

# The Golden Hour (Minutes)-Neonatal Resuscitation

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# The Role of the Fetal Lung *In Utero*

- The fetal lung is not involved in gas exchange
  - Gas exchange performed by the placenta
  - Lung is fluid filled
  - High pulmonary vascular resistance with only ~10% of the right cardiac output going to the lungs
- Primary role of the fetal lung is growth and development



# Pulmonary Transition at Birth

- Basic requirements for gas exchange
  - Ventilation
    - Rapid fluid clearance
    - Establishment of air-filled functional residual capacity
    - Spontaneous breathing
  - Perfusion
    - Rapid reduction in pulmonary vascular resistance
    - Adequate cardiac output with pulmonary perfusion
    - Delaying cord clamping until the lung is inflated may be an advantage in maintaining cardiac output



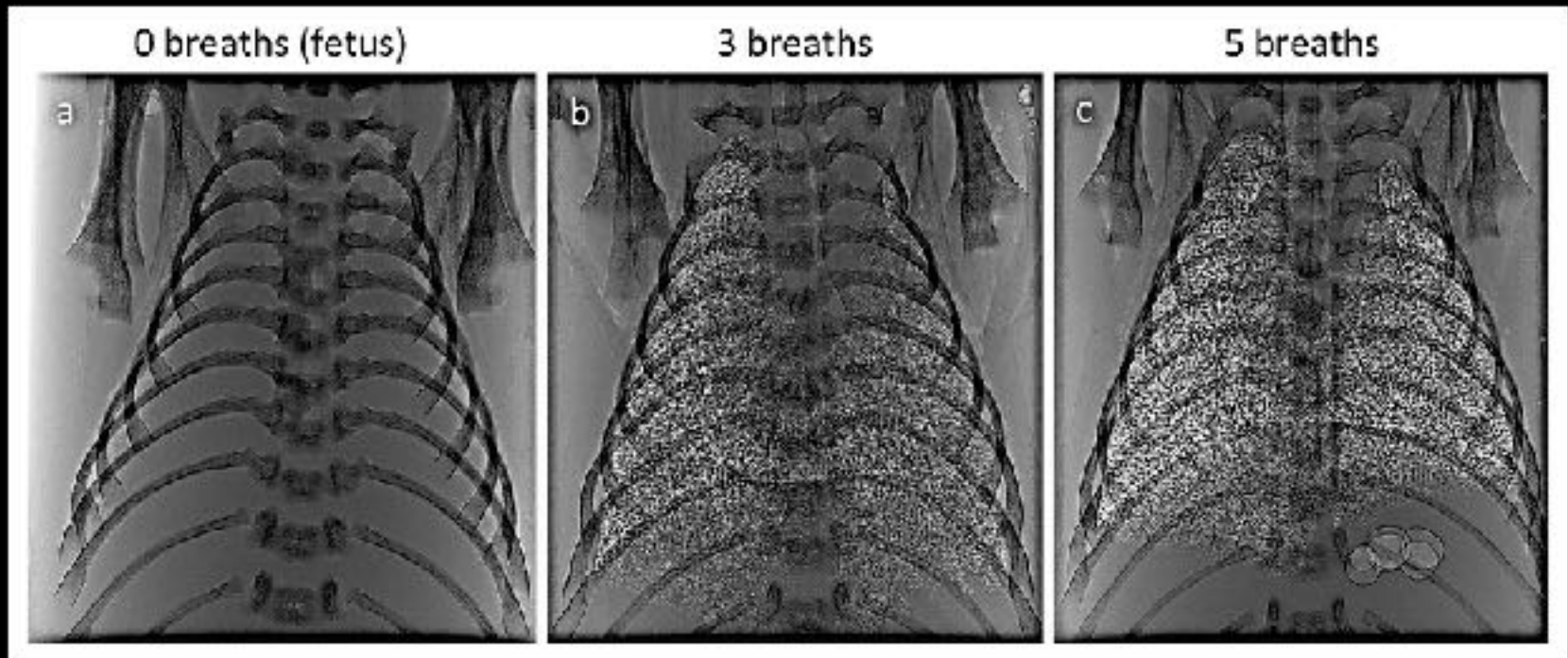
Photo credit: OB-GYN  
Dr. Aris Tsigris



<https://commons.wikimedia.org/w/index.php?title=File:HumanNewborn.JPG&oldid=291359275>

# Initial breaths clear lung fluid

## Newborn Rabbit Pups



**Negative intrathoracic pressure**

# Lung Aeration: THE Key to Successful Transition

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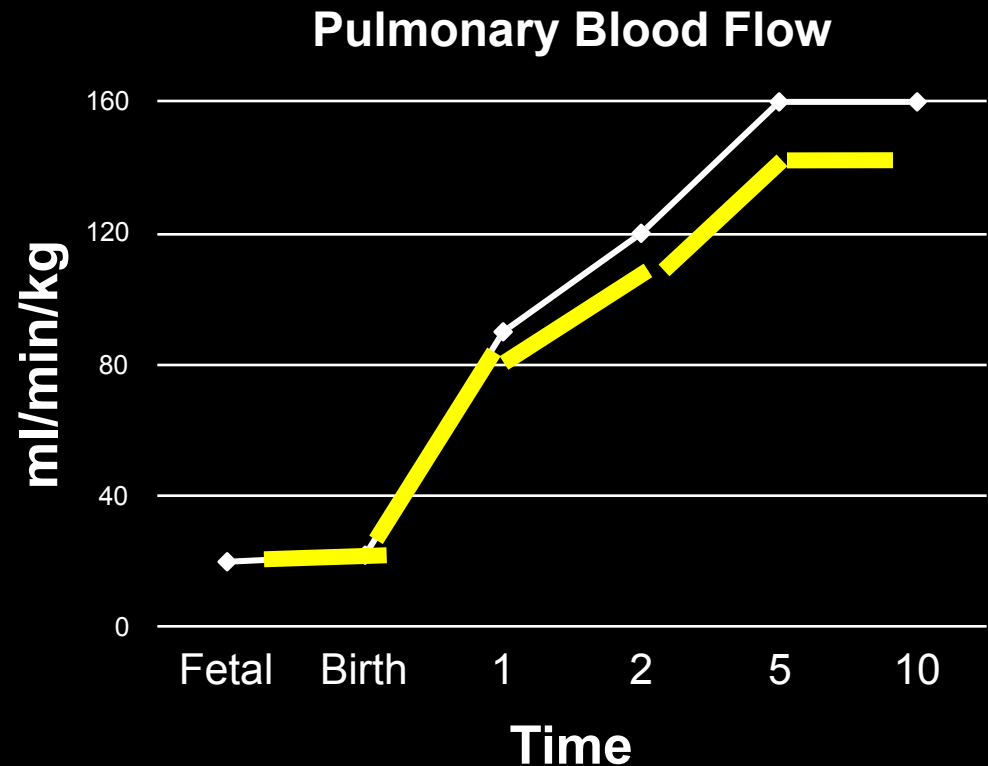
- Lung Aeration
  - Not only critical for gas exchange
  - Also responsible for initiating the cardiovascular changes at birth
- THE critical central step that initiates the sequence of interdependent physiologic changes that enable the infant to transition to life independent of the placenta after birth



AAP-NRP Photo

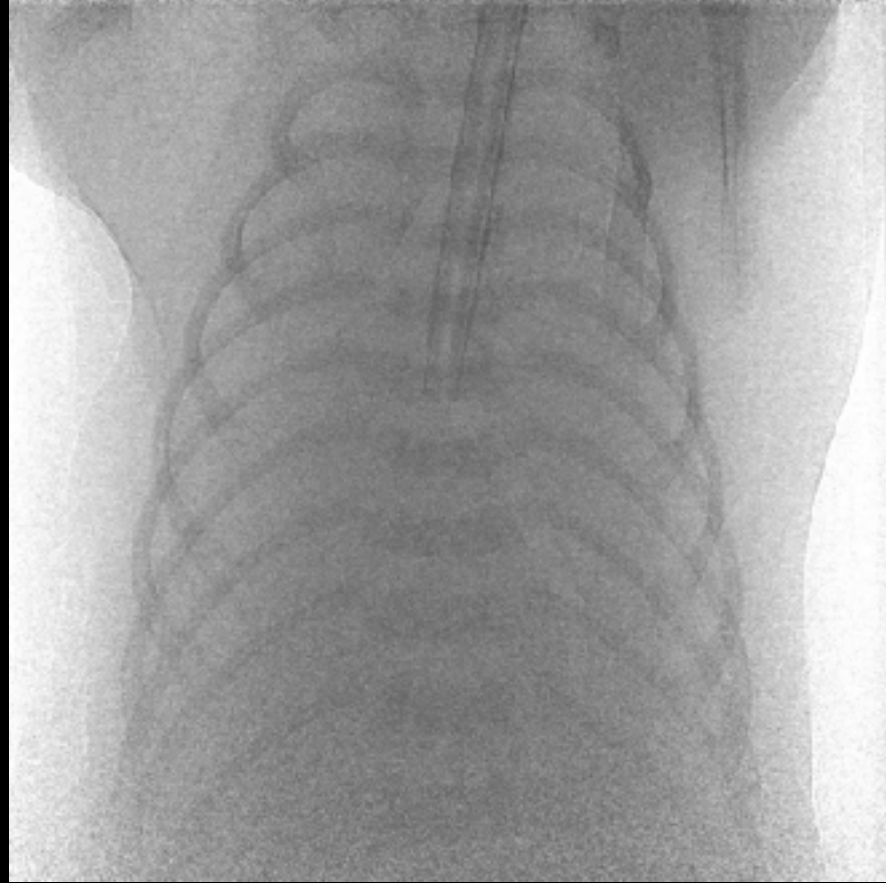
# Lung Aeration Decreases Pulmonary Vascular Resistance

- Blood flow increases 8-10 times in first minutes of life
  - Mechanical distention
  - Oxygen
  - Nitric oxide & prostacyclin
  - Neural pathways?



# Aeration of the lung increases pulmonary blood flow

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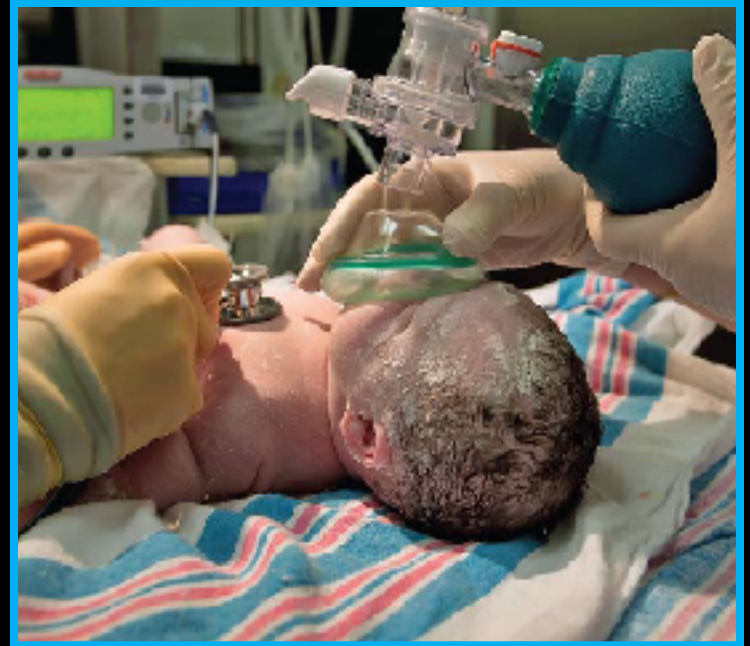




# Ventilation, Ventilation, Ventilation

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“Ventilation of the lungs is the **single most important** and most effective step in resuscitation of the compromised newborn.”





