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Article type : Educational Review

Handling Section Editor Prof :Britta von Ungern-Sternberg

Non-invasive ventilation in children: A review for the pediatric anesthesiologist.

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Conflict of Interest: None.

Statement: Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Abstract

Preserving adequate respiratory function is essential in the perioperative period. Mechanical ventilation with endotracheal intubation is widely used for this purpose. In select patients, non-invasive ventilation (NIV) may be an alternative to invasive ventilation or may complement respiratory management. NIV is used to provide ventilatory support and increase gas exchange at the alveolar level without the use of an invasive artificial airway such as an endotracheal tube or tracheostomy. NIV includes both continuous positive airway pressure (CPAP) and non-invasive positive pressure ventilation. Indications for NIV range from acute hypoxic respiratory failure in the intensive care unit or the emergency department, to chronic respiratory failure in patients with neuromuscular disease with nocturnal hypoventilation. In the perioperative setting, NIV is commonly applied as CPAP, and bilevel positive airway pressure (BPAP). There are limited data on the role of NIV in children in the perioperative setting, and there are no clear guidelines regarding optimal timing of use and pressure settings of perioperative NIV. Contraindications to the use of NIV include reduced level of consciousness, apnea, severe respiratory distress, and inability to maintain upper airway patency or airway protective reflexes. Common problems encountered during NIV involve airway leaks and asynchrony with auto-triggering. High-flow nasal oxygen (HFNO) has emerged as an alternative to NIV when trying to decrease the work of breathing and improve oxygenation in children. HFNO delivers humidified and heated oxygen at rates between 2-70 L/min using specific nasal cannulas, and flows are determined by the patient's weight and clinical needs. HFNO can be useful as a method for preoxygenation in infants and children by prolonging apnea time before desaturation, yet in children with decreased minute ventilation or apnea HFNO does not improve alveolar gas exchange. Clinicians experienced with these devices, such as pediatric intensivists and pulmonary medicine specialists, can be useful resources for the pediatric anesthesiologist caring for complex patients on NIV.

Key words: noninvasive ventilation, pediatric ventilation, high flow nasal oxygen, pediatric airway

Key points:

- NIV aims to decrease work of breathing and support alveolar gas exchange.
- CPAP and BPAP are the most common forms of NIV used in the perioperative settings.
- Pediatric anesthesiologists may encounter complex patients on home NIV and should be comfortable managing these patients and devices.
- HFNO is an alternative to provide respiratory support in patients spontaneously breathing.
- HFNO prolongs apnea time before desaturation but does not improve alveolar gas exchange in children.

1. Introduction

Non-invasive ventilation (NIV) is a ventilatory strategy that aims to increase gas exchange at the alveolar level using different interfaces, without requiring an artificial airway such as an endotracheal tube or tracheostomy. The modern concept of NIV was initially developed in the 1980s, and since, different indications and delivery systems for the NIV have been studied. NIV has applications for children with deteriorating oxygenation and ventilation in the intensive care unit and could be considered in the perioperative setting to temporize children with impending respiratory failure before mechanical intubation is required. Additionally, children with chronic hypercapnic respiratory failure and neuromuscular disease may be prescribed NIV for use at home. Pediatric anesthesiologists often care for complex patients who might be on NIV at baseline and present to the operating room for both airway related and non-airway related procedures. Given their dependance on NIV, many of these patients have physiology involving high oxygen consumption, limited oxygen reserves, and very little apnea tolerance; therefore, interruptions from their baseline NIV interface may be poorly tolerated. It is crucial for pediatric anesthesiologists to become familiar with the range of NIV devices, their capabilities, and settings, how to choose an initial interface to start therapy, as well as limitations of these devices. High-flow nasal oxygen (HFNO) supplementation has also emerged in the past few years as a way to avoid invasive mechanical ventilation and the risks associated with endotracheal intubation in specific patient populations. In this review, we describe the general principle of non-invasive ventilation followed by specific devices and interfaces and their mode of delivery. The perioperative use of NIV will follow. Indications and patient selection, acute versus chronic implementation, contraindications and complications, as well as pitfalls and solutions will be reviewed.

Case: A 6-year-old girl with history of spinal muscular atrophy type 1 and severe sleep apnea presents to the operating room for elective tonsillectomy and adenoidectomy. She is currently on non-invasive ventilation using BPAP (IPAP 14 cm H_2O/EPAP 5 cm H_2O) for 8 hours every night. She

uses a facemask interface. Her parents state that she is compliant with the device that was prescribed for nocturnal hypoventilation a year ago.

What are perioperative implications of her nocturnal non-invasive ventilatory support requirement? Can her home device be used during induction of anesthesia? Can this patient safely have same day surgery and be discharged home?

NIV delivers mechanical ventilatory support without the use of an invasive airway in patients with spontaneous breathing. To improve alveolar ventilation and oxygenation, positive pressure is delivered via an interface such as tight-fitting masks (full facemask, nasal mask) or CPAP hoods or helmets, among others[1]. The benefits of NIV include decreased work of breathing by reducing inspiratory effort[2,3], improving gas exchange while avoiding endotracheal intubation[4] and its associated risks, and decreasing the incidence of respiratory infections. NIV is usually well tolerated and requires minimal to no sedation. In the perioperative setting, NIV includes continuous positive pressure (CPAP), and bilevel positive airway pressure (BPAP). CPAP delivers a set amount of continuous positive airway pressure throughout the respiratory cycle. BPAP delivers a set positive airway pressure during inspiration and maintains a lower positive pressure during the expiratory phase of the respiratory cycle. NIV is intended to be a non-hermetic form of ventilatory support, and it incorporates the upper airway into the breathing pathway. BPAP delivers a set pressure when the machine detects the patient is triggering an inspiratory effort (inspiratory positive airway pressure or IPAP), and then a lower pressure is maintained during the expiratory phase (expiratory positive airway pressure or EPAP). The inspiratory time can be time-cycled or flow-cycled; This modality can also be referred to as BiPAP and non-invasive positive pressure ventilation (NIPPV). Some authors include HFNO as a form of NIV[5], as it has been increasingly used in the perioperative period to avoid invasive mechanical ventilation. However, it is important to note that the physiologic mechanisms to improve oxygenation and delivery methods for HFNO are fundamentally different from NIV. HFNO will be further discussed below. Table 1 summarizes common devices and interfaces with their advantages and limitations.

Medical devices and ventilators to deliver NIV:

There are a variety of devices available that are used for children on home NIV. Most of these devices fall in two general categories: sleep apnea equipment or more sophisticated ventilators or ventilatory devices with NIV capabilities. The later tend to be more expensive but provide additional alarms and regulators to prevent injuries and airway trauma. Brown and colleagues summarize device specific features in detail for home devices frequently prescribed in children[6].

