Intermittent Positive Airway Pressure Devices as a Substitute for Mechanical Ventilators during Ventilator Shortages

Bilevel positive airway pressure (BiPAP®) and continuous positive airway pressure (CPAP) are noninvasive positive pressure ventilation (NIPPV) modes routinely used to treat critically ill patients with respiratory failure. In this context, safe BiPAP and CPAP delivery requires a full-feature mechanical ventilator or a specialized NIPPV ventilator. However, during ventilator shortages caused by the COVID-19 pandemic, some have proposed using “nonventilator” BiPAP and CPAP machines to support critically ill patients until a ventilator becomes available. These machines are greatly simplified versions of NIPPV ventilators and are widely used to treat ambulatory patients with chronic conditions, such as obstructive sleep apnea, on an intermittent and often outpatient basis. These intermittent BiPAP and CPAP therapy machines provide limited monitoring and ventilation capability because they were made for use in patients who do not need life support. This report focuses on the safety and effectiveness of off-label use of these intermittent BiPAP and CPAP machines as temporary ventilator support for critically ill patients during ventilator shortages.

No clinical studies provide direct evidence on the safety and effectiveness of off-label use of intermittent BiPAP and CPAP machines to support critically ill patients during ventilator shortages. Two small randomized controlled trials (RCTs) from Italy and Africa used intermittent CPAP, but full ventilators were either available as backup or not critical for patient care. These studies suggest that intermittent CPAP machine use is feasible for first-line support of acute respiratory failure but need further validation. However, controlled studies to address the question of off-label use of intermittent BiPAP and CPAP machines are limited by ethical barriers, although data collected during critical ventilator shortages may help guide future crisis responses. Two regulatory bodies (FDA and Australia Register of Therapeutic Goods) have endorsed off-label use of intermittent BiPAP and CPAP machines during the 2019-20 Covid-19 outbreak, but medical societies caution that delivering NIPPV with these machines poses risks of airborne infection transmission. Please see this full report for additional safety risks.

Evidence limitations: In 1 RCT, CPAP patients received support with a full-feature ventilator upon meeting intubation or mandatory ventilation criteria; the other RCT did not specify whether patients met such criteria. These RCTs represent experiences in patients with different demographics and etiologies than encountered with COVID-19 and are at risk of bias from small size and/or single-center focus. The feasibility of prospective studies implementing this practice is limited by ethical barriers; however, laboratory studies with human surrogates and data collected during crisis situations would be valuable to guide healthcare provider decisions during critical ventilator shortages.

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Executive Summary

Findings

2 RCTs provide limited indirect evidence on use of intermittent CPAP for severe acute respiratory distress.

- 1 RCT (Brambilla et al. 2014, n = 81) conducted in Italy reported that first-line CPAP using an intermittent Breas CPAP device and a CaStar CPAP helmet allowed successful treatment of adult patients with severe acute respiratory distress. There was less need for intubation and mechanical ventilation than for first-line treatment using high-flow oxygen therapy (16% versus 63%, relative risk 0.24 [95% CI 0.11 to 0.51]. No treatment-related adverse events (AEs) occurred in either group.

- 1 RCT (Wilson et al. 2013, n = 70) conducted in Africa and using 1-hour-delayed treatment as a control reported that CPAP delivered via an intermittent IntelliPAP device and Hudson RCI® nasal prongs successfully achieved breath normalization (rate reduction 16 versus 0 breath/min) in children <5 years old presenting with tachypnea. Authors reported no CPAP-related AEs.

Evidence

Search dates: January 1, 2010, to March 30, 2020. We reviewed full text of 2 RCTs reporting on 81 adults and 70 children.

- We included studies of devices intended for intermittent BiPAP and CPAP in ambulatory patients and excluded studies of NIPPV delivered with full-feature ventilators, NIPPV ventilators, or BiPAP and CPAP machines designed for continuous support of patients with severe respiratory failure. See full text for excluded devices and studies.

