Volume Targeted Ventilation in Newborns ... is their value?

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Disclosure:

• I’ve run a consulting business for over 12 years and have provided neonatal respiratory care education/consultation to/for various health care facilities and companies including EME Medical, Lifetronics Medical, and Draeger Medical
Objectives

• Examine traditional pressure ventilation
• Examine the introduction of volume ventilation
• Discuss a few differences between volume modes and volume targeted strategies
• Discuss the Cochrane Review data on volume targeted versus pressure-limited ventilation
A couple of quotes to keep in mind…

✓ **NO** device is immune to failure of the clinician to use it optimally (Keszler)

✓ …the absence of large RCTs must not be an excuse to ignore an opportunity to tailor technology to the critically ill infant (Mammel)
Unique mechanical ventilation challenges

1. Lung/chest wall mechanics
2. Small VTs, short I times, rapid RR
3. Uncuffed ETT
4. Tidal volume normal values
5. Tidal volume measurements (where and how?)
Pressure Ventilation

- Continues to be the most widely used mode in newborn ventilation,
- something we believed we really understood
- Simplicity!
- ventilation despite ETT leak (?)
- improved intrapulmonary gas exchange and distribution due to the decelerating flow pattern
- **Presumed** benefits of limiting distending pressure and avoiding “BAROTRAUMA”
The major disadvantage!

And it’s a big one…

• Varying tidal volumes with changes in lung compliance

• Lung compliance changes can occur quite rapidly in the newborn period, post clearing of lung fluid/recruitment/surfactant replacement

• Remember the essence of ventilation is minute ventilation ($MV = VT \times RR$)
• Excessive VT displacement, VOLUTRAUMA is thought to be one of the main contributors to VILI

• Large and often inconsistent tidal volumes has been associated with hypocarbia and cerebral perfusion changes, impacting neurological health
Volutrauma

• Increased volume exchange in compliant lung units
• Stretch injury and epithelial and endothelial breaks
• Increased alveolar-capillary permeability (leaky) --- pulmonary edema
Ventilating Premature Lungs

Distal airways, not alveoli, are the most compliant parts of the respiratory tract.
Some Effects of Volutrauma

Dilation of terminal bronchiole

Dilation of alveolar ducts

Over-expanded and coalesced alveoli

Atelectatic alveoli
Another Look at Volutrauma

IMV effects with surfactant

IMV in absence of surfactant
Air Leaks we see include:

- Pneumomediastinum
- Pneumothorax
- Pneumopericardium
- Pneumoretroperitoneum
- Pulmonary Interstitial Emphysema (PIE)
- Subcutaneous emphysema
- Systemic air embolism
If one pushes a big $V_T$ into a critter with a strapped chest, it doesn’t hurt its lungs:

even when PIP is very high!

Courtesy of BUNEL
If one pushes in that same $V_T$ without the strap, it causes the lungs to burst:

even when PIP is not very high!

Courtesy of BUNEL
Newborns are at high risk of volutrauma

- The over compliant chest wall leads them to be less protected to volume injury and overdistension (Clark 2000)
- The newborn lung compliance with HMD can change dramatically with the introduction of surfactant therapy or with the spontaneous resolution of RDS (Goldsmith, 1996)
- The infants own spontaneous contribution to VT and the ventilators recognition of this may also play a role in excessive VT delivery
Why the delay in implementing volume strategies in newborn ventilation

- Technology “fear factor”
- The “work horses” are still working why change
- Lack of large RCTs
- Ventilator variances in volume modes offered and how they work - may be confusing to many
- A lack of clinical understanding of these modes and how best to utilize them
- Nomenclature “mayhem”
Volume targeted ventilation modes (VTV) grouped together but….

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Volume-Controlled</th>
<th>Volume-Guarantee</th>
<th>Volume-Limited</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilator model</td>
<td>1. VIP Bird</td>
<td>Draeger Babylog 8000+</td>
<td>Bear Cub 750 PSV</td>
</tr>
<tr>
<td></td>
<td>2. Siemens Servo 300</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trigger type</td>
<td>1. Pressure sensor</td>
<td>Flow (hot wire anemometer)</td>
<td>Flow (hot wire anemometer)</td>
</tr>
<tr>
<td></td>
<td>2. Pressure or flow sensor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensor position</td>
<td>At ventilator</td>
<td>At Wye piece</td>
<td>At Wye piece</td>
</tr>
<tr>
<td>PIP</td>
<td>Variable, set max</td>
<td>Variable, set max</td>
<td>Pressure-cycled</td>
</tr>
<tr>
<td>Volumes measured that affect ventilation</td>
<td>VTi (displays VTi &amp; VTe)</td>
<td>V Ti, VTe</td>
<td>V Ti (displays VTi, VTe)</td>
</tr>
<tr>
<td>Set maximal VT</td>
<td>Volume-cycled</td>
<td>Inflation stopped if V Ti &gt; 130% set VT</td>
<td>Inflation stops at max set VT</td>
</tr>
<tr>
<td>Adjusts for low VT</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Modes available</td>
<td>IMV, SIMV, AC, Termination sensitivity</td>
<td>SIMV, AC, PSV</td>
<td>SIMV, AC, PSV</td>
</tr>
</tbody>
</table>

Table 1. Comparison of volume-targeted ventilation modes.

