Kliiniline küsimus nr 14

Kas enneaegsete vastsündinute esmasel stabiliseerimisel mõjutab ravitulemusi hingamise toetuse meetodi valik vs mitte?:

- kontrollitud võrreldes kontrollimata rõhuga ventilatsioon
- CPAP võrreldes invasiivne hingamistoetus
- CPAP võrreldes hingamistoetuse puudumine
- prolongeeritud inspiirium võrreldes konventsionaalne ventilatsioon/CPAP

Kriitilised tulemusnäitajad: lapse peamised tulemusnäitajad, hingamistoetuse kestus

Kokkuvõte

At birth, the newborn infant faces immediate and significant challenges for successful transition to the extrauterine environment. The critical physiological tasks to accomplish are to aerate the liquid-filled lung and thereby maintain aerated lung volume to establish a functional residual capacity (FRC). While term infants begin to establish the FRC with the first breath after birth, preterm infants are hampered by a greater instability of the thorax, limited muscle strength, and immature epithelial sodium channels, surfactant composition and production. /Foglia et al 2015

In an extremely preterm lung, eMV (endotracheal mechanical ventilation) triggers an inflammatory cascade, which involves chemokines and other proinflammatory cytokines, transmigration of inflammatory cells to airspaces, secondary lung injury by proteases, and dysregulation of growth factors, leading to fibrosis and abnormal lung development. Animal studies reveal that only 2 hours of postnatal pressure-limited ventilation induced an inflammatory response in the alveolar wash fluid of premature lambs and lambs receiving 2 hours of continuous positive airway pressure were found to have lower indicators of acute lung injury and better lung compliance than lambs that were mechanically ventilated. This supports the hypothesis that avoiding the inflammatory response secondary to eMV may reduce BPD. As preterm lungs appear to be particularly vulnerable during the first few hours of life, early intubation should be avoided. Special caution should be exercised during newborn resuscitation, as seemingly gentle mask ventilation may also overexpand the lungs. /Fischer et al 2013

Centres with high delivery room intubation rates had higher rates of ventilation and bronchopulmonary dysplasia. In the most immature infants, even minimal exposure to supplemental oxygen and mechanical ventilation could be enough to contribute to bronchopulmonary dysplasia. /Schmölzer et al 2013.

Eelnev iseloomustab põhjalikult antud teema kohta leitud tõenduspõhise materjali sisu. Kõik metaanalüüsid, süstemaatilised ülevaated ja randomiseeritud kontrolluuringud väidavad üksmeelselt, et varase CPAP-ravi/NIPPV-ravi (ja seega positiivse lõpp-ekspiratoorse rõhu) kasutamine esmasel stabiliseerimisel on soovitatud kuldne standard. See võimaldab alveoolide „recruitment'i" ehk „lahti puhumist", vältides seeläbi võimalikku baro-volu-traumat, mis võib kaasneda mehaanilise ventilatsiooniga.

Põhjalikult on uuritud ka erinevust mitteinvasiivsete hingamistoetuse meetodite vahel (BiPAP/CPAP vs NIPPV), leitud kaks mõõduka kvaliteediga uuringut kirjeldavad, et NIPPV ravirühmas on enneaegsete vastsündinute intubatsiooni sagedus ja mehaanilise ventilatsiooni vajadus väikesem. Samas leidsin veel kaks uuringut, mis tõestavad vastupidist – NIPPV ja CPAPi meetodite kasutamise vahel ei ole statistiliselt olulist erinevust. Erinevate mitteinvasiivsete hingamistoetuse meetodite teema vajab veel lisauuringuid.

Euroopa vastsündinute elustamise juhend soovitab enneaegsete vastsündinute esmasel stabiliseerimisel pigem kasutada kontrollitud rõhuga ventilatsiooni, vältimaks kopsude ülevenitust ja sellest tulenevaid kahjustusi. Samuti 2014.a avaldatud uuring, Neopuff vs Ambu-mask ventilatsioon (Szyld et al), näitab, et kontrollitud rõhuga ventilatsiooni puhul oli hilisema intubatsiooni vajadus väikesem, kokkuvõtteks kasutati väiksemaid rõhkusid ning subgrupi analüüsist selgub ka väiksem BPD esinemissagedus kontrollitud rõhuga ventilatsiooni grupis.
Ükski leitud materjalidest ei käsitle võrdlusena hingamistoetuse puudumist.

Varasemad uuringud, mis on uurinud prolongeeritud inspiiriumi versus konventsionaalse hingamistoetuse või CPAPi kasutamist enneaegsetel vastsündinutel, on näidanud paljulubavaid tulemusi, kuid nende usaldusväärsus on jäänud madalaks (on olnud enamus vaatlusuuringud, ei ole kasutatud PEEPi kontrollgrupis jne). 2014 a avaldatud metaanalüüs (Schmölzer et al) leidis, et prolongeeritud inspiiriumi (SI) kasutamine esmasel stabiliseerimisel on efektiivne meetod hingamistoetuse rakendamisel lühiajaliselt, vähendades mehaanilise ventilatsiooni vajadust esimese 72 elutunni jooksul. Samas uuringu tulemusena ei esinenud statistiliselt olulist erinevust hilistulemite osas (BPD, suremus). Lisaks esines statistiliselt olulisel määral SI grupis avatud arterioosjuha, mis vajas medikamentoosset või kirurgilist sulgemist.
Sama tulemuseni jõudsid ka Lista et al poolt 2015 a avaldatud uuringu autorid, kus prolongeeritud inspiiriumi kasutamine koos CPAP-raviga vähendas mehaanilise ventilatsiooni vajadust esimese 72 elutunni jooksul, kuid ei vähendanud hingamistoetuse vajadust üldiselt ega ka BPD esinemissagedust. Statistiliselt küll mitteoluline tulemus, kuid prolongeeritud inspiiriumi grupis esines enam pneumotooraksit ja emfüsematoosseid tüsistusi, mis annab aluse, et tegu võib olla liiga agressiivse ravimeetodiga.

Lähiaastatel on valmimas uus suurem randomiseeritud kontrollitud uuring (SAIL study), mis käsitleb prolongeeritud inspiiriumi mõju, seeläbi invasiivse hingamistoetuse vajadust ja hilisema BPD esinemissagedust. Hetkel on põhjapanevate järelduste tegemiseks uuringud ebapiisavad, mistõttu ei soovitata seda manöövrit rutiinselt kasutada.

Kuna kliiniline küsimus käsitleb esmast stabiliseerimist ja tuginedes töörühma poolt püstitatud küsimustele, ei ole antud materjalis käsitletud erinevate invasiivse ventilatsiooni meetodite võrdlust.

Kokkuvõte
Süstemaatilistest ülevaadetest, metaanalüüsidest, randomiseeritud kontrolluuringutest

Antud teema kohta leidsin otsingukriteeriumide järgi 5 metaanalüüsi/süstemaatilist ülevaadet, 5 randomiseeritud kontrolluuringut ja 2 ülevaateartiklit. Kvaliteet kõrge või mõõdukas, enamuse uuringute puuduseks oli *blinding*.

Fischer et al poolt 2013 a koostatud hea kvaliteediga metaanalüüs (7 randomiseeritud kontrolluuringut, 3289 patsienti) käsitleb endotraheaalse mehaanilise ventilatsiooni mittekasutamise efekti BPD esinemissagedusele enneaegsetel lastel, kes on sündinud <30 GN. Vaatamata analüüsi kaasatud uuringute erinevatele uuringustrateegiatele, leidsid autorid statistiliselt olulise efekti suremuse ja BPD vähenemises, kui vältida endotraheaalset mehaanilist ventilatsiooni ning kasutada ”pehmet” mitteinvasiivset ventilatsiooni enneaegsel vastsündinul (odds ratio, 0.83 [95% CI, 0.71–0.96]). Samuti uuriti seost IVH ja võimaliku mitteinvasiivse hingamistoetuse ebaefetiivsusest põhjustatud hüperkapnia vahel. Seost ei leitud ning järeldati, et intubatsiooni vältimine on ohutu.

Schmölzer et al poolt 2013 a koostatud süstemaatiline ülevaade (4 randomiseeritud kontrolluuringut, 2782 patsienti, kellest 1296 vastsündinut nCPAP grupis ja 1486 vastsündinut intubatsiooni grupis) käsitleb varase CPAPi kasutamise mõju BPD esinemissagedusele ja suremusele. Nende analüüsi põhjal selgus, et varane CPAP-ravi vähendab suremust ja BPD esinemissagedust enneaegsetel lastel. Lisaks: „*One additional infant could survive to 36 weeks without bronchopulmonary dysplasia for every 25 babies treated with nasal CPAP in the delivery room rather than being intubated and mechanically ventilated*“. (Relative risk 0.91, 95% confidence interval 0.82 to 1.01, risk difference −0.03, 95% confidence interval −0.07 to 0.01). Analüüsi kitsaskohtadeks peeti asjaolu, et tegemist ei olnud pime-uuringutega, enamus uuritavatest olid saanud antenataalset kortikosteroidi, mistõttu eelduslikult olid vastsündinud sünnimomendil üldseisundilt stabiilsemad, käsitletud ei olnud < 24 GN sündinud lapsi. Tulemuste koondtabel vt viited.