- 1 RCT (Brambilla et al. 2014; n = 81) conducted in Italy compared high-flow oxygen therapy with CPAP in adults with severe acute respiratory failure from pneumonia and reported on patient oxygenation and need for intubation. Full-feature ventilators were available and used as needed when patients met mandatory ventilation criteria.

- 1 RCT (Wilson et al. 2013, n = 70) conducted in Africa compared immediate CPAP with 1-hour delayed CPAP in children younger than age 5 years who had tachypnea and reported on breath normalization.

Guidelines, Position and Consensus Statements


- 3 guidance documents by American, Australian, and European medical societies, 1 by the World Health Organization (WHO), and 1 by the U.S. Department of Defense (DoD) caution healthcare providers that NIPPV may facilitate Covid-19 spread and should be avoided or implemented with adequate risk mitigation strategies.

- 2 guidance documents by FDA and the Australian Registrar of Trade Goods endorse use of ambulatory and intermittent BiPAP and CPAP therapy devices for select patients with Covid-19 as a strategy to mitigate ventilator shortages.

- 2 documents by the U.K. Medicines and Healthcare Products Regulatory Agency list required minimal specifications for devices rapidly manufactured to address ventilator shortages; the specifications may not be met by many commercially available BiPAP and CPAP devices intended for intermittent therapy in ambulatory patients.
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Background

Introduction

Mechanical ventilators are required critical equipment in all emergency and critical care settings. According to a 2010 study, 65,000 full-featured ventilators and 98,000 devices with partial ventilator capabilities, including anesthesia gas machines, transport ventilators, and NIPPV machines, are available in the United States. Understanding the typical pathway for treating respiratory insufficiency for hospitalized patients is important to understand each modality and when it is intended to be used.

For patients admitted with mild respiratory distress, conventional or high-flow oxygen therapy is the first-line therapy. If respiratory distress progresses to or beyond moderate severity, NIPPV in CPAP or BiPAP modes becomes the therapy of choice, provided that patients can protect their airway (e.g., not deeply sedated, paralyzed, or in coma). In critical care settings, clinicians use full-featured ventilators or specialized NIPPV ventilators (e.g., Respironics V60, BiPAP Vision [(Respironics Inc., Murrysville, PA, USA; a subsidiary of Philips NV, Amsterdam, Netherlands)]). Some patients with severe acute respiratory distress may require ventilation modes that only a full-featured ventilator can provide. Full-featured ventilators also become mandatory in patients who are unable to protect their airway and require endotracheal intubation. Clinicians may also choose early intubation for practical reasons—for instance, in patients expected to worsen or to minimize the risk of airborne disease spread by reducing free aerosols.

Crisis situations, such as mass trauma events or disease outbreaks such as COVID-19, can temporarily overwhelm respiratory support capacity at acute care centers, sometimes on a countrywide or global scale. A shortage of full mechanical ventilators and full-feature CPAP or BiPAP machines has led some to propose use of a type of machine that is typically used only for outpatient or home support on an intermittent basis for chronic conditions. This report examines the safety and effectiveness evidence of these intermittent CPAP or BiPAP machines and the risks in the era of COVID-19. Such use constitutes an off-label use these machines were not designed for.

Mechanical Ventilation

Mechanical ventilators are life-support devices that move gas (i.e., air and/or oxygen) to and from a patient's lungs. These devices are intended to sustain patients who are critically ill and cannot breathe on their own or who require assistance to breathe adequately. Circumstances that require mechanical ventilation include severe respiratory illness, trauma, congenital defects, or the effects of drugs (e.g., anesthetics). Mechanical ventilation may be delivered noninvasively with a breathing mask or helmet, but patients who cannot protect their airway (e.g., sedated, comatose, with bulbar paralysis) require endotracheal intubation. Clinicians may also choose early intubation for practical reasons (e.g., when patients are expected to worsen or are infected with an airborne pathogen). (For additional information, see the Medscape article Mechanical Ventilation.)

