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16•17•18 DICEMBRE

NUOVE LINEE GUIDA 2021:
RIANIMAZIONE CARDIOPOLMONARE
POST-LOCKDOWN



Italian
Resuscitation
Council

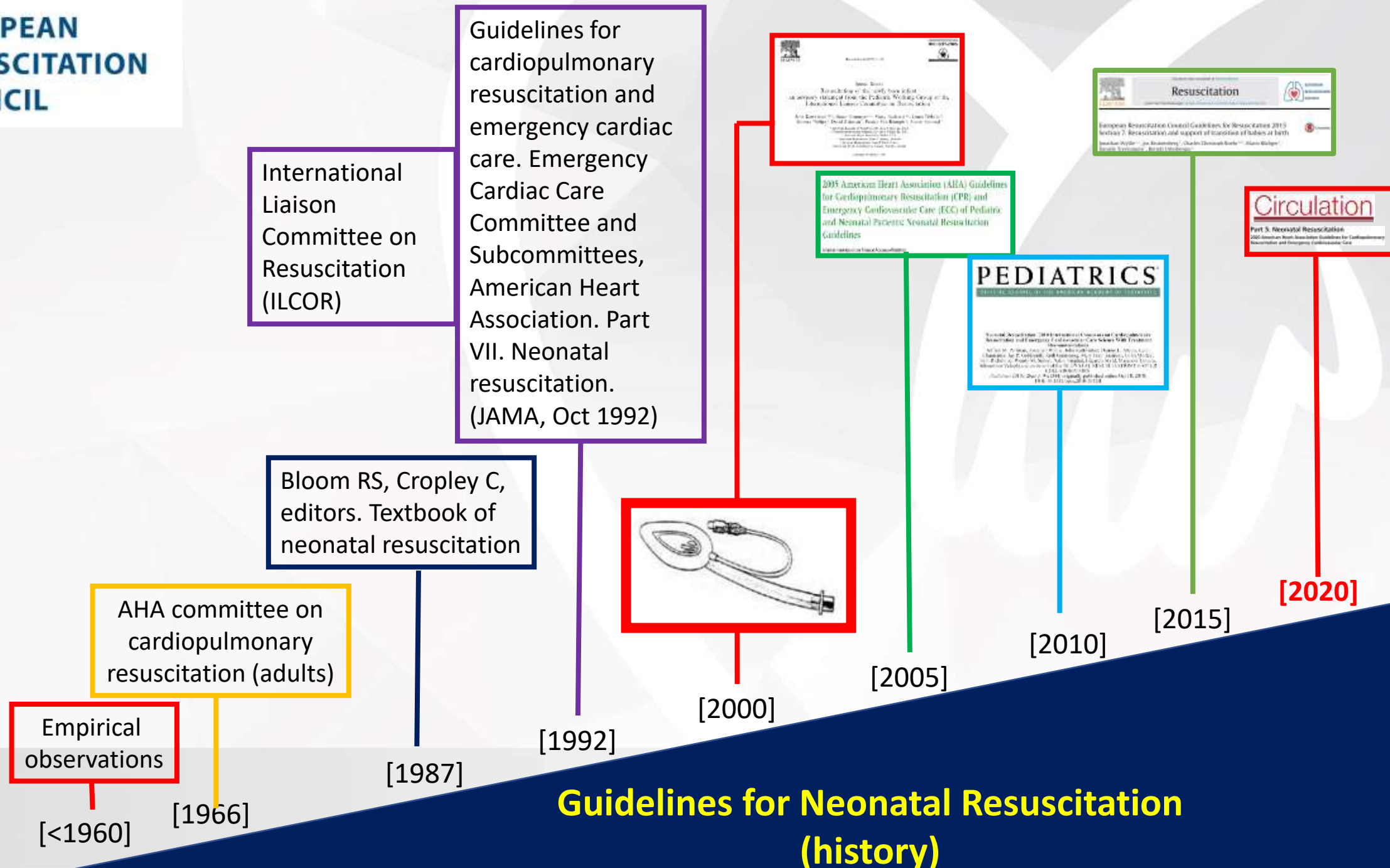
RCP Neonatale

Daniele Trevisanuto
Università degli Studi di Padova



Conflicts of interest

- Member of the ILCOR Neonatal Resuscitation Task Force
- Member of the ERC NLS Science and Education Committee



Guidelines for Neonatal Resuscitation (history)



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Summary of changes since the 2015 guidelines

Summary of changes since the 2015 guidelines

Management of the umbilical cord

Clamping after at least 60 s is recommended, ideally after the lungs are aerated. Where delayed cord clamping is not possible cord milking should be considered in infants >28 weeks gestation.

Infants born through meconium-stained liquor

In non-vigorous infants, recommendations are against immediate laryngoscopy with or without suction after delivery, because this may delay aeration and ventilation of the lungs.

Use of the laryngeal mask

If facemask ventilation is unsuccessful or if tracheal intubation is unsuccessful or not feasible a laryngeal mask may be considered as an alternative means of establishing an airway in infants of >34 weeks gestation (about 2000 g, although some devices have been used successfully in infants down to 1500 g).

Inflation pressure

If there is no response to initial inflations despite an open airway then a gradual increase in the inflation pressure is suggested.

A starting pressure of 25 cm H₂O is suggested for preterm infants <32 weeks gestation.

Air/oxygen for preterm resuscitation

Recommendations are for starting in air at 32 weeks gestation or more, 21-30% inspired oxygen at 28-31 weeks gestation and 30% inspired oxygen at <28 weeks gestation.

The concentration should be titrated to achieve saturations of $\geq 80\%$ at 5 min of age because there is evidence of poorer outcomes where this is not achieved.

Chest compressions

If chest compressions are required, the inspired oxygen concentration should be increased to 100% and consideration given towards securing the airway ideally with a tracheal tube.

Vascular access

The umbilical vein is still favoured as the optimal route of access but, intraosseous access is an alternative method of emergency access for drugs/fluids.

Adrenaline

Where the heart rate has not increased after optimising ventilation and chest compressions an intravenous dose of adrenaline of 10–30 micrograms kg⁻¹ is recommended, repeated every 3–5 min in the absence of a response.

Glucose during resuscitation

An intravenous dose of 250 mg kg⁻¹ (2.5 mL kg⁻¹ of 10% glucose) is suggested in a prolonged resuscitation to reduce the likelihood of hypoglycaemia.

Prognosis

Failure to respond despite 10–20 mins of intensive resuscitation is associated with high risk of poor outcome. It is appropriate to consider discussions with the team and family about withdrawal of treatment if there has been no response despite the provision of all recommended steps of resuscitation and having excluded reversible causes

Madar J. et al. Resuscitation 2021



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Infants born through meconium-stained liquor



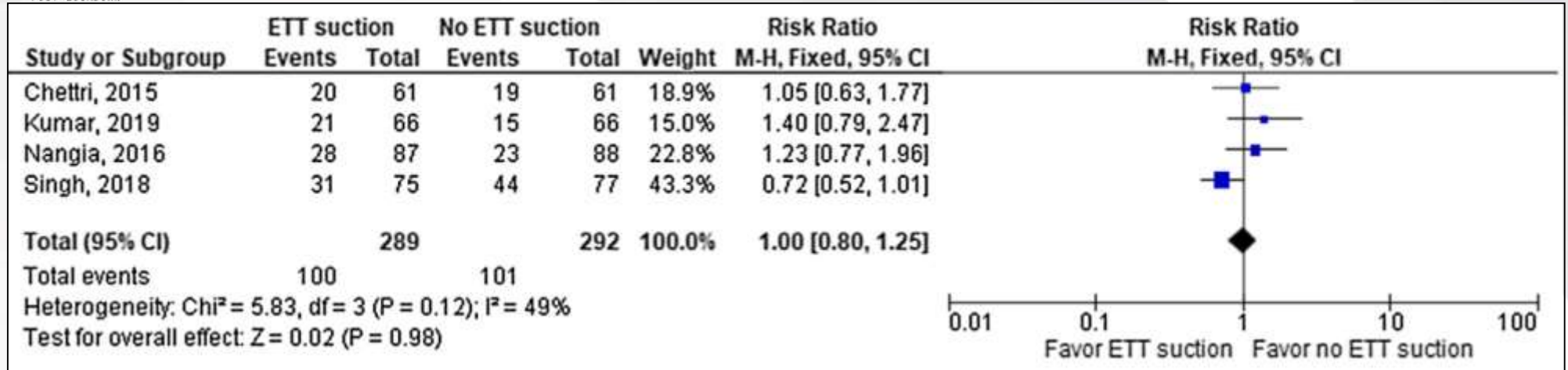
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TABLE 1 ■ Summary of NRP/AHA Recommendation for Delivery Room Management of Meconium-Stained Newborn over the Years

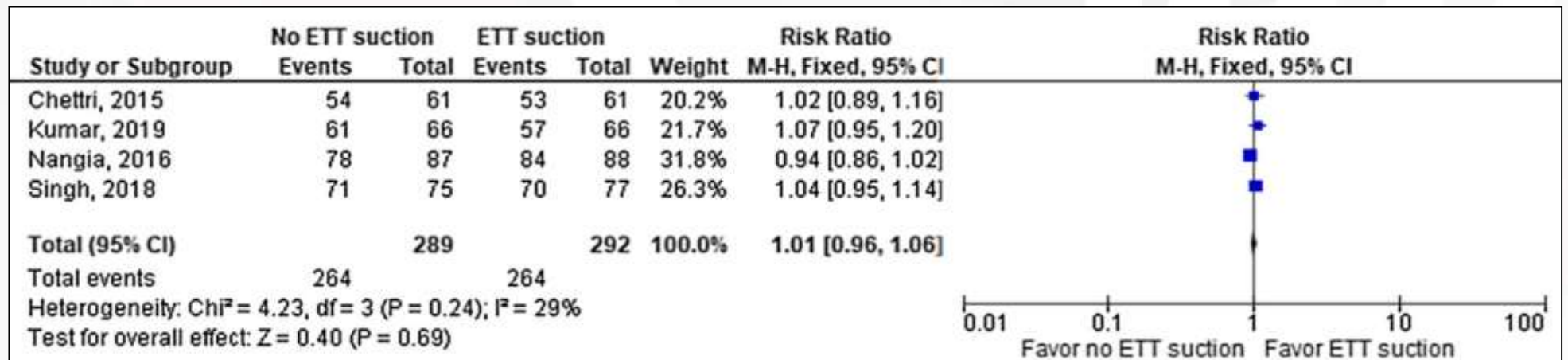
Guidelines	NRP Edition (Year), AHA Guideline						
	First Edition (1987)	Second Edition (1990)	Third Edition (1994)	Fourth Edition (2000), AHA 2000	Fifth Edition (2006) AHA 2005	Sixth Edition (2011), AHA 2010	Seventh Edition (2016), AHA 2015
Intrapartum oro-nasopharyngeal suction after delivery of head	Yes	Yes	Yes	Yes	No	No	No
Endotracheal intubation and suction	Yes for all	Yes for all	Yes for all, notes controversy regarding vigorous infants	Yes for nonvigorous infants, not recommended for vigorous infants (AHA class I)	Yes for nonvigorous infants (AHA class indeterminate), not recommended for vigorous infants	Yes for nonvigorous infants, because insufficient evidence to change practice	No for nonvigorous infants, because insufficient evidence to continue this practice (AHA class IIb)

Abbreviations: AHA = American Heart Association; NRP = Neonatal Resuscitation Program.