Szyld et al avaldasid 2014. aastal uuringu, kus randomiseeriti 1027 (≥26 GN sündinud) patsienti, 11 keskususest ja võrreldi kontrollitud (*T-piece resuscitator, Neopuff*) ja kontrollimata rõhuga (*self-inflating bag, Ambu*) ventilatsiooni kasutamist. Uuringu tulemusena leiti, et mõlemad meetodid toimivad hästi esmasel stabiliseerimisel/elustamisel ja vastsündinu südamelöögisageduse tõstmiseks > 100 x’, samas kontrollitud rõhuga ventilatsiooni puhul oli hilisema intubatsiooni vajadus väikesem. Vt lisatulemused viidetest.

Li et al poolt 2015 a koostatud süstemaatiline ülevaade (5 randomiseeritud kontrolluuringut, 1527 patsienti) võrdleb mitteinvasiivseid hingamistoetuse meetodeid, NIPPV vs nCPAP, RDSiga enneaegsetel vastsündinutel. Süstemaatiline ülevaade leidis, et RDSiga enneaegsetel vastsündinutel, kellele rakendati NIPPV ventilatsiooni, esines oluline invasiivse ventilatsiooni vajaduse vähenemine, kui nCPAP grupis (RR:0.53; 95% CI, 0.33–0.85). Erinevus tuli enam välja nende laste seast, kes olid saanud surfaktanti. Samas kui valim jagati kahte alagruppi (enneaegsed, kes olid sündinud ≤ 30 GN ja kaaluga <1500 g ja enneaegsed sündinud >30 GN ja kaaluga >1500 g), siis NIPPV vs nCPAP ravi vahel (ja hilisem invasiivne ventilatsioon) ei esinenud statistiliselt olulist erinevust. Antud ülevaade uuris ka teisi aspekte (DAP, IVH, NEK, ROP, pneumotooraks, haiglaravi kestus), kuid statistiliselt olulist erinevust ei leitud. Ülevaate kitsaskohtadeks: ebaselge „*blinding*“, erinevad kriteeriumid/vaatlusajad mehaanilise ventilatsiooni rakendamisel, puudulik analüüs lühi- ja kaugtulemi osas.

Samas Shi et al poolt 2014 a avaldatud randomiseeritud kontrolluuring leidis samuti statistiliselt olulise erinevuse NIPPV ja CPAP ravi vahel – NIPPV ravirühmas on enneaegsete vastsündinute intubatsiooni sagedus ja mehaanilise ventilatsiooni vajadus oluliselt väikesem (11.4% vs. 20.9%, P<0.05). Teisalt itaallaste poolt 2014 a avaldatud

randomiseeritud kontrollitud uuring (Salvo et al) ei leidnud statistiliselt olulist erinevust erinevate mitteinvasiivsete hingamistoetuse meetodite vahel (124 WLBW last, NSIPPV vs BiPAP). Samuti ei leidnud statistiliselt olulist erinevust erinevate mitteinvasiivsete meetodite vahel Kirpalani et al 2013 avaldatud uuring, kus randomiseeriti 1009 enneaegset vastsündinut NIPPV vs CPAP gruppi.
Erinevate mitteinvasiivsete hingamistoetuse meetodite teema vajab veel lisauuringuid.

Wilkinson et al avaldasid 2012. aastal süstemaatilise ülevaate, milles võrdlesid 4 randomiseeritud kontrolluuringut – High Flow Nasal Cannula (HFNC) võrdlus teiste mitteinvasiivsete hingamistoetuse meetoditega (CPAP, NIPPV, head box oxygen, low flow nasal cannula). Autorid järeldasid tulemustest, et HFNC puhul on reintubatsiooni tõenäosus suurem kui nt CPAP puhul. Ülevaade ise oli puuduliku kvaliteediga, kuna uuritavate arv oli väike ning subgrupi analüüsides oli mitme püstitatud küsimuse juures analüüsitud vaid ühte uuringut. Põhjapanevate järelduste tegemiseks on vaja täiendavaid uuringuid.

Sama teema kohta on Klingenberg et al avaldanud 2013 a patsiendi rahulolu puudutava ühe keskuse põhise uuringu, milles autorid järeldavad (heaolu osas hinnatud EDIN score): ei esine statistilist olulist erinevust patsiendi heaolu osas niisutatud, soojendatud õhuga High Flow Nasal Cannula versus CPAP-ravi vahel. Samas patsientide vanemad eelistasid HFNC, põhjuseks eeldatud lapse heaolu ja suurem võimalus lapse hoolduses/protseduurides osalemiseks.

Schmölzer et al 2014 a avaldatud prolongeeritud inflatsiooni käsitlev metaanalüüs (4 uuringut, GRADE kvaliteet mõõdukas) leidis, et prolongeeritud inspiiriumi (SI) kasutamine esmasel stabiliseerimisel on efektiivne meetod hingamistoetuse rakendamisel lühiajaliselt, vähendades mehaanilise ventilatsiooni vajadust esimese 72 elutunni jooksul. Samas uuringu tulemusena ei esinenud statistiliselt olulist erinevust hilistulemite osas (BPD, suremus). Lisaks esines statistiliselt olulisel määral SI grupis avatud arterioosjuha, mis vajas medikamentoosset või kirurgilist sulgemist. Vt tulemuste tabel allpool.

Lista et al poolt 2015 a avaldatud randomiseeritud kliiniline uuring, SLI trial, randomiseeris 291 patsienti kahte gruppi, kus võrdlesid prolongeeritud inspiiriumi (25 cm H2O, 15 sekundit) + CPAPi kasutamist ainult CPAPi kasutamisega. Prolongeeritud inspiiriumi kasutamine koos CPAP-raviga vähendas mehaanilise ventilatsiooni vajadust esimese 72 elutunni jooksul, kuid ei vähendanud hingamistoetuse vajadust üldiselt ega ka BPD esinemissagedust.

Viited

Kokkuvõtte (abstract või kokkuvõtlikum info)	**Viide kirjandusallikale**
METHODS: In February 2013, we searched the databases Medline, Embase, and the Cochrane Central Register of Controlled Trials. Study selection criteria included randomized controlled trials published in peer-reviewed journals since the year 2000 that compared preterm infants <30 weeks' GA treated by using a strategy aimed at avoiding eMV with a control group in which mechanical ventilation via an	Fischer, H.S., Bührer, C., 2013. **Avoiding endotracheal ventilation to prevent bronchopulmonary**

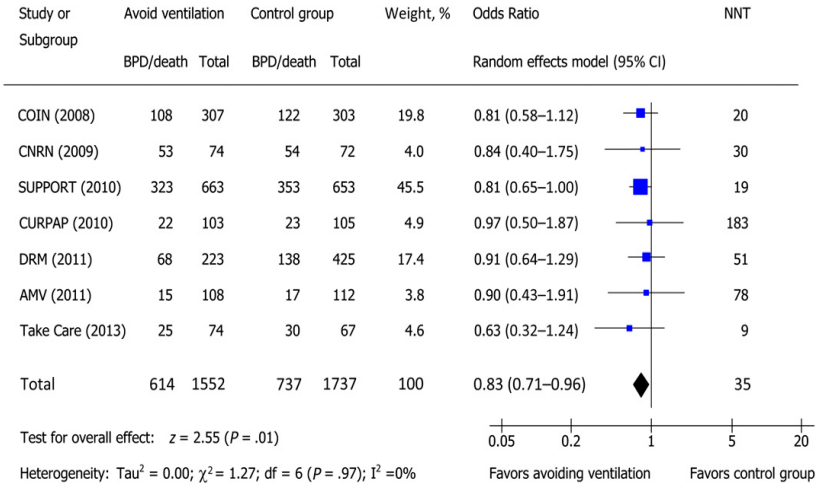
endotracheal tube was performed at an earlier stage. Data were extracted and analyzed by using the standard methods of the Cochrane Neonatal Review Group. The authors independently
assessed study eligibility and risk of bias, extracted data and calculated odds ratios and 95% confidence intervals, employing RevMan version 5.1.6.

RESULTS: We identified 7 trials that included a total of 3289 infants. The combined odds ratio (95% confidence interval) of death or BPD was 0.83 (0.71–0.96). The number needed to treat was 35. The study results were remarkably homogeneous. Avoiding eMV had no influence on the incidence of severe intraventricular hemorrhage.

CONCLUSIONS: Strategies aimed at avoiding eMV in infants <30 weeks' GA have a small but significant beneficial impact on preventing BPD.