# Impending Delivery of ELGAN Infant

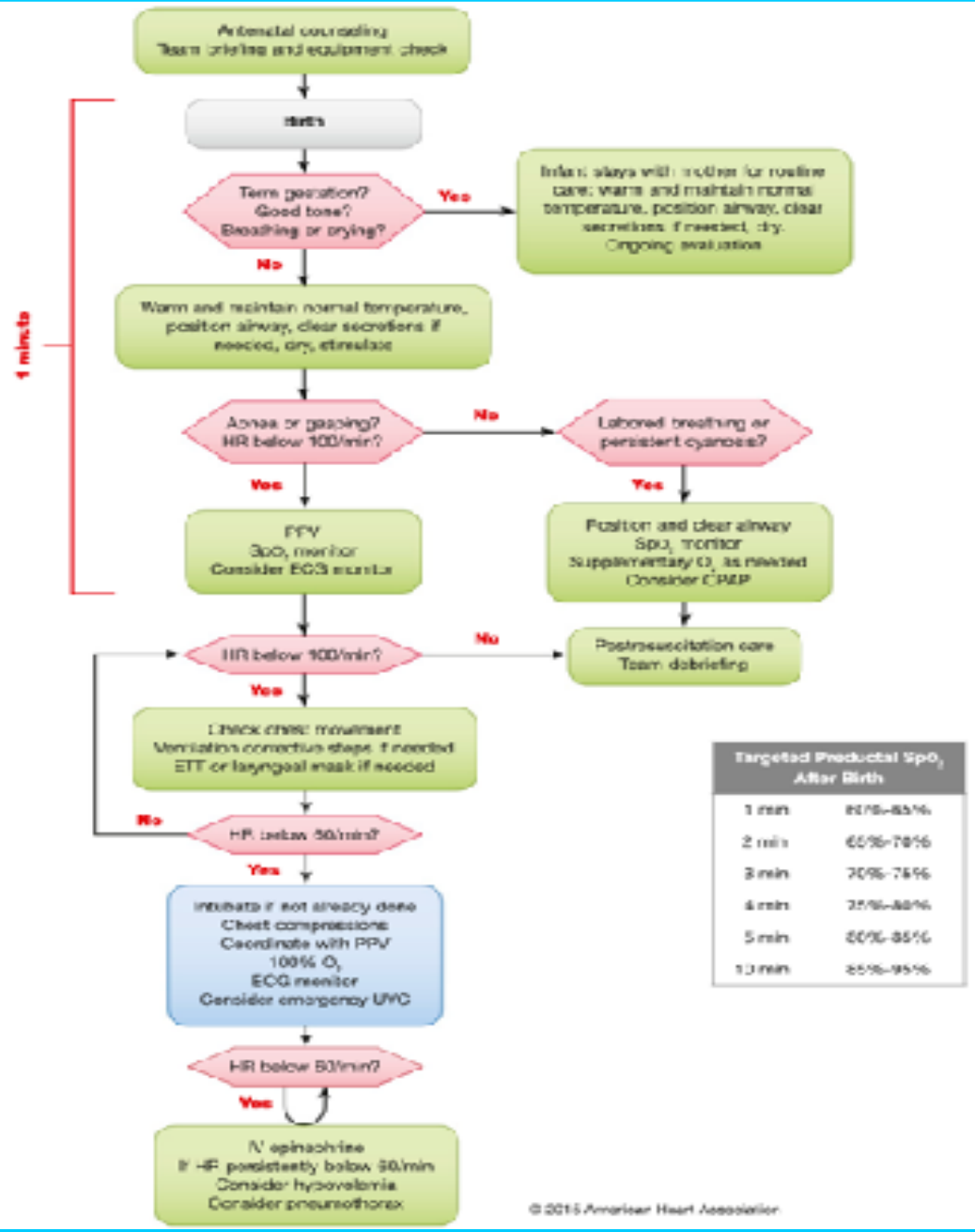
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- 36 yo G1P0 mom
  - severe pre-eclampsia
  - membranes intact
  - no history of trauma
  - Received 1 dose steroids 1 hour ago
- Bedside sono supports her 27 wk EGA dates
  - Estimated fetal weight 820g
  - Female, singleton
- Category 2 Fetal Heart Rate Tracing and breech position
- C/S under epidural anesthesia



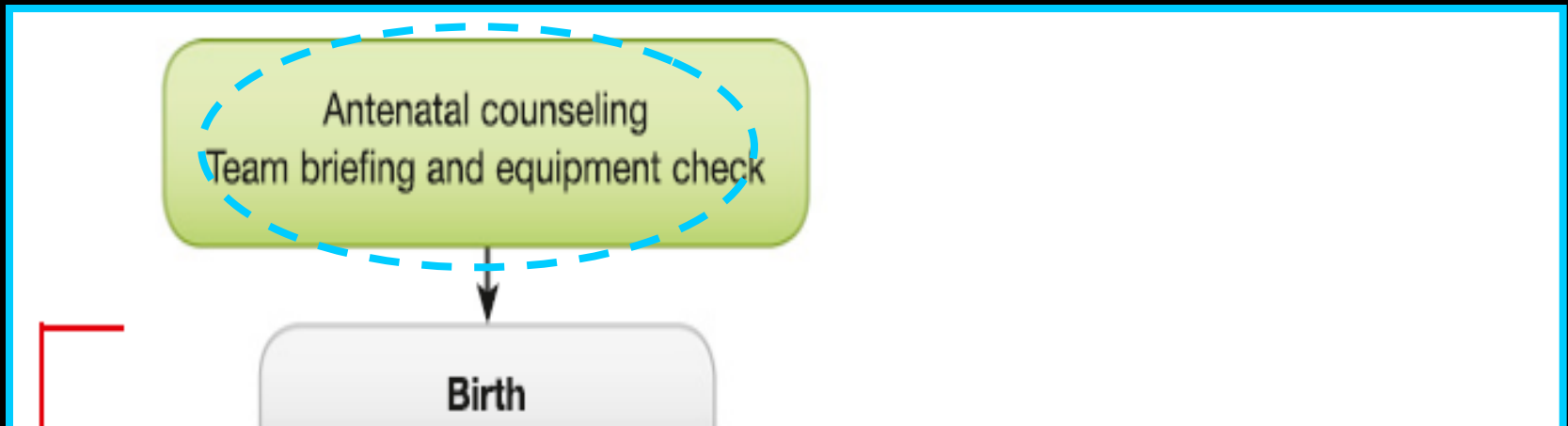
# Current Algorithm For Neonatal Resuscitation for North America

- Adopted across the US and Canada on Jan 1, 2017





- Due to both the maternal and fetal condition delivery will be imminent.



# Antenatal Counseling

- Meeting with parents before the birth of an extremely preterm baby is very important
  - Parents
  - Medical Providers
- These discussions can be difficult
  - Large amount of complex information to convey
  - Parents very stressed
- Need both national and local outcome data and to understand the limitations of each
  - If necessary consult with specialists at your regional referral center to obtain up to date information

# Antenatal Counseling

- Best to consider multiple factors
  - Gestational Age
  - Estimated Fetal Weight
  - Gender
  - Singleton or Multiple
  - Has mother received antenatal steroids
- Ideally, both the obstetric provider and the neonatal provider should be present to talk to the parents
  - Perspectives may differ
  - Such differences should be discussed **BEFORE** meeting with parents so that information is consistent

Preterm Outco... Back

Gestation Select Age

Birth Weight  g

Sex  Male  Female

Singleton Birth  Yes

Antenatal Steroids  Yes

Survival %

Survival without profound neuro-disability %

Survival without med to

Calc Info Algorithm Reference Reset Calc

## United States ELBW Outcome Calculator

Based on a prospectively studied cohort of 4446 extremely premature infants: 18-22 mo outcomes

Tyson JE et al Intensive Care for Extreme Prematurity: Moving Beyond Gestational Age. [N Engl J Med 2008;358:1672-81](#)

Rysavi et al. Evaluation of an updated NICHD extremely preterm birth outcome estimator in the Vermont Oxford Network. [PAS 2018-publication available very soon](#)

# Parkland Hospital Survival & Survival without Severe Illness by OB EGA 2014-2019



	23wk	24wk	25wk	26wk	27wk	28wk	29wk	30wk	31wk	32wk	33wk	34wk
<b>Total Patients</b>	23	59	72	92	89	109	145	160	253	314	473	824

Denominator: all patients excluding those with comfort care

Severe illness includes PDA ligation, severe BPD, surgical NEC, spontaneous intestinal perforation, Grade 3 or 4 IVH, IVH w/surgery for hydrocephalus, cystic PVL, severe ROP (Stage $\geq$ 4, Avastin or laser therapy)

**(Stage $\geq$ 4, Avastin or laser therapy)**



# Preparation for ELGAN Delivery

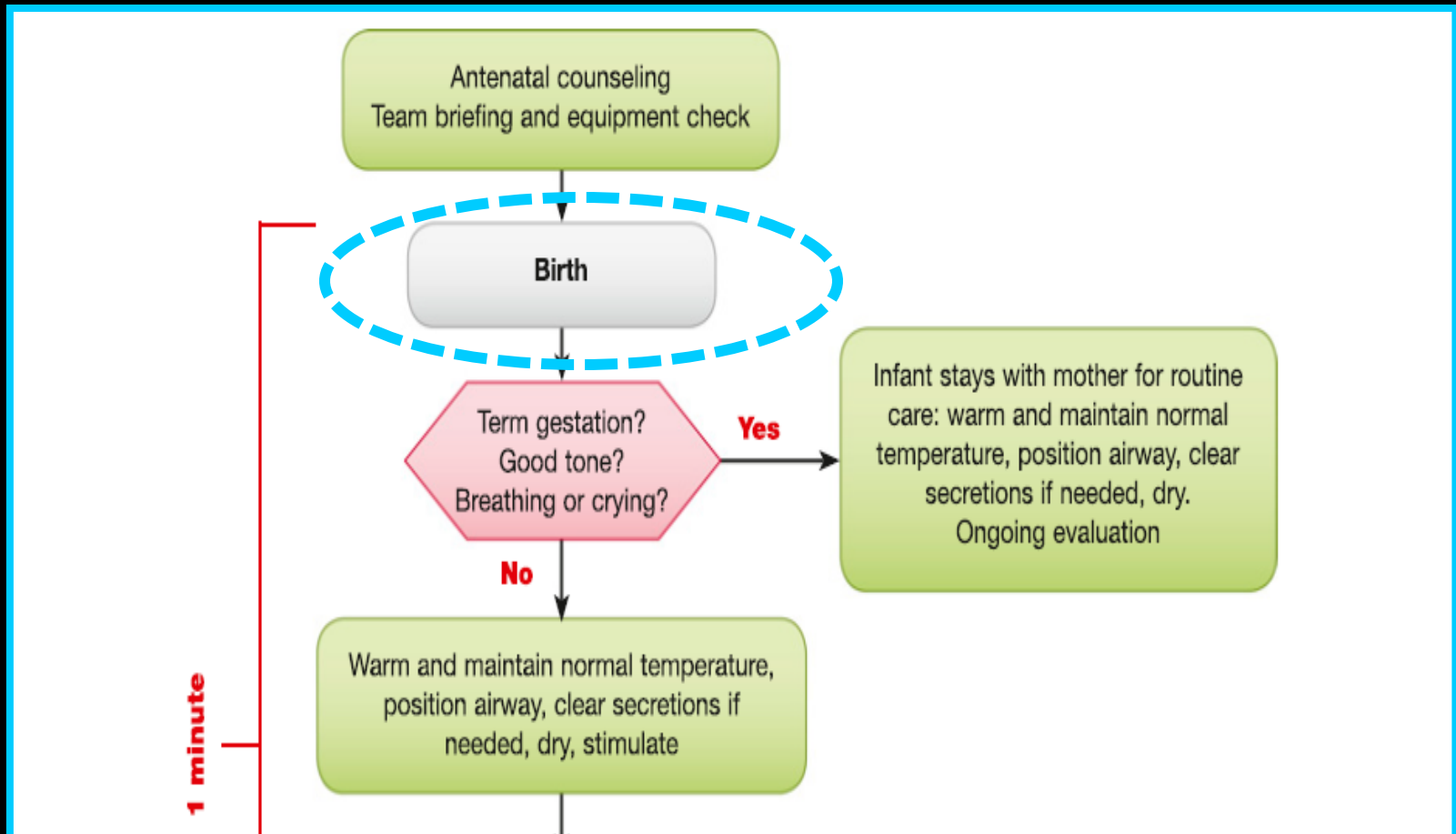


AAP-NRP photo

- Adequate trained personnel (basic team)
  - Neonatologist, Nurse, Respiratory Therapist, Recorder
- Thermal Protection (warm environmental temperature, radiant warmer, plastic wrap, thermal mattress, warm humidified gas)
- PPV device that can provide PEEP/CPAP
- Zero blade and 2.5 endotracheal tube (No laryngeal mask)
- Adjust starting O<sub>2</sub> concentration (FiO<sub>2</sub> 0.21-0.3)
- Pulse Oximetry
- Discussion with OB regarding plans for delayed cord clamping if infant active at delivery



