Standardized Weaning of Positive Pressure Respiratory Support in Preterm Infants

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Abstract

Non-invasive respiratory support is a mainstay of therapy in treating critically ill preterm infants. The optimal method of weaning non-invasive support is not well established. Weaning too quickly can lead to clinical decompensation events, increasing antibiotic exposure and the risk for significant morbidity and mortality including bronchopulmonary dysplasia. The purpose of the evidence-based project was to assess the impact of a protocol for CPAP weaning in infants born at less than 32 weeks gestational age. A total of 53 infants were included in the project, 34 in the pre-protocol group and 19 in the intervention or protocol group at a hospital in the Midwest with a level III neonatal intensive care unit. The protocol was an evidence-based guideline directing the timing and criteria for weaning CPAP. The primary outcome of interest was decompensation events in the 7 days after weaning off CPAP, with a secondary outcome of bronchopulmonary dysplasia at 36 weeks gestational age. Neither outcome met statistical significance due to limited numbers but a clinically relevant decrease in bronchopulmonary dysplasia was seen in the protocol group. Cautious evidence-based respiratory support weaning may have the potential to improve short-term clinical stability, reduce unnecessary medical intervention, and decrease the rate of bronchopulmonary dysplasia in this at-risk population.

Keywords: preterm infant, neonatal, CPAP, high flow nasal cannula, weaning, protocol

Standardized Weaning of Positive Pressure Respiratory Support in Preterm Infants for the Prevention of Clinical Decompensation

Premature infants often require respiratory support after birth due to varying degrees of pulmonary immaturity. Respiratory distress and the long-term complications of neonatal respiratory problems lay the groundwork for ongoing medical complexity into childhood. Preterm babies are at risk of developing bronchopulmonary dysplasia (BPD), setting the stage for lifelong pulmonary diseases (Gough et al., 2014; Um-Bergstrom et al., 2019). Appropriate respiratory support during postnatal development may prevent clinical deterioration events associated with inadequate support and thereby may impact rates of BPD. Current practices for weaning non-invasive respiratory support in this population lack standardization, and little consensus is available about the safety and efficacy of different weaning methodologies. The project introduces an evidence-based protocol for the standardized weaning of respiratory support in premature infants to reduce episodes of clinical decompensation after weaning and the incidence of BPD.

Significance

Very preterm infants, born at less than 32 completed weeks of gestation, often require respiratory support in the early neonatal period. This support, although lifesaving, can cause barometric and volumetric trauma which alters lung development and sets the stage for BPD (Hwang & Rehan, 2019). To avoid lung injury, general practice is early extubation to non-invasive support and early weaning from positive pressure (Dumpa & Bhandari, 2018). Further complicating management, weaning off positive pressure too quickly can increase cardiorespiratory instability, tachypnea, and energy expenditure. These non-specific symptoms of clinical decompensation drive escalations in the provision of critical care. Standardized

approaches to respiratory weaning, when consistently applied to all at-risk patients, are associated with greater success in respiratory support weaning (Amatya et al., 2017).

Local Issue

The clinical setting for the project is a level III neonatal intensive care unit (NICU) in a large suburban area in the Midwest. This NICU is within the largest volume delivery hospital in the area. The unit routinely cares for infants born as early as 27 weeks completed gestation and is equipped to provide high levels of invasive and non-invasive respiratory support, except for high frequency oscillatory ventilation (HFOV). The absence of HFOV is relevant, as infants who are the sickest in terms of respiratory support needed would require transfer to a regional referral center.

The setting is affected by considerable variation in clinical practice among providers, especially in the weaning of respiratory support. Preterm infants at the center are routinely weaned from continuous positive airway pressure (CPAP) to a high flow nasal cannula (HFNC) within the first 2 weeks of life. Some infants subsequently exhibit an increase in apnea, bradycardia, and desaturation events in the days after support weaning. These events prompt clinical concern and lead to the collection of a complete blood count (CBC) or blood culture to rule out infection. This is often accompanied by the prophylactic administration of antibiotics. To rule out respiratory etiologies of the clinical change, a chest radiograph (CXR) is usually obtained and the infant is placed on a higher level of respiratory support. The short-term goal of a standardized approach to respiratory weaning is cardiorespiratory stability at the individual patient level. The long-term goal is to decrease the rate of BPD in the population at this center.

Diversity

Ethnic diversity had the potential to meaningfully influence the project. Premature babies are more likely than term-born infants to have respiratory distress after birth. The rate of preterm birth in the United States continues to rise, with black mothers twice as likely to deliver prematurely than non-Hispanic white mothers, even when controlling for other socioeconomic factors (Manuck, 2017). This project population is infants born at less than 32 weeks gestational age (GA), making it possible that a higher proportion of black infants would be included in the study than expected in a similar population of term neonates. It remained crucial to ensure that the project steps and rationale were transparent to all parents and families, respecting any relevant cultural differences, especially in family participation in health care and trust in medical providers.

Another social consideration was the socioeconomic makeup of the local patient population. The hospital is located in an affluent suburban area, although patients do travel from surrounding areas to deliver in the facility. The patient population within the site's birth center may be demographically different from other hospitals with NICUs in the region. These differences can potentially impact maternal access to appropriate prenatal care, which in turn can affect the fetal and neonatal health of their babies.

Problem and Purpose

Problem

Clinical decompensation events increase the risk of airway trauma, antibiotic exposure, necrotizing enterocolitis, and BPD. Bronchopulmonary dysplasia is linked to increased length and cost of initial hospitalization and asthma and chronic obstructive pulmonary disease (COPD) in adulthood.

Preterm infants are often weaned from respiratory support within the first 2 weeks of life within the project site. This can increase energy expenditure, lead to clinical decompensation, and lay the stage for the development of BPD. Energy expenditure in excess of caloric intake, through tachypnea and increased work of breathing, can lead to inadequate somatic growth, which has been associated with suboptimal lung development (Underwood et al., 2019). Respiratory distress after weaning may necessitate a return to more invasive forms of support, including reintubation and mechanical ventilation. Repeat and prolonged intubations increase the incidence of acute airway damage (Wei & Bond, 2011). This is often accompanied by an antibiotic course to treat possible septic etiologies of decompensation. Antibiotic exposure following an acute deterioration increases the risk of necrotizing enterocolitis, a serious gastrointestinal disease of the preterm infant, and death (Cantey et al., 2018). Together, these complications of respiratory support weaning can increase the likelihood of a BPD diagnosis. Bronchopulmonary dysplasia has both short and long-term impacts, increasing the length and cost of initial hospitalization and the rates of asthma and COPD in adulthood (Gough et al., 2014; Um-Bergstrom et al., 2019; Lapcharoensap et al., 2019).

Purpose

The purpose of the positive pressure weaning project was to decrease the incidence of cardiorespiratory decompensation events and BPD by applying an evidence-based protocol for weaning CPAP in infants born at less than 32 weeks GA in a level III NICU.

Facilitators and Barriers

The implementation of a respiratory support weaning protocol was feasible within the clinical site. The needed equipment was already available, the nursing staff was familiar with the support devices, and the unit routinely included patients fitting the study population. To increase

project sustainability, tailored nursing education was provided with separate presentations of evidence to providers. Additional facilitators of the project included strong support from the medical director of the NICU and a drive to increase the provision of evidence-based care at the hospital organizational level. Improved respiratory management could reduce the number of outgoing patient transfers from the NICU, which would increase revenue for the organization.

Several barriers impacted the implementation of the project at the site. The most significant barrier was staff preparation and education. The respiratory care staff within the project site is variable in terms of knowledge and expertise with existing respiratory support devices and methods. Any change in practice could be unsuccessful without addressing deficits prior to implementation. Other barriers included stagnation among tenured nursing staff and providers.

Review of Evidence

Inquiry

In infants born at less than 32 completed weeks of gestation, does a standardized respiratory support weaning protocol, compared to weaning at provider discretion, decrease the incidence of cardiorespiratory decompensation in the 7 days after weaning off positive pressure, within a level III Neonatal Intensive Care Unit? Does the protocol decrease the rate of BPD at 36 weeks GA in the population and site?

Search Strategies

The review of literature began with a search for evidence-based practice guidelines from applicable groups. Neither the Vermont Oxford Network nor the American Academy of Pediatrics has a guideline for weaning respiratory support in neonates. Database searches were then performed via the Cochrane Database of Systematic Reviews, Pubmed, Medline/NLM, and

CINAHL. The keywords used in the search were respiratory support, positive pressure, CPAP, weaning, protocol, approach, guideline, and bronchopulmonary dysplasia. Each of the terms was associated with the term preterm infant or neonatal. Initial searches with the term premature or premature infant yielded excess unrelated articles due to other uses of the word premature, usually associated with death.

Inclusion was determined based on applicability to the population and clinical question. The review was limited to English language articles published within the previous 10 years. An exception was made to include one article published within the preceding 15 years, as no recent studies were available addressing the relative comfort of patients treated with various support modalities. A total of 127 articles were identified with potential application to the population and topic (See Appendix A). Of those, 30 were relevant to the inquiry, including eight systematic reviews of randomized controlled trials (RCTs) or meta-analyses, representing level I evidence. Nineteen studies were RCTs, representing level II evidence. Three studies were prospective or retrospective quasi-experimental studies, representing level III evidence (See Appendix B).

Synthesis of Evidence

Studies relevant to the clinical inquiry were reviewed and analyzed for relevant contributions (See Appendix C). The studies of non-invasive respiratory support in preterm infants focused on two different support methodologies, high flow nasal cannula (HFNC) and CPAP. The modalities were addressed separately and in comparison to one another. Ultimately seven themes were identified. Themes were the safety of HFNC, the safety of CPAP, comfort on CPAP, comparison of CPAP and HFNC, cardiorespiratory stability on CPAP and HFNC, and finally, weaning strategies and protocols (See Appendix D).

Safety and Efficacy of HFNC

High flow nasal cannula is used in some centers as primary non-invasive support and post-extubation respiratory support, including in preterm infants. Within the last 10 years, three meta-analyses were identified addressing the safety of HFNC use in infants. The unifying outcome among the analyses was the reduction in risk of nasal trauma in infants treated with HFNC compared to those treated with CPAP. A 2015 meta-analysis of 9 RCTs showed that HFNC was comparable in safety to other non-invasive forms of respiratory support and caused less nasal trauma (Kotecha et al., 2015; *n*=1112). Another meta-analysis of 15 RCTs reinforced that HFNC use was associated with a decreased incidence of nasal injury when compared to CPAP (*n*=645) and had similar longer-term respiratory outcomes (Wilkinson et al., 2016; *n*=893). Recently, a third meta-analysis of 21 RCTs indicated that HFNC was similar in safety to CPAP when used as primary support and underscored the reduced incidence of nasal trauma and pulmonary air leak in infants treated with HFNC (Murki et al., 2018; *n*=2886). Each meta-analysis reviewed had limited data to support the safety of HFNC use in infants of lower gestational ages and birthweights.

High flow nasal cannula can provide peak end expiratory pressure (PEEP) comparable to CPAP, especially at higher flow rates. In preterm infants, this effect can be unpredictable. One RCT showed that the PEEP provided by HFNC was especially variable in preterm infants and that the alterations in PEEP were most pronounced in infants with the lowest body weight (Liew et al., 2020). Another study demonstrated that neurologic measures indicative of work of breathing were increased in preterm infants treated with HFNC compared to CPAP, despite clinical stability, indicating that the PEEP provided on HFNC may be inadequate to support premature babies long-term (Nasef et al., 2015).

A common use of HFNC is as a weaning step between CPAP and room air. Weaning with or without HFNC is comparable in outcomes, but studies are mixed on whether it is a beneficial tool or prolongs the total duration of respiratory support. An RCT evaluating HFNC as a weaning tool in preterm infants showed that those weaned with the use of a HFNC required a greater total duration of oxygen therapy (Abdel-Hady et al., 2011). Another study of preterm and term infants found that those treated with HFNC required more total days of respiratory support (Yoder et al., 2013). This data carries significance, as the length of supplemental oxygen and respiratory support are diagnostic criteria for BPD. Additional studies attempted to demonstrate superiority of HFNC in achievement of other important milestones, such as the time to attainment of full oral feeds. A study assessed this outcome but showed no improvement in oral feeding goals in infants treated with HFNC (Tang et al., 2015).

Safety and Efficacy of CPAP

Continuous positive airway pressure is a widely used form of non-invasive respiratory support in infants. Few recent studies evaluate the safety of this therapy, likely because of widespread use and generally accepted safety in the population. Present research is focused on the prophylactic use of CPAP in the delivery room to avoid mechanical ventilation. To address this application of CPAP, a meta-analysis of seven RCTs involving preterm infants was included in the review. The meta-analysis showed that CPAP was useful in reducing the need for mechanical ventilation and exogenous surfactant administration when used as prophylaxis immediately after birth in preterm infants (Subramaniam, Ho & Davis 2016; n=3123). The RCTs in the meta-analysis did not include sufficient data to compare CPAP to other forms of non-invasive respiratory support. A retrospective cohort study was included, comparing CPAP to non-invasive positive pressure ventilation (NIV) with regard to the rate of BPD. Preterm infants

who were extubated to CPAP had a lower incidence of BPD than those extubated to NIV, even after controlling for gestational age and weight (Abu-Shaweesh et al., 2020).

Studies comparing CPAP to low flow nasal cannulas (LFNC) have conflicting results regarding the safety of CPAP. One RCT comparing CPAP to LFNC showed that infants treated with CPAP did not have a decreased incidence of BPD or improved weight gain, though few of the variables studied met statistical significance (Heiring et al., 2015). However, another observational cohort study compared the electrical activity of the diaphragm in preterm infants supported with CPAP to those on LFNC. The results indicated that the labor of the diaphragm was decreased when infants were treated with CPAP (Kraaijenga et al., 2019).

Comfort on CPAP

Measures of comfort in preterm infants are inherently subject to bias because they depend on provider interpretation. Objective tools, which often rely on vital sign measurements, have been used to evaluate pain and discomfort in preterm infants in an attempt to standardize treatment. Only one study was available investigating infant comfort on CPAP and was therefore included despite being greater than 10 years old. The study found that objective measurements of discomfort, including heart rate and blood pressure, were increased when infants were placed on CPAP from room air, indicating that CPAP may increase infant discomfort (Kugelman et al., 2008).

CPAP and HFNC Comparison

Ten studies compared the use of HFNC and CPAP in infants. Among these studies, one RCT and a meta-analysis evaluated each as a non-invasive form of respiratory support following extubation from mechanical ventilation. Although the meta-analysis demonstrated that primary CPAP and HFNC use had comparable outcomes, when used after extubation, HFNC was

associated with an increased incidence of treatment failure and respiratory support escalation (Murki et al., 2018; 21 RCTs, *n*=2886). In addition to post-extubation failure, an RCT showed that infants on HFNC had a greater supplemental oxygen requirement and prolonged respiratory pauses (Kanbar et al., 2020).

Further studies examined CPAP and HFNC use outside of the initial post-extubation period. A systematic review was identified, comparing the two as primary non-invasive respiratory support modes in preterm infants. The review found that HFNC was associated with an increased incidence of treatment failure in preterm infants of greater than 28 weeks gestation (Conte et al., 2018; 6 RCTs, *n*=1227). This supports the finding that preterm infants receive insufficient PEEP on HFNC and experience a concomitant increase in work of breathing, potentially driving the need for escalations in respiratory support (Nasef et al., 2015). One final study corroborated the increase in treatment failure in preterm infants on HFNC and added that lower GA and higher oxygen requirements were correlated with failure on HFNC (Manley et al., 2018).