In hospital settings, there are generally three systems to deliver NIV including: high-flow systems, fluidic logic systems, and ventilator CPAP systems; nonetheless, there is no evidence of superiority among any one of these systems.[7] Additionally, ventilators (neonatal, pediatric and portable models) can provide CPAP and BPAP, with a variety of settings to adapt to the patient's respiratory physiology.

Perioperative use of NIV:

No clear guidance is available regarding perioperative use of NIV, its timing in the course of a patient's surgical journey, and specific pressure settings that should be used. NIV might be an option for procedural sedation (e.g., CT scan, lumbar puncture, colonoscopy) in the spontaneous breathing patient, but is more commonly used post-operatively either due to patient comorbidity, or surgery that increases the risk for post-operative pulmonary complications. NIV and HFNO with their possible indications, possibilities and contraindications are summarized in Table 2. Much of the evidence describing the perioperative use of NIV comes from cardiac surgery patients. A retrospective study comparing HFNO and NIV in patients less than 6 months of age showed no superiority between the two strategies for rescue after failed extubation following cardiac surgery with cardiopulmonary bypass[8]. Some authors recommend that hospitalized patients eligible for NIV

should tolerate periods of time without ventilatory support and maintain SpO_2 with modest oxygen requirements and the ability to call for help if needed.[1]

The use of sedatives and opioids in the perioperative period may impair a patient's inherent airway tone and ability to protect their airway. Furthermore, central neuronal breathing control can also be suppressed. Patients should be monitored until these protective mechanisms are restored, particularly after ambulatory surgery or procedure. Patients with continuous NIV therapy at home should be admitted to a high acuity unit or intensive care unit (ICU) postoperatively as they may be at increased risk for complications.[9] The use of home NIV immediately following surgery is recommended in patients with obstructive sleep apnea (OSA) with careful postoperative monitoring.

Following open cardiac surgery, patients are at high risk of postoperative pulmonary complications. To prevent postoperative re-intubation after cardiac surgery NIV has been an area of focus, although with limited evidence. Observational data in children with post-extubation acute respiratory failure in the cardiac ICU setting reported that BPAP prevented re-intubation in approximately two thirds of the cases and was considered a safe alternative during escalation of care.[10,11]

Case series reporting the postoperative use of NIV after non-idiopathic spine surgery in addition to mechanical insufflator-exsufflator found the potential for its safe use after surgery in children with neuromuscular disease.[12] A clinical trial evaluating different strategies of intraoperative recruitment maneuvers during abdominal surgery found that children who receive 5 minutes of CPAP immediately post extubation as part of their alveolar recruitment strategy had improved oxygenation (measured by arterial blood gas and oxygenation indexes) for up to 12 hours after extubation.[13]

Indications and patient selection:

NIV indications in children include moderate to severe dyspnea or tachypnea, hypoxic respiratory failure, and or respiratory acidosis. NIV in the ICU is indicated for patients with hypercapnic or hypoxic respiratory failure who are hemodynamically stable, spontaneously breathing, and do not require immediate intubation[14]. Specific conditions that may fall within this category include pulmonary edema, dynamic upper airway obstruction (e.g. Pierre Robin sequence, tracheomalacia, laryngomalacia, etc.), pneumonia, cystic fibrosis, status asthmaticus, and acute chest syndrome. As mentioned above the evidence for perioperative NIV use is limited, however, NIV may be useful in high-risk patients with impending acute respiratory failure postoperatively, and patients on chronic ventilatory support (neuromuscular disease). When considering NIV use in the postoperative period reversible causes of hypoventilation, such as residual neuromuscular blockade, should be ruled out.

Implementation of NIV in the intensive care vs. home NIV

NIV has been used extensively in the ICU for acute hypoxic respiratory failure and/or hypercapnic respiratory failure. Benefits of NIV include avoidance of mechanical ventilation and its related-nosocomial infections. A multicenter retrospective study in pediatric ICU patients found supportive evidence in the use of NIV as an alternative to immediate tracheal intubation in patients in whom efforts to avoid tracheal intubation were being made[15]. Another multicenter prospective study found a reduction in mortality, length of ventilation and length of PICU stay when NIV was used as a first line of treatment in patients with unanticipated PICU admission compared to tracheal intubation.[16] Furthermore, another retrospective multicenter study in Italian intensive care units showed that the use of NIV has increased in the past few years to avoid invasive ventilation in children with less severe health status admitted to intensive care with bronchiolitis, pneumonia, prevention of postoperative failure and acute on chronic respiratory failure[17]. The same study reported that the rate of failure with NIV in postoperative patients was close to 20% and that subgroup represented approximately 8.2% of all the patients receiving NIV during the years included in the study.

Home NIV has been prescribed for various chronic diseases affecting respiratory function in children, especially in patients with decreased respiratory muscle strength and decrease respiratory drive due to neuronal disease[9]. A common indication for home CPAP in children is obstructive sleep apnea refractory to adenotonsillectomy[18], where CPAP functions as a "splint" to maintain patency of the pharynx and upper airway, to improve airway obstruction, decrease respiratory muscle load, and reduce the work of breathing. Home NIV may also be prescribed for patients with chronic hypercapnic respiratory failure, specifically in patients with neuromuscular and chest wall disease such as children with Duchenne's muscular dystrophy [19].

Clinicians caring for children on home NIV devices in the perioperative period should be comfortable using these devices, with special attention to the specific capabilities for maximum inspired fraction of oxygen (usually limited). Most devices need to be connected to a power source, although in some countries portable battery-powered devices may be available. Of note, battery life may be difficult to predict, and the device might not have the necessary delivery and monitoring capabilities needed for the perioperative setting[6]. Some families with children in advanced stage of neuromuscular disease may choose NIV as temporizing measure or alternative to avoid tracheostomy, which emphasizes the importance of a thorough preoperative assessment and discussion between the patient's family and the pediatric anesthesiologist.

In our experience, patients with chronic dependence on NIV are transferred to the ICU for postoperative recovery. NIV at typical baseline settings is reinitiated as soon as possible in the postoperative period, although some surgical procedures such as craniofacial surgery or adenotonsillectomy may preclude its application.

Contraindications:

General contraindications to NIV include reduced level of consciousness, apnea (poor respiratory drive), severe respiratory distress, inability to maintain upper airway patency, or airway protective

reflexes. Additional contraindications in children include severe respiratory distress with paradoxical abdominal muscles or thoracic muscle use, increased or inability to clear secretions, severe hypoxemia requiring endotracheal intubation, upper airway obstruction by a mass or tumor, inability to protect the airway (patient is unable to cough or gag), nausea or vomiting, hemodynamic instability, or significantly altered mental status. Relative contraindications include surgery, facial trauma, or facial deformity[14].

