Neonatal Resuscitation

Clinical Paper Summaries
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## DEFINITIONS

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Neopuff™ Key References

T-PIECE RESUSCITATION


HUMIDIFIED RESUSCITATION


SUSTAINED LUNG INFLATION (SLI)


COMPARISONS TO OTHER MECHANICAL VENTILATION DEVICES


Effect of flow rate, humidifier dome and water volume on maximising heated, humidified gas use for neonatal resuscitation

**AIM**
To determine the optimal flow rate and humidifier set-up which allows the T-piece used in neonatal resuscitation to reach an optimal temperature of 36°C and circuit relative humidity (RH) of 100% as quickly as possible.

**METHOD**
During this bench study a flowmeter delivered oxygen to a humidification chamber through a heated patient circuit to a T-piece. Gas flowed freely through the T-piece in all experiments except one, where a test lung was attached. Positive end-expiratory pressure (PEEP) was set at 5 cm H2O. The humidification chambers used were the MR290 (Fisher & Paykel Healthcare) with 108 mL or 30 mL of water (at flow rates of 6, 8 and 10 L/min, respectively), and the MR225 (Fisher & Paykel Healthcare) with 30 mL of water (at flow rates of 8 and 10 L/min).

Gas temperatures were measured at the following three points: the exit of the humidification chamber (T1), 112 cm distal to the chamber along the patient circuit (T2) and at the T-piece (T3). Three humidifier and patient circuit set-ups were used, these were allowed to dry and cool between tests. Data recording started when the humidifier was switched on and continued for 20 minutes. Target temperatures for T1, T2 and T3 were 36°C, 39°C and 36°C, respectively. It was assumed that gas leaving the humidification chamber was at 100% RH, and that 100% RH at the T-piece was achieved if T1 and T2 were within ±1°C of each other.

**RESULTS**
For the MR290 filled with 108 mL of water there was no significant difference between flow rates of 8 and 10 L/min with respect to achievement of target temperatures (p=0.091) or humidity (p=0.631). There was a significant relationship between the gas flow rate and the success of achieving T3 target temperature (p=0.028) and a T1–T3 temperature difference of ±1°C (p<0.001). The time taken to reach the target T3 temperature was significantly slower at flow rates of both 6 and 8 L/min compared with 10 L/min. The performance of different combinations of humidifier chambers, flow rates (8 and 10 L/min) and water volumes are shown in the table below. Target temperature and humidity were not reached when the test lung was added to the circuit.
<table>
<thead>
<tr>
<th></th>
<th>Gas flow rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8 L/min</td>
</tr>
<tr>
<td><strong>Success rate for reaching T3 target, %</strong></td>
<td></td>
</tr>
<tr>
<td>MR290 108 mL water</td>
<td>88.9</td>
</tr>
<tr>
<td>MR290 30 mL water</td>
<td>66.7</td>
</tr>
<tr>
<td>MR225 30 mL water</td>
<td>100</td>
</tr>
<tr>
<td><strong>Time to reach T3 target, sec [median (IQR)]</strong></td>
<td></td>
</tr>
<tr>
<td>MR290 108 mL water</td>
<td>540 (273)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>MR290 30 mL water</td>
<td>600 (617)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>MR225 30 mL water</td>
<td>360 (255)&lt;sup&gt;ab&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Time to reach temperature stability at T3, sec [median]</strong></td>
<td></td>
</tr>
<tr>
<td>MR290 108 mL water</td>
<td>540</td>
</tr>
<tr>
<td>MR290 30 mL water</td>
<td>660</td>
</tr>
<tr>
<td>MR225 30 mL water</td>
<td>690</td>
</tr>
<tr>
<td><em><em>Time to reach T1–T3 difference ±1°C</em>, sec [mean (SD)]</em>*</td>
<td></td>
</tr>
<tr>
<td>MR290 108 mL water</td>
<td>267 (59)</td>
</tr>
<tr>
<td>MR290 30 mL water</td>
<td>193 (34)</td>
</tr>
<tr>
<td>MR225 30 mL water</td>
<td>157 (72)</td>
</tr>
<tr>
<td><em><em>Time to reach stability of T1–T3 difference ±1°C</em>, sec [mean]</em>*</td>
<td></td>
</tr>
<tr>
<td>MR290 108 mL water</td>
<td>540</td>
</tr>
<tr>
<td>MR290 30 mL water</td>
<td>570</td>
</tr>
<tr>
<td>MR225 30 mL water</td>
<td>360</td>
</tr>
</tbody>
</table>

IQR interquartile range.

<sup>a</sup> At or near 100% RH.

<sup>b</sup> p<0.02 for between-group comparison; <sup>ab</sup> Post hoc analysis p<0.05.
CONCLUSION

This is the first published study to test the performance of heated patient circuits for neonatal resuscitation under different experimental conditions. The results show that it is possible to deliver heated and humidified gases during neonatal resuscitation within a clinically-acceptable timeframe.

Based on these findings, a gas flow rate of $\geq 8$ L/min was recommended for achieving target temperature and humidity, which is consistent with new guidelines from the manufacturer that state that the gas flow rate be maintained at 8–15 L/min. The best set-up for achieving optimal temperature and humidity during neonatal resuscitation was defined as a MR290 humidification chamber with 30 mL of water and a flow rate of 10 L/min. Use of the MR225 humidification chamber was not recommended.

KEY POINTS

- Use of the less invasive CPAP/INSURE strategy to treat VLBW infants with RDS is a feasible strategy.
- It is possible to deliver heated and humidified gases during neonatal resuscitation in a clinically-acceptable timeframe.
- The best set-up for achieving optimal temperature and humidity during neonatal resuscitation consists of an MR290 humidification chamber with 30 mL of water and using a flow rate of 10 L/min.
- Use of the MR225 humidification chamber is not recommended.
Measurements from preterm infants to guide face mask size

AIM
To measure facial dimensions in preterm infants at birth and over the first weeks of life and compare these with the diameter of commonly available round masks used to deliver positive pressure ventilation.

METHOD
Preterm infants with a gestational age <34 weeks admitted to the neonatal intensive and special care unit were eligible for inclusion. Each infant was photographed within 72 hours of birth and weekly until they reached 33 weeks and 6 days' postmenstrual age (or until discharge/transfer). Photographs were taken when the infant was lying down with their head and jaw in neutral positions (as they would be to receive mask positive pressure ventilation). The distance from the nasofrontal groove to the mental protruberance was measured. Measurements were compared against three round masks: Laerdal 0/0 (Laerdal), diameter 50 mm; and Infant Resuscitation Masks (Fisher & Paykel Healthcare), diameter 42 mm (small size) or 35 mm (extra small size).

RESULTS
A total of 107 infants from 24–33 weeks' gestational age were enrolled in the study between September 2011 and September 2013. Photographs were used to make 347 facial measurements (median 3 per infant). Initial facial measurements are shown in the table. There was no difference in measurements between males and females, or when small for gestational age infants were excluded. Initial measurements for each gestational age were similar to serial measurements based on postmenstrual age, indicating that postnatal facial growth in preterm infants occurs at a similar rate to antenatal facial growth.

<table>
<thead>
<tr>
<th>Gestation, completed weeks</th>
<th>Initial measurement, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>32±2</td>
</tr>
<tr>
<td>25</td>
<td>35±3</td>
</tr>
<tr>
<td>26</td>
<td>36±3</td>
</tr>
<tr>
<td>27</td>
<td>37±3</td>
</tr>
<tr>
<td>28</td>
<td>38±4</td>
</tr>
<tr>
<td>29</td>
<td>40±4</td>
</tr>
<tr>
<td>30</td>
<td>41±2</td>
</tr>
<tr>
<td>31</td>
<td>39±4</td>
</tr>
<tr>
<td>32</td>
<td>43±4</td>
</tr>
<tr>
<td>33</td>
<td>42±5</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation.
CONCLUSION
Round masks with a 50-mm external diameter may be too large for a high proportion of preterm infants. Smaller masks with an external diameter of 35 mm and 42 mm are more appropriate for infants of <29 or 29–33 weeks’ gestation, respectively.