One meta-analysis and three RCTs contributed data comparing the duration of respiratory therapy on HFNC and CPAP. One RCT showed that infants treated with HFNC as a weaning tool from CPAP experienced fewer total CPAP days than those weaned directly to room air from CPAP (Tang et al., 2015). Other studies of the two modes as primary support showed that infants supported with HFNC experienced a longer duration of total respiratory support, as demonstrated by a meta-analysis and one RCT (Wilkinson et al., 2016; Yoder et al., 2013). A final RCT examining the length of respiratory therapy found that infants under 32 weeks GA took an average of 11 days to wean to room air regardless of which non-invasive respiratory support

mode was used (Soonsawad et al., 2016). None of these studies found a difference in morbidity and mortality between the two groups.

Two studies examined other outcomes commonly believed to be impacted by CPAP therapy. Oral feedings are not universally attempted in infants being treated with CPAP, prompting use of HFNC to provide respiratory support while encouraging oral feeding skills in preterm babies. The two RCTs that examined oral feeding found no difference in the length of time to full oral feeds between babies on CPAP or HFNC (Glackin et al., 2017; Tang et al., 2015). Additionally, no adverse events were noted in the infants who attempted oral feeds while being treated with CPAP (Glackin et al., 2017).

Cardiorespiratory Stability on Non-invasive Support

Three RCTs, one meta-analysis, and one systematic review examined cardiorespiratory stability when CPAP was used as non-invasive respiratory support. The meta-analysis favored the use of CPAP as initial delivery room support, finding decreased rates of mechanical ventilation and exogenous surfactant administration, and a modest decrease in BPD and death (Subramaniam et al., 2016; 7 RCTs, *n*=3123). One RCT comparing CPAP and HFNC found that infants placed on CPAP had shorter respiratory pauses after extubation (Kanbar et al., 2020). Premature infants are at risk of apnea of prematurity, a common problem that often prompts respiratory support escalation. Decreased respiratory pauses may indicate a reduced incidence of apnea in the population. Another small RCT measured the neural drivers of breathing activity, noting lower electrical activity of the diaphragm in infants treated with CPAP compared to HFNC, indicative of superior breathing comfort on CPAP (Nasef et al., 2015). A third, more recent RCT found that preterm infants treated with prolonged CPAP showed sustained improvement in functional residual capacity (FRC) compared to controls, which may indicate

improved long-term pulmonary function (Lam et al., 2020). Finally, a systematic review of CPAP weaning methods noted that infants on sustained CPAP, without cycled times off non-invasive support, had a shorter total duration of oxygen therapy (Jardine et al., 2011; 3 RCTs, *n*=364). The need for supplemental oxygen is a defining criterion of BPD, so this reduction in length of therapy could be extrapolated to a potential reduction in risk of BPD.

One systematic review and one RCT specifically examined treatment failure on HFNC in preterm infants. Each found that HFNC was associated with greater incidence of subsequent escalation in respiratory support. A 2018 systematic review noted that preterm infants of greater than 28 weeks GA were more likely to require intubation when HFNC was attempted as first line respiratory support (Conte et al., 2018; 6 RCTs, *n*=1227). The RCT examining HFNC use noted that those born at greater than 30 weeks GA were more likely to be successfully treated with HFNC than those born earlier; however, preterm infants of all ages were more successfully treated with CPAP (Manley et al., 2018).

Weaning Strategies and Protocols

Few studies addressed the value of respiratory support weaning protocols. One systematic review attempted to could not locate sufficient evidence to support or refute such measures (Wielenga et al., 2016). One RCT addressing weaning from mechanical ventilation to non-invasive support showed that preterm infants extubated to CPAP required less supplemental oxygen than those extubated to HFNC (Kanbar et al., 2020). Although the RCT did not directly address protocols for weaning, the results favored CPAP as a weaning step from mechanical ventilation.

Little standardization exists to direct weaning from non-invasive respiratory support to room air in the preterm infant. One included systematic review and six RCTs compared methods

of weaning off non-invasive support. The 2011 systematic review was limited to three RCTs and compared cycled windows off CPAP to gradual weans in CPAP pressure to a predetermined level before weaning to room air. The review found that gradual weaning was associated with fewer total CPAP days, decreased length of supplemental oxygen therapy, and shorter total length of hospitalization (Jardine et al., 2011; *n*=364). One RCT of similar size to the systematic review (*n*=372) compared gradual CPAP pressure weaning to abrupt weaning from higher pressure directly to room air. The study demonstrated that preterm infants under 28 weeks GA were more likely to remain in room air when weaned gradually (Jensen et al., 2018). Another smaller RCT similarly favored gradual weans, showing that infants were more successfully weaned on the first attempt when pressure was decreased gradually (Amatya et al., 2017). A recent larger RCT examining gradual and abrupt CPAP pressure weaning noted that total length of stay and length of oxygen therapy were similar in both groups, though gradual weans were associated with greater weaning success on the first attempt (Kakkilaya et al., 2020).

Another method of gradual non-invasive support weaning is the stepwise decrease in CPAP pressure with a transition to HFNC or low flow nasal cannula prior to weaning to room air. Two RCTs evaluated weaning with the use of nasal cannulas. One compared weaning directly from CPAP to room air against weaning from CPAP to HFNC and then to room air. The study included only preterm infants and found that the total length of supplemental oxygen therapy was approximately 5 days in the CPAP group compared to 14 days in the group weaned with HFNC (Abdel-Hady et al., 2011). The second RCT evaluated weaning directly to room air from CPAP against weaning from CPAP to LFNC. Weaning success was similar in the two groups, with only a small increase in respiratory rates found in the group weaned without the use of nasal cannula (O'Sonnell et al., 2013). A final RCT examined extended consistent CPAP for

two weeks compared to gradually weaned CPAP during the same timeframe. The study compared measures of pulmonary function in infants born at less than or equal to 32 weeks GA and noted improved FRC in the extended CPAP group, favoring prophylactic continuation of CPAP even in stable preterm infants (Lam et al., 2020)

Three RCTs examined the average length of the need for non-invasive respiratory support in preterm infants. One study of a non-invasive support weaning protocol noted that infants born at less than 27 weeks GA and with birthweights of less than 900 grams experienced more failed attempts at weaning and an increased total length of CPAP therapy, noting that birthweight was even more predictive of weaning failure than GA (Yin et al., 2016). Another RCT studying weaning methods compared windows off CPAP with the use of HFNC to gradual CPAP pressure weans found that both methods were comparable, with each group averaging 7 days of CPAP therapy (Eza et al., 2018). A final study comparing CPAP weaning, with and without the use of HFNC as a step-down tool, found minimal difference in success between methods and that each group required approximately 11 days to reach room air from the time weaning began (Soonsawad, 2016).

Finally, one systematic review, three RCTs, and one retrospective study contributed data associating GA with successful weaning to room air. A 2015 systematic review of 7 RCTs demonstrated that most preterm infants were successfully weaned to room air between 32 and 33 weeks GA regardless of weaning method (Amatya et al., 2015, n=1015). One large RCT compared two weaning protocols and found that both groups averaged 33 weeks GA at the time of successful weaning to room air (Kakkilaya et al., 2020). An earlier RCT comparing abrupt and gradual CPAP pressure weans also noted that infants in both groups averaged 33 weeks GA and 1600 grams of weight at the time of successful weaning (Amatya et al., 2017). A final RCT

examining data before and after implementation of a standardized weaning protocol showed that, after protocol use, babies were successfully weaned approximately one week earlier than pre-protocol. The study showed successful weaning usually occurred near 32 weeks GA and 1450 grams in weight (Kidszun et al., 2016). A large retrospective cohort study examined the mean duration of respiratory support in preterm infants. The study underscored the findings in the RCTs, showing that infants born at 27 weeks GA, the oldest infants included in the study, remained on CPAP until approximately 33 weeks GA (Weisz et al., 2021, *n*=2601).

Evidence Discussion

Continuous positive airway pressure is widely used as non-invasive respiratory support for babies needing positive pressure but not mechanical ventilation. Prophylactic CPAP use in the delivery room for preterm infants is safe and associated with a decreased need for mechanical ventilation and lower rates of BPD (Subramaniam et al., 2016). Available literature contains conflicting information, with some studies indicating that CPAP does not improve lung function, while others show prolonged improvement in functional residual capacity in infants treated with several weeks of CPAP (Heiring et al., 2015; Lam et al., 2020). Efforts to decrease time spent on CPAP are supported by evidence that infants are less comfortable on CPAP and nasal mucosal breakdown is increased on CPAP compared to HFNC (Kugelman et al., 2008; Kotecha et al., 2015). Two of the studies addressing the benefits and risks of CPAP in this population were level I evidence.

Concern over the safety of HFNC use in preterm infants is driving an increase in studies on the use of HFNC in the population. Studies supporting HFNC use have limited data in the preterm infant population. HFNC delivers unpredictable distending airway pressure, especially in the smallest babies (Liew et al., 2020). At best, studies show that HFNC is not inferior to CPAP

in neonates from preterm to post-term gestation (Kotecha et al., 2015; Wilkinson et al., 2016; Yoder et al., 2013). Other efforts to demonstrate superiority of HFNC show no decrease in the time spent on respiratory support or supplemental oxygen when HFNC is used in place of CPAP or as a weaning tool (Soonsawad et al., 2016; Tang et al., 2015). Finally, HFNC use in preterm infants likely increases work of breathing and the need for subsequent escalation in respiratory support (Conte et al., 2018; Kanbar et al., 2020; Manley et al., 2018; Murki et al., 2018; Nasef et al., 2015). Direct comparisons of CPAP to HFNC fail to show a decrease in time to attainment of full oral feeds with HFNC use, which historically has been a supportive rationale for weaning infants from CPAP (Glackin et al., 2017). Four studies examining HFNC use represented level I evidence.

No consensus exists about the safest and most effective method of transitioning an infant from CPAP to room air. Protocols may have no impact on the length of time to achieve weaning goals (Kidszun et al., 2016; Wielenga et al., 2016). Weaning strategies studied in preterm infants demonstrated that gradually weaning CPAP to a predetermined low pressure before transitioning straight to room air is more successful than abrupt weaning, cycled windows off CPAP, or stepping down to HFNC (Amatya et al., 2017; Jensen et al., 2018; Eze et al., 2018; Kakkilaya et al., 2020; O'Sonnell et al., 2013; Soonsawad et al., 2016). Remaining on CPAP until ready to wean directly to room air may decrease the length of supplemental oxygen therapy, which is a diagnostic criterion for BPD (Abdel-Hady et al., 2011; Jardine et al., 2011). Irrespective of the weaning method, infants with higher birthweights and of higher GA experience greater success at weaning off CPAP on the first attempt (Yin et al., 2016). At the time of successful weaning to room air, babies usually have reached at least 32 weeks GA and 1450-1600 grams in weight (Amatya et al., 2017; Amatya et al., 2015; Kidszun et al., 2016; Weisz et al., 2021). Prior to this

age and weight, attempts to wean are often unsuccessful. Two studies of weaning methods were level I evidence, though one found insufficient studies were available to conduct the analysis supporting or refuting the utility of protocols.

Gaps

Available research comparing CPAP and HFNC provides a conflicting picture, with evidence that supports each method as superior to the other. The studies which favor HFNC include term and post-term infants, and the results are likely less applicable to the preterm population. High flow nasal cannulae provide unreliable positive pressure which may be insufficient to meet the increased respiratory support need of a preterm infant. More studies are needed to demonstrate the safety and efficacy of HFNC use in preterm infants. A paucity of evidence exists to support the efficacy of protocols, although most literature comparing multiple weaning strategies involves at least one study weaning protocol. Specific studies of protocols have not demonstrated improved outcomes with protocol implementation and more research is recommended.

Summary and Recommendations

Infants born at less than 32 completed weeks of gestation should be treated with CPAP, beginning in the delivery room (Subramaniam et al., 2016). Although no weaning method is objectively superior to others, studies support that CPAP pressure should be gradually weaned as predetermined stability criteria are met to avoid weaning failure and the need for escalations in respiratory support. An initial attempt to wean an infant off CPAP and directly to room air can be trialed if the infant has met stability criteria, reached 32 weeks GA, and weight is at least l500 grams. CPAP therapy for at least two weeks is suggested, even if the recommended age and weight have been met (Lam et al., 2020).

Theory

The theoretical model that informed the project is Mefford's Theory of Health Promotion for Preterm Infants (2004). The theory has direct application to the unique population of interest and explores the contributors to achieving specific health goals. The theory of Health Promotion for Preterm Infants was developed by Linda Mefford and originally published in 2004. Dr. Mefford is a Ph.D. prepared and board certified Neonatal Nurse Practitioner and Clinical Professor with a background in NICU nursing. The theory of Health Promotion for Preterm Infants predicts the impact of nursing interventions on preterm infants and the family unit and prescribes nursing actions and areas of focus at the nursing practice level.

Mefford's theory contains three major concepts. The first concept is adaptation. A preterm infant must change from physiologic adaptation to the uterine environment to prepare for the extrauterine NICU environment. The family is challenged with adaptation from the expected birth and family dynamic to the new reality of preterm birth and NICU care. The second concept is nursing care, which Mefford describes as existing at the boundary of the patient's internal and external environments. Nursing care in this setting consists of supporting preterm patients in the conservation of energy, structural integrity, personal integrity, and social integrity (Mefford, 2004). The third concept is health, defined within the theory as the successful attainment of the health status of a well newborn who delivered at term gestation (Mefford, 2004).

The theory of Health Promotion for Preterm Infants has been used by nursing researchers. It was retrospectively validated within the original publication and has been used as the framework for other studies. In 2011 Mefford and Alligood again applied the theory to a retrospective review of the impact of nursing interventions on the age and attainment of health

status at hospital discharge in former preterm infants. In 2015 Spilker used the theory to support the creation of a tool for nursing to enhance developmentally supportive patient positioning in preterm infants. The concepts, assumptions, and propositions within the theory are relevant to any preterm infant and family unit within a NICU setting, with application across genders, cultures, languages, and socioeconomic statuses.

The application of Mefford's theory of Health Promotion for Preterm Infants to the project for the weaning of respiratory support in preterm infants is direct and intuitive (See Appendix E). The concepts within the theory, adaptation, nursing care, and health, are inherent in the project and critical to its goal. Adaptation is defined in Mefford's theory as a process of changing the self to better fit with a recently changed environment. This adaptation specifically refers to the maturational physiologic changes that occur within the infant to independently survive outside of the womb (Mefford, 2004). Infants born under 32 weeks of completed gestation are not physiologically mature enough to breathe unassisted and may not ventilate or oxygenate appropriately at the alveolar level. To survive to hospital discharge, infants must mature and attain the health goal of adequate independent respiration for gas exchange. Successful extrauterine adaptation is a foundational goal of the project, decreasing the rates of decompensation events and BPD in the population.

Methods

IRB, Ethics, and Funding

The primary institutional review board (IRB) was the affiliated regional children's hospital IRB. Although the project site's hospital organization has an IRB, it does not approve pediatric studies or projects. Other projects previously implemented within the site were approved through the children's hospital's IRB, as the neonatologists and nurse practitioners at

the site are contracted through that institution. The project sought IRB determination as not human subjects research.

