



**ANNUAL MEETING  
of the SSN 2025**

**NEWBORN RESUSCITATION**



**TUESDAY, MAY 13, 2025**  
Kultur und Kongresshaus Aarau

# The newborn delivery room of tomorrow

Peter Davis

The Royal Women's Hospital  
University of Melbourne

Hey ChatGPT, what will the  
delivery room of tomorrow look  
like?



What will neonatal resuscitation  
look like in 25 years?

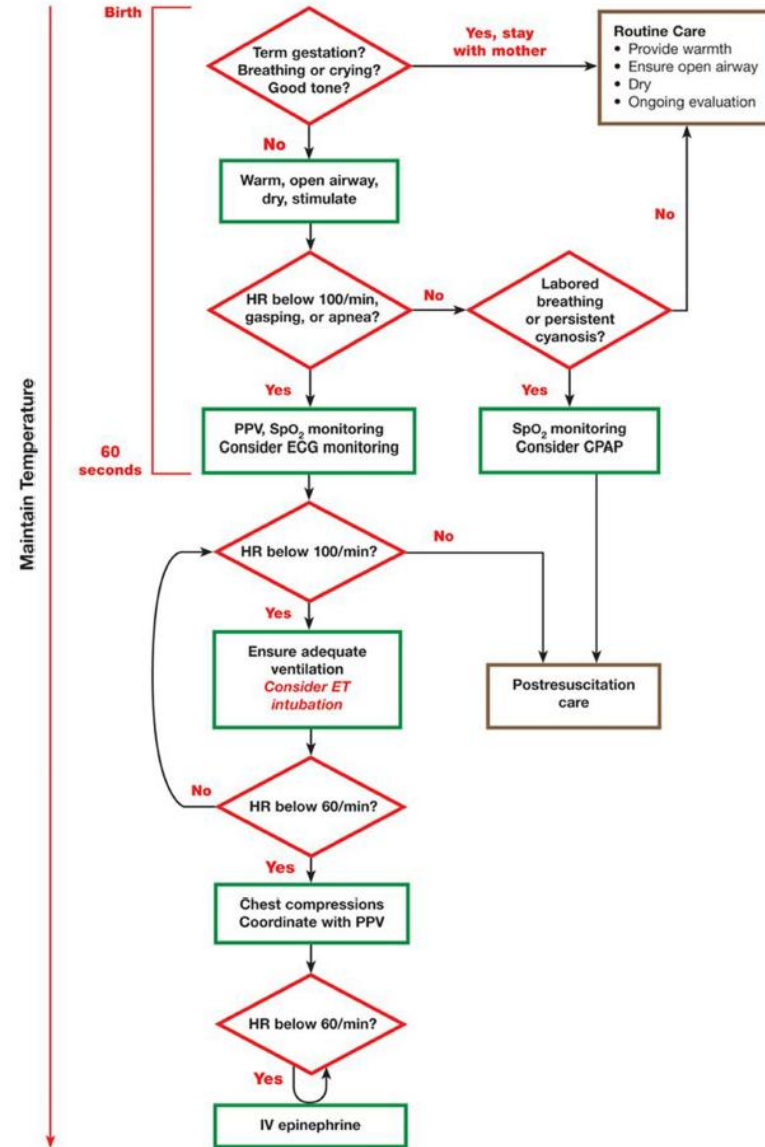
# “Here are some possibilities”

1. **Smart Equipment:** Incorporating AI to monitor vital signs in real-time, providing instant feedback and recommendations to healthcare providers
2. **Telemedicine Integration:** Remotely guide resuscitation allowing for expert input even in underserved areas
3. **Advanced Simulation Training:** Using virtual or augmented reality simulations, providing realistic scenarios to enhance skills
4. **Personalized Care:** Tailored based on genetic and health data of the infant, leading to more effective and individualized treatment
5. **Robotics and Automation:** Automated systems to reduce the physical strain on healthcare providers

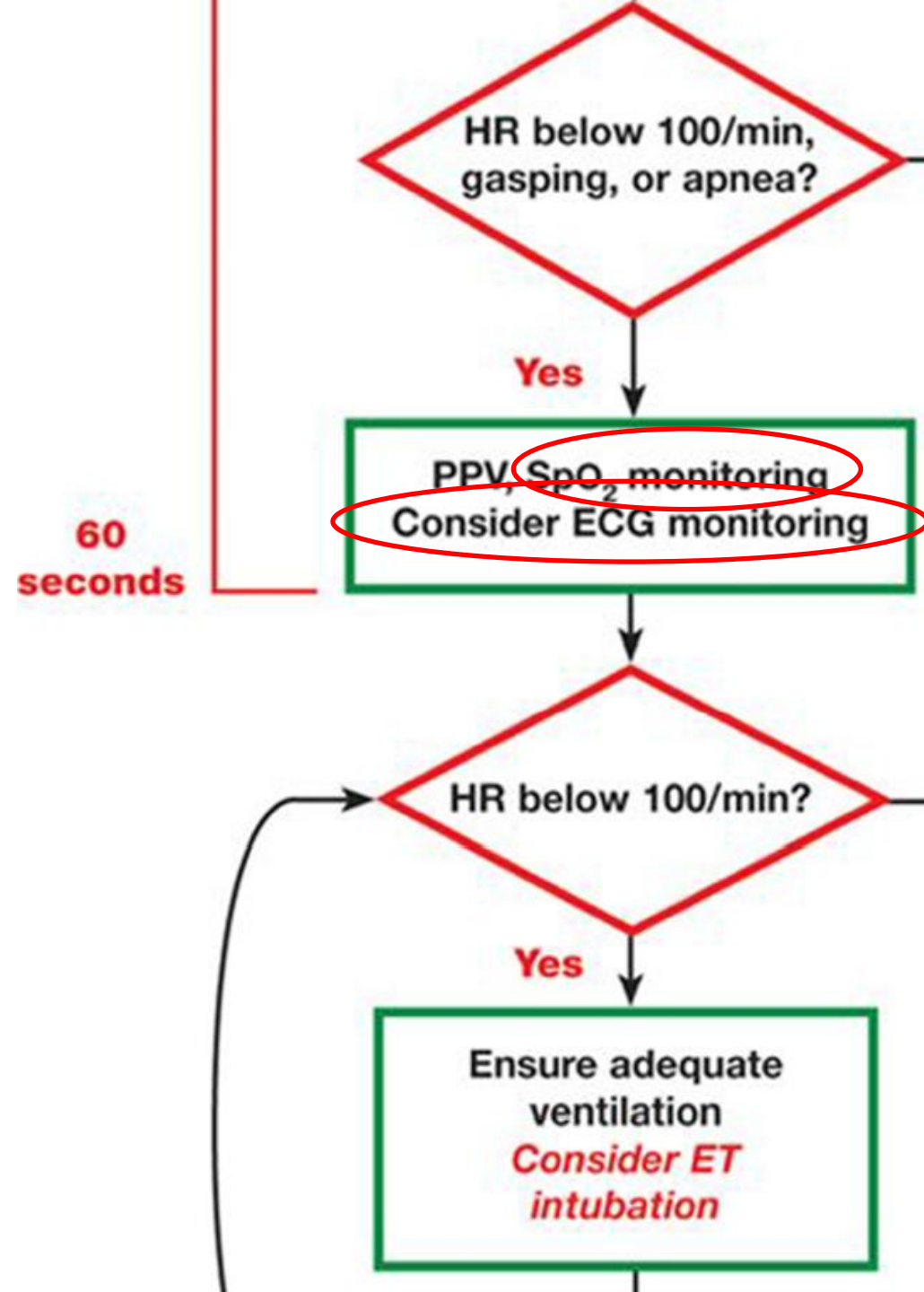
# The Program

- Some better equipment on the horizon
- How do we get to a better future
  - As quickly as possible!
  - Safely!

# ILCOR resuscitation algorithm (since 2020)



ILCOR  
Resuscitation  
algorithm  
(since 2020)



# **SMART EQUIPMENT: HEART RATE**

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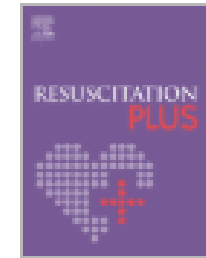
# Some observations about heart rate

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“Heart rate is the most important, objective clinical indicator of the health of newly born infants”



*Apgar V. A proposal for a new method of evaluation of the newborn infant. Curr Res Anesth Analg 1953;32:260–7.*





Review

# Fast and accurate newborn heart rate monitoring at birth: A systematic review ☆

Vishal S. Kapadia<sup>a</sup>  , Mandira D. Kawakami<sup>b</sup>, Marya L. Strand<sup>c</sup>, Cameron Paul Hurst<sup>d</sup>,  
Angela Spencer<sup>e</sup>, Georg M. Schmölzer<sup>f</sup>, Yacov Rabi<sup>g</sup>, Jonathan Wyllie<sup>h</sup>, Gary Weiner<sup>i</sup>,  
Helen G. Liley<sup>j</sup>, Myra H. Wyckoff<sup>a</sup>,  
International Liaison Committee on Resuscitation Neonatal Life Support Task Force<sup>1</sup>

# Conclusions

- ECG is the gold standard but
  - Some delay in obtaining reliable heart rate readings
  - Possibility of false signals or delayed recognition of pulseless electrical activity
  - Electrodes may not adhere well to newborns' skin, especially preterm infants,
- Pulse oximetry is slower to achieve signal and less precise than ECG for HR assessment (but provides oxygen saturation)
- Auscultation and palpation add no additional cost to the delivery room care but are imprecise for HR assessment
  - Both help recognize pulseless electrical activity

**AN  
ALTERNATIVE**

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**Dry  
electrode  
ECG**

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# Neobeat

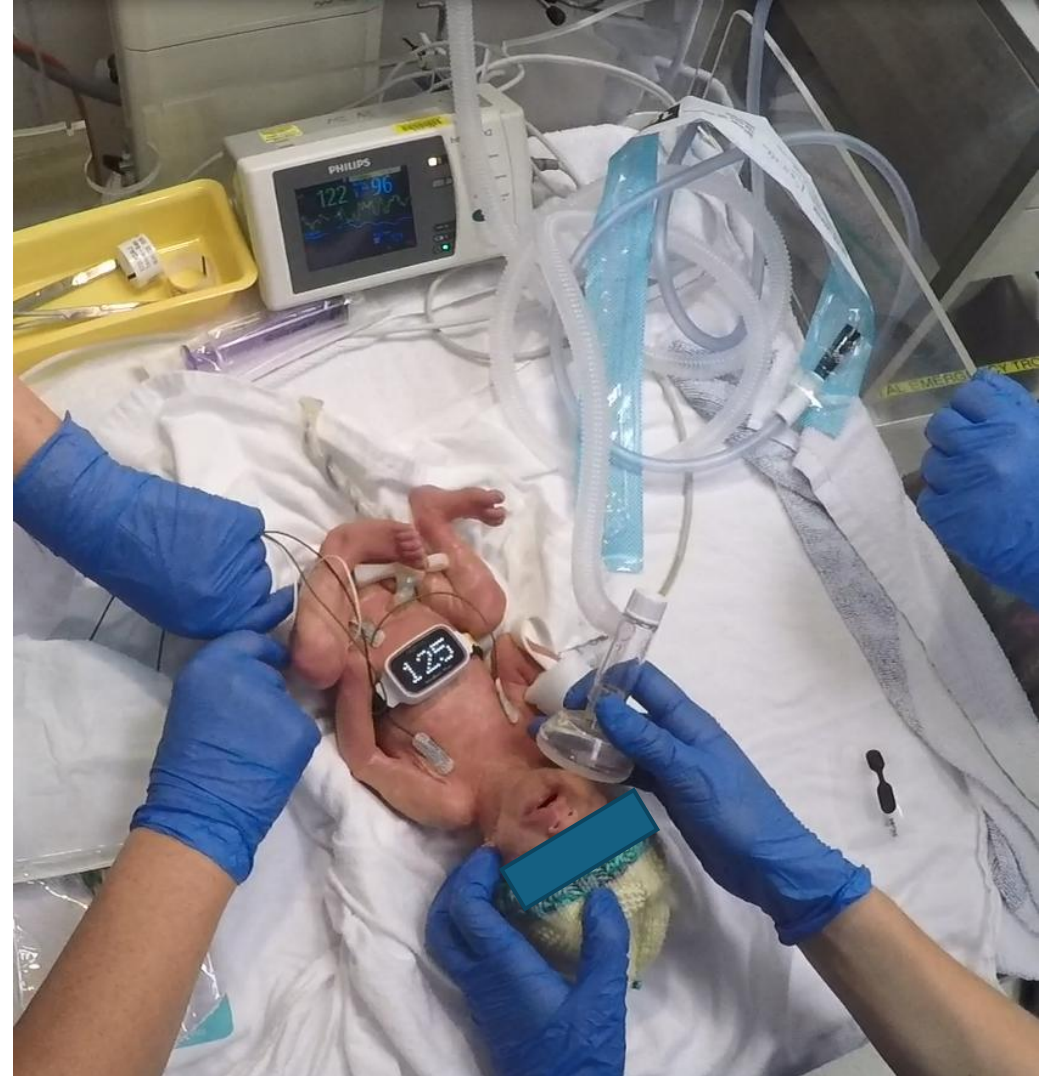
(Laerdal Global Health)