Mechanical ventilators used in critical care are electrically powered, microprocessor-controlled, gas-flow systems that use blowers, bellows, or fans to deliver cyclic (inspiratory and expiratory) airflow from a pressurized gas source, such as a compressor, tank, or wall-mounted supply line to the patient's airway. Current ventilators can use many different algorithms, or ventilation modes, to provide full or partial support depending on the patient's condition and needs. Clinicians broadly classify ventilation based on the supported breathing parameter (volume or pressure) and the breathing cycle control (patient-initiated, machine-initiated, or hybrid). Patients are connected to the ventilator with a breathing circuit consisting of disposable tubing and valves and accessory devices such as heaters, humidifiers, nebulizers, and gas monitors. (For additional information, see the ECRi Product Comparison, Ventilators, Intensive Care.)
NI PPV Devices: NI PPV Ventilators and Intermittent BiPAP and CPAP Devices

NI PPV devices encompass a variety of pressure-controlled ventilation modes with a broad application range that includes acute and chronic respiratory conditions. NI PPV may involve cyclic inspired/expired pressures (BiPAP) or continuous pressure against which the patient breathes (CPAP). BiPAP modes are intended to facilitate inspiration and can substitute for spontaneous breathing if set to timed control. BiPAP may be suitable for patients with compromised motion (e.g., patients with neuromuscular diseases). CPAP does not support breathing motion; rather, the pressure helps maintain the airways open in patients prone to airway or alveolar collapse (e.g., patients with sleep apnea). (For more information, see the 2018 Medscape article by Kaynar and Sharma and the 2017 Medscape article by Soo Hoo).

Devices for NI PPV vary in design and specifications according to their intended application but fall into two broad and sometimes overlapping categories. One type is intended for inpatient, the other for outpatient ambulatory use at home are in an overnight sleep clinic for intermittent support.

- **NI PPV ventilators:** These devices are intended for continuous support in hospitalized patients who have acute, moderate-to-severe respiratory failure. To be classified as a “ventilator,” an NI PPV device must be capable of timed BiPAP with breath rate monitoring and 100% oxygen supplementation. NI PPV ventilators are intended to also detect and compensate for air circuit leaks and track inhaled/exhaled pressures and volumes. The Respironics V60 ventilator, considered the gold standard NI PPV device for critical care, is cleared for marketing by FDA under Product Code MNT (Ventilator, Continuous, Minimal Ventilatory Support, Facility Use). FDA has also cleared ventilators with similar capabilities, but simplified interfaces and portable design, for continuous at-home or in-hospital use under Product Code MNS (Ventilator, Continuous, Non-Life-Supporting).

- **Intermittent BiPAP and CPAP therapy machines for at-home or outpatient use:** These devices are intended to support daily activities on an intermittent basis in patients with chronic respiratory conditions such as chronic obstructive pulmonary disease and obstructive sleep apnea. These devices are not required to deliver timed BiPAP or to possess an inflow port for oxygen supplementation from a concentrated source (e.g., tank or wall outlet). These devices may include alarms to detect therapy interruption, but they do not monitor breath. Typically, the devices have simple interfaces and a small footprint for at-home use. Some are used in hospitals but rarely in a critical care setting. Many such devices are available in the United States with FDA clearance under Product Code BZD (Ventilator, Non-Continuous [Respirator]), which requires performance and safety standards less stringent than those for MNT and MNS devices.

(See the ECRI reports Positive Airway Pressure Units, Noninvasive and Ventilators, Sub-acute/home care for additional information and descriptions of representative devices.)

Safety and Ethical Concerns of Intermittent BiPAP and CPAP Devices as Ventilator Substitutes

When options for ventilation with conventional intensive care unit (ICU) equipment are exhausted, some experts and healthcare agencies advocate using intermittent BiPAP and CPAP therapy machines as bridge devices to support critically ill patients until a full mechanical ventilator becomes available. This practice may, in principle, allow healthcare centers to treat more patients and to optimize ventilator use during a crisis. However, significant drawbacks are likely to complicate implementation and patient selection.

**Safety Risks**

- Suboptimal ventilation with pressure-controlled BiPAP and CPAP in patients with severe respiratory failure may result in disease progression, injury, or death. In the context of critical ventilator shortages, this risk is assumed and considered to be lower than the risk of providing only minimal support with low-flow oxygen while awaiting a ventilator.