Privacy was the primary ethical concern related to the project. It was necessary to collect demographic data on the pre- and post-intervention groups. Although most data needed was specific to the infant, some were collected from maternal medical records. Maternal medical data included maternal risk factors or therapies which impact infant respiratory development, such as antenatal steroid dosing and the timing of steroid treatment. To respect the privacy of babies and mothers, records needed to be only reviewed for the specific data needed for the study. Ethical considerations of the unequal application of the QI intervention were minimized by the pre- and post-intervention project implementation and data collection.

The project team leader has no conflict of interest. The clinical site already employed the devices and services utilized within the project. No outside financial interests impacted the project. Minimal funding was required to implement the project. Small stipends for printing physical materials were necessary, and budgeting allowed for unforeseen miscellaneous costs incurred during the project. The project budget was approved by the clinical site in advance of implementation and was approved for inclusion within the NICU unit budget (See Appendix F).

Setting and Participants

The participants in the project were infants born onsite within the birth center at less than 32 weeks GA at the time of birth. The primary inclusion criteria were gestational age and birthweight. All infants who met the protocol criteria were included in the EBPQI project protocol. The protocol represents a change in the standard of care within the setting and was applied to positive pressure weaning when applicable, regardless of the level of respiratory support needed immediately after birth. Exclusion criteria included known or suspected

congenital anomalies, as such differences can impact respiratory health beyond the scope of the respiratory morbidities associated with preterm birth. The study design was quasi-experimental with a goal of at least 44 infants in a pre-intervention group and 44 infants in a post-intervention or protocol group. Baseline data were collected from the pre-intervention group and compared to data collected from the protocol group. The groups were compared for demographics including gender, ethnicity, gestational age at birth, antenatal steroids, and postnatal surfactant administration.

Intervention

The project intervention consisted of developing and implementing a weaning protocol for the discontinuation of non-invasive positive pressure respiratory support in preterm NICU patients. The protocol was derived from the best available evidence and the project was considered evidence-based practice quality improvement (QI). The protocol, evidence, and rationale were presented by the project team leader separately to providers and then nursing staff at monthly meetings prior to implementation. Nursing education focused on the importance of CPAP maintenance from the delivery room through NICU admission with further emphasis on consistent CPAP during nursing interventions and handling. Provider education elaborated upon the evidence support for the project. The protocol had a planned implementation of August 1, 2021.

Procedure

Infants born at less than 32 weeks or 1500 grams at birth had CPAP prophylactically applied in the delivery room. After the initial delivery room resuscitation, support was provided via a Ram cannula interface with CPAP delivered via a mechanical ventilator, both of which were already available and currently in use within the site. There was an emphasis on consistent

CPAP during nursing care and patient transfer to maintain an infant's FRC. Once infants were included in the protocol based on the entry criteria, they remained on CPAP until meeting all the cessation criteria, though PEEP could be weaned as low as 5 cmH_2O as clinically indicated. Continuous positive airway pressure cessation could be considered when an infant had reached 32 weeks GA and attained and maintained for at least 3 days a weight greater than 1500 grams. Once the necessary weight and GA were reached, an infant was required to meet stability criteria before CPAP could be discontinued. Stability criteria were met when, for 48 hours, an infant had not required supplemental oxygen and had fewer than five bradycardia or desaturation episodes per day (See Appendix G). When the criteria were met, the infant could be weaned directly to room air, though HFNC could be used as a step-down measure at provider discretion.

Baseline data were collected from the pre-intervention group for infants fitting the intervention criteria born in the 12 months prior to the protocol start date. Data collection began with infants born August 1, 2020 and continued until sufficient numbers were obtained. Baseline data collection could span birth dates through July of 2021 if necessary. The protocol was approved by faculty with planned implementation August 1, 2021 and data collection to continue for 6 months through January 31, 2022 (See Appendices H, I, J). Data collection was completed by the project team leader.

Change Process and EBP Models

To achieve evidence-based practice change within the facility, the Stetler Model of evidence-based practice was used in the project. The Stetler Model is a nursing model that originated as a method of research utilization and was adapted over time to facilitate evidence-based practice (Stetler, 2001). The Change Curve Model was used to affect organizational

change within the unit and the facility, as the project impacted several nursing units within the birth center at the project site.

The project is sustainable beyond the initial data collection period. The hospital organization and facility have a focus on QI and various protocols already exist for different clinical problems. Once staff is educated that a protocol exists for a problem, protocols are easy to access via a computer program. Compliance for existing protocols is high within the site, and this project could be expected to have the same success.

Project Design

The project is evidence-based QI with a quasi-experimental, two group design. The protocol was applied to infants born within the site's birth center at birthweights of less than 1500 grams or less than 32 weeks completed GA. These infants were included because research supports that infants born at this stage of development benefit from the prophylactic use of CPAP to avoid the need for mechanical ventilation (Subramaniam, Ho & Davis, 2016).

A clinical decompensation event following CPAP discontinuation was the primary outcome measure. Decompensation was measured as clinical concern resulting in the unplanned procurement of a CBC or blood culture with or without antibiotic administration, obtaining a CXR, or the return to CPAP or greater respiratory support in the 7 days following the initial wean from CPAP. In the absence of another etiology, such a decompensation event could indicate that CPAP was weaned ahead of physiologic maturity. The secondary outcome of interest, BPD, was measured as the need for supplemental oxygen at 36 weeks GA. This outcome would only be observed for those infants who had reached 36 weeks GA by the end of the data collection period.

Validity

Internal validity was promoted by comparison of pre- and post-intervention groups and eliminating the potential for selection bias, as all infants in the designated timeframe who met the inclusion criteria were included in the project. Pre- and post-intervention groups were compared with regard to predetermined demographic data and perinatal historical data to ensure parity between the two. Several threats to internal validity existed, one was attrition. Infants who are very premature, less than 27 weeks GA at birth, and those who require alternative ventilation modes, such as HFOV, are transferred to a regional pediatric referral center. This had the potential to skew the population, favoring the less severely ill preterm infants who remain at the site. However, this skewness was likely to affect both groups equally. Another major threat to internal validity was early intermittent adoption of some of the protocol guidelines in advance of the implementation start date. To control for incomplete early implementation, the pre-intervention historical sample needed to span one full year prior to the implementation of the protocol and a second pre-intervention data set of infants born August 1, 2018 through July 30 2019 was obtained for the project.

External validity was promoted by gathering demographic and historical data about the groups. This ensured similarity of the pre- and post- intervention groups but also reported population data for comparison to preterm infant populations in other centers. This enhanced control for other factors that could potentially impact the outcomes of the project, increasing replicability. Centers with similar patient populations could consider utilizing this or similar protocols. The CPAP patient interface used at the site is the RAM cannula. The RAM cannula is a short binasal prong and is not a sealed CPAP method by design. With RAM cannula use, the delivered CPAP may be less than the pressure ordered (Green et al., 2019). Sometimes this is

accounted for by increasing PEEP to support patients struggling with this support method. Centers with different interfaces for the delivery of CPAP could modify protocol criteria, especially regarding the lowest allowable PEEP before weaning off CPAP.

Outcomes

The primary outcome measured was cardiorespiratory decompensation in the 7 days following weaning off CPAP, either to HFNC or to room air. This data was nominal, yes or no. A decompensation event could be indicative of weaning in advance of physiologic maturity. The secondary outcome was the incidence of BPD. Secondary outcome data were unlikely to be available on all infants at the end of the data collection period but were obtained on any infant who had reached 36 weeks GA by the end of the data collection period. This secondary outcome data was also nominal. The rate of BPD in the population can be indicative of improvements or declines in postnatal respiratory management.

Measurement Instruments

Cardiorespiratory Decompensation

No validated measurement tool exists that can be applied to the primary outcome, decompensation events. For the purposes of the project, a decompensation event was defined as clinical concern resulting in the unplanned procurement of a CBC, blood culture, or CXR, the initiation of antibiotics, or an increase in respiratory support to CPAP or greater. Such management decisions are indicative of a change in the clinical status of an infant and, although they are non-specific, may indicate intolerance to respiratory weaning. This definition was adapted from that used by Kakkilaya and colleagues (2018) to measure failure of CPAP weaning. Within the study, intolerance was defined by increases in apnea, bradycardia, and

desaturation event frequency. The definition for the current project was extrapolated to more specific responsive clinical steps to facilitate collection of historical data.

Bronchopulmonary Dysplasia

Likewise, tools are limited for the measurement of the secondary outcome, BPD. A generally accepted definition is the need for supplemental oxygen at 28 days of life with severity of the disease categorized based on the level of respiratory support needed at 36 weeks GA (Jobe & Bancalari, 2001). The definition of BPD is further refined by the National Institute of Child Health and Development (NICHD) as the need for supplemental oxygen at 36 weeks GA for those born at less than 32 weeks GA and at 28 days of life for those born at greater than 32 weeks GA. Similarly but less specific, the Vermont Oxford Network (VON) defines BPD as the need for supplemental oxygen at 36 weeks GA regardless of age at birth (Concina, Samide, & Bada, 2018). For the purposes of the project, BPD was measured as the need for supplemental oxygen at 36 weeks GA which is consistent with both the NICHD and VON definitions, as the population consisted only of infants born at less than 32 weeks GA (See Appendix K).

Quality of Data

An a priori power analysis was conducted using G*Power with a power of 80%, alpha .05, allocation 1:1, and a two-tailed difference between two independent proportions z-test. With an anticipated proportion of successful weaning without decompensation events in the pre-intervention group of .65 and the post-intervention group of .9, the sample size needed was 88, with 44 in each group. The secondary outcome analysis of BPD was planned via Fischer's exact test. The number of infants in the post-intervention group for whom secondary outcome data would be available was limited by the need to reach 36 weeks GA for measurement. Baseline data from a pre-intervention cohort was collected from infants born at the site, meeting the

protocol entry criteria, and discharged from the hospital within the 12 months preceding the implementation of the protocol. Intervention data were to be collected on all infants meeting the protocol criteria born on or after August 1, 2021.

No benchmark studies were identified measuring the same primary outcome and intervention. Studies comparing two methods of weaning and the success of each are abundant in the literature, so the results of the data collected for this project can be compared to the demographic data and weaning success rates detailed in a large study comparing the success of gradual versus sudden CPAP pressure weaning by Kakkilaya and colleagues in 2018 (n=226). This study was chosen for consistency with the project site in the reported delivery room management and population similarity. Demographic data would be compared to the data from 3 other studies that reported average GA and weight at the time of weaning success (Amatya et al., 2015; Amatya et al, 2017; Kidszun et al, 2016).

Analysis

Primary outcome data were to be analyzed with chi-square for proportions. If the numbers enrolled did not meet criteria, Fischer's exact test would be used in determining statistical results. The primary outcome data were nominal, yes or no, indicating whether or not a decompensation event occurred in the 7 days following weaning off CPAP. Secondary outcome data were also nominal and analyzed with Fischer's exact test, as numbers were expected to be small for this outcome (See Appendices L and M).

Demographic data were collected to ensure that the pre- and post-intervention groups were comparable. The demographic data collected were gender, GA at birth, birthweight, and maternal ethnicity. Medical historical data included maternal antenatal steroid exposure, whether or not an infant required intubation, and surfactant administration. Additional data were collected

for potential outcome importance, including GA at initial and successful weaning off CPAP and weight at initial and successful weaning off CPAP (See Appendix N). T-tests or chi-square tests were anticipated to compare the demographic and historical data between groups and GA and weight at the time of initial and successful weans from CPAP.

Results

Setting and Participants

The project was initiated on August 23, 2021 at the site. The site was a level III NICU with an onsite birth center in a large suburban area with an average daily patient census of 20 neonates. The participants in the project consisted of infants born onsite within the birth center at less than 32 weeks GA or at less than 1500 gram birthweight. Pre-intervention data was collected for infants meeting the same criteria with birthdates from August 1, 2020 to July 31, 2021. After determining that some aspects of the protocol were implemented earlier, affecting the data for the planned pre-intervention cohort, a second pre-intervention data set was collected for infants meeting criteria with birthdates August 1, 2018 through July 31 2019. The 2018-2019 group was ultimately used and will be referred to as the pre-intervention group. Data were collected for 6 months, through February 23, 2022.

The pre-intervention group consisted of 34 infants (n=34). During the study period, 20 infants were born who met criteria and were placed on the protocol. One infant who met protocol criteria was lost to analysis after being inadvertently weaned from CPAP ahead of protocol guidelines (n=19). The two groups did not differ in maternal ethnicity, gender, or the need for intubation and surfactant. The protocol group was younger in mean gestational age at birth (p = .189) and smaller in birthweight (p = .166) than those in the pre-intervention group (See Appendix O). Though these differences did not meet statistical significance, they may be

clinically relevant and do reflect a trend at the center toward keeping infants of younger GA rather than transferring them to a regional referral center.

Intervention Course, Actual

The intervention standardized the weaning from positive pressure respiratory support for infants of low birthweight and low GA. Infants born at less than 32 weeks GA or less than 1500 grams were placed on CPAP or greater support at the time of delivery and maintained on at least CPAP until they reached 32 weeks GA and had maintained a weight of at least 1500 grams for 3 consecutive days. After an infant reached the necessary age and weight criteria, stability criteria needed to be met prior to weaning. Stability criteria consisted of 48 consecutive hours during which an infant did not require supplemental oxygen and had fewer than five bradycardia and/or desaturation events per day.

During the protocol implementation, infants were enrolled regularly. Greater increases in numbers were seen with the births of several sets of premature infants of multiple gestation in the final months of 2021. Very few infants meeting the protocol criteria were born in the final months of the data collection period in early 2022. Although this limited the anticipated numbers, it enabled complete collection of data regarding the secondary outcome of interest, BPD, for all infants in the protocol group.

Outcome Data

The implementation of the protocol resulted in a significant change in practice as evidenced by the difference in GA and weight at initial attempts to wean from CPAP, both analyzed by one-way ANOVA. The protocol group remained on CPAP longer than the pre-intervention group, averaging 33 and 4/7 weeks compared to 32 and 6/7 weeks at first weaning attempt ($p = .021$). The protocol group had higher weight at initial wean from CPAP as well,

reaching 1780 grams compared to 1665 grams at the time of initial weaning attempt (p = .182). Although the difference in average weight did not meet statistical significance, it correlated well with the increased GA which did meet significance (See Appendix O).

The primary outcome of interest was decompensation in the 7 days after weaning off CPAP. In the pre-intervention group, 23.5% of infants met the project definition of decompensation after weaning compared to 36.8% in the protocol group. The greater incidence of decompensation in the protocol group did not meet statistical significance (p = .351) by Fisher's exact test (See Appendix P).

The secondary outcome of interest was BPD as measured by oxygen requirement at 36 weeks GA. The pre-intervention group saw 32.4% of infants meet the definition for BPD diagnosis. In the protocol group 26.3% of infants met the criteria for BPD. The decreased incidence of BPD in the protocol group was not statistically significant by Fisher's exact test (p = .760) but may have clinical relevance because of the differences in GA and birthweight between the groups, as low birthweight and decreasing GA increase a population's risk of BPD (See Appendix P).

One infant from the protocol group was omitted from analysis after being weaned from CPAP outside of the protocol guidelines. The groups were smaller than desired during project planning, so outcome analysis was done by Fisher's exact test for both outcomes.

