HFNC is in use.
- Do not recommend NiPPV for routine use as the transmission risk, especially with a poor mask fit, may be higher.
- Call for mechanical ventilation in cases of acute respiratory failure.

The U.S. Department of Defense (DoD)[15]

Given the scope of the pandemic, a team at the DoD released their "COVID-19 Practice Management Guide" on March 23, 2020. These highlights regard adult patient recommendations.

- Call for supplemental oxygen for patients in respiratory distress, hypoxemia or shock. Recommend a target SpO_2 of 92-96%.

13. Bouadma L, Lescure FX, Lucet JC, Yazdanpanah Y, Timsit JF. Severe SARS-CoV-2 infections: practical considerations and management strategy for intensivists. Intensive care medicine. 2020.

14. The Australian and New Zealand Intensive Care Society (ANZICS). COVID-19 Guidelines. Version 1. 16 March 2020. https://www.anzics.com.au/wp-content/uploads/2020/03/ANZICS-COVID-19-Guidelines-Version-1.pdf

15. Lt Col Renee I. Matos and COL Kevin K. Chung et al. DoD COVID-19 PRACTICE MANAGEMENT GUIDE. 23 March 2020.

Section 2: Guidance for Respiratory Symptom Management

- Recommend consideration of early intubation for patients that require 5-6 L/min consistently to maintain target saturation. Rapid sequence intubation (RSI) is recommended.
- If intubation/mechanical ventilation resources are limited or unavailable, they recommend HVNI/HFNC or a facemask with a reservoir bag at 10-15L/min if the patient is in critical condition.
- They do not recommend NiPPV due to higher risk of transmission, and higher need for staff intervention. Note that if high velocity therapy/HFNC fails, NiPPV should be avoided and intubation should be considered.

Intubation Discussion

Some of the early studies from the Wuhan Province noted the very high mortality rates of COVID-19 patients who were put on mechanical ventilation (MV)—81%[16] and 97%[17]. The authors of those studies urged the need for further studies and discussed that those outcomes could be correlated with the fact that those patients needing MV already had very severe disease progression. And as previously mentioned, we now have a better sense that overall global ICU mortality rates around the world are about 42%, significantly lower than those initially reported.[5] Nevertheless, the initial numbers were stark and as the pandemic continues, clinical circles have largely accepted that COVID-19 patients on ventilators don't do very well. Even popular media outlets have begun diversifying the narrative from 'more ventilators needed' to adding headlines like "Some doctors moving away from ventilators for virus patients."[18]

Type H patients may benefit from intubation while Type L patients could benefit from noninvasive modalities as a first-line option.

As shown in the previous section, avoiding intubation as a front-line treatment is already suggested by medical organizations across the world. The guidelines largely suggest trying non-invasive options, including high-flow oxygen (like high velocity therapy or high flow nasal cannula). They provide limitations to these trials and MV is recommended if the patient cannot be stabilized with non-invasive modes of oxygen support.

16. Yang X Yu Y Xu J et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020; (published online Feb 24.) https://doi.org/10.1016/S2213-600(20)30079-5

17. Zhou F Yu T Du R et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020; (published online March 9.) https://doi.org/10.1016/S0140-6736(20)30566-3

18. Stobbe, Mike. "Some doctors moving away from ventilators for virus patients." Associated Press. April 8, 2020. Last accessed: April 9, 2020. https://apnews.com/8ccd325c2be9bf454c2128dcb7bd616d

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MV is a key, life-saving tool, but it carries known risks, including the need to sedate the patient, an increased risk of inflammation, a risk of pneumothorax and barotrauma among others.[19] Once on MV, the patient cannot speak, or eat or drink and may require more contact from the healthcare provider (HCP), which in turn exposes the HCP more frequently to an infected patient.

In contrast, application of high flow oxygen carries significantly fewer and less serious side effects. The patient can remain unsedated and can interact with the clinician. Regarding HCP transmission risk, computer modeling suggests that use of a surgical mask over high velocity therapy may reduce the risk of particle dispersion and therewith the potential for HCPs to come into contact with infected particles.[20]

Having high velocity therapy as a tool is not a silver bullet, of course. Some patients do deteriorate and require MV. This raises the question: Which patients are good candidates for which tool?

Gattinoni and colleagues published a letter in Intensive Care Medicine that could help answer this question. The piece is titled "COVID-19 pneumonia: different respiratory treatment for different phenotypes?" and identifies two different types of COVID-19 patients.[21] Both types are diagnosed via a CT scan. One, the authors call Type L—and also refer to it as 'silent hypoxemic,'—and the other Type H, which more classically resembles severe ARDS. Their characteristics as described by the authors are shown in Table 2.

Table 2: COVID-19 Phenotypes

TYPE L (SILENT HYPOXEMIA) -> CONSIDER HIGH FLOW, CPAP, NIPPV	TYPE H (SEVERE ARDS) -> USE MV
Low elastance (High lung compliance)	**High** elastance (low lung compliance)
Low ventilation/perfusion ratio	**High** right to left shunt
Low lung weight	**High** lung weight
Low lung recruitability	**High** lung recruitabiulity

The authors note that in their patient sample (n=150) Type L accounted for 70-80% of patients and Type H for 20-30%. They suggest that Type H could benefit from immediate intubation while for Type L, the suggested first-line tools are high flow, CPAP and NiPPV. Though they refer to them as phenotypes, given that the authors acknowledge that one can progress to the other, it may also be helpful to think of these presentations as a continuum rather than distinct presentations.

19. Pierson, DJ. Complications associated with mechanical ventilation. Crit Care Clin. 1990 Jul;6(3):711-24.

20. Leonard S, Atwood CW Jr, Walsh BK, DeBellis RJ, Dungan GC, Strasser W, Whittle JS, Preliminary Findings of Control of Dispersion of Aerosols and Droplets during High Velocity Nasal Insufflation Therapy Using a Simple Surgical Mask: Implications for High Flow Nasal Cannula, CHEST (2020), doi:https://doi.org/10.1016/j.chest.2020.03.043.

21. Gattinoni L. et al. COVID-19 pneumonia: different respiratory treatment for different phenotypes? (2020) Intensive Care Medicine; DOI: 10.1007/s00134-020-06033-2 for respiratory distress syndrome of prematurity – a randomized clinical noninferiority trial." JAMA Pediatr. 2016 Aug 8.

Section 3: Understanding the Role of High Velocity Therapy for Respiratory Distress Management in COVID-19 Patients

What is Mask-Free NIV®?

With Mask-Free NIV, clinicians can treat hypercapnia, hypoxemia, and dyspnea, all with the comfort of a nasal cannula.

Clinicians managing patients in respiratory distress traditionally have had three categories of tools to relieve symptoms. There is oxygen therapy for low severity patients, non-invasive positive pressure ventilation (NiPPV) for moderate distress, and then mechanical ventilation for severe cases of respiratory distress. Vapotherm high velocity therapy offers clinicians a new tool to treat a broad range of patients experiencing respiratory distress: Mask-Free NIV. As an advanced form of high flow, it provides humidified oxygenation through the comfort of a nasal cannula. As an FDA cleared form of NIV, it provides ventilatory support.

This therapy has been clinically shown to be noninferior to NiPPV in treating adults in undifferentiated respiratory distress.[22] has also been demonstrated to have comparable outcomes to CPAP when it comes to neonatal patients.[23]

While it doesn't entirely replace NiPPV in the clinical toolkit, it offers an appealing alternative for clinicians treating most patients in undifferentiated respiratory distress, including distress associated with COVID-19. In particular, it's appealing for those patients who have difficulty tolerating a mask, are difficult to fit, or have a risk of vomiting and aspiration. It is also a good choice for patients where clinicians feel there is benefit to the patient being able to talk, eat, and drink while receiving therapy.

Mechanisms of Action

The idea of Mask-Free NIV may at first sound counter intuitive, but this section will break down how it achieves its efficacy without the use of pressure as a primary mechanism.

22. Doshi, Pratik et al. High-Velocity Nasal Insufflation in the Treatment of Respiratory Failure: A Randomized Clinical Trial. Annals of Emergency Medicine, 2018. Published online ahead of print. https://www.ncbi.nlm.nih.gov/pubmed/29310868

23. Lavizarri A, Colnaghi M, Ciuffini F, Veneroni C, Musumeci S, Cortinovis I, Mosca F. "Heated, humidified high-flow nasal cannula vs nasal continuous positive airway pressure for respiratory distress syndrome of prematurity – a randomized clinical noninferiority trial." JAMA Pediatr. 2016 Aug 8.

