# Strategies that help Avoid Ventilation whenever possible

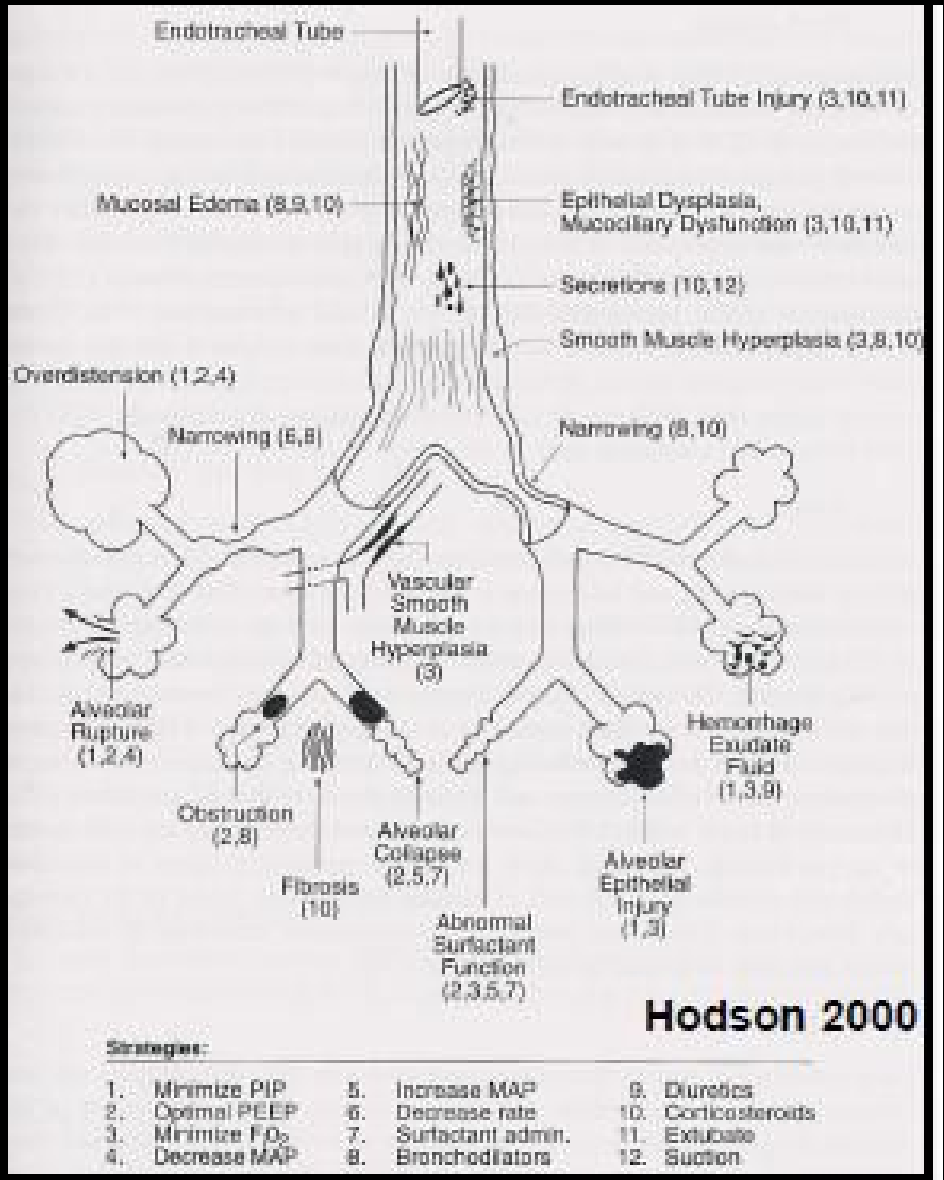
Dr Dinesh Kumar Chirla
MD; DM; FRCPCH(UK),
Fellow in Neonatology (Australia)
Fellow in Paediatric Intensive Care ( UK)
***Director, Neonatal & Paediatric Intensive Care***
***Rainbow Children Hospital & Perinatal Centre***

# WHY NOT ENDOTRACHEAL INTUBATION?

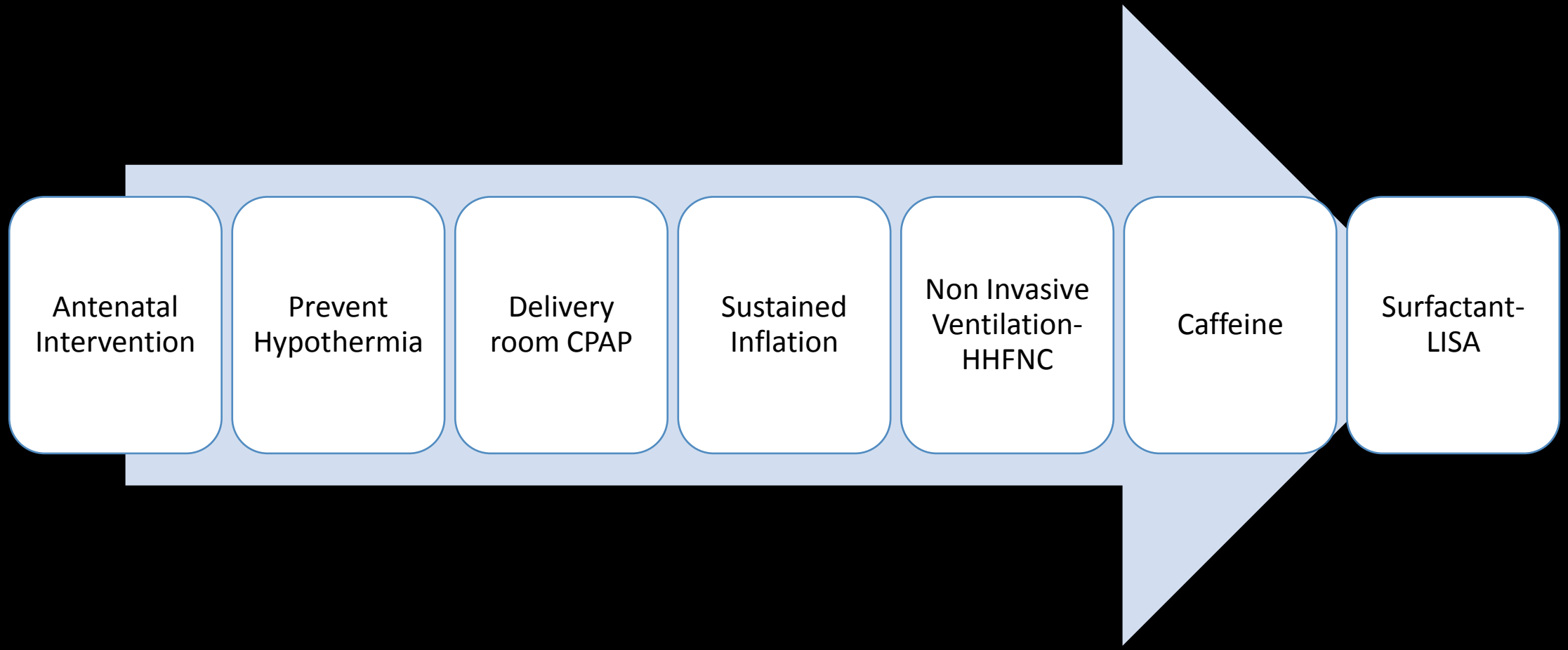
- During intubation
  - Hypoxia, bradycardia
  - Esophageal intubation
  - Pharyngeal perforation
- Increased airway resistance with spontaneous, unassisted breaths ↑ WOB
- Obstruction of endotracheal tube (ETT)
- Malpositioning of the ETT
- Nasal septal damage with nasotracheal tube
- Acquired palatal groove with orotracheal tube
- Vocal cord injury
- Subglottic edema, Subglottic stenosis
- Tracheomalacia, Tracheal stenosis
- Release of plasticizer (di-2-ethylhexyl phthalate)