The use of NIV in patients with recent upper airway surgery, such as tonsillectomy, has been an area of controversy. A major risk of tonsillectomy is postoperative hemorrhage from the exposed surgical bed. Concern exists with the use of NIV and positive pressure following tonsillectomy due to potential expansion of the dissection plane resulting in subcutaneous emphysema and pneumothorax. Buzzi and colleagues studied 69 patients with extracapsular tonsillectomy performed over the course of 6.5 years who required NIV. A bleeding rate of 10.29% was found in these patients, with 5.9% requiring a second operation to control the bleeding. In this cohort, NIV was not associated with an increase in the risk of bleeding or other complications. The authors conclude that NIV may be a reasonable option to provide post-operative respiratory support to these patients although caution must be exercised due to their small sample size[20].

Complications:

NIV is considered safe and is widely used in the pediatric ICU[16] as well as for home therapy in patients with neuromuscular and chest wall disease[6]. Complications can be related to the interface, the degree of positive pressure support needed, as well as the device. These include: facial skin irritation, nasal discomfort, conjunctivitis, pneumothorax, air-leak, and auto-triggering with asynchrony[14]. Retrospective data has associated the use of NIV with an increased incidence of anastomotic leak and mediastinitis in neonates during the postoperative period following tracheoesophageal surgery.[21]

Feeding and nutrition may be affected with the use of NIV. The application of nasal CPAP in neonates can limit the use and advancement of tube feeds in the neonatal ICU. This is important to consider given that NIV is commonly prescribed in neonates due to the benefits seen with acute respiratory distress syndrome[22].

Initial settings:

Although there is no consensus on initial settings for NIV in the perioperative period, based on experience from pediatric ICUs, it is generally considered safe to start with initial IPAP between 6-8 cm H_2O and EPAP between 3-5cm H_2O for BPAP; and with an initial pressure of 5-8 cm H_2O for CPAP[14]. Another approach may be to start with a IPAP of 5 cm H_2O and EPAP of 5 cm H_2O in the cooperative and conscious patient while assessing the level of comfort as well as the degree of respiratory relief provided with these settings. Table 3 summarizes possible initial settings for NIV and HFNO. Then changes in the IPAP, EPAP and trigger can be titrated to maximize patient's comfort and clinical benefit. Brown and colleagues recommend starting with IPAP levels of 10-16 cm H_2O as initial support with an upper limit at 20 cm H_2O for pre-adolescents and 30 cm H_2O for adolescents. However, a physiological tidal volume should be targeted, not exceeding 10 ml/kg ideal bodyweight.[23] FiO_2 can be started at 0.4-0.6. The goals include to increase to a maximal IPAP between 8-15 cm H_2O and to keep and SpO_2 >95%. Other important settings when using BPAP include inspiratory trigger, pressure rise time, and expiratory trigger.

In our institutions, patients on home NIV undergoing thoracic, abdominal or ENT procedures other than myringotomies are routinely admitted to the ICU postoperatively where appropriate monitoring and adequate staff are available and familiar with the management of their NIV devices. This level of care is recommended until the patient has returned to their baseline mental status and analgesic drugs that can impair their respiratory function are no longer required. Clinicians experienced with these devices in the pediatric ICU and pulmonary medicine specialists can be useful resources for the pediatric anesthesiologist caring for complex patients on NIV.

Pitfalls and solutions:

The most common problem after starting NIV is an excessive airway leak between the interface and the patient, which emphasizes the importance of choosing the appropriate interface for the child and ongoing reassessment. Auto-triggering is also one of the most common issues encountered in children. Asynchrony can also be a challenge, and some authors suggest setting low inspiratory triggers while avoiding auto-triggering, presetting limited inspiratory time to avoid prolonged inspiratory time; and adjusting the flow threshold for the expiratory trigger.[14] For small children, apparatus dead space needs to be considered and minimized as much as possible particularly if additional equipment is included with the breathing circuit (e.g. heat and moisture exchanger). Of note, some home devices commonly used to deliver positive pressure ventilation using CPAP or BPAP are programmed with high flows to account for the airway leaks anticipated with the various interfaces used. These preset high flows can be dangerous when ventilating via an endotracheal tube due to the risk of barotrauma, volutrauma, and lung tissue injury. Another consideration is nasal congestion or bleeding, which can interfere with the delivery of NIV in the postoperative period.

End tidal carbon dioxide is commonly used to monitor patients on NIV. The use of this monitor may be limited by the respiratory apparatus dead space, leaks, fresh gas flow rates and tidal volumes. Transcutaneous carbon dioxide monitors can be useful in the hospital setting, especially when arterial blood gases may be impractical or difficult to obtain.[24] Frequent calibration is recommended for these devices.

HFNO:

The use of HFNO was first introduced in 1986 for children with severe upper airway obstruction[25]. It was then described in neonatal intensive care units (NICU) as an alternative to CPAP for apnea of

prematurity [26]. More recently, HFNO has emerged as an alternative to provide oxygenation in patients in the perioperative period. HFNO delivers completely humidified and heated oxygen at rates between 2-70 L/min using specific nasal cannulas, and the flows are determined by the patient's weight and clinical needs; usually, at a rate of 2 L/kg per minute. In pediatric anesthesia, the use of HFNO began after its first description in a case series of 25 patients in 2015[27]. Since then, the application of HFNO in adults and children during anesthesia is referred to as transnasal humidified rapid-insufflation ventilatory exchange (THRIVE). The alleged ventilatory effect of THRIVE is absent in both apneic adults[28] and children[29,30]. The use of the acronym THRIVE should be abandoned in favour of HFNO. In the United States HFNO devices available are only approved for use in spontaneously breathing patients.

High-flow nasal cannula system:

Oxygen is delivered using a system composed of a humidifier base, a heater wire, a temperature probe and a circuit which includes a humidifier chamber, tubing system and a pressure relief valve for the pediatric circuit. A blender added to the tubing system allows FiO_2 variation between 0.21 and 1.0 (Figure 1). It is imperative to ensure patency of nostrils during the use of HFNO. Greater than 50% occlusion of the nostrils by the cannula can risk barotrauma. Specific low resistance cannulas must be used to allow accurate flow titration according to the patient's weight, and thus avoid a dangerous increase in airway and circuit pressure. Should this occur in the pediatric breathing system, a pop-off safety valve is incorporated to prevent a pressure rise in the circuit of more than 40 cm H_2O.