KEY POINTS
• A round mask with an external diameter of 50 mm may be too large for preterm infants of <34 weeks’ gestation.
• A round mask with an external diameter of 42 mm is suitable for preterm infants of 29–33 weeks’ postmenstrual age or weighing 1000–2500 g.
• A round mask with an external diameter of 35 mm is suitable for preterm infants of <29 weeks' postmenstrual age or weighing <1000 g.
Equipment and operator training denote manual ventilation performance in neonatal resuscitation

**AIM**
To investigate the effect of operator training in neonatal manual ventilation on the level of peak inspiratory pressure (PIP) and tidal volume (VT) during simulated neonatal resuscitation.

**METHOD**
Eighty-four health care professionals (10 paediatricians; 22 anaesthetists; 30 neonatal nurses; 22 midwives) were recruited in this prospective, crossover trial. Participants were defined by four levels of training: level 0 = no previous training; level 1 = training on manual ventilation in neonates; level 2 = level 1 plus history of tutorial on lung protective management; level 3 = level 2 plus specific manometer training.

Neonatal resuscitation was simulated using a leak-free neonatal mannequin resembling an infant with very low birth weight (VLBW; birth weight <1500 g), equivalent to a 1.0 kg infant lung with a compliance of 0.2 mL kPa⁻¹ [Fisher & Paykel Healthcare]. Two different manual resuscitation devices were used: a self-inflating (SI) bag consisting of a new 240 mL Laerdal®-bag [Laerdal] with a new Ambu®-10-PEEP-valve [Ambu] set at 5 cm H2O; and a T-piece resuscitator [Neopuff; Fisher & Paykel Healthcare] with the positive end-expiratory pressure (PEEP) set at 5 cm H2O. A brief tutorial on the theoretical background and means of operation of the devices prior to testing was conducted to ensure that each participant had an equal understanding of the use of both devices.

Wall-mounted medical air provided a continuous gas flow of 8 L/min and participants were asked to manually ventilate to a target PIP of 20 cm H2O and a PEEP of 5 cm H2O with a rate of 60 breaths/min. Applied PIP and the resulting VT were measured using a pneumotachograph [CO₂SMO+®; Novametrix Inc.].

**RESULTS**
Operator training significantly affected the level of PIP and VT when using SI-bags for manual ventilation but not when using a T-piece device (see Table). The level of operator training also had a significant effect on inspiratory time when using an SI-bag (p=0.048).

<table>
<thead>
<tr>
<th>Training level</th>
<th>SI-bag</th>
<th>T-piece device</th>
<th>P value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PIP (cm H₂O)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>34.5 (8)</td>
<td>19.7 (0.43)</td>
<td>&lt;0.001</td>
<td>0.556</td>
</tr>
<tr>
<td>1</td>
<td>32.9 (12.8)</td>
<td>19.6 (0.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>24.7 (15.3)</td>
<td>19.6 (0.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>18.3 (11.8)</td>
<td>19.7 (0.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VT (mL)</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td>0.661</td>
</tr>
<tr>
<td>0</td>
<td>7.3 (8)</td>
<td>3.5 (0.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>6.4 (2.7)</td>
<td>3.5 (0.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4.8 (2.2)</td>
<td>3.4 (0.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3.8 (2.3)</td>
<td>3.5 (0.3)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IQR = interquartile range; PIP = peak inspiratory pressure; SI = self-inflating; VT = tidal volume.

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S3  CC ROEHR, M KELM, H PROQUITTÉ, G SCHMALISCH
AMERICAN JOURNAL OF PERINATOLOGY 2010; 27 (9): 753-758
DISCUSSION
VLBW infants often require noninvasive respiratory support. However, excessive PIP and high VT during manual ventilation can cause volutrauma and barotrauma in the neonatal lung. In order to reduce neonatal lung injury, the avoidance of high PIP and VT is essential. The International Liaison Committee on Resuscitation (ILCOR) and European Resuscitation Council (ERC) guidelines equally recognize SI-bags and T-piece devices for manual neonatal resuscitation. While SI-bags are the most commonly used in neonatal resuscitation units worldwide (83%), most are used without pressure manometers or appropriate pressure control. In contrast, T-piece devices (used by 30-40% of units) used during manual ventilation deliver consistent predefined PIP compared with SI-bags. Data from this study indicate that the level and consistency of delivered PIP and VT depends on the resuscitation device and the level of operator training. There was large intersubject variability in levels of applied PIP and VT with the SI-bag for all training levels. However, the higher the operator’s level of training, the better the adherence to the targeted PIP. In comparison, the use of a T-piece device provided consistent delivery of a defined PIP and VT in a simulated neonatal resuscitation scenario, irrespective of operator training level.

CONCLUSION:
PIP and VT are strongly influenced by choice of manual ventilation device during simulated neonatal resuscitation. For operators with no specific training in manual ventilation, use of T-piece devices is advised to control for excessive PIP and VT application.

KEY POINTS
• PIP and VT are strongly influenced by choice of manual ventilation device during simulated neonatal resuscitation.
• T-piece devices provide more reliable and constant PIP and VT than SI-bags, irrespective of prior experience or level of profession of the operator.
• The higher the operator’s level of training in manual neonatal resuscitation, the better the adherence to the targeted PIP and VT when using SI-bags, however larger inter-individual variation is still a problem at all training levels.
A randomized, controlled trial of delivery-room respiratory management in very preterm infants

AIM
To determine whether a sustained inflation followed by early nasal continuous positive airway pressure (CPAP) is more effective and less injurious than the conventional intervention with repeated manual inflations with a self-inflating bag and mask followed by nasal CPAP as a ventilatory strategy in very preterm infants.

METHOD
Two hundred and seven very preterm infants (25–32 weeks’ gestation) were randomized to receive ventilation with an early functional residual capacity intervention (EFURCI) or a conventional intervention.

The EFURCI group received ventilation with a sustained pressure-controlled (20 cm H2O) inflation for 10 seconds using a nasopharyngeal tube and a T-piece ventilator (Neopuff Infant Resuscitator; Fisher & Paykel). This inflation was repeated with increased pressure (25 cm H2O) if breathing remained insufficient, the infant’s heart beat was <100 beats/minute or the infant was cyanotic. After the inflation, early nasal CPAP was initiated at 5–6 cm H2O. Subsequently, if breathing remained insufficient, the infant’s heart rate was <100 beats/minute, the infant was cyanotic, breathing was absent or marked dyspnoea occurred, endotracheal intubation and mechanical ventilation was initiated.

The conventional intervention group was treated with a self-inflating bag and mask with a built-in pressure limitation (Ambu Infant Resuscitators; Ambu) and an oxygen reservoir. Initial inflation pressures of 30–40 cm H2O were used followed by pressures of ≤20 cm H2O. Early nasal CPAP was given on arrival to the neonatal intensive care unit (NICU) if needed. If breathing remained insufficient, the infant’s heart rate was <100 beats/minute, the infant was cyanotic or inflation was not possible, endotracheal intubation and mechanical ventilation were performed.

The primary endpoint of the study was the proportion of infants intubated within 72 hours of age; secondary endpoints included intubation in the delivery room, the need for mechanical ventilation and surfactant treatment, death during admission or bronchopulmonary dysplasia (BPD) based on the National Institute of Child Health and Human Development definition and other neonatal morbidity outcomes.
RESULTS

Data for the primary and secondary endpoints are reported in the table.