- Using intermittent BiPAP and CPAP therapy in patients with severe respiratory failure involves additional risks because the machines are not designed to operate for days or weeks and may become prone to failure. High-flow oxygen therapy (HFOT) is an alternative form of support intended for continuous use.
HFOT involves using a nonsealing mask or nasal cannula to deliver a pressurized oxygen-air stream to the patient. Like CPAP, HFOT may keep airways open and facilitate alveolar recruitment, but HFOT does not guarantee a positive airway pressure at the end of expiration. Thus, HFOT may not be suitable for all CPAP candidates.

- Both HFOT and NIPPV involve increased risks of airborne disease spread compared with those of endotracheal intubation, and risks and benefits must be considered carefully during airborne disease outbreaks. Using filters and environmental infection risk controls (e.g., air purifiers) may mitigate infection risks. Intermittent BiPAP and CPAP therapy devices, however, are typically not designed for use with environmental filters and may require custom and haphazard modifications.

**Ethical Concerns**

- Using devices outside their labeled indication during a time of crisis is generally considered appropriate; however, a legal framework to protect healthcare providers from legal liabilities may not be available at the time and place of a crisis. In addition, patient selection criteria in the context of ventilator allocation optimization are unclear. Patients with early or less severe dysfunction are most likely to tolerate suboptimal support; allocating intermittent BiPAP and CPAP therapy machines to these patients may free ventilators for use in patients with more severe or advanced disease. However, triage-based ventilator allocation also prioritized patients who are most likely to benefit from treatment and survive the disease. Thus, candidate overlap may result in conflict between intermittent BiPAP and CPAP and ventilator-allocation policies.

For additional information, see the following documents:
- Expanding the Use of Noninvasive Ventilation During an Epidemic
- For Critically Ill Patients, Is High-Flow Nasal Cannula Oxygen Delivery a Suitable Alternative to Mechanical Ventilation?
- Ventilator shortage - CPAP Machines to the Rescue?
- CPAP Machines Were Seen as Ventilator Alternatives, But Could Spread COVID-19
- FDA communication: Ventilator Supply Mitigation Strategies: Letter to Health Care Providers

**Alternative and Complementary Crisis Ventilation Capacity Management Strategies**

Using intermittent BiPAP and CPAP in critical care is intended as a last-resort resource management measure. When ventilation demand is expected to exceed capacity, healthcare providers have also considered the following measures in advance or in parallel to off-label BiPAP and CPAP device use:

- **Use of non-FDA-cleared ventilators:** Full-featured and NIPPV ventilators available with a CE mark in Europe and registered with the Australia Register of Therapeutic Goods are subject to stringent safety and performance evaluation requirements and may readily replace FDA-approved devices. Some manufacturers, such as Medtronic (Dublin, Ireland), have also made their designs available for assembly by third parties, and open-source designs are also available. (For additional information, see the FDA Enforcement Policy for Ventilators and Accessories and Other Respiratory Devices during the Coronavirus Disease 2019 (COVID-19) Public Health Emergency.)

- **Ventilator sharing:** Contemporary ventilators feature a single internal airflow circuit and are designed to support one patient at a time. Connecting a ventilator to several patient circuits is feasible, but careful patient selection and close monitoring are needed because operators have no direct control on individual airflow to each patient. Nonetheless, some centers have reported success with this strategy. (For more information, see the ECRISpecial Report Single Ventilator Use to Support Multiple Patients, the ECRI Webinar Strategies to Mitigate Ventilator Shortages, and the news article ‘The Other Option Is Death’: New York Starts Sharing of Ventilators.)