Physiology during spontaneous breathing:

The administration of heated and humidified gas protects the airway mucosa, preventing acute trauma and inflammation caused by normal oxygen, which is usually cold and dry. This airway inflammation usually results in a disruption of mucociliary flow and retention of secretions. In

addition, the bronchial tree reacts with a bronchoconstrictor reflex to protect the lungs. Heated and humidified oxygen decreases the negative effect of high flow oxygen on the airway and the ciliary apparatus and decreases the patient's metabolic demands related to gas adjustment in the lower airways. Observational studies found a flow-dependent increase in pressure and a clear absence of clinically relevant pressure while the mouth remained open[31]. The mechanism for the positive airway pressure generation in spontaneously breathing patients is a result of the resistance to expiration caused by high velocity incoming gases which pressurize the upper airway above atmospheric pressure. In patients breathing with their mouth closed, this effect generates higher airway pressures. [32] This increase in mean pharyngeal pressure delivers some degree of positive pressure into the airway by "splinting" (4-6 cm H_20), maintains a higher functional residual capacity, and improves oxygenation. Furthermore, HFNO reduces air dilution of the delivered oxygen [33], increases the clearance of the dead space [34] with an increased clearance of carbon dioxide.

During the inspiratory phase the important physiological effect of high flow is based on matching of the inspiratory demand of the patient with the delivered flow rate. This contributes to decrease the work of breathing. If the correct flow rate is applied, patients experience facilitated inspiration. If the inspiratory demand increases such as during respiratory distress, the flow rate applied needs to be adjusted. Although HFNO is considered useful as an alternative to deliver oxygen supplementation in children with dyspnea, asthma, tracheomalacia and hypoxemic respiratory failure, there is limited evidence showing benefits over other non-invasive ventilation modalities.

Physiology of apneic oxygenation:

As oxygen passes through the unobstructed upper airways in the direction of the alveoli, apneic oxygenation occurs. The difference between alveolar oxygen extraction and carbon dioxide replacement generates a diffusion gradient resulting in subatmospheric alveolar pressures which initiate a subsequent aventilatory mass flow towards the alveoli [35]. A turbulent supraglottic gas flow which loops around the soft palate and exits the open mouth (keeping the mouth open is an

essential condition for safety) [36], is responsible for continuous flushing of the oral and pharyngeal cavity with gas from the cannula.

This gas movement is supported by cardiac oscillations which trigger a bi-directional air movement of around 10 to 30 ml per heartbeat in adults [37]. The mechanism of positive airway pressure generation as an important physiological mechanism of airway splinting supporting the oxygenation and ventilation in spontaneously breathing patients is absent in apneic patients[38]. The airway pressure during apnea with an open airway remains at atmospheric levels. HFNO allows extension of the safe apnoea period, and it is used clinically with increasing popularity[29].

Clinical applications of HFNO

HFNO can be used in spontaneously breathing and apneic patients in different age groups and in different clinical settings. HFNO might be used during procedural sedation (e.g., for gastroscopy) in the spontaneously breathing. In preterm infants, it is used for respiratory support after extubation [39] and for treatment of respiratory distress of different etiologies[40]. In infants, it has been described for use in the treatment of bronchiolitis and other respiratory illnesses. HFNO in patients with bronchiolitis decreases the rate of endotracheal intubation and the need for escalation of care, although its benefit over other non-invasive ventilation techniques has not been established in randomized clinical trials[41].

In pediatric anesthesia, HFNO has been used during induction of anesthesia for healthy children [29] and during pediatric pharyngo-tracheal surgery [42]. HFNO can be useful as a method for preoxygenation in infants and children[43]. During apneic oxygenation use, consideration should be given to maintaining airway patency, which could be achieved by means of suspension laryngoscopy or continuous application of jaw-thrust. An additional consideration when using these methods intraoperatively, is the rapid washout of the upper airway, and therefore maintenance of anesthesia should be provided with total intravenous agents.

HFNO prolongs apnea time before desaturation, however, in children with decreased minute ventilation or apnea HFNO does not improve alveolar gas exchange and can lead to increased hypercarbia.[44] Therefore, we suggest combined monitoring of standard vital signs such as pulse oximetry, ECG, non-invasive blood pressure, and end-tidal CO_2 with transcutaneous CO_2 monitoring. This can provide useful information about the increase in carbon dioxide during the apnea phase or about possible hypoventilation if used during spontaneous breathing.

While in spontaneous breathing usual initiation of therapy starts with 0.5 to 1 L/kg per minute of oxygen flow and can be raised stepwise to 2 L/kg per minute, in apnea flows of 2 L/kg per minute can be used for children up to 35 kg. Above 35 kg flows do not exceed 70 L/min. Flows of up to 4 L/kg per minute, although potentially safe, showed no clinical benefit compared to flows of 2 L/kg per minute[30]. Like CPAP or BPAP, the effect of HFNO can be evaluated by changes in heart rate, respiratory effort, and work of breathing 1 or 2 hours after therapy initiation. During preoxygenation on induction of anesthesia HFNO might maintain normal SpO_2 in the presence of apnea but end tidal carbon dioxide may continue to rise[45]. Reasons to consider HFNO for support after extubation, especially in the postanesthesia care unit, include reducing respiratory rate and work of breathing, preventing excessive CO_2 accumulation, ease of use, and convenience. Additionally, HFNO is generally well tolerated in young patients who can partially feed themselves and communicate despite the ongoing therapy. Furthermore, HFNO ensures adequate clearance of secretions and limits hypothermia and insensible water loss, keeps mucus more fluid and assists airway recovery (after surgery).

Contraindications for HFNO include hypercapnic respiratory failure, emergent need for invasive mechanical ventilation if not used for apneic oxygenation during intubation, facial injuries or anomalies preventing placement of nasal prongs, increased nasal or oral secretions, and agitation or inability to tolerate the interface. Complications are rare when proper setup and careful monitoring is applied, but there are case reports of pneumocephalus, pneumothorax and abdominal distension.[46]

NIV and HFNO in patients with aerosol-borne diseases

The ongoing advent of the Coronavirus Disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) has directed much attention to the use of respiratory devices. Possible routes of SARS-CoV-2 transmission are contact, droplets and aerosols. NIV and HFNO have been used in patients with COVID-19 in the effort to avoid tracheal intubation, but both therapies were initially limited in patients with COVID-19 due to concern of further airborne spread of aerosolizing virus. However, more recent data suggest that NIV and HFNO do not increase the risk of aerosol generation (Figure 2)[47]. Westafer and collaborators[48], in a retrospective evaluation, found no evidence of increased COVID-19 infections in healthcare workers after the introduction of a respiratory protocol using HFNO in patients with COVID-19. Another prospective observational study comparing the use of supplemental oxygen, CPAP, and HFNO to treat moderate or severe COVID-19 did not find an association with higher levels of viral contamination in the immediate care environment.[50] Furthermore, using an experimental chamber aimed to count total aerosol emissions, Wilson and colleagues[49] measured particle count of exhaled particles with an optical particle counter during six respiratory activities and compared them to the emissions during the same activities with a facemask, while using noninvasive positive pressure ventilation, and during HFNO. The study revealed that compared to quiet breathing, coughing increased the emission of particles 370-fold. The increase in particle emission with NIV and HFNO was modest compared to coughing or forced expiration. Also, HFNO reduced particle emission during coughing by half, and the use of facemask significantly decreased the number of particles generated during these activities. In summary, NIV and HFNO as a therapeutic option to provide respiratory support, should not be banned by clinicians in patients with aerosol-borne disease. The major aerosol-generating risk appears to be the coughing patient.[51] To avoid further confusion, we might reconsider the definition of aerosol-generating procedures and rather speak about aerosol-generating patients. Nevertheless, appropriate personal protective equipment for healthcare workers involved in care of COVID-19 patients remains crucial."