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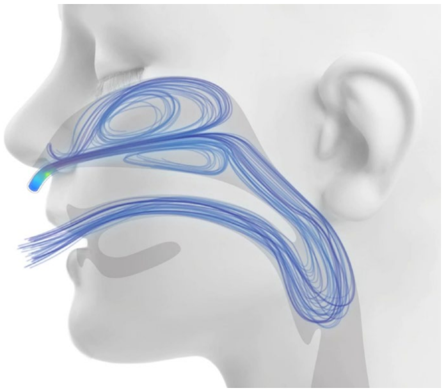

Primary Mechanism

The primary mechanism of action of high velocity therapy, is the flushing of end-expiratory CO_2 from the upper airway between breaths. This is accomplished rapidly and efficiently with a high velocity stream of optimally conditioned breathing gas. Because it is an open system, the fresh gas is insufflated through the nares and the end-expiratory CO_2 is flushed out through the mouth. This reduces the CO_2 content of the next inspiration and fills the nasopharyngeal cavity with fresh gas. **Like a tracheostomy that *mechanically* bypasses the dead space, the high velocity purge *functionally* minimizes it by changing the dead space to a fresh gas reservoir.**

Other Mechanisms

High velocity therapy also achieves its efficacy in part through the following[24]:

- Some distending airway pressure
  - Primarily during exhalation against the high velocity flow
- Warming gas flow (typically 33-37°C)
  - Which decreases inspiratory resistance
- Humidification
  - Optimal humidity preserves mucociliary function and aids in mucus clearance from airways

24. Dysart K, Miller TL, Wolfson MR, Shaffer TH. Research in high flow therapy: Mechanisms of action. Respir Med 2009; 103:1400-1405

Section 3: Understanding the Role of High Velocity Therapy for Respiratory Distress Management in COVID-19

Difference between Vapotherm High Velocity Therapy and NiPPV

Clinicians used to NiPPV as the gold standard treatment for patients with hypercapnia may be skeptical about how a mask-free device that does not deliver pressure as a primary mechanism of action could achieve alveolar ventilation in patients. In reality NiPPV and high velocity therapy are just two different approaches toward the same goal. Let's look at the basics:

Ventilation with NiPPV:

Alveolar Ventilation = (**Tidal Volume** — Dead Space) x Respiratory Rate

In order to achieve ventilation, NiPPV most greatly affects the Tidal Volume aspect of the above equation. The machine ensures ventilation by using positive pressure to deliver target Tidal Volume. Because there is a risk of over-pressurization, clinicians generally start low and adjust up for effect to stabilize a patient.[25]

Ventilation with Vapotherm high velocity therapy:

However, it is also possible to achieve alveolar ventilation by affecting the other parameter in the equation:
Dead Space.

Alveolar Ventilation = (Tidal Volume — **Dead Space**) x Respiratory Rate

The rapid flushing out of the upper airway Dead Space is the mechanism of action by which high velocity therapy facilitates alveolar ventilation.[24, 26]

Unlike NiPPV, it is an open system de-escalation therapy—it is safe to turn on high and stabilize the patient fast. The clinician can then titrate down upon patient response

25. Mehta, Sangeeta and Nicholas S. Hill. Noninvasive Ventilation. American Journal of Respiratory and Critical Care Medicine 163(2).

26. Miller TL, Saberi B, Saberi S (2016) Computational Fluid Dynamics Modeling of Extrathoracic Airway Flush: Evaluation of High Flow Nasal Cannula Design Elements. J Pulm Respir Med 6:376. doi: 10.4172/2161-105X.1000376

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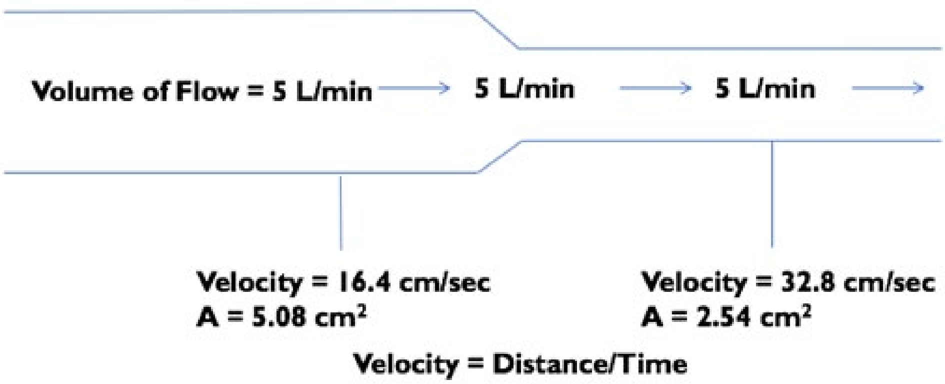
Difference between High Velocity Therapy and Commodity High Flow Oxygen Systems

High velocity therapy is frequently confused with commodity high flow oxygen systems, also commonly known as high flow nasal cannula (HFNC). This comparison is understandable at first glance—both deliver high liter flows of conditioned gas though a cannula interface. However, there are some significant differences between these devices and the likely explanation for the difference in clinical outcomes. As established, high velocity therapy has been clinically demonstrated to be comparable to NiPPV in treating patients in undifferentiated respiratory distress.

As the name suggests, velocity is a key component of the efficacy of high velocity therapy. Unlike most conventional large-bore HFNC, Vapotherm high velocity therapy uses small-bore cannulas. This matters because velocity, at a constant volume of flow, varies inversely with the cross sectional area of a tube, as depicted below.



In other words, the smaller the diameter of the cannula, the faster the gas will travel so long as the volume remains constant. Vapotherm Precision Flow® systems are specifically designed to withstand the back pressure high velocity creates.

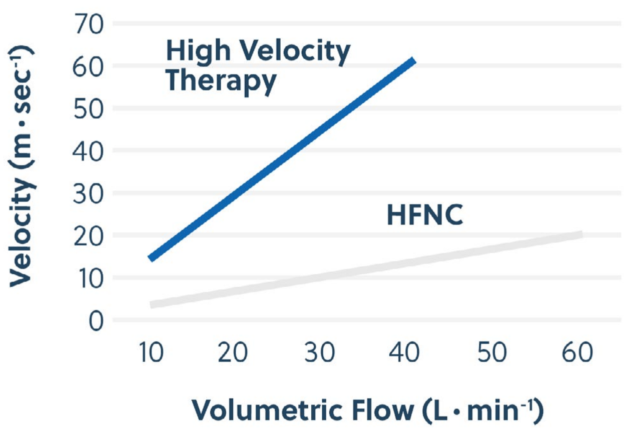
A helpful way to think about it is to envision a garden hose with water flowing out/ If you place your thumb to narrow the diameter of the hose, the water instantly moves faster.

Section 3: Understanding the Role of High Velocity Therapy for Respiratory Distress Management in COVID-19

The Greater the Velocity, The Faster the Flush

In the 2016 study "Computational Fluid Dynamics Modeling of Extrathoracic Airway Flush: Evaluation of High Flow Nasal Cannula Design Elements" Miller and colleagues demonstrated that small-bore cannula prongs flush the upper airway dead space faster than large-bore cannulas. More precisely, the high velocity small-bore cannula achieves a flush in 2.2 seconds while the large-bore cannulas flush in 3.6 seconds.[26]

Figure 1



This is clinically meaningful because with the velocity the small-bore cannulas generate, a lower flow rate is needed to achieve an effective flush. Figure 1 illustrates how high velocity therapy compares to commodity high flow oxygen systems when generating velocity. For example, high velocity therapy achieves the same velocity at approximately 15 L/min that HFNC systems require 60 L/min to achieve.

We are sometimes asked why high velocity therapy only goes up to 40 L/min in its settings when some commodity high flow oxygen systems require higher flow rates. As illustrated, the answer is that it is clinically effective below 40 L/min.

Potential Implications for Oxygen Conservation in COVID-19 Patients

One of the reported challenges during the COVID-19 pandemic has been the increased demand for oxygen in patient treatment, leading to possible shortages at some institutions. In a context such as this, it is important for healthcare providers to understand the distinction between high velocity and high flow systems. Many commodity HFNC go up to 60 L/min, which when placed on maximum settings to treat very hypoxemic patients with COVID-19, uses up significant amounts of oxygen. In contrast, high velocity therapy on maximum settings could possibly help hospitals conserve oxygen. As previously discussed, with a higher velocity, more of the dead space is replaced more quickly with fresh oxygenated gas for the patient to breathe from.

Section 3: Understanding the Role of High Velocity Therapy for Respiratory Distress Management in COVID-19

Not all high flow systems are the same. Vapotherm high velocity therapy can treat hypercapnia along with hypoxemia and dyspnea.

COPD Comorbidities in COVID-19 Patients

We've known that people with underlying conditions are at greater risk for worse COVID-19 outcomes. Thanks to the research of Leung and colleagues, we now better understand some of the mechanisms that may be exacerbating the outcomes for smokers and COPDers who contract COVID-19.

In their recently published article, "ACE-2 Expression in the Small Airway Epithelia of Smokers and COPD Patients: Implications for COVID-19", the researchers conclude that smokers and COPD patients have greater quantities of a cell receptor— Angiotensin-converting enzyme (ACE)-2— in their lower airway tract.[27] This has significant implications because this specific receptor is the entryway through which the SARS-CoV-2 virus— which causes COVID-19—enters and infects the cell.

The combination of COVID-19 on top of COPD presents several management challenges. Traditionally, a COPD patient in respiratory distress would have been treated with Noninvasive Positive Pressure Ventilation (NiPPV) to address hypercapnia. NiPPV is one of the tools suggested for COVID-19 respiratory management in several guidelines across the world, but it is not uniformly recommended. As discussed in Section 2, some organizations[7,14] suggest trial of high flow nasal oxygen on patients not requiring intubation and use of NiPPV only if high flow therapy is unavailable or failed.