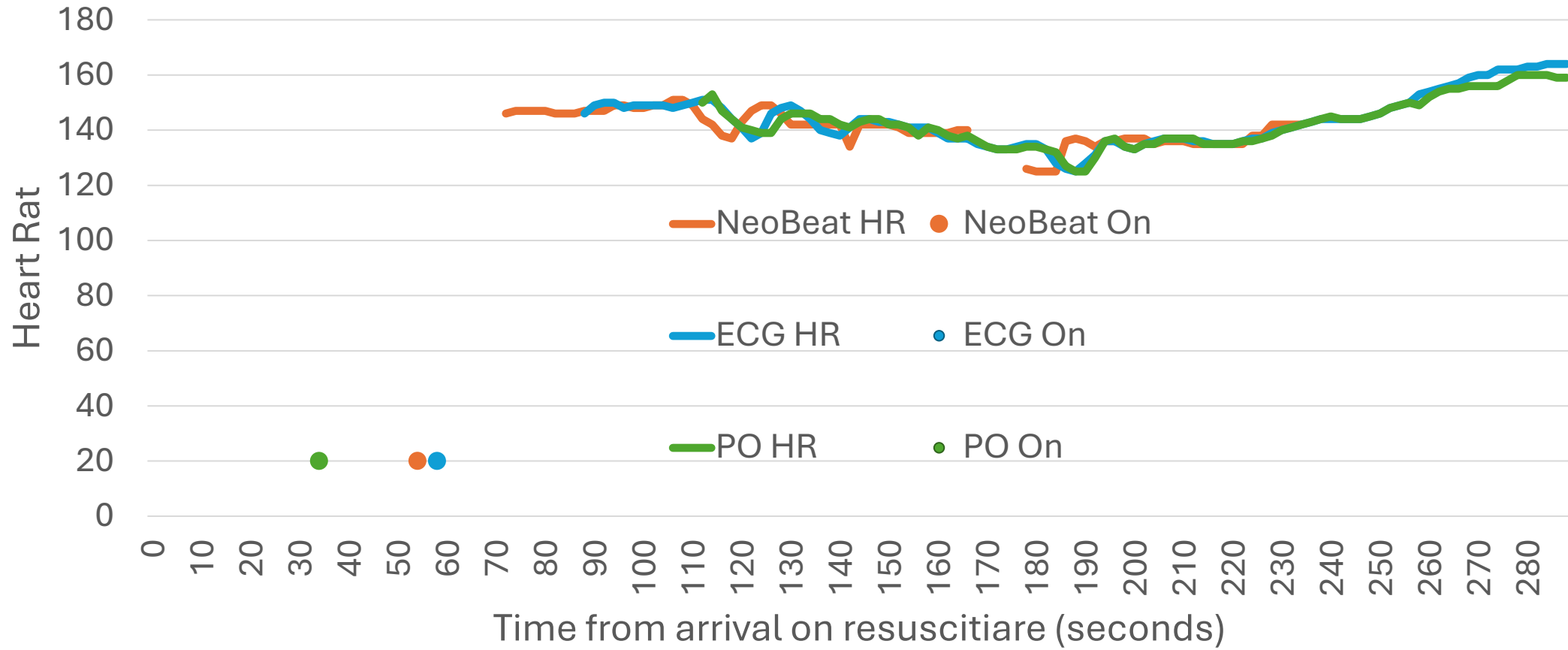
NeoBeat  
(newborns 1.5 – 5 kg)



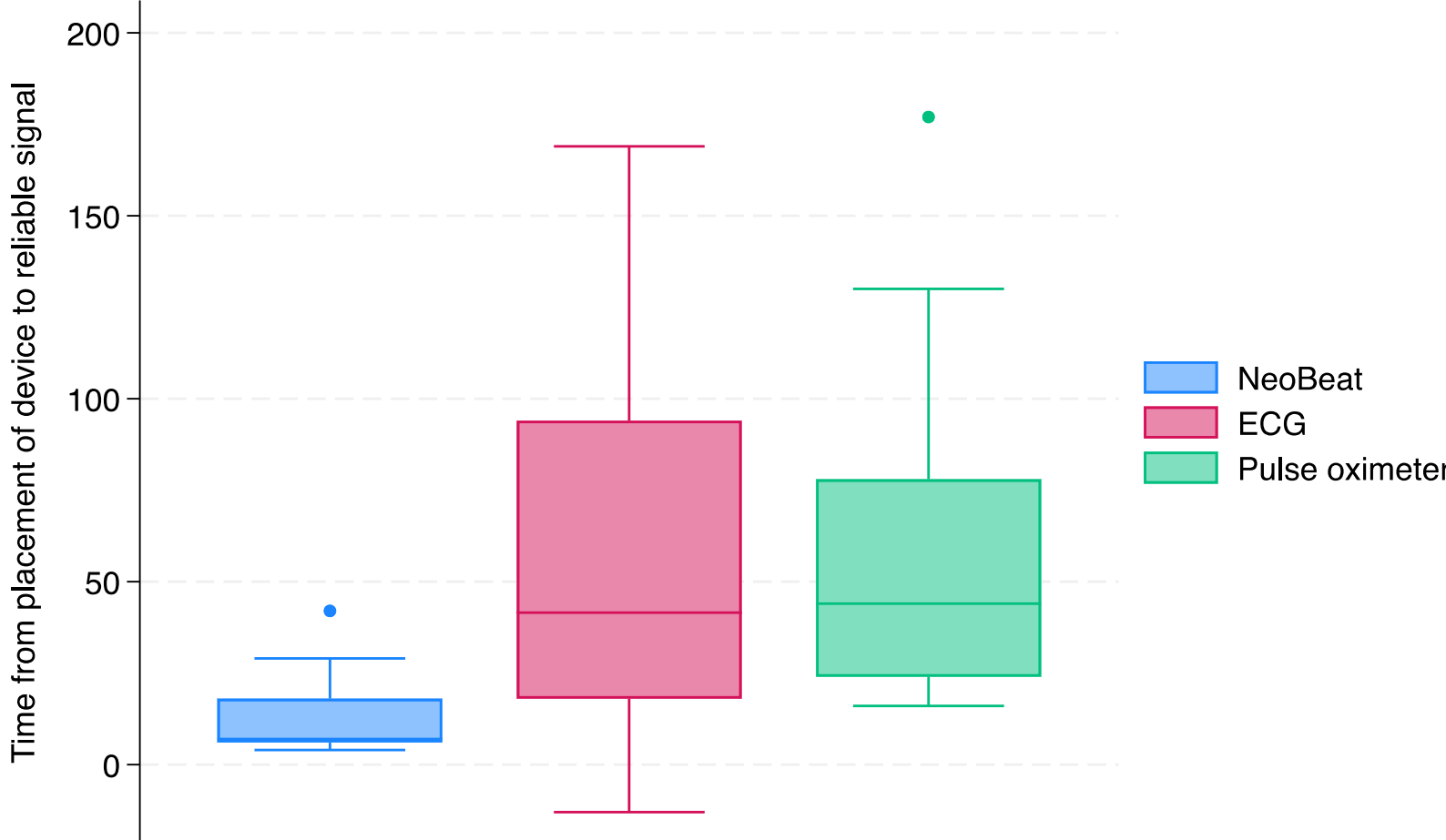
NeoBeat Mini  
(newborns 0.8 – 2 kg)



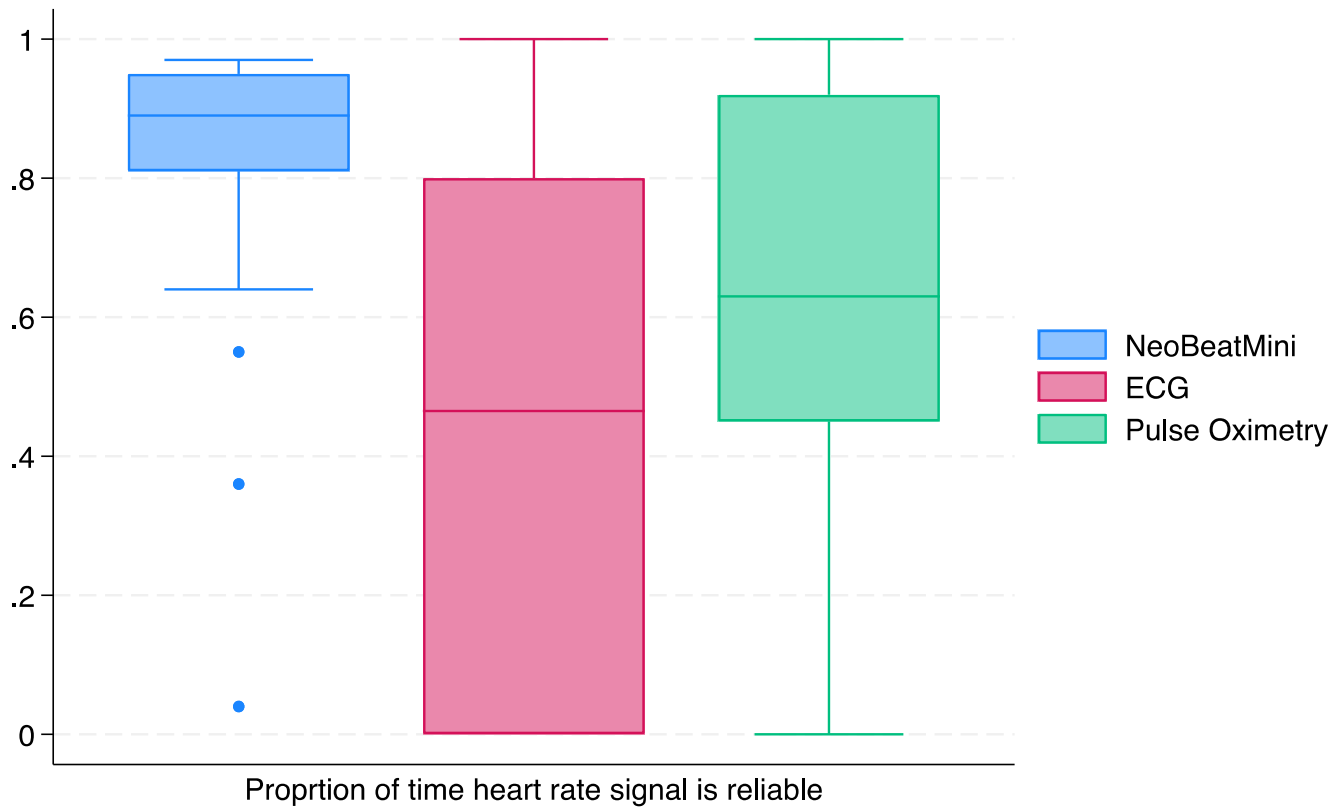
Infant 21  
BW 494g



# Time from placement to reliable signal



# Reliability



Device	Proportion of time signal is reliable (median, IQR)
NEOBEAT	0.89 (0.81, 0.95)
ECG	0.47 (0, 0.8)
Pulse Ox	0.63 (0.45, 0.92)

# Summary

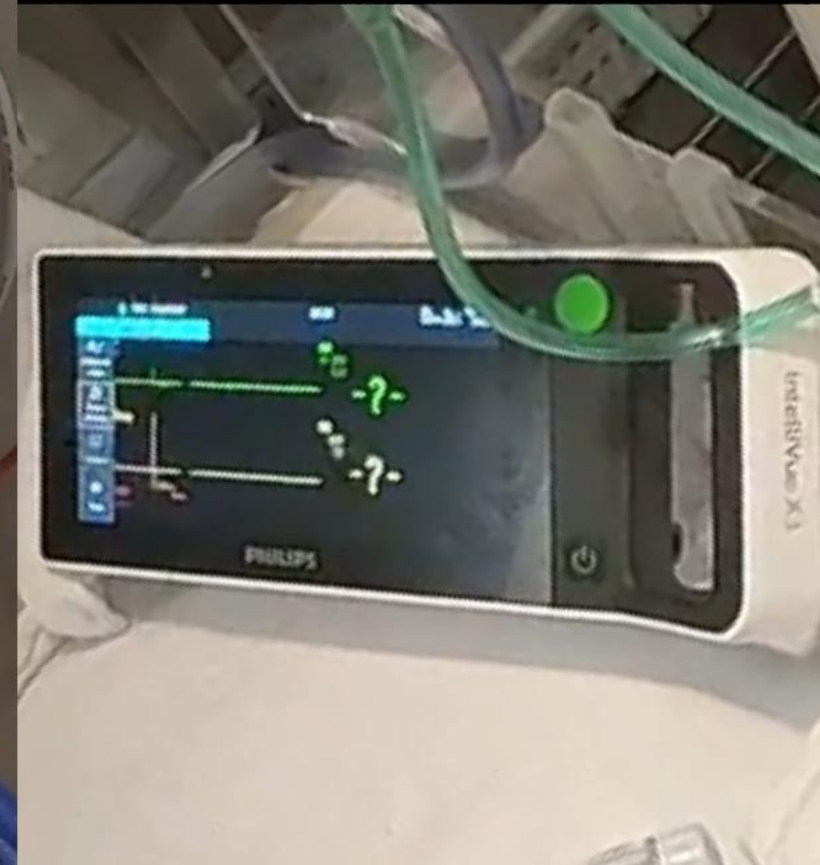
## Neobeat

- Is reusable and consumable-free
- Is accurate
- Is much quicker to apply than ECG (and PO)
- Displays data faster
- Is less "temperamental"

