

# Balancing Brain and Lung Protection in the NICU using Transcutaneous CO<sub>2</sub>

## INTRODUCTION AND DISCLOSURES



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### DISCLOSURES

- Margie White BS, RRT-NPS
  - Clinical Application Specialist for Sentec



# Objectives

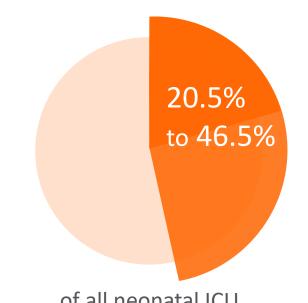
Participants will be able to:

- Identify the percentage of neonatal ICU admissions that have a respiratory component
- Explain how CO<sub>2</sub> levels can influence cerebral blood flow and IVH
- Discuss the effects of blood loss, pain, and infection on premature infants
- Identify how continuous transcutaneous CO<sub>2</sub> monitoring can help support brain function and protect the lung of the neonate

#### What level NICU do you currently work in?



### **Respiratory Distress Causes in Neonates and Infants<sup>1</sup>**



of all neonatal ICU admissions have a respiratory component<sup>2,3</sup>

#### Preterm

- Respiratory distress syndrome
- Pneumonia
- Pneumothorax
- Pulmonary hemorrhage
- Aspiration
- Surfactant protein deficiency

#### Term

#### Preterm list plus:

- Transient tachypnoea of the newborn
- Meconium aspiration
- Primary or secondary persistent pulmonary hypertension of the newborn
- Pleural effusion (chylothorax)
- Alveolar capillary dysplasia

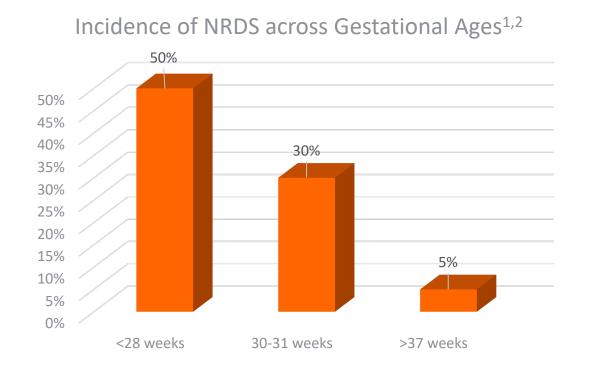
Congenital Anomalies, etc.

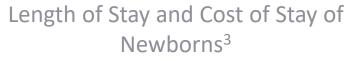
1. Gallacher et al. Breathe (Sheff). 2016;12(1):30-42.

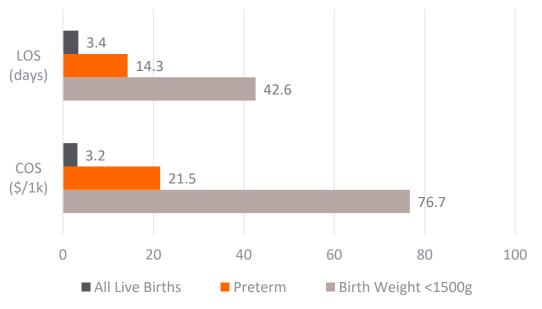
- Qian et al. Chin Med J (Engl) 2010; 123: 2769–2775.
- 3. Baseer et al. Annals of Global Health, 2020, 86(1), p.22.

#### About 12% of babies born in the U.S. are born prematurely—a higher rate than in other developed countries.<sup>2</sup>

# **Preterm Birth and Respiratory Distress Syndrome**







1. Pramanik, A. Medscape.com. Article 976034

2. Dyer et al. P T. 2019;44(1):12-14.

3. Kowlessar et al. HCUP Statistical Brief #163. October 2013. Agency for Healthcare Research and Quality, Rockville, MD.

# **CO**<sub>2</sub> & the Brain

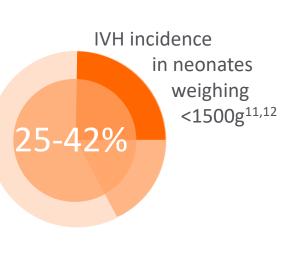
CO<sub>2</sub> levels are of major clinical importance.<sup>1</sup>

> It may be prudent to avoid significant hypocarbia and hypercarbia and CO<sub>2</sub> fluctuations especially during the first 3 days of life, when the risk for IVH is the highest.<sup>1</sup>



HYPERCARBIA Increases cerebral blood flow

 Intraventricular hemorrhage (IVH)<sup>2,4,5,9</sup>





FLUCTUATIONS Sharp changes in PaCO2

- Intraventricular hemorrhage (IVH)<sup>2,4,5,9</sup>
- Cerebral oxygenation changes<sup>10\*</sup>

\*in the first 72 hours of life

 Cerebral electrical activity changes<sup>10\*</sup>



HYPOCARBIA Decreases cerebral blood flow

- Intraventricular hemorrhage (IVH)<sup>2,3,4</sup>
- Periventricular leukomalacia (PVL)<sup>5,6,7,8</sup>
- Cerebral Palsy<sup>13</sup>

 Hochwald et al. Pediatrics. 2019:144(1):e20183640.

- 2. Erickson et al. J Paediatr Child Health.
   7. Shani

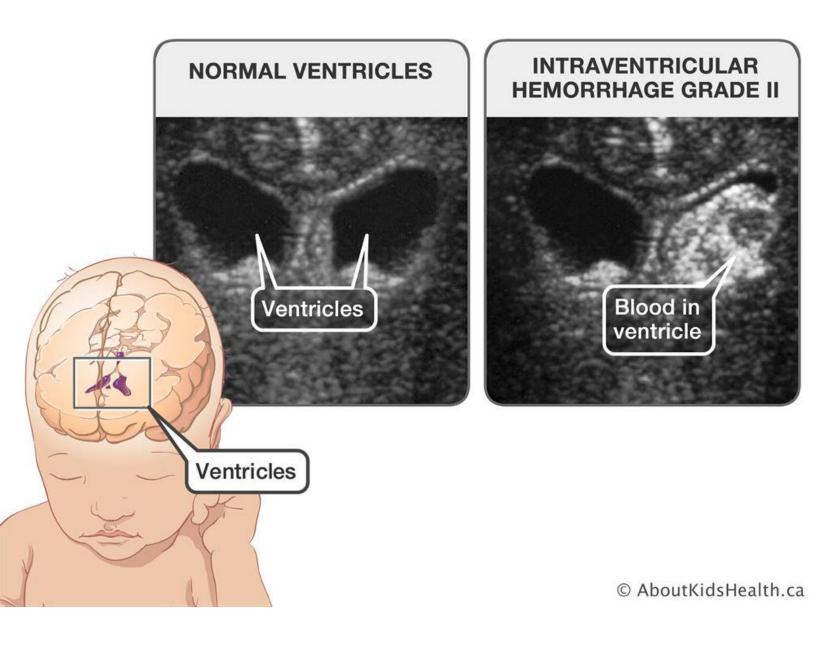
   2002;38(6):560–562.
   2006
- 3. Van de Bor M, et al. Am J Dis Child. 1986;140(11):1125–1130.
- 4. Wallin et al. Early Hum Dev. 1990;23(2):129–137.
  - Resch et al. Early Hum Dev. 2012;88(1):27–31.

