Non-invasive ventilation: An Update

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Non-invasive ventilation

Techniques

- CPAP (mask or prong)
- NIPPV
- High flow subnasal cannulae

Indications

- Primary support
- Post-extubation care

In the beginning

- George Gregory (1971): response to poor outcomes of ventilating babies <1500g
  - ETT CPAP

The New England
Journal of Medicine

Volume 284 JUNE 17, 1971 Number 24

TREATMENT OF THE IDIOPATHIC RESPIRATORY-DISTRESS SYNDROME WITH CONTINUOUS POSITIVE AIRWAY PRESSURE*

GEORGE A. GREGORY, M.D., JOSEPH A. KITTERMAN, M.D., RODERIC H. PHIBBS, M.D., WILLIAM H. TOOLEY, M.D., AND WILLIAM K. HAMILTON, M.D.

Abstract We applied a continuous positive airway pressure to 20 infants (birth weight 930 to 3800 g) severely ill with the idiopathic respiratory-distress syndrome. They breathed spontaneously. Pressure, up to 12 mm of mercury, was delivered through an endotracheal tube to 18 infants and via a pressure chamber around the infant's head to two. Arterial oxygen tension rose in all, permitting us to lower the inspired oxygen an average of 37.5 per cent within 12 hours. Minute ventilation decreased with increased continuous positive airway pressure, but this had little effect on arterial carbon dioxide tension, pH, arterial blood pressure and lung compliance. Sixteen infants survived, including seven of 10 weighing less than 1500 g at birth.

Gregory: ETT CPAP

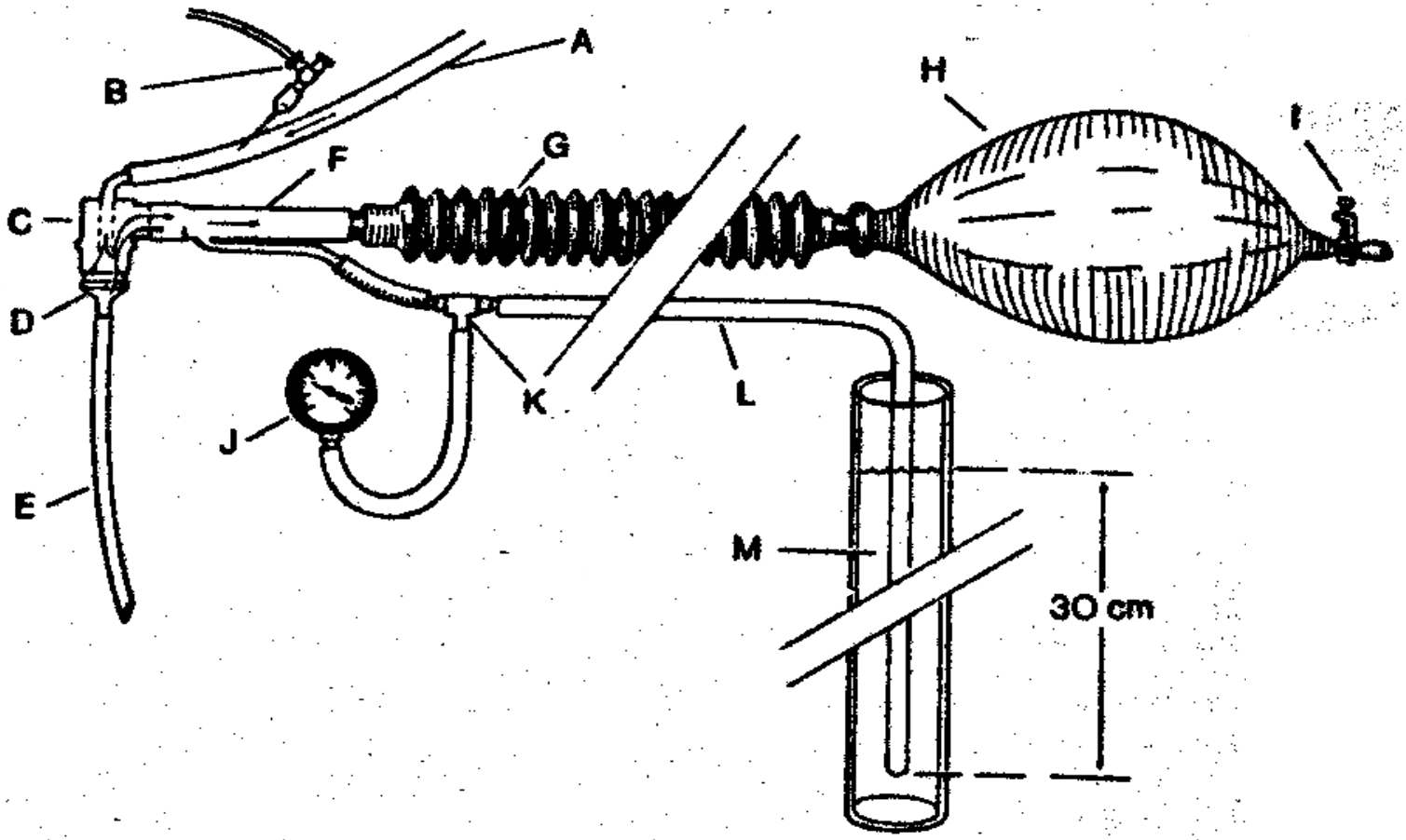
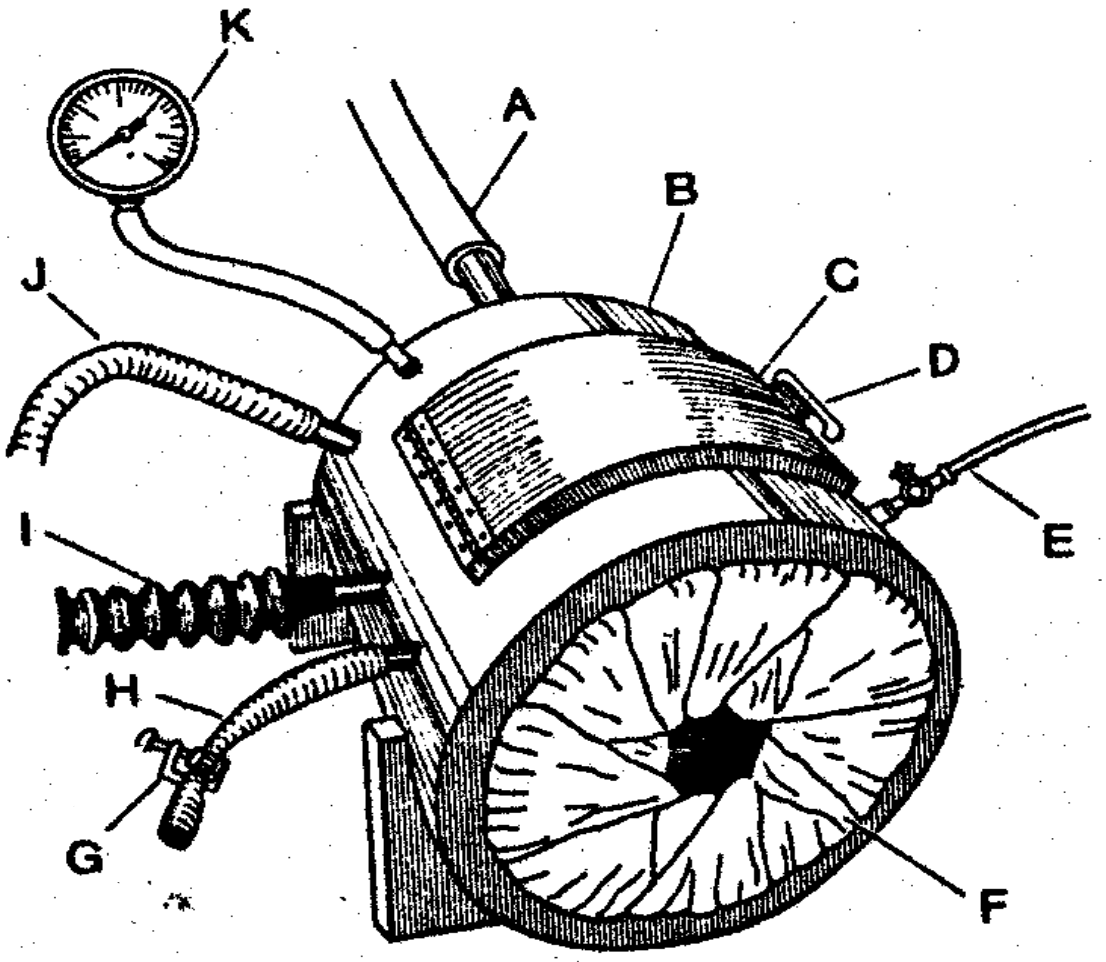


Figure 1. System for Applying Continuous Positive Airway Pressure through an Endotracheal Tube.

“Gregory Box”



And then...

- Better ventilators
- More expertise
- Surfactant

“Intubation and IPPV should be used routinely on all extremely low birth weight neonates and should be started as soon as the infant is on the resuscitation trolley”

Roberton: “The baby under 1000g” 1989

The problems of endotracheal intubation

- Acute and chronic lung damage - volutrauma
- Local airway damage – subglottic stenosis
- Infections – pulmonary and systemic

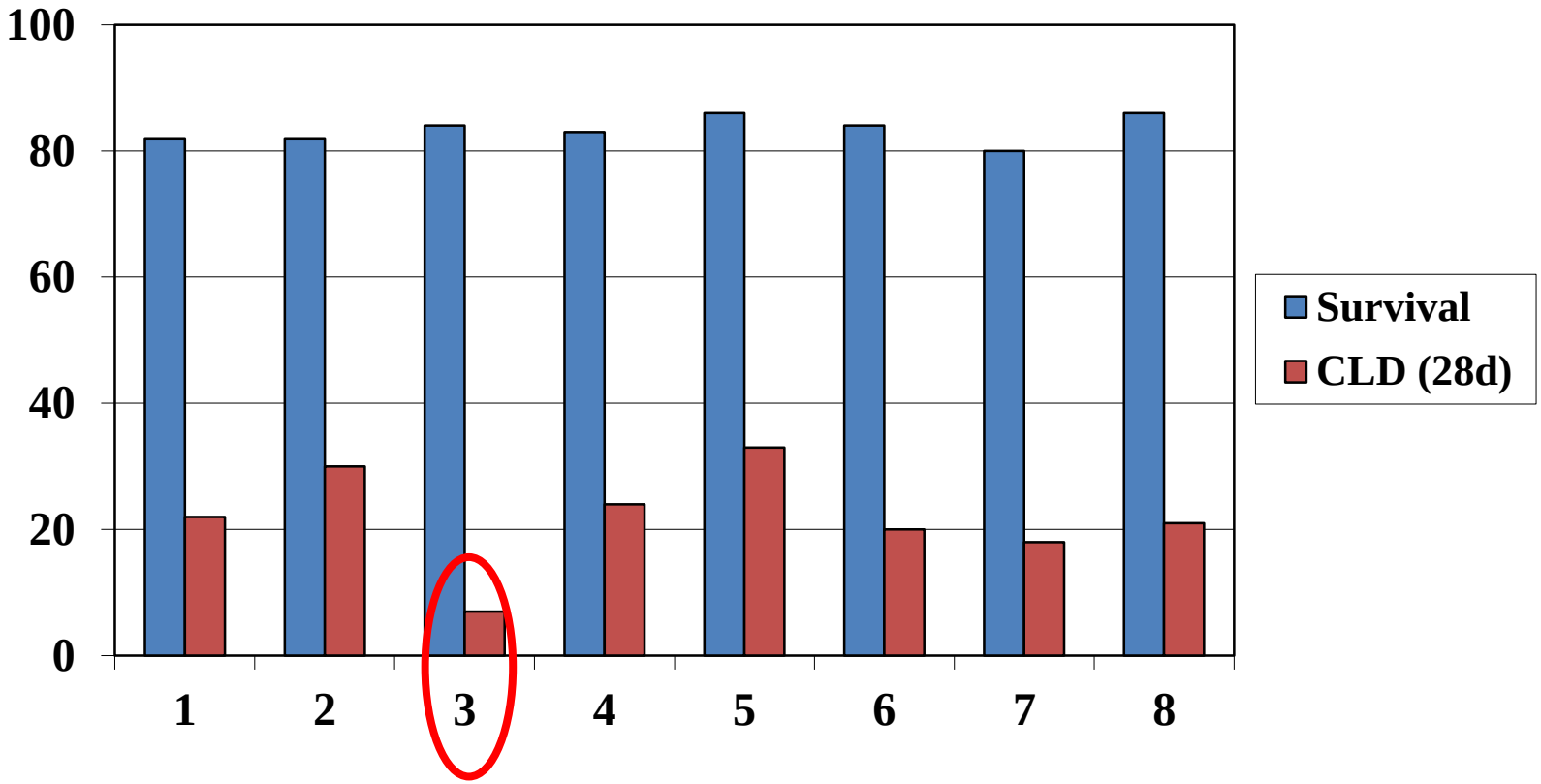
How might CPAP help?

- Increase pharyngeal cross sectional area – decreases upper airway obstruction
- Reduce obstructive apnoea
- Increase Functional Residual Capacity (FRC)

How might CPAP help?

- Reduces resistance and “work of breathing”
- Improves ventilation-perfusion mismatch – and therefore oxygenation
- Conserves surfactant

“Is chronic lung disease preventable” Avery 1987



Spontaneous effort in extremely preterm babies (2010)

	Breathed	Cried
Total (n=61)	80%	69%
<26 weeks	67%	56%
≥26 weeks	86%	74%
<750g	60%	44%
≥750g	94%	86%

THE JOURNAL OF PEDIATRICS • www.jpeds.com

CLINICAL AND LABORATORY OBSERVATIONS

Crying and Breathing by Extremely Preterm Infants Immediately After Birth

Colm P. F. O'Donnell, MB, MRCPI, MRCPCH, FRACP, PhD, C. Omar F. Kamlin, MB, MRCPCH, Peter G. Davis, MD, FRACP, and Colin J. Morley, MD, FRACP, FRCHCP

CPAP in the Delivery Room

COIN, SUPPORT and VON…

Schmoelzer et al, BMJ 2013

Study or subgroup	No of events/total: Nasal CPAP	No of events/total: Intubation	Risk ratio (Mantel-Haenszel) random (95% CI)	Weight (%)	Risk ratio (Mantel-Haenszel) random (95% CI)
Death or BPD					
Dunn 2011[9]	68/223	138/425		12.6	0.94 (0.74 to 1.19)
Morley 2008[7]	108/307	118/303		17.0	0.90 (0.73 to 1.11)
Sandri[10]	33/103	32/105		4.5	1.05 (0.70 to 1.57)
SUPPORT[8]	323/663	353/653		65.9	0.90 (0.81 to 1.00)
Total (95% CI)	532/1296	641/1486			

Test for heterogeneity: $\tau^2=0.00$, $\chi^2=0.60$, df=3, P=0.90, $I^2=0\%$

Test for overall effect: z=2.10, P=0.04

n=2782

RR 0.91 (0.84, 0.99)

RD −0.04 (−0.07 to −0.00)

NNT of 25

$I^2=0\%$

My response to the current evidence

- For preterm babies breathing well at birth NCPAP is an appropriate first line treatment
- I "rescue" babies earlier than previously (COIN): 8 cm H_20 pressure/40% oxygen
  - Is this right?
- CPAP is not the "magic bullet" for BPD
  - the search continues
- CPAP *and* Surfactant *without* ETT?

How can we minimise CPAP failure?

