# EPIQ REVIEW

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# Does the use of primary continuous positive airway pressure reduce the need for intubation and mechanical ventilation in infants ≤32 weeks' gestation?

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WH Yee, J Scotland, Y Pham, R Finch; Evidence-based Practice for Improving Quality (EPIQ) Evidence Review Group. Does the use of primary continuous positive airway pressure reduce the need for intubation and mechanical ventilation in infants  $\leq$ 32 weeks' gestation? Paediatr Child Health 2011;16(10):633-637.

**BACKGROUND:** Ventilator-induced lung injury is a recognized risk factor for bronchopulmonary dysplasia.

**OBJECTIVE:** To determine whether primary continuous positive airway pressure (CPAP), defined as CPAP without previous endotracheal intubation for any indication, can reduce the need for intubation and mechanical ventilation in infants born at  $\leq$ 32 weeks' gestational age.

**METHODS:** The literature was reviewed using the methodology for systematic reviews for the Consensus on Resuscitation Science adapted from the American Heart Association's International Liaison Committee on Resuscitation.

**RESULTS:** Fourteen studies were reviewed. Eleven studies provided varying degrees of supportive evidence (level of evidence 3 to 4) that the use of primary CPAP can reduce the need for intubation and mechanical ventilation.

**CONCLUSION:** The use of CPAP as a primary intervention and mode of respiratory support is an option for infants  $\leq$ 32 weeks' gestation, but avoidance of intubation and mechanical ventilation is more likely in mature infants >27 weeks' gestation.

Key Words: CPAP; Evidence review; Preterm infant

# BACKGROUND

Bronchopulmonary dysplasia (BPD) is a significant morbidity among surviving preterm infants (1). Rates of BPD vary widely across centres and range from 4.0% to 58.3% (2-4). The pathogenesis is multifactorial, with multiple risk factors such as early volutrauma, barotrauma and oxygen exposure superimposed on immature, developing lungs (1,5-7). Therefore, strategies to minimize these factors would be advantageous. One such strategy is the use of primary continuous positive airway pressure (pCPAP) after delivery to avoid ventilator-induced lung injury.

### **OBJECTIVE**

We reviewed the literature to determine whether pCPAP, defined as CPAP without previous endotracheal intubation for any indication, as a mode of respiratory support after delivery reduces the need for intubation and mechanical ventilation in infants  $\leq$ 32 weeks' gestational age. L'utilisation de la pression positive continue primaire réduit-elle le recours à l'intubation et à la ventilation mécanique chez les nourrissons de 32 semaines d'âge gestationnel ou moins?

HISTORIQUE : Les lésions pulmonaires induites par les respirateurs constituent un facteur de risque connu de dysplasie bronchopulmonaire. OBJECTIF : Déterminer si la pression positive continue (PPC) primaire, définie comme une PPC sans intubation trachéale antérieure pour quelque indication que ce soit, peut réduire la nécessité d'intuber et d'administrer une ventilation mécanique aux nourrissons nés à 32 semaines d'âge gestationnel ou moins.

**MÉTHODOLOGIE :** Les chercheurs ont analysé les publications au moyen de la méthodologie d'analyse systématique du *Consensus on Resuscitation Science* adapté de l'*International Liaison Committee on Resuscitation de l'American Heart Association*.

**RÉSULTATS :** Les chercheurs ont analysé 14 études. Onze ont fourni des degrés divers de données probantes (qualité des preuves 3 à 4), appuyant le fait que le recours à la PPC primaire peut réduire la nécessité de procéder à une intubation et à la ventilation mécanique. **CONCLUSION :** Le recours à la PPC comme intervention primaire et mode de soutien respiratoire constitue une possibilité chez les nourrissons de 32 semaines d'âge gestationnel ou moins, mais il est davantage possible d'éviter l'intubation et la ventilation mécanique chez les nourrissons matures de plus de 27 semaines d'âge gestationnel.

# METHOD

Key words selected with synonyms were "continuous positive airway pressure" OR "CPAP" OR "nasal CPAP" OR "early CPAP"; "preterm" OR "premature infant" OR "neonate" OR "newborn"; "resuscitation" OR "delivery room". These concepts were combined with the Boolean operator "AND". Exclusion criteria were nonhuman subjects; non-English language; abstract only; review articles; CPAP as nonprimary intervention; children/adult subjects; late preterm or term infants; >32 weeks' gestation; extubation to CPAP; and surfactant administration with CPAP.

Databases searched were Ovid Medline (1950 to 2009), Scopus (1997 to 2009), Web of Science (1997 to 2009), Embase (1987 to 2008), PubMed (1975 to 2009), CINAHL (1996 to 2008), Cochrane Central Register of Controlled Trials (first quarter of 2009) and Cochrane Database of Systematic Reviews (first quarter of 2009). The abstracts of all available reports and studies were reviewed including single-centre case series, observational studies with

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Figure 1) Flow diagram for study selection. CPAP Continuous positive airway pressure; EPIQ Evidence-based Practice for Improving Quality; pCPAP Primary CPAP

historical and other centre controls, and randomized controlled trials (RCTs). The bibliographies of all selected articles and several review articles were manually searched for additional studies.

From an initial review of 1638 citations and 46 full-text articles (Figure 1), 14 studies were eligible for inclusion in the present review. They were scored using the Evidence Evaluation Worksheet adapted from the American Heart Association's International Liaison Committee on Resuscitation (<www.americanheart.org/presenter.jhtml?identifier=3052119>) (8). Four reviewers independently assigned level of evidence (LOE), direction of support and quality (<www.cebm.net/index.aspx?o=1157>) (9). Inconsistencies were resolved by consensus.

#### RESULTS

The process for selection of the studies is outlined in Figure 1. With the exception of one, all studies included were published between 1999 and 2010. Included studies reported data that described the need for intubation and mechanical ventilation in infants  $\leq$ 32 weeks' gestation who were treated with pCPAP.

#### Characteristics of studies

In 1987, Han et al (10) reported an RCT with a population of infants (n=82) managed in the preantenatal corticosteroid and presurfactant era, using a nasopharyngeal continuous distending pressure device compared with headbox oxygen. They concluded that this mode of respiratory support was not beneficial and "may

worsen the severity of RDS [respiratory distress syndrome]". Only one other RCT addressed the question of our review. In 2004, Sandri et al (11) randomly assigned 230 infants, 28 to 31 weeks' gestation, to early CPAP in the delivery room or delayed/rescue CPAP provided at 30 min of age. They concluded that the incidence of subsequent intubation in both groups was the same. Subramaniam et al (12) reviewed these two RCTs in a Cochrane systematic review and concluded that there was "insufficient information to evaluate the effectiveness of CPAP to reduce the need for IPPV [intermittent positive pressure ventilation]". The remaining studies (n=2824 subjects) included six observational studies (13-18) in centres using historical controls 'before-and-after' implementing routine use of early CPAP (LOE 3), one study (19) reporting a national cohort's experience with increasing use of CPAP over time and a parallel decrease in the use of intubation and mechanical ventilation (LOE 4), and one study (20) reporting a comparison between two centres with different resuscitation and ventilation practices (LOE 4). Additional observational data were identified from two RCTs (21,22). These studies were designed to address the primary outcome of death and/or BPD in patients treated with pCPAP compared with intubation and surfactant, rather than our primary question of pCPAP versus no prophylactic intervention. The group of infants (n=965) from the 'CPAP arm' of these studies (LOE 4) provided additional data regarding the effect of pCPAP. Another RCT (23) designed to address the feasibility of using a T-piece resuscitator in the delivery room before implementing CPAP as a mode of primary respiratory support also provided observational data (n=104) regarding the outcome of patients treated with pCPAP (LOE 4). These studies are presented in Table 1.