 Fujimoto et al. Arch Dis Child Fetal Neonatal Ed. 1994;71(2):F107–F110

- Shankaran et al. Pediatrics. 2006;118(4):1654–1659
   Wiswell et al. Pediatrics. 1996;98(5):918–924
- 1996;98(5):918–924 9. Fabres et al. Pediatrics. 2007;119(2):299–305
- 10. Dix et al. J Pediatr. 2017;187:66-72.e1. 11. Database of VLBW Infants Born in
- 2012. Vermont Oxford Network, 2013.
  12. Ahn et al. J Korean Med Sci. 2015; 30 Suppl 1:552-558.
  13. Rainaldi et al. Assisted Ventilation of the Neonate (Sixth Edition), 2017, 451-458.e2

# IVH: Intraventricular hemorrhage

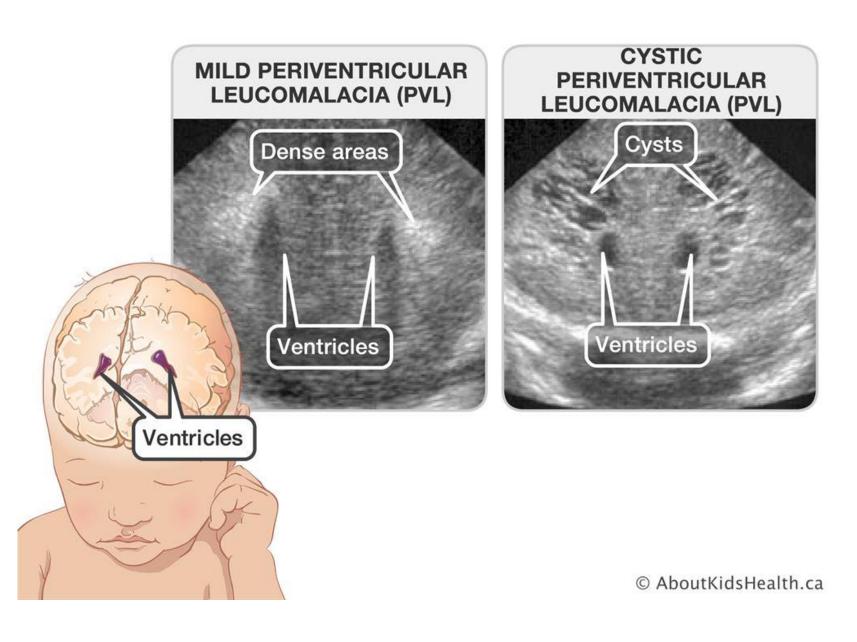
- Bleeding into the fluid filled areas (ventricles) in the brain
- Most common in premature babies, occurring in the first several days of life
- More common in babies with RDS, unstable blood pressure, other medical conditions
- 4 stages called "grades" relative to the degree of bleeding, stage 1 being least severe and stage 4 being most severe



# PVL: Periventricular leukomalacia

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- White matter around the ventricles dies and creates 'holes' and/or cysts in the brain
- Most common in premature infants
- More common in babies who are more premature and more unstable at birth
- More common in babies who also have IVH



# CO<sub>2</sub> & the Lungs

While ventilation support is crucial to protect the brain from hypercarbia, hypocarbia, and  $CO_2$  fluctuations, ventilation itself can also cause lung damage in the absence of finely-tuned care.

**Overdistention &** Volume Duration of mechanical ventilation in VLBW Volutrauma infants has been associated with: increased odds of BPD Increased odds of Pulmonary Hypertension increased risk of neurodevelopmental impairment<sup>2</sup> Safe CO<sub>2</sub> can help titrate care to window deliver the gentlest efficacious ventilatory Implementing strategies to avoid endotracheal support for the individual mechanical ventilation has been shown to Derecruitment and patient. reduce the incidence of BPD.<sup>1</sup> atelectasis

- Fischer et al. Pediatrics Nov 2013, 132 (5) e1351-e1360;
- 2. Choi et al. The Journal of Pediatrics, 2017, Volume 194, 34 39.e3
- 3. Erickson et al. J Paediatr Child Health. 2002;38(6):560–562.

## Continuous, accurate CO<sub>2</sub> measurement enables balanced brain and lung protection

#### Ventilator Support

- + Intraventricular/ Periventricular Hemorrhage (IVH/PVH)
- + Periventricular Leukomalacia (PVL)
- + Cerebral Palsy

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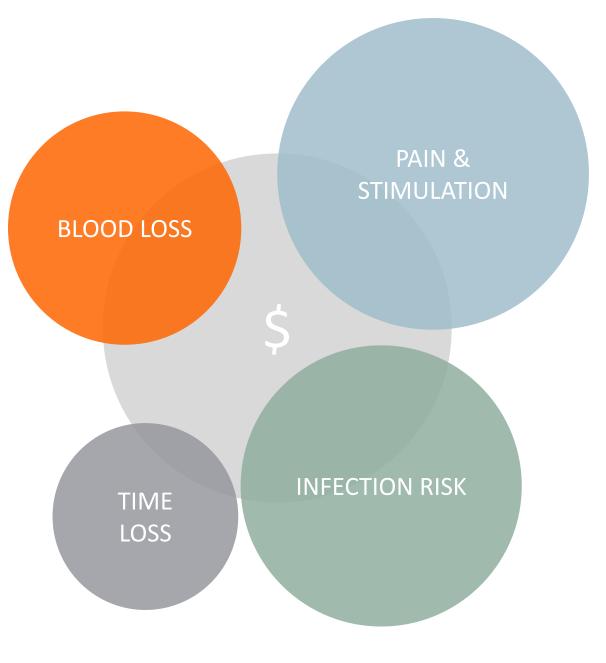
Consistent with lung protection strategies

- + Ventilator Induced Lung Injury (VILI)
- + Bronchopulmonary Dysplasia (BPD)
- + Chronic Lung Disease (CLD)

# What does a blood draw cost?

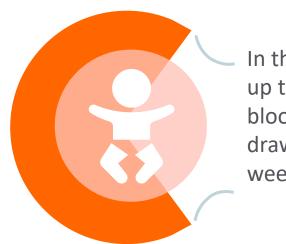
The true cost of an arterial blood gas is measured by more than dollars and cents.

