Ventilator Support in Extremely Low Gestation Neonates

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Dr. Yoder has the following conflicts to disclose w/in past 10 years:

Research Support:
- NHLBI, NICHD
- Drager
- Vapotherm
- INO Therapeutics

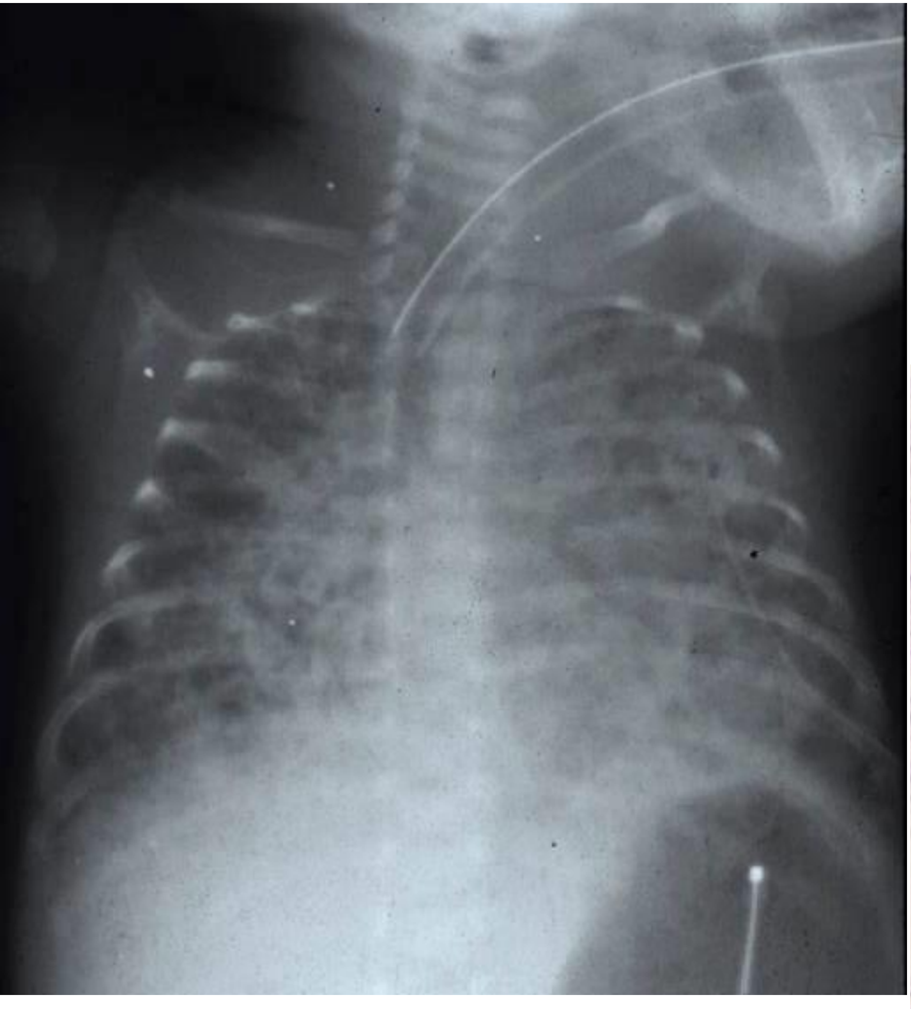
Speakers Bureau:
Fisher & Paykel
(unpaid, except travel support)

Objectives

- Describe lung development at 22-25 weeks and "multi-hit" injuries to lung
- Understand approaches to early sustained lung inflation that minimize VILI
- Review evidence for current approaches to early ventilator care in very preterm infants

Ventilating the extremely preterm infant……..in 40 minutes!!

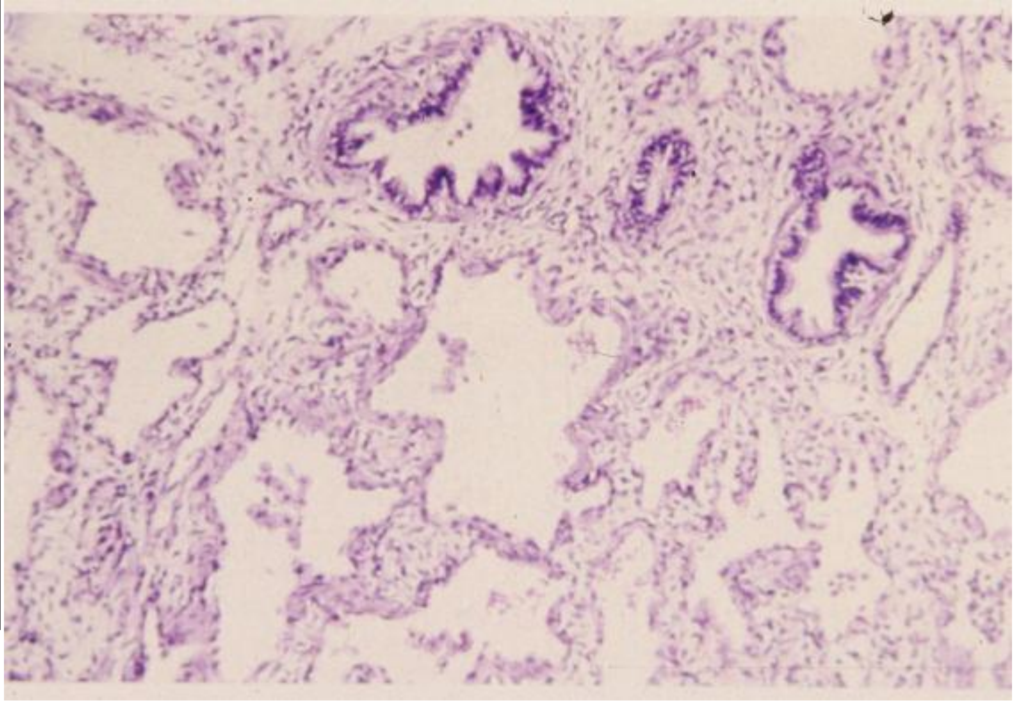
Bronchopulmonary Dysplasia



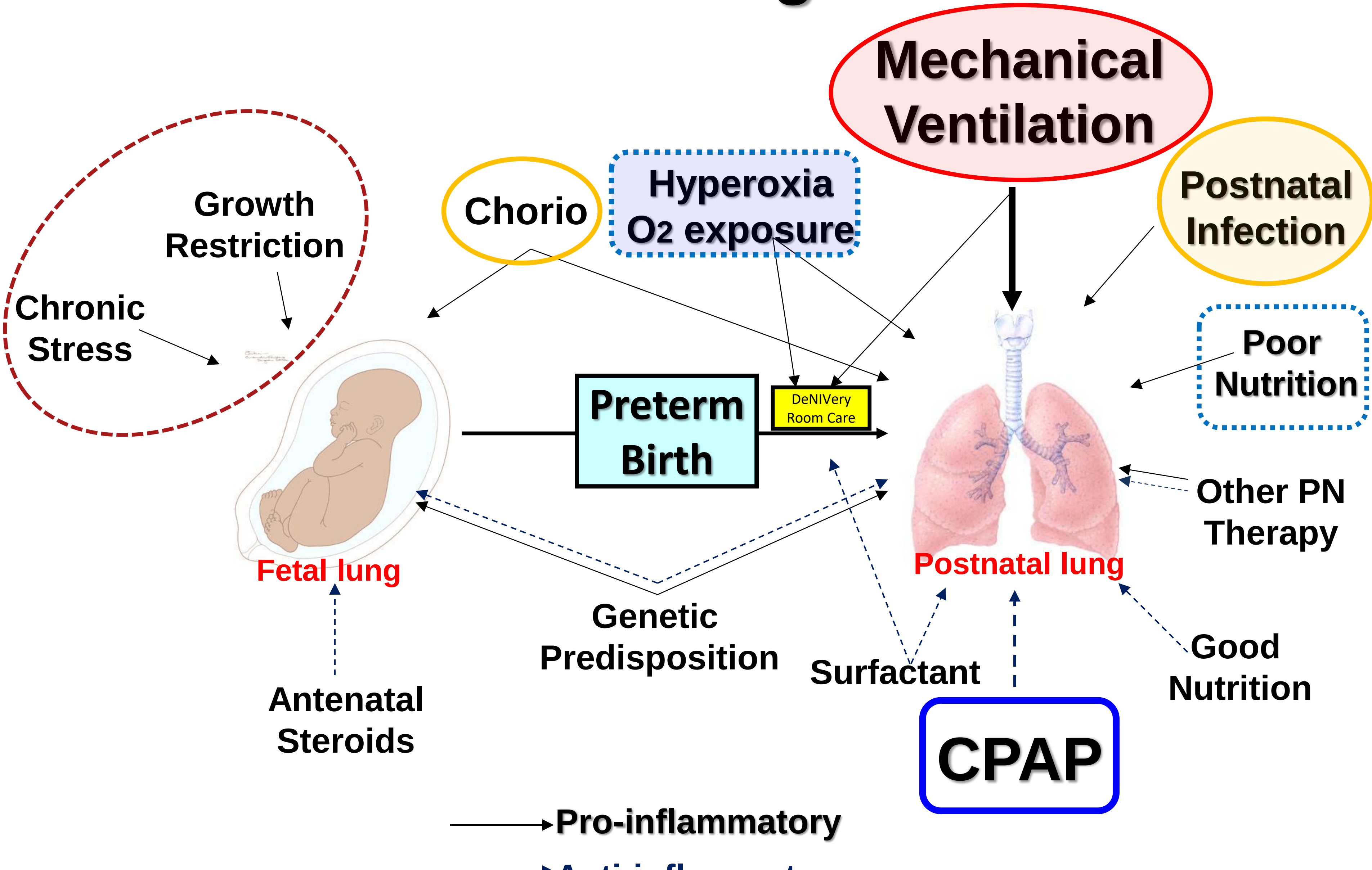
Most common ELGAN morbidity

> 21,000 PubMed citations

Much has changed in > 50 years!