Conclusion

In summary, NIV is a means of providing mechanical ventilation without an artificial airway. General indications for NIV use include moderate to severe dyspnea or tachypnea, hypoxic respiratory failure, and or respiratory acidosis. Contraindications include severe hypoxemia requiring endotracheal intubation, reduced level of consciousness, apnea (poor respiratory drive), upper airway obstruction by a mass or tumor, absence of airway protective reflexes, nausea or vomiting, and hemodynamic instability. Relative contraindications include facial surgery, trauma, or facial deformity, failure to maintain upper airway patency, and inability to clear secretions, cough or gag. No clear guidance exists regarding optimal timing of NIV and pressure settings that should be used in the perioperative period. HFNO is being more frequently used in the perioperative setting as a well-tolerated supportive device for patients with hypoxemic respiratory failure. Its use has also increased for procedures in which spontaneous breathing can be maintained, as well as for apneic oxygenation. Some limitations with its use include patients with facial injuries or increased nasal secretions. It is important to recall that HFNO does not improve alveolar gas exchange in children with decreased minute ventilation or apnea and careful monitoring is required when used in these patients. Clinicians prescribing NIV or HFNO should be familiar with the different devices and interfaces; preparation to establish a definitive airway if NIV fails is fundamental.

Case development

The patient is clearly not eligible for ambulatory tonsillectomy surgery. Postoperative recovery in PICU was planned in anticipation to the procedure. On the day of surgery, inhalational induction using sevoflurane during spontaneous ventilation was chosen. After establishing intravenous access in the anesthetized child, intubation was performed with apneic oxygenation during laryngoscopy without the use of neuromuscular blockade. Surgery was accomplished without complications. Extubation and initiation of NIV occurred in the operating room. The patient's home NIV settings were initially modified by increasing IPAP and FiO_2. The patient was admitted to PICU for further

surveillance. Assistance managing secretions was provided using careful suction of the airway without any further bleeding. NIV was titrated back to home settings before discharge from PICU.

Reflective questions

1. What are the goals of applying non-invasive ventilation in children?

2. What are the main contraindications for NIV in pediatric patients?

3. How can the therapeutic benefit of the treatment with NIV be assessed after initiation of therapy?

References:

1. Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. *Lancet (London, England).* 2009;374(9685):250-259.
2. Essouri S, Durand P, Chevret L, et al. Physiological effects of noninvasive positive ventilation during acute moderate hypercapnic respiratory insufficiency in children. *Intensive Care Med.* 2008;34(12):2248-2255.
3. Stucki P, Perez MH, Scalfaro P, de Halleux Q, Vermeulen F, Cotting J. Feasibility of non-invasive pressure support ventilation in infants with respiratory failure after extubation: a pilot study. *Intensive Care Med.* 2009;35(9):1623-1627.
4. Bernet V, Hug MI, Frey B. Predictive factors for the success of noninvasive mask ventilation in infants and children with acute respiratory failure. *Pediatr Crit Care Med.* 2005;6(6):660-664.
5. Bauchmuller K, Glossop A. Non-invasive ventilation in the perioperative period. *BJA Education.* 2016;16(9):299-304.
6. Brown KA, Bertolizio G, Leone M, Dain SL. Home noninvasive ventilation: what does the anesthesiologist need to know? *Anesthesiology.* 2012;117(3):657-668.
7. Thille AW, Lyazidi A, Richard JC, Galia F, Brochard L. A bench study of intensive-care-unit ventilators: new versus old and turbine-based versus compressed gas-based ventilators. *Intensive Care Med.* 2009;35(8):1368-1376.
8. Richter RP, Alten JA, King RW, et al. Positive Airway Pressure Versus High-Flow Nasal Cannula for Prevention of Extubation Failure in Infants After Congenital Heart Surgery. *Pediatr Crit Care Med.* 2019;20(2):149-157.
9. Ward S, Chatwin M, Heather S, Simonds AK. Randomised controlled trial of non-invasive ventilation (NIV) for nocturnal hypoventilation in neuromuscular and chest wall disease patients with daytime normocapnia. *Thorax.* 2005;60(12):1019-1024.
10. Kovacikova L, Skrak P, Dobos D, Zahorec M. Noninvasive positive pressure ventilation in critically ill children with cardiac disease. *Pediatr Cardiol.* 2014;35(4):676-683.

11. D SR, Galas FRB, Faria LS, Amorim EF, Regenga MM, Troster EJ. Use of Noninvasive Ventilation in Respiratory Failure After Extubation During Postoperative Care in Pediatrics. *Pediatr Cardiol.* 2020;41(4):729-735.
12. Khirani S, Bersanini C, Aubertin G, Bachy M, Vialle R, Fauroux B. Non-invasive positive pressure ventilation to facilitate the post-operative respiratory outcome of spine surgery in neuromuscular children. *Eur Spine J.* 2014;23 Suppl 4:S406-411.
13. Abdel-Ghaffar HS, Youseff HA, Abdelal FA, et al. Post-extubation continuous positive airway pressure improves oxygenation after pediatric laparoscopic surgery: A randomized controlled trial. *Acta Anaesthesiol Scand.* 2019;63(5):620-629.
14. Calderini E, Chidini G, Pelosi P. What are the current indications for noninvasive ventilation in children? *Curr Opin Anaesthesiol.* 2010;23(3):368-374.
15. Emeriaud G, Napolitano N, Polikoff L, et al. Impact of Failure of Noninvasive Ventilation on the Safety of Pediatric Tracheal Intubation. *Crit Care Med.* 2020;48(10):1503-1512.
16. Morris JV, Ramnarayan P, Parslow RC, Fleming SJ. Outcomes for Children Receiving Noninvasive Ventilation as the First-Line Mode of Mechanical Ventilation at Intensive Care Admission: A Propensity Score-Matched Cohort Study. *Crit Care Med.* 2017;45(6):1045-1053.
17. Wolfler A, Calderini E, Iannella E, et al. Evolution of Noninvasive Mechanical Ventilation Use: A Cohort Study Among Italian PICUs. *Pediatr Crit Care Med.* 2015;16(5):418-427.
18. Xanthopoulos MS, Williamson AA, Tapia IE. Positive airway pressure for the treatment of the childhood obstructive sleep apnea syndrome. *Pediatr Pulmonol.* 2021.
19. Pascoe JE, Sawnani H, Hater B, Sketch M, Modi AC. Understanding adherence to noninvasive ventilation in youth with Duchenne muscular dystrophy. *Pediatr Pulmonol.* 2019;54(12):2035-2043.
20. Buzi A, Coblens OM, MacGillivray M, Elden L. The Use of Noninvasive Positive Pressure Ventilation following Pediatric Tonsillectomy. *Otolaryngol Head Neck Surg.* 2017;157(2):297-301.