Meconium Aspiration Syndrome



Survival at discharge



Infants born through meconium-stained liquor

In non-vigorous infants, recommendations are against immediate laryngoscopy with or without suction after delivery, because this may delay aeration and ventilation of the lungs.



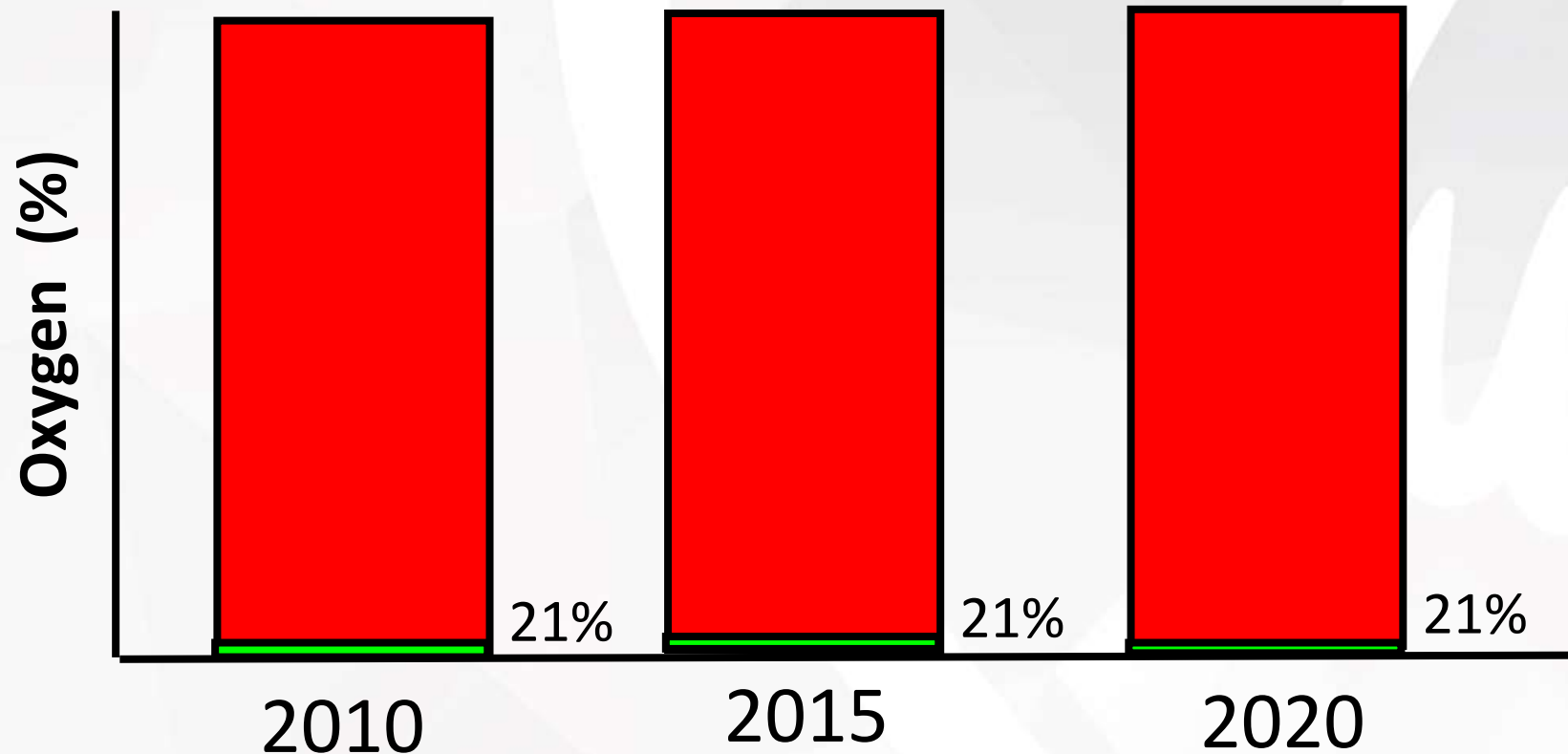
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Air/oxygen for preterm resuscitation



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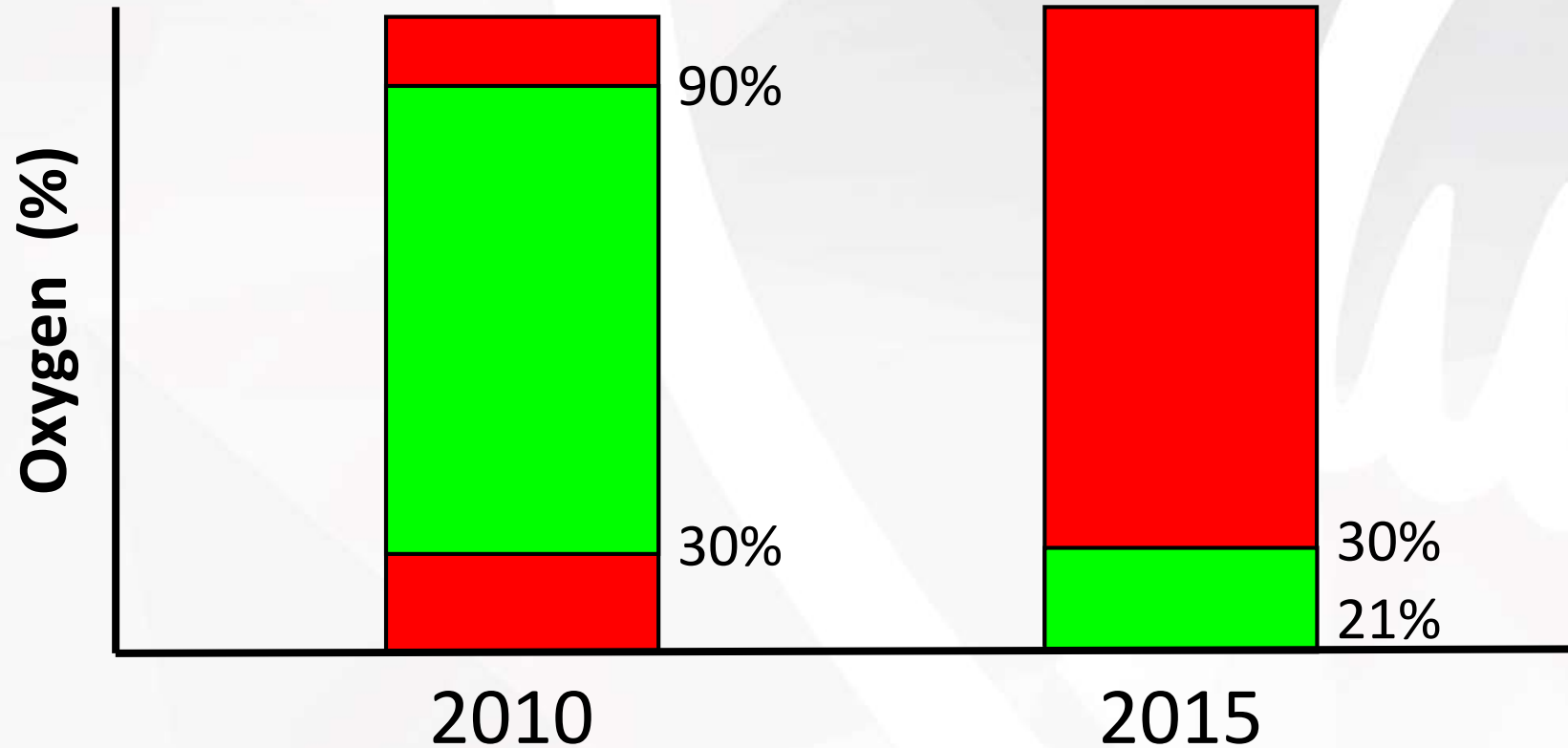
Oxygen to initiate resuscitation in near-term & full-term infants



Wyckoff MH et al. 2015, 2020 AHA Guidelines

Wyllie J et al. 2015, Madar J et al. 2021 ERC Guidelines

Oxygen to initiate resuscitation in preterm infants (<35 wks)



Wyckoff MH et al. 2015 AHA Guidelines
Wyllie J et al. 2015 ERC Guidelines

Torpedo Study

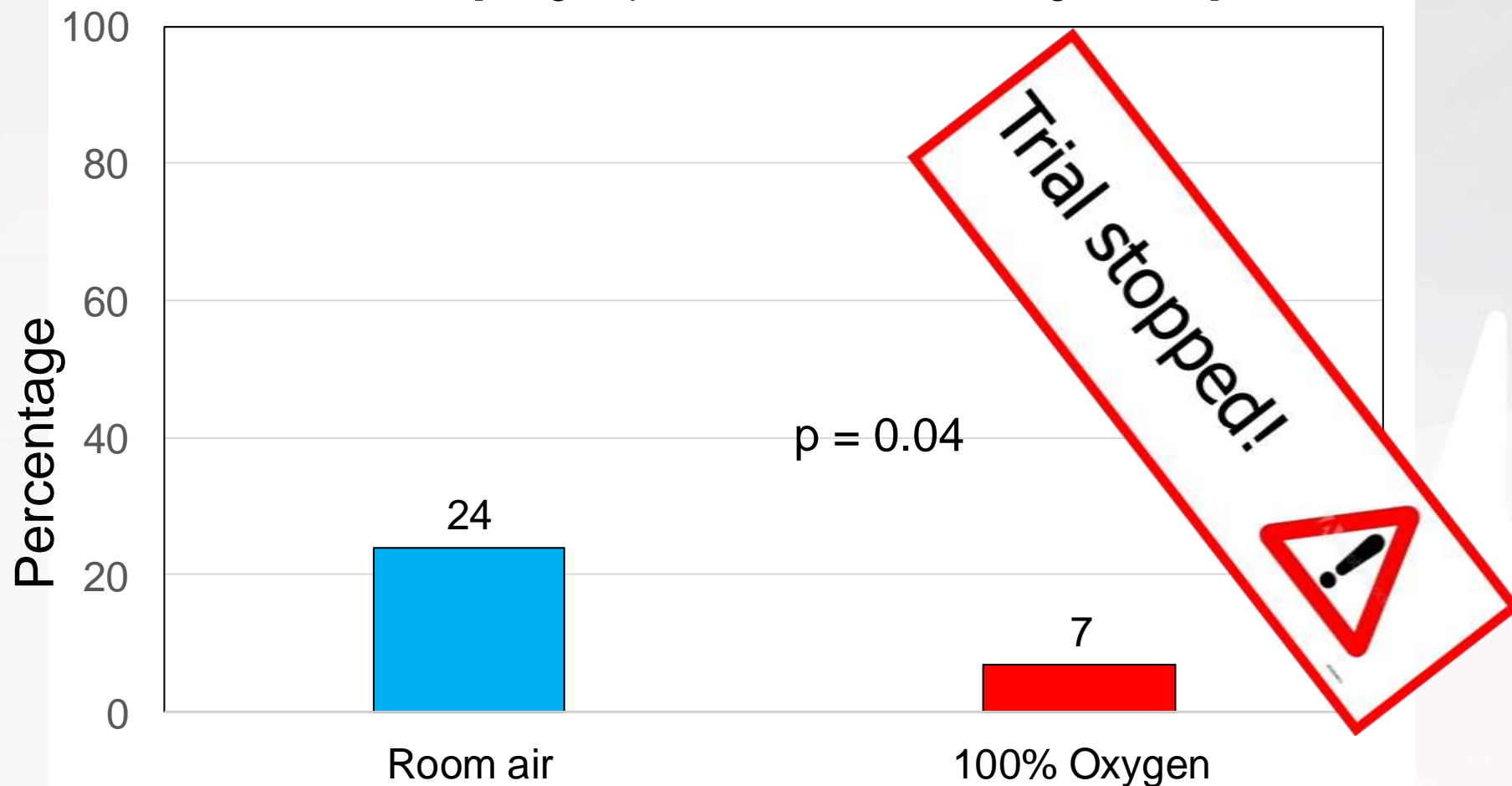
- Study design: RCT
- GA: <32 weeks' gestation
- Treatment: RA versus 100% oxygen
- SpO₂ targets: 65-95% up to 5 min and 85-95% until admission