In their letter "High flow nasal cannula is a good treatment option for COVID-19", Geng and colleagues further point out that NiPPV "requires man-machine cooperation and is uncomfortable."[28]

With certain guidelines and practitioners expressing a preference for high flow in COVID-19 patients, it's important for clinicians to understand that not all high flow is the same. Because high velocity therapy is Mask-Free NIV and provides ventilatory support, it may be an attractive tool for clinicians managing COVID-19 patients with COPD who don't need to be intubated. Having a comfortable ventilatory support tool as an option could also prove useful when we consider that only about 19% of COVID-19 patients experience solely hypoxemic respiratory failure.[29]

27. Leung, Janice M. et al. ACE-2 Expression in the Small Airway Epithelia of Smokers and COPD Patients: Implications for COVID-19. European Respiratory Journal 2020. DOI: 10.1183/13993003.00688-2020

28. Geng, Shike et al. High flow nasal cannula is a good treatment option for COVID-19. Heart & Lung: The Journal of Cardiopulmonary and Acute Care. April 13, 2020. DOI:https://doi.org/10.1016/j.hrtlng.2020.03.018

29. Wu Z, McGoogan JM, (2020) Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. JAMA; doi: 10.1001/jama.2020.2648

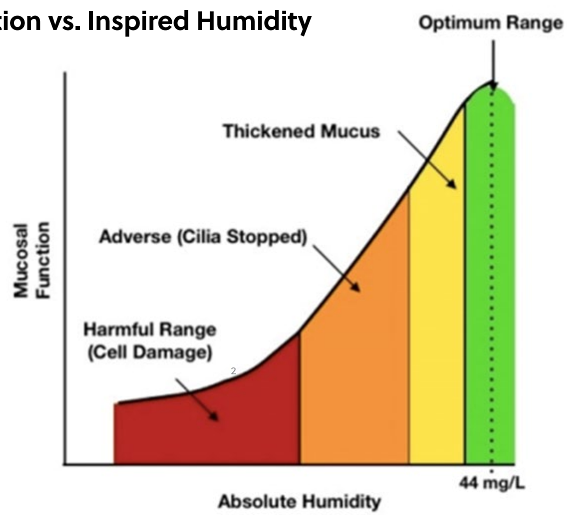
Section 3: Understanding the Role of High Velocity Therapy for Respiratory Distress Management in COVID-19

The Need for Humidification in COVID-19 Patients

The primary clinical concern in many COVID-19 pneumonia cases is meeting the patients' oxygen needs. But as with respiratory infections in general, ensuring proper airway humidification could also be crucial in successfully managing these patients.

It is well-known that for the respiratory system to function optimally and for alveolar gas exchange to happen, the inhaled gas has to be near 100% relative humidity.[30] A healthy airway heats and humidifies each breath in order to preserve its functionality and ability to defend from pathogens through mucociliary clearance. If there is insufficient heat and humidity, the mucociliary elevator can become compromised and even damaged. Figure 2 shows this relationship between humidity and optimal mucosal function.

Figure 2. Mucociliary Function vs. Inspired Humidity



The symptoms of a viral pneumonia can compromise mucosal function in and of themselves. In the case of COVID-19, current recommendations for management call for the restriction of fluids under certain conditions[7]—something that could further challenge that patient's ability to heat and humidify their airway.

High flow oxygen could help address this management challenge. A recent literature review noted that heated and humidified high flow oxygen provided to adults in respiratory distress is associated with better tolerance/comfort, improved mucociliary function, greater secretion clearance, and prevention of lung collapse, among other benefits.[31]

30. Williams R, Rankin N, Smith T, Galler D, Seakins P. Relationship between the humidity and temperature of inspired gas and the function of the airway mucosa. Critical care medicine. 1996;24(11):1920-1929.

31. Roca O, Hernandez G, Diaz-Lobato S, et al. Current evidence for the effectiveness of heated and humidified high flow nasal cannula supportive therapy in adult patients with respiratory failure. Critical care. 2016;20(1):109.

Section 3: Understanding the Role of High Velocity Therapy for Respiratory Distress Management in COVID-19

As with the matter of COPD co-morbidities in COVID-19 patients, when it comes to humidification, it is also important for healthcare workers to know that not all devices which fall under the high flow oxygen umbrella deliver humidification in the same way.

Membrane Humidification vs. Passover Humidification

The difference between high velocity therapy and commodity high flow oxygen systems is that the temperature in the Vapotherm system never exceeds the gas delivery temperature in order to create or maintain humidification. High flow oxygen products use higher than set temperatures in both the creation and maintenance of humidification.

While Vapotherm high velocity therapy uses membrane humidification, high flow oxygen humidifiers use a pass-over humidification system. With pass-over humidification, breathing gas passes over highly heated water to add moisture and humidify the gas. Vapotherm high velocitytherapy, on the other hand, uses a vapor transfer cartridge to deliver water molecules to the gas path across a membrane to create vapor without high heat.

When we look at a cross section of the Vapor Transfer Cartridge in Vapotherm high velocity therapy, we see hundreds of tiny, semi-permeable "straws". The straws are surrounded by water and as gas flows down these fibers, it becomes optimally humidified.[32] This method is quite different from pass-over humidification. Water molecules enter the gas pathway through tiny .05 micron pores in the fibers by osmotic pressure.

32. Waugh J, Granger W. An evaluation of 2 new devices for nasal high-flow gas therapy. Respiratory Care. 2004 Aug; 49(8): 902-906.

Section 3: Understanding the Role of High Velocity Therapy for Respiratory Distress Management in COVID-19

Delivering Optimally Conditioned Gas to the Patient

Generating optimally conditioned gas is just the first step. To be clinically effective, the gas also needs to be delivered in its humidified state all the way to the patient. This is where yet another difference between Vapotherm high velocity therapy and commodity high flow oxygen products comes in.

The oxygen systems largely use a heated wire circuit for dewpoint control as they deliver the gas. As the heat mapping image in Figure 3 illustrates, the wire circuit does not provide uniform heating and leaves parts of the tubing cooler. Each time the humidified gas hits a cold spot in the tubing, there is an opportunity for water to condense out and create rainout. The patient may receive less than optimally humidified breathing gas, and may also experience the discomfort of water droplets being delivered through the cannula.

Figure 3
Heated wire circuit of commodity high flow oxygen systems.

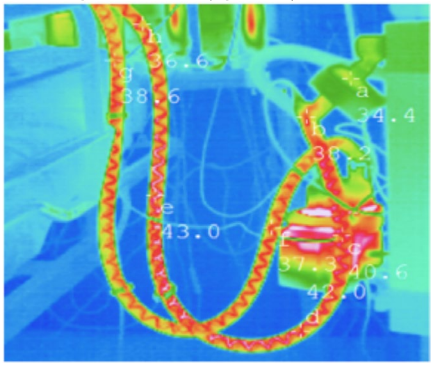
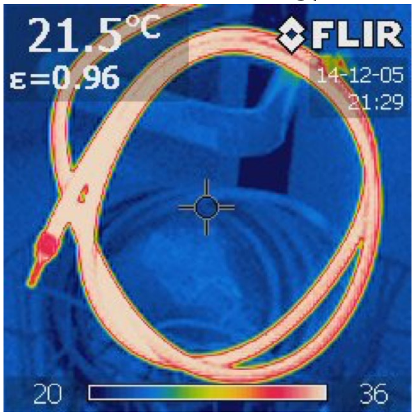
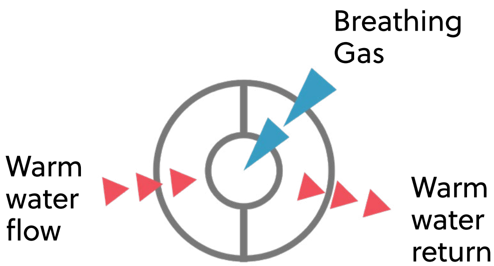


Figure 4
Triple lumen delivery tube of Hi-VNI Technology



In contrast, high velocity therapy ensures that the delivery tubing is uniformly heated and thereby reduces the chance of rainout, as shown in Figure 4. This is accomplished through a triple-lumen—or three-channel—delivery tube. In essence, the tube creates a warm-water jacket that keeps the Medical Grade Vapor energetically stable all the way from the Vapor Transfer Cartridge to the High Velocity Cannula, where the short supply tubing continues to ensure that the possibility of rainout is further reduced.

Section 3: Understanding the Role of High Velocity Therapy for Respiratory Distress Management in COVID-19



Cross-section of tubing

An added benefit to the triple-lumen delivery tube is that it's safe to touch and will not cause burns.

Understanding the importance of optimal airway humidification is one of the factors that could help healthcare workers in successful management of complex patients, like COVID-19 patients.