# The problem of Endotracheal Intubation

- Acute and chronic lung damage - volutrauma
- Infections – pulmonary and systemic



# Strategies to Avoid Ventilation



# Thermoregulation

- Skin to skin contact (KMC)
- Radiant warmer
- Plastic wrap up to the level of neck with cap
- Increased room temperature
- Thermal mattresses
- Use of warmed humidified resuscitation gases

**Various combinations of these strategies may be reasonable to prevent hypothermia in infants born at < 32 weeks of gestation**

# Hypothermia A Risk Factor For Respiratory Distress Syndrome In Premature Infants?

- 593 infants of < 32 weeks GA
- 64% (n = 381) had hypothermia (< 36.5$^{o}$C)
- 33% (n = 197) had a rectal temperature within the normal range (36.5$^{o}$C - 37.5$^{o}$C)
- 3% (n = 15) had hyperthermia (> 37.5$^{o}$C).
- The unadjusted odds for need for surfactant if hypothermic were almost twice the odds in normothermic newborns at admission (OR 1.92 95% CI: 1.34; 2.76).

*Arch Dis Child* 2014;**99**:A498

# Thermoregulation



# Delivery room CPAP

COIN, SUPPORT and VON

# Delivery room CPAP

- Diminishing atelectasis
- Improving Functional residual capacity
- Correcting ventilation-perfusion abnormalities
- Decreasing pulmonary edema
- Reducing intrapulmonary shunting

# CPAP

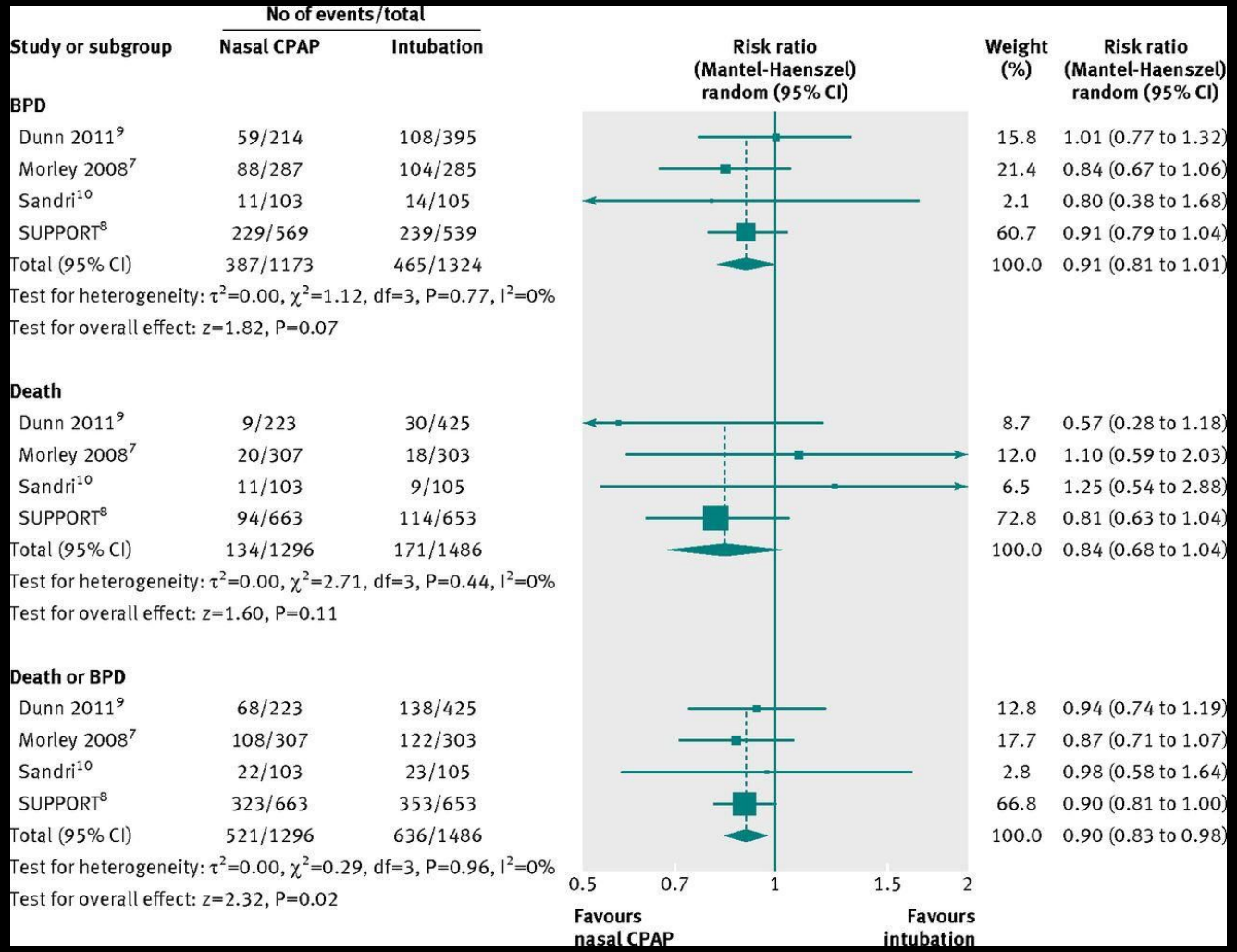
3 RCT enrolling 2358 preterm infants born at <30 weeks of gestation demonstrated that starting newborns on CPAP may be beneficial when compared with endotracheal intubation and PPV