TABLE 4 Mortality

Variable	All Infants		
	RA, <i>n</i> = 144	100% O ₂ , <i>n</i> = 143	RR (95% CI)
All deaths	14 (10)	6 (4)	2.3 (0.9–5.7), <i>P</i> = .10
Neonatal death (death <28 d)	12 (8)	5 (3)	3.1 (0.9–11.1), <i>P</i> = .08
Death before hospital discharge	14 (10)	5 (3)	2.6 (0.9–7.1), <i>P</i> = .06
Age of death, d	12 (2–95)	4 (1–11)	<i>P</i> = .24
Causes of death ^c			

Mortality rate

[subgroup of babies <28 weeks' gestation]



Adjusted OR for Outcome - Room Air as reference

<u>Outcome</u>	<u>Intermediate</u>	<u>100% O₂</u>
<i>Primary</i>		
Death or NDI	1.01 (0.77-1.34)	1.03 (0.78-1.35)
Death or severe NDI	1.14 (0.82-1.58)	1.22 (0.90-1.67)
<i>Secondary</i>		
Death	1.03 (0.68-1.56)	0.93 (0.63-1.37)
NDI	1.00 (0.74-1.35)	1.08 (0.81-1.45)
Severe NDI	1.22 (0.78-1.91)	1.57 (1.05-2.35)
Language score < 70	1.54 (0.89-2.67)	1.73 (1.02-2.91)

No significant differences: CP, Cognitive score < 85, Cognitive score < 70, Visual impairment, Hearing impairment

Initial Oxygen Concentration for Preterm Neonatal Resuscitation

CONCLUSIONS: The ideal initial F_{IO_2} for preterm newborns is still unknown, although the majority of newborns ≤ 32 weeks' gestation will require oxygen supplementation.

Recommendation of FiO₂ and newborn resuscitation

- Term and near term infants

OR for mortality: 0.69 (95%CI 0.54-0.88) in favour of air

→ Start with room air – adjust according to SpO₂

- Preterm infants 28-31 weeks GA

OR for mortality: 1.9 (95%CI 0.33-11.1)

→ Start with 21-30% – adjust according to SpO₂

- Preterm infants <28 weeks GA

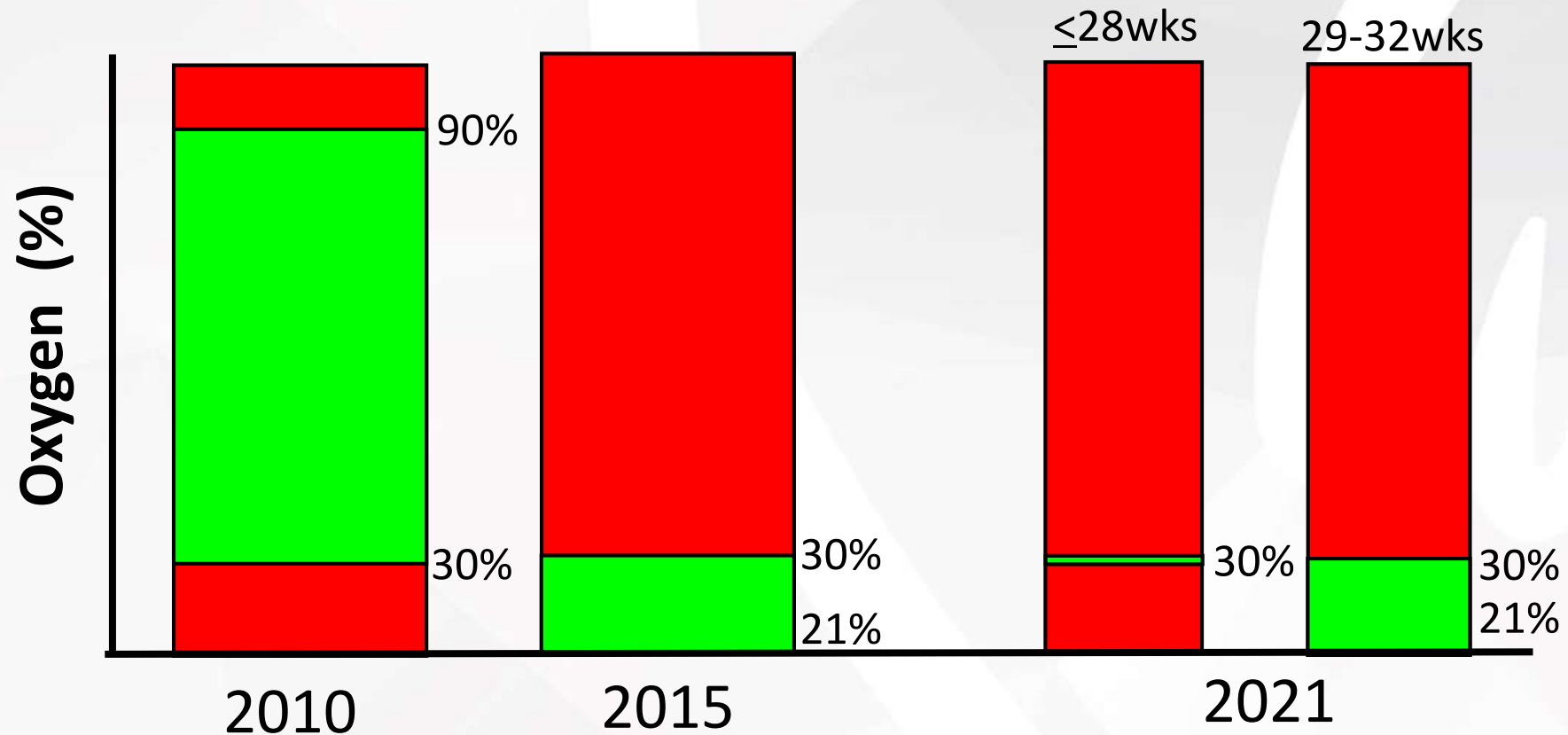
OR for mortality: 5.3 (95% CI 1.35-20)

→ Don't start with 21%

→ Start with 30% – adjust according to SpO₂

Until more data are available from randomized studies aim at a SpO₂ of 80-85% within 5 minutes

Oxygen to initiate resuscitation in preterm infants



SpO₂ >80% at 5 minutes!

Wyckoff MH et al. 2015 AHA Guidelines

Wyllie J et al. Resuscitation 2020

Madar J et al. Resuscitation 2021



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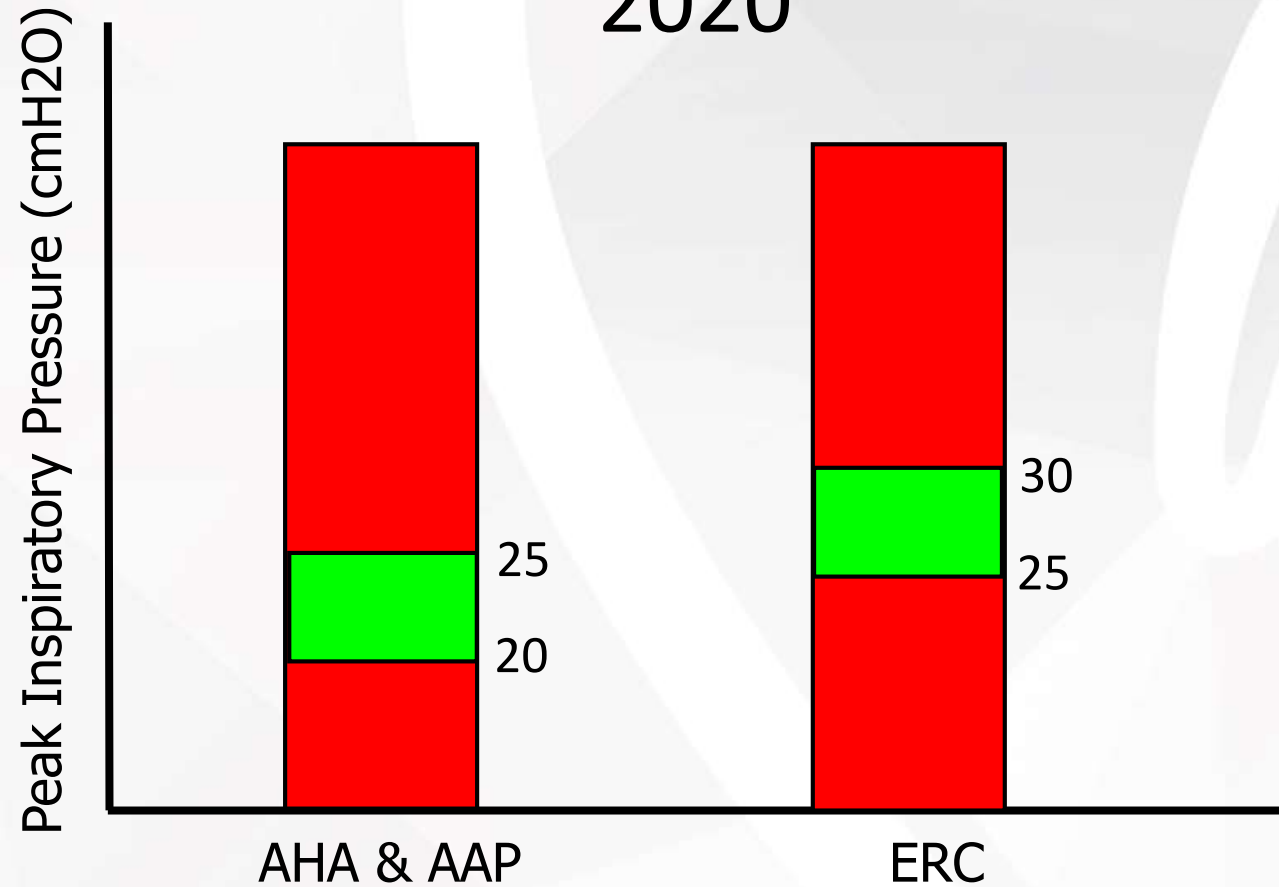
Inflation pressure



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Inspiratory Pressure for Preterm Infants (GA < 32 weeks)

2020

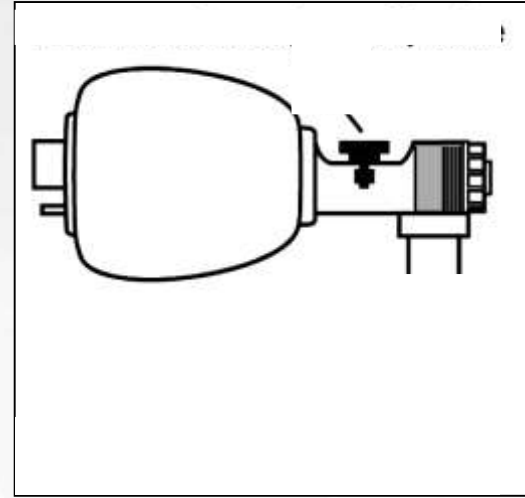


Kalid A et al. Circulation 2020
Madar J et al. Resuscitation 2021



T-piece

or



Self-inflating bag

Guidelines 2015

Treatment Recommendation

“There is insufficient evidence so that a recommendation of one device over another would be purely speculative...”