# At birth, collaborate with obstetrical team to decide whether to perform delayed cord clamping





# Delayed Cord Clamping (DCC) Preterm Infants?

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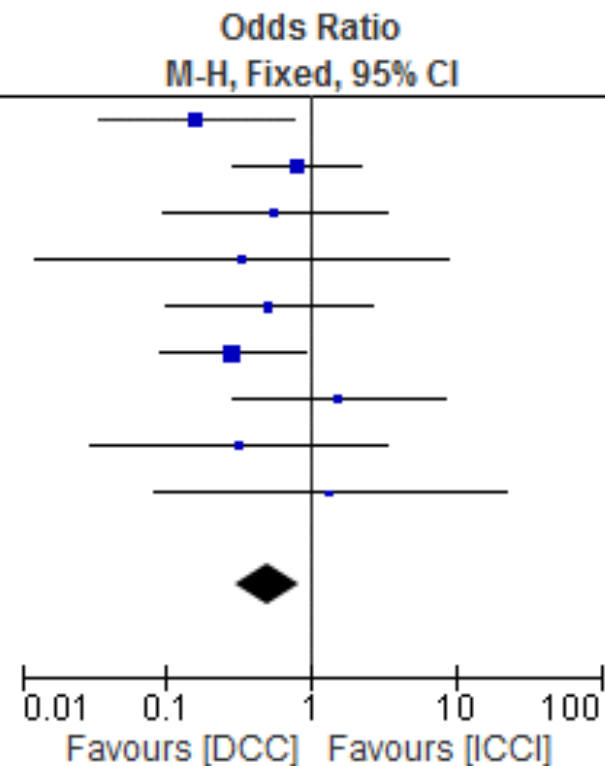
- Outcomes examined: mortality, severe IVH, any IVH, hemodynamic stability, neurodevelopment
- Sixteen studies included
  - 12 RCTs (691 cases)
  - 4 Observational Studies (811 cases)
- No difference in mortality or severe IVH
- No data for neurodevelopment
- DCC improved any IVH, hemodynamic stability

# Outcome: PVH/IVH (gr I-IV)

<RCT>

Study or Subgroup	DCC		ICC		Weight	Odds Ratio
	Events	Total	Events	Total		M-H, Fixed, 95% CI
Hofmeyr 1988	8	23	10	13	19.6%	0.16 [0.03, 0.75]
Hofmeyr 1993	8	40	11	46	19.3%	0.80 [0.28, 2.23]
Kugelman 2007	2	30	4	35	8.1%	0.55 [0.09, 3.26]
McDonnell 1997	0	15	1	16	3.3%	0.33 [0.01, 8.83]
Mercer 2003	3	16	5	16	9.6%	0.51 [0.10, 2.62]
Mercer 2006	5	36	13	36	26.4%	0.29 [0.09, 0.91]
Oh 2011	4	16	3	17	5.1%	1.56 [0.29, 8.38]
Rabe 2000	1	19	3	20	6.5%	0.31 [0.03, 3.33]
Strauss 2008	1	45	1	60	2.0%	1.34 [0.08, 22.03]
<b>Total (95% CI)</b>		<b>240</b>		<b>259</b>	<b>100.0%</b>	<b>0.49 [0.29, 0.82]</b>

Total events 32 51  
 Heterogeneity:  $\text{Chi}^2 = 6.20$ ,  $\text{df} = 8$  ( $P = 0.63$ );  $I^2 = 0\%$   
 Test for overall effect:  $Z = 2.70$  ( $P = 0.007$ )





# 2015 Guidelines for Delayed Cord Clamping

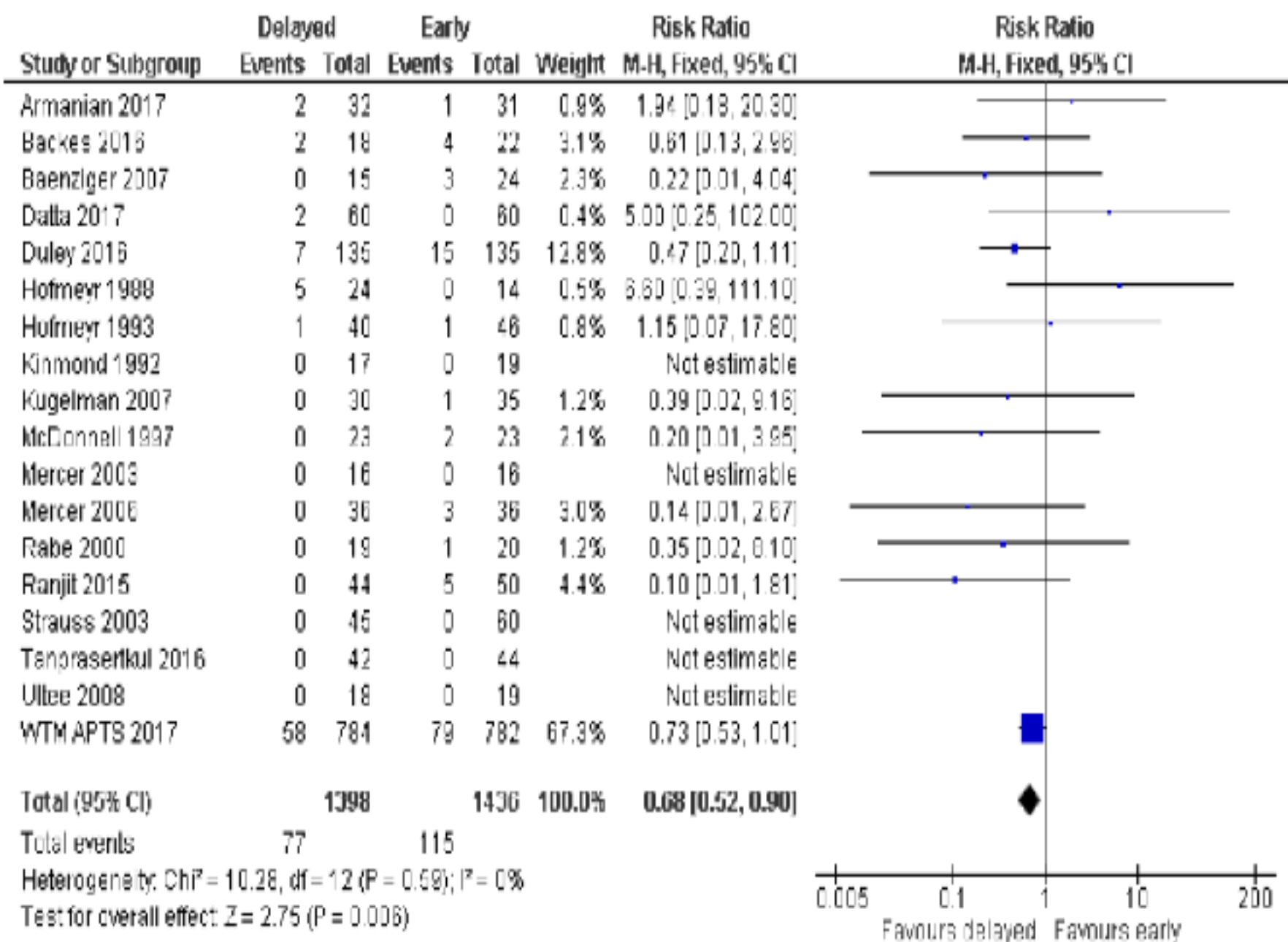
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- Delayed cord clamping is suggested for 30-60 seconds for most preterm newborns showing some signs of vigor (some respiratory effort, some tone/movement)
  - Place skin to skin with mom or OB securely hold in a warm, dry towel or blanket
  - Very preterm newborns may be wrapped in a warm blanket or polyethylene plastic
- No delay if infant appears lifeless or placental circulation disrupted (abruption, cord avulsion, bleeding placenta previa, bleeding vasa previa)
- Need good communication and teamwork with OBs

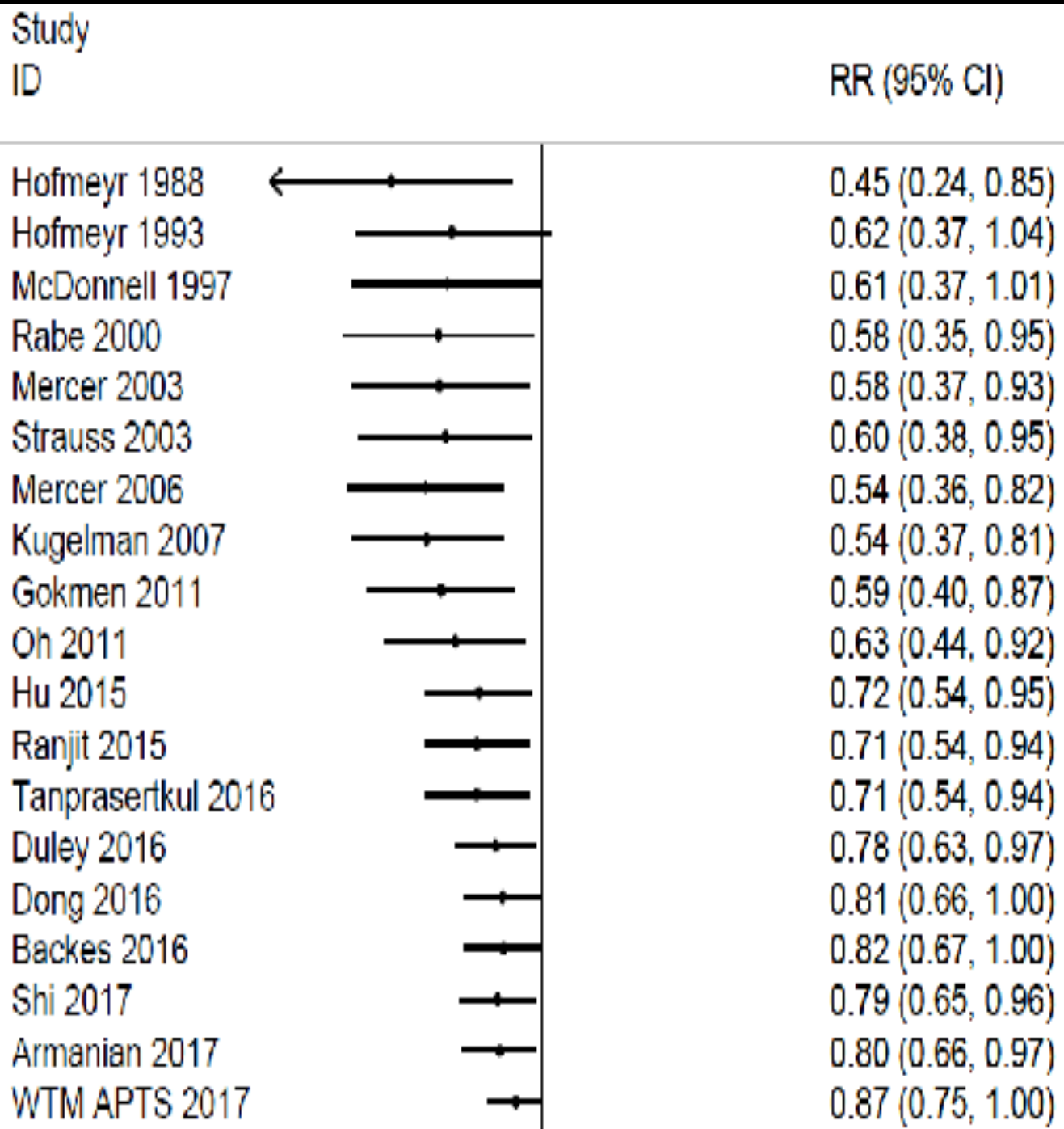
# New Evidence since 2015

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- 30 additional trials! (>3000 additional babies)
- Tarnow-Mordi et al. *N Engl J Med.* 2017;377(25):2445-2455.
  - N=1566 <30 week EGA infants randomized to immediate versus delayed cord clamping (>60s) (DCC)
  - Primary outcome: Death or major morbidity ((defined as severe brain injury on postnatal ultrasonography, severe retinopathy of prematurity, necrotizing enterocolitis, or late-onset sepsis) by 36 weeks of postmenstrual age.
  - DCC (37.0%) vs ICC (37.2%) (relative risk, 1.00; 95% confidence interval, 0.88 to 1.13; P = 0.96).