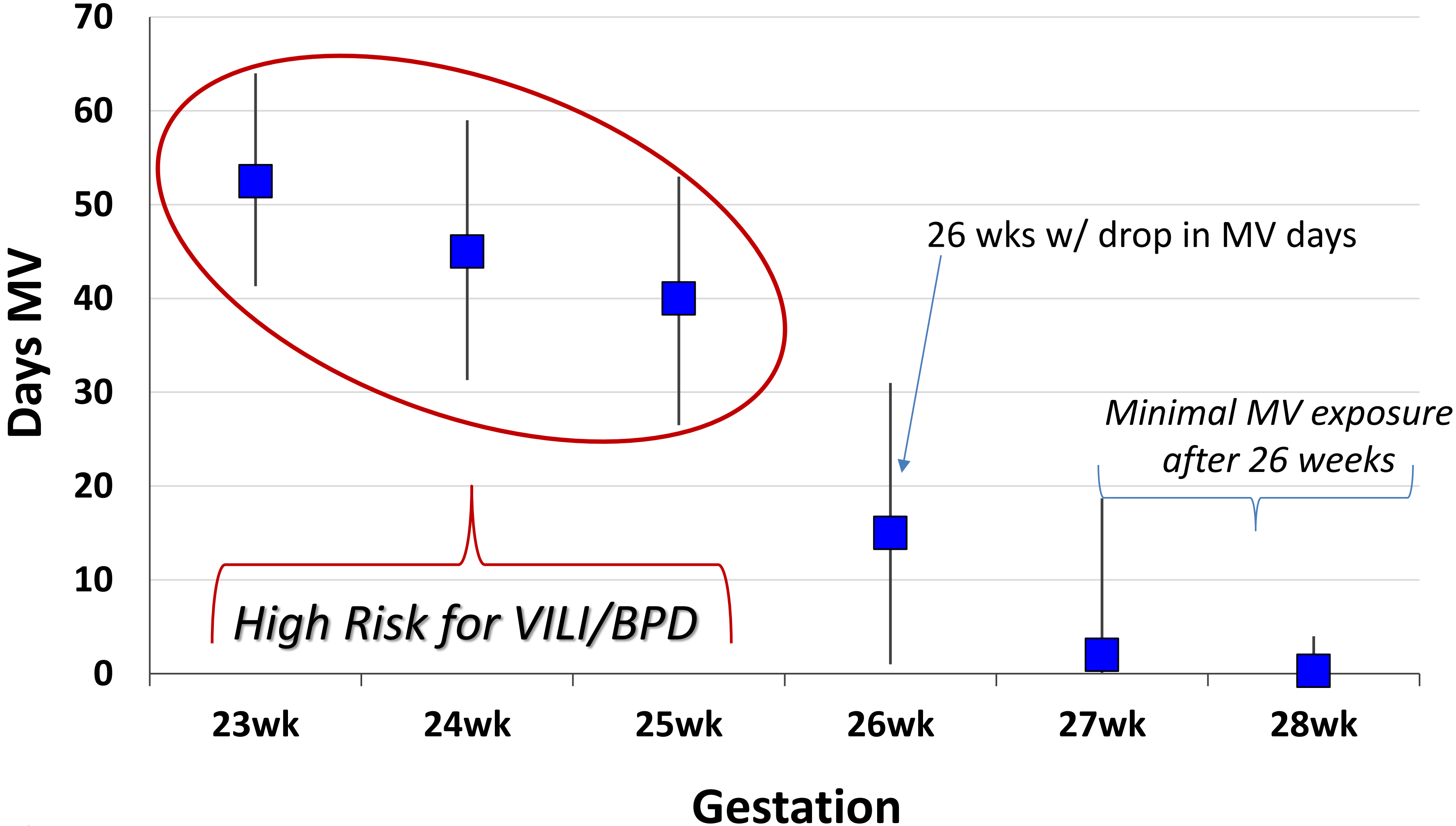


Factors Contributing to BPD Risk



Yoder BA, NeoRev 2008

Median (IQR) Vent Days by GA

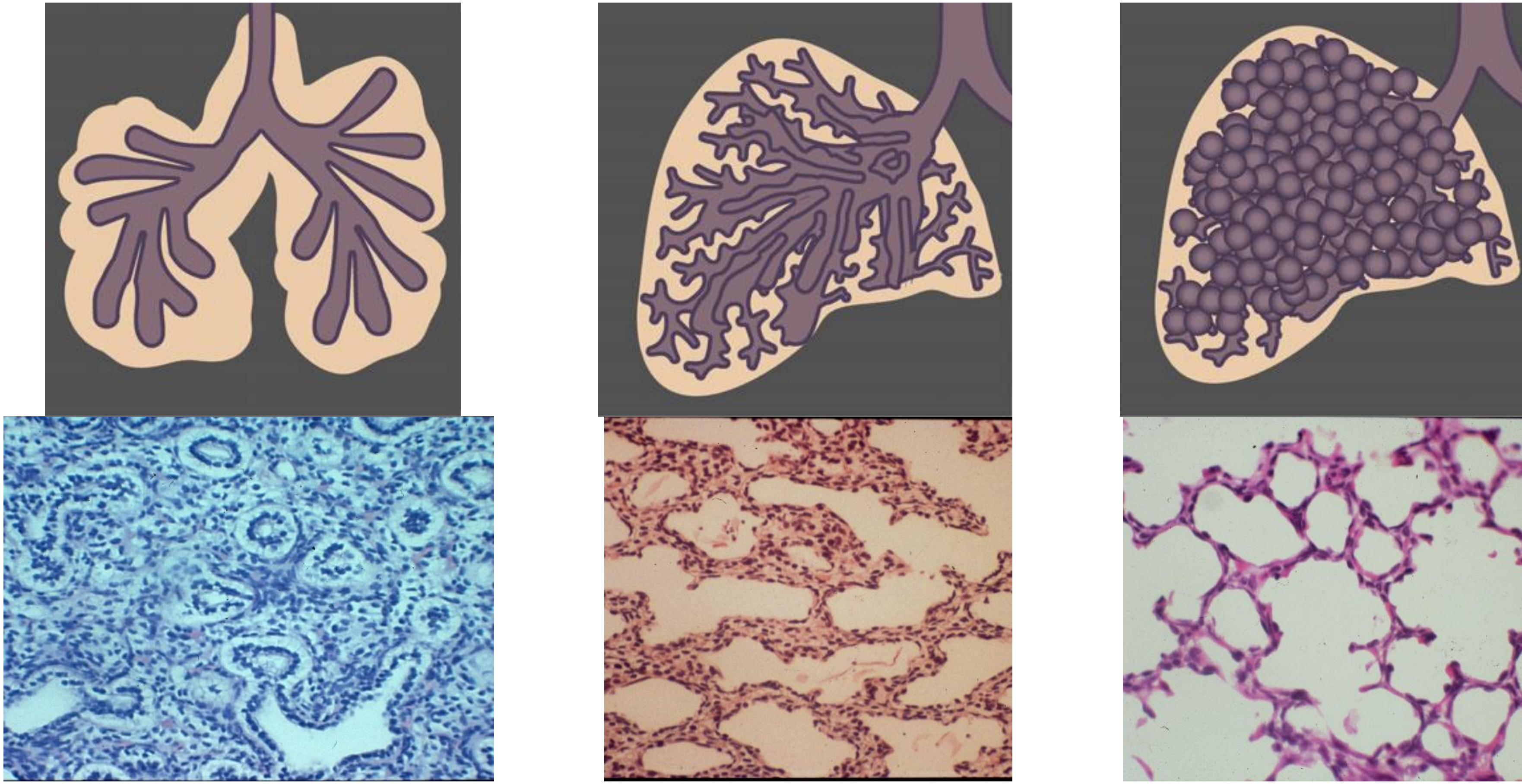


UofU n = 695

Pseudoglandular
~5-18 wk

Canalicular
~16-26 wk

Saccular
~26-36 wk



Pseudoglandular

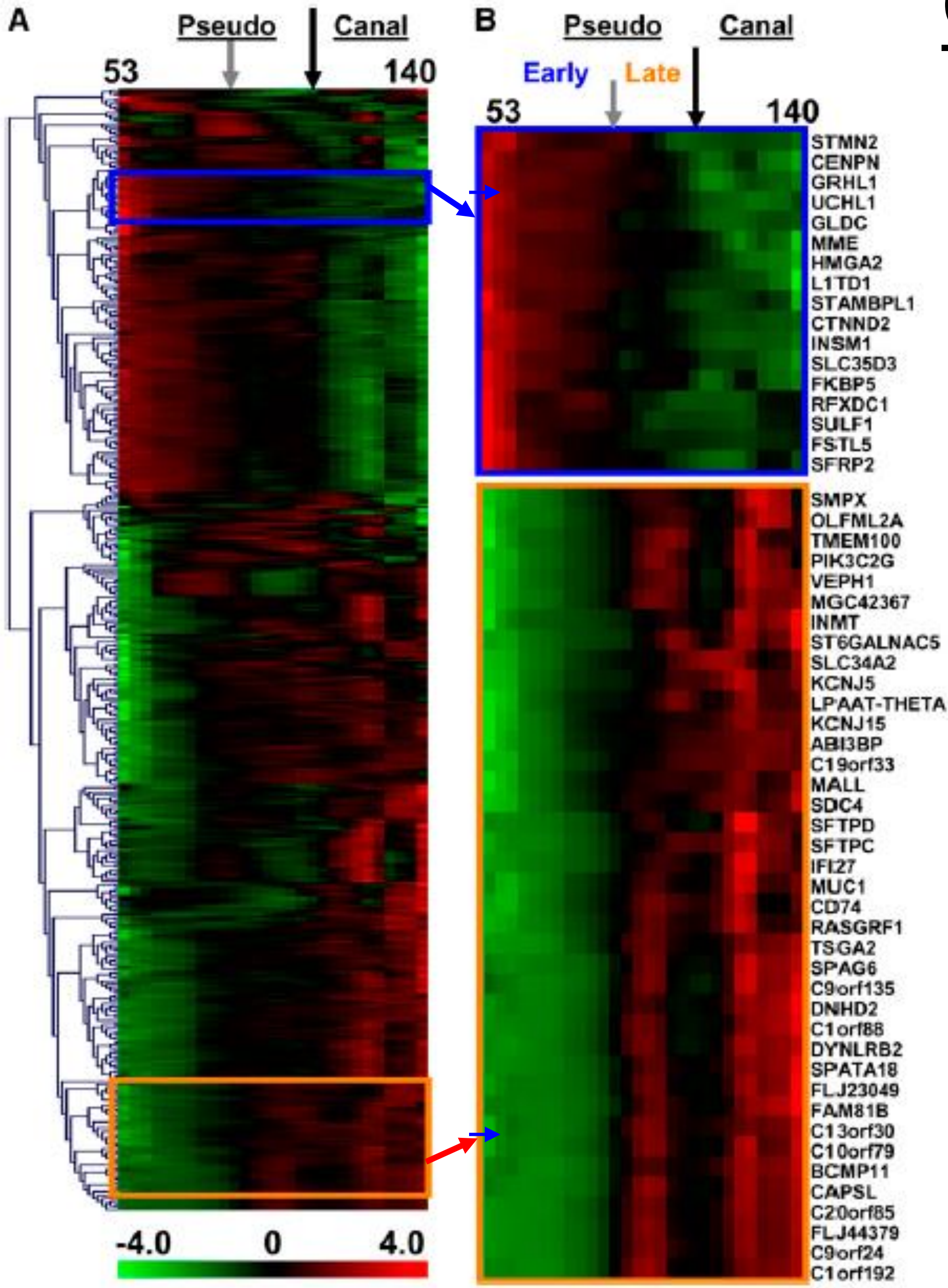
Canalicular

Saccular

BPD primarily occurs in baby's born in the canalicular stage of lung development

Nikoloc MZ, Development, 2018

Gene expression from ~ 7-20 weeks GA



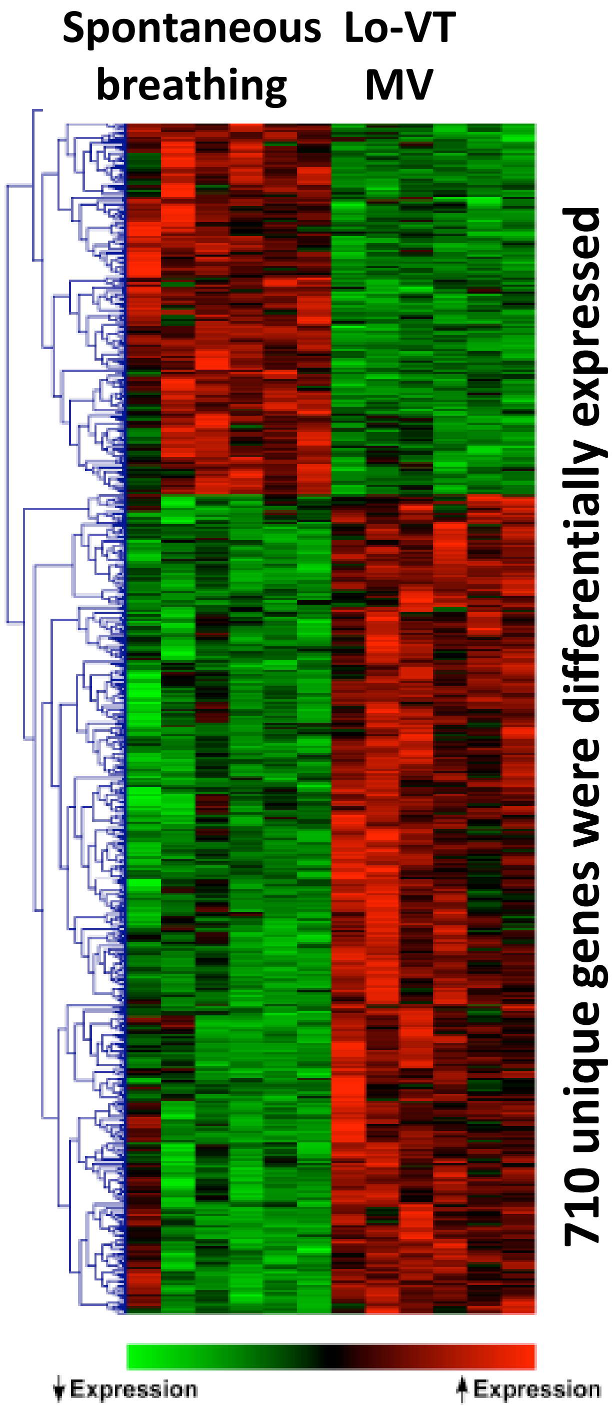
Lung development is highly orchestrated

Gene expression changes dramatically during lung development

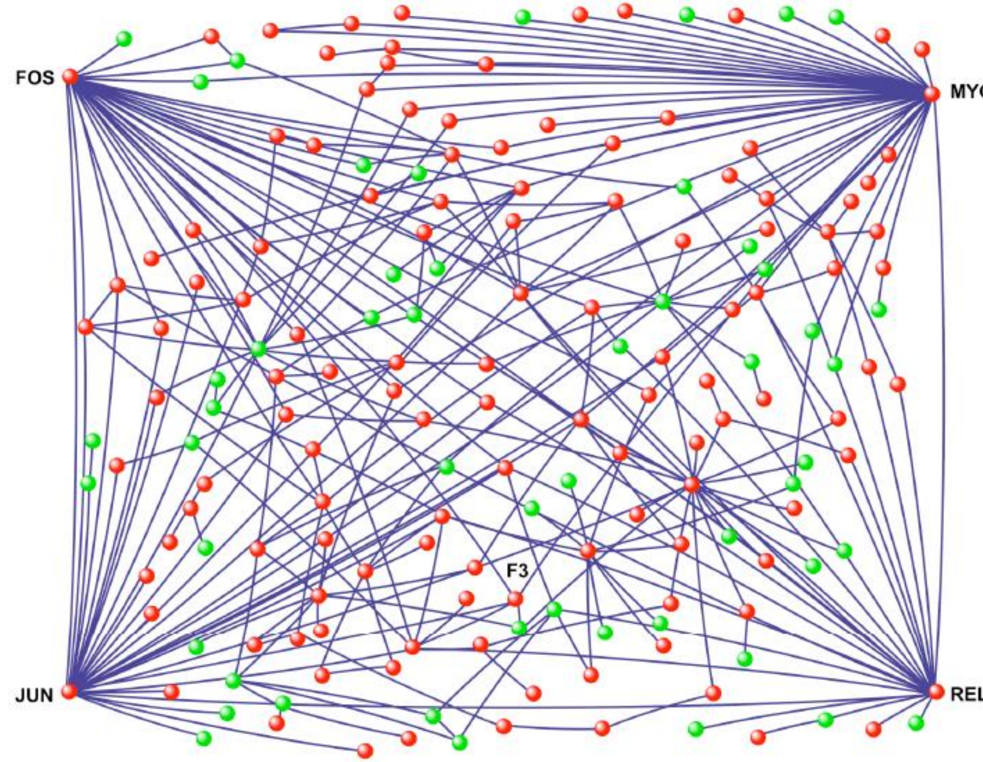
Fetal perturbations interrupt the normal developmental process

Kho AL et al, AJRCCM 2010

“Multi-Hit” Insults & Neonatal Lung Injury



710 unique genes were differentially expressed during MV as compared to spontaneous breathing

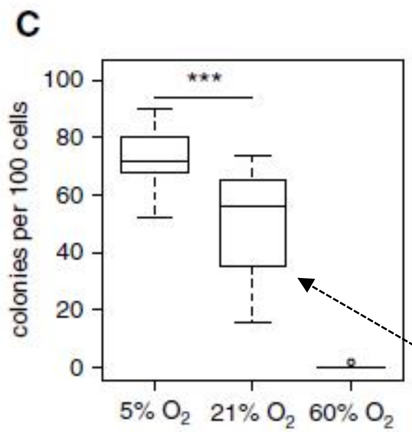


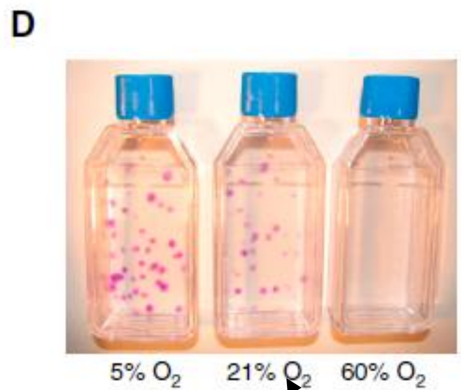
Non-injurious MV activates a diffuse transcriptional network of pro-inflammatory molecules & immune-mediated pathways

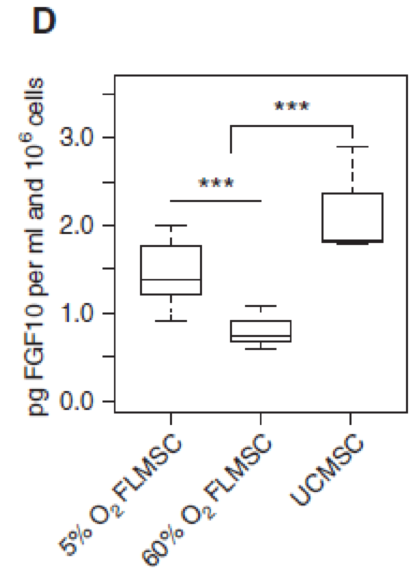
Gharib SA et al, *Physiol. Genomics* 2009

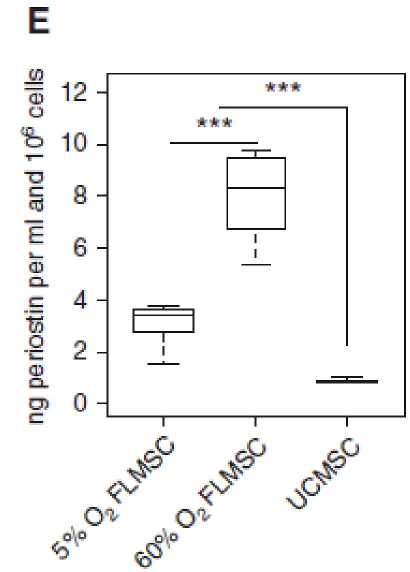
21% O2 Disrupts Human Fetal Stem Cells

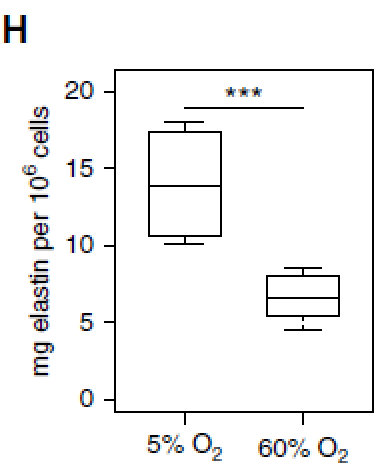
Mobius MA et al, Am J Respir Cell Mol Biol, May 2019

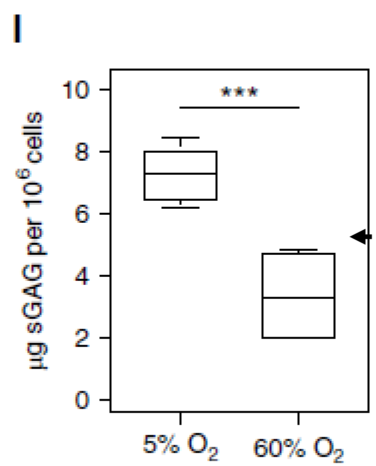












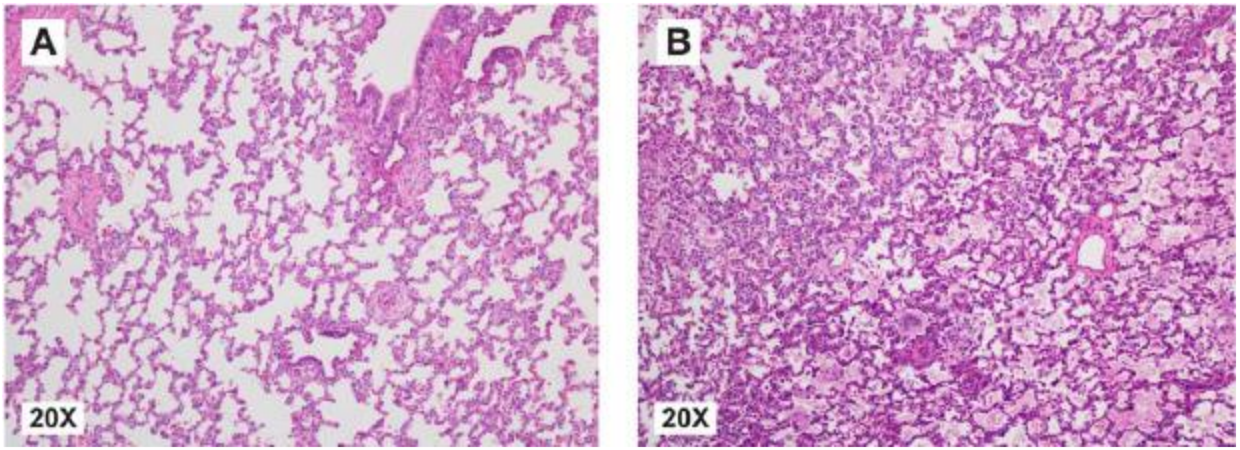
Even RA O2 alters fetal lung MSC's

Contributes to fl-MSC secrotome that interrupts normal lung development

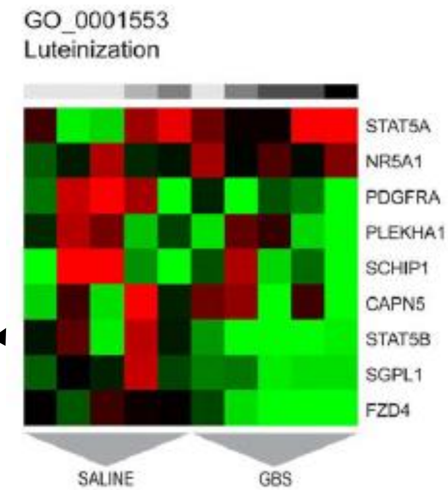
UC-MSC's appear to be less affected by exposure to oxygen than fetal lung MSC's

Chorio-decidual Infection Disrupts Morphogenesis & Angiogenesis Pathways in Fetal Macaque Lungs

McAdams RM et al, *PLOS ONE* 2012

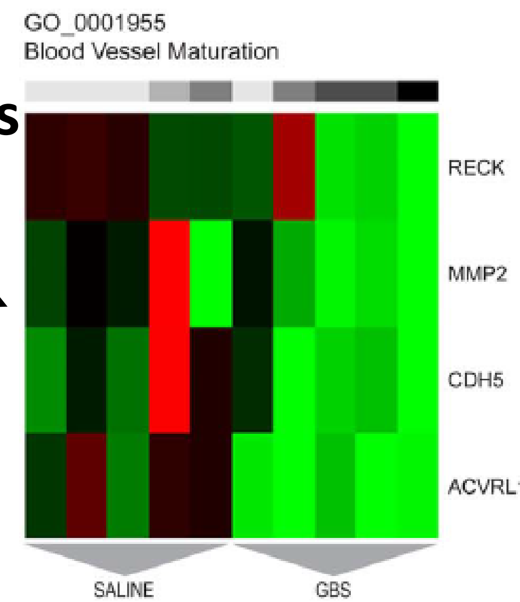


Control **GBS exposed (not infected)**

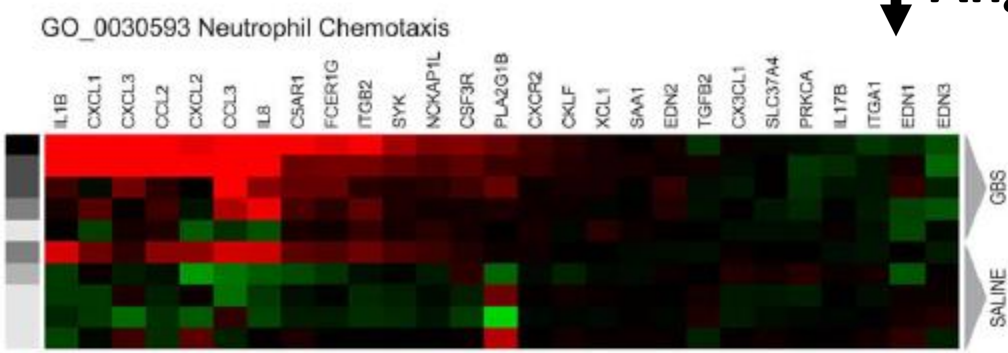


↓ **Morphogenesis**

↓ **Angiogenesis**



↑ **Inflammatory pathways**



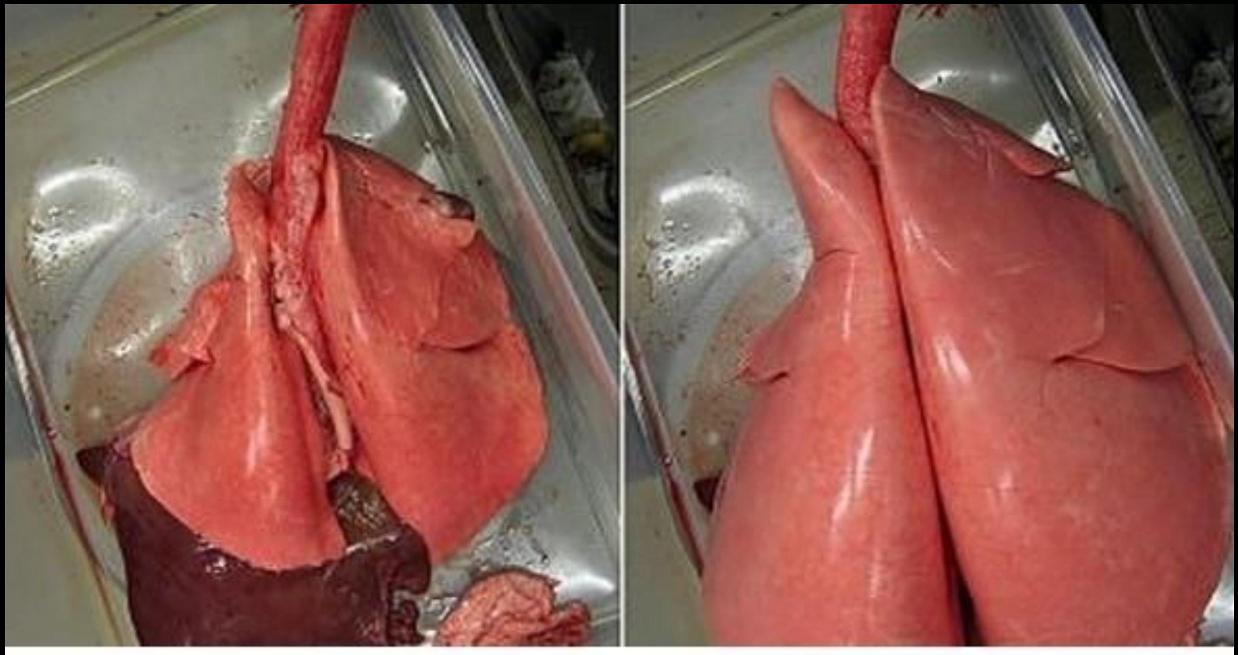
Interim Summary # 1

Lung development is highly sophisticated

Canalicular lung stage at threshold of viability

Preterm birth & neonatal care practices disrupt lung development & lead to impaired alveolization/vasculogenesis