- **Triage-based allocation:** As a last resort, clinicians can follow triage principles to maximize effective ventilator use by not ventilating or terminating ventilation in patients who are not expected to recover. This approach operates, in principle, in opposition to that of ventilator sharing and raises ethical concerns of its
Response to Ventilator Shortages during the 2019-2020 COVID-19 Outbreak

On March 24, 2020, FDA issued an Emergency Use Authorization covering non-FDA-approved ventilators, alternative devices not approved or cleared for critical respiratory support, and devices intended to facilitate ventilator sharing. The document reflects final adoption for Enforcement Policy Guidelines that FDA issued earlier in March 2020.

On March 22, 2020, FDA issued Ventilator Supply Mitigation Strategies: Letter to Health Care Providers that outlines and endorses the strategies discussed on the later EUA and recommends providers consult with manufacturers regarding approved indications and potential device modification and off-label use to face ventilator demands during the outbreak.

Guidelines, Position and Consensus Statements

Searches of PubMed, EMBASE, EGT, and other web-based resources identified the following eight relevant guidelines published between January 1, 2015, and March 30, 2020:

- **American Society of Anesthesiologists. COVID-19: Information for Healthcare Professionals.** 2020. This online guidance document does not address ventilator shortages but states "in patient with acute respiratory failure, it may be prudent to proceed directly to endotracheal intubation, because non-invasive ventilation (e.g. CPAP or BiPAP) may increase the risk of infectious transmission."

- **Australian Government Department of Health. COVID-19 Information for Clinicians on Ventilators and Alternative Strategies When in Short Supply.** 2020. Off-label use and modifications may be applied to ventilators, anaesthesia gas machines and other devices intended for respiratory support, in response to the COVID-19 pandemic. Although inclusion in the Australian Register of Therapeutic Goods (ARTG) is required for a medical device to be lawfully supplied, the TGA takes a proactive stance with respect to repurposing of alternative devices (such as veterinary devices) and rapid establishment of new manufacturing capability.

  The TGA believes that modifications would not create undue risks in the following scenarios...

  - The potential advantages of using HFNO [high-flow nasal oxygenation] and NIV [noninvasive ventilation] need to be balanced against the risk of virus aerosolization. It should be assumed that NIV and HFNO are aerosol generating. Patients receiving these therapies should be cared for in airborne isolation rooms and staff should wear full PPE [personal protection equipment] (including N95/P2 masks) while in the patient's room.


  - In the event of more patients than ventilators, then patients requiring intubation can be intubated and bag valve mask ventilated until a lower acuity patient can be extubated. Splitting ventilators with use of viral filters in patients with similar pulmonary compliance has also been proposed.

- **FDA. Ventilator Supply Mitigation Strategies: Letter to Health Care Providers.** 2020. FDA states:

  - If the number of ventilators in your facility is running low, consider alternative devices capable of delivering breaths or pressure support to satisfy medically necessary treatment practices for patients requiring such ventilatory support.
Continuous Positive Airway Pressure (CPAP), auto-CPAP, and bilevel positive airway pressure (BiPAP or BPAP) machines typically used for treatment of sleep apnea (either in the home or facility setting) may be used to support patients with respiratory insufficiency provided appropriate monitoring (as available) and patient condition.


- It is beyond the scope of this document to discuss the efficacy of NIV and HFNO for the treatment of respiratory failure in the COVID-19 patient group. We have, however, considered the risks and benefits of these therapies as an adjunct to tracheal intubation, in order to make the recommendations below.

- Until further data become available, it should be assumed that NIV and HFNO are aerosol generating. Patients receiving these therapies should be cared for in airborne isolation rooms and staff should wear close contact aerosol protective PPE (including N95/P2 masks) while in the patient room.

- If NIV is used for pre-oxygenation, any perceived advantage over the technique outlined above should be balanced against increased complexity and risk of aerosolisation. A viral filter should be inserted between the face mask and the circuit, and the ventilator placed on standby prior to removing the mask.


- In adults with COVID-19 and acute hypoxemic respiratory failure, we suggest using HFNC over NIPPV (weak recommendation, low quality evidence).

- Given the evidence for a decreased risk of intubation with HFNC compared with NIPPV in acute hypoxemic failure, and studies suggesting that NIPPV may carry a greater risk of nosocomial infection of healthcare providers, we suggest HFNC over NIPPV.