- 19 trials
- DCC 10%
- ICC 13%
- RR 0.87 [0.75, 1.00]



# What about Cord Milking?

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- Appealing as can be done quickly so that resuscitation could commence quickly for babies who are not breathing
- At time of 2015 ILCOR review, ~200 babies randomized to either cord milking or immediate cord clamping in 4 small RTCs, 1 cohort study
- At the time of review 1 small study comparing cord milking to delayed cord clamping



# 2015: Cord Milking Science Still Too Limited to Adapt for Routine Use

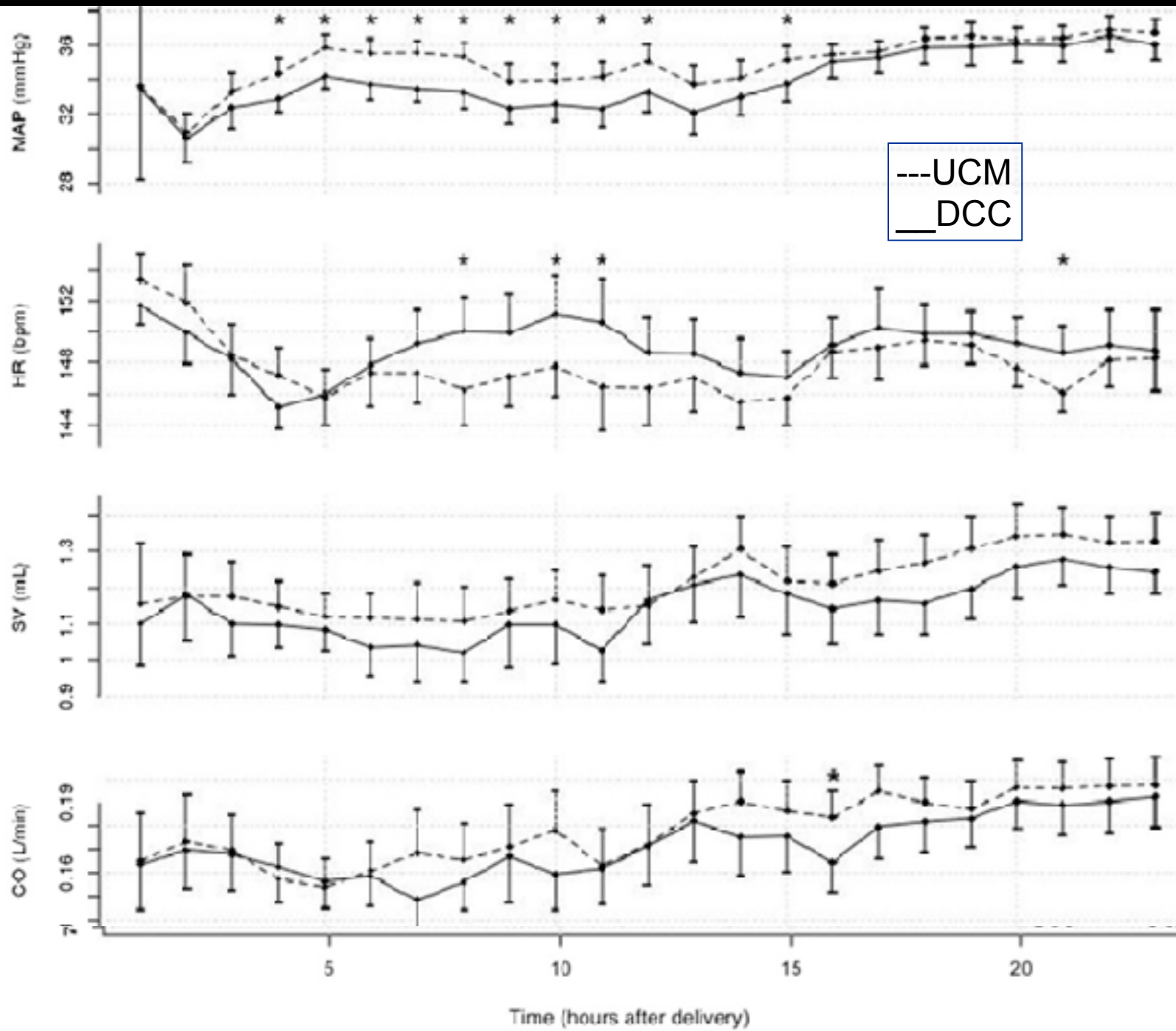
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- Currently, ILCOR **suggests against the routine use** of cord milking for infants born at less than 29 weeks of gestation but cord milking may be considered a reasonable alternative to immediate cord clamping to improve initial mean blood pressure, hematological indices and ICH. However, there is no evidence for improvement or safety in long term outcomes.
- If new compelling science is available in the coming years, a new recommendation would be made using the new ILCOR process of continuing review

# Umbilical Cord Milking (UCM) Versus Delayed Cord Clamping (DCC) in Preterm Infants (<32 wks EGA)

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- Katheria et al. *Pediatrics*. 2015;136(1):61-69.
  - 2-center pilot trial powered for Superior Veno-Caval flow differences
  - Infants delivered by C/S randomly assigned to undergo UCM or DCC
  - N=154
  - UCM (4 strippings) or DCC (45–60 seconds) were performed

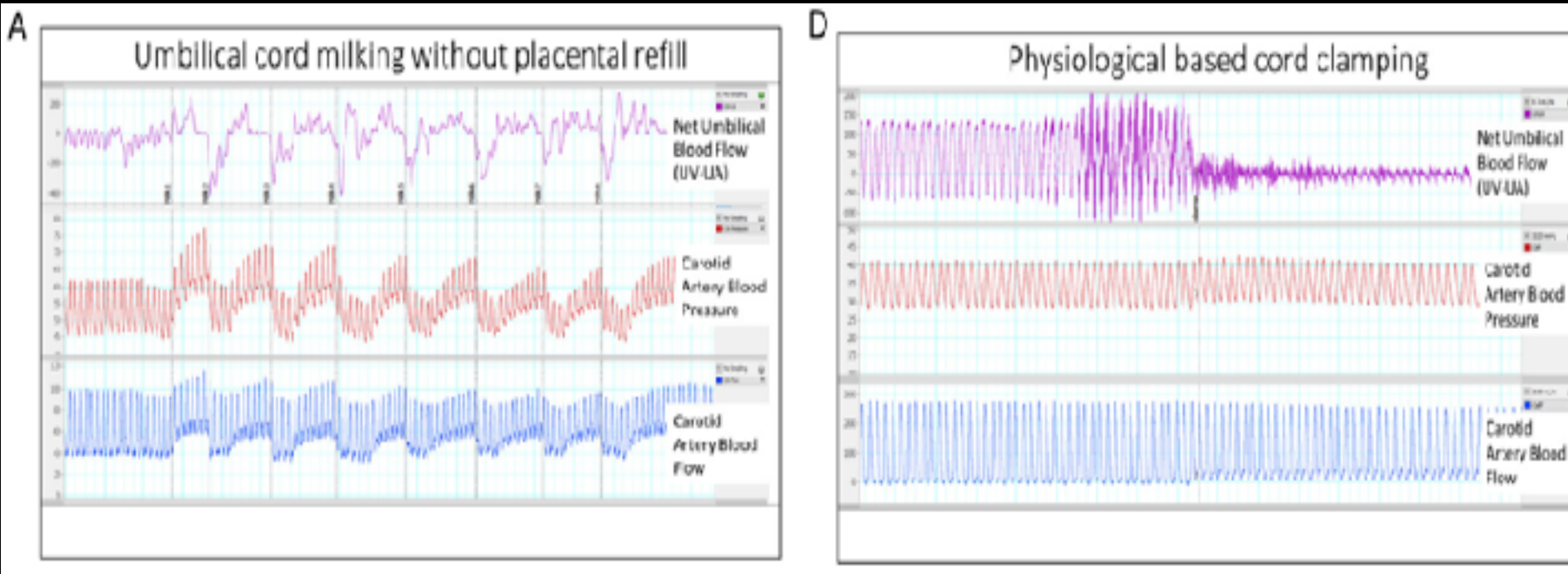


# A Randomized Clinical Trial of Umbilical Cord Milking vs Delayed Cord Clamping in Preterm Infants: Neurodevelopmental Outcomes at 22-26 Months of Corrected Age

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- Katheria et al. *J Pediatr* 2018.194;76-80
  - N=135 (74% F/U rate for the pilot trial participants)
  - Infants randomized to umbilical cord milking at birth
    - significantly higher cognitive and language composite
    - less likely to have a cognitive composite score of <85 (4% vs 15%;  $P = .04$ ).
    - Motor function was similar in both groups
    - No differences in the incidences of mild or moderate to severe neurodevelopmental impairment, hearing or visual impairments, pulmonary morbidities, or rehospitalizations between the 2 groups

# Hemodynamic effects of umbilical cord milking in preterm sheep during transition



- Blank DA, et al. Arch Dis Child Fetal Neonatal Ed 2017;0:F1–F8.
  - 126 day fetal lambs were exteriorized, intubated and instrumented
  - Randomized to 4 different cord management strategies
  - Umbilical, pulmonary and cerebral blood flows and arterial pressures measured
  - Measured hemodynamic effects on carotid artery BP and blood flow



# Katheria et al. JAMA 2019;322:1877-1886

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- Multi-national, randomized controlled non-inferiority trial enrolled preterm infants of 23-31 weeks gestation.
- UCM (4 times) or DCC (at least 60 seconds) stratified by mode of delivery and gestational age, lower gestational age (GA) strata: 23 -27 weeks and higher GA strata: 28 - 31 weeks gestation
- Planned enrollment: n=1500
- Trial halted at n=474 for safety concerns
- No difference in primary outcome of death or severe IVH for the whole study population

# Umbilical Cord Milking versus Delayed Cord Clamping 23-27 wk GA Infants

Delivery Room and Neonatal Outcomes	DCC (N=89)	UCM (N=93)	p-value
Time of cord clamp, sec	56.7 (16.4)	21.1 (13.8)	<0.0001
Crying or breathing b/f cord clamping	68 (76%)	48 (52%)	0.0007
Admission temp, °C	36.8 (0.7)	36.8 (0.6)	0.998
Apgar score, 1 min: Median (IQR)	5.0 (2,6)	4.0 (3,7)	0.47
Apgar score, 5 min: Median (IQR)	7.0 (6,8)	7.0 (5,8)	0.91
Received PPV	77 (87%)	79 (85%)	0.899
Intubation in delivery room	54 (61%)	53 (57%)	0.67
Hemoglobin at 4 hours of life	15 (2.4)	15 (2.8)	0.86
Peak bilirubin, mg/dl	7.1 (1.9)	7.3 (2.0)	0.70
Any IVH	27 (30%)	25 (27%)	0.61
Severe IVH (Grade 3 or 4)	4 (4%)	20 (22%)	0.0007
Death	12 (13%)	14 (15%)	0.76

What about delayed cord clamping for the non-vigorous infant who needs resuscitation?