Discussion

Successes

The protocol group experienced a decreased incidence of BPD. Although this was not a statistically significant finding (p = .760) due to limited numbers, the results may have clinical relevance. The protocol group was smaller at birth by weight and younger in GA on average

when compared to the pre-intervention group. The average GA in the pre-intervention group was 30 and 3/7 weeks compared to the protocol group average of 29 and 5/7 weeks (p = .189). The study was underpowered to meet statistical significance, but these differences may have clinical relevance, especially concerning the BPD outcome. Lower birthweight and lower gestational age are risk factors for the development of BPD. The protocol group's lower birthweight and lower birth GA should coincide with an increased risk of BPD among the group compared to the pre-intervention group. The results show a trend toward a decreased incidence of BPD in the protocol group, which may indicate that the protocol was beneficial in preventing the development of BPD. A large sample and ongoing data collection may help to elucidate this finding.

Strengths

The project implementation benefitted from enthusiastic nursing support. After presenting the proposal to nursing staff, charge nurses showed engagement in ensuring that protocol aspects were followed from a nursing perspective. Additional support from the medical director of the NICU ensured that providers remained aware of the protocol and continued to follow the criteria. Before the implementation there was a concern that varying levels of respiratory staff education would be a hindrance to implementation, but this was not experienced. Respiratory staff remained supportive and adaptive to the changes in practice through the protocol.

Protocol implementation was largely successful. All infants born within the protocol period who met criteria were appropriately placed on the protocol. Only one infant was lost to follow up for having CPAP discontinued earlier than 32 weeks GA. This failure provided an

opportunity to reeducate staff and renew interest in the project for the remainder of the data collection period.

Results Compared to Evidence

Little evidence was available to address the outcomes of interest in the project. Decompensation events are variably defined and not the topic of available studies. There is support in the literature for prophylactic CPAP use after delivery to reduce BPD, but this data was not collected in the project, as most infants in the target population require at least CPAP as initial support regardless of subsequent resuscitation steps.

Many studies addressed the GA and weight at successful CPAP weaning and one addressed the relative success of protocolized weaning in preterm infants. An RCT evaluating standardized weaning tools found that the use of a protocol for respiratory weaning resulted in successful weaning approximately one week earlier than before the protocols were implemented (Kidszun et al., 2016). In this project successful weaning occurred at an average of 33 and 6/7 weeks compared to 33 and 0/7 weeks in the pre-intervention group (p=0.028, See Appendix O). This represents weaning success at almost one week later in the protocol group than in the pre-intervention group, in contrast to what the available evidence suggested.

The GA and weight required to begin CPAP weaning in the protocol were derived from evidence suggesting that weaning success, regardless of the method used, tended to occur between 32 and 33 weeks GA (Amatya et al., 2015). Several other large RCTs noted that infants averaged 33 weeks GA at the time of weaning success (Amatya et al., 2017, Kakkilaya et al., 2020). The project data show that infants in the pre-intervention group were weaned successfully at a mean age of 33 and 0/7 weeks and those in the protocol group at 33 and 6/7 weeks (p = .028). Evidence regarding weight at the time of weaning success showed that infants were

successfully weaned between 1450 and 1600 grams (Amatya et al., 2017, Kidszun et al., 2016). This evidence informed the project requirement of 1500 gram weight prior to attempting weaning. The actual weight achieved at the time of successful weaning in the pre-intervention group was a mean of 1687 grams, compared to 1842 grams in the protocol group (p = .172). The project findings related to weight and GA at weaning success are consistent with the literature and tend toward greater GA and weight in both groups than available evidence had indicated.

Limitations

Internal Validity Effects

Internal validity was enhanced by strong adherence to the protocol. All infants meeting criteria were placed on the protocol and only one was weaned outside of the parameters. The factors with the greatest negative influence on internal validity related to the definitions of decompensation and BPD.

Decompensation was defined as the unplanned procurement of a CBC, blood culture, or CXR, the initiation of antibiotics, or an increase in respiratory support to CPAP or greater. This definition became problematic, both increasing and decreasing the incidence of recorded decompensation in the data, and affected both groups. Preterm and low birthweight infants are at increased risk of gastrointestinal (GI) illness. Infants who exhibited signs of feeding intolerance or hematochezia in the week following CPAP weaning received CXR in conjunction with abdominal imaging, as well as blood cultures and antibiotics. This accounted for several instances of recorded decompensation in the data. While it is possible that symptoms of respiratory decompensation and GI illness could overlap, these clinical changes may have occurred independent of CPAP weaning and could have erroneously affected the outcome data. A refined definition in future analysis of data would be necessary.

Bronchopulmonary dysplasia was defined for the project purposes as the need for supplemental oxygen at 36 weeks GA. This definition is well accepted in the literature, but within the project may have been excessively precise, limiting understanding of the entire clinical picture. In both groups, there were infants who did not meet the definition of BPD but days or weeks later required a return to small amounts of supplemental oxygen. This would indicate the actual rate of BPD in both groups may be higher than that observed. There was one infant in the protocol group who met the BPD definition prior to any attempts to wean off CPAP. While the diagnosis of BPD in this infant is valid, it is not an indicator of the effect of the protocol and, with limited numbers in the protocol group, may have had a significant impact on the results observed.

External Validity Effects

The infants included in the protocol were predominantly born to white mothers, and all were within an affluent suburban area. This may negatively impact the transferability of the project intervention to centers with different patient populations. All other demographic data that were collected serve to enhance transferability, allowing interested sites to compare birthweight, GA, incidence of maternal steroid dosing, and infant intubation and surfactant rates. Centers with similar demographics could expect to see similar protocol utility.

Equipment usage has the potential to impact intervention transferability. The project site utilizes a RAM cannula as the only available CPAP interface. This interface is designed with a substantial leak, often necessitating an increase in PEEP compared to other, more occlusive, devices. The use of RAM cannula influenced the protocol decision not to wean CPAP below a PEEP of 5 cm/H_2O, understanding that the actual PEEP delivered was likely to be lower than the

ordered PEEP. Centers utilizing different support devices would need to adapt the protocol guidelines to better align with available equipment within a facility.

Sustainability of Effects

Although the project outcomes did not meet statistical significance, any improvement in the rate of BPD among preterm infants is clinically relevant and may prevent morbidity and mortality. The continued use of the protocol at the site could enhance infant population health and is not demonstrated to be harmful. The CPAP weaning protocol will be sustained at the site and further evaluated and adapted over time.

Protocol adherence is likely to wane over time without continued engagement and staff updates. To increase compliance with the protocol, providers will be updated at semi-annual meetings, and nursing staff will receive new education on a quarterly basis. The NICU unit educator will include protocol training in new hire nursing education and in annual ongoing education.

Efforts to Minimize Limitations

Although the outcome definitions were likely to have erroneously impacted the results, the definitions were consistently applied as originally planned. This minimized the undue impact upon either group, keeping the impact on outcome data consistent between the groups. Racial and ethnic diversity was minimal in both groups and although transferability is thus limited, the pre- and post-intervention groups were similar in composition. Although a difference in GA and birthweight was noted that did not meet statistical significance, other demographic data supported that the two groups were not different in other ways that could impact the rates of decompensation or BPD. This similarity between groups mitigates potential outside influences on the outcome data.

Interpretation

Expected and Actual Outcomes

The goal of the protocol was to decrease the incidence of decompensation and BPD in the population. The expectation was that protocol use would result in a decrease in episodes of decompensation, but this was not seen. The protocol group experienced an increased rate of decompensation, 36.8% compared to 23.5% in the pre-intervention group ($p = .351$). This result was not statistically significant, and further collection of data to increase the size of the protocol group is necessary. Additionally, refinement of the definition of decompensation is needed to ensure that the decompensation seen is likely to be related to respiratory support weaning.

Bronchopulmonary dysplasia incidence data were available on all patients in the protocol group, which was not an expectation prior to protocol implementation. The data showed a decreased incidence of BPD in the protocol group, 26.3% compared to 32.4% in the pre-intervention group ($p = .760$). This finding was expected, though the results were not statistically significant. Limited numbers in the protocol group impact the usefulness of this outcome finding, but the preliminary data suggest that continuing the protocol with ongoing data collection has potential value.

Intervention Effectiveness

Standardization of CPAP weaning in preterm infants has the potential to decrease the rate of BPD in the population. Infants in the protocol group were generally younger and smaller than those in the pre-intervention group. If the use of the protocol conferred no effect, the expectation would be that rates of BPD would at least be the same between the two groups or would be higher in the more at-risk protocol group. The actual data indicate a clinically significant trend toward less BPD in the protocol group. With a larger protocol group and more data, it may be

possible to show that the rate of BPD would be statistically decreased with the use of standardized weaning.

The use of a standardized CPAP weaning protocol is most likely to be effective in NICU settings that routinely care for infants less than 32 weeks GA at birth. Additionally, centers which consistently utilize one respiratory interface, allowing staff to be familiar with and adept at using equipment, are more likely to experience respiratory weaning success. A strong culture of protocol use will also contribute to the successful implementation of a new respiratory support weaning protocol.

Intervention Revision

Data for both groups suggest that weaning success at the site tends to occur at 33 weeks GA or greater and at greater than 1600 grams in weight. The protocol indicates that weaning can be attempted at 32 weeks GA and 1500 grams, which is significantly younger and smaller than is generally successful within the setting. In revising the intervention, it may be prudent to increase the age and weight necessary for initial CPAP weaning. This change could enhance success at the first attempt to wean support.

Expected and Actual Impact

The project implementation was associated with a potential decrease in the rate of BPD. If this outcome is verified through further study, the potential decrease in morbidity and mortality for preterm infants would be meaningful in many ways. The health system would see fewer babies and children with ongoing complications related to BPD. The societal burden on hospitals and cost of care could also be decreased with fewer children in the community affected by ongoing respiratory conditions.

The cost of the project was initially budgeted at $100. The actual cost was far less than anticipated. Because of the COVID-19 pandemic mitigation strategies, a great deal of the education was remote or online. This negated the need for printed materials. The time spent on data collection greatly outpaced what was anticipated. This could increase the ongoing costs if required to compensate an individual for time spent in future data collection. Outside of data collection, the project cost did not meaningfully add to the site's budget, as the equipment needed was already in use.

Opportunities

In addition to adapting the definition for decompensation, and possibly BPD, adjustments to the demographic data collected may enhance understanding of the results. Maternal steroid dosing prenatally is meant to enhance fetal lung maturity and improve infant respiratory outcomes. Steroids are shown to be beneficial when administered as two doses given 14 days to 24 hours before delivery. In many instances and in both groups, steroids were given to mothers as a single dose immediately prior to imminent preterm delivery. These doses were unlikely to impact fetal respiratory health, so in future data collection a more specific definition should be used. Another factor that may need to be addressed is demographic data collection regarding infants of multiple gestation. Several infants included in both groups were from pregnancies of multiples, which may impact the risk of prematurity and its comorbidities, including BPD.

Data collection in the pre-intervention group focused on age and weight at the time of CPAP weaning but did not include other aspects which were part of the protocol. Stability criteria were required of the protocol group prior to CPAP weaning and included the requirement to not be utilizing supplemental oxygen. Data regarding supplemental oxygen level at the time of

CPAP weaning in the pre-intervention group were not collected. This additional data could further demonstrate the differences in stability between groups at the time of CPAP weaning.

Conclusion

Practical Usefulness

Protocols standardizing approaches to care ensure consistency within a clinical site. The protocol for weaning positive pressure respiratory support in preterm infants, at the very least, does not harm infants and may improve the rate of BPD in the population. Infants with BPD often require longer initial hospital stays and ongoing care related to associated morbidities throughout childhood. If consistently used, the protocol may improve outcomes in the population at the site, and the data gathered adds to the body of literature supporting the successful weaning of respiratory support in premature infants.

Further Study of Intervention

The site will continue to implement the protocol. Ongoing data collection to increase the protocol group size would allow for reanalysis of the outcome data in hope of achieving statistical significance. Based on the historical data, the protocol group could be expected to reach the same size as the historical group by August 2022. After a complete data set is analyzed, the protocol can be further refined.

Dissemination

The project outcome data is being presented to the group of providers at CMH in a series of update meetings in Spring 2022. The project will be presented in a podium presentation at the Academy of Neonatal Nursing Spring 2022 conference in Orlando, FL, on May 13, 2022. A manuscript reporting the project and outcomes will be submitted to Neonatal Network for consideration for publication.

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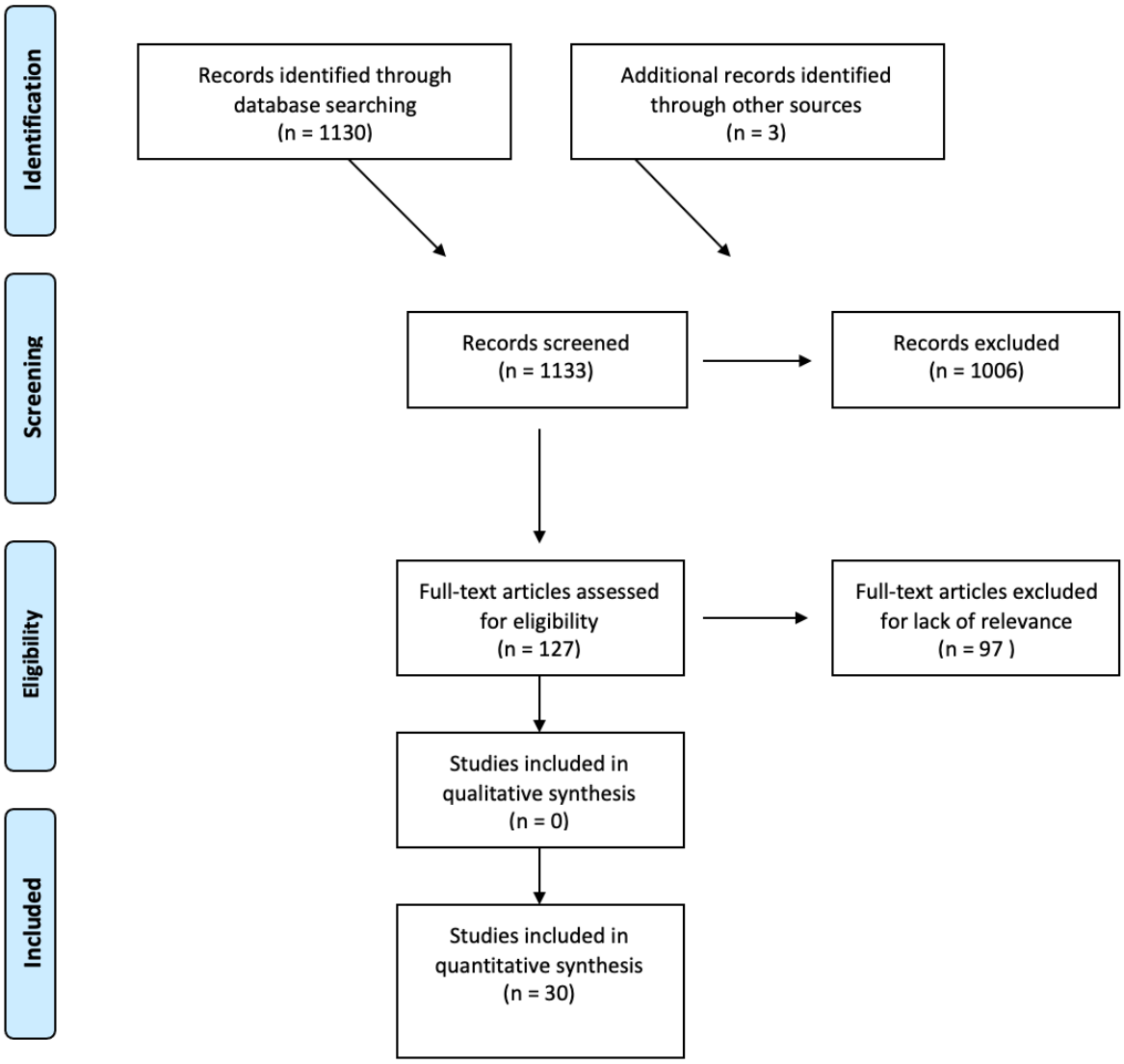
Appendix A