Post-Extubation of COVID-19 Patients

As established, some COVID-19 patients will appropriately, but unfortunately have to be intubated. Eventually those patients are being extubated and it's well-known that failed extubation is associated with an increased risk of mortality and morbidity.[33]

Traditionally, low flow oxygen therapy and noninvasive positive pressure ventilation (NiPPV) have been the devices to help support patients through post-extubation. In recent years, high flow nasal cannula (HFNC) has become a more widely accepted tool for this procedure. Studies by Hernandez and colleagues show that HFNC is superior to conventional oxygen therapy at preventing reintubation[34] and similar in efficacy to NiPPV for reintubation prevention as well.[35] Furthermore, Stephan and colleagues found that in cardiothoracic surgery patients, HFNC has similar efficacy to NiPPV in preventing or resolving acute respiratory distress during post-extubation.[36]

However, it's important to note that these studies exclude hypercapnic patients and are solely focused on hypoxemic patients. Although commodity HFNC has attractive advantages over NiPPV—such as a more comfortable interface that allows patients to talk, eat, and take oral medication—it does have limitations when managing hypercapnic patients. This is why some clinicians implement HFNC in concert with NiPPV.

33. Epstein SK et al, Effects of Failed Extubation on Outcome of Mechanical Ventilation. CHEST. 1997; 112(1); 186-192.

34. Hernandez et al, Effect of Postextubation High-Flow Nasal Cannula vs Conventional Oxygen Therapy on Reintubation in Low-Risk Patients: A Randomized Control Trial. JAMA. 2016; 315(113);1354-1361.

35. Hernandez et al, Effects of Postextubation High-Flow Nasal Cannula Cannula vs Noninvasive Ventilation on Reintubation and Postextubation Respiratory Failure in High Risk Patients; A Randomized Controlled Trial. JAMA. 2016; 316(15):1565-1574.

36. Stephan et al, High-Flow Nasal Oxygen vs Noninvasive Positive Airway Pressure in Hypoxemic Patients After Cardiothoracic Surgery: A Randomized Clinical Trial. 2015; 313(23): 2331-2339.

Section 3: Understanding the Role of High Velocity Therapy for Respiratory Distress Management in COVID-19

Thille and colleagues recently published a study in JAMA, titled "Effect of Postextubation High-Flow Nasal Oxygen With Noninvasive Ventilation vs High-Flow Nasal Oxygen Alone on Reintubation Among Patients at High Risk of Extubation Failure: A Randomized Clinical Trial." This trial found that when both HFNC and NiPPV were used on patients of high risk of extubation failure, the risk of reintubation was significantly decreased when compared to use of HFNC alone.[37]

In the discussion, the authors note that "noninvasive ventilation [NIV] may be beneficial on outcomes of hypercapnic patients ..." They also note that "patients older than 65 years or with underlying chronic cardiac or respiratory disease are also at high risk of reintubation and could benefit from noninvasive ventilation."[37] This interpretation is in line with our understanding that hypercapnia is a symptom that leads to increased work of breathing that calls for ventilatory support intervention.

Given the chances of extubation success by using a combination of NIV and HFNC, clinicians should be aware of high velocity therapy as a Mask-Free NIV post-extubation support tool.

37. Thille, A.W. et al. Effect of Postextubation High-Flow Nasal Oxygen With Noninvasive Ventilation vs High-Flow Nasal Oxygen Alone on Reintubation Among Patients at High Risk of Extubation Failure: A Randomized Clinical Trial. JAMA. 2019 Oct 2;322(15):1465-1475. doi: 10.1001/jama.2019.14901.

Section 4: Preventing Transmission When Using High Velocity Therapy

Now that we've covered how Vapotherm high velocity therapy can be used in the management of COVID-19 patients, we'll discuss the key concern of precautions healthcare workers (HCPs) can take in preventing infection during the course of patient treatment.

Though it's important to understand different risk levels of different procedures, standard precautions when treating suspected or confirmed COVID-19 patients should always include proper personal protective equipment (PPE) such as a N95 or equivalent respirator, gloves, and gowns among other equipment.

WHO and CDC guidelines also recommend performing procedures in an adequately ventilated room, preferably an Airborne Infection Isolation Room (AIIR) or Negative Pressure room.

As a mask-free modality that delivers high flows of oxygen to patients, Vapotherm high velocity therapy has a low risk of transmission by comparison to NiPPV. Nevertheless, given the infectiousness of this novel coronavirus the already low risk can and should be further reduced with a few simple precautions.

Not All AGPs Are the Same

All respiratory support interventions are AGPs. The act of changing the airway or its function in some way has the risk of generating potentially infectious droplets. However, not all AGPs present the same level of risk.

In a systematic review of the transmission risk of acute respiratory infections from aerosol generating procedures, Tran and colleagues found that the risk of transmission for high flow was not significant, when compared to significant increased risk associated with tracheal intubation, non-invasive positive pressure ventilation, tracheostomy, and manual ventilation.[38] Table 3 shows some select findings from Tran et al.'s meta-analysis.

38. Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J (2012) Aerosol Generating Procedures and Risk of Transmission of Acute Respiratory Infections to Healthcare Workers: A Systematic Review. PLoS ONE 7(4): e35797. doi:10.1371/journal.pone.0035797

Section 4: Preventing Transmission When Using High Velocity Therapy

Table 3: Aerosol Procedures as Risk Factors of SARS Transmission

AGP	ESTIMATE (ODDS RATIO 95% CL)
Tracheal intubation (4 cohort studies)	6.6 (2.3, 18.9); 39.6% [pooled estimate]
Tracheal intubation (4 case-control studies)	6.6 (4.1, 10.6); 61.4% [pooled estimate]
Suction before intubation (2 cohort studies)	3.5 (0.5, 24.6); 59.2% [pooled estimate]
Suction after intubation (2 cohort studies)	1.3 (0.5, 3.4); 28.8% [pooled estimate]
Manual ventilation before intubation (1 cohort study)	2.8 (1.3, 6.4) [point estimate]
High flow oxygen (1 cohort study)	0.4 (0.1, 1.7) [point estimate]

Adapted from Tran K et al.

It becomes clear, that high flow oxygen modalities, such as high velocity therapy may have a lower risk of SARS transmission than any of the procedures associated with intubation. This risk difference is also reflected in some of the medical organization guidelines. For example, SCCM recommends the use of high flow oxygen as a front-line therapy over the use of NiPPV for COVID-19 patients not requiring intubation.[7] This recommendation—Surviving Sepsis Campaign COVID-19 Guidelines—states:

> "patients may find HFNC more comfortable than NIPPV. Given the evidence for a decreased risk of intubation with HFNC compared with NIPPV in acute hypoxemic respiratory failure and studies suggesting that NIPPV may carry a greater risk of nosocomial infection of healthcare providers, we suggest HFNC over NIPPV."

However, even though high velocity therapy already has a low risk of COVID-19 infectiousness compared to many other respiratory procedures, the already low risk can and should be further reduced with a few simple precautions.

Simulation of Surgical Mask Precaution

As noted in Section 2 of this book, the Respiratory Care Committee of the Chinese Thoracic Society specifically recommended use of a simple surgical mask over the face of the patient, covering the mouth and nose while that patient is on a high flow modality.[9] This seems to be a sensible and intuitive precaution. To see exactly to what degree it might work for Vapotherm high velocity therapy, our Science & Innovation team conducted computational fluid dynamics (CFD) modeling. The preliminary results were published in CHEST[39] and the full results in JACEP Open[40].

39. Leonard S, Atwood CW Jr, Walsh BK, DeBellis RJ, Dungan GC, Strasser W, Whittle JS, Preliminary Findings of Control of Dispersion of Aerosols and Droplets during High Velocity Nasal Insufflation Therapy Using a Simple Surgical Mask: Implications for High Flow Nasal Cannula, CHEST (2020), doi: https://doi.org/10.1016/j.chest.2020.03.043

40. Leonard S, Strasser W, WhittlHigh resolution computational fluid dynamics simulations of particle behavior during high velocity nasal insufflation with asimple surgical maske J, Volakis LI, DeBellis RJ, Prichard R, Atwood CW, Dungan GC. Reducing aerosol dispersion by high flow therapy in COVID-19:. JACEP

Section 4: Preventing Transmission When Using High Velocity Therapy

The CFD model was performed in ANSYS Fluent CFD (ANSYS, Inc, Canonsburg, PA, USA) and simulated several cases of a patient breathing at 32 bpm at a tidal volume of 500ml. Table 4 shows the breakdown of all studied scenarios.

Table 4: Computational Fluid Dynamics Modeling Scenarios

CASE	THERAPY FLOW (L/MIN)	MASK	BREATHING	PARTICLE RANGE
High Velocity Therapy w/ Mask	40	Yes	32bpm, 500ml V_t	.1 µm - 100 µm
Low Flow O_2 w/ Mask	6	Yes	32bpm, 500ml V_t	.1 µm - 100 µm
No Therapy w/ Mask	None	Yes	32bpm, 500ml V_t	.1 µm - 100 µm
HVNI w/o Mask	40	No	32bpm, 500ml V_t	.1 µm - 100 µm
Low Flow O_2 w/o Mask	6	No	32bpm, 500ml V_t	.1 µm - 100 µm
No Therapy w/o Mask	None	No	32bpm, 500ml V_t	.1 µm - 100 µm

The testing found that with a surgical mask in place over the high velocity cannula, the surgical mask captured the majority of all particles leaving the patient's nose and mouth. The mask reduced the velocity of gas leaving the patients face significantly. (Figure 5)

Figure 5: Velocity Maps of Particle Dissemination in This Simulation

The image on the left depicts a patient simulation without the mask during high velocity therapy. The one in the middle shows the velocity map of particle dispersion with a mask on during therapy while the one on the right shows a patient breathing with a mask, but without therapy. It becomes apparent that the last two images show comparable particle containment.