- Rapidly Manufactured CPAP System (RMCPAP):
  Mechanical ventilation with PEEP through an endotracheal tube remains the mainstay of respiratory treatment in patients with severe respiratory failure from COVID-19. There is however some recent evidence that less invasive means of ventilation may have a role...
  This is a specification of the minimally (and some preferred options) clinically acceptable CPAP system.

  RMCPAP [rapidly manufactured CPAP] must deliver inspired oxygen concentration in the range 35 – 80% to the patient, selectable by the user.

  Should consume less than 5 L/m of oxygen, but could consume up to 10 L/m. Must not consume more than 15 L/m of oxygen (this may require the use of a reservoir).

  Must maintain a nearly constant airway pressure of between 5–15 cmH2O, with the ability to adjust the pressure.

  Must either alarm or be provided with a suitable air entrainment system if the fresh gas supply fails which prevents significant rebreathing.

  Must be reliable. RMCPAP must be capable of continuous operation (100% duty cycle) for 14 days.

- Rapidly Manufactured Ventilator System Specification:
  Must have mandatory ventilation (for the deeply sedated and paralysed).

  Optional pressure support mode for those patients breathing to some extent themselves, for example, BiPAP.

  If the patient stops breathing in pressure support mode, it must failsafe automatically onto mandatory ventilation.
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User must be able to control inspired oxygen proportion (FiO2). The percentage of oxygen in the gas being breathed in by the patient. Room air is 21% oxygen.

At least 50% and 100% [oxygen] options.

The following should be continuously displayed so the user can verify:

- current settings of tidal volume, frequency, PEEP, FiO2, ventilation mode
- actual achieved rates of tidal volume, breathing rate, PEEP, plateau pressure, FiO2
- if it exists, in pressure support mode there must be real-time confirmation of each patient breath and an alarm if below acceptable range
- optionally CO2 monitoring included

WHO. Clinical Management of Severe Acute Respiratory Infection when COVID-19 Is Suspected. 2020. This interim guidance document reads: "Due to uncertainty around the potential for aerosolization, HFO, NIV, including bubble CPAP, should be used with airborne precautions until further evaluation of the safety can be completed."

Clinical Literature

We searched PubMed, EMBASE, the Cochrane Library, and selected web-based resources for clinical studies of respiratory support in patients with acute respiratory failure using positive airway pressure therapy devices not intended for this patient population. To reflect contemporary technology and clinical practices, we searched for studies published between January 1, 2010, and March 30, 2020. Our search strategies included the following keywords: ventilator, invasive, noninvasive, cpap, bipap, sars, covid-19, coronavirus, respiratory distress, pandemic, epidemic, supply shortage, intubation, apap. Please see the Selected Resources and References section for detailed search strategies.

We excluded from review studies of NIPPV with standard ICU ventilators or with NIPPV devices specifically intended or designed for continuous support in patients with acute respiratory failure. We defined these devices as those having the following minimal capabilities:

- Mandatory ventilation mode with breath monitoring and automatic switch to mandatory ventilation if the patient stops breathing on his/her own
- Air leak detection and compensation
- Oxygen supplementation to FiO2 100%
- Continuous 24-hour operation

We identified the following such devices in our searches but excluded them from assessment:

- 3 NIPPV ventilators cleared by FDA under Product Code MNT: Respironics V60, BiPAP S/T, and BiPAP Vision.
- 3 non-life-support NIPPV devices cleared by FDA under Product Code MNS: BiPAP AVAPS and BiPAP Synchrony (Respironics) and Resumed VPAP III ST-A (ResMed, Inc., San Diego, CA, USA).
- VENTIlogic LS (Löwenstein Medical GmbH & Co. KG, Bad Ems, Germany), a CE-marked device with capabilities similar to those of FDA-cleared MNS devices, including mandatory breath mode, breath monitoring, and oxygen supplementation.

We also excluded studies of neonates, in whom standard ICU ventilators are not routinely used because of their physiology.