This record should be cited as: McCallion N, Davis PG, Morley CJ. Volume-targeted versus pressure-limited ventilation in the neonate. Cochrane Database of Systematic Reviews 2005, Issue 3. Art. No.: CD003666. DOI: 10.1002/14651858.CD003666.pub2.

Differences do exist
Only till recently,

• Has there been a significant appreciation on the importance of understanding volutrauma and the dangers of inadvertent hypocapnea in the very fragile newborns we care for

• There has been a renewed interest from clinicians across the globe at ways of controlling tidal volumes in neonatal ventilation
What is the literature telling us?

• To date there are a growing number of papers looking at volume targeted techniques in Neonatal Ventilation

• None of the studies are sufficiently large enough to unequivocally demonstrate the ultimate benefit of volume targeting

• Individual practices still vary significantly

• Open lung approaches are not universal

• “PEEP-a-phobia” still exists (Riemsberger)
Deflation
(inadequate PEEP)

Inflation
(adequate PIP)
Low lung volumes are also damaging
A BRIEF REVIEW OF COMMONLY UTILIZED VOLUME MODES/ADJUNCTS
Volume Guarantee (Draeger Babylog) AUTOFLOW (EVITA XL-NEO)

- An option which utilizes previous breath exhaled volume to deliver the VG set within a user determined pressure limit
- The VTs are measured at the patient ETT via heated wire flow sensor
- It delivers the VG based on changes in R, compliance and pt effort
- This option can be added to A/C, SIMV or PSV ventilation modes
Figure 7: Working Principle of Volume

Guarantee: inspiratory pressure is automatically regulated by the ventilator to achieve set tidal volume. The Babylog 8000plus may take up to 6-8 breath to reach set tidal volume.
Volume Controlled (BIRD VIP, S300)

- A tidal volume is set on the machine and the flow and I time limit to deliver the tidal volume
- The pressures can be limited
- The VT is a delivered from the machine and measured exiting the machine
- The user adjust the VT to target an exhaled VT measured by the proximal flow sensor
PRVC (s300 / servo-i)

- Pressure regulated volume control an A/C mode which analyzes the inspiratory tidal volume and delivers the next VT based on R and C of the lung properties
- Uses 4 test breaths to determine how to alter the decelerating flow to deliver the VT at the lowest PIP possible
2005 Cochrane Review
McCallion, Davis and Morley

- Included 4 RCT in the meta-analysis
- 178 preterm infants entered during the first 72 hours of life
- 2 studies were based on VCV and 2 used VG
- these modes were classified as volume targeted modes for the purpose of the review
PRVC (S300)

- Piotrowskis group 1997
- Sealed envelopes were used for study allocation
- study comparing PRVC (servo) (27) vs control TCPL group (30)
- all 57 infants BW less than 2500 gms
- Excluded airleaks, sepsis and MAS
- Outcomes: Death, BPD, Airleaks, IVH, PDA, sepsis, use of MR and duration of MV
VCV (BIRD VIP)

• Sinha 1997
• Sealed envelopes for study allocation
• Experimental group N=25 VCV VT set (5-8ml/kg) and the control group TCPL with PIP adjusted to achieve 5-8mls/kg
• Outcomes death, IVH or PVL, BPD, PTX, PDA or improved A-a gradient
Volume Guarantee (Babylog 8000)

- Keszler 2004
- Sealed envelopes for study allocation
- N18 <34 wks (RDS ventilated by 6 hours and expected to require ventilation for >24 hours)
- Exclusion: leak >30% cong heart, resp of CNS anomalies, paralysis or sedation
- Experimental group A/C VG vs Control group A/C
- Outcomes: Death, PTX, PIE, Tidal volumes
• Lista 2004
• Random number sequence allocation
• N=53 (2 sites) 25-32 wks vented for RDS in 1st 24 hrs treated with surfactant within 3 hrs.
• Exclusion: lethal anomalies, IVH >gr2, sepsis, use of MR
• Experimental group (30) PSV VG (5mls/kg) control group(23) PSV with set PIP to achieve (5mls/kg) PIP weaned to achieve blood gas goals
• Outcomes: death, PDA, BPD, IVH, PVL, ROP, PIE need for post natal steroids
• ALSO compared inflammatory markers in 2 groups
Lista 2004- significant results