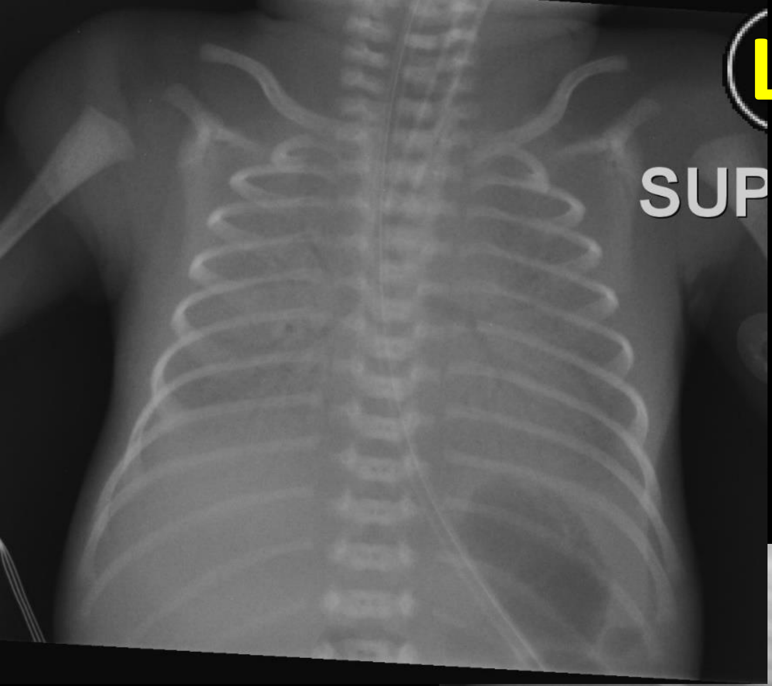
The “Open Lung” Concept



Optimal Lung Volume

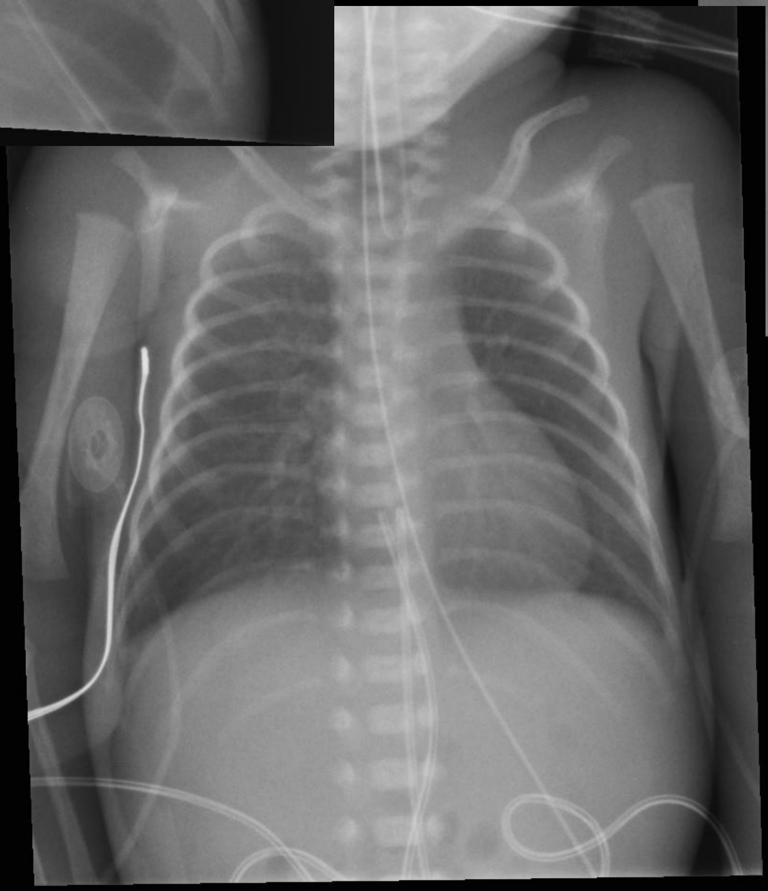
That level of lung inflation where matching of ventilation-perfusion + pulmonary blood flow result in maximum O2 uptake and delivery

Achieving & maintaining OLV is a dynamic process



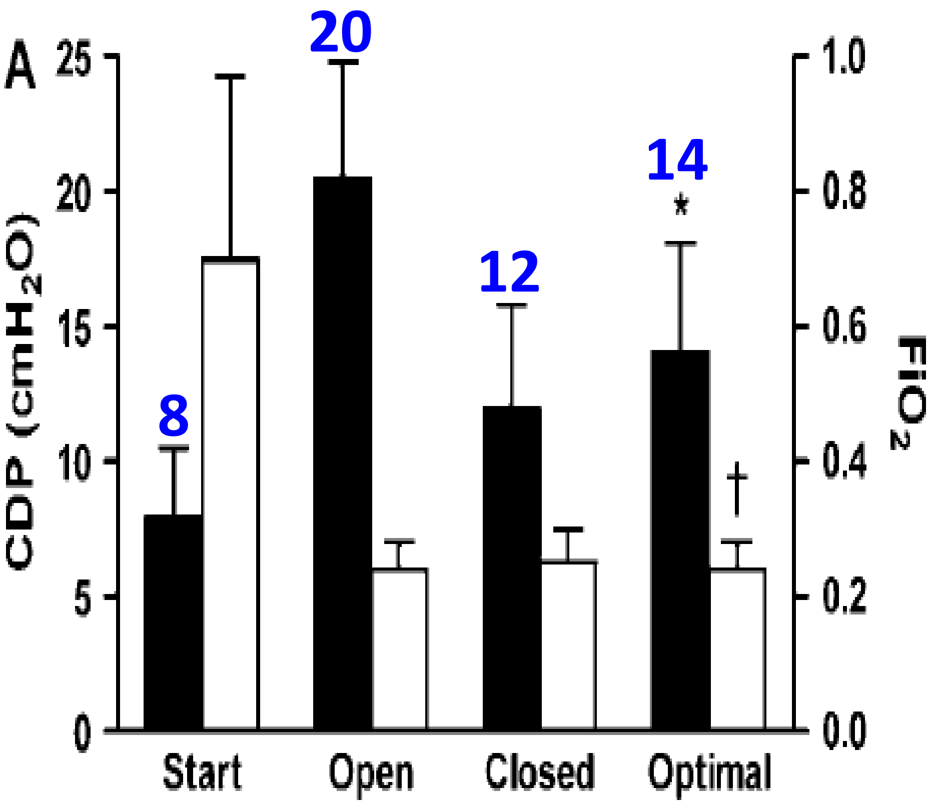
LOW

HIGH



"Optimal"

FiO2 as Guide for Lung Recruitment



Pre-surfactant Recruitment

Mean CDP_{olv} = 20 ± 4

Mean CDP_{opt} = 14 ± 4

Mean $FiO2_{olv}$ = 0.24 ± 0.04

Mean $FiO2_{opt}$ = 0.24 ± 0.04

(96% infants w/ FiO2 < 0.30)

■ = Pressure

□ = FiO2

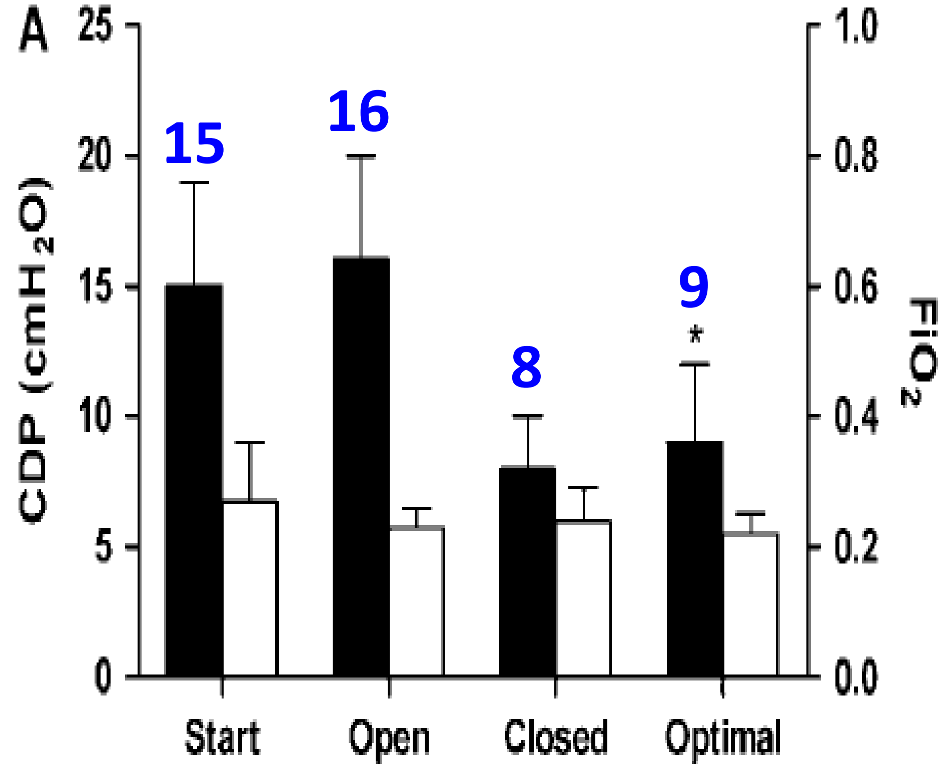
De Jaegre A et al, AmJRCCM 2006

FiO2 as Guide for Lung Recruitment

<u>Post-surfactant Rx</u>

Recruitment maneuvers show much lower Paw

Post-surf CDP_{opt} = 9 ± 3
vs
Pre-surf CDP_{opt} = 14



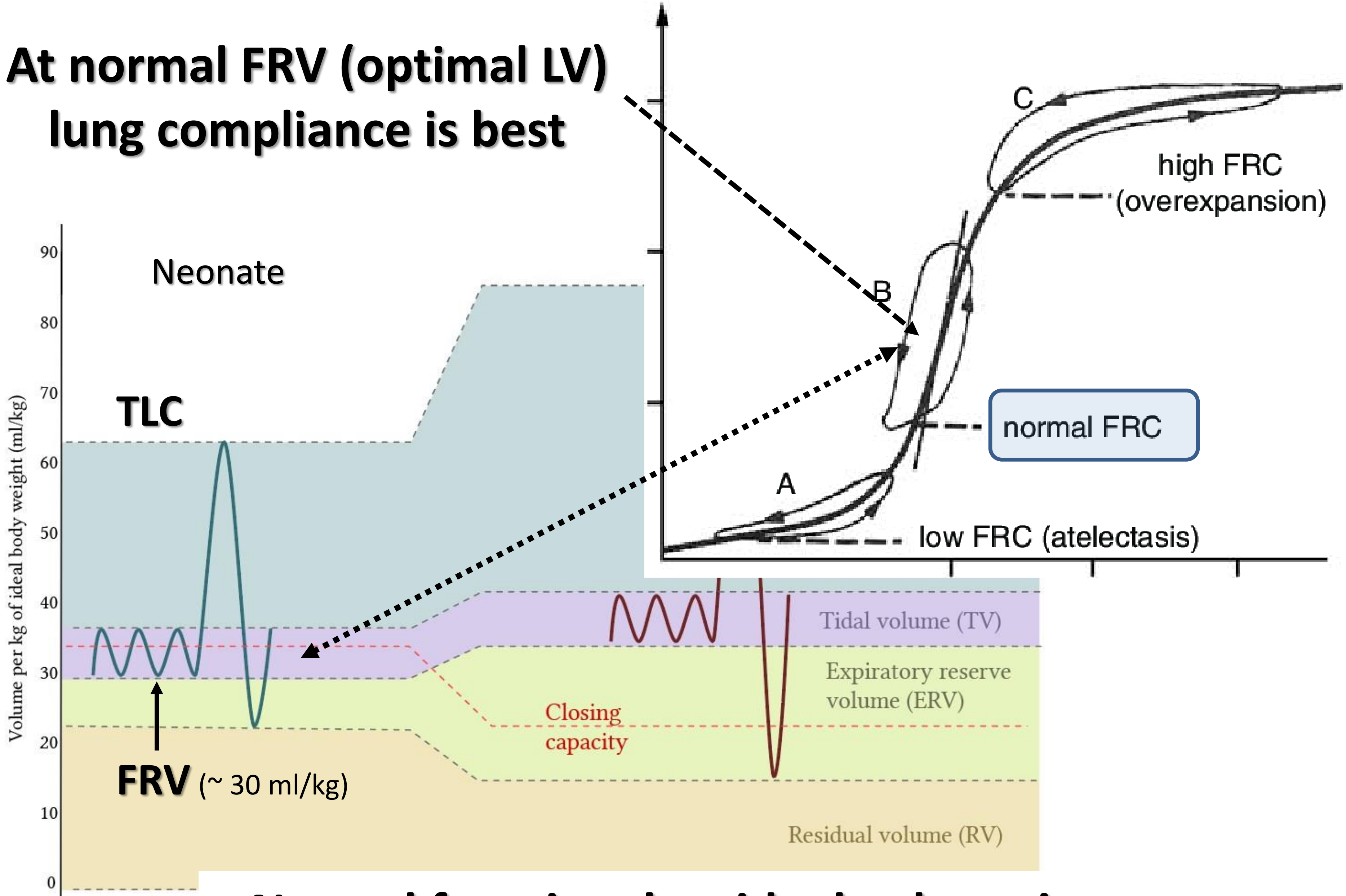
Post-surfactant Recruitment

■ = Pressure
□ = FiO2

De Jaegre A et al, AmJRCCM 2006

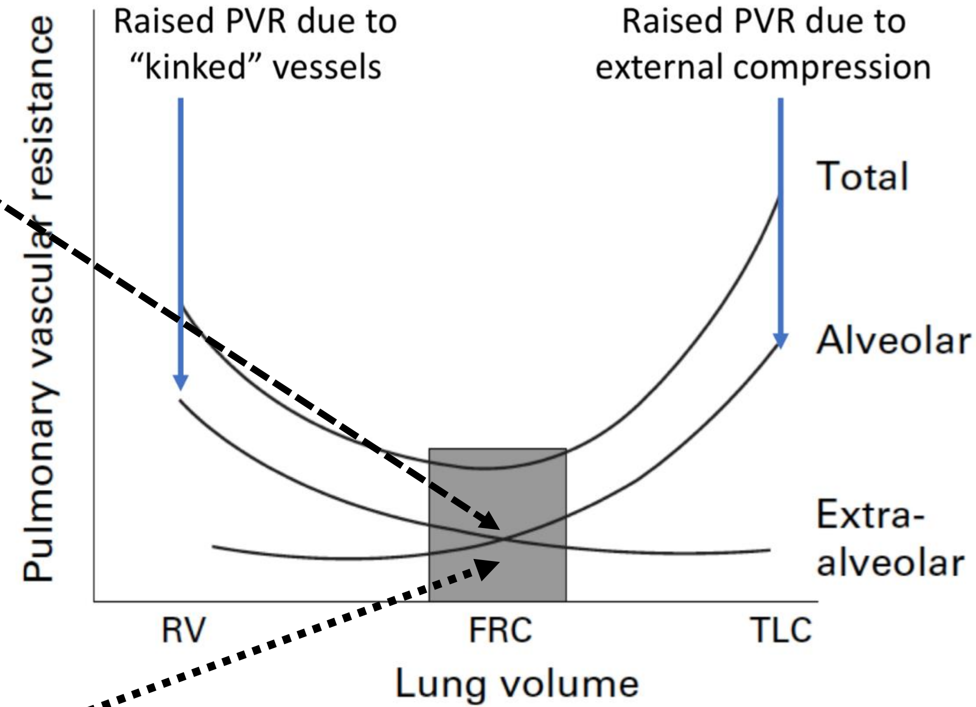
How can we sustain oxygenation when Paw is lowered?