Adapted PRISMA Flow Diagram



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Appendix B

Hierarchy of Evidence

Rating System for the Hierarchy of Evidence For an Interventional Inquiry (Modification by Dr. Lindholm for course N5613)	
Level I	Evidence from a systematic review or meta-analysis of all relevant RCTs. *Evidence-based clinical practice guidelines based on systematic reviews of RCTs).**
Level II	Evidence obtained from well-designed RCT. *Quantitative systematic review of well-designed controlled trial without randomization.*
Level III	Evidence obtained from well-designed controlled trial without randomization *(quasi-experimental).* *Quantitative systematic review of case-control, cohort, or correlational studies.*
Level IV	Evidence from well-designed case-control or cohort study *(or cross-sectional study)*
Level V	Evidence from systematic review of *quantitative* descriptive *(no relationships to examine)* or qualitative studies.
Level VI	Evidence from a single *quantitative* descriptive *(no relationships to examine in the study) or* qualitative study
Level VII	Evidence from the opinion of authorities and/or reports of expert committees

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Appendix C

Evidence Table

First author, Year, Title, Journal	Purpose	Research Design[1], Evidence Level[2] & Variables	Sample & Sampling, Setting	Measures & Reliability (if reported)	Results & Analysis Used	Limitations & Usefulness
Kanbar, Shalish, Latrmouille, Rao, Brown, Kearney, Sant'Anna (2020) Cardiorespiratory behavior of preterm infants receiving continuous positive airway pressure and high flow nasal cannula post extubation: randomized crossover study	Compare respiratory behavior in newly extubated preterm infants on CPAP to those on high flow nasal cannula (HFNC)	Quantitative, unblinded, paired RCT Level II evidence HFNC first, CPAP first, respiratory pauses, desaturation, apnea, asynchronous breathing, movement	30 infants <1250 gram birthweight who were intubated at birth (n=14 CPAP first, n=16 HFNC first) 2 neonatal units in Montreal, Canada. Random assignment, paired case-control.	Wilcoxon's rank-sum and signed-rank nonparametric tests for paired comparisons Significant results for maximum respiratory pause length (p=0.04) and lowest (p=0.02) and highest (p=0.05) FiO2 requirement.	When on HFNC infants had increased maximum respiratory pause length compared to CPAP. Time on HFNC also associated with increased FiO2 requirement. Extubation failure was higher in the HFNC first group.	Study done immediately after extubation from mechanical ventilator. May have limited application to population never requiring intubation.
Soonsawad, Tongsawang, Nuntnarumit (2016). Heated Humidified High-Flow Nasal Cannula for Weaning from Continuous Positive Airway Pressure in Preterm Infants: A Randomized Controlled Trial	Compare time to wean off CPAP directly to weaning by using high flow nasal cannula (HFNC)	Quantitative unblinded RCT Level II evidence Wean from CPAP directly, wean from CPAP to HFNC, length of respiratory support, bronchopulmonary dysplasia, retinopathy of prematurity, intraventricular hemorrhage, necrotizing enterocolitis, patent ductus arteriosus, need to escalate respiratory support/intubate	101 preterm infants <32 weeks gesatational age (n=51 in HFNC group and n=50 in CPAP group) Single center study, Thailand	Chi square and Fisher's exact for categorial variables, Mann-Whitney U for continuous Length of respiratory support did not differ between CPAP and HFNC groups (p=0.12).	Infants took about 11 days to wean off respiratory support once weaning began in both CPAP and HFNC groups. There was no difference in morbidities between the groups.	Limited study size and single center design. Fixed 24 hour weaning schedules may have prolonged the weaning time.
Yoder, Stoddard, King, Dirnberger, Abbasi (2013). Heated, humidified high-flow nasal cannula versus nasal CPAP for respiratory support in neonates	Assess efficacy of safety of high flow nasal cannula (HFNC) compared to CPAP	Quantitative unblinded RCT Level II evidence HFNC support, CPAP support, failure on support mode, total ventilator and non-invasive support days, need for delayed intubation, frequency of adverse events, nasal mucosal injury, overall comfort, incidence of bronchopulmonary dysplasia	432 infants 28-42 weeks gestational age (n=220 in CPAP group, n=212 in HFNC group) Seven centers in the United States and China	Chi square intention to treat analysis, categorial variables via Chi square of Fischer's exact. Student's t test for normally distributed or Mann-Whitney U for non-normal distribution. No difference in early failure between groups (p=0.521),	HFNC was as safe as CPAP but infants tended to remain on respiratory support longer in HFNC group (p<0.01).	Study underpowered to demonstrate statistical significance. No standardization of CPAP or HFNC interfaces between centers.

				need for intubation (p=0.252), or any morbidity studied.		
Wilkinson, Andersen, O'Donnell, De Paoli (2016). High flow nasal cannula for respiratory support in preterm infants	Compare efficacy of high flow nasal cannula (HFNC) with other non-invasive respiratory support	Meta analysis of 15 RCTs and quasi-randomised controlled trials Level I evidence HFNC, CPAP, non-invasive positive pressure ventilation, chronic lung disease (CLD), death, treatment failure/reintubation, length of respiratory therapy, length of hospitalization, air leak syndrome, nasal trauma, sepsis, GI illness, weight gain, days to attain full feeds	HFNC as primary support compared to CPAP, primary outcome/death, and CLD (4 studies, n= 439), difference as primary support (1 study, n=75), post extubation compared to CPAP (6 studies, n=934), death or CLD (5 studies, n=893), treatment failure (5 studies, n=786), reintubation (5 studies, n=934), nasal trauma (4 studies, n=645)	Chi square with Z scores for overall effect for each outcome. HFNC comparable to CPAP as post-extubation support/ death (p=0.61), as post-extubation support/ CLD (p=0.56), as delivery room prophylactic support (p=0.34), worse than CPAP at preventing extubation failure (p=0.12), less nasal trauma on CPAP (p=0.17), decreased incidence of pneumothorax on HFNC (p=0.99)	HFNC is associated with reduced nasal trauma, is associated with longer duration of respiratory support, outcomes and CLD were essentially the same between HFNC and CPAP	Limited numbers of extremely preterm and late preterm infants included in studies. In some of the included studies, the flow delivered by HFNC was at discretion of clinicians. Secondary outcomes were taken from medical records and subject to bias
Glackin, O'Sullivan, George, Semberova, Miletin (2017). High flow nasal cannula versus NCPAP, duration to full oral feeds in preterm infants: a randomised controlled trial	Compare the time taken by preterm infants to achieve full oral feeds when supported with HFNC or CPAP	Quantitative unblinded RCT Level II evidence HFNC, CPAP, number of days to full oral feeds, duration of respiratory support	44 preterm infants <1500 grams and <30 weeks gestation at birth, who remained on respiratory support with/without supplemental oxygen at 32 weeks (n=22 in CPAP group, n=22 in HFNC group) Single center study, Ireland	Student's t-test, Fischer's exact, and Mann-Whitney U. Infants on HFNC achieved full feeds in about 36 days and those on CPAP in about 34 days (p=0.61)	Preterm infants on HFNC and CPAP reached full oral feeds at similar times, there was no improvement in those treated with HFNC. No aspiration was noted in infants orally fed while on CPAP	Limitated by lack of blinding and noted staff preference for handling infants on HFNC which may have favored earlier and more consistent oral feeding practice in the HFNC group.
Murki, Singh, Khant, Dash, Oleti, Joy, Kabra (2018). High-flow nasal cannula versus nasal continuous positive airway pressure for primary respiratory support in preterm infants with respiratory distress:	Compare safety and efficacy of HFNC and CPAP for use premature infants	Meta analysis of 21 RCTs Level I evidence HFNC, CPAP, treatment failure, nasal trauma, pneumothorax	21 studies with total n=2886, treatment failure (n=2772),	Weighted mean differences for continuous outcomes, relative risk for non-continuous. Treatment failure rate was similar	HFNC was similar in efficacy and safety to CPAP as primary support, was less successful at post-extubation support, and was associated with less nasal	Lack of standardized definition of treatment failure and nasal trauma. Limited representation of preterm infants <28 weeks and with birthweight <1000 grams

A randomized controlled trial				between HFNC and CPAP (RR 1.03, p= 0.84), HFNC showed decreased nasal trauma incidence (p<0.00001), CPAP associated with less treatment failure when used after extubation (RR 1.23, p=0.04), similar number of days on respiratory support between CPAP and HFNC (p=0.54)	trauma and fewer pneumothoraces	
Nasef, El-Gouhary, Schurr, Reilly, Beck, Dunn, Ng (2015). High-flow nasal cannulae are associated with increased diaphragm activation compared with nasal continuous positive airway pressure in preterm infants	Comparing diaphragm activity in infants on HFNC vs CPAP	Unblinded, randomized crossover study Level II evidence HFNC, CPAP, neural inspiratory/expiratory time, electronic activity of the diaphragm peak/minmum, heart rate, respiratory rate, FiO2	10 preterm infants <1500 g at birth (mean gestational age 26 weeks and birthweight 900 g) Single center study	Paired t-test, chi square, Fischer's exact Increase in electrical activity of the diaphragm noted on HFNC (p=0.1) and longer neural inspiratory time (p=0.01)	Infants showed no difference in clinical measures of respiratory distress on HFNC vs CPAP, but increase in neurologic measures indicating greater work of breathing on HFNC. PEEP delivered by HFNC may be too little for preterm infants.	Small sample size, short study period on each support method(2 hours). Results may underestimate the difference between HFNC and CPAP in population
Tang, Reid, Lutz., Malcolm, Oliver, Osborn (2015). Randomised controlled trial of weaning strategies for preterm infants on nasal continuous positive airway pressure	Determine optimal strategy for successfully weaning preterm babies off of CPAP	Quantitative unblinded RCT Level II evidence Abrupt CPAP wean with HFNC, abrupt CPAP wean without HFNC, gradual CPAP wean with HFNC, gradual CPAP wean without HFNC, chronic lung disease, days of respiratory support, length of hospital stay, day to full oral feeds, corrected gestational age off various types of respiratory support, weight at 36 weeks	60 preterm infants < 30 weeks gestation (n=15 in each of four study arms) Single center study, Australia	ANOVA, student's t-test, Kruskal-Wallis, Mann-Whitney U, Pearson chi, Fischer exact No significant difference in primary outcomes, duration of CPAP was decreased in abrupt wean with HFNC group, 1 day compared to 15-24 days (p= 0.002). Infants with any HFNC	Duration of CPAP was decreased in infants treated with HFNC, but there was no difference in any other primary or secondary outcome. Infants with HFNC did not fully wean from respiratory support or achieve full oral feeds sooner. Abrupt wean with HFNC is effective and may be most acceptable to parents.	Pilot study, further research needed to support conclusions

				had reduced duration of CPAP (p=0.009)		
Conte, Orfeo, Gizzi, Massenzi, Fasola (2018). Rapid systematic review shows that using a high-flow nasal cannula is inferior to nasal continuous positive airway pressure as first-line support in preterm neonates	Assess the efficacy of HFNC as first line respiratory support for preterm infants	Systematic review of 6 RCTs Level I evidence HFNC, CPAP, non-invasive positive pressure ventilation (NIPPV), treatment failure, intubation, BPD	6 studies with total n=1227 preterm infants <37 weeks gestation	RR with Mantel-Haenszel model, mean differences with inverse variance method CPAP was associated with lower risk of treatment failure (p<0.001), intubation (p=0.15), and BPD (p=0.54)	HFNC is associated with greater treatment failure than CPAP in preterm infants >28 weeks gestation	English language studies only, rapid review with limited results from just 3 databases searched
Manley, Roberts, Froisland, Doyle, Davis, Owen (2018). Refining the use of nasal high-flow therapy as primary respiratory support for preterm infants	Identify variables that predict failure of HFNC as first line respiratory support	Quantitative analysis of unblinded RCT Level II evidence HFNC, CPAP, failure of support within 72 hours,	278 preterm infants with mean gestational age 32 weeks and mean birthweight about 1750 g Multicenter trial, Australia and New Zealand	Chi square, t-test, Mann-Whitney U Infants who failed HFNC had lower gesatational age and higher supplemental FiO2 need before study began (both p<0.01)	Lower gestational age and higher FiO2 requirement are moderately predictive of HFNC treatment failure. CPAP is superior in all groups studied at preventing treatment failure	Study includes few extremely preterm infants and a cohort that was mostly exposed to antenatal corticosteroids to improve pulmonary outcomes
Abdel-Hady, Shouman, Aly (2011). Early weaning from CPAP to high flow nasal cannula in preterm infants is associated with prolonged oxygen requirement: a randomized controlled trial	Determine which approach is superior for CPAP weaning, with or without transition to nasal cannula (NC)	Quantitative, unblinded RCT Level II evidence No NC, NC, total oxygen days, duration of respiratory support, success of weaning off CPAP, length of hospitalization	60 preterm infants > or = 28 weeks gestation (n=30 in each group) Single center study, Egypt	T-test or Mann Whitney U, depending on distribution. Chi square and Fischer's exact test for categorical data. Length of oxygen therapy differed significantly (p<0.001), as did total CPAP days (p=0.04) avg 11 days vs 8 days in NC group.	Weaning directly from CPAP to room air after 24 hours of stability on FiO2 0.21 was associated with fewer supplemental oxygen days (5 days vs 14 days in NC group). No difference in successful weaning between groups. Total days on CPAP increased in the no NC group (11 days vs 8 days).	No infants less than 28 weeks were included in the study, potentially skewing results by sampling infants with decreased incidence of significant respiratory disease of prematurity
Liew, Fenton, Harigopal, Gopalakaje, Brodlie, O'Brien (2020). Physiological effects of high-flow nasal cannula therapy in preterm infants	Understand respiratory physiology effects of HFNC use in preterm infants	Unblinded, randomized crossover study Level II evidence HFNC, CPAP, PEEP, tidal volume, deadspace washout, SpO2, vital signs	44 preterm infants with birthweight 500-1900 g Single center study, England	ANOVA, Tukey, Spearman correlation, multiple linear regression Weight negatively correlated	HFNC provides PEEP but with wide ranging variability, especially in infants <1000 g. CPAP delivers effective PEEP more consistent with desired	No esophageal pressure measurements which would have provided data on lung compliance and work of breathing. Increase in FiO2