Starting CPAP resulted in decreased rate of intubation in the delivery room, decreased duration of mechanical ventilation with potential benefit of reduction of death and/or bronchopulmonary dysplasia & no significant increase in air leak or severe IVH


* Morley CJ, Davis PG, Doyle LW, Brion LP, Hascoet JM, Carlin JB; COIN Trial Investigators. Nasal CPAP or intubation at birth for very preterm infants. N Engl J Med. 2008;358:700–708. doi: 10.1056/ NEJMoa072788.
* SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network, Finer NN, Carlo WA, Walsh MC, Rich W, Gantz MG, Laptook AR, Yoder BA, Faix RG, Das A, Poole WK, Donovan EF, Newman NS, Ambalavanan N, Frantz ID 3rd, Buchter S, Sanchez PJ, Kennedy KA, Laroia N, Poindexter BB, Cotten CM, Van Meurs KP, Duara S, Narendran V, Sood BG, O'Shea TM, Bell EF, Bhandari V, Watterberg KL, Higgins RD. Early CPAP versus surfactant in extremely preterm infants. N Engl J Med. 2010;362:1970–1979.
* Dunn MS, Kaempf J, de Klerk A, de Klerk R, Reilly M, Howard D, Ferrelli K, O'Conor J, Soll RF; Vermont Oxford Network DRM Study Group. Randomized trial comparing 3 approaches to the initial respiratory management of preterm neonates. Pediatrics. 2011;128:e1069– e1076. doi: 10.1542/peds.2010-3848.

# Non-invasive versus invasive respiratory support in preterm infants at birth: systematic review and meta-analysis-

*Georg M Schmölzer, BMJ 2013*



*Georg M Schmölzer, BMJ 2013*

- Surfactant: All trials assessed surfactant, with a significant reduction in administered surfactant in the nasal CPAP group (relative risk 0.40, 0.23 to 0.70, risk difference −0.51, −0.79 to −0.23, with 98% heterogeneity).
- **Need for Mechanical Ventilation**: All trials assessed the need for any mechanical ventilation, with a significant reduction in the nasal CPAP group (relative risk 0.56, 0.32 to 0.97, risk difference −0.34, −0.68 to −0.01, with 99% heterogeneity).

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

# Respiratory Support in Preterm Infants at Birth

COMMITTEE ON FETUS AND NEWBORN

*Pediatrics* 2014;133;171; originally published online December 30, 2013;
DOI: 10.1542/peds.2013-3442

# Conclusion

1. Early use of CPAP with subsequent selective surfactant administration in extremely preterm infants results in ***lower rates of BPD/death*** when compared with treatment with prophylactic or early surfactant therapy (Level of Evidence: 1)

2. Preterm infants treated with early CPAP alone are ***not at increased risk of adverse outcomes*** if treatment with surfactant is delayed or not given (Level of Evidence: 1)

# Conclusion

3. Early initiation of CPAP may lead to a ***reduction in duration of ventilation and postnatal steroid therapy*** (Level of Evidence: 1)

4. Infants with RDS are a ***heterogeneous population***, it is necessary to ***individualize*** patient care. Care for these infants is provided in a variety of care settings, and thus the capabilities of the health care team need to be considered.

# Recommendation

- CPAP immediately after birth with later selective surfactant administration is an alternative to routine intubation and surfactant administration in preterm infants (Level of Evidence: 1, Strong Recommendation)
- If it is likely that respiratory support with a ventilator will be needed, early administration of surfactant followed by rapid extubation is preferable to prolonged ventilation (Level of Evidence: 1, Strong Recommendation)

# Sustained Lung Inflation at Birth for Preterm Infants: A Randomized Clinical Trial

Gianluca Lista, Pediatrics 2015

- Randomly assigned infants born at 25 weeks 0 days to 28 weeks 6 days of gestation to receive
  - SLI (25 cm $H_2O$ 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.