21. Ferrand A, Roy SK, Faure C, Moussa A, Aspirot A. Postoperative noninvasive ventilation and complications in esophageal atresia-tracheoesophageal fistula. *J Pediatr Surg.* 2019;54(5):945-948.
22. Canning A, Clarke S, Thorning S, Chauhan M, Weir KA. Oral feeding for infants and children receiving nasal continuous positive airway pressure and high flow nasal cannula: a systematic review. *BMC Pediatr.* 2021;21(1):83.
23. Kneyber MCJ, de Luca D, Calderini E, et al. Recommendations for mechanical ventilation of critically ill children from the Paediatric Mechanical Ventilation Consensus Conference (PEMVECC). *Intensive Care Med.* 2017;43(12):1764-1780.
24. Storre JH, Steurer B, Kabitz HJ, Dreher M, Windisch W. Transcutaneous PCO2 monitoring during initiation of noninvasive ventilation. *Chest.* 2007;132(6):1810-1816.
25. Klein M, Reynolds LG. Relief of sleep-related oropharyngeal airway obstruction by continuous insufflation of the pharynx. *Lancet.* 1986;327(8487):935-939.
26. Sreenan C, Lemke RP, Hudson-Mason A, Osiovich H. High-flow nasal cannulae in the management of apnea of prematurity: a comparison with conventional nasal continuous positive airway pressure. *Pediatrics.* 2001;107(5):1081-1083.
27. Patel A, Nouraei SA. Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE): a physiological method of increasing apnoea time in patients with difficult airways. *Anaesthesia.* 2015;70(3):323-329.
28. Riva T, Greif R, Kaiser H, et al. Carbon Dioxide Changes during High-flow Nasal Oxygenation in Apneic Patients: A Single-center Randomized Controlled Noninferiority Trial. *Anesthesiology.* 2021.
29. Riva T, Pedersen TH, Seiler S, et al. Transnasal humidified rapid insufflation ventilatory exchange for oxygenation of children during apnoea: a prospective randomized controlled trial. *British journal of anaesthesia.* 2018;120(3):592-599.
30. Riva T, Préel N, Theiler L, et al. Evaluating the ventilatory effect of Transnasal Humidified Rapid Insufflation Ventilatory Exchange (THRIVE) in apnoeic small children with two different oxygen flow rates: a randomised controlled trial. *Anaesthesia.* 2020;in press.

31. Ritchie J, Williams AB, Gerard C, Hockey H. Evaluation of a humidified nasal high-flow oxygen system, using oxygraphy, capnography and measurement of upper airway pressures. *Anesth Intensive Care.* 2011;39:1103-1110.
32. Parke RL, Eccleston ML, McGuinness SP. The Effects of Flow on Airway Pressure During Nasal High-Flow Oxygen Therapy. *Respiratory Care.* 2011;56(8):1151-1155.
33. Ward JJ. High-Flow Oxygen Administration by nasal cannula for adult and perinatal patients. *Respir Care.* 2013;58(1):98-122.
34. Moller W, Feng S, Domanski U, et al. Nasal high flow reduces dead space. *J Appl Physiol (1985).* 2017;122(1):191-197.
35. Bartlett RG, Jr., Brubach HF, Specht H. Demonstration of aventilatory mass flow during ventilation and apnea in man. *J Appl Physiol.* 1959;14(1):97-101.
36. Hermez LA, Spence CJ, Payton MJ, Nouraei SAR, Patel A, Barnes TH. A physiological study to determine the mechanism of carbon dioxide clearance during apnoea when using transnasal humidified rapid insufflation ventilatory exchange (THRIVE). *Anaesthesia.* 2019;74(4):441-449.
37. Slutsky AS, Brown R. Cardiogenic oscillations - A potential mechanism enhancing oxygenation during apneic respiration. *Medical Hypotheses.* 1982;8:393-400.
38. Riva T, Meyer J, Theiler L, et al. Measurement of airway pressure during high-flow nasal therapy in apnoeic oxygenation: a randomised controlled crossover trial(). *Anaesthesia.* 2021;76(1):27-35.
39. Manley BJ, Owen LS, Doyle LW, et al. High-flow nasal cannulae in very preterm infants after extubation. *N Engl J Med.* 2013;369(15):1425-1433.
40. Sztrymf B, Messika J, Mayot T, Lenglet H, Dreyfuss D, Ricard JD. Impact of high-flow nasal cannula oxygen therapy on intensive care unit patients with acute respiratory failure: a prospective observational study. *J Crit Care.* 2012;27(3):324.e329-313.
41. Milesi C, Essouri S, Pouyau R, et al. High flow nasal cannula (HFNC) versus nasal continuous positive airway pressure (nCPAP) for the initial respiratory management of acute viral

bronchiolitis in young infants: a multicenter randomized controlled trial (TRAMONTANE study). *Intensive Care Med.* 2017;43(2):209-216.