Wyckoff MH et al. Circulation 2015

Wyllie J et al. Resuscitation 2015



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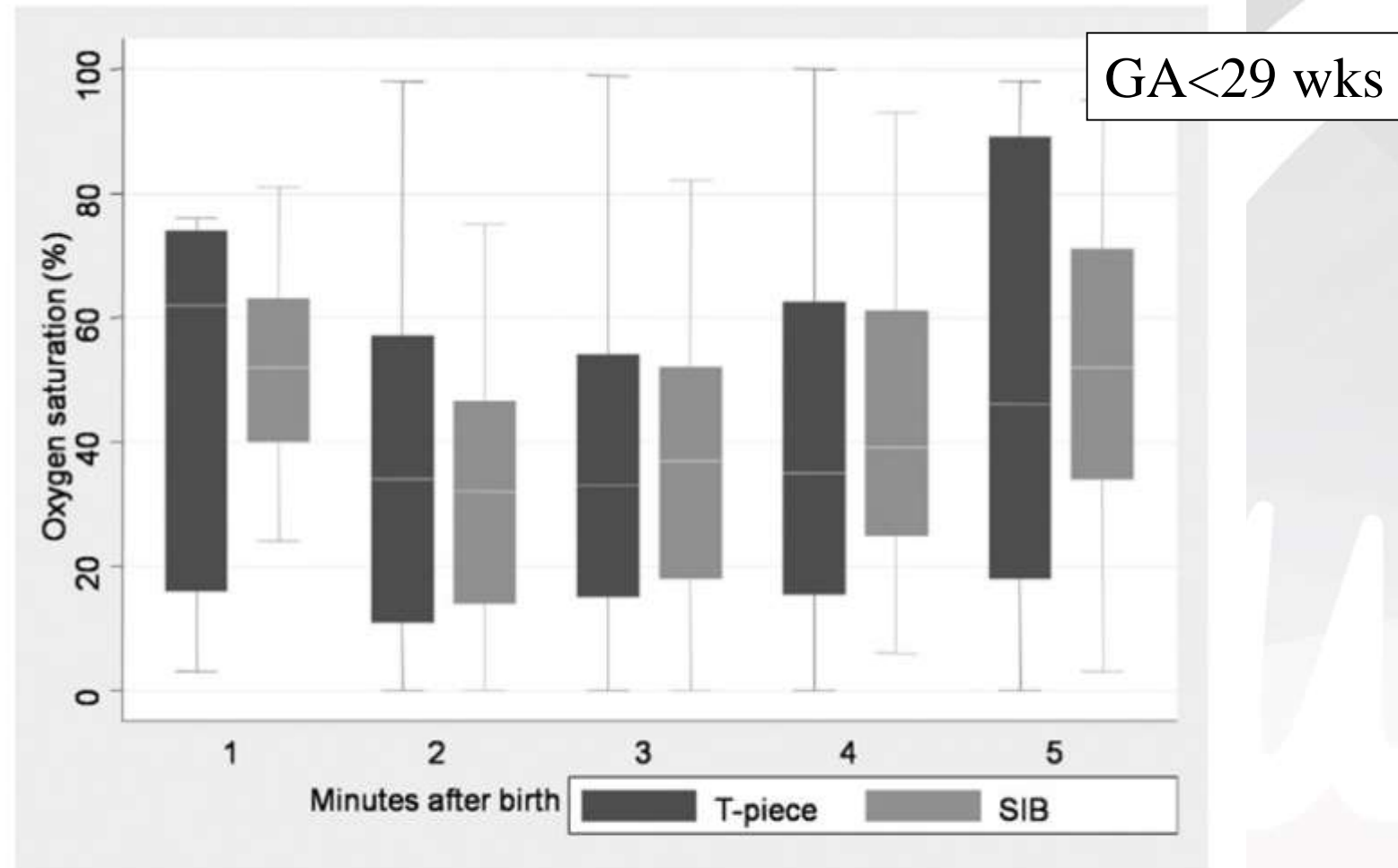


Figure 4. SpO₂ shown at each minute, for the first 6 minutes after birth, in the T-piece and SIB group. The *box plots* show the median, IQR, and range.

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 \pm SD [†]	2.7 \pm 36	3.05 \pm 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 \pm SD [‡] variability	25.58 \pm 1.9	28 \pm 4.9	-	<.001
PIP >25 cm H ₂ O, n (%)	52 (10)	184 (37)	5.0 (3.6-7.0)	<.001
Mean maximum FiO ₂ in delivery room, mean \pm SD	0.46 \pm 0.19	0.50 \pm 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 \pm SD	5.0 \pm 7.6	8.3 \pm 13.3	-	.007
Days on CPAP, mean \pm SD	7.83 \pm 11.3	7.96 \pm 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 \pm SD	13.8 \pm 17	22.8 \pm 25	-	<.001

GA > 26 weeks

GA > 26 weeks

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 \geq 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 \pm SD	21 \pm 20	35 \pm 27	-	.0007

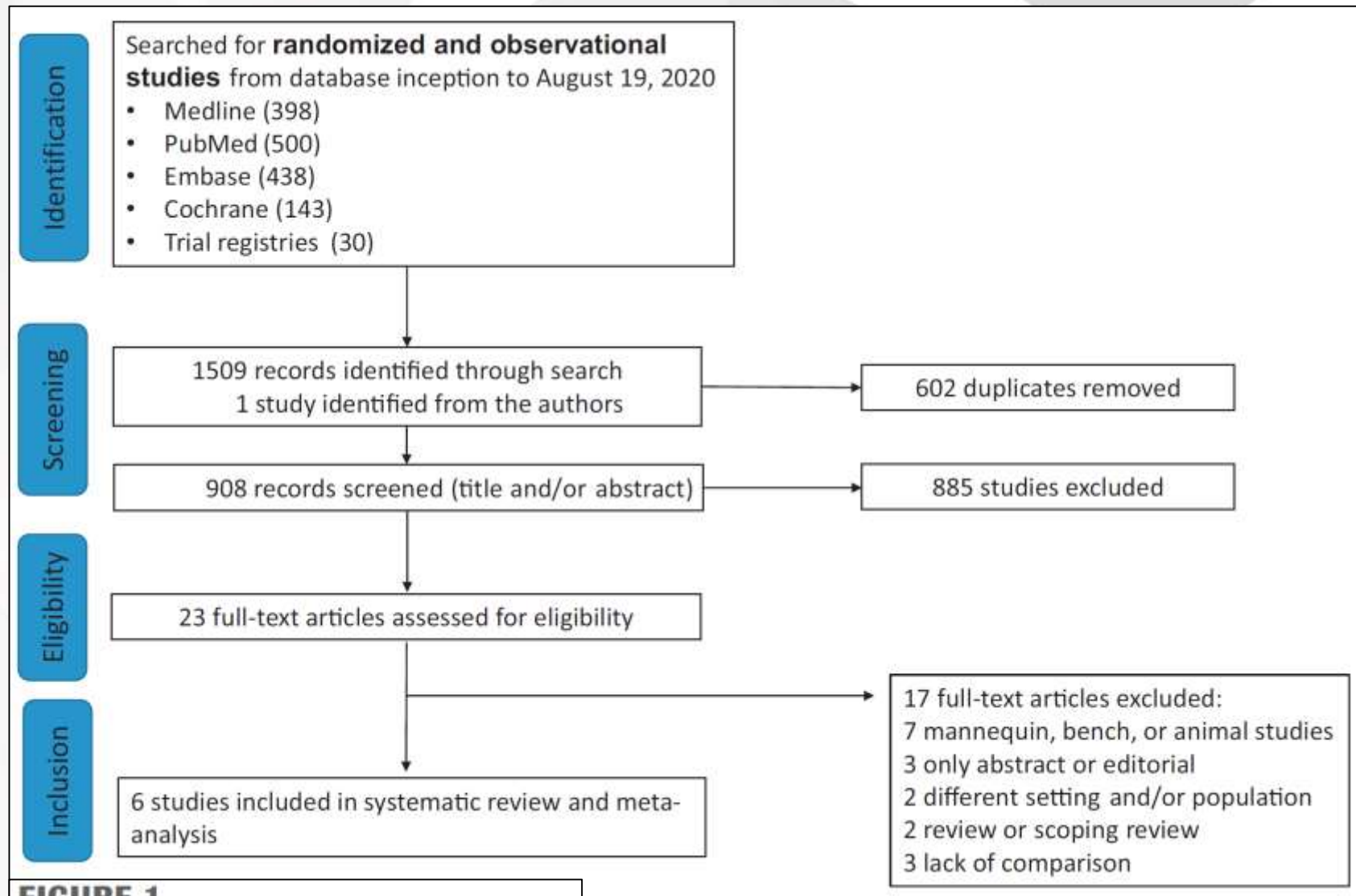
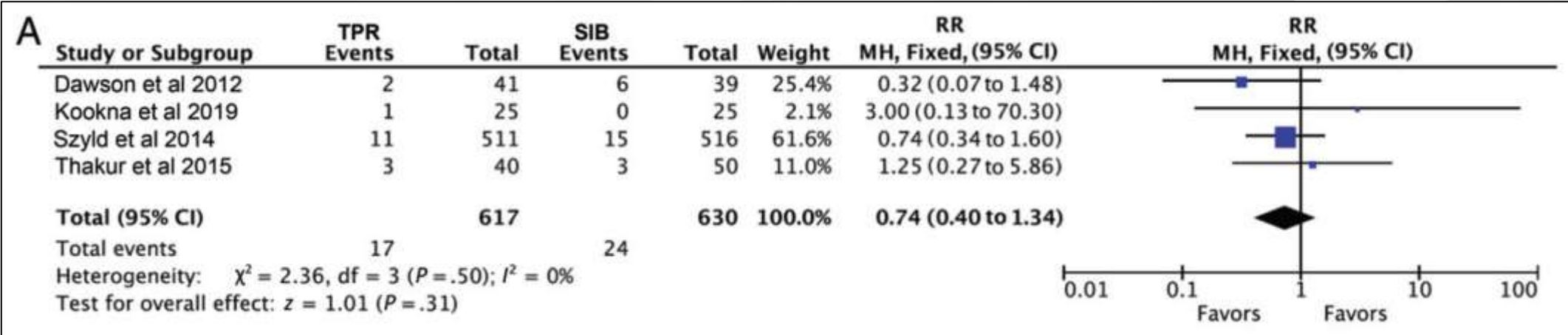
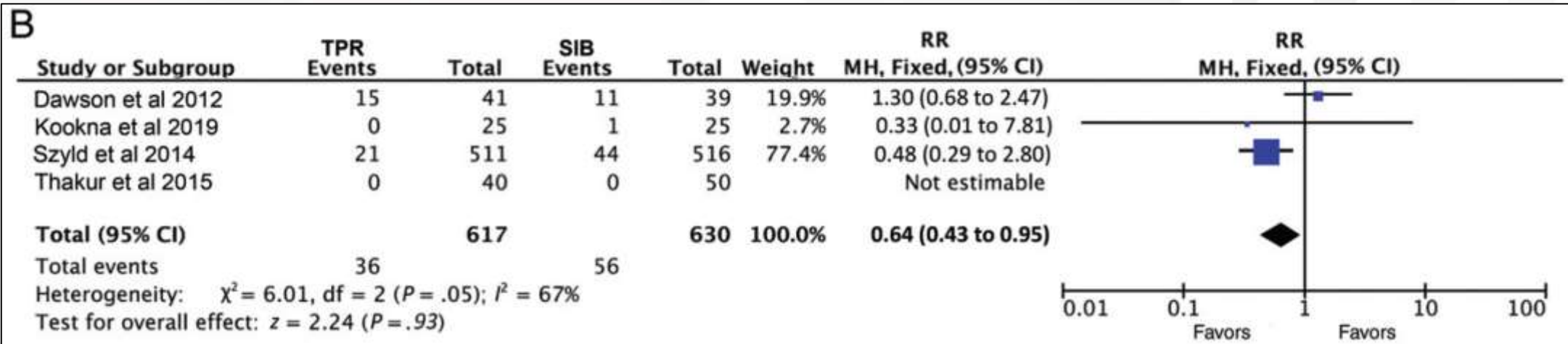