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AAP-NRP photo

## Delaying cord clamping until ventilation onset improves cardiovascular function at birth in preterm lambs

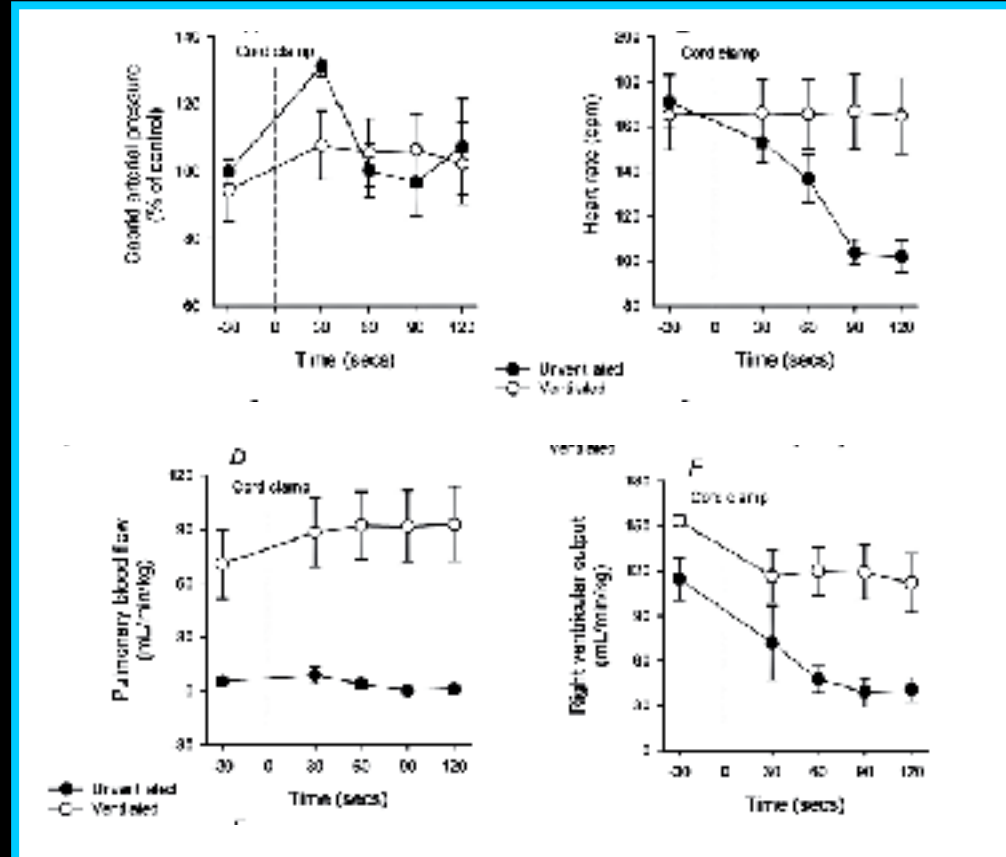
Sasmira Bhatt<sup>1,2</sup>, Beth J. Alison<sup>1</sup>, Euan M. Wallace<sup>1,2</sup>, Kelly J. Crossley<sup>1,2</sup>, Andrew W. Gill<sup>3</sup>, Martin Kluckow<sup>4</sup>, Arjan B. de Pas<sup>5</sup>, Colin J. Murley<sup>6</sup>, Graeme R. Polglase<sup>1,2</sup> and Stuart B. Hooper<sup>1,2</sup>

- Preterm lambs prenatally operated
  - At 123 days (84% of term=32 weeks in human infants)
- Catheters implanted
  - into the PA, CA and Doppler probes around PA & CA
- Lambs delivered at 126±1 days
- Two groups:
  - Clamp 1<sup>st</sup> : Cord was clamped at delivery and ventilation delayed for ~2 min ( $n = 6$ )
  - Vent 1<sup>st</sup> : Cord clamping delayed, until 2 min after ventilation was established ( $n = 6$ ).

■ Pressure and flow.

# Ventilation prior to cord clamping results in more stable transition

- 30-50% of cardiac output goes to placenta
- Immediate cord clamp before lung ventilated results in unstable carotid pressure
- Delaying cord clamp until lungs ventilated allows smoother transition
  - UVC flow maintains ventricular preload until pulmonary blood flow established
  - Prevents carotid pressure spike and drop

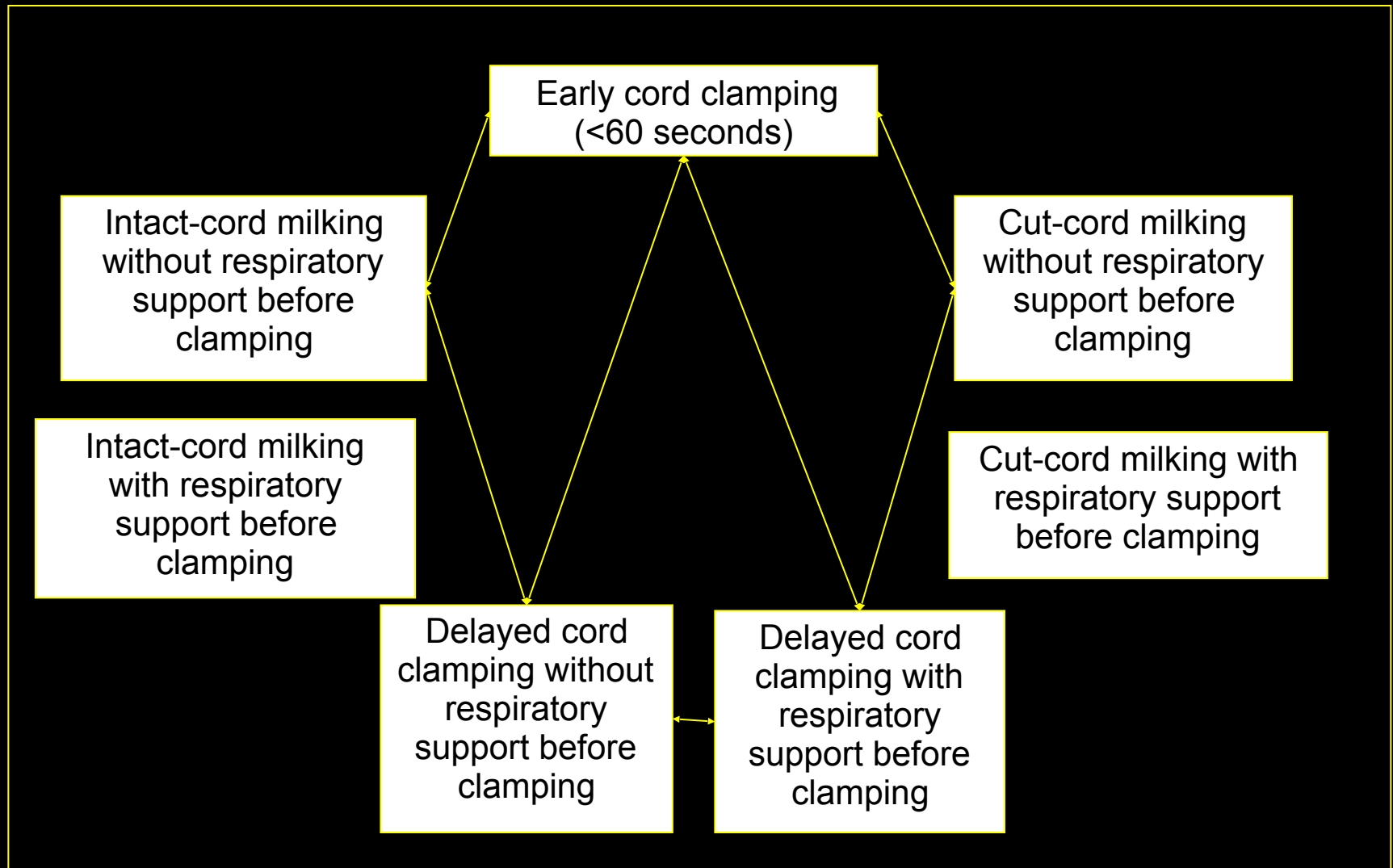


# Ventilation First Trials for Non-Vigorous Infants



- 3 on-going international trials examining delayed cord clamping while resuscitation commences with a mobile resuscitation trolley pulled up next to mom

# Cord Management Strategy Comparisons in the Literature





# Work in Progress

- Neonatal Life Support Task Force of ILCOR is working with Cochrane Collaboration to complete a systematic review with meta-analysis regarding all available evidence for cord management strategies
  - Term vs Preterm
  - Immediate Cord Clamping vs Delayed
  - Delayed Cord Clamping versus Ventilation Prior to Clamping of Cord for newborns in need of resuscitation
  - Length of delay prior to clamping
  - Immediate Cord Clamping vs Cord Milking
  - Delayed vs Cord Milking
  - Type of cord milking (after cord clamping or with placenta still perfusing)



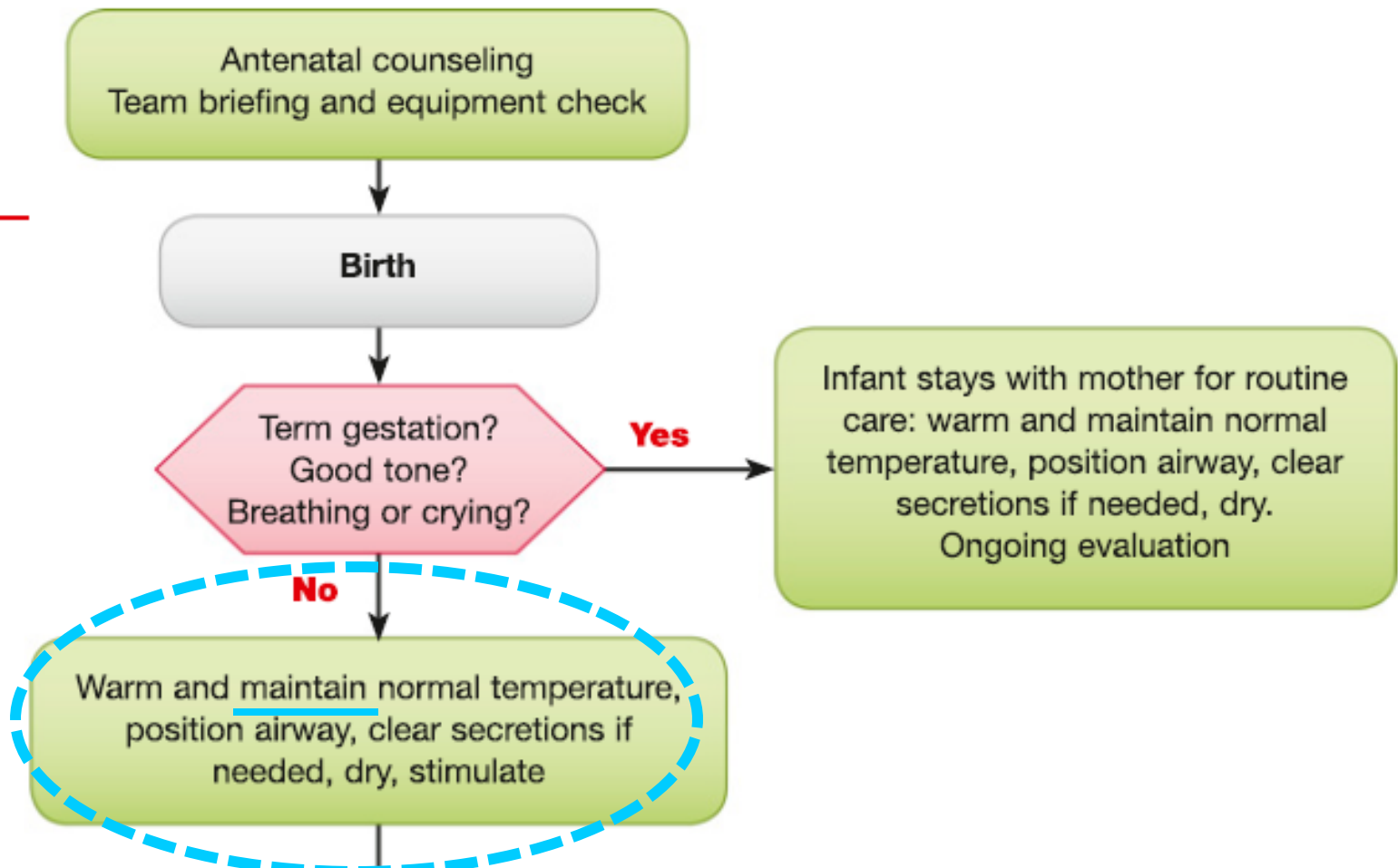
# At Delivery: Our baby has some respiratory effort but not great tone

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- Delayed Cord Clamping attempted for 60 seconds
- Infant brought to the radiant warmer