- Decreased levels of pro-inflammatory cytokines in the tracheal aspirate from VG group
- Vent days 12 in the PSV group vs 9 in the PSV VG group
Combined look at results from Cochrane review

- No significant difference for death at hospital discharge
- Secondary outcomes: pooled data
- None of the 4 trials addressed growth, death after d/c or neurodevelopmental outcome
The volume group showed a **significant** reduction in the following:
### Analysis 1.4. Comparison 1 Volume-targeted vs pressure limited ventilation, Outcome 4 Duration of Intermittent positive pressure ventilation (days).

**Review:** Volume-targeted versus pressure-limited ventilation in the neonate

**Comparison:** 1 Volume-targeted vs pressure limited ventilation

**Outcome:** 4 Duration of intermittent positive pressure ventilation (days)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Volume targeted</th>
<th>Pressure limited</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
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<tbody>
<tr>
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<td>N</td>
<td>Mean (SD)</td>
<td>N</td>
<td>Mean (SD)</td>
<td>IV/Fixed, 95% CI</td>
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<td>1 Volume guarantee</td>
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<td></td>
</tr>
<tr>
<td>Lista 2004</td>
<td>30</td>
<td>8.8 (3)</td>
<td>23</td>
<td>12.3 (3)</td>
<td>-3.50 [-5.13, -1.87]</td>
</tr>
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<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>30</strong></td>
<td></td>
<td><strong>23</strong></td>
<td></td>
<td><strong>69.0%</strong> [-5.13, -1.87]</td>
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<tr>
<td></td>
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<tr>
<td>2 Volume controlled</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Sinha 1997</td>
<td>25</td>
<td>5.1 (2.72)</td>
<td>25</td>
<td>6.75 (5.58)</td>
<td>-1.65 [-4.08, 0.78]</td>
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<tr>
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<td></td>
<td><strong>25</strong></td>
<td></td>
<td><strong>31.0%</strong> [-4.08, 0.78]</td>
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<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>55</strong></td>
<td></td>
<td><strong>48</strong></td>
<td></td>
<td><strong>100.0%</strong> [-4.28, -1.57]</td>
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</table>

Heterogeneity: not applicable

Test for overall effect: Z = 4.21 (P = 0.000026)

Test for subgroup differences: Chi² = 1.53, df = 1 (P = 0.22); I² = 35%

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This record should be cited as: McCallion N, Davis PG, Morley CJ. Volume-targeted versus pressure-limited ventilation in the neonate. Cochrane Database of Systematic Reviews 2005, Issue 3. Art. No.: CD003666. DOI: 10.1002/14651858.CD003666.pub2.
Analysis 1.7. Comparison 1 Volume-targeted vs pressure limited ventilation, Outcome 7 Pneumothorax.

Review: Volume-targeted versus pressure-limited ventilation in the neonate

Comparison: 1 Volume-targeted vs pressure limited ventilation

Outcome: 7 Pneumothorax

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Volume targeted</th>
<th>Pressure limited</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
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</thead>
<tbody>
<tr>
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<td>n/N</td>
<td>n/N</td>
<td>M-H,Fixed,95% CI</td>
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<td>M-H,Fixed,95% CI</td>
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<td>1 Volume guarantee</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kessler 2004</td>
<td>0/9</td>
<td>0/9</td>
<td>*</td>
<td>0.0%</td>
<td>0.0 [0.0, 0.0]</td>
</tr>
<tr>
<td>Lista 2004</td>
<td>0/30</td>
<td>3/23</td>
<td></td>
<td>30.0%</td>
<td>0.11 [0.01, 2.04]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>39</td>
<td>32</td>
<td></td>
<td>30.0%</td>
<td>0.11 [0.01, 2.04]</td>
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<td></td>
<td></td>
<td></td>
<td>Heterogeneity: Chi² = 0.0, df = 0 (P = 1.00); I² = 0.0%</td>
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<td>Test for overall effect: Z = 1.48 (P = 0.14)</td>
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<td>2 Volume controlled</td>
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<tr>
<td>Piotrowski 1997</td>
<td>2/27</td>
<td>6/30</td>
<td></td>
<td>43.3%</td>
<td>0.37 [0.08, 1.68]</td>
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<tr>
<td>Sinha 1997</td>
<td>0/25</td>
<td>3/25</td>
<td></td>
<td>26.7%</td>
<td>0.14 [0.01, 2.63]</td>
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<tr>
<td><strong>Subtotal (95% CI)</strong></td>
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<td>55</td>
<td></td>
<td>70.0%</td>
<td>0.28 [0.08, 1.07]</td>
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<td>Total events: 2 (Volume targeted), 9 (Pressure limited)</td>
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<td>Heterogeneity: Chi² = 0.33, df = 1 (P = 0.56); I² = 0.0%</td>
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<td>Test for overall effect: Z = 1.86 (P = 0.063)</td>
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<tr>
<td><strong>Total (95% CI)</strong></td>
<td>91</td>
<td>87</td>
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<td>100.0%</td>
<td>0.23 [0.07, 0.76]</td>
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<td>Total events: 2 (Volume targeted), 12 (Pressure limited)</td>
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<td></td>
<td></td>
<td>Heterogeneity: Chi² = 0.72, df = 2 (P = 0.70); I² = 0.0%</td>
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<td>Test for overall effect: Z = 2.40 (P = 0.016)</td>
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</tbody>
</table>