In this simulation, using the mask during high velocity therapy contained 88.8% of the particles. This was slightly greater than using a mask without treatment, as shown in Table 4.

Table 5: Comparison of Particles Caught by Surgical Mask In This Simulation[40]

SIMULATED CASE	MASK STATUS	CAUGHT IN MASK OR ON PATIENT FACE	TRAPPED NEAR FACE (< 1m)	ESCAPED TO REST OF ROOM (>1m)
High Velocity Therapy	No	N/A	23.0%	77.0%
No Therapy	No	N/A	47.7%	52.3%
High Velocity Therapy	Yes	88.8%	2.95%	8.23%
No Therapy	Yes	73.4%	6.81%	19.8%

It may seem counter-intuitive that more particles were captured by the mask during therapy than without therapy. In the discussion, the authors note that it could be explained through the high velocity exiting the patient's nares and mouth. Basically, the mask is designed to capture particles that are pushed into the mask material. With high velocity therapy there is a lot of momentum to the gas flow which essentially directs the gas into the mask matrix. In this way, it allows the mask to do what the mask is designed to do—capture particles. With spontaneous breathing or low flow oxygen, there is much less exit velocity and more opportunity for the gas-borne particles to avoid impacting the mask material, and thereby avoid potential capture.

It's worth noting that the most obvious particulate movement occurred via the leaks in the mask. The authors recommend minimizing mask leaks to further reduce the risk of transmission.

The modeling also found that using a surgical mask with high velocity therapy still achieved significant clearance of CO_2 from the upper airway. However, the mask did lead to a 37% reduction of CO_2 clearance at 35 L/min. Clinicians using high velocity therapy for ventilatory support should consider adjusting starting flows higher because the high velocity flush is a key mechanism of achieving that ventilatory support. (see Section 3 of this book)

Conclusion

HCPs should apply a surgical mask over the nose and mouth of a patient with a properly fitted cannula before initiating high velocity therapy. Based on this CFD model, such use of a surgical face mask may greatly reduce the spread of potentially infectious particles during high velocity treatment.

Section 4: Preventing Transmission When Using High Velocity Therapy

Simulation of Negative Pressure Scavenger Kit Precaution

Another precaution HCPs can use on patients with infectious droplet transmitted diseases is creating a localized area of negative pressure at the patient's face. The idea for this was brought to Vapotherm by Felix Khusid. Khusid is an RRT out of New York, one of the epicenters of the pandemic in the US. He proposed a system to Vapotherm that paired a modified face-tent with hospital suction to create an area of negative pressure at the patient's face. It was designed to help suction away potentially infectious particles and trap them in a suction canister. We thought it was a good idea that could help customers and thus, the FELIX-1 came about, named in honor of Khusid. (Figure 6)

Figure 6: FELIX-1 over Vapotherm high velocity cannula

This concept of creating localized negative pressure has been executed in hospitals before. We conducted CFD modeling to determine its efficacy and found that for this particular simulation, there was a comparable or better potential for particle capture when compared to the face mask model discussed previously. Table 6 shows the comparison.

Table 6: Particle Capture During A Computer Simulation of Vapotherm High Velocity Therapy

CONFIGURATION	CAPTURE EFFICIENCY (IN THESE MODELS)
Patient on high velocity therapy wearing face mask only	88.8%[40]
Patient on high velocity therapy wearing FELIX-1	97.1%[41]

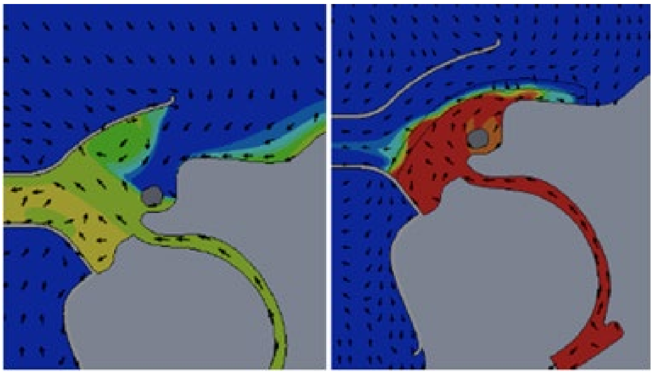
It should be noted that there was a reasonably high flow of vacuum in this simulation. The It should be noted that there was a reasonable high flow of cavuum in this simulation. The performance will vary with different patients and degrees of vacuum flow available in each individual hospital setting.

Additionally, the simulation suggested that compared to a surgical face mask, the FELIX-1 had less heat retention around the patient's face in this model (Figure 7).

41. Data on file with Vapotherm.

Section 4: Preventing Transmission When Using High Velocity Therapy

Figure 7: Simulation of FELIX-1 without (left) and with (right) surgical mask on patient during high velocity therapy



As the heat map in Figure 6 indicates, in this model, the FELIX-1 maintained cooler air around the patient's face. This could be more comfortable for patients.

Section 5: A COVID-19 Patient Case Study with Vapotherm High Velocity Therapy

Vapotherm's high velocity therapy is a tool for treating respiratory distress. The following case study describes certain outcomes in relation to the use of Vapotherm's high velocity therapy, but individual results may vary. Practitioners should refer to the full indications for use and operating instructions of any products referenced herein before prescribing them.

Use of Vapotherm High Velocity Therapy in a COVID-19 Patient with a History of COPD and Mask-Intolerance

Jeremy A. Greenberg, MD - Assistant ICU Medical Director

A 56-year-old male with a history of COPD and Hypertension was admitted to the intensive care unit (ICU) with acute respiratory distress syndrome (ARDS) due to COVID-19.

The patient had been in his normal state of health until 4 days prior to this admission, when he developed gradual onset, progressively worsening dyspnea. He had a non-productive cough. He had no fever, chills, congestion, or sore throat. The day of admission, he presented to a local urgent care where his oxygen saturation was 83% while breathing ambient air. Emergency medical services were dispatched, and the patient was transported by ambulance to our emergency department.

On examination, his temperature was 36.7°C, the heart rate (HR) 112 beats per minute, the blood pressure 113/73 mmHg, the respiratory rate (RR) 33 breaths per minute, and the oxygen saturation (SpO_2) 87% while receiving supplemental oxygen with a nasal cannula at 6 liters per minute. He was in extremis and communication was limited to single word sentences. He had sternal retractions with inspiration and tensing of his abdominal wall musculature with exhalation. Inspiratory and expiratory wheezes were heard on bilateral lung auscultation.

An arterial blood gas showed a pH of 7.32, a partial pressure of carbon dioxide ($PaCO_2$) of 52 mmHg, and a partial pressure of oxygen (PaO_2) of 58 mmHg. Testing for SARS-CoV-2 was positive. Chest x-ray showed bilateral, multifocal patchy airspace disease. He received 3 successive nebulized bronchodilator treatments with ipratropium bromide and albuterol sulfate. The initial plan for his acute respiratory failure was support with bi-level positive airway pressure non-invasive ventilation. However, the patient expressed that he had previously been placed on that therapy during a hospitalization approximately 1.5 years ago for an acute exacerbation of his COPD and had been unable to tolerate the device due to discomfort as well as intense feelings of claustrophobia. He requested an alternative therapy and was placed on Vapotherm high velocity therapy (Precision Flow Hi-VNI, Vapotherm, Exeter, NH USA) with Vapotherm at a flow of 30 liters per minute and an inspired oxygen of 60%. He additionally received methylprednisolone 125 mg IV and empiric anti-infectives for possible co-infection with bacterial community acquired pneumonia after blood cultures, respiratory culture, and respiratory viral panel were obtained.

Approximately 2 hours following, a reassessment by the ICU team revealed his heart rate had decreased to 85 beats per minute, the blood pressure 143/77 mmHg, the respiratory rate 24 breaths per minute, and the oxygen saturation 94%. He subjectively felt improved. His work of breathing was improved. A repeat arterial blood gas showed a pH of 7.38, a partial pressure of carbon dioxide of 49 mmHg, and a partial pressure of oxygen of 77 mmHg (Table 6). He was admitted to a negative pressure room in the newly created COVID ICU.

Table 7: Vital signs and arterial blood gas results before and after 2 hours of Vapotherm high velocity therapy.

	HR	RR	$SpO2_2$	BLOOD PRESSURE	pH	$PaCO2_2$	PaO_2
Initial presentation on 6 L/min low flow oxygen	112	33	87%	113/73 mmHg	7.32	52 mmHg	58 mmHg
2 hours after high velocity therapy initiation (30L/min .60 FiO_2)	85	24	94%	143/77 mmHg	7.38	44 mmHg	77 mmHg

He was managed in the COVID ICU from hospital days 0 through 12. His acute respiratory failure with hypoxemia and hypercapnia was managed with high velocity therapy. From days 0 to 2, he remained on the initial settings at 30 liters per minute of flow and an inspired oxygen of 60%. His respiratory rate ranged from 16 to 24 breaths per minute during this time. On hospital day 3, his oxygen saturation decreased to 85%. His flow was increased to 40 liters per minute and inspired oxygen to 80%. He remained on these settings from hospital day 3 to hospital day 9. During this time, his respiratory rate ranged from 22 to 27 breaths per minute and his oxygen saturation 86 – 93%. Starting on hospital day 10, his oxygen saturation and ventilatory work of breathing improved. From hospital day 10 to hospital day 12 the high velocity therapy settings were decreased every 4 hours while targeting an oxygen saturation of 88-95%. On hospital day 12, high velocity therapy was discontinued and he was placed on supplemental oxygen with a nasal cannula at 5 liters per minute. He was transferred from the ICU to a COVID-19 ward with telemetry monitoring.