#### Quality of the studies

The majority of studies were observational, using historical controls or no controls in the context of observational data within a subset of subjects from an RCT designed to address a different primary outcome. The quality of the studies was generally good to fair, but was variable based on a clear definition of the comparison groups, outcomes measured objectively, known confounders identified and controlled for, and sufficient follow-up.

#### DISCUSSION

The overall observed rate of avoiding intubation and mechanical ventilation by using pCPAP in these studies ranged from 12% to 92.6%. This broad range reflects the heterogeneity of the observational studies along with the temporal changes in neonatal care that likely occurred over the reported time periods.

Some studies attempted to determine whether the use of pCPAP was associated with a decrease in the incidence of BPD. With the exception of the study by Aly et al (13), none of the studies identified a statistically significant decrease in the incidence of BPD, or differences in other neonatal morbidities including air leak and necrotizing enterocolitis. Aly et al reported avoiding intubation in 92.6% of patients and a decrease in BPD, but this was the result of a single centre's experience at the end of four successive time periods, after implementing a policy for use of early nasal CPAP in extremely low birth weight infants, and incorporating an education and training program. They specifically assigned experienced nurses to provide care in the first week with a 'minimal handling' strategy. It is of note that the outcomes were actually worse in the first time period than at baseline, suggesting that there was a 'learning curve', with sequential improvement over the three time periods after the change in practice. Only the data from the 'CPAP arm' of one RCT (22) reported a higher

TABLE 1

Studies of primary continuous positive airway pressure (pCPAP) in infants ≤32 weeks' gestation