FIGURE 1
PRISMA flow diagram of study selection.

In-hospital mortality



BPD



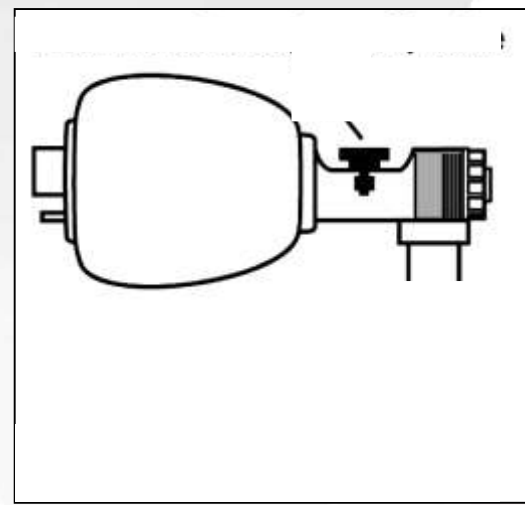
COMPARISON 1: T-PIECE RESUSCITATOR vs SELF-INFLATING BAG

Where resources permit, we suggest the use of a T-Piece resuscitator over the use of a self-inflating bag in infants receiving positive pressure ventilation at birth. (Weak recommendation, very low certainty of evidence). A self-inflating bag should be available as a back-up device for the T-piece resuscitator in case of gas supply failure (technical remark).



T-piece

>



Self-inflating bag

Which T-piece?

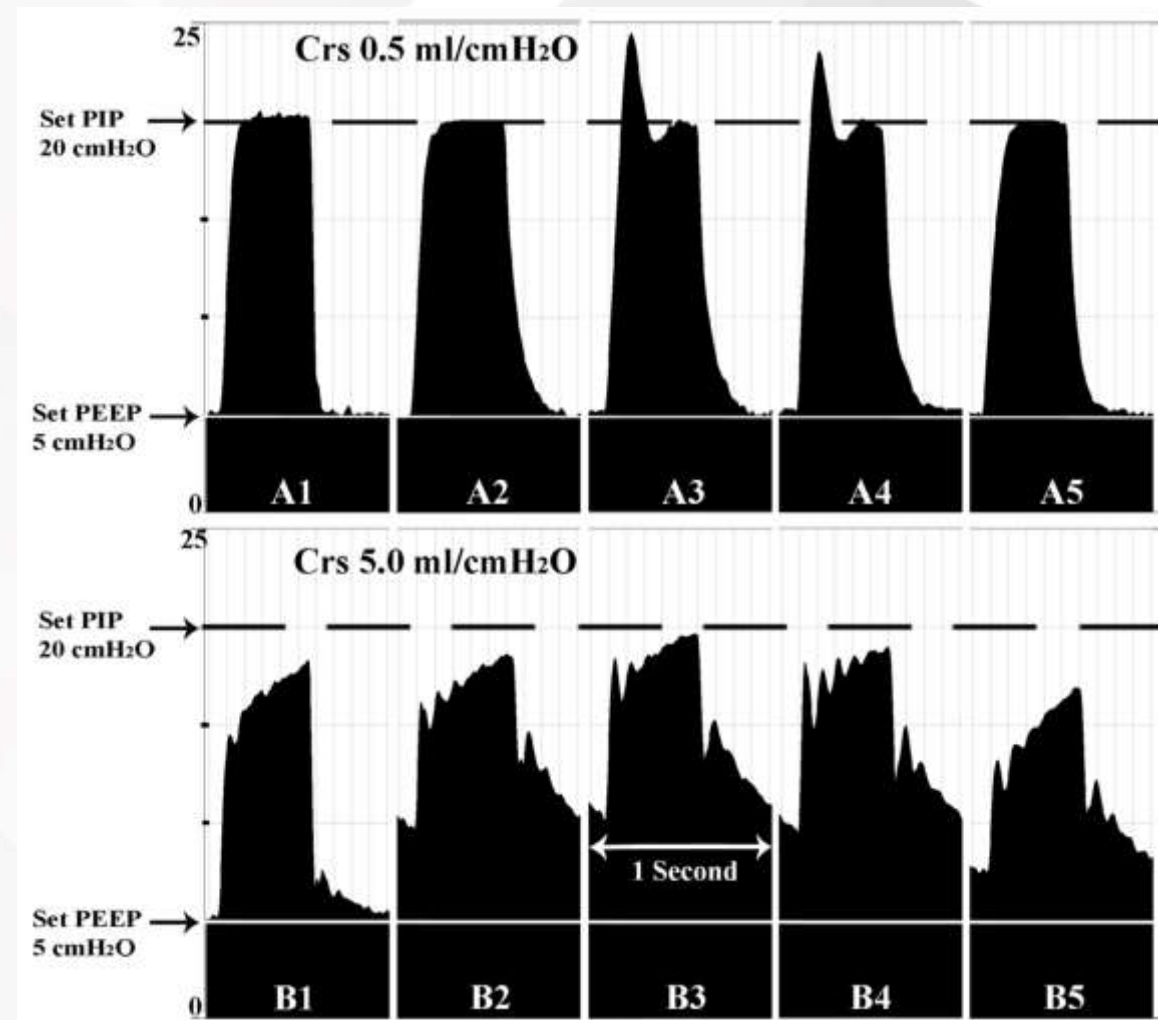


Figure 4 Examples of recorded pressure waveforms for each TPR device tested: 1: rPAP; 2: Neopuff; 3: GE Panda; 4: Draeger Resuscitaire; and 5: Atom at test lung compliances: A: 0.5 mL/cmH₂O and B: 5.0 mL/cmH₂O. Time scale 1 s per segment. PEEP, positive-end expiratory pressure; PIP, peak inflation pressure; TPR, T-piece resuscitator.

Single NF prong



Double NF prong



Short binasal prongs
(Judson)



Short binasal cannulae
(Fisher&Paykel / RAM)