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How much blood is drawn?



In the first 6 weeks of life, up to 30% of the circulating blood volume of neonates is drawn for lab work each week.<sup>1</sup>



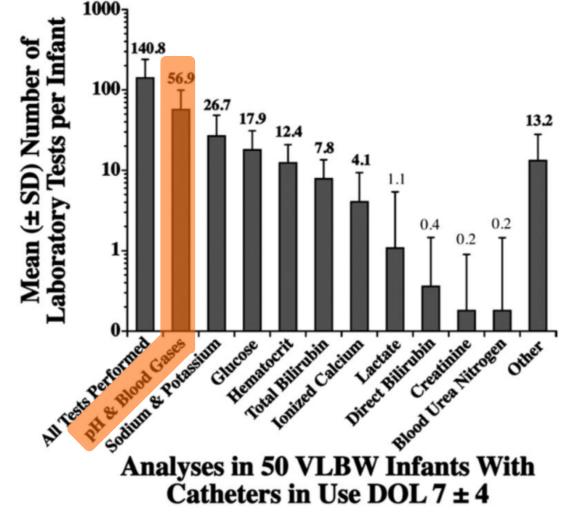
To further place this in perspective, 6–7 mL of blood drawn from an infant weighing 1 kg is equivalent to a 450 mL blood loss in an adult.<sup>2</sup>



2. Carroll et al. Semin Perinatol. 2012;36(4):232-243. doi:10.1053/j.semperi.2012.04.003



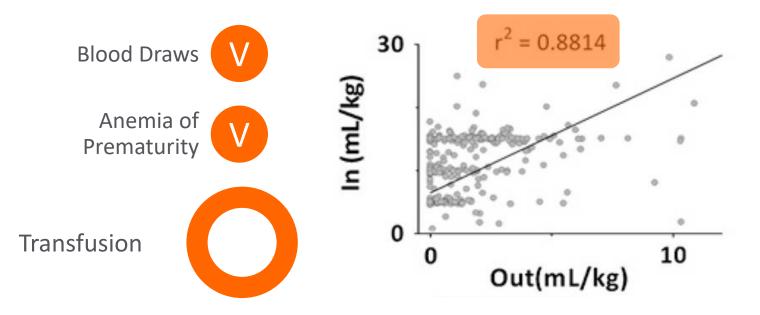
How much blood is drawn? What is the blood drawn for? pH and Blood Gas measurements are the highest driver of blood draws in the NICU.<sup>1</sup>







Phlebotomy is well established as the main cause of anemia of prematurity shown through the direct relationship and high correlation values between volume of blood drawn and volume of blood transfused.<sup>1,2</sup>



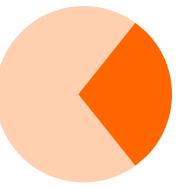
How much blood is drawn? What is the blood drawn for? Is all the blood being used? Why does it matter?

- 1. Widness et al. Neoreviews. 2008;9(11):e520. doi:10.1542/neo.9-11-e520
- 2. Valieva et al. J Pediatr. 2009;155(3):331-37.e1. doi:10.1016/j.jpeds.2009.02.026



How much blood is drawn? What is the blood drawn for? Is all the blood being used? Why does it matter? Why avoid transfusion? Transfusion may as much as double the risk of developing NEC.<sup>1</sup>

Up to 30% of NEC cases are estimated to be transfusionrelated.<sup>2</sup>



Transfusion associated NEC (TANEC) patients generally have higher mortality, longer hospital stays, and are more likely to require surgery.<sup>1</sup>







Transfusion may be associated with IVH extension from Stage 1 to Stage 3 or 4.<sup>4</sup> Transfusion [increases] the risks of infection, vascular overload, lung injury, sensitization, and transfusion reaction.<sup>3</sup>

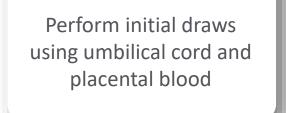
- 1. Mohamed et al. *Pediatrics*. 2012;129(3):529-540. doi:10.1542/peds.2011-2872
- 2. Gephart et al. Adv Neonatal Care. 2012;12(4):232-236.
- 3. Whitehead et al. Crit Care. 2019;23(1):278. Published 2019 Aug 9. doi:10.1186/s13054-019-2511-9
- 4. Baer et al. Transfusion. 2011;51(9):1933-1939. doi:10.1111/j.1537-2995.2011.03081.x

How much blood is drawn? What is the blood drawn for? Is all the blood being used? Why does it matter? Why avoid transfusion? What can be done?

#### Counsilman, et al.

latrogenic blood loss in extreme preterm infants due to frequent laboratory tests and procedures.

*The Journal of Maternal-Fetal & Neonatal Medicine, 2019.* 



4

Adhere to a strict

transfusion protocol.

(Whyte 2011)

7

Implement transcutaneous to reduce

the frequency of blood

gases

Implement a robust delayed cord clamping program.

2

Adhere to strict protocols on amount of blood required for each specific test.

5

8

Educate caregivers on iatrogenic anemia and importance of reducing lab tests Give supplemental iron.

3

Use bedside point of care testing with lowest volumes needed.