# 2015 Neonatal Resuscitation Guidelines: Increased Focus on Maintaining Normal Temperature



# Why Prematures Are at Particular Risk for Hypothermia

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- Immature epidermal barrier
  - High evaporative heat loss
- Limited subcutaneous fat
- Increased surface area/weight ratio
- Ineffective non-shivering thermogenesis





# 2015: ILCOR Systematic Reviews Regarding Temperature Stabilization

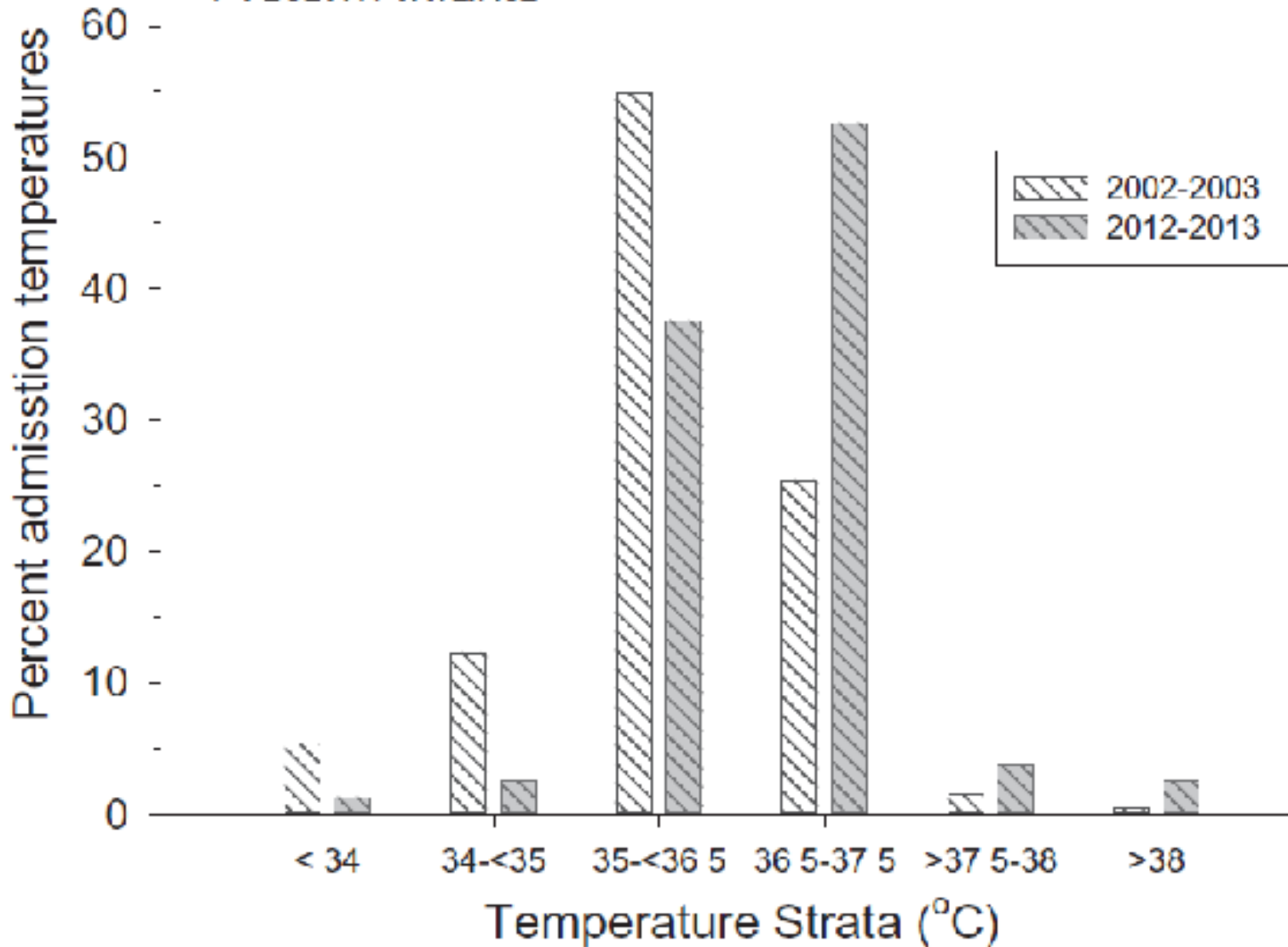
- 36 observational studies demonstrate increased risk of mortality associated with hypothermia at admission
- Hypothermic infants have increased morbidity
  - Hypoglycemia, Respiratory Distress, Intraventricular hemorrhage, Late onset sepsis
- Temperature should be monitored and maintained between 36.5-37.5°C after delivery

# Admission Temp by for Infants $\leq 28$ wks Gestational Age

Gestational Age (wks)	n	Birth Weight (g)	Admission Temp	
			< 35 °C	< 36 °C
28	643	1088 $\pm$ 201	10%	38%
27	609	977 $\pm$ 182	11%	42%
26	539	840 $\pm$ 163	13%	44%
25	468	751 $\pm$ 130	21%	57%
24	397	655 $\pm$ 100	34%	64%
<24	187	598 $\pm$ 118	44%	72%

- For every 1°C decrease in admission temperature
  - Odds of late onset sepsis  $\uparrow$  by 11% (OR 1.11; CI:1.02-1.20)
  - Odds of death  $\uparrow$  by 28% (OR 1.28; CI: 1.16-1.41)

## Extreme Preterm Infants



- Fewer low admission temperatures but more elevated temperatures.
- Inverse association between temperature and mortality risk persists.

# Increased Ambient Temperature in OR Improves Infant Temperatures

	<u>Standard management</u>	<u>Study group</u>	<i>P</i> value	RR (95% CI)
	20°C (67°F)	23°C (73°F)		
	N = 419	N = 406		
<b>Abnormal temperature</b>				
Hypothermia, <sup>a</sup> <36.5°C	208 (50)	143 (35)	<.001	1.4 (1.2 1.7)
Moderate/severe hypothermia, <sup>a</sup> <36.0°C	79 (19)	20 (5)	<.001	3.8 (2.4 6.1)
Hyperthermia, <sup>a</sup> >38.0°C	2 (0.5)	8 (2.0)	.05	0.2 (0.05 1.1)
<b>Infant morbidity</b>				
Intubation in OR	3 (0.7)	9 (2.2)	.07	0.3 (0.1–1.2)
Ventilator use in first 24 h	4 (1.0)	8 (2.0)	.2	0.5 (0.2–1.6)
Hypoglycemia	6 (1.4)	4 (1.0)	.6	1.5 (0.4–5.1)
Umbilical artery pH <7.0	2 (0.5)	2 (0.5)	1	1.0 (0.1–6.9)
Sepsis	2 (0.5)	0 (0.0)	.2	4.9 (0.2–100.6)
Hyperbilirubinemia	31 (7.4)	39 (9.6)	.3	0.8 (0.5–1.2)

Data reported as N (%) unless otherwise indicated.

CI, confidence interval; OR, operating room; RR, relative risk.

<sup>a</sup> Neonatal hypothermia and temperatures reported were measured on arrival to admitting nursery.

# A Randomized Trial of Conditioned or Unconditioned Gases for Stabilizing Preterm Infants at Birth

- McGrory et al. *J Pediatr* 2018;193:47-53
  - Infants < 30 weeks gestation
  - Randomized (not blinded)
  - Heated, humidified vs unconditioned gases for respiratory support in the delivery room
- Fewer infants in the heated-humidified group were hypothermic on admission to NICU
  - 36/132 [27%] compared with controls (61/141 [43%],  $P < .01$ ).
  - No difference in rates of hyperthermia ( $>37.5^{\circ}\text{C}$ )



# Combinations of Strategies to Provide Warmth May Be Used

- For all newborns

- Environmental Temperature at least 23-25°C (77°F)
- Warm Blankets for Drying
- Hats



- For **Monitor temperature in the delivery room and adjust as needed**  
– R **Avoid hyperthermia!!**  
– W



- For Preemies

- Polyethylene Occlusive wrapping
- Heated (NaAcetate) Mattresses



# We Don't Skimp on the Initial Steps!!

- Provide warmth: Warm room, Radiant Warmer, Thermal Mattress, Plastic Poncho, Wool Hat

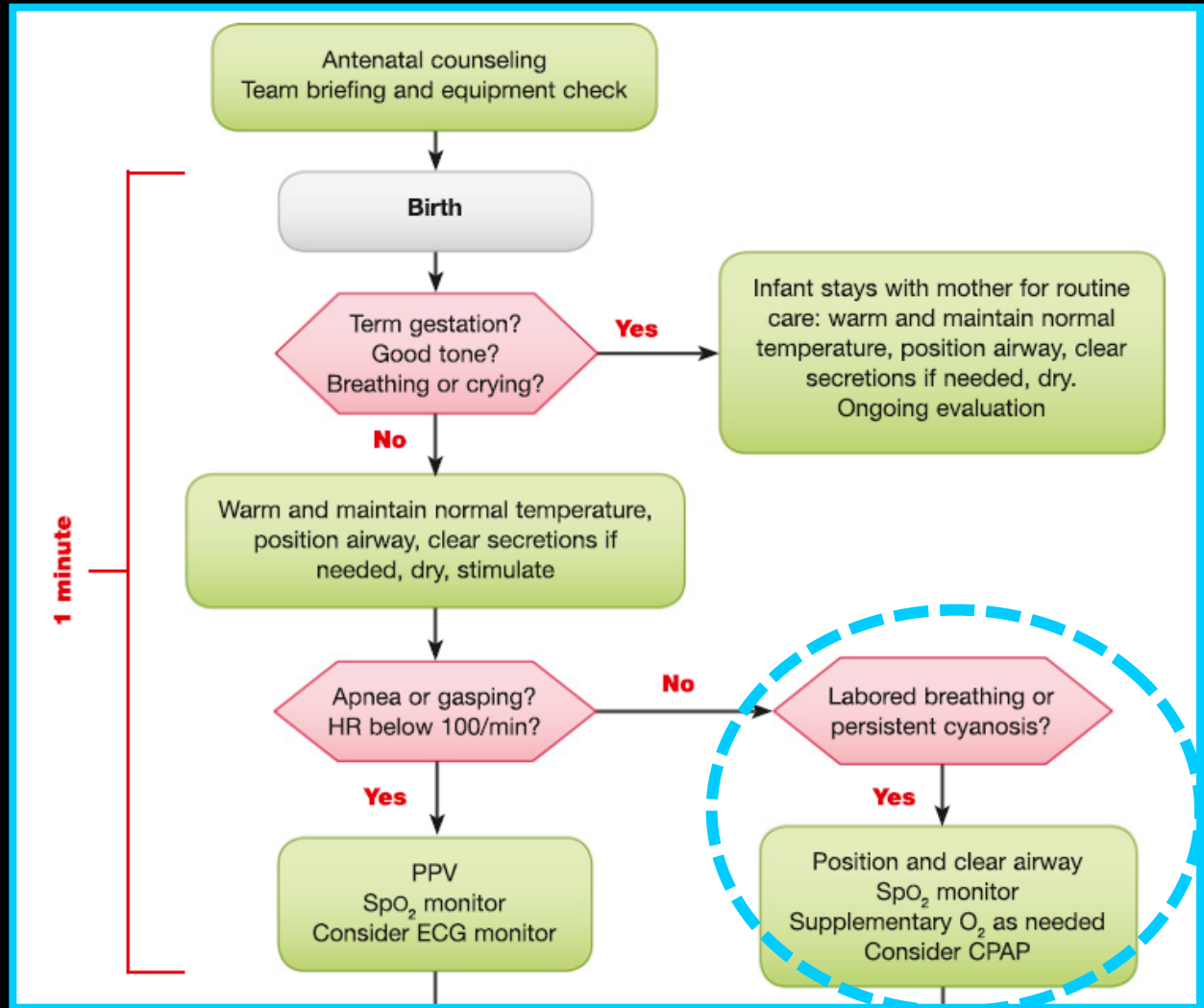


- Position in the open airway position, clear the airway (if needed) and stimulate



# 2015 Neonatal Resuscitation Guidelines

If baby is breathing and maintains heart rate.....