<table>
<thead>
<tr>
<th>Type of ventilation</th>
<th>EFURCI (n=104)</th>
<th>Conventional (n=103)</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intubated within 72h of age, n (%)</td>
<td>38 (37)</td>
<td>52 (51)</td>
<td>0.57 (0.32–0.98)</td>
<td>0.04</td>
</tr>
<tr>
<td>Intubated in the delivery room, n (%)</td>
<td>18 (17)</td>
<td>37 (36)</td>
<td>0.37 (0.20–0.70)</td>
<td>0.002</td>
</tr>
<tr>
<td>Total period of mechanical ventilation of intubated infants &lt;72h of age, days [median (IQR)]</td>
<td>2.5 (1–8.3)</td>
<td>4.5 (2–11.5)</td>
<td>0.2</td>
<td></td>
</tr>
<tr>
<td>Total period of NCPAP of total group, days [median (IQR)]</td>
<td>2 (0.3–8)</td>
<td>2 (0–11)</td>
<td>0.038</td>
<td></td>
</tr>
<tr>
<td>Surfactant doses, mean (SD)</td>
<td>0.4 (0.8)</td>
<td>0.6 (1.0)</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Surfactant &gt;1 dose, n (%)</td>
<td>10 (10)</td>
<td>22 (21)</td>
<td>0.39 (0.18–0.88)</td>
<td>0.02</td>
</tr>
<tr>
<td>Mortality, n (%)</td>
<td>2 (2)</td>
<td>4 (4)</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>BPD, n (%):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>22 (22)</td>
<td>34 (34)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Moderate to severe</td>
<td>9 (9)</td>
<td>19 (19)</td>
<td>0.41 (0.18–0.96)</td>
<td>0.04</td>
</tr>
<tr>
<td>PDA needing treatment, n (%)</td>
<td>21 (20)</td>
<td>16 (16)</td>
<td>0.4</td>
<td></td>
</tr>
</tbody>
</table>

95% CI = 95% confidence interval; BPD = bronchopulmonary dysplasia; EFURCI = early functional residual capacity intervention; h = hours; IQR = interquartile range; n = number; NCPAP = nasal continuous positive airway pressure; OR = odds ratio; PDA = patent ductus arteriosus; SD = standard deviation.

DISCUSSION

This is the first prospective, randomised trial in very preterm infants comparing an EFURCI ventilation strategy with conventional intervention using a bag and mask. The intubation rate, surfactant requirement and incidence of BPD were all reduced by the new strategy. Potential reasons for the beneficial effects of EFURCI include avoiding the use of potentially dangerous high inspiratory pressures, preservation of surfactant and allowing time to differentiate between RDS and transition problems. The latter reduces the number of infants undergoing unnecessary intubation. While this study shows the importance of early respiratory management for pulmonary outcome in very preterm infants, further randomised controlled trials are needed to develop an optimal strategy for these patients.
CONCLUSION
The EFURCI ventilation strategy, which consisted of a sustained inflation followed by early nasal CPAP delivered through a nasopharyngeal tube, is a more efficient strategy than the conventional intervention with repeated manual inflations with a self-inflating bag and mask followed by nasal CPAP in very preterm infants.

KEY POINTS
• Use of an EFURCI ventilation strategy in very preterm infants reduced the rate of intubation at <72 hours of age, surfactant usage and the incidence of BPD compared with a conventional ventilation strategy.
• Further randomised controlled trials are needed to develop an optimal strategy for these patients.
Humidified and heated air during stabilization at birth improves temperature in preterm infants

**AIM**
To investigate the effect of using humidified and heated gas during respiratory support at birth on body temperature in very preterm infants admitted to the neonatal intensive care unit (NICU).

**METHOD**
This prospective observational study compared two cohorts of infants born at ≤32 weeks’ gestation who required respiratory support in the delivery room. The first cohort was born from February to July 2008 (cold group; n=58) and the second was born from October 2008 to May 2009 after a change to hospital policy specified the use of humidified and heated gas (heat & humidification group; n=54). Humidification of inspired gases during respiratory support in the delivery room was provided using a heated humidifier [MR850; Fisher & Paykel Healthcare] set to 37°C. Respiratory support was provided using a T-piece ventilator [Neopuff infant resuscitator; Fisher & Paykel Healthcare]. After stabilization, infants were transferred to the NICU.

The primary endpoint of the study was rectal temperature which was taken on arrival at the NICU using a digital thermometer [Thermoval; Hartmann]. Secondary endpoints were requirement for mechanical ventilation and surfactant, oxygen treatment 28 days after birth, patent ductus arteriosus that required treatment, hypotension needing inotropic support, ≥ grade 2 necrotising enterocolitis, ≥ grade 2 intraventricular haemorrhage and/or cystic periventricular leukomalacia, and death during admission.

**RESULTS**
There were no significant differences in baseline characteristics between the two groups of infants. Data for the primary and secondary endpoints are reported in the table.
### Primary endpoint

<table>
<thead>
<tr>
<th></th>
<th>Cold group (n=58)</th>
<th>Heat and humidification group (n=54)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean body temperature on arrival at the NICU (°C)</td>
<td>35.9</td>
<td>36.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Normothermia (patients)</td>
<td>12%</td>
<td>43%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mild hypothermia (patients)</td>
<td>33%</td>
<td>35%</td>
<td>NS</td>
</tr>
<tr>
<td>Moderate hypothermia (patients)</td>
<td>53%</td>
<td>19%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mild hyperthermia (patients)</td>
<td>2%</td>
<td>4%</td>
<td>NS</td>
</tr>
<tr>
<td>Moderate hyperthermia (patients)</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
</tbody>
</table>

### Secondary endpoints (patients)

<table>
<thead>
<tr>
<th></th>
<th>Cold group (n=58)</th>
<th>Heat and humidification group (n=54)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surfactant treatment</td>
<td>31%</td>
<td>43%</td>
<td>0.24</td>
</tr>
<tr>
<td>Oxygen treatment at age 28 days</td>
<td>26%</td>
<td>15%</td>
<td>0.23</td>
</tr>
<tr>
<td>PDA needing treatment</td>
<td>12%</td>
<td>22%</td>
<td>0.11</td>
</tr>
<tr>
<td>Hypotension needing treatment</td>
<td>19%</td>
<td>7%</td>
<td>0.07</td>
</tr>
<tr>
<td>NEC ≥ grade 2</td>
<td>2%</td>
<td>4%</td>
<td>0.21</td>
</tr>
<tr>
<td>IVH ≥ grade 2 and/or cystic PVL</td>
<td>18%</td>
<td>15%</td>
<td>0.77</td>
</tr>
<tr>
<td>Death during admission</td>
<td>7%</td>
<td>6%</td>
<td>0.77</td>
</tr>
</tbody>
</table>

Normothermia = core body temperature 36.5-37.5°C; Mild hypothermia = core body temperature 36.0-36.4°C; Moderate hypothermia = core body temperature <36.0°C; Mild hyperthermia = core body temperature 37.6-38.0°C; Moderate hyperthermia = core body temperature >38.0°C; PDA = patent ductus arteriosus; NEC = necrotizing enterocolitis; IVH = intraventricular haemorrhage; PVL = periventricular leukomalacia; NS = not significant.

### Discussion

Delivery of dry, cold gases has a number of deleterious physiological effects. The use of humidified and heated gas has been defined as the standard of care during respiratory support for preterm infants in the NICU. However, there is no such recommendation for respiratory support provided in the delivery room. Preterm infants are at risk of heat loss after delivery, and can develop hypothermia, which is associated with increased morbidity and mortality. In this study, heating and humidifying respiratory gases given in the delivery room prevented the postnatal fall in body temperature and there was a significant reduction in the incidence of moderate hypothermia on admission to the NICU. There was no significant effect on morbidity and mortality, although this study was not adequately powered to assess these endpoints. More data are needed to determine whether reducing hypothermia in very preterm infants translates into a clinical benefit, and offsets the additional cost of providing heat and humidification (approximately €50 per patient in this study).
CONCLUSION

Adding heat and humidification to inspired gases during respiratory support in the delivery room appears to have a beneficial effect on body temperature at admission to NICU in very preterm infants. Further study of the effect of different gas conditions on lung physiology in preterm infants is required before the use of heated and humidified gas can be recommended as the standard of care in this setting.

KEY POINTS

• Use of heated and humidified gases for respiratory support of very preterm infants in the delivery room prevents the postnatal decrease in temperature.