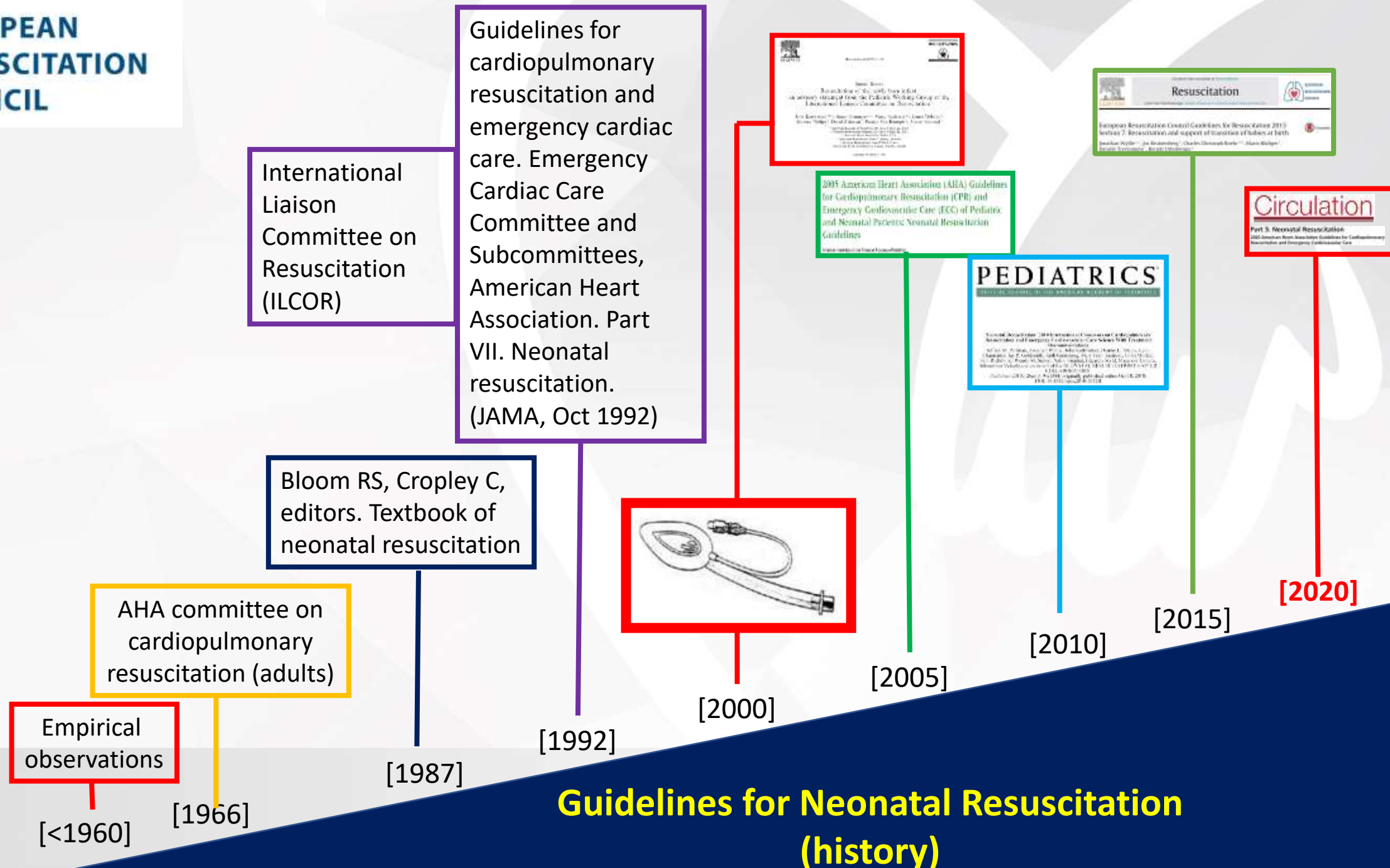


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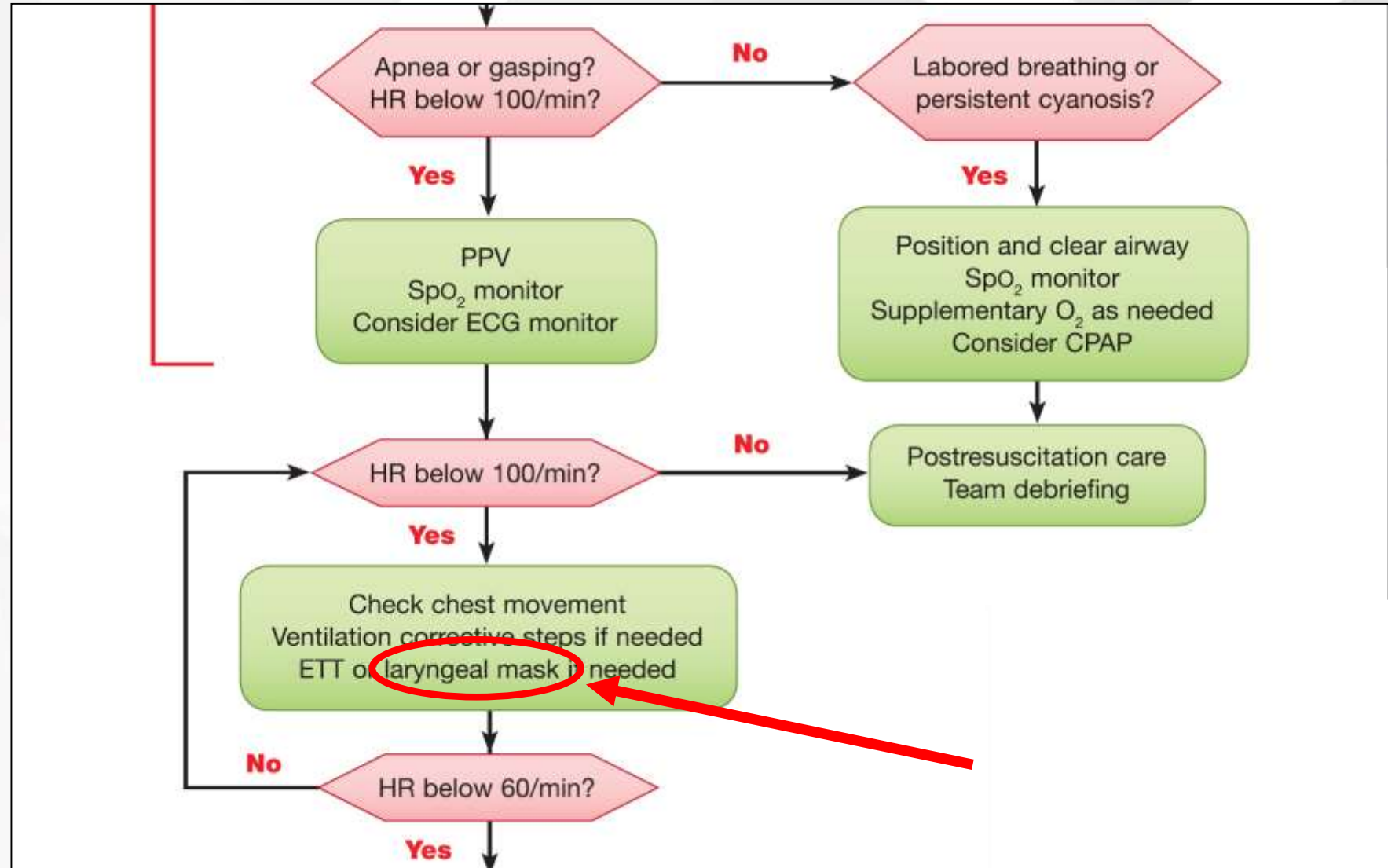
Use of the laryngeal mask



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Guidelines for Neonatal Resuscitation (history)





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Cochrane
Library

Cochrane Database of Systematic Reviews

Laryngeal mask airway versus bag-mask ventilation or endotracheal intubation for neonatal resuscitation (Review)

Qureshi MJ, Kumar M

Qureshi MJ, Kumar M, Cochrane Library 2018



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	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias and detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Esmail 2002	?	?	-	+	?	
Feroze 2008	?	?	-	?	?	
Pejovic 2015	+	+	-	+	+	
Singh 2005	+	+	-	+	?	
Trevisanuto 2015	+	+	-	+	+	
Yang 2016	-	-	-	+	+	
Zhu 2011	-	-	-	+	?	

7 RCT
Very low- to low-quality evidence
[794 infants]

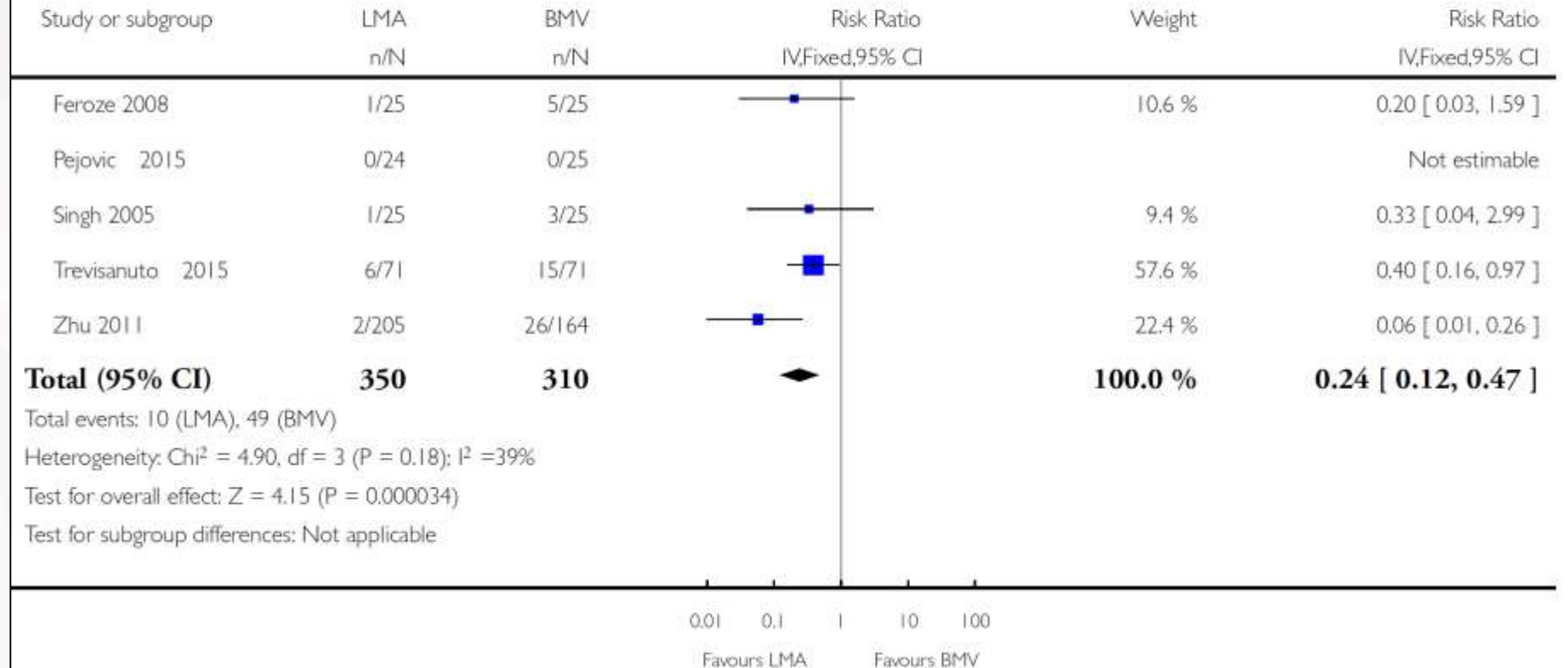
Analysis 1.2. Comparison 1 LMA versus BMV, Outcome 2 Need for intubation.

Review: Laryngeal mask airway versus bag-mask ventilation or endotracheal intubation for neonatal resuscitation

Comparison: 1 LMA versus BMV

Outcome: 2 Need for intubation

Need for intubation



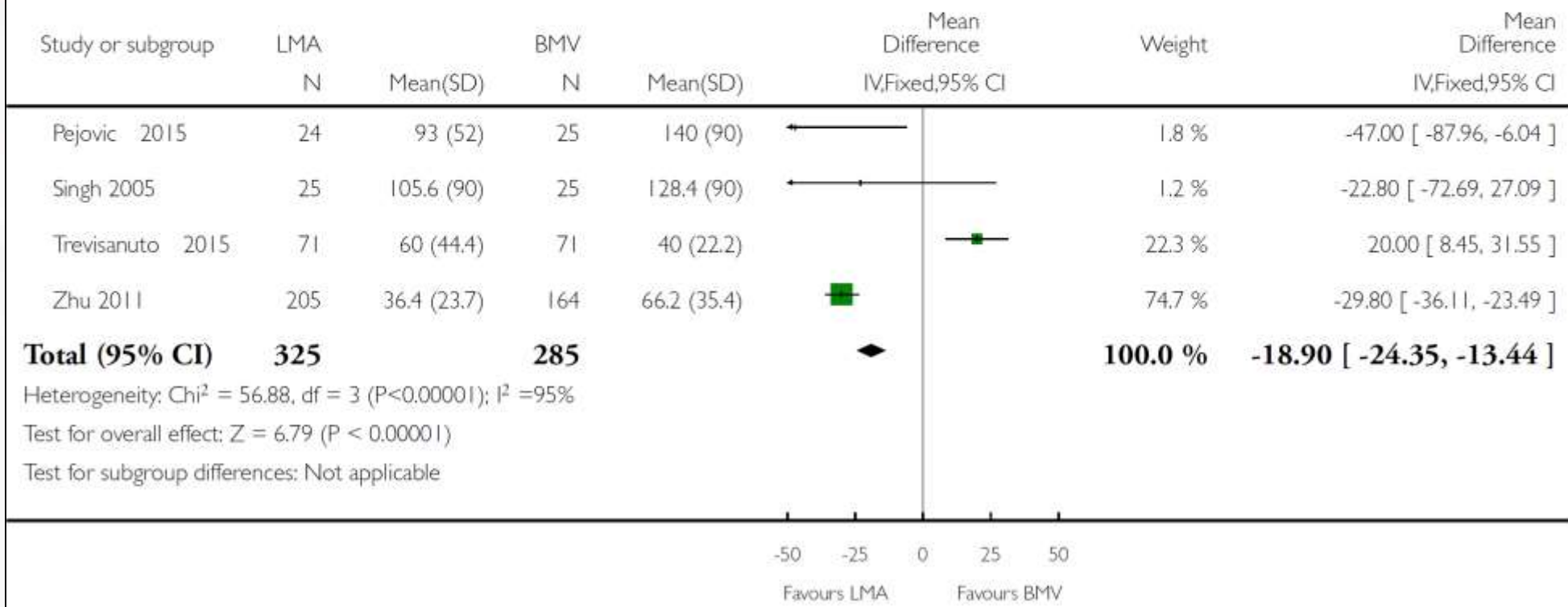
Analysis 1.4. Comparison 1 LMA versus BMV, Outcome 4 Ventilation time [seconds].