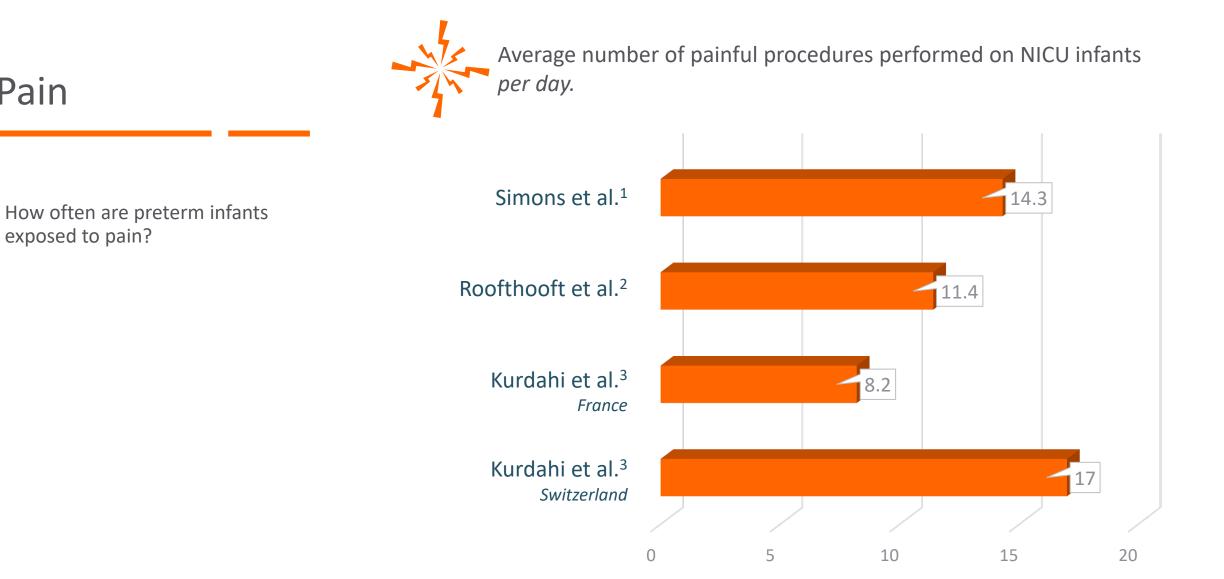
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Control Provide the Action of the Action

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#### COUNSILMAN ET AL, 2019

latrogenic blood loss in extreme preterm infants due to frequent laboratory tests and procedures The Journal of Maternal-Fetal & Neonatal Medicine.



1. Simons et al. Arch Pediatr Adolesc Med. 2003;157(11):1058–1064. doi:10.1001/archpedi.157.11.1058

Roofthooft et al. Neonatology. 2014;105(3):218-226. doi:10.1159/000357207 2.

3. Lina Kurdahi Badr et al. Volume 13, Issue 2, 2013, Pages 82-86,

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Pain

How often are preterm infants exposed to pain?

Which painful procedure is most common?

Heel punctures comprise 61% to 87% of the invasive procedures performed on ill infants.<sup>1</sup>



Analgesics are rarely given for blood sampling, and few seem to be effective.<sup>1,2,3,4</sup>

- 1. Kapellou et al. BMJ Clin Evid. 2009;2009:0313. Published 2009 Jan 7.
- 2. Bellieni et al. (2014). The Journal of Maternal-Fetal & Neonatal Medicine. 29. 10.3109/14767058.2014.992334.
- 3. Johnston et al. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD008435. DOI: 10.1002/14651858.CD008435.pub3.
- 4. Shah et al. Cochrane Database Syst Rev. 2011;2011(10):CD001452. Published 2011 Oct 5. doi:10.1002/14651858.CD001452.pub4

How often are preterm infants exposed to pain?

Which painful procedure is most common?

How do preterm infants process pain?

# The short-term consequences of pain are well documented. An increase in HR, a decrease in $SpO_2$ , heart rate variability, blood pressure fluctuations and increased secretion of stress hormones are noted in many studies.<sup>1</sup>

Preterm infants are more sensitive to pain, in part because they lack the neuro-development to comfort themselves.<sup>2</sup>

Pain in the first few days of life has been shown to magnify the pain response to later stimuli.<sup>3</sup>

- 1. Lina Kurdahi Badr, Newborn and Infant Nursing Reviews, Volume 13, Issue 2, 2013, Pages 82-86,
- 2. Fitzgerald, M. Nat Rev Neurosci 6, 507–520 (2005). https://doi.org/10.1038/nrn1701
- 3. Gokulu et al. Acta Paediatr. 2016;105(11):e520-e525. doi:10.1111/apa.13557

How often are preterm infants exposed to pain?

Which painful procedure is most common?

How do preterm infants process pain?

What are the long term effects of neonatal pain?

Higher number of neonatal skin breaks predicted lower Mental Development Index<sup>5</sup>

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More early "skin breaks" were associated with:

• reduced lateral thalamic volume,

8

Μ

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W

- slower metabolic thalamic growth,
- altered/reduced white matter microstructure<sup>1,2</sup>

Cognitive and motor scores were predicted by thalamic volumetric growth, regardless of sex and GA at birth.<sup>1</sup> Greater number of invasive procedures were associated with reduced white matter and lower IQ<sup>3</sup>

More neonatal invasive procedures was associated with smaller amygdala and thalamus volumes, in turn related to poorer cognitive, visual-motor, and behavioral outcomes.<sup>4</sup>

- 1. Duerden et al. J Neurosci. 2018;38(4):878-886.
- 2. Brummelte et al. Ann Neurol. 2012;71(3):385-396.
- 3. Vinall et alPediatrics. 2014;133(3):412-421.

4. Chau et al. Front Behav Neurosci. 2019;13:51. Published 2019 Mar 19.

Cumulative neonatal pain-related stress

was independently associated with

negatively correlated with visual-

perceptual abilities at school-age.<sup>6</sup>

changes in brain activity, which were

- 5. Grunau et al.. Pain. 2009;143(1-2):138-146.
- 6. Doesburg et al. Pain. 2013;154(10):1946-1952.

How often are preterm infants exposed to pain?

Which painful procedure is most common?

How do preterm infants process pain?

What are the long term effects of neonatal pain?

What can be done?

Hall, et al.

Pain Management in Newborns

Clinics in Perinatology, 2014.

Decrease bedside disruptions by timing routine medical interventions with other care procedures

Place peripheral arterial or central venous catheters in patients who need more than 3-4 heelsticks per day. Use adequate analgesia.

4

Anticipate laboratory testing to minimize the frequency of blood sampling.

2

Use hand-held devices that can perform several analyses from a single blood sample, reducing the number of heelsticks required for lab testing.

3

Consider noninvasive therapeutic approaches for providing analgesia in newborns

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monitoring such as transcutaneous PaO<sub>2</sub>, PaCO<sub>2</sub>, SpO<sub>2</sub>, glucose or bilirubin levels, or NIRS to avoid the need for blood

sampling.