42. Riva T, Theiler L, Jaquet Y, Giger R, Nisa L. Early experience with high-flow nasal oxygen therapy (HFNOT) in pediatric endoscopic airway surgery. *International journal of pediatric otorhinolaryngology.* 2018;108:151-154.
43. Humphreys S, Rosen D, Housden T, Taylor J, Schibler A. Nasal high-flow oxygen delivery in children with abnormal airways. *Paediatric anaesthesia.* 2017;27(6):616-620.
44. Humphreys S, Lee-Archer P, Reyne G, Long D, Williams T, Schibler A. Transnasal humidified rapid-insufflation ventilatory exchange (THRIVE) in children: a randomized controlled trial. *British journal of anaesthesia.* 2017;118(2):232-238.
45. Humphreys S, Schibler A. Nasal high-flow oxygen in pediatric anesthesia and airway management. *Paediatric anaesthesia.* 2020;30(3):339-346.
46. Lin J, Zhang Y, Xiong L, Liu S, Gong C, Dai J. High-flow nasal cannula therapy for children with bronchiolitis: a systematic review and meta-analysis. *Arch Dis Child.* 2019;104(6):564-576.
47. Gaeckle NT, Lee J, Park Y, Kreykes G, Evans MD, Hogan CJ, Jr. Aerosol Generation from the Respiratory Tract with Various Modes of Oxygen Delivery. *Am J Respir Crit Care Med.* 2020;202(8):1115-1124.
48. Westafer LM, Soares WE, 3rd, Salvador D, Medarametla V, Schoenfeld EM. No evidence of increasing COVID-19 in health care workers after implementation of high flow nasal cannula: A safety evaluation. *Am J Emerg Med.* 2021;39:158-161.
49. Wilson NM, Marks GB, Eckhardt A, et al. The effect of respiratory activity, non-invasive respiratory support and facemasks on aerosol generation and its relevance to COVID-19. *Anaesthesia.* 2021;76(11):1465-1474.
50. Winslow RL, Zhou J, Windle EF, et al. SARS-CoV-2 environmental contamination from hospitalised patients with COVID-19 receiving aerosol-generating procedures. *Thorax.* 2021.
51. Hamilton FW, Gregson FKA, Arnold DT, et al. Aerosol emission from the respiratory tract: an analysis of aerosol generation from oxygen delivery systems. *Thorax.* 2021.

Figures:

Figure 1. High-flow nasal oxygenation (HFNO) device. Nasal interface can be exchanged to adapt for use in adult and pediatric patients. (Permission obtained from manufacturer).

Figure 2. Graphic showing the particle number concentration with various modes of oxygen delivery[47]. Particle number concentration with various modes of oxygen delivery. Box-and-whisker plots demonstrate the median and interquartile ranges. Note the change in scale of the y-axis in coughing. The horizontal dashed line represents the average baseline particle number concentration of the room (0.060 particles/cm^3). FM= face mask; HFNC= heated and humidified high-flow nasal cannula; NC= nasal cannula; NIPPV = noninvasive positive pressure ventilation. (Reprinted with permission of the American Thoracic Society. Copyright © 2021 American Thoracic Society. All rights reserved)

Table 1. Advantages and limitations of non-invasive ventilation interfaces and high-flow nasal oxygen (HFNO).

Device/Interface	Advantages	Limitations
Nasal cannula/ prongs	- Easy to use and well tolerated in neonates, infants, and children - Available in most clinical settings	- Efficacy can be limited by significant airway leaks through the mouth
Nasal mask	- Located only around the contour of the nose - Good acceptance in infants, toddlers, and older children - Helps to minimize apparatus dead space and the triggering function of the devices	- Air leaks either through the mouth or due to a poor interface seal can limit its benefit
Face mask	- Located around the mouth and nose, provides more reliable delivery of positive pressure - Good tolerance in older children	- Requires more compliance; younger children and infants may become agitated when the mask is applied
Total/Scuba mask	- The whole face becomes part of the interface - Better acceptance in older children	- May increase dead space - Needs a higher flow rate to mitigate rebreathing
Helmet	- More commonly used in neonates in the ICU with good tolerance	- Regional availability may vary depending on the country.
High-flow nasal cannula	- Well tolerated by neonates, infants and children. - Allows to provide oral intake during therapy	- Increased oxygen consumption depending on the oxygen fraction and flow rate

ICU=intensive care unit.

Table 2. Indications, possible applications, and contraindications for non-invasive ventilation (NIV) and high-flow nasal oxygen (HFNO).

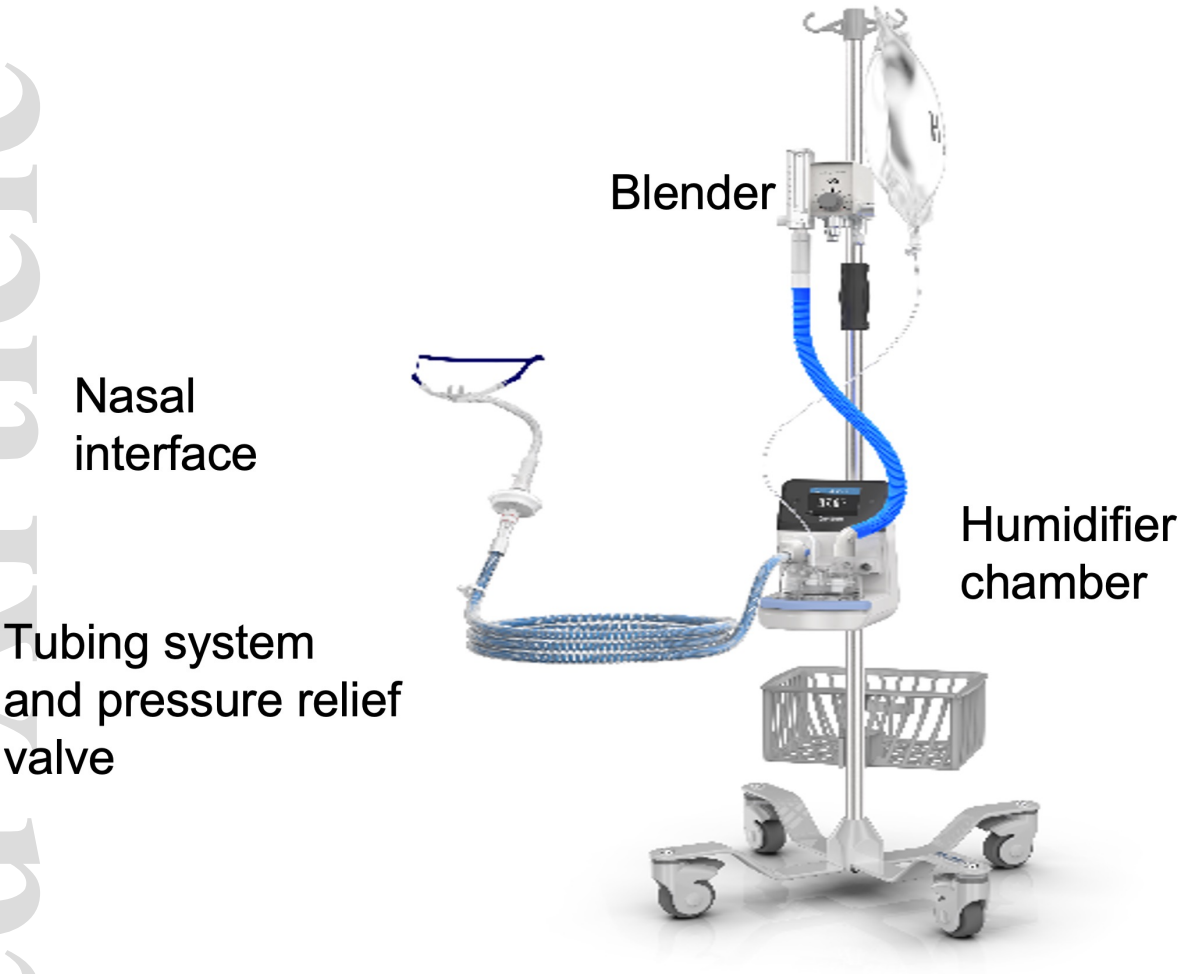
	NIV	HFNO
Indications	- Moderate to severe dyspnea or tachypnea - Hypoxemic or hypercapnic respiratory failure	- Moderate to severe dyspnea or tachypnea - Hypoxemic respiratory failure
Possible applications	- Procedural sedation in spontaneously breathing patients - Pre-oxygenation for intubation (only BPAP and time-cycled)	- Procedural sedation in spontaneously breathing patients - Apneic oxygenation during laryngoscopy for intubation - Apneic oxygenation during procedures (ensure CO_2 monitoring, ventilation needed for CO_2 elimination
Absolute contraindications	- Need for endotracheal intubation - Reduced level of consciousness - Severe respiratory distress with paradoxical abdominal muscles or thoracic muscle use - Absence of protective airway reflexes - Upper airway obstruction by a mass or tumor - Nausea or vomiting, hemodynamic instability	- Severe hypoxemia requiring endotracheal intubation - Hypercapnic respiratory failure - Reduce level of consciousness with inability to maintain ventilation
Relative Contraindications	- Facial surgery or trauma, or facial deformity - Inability to maintain upper airway patency - Inability to cough or gag, increased or inability to clear secretions	- Nasal surgery, facial trauma, or facial deformity - Increased nasal secretions