- Minimally-invasive surfactant therapy
  - Concept: Deliver surfactant to a spontaneously ventilating infant who can then continue on nasal CPAP
  - Methods:
    - Nasopharyngeal instillation (Kattwinkel 2004)
    - Laryngeal mask (Trevisanuto 2005)
    - Aerosolisation (Finer 2010)
    - Tracheal catheterisation
      - Flexible feeding tube vs Semi-rigid vascular catheter

Surfactant via tracheal catheterisation

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

Wolfgang Göpel, Angela Kribs*, Andreas Ziegler, Reinhard Laux, Thomas Hoehn, Christian Wieg, Jens Siegel, Stefan Avenarius, Axel von der Wense, Matthias Vochem, Peter Groneck, Ursula Weller, Jens Möller, Christoph Härtel, Sebastian Haller, Bernhard Roth, Egbert Herting, on behalf of the German Neonatal Network*

Lancet 2011; 378: 1627–34

	Intervention group (n=108)	Standard treatment group (n=112)	Absolute risk reduction (95% CI)	Number needed to treat (95% CI)	p value*
All infants (%)	30 (28%)	51 (46%)	−0·18 (−0·30 to −0·05)	6 (3 to 20)	0·008

The primary outcome was any mechanical ventilation between 25 h and 72 h of age.

Table 2: **Primary outcome**

"More information is needed before [this technique] can be used in clinical practice…"

Cools *Lancet* 2011

Tracheal catheterisation

The Cologne method

- Verder 1992, Kribs 2007, Herting 2010, Göpel 2011
- Direct laryngoscopy
- 5-6 FG feeding tube inserted into trachea with Magill's forceps
- Surfactant instilled, catheter removed
- Problems – highly flexible tube, need for Magill's forceps

Tracheal catheterisation

The Hobart method

- Dargaville ADCF&N 2011
- Direct laryngoscopy
- 16G vascular catheter (Angiocath, Becton Dickinson) inserted into trachea
- Surfactant (100-200 mg/kg Curosurf) instilled

Surfactant instillation
The Hobart method

Surfactant instillation
The Hobart method

Less invasive surfactant administration versus intubation for surfactant delivery in preterm infants with respiratory distress syndrome: a systematic review and meta-analysis

Jose C Aldana-Aguirre,[1] Merlin Pinto,[1] Robin M Featherstone,[2] Manoj Kumar[1,3]

Aldana-Aguirre JC, *et al*. *Arch Dis Child Fetal Neonatal Ed* 2017;**102**:F17–F23. doi:10.1136/archdischild-2015-310299

Table 2 Risk of bias assessments

Study	Random sequence generation	Allocation concealment	Blinding of participant and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other biases
Göpel *et al*[27]	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Criteria for providing surfactant were not similar across the two groups
Kanmaz *et al*[28]	Unclear	Low risk	High risk	High risk	Low risk	Low risk	
Mirnia *et al*[29]	Unclear	Unclear	High risk	High risk	Low risk	Unclear*	
Bao *et al*[30]	Low risk	Unclear	High risk	High risk	Low risk	Unclear†	Trial stopped early
Mohammadizadeh *et al*[31]	Unclear	Low risk	High risk	High risk	Low risk	High‡	
Kribs *et al*[32]	Low risk	Low risk	High risk	High risk	Low risk	Low risk	

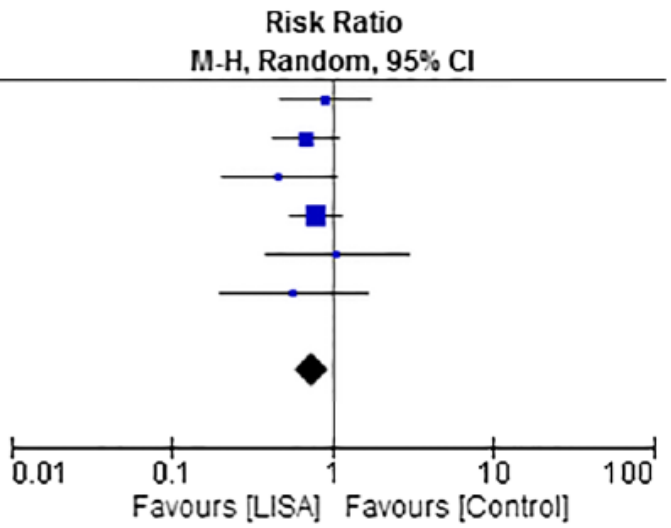
*Trial protocol not registered in a public trial registry.
†Trial protocol registered after completion of the study.
‡Outcomes of common neonatal morbidities, that is, NEC, ROP and PDA requiring treatment not provided.
NEC, necrotising enterocolitis; PDA, patent ductus arteriosus; ROP, retinopathy of prematurity.

Death or BPD

Study or Subgroup	LISA Events	LISA Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Gopel 2011	15	108	17	112	13.3%	0.92 [0.48, 1.74]
Kanmaz 2013	22	100	32	100	25.1%	0.69 [0.43, 1.10]
Mirnia 2013	7	66	16	70	8.1%	0.46 [0.20, 1.06]
Kribs 2015	35	107	43	104	43.3%	0.79 [0.55, 1.13]
Bao 2015	7	47	6	43	5.4%	1.07 [0.39, 2.93]
Mohammadizadeh 2015	4	19	7	19	4.9%	0.57 [0.20, 1.63]
Total (95% CI)		**447**		**448**	**100.0%**	**0.75 [0.59, 0.94]**
Total events	90		121			

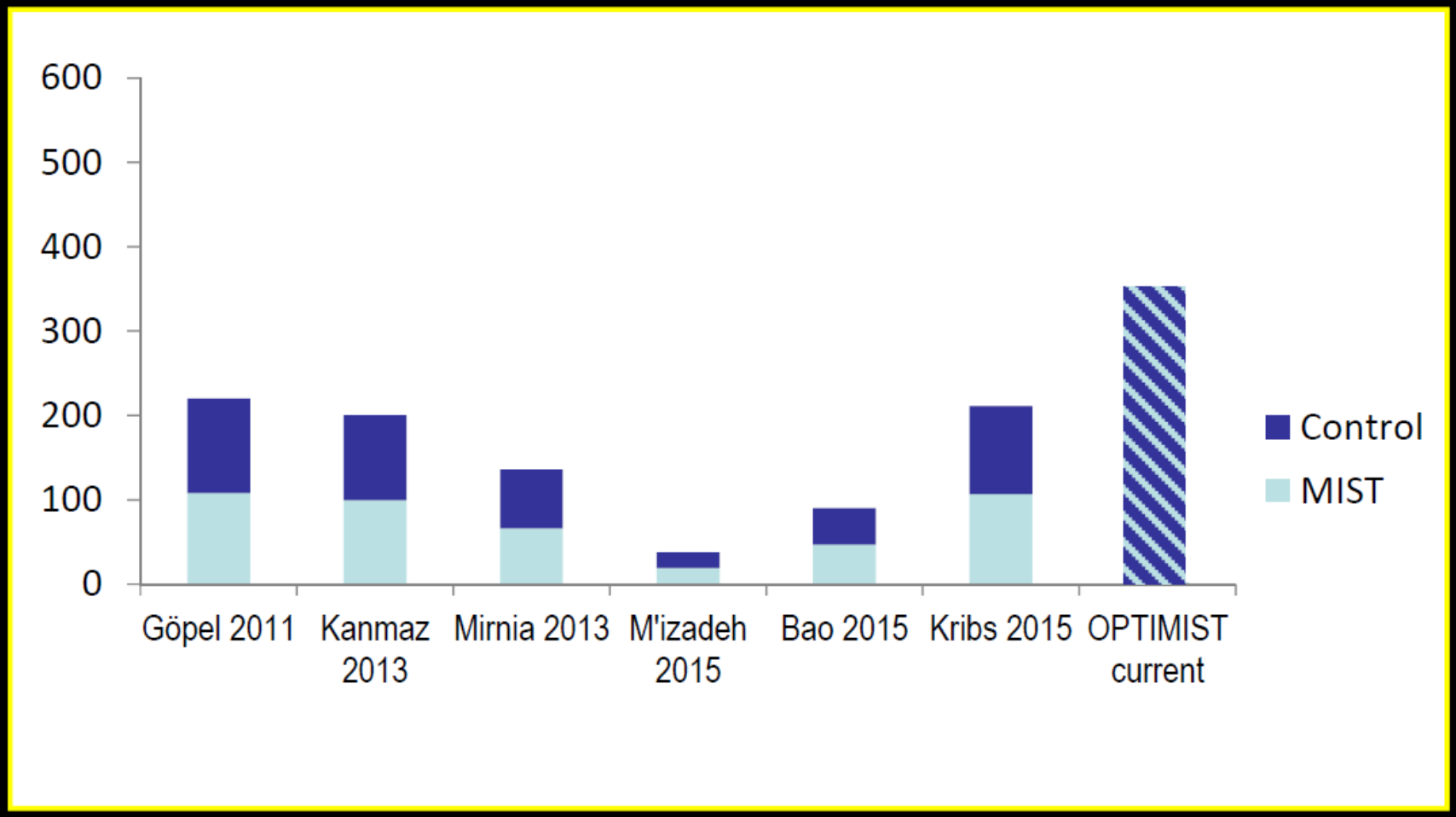
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.63$, $df = 5$ ($P = 0.76$); $I^2 = 0\%$

Test for overall effect: $Z = 2.46$ ($P = 0.01$)



Surfactant via brief tracheal catheterisation

Completed clinical trials



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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

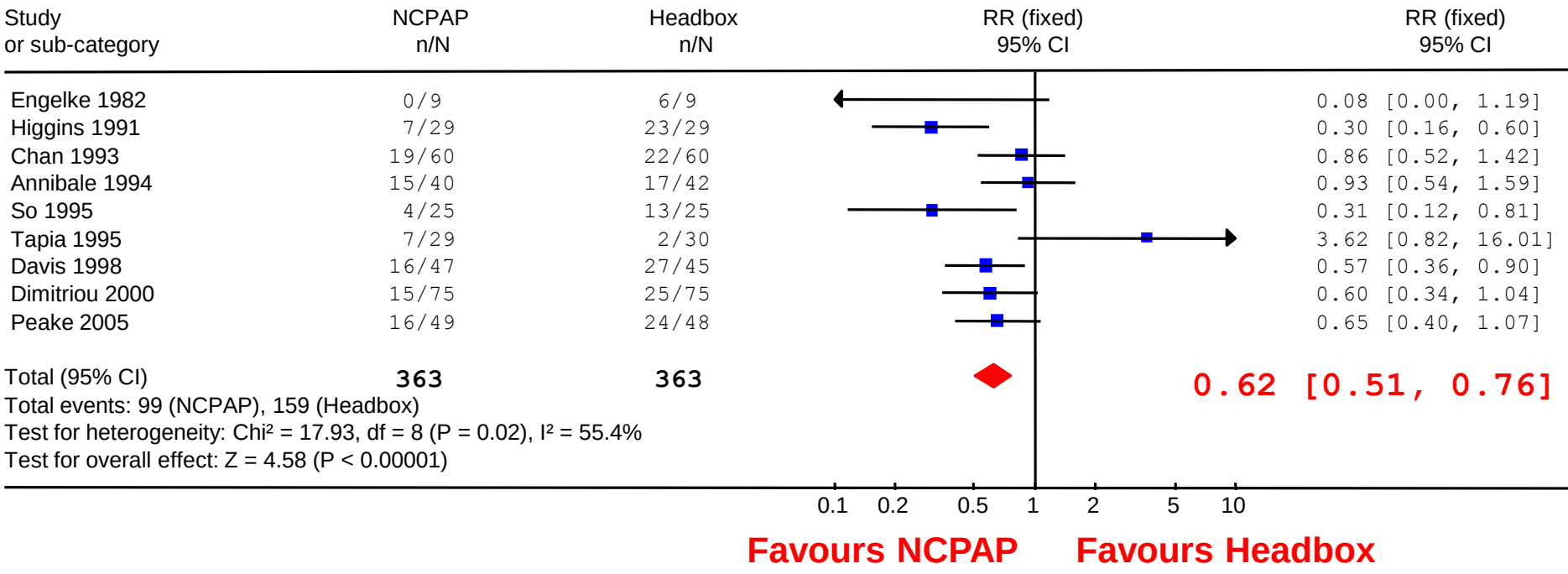
RECOMMENDATION

- 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)

Getting babies off an ETT

NCPAP immediately after extubation for preventing morbidity in preterm infants

Outcome: Failure



Treat 6 babies to prevent 1 failure

Can we do better than CPAP?

NIPPV

What is NIPPV?

- Combines CPAP with ventilator breaths
- Has a set PIP, rate and IT
- Many names
  - Cycling
  - CPAP+BUR= back up rate
  - NV = nasal ventilation
  - N-SIMV = nasal synchronised IMV
  - N-IMV = nasal IMV
  - N-BiPAP = nasal bipap
- Unifying name NIPPV

Why use NIPPV?
Isn't CPAP enough?

Optimal CPAP:

≥ 5 cmH_2O

short bi-nasal prongs

caffeine

≈30% LBW infants fail extubation to CPAP

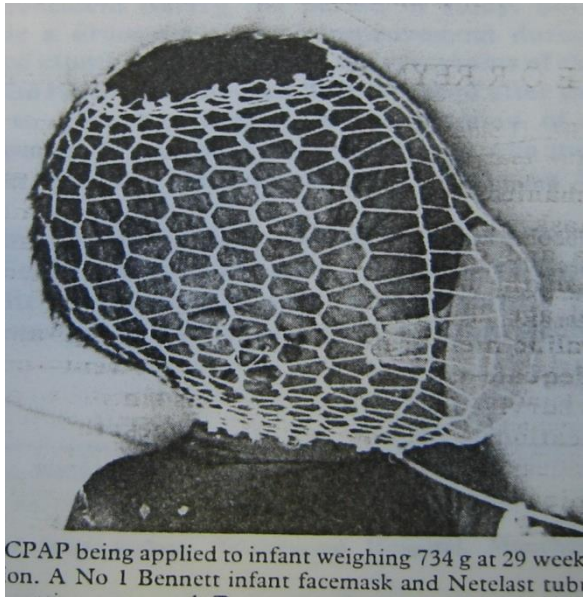
≈50% VLBW fail initial CPAP support

How does NIPPV work?