During his ICU course he additionally received scheduled, nebulized ipratropium bromide and albuterol sulfate every 4 hours. This was continued from hospital day 0 through hospital day 5. He was subsequently transitioned to twice daily inhaled tiotropium and twice daily inhaled budesonide-formoterol. He received 10 days of Decadron, 5 days at a dose of 20 mg IV followed by 5 days at 10 mg IV. 5 doses of Remdesivir were administered. He additionally received convalescent plasma as part of an investigational study on hospital day 3. Empiric antibiotics were discontinued on hospital day 3 after blood cultures, respiratory culture, and respiratory viral panel resulted negative.

He was discharged home on hospital day 14 without need for supplemental oxygen. He did not attend referral Telemedicine appointments arranged prior to hospital discharge with primary care and pulmonology. He was reached by phone approximately 2 months following hospital discharge and reported that he had returned to work, though with some limitations. He described persistent fatigue, cognitive slowing, and exertional dyspnea though felt these issues were gradually improving and expressed confidence he would return to his pre-hospitalization functional status. He agreed to see a pulmonologist for further management of his COPD and to consider smoking cessation interventions.

Section 6: Key Take-Aways

Section 6: Key Take-Aways

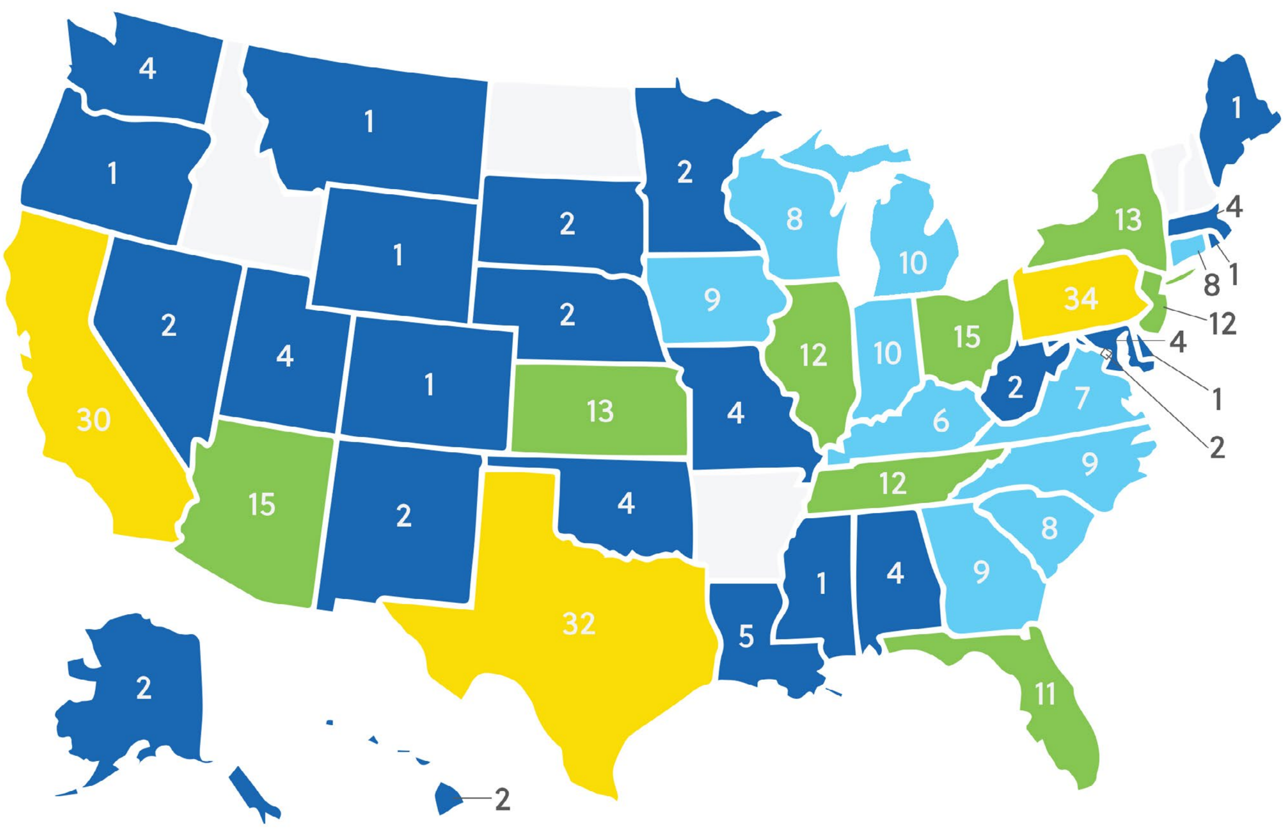
- High velocity therapy has low risk of transmission by comparison to some other ventilatory support
- To capture particles, a surgical mask or a negative pressure scavenger kit can be used over the patient's mouth and nose with the high velocity cannula in place
- High velocity therapy is a form of mask-free NIV and can provide ventilatory support in addition to oxygenation
- High velocity therapy is appropriate for post-extubation
- The design of the device delivering high velocity therapy may help you conserve oxygen even at maximum settings by comparison to conventional high flow

Survey Results: COVID-19 Survey of US Healthcare Workers

Results

In order to help you and ourselves get a sense of how this pandemic is impacting HCPs across U.S. hospitals, we sent out a survey in July of 2020. 344 HCPs practicing in the U.S. took it. We hope the below results help you see how your institution might compare to your colleagues'. *

Graphic Distribution of Respondents

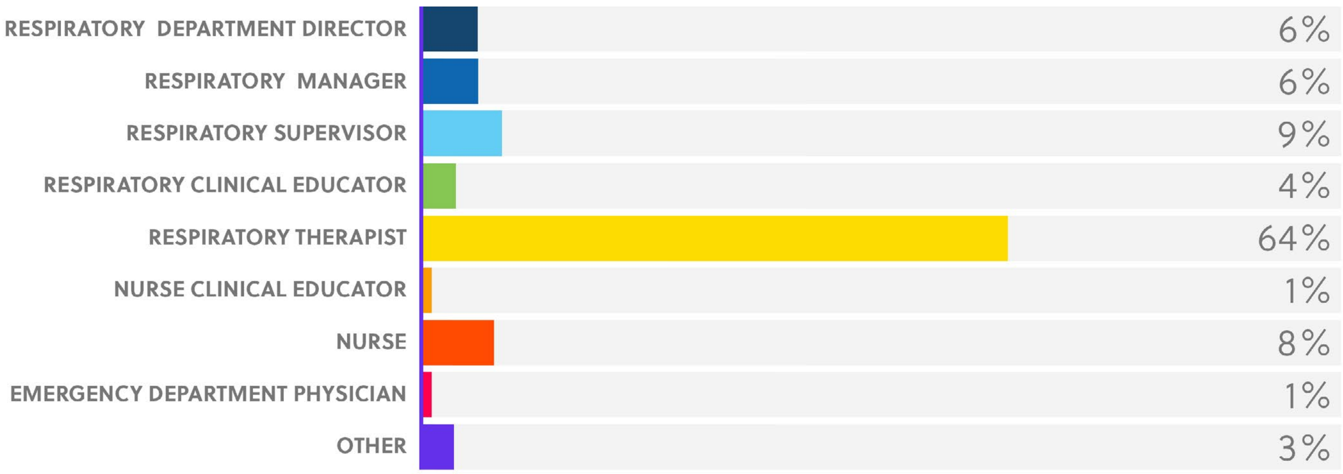


* Results have been rounded to the nearest percentage point.

Survey Results: COVID-19 Survey of US Healthcare Workers

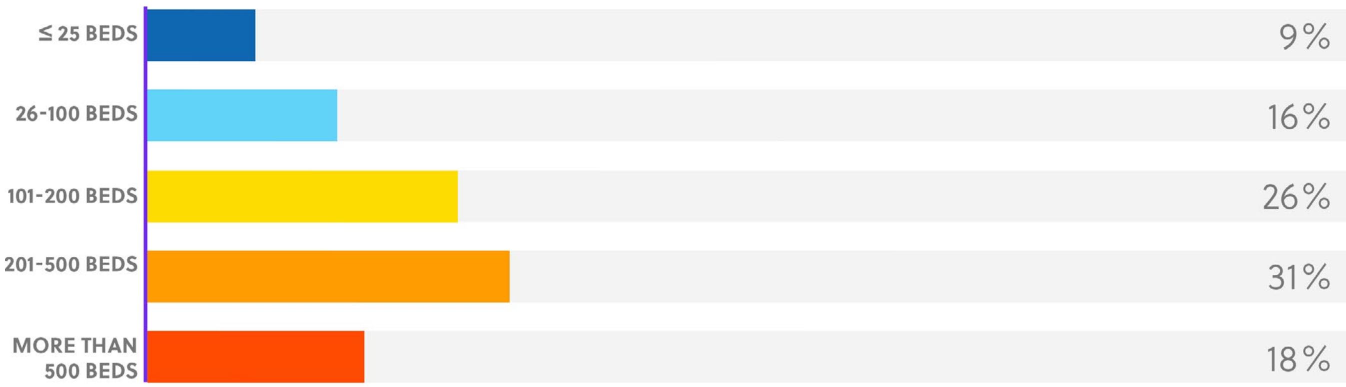
Question 1

What is your job title?