• Morbidity and mortality rates are similar when either cold or heated and humidified gases are used for delivery room respiratory support in very preterm infants.
Initial respiratory support with cold, dry gas versus heated humidified gas and admission temperature of preterm infants

AIM
To compare the effects of heated humidified gas (HHG) versus cold, dry gas as initial respiratory support (from delivery until arrival at the neonatal unit) on admission temperatures in preterm infants.

METHOD
This multicenter, non-blinded trial was conducted at Middlemore Hospital, Auckland, New Zealand (NZ) and Lieden University Medical Center, Leiden, The Netherlands (NL). Preterm infants of <32 weeks’ gestation who required respiratory support at delivery were randomized to receive respiratory support with either unconditioned cold, dry gas or HHG at delivery and during transport. Randomization was stratified by center and gestational age (<28 weeks’ and ≥28 weeks’). Respiratory support was initially provided with a T-piece ventilator (Fisher & Paykel Healthcare), which was used to provide continuous positive airway pressure (CPAP) or positive pressure ventilation. A humidifier (MR225 or MR850; Fisher & Paykel Healthcare) and heated resuscitation circuit (900RD110; Fisher & Paykel Healthcare) were used, with a gas flow rate of 8 L/min. The delivery room temperatures were 25–26°C, and infants were either wrapped or dried after delivery, and received head covering. During 40 s delayed cord clamping (DCC), which was performed in NZ only, there was no ventilator support. All infants were transported to the neonatal unit in a preheated radiant warmer or incubator at 35°C. Oxygen saturation and heart rate were monitored by pulse oximetry. The primary endpoint was an axillary admission temperature within the desired range of 36.5–37.5°C (i.e. normothermia), as measured by a digital electronic thermometer (Welch Allyn, Skaneateles Falls, New York, USA or Thermoval, Hartmann, Heidenheim, Germany). Secondary endpoints included the receipt of respiratory support during transport and after admission, the fraction of inspired oxygen (FiO₂) at 30 and 60 min, and the total minutes of oxygen exposure in the first hour. Signs of neonatal morbidity, including bronchopulmonary dysplasia, grade 3 or 4 intraventricular hemorrhage, necrotizing enterocolitis, and retinopathy of prematurity were also recorded.

RESULTS
Significantly higher rates of normothermia on admission were observed in preterm infants when HHG was used as initial respiratory support compared with cold, dry gas (Table). Across all infants (n=203), admission temperatures were >37.5°C in 8 patients (4%) and <36.5°C in 69 patients (34%). The proportion of infants with temperatures above or below the desired range was not significantly different between groups, although admission temperatures were <35.5°C in significantly fewer infants in the HHG than cold, dry gas group (Table). Significantly more infants at <28 weeks’ gestation were normothermic in the HHG than cold, dry gas group (Table). Based on binary logistic regression, humidification and hospital site were significant factors in predicting normothermia on admission. HHG reduced the number of infants outside the desired temperature range by 43% (from 23% to 13%) in NZ and by 24% (from 67% to 51%) in NL. Univariate analysis showed that mean birth weight was significantly higher in NZ than NL (392 g vs. 342 g; p<0.05). The use of DCC was not associated with significant changes in admission temperatures in either univariate or multivariate regression analysis. Secondary measures of respiratory outcomes were not significantly different between groups.
### Outcome Summary

<table>
<thead>
<tr>
<th>Outcome</th>
<th>HHG (n=100)</th>
<th>Cold, dry gas (n=103)</th>
<th>Unadjusted OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normothermia&lt;sup&gt;a&lt;/sup&gt; (%)</td>
<td>69</td>
<td>55</td>
<td>1.8 (1.01–3.19)</td>
<td>NR</td>
</tr>
<tr>
<td>Infants &lt;28 weeks' (%)</td>
<td>69</td>
<td>42</td>
<td>NR</td>
<td>0.03</td>
</tr>
<tr>
<td>Severe hypothermia&lt;sup&gt;b&lt;/sup&gt; (%)</td>
<td>2</td>
<td>12</td>
<td>NR</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Results are shown as percentages. CI, confidence interval; OR, odds ratio

<sup>a</sup> Defined as an admission axillary temperature of 36.5–37.5°C

<sup>b</sup> Admission axillary temperature of <35.5°C

### DISCUSSION

The favorable effects of HGG as respiratory support from birth in preterm infants were consistent with previous observational study findings. In addition to an increase in normothermia on admission (including in infants <28 weeks' gestation), HHG was more effective in reducing severe hypothermia than cold, dry gas in preterm infants. The potential benefits of HHG will need to take into consideration the extra costs of the circuit (~$US50). Differences in the admission temperatures between the NZ and NL sites may be due to differences in birth weight and the use of wrapping after delivery. The use of DCC in NZ did not significantly affect admission temperatures in this study. Both sites showed improvement over time in the proportion of patients with normothermia on admission, which was likely due to ongoing quality improvement and technique familiarity. In 2008, 88% of infants in the NL were outside the desired temperature range compared with 68% of infants in the non-humidified group during this study (p=0.01). Similarly in NZ, the proportion of patients outside the desired temperature decreased from 30% in 2008 to 23% during this study. Although the use of HHG in preterm infants requiring respiratory support is standard practice in nurseries, the optimal temperature and humidity have not been established. Clinical effects of cold, dry gas ventilation on preterm infants, including increased airway resistance, increased work of breathing, and decreased compliance, have been previously observed. In this study, the respiratory status in the first hour or during the neonatal period showed no significant difference between the HHG and cold, dry gas groups; however, the trial was insufficiently powered to assess these outcomes.

### CONCLUSION

This study indicates that addition of HHG to respiratory support from delivery, in combination with other measures to prevent hypothermia, may be beneficial with regard to normothermia in preterm infants <32 weeks' gestation, particularly in those <28 weeks’. Differences in respiratory outcomes, morbidity, and mortality were not observed in this study, and larger studies are needed to fully assess these outcomes.
Effect of sustained inflation duration; resuscitation of near-term asphyxiated lambs

AIM
To compare the effects of three different initial ventilation strategies delivered immediately after birth on the amount of additional complications seen in near-term asphyxiated lambs.

METHOD
This experimental animal study used a previously-validated lamb model of induced near-term asphyxiation. Eighteen near-term lambs were intubated and randomized to receive initial ventilation according to one of three different protocols: inflation time of 0.5 second at a rate of 60 per minute (no sustained inflation); five inflations of 3 seconds duration with a 1-second expiratory time; or a single 30 second inflation. The peak inflating pressure (PIP) was 35 cm H2O, peak end-expiratory pressure (PEEP) was 5 cm H2O and the fraction of inspired oxygen (FiO2) was 0.21. The first two strategies were delivered using a ventilator (Dräger Babylog 8000plus), and in the third group (30-second inflation) ventilation was delivered with a T-piece device (Neopuff; Fisher & Paykel Healthcare). The endotracheal tubes were clamped during disconnection from the T-piece and connection to the ventilator. After the different initial ventilation strategies, all animals received pressure-limited ventilation for 10 minutes, then the settings were changed to volume-guaranteed ventilation with a target expiratory tidal volume of 8 mL/kg; ventilation was continued for another 30 minutes before animals were euthanized. Heart rate (HR), carotid blood pressure (CBP), tidal volume and PIP were monitored continuously. Arterial blood gas samples were collected at 1, 2.5, 5, 7.5, 10, 15, 20 and 30 minutes after the onset of ventilation.

The primary outcome was the time taken from the start of ventilation to circulatory recovery (HR ≥120 bpm and a mean CBP ≥40 mmHg). The secondary outcome measured was change in lung compliance.