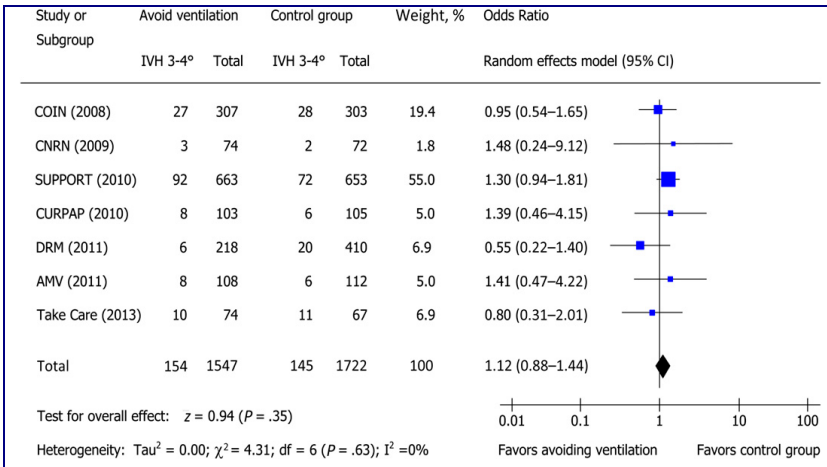
dysplasia: a meta-analysis. Pediatrics 132, e1351–1360. doi:10.1542/peds.2013-1880

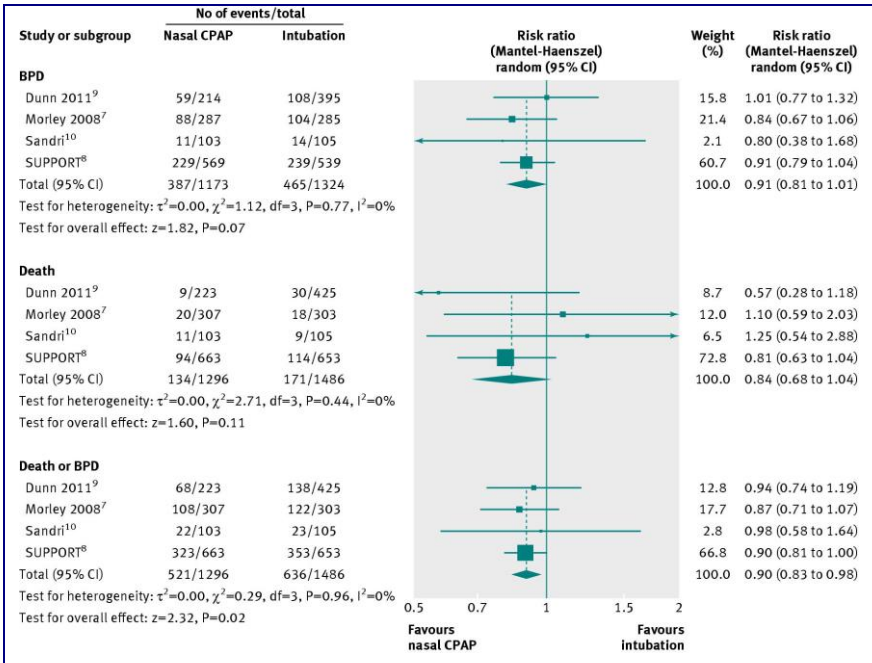
BPD/Death



Avoiding eMV in very premature infants means that a considerable number of
them will later need rescue intubation because of hypercapnic respiratory failure. On the one hand, there are substantiated concerns about the association between hypercapnia and IVH in preterm infants, especially during the first days of life. On the other hand, mild hypercapnia has long been regarded as safe in premature infants <1000 g, and permissive hypercapnia can be used as a way of reducing eMV and improving pulmonary outcomes. The results of the present meta-analysis revealed no difference in the incidence of severe IVH between the intervention group and the control group, which indicates that the strategies applied to avoid eMV in the included RCTs were generally safe.

IVH

 Assessment of the included RCTs indicated that all studies were of good methodological quality with mostly low risk for bias. The only major issue was the lack of blinding.	
Objective: To assess the role of nasal continuous positive airway pressure (CPAP) initiated at birth for prevention of death and bronchopulmonary dysplasia in very preterm infants. **Data sources** PubMed, Embase, the Cochrane Central Register of Controlled Trials, and online Pediatric Academic Society abstracts from the year of inception to June 2013. Eligibility criteria for selecting studies Randomised controlled trials evaluating the effect of nasal CPAP compared with intubation in preterm infants born at less than 32 weeks' gestation and presenting the outcomes of either death or bronchopulmonary dysplasia, or both (defined as the need for oxygen support or mechanical ventilation at 36 weeks corrected gestation), during hospital stay. **Results** Four randomised controlled trials (2782 participants) met the inclusion criteria, with 1296 infants in the nasal CPAP group and 1486 in the intubation group. All the trials reported bronchopulmonary dysplasia independently at 36 weeks corrected gestation, with borderline significance in favour of the nasal CPAP group (relative risk 0.91, 95% confidence interval 0.82 to 1.01, risk difference −0.03, 95% confidence interval −0.07 to 0.01). No difference in death was observed (relative risk 0.88, 0.68 to 1.14, risk difference −0.02, −0.04 to 0.01, respectively). Pooled analysis showed a significant benefit for the combined outcome of death or bronchopulmonary dysplasia, or both, at 36 weeks corrected gestation for babies treated with nasal CPAP (relative risk 0.91, 0.84 to 0.99, risk difference −0.04, -0.07 to 0.00), number needed to treat of 25). **Conclusion** One additional infant could survive to 36 weeks without bronchopulmonary dysplasia for every 25 babies treated with nasal CPAP in the delivery room rather than being intubated.	Schmölzer, G.M., Kumar, M., Pichler, G., Aziz, K., O'Reilly, M., Cheung, P.-Y., 2013. **Non-invasive versus invasive respiratory support in preterm infants at birth: systematic review and meta-analysis.** BMJ 347, f5980.



Objective: To evaluate whether nasal intermittent positive pressure ventilation (NIPPV) would decrease the requirement for endotracheal ventilation compared with nasal continuous positive airway pressure (NCPAP) for preterm infants with respiratory distress syndrome (RDS) and compare the related complications between these two noninvasive variations of respiratory support. **Methods:** A search of major electronic databases, including Medline (1980–2013) and the Cochrane Central Register of Controlled Trials, for randomized controlled trials that compared NIPPV versus NCPAP for preterm infants with RDS was performed. **Main Results:** Six randomized controlled trials met selection criteria (n=1,527). The meta-analyses demonstrated significant decrease in the need for invasive ventilation in the NIPPV group (RR:0.53; 95% CI, 0.33–0.85). In the subgroup of infants who received surfactant also demonstrated a significant rate of failure of nasal support in the NIPPV group (RR:0.57; 95% CI 0.42–0.78). However, the subgroup of infants whose gestational age (GA) ≤30 weeks or birth weight (BW)<1,500 g showed no difference between the two groups (RR:0.59; 95% CI 0.27–1.26); and the subgroup of infants whose GA>30 weeks or BW>1,500 g also showed no difference between the two groups (RR:0.63; 95% CI 0.29–1.39). No differences in other outcome variables were observed between the two groups. **Conclusions:** Among preterm infants with RDS, there was a significant decrease in the need for invasive ventilation in the NIPPV group as compared with NCPAP group, especially for the infants who received surfactant. However, NIPPV could not decrease the need for invasive ventilation both in the subgroup of infants whose GA ≤30 weeks or BW<1,500 g and the subgroup of infants with BW of >30 weeks or BW>1,500 g. It is limited to analysis the primary outcome generally. Larger trials of this intervention are needed to assess the	Li, W., Long, C., Zhangxue, H., Jinning, Z., Shifang, T., Juan, M., Renjun, L., Yuan, S., 2015. **Nasal intermittent positive pressure ventilation versus nasal continuous positive airway pressure for preterm infants with respiratory distress syndrome: a meta-analysis and up-date.** Pediatr. Pulmonol. 50, 402–409. doi:10.1002/ppul.23130

difference in this primary outcome and the related complications between both forms of noninvasive respiratory support.