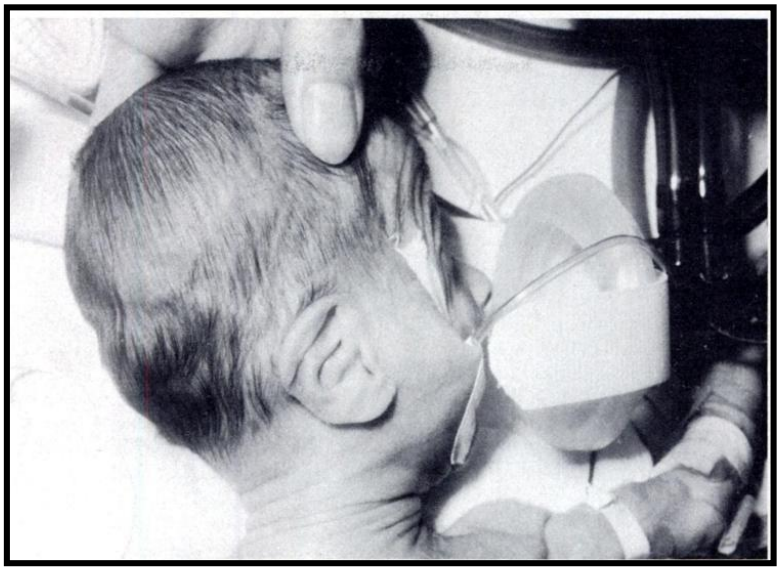
- We don’t know!
- Hypotheses include:
  - Induce Head’s paradoxical reflex
  - Increase MAP and thereby alveolar recruitment
  - Increase tidal volume
  - Pharyngeal dilatation
  - Improved respiratory drive

A short history of NIPPV

- Started in 1970s
- Abandoned because of head moulding and cerebellar haemorrhages



CPAP being applied to infant weighing 734 g at 29 week
on. A No 1 Bennett infant facemask and Netelast tub



A short history of NIPPV

- Popular in the 1980s: used in ~50% of Canadian units
- Became unpopular because of reports of GI perforations

A short history of NIPPV

- Re-emerged in the 1990s with synchronisation
- By 2007 (Owen, ADC)
  - Used by ~50% of units
  - 77% synchronised
  - 80% used as rescue for babies failing CPAP
  - 59% used routinely post-extubation
  - Large variability in pressures and rates used

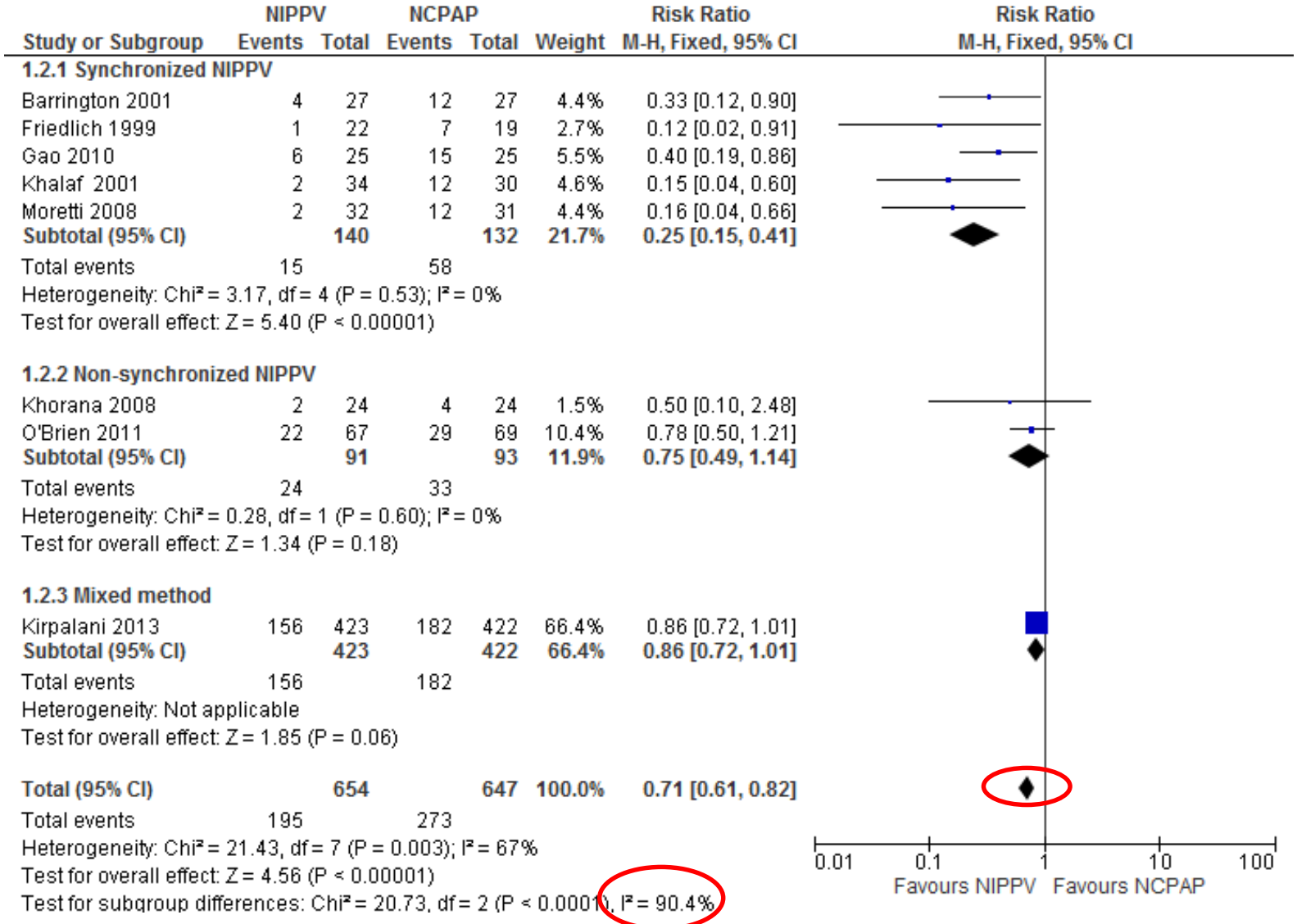
Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation (Review)

Lemyre B, Davis PG, De Paoli AG, Kirpalani H

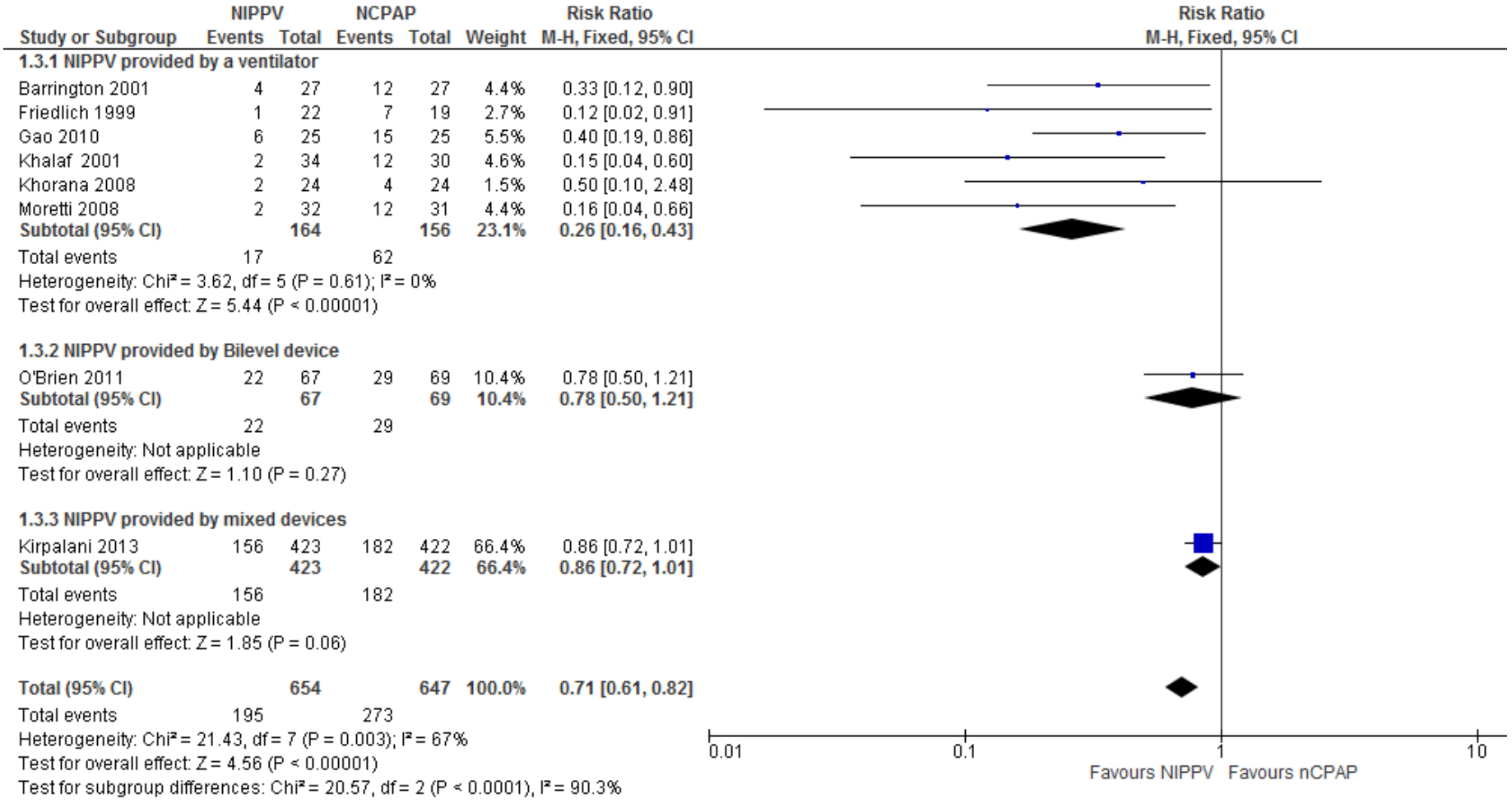
THE COCHRANE COLLABORATION®

Respiratory failure post-extubation

(by synchronisation)



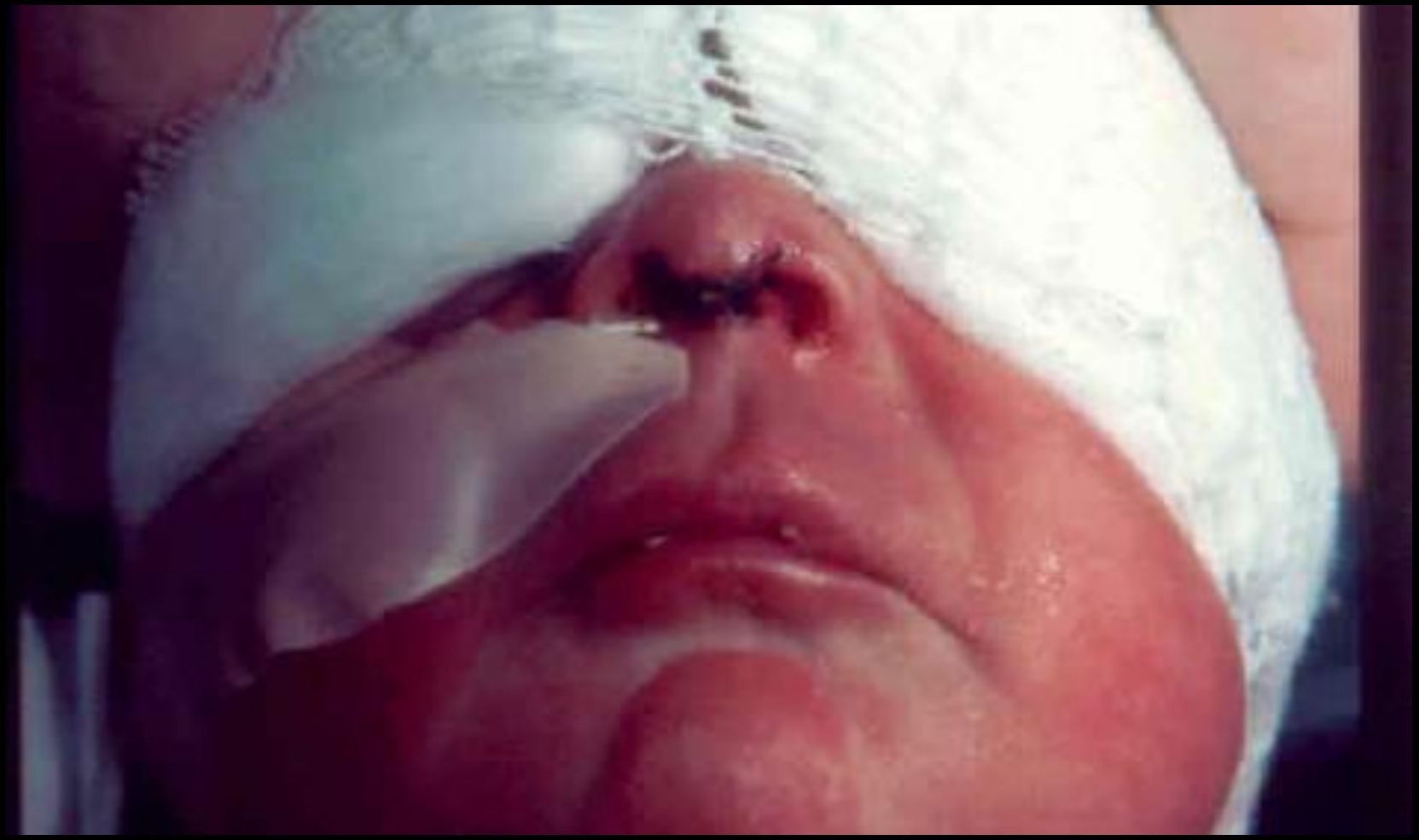
Respiratory failure post-extubation
(by device)



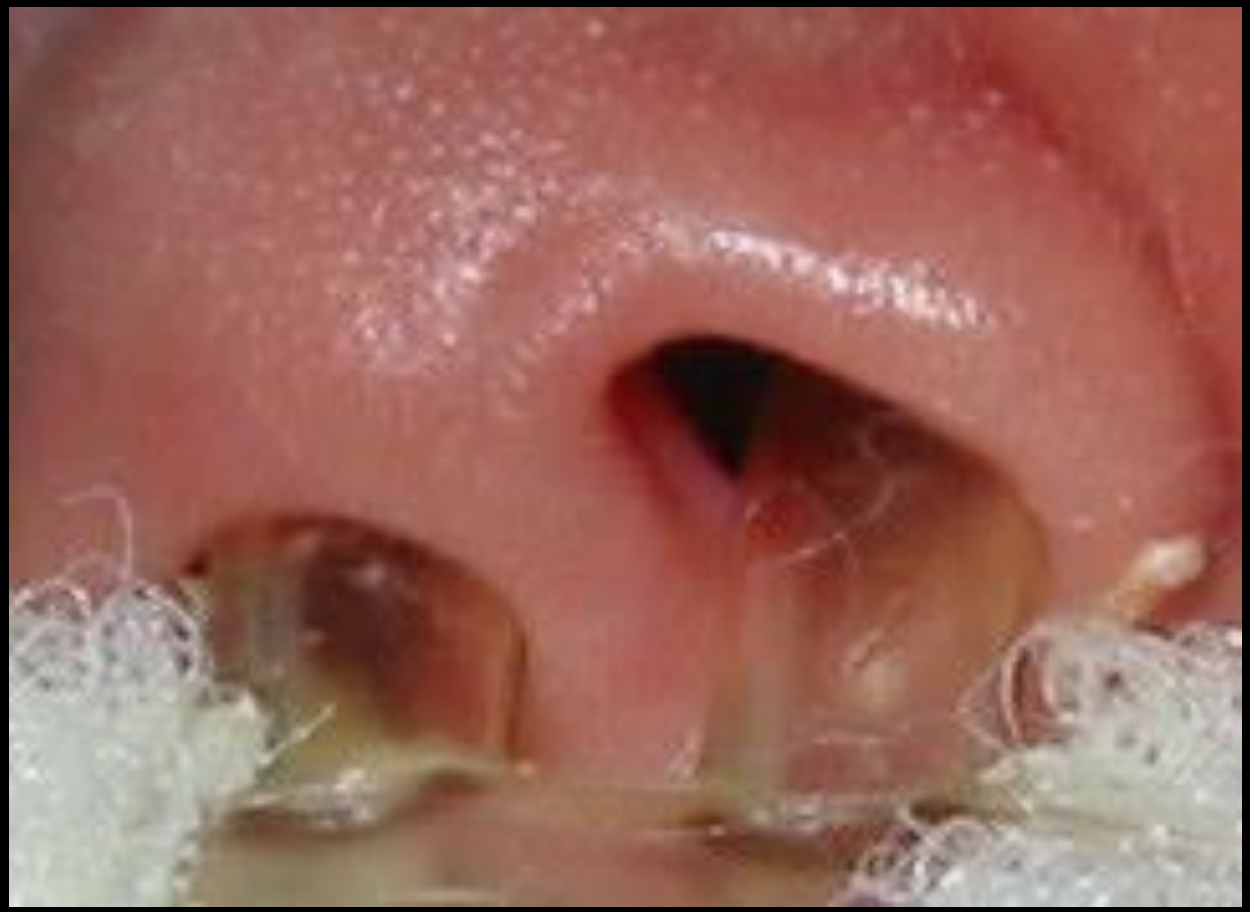
My response to the current evidence

- NIPPV may offer advantages over CPAP
- Synchronisation and the device used may be important (might NAVA be useful?)
- NIPPV does not appear to be associated with increased side effects
- The best combination of settings for NIPPV needs to be established in future trials