App et al (13)         2004         Study polyticition         App et al (13)         Comments         Com	Deferre	Veen	04	Oturtu	Percented entreme	0	
Page et al (1,3)         2005         Single control         Control interest         <	Reference	Year	Study population	Study	Reported outcome	Comment	
He to finalities       accordination of the second provide construction of the se	Aly et al (13)	2004	Single centre	Ubservational study over	Increasing use of CPAP (17.6%, 61.8%	ENCRAP with education and	3 (S)
File         2100 g         compared with substration increasing with particulation with with with with with with with with			n=101 Infants	2002 (n-34 n-34 n-33)	decrease in intubation and use of	training program Assigned	Q: fair
Prove care and a part of media (infinites in baseline period).         accided in first week (10.5%, 852% and baseline period).         prove care in the week (with mining handling)         prove care in the week (with mining handling)           (23)         200         Five-conte RCT (23)         Status (10,5%, 82%) over the three into periods.         Charla in Contexponent (10,5%) over the three into periods.         Charla into pe			<1000 g	compared with a historical	surfactant Intubation increasingly	experienced nurses to	
Fire et al (23)         2004 (23)         Fire et al (23)         Support (23)         Support (2				cohort of $n=45$ infants in	avoided in first week (61 5% 86 2% and	provide care in first week	
First et al.         2004         First et al.         Unit accided a policy forum         Described trend to increase nearrange inflation in unit image in individue of inflation in unit image.         Single control inflation unit image.         Single contro intin unit in unit image.         Single contr				baseline period 1995–1997	92.6%) over the three time periods	with 'minimal handling'	
Fine et al (23)         2004         Five-centre RCT n=104 inflams (A 22-28 weeks)         Study to address feasibility of radomization to use of the radomization compand with sessicitation compand with sessicitation compand with sessicitation compand with rescaled mask positive (PAP/PEEP (-48))         Study to address feasibility of radomization to use of the radomization compand with sessicitation compand with delivery room         Final as 22 weeks and the compand with sessicitation compand with delivery room         Final sessicitation resultation compand with heads the delivery room         Compand resultation resultatin resultation resultation resultatin resultation result				Unit adopted a policy for use of	Described trend to increase necrotizing	strategy. Small number of	
Finer et al2004File-centre RCT n=104 intrants (GA 22-28 weeks)Study is address feasibility of randomization to use of the in declivery room to delivery in the delivery room to delivery pressure values of transfers feasibility of in the delivery room to delivery in the delivery room to delivery pressure values of transfers feasibility of in the delivery room to delivery resultation to use of the indication. Overall. 20% of inferess. text of the delivery room text of the delivery roomChaines feasibility of pressure values of the delivery room text of the delivery roomChaines feasibility of pressure values of the delivery room text of the delivery roomChaines feasibility of pressure values of the delivery room text of t				ENCPAP in the delivery room	enterocolitis. P=0.72	infants in each time period	
Prior et al2004 n = 104 infrared met of 104 i				,,,	Decrease in BPD over the three time	Criteria for CPAP failure not	
Fine et al (23)         200         Fine centre RCT in 500 (infants GA 22-28 weeks in price resuscitation to use of the price resuscitation (Neentll 20% of Infants CPAP/PEEP (n=55) during resuscitation compared with standard maxpapative pressure variitation without PEEP (n=65)         One-Infants 227 weeks weeks in standard maxpapative pressure variitation without pressure variitation without PEEP (n=63)         One-Infants 227 weeks weeks in standard maxpapative pressure variitation without pressure variitation with pressure variitation with pressure variitation variitation in the second tensor of finants variitation in the second tensor of thenepressure variitation					periods (definition of BPD not stated)	well defined	
(23)       n=104 istatus GA 23-28 weeks       n=100 istatus GA 23-28 weeks       n=104 istatus G	Finer et al	2004	Five-centre RCT	Study to address feasibility of	One-half of patients <28 weeks intubated	Criteria for CPAP failure.	4 (S)
GA 23-39 weeks       Comparing two periods before (14)       Figure 24 weeks and the second of inflatts and the second and these the second and thesecond and the second and thesecond and the	(23)	2001	n=104 infants	randomization to use of the	in delivery room for resuscitation	$PCO_{2}>55-60$ mmHq.	0. doop
Wared as in the delivery room to deliver resultation compared with standard mask positive pressure ventilation without pressure ventilation compared with possible rescue compared with possible rescue problem of early nCPAP in Neuconference fr02, 000 results and use of and use of antenation the delivery room in the second time period 250%, n=252 mmHg, pH<7.25, 0; 1air FO_2=06.0, apnea intubation in the delivery room in the second time period 25% in second profice of early nCPAP in the the second time period 25% in second profice of early nCPAP in the second time period 25% in second profice of early nCPAP in the second time period 25% in second profice of early nCPAP in the second time period 25% in second profice of CPAP failure: 25% exek infants the CPAP group pressure via NFT flowed VFT CPAP delivered by pressure via NFT flowed VFT CPAP delivered by pressure via NFT flowed VFT CPAP delivered by pressure via NFT flowed VFT CPAP delivered VFT Pop-100, nemeretail VFT Pop-100, nemerial VFT Pop-100, n	( )		GA 23–28 weeks	T-piece resuscitator (Neopuff <sup>†</sup> )	indication. Overall, 20% of infants	pH<7.25, apnea or	a. good
Han et al (10)         1987         Single-centre RCT         Nasopharyngeal CDP (n-43)         Nasopharyngeal CDP (n-43)         Single CATE         NC (2) Single RCT         NC (2) Single RCT </td <td></td> <td></td> <td>0/120 20 100/0</td> <td>in the delivery room to deliver</td> <td>&lt;28 weeks avoided intubation within the</td> <td>FiO<sub>2</sub>&gt;0.30 for surfactant</td> <td></td>			0/120 20 100/0	in the delivery room to deliver	<28 weeks avoided intubation within the	FiO <sub>2</sub> >0.30 for surfactant	
Hane at al (10)         Single-centre RCT         Resultation compared with standard mask positive pressure ventilation withou pEEP (n=49)         Chara in (not intubated in delivery room         CPAP in (NCL) date in time resuscitation, if not intubated in delivery room         CPAP in (NCL) date resuscitation, if not intubated in delivery room         Indivery room <thindivery room<="" th="">         Indivery room         In</thindivery>				CPAP/PEEP (n=55) during	first 7 days, regardless of mode of initial	administration	
Han et al (1)         IPAP is NLCQ after initial resuscitation, if no initiability resuscitation, if no initiability resuscitation, if no initiability resuscitation, if no initiability and elevery room         PAP is NLCQ after initial resuscitation, if no initiability resuscitation, if no initiability and elevery room         Produces current NLCQ area in delivery room         Produces current NLCU area in area area in and sector in delivery room         Produces current NLCU area in and sector in delivery room         Produces current NLCU area in and sector in delivery room         Produces current NLCU area				resuscitation compared with	resuscitation. Infants >27 weeks were	Both groups treated with	
Han et al (10)         1967         Regeneration of the pressure verification with peadback of the pressure verification				standard mask positive	less likely to require intubation. All	CPAP in NICU after initial	
Han et al (10)         1987         Single-centre RCI n=82 infants         PEEP (m-49) use compared with headbox oxygen with possible rescue CDP (m-43)         Unable to demonstrate advantage to early CDP in reducing RDS. Higher CDP (m-43)         in delivery room         Core of and use of antenatal conticostancids         O; good and use of antenatal conticostancids         O; good ante continues (CDP (m-43))           Jegatheesan         2006         Ringle centre on-171 infants         O; pomoticostancids         Create industry proor antity Infants         Create and 3%, respectively for infants avoided intubation and mechanical ventilation, 4%, increase in dosage of mechanical ventilation; Parsar with PT followed by NPT CPAP delivered by mechanical ventilation; COIN trial         Crease in dosage of mechanical ventilation; CPAP group, n=307         Crease in dosage of mechanical ventilation; Parsar with PT followed by NPT CPAP delivered by mechanical ventilation; Parsar with PT followed by NPT CPAP delivered by mechanical ventilation; CPAP group, n=307         Crease in dosage of mechanical ventilation; Parsar with PT followed by NPT CPAP delivered by mechanical ventilation; Parsar with PT followed by NPT CPAP delivered by mechanical ventilation; CPAP group, n=307         Crease in dosage of mechanical ventilation; Parso				pressure ventilation without	infants at 23 weeks were intubated in	resuscitation, if not intubated	