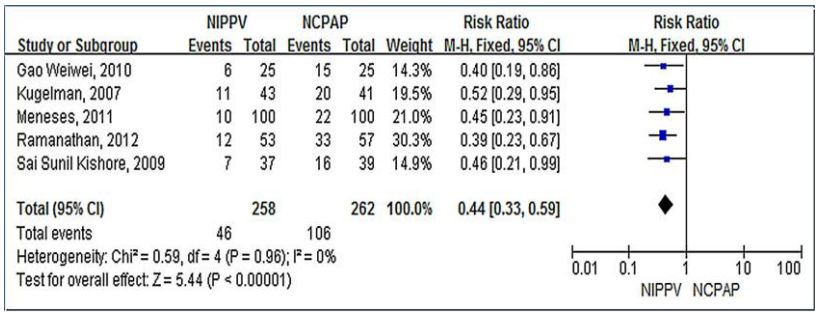
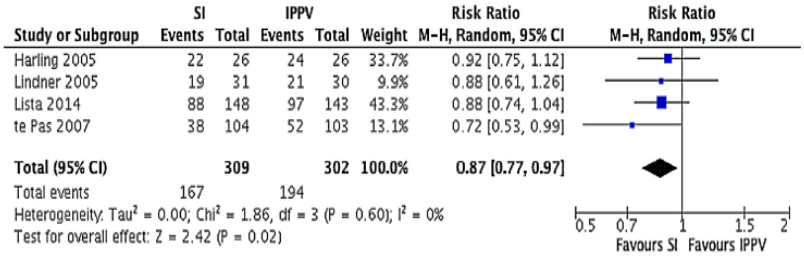


TABLE 3— Bias Assessment of 5 Included RCTs

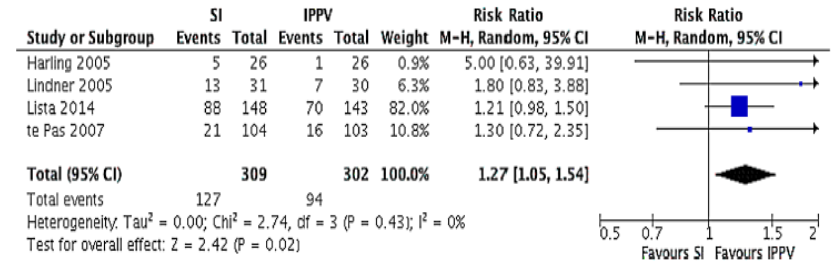
	Kugelman	Ramanathan	Sai Sunil Kishore	Meneses	Gao WW	Haresh Kirpalani
Allocation concealment	Yes	Yes	Yes	Yes	Yes	Yes
Sequence generation	Yes	Yes	Yes	Yes	Unclear	Yes
Blinding (participants)	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Blinding (outcome assessors)	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Incomplete data address	Yes	Yes	Yes	Yes	Yes	Yes
Free of selective reporting	Yes	Yes	Yes	Yes	Yes	Yes
Free of other Bias	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear

Study selection: Randomised clinical trials comparing the effects of SI with IPPV at birth in preterm infants for neonatal outcomes. Data extraction and synthesis Descriptive and quantitative information was extracted; data were pooled using a random effects model. Heterogeneity was assessed using the Q statistic and I2.
Results: Pooled analysis showed significant reduction in the need for mechanical ventilation within 72 h after birth (relative risk (RR) 0.87 (0.77 to 0.97), absolute risk reduction (ARR) −0.10 (−0.17 to −0.03), number needed to treat 10) in preterm infants treated with an initial SI compared with IPPV. However, significantly more infants treated with SI received treatment for patent ductus arteriosus (RR 1.27 (1.05 to 1.54), ARR 0.10 (0.03 to 0.16), number needed to harm 10). There were no differences in BPD, death at the latest follow-up and the combined outcome of death or BPD among survivors between the groups.
Conclusions: Compared with IPPV, preterm infants initially treated with SI at birth required less mechanical ventilation with no improvement in the rate of BPD and/or death. The use of SI should be restricted to randomised trials until future studies demonstrate the efficacy and safety of this lung aeration manoeuvre.



Outcome of mechanical ventilation <72 h after birth. IPPV, intermittent positive pressure ventilation; SI, sustained inflation.

Schmölzer, G.M., Kumar, M., Aziz, K., Pichler, G., O'Reilly, M., Lista, G., Cheung, P.-Y., 2014. **Sustained inflation versus positive pressure ventilation at birth: a systematic review and meta-analysis.** Arch. Dis. Child. Fetal Neonatal Ed. doi:10.1136/archdischild-2014-306836



Outcome of patent ductus arteriosus. IPPV, intermittent positive pressure ventilation; SI, sustained inflation.

Table 1 Assessment of risk of bias in the included studies

Study	Year	Sequence generation	Allocation concealment	Blinding of caregivers	Incomplete outcome data addressed	Selective outcome reporting	Other biases
Harling *et al*[17]	2005	Unclear	Low	High	High	Unclear	Post-randomisation exclusions. Data for interaction effect with other intervention in factorial design not presented
Lindner *et al*[14]	2005	Unclear	Unclear*	High	Low	Unclear	Study terminated prematurely. Conflict of interest statement missing; source of funding not declared
te Pas *et al*[16]	2007	Unclear	Low	High	Low	Low	
Lista *et al*[15]	2014	Low	Low	High for clinical staff, low for outcome assessor	Low	Low	

*A small fixed block size could have put allocation concealment at risk.

METHODS: We randomly assigned infants born at 25 weeks 0 days to 28 weeks 6 days of gestation to receive SLI (25 cm H2O for 15 seconds) followed by nasal continuous positive airway pressure (nCPAP) or nCPAP alone in the delivery room. SLI and nCPAP were delivered by using a neonatal mask and a T-piece ventilator. The primary end point was the need for MV in the first 72 hours of life. The secondary end points included the need for respiratory supports and survival without bronchopulmonary dysplasia (BPD).
RESULTS: A total of 148 infants were enrolled in the SLI group and 143 in the control group. Significantly fewer infants were ventilated in the first 72 hours of life in the SLI group (79 of 148 [53%]) than in the control group (93 of 143 [65%]); unadjusted odds ratio: 0.62 [95% confidence interval: 0.38–0.99]; P = .04). The need for respiratory support and survival without BPD did not differ between the groups. Pneumothorax occurred in 1% (n = 2) of infants in the control group compared with 6% (n = 9) in the SLI group, with an unadjusted odds ratio of 4.57 (95% confidence interval: 0.97–21.50; P = .06).
CONCLUSIONS: SLI followed by nCPAP in the delivery room decreased the need for MV in the first 72 hours of life in preterm infants at high risk of respiratory distress syndrome compared with nCPAP alone but did not decrease the need for respiratory support and the occurrence of BPD.
In the present study, the frequency of pneumothorax (6% vs 1%) and interstitial emphysema (5% vs 1%) was higher in the SLI group than in the control group. Although the difference was not statistically significant, we believe that this finding deserves consideration because it might suggest that our SLI maneuvers (25 cm H2O for 15 seconds) might be too aggressive.

Lista, G., Boni, L., Scopesi, F., Mosca, F., Trevisanuto, D., Messner, H., Vento, G., Magaldi, R., Del Vecchio, A., Agosti, M., Gizzi, C., Sandri, F., Biban, P., Bellettato, M., Gazzolo, D., Boldrini, A., Dani, C., SLI Trial Investigators, 2015. **Sustained lung inflation at birth for preterm infants: a randomized clinical trial.** Pediatrics 135, e457–464. doi:10.1542/peds.2014-1692

We believe that other clinical studies are necessary to investigate the effectiveness of SLI in improving outcomes in extremely preterm infants. Until these studies are available, the SLI maneuver cannot be recommend as routine prophylactic assistance in preterm infants in the delivery room.

TABLE 2 Primary and Secondary Outcomes

Outcome	Control Group (n = 143)	SLI Group (n = 148)	Unadjusted Odds Ratio (95% CI)	P	Adjusted Odds Ratio (95% CI)[a]
Primary outcome, n (%)					
MV within the first 72 h of life	93 (65)	79 (53)	0.62 (0.38–0.99)	.04	0.57 (0.33–0.96)
Secondary outcomes, n (%)					
MV within the first 3 h of life	73 (51)	66 (45)	0.77 (0.49–1.22)	.27	0.72 (0.43–1.22)
BiPAP	47 (33)	63 (43)	1.51 (0.94–2.44)	.09	1.51 (0.93–2.43)
Nasal IMV	36 (25)	39 (26)	1.06 (0.63–1.80)	.85	1.07 (0.63–1.81)
Surfactant	110 (77)	109 (74)	0.84 (0.49–1.43)	.52	0.88 (0.50–1.56)
SIMV/SIPPV/PSV	90 (63)	86 (58)	0.82 (0.51–1.31)	.43	0.84 (0.51–1.39)
HFV	31 (22)	32 (22)	1.00 (0.57–1.74)	.99	1.03 (0.58–1.83)
Any mechanical ventilation	98 (69)	88 (59)	0.67 (0.42–1.10)	.11	0.68 (0.41–1.13)
BPD[b,c]	50 (35)	57 (39)	1.17 (0.80–1.71)[d]	.42	1.14 (0.78–1.69)[d]
Death[c]	12 (8)	17 (11)	1.37 (0.66–2.88)[d]	.40	1.39 (0.66–2.93)[d]

BiPAP, bilevel positive airway pressure; HFV, high-frequency ventilation; PSV, pressure support ventilation; SIMV, synchronized intermittent MV; SIPPV, synchronized intermittent positive pressure ventilation.
[a] Adjusted for center and gestational age.
[b] Defined by the use of supplemental oxygen at a postmenstrual age of 36 weeks.
[c] Proportions are estimates of cumulative incidence of events in the presence of competing risks.
[d] Unadjusted hazard ratio (95% confidence interval).