Table 3. Initial settings and goals suggested for non-invasive ventilation (NIV) and high-flow nasal oxygen (HFNO).

	NIV		**HFNO**
	BPAP	CPAP	
Initial settings	IPAP: 5-8 cm H_2O EPAP: 3-5 cm H_20	5-8 cm H_20	0.5 – 1 L/kg per minute
Suggested maximal pressures	IPAP: 8-15 cm H_2O EPAP: 4-8 cm H_2O	8-15 cm H_2O	2-4 L/kg per minute* Total max. 70 L/min
FiO_2	0.4-0.6. Titrate with the aim of SpO_2 >95%		
Aim	4-7ml/kg tidal volume		2 L/kg per minute
Comments	- Reevaluate therapy after 1-2 hours - Leakage can increase with high pressure settings - Do not titrate too fast, to improve patient's cooperation		- Reevaluate therapy after 1-2 hours - Do not titrate flow too fast in conscious patients - Does not provide CO_2 elimination in apneic patients

BPAP= bilevel positive airway pressure; CPAP= continuous positive pressure; IPAP=inspiratory positive airway pressure; EPAP=expiratory positive airway pressure.

* 4 L/kg per minute is considered safe but has no clinical benefit.



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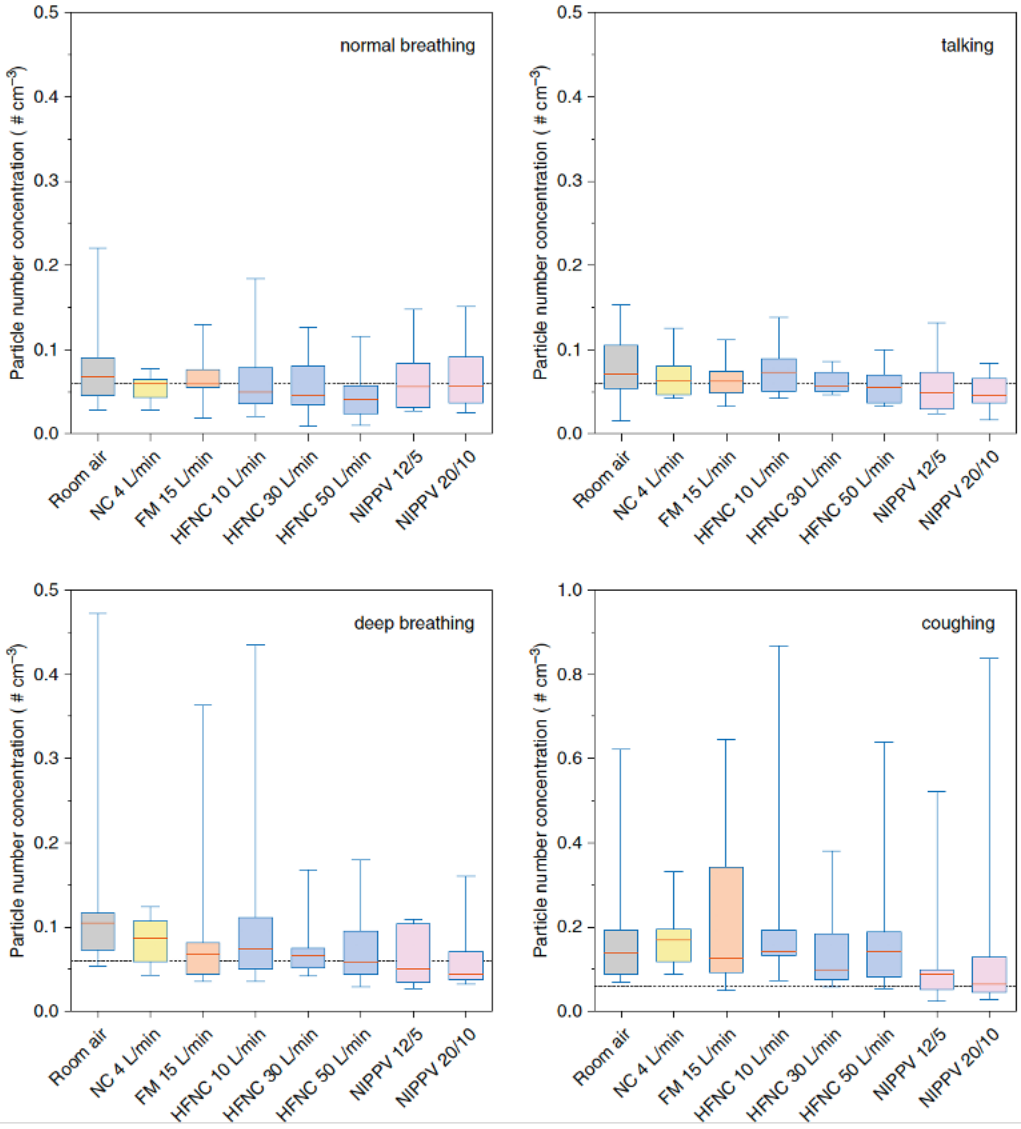

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