5

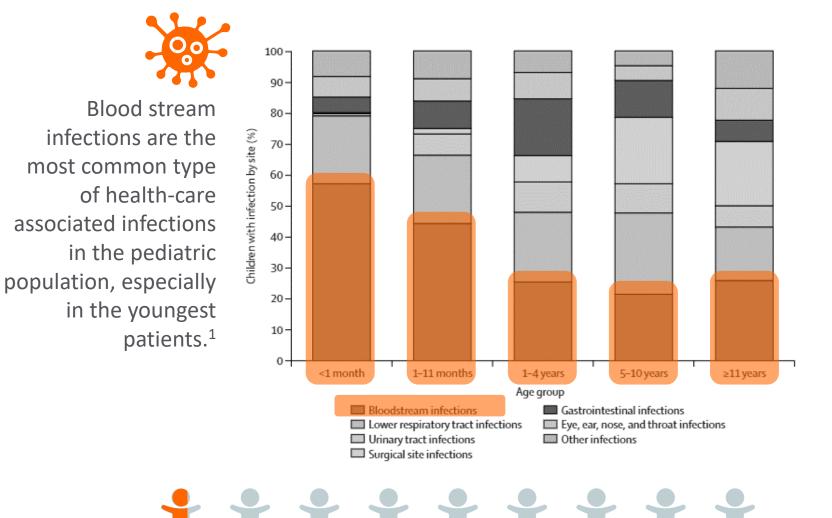
Use noninvasive

[...]"everyday" clinical exposures are now also recognized as key predictors of brain maturation in preterm infants. Pain is one such "everyday" clinical exposure. Increasing evidence suggests that pain is a central factor that predicts dysmaturation, especially in babies born very preterm and in those with many early exposures to pain.

#### MCPHERSON ET AL, 2020

The influence of pain, agitation, and their management on the immature brain. Pediatric Research

#### Distribution of health-care-associated infections in children, by age group



Globally, NICUs were found to have a hospital acquired infection rate of 10.7%<sup>1</sup>

#### Infection

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How common are blood stream infections?



CLABSI are the most common cause of late onset sepsis in neonates and thus constitute one of the leading causes of both morbidity and mortality in this age group.<sup>2</sup>

1. Karagiannidou et al. J Infect Public Health. 2019;12(3):372-379. doi:10.1016/j.jiph.2018.12.004

- 2. Bannatyne et al. Int J Pediatr. 2018;2018:4658181. Published 2018 Sep 2. doi:10.1155/2018/4658181
- 3. Kime et al. Adv Neonatal Care. 2011 Aug;11(4):242-8; quiz 249-50
- 4. Lilien et al. J Paediatr 1976;88:478-80.



#### Infection

How common are blood stream infections?

How do infections impact outcomes?

What can be done?

Kime, et al.

Central Line "Attention" Is Their Best Prevention

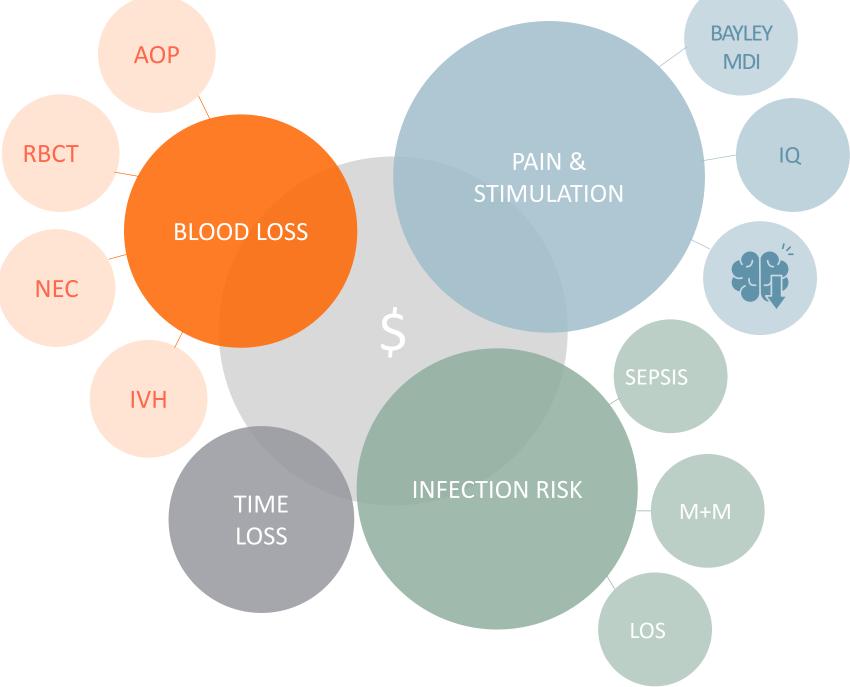
Advances in Neonatal Care, 2011.



# What does a blood draw cost?

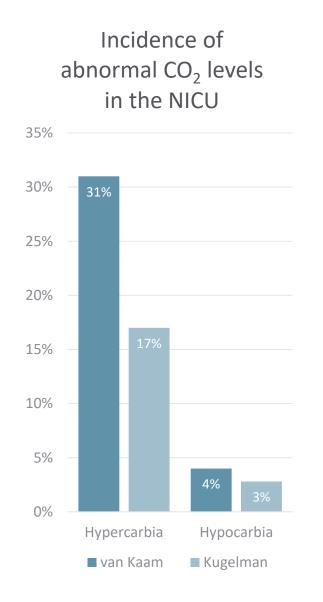
The true cost of an arterial blood gas is measured by more than dollars and cents.

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# Continuous CO<sub>2</sub> monitoring as a solution

- CO<sub>2</sub> values outside the ideal range are common in the NICU
- Blood gases only offer a point-in-time measurement, which can misrepresent the patient course
- 1. van Kaam et al. Neovent Study Group. Arch Dis Child Fetal Neonatal Ed. 2013;98(4):F323-F326. doi:10.1136/archdischild-2012-302649
- 2. Kugelman et al. *J Pediatr*. 2016;168:56-61.e2. doi:10.1016/j.jpeds.2015.09.051
- 3. Storre et al. J. H., & Dellweg, D. (2014). In *Pneumologie*. Stuttgart: Georg Thieme Verlag.