# SLI trial

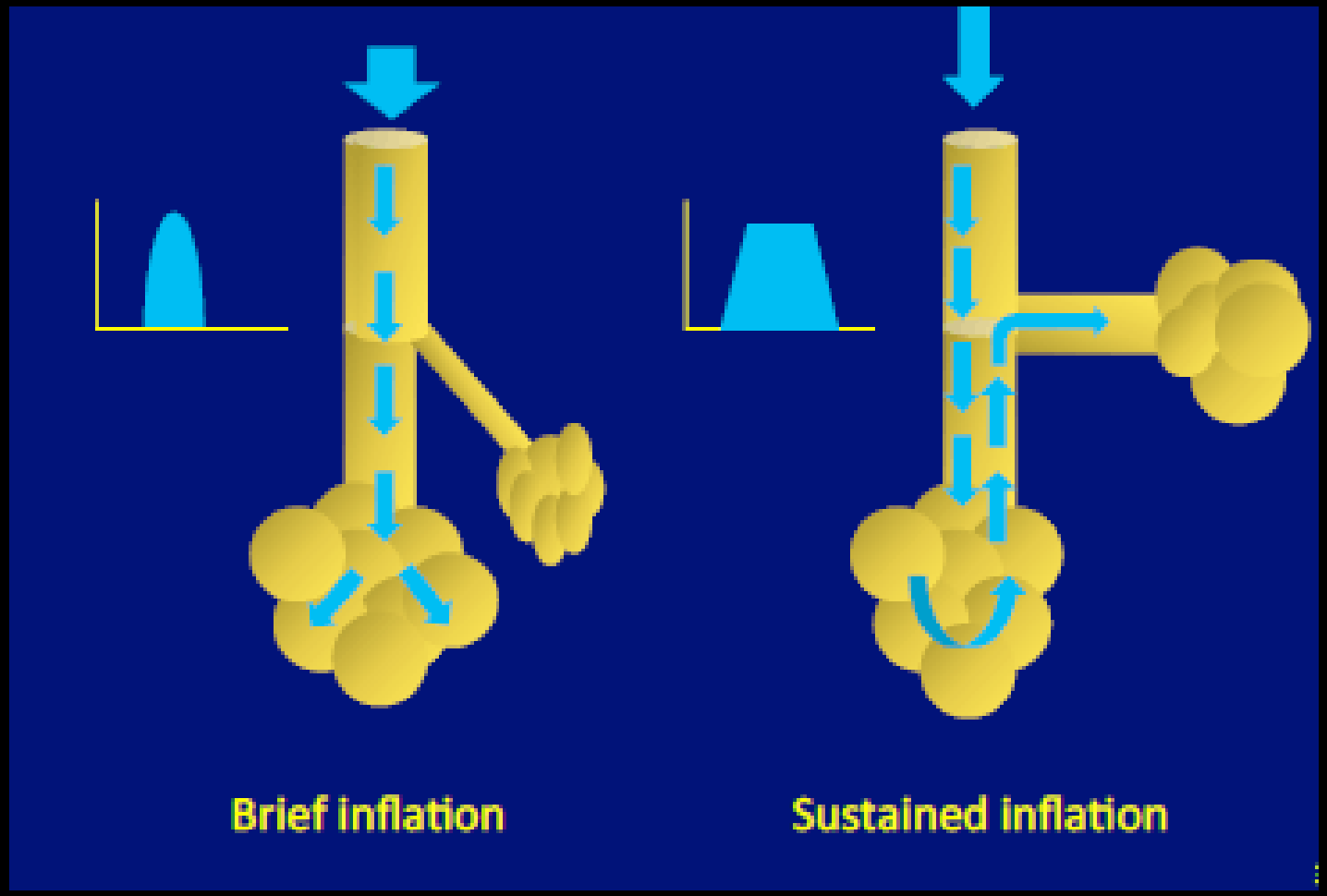
- Total of 148 infants were enrolled in the SLI group and 143 in the control group.
- Significantly fewer infants were ventilated in the first 72 hours of life in the SLI group (79 of 148 [53%]) than in the control group (93 of 143 [65%]); unadjusted odds ratio: 0.62 [95% confidence interval: 0.38–0.99]; *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).

# Sustained Lung Inflation at Birth for Preterm Infants: A Randomized Clinical Trial

Gianluca Lista, Pediatrics 2015

- Sustained inflation at birth in preterm infants with respiratory distress
  - Decrease the need for Intubation in DR
  - Decrease Need for surfactant
  - Shortened the TIME of MV/Respiratory support
  - Reduce the incidence in BPD

# Sustained Lung inflation

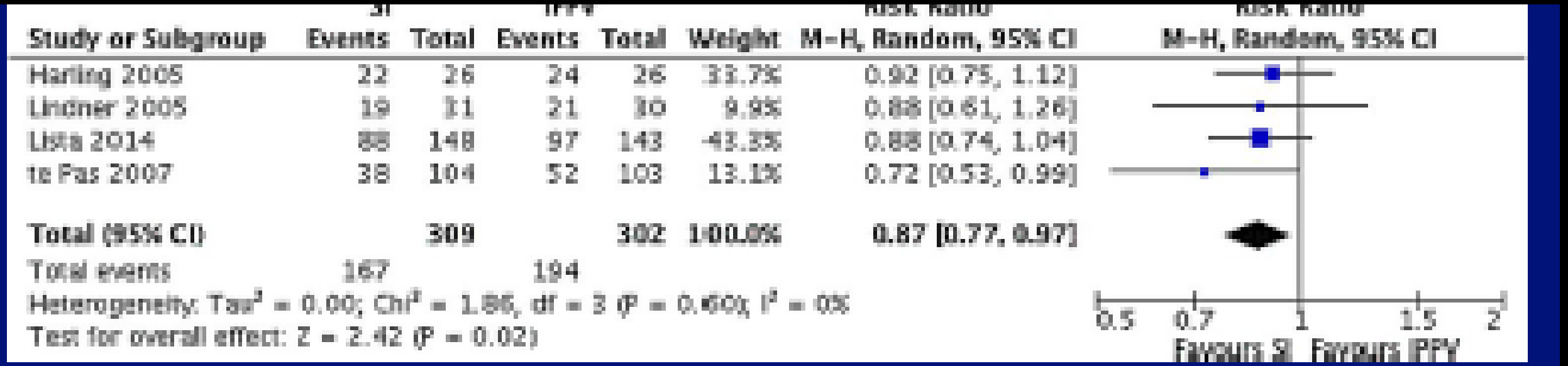


# SLI at birth v/s MV- meta analysis

Arch Dis Child Fetal Neonatal Ed. 2015 July

- 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.

# Outcome of MV at 72 hours



# Mask versus Nasal tube for stabilization of preterm neonates

Kamlin C Pediatrics 2013

- One hundred forty-four infants were enrolled.
- Infants <31 weeks' gestation were randomized just before delivery to SNP (endotracheal tube shortened to 5 cm) or FM
- The rate of intubation in the DR was the same in both groups (11/72 [15%] vs 11/72 [15%], *P* = 1.000].
- Infants assigned to SNP had lower $SpO_2$ at 5 minutes and received a higher maximum concentration of oxygen in the DR.

# HHFNC

CPAP

HFNC

# How does HHFNC work?

- Positive distending pressure
  - not ‘set’ or monitored like CPAP devices
- Oxygen delivery
  - higher concentrations than ‘low flow’
- Heating and humidification
  - better ‘conditioning’ of gases
- Supports inspiration with high flow of gas
  - ?reduces ‘work of breathing’
- ‘Washout’: Reduces the ‘dead space’ re-breathing
  - better/more efficient ventilation

# Why are HFNC used

- ‘easy to use’
- ‘safe’
- ‘decreases WOB’
- ‘nurses love it’
- ‘babies more settled’
- ‘less “CPAP belly”’
- ‘less nasal trauma’
- ‘no pneumothoraces

# Safety and Efficacy of High-Flow Nasal Cannula Therapy in Preterm Infants: A Meta-analysis.

Kotecha SJ, Pediatrics. 2015;136(3):542.