Review: Laryngeal mask airway versus bag-mask ventilation or endotracheal intubation for neonatal resuscitation

Comparison: 1 LMA versus BMV

Outcome: 4 Ventilation time [seconds]

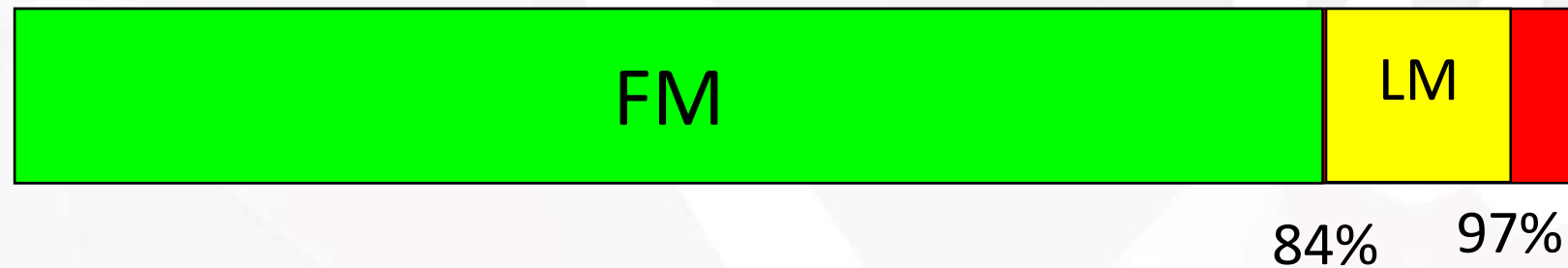
Ventilation time



Effective PPV

LM vs. FM

[late-preterm and full-term infants]



[7 RCT]

1 **Original Article**

2 **A Randomized Trial of Laryngeal Mask
3 Airway in Neonatal Resuscitation**

4 Nicolas J. Pejovic, M.D., Ph.D., Susanna Myrnerets Höök, M.D., M.Med.,
5 Josaphat Byamugisha, M.D., Ph.D., Tobias Alfvén, M.D., Ph.D.,
6 Clare Lubulwa, M.D., M.Med., Francesco Cavallin, M.Sc.,
7 Jolly Nankunda, M.D., Ph.D., Hege Ersdal, M.D., Ph.D.,
8 Mats Blennow, M.D., Ph.D., Daniele Trevisanuto, M.D., and
9 Thorkild Tylleskär, M.D., Ph.D.



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Kampala, Uganda



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November 26, 2020

RANDOMIZATION: day-by-day cluster randomization



or



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PRIMARY OUTCOME: early neonatal death (within 7 days) or admission to NICU with moderate-to-sever HIE (Thomson score >11) at day 1 to day 5 during hospitalization.

Table 2. Outcome Measures.*

Outcome	Laryngeal Mask Airway	Face Mask	Unadjusted Analysis		Adjusted Analysis†	
			Relative Risk (95% CI)	P Value	Relative Risk (95% CI)	P Value
	<i>no./total no. (%)</i>					
Primary outcome	154/563 (27.4)	144/591 (24.4)	1.12 (0.92–1.37)	0.27	1.16 (0.90–1.51)	0.26
Secondary outcomes						
Advanced resuscitation	39/566 (6.9)	39/597 (6.5)	1.05 (0.69–1.62)	—	1.08 (0.63–1.86)	—
Early neonatal death	122/563 (21.7)	109/591 (18.4)	1.17 (0.93–1.48)	—	1.21 (0.90–1.63)	—
Very early neonatal death	89/563 (15.8)	85/591 (14.4)	1.10 (0.84–1.45)	—	1.13 (0.80–1.58)	—
Admission to NICU with Thomson score of ≥11 at days 1–5 during hospitalization	53/474 (11.2)	51/504 (10.1)	1.13 (0.89–1.70)	—	1.27 (0.84–1.93)	—
Admission to NICU with Thomson score of ≥7 at days 1–5 during hospitalization	100/474 (21.1)	115/504 (22.8)	0.97 (0.78–1.21)	—	0.94 (0.70–1.27)	—
Any hospital admission during first 7 days of life	496/519 (95.6)	530/554 (95.7)	0.99 (0.97–1.02)	—	—	—

Table 2. Outcome Measures.*

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Any hospital admission during first 7 days of life	496/519 (95.6)	530/554 (95.7)	0.99 (0.97–1.02)	—	—	—

Conclusions

In neonates with asphyxia, the LMA was safe in the hands of midwives but was not superior to face-mask ventilation with respect to early neonatal death and moderate-to-severe hypoxic–ischemic encephalopathy.



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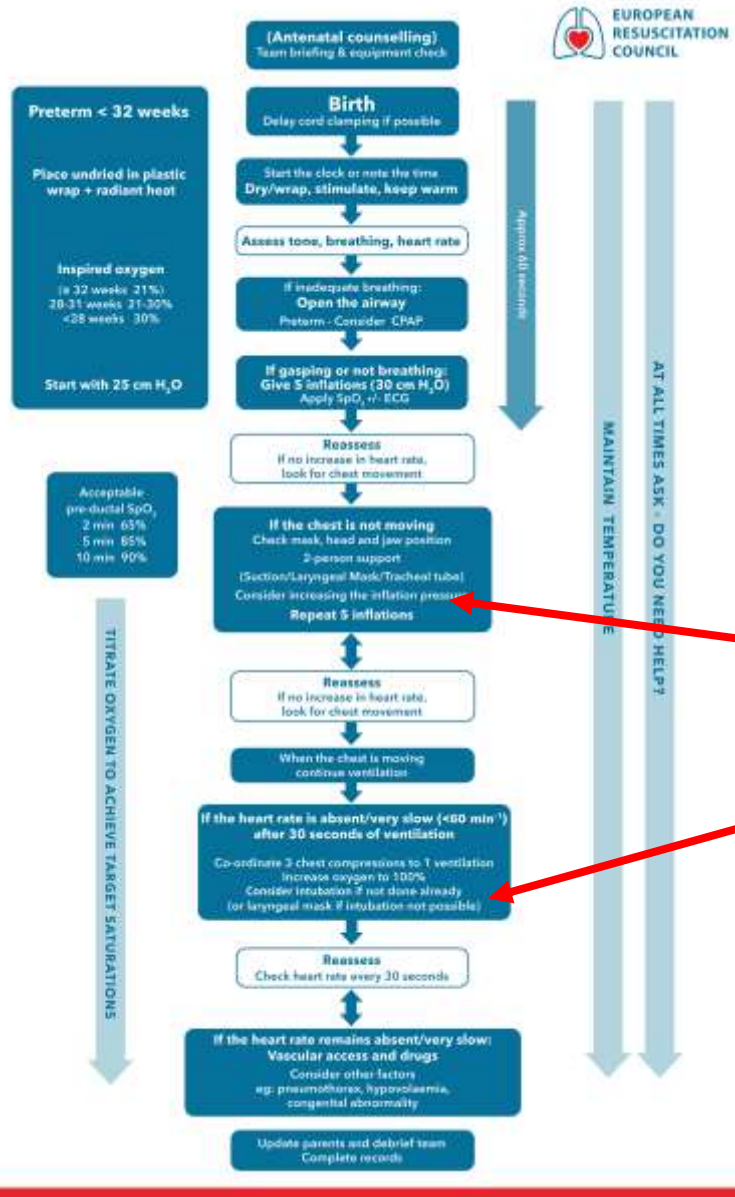
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Laryngeal mask

Use of the laryngeal mask

If facemask ventilation is unsuccessful or if tracheal intubation is unsuccessful or not feasible a laryngeal mask may be considered as an alternative means of establishing an airway in infants of >34 weeks gestation (about 2000 g, although some devices have been used successfully in infants down to 1500 g).



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Management of the umbilical cord



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~~ICC~~

DCC

UCM?



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Guidelines 2015

Cord milking

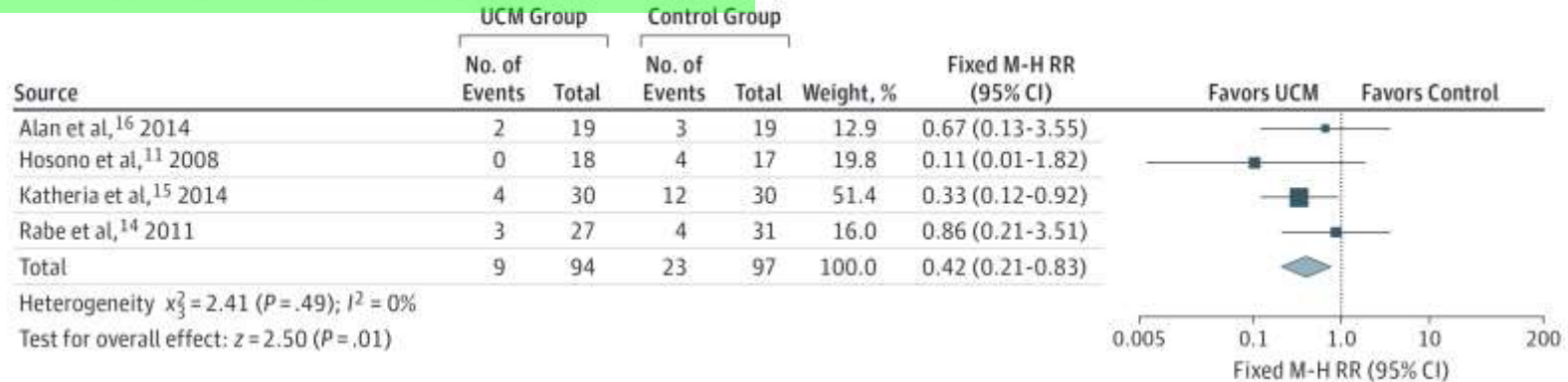
Treatment Recommendation

“We **suggest against** the routine use of cord milking for infants born at less than 29 weeks of gestation because there is insufficient published human evidence of benefit.”