RESULTS
A single 30 second inflation was significantly more effective than the other 2 ventilation strategies with respect to achievement of lower HR and CBP (see table). In addition, partial pressure of carbon dioxide (PaCO2) decreased earlier and partial pressure of oxygen (PaO2) was significantly higher from 5 to 10 minutes after the start of ventilation in the single 30-second inflation group compared with the other interventions. With the PIP set at 35 cm H2O there was a steady increase in tidal volume after resuscitation using a single 30 second inflation, and values were greater than in the other treatment groups from 8 to 10 minutes post-intervention. This increase in tidal volume was deemed to be secondary to improved lung compliance. After the switch to volume-guaranteed ventilation, those animals resuscitated with a single 30 second inflation required a lower PIP to achieve the same tidal volume and in addition had significantly higher lung compliance compared with the other two groups.

<table>
<thead>
<tr>
<th>Median (IQR)</th>
<th>Time to reach circulatory recovery (seconds)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR 120 beats/min</td>
</tr>
<tr>
<td>No sustained inflation</td>
<td>64 (35–110)</td>
</tr>
<tr>
<td>3-sec inflations x5</td>
<td>38 (20–134)</td>
</tr>
<tr>
<td>30-sec inflation</td>
<td>8 (5–11) (a,b)</td>
</tr>
</tbody>
</table>

CBP, carotid blood pressure; HR, heart rate; IQR, interquartile range.
\(a\) p<0.05 vs no sustained inflation; \(b\) p<0.05 vs 3-sec inflations x5.
CONCLUSION

Appropriate inflation times for initial lung inflations in apneic newborn infants are not currently specified in available guidelines and there is regional variation in recommendations. This study is the first to compare different initial ventilation strategies for near-term animals with severe perinatal asphyxia. The results of this study showed that a single 30 second inflation was associated with significant increases in HR and CBP, suggesting that this approach might facilitate a faster circulatory transition. However, it will be important to examine cerebral hemodynamics after use of the single 30 second inflation strategy to determine whether the marked increase in HR and CBP is associated with damaging increases in cerebral blood flow. The persistent improvement in lung compliance observed with the 30 second single inflation strategy and parallel improvement in oxygenation was probably due to better lung aeration and this continued beyond the period of stabilization. The promising results of this animal study suggest that investigation of the use of a single 30 second inflation for resuscitation after perinatal asphyxia in newborn infants is warranted.

KEY POINTS

- A single 30 second inflation is associated with significantly improved increases in HR and CBP in an animal model of near-term neonatal asphyxia.
- A single 30 second inflation is more effective than five 3-second inflations and inflations of 0.5 second at a rate of 60 per minute (no sustained inflation).
- A single 30 second inflation was associated with improvements in lung compliance that persisted beyond the stabilization period.
- Investigation of the use of a single 30 second inflation for resuscitation after perinatal asphyxia in newborn infants is warranted.
Sustained lung inflation at birth for preterm infants: a randomized clinical trial

AIM
To compare the use of prophylactic sustained lung inflation (SLI) followed by nasal continuous positive airway pressure (nCPAP) with nCPAP alone in the delivery room, in order to determine whether SLI plus early nCPAP used shortly after birth in preterm infants at high risk of respiratory distress syndrome (RDS) would reduce the need for mechanical ventilation and improve respiratory outcomes.

METHOD
This randomized, controlled, multicenter, single-blinded study was conducted in perinatal centers across Italy. Infants aged between 25 weeks 0 days and 28 weeks 6 days at the time of birth were eligible for the study. Infants were randomized in a 1:1 ratio to either SLI plus nCPAP or nCPAP alone immediately after birth (before the first breath), stratified according to center and gestational age (25/26 weeks and 27/28 weeks). In the SLI group, infants underwent oropharyngeal and nasal suctioning, and then a 15-second, pressure-controlled (25 cm H2O) inflation, followed by 5 cm H2O nCPAP at a flow rate of 8–10 L/min using a neonatal mask and T-piece ventilator (Neopuff™ Infant Resuscitator; Fisher & Paykel Healthcare). If respiratory failure persisted and/or the heart rate was >60 and <100 bpm, the SLI was repeated as above. If the heart rate was still >60 and <100 bpm after the second SLI, infants were resuscitated according to American Academy of Pediatrics (AAP) guidelines. The control group received nCPAP at 5 cm H2O and assistance according to AAP guidelines. Infants who were not intubated in the delivery room were transferred on nCPAP at 5 cm H2O to the NICU. Criteria for starting mechanical ventilation in the delivery room was a heart rate of <60 bpm despite proper positive pressure ventilation; in the NICU, mechanical ventilation was started when: pH was <7.20 with PaCO2 >65 mmHg; when PaO2 was <50 mmHg with FiO2 ≥0.50; after surfactant treatment; or if there were frequent (>4 episodes in 1 hour or >2 episodes requiring bag-and-mask ventilation) episodes of apnea despite adequate nCPAP delivery and oxygenation. The primary endpoint was mechanical ventilation within the first 72 hours of life. Secondary endpoints included mechanical ventilation within the first 3 hours of life, the need for various types of mechanical ventilation, duration of nCPAP, duration of hospitalization, need for and doses of surfactant, and occurrence of RDS, bronchopulmonary dysplasia (BPD), and death.

RESULTS
The use of SLI significantly decreased the need for mechanical ventilation within the first 72 hours after birth (see Table). The SLI procedure did not alter the frequency of use of other respiratory support during hospitalization, nor did it affect the duration of the non-invasive support/ventilation required. The need for and number of doses of surfactant did not differ between groups, nor did the duration of hospitalization. The rates of RDS, BPD, or death were not different between groups (see Table); however, there was a trend towards an increase in pneumothorax (6% vs 1%; p=0.06) and interstitial emphysema (5% vs 1%; p=0.09) in the SLI group versus controls. When analyses according to maternal and infant characteristics were performed, there were no factors that significantly influenced the effects of the SLI procedure.
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control (n=143)</th>
<th>SLI (n=148)</th>
<th>Unadjusted odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MV within 72 hours, n (%)</td>
<td>93 (65)</td>
<td>79 (53)</td>
<td>0.62 (0.38–0.99)</td>
<td>0.04</td>
</tr>
<tr>
<td>MV within 3 hours, n (%)</td>
<td>73 (51)</td>
<td>66 (45)</td>
<td>0.77 (0.49–1.22)</td>
<td>0.27</td>
</tr>
<tr>
<td>Nasal IMV, n (%)</td>
<td>36 (25)</td>
<td>39 (26)</td>
<td>1.06 (0.63–1.80)</td>
<td>0.85</td>
</tr>
<tr>
<td>SIMV/SIPPV/PSV, n (%)</td>
<td>90 (63)</td>
<td>86 (58)</td>
<td>0.82 (0.51–1.31)</td>
<td>0.43</td>
</tr>
<tr>
<td>HFV, n (%)</td>
<td>31 (22)</td>
<td>32 (22)</td>
<td>1.00 (0.57–1.74)</td>
<td>0.99</td>
</tr>
<tr>
<td>Any MV, n (%)</td>
<td>98 (69)</td>
<td>88 (59)</td>
<td>0.67 (0.42–1.10)</td>
<td>0.11</td>
</tr>
<tr>
<td>BiPAP, n (%)</td>
<td>47 (33)</td>
<td>63 (43)</td>
<td>1.51 (0.94–2.44)</td>
<td>0.09</td>
</tr>
<tr>
<td>Surfactant, n (%)</td>
<td>110 (77)</td>
<td>109 (74)</td>
<td>0.84 (0.49–1.43)</td>
<td>0.52</td>
</tr>
<tr>
<td>Dose of surfactant, hours</td>
<td>1 (1–2)</td>
<td>1 (1–2)</td>
<td>NR</td>
<td>0.55</td>
</tr>
<tr>
<td>Duration of nCPAP, hours</td>
<td>190 (47–500)</td>
<td>218 (42–480)</td>
<td>NR</td>
<td>0.88</td>
</tr>
<tr>
<td>Duration of hospitalization, days</td>
<td>75 (60–101)</td>
<td>83 (61–107)</td>
<td>NR</td>
<td>0.22</td>
</tr>
<tr>
<td>RDS</td>
<td>134 (94)</td>
<td>133 (90)</td>
<td>0.60 (0.25–1.41)</td>
<td>0.23</td>
</tr>
<tr>
<td>BPD, n (%)</td>
<td>50 (35)</td>
<td>57 (39)</td>
<td>1.17 (0.80–1.71)</td>
<td>0.42</td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>12 (8)</td>
<td>17 (11)</td>
<td>1.37 (0.66–2.88)</td>
<td>0.40</td>
</tr>
</tbody>
</table>

a. mean (interquartile range)
b. Hazard ratio (95% CI)

BiPAP, bi-level positive airway pressure; BPD, bronchopulmonary dysplasia; HFV, high-frequency ventilation; IMV, intermittent mechanical ventilation; MV, mechanical ventilation; nCPAP, nasal continuous positive airway pressure; NR, not reported; PSV, pressure support ventilation; RDS, respiratory distress syndrome; SIMV, synchronized intermittent mechanical ventilation; SIPPV, synchronized intermittent positive pressure ventilation; SLI sustained lung inflation.