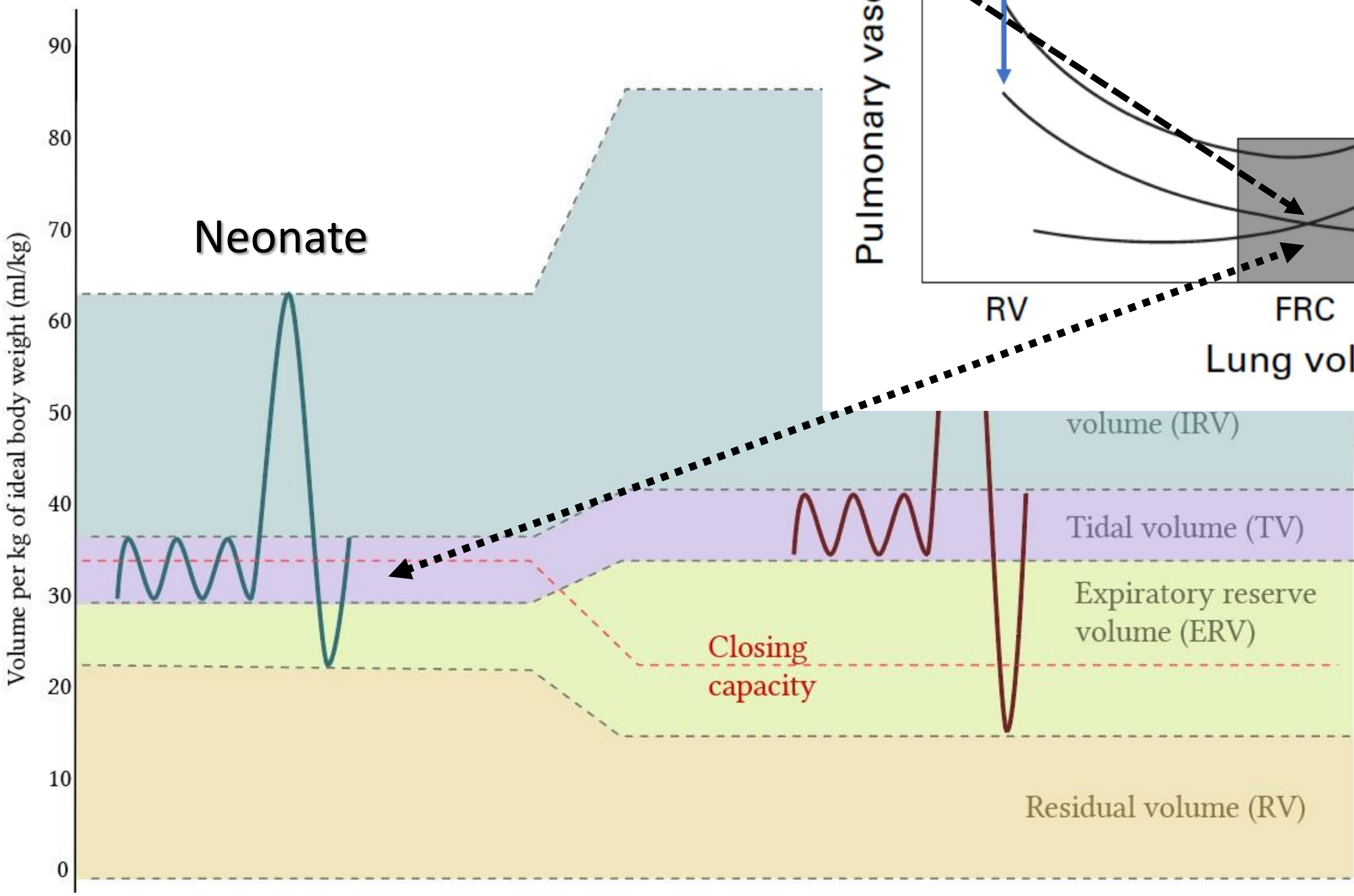
At normal FRV (optimal LV) lung compliance is best



Normal functional residual volume is significantly less than total lung capacity

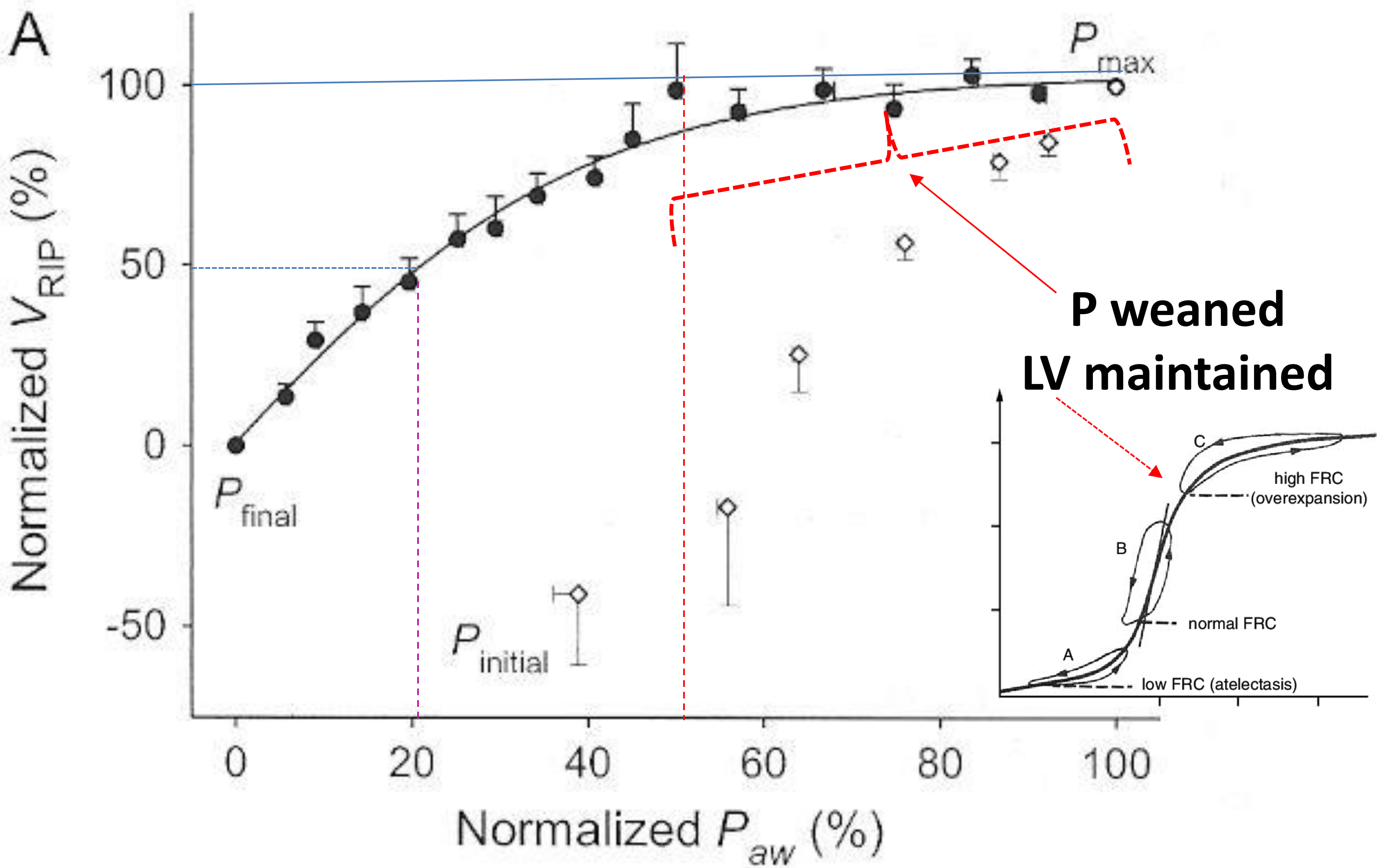
At normal/optimal FRV, PVR is at nadir





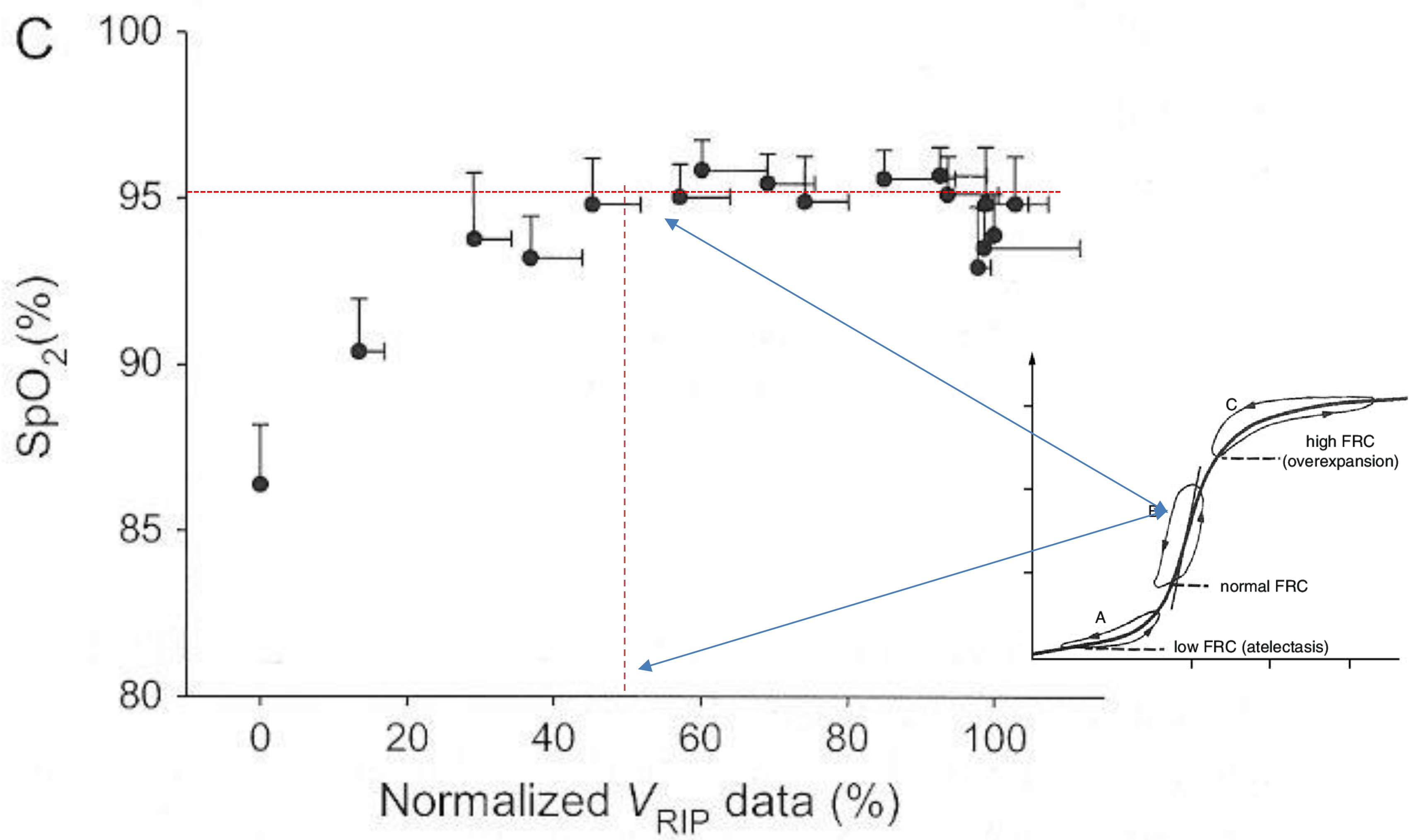
Once recruited…EELV maintained as pressure ↓

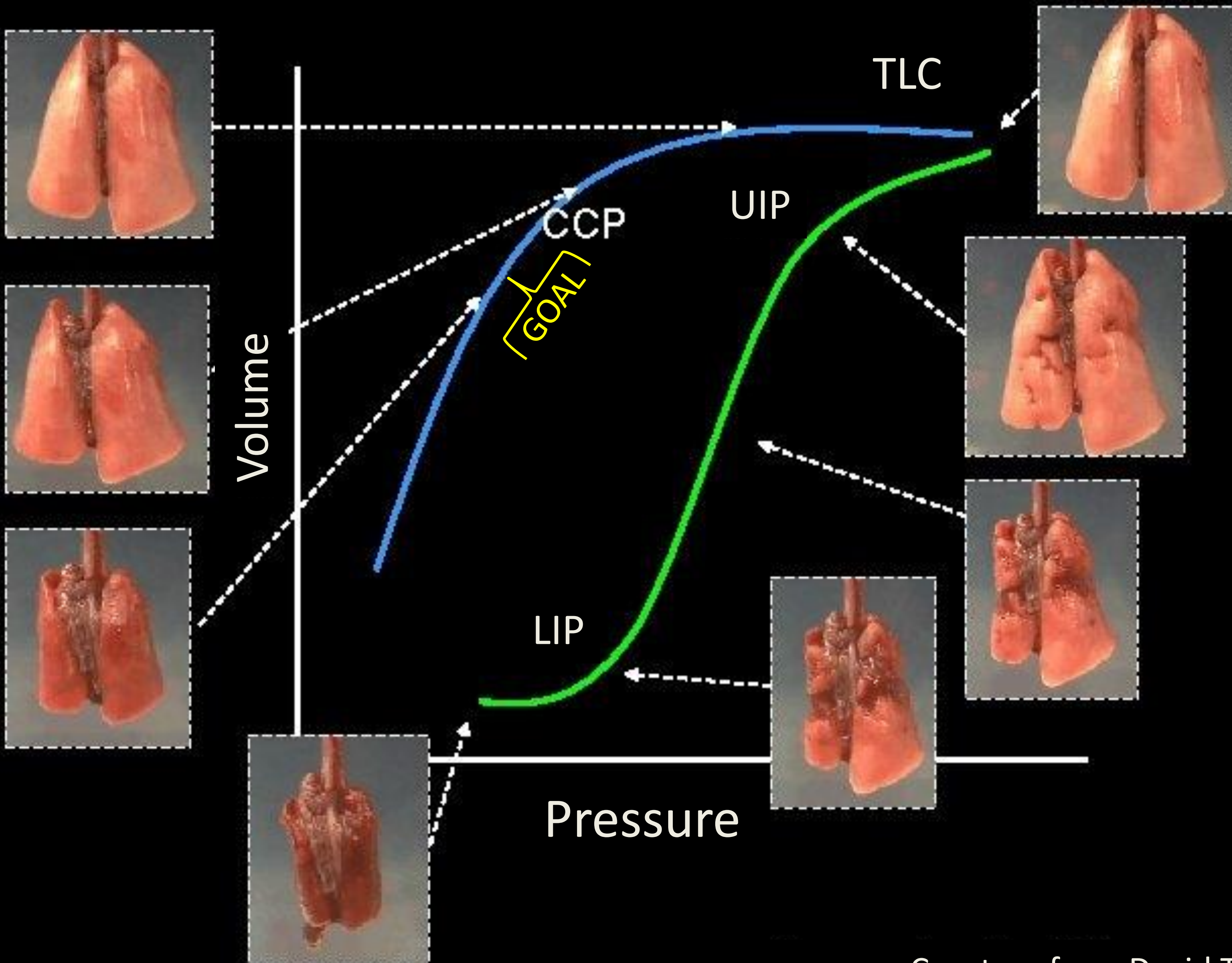
Tingay et al. Am J Respir Crit Care Med 2006; 173: 414-420



SpO2 remains stable as Paw decreases because OLV is maintained

Tingay et al. Am J Respir Crit Care Med 2006; 173: 414-420





Courtesy from David Tingay
Royal Children’s Hospital Melbourne

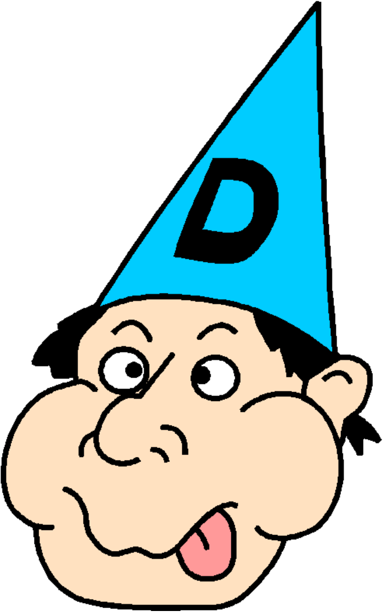
Interim Summary # 2

OLV, best measured by O2/FiO2 response, supports gas exchange & minimizes VILI

At OLV, improved C_L allows support at lower P_{AW}

OLV can be safely achieved/maintained via conventional &/or high-frequency modes

On-going inflammatory “hits” → lung injury ….requiring constant readjustments in MV



PRVC

A/C

SIMV

CMV

HFJV

PS-VG

MMV

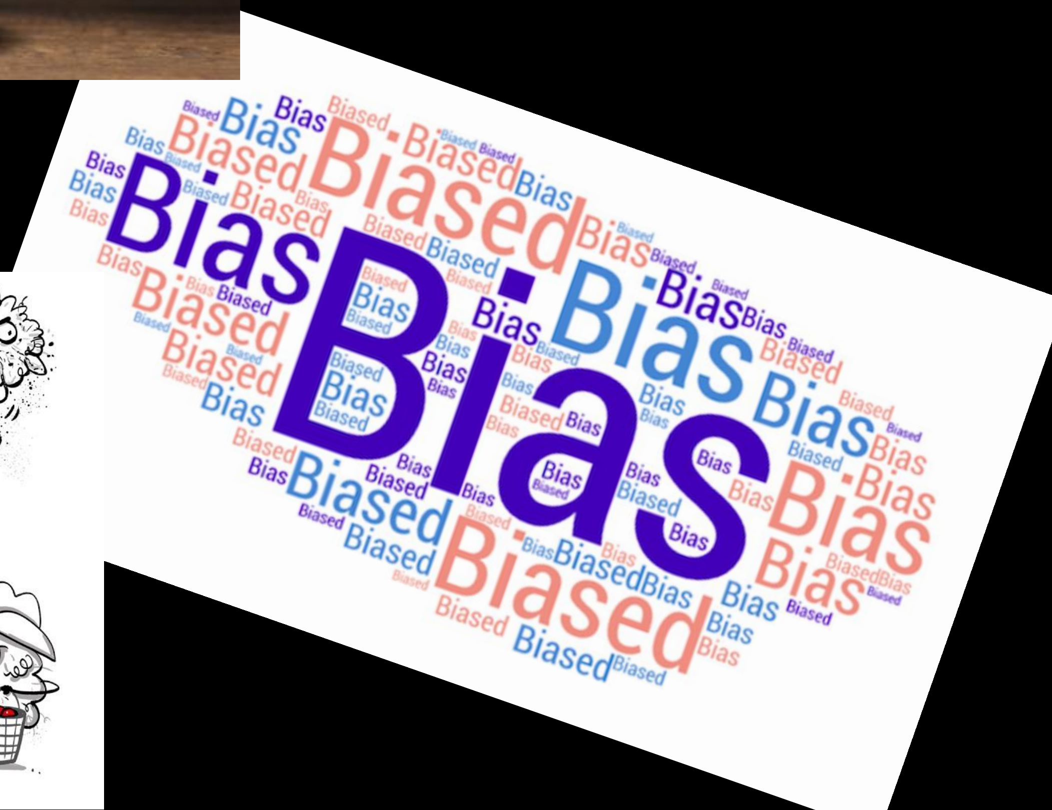
PSV

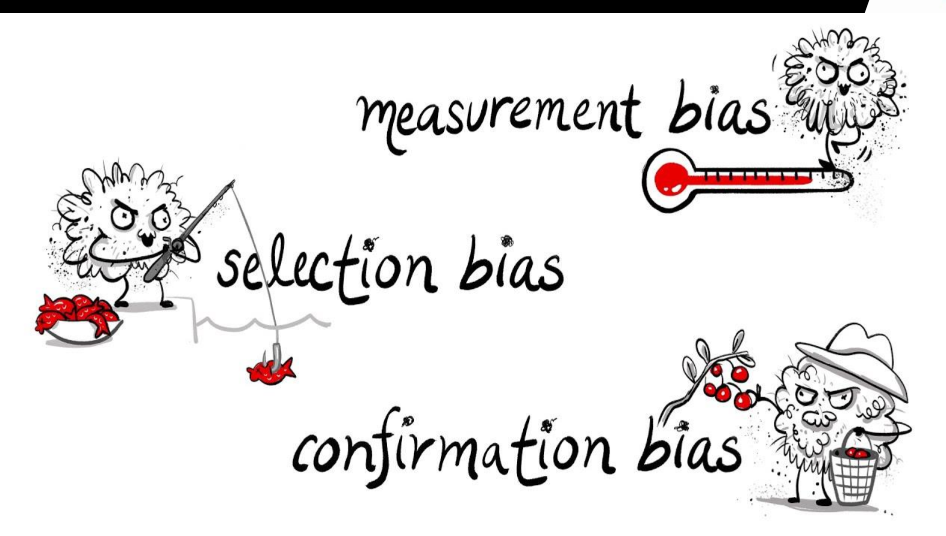
APRV

HFOV

VAPS


We won't be needing that sample...