				with PEEP on HFNC (p=0.0001), CPAP delivered more consistent PEEP (set and achieved 6 mmH2O) and was > HFNC 2-7 lpm (p <0.05)	PEEP. Weight is associated with greater alterations in PEEP on HFNC than gestational age.	requirement in 30% of infants, most <1000 g, was seen but not included in analysis
Kotecha, Adappa, Gupta, Watkins, Kotecha, Chakraborty (2015). Safety and efficacy of high-flow nasal cannula therapy in preterm infants: a meta-analysis	Compare safety of HFNC to other forms of non-invasive respiratory support	Meta analysis of 9 RCTs Level I evidence HFNC, CPAP, non-invasive positive pressure ventilation (NIPPV), treatment failure, death, pulmonary air leak, nasal trauma	9 studies with total n=1112 preterm infants < 37 weeks gestation	Weighted mean differences, odds ratios HFNC is associated with a very slightly increased risk of treatment failure (OR 1.09), risk of nasal trauma was significantly reduced on HFNC (OR 0.13, p=0.02)	HFNC use is comparable in safety to other non-invasive support methods and is associated with lower risk of nasal trauma	Unable to stratify results based on gestational age, limited data to support safety in infants <32 weeks gestation
Heiring, Steensberg, Bjerager, Greisen (2015). A Randomized Trial of Low-Flow Oxygen versus Nasal Continuous Positive Airway Pressure in Preterm Infants	Compare lung function at 28 days in infants on CPAP versus those on low flow nasal cannula (NC)	Quantitative, multicenter, unblinded RCT Level II evidence Prolonged CPAP, low flow nasal cannula, a/A pO2 at 28 days, respiratory support at 36 weeks, weight gain, length of CPAP therapy	52 preterm infants >26 weeks GA and <1500 g birthweight infants (n=30 in CPAP group and n=22 in low flow NC group) 7 neonatal units in Denmark, random assignement, two arms.	T test, ANOVA and Mann Whitney U tests. Categorical variables compared with chi square or Fisher's exact test. Very few variables met statistical significance, only length of time of CPAP (p<0.001)	CPAP group did not have decreased need for respiratory support or supplemental oxygen at 36 weeks GA compared to low flow oxygen group. Total length of time on CPAP was increased in CPAP group. No difference in weight at 28 days or discharge between groups.	Data collected in 2003-2005 but not published due to organizational problems. Ultimately published in 2015 due to increasing use of CPAP in population. Match between groups poor. Greater number in CPAP group had been intubated and received surfactant, indicative of greater degree of respiratory disease. Limited statistical power
Kugelman, Bar, Riskin, Chistyakov, Mor, Bader (2008). Nasal respiratory support in premature infants: short-term physiological	Compare object comfort assessment on and off of nasal respiratory support	Unblinded, randomized crossover study Level II evidence Spontaneous breathing in room air, CPAP, nasal intermittent positive	54 preterm infant (mean birthweight 1500 g and 30.5 weeks gesatational age) Single center study, Israel	Paired t-test, Wilcoxon rank-sum, chi square, regression analysis BP and discomfort scores were	Heart rate was the same on and off respiratory support, respiratory rate was higher without support. BP and discomfort scores were	Discomfort assessment is subjective and may be biased in unblinded study. No continuous monitoring of BP and no blood gases included in study. BP

effects and comfort assessment		pressure ventilation, heart rate, respiratory rate, blood pressure (BP), discomfort score		higher when on respiratory support ($p < 0.001$). Respiratory rate higher off support ($p<0.001$)	increased which may indicate discomfort, however no nasal breakdown noted on respiratory support.	could be higher on support due to increased lung recruitment, reflecting overall improved stability
Subramaniam, Ho, Davis (2016). Prophylactic nasal continuous positive airway pressure for preventing morbidity and mortality in very preterm infants	Investigate whether prophylactic CPAP in the delivery room reduces need for mechanical ventilation and BPD in preterm infants	Meta analysis of 7 unblinded RCTs Level I evidence CPAP, assisted ventilation, failure of treatment, rate of BPD, mortality, surfactant use, air leak, feeding intolerance, neurologic injury, necrotizing enterocolitis, sepsis, retinopathy of prematurity, length of hospital stay, neurodevelopmental outcome	7 studies with total n=3123	Weighted mean differences for continuous outcomes, relative risk for non-continuous CPAP compared to mechanical ventilation with or without surfactant showed small reduction in BPD or death in CPAP group (RR 0.89). Decreased need for mechanical ventilation (RR 0.5) and surfactant (RR 0.54) in CPAP group	Prophylactic CPAP in the delivery room reduces the need for mechanical ventilation and surfactant use in preterm babies	Insufficient evidence to compare CPAP to other non-invasive forms of respiratory support Studies were unblinded, in some studies a few participants were excluded from results after randomization and treatment plans were not adhered to
Kraaijenga, de Waal, Hutten, de Jongh, van Kaam (2017) Diaphragmatic activity during weaning from respiratory support in preterm infants	Determine the effect of weaning from CPAP to low flow nasal cannula (LFNC) on the electrical activity of the diaphragm (edi) in neonates	Prospective observational cohort study Level III evidence CPAP edi, LFNC edi, success or failure of weaning	59 infants < 36 weeks gestation, for a total of 74 weaning attempts measured Single level 3 NICU in Amsterdam, Netherlands	Repeated measures ANOVA, and group comparisons with Mann-Whitney U or t-test Infants who failed first attempt had lower gestational age ($p<0.05$) or higher number of apnea and bradycardia events in the prior 24 hours ($p<0.05$)	Edi increased in all infants after weaning off CPAP to LFNC, most significantly in those who went on to fail wean. Frequent apnea and bradycardia events in the prior 24 hours may be predictive of weaning failure.	High number of infants dropped out during the first 2 hours of planned 3 hour measurement, limiting power. Study only included relatively stable neonates
Abu-Shaweesh, Khasawneh, Tang, Worley, Saker, (2020). Compared to CPAP extubation to non-invasive ventilation is associated with higher risk of	Compare rates of BPD between infants extubated to CPAP versus extubated to Non-invasive intermittent positive	Retrospective cohort study Level III evidence Extubation to CPAP, extubation to NIV, BPD, gestational age, birthweight	122 preterm infants with birthweight < 1000 grams (n=46 CPAP group, n=74 NIV group)	Wilcoxon rank-sum and Chi square, logistic regression for data correction and presented as medians	Those extubated to CPAP experienced a lower rate of BPD when compared to multiple different forms of NIV,	Retrospective study, no definitive extubation readiness criteria at center, provider discretion for which post-

bronchopulmonary dysplasia in extremely low birth weight infants	pressure ventilation (NIV)		Cleveland Clinic Children's Hospital, OH	Lower incidence of BPD in CPAP group (p=0.011), result remained after adjusting for weight and age (p=0.029)	including neural adjusted ventilator assist (synchronized mode). The finding remained after controlling for GA and birthweight	extubation support mode to use
Jardine, Inglins, Davies (2011). Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants	Determine risks and benefits of different strategies for CPAP withdrawal	Systematic review including 3 RCTs and quasi randomized trials Level I evidence Stopping CPAP abruptly, weaning to predefined level and then stopping completely, cycling times off CPAP, weaning from CPAP to HFNC, time to successfully weaning off CPAP, treatment failure, intubation	3 studies with total n=364	Weighted mean differences, relative risk for categorical outcomes for planned meta analysis. Results were limited to review of studies due to limited number of studies meeting criteria	Weaning CPAP to predefined pressure and then stopping completely is associated with less total time on CPAP, shorter duration of oxygen therapy, and shorter hospital stay compared to cycling off CPAP	One included study is published only as an abstract
Lam, Schilling, Scottoline, Platteau, Niederhausen, Lund, Schelonka, MacDonald, McEvoy (2020). The effect of extended continuous positive airway pressure on changes in lung volumes in stable premature infants: a randomized controlled trial	Evaluate impact of 2 weeks of CPAP vs discontinuation of CPAP on lung volume through discharge	Quantitative unblinded RCT Level II evidence CPAP 2 weeks, CPAP discontinuation, functional residual capacity (FRC) at 2 weeks, FRC at discharge	44 infants <32 weeks gestation (CPAP 2 weeks n=24, discontinuation CPAP n=26) Single center study	t-test, Mann-Whitney U, chi square Infants on 2 weeks of CPAP had greater FRC at 2 weeks (p=0.03) and at discharge (p=0.01)	Preterm infants who remained on prophylactic CPAP for 2 weeks had improved lung function	Small sample, single center study
Weisz, Yoon, Dunn, Emberley, Mukerji, Read, Shah (2021). Duration of and trends in respiratory support among extremely preterm infants	Describe the duration of the need for different forms of respiratory support in neonates based on gestational age.	Retrospective cohort study Level III evidence Gestational age (GA), length of mechanical ventilation, length of positive pressure support, length of oxygen therapy	8881 preterm infants born at 23 0/7 to 27 6/7 weeks gestation, fron 1/1/2010-12/31/2017. Tertiary NICUs in the Canadian Neonatal Network	Interquartile ranges for support types, descriptive statistics for antenatal and perinatal characteristics Infants born at 27 weeks GA were successfully weaned off positive pressure support at a mean age of 33 4/7 weeks (31 4/7- 35 6/7 weeks) (n=2601)	Lower gestational age is associated with a longer duration of mechanical ventilation, though trended toward earlier extubation over time. Length of positive pressure support increased over the study period, authors speculated due to earlier extubation trend.	Multi center study with different practices, techniques, and modalities. Limited to infants of extremely low GA
Yin, Broom, Wright, Hovey, Abdel-Latif,	Identify factors influencing number of	Quantitative, post-hoc analysis of RCT.	50 preterm babies (PB) (26 in fast wean	Independent sample t-tests, chi-squares or	PB in fast wean group spent less time on CPAP.	Small sample size, post-hoc analysis,

Shadbolt (2016). CeasIng Cpap At standarD criteriA (CICADA): predicting a successful outcome	attempts before successful CPAP wean	Level II evidence Gestational age (GA), birthweight (BW), gender, patent ductus arteriosus (PDA), on corrected GA (CGA) at time of initial CPAP wean and successful CPAP wean	arm, 24 in slow wean arm) One center Random assignment, two groups	Fisher's exact tests to compare categorical variables among groups. Correlation study and linear regression. BW to duration of CPAP r = -0.497, p=0.001	PDA, GA <27 weeks and BW <900 grams increased length of CPAP and number of weaning attempts before success.	between-group differences in GA and BW
Eze, Murphy, Dhar, Rehan (2018). Comparison of sprinting vs non-sprinting to wean nasal continuous positive airway pressure off in very preterm infants	Compare successful weaning off CPAP in a sprinting wean (scheduled intervals off CPAP and on HFNC) vs gradual pressure wean	Quantitative, unblinded RCT Level II evidence Sprinting wean, gradual pressure wean, successful wean off CPAP on first attempt, number of attempts to wean, number of day to successful wean, and incidence of BPD, severe ROP, and PVL. Length of stay and gestation age at discharge	80 infants, 23-31 weeks gestation at birth (n=40 in each group) 2 neonatal units in California. Random assignment.	Chi square or Fischer's exact test for between group data. Two sample t-test or Wilcoxon rank-sum for continuous variables. No significant differences were found. between groups for any variable	Sprinting and gradual pressure wean were comparable. Each group required avg 1.3 attempts to wean off CPAP and 7 days total CPAP therapy.	Imbalance in number of infants included from each site. Insufficient sample size to stratify results by gestational age
Kakkilaya, Tang, Wagner, Ridpath, Ibrahim, Brown, Rosenfeld (2020). Discontinuing Nasal Continuous Positive Airway Pressure in Infants ≤32 Weeks of Gestational Age: A Randomized Control Trial	Compare immediate cessation v. stepwise decrease in pressure of CPAP	Quantitative, single center, unblinded RCT Level II evidence Abrupt CPAP discontinuation, gradual pressure wean, and total CPAP days	226 preterm infants <32 weeks GA (116 control group, 110 gradual wean group) One high volume delivery center, random assignment, two groups	Independent t test, Chi square, and Mann Whitney U tests. Very few variables compared met statistical significance	Abrupt weaning associated with more failed attempts prior to successful wean. No difference in total CPAP duration, length of O2 therapy, length of stay. Both groups avg 33 wks at time of successful wean.	Unblinded groups, no specified cessation criteria in control group, and 10% attrition from each arm
Wielenga, van den Hoogen, van Zanten, Helder, Bol, Blackwood (2016). Protocolized versus non-protocolized weaning for reducing the duration of invasive	Assess efficacy of protocolized weaning in reducing the duration of mechanical ventilation	Systematic review of RCTs Level I evidence Weaning with protocol, weaning without protocol, days of mechanical ventilation	Only 2 studies met inclusion criteria but those we unable to provide data on subgroup analysis and thus were excluded		There is insufficient evidence to support or refute the value of protocolized weaning	Limited studies available to address research question

mechanical ventilation in newborn infants						
Kidszun, Plate, Arnold, Winter, Gerhold-Ay, Mildenberger (2016). Standardized weaning of infants <32 weeks of gestation from continuous positive airway pressure - a feasibility study	Evaluate the feasibility of a standardized approach to CPAP weaning in preterm babies	Quasi-experiemental pre and post intervention feasibility study Level II evidence Weaning without protocol, weaning with protocol, success of weaning at first attempt	Pre intervention cohort n=36, post intervention cohort n=41 Single center study	Chi square, Mann-Whitney U No significant difference in gestational age at time off CPAP (p=0.405), or weight off CPAP (p=0.927). Infants post intervention weaned off respiratory support sooner (p=0.171)	Most babies were successfully weaned off CPAP by about 32 weeks gestation and 1450 grams, both pre and post intervention. After intervention infants weaned off respiratory support of any kind about 1 week sooner (32 weeks compared to 33 weeks)	Pre and post study, possible bias and confounding variables
Amatya, Macomber, Bhutada, Rastogi, Rastogi (2017). Sudden versus gradual pressure wean from Nasal CPAP in preterm infants: a randomized controlled trial	Determine whether gradually pressure weaning of CPAP or abrupt weaning to room air is more successful	Quantitative unblinded RCT Level II evidence Sudden wean off CPAP to room air, gradual CPAP pressure wean, success at weaning on first attempt, gestational age at successful wean, weight at successful wean	70 preterm infants <32 weeks gestation (sudden cessation n=35, gradual wean n=33) Single center study	Student's t-test, chi square, Fisher's exact Greater success off CPAP at first attempt in gradual pressure group (p=0.03), no significant difference in age or weight at time of successful wean	Infants in gradual wean group were more successfully weaned on first attempt. Both groups weaned off CPAP at about 33 weeks gestation and 1600 grams	Unblinded study, but compensated for with strict weaning algorithm and parameters
Jensen, Sellmer, Ebbesen, Cipliene, Johansen, Hansen, Nielsen, Nikitina, Petersen, Henriksen (2018). Sudden vs pressure wean from nasal continuous positive airway pressure in infants born before 32 weeks of gestation: a randomized clinical trial	Compare sudden weaning of CPAP with gradual pressure weaning in preterm infants	Quantitative unblinded RCT Level II evidence Gradual pressure wean, abrupt wean to room air, success on first wean attempt, weight gain velocity, total duration of CPAP	372 infants <32 weeks gesatation (sudden wean group n=185, gradual wean n=187) 6 centers in Denmark	Linear model with risk ratios No statistical difference in weight gain velocity between groups, no difference in secondary outcomes. Gradual pressure group more successfully weaned on first attempt (41% vs 11%)	Infants <28 weeks gestation were more successfully weaned on first attempt in the gradual pressure wean group	Unblinded study, accounted for with strict weaning criteria
O'Sonnell, Curry, Buggy, Moynihan, Sebokova, Janota, Miletin (2013). The NOFLO trial: low-flow nasal prongs therapy in weaning nasal	Determine if low flow nasal cannula (NC) room air aids weaning off CPAP in low birthweight infants	Quantitative unblinded RCT Level II evidence NC wean, spontaneous room air	78 infants <1500g (NC group n=39, spontaneous breathing n=39)	t-test, Mann-Whitney U, Fisher's exact No significant difference in success between	No benefit of weaning from CPAP to NC compared to weaning directly to room air	Study underpowered to evaluate the secondary outcome of CLD

continuous positive airway pressure in preterm infants	compared to room air	breathing, chronic lung disease (CLD)	2 centers in Ireland and Czech Republic	groups (p=0.48). Mild increase in respiratory rate in room air group (p=0.05)		
Amatya, Rastogi, Bhutada, Rastogi (2015). Weaning of nasal CPAP in preterm infants: who, when and how? A systematic review of the literature	Determine the gestational age (GA), weight, and weaning method for which weaning off CPAP is most successful	Systematic review of 7 studies Level I evidence Gestational age, weight, sudden wean to room air, gradual pressure wean, cycled time off CPAP	Total n=1015 preterm infants	RCT of 6 of the 7 studies included GA at time of successful wean 31.9-33.8 weeks	Weaning off CPAP is most successful at 32-33 weeks GA and 1600 g. Unclear which weaning method is optimal	Insufficient studies available focusing on weaning methods off CPAP