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In rates of severe gr 3 or 4 IVH

### Analysis 1.11. Comparison of Volume-targeted vs pressure limited ventilation, Outcome 11 Severe IVH (grade 3 or 4)

**Review:** Volume-targeted versus pressure-limited ventilation in the neonate

**Comparison:** 1 Volume-targeted vs pressure limited ventilation

**Outcome:** 11 Severe IVH (grade 3 or 4)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Volume targeted r/N</th>
<th>Pressure limited r/N</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume guarantee</td>
<td></td>
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<tr>
<td>Lista 2004</td>
<td>1/30</td>
<td>2/23</td>
<td></td>
<td>17.8%</td>
<td>0.38 [0.04, 3.97]</td>
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<tr>
<td><strong>Subtotal (95% CI)</strong></td>
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<td><strong>23</strong></td>
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<tr>
<td>Total events</td>
<td>1 (Volume targeted), 2 (Pressure limited)</td>
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<tr>
<td>Heterogeneity: not applicable</td>
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<tr>
<td>Test for overall effect: ( Z = 0.80 ) ( (P = 0.42) )</td>
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<tr>
<td>2 Volume controlled</td>
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<td></td>
</tr>
<tr>
<td>Potrowski 1997</td>
<td>3/27</td>
<td>11/30</td>
<td></td>
<td>82.2%</td>
<td>0.30 [0.09, 0.97]</td>
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<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>27</strong></td>
<td><strong>30</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>3 (Volume targeted), 11 (Pressure limited)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Heterogeneity: not applicable</td>
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</tr>
<tr>
<td>Test for overall effect: ( Z = 2.01 ) ( (P = 0.045) )</td>
<td></td>
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</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>57</strong></td>
<td><strong>53</strong></td>
<td></td>
<td>100.0%</td>
<td>0.32 [0.11, 0.90]</td>
</tr>
<tr>
<td>Total events</td>
<td>4 (Volume targeted), 13 (Pressure limited)</td>
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</tr>
<tr>
<td>Heterogeneity: ( \chi^2 = 0.03 ), df = 1 ( (P = 0.86) ); ( I^2 = 0.0% )</td>
<td></td>
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<tr>
<td>Test for overall effect: ( Z = 2.16 ) ( (P = 0.031) )</td>
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</table>

This record should be cited as: McCallion N, Davis PG, Morley CJ. Volume-targeted versus pressure-limited ventilation in the neonate. *Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD003666. DOI: 10.1002/14651858.CD003666.pub2.
Borderline statistical significance in reduction of BPD

**Analysis 1.13. Comparison of Volume-targeted vs Pressure Limited Ventilation, Outcome 13 BPD (supplemental oxygen at 28 days)**