# Role of CPAP in the Delivery Room

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- If heart rate and respiratory effort are adequate but there is increased work of breathing or a perception of cyanosis then CPAP can be considered
- CPAP may help establish functional residual capacity
  - CPAP can be delivered with a flow-inflating bag or a T-piece resuscitator, but NOT a self-inflating bag





# CPAP vs Intubation for Preterm Newborns in the Delivery Room

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- 3 RCTs (n=2358)
- Potential benefit for reducing death or BPD (RR, 0.91; 95% CI, 0.83–1.00)
- No advantage for death alone, BPD alone, air leak, severe IVH, NEC, ROP
- Tx Recommendation: For spontaneously breathing preterm infants with respiratory distress requiring respiratory support in the delivery room, we suggest initial use of CPAP rather than intubation and PPV

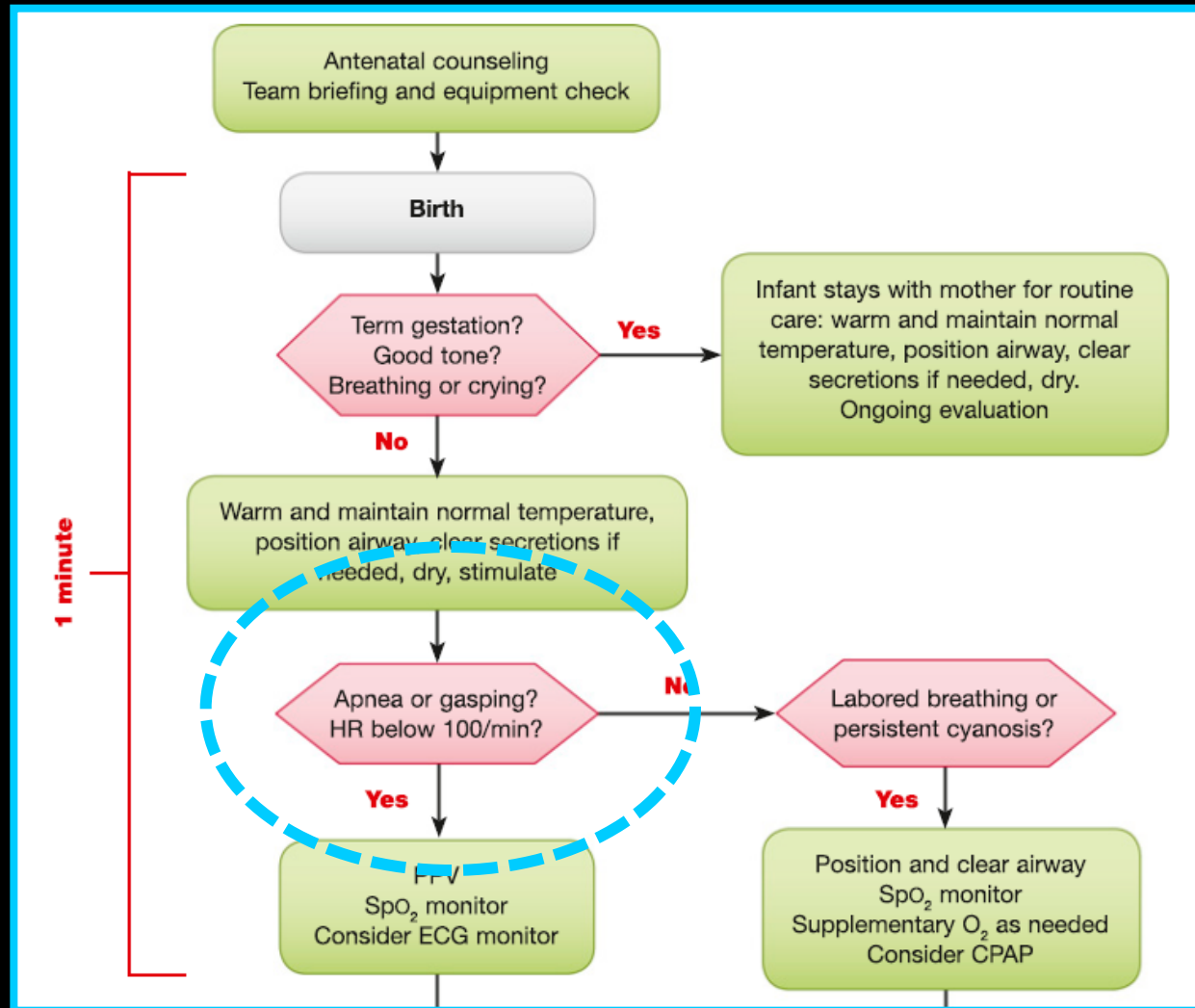


# CPAP Started, Pulse Ox Placed on Right Hand

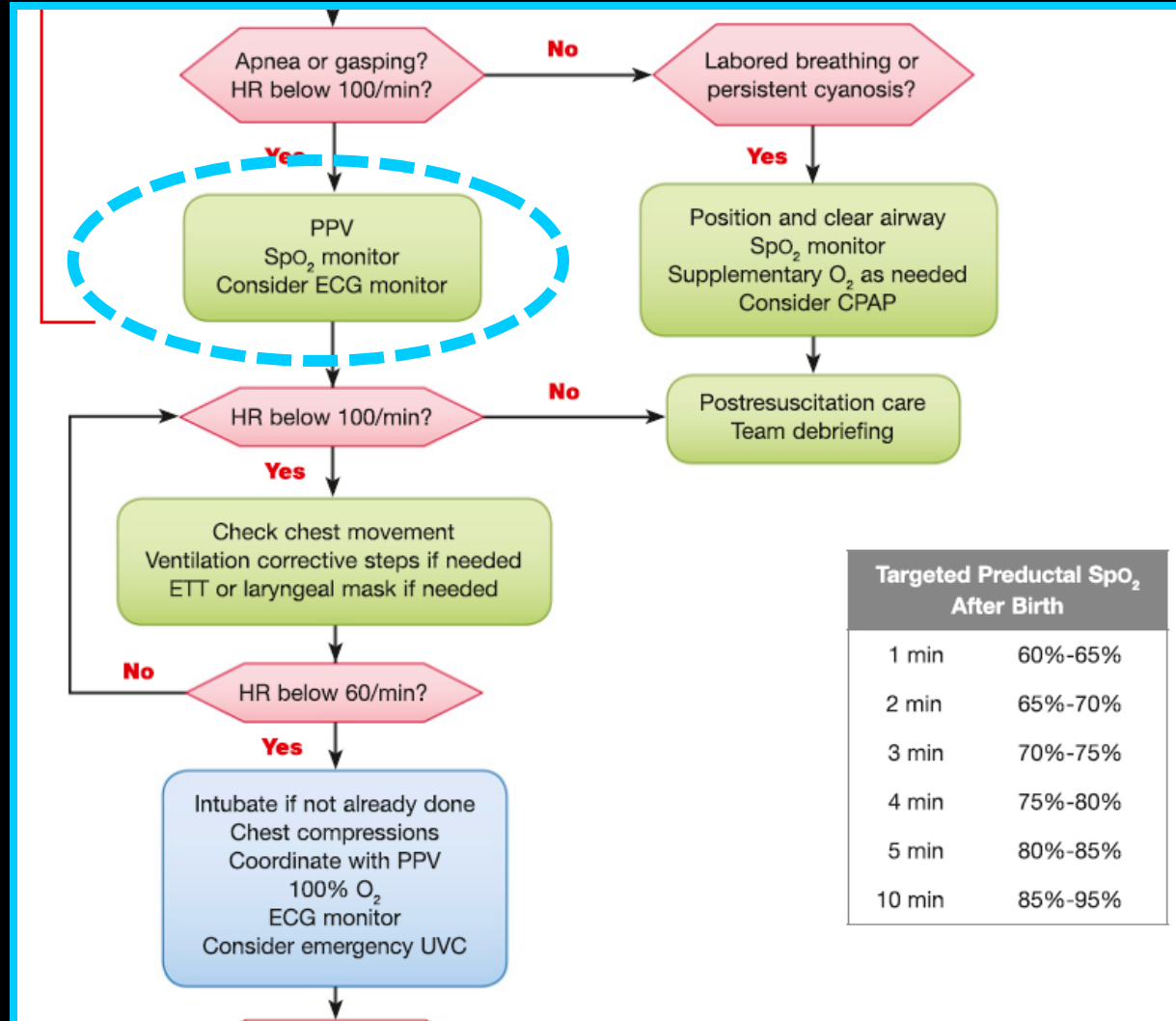


# Respiratory Effort and Heart Rate?

Heart Rate = 80  
Ineffective  
Respiratory Effort



# 2015 Neonatal Resuscitation Guidelines



Targeted Productal SpO <sub>2</sub> After Birth	
1 min	60%-65%
2 min	65%-70%
3 min	70%-75%
4 min	75%-80%
5 min	80%-85%
10 min	85%-95%

- PPV started with T-piece set at 25/5 cm H<sub>2</sub>O
- FiO<sub>2</sub> .3



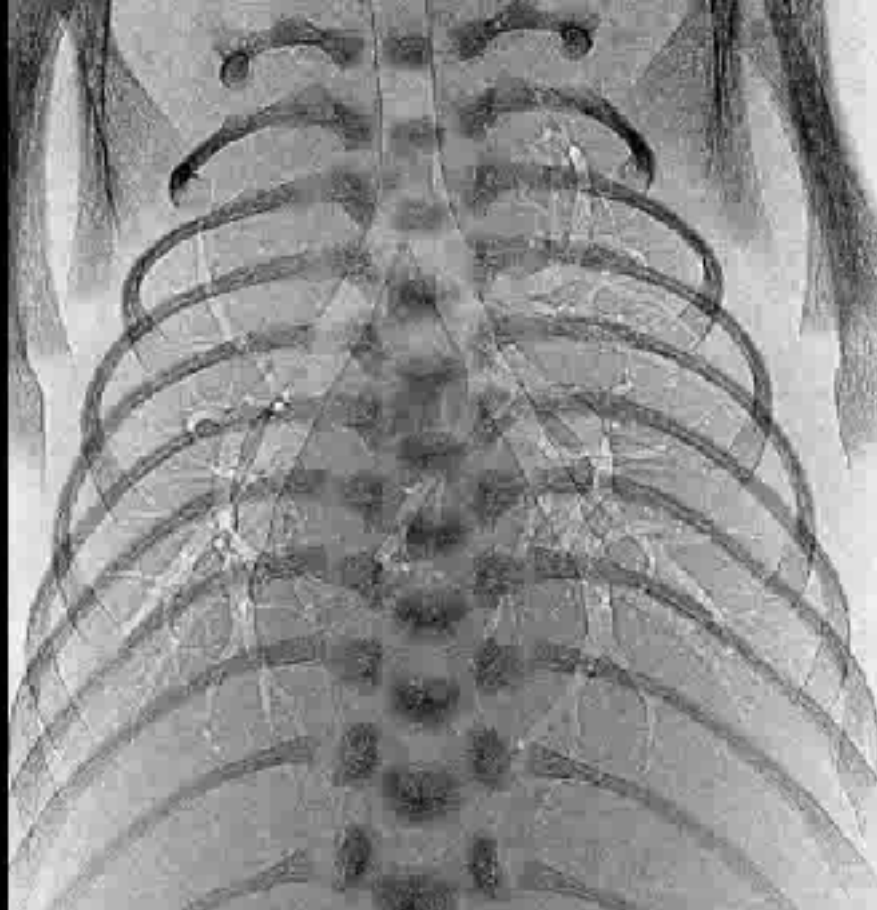
# So is one PPV device better than another for delivering PEEP?