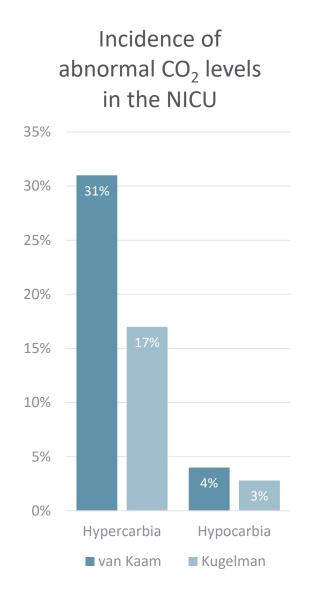


Van Kaam: >52mmHg; <30mmHg

Kugelman: >60mmHg; <30mmHg

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- 2. Kugelman et al. *J Pediatr*. 2016;168:56-61.e2. doi:10.1016/j.jpeds.2015.09.051
- 3. Storre et al. J. H., & Dellweg, D. (2014). In *Pneumologie*. Stuttgart: Georg Thieme Verlag.



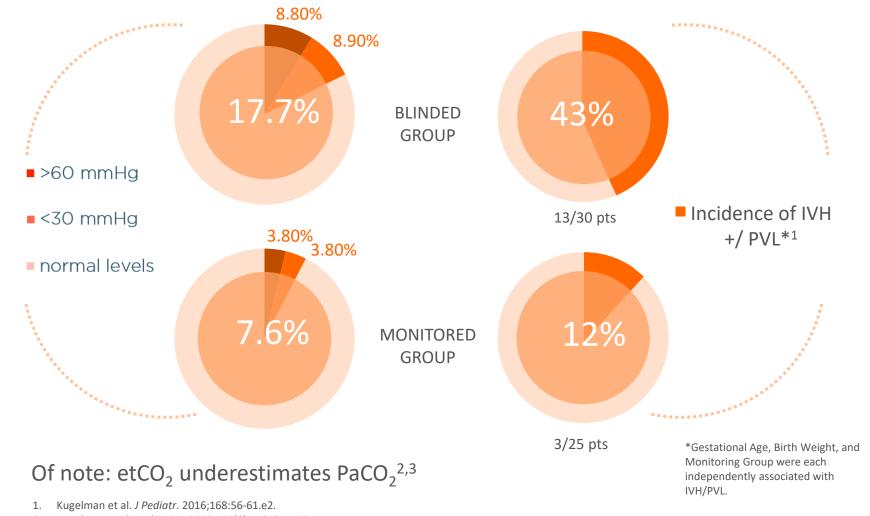
Van Kaam: >52mmHg; <30mmHg

Kugelman: >60mmHg; <30mmHg

# **Continuous** monitoring and outcomes

We speculate that avoiding hypercarbia or hypocarbia and optimizing mechanical ventilation based on continuous CO<sub>2</sub> monitoring could decrease the rates of neurologic and respiratory complications.<sup>1</sup>

Percentage of time spent at different levels of distal etCO<sub>2</sub>. Safe range defined as 30-60 mmHg<sup>1</sup>



- - Kugelman et al. Pediatrics. 2008;122(6):e1219-e1224. 2.
  - Rozycki et al. Pediatrics. April 1998, 101 (4) 648-653; 3.

# tcPCO<sub>2</sub> vs etCO<sub>2</sub>

Unlike  $etCO_2$ measurement,  $tcCO_2$ measurement is not influenced by ventilationperfusion mismatch and was found to be as good as or more accurate than  $etCO_2$  measurement in preterm infants.<sup>1</sup>

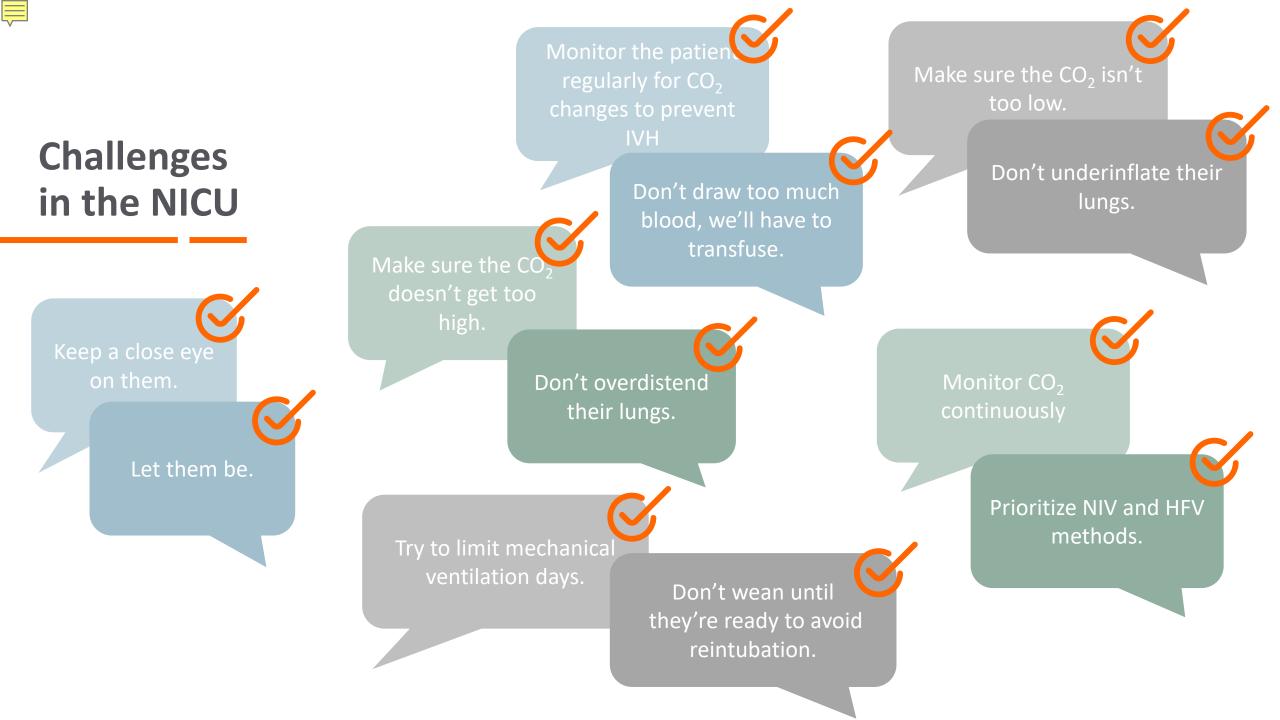
#### End Tidal

- Faster discrimination of tracheal vs esophageal intubations than standard clinical assessment<sup>1</sup>
- Provides waveform for skilled clinicians to interpret compliance and resistance issues
- Leakage around uncuffed ETTs > mixing of measured CO<sub>2</sub> with inhaled air
- Ineffective with small tidal volumes and higher respiratory rates/short exhalation time<sup>5</sup>
- Direct relationship between degree of inaccuracy and severity of ventilationperfusion mismatch<sup>2,3,4</sup>
- Not feasible for High Flow Ventilation modalities
- No device suitable for noninvasive ventilation
- Adds airway dead space
- Added weight of mainstream adaptor