Question 2

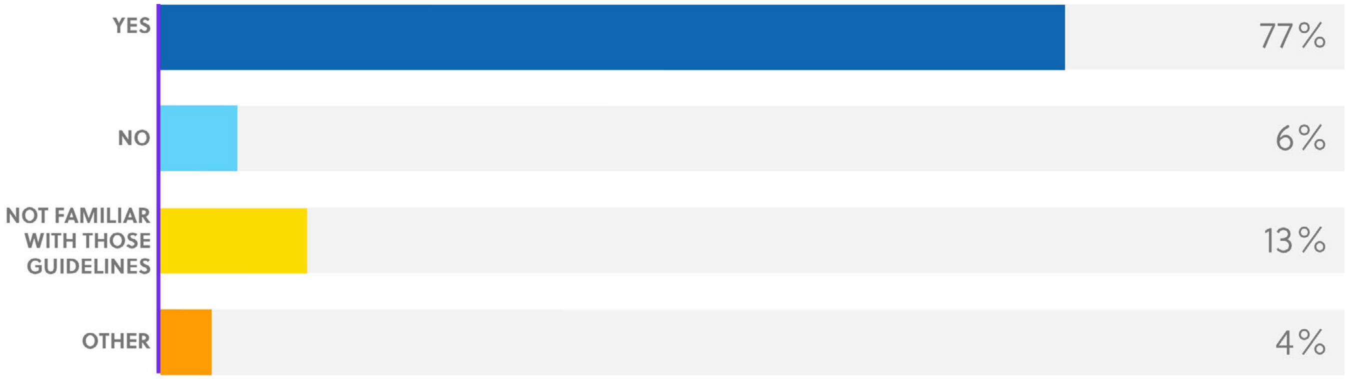
What is your hospital size?



Survey Results: COVID-19 Survey of US Healthcare Workers

Question 3

Are you following WHO, SCCM, and other organizations' guidelines and including the use of heated high flow oxygen on COVID-19 patients not requiring immediate intubation?



Question 4

Approximately, how many COVID-19 patients has your institution put on some form of respiratory support to date?

Survey Results: COVID-19 Survey of US Healthcare Workers

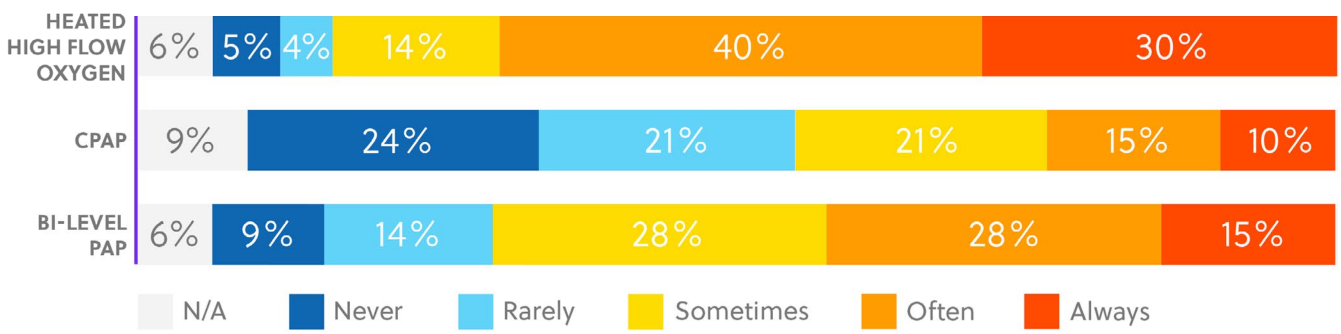
Question 5

Approximately what percentage of your COVID-19 patients have required intubation and invasive mechanical ventilation?

The average of all responses was 29%.

Question 6

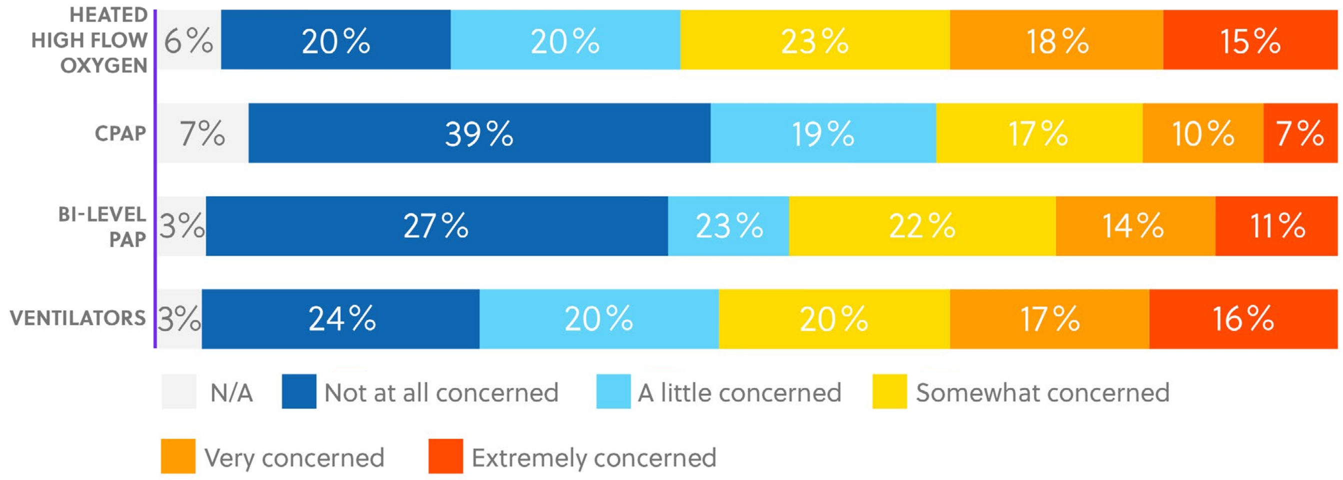
How frequently are you attempting the following non-invasive forms of respiratory support to avoid intubation and invasive mechanical ventilation of COVID-19 patients?



Survey Results: COVID-19 Survey of US Healthcare Workers

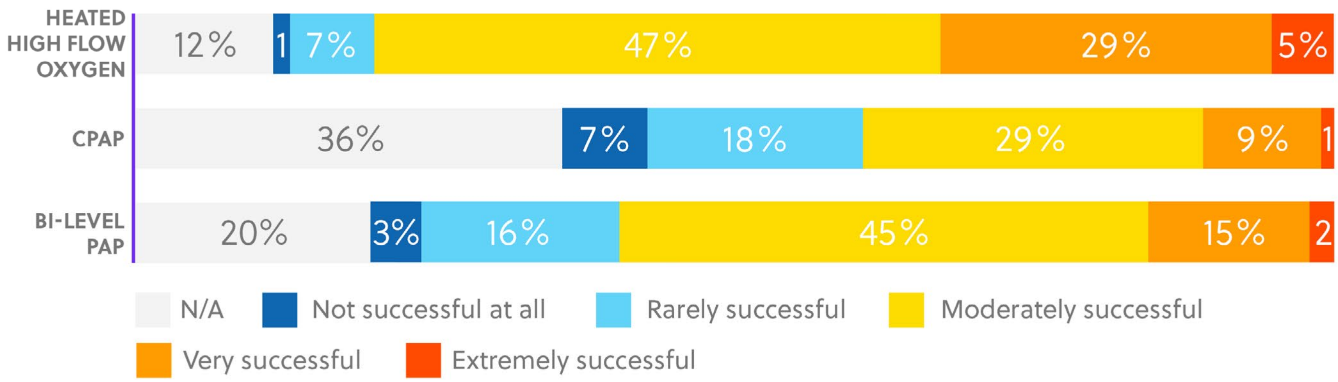
Question 7

How concerned are you about possibly running out of the following equipment due to COVID-19?



Question 8

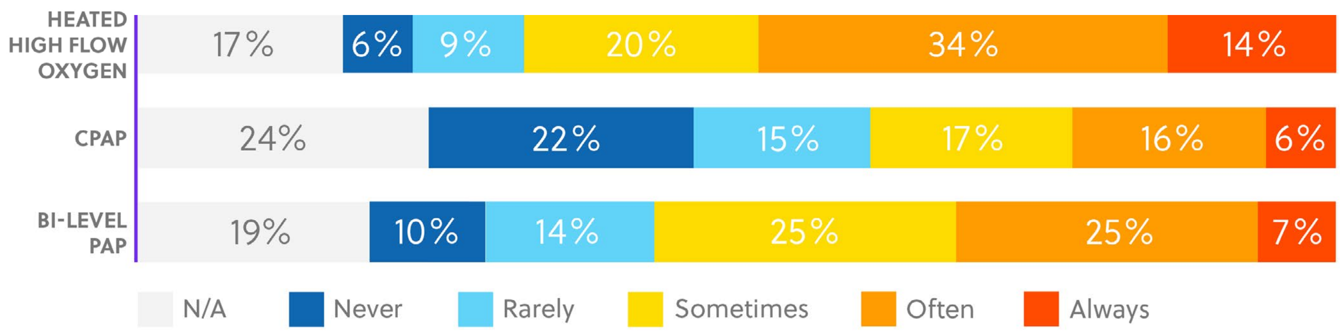
How successful are these non-invasive forms of respiratory support in helping to prevent intubation and mechanical ventilation in COVID-19 patients?