Bias
Biased


measurement bias
selection bias
confirmation bias

Basic Modes of Conventional Ventilation

Volume-targeted

Pressure-limited

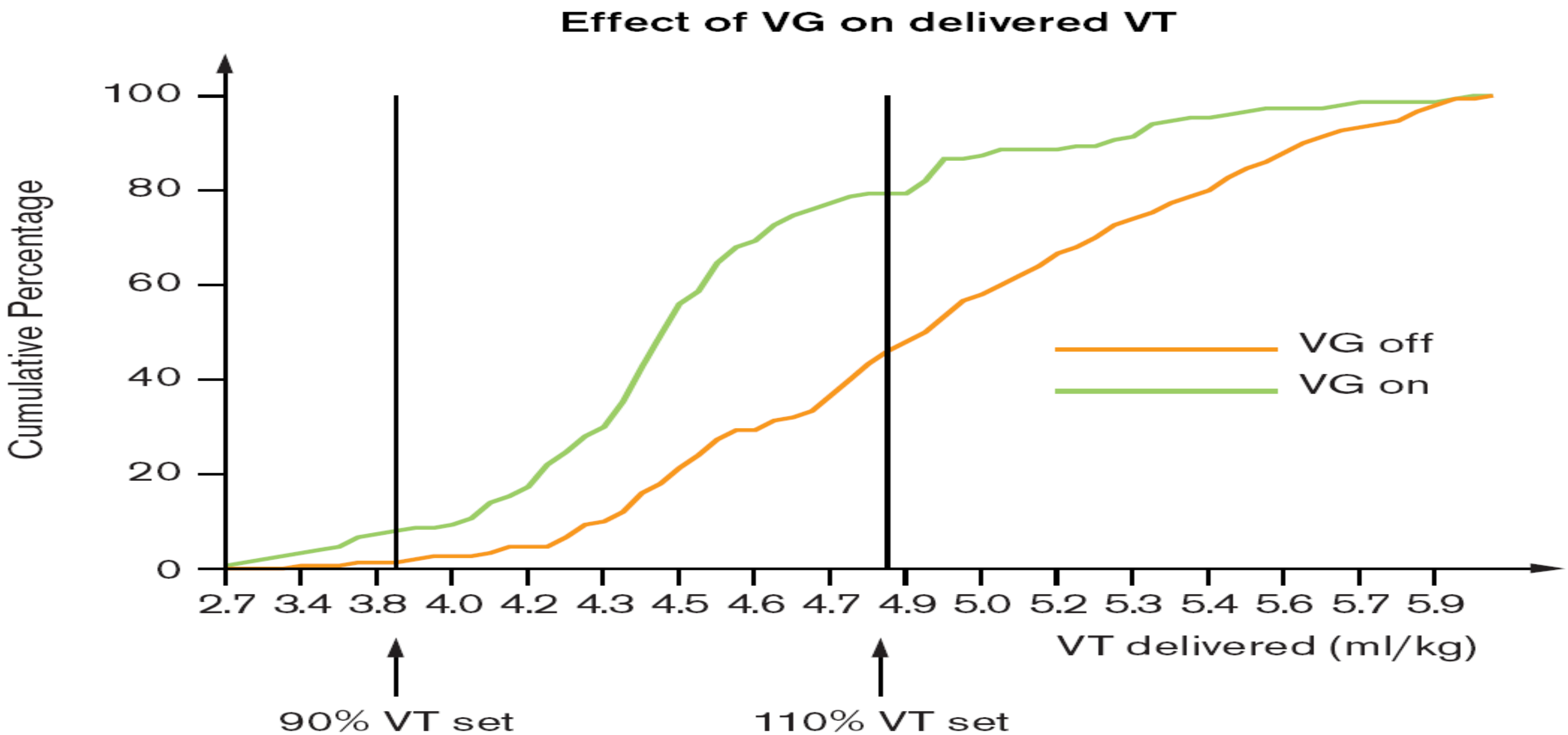
Volume Targeted Ventilation

- **<u>ADVANTAGES</u>**
  - Consistent V_T delivery
  - Auto-weaning of PIP as compliance improves
  - Linear increase in MV as V_T increases

- **<u>DISADVANTAGES</u>**
  - May need high airway pressures → *"scary"*
  - Pt-Vent dysynchrony w/ inadequate inspiratory flow
  - Excess ETT air leak can affect V_T delivery

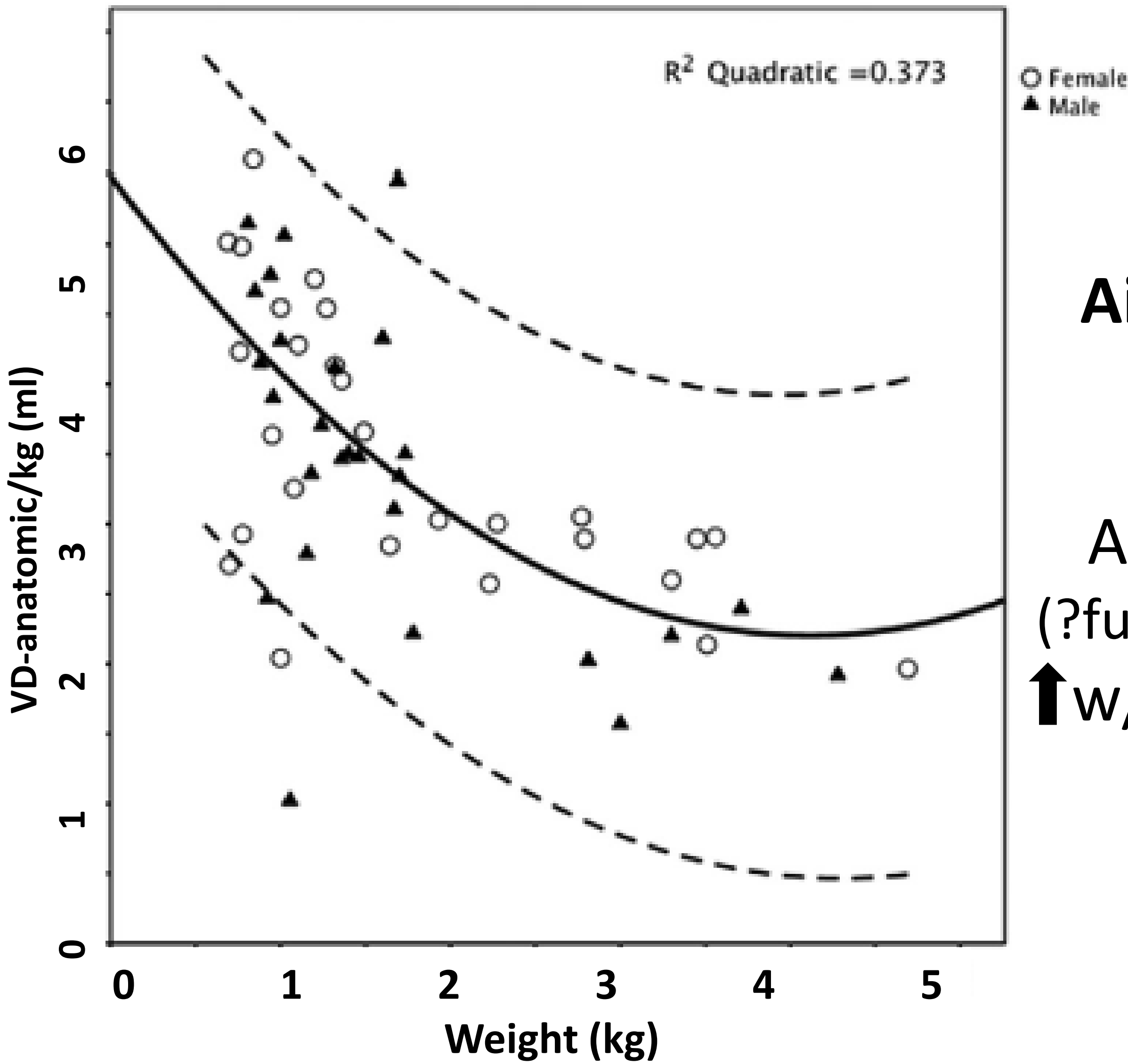
VG Improves Stability of V_T

Ahluwali J et al, Primer on VG



~ 80% of breaths w/in 90-110% of set V_T w/ VG vs < 50% during PC support mode

Anatomic D_{sp} by Birth Weight



Airway dead space⬆ as GA⬇

Airway dead space (?functional & anatomic?) ⬆w/ longer time on MV

Dassio T, Peds Pulm 2018
Neumann R, Neo 2015
Nassabeh-Montazamis S, Peds Pulm 2009

Original Paper

Neonatology

Neonatology 2015;107:43–49
DOI: 10.1159/000366153

Received: March 24, 2014
Accepted after revision: July 27, 2014
Published online: November 6, 2014

Influence of Gestational Age on Dead Space and Alveolar Ventilation in Preterm Infants Ventilated with Volume Guarantee

Roland P. Neumann[a, b] Jane J. Pillow[b–d] Cindy Thamrin[f] Alexander N. Larcombe[e]
Graham L. Hall[e] Sven M. Schulzke[a, b]

- **Cannot recommend specific target V_T in very preterm infants**
- V_T depends on variety of patient and device specific factors
- Adjusting set V_T to target physiologic RR may be optimal
  - But this is an unstudied hypothesis

VG-MV: Where do you start?

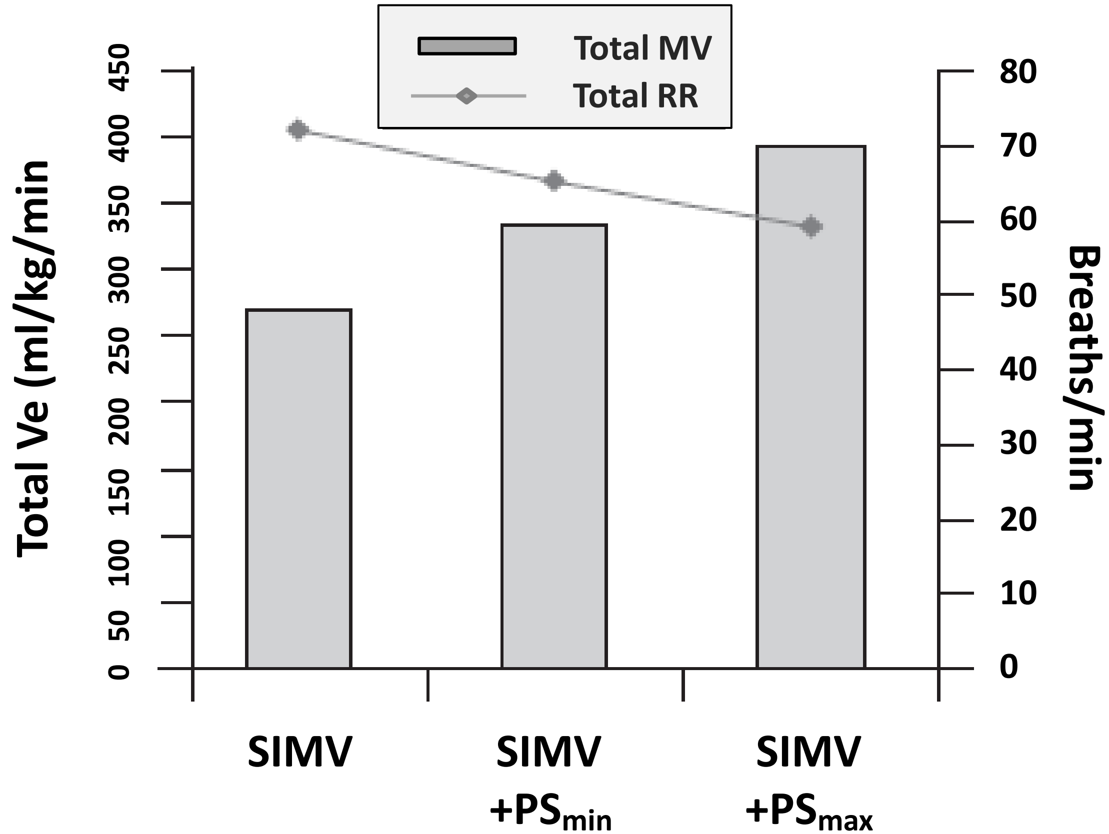
- **What is “best” mode for VG-MV?**
  - SIMV + PS
    - How much PS ?
  - PSV only
  - AC only
  - NAVA
  - Other
- **Limited RCT’s comparing different modes**

PSV w/ SIMV

↑ VT, MV, Paw

↓ RR & FiO2

↓ WOB



Vtexh	SIMV	+ PSmin	+ PSmax
VT_{exh} (ml/k)	3.9 (0.7)*	5.2 (1.3)	6.7 (0.7)
Mvexh (ml/k/m)	270 (47)*	332 (53	392 (63)
RR (bpm)	72 (6)*	65 (9)	59 (10)
Paw (cmH2O)	5.6 (0.8)*	6.8 (0.9)	7.9 (1.3)
FiO2 (%)	24.2 (2.2)*	23.6 (1.5)	21.5 (1.2)

Psmin - target VT ~ 3-4 ml/kg

Psmax - target VT ~ 5-6 ml/kg

Gupta S, ADCFNE 2008

FACT or FICTION?

Volume-targeted approaches are

better than pressure-limited modes

for conventional neonatal ventilation

Meta-Analysis: VG vs PC MV

Outcome	RR or Mean Δ	95% CI	NNTB (95% CI)
Death/BPD	0.75	0.53 – 1.07	
BPD 36 wks	0.73	0.59-0.89	8 (5-20)
G 3-4 IVH	0.53	0.37-0.77	11 (7-25)
PVL/sIVH	0.47	0.27-0.80	11 (7-33)
Pneumothorax	0.52	0.31-0.87	20 (11-100)
Hypocapnia	0.49	0.33-0.72	3 (2-5)
Days MV	-1.35	-1.83, -0.86	

Klingenberg C et al, Cochrane Rev 2017

FACT

In general, volume-targeted SIMV

is best mode for

conventional neonatal ventilation

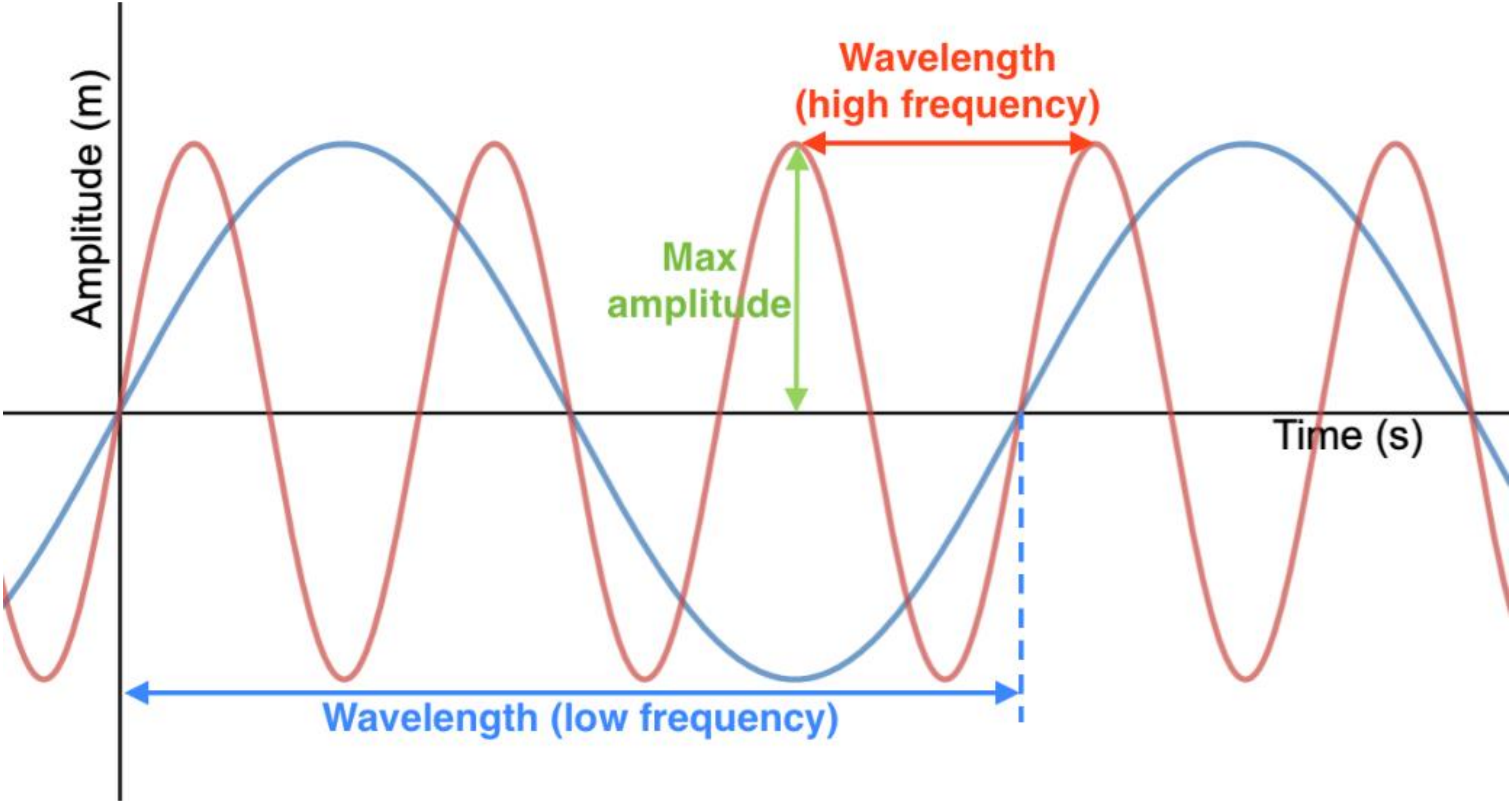
Interim Summary # 3

Volume targeted approach to conventional mechanical ventilation is preferred

Typical starting V_T is ~ 5 ml/kg, but varies by gestational and postnatal age

No specific ventilator or V_T mode shown to be better than another

So What About High Frequency??



High Frequency Ventilation

Suggested advantage

adequate gas exchange w/ much smaller V_T

? Lower risk for VILI ?