Han et al (10)       Isolale-centre RCT       Nasopharyngeal CDP (n=43) (n=42 infants GA <32 weeks       Unable to demonstrate advantage to corticosteroids       Predates current NICU care CDP (n=40)       1 (0)         Jegatheesan       2006       Single centre n=171 infants       Observational study of two periods, before (2000- periods, before (2000- cort and period, before (2000- policy of arth (CAPA infants at policy of arth (CAPA infants at CDP (n=40))       Observational study of two periods, before (2000- rol arth (CAPA infants at CAP system       Using nCPAP in second period, 24% of infants were never inubated, proportions decrease to 10% and 40%, verspectively for infants at CAPA failure: policy of arth (CAPA infants at CAP system       3 (S)         Lindner et al (15)       1999       Single centre n=123 infants       Observational study of two periods before (1994, n=50 and after (1996, n=67) implementation of lung recultiment with policy pressure via NPT followed by NPT CPAP delivered by weeks       Not difference in CLD at 36 weeks       Increase in dosage of antenstatio batter two services (1994, n=67)       3 (S)         Mortey et al (22):       2006       Multicentre RCT       Roductare the inte delivery room with infant in the delivery room at 5 min of all set for PAP group. No difference in primary outnome of details or BPD at 36 weeks       Criteria for CPAP failure: PO_2-960 mmHg, pH-7.25, Q: good       4 (S)         Norder et al (22):       2006       Single centre et al (16)       Comparing two periods before et al (16)       No difference in primary outnome of details or BPD at 36 weeks       Criteria for CPAP failur				PEEP (n=49)	the delivery room	in delivery room	
Image: Infants       use compared with headbox       early CDP in reducing RDS. Higher       and use of antendal       C: good         Jegatheesa       2006       Single centre       Observational study of       Using nCPAP in second period, 24% of       Citeria for CPAP failure:       3 (S)         at 1(14)       n=171 infants       Two periods, before (2000- n=171 infants       2004, n=96) and after (2002- indats were not inubated in delivery room and, overall, 12% were newers       Citeria for CPAP failure:       3 (S)         Inductor proportion of infants       n=172 infants       Two periods before (1994, n=125 infants       No difference in CD at 36 weeks       Increase in dosage of antenatal betamethasone in the second time period;       Single centre       Observational study of wroperiods before (1994, n=56) and after (1996, n=67) mechanical ventilation       No difference in CD at 36 weeks       Increase in dosage of antenatal betamethasone in the second time period;       Single centre       3 (S)         Morley et al       2008       Multicentre RCT       Radomized to use of CPAP wersus endotracheal intubation age. Study conducted 1999- versus endotracheal intubation       Overall, 54% of infants in the CPAP grow       FC0_2-600 mm4g, pH<7.25, C	Han et al (10)	1987	Single-centre RCT	Nasopharyngeal CDP (n=43)	Unable to demonstrate advantage to	Predates current NICU care	1 (O)
GA - 32 weeks         oxygen with possible rescue CDP (n-39)         FrO <sub>2</sub> lower 4A ratio in CDP early CDP (n-39)         control CDP early control A ratio in CDP early A ratio in CDP early CDP (n-39)         control CDP early CDP (n-39)         contro CDP early CDP (n-39) </td <td></td> <td></td> <td>n=82 infants</td> <td>use compared with headbox</td> <td>early CDP in reducing RDS. Higher</td> <td>and use of antenatal</td> <td>Q: good</td>			n=82 infants	use compared with headbox	early CDP in reducing RDS. Higher	and use of antenatal	Q: good
CDP (n-33)       treated group, "worsen severity of RDS"         et al (14)       2006       Single centre (A23-32 weeks)       Observational study of (A 23-32 weeks)       Using CPAP in second period, 24% of (A 23-32 weeks)       Criteria for CPAP failure: Policy of early nCPAP in the delivery room with Intent Flow and 3%, respectively for infants at GA (A 25-28 weeks)       Core and the centre (B22-0.60, apnea       Criteria (A23-32 weeks)       Core and the centre delivery room with Intent Flow A2004, n=75) implementing a noCPAP system       No difference in CLD at 36 weeks       Increase in dosage of antenatal betamethason in the second time period: 25% in second period and 7% in first period       Increase in dosage of antenatal betamethason in the second time period. 25% in second period and 7% in first period       Increase in dosage of antenatal betamethason in the delivery room at 5 mind (Criteria for CPAP failure: pressure via NPT foilowed by NPT CPAP delivered by weeks)       Coreal, 54% of infants in the CPAP group.       Criteria for CPAP failure: PCO_2-60 mmHg, pH<7.25, period and 7% in first period       4 (S)         Narendrian et al (16)       Single centre (33% Ca52-26 weeks at (17)       Coreal, 54% of infants in the CPAP group.       Criteria for CPAP failure: PCO_2-60 mmHg, pH<7.25, period and 7% in first period       A (S)         Narendrian et al (16)       Single centre (2006       Comparing two periods before (2006-2001, n=79) use of ENCPAP       Corease in itubation in the delivery avoided intubation in the delivery period       FCO_2-60 mmHg, pH<7.15, period       G (S)         Narendrian et al (16)       Single centre n=1			GA <32 weeks	oxygen with possible 'rescue'	FiO <sub>2</sub> , lower a/A ratio in CDP early	corticosteroids	
Jegathesan 2006 Single centre et al (14) n=717 infrants coll viewers (17) n=42 (14) n=				CDP (n=39)	treated group, "worsen severity of RDS"		
et al (14)       n=171 infants       two pendes, berofe (2000- 51000 g       2004, n=89) and flater (2002- 2004, n=89) and flater (1994, negotive) for infants avoided intubation and mechanical ventilation n=123 infants       Increase in dosage of anternati betamethasone in second time period. 25% in second second time period. 25% in second detailed       Increase in dosage of anternati betamethasone in asecond time period. 25% in second second time period. 25% in second detailed       3 (5)         Morley et al (22): COIN trial       2008       Multicentre RCT       Reductacheal intubation age. Study conducted 1999- 2006       Overall, 54% of infants in the CPAP group.       Criteria for CPAP failure: to 28 week infants. Use of surfactant halved in the delivery room one arm of RCT       4 (5)         Narendran et al (16)       2003       Single centre n=171 infants Comparing two periods before infants       Decreased intubation and efference in primary outcome of dath or BPD at 36 weeks       Criteria for CPAP failure: PCO_2=60 mmHg, pH<7.15, 0.2, 90.060       3 (5)         Narendran et al (16)       Single centre n=171 infants       Comparing two periods before infants       Decreased intubation in the delivery room one arm of RCT       Criteria for CPAP failure: PCO_2=60 mmHg, pH<7.15, 0.2, 90.060       3 (5)	Jegatheesan	2006	Single centre	Observational study of	Using nCPAP in second period, 24% of	Criteria for CPAP failure:	3 (S)
S1000 g       2004, n=350 jaild alter (2002- gold, n=75) implementing a policy of early nCPAP in the delivery room with Infant Flow4       1001 alter (2002- comparing two periods before et al (16)       1002 s200, appead policy of early nCPAP in the delivery room with Infant Flow4       1001 alter (2002- comparing two periods before et al (16)       1002 s200, appead policy of early nCPAP in the delivery room with Infant Flow4       268 weeks         Lindner et al (15)       1999       Single centre a=123 infants versus endorthcel by implementation of lung reclamical versitiation (22):       Observational study of methanical versitiation periods before et al (16)       GR 252-28 weeks (33% GA 25-26 weeks)       No difference in primary outcome of deating (33% GA 25-26 weeks)       No difference in primary outcome of deating and 3%, respectively for infants in the cPAP group. No mechanical versitiation.       Coverall, 54% of infants in the cPAP group. Criteria for CPAP failure: avoided intubation and ventilation.       4 (S)         Morley et al (22):       2008       Multicentre RCT       Randomized to use of CPAP age. Study conducted 199- 2006       Overall, 54% of infants in the CPAP group. No difference in primary outcome of deating or 15 to 26-week infants. Use of suffactant or BPD at 36 weeks       FIO_2>0.60, apnea despite adferie. Higher incidence of pneumotrox in the CPAP advide untractant use. Observational data from one arm of RCT       Griteria for CPAP failure: 3 (S)         Narendram       2008       Single centre (1998-1999, n=929) and after (1000 g       Comparing two periods before (2000-2001, n=77) use of unafter exothapriced, 14% in the first period worided in 17.4% in the first per	et al (14)		n=171 infants	two periods, before (2000-	Infants were not intubated in delivery	$PCO_2>65$ mmHg, pH<7.25,	Q: fair