We identified and reviewed full text of two studies, as follows:

- 1 RCT (n = 81) conducted in Italy compared HFOT with CPAP in adults with severe acute respiratory failure and reported on patient oxygenation and need for intubation.(1) CPAP involved use of a Breas flow generator (Vital Signs, Inc., now Breas Medical AB, Mölnlycke, Sweden) and a CaStar CPAP helmet interface (StarMed S.r.l, Mirandola, Italy).
1 RCT (n = 70) conducted in Africa used delayed treatment as a control and reported on breathing normalization in children younger than 5 years presenting with tachypnea and treated with CPAP using an IntelliPAP device (DeVilbiss Healthcare GmbH, Mannheim, Germany) and Hudson RCI CPAP nasal prongs (Teleflex Inc., Morrisville, NC, USA). (2)

We reviewed full-text articles available with open access or our library subscriptions. We also identified but excluded from review three studies that reported on pooled groups of patients treated with ambulatory, intermittent BPAP and CPAP devices and with intensive NIPPV machines or full-featured ventilators. (3-5) See Table 1 for a study details.

Evidence limitations. The RCTs provide only indirect evidence on the safety and effectiveness of using intermittent BiPAP and CPAP devices for NIPPV that were designed for intermittent ambulatory support as an ICU ventilator substitute. In one study, patients received support with a full-featured ventilator upon meeting intubation or mandatory ventilation criteria. The other study does not specify whether patients met such criteria. The studies represent experiences in patients with different demographics and etiologies, and they are at risk of bias from small size and/or single-center focus. Thus, findings requires independent validation. The feasibility of prospective studies implementing this practice is limited by ethical barriers; however, laboratory studies with human surrogates and data collected during crisis situations would be valuable to guide healthcare provider decisions during critical ventilator shortages.
### Table 1. Clinical Trials

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Study Type and Patients</th>
<th>Intervention</th>
<th>Findings Reported by Authors</th>
<th>Authors’ Conclusions</th>
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<tr>
<td>Brambilla et al. 2014(1)</td>
<td>Open-label, single-center randomized controlled trial (RCT) of 81 adult patients with severe hypoxemic respiratory failure (hARF)</td>
<td>Continuous positive airway pressure (CPAP) therapy with a Breas CPAP generator (Breas Medical) and a helmet interface (StarMed) (n = 41) or low-flow oxygen therapy with a Venturi mask (n = 40), Patients were switched to full ventilators as needed.</td>
<td>&quot;The proportion of patients meeting ETI [endotracheal intubation] criteria in the CPAP group was significantly lower compared to those in the control group (6/40 = 15% vs. 26/41 = 63%, respectively, p &lt; 0.001; relative risk 0.24, 95% CI 0.11-0.51; number needed to treat, 2) two patients were intubated in the CPAP group and one in the control group. The CPAP group showed a faster and greater improvement in oxygenation in comparison to controls (p &lt; 0.001). In either study group, no relevant adverse events were detected.&quot;</td>
<td>&quot;Helmet CPAP reduces the risk of meeting ETI criteria compared to oxygen therapy in patients with severe hARF due to pneumonia.&quot;</td>
</tr>
<tr>
<td>Wilson et al. 2013(2)</td>
<td>Open-label, multicenter RCT of 70 children (age 3 months to 5 years) presenting with tachypnea</td>
<td>Immediate or 1-hour delayed CPAP with an IntelliPAP generator (DeVilbiss Healthcare) and Hudson RCI CPAP nasal cannula (Teleflex)</td>
<td>&quot;The study was stopped after the enrollment of 70 subjects because of a predetermined stop value of P &lt; .001. Mean respiratory rate of children who received immediate CPAP fell by 16 breaths/min (95% CI 10-21) in the first hour compared with no change in children who had CPAP delayed by 1 hour (95% CI -2 to +5). Thirty-five of the patients had a positive malaria blood smear. There were 3 deaths as a result of severe malaria. No major complications of CPAP use were noted.&quot;</td>
<td>&quot;CPAP decreases respiratory rate in children with respiratory distress compared with children not receiving CPAP. The technology was successfully used by local nurses. No complications were associated with its use.&quot;</td>
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Selected Resources and References

Search Summaries

The following databases were used to identify the literature and related materials.