**...Video review is badly needed for all babies !**



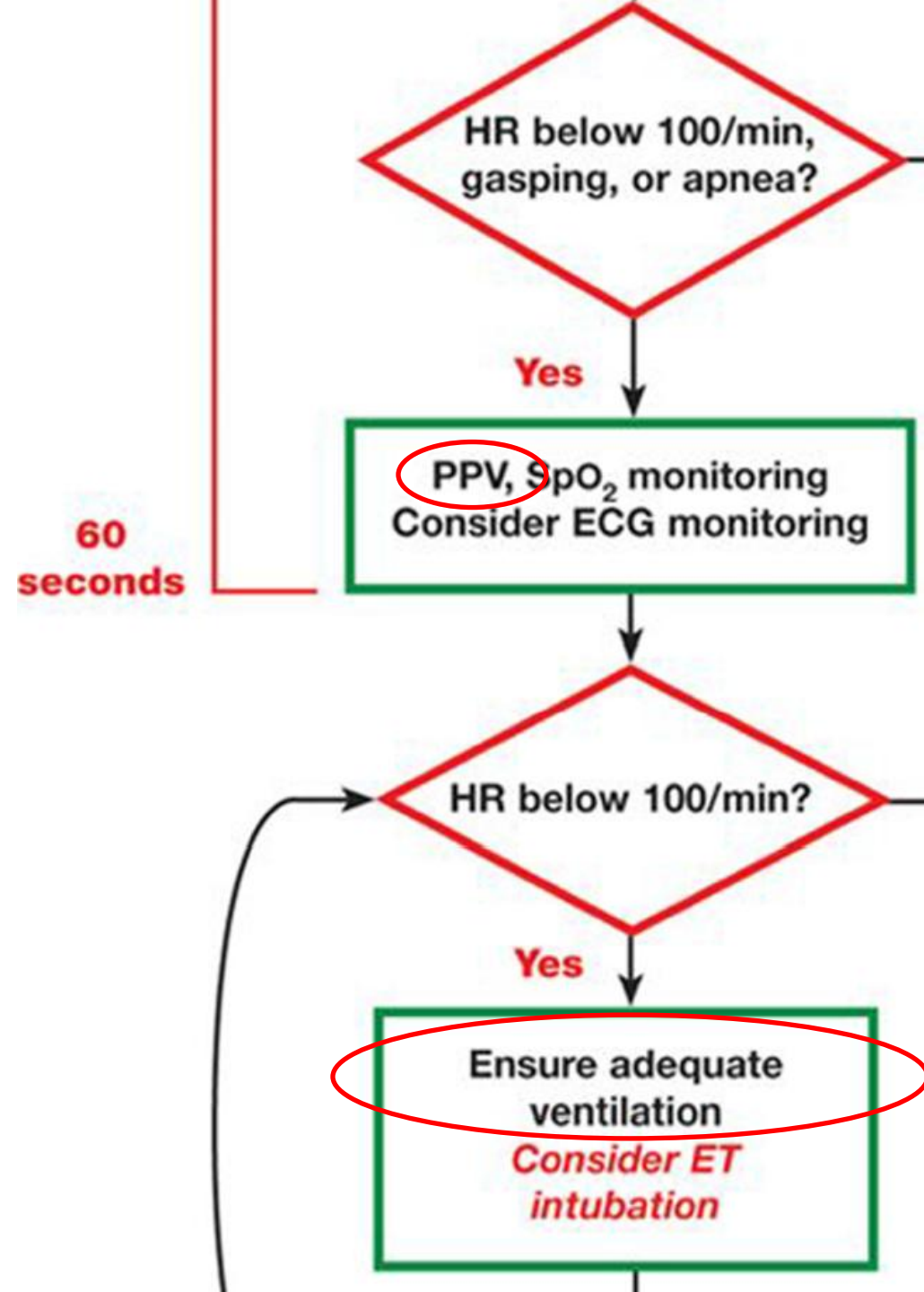
**APGAR**  
**00:26**



# **SMART EQUIPMENT: RESPIRATORY FUNCTION MONITORS**

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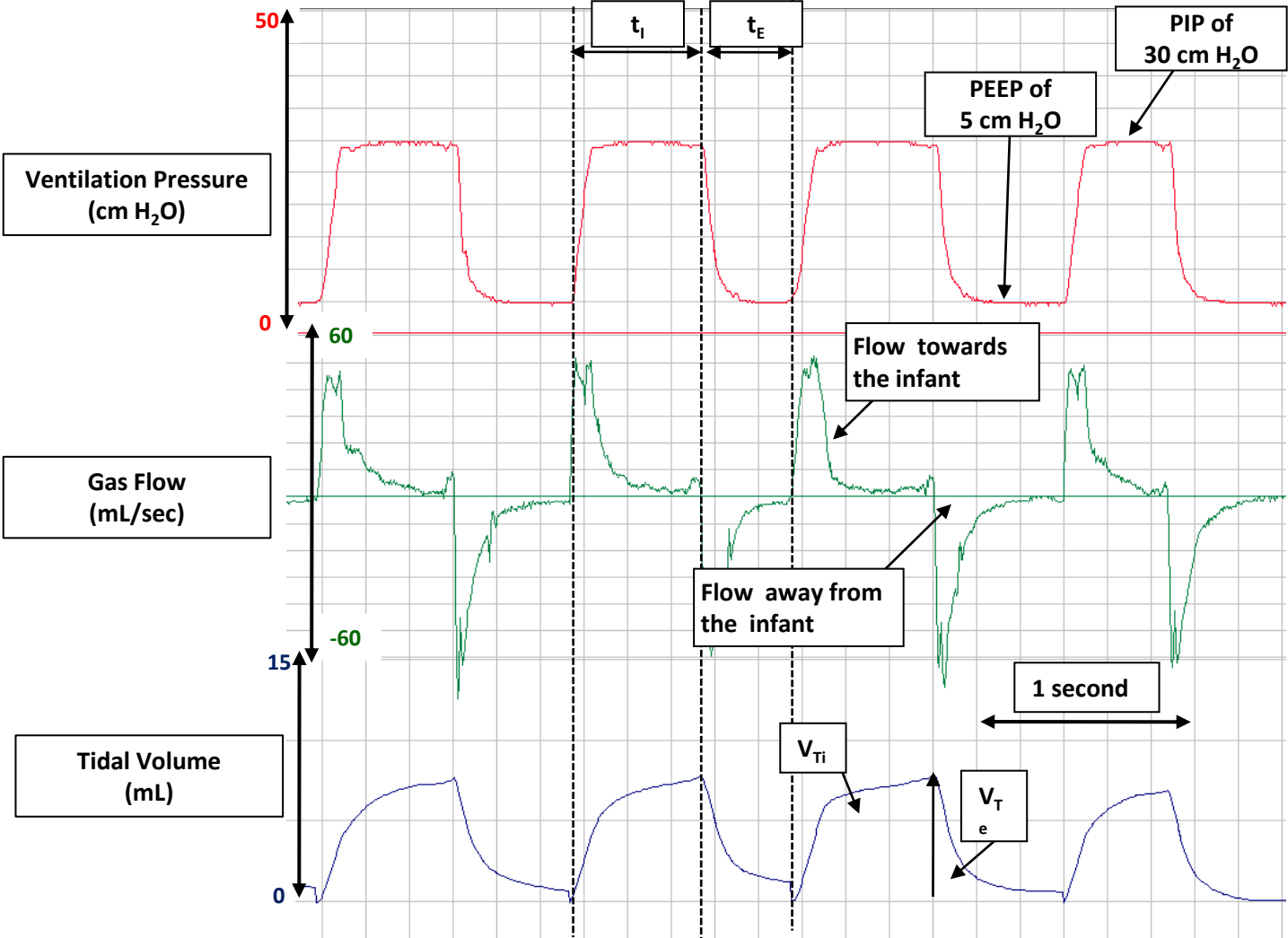
ILCOR  
Resuscitation  
algorithm  
(since 2020)



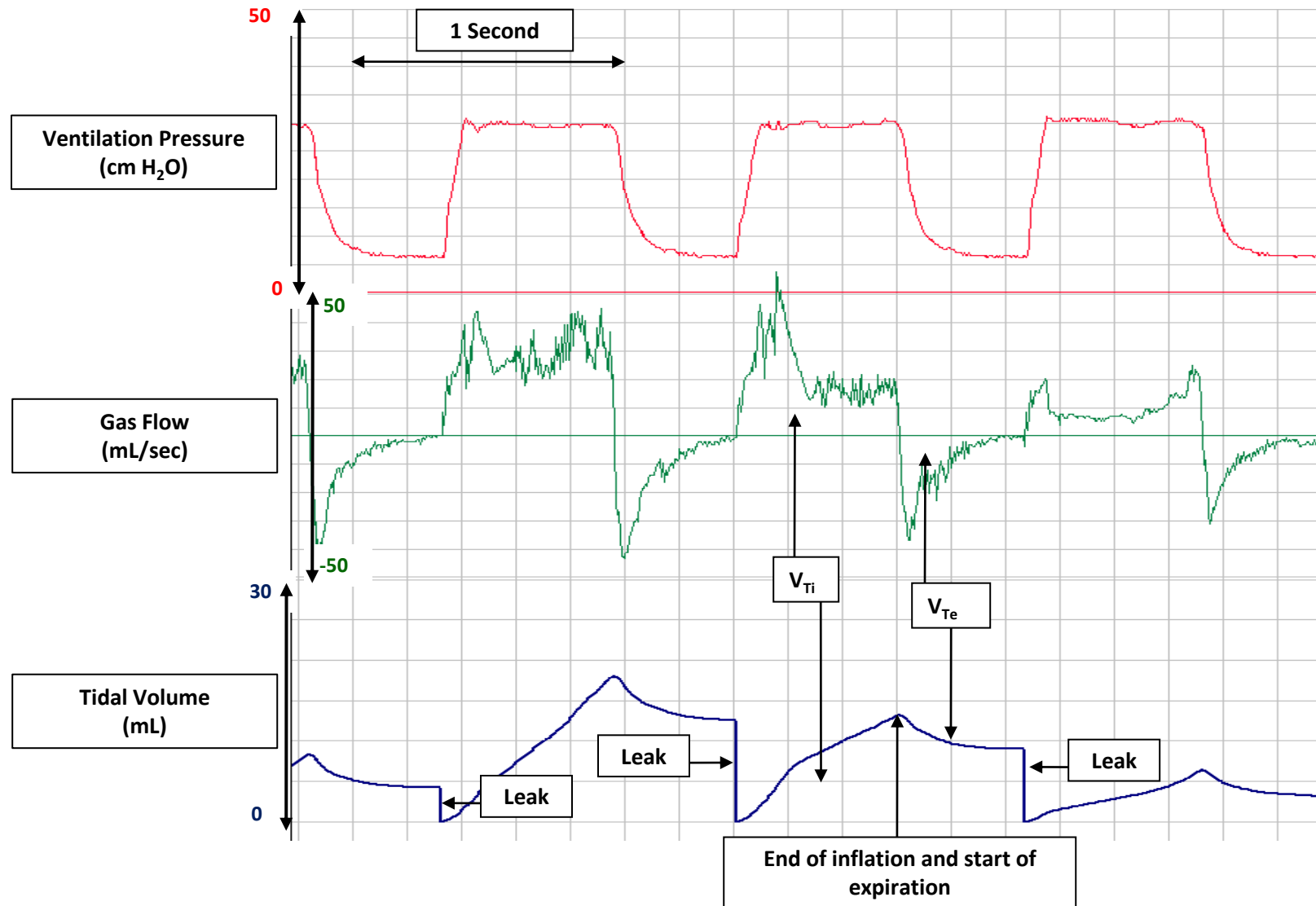
# Uses of a Respiratory Function Monitor

- Diagnose problems with mask ventilation
  - Leak
  - Obstruction
- Ensure delivery of effective and safe tidal volume