GA 23-32 weeks       2004, IL-10, Intermental and 3%, respectively for infants at GA         Lindner et al       1999       Single centre       Observational study of       Greater proportion of infants avoided intubation and mechanical ventilator       Increase in dosage of       3 (S)         (15)       n=123 infants       two periods before (1994, n=67)       No difference in CLD at 36 weeks       Increase in dosage of       3 (S)         (15)       n=123 infants       two periods before (1994, n=67)       implementation of lung recruitment with positive pressure via NPT followed by NPT CPAP delivered by NPT contantiator 4000 g       Overall, 64% of infants in the CPAP group. Criteria for CPAP failure:       4 (S)         (22);       n=610 infants       GA 252-80 weeks       asc. Sudy conducted 1999-       2006       Verall, 64% of infants in the CPAP group. No       FiO_2-60.0, apnea despite veraitiator, 44%, 76, 25% on group. No       FiO_2-50.0, apnea despite veraitiator, 44%, 76, 25%, 07, 20, 200, 200, apnea despite veraitiator, 44%, in the delivery room on a form on an inferventilation, 44% in the delivery room on a form on earm of RCT       Societaria for CPAP failure:       3 (S)         Narendran       2008       Single centre       Comparing two periods before tent primer veraitiation; mechanical veraitiation; mechanical veraitiation; mechanical veraitiation; mechanical veraitiation; mechanical veraitiation; mech			≤1000 g	2004, $n=96$ ) and after ( $2002-$	intubated propertiens decrease to 15%	FIO <sub>2</sub> >0.60, aprilea	
Lindner et al       1999       Single centre n=123 infants <1000 g			GA 23–32 weeks	policy of early nCPAP in the	and 3% respectively for infants at GA		
Lindner et al (15)       1999       Single centre n=123 infants s-1000 g GA ≥24 weeks       Observational study of two periods before (1994, mechanical ventilation pressure via NPT followed by NPT CPAP delivered by mechanical ventilation       Greater proportion of infants avoided intubation and mechanical ventilation in the second time period 225% in second period and 7% in first period       Increase in dosage of antenatal betamethasone in the second time period Criteria for CPAP failure not detailed       3 (\$)         Morley et al (22); COIN trial       2008       Multicentre RCT (33% GA 25–26 weeks)       Randomized to use of CPAP or sus endotracheal intubation age. Study conducted 1999- weeks)       Overall, 54% of infants in the CPAP group recruitment with positive pressure via NPT followed by NPT CPAP delivered by mechanical ventilator       Overall, 54% of infants in the CPAP group recruitment with positive pressure via NPT followed by NPT CPAP delivered by mechanical ventilator       Overall, 54% of infants in the CPAP group recruitment with positive pressure via NPT followed by nechanical ventilator       Overall, 54% of infants in the CPAP group recruitment with positive pressure via NPT followed by nechanical ventilation; 45% (33% GA 25–26 weeks)       PCO_2+60 mmHg, pH-7.25, or BPD at 36 weeks       PCO_2+60, prene despite caffeine. Higher incidence of pneumothorax in the CPAP group. NNH 16. NNT 2.5 to avoid surfactant use.       Qos observational study of ENCPAP         Narendran (17)       Single centre n=1526 infants GA <32 weeks				delivery room with Infant Flow <sup>‡</sup>	<26 weeks		
Lindner et al 1999 Single centre (15)				nCPAP system	No difference in CLD at 36 weeks		
(15)       n=123 infants <1000 g GA ≥24 weeks       two periods before (1994, n=56) and after (1996, n=67) implementation of lung recruitment with positive pressure via NPT followed by NPT CPAP delivered by mechanical ventilation;       intubation and mechanical ventilation in the second time period: 25% in second period and 7% in first period       antenatal betamethasone in second time period: 22%, COIN trial       Q: fair         COIN trial       2008       Multicentre RCT (33%, GA 25–28 weeks)       Randomized to use of CPAP versus endotracheal intubation in the delivery room at 5 min of age. Study conducted 1999- 2006       Overall, 54% of infants in the CPAP group versus endotracheal intubation in 25 to 26-week infants and 60% in 27 to 28-week infants and 60% in 27 to 2	l indner et al	1999	Single centre	Observational study of	Greater proportion of infants avoided	Increase in dosage of	3 (S)
e1000 g GA ≥24 weeks       n=56) and after (1996, n=67) implementation of lung recruitment with positive pressure via NPT followed by NPT CPAP delivered by mechanical ventilator       the second time period: 25% in second period and 7% in first period       second time period       Criteria for CPAP failure: 4 (S)         Morley et al       2008       Multicentre RCT       Randomized to use of CPAP weeks)       Overall, 54% of infants in the CPAP group consultation and ventilation; in 25 to 26-week infants. Use of surfactant halved in the CPAP group. No difference in primary outcome of deat weeks)       PCO_2+60 mmHg, pH<7.25, 2006       Q: good         Narendran et al (16)       2003       Single centre n=171 infants <1000 g	(15)		n=123 infants	two periods before (1994.	intubation and mechanical ventilation in	antenatal betamethasone in	O: fair
GA >24 weeks       implementation of lung recruitment with positive pressure visit wisit with positi preserind presure visit with posint pressure visi	()		<1000 g	n=56) and after (1996, n=67)	the second time period: 25% in second	second time period	G. Iuli
Morley et al     2008     Multicentre RCT     Randomized to use of CPAP     Overall, 54% of infants in the CPAP group     Criteria for CPAP failure:     4 (5)       (22);     GA 25-28 weeks     in the delivery room at 5 min of (33% GA 25-26     in the delivery room at 5 min of (33% GA 25-26     in the delivery room at 5 min of (33% GA 25-26     in the delivery room at 5 min of (33% GA 25-26     in the delivery room at 5 min of (33% GA 25-26     in the delivery room at 5 min of (33% GA 25-26     in the delivery room at 5 min of (33% GA 25-26     in the delivery room at 5 min of (33% GA 25-26     in the delivery room at 5 min of (33% GA 25-26     in the delivery room at 5 min of (33% GA 25-26     in the delivery room at 5 min of (33% GA 25-26     in 25 to 26-week infants. Use of surfactant halved in the CPAP group. No one arm of RCT     PCO_2>60 mmHg, pH-7.15, or BPD at 36 weeks     preumothorax in the CPAP group, NNH 16, NNT 15, NNT 15, NNT 15, NNT 15, NNT 15, NNT 16, NNT 15, NNT 16, NNT 15, NNT 16, NNT 16, NNT 15, NNT 16, NNT			GA >24 weeks	implementation of lung	period and 7% in first period	Criteria for CPAP failure not	
Morley et al       2008       Multicentre RCT       Randomized to use of CPAP       Overall, 54% of infants in the CPAP group       Criteria for CPAP failure:       4 (S)         (22):       n=610 infants       versus endotracheal intubation       avoided intubation and ventilation; 45%       PCQ_2>60 mmHg, pH<7.25,			0,1121 1100110	recruitment with positive		detailed	
Morley et al (22); COIN trial       2008       Multicentre RCT n=610 infants       Randomized to use of CPAP versue endotracheal intubation in the delivery room at 5 min of (3% GA 25–28 weeks) weeks)       outded intubation and ventilation; 45% (3% GA 25–28 weeks)       PCO <sub>2</sub> >60 mmHg, pH<7.25, FIO <sub>2</sub> >0.60, apnea despite in the delivery room at 5 min of (3% GA 25–28 weeks)       Q: good         COIN trial       GA 25–28 weeks (3% GA 25–27) weeks)       age. Study conducted 1999- 2006       avoided intubation and ventilation; 45% in the delivery room at 5 min of (3% GA 25–28)       PCO <sub>2</sub> >60 mmHg, pH<7.25, (3% GA 25–28)       Q: good         Versue       GA 25–28 weeks       age. Study conducted 1999- 2006       balved in the CPAP group. No difference in primary outcome of death or BPD at 36 weeks       proumothorax in the CPAP group, NNH 16. NNT 2.5 to avoid surfactant use. Observational data from one arm of RCT       Oservational data from one arm of RCT         Narendran et al (16)       2008       Single centre n=171 infants       Comparing two periods before ENCPAP       Decreased intubation in the delivery room enitation; mechanical ventilation avoided in 17.4% in the first period compared with 27.8% in the second period.       FCO <sub>2</sub> >65 mmHg, pH<7.15, No difference in CLD at 36 weeks       Q: fair         Pelligra et al (17)       FIO <sub>2</sub> >0.60       Single centre boble' CPAP) as a delivery room intervention       Reduction in use of surfactant and need compared with 27.8% in the second period.       Criteria for CPAP failure: No difference in BPD at 36 weeks       Q: good FiO <sub>2</sub> >0.50, apnea				pressure via NPT followed by			