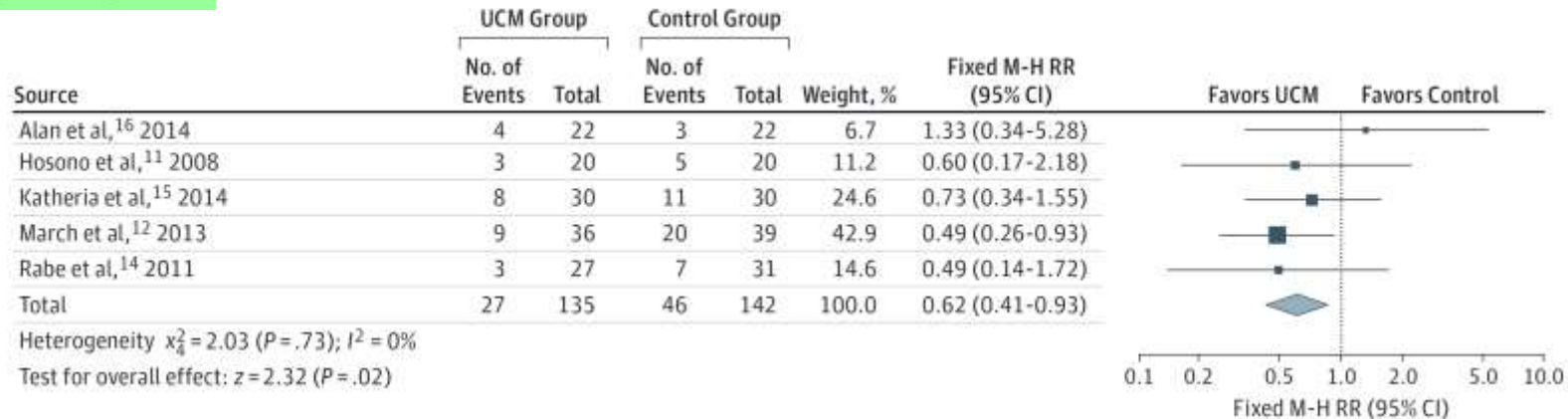
“Cord milking may be considered on an individualized basis or in a research setting as it may improve initial mean blood pressure, hematological indices and intracranial hemorrhage. There is no evidence for improvement or safety in long-term outcomes. (Weak recommendation, low level of evidence).”

Efficacy and Safety of Umbilical Cord Milking at Birth A Systematic Review and Meta-analysis

B Oxygen requirement at 36 wk, postmenstrual age in preterm infants^a



C IVH of all grades^a



Benefits of umbilical cord milking versus delayed cord clamping on neonatal outcomes in preterm infants: A systematic review and meta-analysis

Conclusions

UCM wasn't reduced in-hospital mortality and need for transfusion compared to DCC. But our study suggests that UCM may lower the risk of IVH and improve certain neurodevelopmental outcomes compared to DCC in preterm infants.

Premature Infants Receiving Cord Milking Or Delayed Cord Clamping: A Randomized Controlled Non-inferiority Trial

P: In infants with GA 23-31 weeks

I: does Umbilical Cord Milking

C: Delayed Cord Clamping

O: reduce Intraventricular hemorrhage (IVH) or Death

Premature Infants Receiving Cord Milking Or Delayed Cord Clamping: A Randomized Controlled Non-inferiority Trial


Primary outcome

Intraventricular hemorrhage (IVH) or death

DDC	UCM	p-value
19/238 (8%)	28/236 (12%)	0.16

Premature Infants Receiving Cord Milking Or Delayed Cord Clamping: A Randomized Controlled Non-inferiority Trial

Trial stopped!



[23-27 wks]

Severe intraventricular hemorrhage (IVH)

DDC	UCM	p-value
(6%)	20/93 (22%)	0.0019

Management of the umbilical cord

Clamping after at least 60 s is recommended, ideally after the lungs are aerated. Where delayed cord clamping is not possible cord milking should be considered in infants >28 weeks gestation.



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POST-LOCKDOWN

Prognosis



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Discontinuing Resuscitative Efforts

An Apgar score of 0 at 10 minutes is a strong predictor of mortality and morbidity in late preterm and term infants.

We suggest that, in infants with an Apgar score of 0 after 10 minutes of resuscitation, if the heart rate remains undetectable, it may be reasonable to stop assisted ventilation; however, the decision to continue or discontinue resuscitative efforts must be individualized.

Discontinuing Resuscitative Efforts

“Newborns immediately after birth presenting with at least 10 minutes of asystole, bradycardia, or pulseless electrical activity for which CPR is indicated.”

Discontinuing Resuscitative Efforts

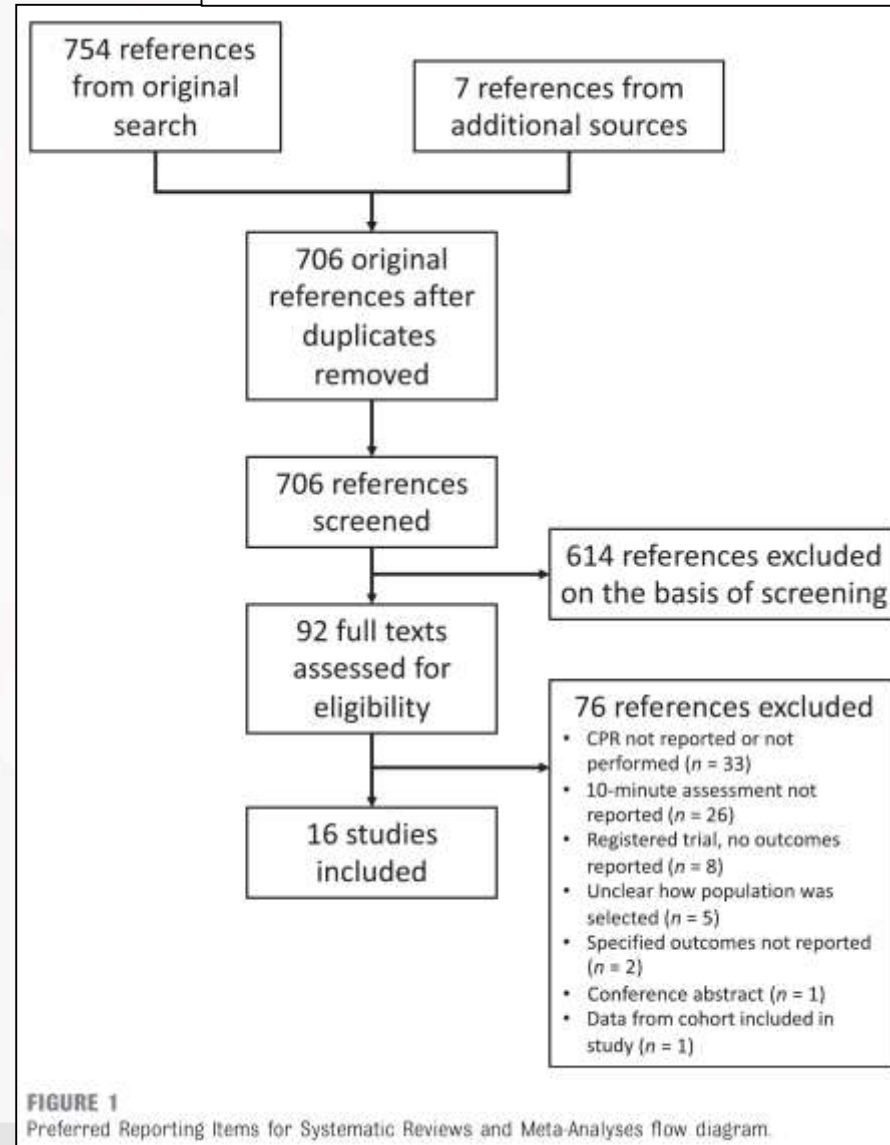


FIGURE 1
Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

Discontinuing Resuscitative Efforts

TABLE 5 Subgroup Analyses for Survival and Neurodevelopmental Outcomes

Subgroup	Studies Contributing	Infants, <i>N</i>	Survival to Last Follow-up, <i>n</i> (%)	Infants Assessed for Neurodevelopment, <i>n</i>	Survival Without Moderate or Severe NDI	
					<i>n</i> (% of Survivors Assessed)	<i>n</i> (% of All Enrolled)
Population level studies	6 ^{12,13,15,16,23,24}	240	67 of 240 (28)	15	9 of 15 (60)	9 of 131 ^a (7)
Therapeutic hypothermia treatment	9 ^{10,11,17,19-21,23-25}	206	122 of 206 (59)	57	21 of 57 (37)	21 of 105 ^b (20)
Gestational age \geq 36 wk	13 ^{10-13,15,17-21,23-25}	350	189 of 350 (54)	73	23 of 73 (32)	23 of 166 ^c (14)
Gestational age $<$ 36 wk	7 ^{12,13,15,20,23-25}	144	41 of 144 (28)	8	5 of 8 (63)	5 of 42 ^d (12)
Heart rate detection reported \geq 20 min after birth	5 ^{11,20,21,23,24}	39	15 of 39 (38)	15	6 of 15 (40)	6 of 39 (15)

Discontinuing Resuscitative Efforts

If the heart rate of a newly born term infant remains undetectable for more than 20 minutes after birth despite the provision of all recommended steps of resuscitation and excluding reversible causes, discuss with the clinical team and family and consider stopping resuscitation.



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Summary of changes since the 2015 guidelines

Summary of changes since the 2015 guidelines

Management of the umbilical cord

Clamping after at least 60 s is recommended, ideally after the lungs are aerated. Where delayed cord clamping is not possible cord milking should be considered in infants >28 weeks gestation.

Infants born through meconium-stained liquor

In non-vigorous infants, recommendations are against immediate laryngoscopy with or without suction after delivery, because this may delay aeration and ventilation of the lungs.

Use of the laryngeal mask

If facemask ventilation is unsuccessful or if tracheal intubation is unsuccessful or not feasible a laryngeal mask may be considered as an alternative means of establishing an airway in infants >28 weeks gestation (about 2000 g, although some data suggest successful use in infants down to 1500 g).

Inflation pressure

If there is no response to initial inflation, a gradual increase in the inflation pressure may then be considered. A starting pressure of 25 cm H₂O is suggested for preterm infants <32 weeks gestation.

Air/oxygen for preterm resuscitation

Recommendations are for starting in air at 32 weeks gestation or more, 21-30% inspired oxygen at 28-31 weeks gestation and 30% inspired oxygen at <28 weeks gestation.

The concentration should be titrated to achieve saturations of $\geq 80\%$ at 5 min of age because there is evidence of poorer outcomes where this is not achieved.

Chest compressions

If chest compressions are required, the inspired oxygen concentration should be increased to 100% and consideration given towards securing the airway ideally with a tracheal tube.

Vascular access

The umbilical vein is still favoured as the optimal route of access but, intraosseous access is a viable alternative method of emergency access for drugs/fluids.

Adrenaline

There is an increased response to adrenaline after optimising ventilation. An intravenous dose of adrenaline of 0.1 mg kg⁻¹ (10 µg kg⁻¹) is recommended, repeated every 3-5 min in the absence of a response.

Glucose during resuscitation

An intravenous dose of 250 mg kg⁻¹ (2.5 mL kg⁻¹ of 10% glucose) is suggested in a prolonged resuscitation to reduce the likelihood of hypoglycaemia.

Prognosis

Failure to respond despite 10-20 mins of intensive resuscitation is associated with high risk of poor outcome. It is appropriate to consider discussions with the team and family about withdrawal of treatment if there has been no response despite the provision of all recommended steps of resuscitation and having excluded reversible causes.

Work in progress...



Italian Resuscitation Council

♥♥♥.ircouncil.it

Grazie!

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