Appendix D

Evidence Grid by Theme

	HFNC and CPAP comparison	Safety/Efficacy of HFNC in population	Safety/Efficacy of CPAP in population	Comfort on CPAP	Cardiorespiratory stability on CPAP/HFNC	Weaning strategies (protocols)
A Randomized Trial of Low-Flow Oxygen versus Nasal Continuous Positive Airway Pressure in Preterm Infants (Heiring, 2015)			X			
Cardiorespiratory behavior of preterm infants receiving continuous positive airway pressure and high flow nasal cannula post extubation: randomized crossover study (Kanbar, 2020)	X				X	X
CeasIng Cpap At standarD criteriA (CICADA): predicting a successful outcome (Yin, 2016)						X
Comparison of sprinting vs non-sprinting to wean nasal continuous positive airway pressure off in very preterm infants (Eze, 2018)						X
Discontinuing Nasal Continuous Positive Airway Pressure in Infants ≤32 Weeks of Gestational Age: A Randomized Control Trial (Kakkilaya, 2020)						X
Early weaning from CPAP to high flow nasal cannula in preterm infants is associated with prolonged oxygen requirement: a randomized controlled trial (Abdel-Hady, 2011)		X				X
Heated Humidified High-Flow Nasal Cannula for Weaning from Continuous Positive Airway Pressure in Preterm Infants: A Randomized Controlled Trial (Soonsawad, 2016)	X	X				X
Heated, humidified high-flow nasal cannula versus nasal CPAP for respiratory support in neonates (Yoder, 2013)	X	X				
High flow nasal cannula for respiratory support in preterm infants (Wilkinson, 2016)	X	X				
High flow nasal cannula versus NCPAP, duration to full oral feeds in	X					

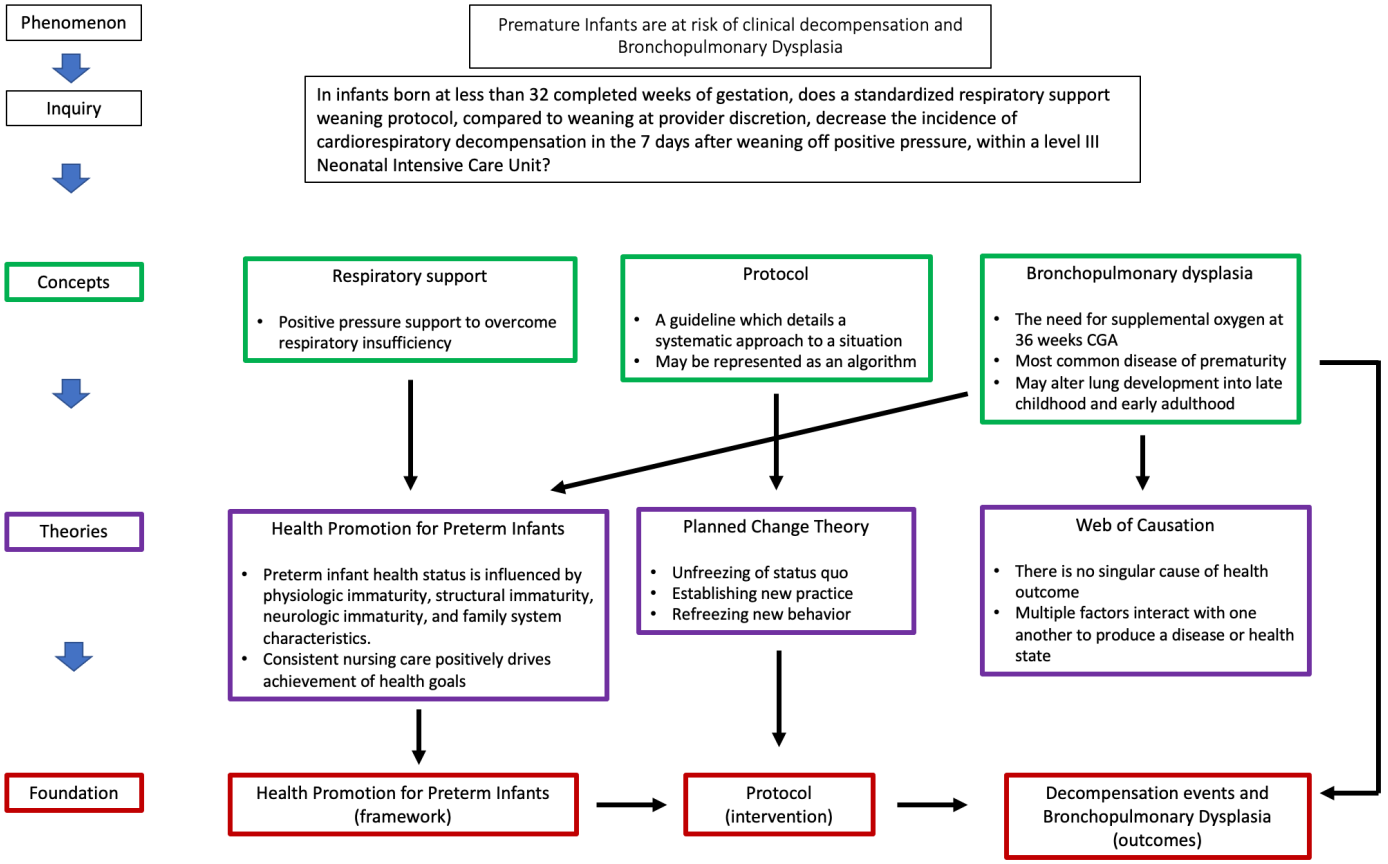
	HFNC and CPAP comparison	Safety/Efficacy of HFNC in population	Safety/Efficacy of CPAP in population	Comfort on CPAP	Cardiorespiratory stability on CPAP/HFNC	Weaning strategies (protocols)
A Randomized Trial of Low-Flow Oxygen versus Nasal Continuous Positive Airway Pressure in Preterm Infants (Heiring, 2015)			X			
preterm infants: a randomised controlled trial (Glackin, 2017)						
HIgh-flow nasal cannula versus nasal continuous positive airway pressure for primary respiratory support in preterm infants with respiratory distress: A randomized controlled trial (Murki, 2018)	X	X				
High-flow nasal cannulae are associated with increased diaphragm activation compared with nasal continuous positive airway pressure in preterm infants (Nasef, 2015)	X	X			X	
Nasal respiratory support in premature infants: short-term physiological effects and comfort assessment (Kugelman, 2008)			X	X		
Physiological effects of high-flow nasal cannula therapy in preterm infants (Liew, 2020)		X				
Prophylactic nasal continuous positive airway pressure for preventing morbidity and mortality in very preterm infants (Subramaniam, 2016)			X		X	
Protocolized versus non-protocolized weaning for reducing the duration of invasive mechanical ventilation in newborn infants (Wielenga, 2016)						X
Randomised controlled trial of weaning strategies for preterm infants on nasal continuous positive airway pressure (Tang, 2015)	X	X				
Rapid systematic review shows that using a high-flow nasal cannula is inferior to nasal continuous positive airway pressure as first-line support in preterm neonates (Conte, 2018)	X				X	
Refining the use of nasal high-flow therapy as primary respiratory	X	X			X	

	HFNC and CPAP comparison	Safety/Efficacy of HFNC in population	Safety/Efficacy of CPAP in population	Comfort on CPAP	Cardiorespiratory stability on CPAP/HFNC	Weaning strategies (protocols)
A Randomized Trial of Low-Flow Oxygen versus Nasal Continuous Positive Airway Pressure in Preterm Infants (Heiring, 2015)			X			
support for preterm infants (Manley, 2018)						
Safety and efficacy of high-flow nasal cannula therapy in preterm infants: a meta-analysis (Kotecha, 2015)		X				
Standardized weaning of infants <32 weeks of gestation from continuous positive airway pressure - a feasibility study (Kidszun, 2016)						X
Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants (Jardine, 2011)					X	X
Sudden versus gradual pressure wean from Nasal CPAP in preterm infants: a randomized controlled trial (Amatya, 2017)						X
Sudden vs pressure wean from nasal continuous positive airway pressure in infants born before 32 weeks of gestation: a randomized clinical trial (Jensen, 2018)						X
The effect of extended continuous positive airway pressure on changes in lung volumes in stable premature infants: a randomized controlled trial (Lam, 2020)					X	X
The NOFLO trial: low-flow nasal prongs therapy in weaning nasal continuous positive airway pressure in preterm infants (O'Sonnell, 2013)						X
Weaning of nasal CPAP in preterm infants: who, when and how? A systematic review of the literature (Amatya, 2015)						X
Diaphragmatic activity during weaning from respiratory support in preterm infants (Kraaijenga, 2017)			X			
Duration of and trends in respiratory support						X

	HFNC and CPAP comparison	Safety/Efficacy of HFNC in population	Safety/Efficacy of CPAP in population	Comfort on CPAP	Cardiorespiratory stability on CPAP/HFNC	Weaning strategies (protocols)
A Randomized Trial of Low-Flow Oxygen versus Nasal Continuous Positive Airway Pressure in Preterm Infants (Heiring, 2015)			X			
among extremely preterm infants (Weisz, 2021)						
Compared to CPAP extubation to non-invasive ventilation is associated with higher risk of bronchopulmonary dysplasia in extremely low birth weight infants (Abu-Shaweesh, 2020)			X			

Appendix E

Theory Application



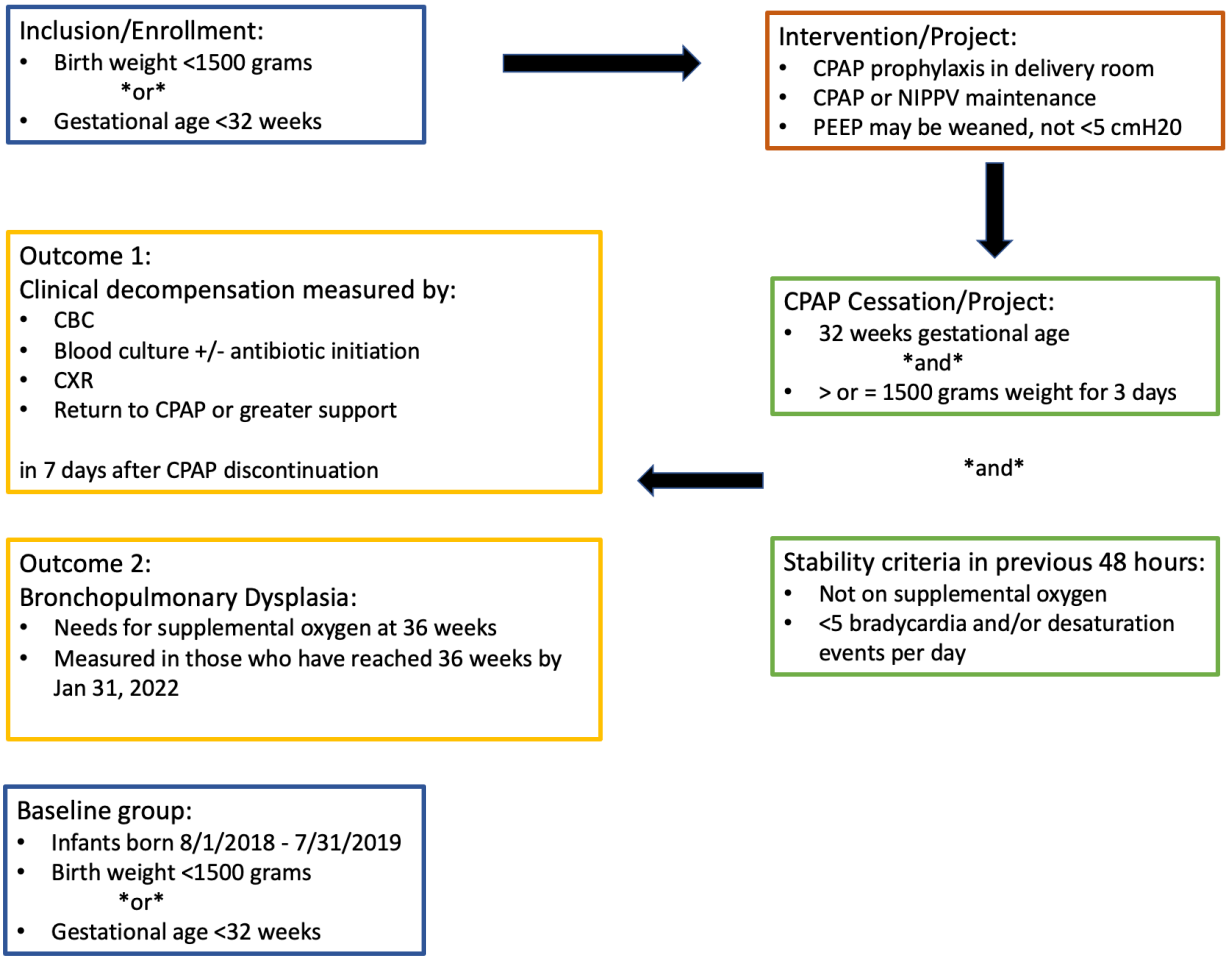
Appendix F

Budget Table

Item	**Item Description**	**Quantity**	**Unit Cost**	**Anticipated Cost**
Print materials	Protocol Diagrams	20	$0.03	Up to $1
Equipment	None that is not already employed in the unit			$0
Miscellaneous	Allocation for unforeseen educational materials			Up to $100
Student Time	Protocol development, presentations at staff meetings, data collection	132 hours	Not billed	$0
Total				$101

Appendix G

Intervention Flow Diagram



Appendix H

Faculty Approval Letter

UMKC School of Nursing and Health Studies

June 28, 2021

UMKC DNP Student: Michelle Marshall

Congratulations. The UMKC Doctor of Nursing Practice (DNP) faculty has approved your DNP project proposal, *A protocol for weaning preterm infants off of respiratory support.*

You may proceed with IRB application

Sincerely,

Cheri Barber, DNP, RN, PPCNP-BC, FAANP
Clinical Assistant Professor
DNP Program Director
UMKC School of Nursing and Health Studies barberch@umkc.edu

Lyla Lindholm, DNP, RN, ACNS-BC
Clinical Assistant Professor, DNP Faculty
MSN-DNP Program Coordinator
UMKC School of Nursing and Health Studies lindholml@umkc.edu

Debbie C. Pankau DNP, APRN, FNP-BC
Clinical Assistant Professor
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DNP Faculty Mentor Daphne A Reavey PhD, RN, NNP-BC
UMKC School of Nursing and Health Studies

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Appendix I

IRB Approval Letter

Children's Research Institute
CHILDREN'S MERCY KANSAS CITY

NOT ENGAGED IN HUMAN SUBJECTS RESEARCH

August 16, 2021

Michelle Marshall: memarshall@cmh.edu

Dear Dr. Marshall:

On 8/16/2021, the ORI staff reviewed the following protocol:

Type of Review:	Initial Study
Title:	Standardized Weaning of Positive Pressure Support in Preterm Infants
Investigator:	Michelle Marshall
myIRB ID:	STUDY00001904
Funding:	None
Documents Reviewed:	• CPAP Weaning Protocol in Preemies, Intervention, Category: IRB Protocol; • Data Collection Template, Category: Data Collection Sheet; • QI Project Template Form, Category: IRB Protocol

ORI staff determined that the proposed activity does not involve research as defined by DHHS regulations.