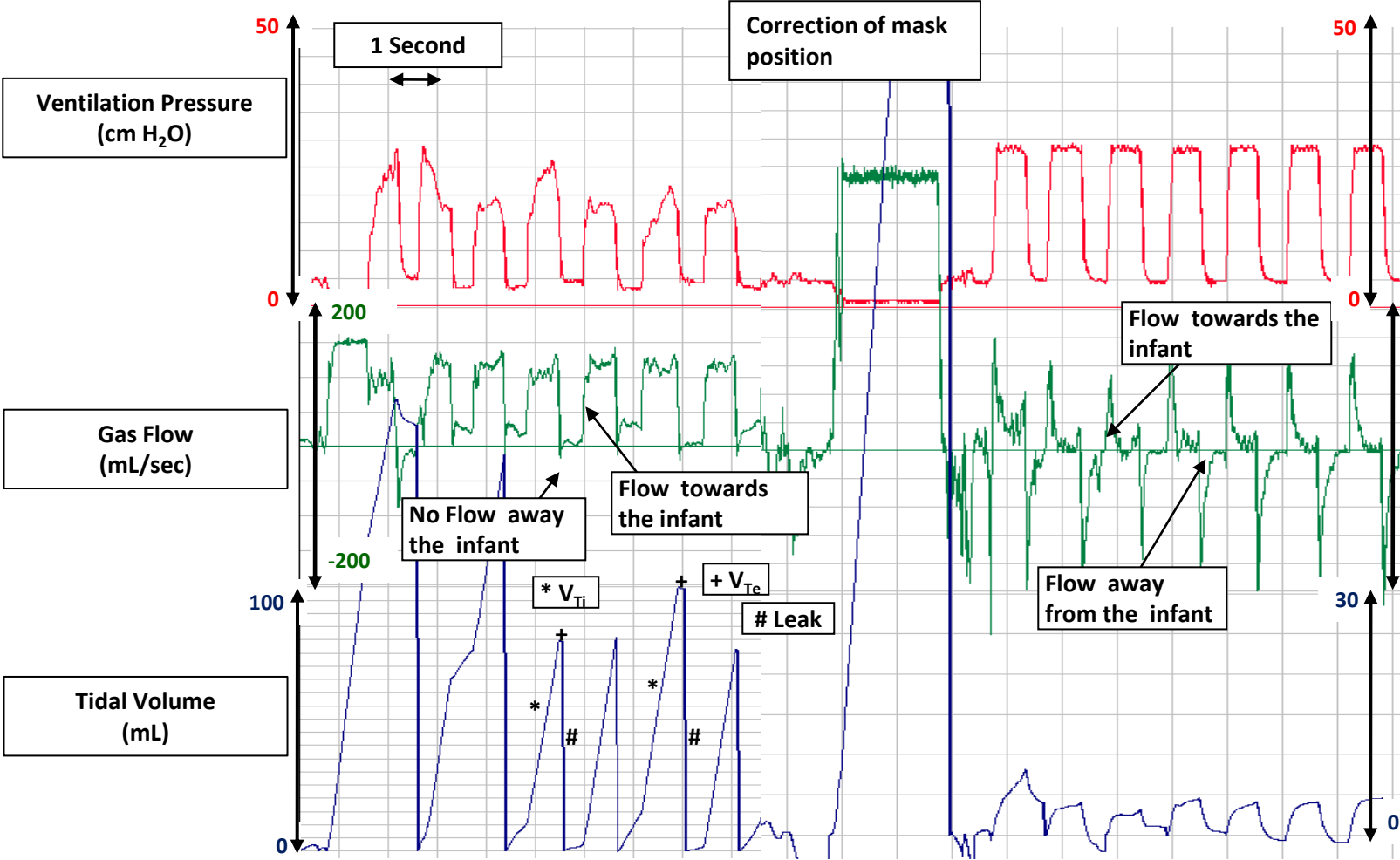
# Good mask ventilation



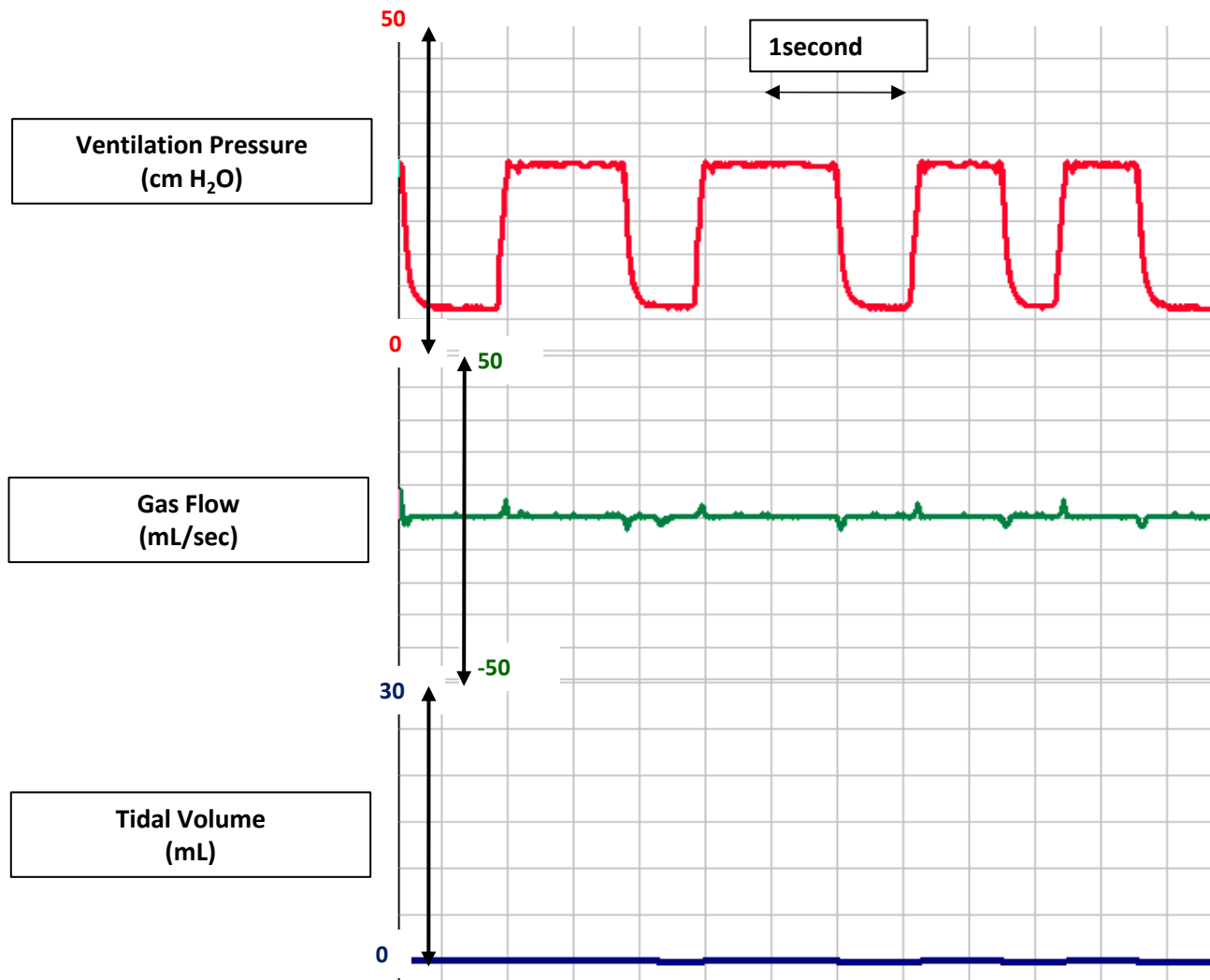
# Problem 1: Face mask leak



# Face mask leak and correction



# Problem 2: Airway obstruction



# How common?

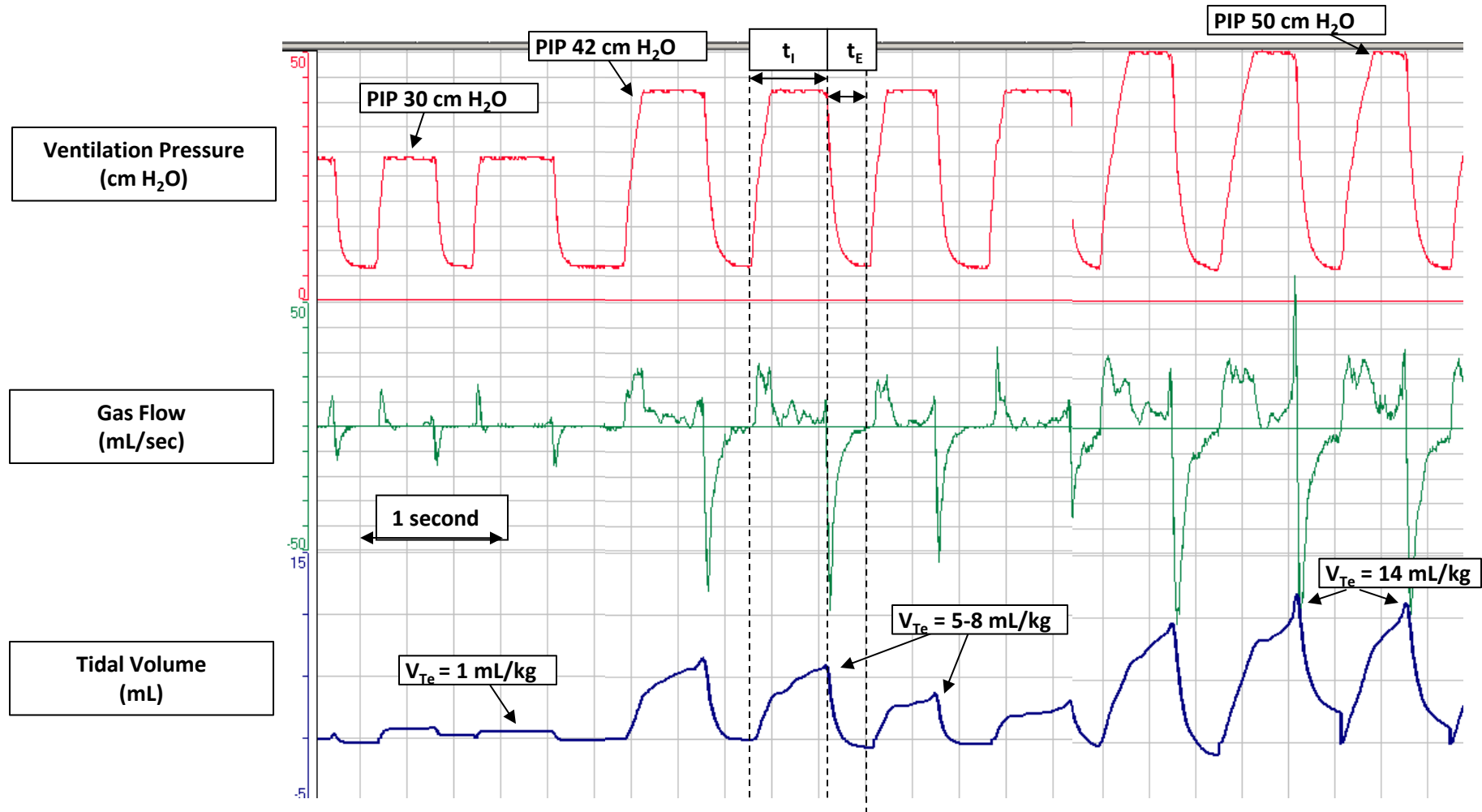
## Airway obstruction

- A 75% reduction in expired tidal volume (V<sub>Te</sub>)
- Occurred in **25%** of resuscitations

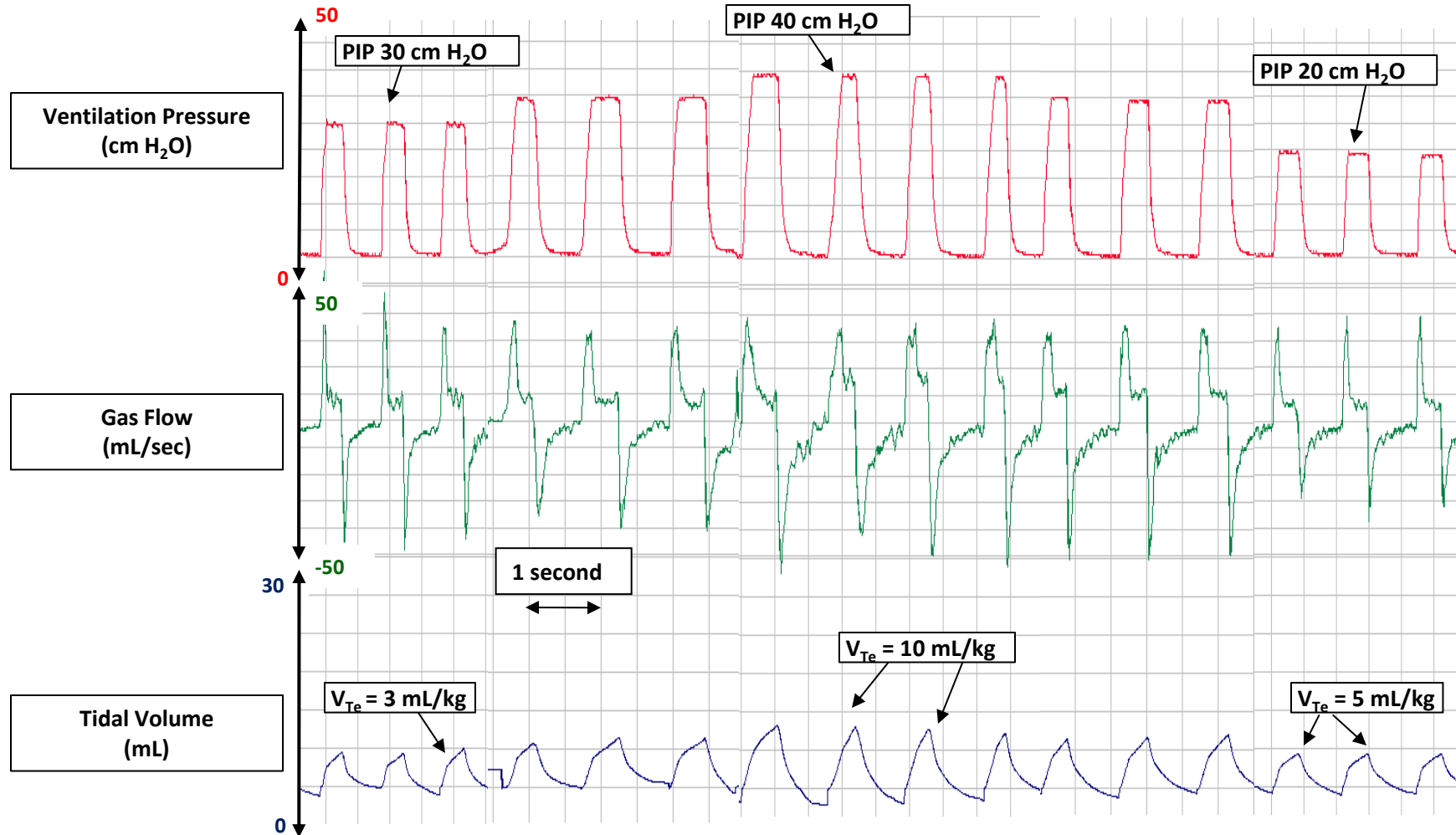
## Face-mask leak

- Mask leak of >75% defined as clinically important
- Occurred in **48%** of resuscitations

# Problem 3: Overventilation



# Targeting tidal volume



# Respiratory function monitors

Florian

A



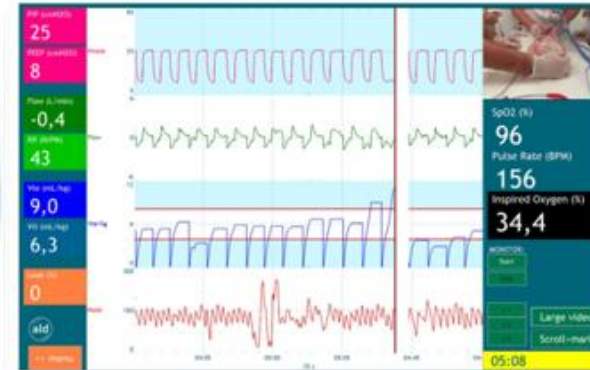
Respironics NM3

B



Lifebox

C



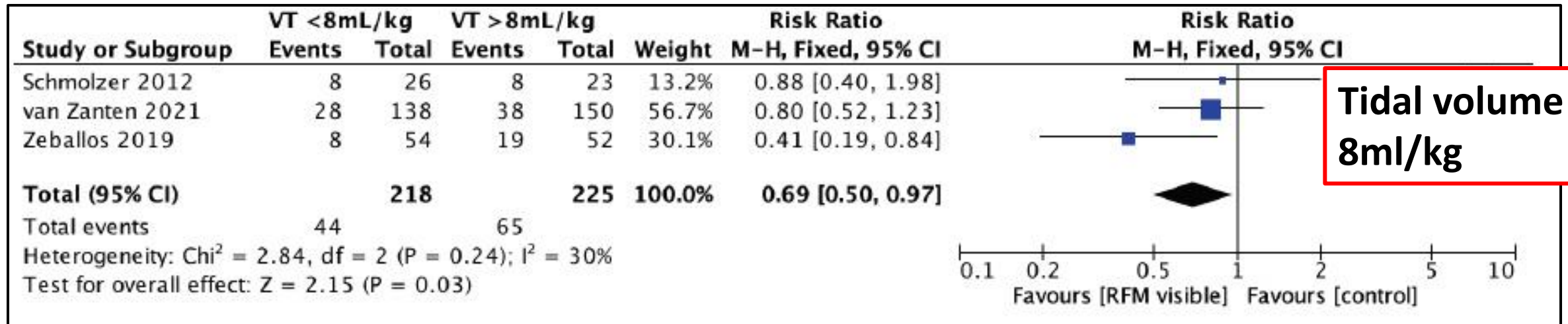
RFMs used in studies (Source: Schmölder *et al.*, Zeballos *et al.*, van Zanten *et al.*)