- 1112 preterm infants, participating in 9 clinical trials.
- High-flow therapy was similar in efficacy to other modes of NIV in preterm infants when used as primary support (odds ratio of failure of therapy, 1.02 [95% confidence interval: 0.55 to 1.88]), as well as after extubation (1.09 [0.58 to 2.02]).
- There were no significant differences in odds of death (0.48 [0.18 to 1.24]) between the groups.
- Preterm infants supported on high-flow had significantly lower odds of nasal trauma (0.13 [0.02 to 0.69]).
-

# High flow nasal cannula for respiratory support in preterm infants

Wilkinson D, Cochrane Database Syst Rev. 2016;2:CD006405

When used as primary respiratory support after birth compared to CPAP (4 studies, 439 infants)

- there were no differences in the primary outcomes of death (typical risk ratio (RR) 0.36, 95% CI 0.01 to 8.73, 4 studies, 439 infants)
- chronic lung disease (CLD) (typical RR 2.07, 95% CI 0.64 to 6.64; 4 studies, 439 infants).

HFNC use resulted in longer duration of respiratory support, but there were no differences in other secondary outcomes.

# Conclusion

- HFNC has similar rates of efficacy to other forms of non-invasive respiratory support in preterm infants for preventing treatment failure, death and CLD.
- Most evidence is available for the use of HFNC as post-extubation support.
- Following extubation, HFNC is associated with less nasal trauma, and may be associated with reduced pneumothorax compared with nasal CPAP.
- Further adequately powered randomised controlled trials should be undertaken in preterm infants comparing HFNC with other forms of primary non-invasive support after birth and for weaning from non-invasive support.
- Further evidence is also required for evaluating the safety and efficacy of HFNC in extremely preterm and mildly preterm subgroups, and for comparing different HFNC devices.

# Nasal High-Flow Therapy for Primary Respiratory Support in Preterm Infants.

. N Engl J Med. 2016 Sep 22;375(12):1142-51

- 564 preterm infants (gestational age, ≥28 weeks 0 days) with early respiratory distress who had not received surfactant replacement to treatment with either nasal high-flow therapy or nasal CPAP.
- The primary outcome was treatment failure within 72 hours after randomization.
- Trial recruitment stopped early at the recommendation of the independent data and safety monitoring committee because of a significant difference in the primary outcome between treatment groups.
- Treatment failure occurred in 71 of 278 infants (25.5%) in the high-flow group and in 38 of 286 infants (13.3%) in the CPAP group (risk difference, 12.3 percentage points; 95% confidence interval [CI], 5.8 to 18.7; P<0.001).
- The rate of intubation within 72 hours did not differ significantly between the high-flow and CPAP groups (15.5% and 11.5%, respectively; risk difference, 3.9 percentage points; 95% CI, -1.7 to 9.6; P=0.17), nor did the rate of adverse events.
- Conclusions When used as primary support for preterm infants with respiratory distress, high-flow therapy resulted in a significantly higher rate of treatment failure than did CPAP

# Caffeine

Clinics in Perinatology 2016

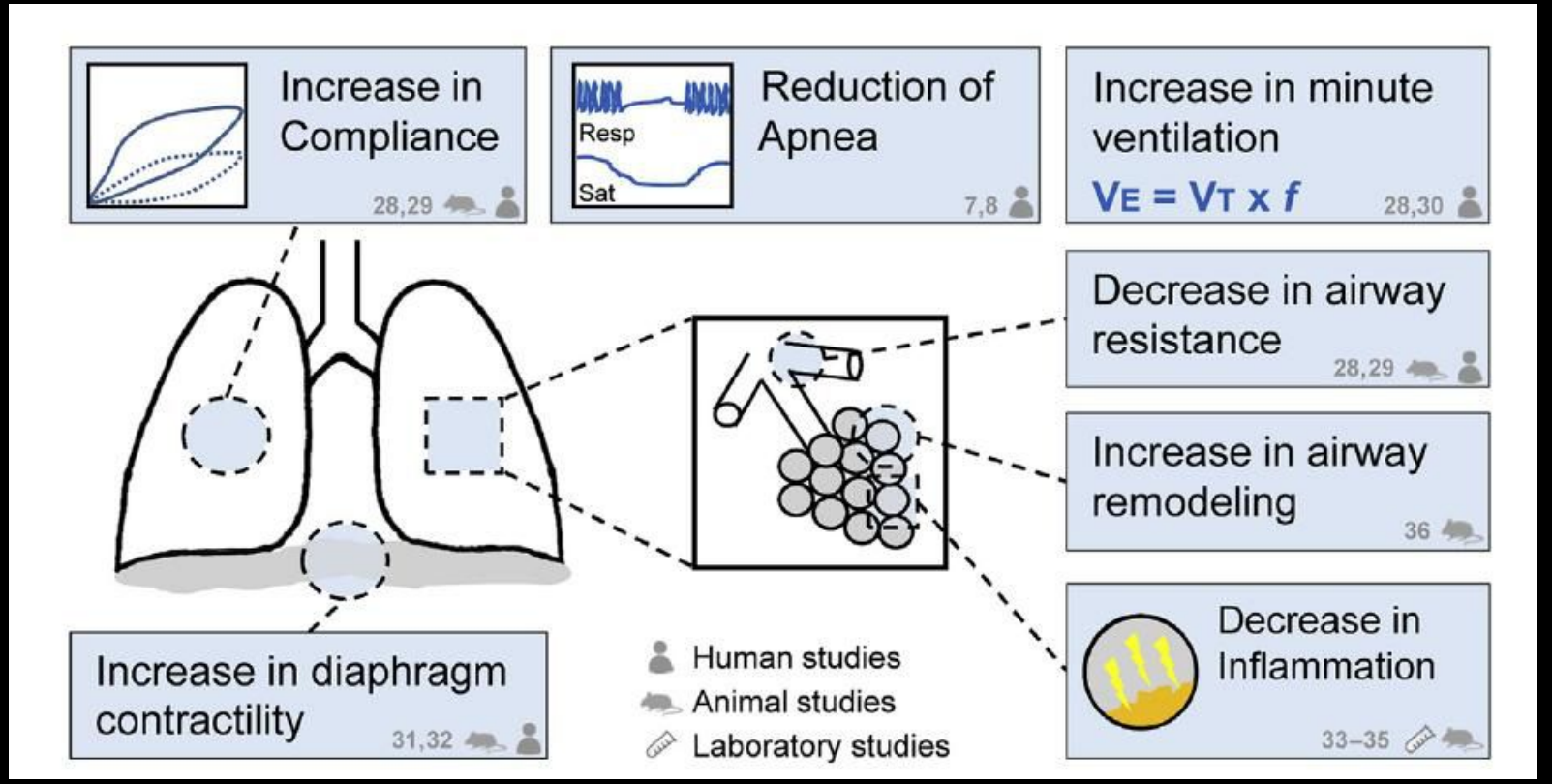
## Known respiratory benefits of caffeine in infants weighing less than 1250 g at birth