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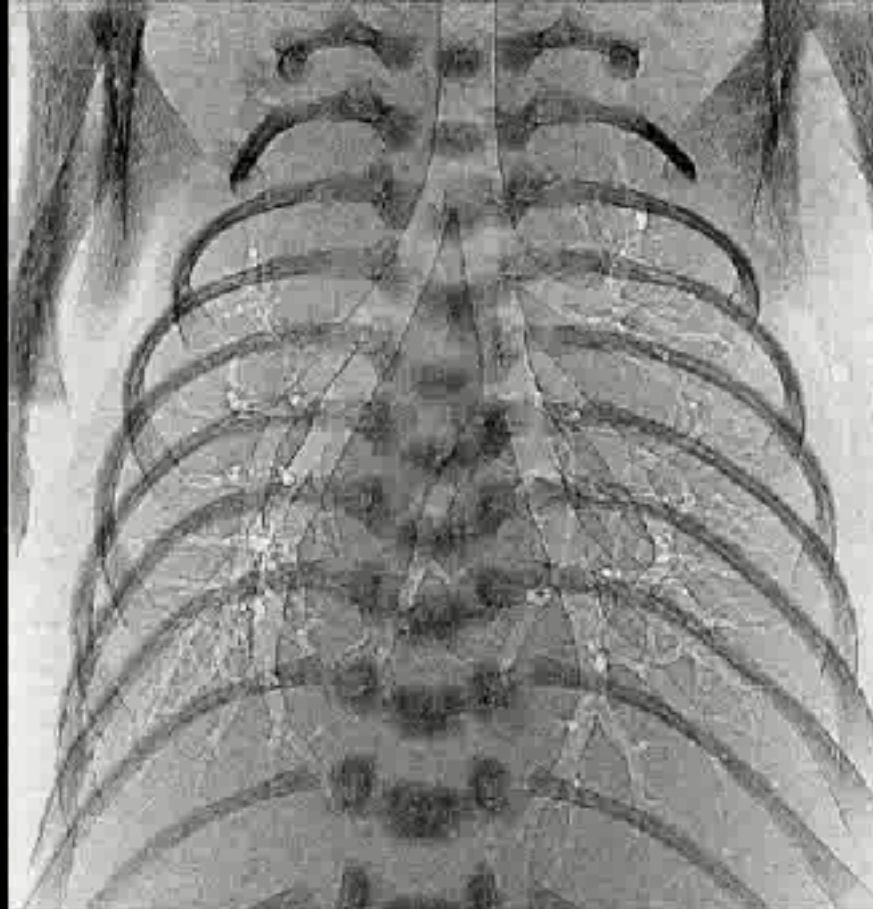
# PPV WITHOUT PEEP

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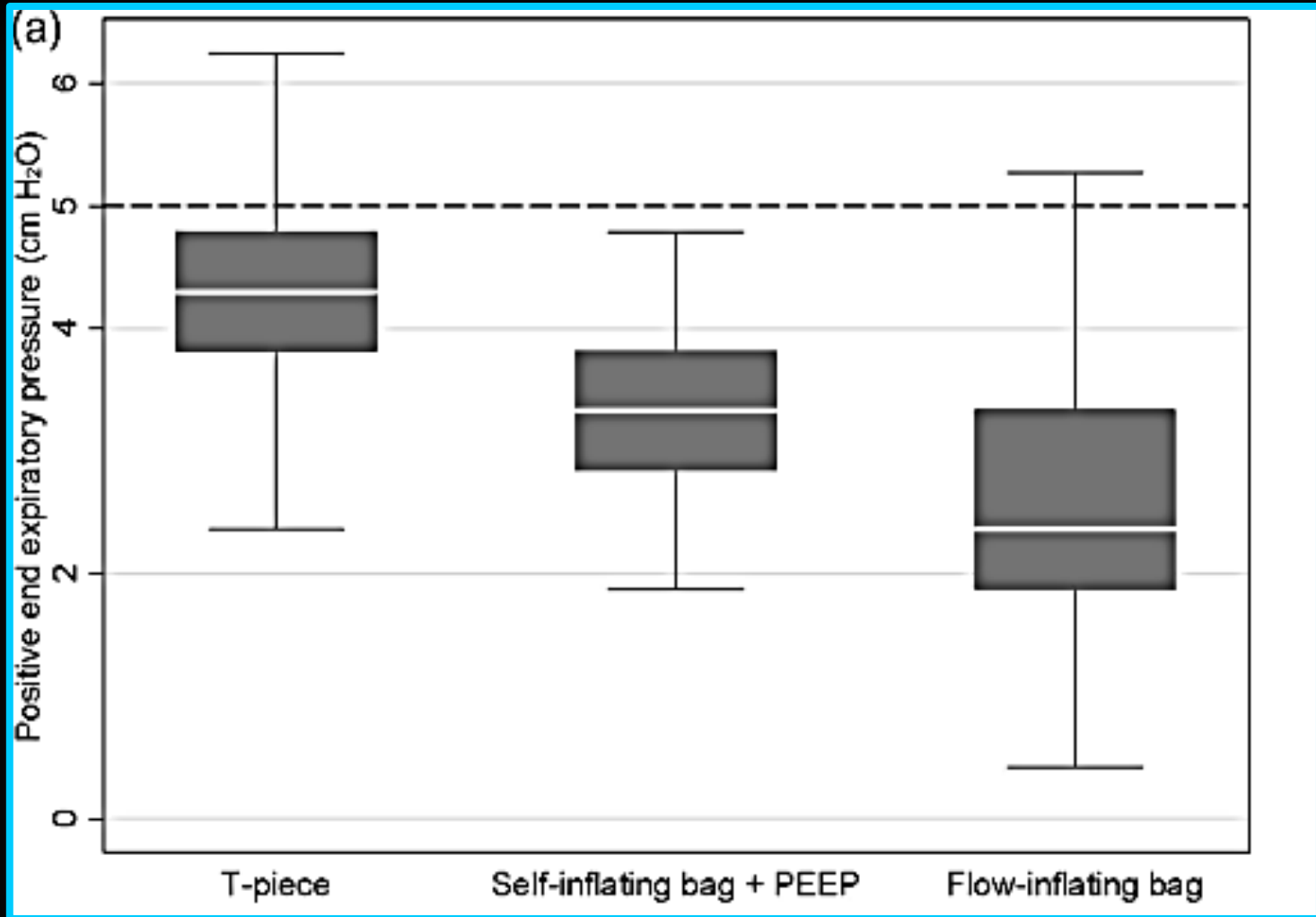
# PPV WITH PEEP

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# PEEP: Which device?

“Ventilate 30/5 x 40/min.” Face mask manikin



# Clinical application?

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- Szyld et al, J Pediatr 2014. Randomized trial of T-piece vs. Self-inflating Bag
  - N=1027 newborns (195 VLBWs)
  - In VLBW subgroup: T-piece group had fewer with HR < 100 bpm at 2-minutes, fewer intubated, fewer with BPD and fewer days on oxygen
- Guinsburg et al. ADC-FN 2018. Prospective cohort study of T-piece vs. Self-inflating Bag
  - N = 1962 VLBWs
  - T-piece use associated with greater chance of survival without major morbidity (OR 1.38)



# Current Oxygen Recommendations for the Delivery Room

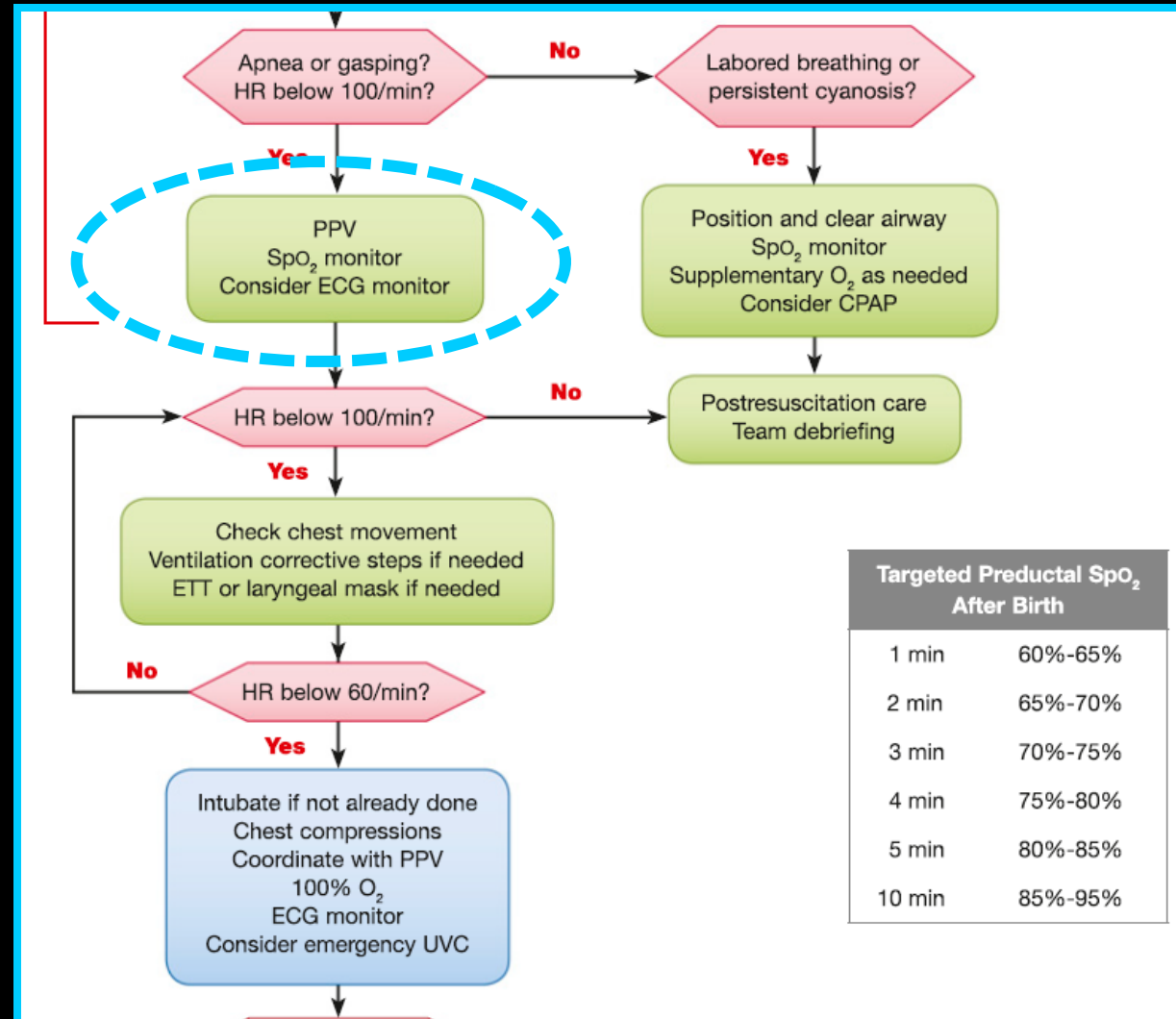
- Preterm Infants < 35 weeks: Initiate resuscitation with a low-oxygen concentration (21–30%) (weak recommendation, very low-certainty evidence).
  - Very low certainty evidence from 10 RCTs and 4 observational studies enrolling 5697 subjects found no statistically significant benefit or harm in preventing mortality when beginning resuscitation with low-oxygen as compared with high-oxygen concentration (RR, .83; 95%CI, 0.5–1.37). {Welsford et al. 2019 Pediatrics}
- Value on not exposing preterm newborns to additional oxygen without proven benefit for critical or important outcomes.

# Current Oxygen Recommendations for the Delivery Room

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- Balance between the need to give sufficient oxygen to correct hypoxemic state and the desire to avoid excessive oxygen exposure.
- The goal of current strategy resuscitation is to titrate oxygen amount to achieve a target SpO<sub>2</sub>.
- Target SpO<sub>2</sub> for delivery room resuscitation is the approximated median preductal saturation of healthy term babies (even for preterm infants).

# 2015 Neonatal Resuscitation Guidelines



Targeted Productal SpO <sub>2</sub> After Birth	
1 min	60%-65%
2 min	65%-70%
3 min	70%-75%
4 min	75%-80%
5 min	80%-85%
10 min	85%-95%

- Heart rate quickly rises
- O<sub>2</sub> adjusted to meet goal saturations
- Transitioned to CPAP
- Prepared for transport





## Conclusions



- An immense number of complex decisions and tasks must be accomplished in a short period of time following the birth of an ELBW infant
- A standardized approach, using the best possible evidence should be used
  - Allow for individual variation in the response of the neonate
- Goal is to provide the least invasive support needed BUT must be prepared for the worst
- Strong communication, teamwork, medical knowledge and clinical skills are essential