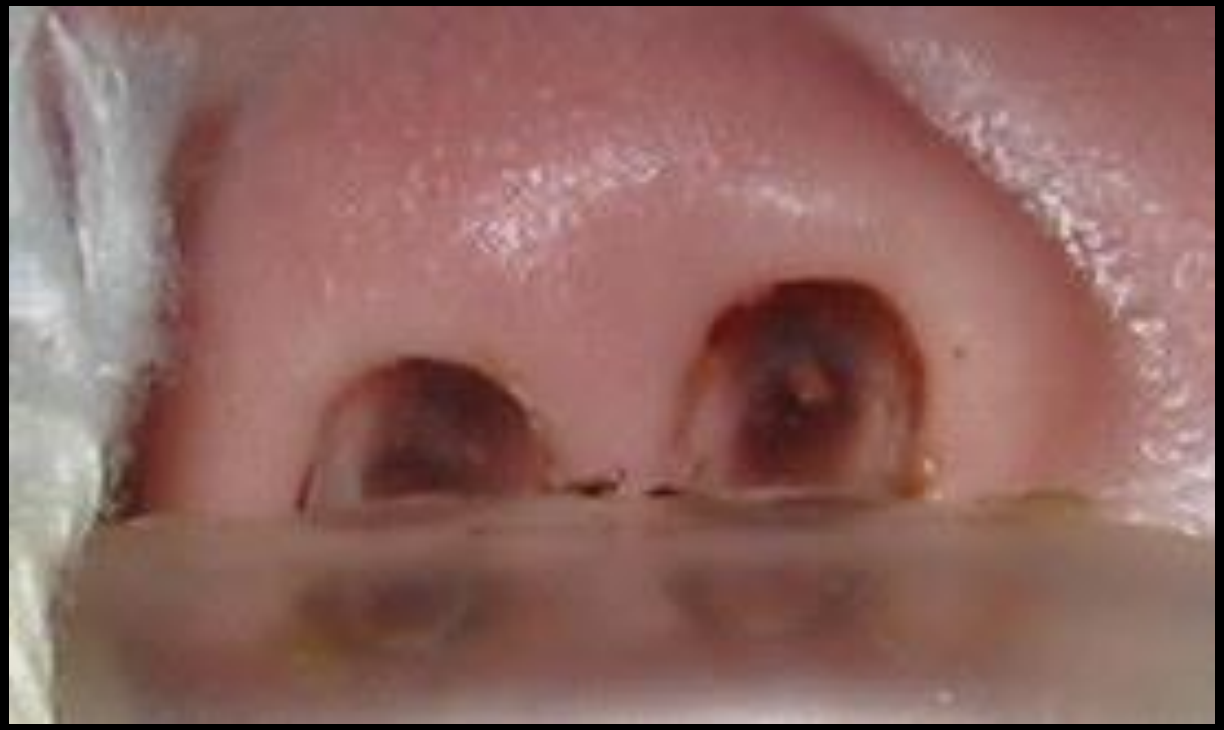
CPAP is difficult



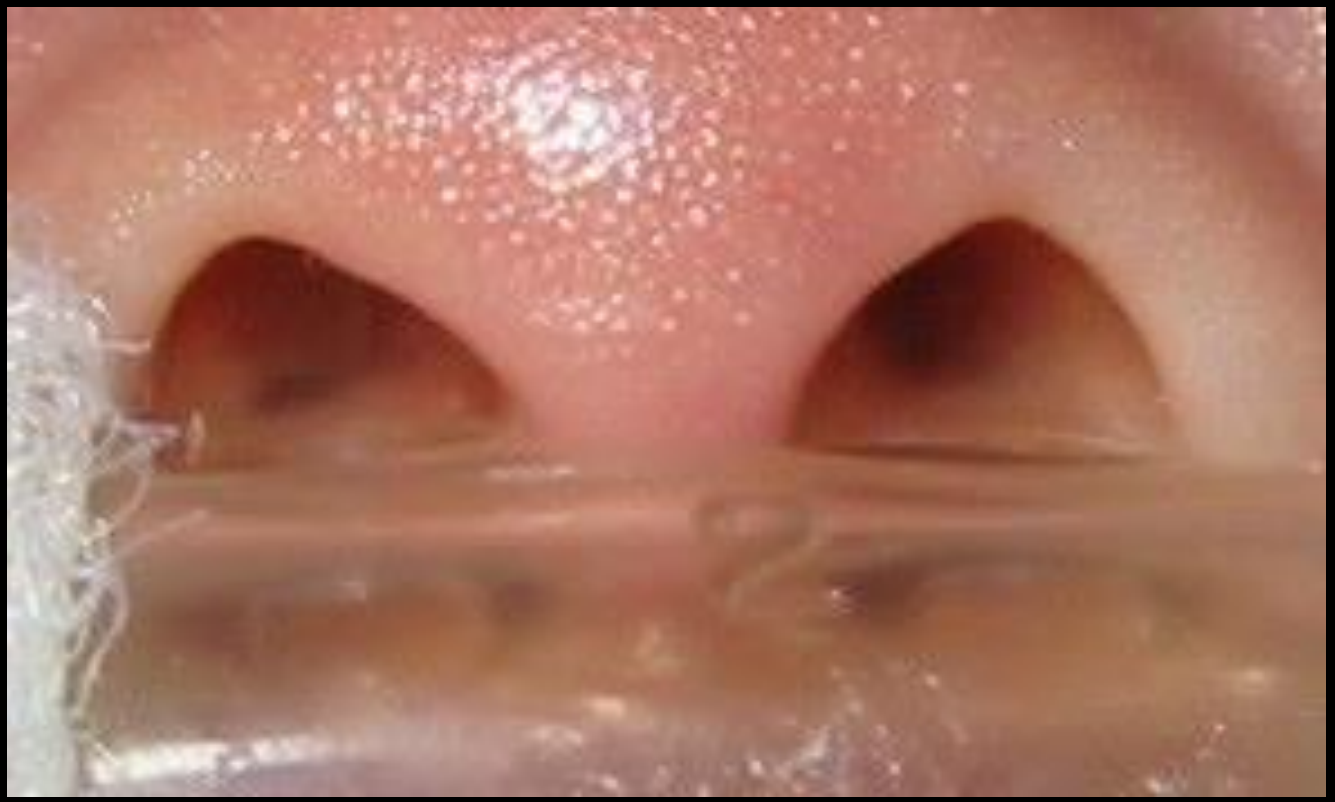
Prongs too small - leak



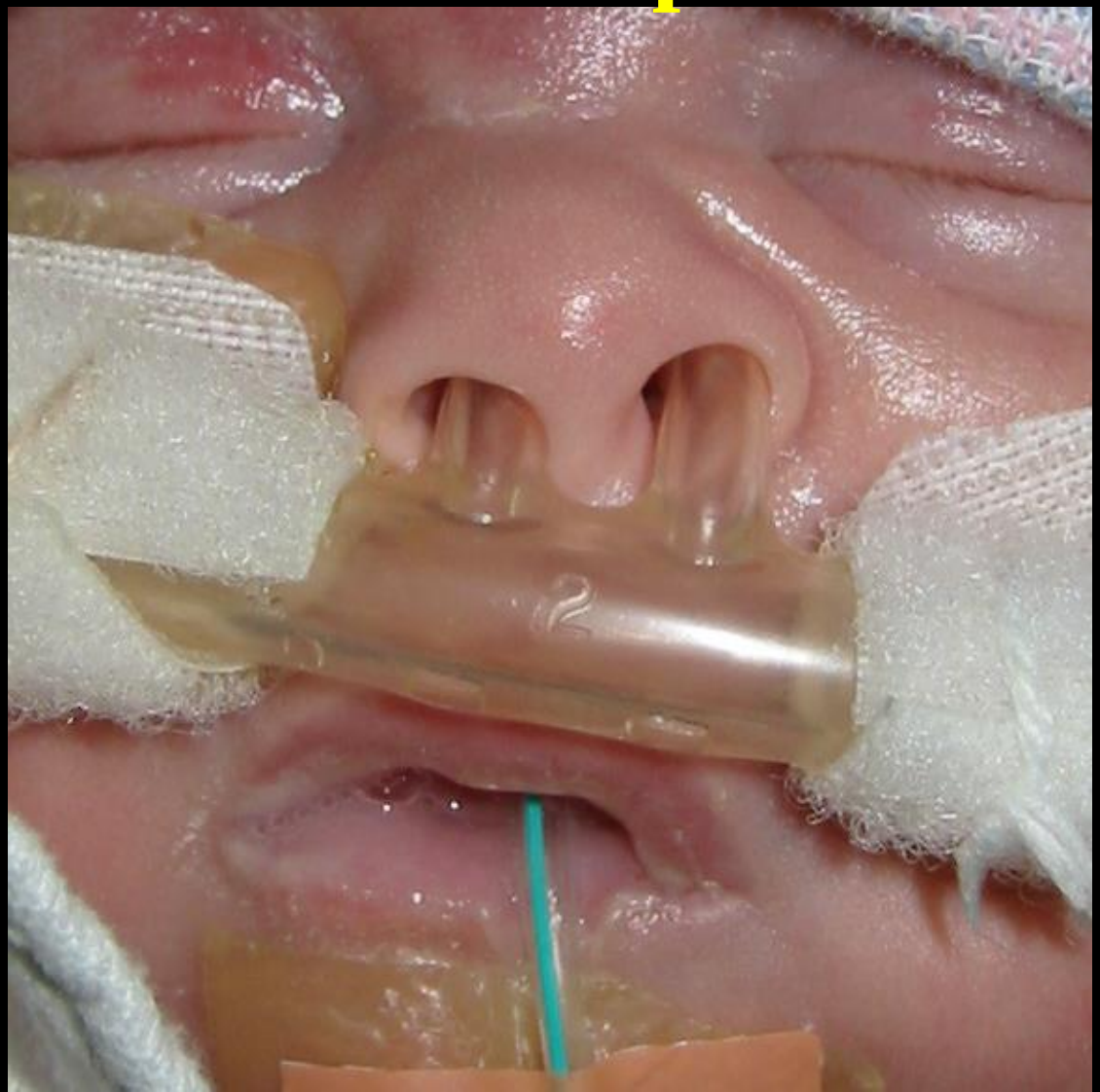
Prongs too large – blanching/trauma



Fundamental design flaw: Round prongs/triangular nostrils

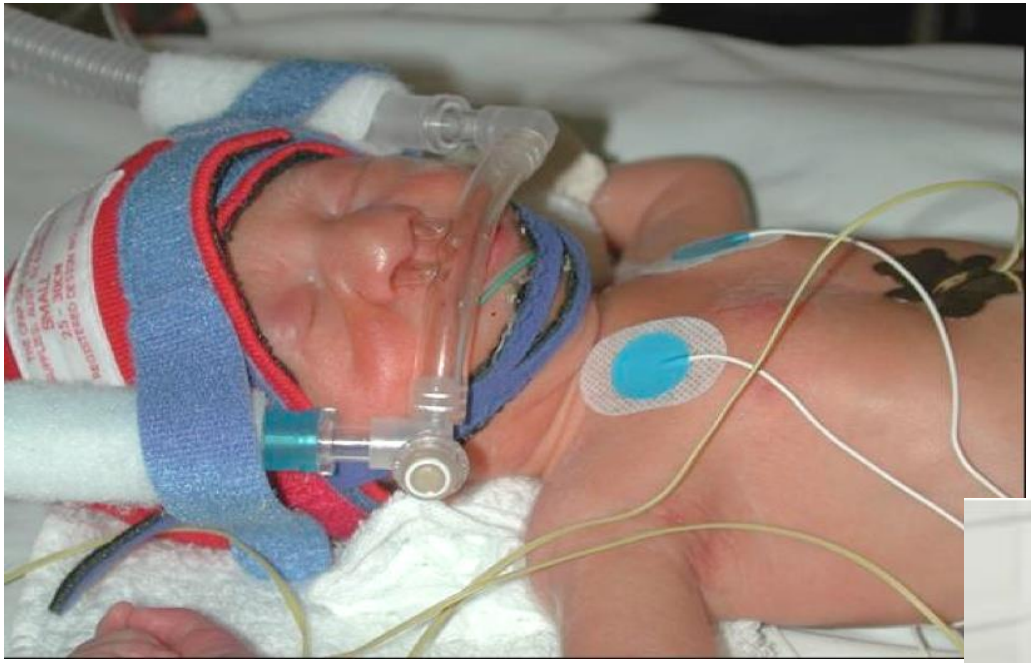


Poor position:
Trauma to nasal septum and leak



High Flow Subnasal Cannulae

A safe, effective alternative?