- Decreases apnea episodes in preterm infants
- Decreases risk of bronchopulmonary dysplasia
- Decreases duration of positive airway pressure support
- Decreases treatment of a patent ductus arteriosus
- Increases successful extubation within 1 week of initiation of treatment

## Potential additional respiratory benefits of early initiation of caffeine in VLBW infants

- May further decrease risk of bronchopulmonary dysplasia
- May further decrease duration of invasive respiratory support
- May further decrease duration of noninvasive respiratory support
- May further decrease treatment of a patent ductus arteriosus

# Physiologic effects of Caffeine on Pulmonary function



# A pilot randomized controlled trial of early versus routine caffeine in extremely premature infants

. Katheria AC, et al. Am J Perinatol2015;32(9):879–86

- In this study, infants less than 29 weeks' gestation were randomized to early prophylactic use of caffeine before 2 hours of age or caffeine initiation at 12 hours of age.
- The study reported fewer infants in the early caffeine treatment arm required intubation by 12 hours of age, compared with those receiving caffeine at 12 hours of age, although this was not a statistically significant difference (27% vs 70%, P5.08).
- By contrast, there was no reduction in days of mechanical ventilation between infants receiving caffeine before 2 hours versus 12 hours of age (mean 6 days vs 3 days; P 5 .40).
- Additional studies are necessary to determine if prophylactic caffeine can successfully prevent the need for intubation among preterm infants initially supported with noninvasive respiratory modalities

# Avoiding Endotracheal Ventilation to prevent BPD- a meta analysis Pediatrics 2013

**TABLE 1** Characteristics of Included Studies

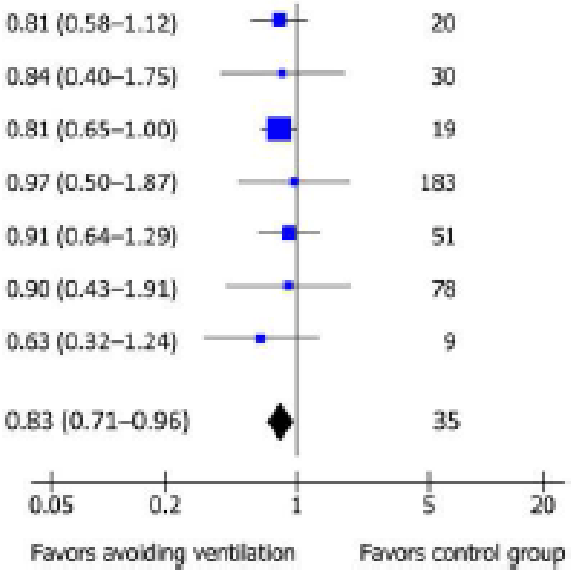
| Author | Study Name | Year | Intervention | Any eMV Except INSURE, % | GA | Randomization | *n* | Recruitment |
|---|---|---|---|---|---|---|---|---|
| Morley et al[13] | COIN | 2008 | nCPAP versus mechanical ventilation | 59 vs 100 | $25\ ^{0}/_{7}$–$28^{6}/_{7}$ | At 5 min of age | 610 | 1999–2006 |
| Rojas et al[37] [a] | CNRN | 2009 | nCPAP versus INSURE | 43 vs 39 | $27\ ^{0}/_{7}$–$29^{6}/_{7}$ | 15–60 min of age | 146[b] | 2004–2006 |
| Finer et al[14] | SUPPORT | 2010 | nCPAP versus mechanical ventilation | 83 vs 100 | $24\ ^{0}/_{7}$–$27^{6}/_{7}$ | <1 h of age | 1316 | 2005–2009 |
| Sandri et al[16] | CURPAP [d] | 2010 | nCPAP versus INSURE | 31 vs 33[c] | $25\ ^{0}/_{7}$–$28^{6}/_{7}$ | <30 min of age | 208 | 2007–2008 |
| Dunn et al[15] | DRM | 2011 | 3 groups: nCPAP versus INSURE versus mechanical ventilation | 52 vs 59 vs 96 | $26\ ^{0}/_{7}$–$29^{6}/_{7}$ | Before delivery | 648 | 2003–2009 |
| Göpel et al[36] | AMV | 2011 | nCPAP ± surfactant during spontaneous breathing versus nCPAP ± mechanical ventilation | 33 vs 73 | $26\ ^{0}/_{7}$–$28^{6}/_{7}$ | <12 h of age | 220 | 2007–2009 |
| Kanmaz et al[19] [a] | Take Care | 2013 | nCPAP ± surfactant during spontaneous breathing versus nCPAP ± INSURE | 42 vs 52[a] | $\leq 29^{6}/_{7}$ | <2 h of age | 141[b] | 2010–2011 |