# Respiratory function monitoring to improve the outcomes following neonatal resuscitation: a systematic review and meta-analysis

Sarah Marie de Medeiros,<sup>1</sup> Avneet Mangat,<sup>2</sup> Graeme R Polglase ,<sup>3</sup>  
G Zeballos Sarrato,<sup>4</sup> Peter G Davis ,<sup>5</sup> Georg M Schmölzer  <sup>1,2</sup>

**Arch Dis Child Fetal Neonatal Ed 2022;0:F1–F8. doi:10.1136/archdischild-2021- 323017**

# Secondary outcome: excessive tidal volume



# Primary outcome: Death before discharge

Study or Subgroup	RFM visible		RFM masked		Weight	Risk Ratio
	Events	Total	Events	Total		M-H, Fixed, 95% CI
Schmolzer 2012	4	26	4	23	11.4%	0.88 [0.25, 3.14]
van Zanten 2021	11	54	9	52	24.5%	1.18 [0.53, 2.60]
Zeballos 2019	21	138	25	150	64.1%	0.91 [0.54, 1.55]
<b>Total (95% CI)</b>		<b>218</b>		<b>225</b>	<b>100.0%</b>	<b>0.97 [0.64, 1.48]</b>

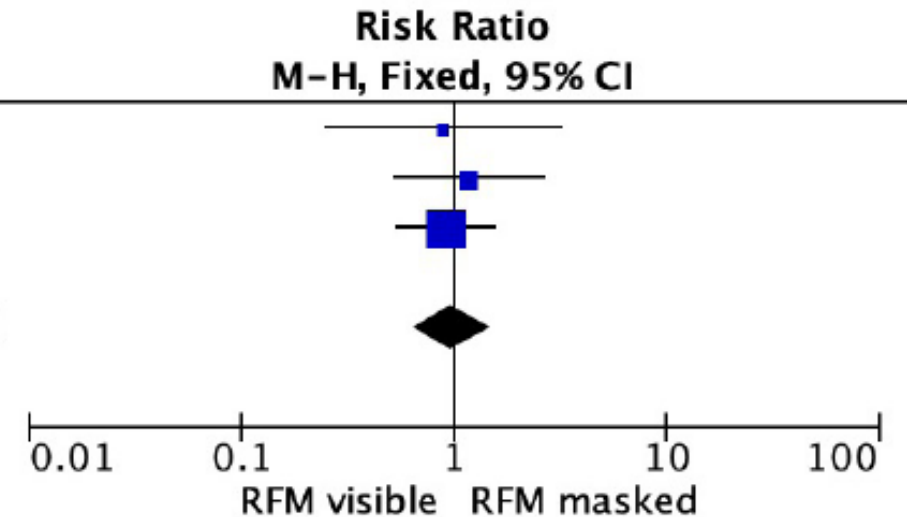
Total events

36

38

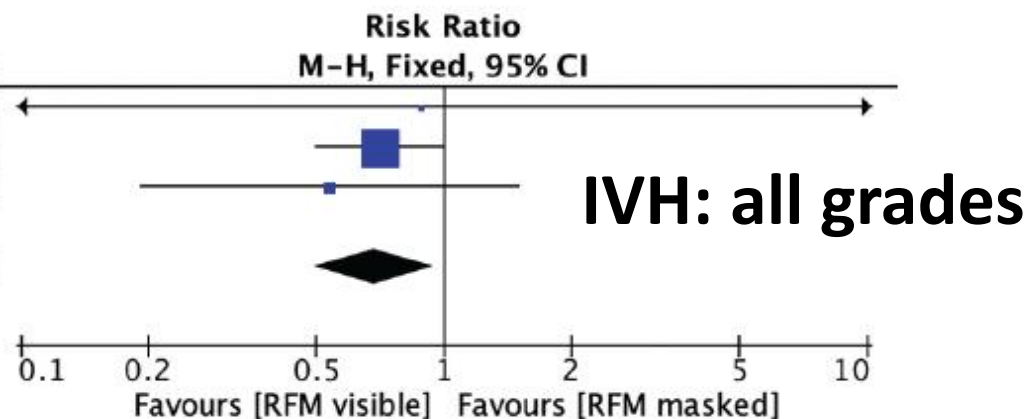
Heterogeneity:  $\text{Chi}^2 = 0.30$ ,  $\text{df} = 2$  ( $P = 0.86$ );  $I^2 = 0\%$

Test for overall effect:  $Z = 0.12$  ( $P = 0.90$ )

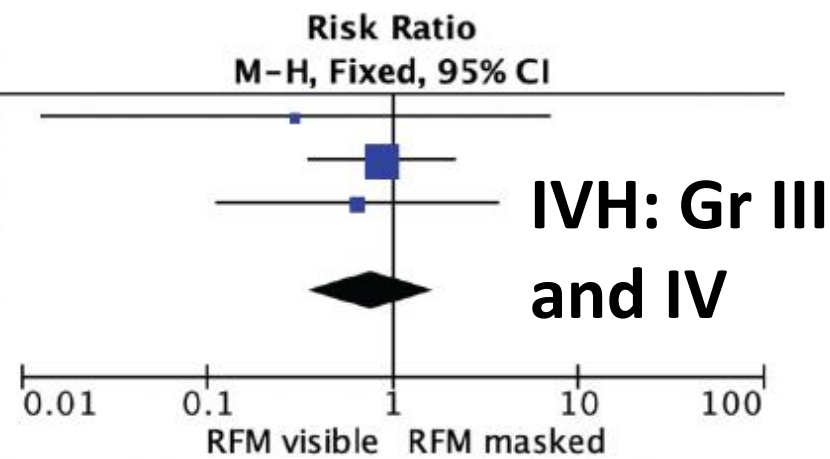


# Secondary outcome: Intraventricular hemorrhage

Study or Subgroup	RFM visible		RFM masked		Weight	Risk Ratio
	Events	Total	Events	Total		M-H, Fixed, 95% CI
Schmolzer 2012	1	26	1	23	1.7%	0.88 [0.06, 13.35]
van Zanten 2021	36	138	55	149	83.8%	0.71 [0.50, 1.00]
Zeballos 2019	5	54	9	52	14.5%	0.53 [0.19, 1.49]
<b>Total (95% CI)</b>		<b>218</b>		<b>224</b>	<b>100.0%</b>	<b>0.68 [0.49, 0.95]</b>
Total events	42		65			
Heterogeneity: $\text{Chi}^2 = 0.29$ , $\text{df} = 2$ ( $P = 0.87$ ); $I^2 = 0\%$						
Test for overall effect: $Z = 2.25$ ( $P = 0.02$ )						



Study or Subgroup	RFM visible		RFM masked		Weight	Risk Ratio
	Events	Total	Events	Total		M-H, Fixed, 95% CI
Schmolzer 2012	0	26	1	23	11.2%	0.30 [0.01, 6.94]
van Zanten 2021	8	138	10	150	67.4%	0.87 [0.35, 2.14]
Zeballos 2019	2	54	3	52	21.5%	0.64 [0.11, 3.69]
<b>Total (95% CI)</b>		<b>218</b>		<b>225</b>	<b>100.0%</b>	<b>0.76 [0.35, 1.63]</b>
Total events	10		14			
Heterogeneity: $\text{Chi}^2 = 0.47$ , $\text{df} = 2$ ( $P = 0.79$ ); $I^2 = 0\%$						
Test for overall effect: $Z = 0.71$ ( $P = 0.48$ )						



# Conclusions

- In infants <37 weeks, an RFM in addition to clinical assessment compared with clinical assessment during mask ventilation resulted in **similar in-hospital mortality**
  - significant reduction for any intraventricular hemorrhage
- Further trials are required to determine whether RFMs should be routinely available for neonatal resuscitation
- Have we got the design right?

# Respiratory function monitors

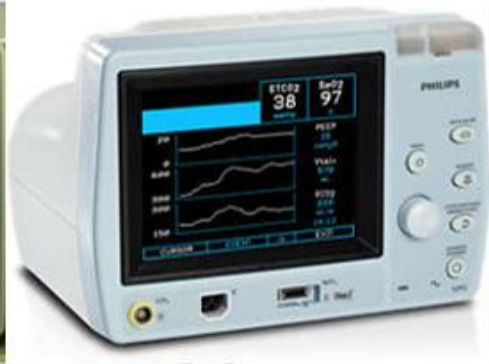
Florian

A



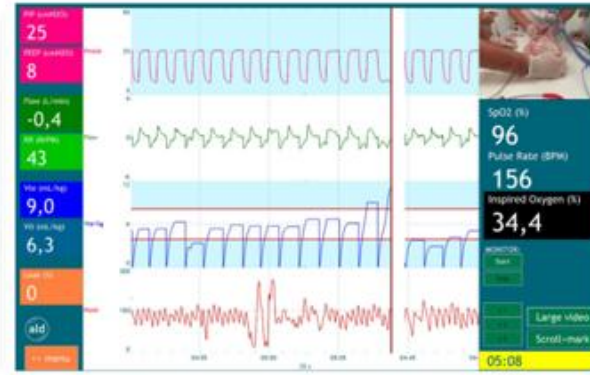
Respironics NM3

B



Lifebox

C



RFMs used in studies (Source: Schmölzer *et al.*, Zeballos *et al.*, van Zanten *et al.*)

**Human factors  
*must* be  
considered:  
Too much  
information?  
Distract from the  
baby?  
Need for  
training/retraining?**

# Next generation RFM

The JUNO Monitor (Australia)



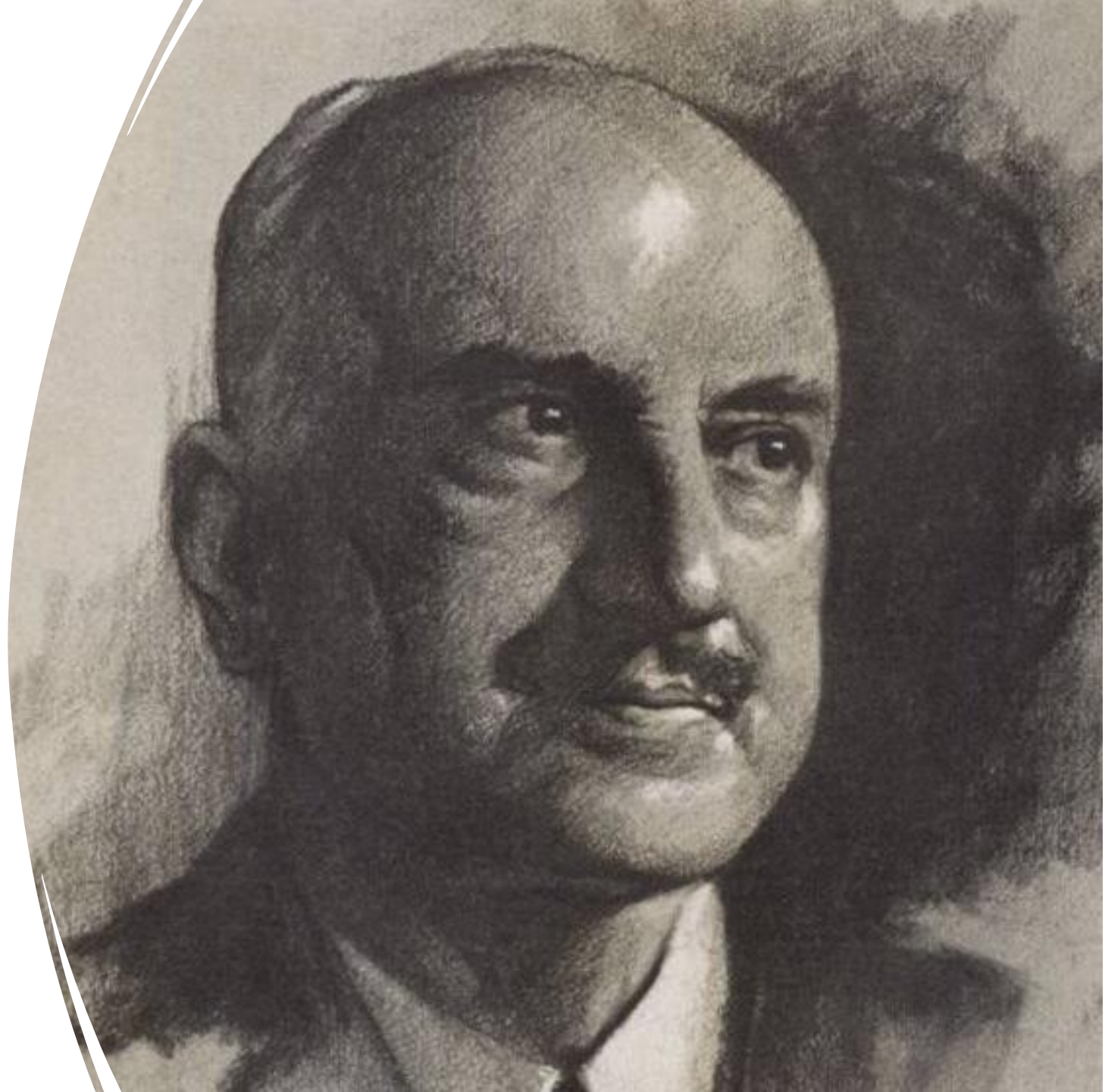
**LOOKING BACK BEFORE WE  
LOOK FORWARD**