Morley et al (22);         2008         Multicentre RCT n=610 infants         Randomized to use of CPAP or sus endotracheal intubation in the delivery room at 5 min of (33% GA 25–28 weeks)         versus endotracheal intubation age. Study conducted 1999– 2006         versus endotracheal intubation age. Study conducted 1999– 2006         versus endotracheal intubation in the delivery room at 5 min of age. Study conducted 1999– 2006         versus endotracheal intubation in 25 to 26-week infants. Use of surfactant to 28-week infants. Use of surfactant or BPD at 36 weeks         FO2_2-60, apnea despite caffeine. Higher incidence of group, NNH 16. NNT 2.5 to avoid surfactant use. Observational data from one am of RCT           Narendran et al (16)         2003         Single centre tal (16)         Comparing two periods before en-171 infants <1000 g				NPT CPAP delivered by			
Morley et al       2008       Multicent RCT       Randomized to use of CPAP       Overall, 54% of infants in the CPAP group. Criteria for CPAP failure:       4 (S)         (22);       n=610 infants       GA 25–28 weeks       avoided intubation and ventilation; 45%       PCO_2>60 mmHg, pH<7.25,				mechanical ventilator			
(22);       n=610 infants       versus endotracheal intubation       avoided intubation and ventilation; 45%       PCO <sub>2</sub> >60 mmHg, pH<7.25,	Morley et al	2008	Multicentre RCT	Randomized to use of CPAP	Overall, 54% of infants in the CPAP group	Criteria for CPAP failure:	4 (S)
COIN that       GA 25-28 weeks (33% GA 25-26 weeks)       in the delivery room at 5 min of (33% GA 25-26 weeks)       in the delivery room at 5 min of age. Study conducted 1999- 2006       in 25 to 26-week infants. Use of surfactant halved in the CPAP group. No difference in primary outcome of death or BPD at 36 weeks       FIO_2>0.60, aphea despite caffeine. Higher incidence of avoid surfactant use. Observational data from one arm of RCT         Narendran       2003       Single centre et al (16)       Comparing two periods before et al (16)       Decreased intubation in the delivery room (1998–1999, n=929) and after <1000 g	(22);		n=610 infants	versus endotracheal intubation	avoided intubation and ventilation; 45%	<i>P</i> CO <sub>2</sub> >60 mmHg, pH<7.25,	Q: good
(33% GA 25-26 weeks)       age. Study conducted 1999- 2006       to 28-week intants. Use of suffactant halved in the CPAP group. No       carteine. Higher incidence of preumothorax in the CPAP group, NNH 16. NNT 2.5 to avoid suffactant use. Observational data from one arm of RCT         Narendran       2003       Single centre       Comparing two periods before (1998–1999, n=929) and after <1000 g	COIN trial		GA 25–28 weeks	in the delivery room at 5 min of	in 25 to 26-week infants and 60% in 27	$F_{10}O_{2}>0.60$ , apnea despite	
weeks)       2006       Indexending Graph (Notional and the Graph group). Notional and the Graph group, NNH 16. NNT 2.5 to avoid surfactant use.         CPAP group n=307       Comparing two periods before et al (16)       Comparing two periods before (1998–1999, n=929) and after < (2000–2001, n=79) use of ENCPAP			(33% GA 25–26	age. Study conducted 1999-	to 28-week Infants. Use of surfactant	carreine. Higher Incidence of	
CPAP group n=307       Unitedence in primary outcome of deal in group, run, run, run, run, run, run, run, run			weeks)	2000	difference in primary outcome of death	aroup NNH 16 NNT 2.5 to	
Narendran       2003       Single centre       Comparing two periods before       Decreased intubation in the delivery room       Criteria for CPAP failure:       3 (S)         et al (16)       n=171 infants       (1998–1999, n=929) and after       and reduced need for mechanical       PCO <sub>2</sub> >65 mmHg, pH<7.15,			CPAP group n=307		or BPD at 36 weeks	avoid surfactant use	
Narendran et al (16)2003 n=171 infants <1000 gSingle centre (1998–1999, n=929) and after (2000–2001, n=79) use of ENCPAPDecreased intubation in the delivery roomCriteria for CPAP failure: PCO2>65 mmHg, pH<7.15, G2 so 603 (S)Pelligra et al (17)2008Single centre n=1526 infants GA <32 weeks						Observational data from	
Narendran et al (16)2003Single centre n=171 infants <1000 gComparing two periods before (1998–1999, n=929) and after (200–2001, n=79) use of ENCPAPDecreased intubation in the delivery roomCriteria for CPAP failure: 3 (S)3 (S)Pelligra et al (17)2008Single centre n=1526 infants GA <32 weeks						one arm of RCT	
et al (16) n=171 infants <1000 g Pelligra et al 2008 Single centre (17) n=1526 infants GA <32 weeks GA <32 weeks No difference in CPAP (underwater 'bubble' CPAP) as a delivery rom intervention	Narendran	2003	Single centre	Comparing two periods before	Decreased intubation in the delivery room	Criteria for CPAP failure:	3 (S)
<ul> <li>&lt;1000 g</li> <li>(2000–2001, n=79) use of ENCPAP</li> <li>Pelligra et al 2008</li> <li>Single centre (17)</li> <li>n=1526 infants</li> <li>GA &lt;32 weeks</li> <li>GA &lt;32 weeks</li> <li>GA &lt;32 weeks</li> <li>A dafter (2000–2004, n=851) and after (2000–2004, n=851) the centre adopted practice of using nCPAP (underwater 'bubble' CPAP) as a delivery room intervention</li> <li>ventilation; mechanical ventilation avoided in 17.4% in the first period compared with 27.8% in the second period</li> <li>No difference in CLD at 36 weeks</li> <li>FiO<sub>2</sub>&gt;0.60</li> <li>FiO<sub>2</sub>&gt;0.60</li> <li>Criteria for CPAP failure: 3 (S)</li> <li>PCO<sub>2</sub>&gt;60 mmHg, pH&lt;7.25, Q: good</li> <li>FiO<sub>2</sub>&gt;0.50, apnea</li> <li>FiO<sub>2</sub>&gt;0.50, apnea</li> </ul>	et al (16)		n=171 infants	(1998–1999, n=929) and after	and reduced need for mechanical	<i>P</i> CO <sub>2</sub> >65 mmHg, pH<7.15,	Q: fair
Pelligra et al 2008       Single centre (17)       Observational study of n=1526 infants       Reduction in use of surfactant and need before (1996–2000, n=675)       Criteria for CPAP failure: (17)       3 (S)         GA <32 weeks			<1000 a	(2000–2001, n=79) use of	ventilation; mechanical ventilation	FiO <sub>2</sub> >0.60	
compared with 27.8% in the second period No difference in CLD at 36 weeks Pelligra et al 2008 Single centre (17) n=1526 infants (A <32 weeks GA <32 weeks before (1996–2000, n=675) and after (2000–2004, n=851) the centre adopted practice of using nCPAP (underwater 'bubble' CPAP) as a delivery room intervention			0	ENCPAP	avoided in 17.4% in the first period		
Pelligra et al 2008 Single centre (17) n=1526 infants GA <32 weeks GA <43 weeks GA <44 weeks GA					compared with 27.8% in the second		
Pelligra et al       2008       Single centre       Observational study of       Reduction in use of surfactant and need       Criteria for CPAP failure:       3 (S)         (17)       n=1526 infants       two sequential time periods       for mechanical ventilation in second       PCO <sub>2</sub> >60 mmHg, pH<7.25, Q: good					period		
Pelligra et al       2008       Single centre       Observational study of       Reduction in use of surfactant and need       Criteria for CPAP failure:       3 (S)         (17)       n=1526 infants       two sequential time periods       for mechanical ventilation in second       PCO <sub>2</sub> >60 mmHg, pH<7.25, Q: good					No difference in CLD at 36 weeks		
(17)       n=1526 infants       two sequential time periods       for mechanical ventilation in second       PCO2>60 mmHg, pH<7.25, Q: good	Pelligra et al	2008	Single centre	Observational study of	Reduction in use of surfactant and need	Criteria for CPAP failure:	3 (S)
GA <32 weeks before (1996–2000, n=675) period. In the second period, 19% of FiO <sub>2</sub> >0.50, apnea and after (2000–2004, n=851) infants avoided intubation compared the centre adopted practice of using nCPAP (underwater 'bubble' CPAP) as a delivery room intervention	(17)		n=1526 infants	two sequential time periods	for mechanical ventilation in second	<i>P</i> CO <sub>2</sub> >60 mmHg, pH<7.25,	Q: good
and after (2000–2004, n=851) Infants avoided intubation compared the centre adopted practice of using nCPAP (underwater 'bubble' CPAP) as a delivery room intervention			GA <32 weeks	before (1996–2000, n=675)	period. In the second period, 19% of	FiO <sub>2</sub> >0.50, apnea	
using nCPAP (underwater bubble' CPAP) as a delivery room intervention				and after (2000–2004, n=851)	with 0% of infonto in the first period		
'bubble' CPAP) as a delivery room intervention				using nCPAP (underwater	No difference in PDD at 26 weeks		
room intervention				'bubble' CPAP) as a delivery	NO UNETERICE III DPD at 30 WEEKS		
				room intervention			