# Effect on BPD

## Avoiding Endotracheal Ventilation to Prevent Bronchopulmonary Dysplasia: A Meta-analysis

Fischer HS, Bührer C; Pediatrics 2013; 132:e1351-60

| Study or Subgroup | Avoid ventilation BPD/death | Avoid ventilation Total | Control group BPD/death | Control group Total | Weight, % | Odds Ratio Random effects model (95% CI) | NNT |
|---|---|---|---|---|---|---|---|
| COIN (2008) | 108 | 307 | 122 | 303 | 19.8 | 0.81 (0.58–1.12) | 20 |
| CNRN (2009) | 53 | 74 | 54 | 72 | 4.0 | 0.84 (0.40–1.75) | 30 |
| SUPPORT (2010) | 323 | 663 | 353 | 653 | 45.5 | 0.81 (0.65–1.00) | 19 |
| CURPAP (2010) | 22 | 103 | 23 | 105 | 4.9 | 0.97 (0.50–1.87) | 183 |
| DRM (2011) | 68 | 223 | 138 | 425 | 17.4 | 0.91 (0.64–1.29) | 51 |
| AMV (2011) | 15 | 108 | 17 | 112 | 3.8 | 0.90 (0.43–1.91) | 78 |
| Take Care (2013) | 25 | 74 | 30 | 67 | 4.6 | 0.63 (0.32–1.24) | 9 |
| Total | 614 | 1552 | 737 | 1737 | 100 | 0.83 (0.71–0.96) | 35 |




Test for overall effect: $z = 2.55$ ($P = .01$)

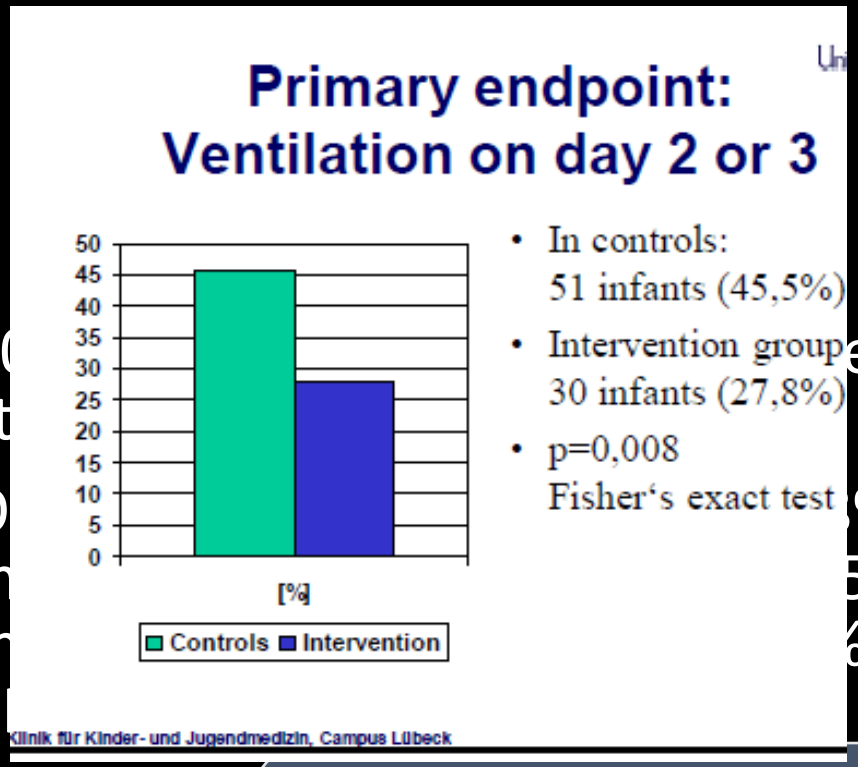
Heterogeneity: $Tau^2 = 0.00$; $\chi^2 = 1.27$; $df = 6$ ($P = .97$); $I^2 = 0\%$

# Avoidance of mechanical ventilation by surfactant treatment of spontaneously breathing preterm infants (AMV): an open-label, randomised, controlled trial.

**Lancet 2011, Herting**

- 220 preterm infants with a gestational age between 26 and 28 weeks and a birthweight less than 1·5 kg were enrolled in 12 German neonatal intensive care units.
- Infants were stabilised with continuous positive airway pressure and received rescue intubation if necessary.
- In the intervention group, infants received surfactant treatment during spontaneous breathing via a thin catheter inserted into the trachea by laryngoscopy if they needed a fraction of inspired oxygen more than 0·30.
- The primary endpoint was need for any mechanical ventilation,

- 108 infants were assigned to the intervention group and 112 infants to the standard treatment group.
- On day 2 or 3 after birth, 30 (28%) infants in the intervention group were mechanically ventilated versus 51 (46%) in the standard treatment group (number needed to treat 6, 95% CI 3-20, absolute risk reduction 0·18, 95% CI 0·30-0·05, p=0·008).
- 36 (33%) infants in the intervention group were mechanically ventilated during their stay in the hospital compared with 82 (73%) in the standard treatment group (number needed to treat: 3, 95% CI 2-4, p<0·0001).
- No differences between groups for mortality (seven deaths in the intervention group vs five in the standard treatment group) and serious adverse events (21 vs 28).




- 1( e intervention group and 112 infants to the st
- O %) infants in the intervention group were m 51 (46%) in the standard treatment group (r % CI 3-20, absolute risk reduction 0·18, 95% C
- 36 (33%) i ted during the ard treatment
- No differe intervention group vs five in the standard treatment group) and serious adverse events (21 vs 28).

CONCLUSION

The application of surfactant via a thin catheter to spontaneously breathing preterm infants receiving continuous positive airway pressure reduces the need for mechanical ventilation.