TABLE 4 Comparison of Other Collected Data

Outcome	Control Group (n = 143)	SLI Group (n = 148)	Unadjusted Odds Ratio (95% CI)	P
RDS	134 (94)	133 (90)	0.60 (0.25–1.41)	.23
Pneumothorax	2 (1)	9 (6)	4.57 (0.97–21.50)	.06
Interstitial emphysema	2 (1)	7 (5)	3.50 (0.72–17.10)	.09
Pharmacologic treatment of PDA	70 (49)	88 (59)	1.53 (0.96–2.43)	.07
Surgical closure of PDA	8 (6)	5 (3)	0.59 (0.19–1.85)	.36
IVH	28 (20)	37 (25)	1.37 (0.79–2.39)	.27
Grade ≥3	8 (6)	12 (8)	1.49 (0.59–3.76)	.39
PVL	5 (4)	1 (1)	0.19 (0.02–1.63)	.08
NEC	4 (3)	7 (5)	1.73 (0.49–6.03)	.38
ROP[a]	58 (41)	60 (41)	0.99 (0.63–1.60)	.99
Grade ≥3	12 (8)	14 (9)	1.14 (0.51–2.56)	.75
Sepsis	44 (31)	54 (36)	1.29 (0.79–2.11)	.30

Data are presented as n (%). IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; PDA, patent ductus arteriosus; PVL, periventricular leukomalacia; ROP, retinopathy of prematurity.
[a] Proportions are estimates of cumulative incidence of events in the presence of competing risks.

Methods: This was a single center, randomized, controlled trial. A total of 179 preterm and term infants with RDS were randomized to NIPPV (n=88) or nCPAP (n=91). The clinical data of enrolled infants including blood gas analysis, PaO2/FiO2 ratio, incidence of intubation, and complications, if occurred, were recorded. The primary outcome was the need for endotracheal ventilation. The secondary outcome was the measurement of favorable outcome, which was defined as discharged without any respiratory support and feeding well and gaining weight. Analysis followed slightly modified intention to treat principle.
Results: Significantly less number of infants randomized to NIPPV group required intubation and mechanical ventilation compared with nCPAP group (11.4% vs. 20.9%, P<0.05). A favorable outcome was

Shi, Y., Tang, S., Zhao, J., Shen, J., 2014. **A prospective, randomized, controlled study of NIPPV versus nCPAP in preterm and term infants with respiratory distress syndrome.** Pediatr. Pulmonol. 49, 673–678. doi:10.1002/ppul.228

more likely in infants randomized to NIPPV (93.2% vs. 84.6%, P<0.05). In subgroup analysis, NIPPV was associated with reduced need for intubation in preterm (9.9% vs. 19.2%) and term (17.6% vs. 27.8%) infants, but the difference was statistically significant only in preterm infants (P<0.05). **Conclusion:** Treatment with NIPPV compared with nCPAP decreased the need for endotracheal ventilation and increased favorable outcome in preterm and term infants with RDS.	83
METHODS: We randomly assigned 1009 infants with a birth weight of less than 1000 g and a gestational age of less than 30 weeks to one of two forms of noninvasive respiratory support — nasal intermittent positive-pressure ventilation (IPPV) or nasal continuous positive airway pressure (CPAP) — at the time of the first use of noninvasive respiratory support during the first 28 days of life. The primary outcome was death before 36 weeks of postmenstrual age or survival with bronchopulmonary dysplasia. **RESULTS:** Of the 497 infants assigned to nasal IPPV for whom adequate data were available, 191 died or survived with bronchopulmonary dysplasia (38.4%), as compared with 180 of 490 infants assigned to nasal CPAP (36.7%) (adjusted odds ratio, 1.09; 95% confidence interval, 0.83 to 1.43; P = 0.56). The frequencies of air leaks and necrotizing enterocolitis, the duration of respiratory support, and the time to full feedings did not differ significantly between treatment groups. **CONCLUSIONS:** Among extremely-low-birth-weight infants, the rate of survival to 36 weeks of postmenstrual age without bronchopulmonary dysplasia did not differ significantly after noninvasive respiratory support with nasal IPPV as compared with nasal CPAP.	Kirpalani, H., Millar, D., Lemyre, B., Yoder, B.A., Chiu, A., Roberts, R.S., NIPPV Study Group, 2013. **A trial comparing noninvasive ventilation strategies in preterm infants.** N. Engl. J. Med. 369, 611–620. doi:10.1056/NEJMoa1214533
BACKGROUND: This study evaluates the efficacy of 2 different NIV strategies for RDS treatment in very low birth weight (VLBW) infants: nasal synchronized intermittent positive pressure ventilation (NSIPPV), which is a modality of conventional ventilation with intermittent peak inspiratory pressure, and bilevel continuous positive airway pressure (BiPAP), not synchronized, with 2 alternate levels of continuous positive airway pressure. **METHODS:** We conducted a 2-center randomized control study in 124 VLBW infants (<1500 g and <32 weeks of gestational age) with RDS who received NIV support (NSIPPV, n = 62; BiPAP, n = 62) within 2 hours of birth. We evaluated the performance of NIV strategies by selected primary outcomes (failure rate and duration of ventilation) and secondary outcomes. **RESULTS:** The number of failures and duration of ventilation support did not differ between NSIPPV and BiPAP strategies (P> 0.05 for both). Moreover, no differences between groups were found regarding secondary outcomes (P>0.05 for all).	Salvo, V., Lista, G., Lupo, E., Ricotti, A., Zimmermann, L.J.I., Gavilanes, A.W.D., Barberi, I., Colivicchi, M., Temporini, F., Gazzolo, D., 2015. **Noninvasive ventilation strategies for early treatment of RDS in preterm infants: an RCT.** Pediatrics 135, 444–451. doi:10.1542/peds.2014-0895

CONCLUSIONS: The present data show no statistically significant differences between NSIPPV and BiPAP strategies in terms of duration of ventilation and failures, suggesting that both NIV techniques are effective in the early treatment of RDS in VLBW infants. Further randomized investigations on wider populations are needed to evaluate the effect of NIV techniques on long-term outcomes.	
Background High flow nasal cannulae (HFNC) are small, thin, tapered cannulae used to deliver oxygen or blended oxygen and air at flow rates of > 1 L/min. HFNC can be used to provide high concentrations of oxygen and may deliver positive end-expiratory pressure. **Objectives** To compare the safety and efficacy of HFNC with other forms of non-invasive respiratory support in preterm infants. **Search methods** The strategy included searches of the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2010), MEDLINE, CINAHL, EMBASE and abstracts from conference proceedings. **Selection criteria** Randomised or quasi-randomised trials comparing HFNC with other non-invasive forms of respiratory support in preterm infants immediately after birth or following extubation. **Data collection and analysis** Data were extracted and analysed by the authors. Relative risk, risk difference and number needed to treat were calculated. **Main results** Four studies were identified for inclusion in the review. The studies differed in the interventions compared (nasal continuous positive airway pressure (CPAP), humidified HFNC, non-humidified HFNC), the flow rates provided and the indications for respiratory support. Meta-analysis and subgroup analysis were not possible. When used as primary respiratory support after birth, one trial found similar rates of treatment failure in infants treated with HFNC and nasal CPAP. Following extubation, one trial found that infants treated with HFNC had a significantly higher rate of reintubation than those treated with nasal CPAP. Another trial found similar rates of reintubation for humidified and non-humidified HFNC, and the fourth trial found no difference between two different models of equipment used to deliver humidified HFNC.	Wilkinson, D., Andersen, C., O'Donnell, C.P., De Paoli, A.G., 2011. **High flow nasal cannula for respiratory support in preterm infants.** Cochrane Database Syst Rev CD006405. doi:10.1002/14651858.CD006405.pub2