Potential risks

adverse effects 2^{nd} to inadequate understanding of device(s) & lung pathophysiology

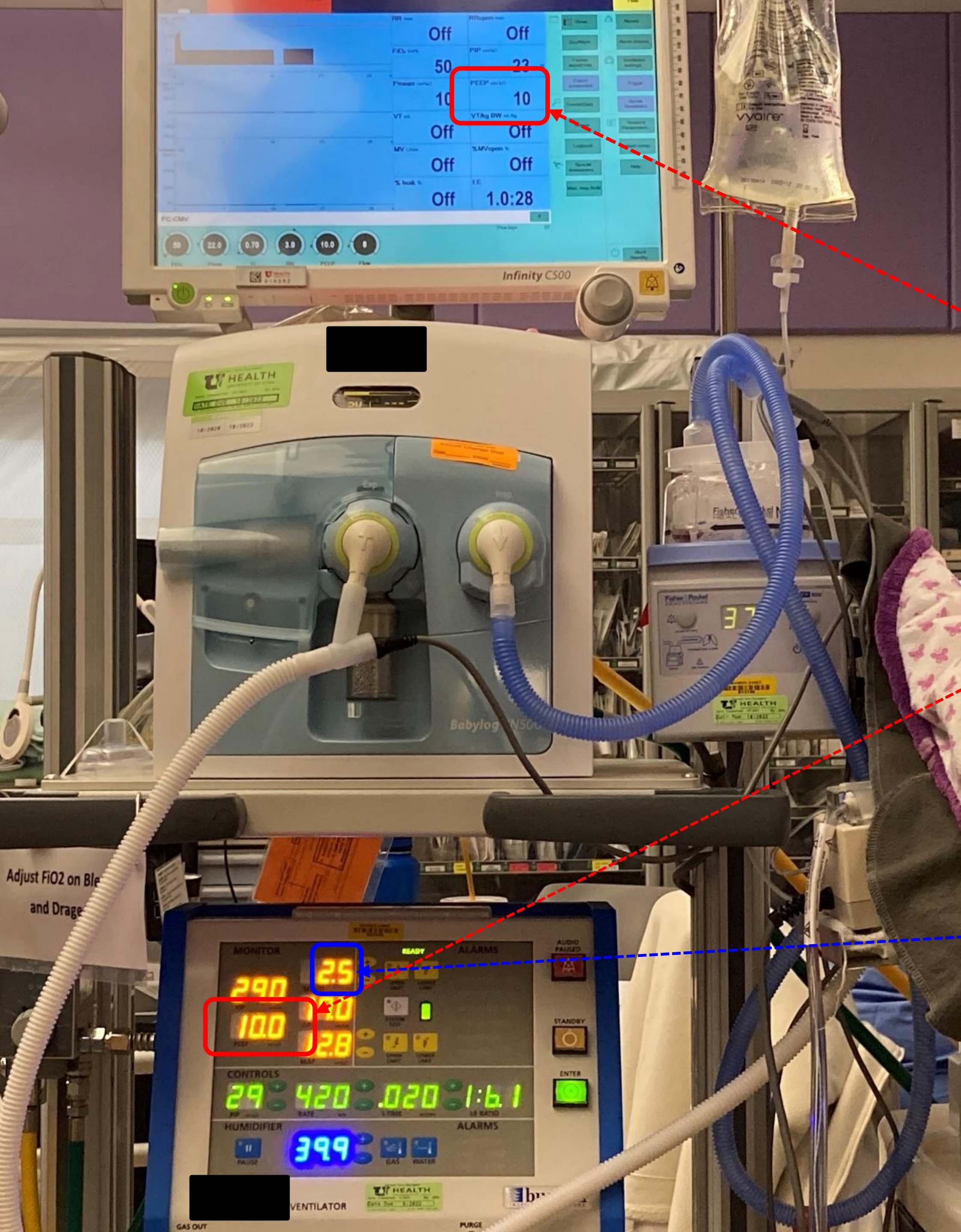
Classification by Device

- **Oscillation (HFOV)**
  - SensorMedics 3100A (Vyaire Medical)
  - Drager, Leoni +, Stephanie, SLE500, others
    - VT-HFOV devices currently not approved in US
- **Jet (HFJV)**
  - Bunnell Life Pulse
- **Flow-Interruption (HFFI)**
  - VDR4 (Percussionaire)

Characteristics by Mode

	SM3100A	HFJV	Drager VN500*
Exhalation	**Active**	**Passive**	**Active**
Rates	5-15 Hz	240-480	5-20 Hz
I:E	1:2	1:4 – 1:12	1:1 – 1:2
Insp time	22 – 67 msec	20 msec	16-67 msec
Waveform	Square	Peaked	Sinusoidal
CMV breaths	No	Yes	Yes
Vol-Targeted	No	No	Yes

* Currently not FDA approved in US



Additional JET features

CMV set PEEP should be + 2 measured “Jet PEEP”

(Monitor for “inadvertent” PEEP)

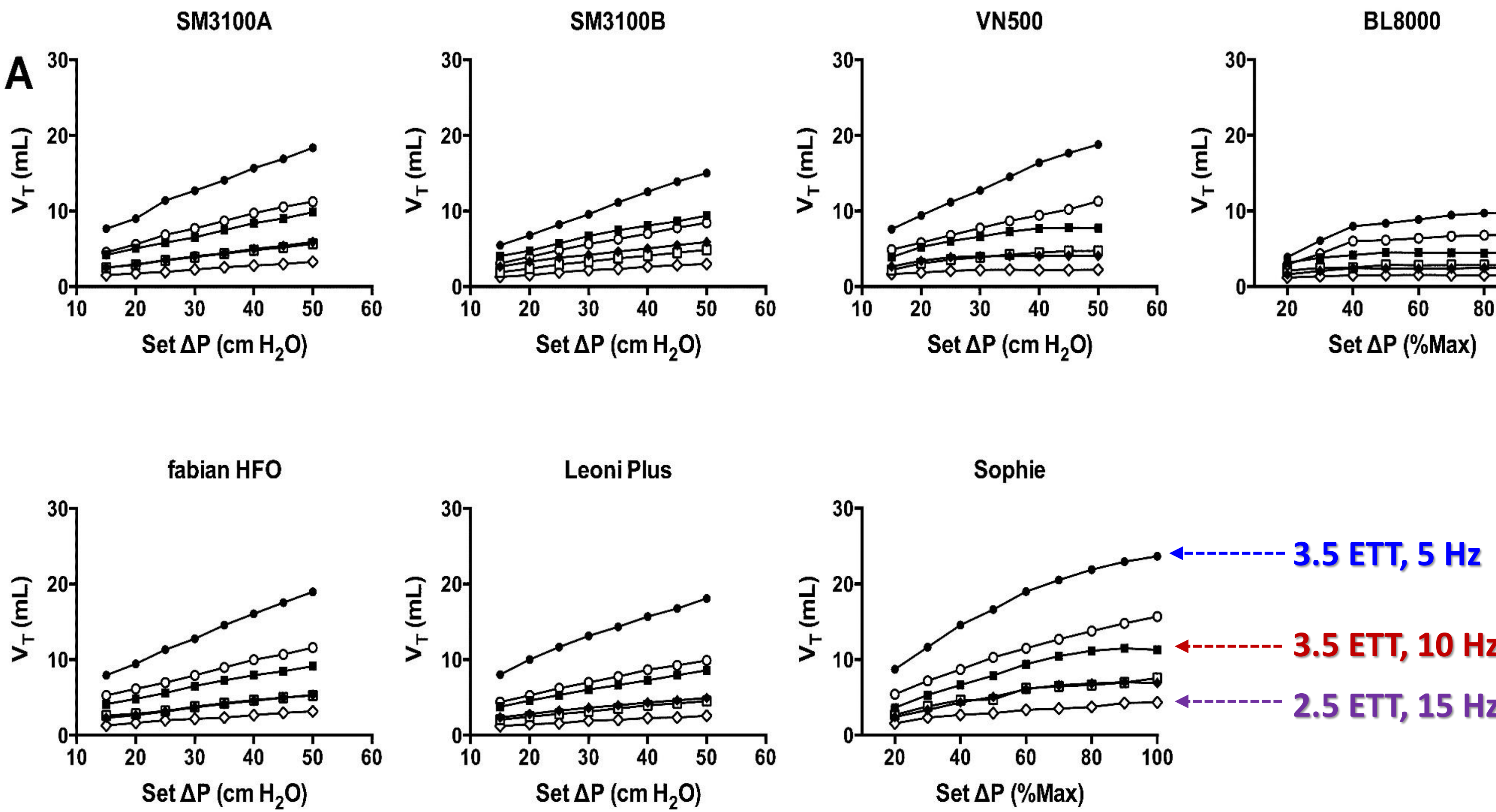
“Servo pressure” relative estimate of system compliance

General Concepts of HFV

- **Ventilation** – usually easily established
  - **V_T changes have greater effect than rate**
    - **HFV theory:** $V_{CO_2} = f^a \times (V_T)^b$

      where a = 0.7-1.0 & b = 1.5-2.2
  - **Must be cautious to minimize hypocarbia**
  - **Gas-trapping pathophysiology requires slower HFV rates / longer exhalation times**

Tidal volume changes similarly in all devices w/ increasing ΔP, ETT size, and *f*



Tingay, et al Neonatology 2015

General Concepts of HFV

- **Oxygenation – dependent on OLV**
  - No easy method to identify OLV
  - Assume inflation to ~ 9^{th} posterior rib
  - Must also include overall “good” inflation
  - Absence of diaphragm flattening
  - FiO_2 consistently < 0.30
- more difficult to assess w/ lung hypoplasia

OLV – optimal lung volume

Does One HFV Mode Have An Advantage?

Does It Vary By Disease?

WHAT DO CLINICAL TRIALS COMPARING HFOV TO HFJV SHOW?


Nothing

Despite over 40 years of HFV practice

NO randomized controlled trials

have compared HFOV to HFJV

for any neonatal respiratory disorder

WHAT ABOUT TRIALS COMPARING HFV TO CMV?

FACT or FICTION?

HFV leads to better lung

outcomes than conventional MV

for treatment of preemies with RDS

Cochrane
Library

2015

Cochrane Database of Systematic Reviews

Elective high frequency oscillatory ventilation versus Conventional ventilation for acute pulmonary dysfunction in preterm infants (Review)

Cools F, Offringa M, Askie LM

Sample size

- Nineteen eligible studies involving 4096 infants

Authors' conclusions

- Elective HFV compared with CV showed a small reduction in risk of CLD

Analysis 1.7. Comparison 1 HFOV versus CV (all trials), Outcome 7 CLD at 36 to 37 weeks PMA or discharge in survivors.

Review: Elective high frequency oscillatory ventilation versus conventional ventilation for acute pulmonary dysfunction in preterm infants

Comparison: 1 HFOV versus CV (all trials)

Outcome: 7 CLD at 36 to 37 weeks PMA or discharge in survivors

HFOV w/ lower rate of BPD at 36 wks

Study or subgroup	HFOV n/N	CV n/N	Weight	Risk Ratio M-H,Fixed,95% CI
Clark 1992	[illegible]	[illegible]	2.3 %	0.23 [0.07, 0.73]
[illegible]	[illegible]	[illegible]	5.8 %	0.58 [0.35, 0.95]
[illegible]	[illegible]/41	0/46		Not estimable
[illegible] 1998	32/126	30/129	6.1 %	1.09 [0.71, 1.68]
Plavka 1999	3/19	8/18	1.7 %	0.36 [0.11, 1.13]
Durand 2001	5/19	14/20	2.8 %	0.38 [0.17, 0.84]
Moriette 2001	24/108	30/107	6.2 %	0.79 [0.50, 1.26]
Courtney 2002	70/201	93/210	18.7 %	0.79 [0.62, 1.00]
Johnson 2002	165/300	163/292	33.9 %	0.99 [0.85, 1.14]
Van Reempts 2003	24/122	19/133	3.7 %	1.38 [0.79, 2.39]
Schreiber 2003	43/84	34/84	7.0 %	1.26 [0.91, 1.76]
Craft 2003	13/19	13/21	2.5 %	1.11 [0.70, 1.74]
Vento 2005	2/19	8/18	1.7 %	0.24 [0.06, 0.97]
Dani 2006	4/11	3/10	0.6 %	1.21 [0.36, 4.14]
Lista 2008	2/18	2/20	0.4 %	1.11 [0.17, 7.09]
Salvo 2012	1/39	3/39	0.6 %	0.33 [0.04, 3.07]
Sun 2014	13/173	28/166	5.9 %	0.45 [0.24, 0.83]
Total (95% CI)	**1392**	**1394**	**100.0 %**	**0.86 [0.78, 0.96**

Cochrane
Library

2015

Cochrane Database of Systematic Reviews

Elective high frequency oscillatory ventilation versus Conventional ventilation for acute pulmonary dysfunction in preterm infants (Review)

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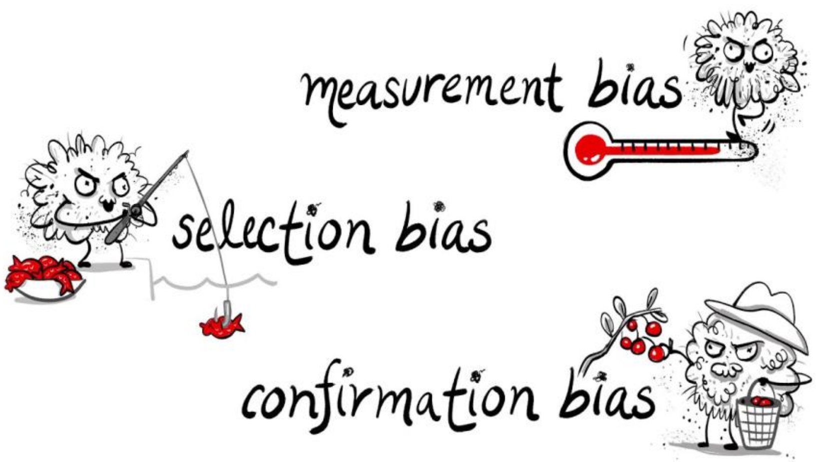
Benefits of HFV lost when studies analyzed by use of surfactant & by use of optimal lung volume strategies

Caveats to HFV vs CMV Trials

- Inconsistent trial designs
  - Pre vs Post surfactant eras
  - Mostly PC CMV approaches
  - Variable HFV approaches
    - ? Open lung methodology
    - ? Duration of HFV support
  - ? Optimized post-extubation NIV support
  - *Mean GA typically 26+ weeks or higher*


We won't be needing that sample...


measurement bias
selection bias
confirmation bias


Bias
Biased

Interim Summary # 4

HFV have unique characteristics that must be understood to optimize performance

There are no RCTs comparing different HFV modes to each other

Meta-analyses & long-term f/u studies do not show benefit for HFV vs CMV

Ventilator Support
in
Extremely Preterm Infants

Common Strategies in Hospitals with Success in Care of 22–24 wk Infants

- Aggressive pre/perinatal support/intervention
- Written guidelines/checklist for initial DR/NICU care
- Initial stabilization w/ DR intubation for 22-23 wks
- **Standardized 1st intent ventilator mode & settings**
- Early surfactant & caffeine administration

General Approaches to Care

	Uppsala	Kanagawa	U Iowa
Perinatal	ANS	ANS	ANS
DR	NO BMV, **2.0 ETT**	**2.0 ETT**	BMV x 30s, **2.0 ETT**
Surfactant	In DR	w/in 6 hrs	w/in 1st hr
Caffeine	Early	Early	Early
Cardiac	No inotropes No PDA Rx 1st week	Early *f*ECHO, *pINDO* Routine low dose Dobu/Dopa	PRN *f*ECHO HC, inotrope *prn*
Sedation	None, Min Stim	PhenoB – *no MS*	None, Min Stim

Sindelar R et al, Semin Perinatol 2022

Specific Ventilator Approaches

Sindelar R et al, Semin Perinatol 2022

	Mode	Settings	Gas goals	Extubation
Uppsala (Sweden)	**VTV** (AC/PSV)	Initial V_T ~ 5 ml/kg PEEP 4-5 AC @ R 60, IT 0.33	90-95% 50-60 torr	~ 29 wks PMA (early as able)
Kanagawa (Japan)	**HFOV** V-targeted	V_{Thf} ~1-2 ml/kg Paw ~ 12 cmH2O *f* 12 Hz, I:E 1:1 ± 3-4 CMV breaths	85-90% 37-52 torr	~ 36 wks (very delayed)
U Iowa (USA)	**JET**	PEEP 4-5, PIP 22-24 *f* 300, IT.020 ± CMV rate @ 4 *prn*	84-93% 45-60 torr	~ 31 wks PMA (goal no failure)

Specific Ventilator Approaches

Sindelar R et al, Semin Perinatol 2022

	Mode	Settings	Gas go[illegible]	[illegible]on
Uppsala (Sweden)	**VTV** (AC/PSV)	Initial V_T ~ [illegible]	[illegible]	[illegible] as able)
K[illegible] ([illegible]	[illegible]	[illegible]H2O [illegible] Hz, I:E 1:1 + 3-4 CMV breaths	85-90% 37-52 torr	~ 36 wks (very delayed)
U Io[illegible]a (USA)	**JET**	PEEP 4-5, PIP 22-24 *f* 300, IT.020 + CMV rate @ 4 *prn*	84-93% 45-60 torr	~ 31 wks PMA (goal no failure)

GOAL: Minimize Volutrauma & Overdistention

Early volume targeted ventilation in preterm infants born at 22–25 weeks of gestational age

Pediatr Pulmonol 2021

Linda Wallström MD | Amanda Sjöberg MD | Richard Sindelar MD, PhD

- Retrospective observational study
- Compared PLV to VTV in two different epochs
  - PLV 2014-2015
  - VTV 2017-2018
- Uppsala Children's Hospital NICU, Sweden
- Both modes applied with *assist control mode*
- 90% + ANS and 100% Rx w/ surfactant

Early volume targeted ventilation in preterm infants born at 22–25 weeks of gestational age

Pediatr Pulmonol 2021

Linda Wallström MD | Amanda Sjöberg MD | Richard Sindelar MD, PhD

- Stephanie or Sophie Ventilator
  - (Fritz Stephan GmbH, Germany)
- Assist control mode w/ initial rate set to 60 bpm
- Inspiratory time set at 0.33 s, w/ I:E ratio 1:2
- VTV initial set tidal volume @ 5.0 ml/kg
- Target PaCO2 during 1st days was 34–45 mmHg

VTV associated w/ lower PIPs over 1st 20 hrs life

VTV group w/ less hypocapnia

&

more extubated by 24 hrs (30% v 13%)

Ultimately…..no differences in survival, BPD, days MV, IVH, etc

VT	2 ± 5 Vt 4.7 ± 1.4	O2 26 ± 7 RR 62 ± 5 Vt 4.7 ± 1.4	EEP 4.2 ± 0.5 FiO2 26 ± 6 RR 61 ± 6 Vt 4.8 ± 1.4	PIP 12.4 ± 2.2 PEEP 4.3 ± 0.4 FiO2 26 ± 4 RR 61 ± 2 Vt 4.9 ± 1.0

Wallstrom L, Peds Pulm 2021

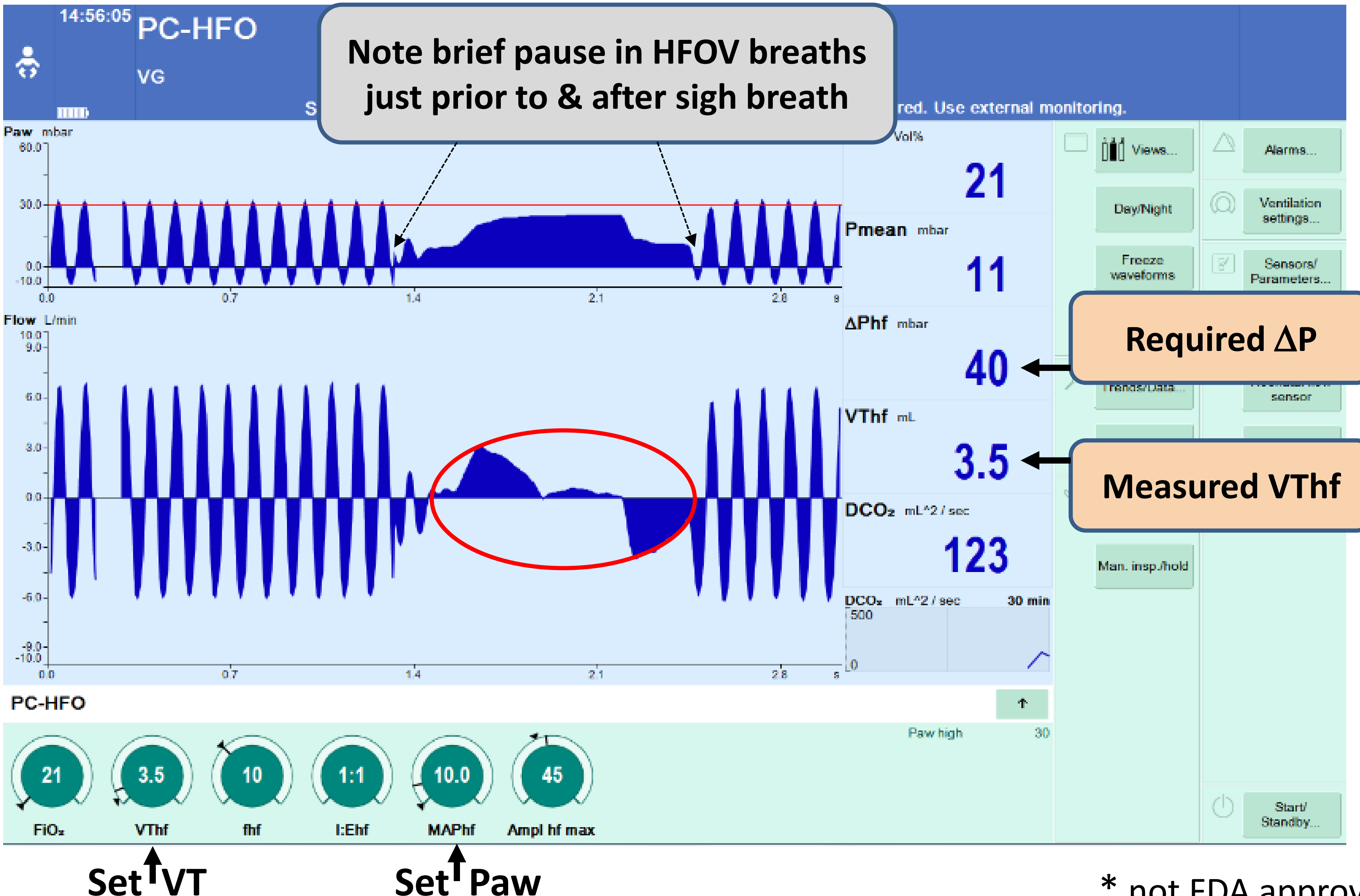
Using very high frequencies with very low V_Thf during high-frequency oscillatory ventilation to protect the immature lung. A pilot study.