CPAP

HFNC

nHF: Mechanisms of action

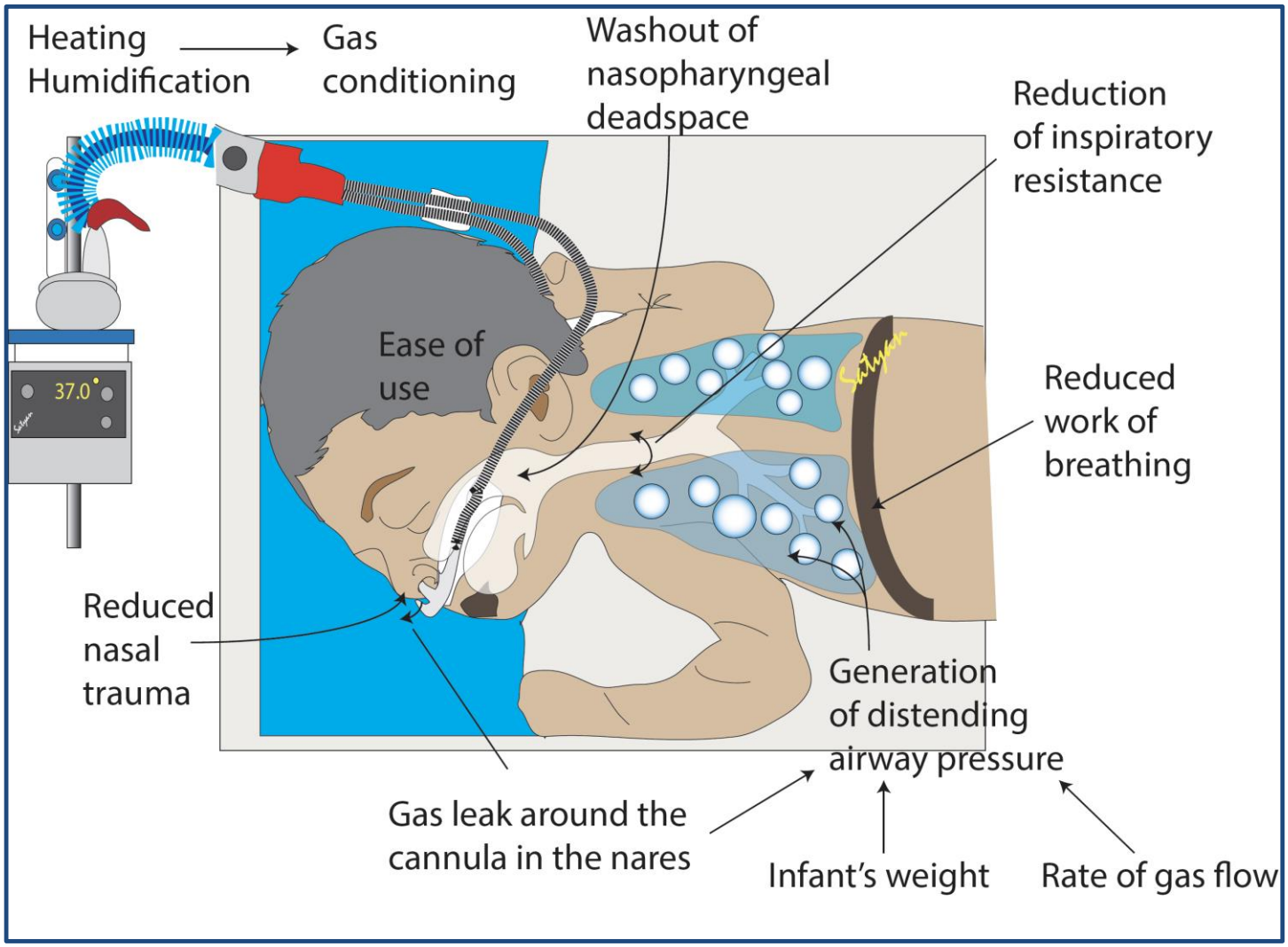


Figure courtesy Dr Satyan Lakshminrusimha, University of Buffalo

Distending pressure

- Concern about unpredictable distending pressures in preterm infants

- Pressures generated by HFNC ≤ those commonly set with nasal CPAP

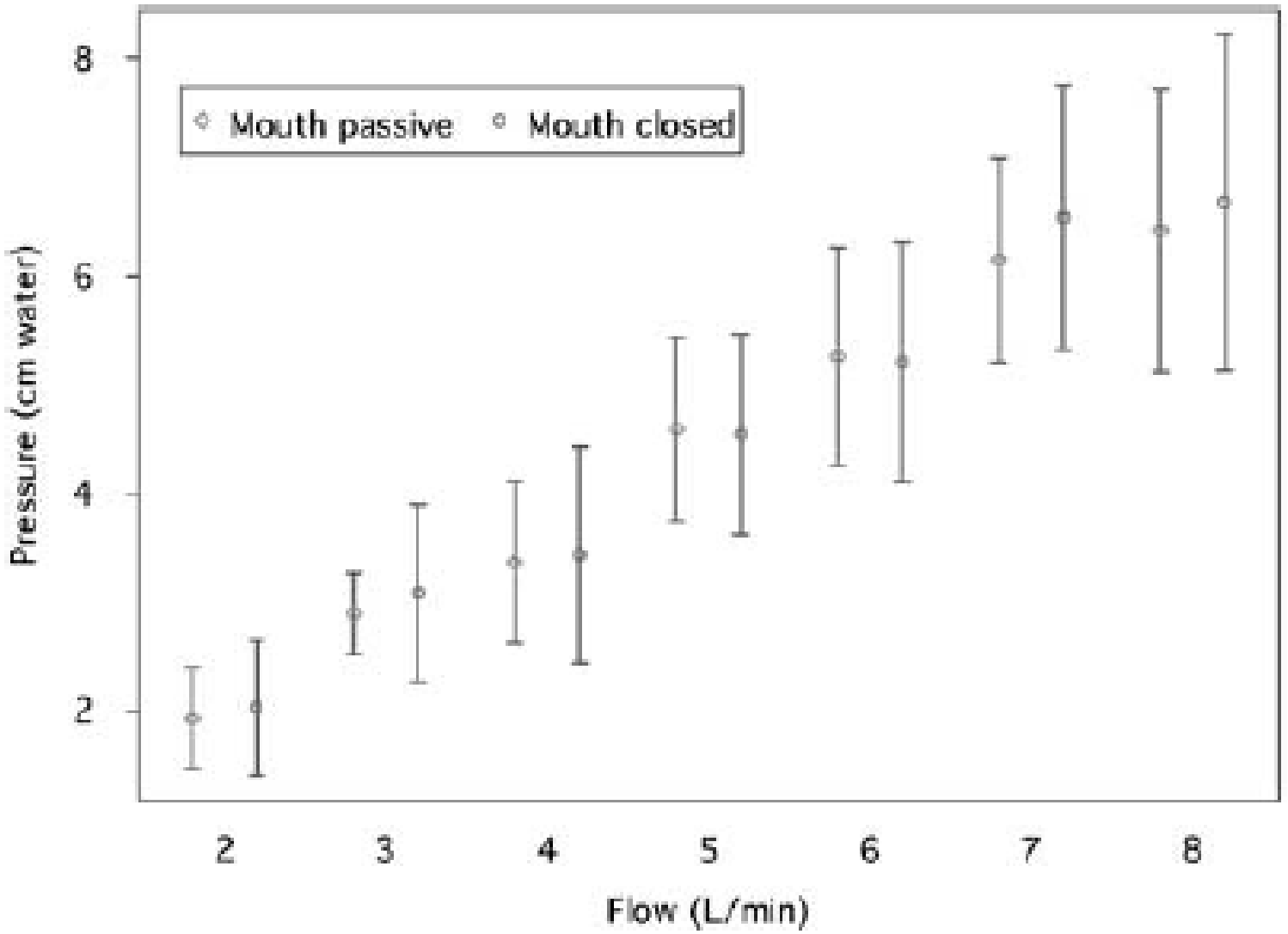


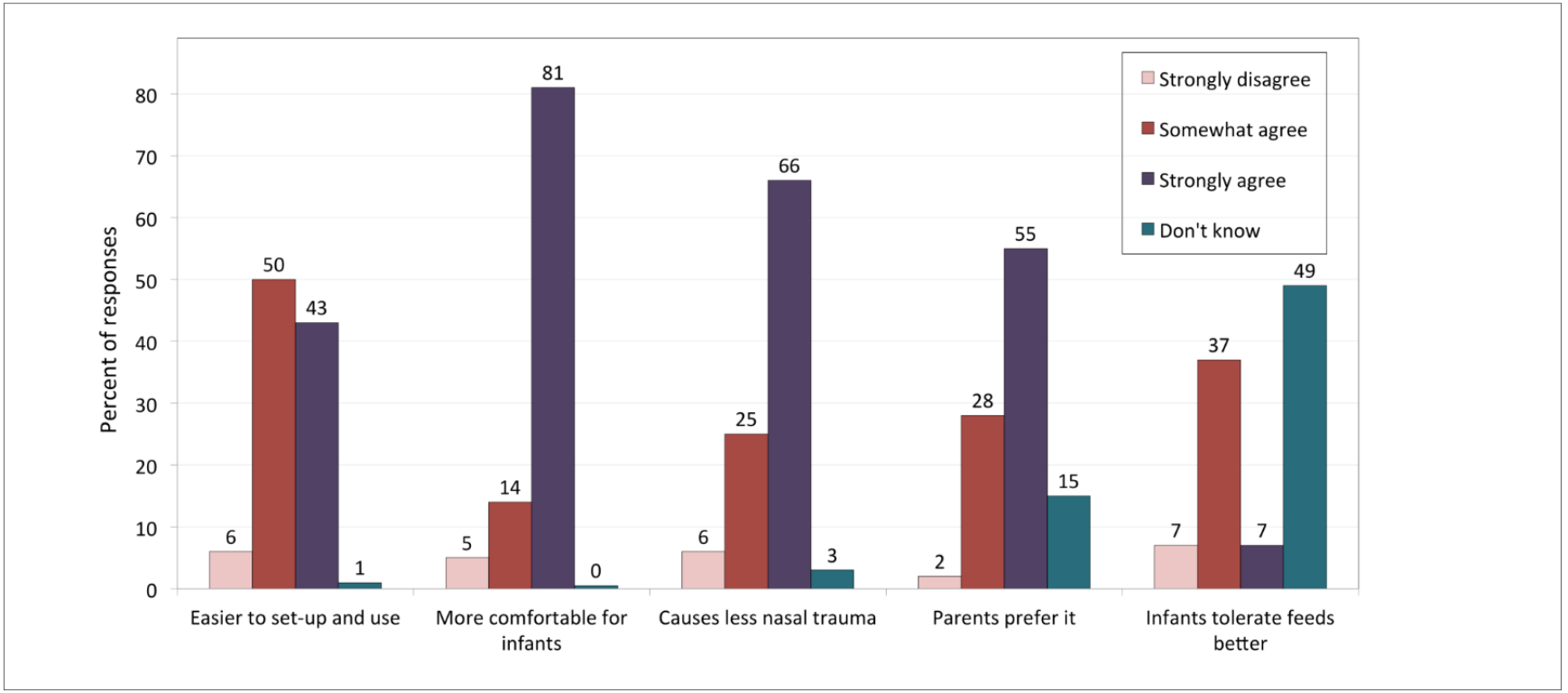
Figure 2 Mean pharyngeal pressure (with 95% confidence intervals) recorded at flow rates 2 to 8 l min^{-1}.

Wilkinson et al, *J Perinatol* 2008

nCPAP vs HF: Who decides?

Nursing Perceptions

Perceptions of HFNC in comparison to NCPAP



Roberts, Journal of Paediatrics and Child Health, 2014

Parental Preference

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

Klingenberg, ADC 2013

Why Nasal HF?

- Easier to set up and use
- Better access to the infant
- More comfortable
- Parents prefer it
- Improved bonding

WHAT ABOUT SOME EVIDENCE?

COCHRANE REVIEW (2011)

Wilkinson, Andersen, O'Donnell and De Paoli

"Insufficient evidence to establish the safety or effectiveness of HFNC… in preterm infants"

COCHRANE REVIEW (2011)

Wilkinson, Andersen, O'Donnell and De Paoli

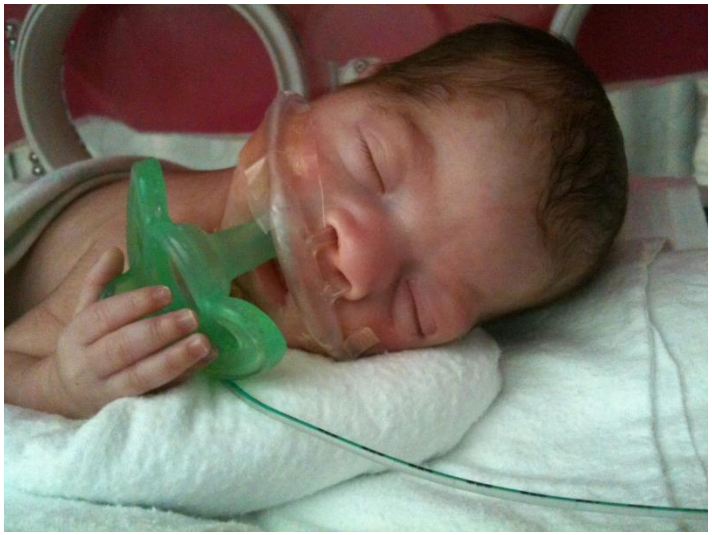
"Further adequately powered RCTs should be undertaken in preterm infants comparing HFNC with NCPAP…"

High-Flow Nasal Cannulae as **P**ost-**E**xtubation **R**espiratory **S**upport in **P**remature Infants: **A** **C**PAP **E**quivalent?

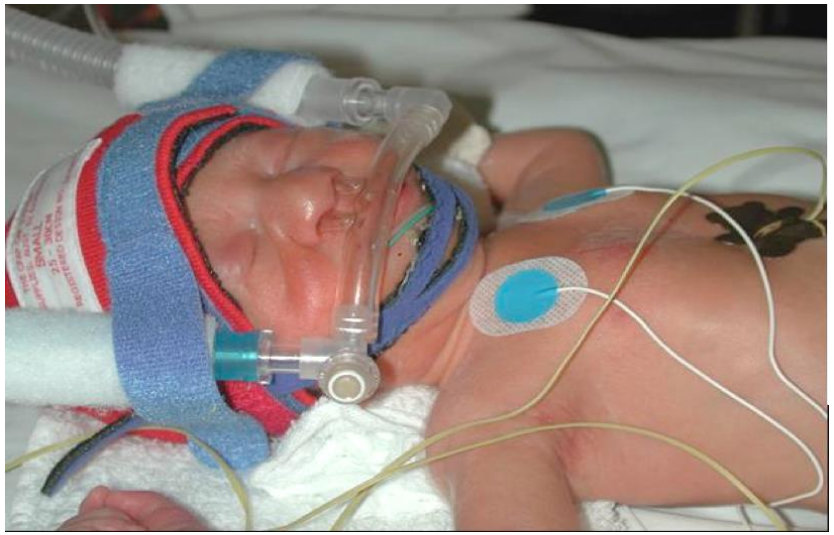
A multicenter, randomized, non-inferiority trial

Manley BJ, Owen LS, Doyle LW, Andersen CC, Cartwright DW, Pritchard MA, Donath SM, Davis PG. N Engl J Med. 2013

PRETERM INFANTS <32 WEEKS' GA
FIRST EXTUBATION



VS



HFNC 5-6 L/min

NCPAP 7 cm H_2O

PRIMARY OUTCOME: FAILURE WITHIN 7 DAYS

FOLLOWED TO DISCHARGE FROM HOSPITAL

NON-INFERIORITY TRIALS

- Most RCTs are *superiority* trials

- *Non-inferiority* trials aim to determine if a new treatment (eg. HFNC) has efficacy that is **similar to or no worse than** an established therapy (eg. NCPAP)

- The premise is usually that the new treatment has some other benefit and might be favored over the standard treatment, **even if the efficacy is the same or lower**