ECRI Institute Resources [searched January 1, 2010, through March 3, 2020]

Search Strategy:

ventilator; (noninvasive OR non-invasive) AND ventilation; CPAP

Results: We identified seven related reports. See also the ECRI COVID-19 Resource Center.

- Continuous positive airway pressure (CPAP) units. [Health Devices Journal]. 2019 Dec 30.
- Portable/Transport ventilators: breathe easier. 2010 March 1.
- Single ventilator use to support multiple patients. [Hotline]. 2020 March.
- Should we reconsider how often we intubate older patients? [Healthcare Risk Control]. 2018 Jun.


Search Strategy:


#3 ("Ventilators, Mechanical"[mj] OR "Respiration, Artificial"[mj]) AND invasive[ti] OR “Intubation”[mj] OR intubation*[ti] OR intubated*[ti])


#6 ("Ventilators, Mechanical"[Mesh] OR "Respiration, Artificial"[Mesh]) AND invasive[tiab] OR “Intubation”[Mesh] OR intubation*[tiab] OR intubated*[tiab])

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#8 (#1 OR (#2 AND #3 AND #5) OR (#4 AND #5 AND #6 AND #7))

Results: We identified 99 records.


Search Strategy:

#1 ('ventilator'/exp OR 'intensive care ventilator'/exp OR ventilator:ti OR ventilators:ti) AND (shortage* OR stockpile* OR shortfall:ti,ab)
#2 "Noninvasive Ventilation"/exp OR 'bipap device'/exp OR 'cpap device'/exp OR 'high flow nasal cannula'/exp OR 'high flow nasal cannula:ti,ab OR apap:ti,ab OR bpap:ti,ab OR cpap:ti,ab OR ((Philips OR respironics) NEXT/2 ("v60" OR "v 60"):ti,ab)
#3 'severe acute respiratory syndrome'/exp OR 'SARS-related coronavirus'/exp OR 'SARS coronavirus'/exp OR 'covid 19'/exp OR 'respiratory distress syndrome'/exp OR 'influenza'/exp OR 'pandemic'/exp OR 'epidemic'/exp OR 'Influenza virus'/exp OR (influenza* OR pneumonia* OR pandemic* OR epidemic* OR COVID* OR coronavirus*:ti,ab)
#4 ('ventilator'/exp OR 'intensive care ventilator'/exp) AND ('respiratory tract intubation'/exp OR invasive:ti,ab OR intubation*:ti,ab OR intubated*:ti,ab)
#5 (#1 OR (#2 AND #3 AND #5) OR (#4 AND #5 AND #6 AND #7))

Results: We identified 7 unique records.


Search Strategy: Searched Cochrane Database of Systematic Reviews; Browsed Cochrane COVID-19 resource page

#1 "noninvasive ventilation" OR "non-invasive ventilation" OR "high flow nasal cannula" OR hfnc OR apap OR bpap OR or bipap OR cpap
#2 (ventilator OR ventilation) AND invasive OR intubat*
#3 #1 AND #2

Results: We did not identify any unique Cochrane Systematic Reviews pertaining to use of CPAP or other noninvasive ventilation in place of invasive ventilation for respiratory infections; however, Cochrane has created the following resource page to address the COVID-19 outbreak.


Guidelines and Standards [searched January 1, 2015, through March 30, 2020]

Search Strategy:

Ventilation; ventilators; CPAP; noninvasive ventilation; COVID-19

Results: We identified eight relevant documents.

Selected Standards and Guidelines

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Selected Web Resources. [searched March 30, 2020]
- Nishimura M. For critically ill patients, is high-flow nasal cannula oxygen delivery a suitable alternative to mechanical ventilation?
- NPR. CPAP Machines were seen as ventilator alternatives, but could spread COVID-19. 2020 Mar 27.

References Reviewed (PubMed and EMBASE search dates were January 1, 2000, through March 30, 2020)

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