**DISCUSSION**

The reduction in the need for mechanical ventilation in the first 3 days of life are likely due to the lung recruitment and functional residual capacity provided by the SLI procedure, and the prevention of lung collapse by the use of positive end-expiratory pressure. The lack of impact of SLI on rates of BPD may be due to the use of nCPAP in the control group, which may have allowed a gradual recruitment of functional residual capacity in the absence of SLI, and therefore lessened any BPD-preventing effect of the SLI procedure in the SLI group. Alternatively, ventilator-induced lung injury that occurred in the days following the SLI procedure may have overcome the beneficial effect conferred by SLI and increased the likelihood that BPD would subsequently develop. Since the development of BPD is multifactorial, it is unlikely that one single procedure can completely prevent it. The increased incidence of pneumothorax and interstitial emphysema in infants who underwent SLI versus controls suggests that the procedure used might be too aggressive in infants of the age group investigated in this study, particularly when SLI is used as prophylaxis as it was here.
CONCLUSION

In this study, use of SLI in the first minutes of life in extremely preterm infants at risk of RDS reduced the need for mechanical ventilation over the first 72 hours, but had no impact on the overall need for and duration of respiratory support during hospitalization, or the incidence of BPD or RDS. Until other clinical studies are performed which investigate the effectiveness of SLI in improving outcomes, SLI should not be recommended for use as routine prophylactic assistance with preterm infants in the delivery room.

KEY POINTS

• The prophylactic use of SLI plus nCPAP in the delivery room with extremely preterm infants decreases the need for mechanical ventilation within the first 72 hours of life compared with nCPAP alone.

• The overall need for non-invasive respiratory support during hospitalization, or the incidence of BPD or RDS, were not decreased by the addition of SLI to nCPAP.

• Until further data is gathered, SLI should not be routinely used as a prophylactic procedure in preterm infants at risk of RDS.
Sustained inflations: comparing three neonatal resuscitation devices

AIM
To evaluate the ability of operators from different professional groups to provide a 10-second sustained inflation to a neonatal mannequin using three manual ventilation devices.

METHOD
The three devices tested were a 500 mL flow-inflating (anaesthesia) bag, a self-inflating bag (Laerdal 240 mL silicone infant resuscitator) fitted with a positive end-expiratory pressure (PEEP) valve and a reservoir (Laerdal), and a T-piece device (Neopuff; Fisher & Paykel Healthcare). Gas flow for all devices was set at 8 L/min and the same round silicone facemask (size 0/1; Laerdal) was used with all devices. Participants included 50 clinical staff members from the Royal Women’s Hospital, Melbourne, Australia (10 neonatal consultants, 10 neonatal fellows, 10 paediatric registrars, 10 neonatal nurses and 10 anaesthetic registrars). Each device was connected to a neonatal mannequin fitted with a 50 mL test lung and then used by each participant in a random order. The instruction was to give a sustained inflation at 30 cm H2O for 10 seconds. Participants were able to view a manometer during the study. A pressure line was connected internally to the mannequin’s airway and pressure and gas flow were recorded using a respiratory function monitor (Florian; Acutronic Medical Systems AG). The duration of inflation was determined from the gas flow curves.

RESULTS
Participants had different levels of experience with each of the devices depending on their role. Before the study, 90% of participants stated a preference for the T-piece device, 6% preferred the flow-inflating bag and 4% preferred the self-inflating bag for use during resuscitation. There were no significant differences between the different professional groups with respect to the mean inflating pressure (MIP) and peak inflating pressure (PIP) although significant differences between devices were observed. Overall values for each device are reported in the table.

<table>
<thead>
<tr>
<th></th>
<th>Flow-inflating bag</th>
<th>Self-inflating bag</th>
<th>T-piece device</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean inflating pressure (cm H2O)</td>
<td>26.9\textsuperscript{a}</td>
<td>23.4\textsuperscript{a,b}</td>
<td>28.8</td>
</tr>
<tr>
<td>Peak inflating pressure (cm H2O)</td>
<td>32.3\textsuperscript{a}</td>
<td>30.6</td>
<td>29.8</td>
</tr>
</tbody>
</table>

\textsuperscript{a} P<0.001 vs T-piece device; \textsuperscript{b} P<0.001 vs flow-inflating device.

Independent of experience, most participants were able to deliver a constant and stable (>25 cm H2O) inspiratory pressure (IP) with the T-piece device. The median duration of IP >25 cm H2O was similar for the flow-inflating bag (but with greater inter-individual variation versus the T-piece device), and IP was significantly lower with the self-inflating bag compared to the other devices (p<0.001). In addition, there were large variations in the ability of different participants to achieve a sustained inflation with a self-inflating bag. There was a significant correlation between months of experience using a self-inflating bag and the ability to provide longer inflation times at an IP >25 cm H2O with this device.

Consistent square-shaped pressure curves with a rapid rise in pressure when inflation started were achieved with the T-piece device. For the flow-inflating bag there was more variation but characteristics usually included an early pressure peak and a slow decline in pressure, but often with substantial mask leak. There was marked variation in the pressure and gas curves generated during use of the self-inflating bag. Unless there was a large facemask leak, gas flow into the test lung occurred mainly during the first part of the sustained inflation with all three devices.
**DISCUSSION**

Physiologically it is logical to facilitate airway liquid clearance and improve lung inflation immediately after birth using sustained inflations. However, there is a paucity of data on the relative effectiveness of different ventilation devices for delivering sustained inflations. The results of this study show that the T-piece device was able to be used by a variety of different operators to deliver a long, constant, pressure-limited sustained inflation. The flow-inflating bag was also useful for providing a relatively consistent IP during sustained inflation whereas sustained inflations of ≥10 seconds can rarely be achieved with a self-inflating bag. However, this study having been performed in a laboratory rather than a clinical setting, and the prior preference for a T-piece device by the majority of participants, are potential sources of bias.

**CONCLUSION**

A T-piece device was more effective than flow-inflating and self-inflating bags for delivering consistent and stable inflation pressures during a 10-second sustained inflation in a neonatal model.

**KEY POINTS**

- A T-piece device provides consistent and stable inflation pressures during a 10-second sustained inflation in a neonatal model.
- A flow-inflating bag can be used to deliver sustained inflation but pressure delivery is variable.
- Sustained inflations >10 seconds are difficult to achieve using a self-inflating bag.

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Comparison of the T-piece resuscitator with other neonatal manual ventilation devices: a qualitative review

AIM
To review published literature regarding the use of a T-piece resuscitator (TPR) for neonatal resuscitation, with a focus on data comparing TPR with other manual ventilation devices (self-inflating bag [SIB] and flow-inflating bag [FIB]).

DETAILS
The proportion of infants requiring resuscitation at birth is approximately 5–10%. Three devices are currently recommended by neonatal resuscitation guidelines: SIB, FIB and TPR. TPR provides pressure-controlled, flow-delivered positive pressure ventilation, and modification of positive end-expiratory pressure (PEEP) is possible by rotating the PEEP valve. A number of different TPR devices are available, but data suggests that the most popular of these is Neopuff (Fisher & Paykel Healthcare); other options are Tom Thumb (Viamed) and Neotee (Mercury Medical).