Authors' conclusions There is insufficient evidence to establish the safety or effectiveness of HFNC as a form of respiratory support in preterm infants. When used following extubation, HFNC may be associated with a higher rate of reintubation than nasal CPAP. Further adequately powered randomised controlled trials should be undertaken in preterm infants comparing HFNC with nasal CPAP and with other means of respiratory support; or of support following extubation. These trials should measure clinically important outcomes.	
Objective To compare patient comfort in preterm infants treated with heated humidified high flow nasal cannulae (HHHFNC) versus nasal continuous positive airway pressure (NCPAP). **Design** Randomised cross-over trial (2×24 h). Setting Single tertiary neonatal unit. Patients 20 infants less than 34 weeks postmenstrual age treated with NCPAP due to mild respiratory illness. **Interventions** After parental consent, infants were randomised to 24 h of treatment with NCPAP or HHHFNC followed by 24 h of the alternate therapy. **Main outcome measures** Primary outcome was patient comfort assessed by the EDIN (neonatal pain and discomfort) scale. Secondary outcomes were respiratory parameters (respiratory rate, FiO2, SpO2, TcPCO2), ambient noise, salivary cortisol and parental assessments of their child. **Results** We found no differences between HHHFNC and NCPAP in mean cumulative EDIN score (10.7 vs 11.1, p=0.25) or ambient noise (70 vs 74 dBa, p=0.18). Parents assessed HHHFNC treatment as significantly better in the three domains, 1) child satisfied, 2) parental contact and interaction and 3) possibility to take part in care. Mean respiratory rate over 24 h was lower during HHHFNC than CPAP (41 vs 46, p=0.001). Other respiratory parameters were similar. **Conclusions** Using EDIN scale, we found no difference in patient comfort with HHHFNC versus NCPAP. However, parents preferred HHHFNC, and during HHHFNC respiratory rate was lower than during NCPAP. Table 2 Primary and secondary outcomes Outcome | HHHFNC | NCPAP | p Value EDIN score, cumulative* | 10.7 (3.3) | 11.1 (3.0) | 0.35 Noise, dBA | 70 (10) | 74 (10) | 0.18 Parental assessment 1. Child satisfied | 8.6 (1.1) | 6.9 (1.6) | <0.001 2. Contact and interaction | 9.0 (1.1) | 6.7 (1.6) | <0.001 3. Possibility to take part in care | 9.1 (1.2) | 8.0 (1.6) | 0.03 $TcPCO_2$ (mean 2 h) kPa | 5.5 (1.1) | 5.5 (1.2) | 0.87 Respiratory rate (mean 24 h) | 41 (7) | 46 (9) | 0.001 FiO_2 (mean 24 h) | 21.8 (1.6) | 21.5 (1.1) | 0.06 SpO_2 (mean 24 h) | 95 (2) | 95 (2) | 0.41 All data are mean (SD). *Cumulative score based on assessment over three nursing shifts (day, evening, night). HHHFNC, heated humidified high flow nasal cannulae; NCPAP, nasal continuous positive airway pressure.	Klingenberg, C., Pettersen, M., Hansen, E.A., Gustavsen, L.J., Dahl, I.A., Leknessund, A., Kaaresen, P.I., Nordhov, M., 2014. **Patient comfort during treatment with heated humidified high flow nasal cannulae versus nasal continuous positive airway pressure: a randomised cross-over trial.** Arch. Dis. Child. Fetal Neonatal Ed. 99, F134–137. doi:10.1136/archdischild-2013-304525

Objective To evaluate the effectiveness and safety of a T-piece resuscitator compared with a self-inflating bag for providing mask ventilation to newborns at birth. **Study design** Newborns at ≥26 weeks *(<26 näd jäeti välja tõenäosema intubatsiooni tõttu*) gestational age receiving positive-pressure ventilation at birth were included in this multicenter cluster-randomized 2-period crossover trial. Positive-pressure ventilation was provided with either a self-inflating bag (self-inflating bag group) with or without a positive end-expiratory pressure valve or a T-piece with a positive end-expiratory pressure valve (T-piece group). Delivery room management followed American Academy of Pediatrics and International Liaison Committee on Resuscitation guidelines. The primary outcome was the proportion of newborns with heart rate (HR) ≥100 bpm at 2 minutes after birth. **Results** A total of 1027 newborns were included. There was no statistically significant difference in the incidence of HR ≥100 bpm at 2 minutes after birth between the T-piece and self-inflating bag groups: 94% (479 of 511) and 90% (466 of 516), respectively (OR, 0.65; 95% CI, 0.41-1.05; P = .08). A total of 86 newborns (17%) in the T-piece group and 134 newborns (26%) in the self-inflating bag group were intubated in the delivery room (OR, 0.58; 95% CI, 0.4-0.8; P = .002). The mean ±SD maximum positive inspiratory pressure was 26 ± 2 cmH2O in the T-piece group vs 28 ± 5 cmH2O in the self-inflating bag group (P < .001). Air leaks, use of drugs/chest compressions, mortality, and days on mechanical ventilation did not differ significantly between groups. **Conclusion** There was no difference between the T-piece resuscitator and a self-inflating bag in achieving an HR of ≥100 bpm at 2 minutes in newborns ≥26 weeks gestational age resuscitated at birth. However, use of the Tpiece decreased the intubation rate and the maximum pressures applied. **Table II. Secondary outcomes** Outcome measure | T-piece group (n = 511) | SIB group (n = 516) | OR (95% CI)* | *P* value* Outcomes in the delivery room Intubation for ventilatory support in the delivery room, n (%) | 86 (17) | 134 (26) | 0.58 (0.4-0.8) | .002 1-min Apgar score ≤3, n (%) | 153 (30) | 177 (34) | 1.3 (0.9-1.7) | .070 5-min Apgar score ≤5, n %) | 30 (6) | 47 (9) | 1.5 (0.9-2.5) | .080 Drugs/chest compressions, n (%) | 8 (1.6) | 17 (3.3) | 0.5 (0.2-1.1) | .090 Time to spontaneous breathing, min, mean ± SD† | 2.7 ± 36 | 3.05 ± 3.9 | - | .100 Time elapsed until HR ≥ 100 bpm, min, median (IQR) | 1 (0.5-1.6) | 1 (0.5-1.8) | - | .068 Maximum PIP, mean ± SD‡ variability | 25.58 ± 1.9 | 28 ± 4.9 | - | <.001 PIP >25 cm H_2O, n (%) | 52 (10) | 184 (37) | 5.0 (3.6-7.0) | <.001 Mean maximum FIO_2 in delivery room, mean ± SD | 0.46 ± 0.19 | 0.50 ± 0.21 | - | .001 Outcomes after the delivery room Mortality, n (%) | 11 (2.2) | 15 (2.9) | 1.1 (0.5-2.5) | .810 Air leaks (pneumothorax and/or pneumomediastinum), n (%) | 13 (2.5) | 8 (1.6) | 0.6 (0.2-1.4) | .250 Mechanical ventilation, n (%) | 116 (22.7) | 147 (28.5) | 1.3 (0.9-1.8) | .160 Days on mechanical ventilation, mean ± SD | 5.0 ± 7.6 | 8.3 ± 13.3 | - | .007 Days on CPAP, mean ± SD | 7.83 ± 11.3 | 7.96 ± 10.1 | - | .901 Hypoxic ischemic encephalopathy, n (%) | 21 (4.1) | 28 (5.4) | 1.3 (0.7-2.4) | .330 Use of oxygen, n (%) | 208 (40.7) | 222 (43.0) | 1.1 (0.8-1.5) | .411 Days on oxygen, mean ± SD | 13.8 ± 17 | 22.8 ± 25 | - | <.001 *CPAP*, continuous positive airway pressure; *PIP*, peak inspiratory pressure. *Corrected by center and birth weight <1500 g. †990 subjects. ‡1007 subjects.	Szyld, E., Aguilar, A., Musante, G.A., Vain, N., Prudent, L., Fabres, J., Carlo, W.A., Delivery Room Ventilation Devices Trial Group, 2014. **Comparison of devices for newborn ventilation in the delivery room.** J. Pediatr. 165, 234–239.e3. doi:10.1016/j.jpeds.2014.02.035

Table III. Analysis in the subgroup of VLBW infants

Outcome measure	T-piece group (n = 85)	SIB group (n = 110)	OR (95% CI)*	P value*
HR ≥100 bpm at 2 min, n (%)	75 (88.2)	84 (76.4)	0.43 (0.19-0.95)	.037
Intubation for ventilatory support, n (%)	45 (52.9)	76 (69.1)	2.01 (1.12-3.60)	.019
Drugs/chest compressions, n (%)	3 (3.5)	5 (4.6)	1.30 (0.30-5.61)	.723
Mechanical ventilation, n (%)	62 (72.9)	85 (77.3)	1.26 (0.66-2.43)	.487
BPD, n (%)	21 (24.7)	44 (40.0)	2.03 (1.09-3.79)	.036
Air leaks (pneumothorax and/or neumomediastinum), n (%)	3 (3.5)	2 (1.8)	0.51 (0.08-3.1)	.461
Use of oxygen, n (%)	71 (83)	101 (92)	2.2 (0.9-5.5)	.082
Days on oxygen, mean ± SD	21 ± 20	35 ± 27	-	.0007

*Corrected by center.