Piaggio et al, JAMA 2006

NON-INFERIORITY TRIALS

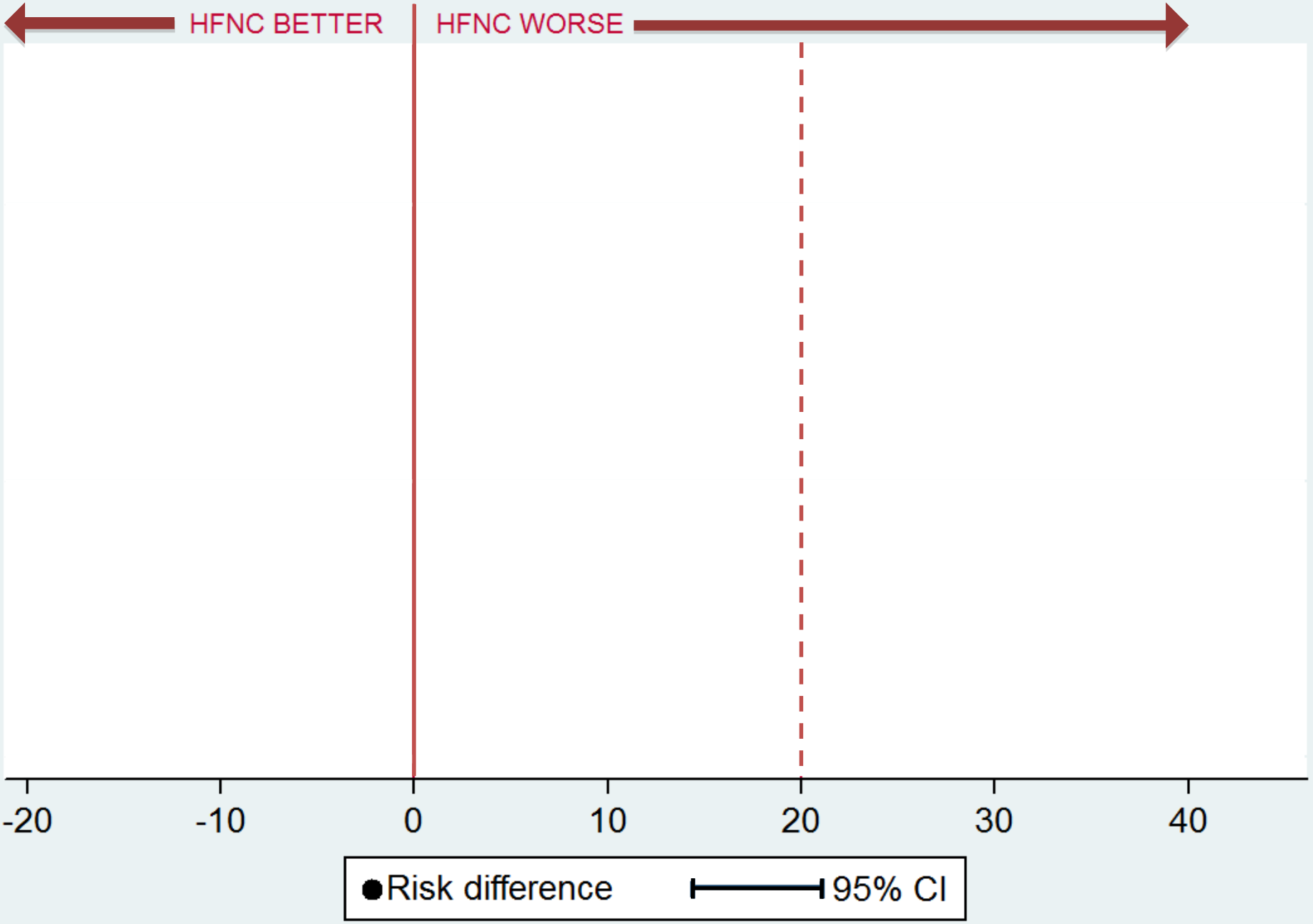
- Non-inferiority is based on the risk difference (95% CI) for the primary outcome between the two treatments

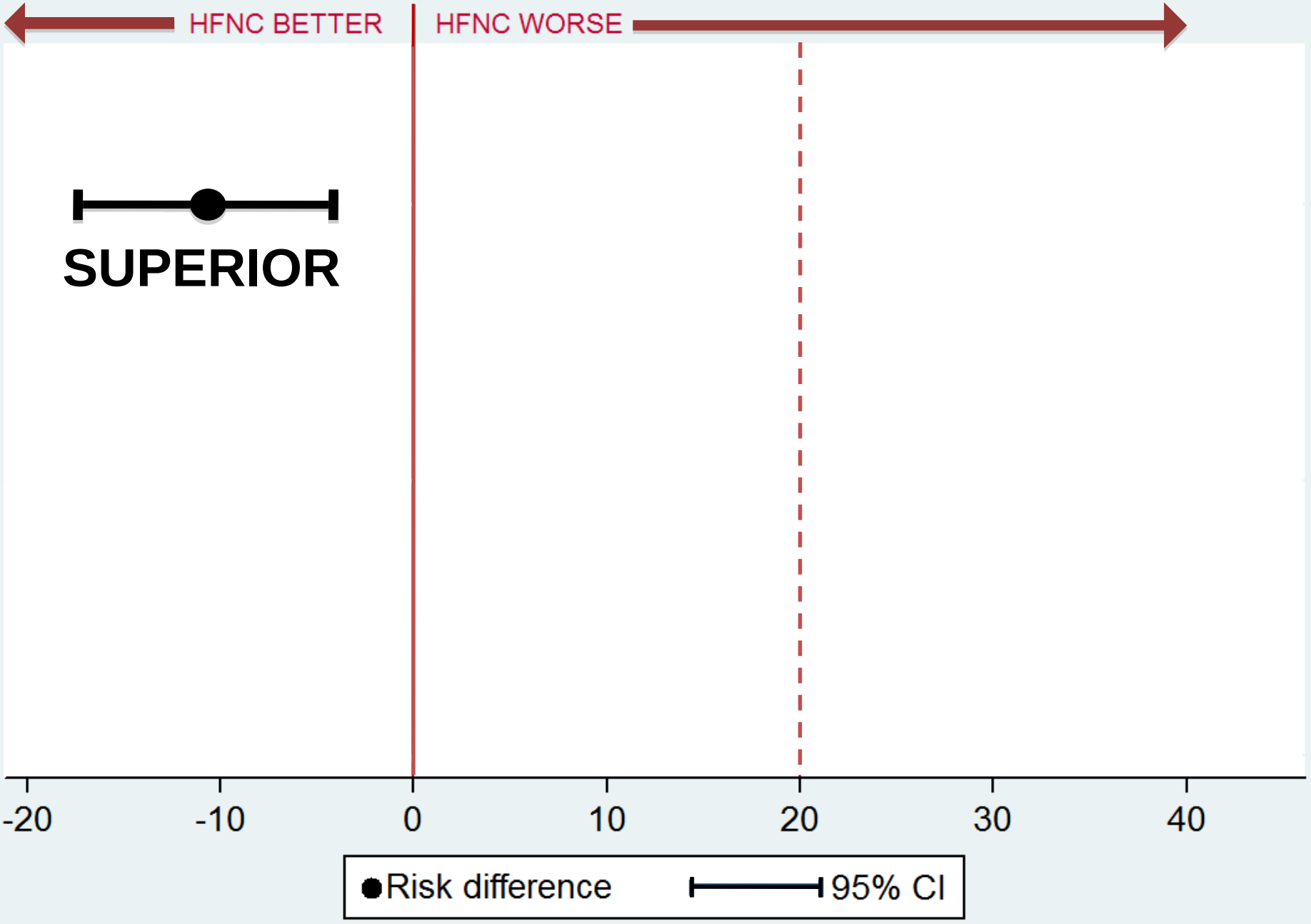
- 'Margin of non-inferiority' is defined

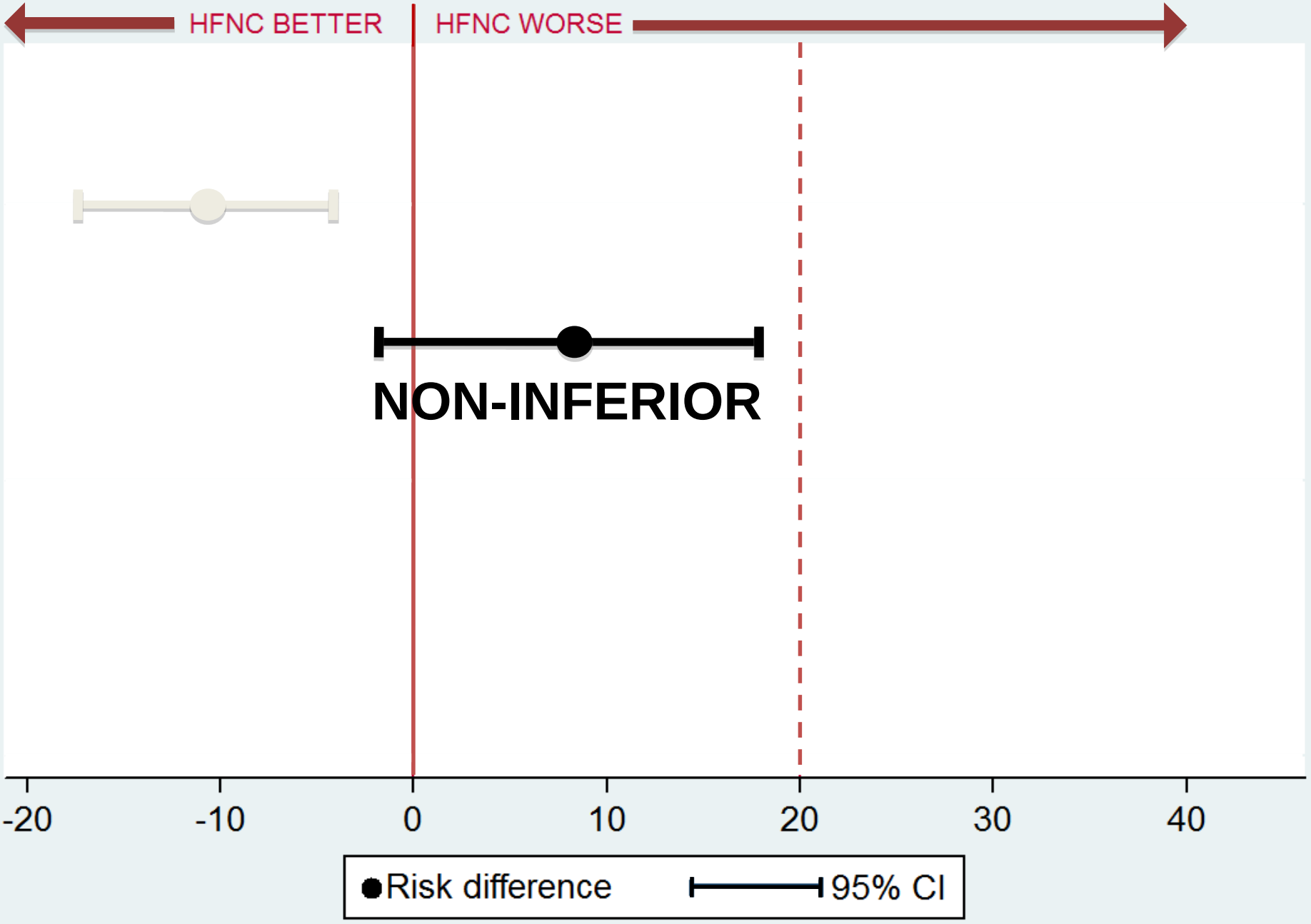
➢ ***We defined the margin as 20%***

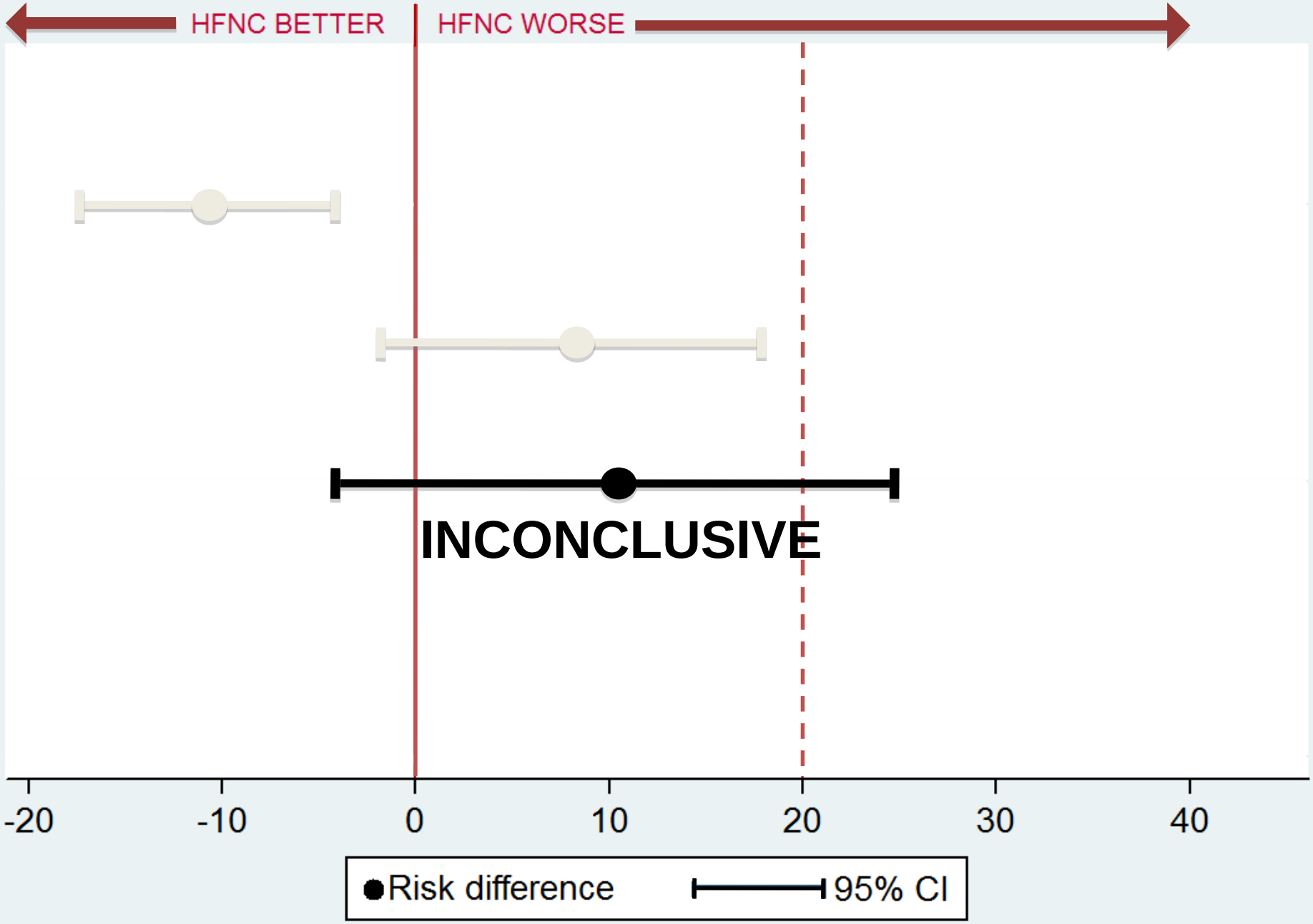
➢ ***If the risk difference for treatment failure and upper limit of its 95% CI is ≤20%, then HFNC is 'non-inferior'***