A literature search was conducted using Medline (1966–2011), EMBASE (1986–2011) and the Cochrane Clinical Trial Register and 50 studies were identified. Thirty studies were included in the review, two studies were conducted in infants, 14 were simulated, one was an observational study and the 13 remaining used TPR without comparison. A number of primary and secondary endpoints were defined a priori including: mortality before discharge home, need for endotracheal intubation in the delivery room, incidence of bronchopulmonary dysplasia (primary determinants of efficacy), provision of predetermined positive inspiratory pressure (PIP), ability to provide predetermined PEEP, ability to alter both pressures during resuscitation, inspiratory time provided, ability to provide a prolonged inflation breath, ability to provide consistent targeted tidal volumes, mask leak and the effect of training on device use (secondary determinants of efficacy).

Primary determinants of efficacy: Data from two studies were available. The first did not report any significant difference between TPR and SIB with respect to mortality, need for endotracheal intubation, need for respiratory support at 28 days and oxygen saturation at 5 minutes. The second study reported a 26% reduction in the incidence of chronic lung disease over a 3-year period following the introduction of Neopuff for delivery room management of infants with a birthweight of <1500g. However, the contribution of TPR to this decrease cannot be definitively determined because of the presence of too many confounding variables.

Provision of predetermined PIP (15 studies): Comparative collated data reported from 11 studies suggested that Neopuff provided less variation in pressures than both SIB and FIB. In another comparative trial the percentage of pressures within the target range was substantially higher for Tom Thumb (89%) versus SIB (5%) and FIB (17%). At a target PIP of 20 cm H₂O, percentage of breaths with a PIP <21 cm H₂O and percentage of breaths with PIP >30 cm H₂O were all significantly lower with Neopuff compared with SIB and FIB. PIP was shown to be flow dependent in a number of studies, while use of a commercially-available gas flow restrictor (Flowtec Model HBD2) allowed the Neopuff to provide appropriate levels of PIP and PEEP without inadvertently delivering excessive pressures.

Provision of predetermined PEEP (12 studies): The comparison between Neopuff and both SIB (with and without a PEEP valve) and/or FIB in the 7 manikin studies was favorable. In the one study conducted in infants, PEEP was closer to the target with Neopuff than with SIB without a PEEP valve. PEEP was shown to increase as gas flow increased, although use of the PEEP valve could reduce the change in PEEP for the same increase in gas flow. In one study, the results suggested that the PEEP valve may be inadvertently turned during resuscitation. When the PEEP valve is fully occluded and the mask loosely at the infant’s face, Neopuff can provide nearly 100% free flow oxygen.
Ability to alter pressures during resuscitation (two studies): The time taken to change pressure from 20 to 40 cm H₂O during resuscitation was longer with Neopuff compared with SIB and FIB (5.7 sec vs. 2.2 and 1.8 sec, respectively). In a manikin study, Neopuff users did not respond to change in compliance during resuscitation whereas those using SIB increased PIP in response to reduced compliance.

Inspiratory time (three studies): Inspiratory time during Neopuff use has been reported to be decreased when the operator is distracted, to be significantly affected by operator experience, and to be slightly longer than that with SIB and FIB when the target was 60 inflations per minute.

Prolonged inflation breaths (three studies): The Neopuff provided more consistent prolonged inflation than SIB (in all three studies reporting this endpoint), and than FIB in two of the three studies. There was no difference reported between Neopuff and FIB in one study.

Tidal volumes (eight studies): The results of all eight comparative manikin studies reported that tidal volumes were lower and more stable during use of Neopuff versus SIB. In one infant study, TPR tended to provide a lower tidal volume than SIB in preterm infants born at <29 weeks’ gestation. Delivery of tidal volume with Neopuff did not vary according to operator experience, but SIB inexperienced operators tended to provide a greater tidal volume than those who had more resuscitation experience.

Mask leak (six studies): Five studies comparing mask leak with TPR versus SIB reported lower mask leak during use of SIB; there was no difference between devices in one manikin study. During use of Neopuff, mask leak was greater with one operator than with two, availability of a manometer decreased mask leak, training in mask handling reduced mask leak, and mask leak increased at higher gas flow rates. One manikin study reported no difference in mouth leak between Neopuff, SIB and FIB.

Training (six studies): Data from three studies reported that operator experience had no effect on the PIP or tidal volume provided during Neopuff use. Operators who had used Neopuff infrequently had difficulty setting up the device, but could provide ventilation with an SIB without assistance. The level of operator experience had no effect on mean airway pressures or tidal volumes during Neopuff use, but inexperienced operators provided a longer inspiratory time whilst mean airway pressures and tidal volumes remained constant.

Ongoing clinical trials (five studies): Use of Neopuff in the delivery room is being investigated in three ongoing randomized controlled trials. Main outcome measures include the incidence of transient tachypnea of the newborn, need for mechanical ventilation and surfactant in very low birthweight infants, and establishment of functional residual capacity. Comparative studies are investigating Neopuff versus SIB, with and without a PEEP valve, in infants born at >26 weeks’ gestation, and Neopuff then continuous positive airway pressure versus intermittent positive pressure ventilation in infants born at 27–33 weeks’ gestation.

CONCLUSION

Overall, there was insufficient data to allow accurate determination of the optimal manual resuscitation device for use in infants at birth. In general, though, TPR is good at providing PIPs close to the target with little variation and PEEP closer to predetermined targets compared with SIB and FIB. In addition, volutrauma appears to be less likely with TPR and inspiratory times are more consistent. However, it is more difficult for users to detect changes in compliance when using TPR for resuscitation, mask leak is higher for TPR versus SIB or FIB, and changes to gas flow during TPR have marked effects on PIP, PEEP and mask leak. In addition, the TPR is more difficult to set up and requires a higher level of operator training. The results of ongoing randomized clinical trials will help to determine whether TPR improves resuscitation outcomes and reduces morbidity compared with SIB, and whether TPR-associated sustained lung inflation is superior to SIB ventilation. Until these data become available it is recommended that healthcare providers are well trained to use the device of choice for their clinical practice, and have a good knowledge of its limitations.
KEY POINTS

• Neonatal resuscitation guidelines recommend three different devices: SIB, FIB and TPR.

• A number of different TPR devices are available, but the most popular of these is Neopuff (Fisher & Paykel Healthcare).

• TPR provides PIPs close to the target with little variation and PEEP closer to predetermined targets compared with SIB and FIB.

• PEEP is likely to be closer to predetermined values when TPR is used compared with SIB and FIB.

• Volutrauma appears to be less likely with TPR versus SIB and FIB.

• Inspiratory times are more consistent during TPR than during SIB or FIB.

• Changes in compliance are more difficult to detect when TPR is being used for resuscitation compared with SIB or FIB.

• Mask leak is higher for TPR versus SIB or FIB.

• Changes to gas flow during TPR have marked effects on PIP, PEEP and mask leak.

• TPR is more difficult to set up than SIB or FIB and requires a higher level of operator training.
Comparison of three manual ventilation devices using an intubated mannequin

**AIM**
To compare the effectiveness and consistency of mechanical ventilation provided by trained healthcare professionals using a self-inflating bag, a disposable flow-dependent anaesthesia bag with attached manometer and a Neopuff device.