J Perinatol 2016

N González-Pacheco, M Sánchez-Luna, C Ramos-Navarro, N Navarro-Patiño and AR-S de la Blanca

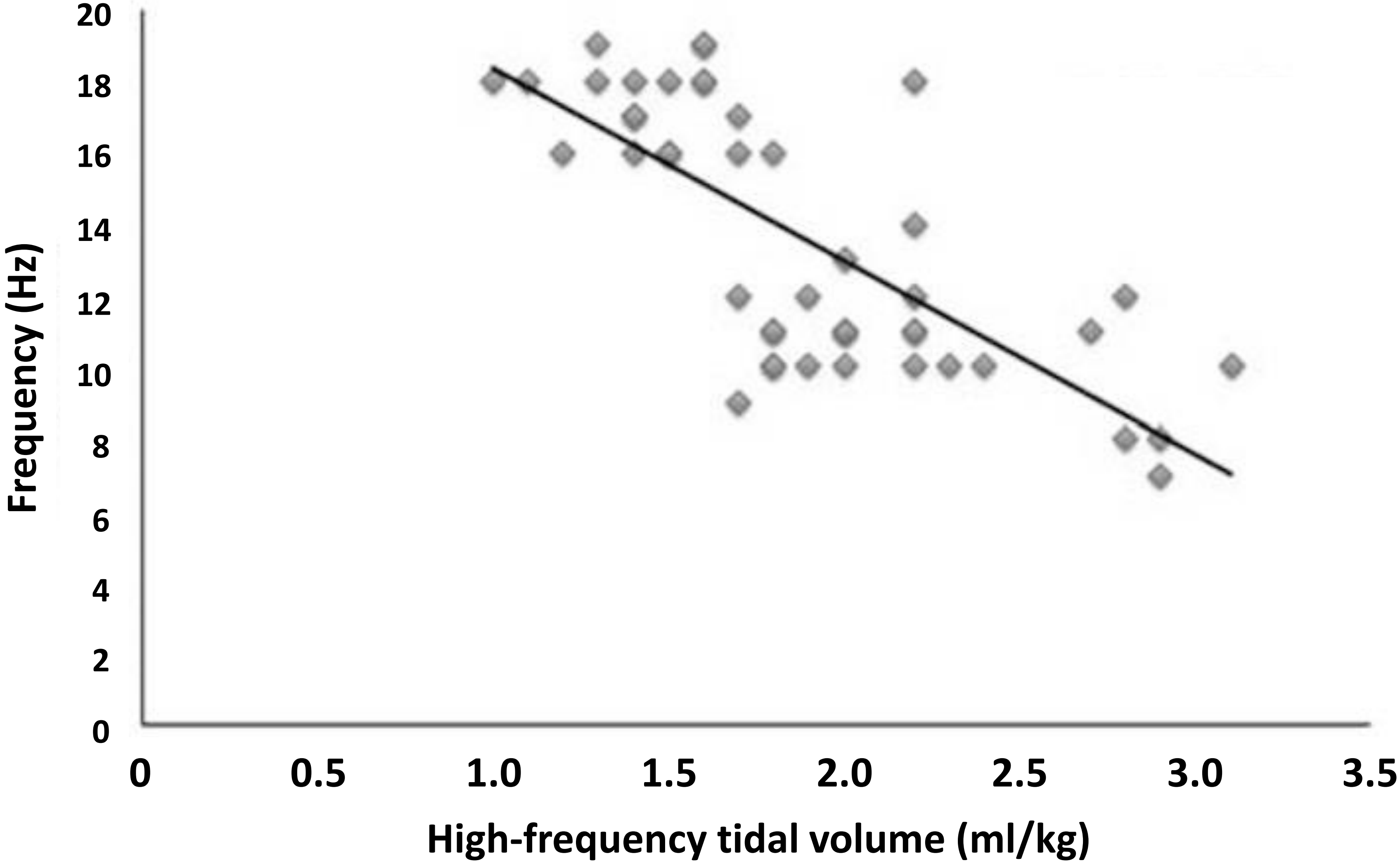
- Prospective, non-randomized trial
- N = 23; mean GA 28 wks; 60% < 1000g
- ELGANs managed by V_T-HFOV
- Aim: assess efficacy of higher *f* and lower V_T to achieve targeted DCO2 ($VThf^2 \times f$) & pCO2

Babylog VN500*
HFO with Volume Guarantee and “Sigh“



* not FDA approved

Higher *f* associated w/ smaller V_T to maintain acceptable pCO_2

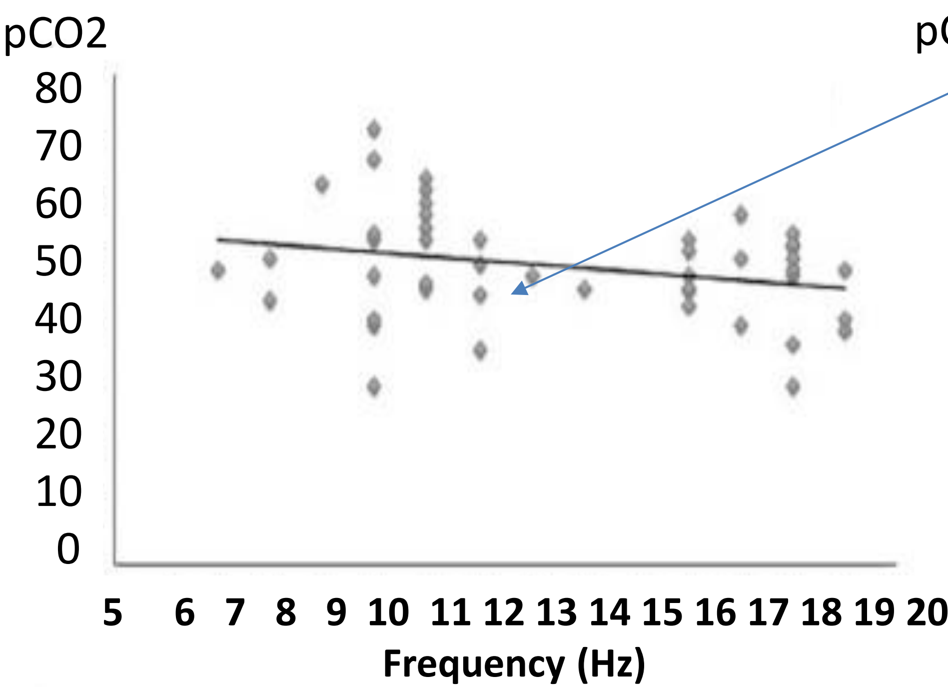


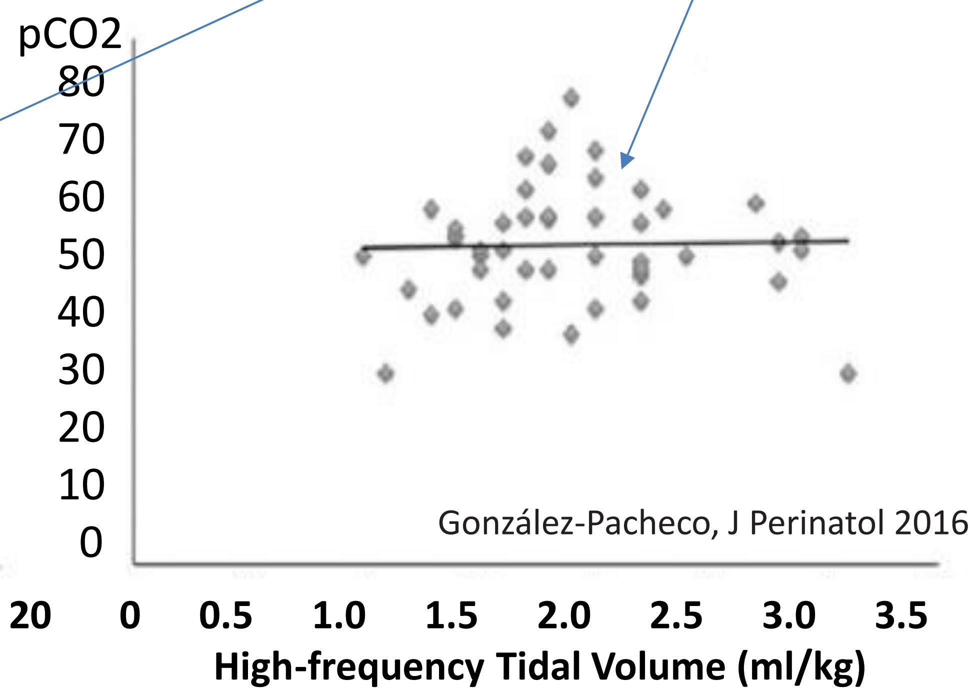
González-Pacheco, J Perinatol 2016

Babies < 1000g	Initial	Final
f (Hz)	11 ± 1	18 ± 1 *
Vt (ml/kg)	2.1 ± 0.3	1.5 ± 0.3 *
ΔP (cmH2O)	18.3 ± 6.4	16.5 ± 5.0
DCO2 (ml^2/sec)	23.4 ± 9.9	18.5 ± 7.5 *
FiO2 (%)	41 ± 19	33 ± 13
SpO2 (%)	90 ± 6	93 ± 2 *
pCO2 (mmHg)	55 ± 10	46 ± 8 *

Gas exchange improved w/ higher *f* & lower VT

No correlation between pCO2 and either *f* or V_T





González-Pacheco, J Perinatol 2016

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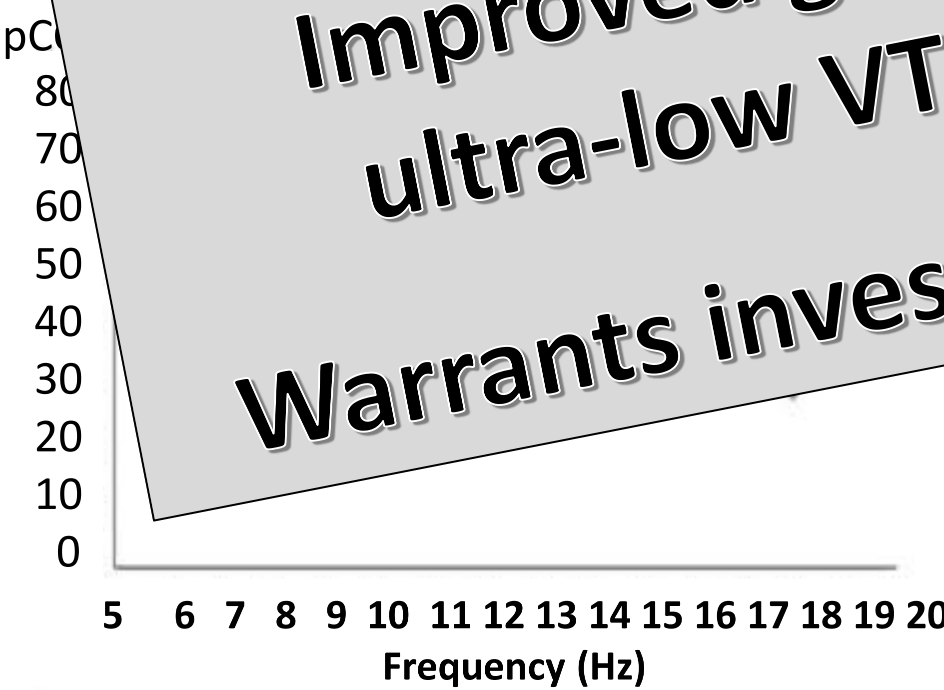
f (Hz)	11 ± 1	18 ± 1 *
Vt (ml/kg)	2.1 ± 0.3	1.5 ± 0.3 *
ΔP (cmH2O)	18.3 ± 6.4	16.5 ± 5.0
DCO2 (ml²/sec)	23.4 + 9.9	[illegible]
FiO2 (%)	[illegible]	[illegible]

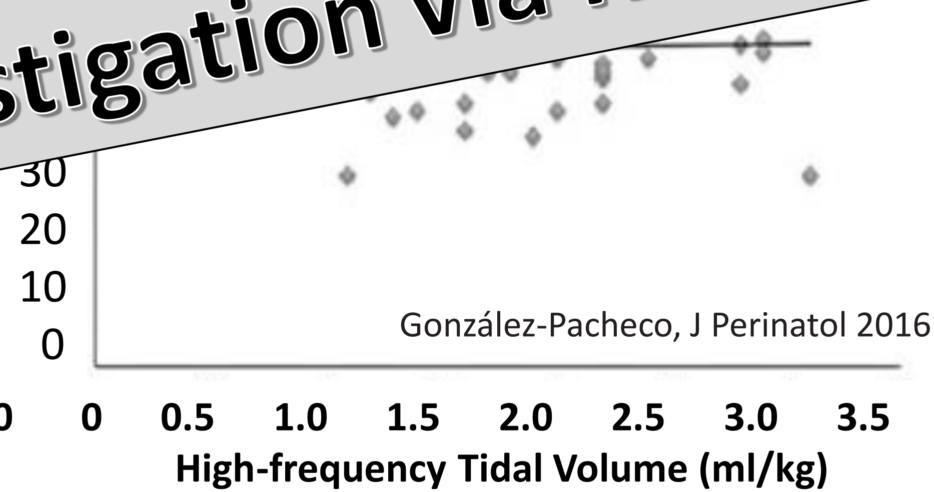
Gas exchange improved w/ higher *f* & lower VT

Essentially "vibratory" CPAP

Improved gas exchange via ultra-low VThf at higher *f*

Warrants investigation via RCT's





González-Pacheco, J Perinatol 2016

“But Master Yoda – What of the **“Jet-I”**?

Survival and short-term respiratory outcomes of <750 g infants initially intubated with 2.0 mm vs. 2.5 mm endotracheal tubes

Jennifer N. Berger[1✉], Timothy G. Elgin[2], John M. Dagle[2], Jonathan M. Klein[2] and Tarah T. Colaizy[2]

J Perinatal 2022

- Retrospective review, 147 infants < 750g
- Standard use of 2.0 ETT at < 24 weeks
- Near universal use of HFJV in this population

Survival and short-term respiratory outcomes of <750 g infants initially intubated with 2.0 mm vs. 2.5 mm endotracheal tubes

Jennifer N. Berger[1✉], Timothy G. Elgin[2], John M. Dagle[2], Jonathan M. Klein[2] and Tarah T. Colaizy[2]

J Perinatal 2022

Initial JET Settings

- *300 bpm if < 24 wks, < 600g*
  - Otherwise ~ 360 bpm
- *I-time 20 msecs (0.02s)*
  - To minimize air trapping
- *PEEP 5 cmH2O*
  - To avoid hyperinflation
  - Increase prn if poor inflation & FiO2 > 0.40 after surf Rx
- PIP 22-24 w/ visible vibration

CMV/"Sigh" Breaths

- Add for lung recruitment
  - Esp w/ "wandering" focal/patchy atelectasis
  - Usually after 1st few days
- Initial R 4 w/ I-time 0.4s
- PIP 6-10 above PEEP
- Do not interrupt jet breaths
- Do not wean unless PIE

Survival and short-term respiratory outcomes of <750 g infants initially intubated with 2.0 mm vs. 2.5 mm endotracheal tubes

Jennifer N. Berger[1✉], Timothy G. Elgin[2], John M. Dagle[2], Jonathan M. Klein[2] and Tarah T. Colaizy[2]

J Perinatal 2022

	Jet PIP	Jet Rate	Jet Paw	Jet FiO2	pCO2
6-12 hrs	27 (22-33)	360 (360-420)	8 (7-9)	0.29 (0.22-0.36)	44 (40-48)
7 days	30 (25-34)	360 (300-360)	8 (7-9)	0.35 (0.30-0.48)	52 (47-56)
Pre-extubation	22 (19-24)	420 (360-480)	10 (8-11)	0.32 (0.28-0.40)	51 (47-55)

- Age at 1st ETT change 27 d (19-32)
- Age 1st extubation try 52 d (43-61); PMA ~ 30-31 wks
- Age success extubation 69 d (51-85); PMA ~ 33 wks
- 74% success rate w/ 1st trial of extubation

Interim Summary # 5

Improving survival & respiratory outcomes for very immature infants

Management via VTV, HFOV, & HFJV modes targeting optimized lung inflation and low volume-targeted approaches

No specific ventilator or V_T mode has been proven better than another

The operator rather than the mode is the most critical factor

DRIVER TEST

Even if he passes sobriety test, I still think he is screwed

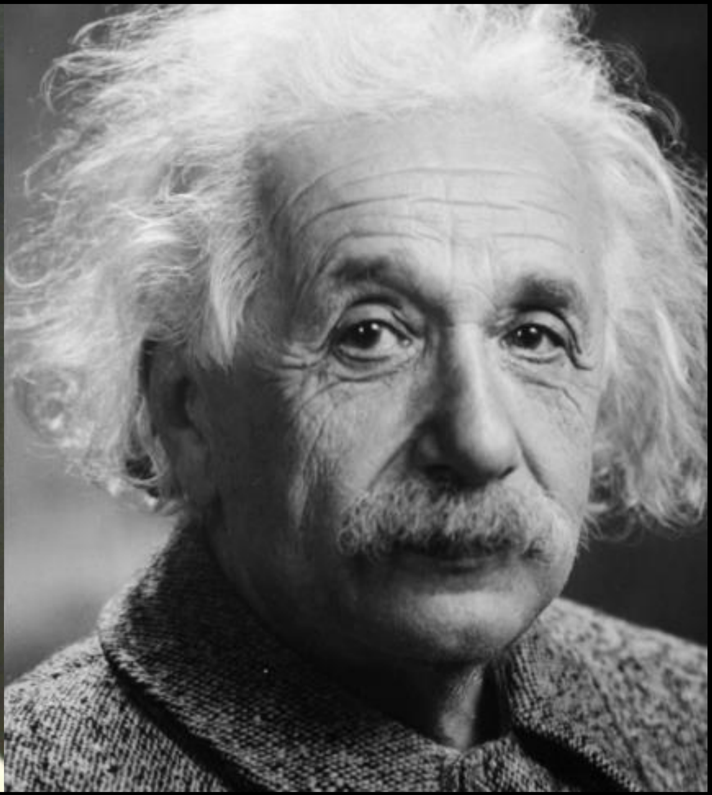
CONCLUSIONS

- Lungs of most immature preterm infants are in canalicular stage at birth

- Multiple pre & postnatal insults contribute to disruption of lung development & injury

- Ventilator support can be achieved using conventional (V-targeted) & high-frequency modes

- Given low patient numbers & existing bias, needed RCTs are unlikely

Learn from yesterday, live for today, hope for tomorrow

The important thing is to not stop questioning

Yoder's Axioms

The sooner you extubate,
the sooner the tube's out!