#### Transcutaneous<sup>1,6,7</sup>

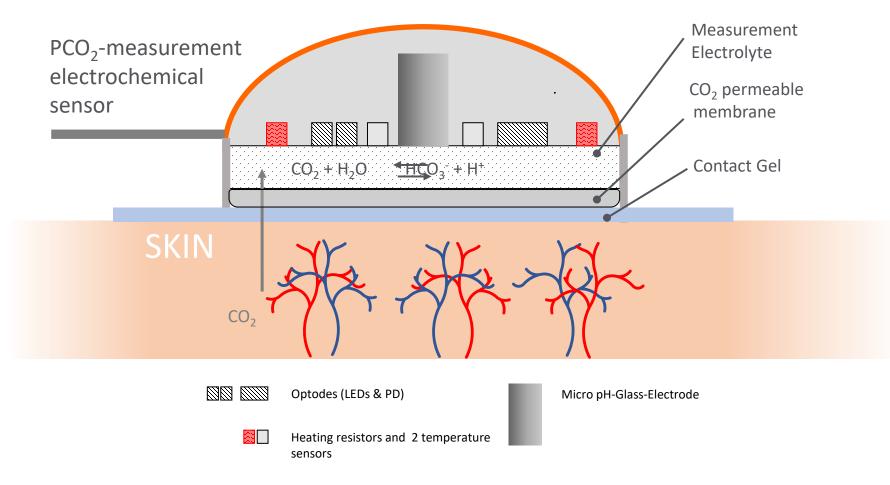
- Compatible with any type of ventilation:
  - + Mechanical Ventilation
  - + HFV, HFOV, HFJV, Percussive Ventilation
  - Noninvasive including HFNC, HHFNC, Bubble CPAP, etc.
  - + spontaneous breathing
- + No dead space issues
- + No weight on ETTs
- + Accurate despite ventilation-perfusion mismatch
- + Accurate independent of respiration rate or tidal volume
- No breath-to-breath waveform
- No rapid assessment of ETT placement
- Poor perfusion at monitoring site can impact measurements
- Requires frequent calibration to maintain accuracy

- 1. Hochwald et al. Pediatrics. 2019;144(1):e20183640.
- 2. Repetto et al. *J Perinatol*. 2001;21(5):284-287.
- 3. Hagerty et al. J Perinatol. 2002;22(3):219-225.
- 4. Proquitté et al. Pediatr Crit Care Med. 2004;5(1):75-80.
- 5. Schmalisch G. Biomed Eng Online. 2016;15(1):104.
- 6. Huttmann et al, Ann Am Thorac Soc. 2014;11(4):645-652.
- 7. Restrepo et al. Respiratory Care Nov 2012;57(11)1955-1962.



### A noninvasive, continuous measurement of PCO<sub>2</sub>

Transcutaneous technology warms the skin at the measurement site to encourage blood flow and diffusion of gases across the skin, through the permeable membrane, and into the specially formulated electrolyte, where a measurable reaction takes place. Algorithms translate the data into an estimate of PaCO<sub>2</sub>

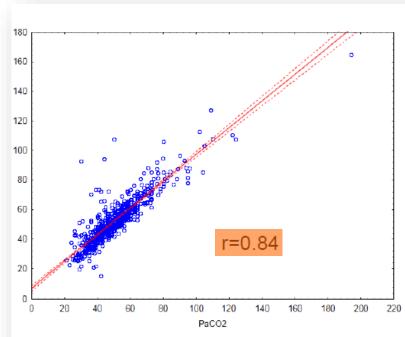




#### Consistent Accuracy



CO<sub>2</sub> trends are helpful, but a trend that accurately reflects traditional blood gases is <u>impactful.</u> Critically III Children <21 y; median age 2.1 years R=0.70 in children <2 years<sup>2</sup>



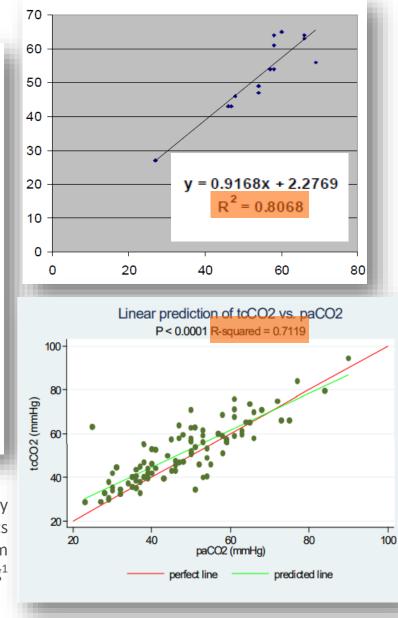
**Figure 2**: Scatterplot of  $P_{TC}CO_2$  and  $PaCO_2$  with graphed 95% confidence intervals represented by dashed lines

Mechanically ventilated infants 27w-term weighing >1000g<sup>1</sup>

1. Schmidt et al. Pediatric Academic Societies Annual Meeting 2009

- 2. Bhalla et al, Pediatric Academic Societies Annual Meeting 2015
- 3. Rowley, et al. AARC National Meeting 2008

Neonatal patients on HFOV Median GA 25 weeks<sup>;</sup> 64% of samples from pts on vasopressors<sup>3</sup>

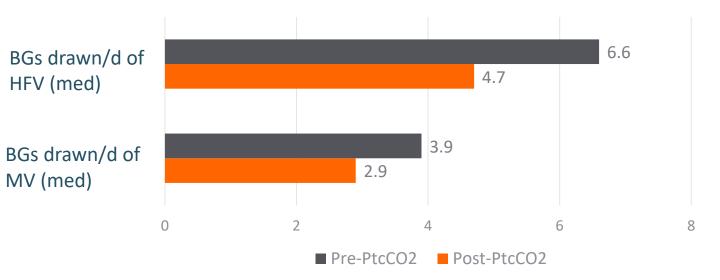


On average how frequently are you getting ABGs in your NICU on your mechanically ventilated patients?