## TABLE 1 - CONTINUED

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Reference	Year	Study population	Study	Reported outcome	Comment	LOE*
Sandri et al	2004	Multicentre RCT	Randomized infants to nCPAP	No difference in the need for intubation or	Criteria for CPAP failure:	1 (N)
(11)		n=230 infants GA 28–31 weeks	within 30 min of age (n=115) or rescue nCPAP if FiO <sub>2</sub> >0.40 beyond 30 min of age (n=115), using the Infant Flow <sup>‡</sup> Driver system. Study conducted 1999–2000	surfactant use in the two groups Practice of routine prophylactic surfactant in infants at GA <28 weeks	<i>P</i> CO <sub>2</sub> >70 mmHg, pH<7.2, apnea or FiO <sub>2</sub> >0.80 in first 30 min	Q: good
Subramaniam	2005	Meta-analysis	Analysis of two RCTs conducted	Concluded that there was "insufficient	Different population, time	2 (N)
et al (12)		2 studies (n=312) GA <32 weeks	in 1987 and 1999, respectively	information to evaluate the effectiveness of CPAP to reduce need for IPPV"	period and NICU practices in two studies	Q: fair
Finer et al (21) (SUPPORT Trial Group)	2010	Multicentre RCT n=1316 GA 24–28 weeks (43% GA 24–25 weeks) CPAP group: n=663	Randomized to CPAP or intubation in delivery room and surfactant treatment (within 1 h after birth). Also randomized to one of two target ranges of oxygen saturation. Study conducted 2005–2009	Within the CPAP group, 65.6% avoided intubation in the delivery room, 32.9% avoided treatment with surfactant and intubation was avoided in 16.9% overall No difference in the primary outcome of death or BPD at 36 weeks	Criteria for CPAP failure: $PCO_2>65 \text{ mmHg},$ $FiO_2>0.50, hemodynamic$ instability Observational data from one arm of RCT	4 (S) Q: good
Swietlinski et al (19)	2007	National cohort 2003 to 2005 Subset of infants <30 weeks' GA, n=236	Observational study after implementing use of the Infant Flow <sup>†</sup> Advance Driver CPAP within a national program across 57 secondary and tertiary care NICUs	In a subset of infants ≤30 weeks' gestation, able to avoid intubation in 157 of 236 (66.5%) Incidence of nasal and facial complications noted to be higher in lower birth weight infants	Multicentre, three modes of CPAP used: standard, bi-level and triggered bi-level. Criteria for CPAP failure: <i>P</i> CO <sub>2</sub> >65 mmHg, pH<7.25, FiO <sub>2</sub> >0.60, apnea	4 (S) Q: poor
Vanpee et al (20)	2007	Two centres n=172 infants GA <28 weeks	Comparison over two years at a European centre (n=102) and a United States centre (n=70) to evaluate differences in resuscitation and ventilation practices	nCPAP (Infant Flow <sup>‡</sup> Driver system) was used initially in 56% of infants in the first centre; overall, 22% avoided intubation during the first week of life. Routine intubation and surfactant use in the second centre	Infants in first centre had higher SNAPPE-II scores, and antenatal steroids used less frequently in second centre	4 (S) Q: poor
Zecca et al (18)	2006	Single centre n=324 infants GA 24–28 weeks	Observational study of two periods before (1992–1997, n=161) and after (1998–2003, n=163) implementation of practice change from immediate intubation to use of nCPAP initiated in delivery room with T-piece resuscitator (NeoPuff <sup>†</sup> )	Overall, intubation avoided in 14% of infants in the second period compared with 3% in the first period. Infants 27–28 weeks' GA, 21.3% avoided intubation in the second period compared with 2.8% in the first period. Infants 24–26 weeks' GA, >95% intubated in both periods	Greater use of antenatal steroids in the second period Prophylactic ibuprofen used in the second period Criteria for CPAP failure: <i>P</i> CO <sub>2</sub> >60 mmHg, pH<7.25	3 (S) Q: fair

\*Letters in parentheses under level of evidence (LOE): N Neutral to intervention; O Oppose intervention; S Support intervention; <sup>†</sup>Fisher & Paykel Healthcare Limited, Canada; <sup>‡</sup>CareFusion, USA. BPD Bronchopulmonary dysplasia; CDP Continuous distending pressure; CLD Chronic lung disease; COIN Nasal CPAP or Intubation at Birth; CPAP continuous positive airway pressure; ENCPAP Early 'bubble' nasal CPAP; FiO<sub>2</sub> Fraction of inspired O<sub>2</sub>; GA Gestational age; IPPV Intermittent positive pressure ventilation; nCPAP Nasal CPAP; NICU Neonatal intensive care unit; NNH Number needed to harm; NNT Number needed to treat; NPT Nasopharyngeal tube; PCO<sub>2</sub> Partial pressure of CO<sub>2</sub>; PEEP Positive end expiratory pressure; Q Quality; RCT Randomized controlled trial; RDS Respiratory distress syndrome; SNAPPE Score for Neonatal Acute Physiology Perinatal Extension; SUPPORT Surfactant, Positive Pressure, and Oxygenation Randomized Trial

incidence of air leak in the CPAP group compared with the group managed with intubation.

The set criteria for 'CPAP failure' resulting in intubation and mechanical ventilation were all very similar in the studies (Table 1), with the exception of the delivery room feasibility study of the T-piece resuscitator (23). Infants requiring a fraction of inspired  $O_2 > 0.30$  could be intubated to receive surfactant, so in the present study, 80% of infants <28 weeks' gestation placed on CPAP were subsequently intubated.