The longer you wait,
the longer the tube's in!!

Getting the Tube Out

- *ANY* written guideline improves outcomes
- Written guidelines in combo with supporting assessment & actions by RT → reduces vent days
  - Who's at highest risk for failure?
  - Is there an "optimal" predictive tool?
  - What is "best" non-noninvasive support mode?

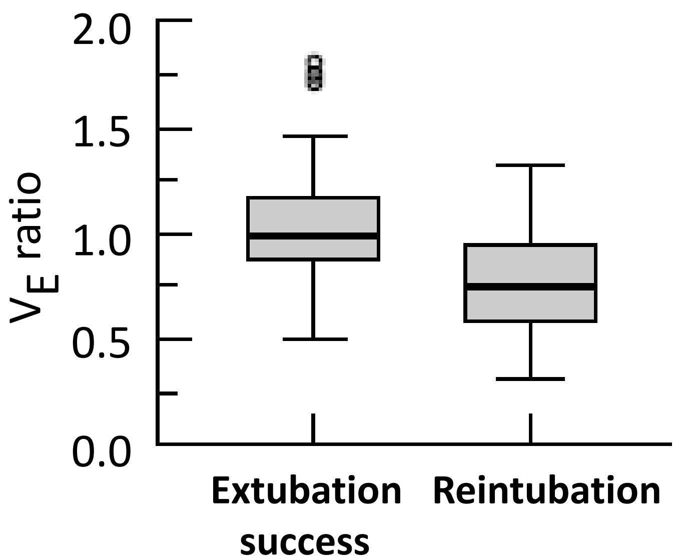
Predicting Extubation Success in VLBWI

Kamlin CO, ADCFNE 2006

- Infants < 1250 g on VG-SIMV
- Compared 3 predictors:
  - V_E - expiratory minute ventilation
  - V_E ratio - ratio of V_{Ecpap} / V_{Event}
  - Spontaneous breathing trial (SBT)
    - ETT CPAP x 3 minutes w/out bradycardia or desats
      - HR < 100 for > 15 sec
      - SpO2 < 85% despite 15% increase in FiO2

Predicting Extubation Success in VLBWI

Kamlin CO, ADCFNE 2006



Mean (SD)

V_{Ecpap} success = 314 (116) ml/k/min

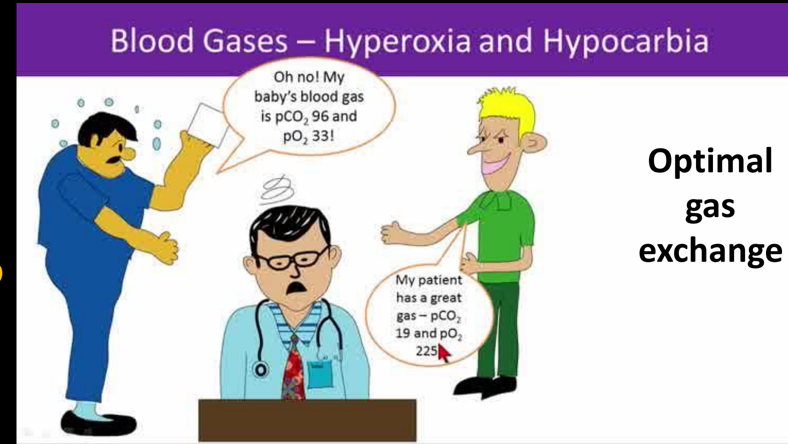
V_{Ecpap} failure = 271 (113) ml/k/min

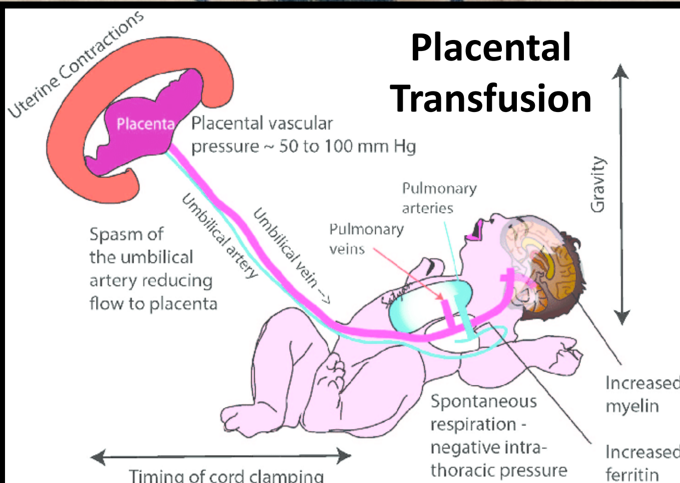
	PPV	NPV	Sensitivity	Specificity
SBT	**93%**	**89%**	**87%**	**73%**
V_{Ecpap}	87%	50%	85%	45%
V_E ratio	87%	55%	87%	54%

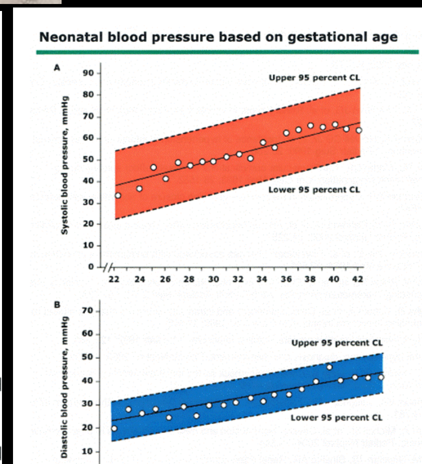
Predicting Extubation Success

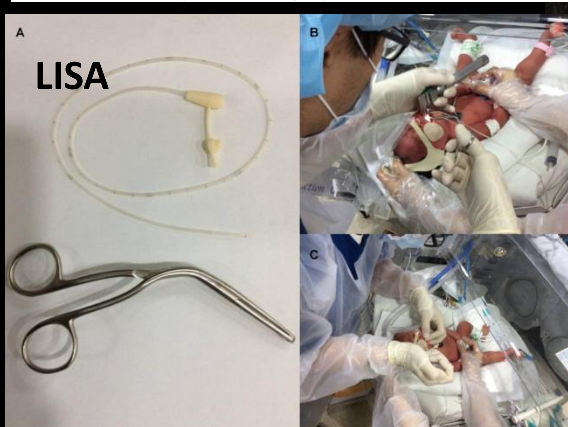
- Better than coin flip
- Written guidelines help
  - *Ask every day*.....can we extubate this baby?
  - If < 26 weeks, consider brief SB trial
- Optimize initial non-invasive support mode
- *Don't be afraid to fail!*

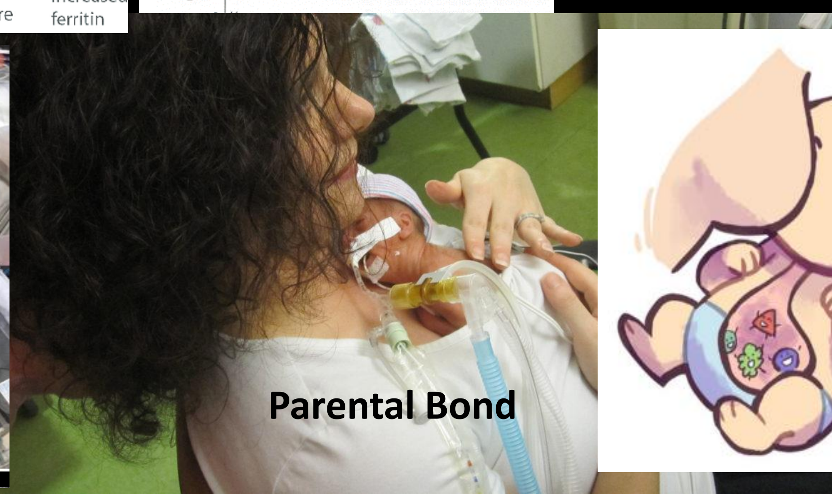
It's bundles of cares









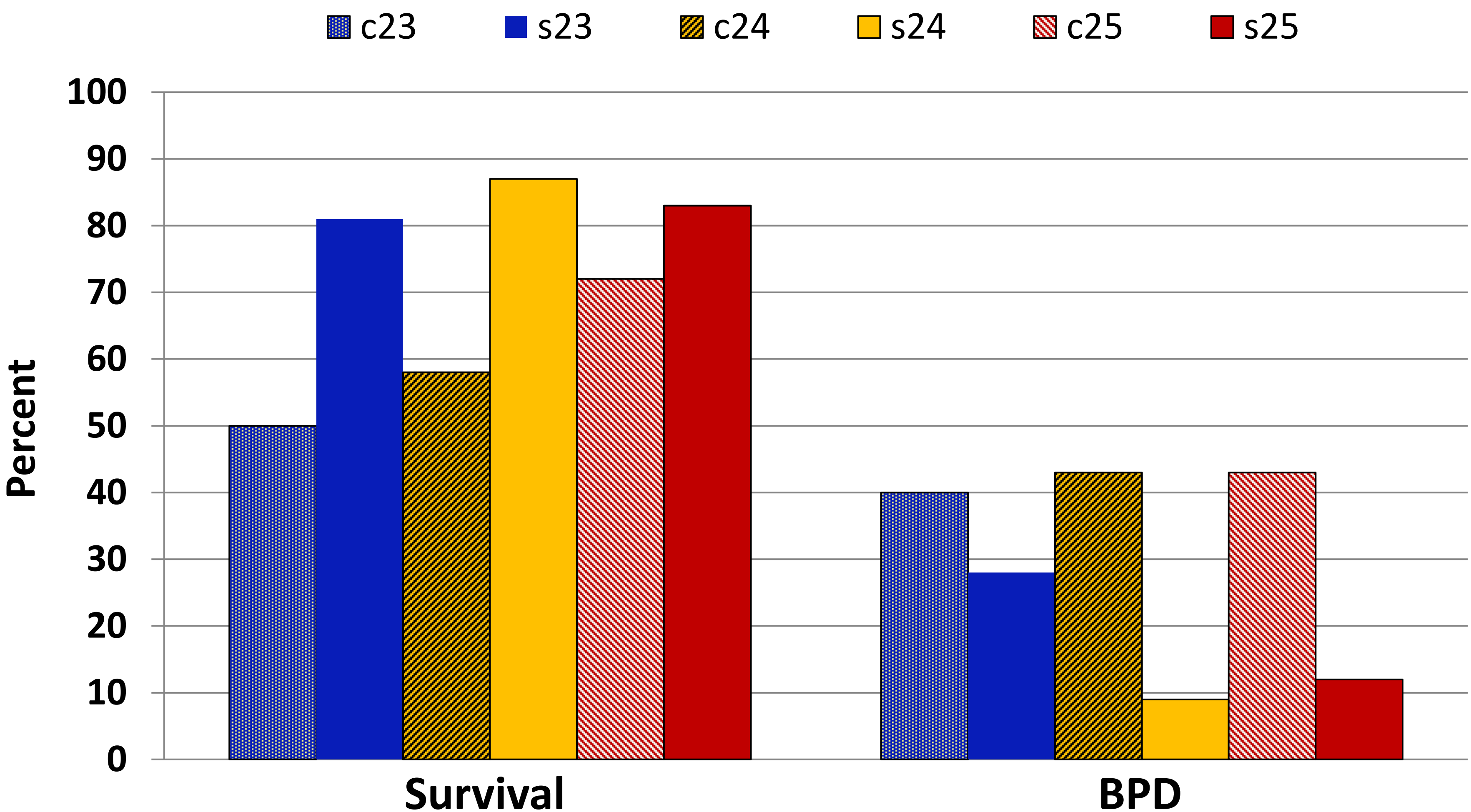


Multi-Pronged Protocol to Assist ELGANs in Transition to Extrauterine Life

Mehler K et al, Acta Paeds 2012

1. Delayed cord clamping
2. Only sxn mouth/airway if blood or MSAF
3. <u>Immediate</u> CPAP @ 8 cm H_2O & 30%
4. CPAP &/or SI (30 sec) if poor response
5. MIST: Distress / FiO_2 > 30% / CPAP > 8
6. HFV if intubated
7. Early PDA screen & treatment

Multiple Changes in Care Accompanied by Improved Survival & Less Morbidity



Mehler K et al, Acta Paeds 2012

A Quality Improvement Bundle to Improve Outcomes in EPIs in the 1^{st} Week

Travers CP et al, Pediatrics 2022

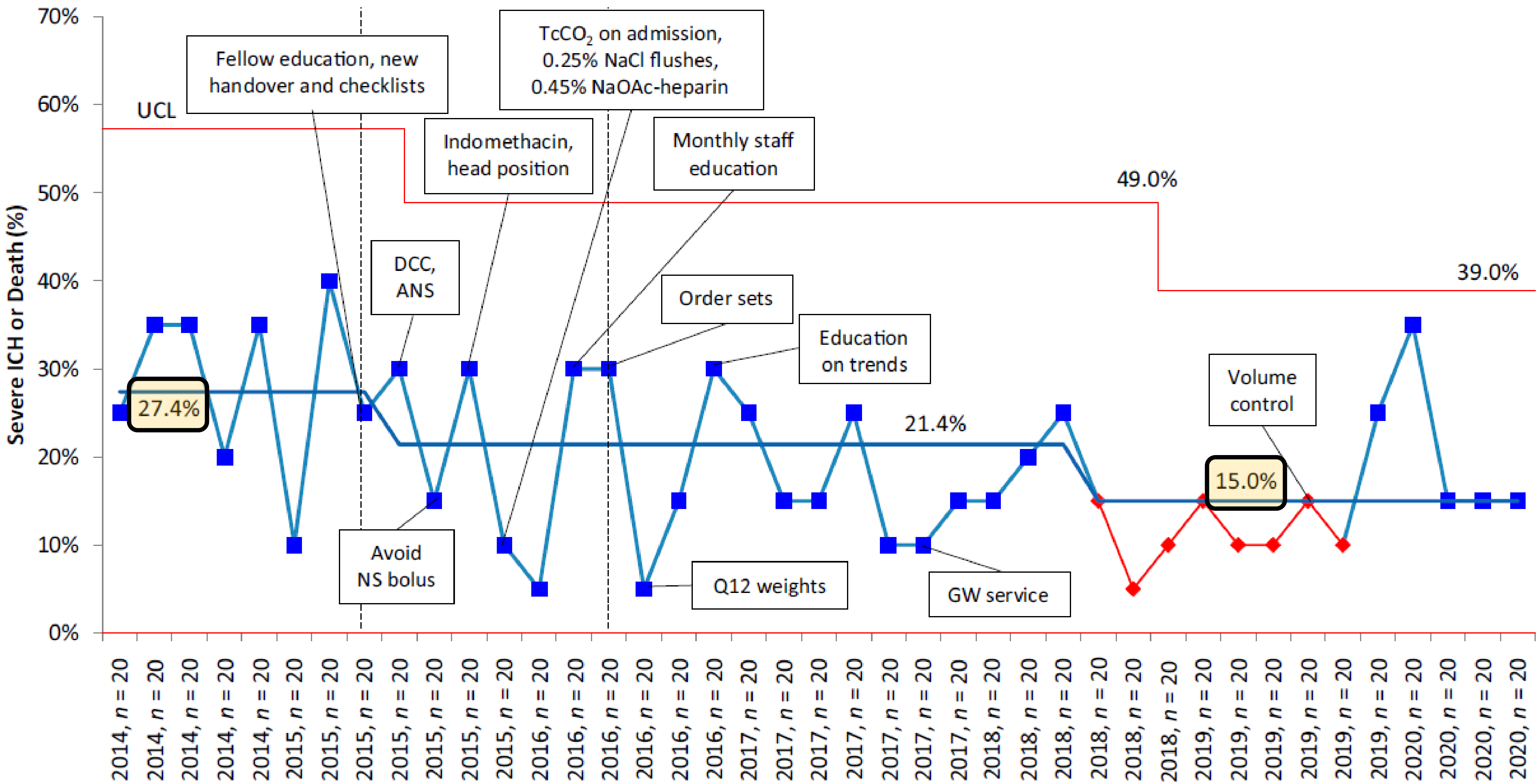
Preterm births $22^{0\text{-}7}$ to $27^{6/7}$

SUPPLEMENTAL TABLE 3 List of Interventions Implemented in the Golden Week

Perinatal	Admission	Days 1–3	Days 1–7
Antenatal corticosteroids from 22 + 0/7 if resuscitating	Head position midline	Limit normal saline bolus	Formal physician handover every 12 h
Delayed cord clamping 30–60 s	Transcutaneous CO_2 monitor	Limit bicarbonate bolus	Minimal handling
Higher (0.60) starting FIO_2 in delivery room	Line placement in first hour	Limit inotrope use	0.25% sodium chloride line flushes
Early CPAP and selective surfactant in delivery room	Evidence-based order sets initiated	Limit transfusion of blood products	Slow flushing and withdrawal from CVLs
Heart rate electrodes in delivery room	Sodium acetate containing line fluids	Wt and serum Na Q12 and urine output Q6	Follow trends in clinical and laboratory values
Thermoregulation with bag and mattress	Single-dose indomethacin prophylaxis	Careful total fluid intake changes ~10/kg per day	Volume control with target of 4/kg if on SIMV

A Quality Improvement Bundle to Improve Outcomes in EPIs in the 1st Week

Travers CP et al, Pediatrics 2022



On-going / Future Approaches to BPD