Table IV. Subgroup analysis comparing the patients from centers using SIB with PEEP and centers using SIB without PEEP vs T-piece

Outcome measure	T-piece (n = 226)	SIB without PEEP valve (n = 226)	P value	T-piece (n = 285)	SIB with PEEP valve (n = 290)	P value
Outcomes in the delivery room						
HR ≥100 bpm at 2 min, n (%)	218 (96)	210 (93)	.099	261 (92)	256 (88)	.192
Intubation for ventilatory support in the delivery room, n (%)	31 (14)	53 (23)	.008	55 (19)	81 (28)	.012
1-min Apgar score ≤3, n (%)	51 (23)	66 (29)	.092	102 (36)	111 (39)	.340
5-min Apgar score ≤5, n (%)	12 (5)	23 (10)	.055	18 (6)	24 (8)	.364
Drugs/chest compressions, n (%)	2 (1)	6 (3)	.175	6 (2)	11 (4)	.239
Time to spontaneous breathing, min, mean ± SD†	2.7 ± 4.4	2.9 ± 3.7	.668	2.7 ± 2.8	3.2 ± 4.1	.114
Time elapsed until HR ≥100 bpm, min, median (IQR)	1 (0.5-2)	1 (0.5-1.9)	.109	1 (0.5-1.5)	1 (0.5-1.8)	.247
Maximum PIP, mean ± SD‡ variability	25.3 ± 1.2	27.3 ± 3.9	<.001	25.8 ± 2.3	28.7 ± 5.5	<.001
PIP >25 cm H_2O, n (%)	11 (5)	73 (33)	<.001	41 (15)	111 (40)	<.001
Maximum FiO_2 in delivery room, mean ± SD	0.47 ± 0.2	0.53 ± 0.2	.005	0.46 ± 0.2	0.48 ± 0.2	.118
Outcomes after the delivery room						
Mortality, n (%)	7 (3)	7 (3)	.999	4 (1)	8 (3)	.265
Air leaks (pneumothorax and/or pneumomediastinum), n (%)	6 (3)	2 (1)	.175	7 (2)	6 (2)	.759
Mechanical ventilation, n (%)	37 (16)	43 (19)	.449	79 (28)	104 (36)	.028
Days on mechanical ventilation, mean ± SD	6 ± 5	12 ± 17	.014	5 ± 8	7 ± 11	.148
Days on CPAP, mean ± SD	41 ± 22	51 ± 31	.030	88 ± 49	86 ± 37	.161
Hypoxic ischemic encephalopathy, n (%)	8 (4)	7 (3)	.793	13 (5)	21 (7)	.169
Use of oxygen, n (%)	93 (41)	96 (42)	.079	115 (40)	126 (43)	.321
Days on oxygen, mean ± SD	13 ± 15	23 ± 22	.014	14 ± 19	23 ± 27	.012
Birth weight <1500 g, n (%)	30 (13)	41 (18)	.146	55 (19)	69 (24)	.180
BPD, n (%)	9 (30)	19 (46)	.153	12 (22)	25 (36)	.090

*Corrected by center and birth weight <1500 g.
†990 subjects.
‡1007 subjects.

Our findings may be partially explained by the fact that a T-piece provides PEEP more effectively than a self-inflating bag with a PEEP valve, enhancing the clearance of fluid from the lungs and establishment of an effective functional residual capacity. Analysis of the VLBW infant subgroup revealed a higher incidence of BPD in the self-inflating bag group.

Our study has several limitations. The trial could not be blinded because its design precluded masking of the intervention and the outcome evaluation. In addition, actual PEEP, lung volumes, tidal volumes, and leaks around the mask were not measured as recommended by some authors, because this trial tested interventions in routine clinical practice.

Background: Extremely preterm infants require assistance recruiting the lung to establish a functional residual capacity after birth. Sustained inflation (SI) combined with positive end expiratory pressure (PEEP) may be a superior method of aerating the lung compared with intermittent positive pressure ventilation (IPPV) with PEEP in extremely preterm infants. The Sustained Aeration of Infant Lungs (SAIL) trial was designed to study this question.
Methods/Design: This multisite prospective randomized controlled unblinded trial will recruit 600 infants of 23 to 26 weeks gestational age who require respiratory support at birth. Infants in both arms will be treated with PEEP 5 to 7 cm H2O throughout the resuscitation. The

Foglia, E.E., Owen, L.S., Thio, M., Ratcliffe, S.J., Lista, G., Te Pas, A., Hummler, H., Nadkarni, V., Ades, A., Posencheg, M., Keszler, M., Davis, P., Kirpalani, H., 2015. **Sustained Aeration of Infant**

study intervention consists of performing an initial SI (20 cm H20 for 15 seconds) followed by a second SI (25 cm H2O for 15 seconds), and then PEEP with or without IPPV, as needed. The control group will be treated with initial IPPV with PEEP. The primary outcome is the combined endpoint of bronchopulmonary dysplasia or death at 36 weeks post-menstrual age.	**Lungs (SAIL) trial: study protocol for a randomized controlled trial.** Trials 16, 95. doi:10.1186/s13063-015-0601-9

Ravijuhendid

Kokkuvõte ravijuhendites leiduvast:

1) European Resuscitation Council Guidelines for Resuscitation 2010

2) European Consensus Guidelines on the Management of Neonatal Respiratory Distress Syndrome (RDS) in Preterm Infants 2013

3) Care of extremely premature infants, The Swedish National Board of Health and Welfare, 2014

Eelnevalt mainitud ravijuhendid oleme hinnanud AGREE juhendiga ning saadud tulemuste põhjal on tegemist kvaliteetsete juhenditega, mida otsustasime käesoleva ravijuhendi koostamisel kasutada.

Hingamise toetuse metoodika valik esmasel stabiliseerimisel:

1) Euroopa vastsündinute elustamise juhend soovitab enneaegsete vastsündinute esmasel stabiliseerimisel pigem kasutada kontrollitud rõhuga ventilatsiooni.

Kopsude avanemiseks, kopsukoe kahjustuse ja alveoolide korduva kollabeerumise vältimiseks on vajalik vältida suurte mahtudega (lubatud maksimaalselt 4–8 ml/kg) ventilatsiooni ja kopsude ülevenitatavust. Tagada stabiilne lõpp-ekspiratoorne rõhk (PEEP), seeläbi paraneb kopsude venitatavus ja gaasivahetus. *Initial inflation pressure* soovitatavalt 20–25 cmH2O.

2) RDSi juhend ütleb: ”*Respiratory support in the form of mechanical ventilation (MV) may be lifesaving but can cause lung injury, and protocols should be directed at avoiding mechanical ventilation where possible by using non-invasive respiratory support such as CPAP*”.

If lung inflation is needed a single sustained inflation of about 25 cmH20 for about 15 s may be better than repeated manual inflations, although more research is needed for this intervention.

*In spontaneously breathing babies stabilize with CPAP of at least 5–6 cmH20 via mask or nasal prongs **(A)***.

*CPAP should be started from birth in all babies at risk of RDS, such as those <30 weeks' gestation who do not need MV, until their clinical status can be assessed **(A)***.

*Intubation should be reserved for babies who have not responded to positive pressure ventilation via face mask. Babies who require intubation for stabilization should be given surfactant **(A)***.

*MV should be used to support babies when other methods of respiratory support have failed **(B)**.*

*Duration of MV should be minimized to reduce its injurious effect on the lung **(B)**.*

*Targeted tidal volume ventilation should be employed as this shortens duration of ventilation and reduces BPD **(A)**.*

*HFOV may be useful as a rescue therapy **(B)**.*

*When weaning from MV it is reasonable to tolerate a moderate degree of hypercarbia, provided the pH remains above 7.22 **(B)**. Avoid hypocarbia as this is associated with increased risks of BPD and periventricular leukomalacia **(B)**.*

Grades of recommendation: GRADE

A	At least one meta-analysis, systematic review or RCT rated as 1++ and directly applicable to the target population or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population and demonstrating consistency of results or Extrapolated evidence from studies such as 1++ or 1+
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating consistency of results or Extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4 or Extrapolated evidence from studies rated as 2+

GRADE = Grading of recommendations assessment, development and evaluation [5]; RCT = randomized controlled trial.

3) Rootsi enneaegse vastsündinu ravijuhend:

Nasal continuous positive airway pressure (nasal CPAP) ought to be the first choice of breathing support for extremely premature infants.

Respirator treatment ought only to be used when other methods for breathing support are inadequate. The care periods in a respirator ought to be as short as possible.