Despite its observational nature, data from the 'CPAP arms' of the large RCTs represent a large sample of similar, extremely premature infants exposed to pCPAP. The lower intubation rate in the Nasal CPAP or Intubation at Birth (COIN) trial (22), in contrast to the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT) (21), likely reflects the lower gestational age of the patients in the SUPPORT trial. This is congruent with observations made in other studies (14,18,23). Collectively, the studies suggest that use of pCPAP is more likely to be successful in infants >27 weeks' gestation.

The success of surfactant in treating respiratory distress in preterm infants led to the strategy of prophylactic surfactant (24). More recently, centres have adopted the practice of intubation for surfactant administration followed by extubation to early CPAP, in efforts to avoid the presumed deleterious effects of positive pressure ventilation (25). These practice strategies have made it difficult to conduct RCTs comparing pCPAP with a true noninterventional control group. With good prenatal care, including administration of antenatal corticosteroids, some extremely premature infants are observed to experience minimal clinical symptoms of respiratory distress, and the chest radiographs do not have the classical reticular granular pattern of RDS. It is in this group of infants that it may be possible to provide respiratory support with pCPAP, and avoid intubation and mechanical ventilation. The present review suggests that intubation may be avoided in some of these infants, but the success rate described is as low as 12% or as high as 92.6%. Most of the observational data report success rates ranging from 12% to 54%, with higher success rates identified in more mature infants >27 weeks' gestation. The observational nature of these studies is confounded by biases that include, but are not limited to, the different types of CPAP systems used, different pressure used and other concurrent practices such as the changing use of antenatal corticosteroids because some of these 'before-and-after' studies spanned several years.

Successful use of pCPAP could circumvent the need for endotracheal intubation. The appeal of this strategy is that it could avoid the deleterious effects of mechanical ventilation and the occurrence of ventilator-induced lung injury.

#### CONSENSUS ON SCIENCE

There is good to fair-quality supportive evidence from 11 studies (LOE 3 to LOE 4) that the use of pCPAP can reduce the need for intubation and mechanical ventilation in infants  $\leq$ 32 weeks' gestation.

#### RECOMMENDATION

The use of CPAP as a primary intervention and mode of respiratory support is an option for infants  $\leq$ 32 weeks' gestation, but avoidance of intubation and mechanical ventilation is more likely in mature infants >27 weeks' gestation.

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#### REFERENCES

- Van Marter LJ. Epidemiology of bronchopulmonary dysplasia. Semin Fetal Neonatal Med 2009;14:358-66.
- Lee SK. Canadian Neonatal Network Annual Report. Toronto: Canadian Neonatal Network, 2007.
- Payne NR, LaCorte M, Karna P, et al. Reduction of bronchopulmonary dysplasia after participation in the Breathsavers Group of the Vermont Oxford Network Neonatal Intensive Care Quality Improvement Collaborative. Pediatrics 2006;118(Suppl 2):S73-7.
- 4. Zeitlin J, Draper ES, Kollee L, et al. Differences in rates and short-term outcome of live births before 32 weeks of gestation in Europe in 2003: Results from the MOSAIC cohort. Pediatrics 2008;121:e936-44.
- Bancalari E, Claure N, Sosenko IR. Bronchopulmonary dysplasia: Changes in pathogenesis, epidemiology and definition. Semin Neonatol 2003;8:63-71.
- Coalson JJ. Pathology of new bronchopulmonary dysplasia. Semin Neonatol 2003;8:73-81.

- Merritt TA, Deming DD, Boynton BR. The 'new' bronchopulmonary dysplasia: Challenges and commentary. Semin Fetal Neonatal Med 2009;14:345-57.
- Morley PT. Evidence evaluation worksheets: The systematic reviews for the evidence evaluation process for the 2010 International Consensus on Resuscitation Science. Resuscitation 2009;80:719-21.
- Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: A proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000;283:2008-12.
- Han VK, Beverley DW, Clarson C, et al. Randomized controlled trial of very early continuous distending pressure in the management of preterm infants. Early Hum Dev 1987;15:21-32.
- Sandri F, Ancora G, Lanzoni A, et al. Prophylactic nasal continuous positive airways pressure in newborns of 28-31 weeks gestation: Multicentre randomised controlled clinical trial. Arch Dis Child Fetal Neonatal Ed 2004;89:F394-8.
- Subramaniam P, Henderson-Smart DJ, Davis PG. Prophylactic nasal continuous positive airways pressure for preventing morbidity and mortality in very preterm infants. Cochrane Database Syst Rev 2005;(3):CD001243.
- Aly H, Milner JD, Patel K, El-Mohandes AA. Does the experience with the use of nasal continuous positive airway pressure improve over time in extremely low birth weight infants? Pediatrics 2004;114:697-702.
- Jegatheesan P, Keller RL, Hawgood S. Early variable-flow nasal continuous positive airway pressure in infants < or =1000 grams at birth. J Perinatol 2006;26:189-96.
- Lindner W, Vossbeck S, Hummler H, Pohlandt F. Delivery room management of extremely low birth weight infants: Spontaneous breathing or intubation? Pediatrics 1999;103(5 Pt 1):961-7.
- Narendran V, Donovan EF, Hoath SB, Akinbi HT, Steichen JJ, Jobe AH. Early bubble CPAP and outcomes in ELBW preterm infants. J Perinatol 2003;23:195-9.
- Pelligra G, Abdellatif MA, Lee SK. Nasal continuous positive airway pressure and outcomes in preterm infants: A retrospective analysis. Paediatr Child Health 2008;13:99-103.
- Zecca E, de LD, Costa S, Marras M, de TP, Romagnoli C. Delivery room strategies and outcomes in preterm infants with gestational age 24-28 weeks. J Matern Fetal Neonatal Med 2006;19:569-74.
- Swietlinski J, Bober K, Gajewska E, et al. Introduction of Infant Flow nasal continuous airway pressure as the standard of practice in Poland: The initial 2-year experience. Pediatr Crit Care Med 2007;8:109-14.
- Vanpée M, Walfridsson-Schultz U, Katz-Salamon M, Zupancic JA, Pursley D, Jonsson B. Resuscitation and ventilation strategies for extremely preterm infants: A comparison study between two neonatal centers in Boston and Stockholm. Acta Paediatr 2007;96:10-6.
- Finer NN, Carlo WA, Walsh MC, et al. Early CPAP versus surfactant in extremely preterm infants. N Engl J Med 2010;362:1970-9.
- Morley CJ, Davis PG, Doyle LW, Brion LP, Hascoet JM, Carlin JB. Nasal CPAP or intubation at birth for very preterm infants. N Engl J Med 2008;358:700-8.
- 23. Finer NN, Carlo WA, Duara S, et al. Delivery room continuous positive airway pressure/positive end-expiratory pressure in extremely low birth weight infants: A feasibility trial. Pediatrics 2004;114:651-7.
- Soll RF, Morley CJ. Prophylactic versus selective use of surfactant in preventing morbidity and mortality in preterm infants. Cochrane Database Syst Rev 2001;(2):CD000510.
- 25. Stevens TP, Harrington EW, Blennow M, Soll RF. Early surfactant administration with brief ventilation vs. selective surfactant and continued mechanical ventilation for preterm infants with or at risk for respiratory distress syndrome. Cochrane Database Syst Rev 2007;(4):CD003063.