This project involves a quality improvement project aimed to improve the weaning of CPAP via standardization. This project involves a measurable, specific goal of evaluating current local practice and implementing ways to directly improve local clinical care at CMH and is not designed to create or contribute to generalizable knowledge. Hence it is not considered a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge according to 45 CFR 46.102(l) (not research).

IRB review and approval by this organization is not required. This determination applies only to the activities described in the myIRB submission listed above and does not apply should any changes be made. If changes are made and there are questions about whether these activities engage CM in human subjects research, please submit a new request in myIRB for a determination. You can create a modification by clicking **Create Modification / CR** within the study.

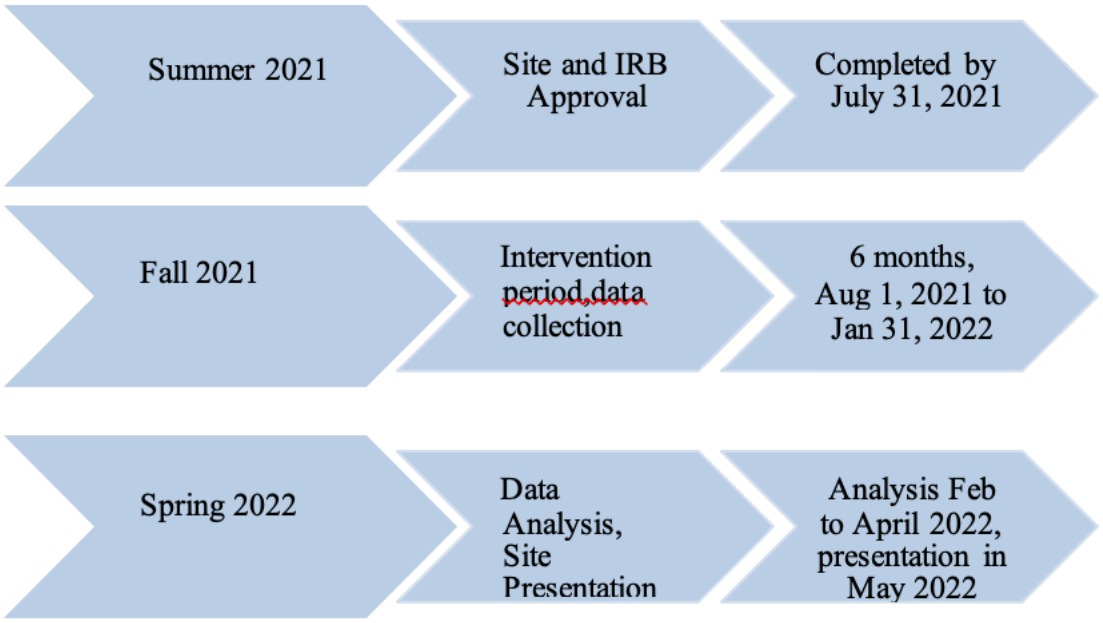
Sincerely,
Dane Sommer, DMin
Co-Chair, CM Institutional Review Board

Doug Swanson, MD
Co-Chair, CM Institutional Review Board

Ryan McDowell
Director, Office of Research Integrity

Appendix J

CPAP Weaning Project Timeline



Appendix K

Definition of Terms

Term	Definition
Antenatal Steroids	Steroids given to a pregnant women to enhance fetal lung maturity within the 2 weeks preceding preterm delivery
Protocol	A guideline outlining a systematic approach to a specific situation, can be represented as an algorithm.
Respiratory Support	Supportive positive pressure sufficient to overcome the respiratory insufficiency characteristic of infants born in the saccular stage of pulmonary development.
Decompensation event	Clinical concern resulting in the unplanned procurement of a complete blood count, chest radiograph, or a blood culture with, antibiotic administration, or the return to CPAP or greater respiratory support.
Bronchopulmonary dysplasia	The need for supplemental oxygen at 36 weeks gestational age.

Appendix L

Statistical Analysis Template

Primary Outcome

Group	Decompensation after wean off CPAP	No decompensation after wean off CPAP	P value
Pre-protocol (n=44)			
Post-protocol (n=44)			
Total			

Secondary Outcome

Group	Bronchopulmonary Dysplasia Diagnosis	No Bronchopulmonary Dysplasia	P value
Pre-protocol (n=?)			
Post-protocol (n=?)			
Total			

Appendix M

Logical Flow of Outcomes to Analysis

Outcome/Demographic	Measurement	Statistical Analysis
Decompensation in 7 days after wean off CPAP	Obtaining CBC or blood culture, starting antibiotics, or escalation in respiratory support	Chi square
Bronchopulmonary Dysplasia	Supplemental oxygen requirement at 36 weeks gestational age	Chi square or Fischer's exact
Gestational age at birth	Weeks/days	T test
Birthweight	grams	T test
Gender	M/F	Chi square
Maternal Ethnicity	NA	T test
Age at successful wean off CPAP	Weeks/days	T test
Weight at successful wean off CPAP	grams	T test
Intubation	Y/N	Chi square
Surfactant	Y/N	Chi square
Maternal steroids	Y/N	Chi square

Appendix N

Data Collection Template

Group		
Gestational Age (GA) at Birth		
Birthweight		
Gender		
GA at Initial Wean Off CPAP		
Weight at Initial Wean Off CPAP		
GA at Successful Wean Off CPAP		
Weight at Successful Wean Off CPAP		
Maternal Ethnicity		
Intubation		
Surfactant		
Maternal Steroids		
Decompensation (Y/N)		
CBC		
Blood Culture		
Antibiotics		
Chest Xray		
Increased Respiratory Support		
Bronchopulmonary dysplasia		

Appendix O

Demographic Data Analysis

Group	Pre-intervention	Protocol	Statistical Test	P value
Gestational Age (GA) at Birth	30.43 weeks	29.80 weeks	ANOVA	0.189
Birthweight	1439 grams	1318 grams	ANOVA	0.166
Gender	M F 19 15	M F 12 7	Fisher's Exact	0.773
GA at Initial Wean Off CPAP	32.81 weeks	33.65 weeks	ANOVA	0.021
Weight at Initial Wean Off CPAP	1665 grams	1780 grams	ANOVA	0.182
GA at Successful Wean Off CPAP	32.93 weeks	33.86 weeks	ANOVA	0.028
Weight at Successful Wean Off CPAP	1687 grams	1842 grams	ANOVA	0.172
Maternal Ethnicity	23 – Caucasian 4 – Black 3 – Hispanic 3 – Asian 1 - Unknown	15 – Caucasian 0 – Black 3 – Hispanic 1 – Asian 0 - Unknown	Chi Square	0.443
Intubation	No Yes 15 19	No Yes 6 13	Fisher's Exact	0.400
Surfactant	No Yes 15 19	No Yes 6 13	Fisher's Exact	0.400
Maternal Steroids	No Yes 0 34	No Yes 1 18	Fisher's Exact	0.358
Decompensation (Y/N)	No Yes 26 8	No Yes 12 7	Fisher's Exact	0.351
Bronchopulmonary dysplasia	No Yes 23 11	No Yes 14 5	Fisher's Exact	0.760

Appendix P

Statistical Analysis Results

	Decompensation		Bronchopulmonary Dysplasia	
Group	Yes	No	Yes	No
Pre-Intervention (n=34)	8	26	11	23
Protocol (n=19)	7	12	5	14
Total (n=53)	15	38	16	37

	Pre-Intervention (n=34)		Protocol (n=19)		
	n	Incidence %	n	Incidence %	P value
Decompensation	8	23.5	7	36.8	0.351
BPD	11	32.4	5	26.3	0.760

Outcome analysis by 2 sided Fisher's Exact Test

Appendix Q

Logic Model

Logic Model for DNP Project					
Student: Michelle Marshall, NNP-BC					
Inquiry: In infants born at less than 32 completed weeks of gestation, does a standardized respiratory support weaning protocol, compared to weaning at provider discretion, decrease the incidence of cardiorespiratory decompensation in the 7 days after weaning off positive pressure, within a level III Neonatal Intensive Care Unit?					
Inputs	**Intervention(s) Outputs**		**Outcomes -- Impact**		
	Activities	***Participation***	**Short**	**Medium**	**Long**
Evidence, sub-topics 1. Safety of HFNC 2. Safety of CPAP 3. Comparison of HFNC and CPAP 4. Cardiorespiratory stability on CPAP/HFNC 5. Comfort on CPAP 6. Weaning protocols Major Facilitators or Contributors 1. Medical director support 2. Organization support for EPBQI 3. Organizational benefit of patient retention at facility Major Barriers or Challenges 1. Respiratory staff preparation 2. Stagnation of tenured staff	EBP intervention Prophylactic CPAP at delivery for infants <32 weeks gestational age followed by weaning protocol of gradual CPAP pressure weaning until 32 weeks age and 1500 gram weight are met Major steps of the intervention 1. Evidence based protocol development 2. IRB and site approval 3. Stakeholder identification 4. Provider education 5. Nursing and respiratory therapy education 6. Protocol implementation 7. Outcome evaluation	The participants Preterm infants born at <32 weeks completed gestational age Site NICU at Advent Health Shawnee Mission (level III) Time Frame 6 months, 8/1/2021-1/31/2022 Consent or assent Needed No Other person(s) collecting data yes Others consenting no	Outcome(s) to be measured during project. Primary: Decompensation in 7 days after wean from CPAP Secondary: bronchopulmonary dysplasia (supplemental oxygen or respiratory support at 36 weeks age) Measurement tool(s) 1. Incidence of obtaining CBC, CRP, blood culture in 7 days after wean from CPAP 2. Increase in respiratory support in 7 days after wean 3. Need for supplemental oxygen or respiratory support at 36 weeks age Statistical analysis to be used 1. chi square for primary outcome 2. Fischer's exact test for secondary outcome 3. T test for demographic data	Bronchopulmonary Dysplasia	None at this time

Appendix R

Executive Summary

Preterm infants often require respiratory support through continuous positive airway pressure (CPAP). There is no consensus as to the safest and most successful method of weaning CPAP. Weaning too quickly may cause morbidity in these patients, specifically increasing episodes of clinical decompensation and rates of bronchopulmonary dysplasia (BPD). Standardized approaches to weaning respiratory support are more successful and may decrease morbidity.

This evidence-based quality improvement (QI) project was planned at a level III neonatal intensive care unit within a large birth center in an affluent suburban area. Respiratory support weaning at the site was inconsistent and discretionary. The purpose of the project was to decrease the incidence of cardiorespiratory decompensation events and BPD by applying an evidence-based protocol for weaning CPAP in infants born at less than 32 weeks gestational age (GA) at the site. The site has an established system of protocol use and good adherence to past QI, making project sustainability at the site likely.

A literature review identified 30 studies with direct application to the project, many of which were high quality evidence. Themes identified in the evidence suggested that infants born at less than 32 weeks GA should be treated with prophylactic CPAP at delivery. Respiratory support may be gradually weaned as predetermined stability criteria are met to improve patient weaning tolerance. An initial attempt to wean an infant off CPAP may be successful at 32 weeks GA, and at a weight of at least l500 grams.

The protocol was implemented for all infants born onsite who met the age and weight guidelines. Infants were placed on CPAP or higher support and maintained on CPAP with a positive end expiratory pressure of at least 5 cm/H_2O until they reached 32 weeks GA and 1500

grams, as well as met the designated stability criteria. The outcomes of interest were cardiorespiratory decompensation within the 7 days after weaning off CPAP and BPD measured at 36 weeks GA. Both outcomes were reviewed nominally, yes or no. Baseline data were collected for infants meeting the criteria born in 2018-2019 and project data was collected from August 2021 to February 2022.

The pre-intervention group consisted of 34 infants (n=34) and the protocol group included 19 infants born during the data collection period (n=19). Demographic data were collected and the groups did not differ in ethnicity, gender, maternal steroid dosing, or infant need for intubation and surfactant. There was a statistically insignificant difference in birthweight and gestational age, with the protocol group having lower means in GA and birthweight (p = .189 and p = .166 respectively). This may be clinically relevant, as the risk of BPD is inversely associated with GA and birthweight.

The two outcomes were analyzed by Fisher's Exact Test due to the discrepancy in size between groups. There was a statistically insignificant increase in decompensation seen in the protocol group (p=0.351) and a decrease in BPD in the protocol group (p=0.760). Although the data was underpowered to meet significance due to low numbers, there may be clinical relevance to the decrease in BPD incidence after protocol implementation. The protocol group was slightly more premature and smaller at birth (mean GA 29.8 weeks and mean birthweight 1318 grams) than the pre-intervention group (mean GA 30.4 weeks and a mean birthweight 1439 grams). These differences increase the risk of BPD in the protocol group, though this group experienced less BPD than the pre-intervention group. Further data collection and study would be needed to show clinical significance of protocol impact on the outcome of BPD.

The project was largely successful, with staff support and consistent application for infants meeting the criteria. The increase in mean GA and weight at the time of weaning after protocol implementation was consistent with the project expectation of keeping infants on CPAP longer before weaning attempts would begin. The evidence review indicated that weaning success tends to occur between 32 and 33 weeks GA. The project protocol group was successfully weaned at a mean age of 33.9 weeks GA, which is older than both the pre-intervention group (32.9 weeks GA) and the available evidence.

Other centers wishing to adopt the protocol would need to ensure population parity and would need to adapt the guidelines to the respiratory support devices available within a particular site. Further data collection at the site is necessary to interpret the effect of the project on the outcomes. Refinement of the definition of decompensation is also needed to ensure clarity of results. If the observed decrease in BPD can be verified through further study, the potential decrease in morbidity and mortality for preterm infants would be meaningful.