## Reducing blood draws

Introduction of transcutaneous CO<sub>2</sub> technology resulted in a >25% reduction in blood gases drawn per day on ventilated patients at The Children's Hospital of Philadelphia's Level IV NICU<sup>1</sup> The use of PtcCO<sub>2</sub> monitoring statistically decreased blood gas frequency among ventilated neonates without impacting the duration of mechanical ventilation or clinical outcomes.



1. Mukhopadhyay S, Maurer R, Puopolo KM. Neonatal Transcutaneous Carbon Dioxide Monitoring--Effect on Clinical Management and Outcomes. *Respir Care*. 2016;61(1):90-97. doi:10.4187/respcare.04212

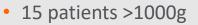
# Safety & Skin Integrity



Transcutaneous technology has evolved since introductory devices resulted in heat and skin integrity issues in the NICU. None of the subjects had any detectable harm to their skin.<sup>1</sup>

- 50 patients
- BW 744-1326g
- GA 25.6-30.4 weeks
- 12 uninterrupted hours monitoring

The device was safe, not causing any adverse skin changes in this limited set of critically ill neonates.<sup>2</sup>



- GA 27-40 weeks
- 21 median hours monitoring (8.5-51 hours)

Not all transcutaneous devices function identically to protect neonatal skin. Always discuss safety and precautions with the device manufacturer.

- . Aly et al. Am J Perinatol. 2017;34(5):480-485.
- 2. Schmidt et al. Pediatric Academic Societies Annual Meeting 2009

#### **Summary**

 $CO_2$  is an integral parameter for lung and brain protection of preterm infants in the NICU. High, low, and large fluctuations in  $CO_2$  values are common and are associated with poor outcomes. Blood gases only offer point-in-time measurement and introduce risks associated with blood loss, pain, infection, and time loss. Continuous monitoring of CO<sub>2</sub> lessens time spent outside of "safe ranges" and may lead to a reduction in associated adverse outcomes

End tidal CO<sub>2</sub> underestimates PaCO<sub>2</sub>, is often infeasible and/or inaccurate in the NICU population and is incompatible with lungfriendly high frequency ventilation methods.

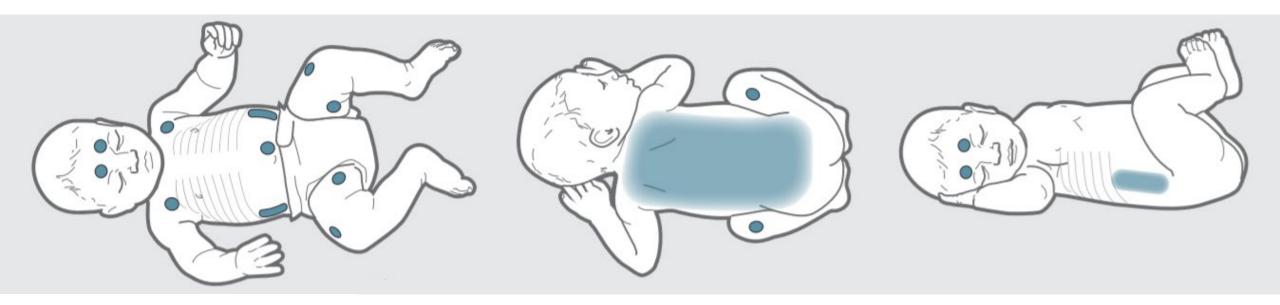
Modern transcutaneous technology overcomes limits of previous devices to offer accurate, continuous, noninvasive  $CO_2$  values regardless of ventilation method or V/Q mismatch, all while supporting neuroprotective efforts to deliver clustered care, protect skin integrity, and reduce the frequency of blood draws.



# Thank you.



## **Neonatal Monitoring Sites**



## **Principles of Correlation**

#### Sensor

- Ensure membrane intact and in good condition
- If needed, change membrane (let monitor and sensor stabilize 90 minutes before placing on patient. Then watch for CO<sub>2</sub> stabilization: "green numbers" and ideally wait 15 more minutes to do a correlating gas)

#### Site

- Good perfusion is essential to accuracy
- External pressure on the sensor? Even clothing/dressings
- Too peripheral?
- NICU Arterio-venous shunt? Ensure ABG and Sentec site are on same anatomical side of shunt.

#### Seal

- Good quality, air-free seal between sensor and skin
- Air can skew measurements
- Ensure sensor is tightly attached with no air or hair in seal
- Adequate contact gel between sensor and skin

#### Status

- Patient conditions such as edema, vasoactive drugs, shock and sepsis impact perfusion, which impacts accuracy.
- Perfusion issues result in tcpCO<sub>2</sub> readings that are higher than ABGs

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#### AARC Clinical Practice Guideline

#### What do the guidelines say?

AARC Clinical Practice Guideline: Transcutaneous Monitoring of Carbon Dioxide and Oxygen: 2012

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#### TCM 3.0 SETTING

TCM may be performed by trained personnel in a variety of settings that include, but are not limited to hospitals, extended care facilities, and patient transport.<sup>20,22,30</sup> It is utilized in the following specific clinical settings to determine the presence of hypoventilation or respiratory depression:

**3.1** Mechanical ventilation, including conventional modes of ventilation,<sup>31-33</sup> high-frequency ventilation,<sup>27,34</sup> steady state high frequency jet ventilation,<sup>35</sup> and noninvasive ventilation.<sup>34-39</sup>

#### TCM 4.0 INDICATIONS

The use of TCM is indicated in patients who either lack arterial access or have the need for continuous monitoring of oxygen and carbon dioxide with minimal blood draws.<sup>60</sup> TCM allows the assessment of:

**4.1** adequacy of oxygenation and/or ventilation<sup>2,9,10,13,22,25,29,30,37,50,73-76</sup>

4.2 response to diagnostic and the rapeutic interventions, as evidenced by  $P_{tcO_2}$  and/or  $P_{tcCO_2}$  values^{2,22,29,30,37,38,64,67,74,77}

**4.2.1** Weaning and extubation decisions may be made based on  $P_{tcCO_2}$  measurement alone.<sup>78,79</sup>