Survey Results: COVID-19 Survey of US Healthcare Workers

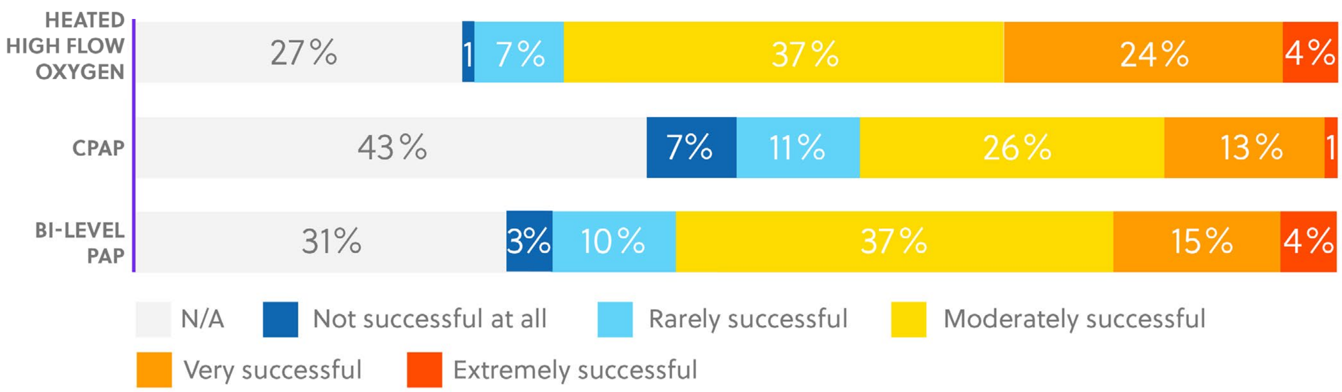
Question 9

How frequently are you attempting the following non-invasive forms of respiratory support to wean COVID-19 patients from invasive mechanical ventilation?



Question 10

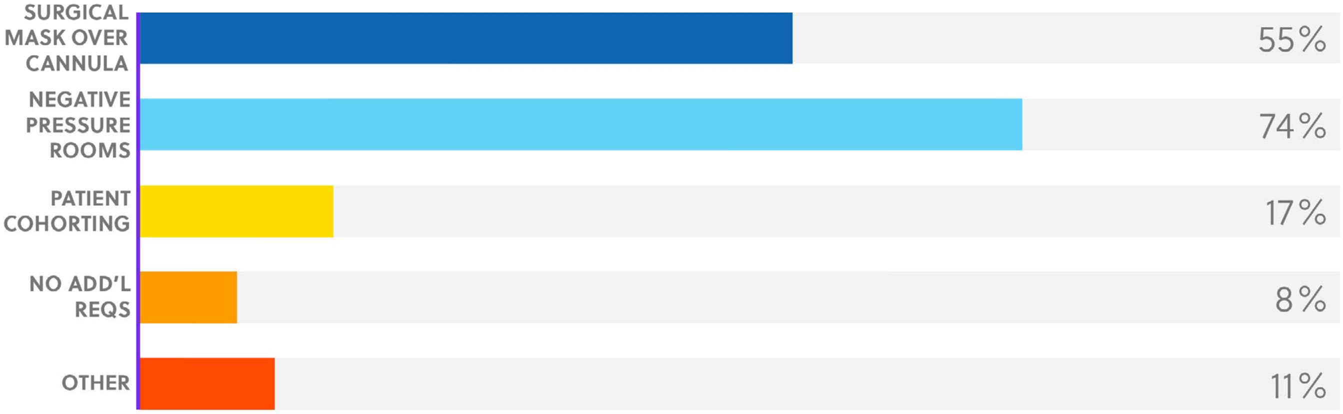
How successful are these non-invasive forms of respiratory support in weaning COVID-19 patients from mechanical ventilation?



Survey Results: COVID-19 Survey of US Healthcare Workers

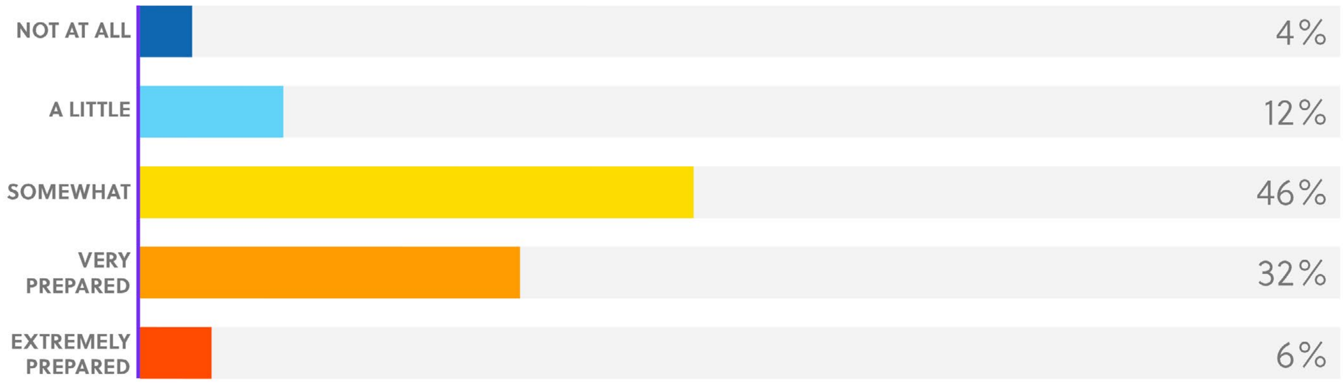
Question 11

How successful are these non-invasive forms of respiratory support in weaning COVID-19 patients from mechanical ventilation?



Question 12

How prepared do you feel for the next COVID-19 surge?



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Question 13

What, if anything, would help you feel more prepared? (Write in answer)

The most common trend in this write-in was more consistent access to PPE without the need to recycle it. The second most common trend was access to accurate information and better communication within the institution.

Results Summary

The methodology for this survey does not lend itself to drawing any definitive conclusions about the performance of certain precautions or respiratory support modalities in the management of COVID-19 patients. Nevertheless, it does provide some interesting and informal insights into potential trends.

The majority of respondents indicated that they were familiar with the guidelines to include high flow modalities for respiratory distress management of COVID-19 patients. This correlates with this survey's trend that, on average, high flow modalities were the primary tool that respondents used to try to prevent intubation. On average they were also more successful in helping patients avoid intubation by comparison to CPAP and Bi-Level PAP modalities. Furthermore, respondents indicated that they were most worried about running out of high flow modalities, closely followed by ventilators. While not significant, this finding indicates a trend away from intubation as a first-line response and a focus on high flow to try to prevent intubation.

Regarding intubation rate, respondents on average noted that 29% of their COVID-19 patients were intubated. This number seems in line with Gattinoni et al.'s observation that about 20-30% of COVID-19 patients are Type H and require mechanical ventilation.[21]

For weaning off mechanical ventilation, respondents on average listed high flow modalities as most successful, closely followed by Bi-level PAP. CPAP was listed as non-applicable for weaning by 43% of respondents.

As for transmission precautions during high flow treatment, in addition to PPE, the two most commonly listed ones were Negative Pressure rooms (75% of all respondents) and patients wearing surgical masks (55% of all respondents). The "other" write-in answers also echoed versions of patient isolation and particle containment.

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For the final questions, a plurality of respondents said they were somewhat prepared. Below are a few select answers to the question of what would make you feel more prepared for the next surge.

Extremely Prepared – "Quality leadership."

Very Prepared — "more PPE and more equipment and more knowledge about COVID by experts"

Somewhat Prepared — "vaccine and better pharmacologic therapy more availability of equipment"

A Little Prepared — "More education regarding PPE; many staff when floated (not respiratory) do not fully understand what to do. More education regarding therapies. More staff availability."

Not At All Prepared — "Sufficient PAPRs for all the staff who want/need to use them. Negative pressure isolation for entire COVID unit, as well as for individual rooms. Right now we have none of our COVID patients under negative pressure. Sufficient PPE and staff education to ensure that all staff are protected at all times. MUCH more testing of staff, especially on COVID units, and contact tracing for staff who get sick (we have no regular staff testing or contact tracing yet). Sufficient staffing to support COVID units. Right now we are expected to treat PCU COVID patients with the same staffing ratios as regular Telemetry patients. It is physically impossible."

It's worth noting that in addition to an emphasis on PPE, there were repeat expressions of frustration about the politicization of the virus and lack of clear and consistent guidelines about best practices. This plea for better communication was consistent with respondents who noted that they felt somewhat or less than somewhat prepared.

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