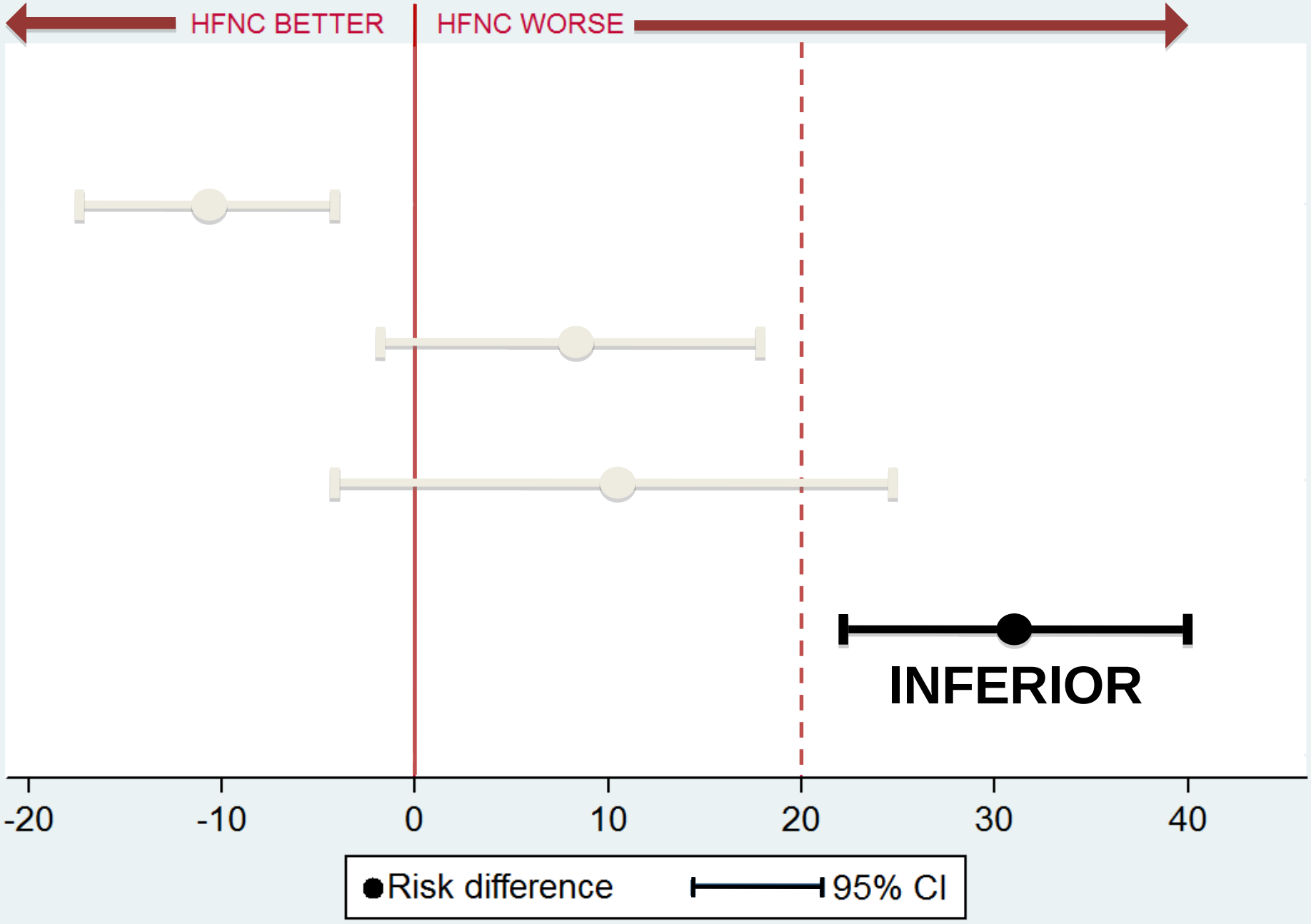
Piaggio et al, JAMA 2006


HFNC BETTER
HFNC WORSE
-20
-10
0
10
20
30
40
Risk difference
95% CI


HFNC BETTER
HFNC WORSE
SUPERIOR
-20
-10
0
10
20
30
40
Risk difference
95% CI


HFNC BETTER
HFNC WORSE
NON-INFERIOR
-20
-10
0
10
20
30
40
Risk difference
95% CI


HFNC BETTER
HFNC WORSE
INCONCLUSIVE
-20
-10
0
10
20
30
40
Risk difference
95% CI


HFNC BETTER
HFNC WORSE
INFERIOR
-20
-10
0
10
20
30
40
Risk difference
95% CI

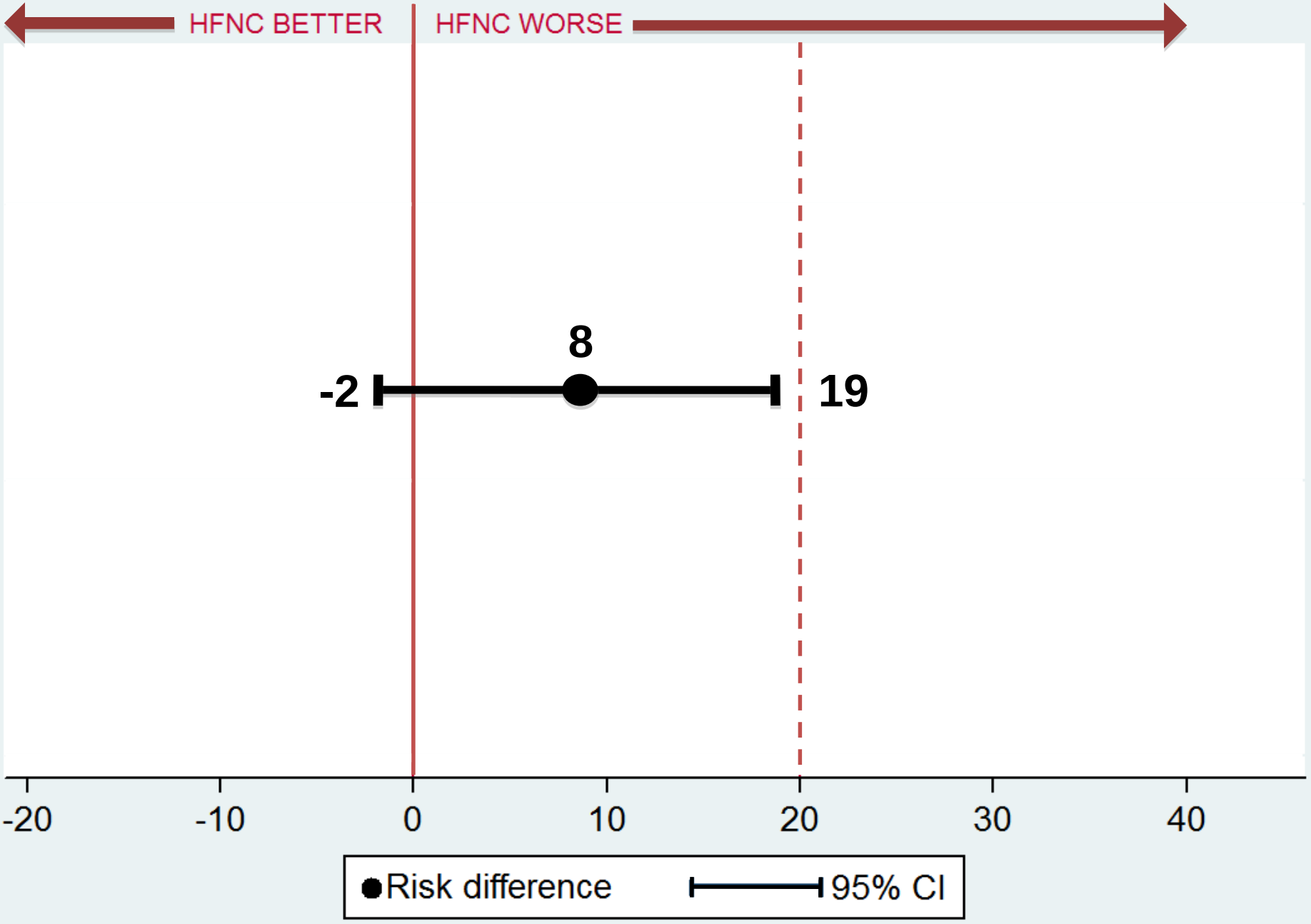
PRIMARY OUTCOME (N=303)

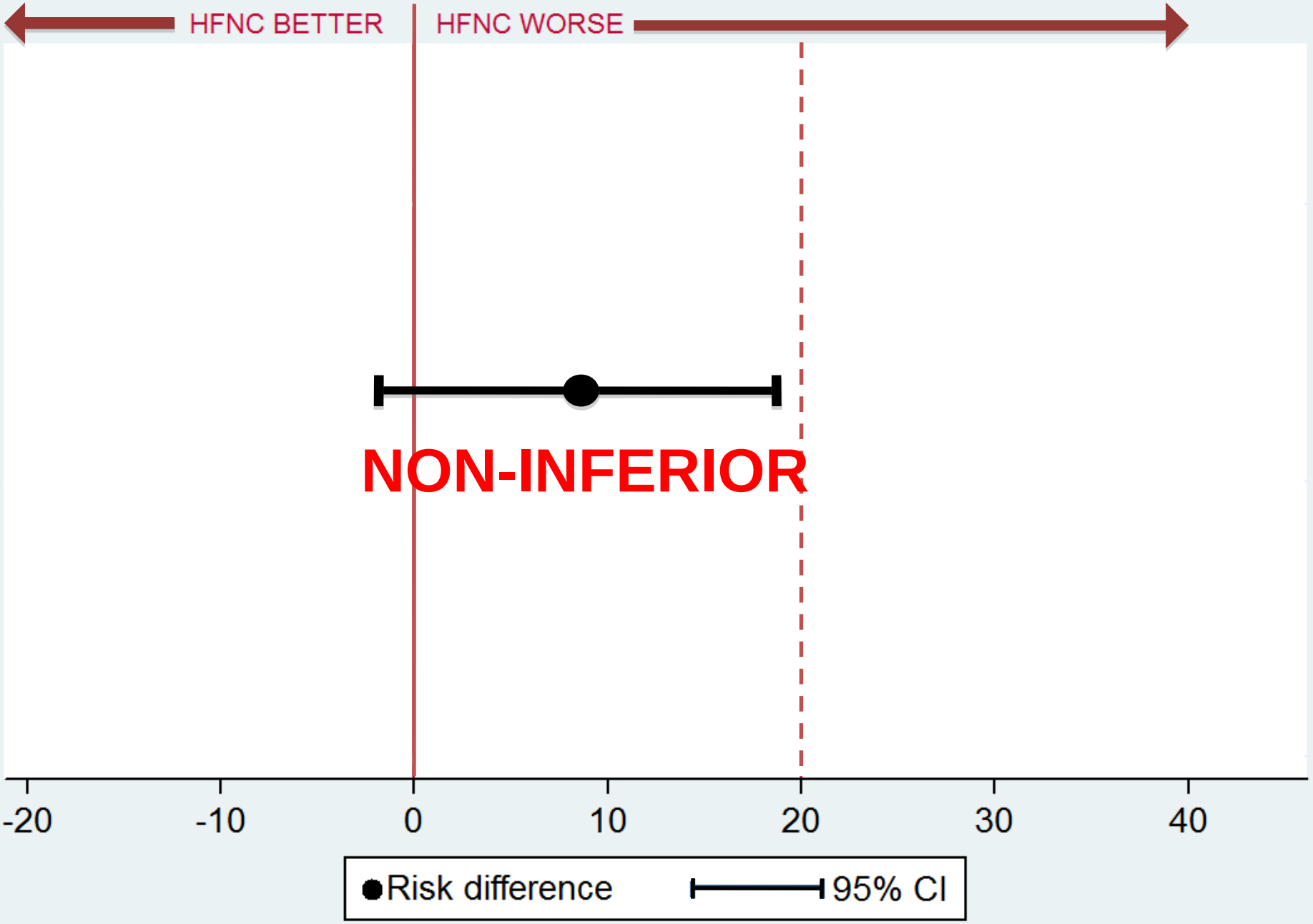
FAILURE OF THE ASSIGNED TREATMENT WITHIN 7 DAYS

HFNC	NCPAP
52/152	39/151
34%	26%

Risk difference 8%

95% CI (-2, 19) %


HFNC BETTER
HFNC WORSE
8
-2
19
-20
-10
0
10
20
30
40
Risk difference
95% CI


HFNC BETTER
HFNC WORSE
NON-INFERIOR
-20
-10
0
10
20
30
40
Risk difference
95% CI

SECONDARY OUTCOMES:

RE-INTUBATION WITHIN 7 DAYS

HFNC	NCPAP
27/152	38/151
18%	25%

Risk difference -7%

95% CI (-17, 2) %

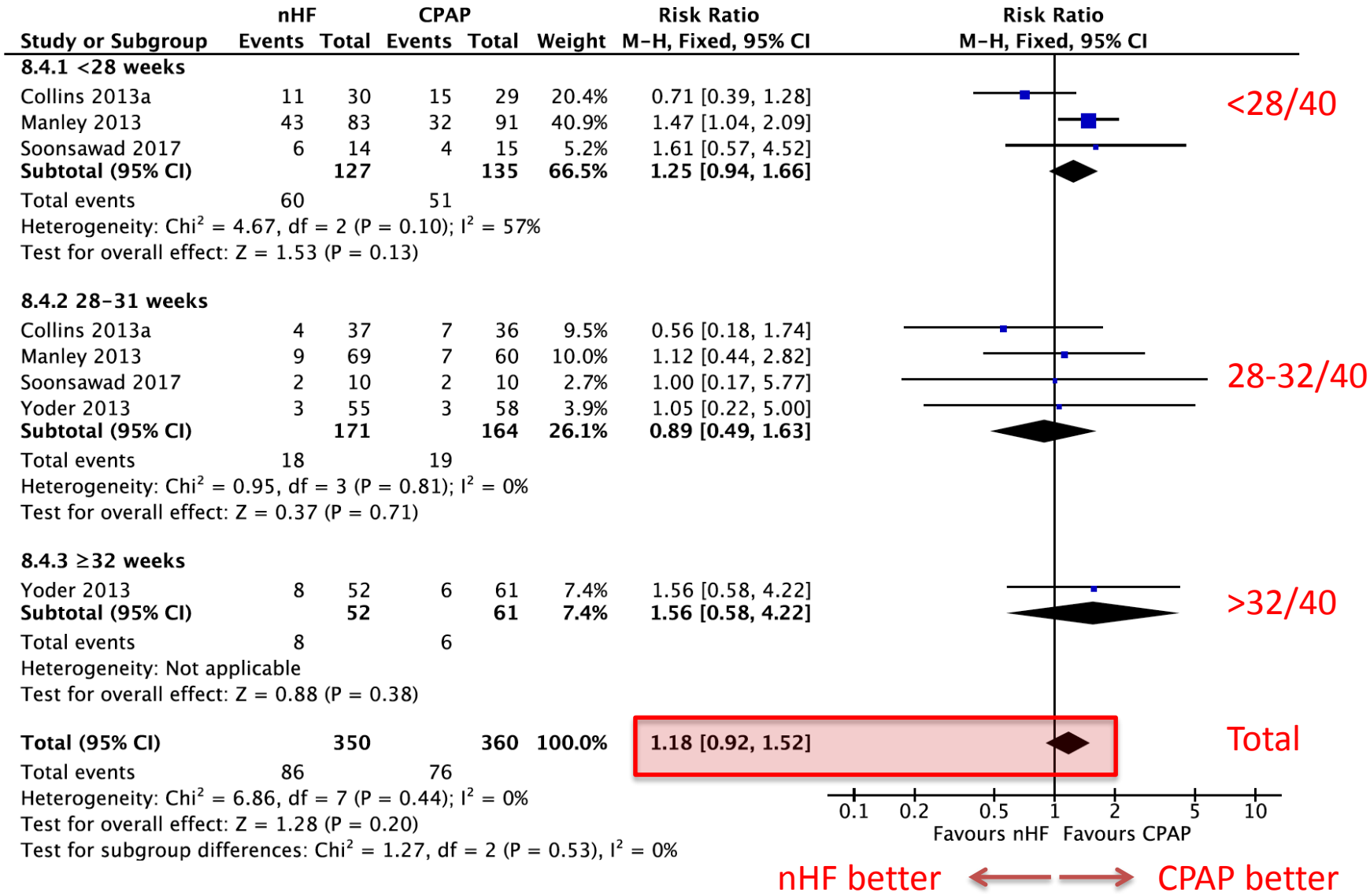
SECONDARY OUTCOMES:

RE-INTUBATION WITHIN 7 DAYS

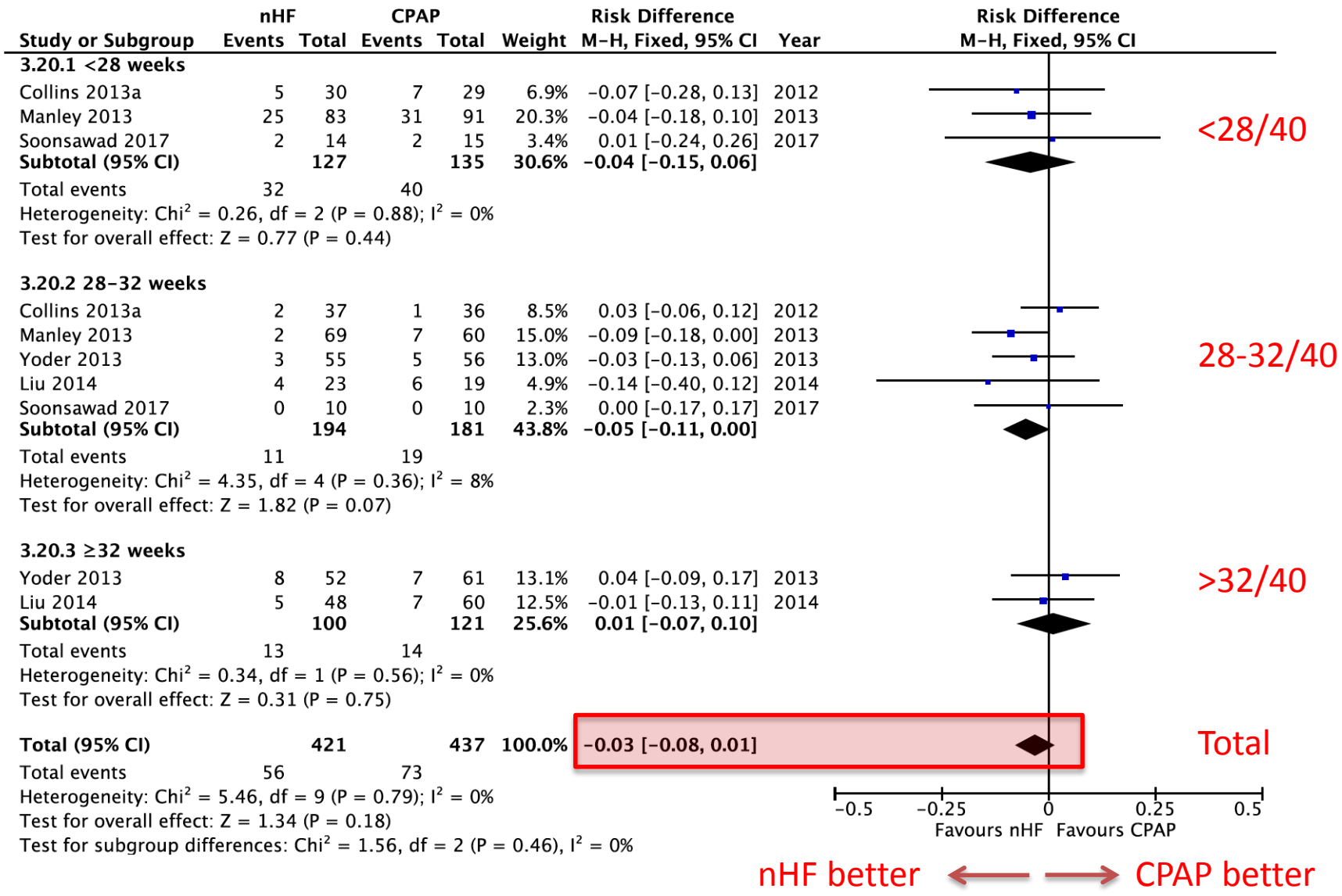
HFNC	NCPAP
27/152	38/151
18%	25%

HALF OF INFANTS IN WHOM HFNC FAILED WERE ‘RESCUED’ BY NCPAP

Post Extubation: Treatment Failure <7 days (without Campbell)



Post Extubation: Intubation <7 days (without Campbell)



PRIMARY THERAPY: HIPSTER (28 TO 36+6 WEEKS' GESTATION)

Roberts CT, Owen LS, Manley BJ, Frøisland DH, Donath SM, Dalziel KM, Pritchard MA, Cartwright DW, Collins CL, Malhotra A, Davis PG; HIPSTER Trial Investigators., N Engl J Med 2016;375:1142-51

Primary Outcome

Treatment failure within 72 hours of randomization

High Flow	VS	CPAP
71/278 25.5%		38/286 13.3%

Risk difference for treatment failure with High Flow, **12.3%**, 95% confidence interval, 5.8 to 18.7% ($P<0.001$)

Intubation

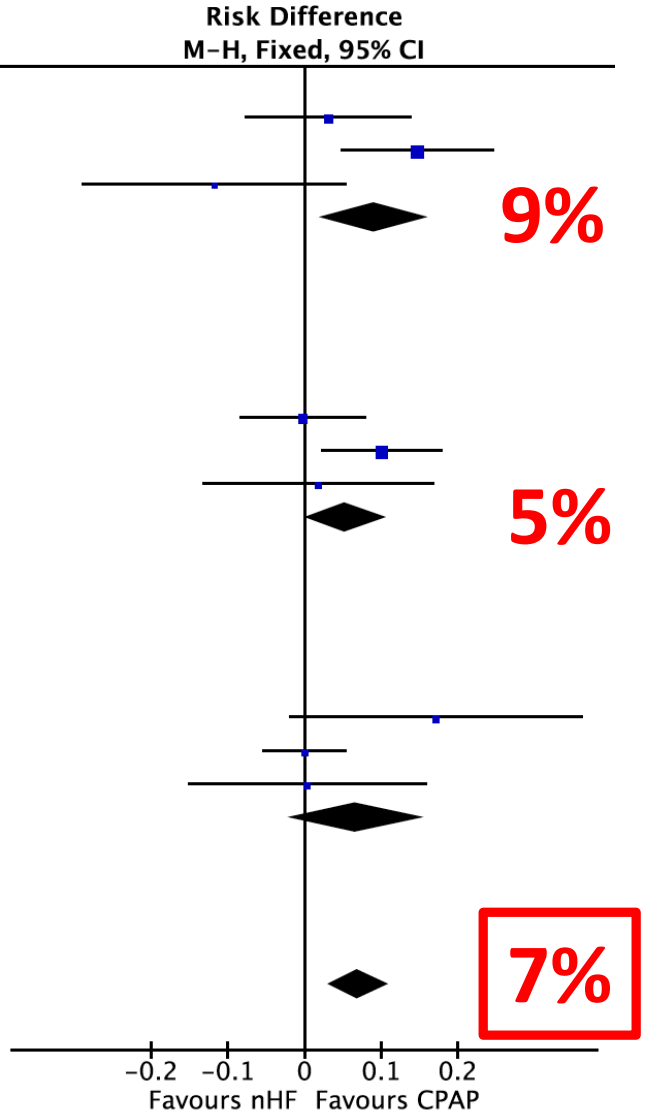
within 72 hours of randomization

High Flow	VS	CPAP
43/278		33/286
15.5%		11.5%

Risk difference for intubation with High Flow, **3.9%**, 95% confidence interval, -1.7 to 9.6% (P=0.17)

Primary support: Treatment failure

Study or Subgroup	nHF Events	nHF Total	CPAP Events	CPAP Total	Weight	Risk Difference M-H, Fixed, 95% CI	Year
1.4.2 28-31 weeks							
Lavizzari 2016	10	71	8	73	11.8%	0.03 [-0.08, 0.14]	2016
Roberts 2016	46	140	27	149	23.6%	0.15 [0.05, 0.25]	2016
Yoder 2013	0	20	2	17	3.0%	-0.12 [-0.29, 0.05]	2013
Subtotal (95% CI)		**231**		**239**	**38.3%**	**0.09 [0.02, 0.16]**	
Total events	56		37				
Heterogeneity: $Chi^2 = 8.03$, df = 2 (P = 0.02); $I^2 = 75\%$							
Test for overall effect: Z = 2.51 (P = 0.01)							
1.4.3 ≥32 weeks							
Lavizzari 2016	7	87	7	85	14.0%	-0.00 [-0.08, 0.08]	2016
Roberts 2016	25	138	11	137	22.5%	0.10 [0.02, 0.18]	2016
Yoder 2013	6	38	7	50	7.1%	0.02 [-0.13, 0.17]	2013
Subtotal (95% CI)		**263**		**272**	**43.5%**	**0.05 [0.00, 0.11]**	
Total events	38		25				
Heterogeneity: $Chi^2 = 3.38$, df = 2 (P = 0.18); $I^2 = 41\%$							
Test for overall effect: Z = 1.96 (P = 0.05)							
1.4.4 <37 weeks' (subgroup data not available)							
Shin 2017	16	42	9	43	6.9%	0.17 [-0.02, 0.36]	2017
Iranpour 2011	0	35	0	35	5.7%	0.00 [-0.05, 0.05]	2011
Nair 2005	4	33	4	34	5.5%	0.00 [-0.15, 0.16]	2005
Subtotal (95% CI)		**110**		**112**	**18.1%**	**0.07 [-0.02, 0.16]**	
Total events	20		13				
Heterogeneity: $Chi^2 = 7.66$, df = 2 (P = 0.02); $I^2 = 74\%$							
Test for overall effect: Z = 1.48 (P = 0.14)							
Total (95% CI)		**604**		**623**	**100.0%**	**0.07 [0.03, 0.11]**	
Total events	114		75				
Heterogeneity: $Chi^2 = 19.78$, df = 8 (P = 0.01); $I^2 = 60\%$							
Test for overall effect: Z = 3.51 (P = 0.0004)							
Test for subgroup differences: $Chi^2 = 0.65$, df = 2 (P = 0.72), $I^2 = 0\%$							

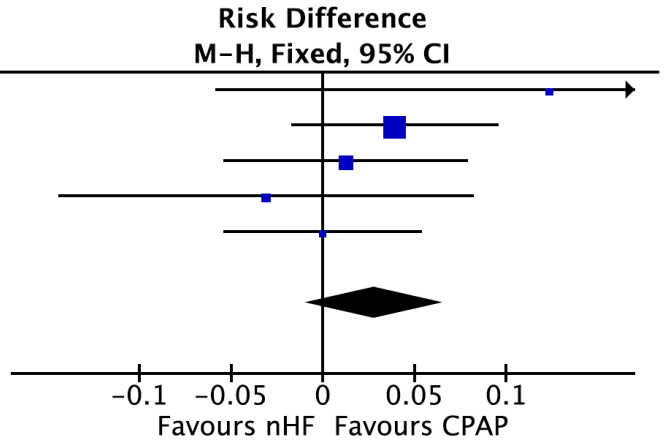


Primary support: Intubation

Study or Subgroup	nHF Events	nHF Total	CPAP Events	CPAP Total	Weight	Risk Difference M-H, Fixed, 95% CI	Year
Shin 2017	13	42	8	43	7.3%	0.12 [-0.06, 0.31]	2017
Roberts 2016	43	278	33	286	48.6%	0.04 [-0.02, 0.10]	2016
Lavizzari 2016	17	158	15	158	27.3%	0.01 [-0.05, 0.08]	2016
Yoder 2013	6	58	9	67	10.7%	-0.03 [-0.14, 0.08]	2013
Iranpour 2011	0	35	0	35	6.0%	0.00 [-0.05, 0.05]	2011
Total (95% CI)		**571**		**589**	**100.0%**	**0.03 [-0.01, 0.07]**	
Total events	79		65				

Heterogeneity: $Chi^2 = 3.51$, df = 4 (P = 0.48); $I^2 = 0\%$

Test for overall effect: Z = 1.47 (P = 0.14)



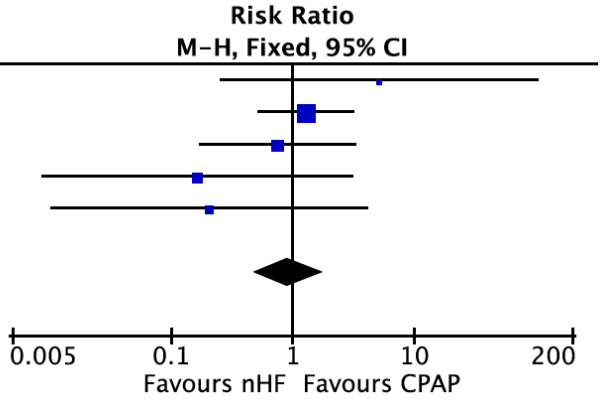
Pneumothorax

Primary support

Study or Subgroup	nHF Events	nHF Total	CPAP Events	CPAP Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Shin 2017	2	42	0	43	2.7%	5.12 [0.25, 103.50]	2017
Roberts 2016	10	278	8	286	43.6%	1.29 [0.52, 3.21]	2016
Lavizzari 2016	3	158	4	158	22.1%	0.75 [0.17, 3.30]	2016
Yoder 2013	0	58	3	67	18.0%	0.16 [0.01, 3.12]	2013
Nair 2005	0	33	2	34	13.6%	0.21 [0.01, 4.13]	2005
Total (95% CI)		**569**		**588**	**100.0%**	**0.92 [0.48, 1.78]**	
Total events	15		17				

Heterogeneity: $Chi^2 = 4.10$, df = 4 (P = 0.39); $I^2 = 3\%$

Test for overall effect: Z = 0.24 (P = 0.81)

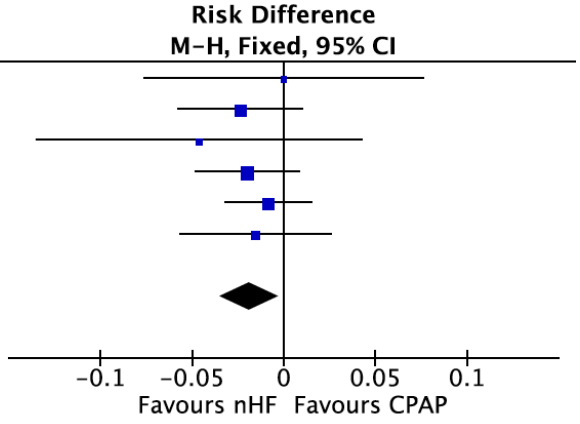


Post-extubation

Study or Subgroup	nHF Events	nHF Total	CPAP Events	CPAP Total	Weight	Risk Difference M-H, Fixed, 95% CI	Year
Soonsawad 2017	0	24	0	25	4.7%	0.00 [-0.08, 0.08]	2017
Liu 2014	1	128	4	127	24.3%	-0.02 [-0.06, 0.01]	2014
Mostafa-Gharehbaghi 2014	1	42	3	43	8.1%	-0.05 [-0.13, 0.04]	2014
Manley 2013	1	152	4	151	28.9%	-0.02 [-0.05, 0.01]	2013
Yoder 2013	0	107	1	119	21.5%	-0.01 [-0.03, 0.02]	2013
Collins 2013a	0	67	1	65	12.6%	-0.02 [-0.06, 0.03]	2012
Total (95% CI)		**520**		**530**	**100.0%**	**-0.02 [-0.03, -0.00]**	
Total events	3		13				

Heterogeneity: $Chi^2 = 1.47$, df = 5 (P = 0.92); $I^2 = 0\%$

Test for overall effect: Z = 2.32 (P = 0.02)



Is CPAP the gold standard?

- If you can have only one form of noninvasive ventilation – choose CPAP
- If you can manage two forms
  - HF is a highly suitable alternative
    - More comfortable
    - Slightly cheaper
    - Makes nurses and parents happy
  - Babies failing HF (primary or post-extubation) can be successfully rescued using CPAP

The Gaps

- Role of High Flow in other (non-tertiary) settings?
- Is one version of High Flow better than the others?
- Can we safely go higher with flow rates?
- Is there a role for High Flow for ELBW babies?