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# George Santayana

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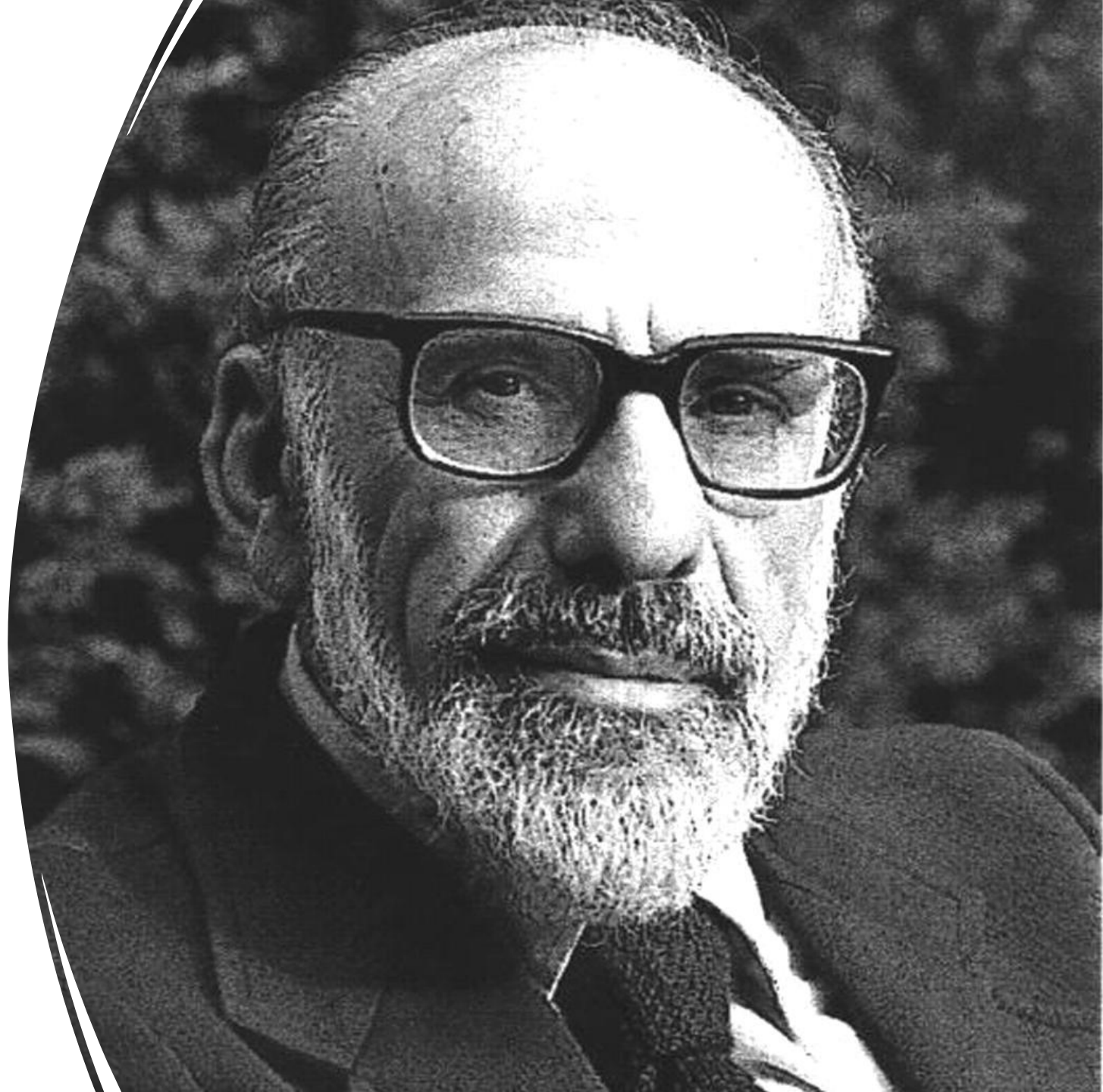
“Those who cannot  
remember the past are  
condemned to repeat it”



William (Bill)  
Silverman  
(1924-2004)

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**“Organized skepticism”**



<http://www.neonatology.org/classics/parable/>

**RETROLENTAL  
FIBROPLASIA**  
*A Modern Parable*

**WILLIAM A. SILVERMAN, M.D.**

**MONOGRAPHS IN  
NEONATOLOGY**

Results of some "Proclaimed" Therapies in the  
Development of Perinatal Medicine

	Consequences*		
	<i>Led to Sounder Practice</i>	<i>Led to Disaster</i>	<i>Misled into Fruitless Byways</i>
Gradual Changes in Therapy			
Testosterone to stimulate growth of prematures		?	
Thyroid hormone . . . ibid . . .			×
DES to prevent miscarriage		×	
Progestins to prevent miscarriage		×	
Exchange transfusion	×		
Supplemental oxygen for periodic breathing		×	
Initial thirsting and starving		× (?)	
Synthetic vitamin K prophylaxis		×	
Low-fat, high-protein feedings		?	
Sulfisoxazole prophylaxis		×	
Chloramphenicol prophylaxis		×	
Gastric emptying to prevent RDS**			×
Sternal traction for RDS			×
Epsom salt enemas for RDS		×	
Rocking-bed for RDS			×
Alevaire for RDS			×
Water mist for RDS			×
Acetylcholine for RDS			×
Respirator support in RDS	×		
Continuous positive airway pressure for RDS	× (?)		
Feeding gastrostomy for prematures		?	×
Ice water resuscitation for asphyxia			×
Sodium bicarbonate bolus infusions in asphyxia	?		
Lowered thermal environment		×	
Routine hexachlorophene bathing		?	
Phototherapy for hyperbilirubinemia	× (?)		

# Results of some “proclaimed” therapies in perinatal medicine (Silverman)

<b>Change in therapy</b>	<b>Led to disaster</b>	<b>Misled into fruitless byways</b>
<b>Diethyl stilbestrol to prevent miscarriage</b>	<b>x</b>	
<b>Supplemental oxygen for periodic breathing</b>	<b>x</b>	
<b>Chloramphenicol prophylaxis</b>	<b>x</b>	
<b>Lowered thermal environment</b>	<b>x</b>	
<b>Iced water resuscitation for asphyxia</b>		<b>x</b>
<b>Water mist for RDS</b>		<b>x</b>
<b>Sternal traction for RDS</b>		<b>x</b>

## Organised scepticism looks like:

- Well designed, adequately powered, (randomised controlled) trials recruiting the spectrum of infants to who the results will be applied

# **BARRIERS TO GOOD RESEARCH IN THE DR: CONSENT**

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# Two Cases

- *A pregnant woman at 24 weeks' presents with pain and bleeding*
- *Pain settles, cervix closed*
- *Admitted and given corticosteroids*
- *Approached for prospective consent for a DR trial in case labour eventuates*
- *Consent is obtained*
- *CS 4 days later for worrying CTG, after first receiving MgSO<sub>4</sub>*
- *After birth her baby is enrolled in the study*



- *A pregnant woman at 24 weeks' presents with pain and bleeding*
- *Cervix 4cm dilated with cord presentation*
- *Rushed directly to theatre for C-section*
- *No corticosteroids or MgSO<sub>4</sub>*
- *No possibility for prospective consent for a DR trial*
- *"Eligible" baby missed for enrolment*



# Selection bias in neonatal DR trials

## IN

Good antenatal care

'Inborn'

Antenatal steroids

Well mother

Preeclampsia

**Good outcome more likely**

## OUT

Limited antenatal care

'Outborn'

No antenatal steroids

Unwell mother

Placental abruption

**Poor outcome more likely**

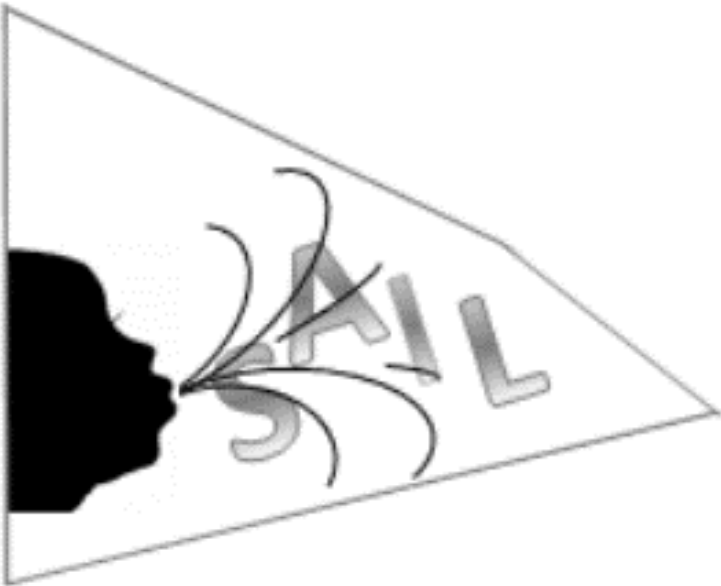
JAMA | **Original Investigation**

# Effect of Sustained Inflations vs Intermittent Positive Pressure Ventilation on Bronchopulmonary Dysplasia or Death Among Extremely Preterm Infants The SAIL Randomized Clinical Trial

Haresh Kirpalani, BM, MSc; Sarah J. Ratcliffe, PhD; Martin Keszler, MD; Peter G. Davis, MD, FRACP; Elizabeth E. Foglia, MD, MSCE; Arjan te Pas, MD, PhD; Melissa Fernando, MPH; Aasma Chaudhary, BS, RRT; Russell Localio, PhD; Anton H. van Kaam, MD, PhD; Wes Onland, MD, PhD; Louise S. Owen, MD, FRACP; Georg M. Schmölzer, MD, PhD; Anup Katheria, MD; Helmut Hummler, MD, MBA; Gianluca Lista, MD, PhD; Soraya Abbasi, MD; Daniel Klotz, MD; Burkhard Simma, MD; Vinay Nadkarni, MD, MS; Francis R. Poulain, MD; Steven M. Donn, MD; Han-Suk Kim, MD, PhD; Won Soon Park, MD, PhD; Claudia Cadet, MD; Juin Yee Kong, MD; Alexandra Smith, MD; Ursula Guillen, MD, MSE; Helen G. Liley, MB, ChB, FRACP; Andrew O. Hopper, MD; Masanori Tamura, MD, PhD; for the SAIL Site Investigators

*JAMA*. 2019;321(12):1165-1175. doi:10.1001/jama.2019.1660

# The SAIL experience



18 centres in 9 countries recruited infants:

- 12 used prospective antenatal consent only
- 6 sites (4 continents) allowed deferred consent

*Unpublished data.*

*Thanks to: Louise Owen, Sarah Ratcliffe, Elizabeth Foglia, Haresh Kirpalani and the SAIL trial investigators*

# Does the use of deferred consent in neonatal clinical trials affect:

- FEASIBILITY?
- GENERALISABILITY?
- PATIENT OUTCOMES?
- TRIAL RESULTS?

Does the use of deferred consent in neonatal clinical trials affect:

1. **FEASIBILITY – Can we get the trial done on time?**
2. GENERALISABILITY?
3. PATIENT OUTCOMES?
3. TRIAL RESULTS?

# SAIL Trial (unpublished data)

Parameter	Prospective consent (12 centres)	Deferred consent available (6 centres)
Eligible	473	315
Randomised and consented	197	229
Randomised and consented	<b>42%</b>	<b>73%</b>

Absolute difference: **31% (95% CI: 24%, 38%), P<0.001**



# Does the use of deferred consent in neonatal clinical trials affect:

1. FEASIBILITY?
2. GENERALISABILITY – Can we apply the results of our trial to all our patients?
3. PATIENT OUTCOMES?
3. TRIAL RESULTS?

# Characteristics

Infant characteristics	Prospective only (n=197)	Deferred available (n=229)	P value
Complete antenatal steroids	84%	73%	0.012
Intubated in DR	64%	46%	0.001

# Does the use of deferred consent in neonatal clinical trials affect:

1. FEASIBILITY?
2. GENERALISABILITY?
- 3. PATIENT OUTCOMES?**
3. TRIAL RESULTS?

# Outcomes

Infant outcome	Prospective only (n=197)	Deferred available (n=229)	Adjusted relative risk
Death or BPD	57%	65%	1.2 (0.98, 1.14)
Any IVH	24%	35%	1.6 (1.1, 2.4)
Necrotising enterocolitis	9%	18%	2.6 (1.5, 4.7)

# Does the use of deferred consent in neonatal clinical trials affect:

1. FEASIBILITY?
2. GENERALISABILITY?
3. OUTCOMES?
- 3. TRIAL RESULTS?**

# Effect on SAIL primary outcome

Death or BPD	Sustained Inflation (intervention)	Standard PPV (control)	Risk Difference (95% CI)	P value
Antenatal consent only	58%	57%	1.0 (-14.6, 14.1)	0.88
Deferred consent available	70%	60%	9.6 (-2.2, 22.9)	0.13



# Effect on early deaths in SAIL

<b>Deaths &lt;48 hours</b>	<b>Sustained Inflation</b>	<b>Standard PPV</b>	<b>Risk Difference (95% CI)</b>	<b>P value</b>
Overall	7.4%	1.4%	5.6 (2.1, 9.1)	0.002
Antenatal consent only	5.9%	2.1%	3.8 (-1.6, 9.2)	0.28
Deferred consent available	8.8%	0.9%	8.0 (2.5, 13.5)	0.005



# Does the use of deferred consent in neonatal clinical trials affect:

- |                      |         |
|----------------------|---------|
| 1. FEASIBILITY?      | Yes     |
| 2. GENERALISABILITY? | Yes     |
| 3. OUTCOMES?         | Yes     |
| 3. TRIAL RESULTS?    | Perhaps |



Leading article

# Deferred consent for the enrolment of neonates in delivery room studies: strengthening the approach

Maria C den Boer,<sup>1,2</sup> Mirjam Houtlosser,<sup>2</sup> Elizabeth E Foglia,<sup>3</sup>  
Peter G Davis,<sup>4</sup> Anton H van Kaam,<sup>5</sup> Camille O F Kamlin,<sup>6</sup>  
Georg M Schmölzer,<sup>7</sup> Martine C de Vries,<sup>2,8</sup> Arjan B te Pas<sup>1</sup>

# Deferred consent is...

- USA: 'Exception from informed consent'
- Canada: 'Exception to consent'
- Australia/UK: 'Research without prior consent'
- European Union: 'Informed consent to participate in a clinical trial after the decision to include the subject in the clinical trial'

# The Delivery Room of the future: A Learning Health System

- Sets a moral priority on continuously evaluating and improving health care
- Knowledge development and translation are integrated into the core of the healthcare delivery process
- Useful for comparative effectiveness studies involving no more than minimal (additional) risk
  - Waiver or deferred consent may be appropriate
- Requires extensive consultation with:
  - Parents, ethics committees, clinicians and investigators

# Summary and implications

- Neonatal clinical research is unique and challenging
- The use of deferred consent may increase enrolment, achieve a more representative sample and increase generalisability (and change trial results!)
- There is ongoing uncertainty/controversy regarding acceptability to clinicians, researchers, ethical review boards, public and **parents**
  - Education
  - Research
- Sensitivity around the process, including consenting bereaved families
- Is deferred consent the best model?
- There is a need to balance patient protection and parental autonomy with the appropriate testing of new and existing therapies