Review: Volume-targeted versus pressure-limited ventilation in the neonate

Comparison: 1 Volume-targeted vs pressure limited ventilation

Outcome: 13 BPD (supplemental oxygen at 28 days)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Volume targeted n/N</th>
<th>Pressure limited n/N</th>
<th>Risk Ratio M-H,Fixed, 95% CI</th>
<th>Weight %</th>
<th>Risk Ratio M-H,Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Volume guarantee</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lista 2004</td>
<td>3/30</td>
<td>4/23</td>
<td></td>
<td>44.3 %</td>
<td>0.58 [0.14, 2.32]</td>
</tr>
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<td><strong>Subtotal (95% CI)</strong></td>
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<td><strong>23</strong></td>
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<tr>
<td>Total events: 3 (Volume targeted), 4 (Pressure limited)</td>
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<tr>
<td>Heterogeneity: not applicable</td>
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<tr>
<td>Test for overall effect: Z = 0.78 (P = 0.44)</td>
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<tr>
<td>2 Volume controlled</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Piotrowski 1997</td>
<td>6/27</td>
<td>6/30</td>
<td></td>
<td>55.7 %</td>
<td>1.11 [0.41, 3.04]</td>
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<tr>
<td><strong>Subtotal (95% CI)</strong></td>
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<td><strong>30</strong></td>
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<tr>
<td>Total events: 6 (Volume targeted), 6 (Pressure limited)</td>
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<td>Heterogeneity: not applicable</td>
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<tr>
<td>Test for overall effect: Z = 0.21 (P = 0.84)</td>
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<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>57</strong></td>
<td><strong>53</strong></td>
<td></td>
<td>100.0 %</td>
<td>0.87 [0.39, 1.96]</td>
</tr>
<tr>
<td>Total events: 9 (Volume targeted), 10 (Pressure limited)</td>
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<tr>
<td>Heterogeneity: Chi² = 0.57, df = 1 (P = 0.45); I² = 0.0%</td>
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<tr>
<td>Test for overall effect: Z = 0.33 (P = 0.74)</td>
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</tr>
</tbody>
</table>

This record should be cited as: McCallion N, Davis PG, Morley CJ. Volume-targeted versus pressure-limited ventilation in the neonate. *Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD003666. DOI: 10.1002/14651858.CD003666.pub2.
• S 300 measuring at the machine does not account for loss in volume due to tubing compliance impossible to assign a fixed figure “additional compressible volume” to account for this given the variance warm circuit and humidifier pot volumes

• Regulates pressure on ease of delivering inspiratory volume ?ETT leak
• Assist Control PRVC is very different in how it ventilates compared to IMV on the sechrist or bear cub IMV
• I time set to 0.5 sec
• Rates of 12 (IMV vs A/C) very different support structure (atelectrauma)
• 1-2 hours of ETT CPAP prior to extubation (atelectrauma)
• PEEP 3-5 cmh20 (atelectrauma)
VG - Keszler

• A/C VG set VT to 5ml/kg (user/software driven)

• A/C PIP targeted to achieve 4-6mls/kg (user driven)
VG -Lister

- PSV back up rates of 40 for both groups 
  ~3 sec before VTR interaction (asynchrony)
- I time limit utilized for PSV breaths ~.3-.4 s
- No mention of Leak around ETT
- Both used VTs of 5 ml/kg
- PEEPs of 3.5 - 4 cmH20 (?atelectrauma)
- PSV possible reduction in MAP and derecruitment
VCV - Sinha

- volume control on the VIP machine vs flow sensor target 5-8 mls/kg
- Volume control waveform vs TCPL differences in opening of the lung
- In the face of variable leaks user intervention to target appropriate exhaled VT was required (less automated)
Ultimately, the waters are very muddy

- Volume control and volume guarantee are not the same thing
- Combining results between the 2 may not be helpful
- Many users interpret them as the same and use similar strategies to ventilate despite inherent differences between devices and algorithms utilized
Why Use Volume Targeted Ventilation?

- Believe that Volutrauma exists
- If one can set an appropriate VT the patient will be ventilated with varying pressures up to the set pressure limit
- More consistent ventilation should ultimately lead to less variability in carbon dioxide levels
- Less Hypocarbia may lead to a decreased risks for developing IVH and PVL
- Improved ventilation should reduce the time on the ventilator and lead to less CLD and BPD
If you plan on volume targeting

- What will be the targets you set and why?
- How accurate does your device measure them?
- Where does it measure them?
- What happens if there is a leak around the ETT – compensation built in?
A few take home messages

• Know your ventilator 1st and foremost
• the algorithms it uses to make decisions
• What volumes are you targeting where are they measured is there any dead space volume to account for…flow sensor location
• Do progressively diseased lungs ie CLD always require the same VT they started out with? Does the gas exchange surface area change
• When evaluating the literature, take into account your currently available technology the similarities used and strategies implemented
• If the results are promising how does your practice differ/similar
• What happens to VT in the face of changes in R/C or patient inspiratory efforts, ETT leak?
• Be aware of randomized control bias’
• The importance of the ventilator circuit and humidifier in VTR performance
In closing,

✓ More studies have been conducted looking at volume targeted techniques in the newborns we care for and the results are favourable

✓ We have made considerable progress in utilizing volume targeted modes in our everyday practice
“In some ways we are as confused as ever, but we believe we are confused on a higher level and about more important things.”

A.R. Feinstein, MD
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