PUBMED otsingud:

Search	Add to builder	Query	Items found	Time
#18	Add	Search (((((("Continuous Positive Airway Pressure"[Mesh]) OR nasal continuous positive airway pressure) OR nasal continuous positive airway) OR CPAP)) AND ((((((((((("premature infant") OR "premature infants") OR "premature newborn") OR "premature newborns") OR "premature neonate") OR "premature neonates") OR "preterm infant") OR "preterm infants") OR "preterm newborn") OR "preterm newborns") OR "preterm neonate") OR "preterm neonates")) OR (("Infant, Premature"[Mesh]) OR "Infant, Low Birth Weight"[Mesh]))	1068	14:43:53
#17	Add	Search (((((("Continuous Positive Airway Pressure"[Mesh]) OR nasal continuous positive airway pressure) OR nasal continuous positive airway) OR CPAP)) AND ((((((((((("premature infant") OR "premature infants") OR "premature newborn") OR "premature newborns") OR "premature neonate") OR "premature neonates") OR "preterm infant") OR "preterm infants") OR "preterm newborn") OR "preterm newborns") OR "preterm neonate") OR "preterm neonates")) OR (("Infant, Premature"[Mesh]) OR "Infant, Low Birth Weight"[Mesh])) Filters: Meta-Analysis; Randomized Controlled Trial; Systematic Reviews; published in the last 5 years	100	14:43:53
#16	Add	Search (((("Continuous Positive Airway Pressure"[Mesh]) OR nasal continuous positive airway pressure) OR nasal continuous positive airway) OR CPAP	9986	14:43:08
#9	Add	Search "Continuous Positive Airway Pressure"[Mesh]	4235	13:29:08
#6	Add	Search nasal continuous positive airway pressure	8673	13:28:34
#7	Add	Search nasal continuous positive airway	2465	13:28:24
#5	Add	Search CPAP	5638	13:27:21
#4	Add	Search ((((((((((("premature infant") OR "premature infants") OR "premature newborn") OR "premature newborns") OR "premature neonate") OR "premature neonates") OR "preterm infant") OR "preterm infants") OR "preterm newborn") OR "preterm newborns") OR "preterm neonate") OR "preterm neonates")) OR (("Infant, Premature"[Mesh]) OR "Infant, Low Birth Weight"[Mesh])	82069	13:26:50

#5	Add	Search (stabilization) AND ((((((((((("premature infant") OR "premature infants") OR "premature newborn") OR "premature newborns") OR "premature neonate") OR "premature neonates") OR "preterm infant") OR "preterm infants") OR "preterm newborn") OR "preterm newborns") OR "preterm neonate") OR "preterm neonates")) OR (("Infant, Premature"[Mesh]) OR "Infant, Low Birth Weight"[Mesh])) Filters: published in the last 5 years	50	16:41:28
#4	Add	Search (stabilization) AND ((((((((((("premature infant") OR "premature infants") OR "premature newborn") OR "premature newborns") OR "premature neonate") OR "premature neonates") OR "preterm infant") OR "preterm infants") OR "preterm newborn") OR "preterm newborns") OR "preterm neonate") OR "preterm neonates")) OR (("Infant, Premature"[Mesh]) OR "Infant, Low Birth Weight"[Mesh]))	197	16:41:28
#2	Add	Search stabilization	72128	15:35:07
#1	Add	Search ((((((((((("premature infant") OR "premature infants") OR "premature newborn") OR "premature newborns") OR "premature neonate") OR "premature neonates") OR "preterm infant") OR "preterm infants") OR "preterm newborn") OR "preterm newborns") OR "preterm neonate") OR "preterm neonates")) OR (("Infant, Premature"[Mesh]) OR "Infant, Low Birth Weight"[Mesh])	82595	15:32:58

#7	Add	Search (((ventilation) OR (("Noninvasive Ventilation"[Mesh]) OR ("Pulmonary Ventilation"[Mesh] OR "Intermittent Positive-Pressure Ventilation"[Mesh] OR "High-Frequency Ventilation"[Mesh] OR "Continuous Positive Airway Pressure"[Mesh] OR "Positive-Pressure Respiration"[Mesh] OR "Respiration, Artificial"[Mesh])))) AND ((((((((((("premature infant") OR "premature infants") OR "premature newborn") OR "premature newborns") OR "premature neonate") OR "premature neonates") OR "preterm infant") OR "preterm infants") OR "preterm newborn") OR "preterm newborns") OR "preterm neonate") OR "preterm neonates")) OR (("Infant, Premature"[Mesh]) OR "Infant, Low Birth Weight"[Mesh]))))	7339	16:20:33
#11	Add	Search (((ventilation) OR (("Noninvasive Ventilation"[Mesh]) OR ("Pulmonary Ventilation"[Mesh] OR "Intermittent Positive-Pressure Ventilation"[Mesh] OR "High-Frequency Ventilation"[Mesh] OR "Continuous Positive Airway Pressure"[Mesh] OR "Positive-Pressure Respiration"[Mesh] OR "Respiration, Artificial"[Mesh])))) AND ((((((((((("premature infant") OR "premature infants") OR "premature newborn") OR "premature newborns") OR "premature neonate") OR "premature neonates") OR "preterm infant") OR "preterm infants") OR "preterm newborn") OR "preterm newborns") OR "preterm neonate") OR "preterm neonates")) OR (("Infant, Premature"[Mesh]) OR "Infant, Low Birth Weight"[Mesh])))) Filters: Meta-Analysis; Systematic Reviews; Randomized Controlled Trial; published in the last 5 years	249	16:20:32
#10	Add	Search (((ventilation) OR (("Noninvasive Ventilation"[Mesh]) OR ("Pulmonary Ventilation"[Mesh] OR "Intermittent Positive-Pressure Ventilation"[Mesh] OR "High-Frequency Ventilation"[Mesh] OR "Continuous Positive Airway Pressure"[Mesh] OR "Positive-Pressure Respiration"[Mesh] OR "Respiration, Artificial"[Mesh])))) AND ((((((((((("premature infant") OR "premature infants") OR "premature newborn") OR "premature newborns") OR "premature neonate") OR "premature neonates") OR "preterm infant") OR "preterm infants") OR "preterm newborn") OR "preterm newborns") OR "preterm neonate") OR "preterm neonates")) OR (("Infant, Premature"[Mesh]) OR "Infant, Low Birth Weight"[Mesh])))) Filters: Meta-Analysis; Systematic Reviews; published in the last 5 years	91	13:47:59
#9	Add	Search (((ventilation) OR (("Noninvasive Ventilation"[Mesh]) OR ("Pulmonary Ventilation"[Mesh] OR "Intermittent Positive-Pressure Ventilation"[Mesh] OR "High-Frequency Ventilation"[Mesh] OR "Continuous Positive Airway Pressure"[Mesh] OR "Positive-Pressure Respiration"[Mesh] OR "Respiration, Artificial"[Mesh])))) AND ((((((((((("premature infant") OR "premature infants") OR "premature newborn") OR "premature newborns") OR "premature neonate") OR "premature neonates") OR "preterm infant") OR "preterm infants") OR "preterm newborn") OR "preterm newborns") OR "preterm neonate") OR "preterm neonates")) OR (("Infant, Premature"[Mesh]) OR "Infant, Low Birth Weight"[Mesh])))) Filters: Meta-Analysis; published in the last 5 years	40	13:47:56
#8	Add	Search (((ventilation) OR (("Noninvasive Ventilation"[Mesh]) OR ("Pulmonary Ventilation"[Mesh] OR "Intermittent Positive-Pressure Ventilation"[Mesh] OR "High-Frequency Ventilation"[Mesh] OR "Continuous Positive Airway Pressure"[Mesh] OR "Positive-Pressure Respiration"[Mesh] OR "Respiration, Artificial"[Mesh])))) AND ((((((((((("premature infant") OR "premature infants") OR "premature newborn") OR "premature newborns") OR "premature neonate") OR "premature neonates") OR "preterm infant") OR "preterm infants") OR "preterm newborn") OR "preterm newborns") OR "preterm neonate") OR "preterm neonates")) OR (("Infant, Premature"[Mesh]) OR "Infant, Low Birth Weight"[Mesh])))) Filters: published in	1544	13:47:31

		the last 5 years		
#6	Add	Search (ventilation) OR (("Noninvasive Ventilation"[Mesh]) OR ("Pulmonary Ventilation"[Mesh] OR "Intermittent Positive-Pressure Ventilation"[Mesh] OR "High-Frequency Ventilation"[Mesh] OR "Continuous Positive Airway Pressure"[Mesh] OR "Positive-Pressure Respiration"[Mesh] OR "Respiration, Artificial"[Mesh]))	282652	13:47:11
#5	Add	Search ("Noninvasive Ventilation"[Mesh]) OR ("Pulmonary Ventilation"[Mesh] OR "Intermittent Positive-Pressure Ventilation"[Mesh] OR "High-Frequency Ventilation"[Mesh] OR "Continuous Positive Airway Pressure"[Mesh] OR "Positive-Pressure Respiration"[Mesh] OR "Respiration, Artificial"[Mesh])	95311	13:46:37
#2	Add	Search ventilation	258531	13:38:23
#1	Add	Search ((((((((((("premature infant") OR "premature infants") OR "premature newborn") OR "premature newborns") OR "premature neonate") OR "premature neonates") OR "preterm infant") OR "preterm infants") OR "preterm newborn") OR "preterm newborns") OR "preterm neonate") OR "preterm neonates")) OR (("Infant, Premature"[Mesh]) OR "Infant, Low Birth Weight"[Mesh]))	82605	13:38:11