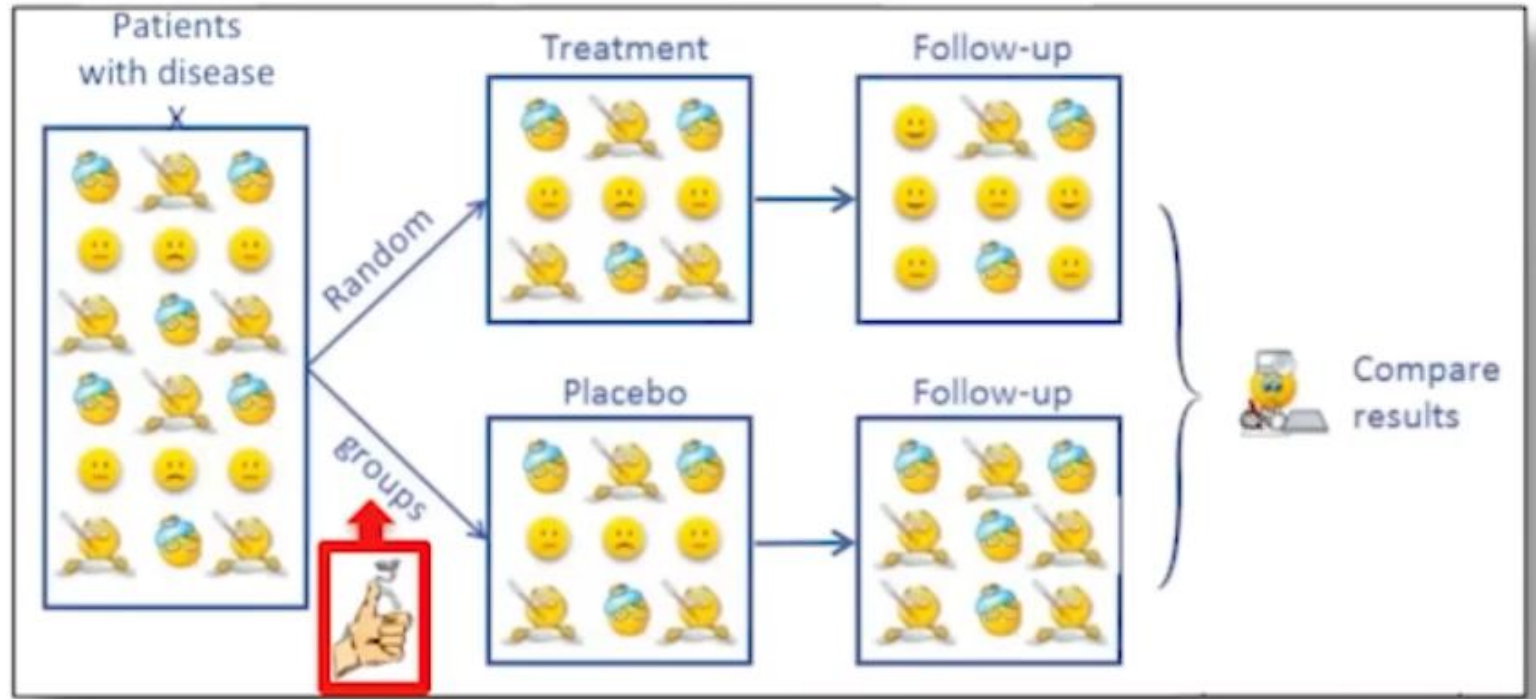


# A New Paradigm

# Traditional RCTs



Traditional fixed-sample design:



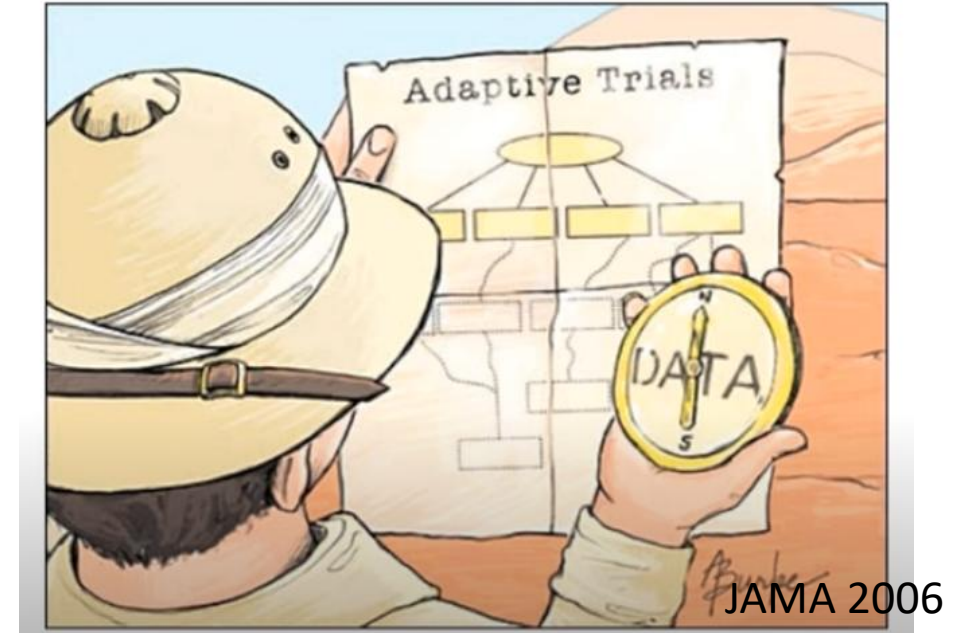
# Limitations of traditional RCTs

- Cost
- Slow progress
  - Time to complete
    - First patient in SUPPORT recruited in 2005, NeOProM published 2018!
  - One question at a time
- “Representativeness”?

# The alternative: Adaptive platform trials?

- Adaptive

- Population
- Sample size
- Multiple interventions
- Defined stop/start rules
- New treatments added
- Interim and final analyses

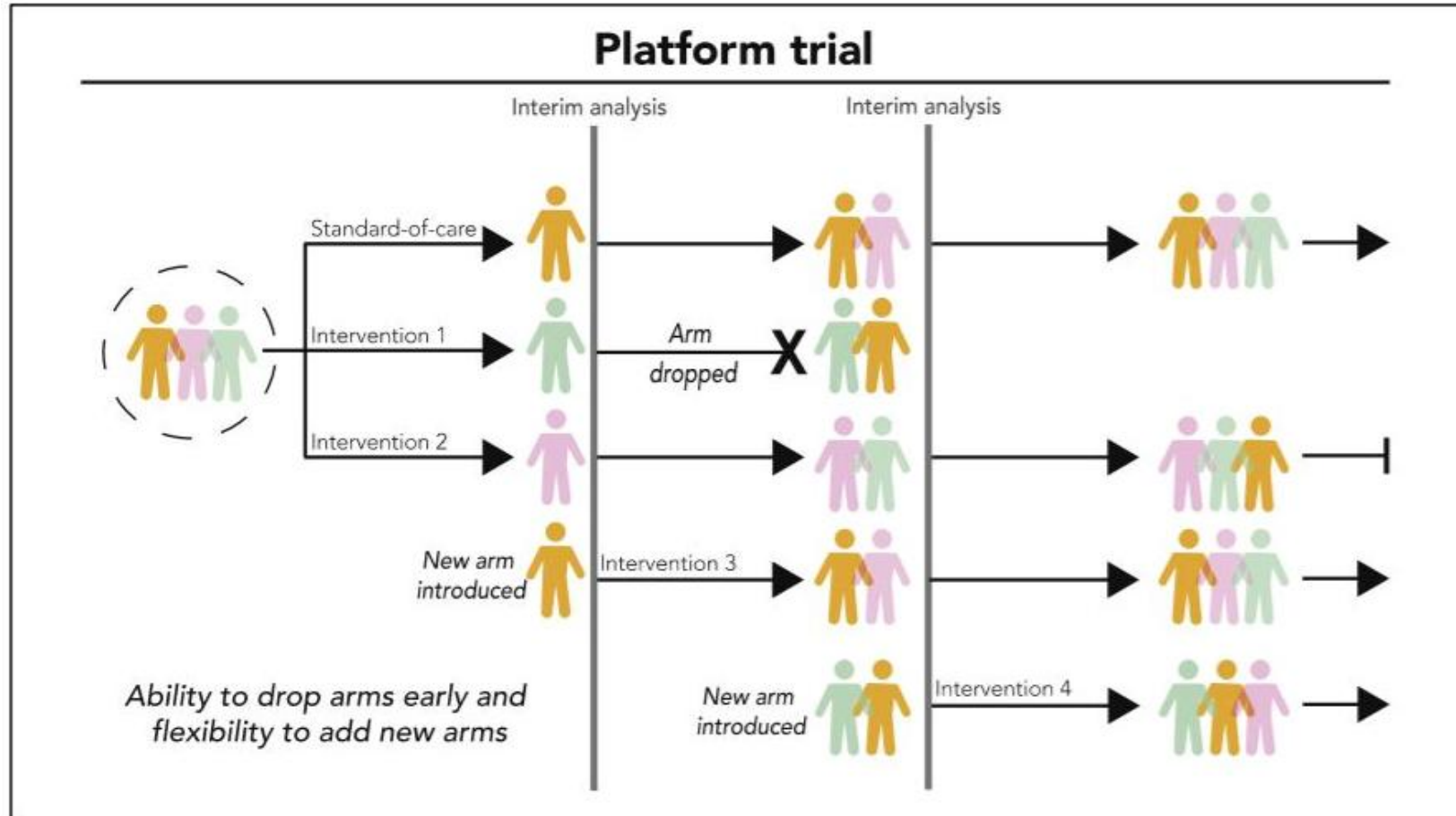


- Platform

- Common master protocol
- Common primary outcome
- Co-ordinated network and trial workforce



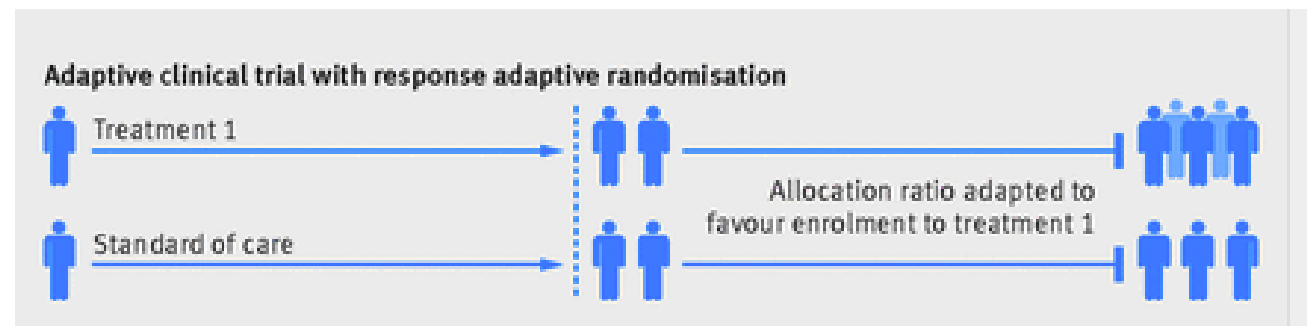
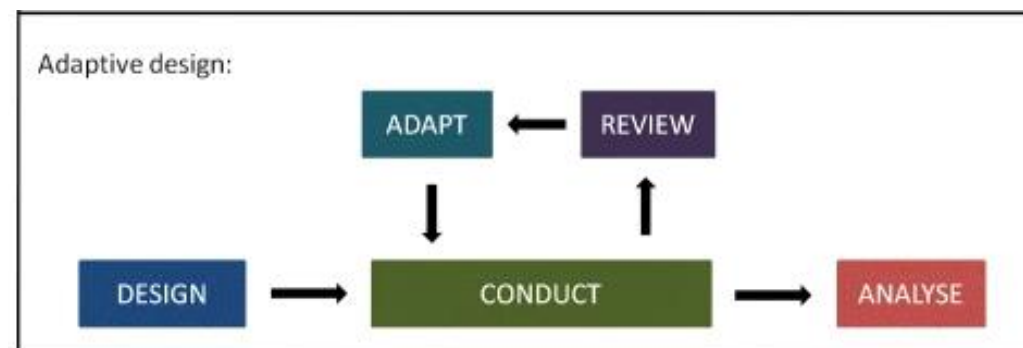
# How does an APT work?