# NINSAPP Trial

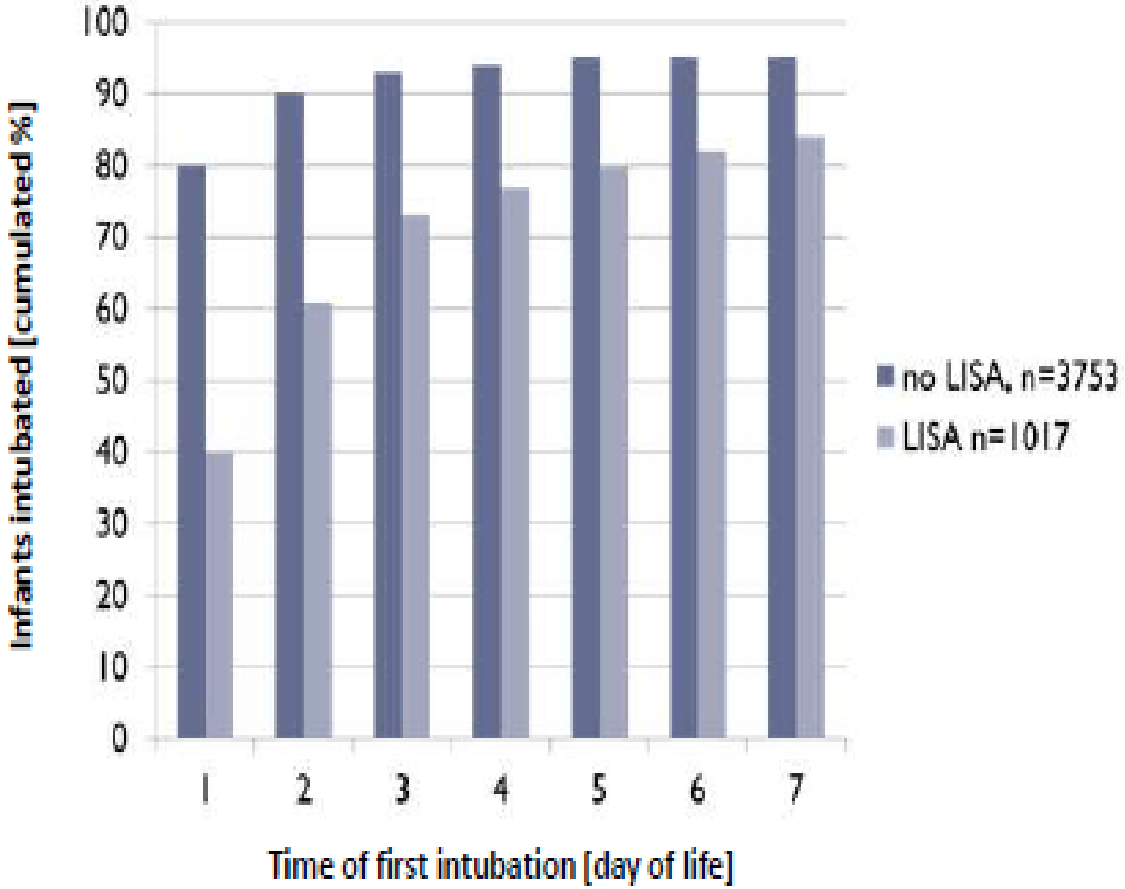
Table 1. Baseline Clinical Characteristics

| Characteristic | Group | |
|---|---|---|
| | Intervention (n = 107) | Control (n = 104) |
| Gestational age, mean (SD), wk | 25.3 (1.1) | 25.2 (0.91) |
| Birth weight, mean (SD), g | 711 (195) | 674 (165) |
| Apgar score, median (IQR) | | |
| 5 min | 8 (7-9) | 8 (7-8) |
| 10 min | 8 (8-9) | 8 (8-9) |
| Cord arterial pH, mean (SD) | 7.34 (0.09) | 7.35 (0.08) |
| Male sex, No. (%) | 63 (58.9) | 52 (50.0) |
| Multiple births, No. (%) | 32 (30.0) | 35 (33.7) |
| Antenatal corticosteroids, No. (%) | | |
| Full course | 88 (82.2) | 79 (76.0) |
| Incomplete course | 17 (15.9) | 23 (22.1) |
| Cesarean section, No. (%) | 94 (87.8) | 96 (92.3) |

Abbreviation: IQR, interquartile range.

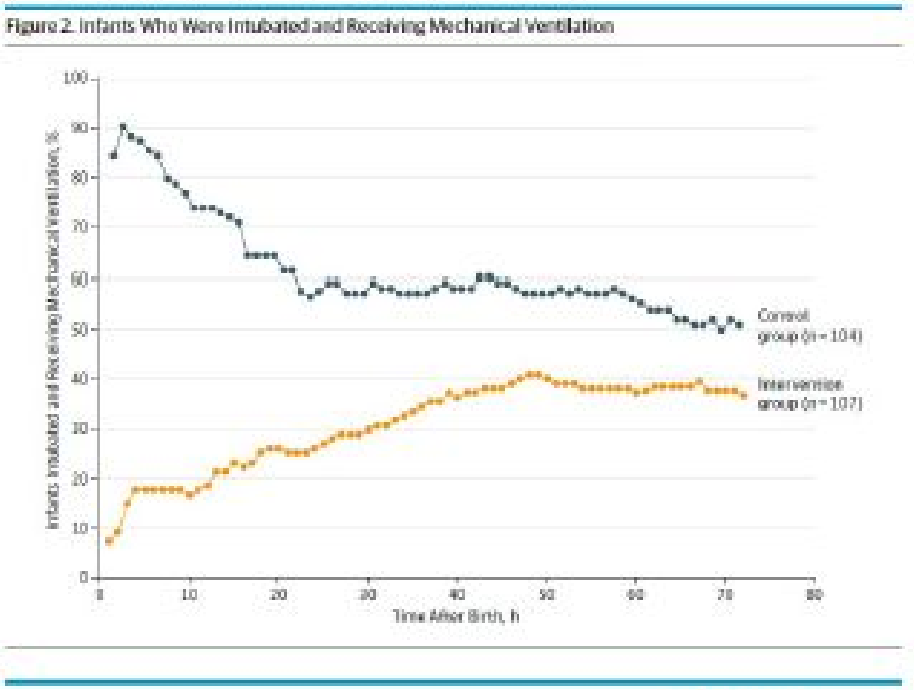
JAMA Pediatr 2015;169:723-730

# LISA- Timing of First Intubation




Göpel, Kribs, Herting LISA for the prevention of BPD, in „BPD" by Bhandari (ed.) Springer 2016

## NINSAPP Trial




Percentage of intervention and control infants who were intubated and received mechanical ventilation in hours 1 to 96 after birth.

JAMA Pediatr 2015;169:723-730

# Summary

- Strategies which potentially reduce need for Ventilaion
  - Antenatal Steroids
  - Prevention of Hypothermia
  - Delivery room CPAP
  - HHFNC
  - Early Caffeine
  - Surfactant-LISA
  - NIV
  - Prevention of INFECTION