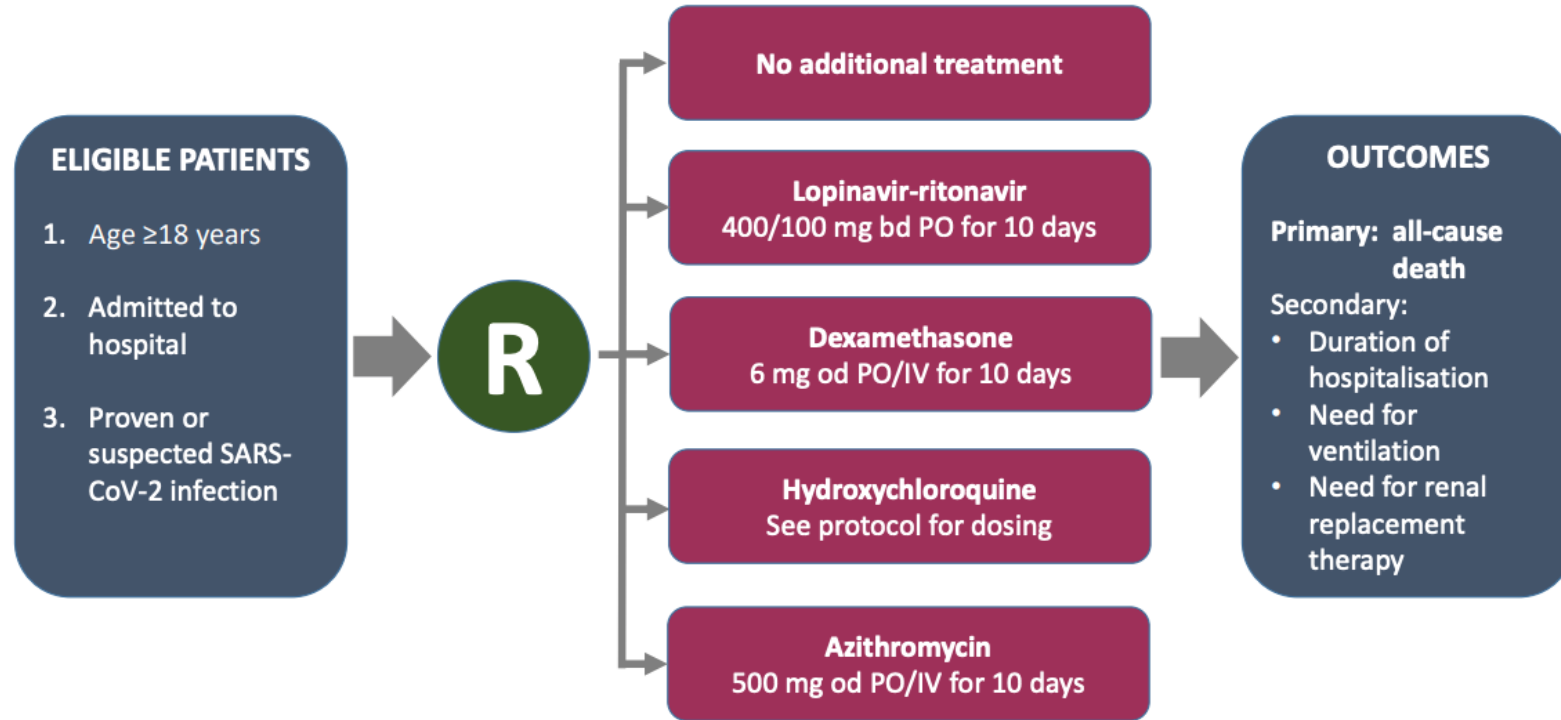
Park JJ, Harari O, Dron L, Lester RT, Thorlund K, Mills EJ.  
An overview of platform trials with a checklist for clinical readers.  
*Journal of Clinical Epidemiology*. 2020 May 13.

# What are the benefits?

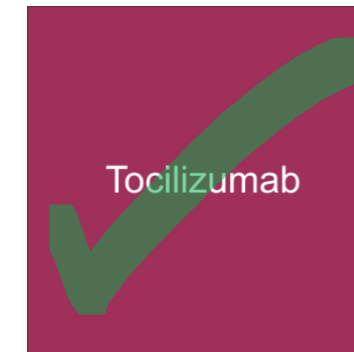
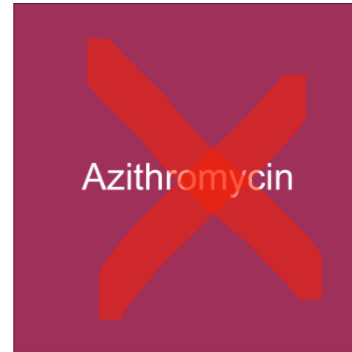
- Improved efficiency
- Cost saving
- Personalised treatments
- Answer multiple questions
- Answer complex questions
- Perpetual
- Ethical



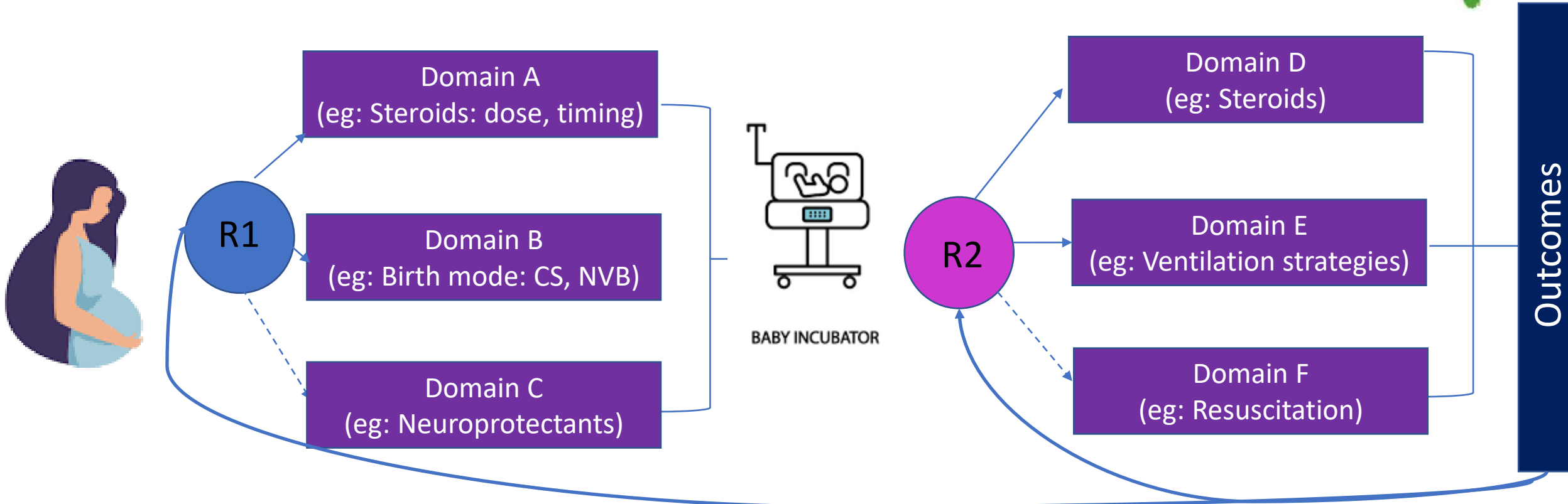
# COVID-19 and APTs



# Recovery



# An APT for preterm birth – are we ready?



Accumulated data helps guide randomization

# Our first attempt

- Antenatal:
  - Women at imminent risk of preterm birth < 35 weeks randomised to betamethasone
    - standard dose (2 x 12mg 24 hours apart)
    - medium dose (4 x 6mg 12 hours apart)
    - low dose (4 x 3mg 12 hours apart)
- Neonatal
  - Very preterm infants randomised to caffeine
    - higher dose (40mg/kg load and 20mg/kg/day maintenance)
    - medium dose 30mg/kg load and 15mg/kg/day maintenance)
    - lower dose (20mg/kg load and 10mg/kg/day maintenance)

# Conclusions

- Moral and ethical imperative to improve the care of newborn babies
- Randomised trials are critical to identify effective treatments
- Successful trials have high quality and power
  - Collaboration is key to recruitment of sufficient numbers (ideally protocols harmonised prospectively)
- Alternative modes of consent may be required for trials in emergency situations
- Alternative trial designs like Adaptive Platform Trials are required to quickly and efficiently advance care

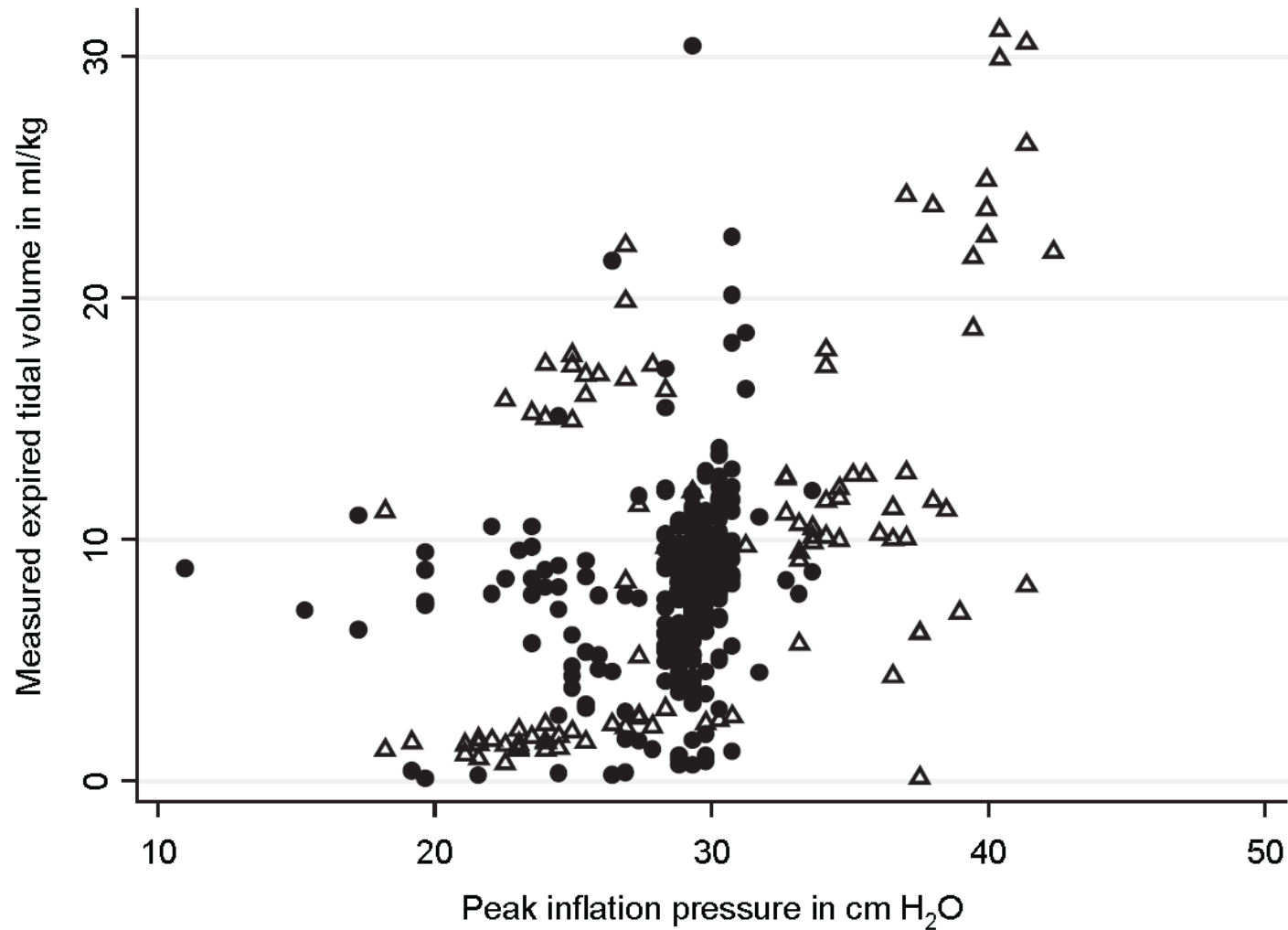


**“Keep it small and you will make a difference”**



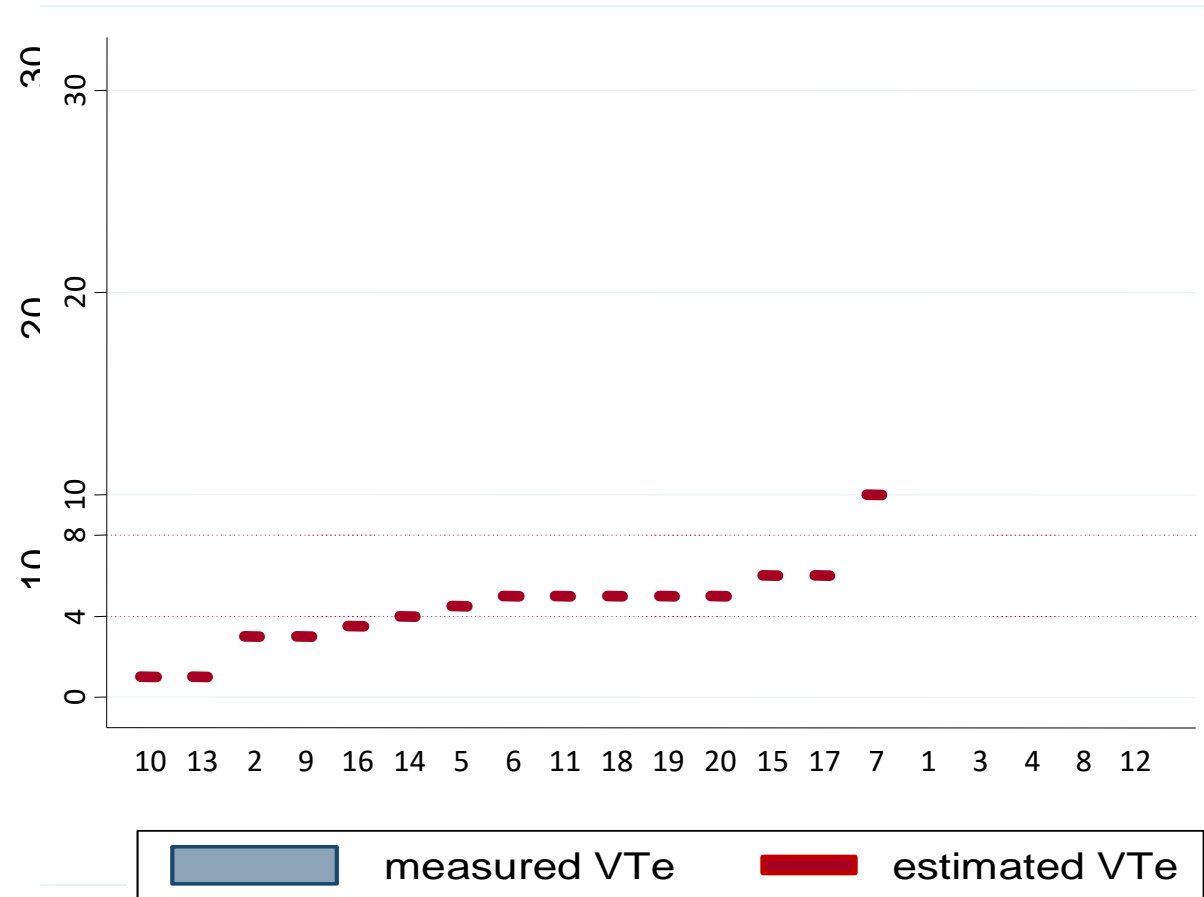
**Pete Seeger (1919-2014)**

# Displayed PIP is a poor surrogate for tidal volume delivered



*Schmoelzer et al, ADC (F&N Ed, 2010)*

# Tidal volume



*Poulton et al, Resuscitation 2011.*

# Tidal volume