**METHOD**
Healthcare professionals (10 neonatal nurses, 11 consultant pediatricians or anesthetists, 11 junior or middle-grade pediatricians or anesthetists, 1 emergency medical technician, 1 public health physician and 1 midwife) were recruited at in-service training days. All were asked to deliver mechanical ventilation to an intubated neonatal mannequin incorporating an endotracheal tube, functional lungs and pressure transducer (Fisher & Paykel Healthcare). Three different devices were used: an infant-size, silicone, self-inflating bag (Laerdal Medical); a disposable, flow-dependent, latex-free anaesthesia bag attached to a manometer (Intersurgical) and a Neopuff device (Fisher & Paykel Healthcare). Participants had to preset the Neopuff settings prior to testing. For all devices, healthcare professionals were asked to provide positive pressure ventilation for a 2-minute period at 40 breaths/min, with peak inspiratory pressure (PIP) of 20 cm H₂O and positive end-expiratory pressure (PEEP) of 4 cm H₂O. Participants were able to observe chest movements during ventilation and a manometer when using the anesthesia bag or Neopuff. No other feedback was provided.

**RESULTS**
Analysis by each specialty was not possible given the small number of participants. Therefore, subjects were allocated to one of two groups: physicians (n=23) or allied health professionals (n=12). There was no significant difference between these groups with respect to delivery of mechanical ventilation via the three different methods. However, there were significant differences in ventilatory variables between the methods, with the self-inflating bag producing much higher mean and maximum PIP, and negligible PEEP (see table). The Neopuff was able to deliver greater airway pressures than the other ventilation options (see table).

<table>
<thead>
<tr>
<th></th>
<th>Self-inflating bag</th>
<th>Anaesthesia bag</th>
<th>Neopuff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean maximum PIP, cm H₂O</td>
<td>44.7 (2.3)</td>
<td>22.6 (0.7)a</td>
<td>20.4 (0.5)a,b</td>
</tr>
<tr>
<td>Mean PIP, cm H₂O</td>
<td>30.7 (1.9)</td>
<td>18.1 (0.4)a</td>
<td>20.1 (0.1)a,b</td>
</tr>
<tr>
<td>Mean PEEP, cm H₂O</td>
<td>0.15 (0.03)</td>
<td>2.83 (0.23)a</td>
<td>4.41 (0.08)a,b</td>
</tr>
<tr>
<td>Mean airway pressure, cm H₂O</td>
<td>7.6 (0.8)</td>
<td>8.5 (0.3)</td>
<td>10.9 (0.3)a,b</td>
</tr>
<tr>
<td>Mean rate, breaths/min</td>
<td>47.1 (3.0)</td>
<td>47.3 (2.7)</td>
<td>39.7 (1.8)c,d</td>
</tr>
<tr>
<td>Total breaths ≤21 cm H₂O PIP, %</td>
<td>39 (0.07)</td>
<td>92 (0.02)a</td>
<td>98 (0.02)a</td>
</tr>
<tr>
<td>Total breaths ≤30 cm H₂O PIP, %</td>
<td>45 (0.07)</td>
<td>0a</td>
<td>0a</td>
</tr>
</tbody>
</table>

Values are mean (standard error of the mean).
a p<0.001 vs self-inflating bag; b p<0.001 vs anaesthesia bag; c p<0.05 vs self-inflating bag; d p<0.05 vs anaesthesia bag.
CONCLUSION
Accurate, reliable and reproducible manual ventilation in very low birth weight infants can be achieved by healthcare professionals using an anaesthetic bag with manometer and a Neopuff device, independent of training or specialty. In contrast, self-inflating bags are not recommended in this patient group.

KEY POINTS
• The ability to perform consistent mechanical ventilation on neonates is not dependent on healthcare professional training.
• The ability to perform consistent mechanical ventilation on neonates depends on the equipment used.
• Achievement of target ventilation rate during manual ventilation of neonates occurs more often when using a Neopuff device compared with an anaesthetic bag or a self-inflating bag.
• Self-inflating mechanical ventilation devices without a manometer should not be considered as first choice for manual ventilation of very low birth weight infants due to high PIP and minimal PEEP.
ANESTHESIA BAG
A soft rubber bag used as part of a gas flow system to monitor and control the patients breathing.

BRONCHOPULMONARY DYSPLASIA (BPD) OR CHRONIC LUNG DISEASE
A chronic lung condition that affects neonates who were born prematurely or required respiratory support after birth.

BI-LEVEL POSITIVE AIRWAY PRESSURE (BIPAP)
Respiratory therapy where two air pressures are applied, one during the inspiratory phase and a lower pressure during expiration.

CAROTID BLOOD PRESSURE (CBP)
Blood pressure measured at the carotid artery.

CLINICAL RISK INDEX FOR BABIES (CRIB) SCORE
An index of initial neonatal risk which takes into account birth weight, gestational age, minimum and maximum FiO2 and maximum base excess during the first 12 hours, and the presence of congenital malformations.

CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP)
A technique of respiratory therapy in which airway pressure is maintained above atmospheric pressure throughout the respiratory cycle by pressurization of the ventilatory circuit.

DEAD SPACE
Volume in the airway path that is common to both the inspiratory and expiratory passages. Volume of gas that does not participate in gas exchange. It is ventilated but NOT perfused by the pulmonary circulation:

• **Alveolar dead space**: Volume of gas ventilating unperfused alveoli that has no blood perfusion (shunt or pulmonary embolism).

• **Anatomic dead space**: Volume of gas within the conducting zone of the lungs and upper airway. (Amount of volume that does not enter the alveoli.)

• **Mechanical dead space**: Expired air that is re-breathed through connecting tubing.

• **Physiologic dead space**: Anatomic and alveolar dead space.

DELAYED CORD CLAMPING (DCC)
A technique where clamping of the umbilical cord is delayed until after the cord has stopped pulsating or after delivery of the placenta.

ENDOTRACHEAL TUBE (ETT)
A tube inserted through the mouth or nose into the trachea to maintain an unobstructed airway.

EXTUBATION
Withdrawing an endotracheal tube (ETT) from a patient’s airway.

FLOW-INFLATING BAG (FIB)
A hand held resuscitation device that fills with gas from a compressed flow source.

FRACTION OF INSPIRED OXYGEN (FiO2):
The proportion of oxygen in the air that is inspired.

FULL-TERM
An infant born between 37 and 40 weeks gestation.

HIGH-FREQUENCY VENTILATION (HFV)
Ventilation that uses respiratory rates that greatly exceed the rate of normal breathing and tidal volumes that are less than dead space.

HYPOTHERMIA
A condition where the body loses heat faster than it can produce it.

INTRAVENTRICULAR HEMORRHAGE
Bleeding into the ventricles of the brain (occurs most often in premature infants).

INTUBATION
The insertion of an ETT or tracheostomy tube into the trachea.

LUNG COMPLIANCE
The ability of the lungs to stretch during a change in volume relative to an applied chamber pressure.

MECHANICAL VENTILATION (MV)
The use of an invasive artificial airway to mechanically assist or replace spontaneous breathing, when patients cannot do so on their own.

NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (nCPAP)
A technique of respiratory therapy in which airway pressure is maintained above atmospheric pressure throughout the respiratory cycle by pressurization of the ventilator circuit.

NORMOTHERMIA
Normal body temperature.
OXYGEN SATURATION (SpO2)
Oxygen saturation as measured by pulse oximetry.

PARTIAL PRESSURE OF CARBON DIOXIDE (PaCO2):
The part of total blood gas pressure exerted by carbon dioxide gas; a measure of how much carbon dioxide is dissolved in the blood and how well carbon dioxide is able to move out of the body.

PARTIAL PRESSURE OF OXYGEN (PaO2)
The part of total blood gas pressure exerted by oxygen gas; a measure of how much oxygen is dissolved in the blood and how well oxygen is able to move from the airspace of the lungs into the blood.

POSITIVE END EXPIRATORY PRESSURE (PEEP)
It is a pressure above atmospheric pressure in the airway throughout the expiratory phase of positive pressure ventilation. PEEP is used during mechanical ventilation to improve oxygenation.

POSITIVE END INSPIRATORY PRESSURE (PIP)
The highest pressure applied to the lungs during inspiration.

PRESSURE SUPPORT VENTILATION (PSV)
Ventilation designed to augment a spontaneously generated breath; the patient has primary control over the frequency of the breathing, the inspiratory time and the inspiratory flow.

PRETERM
An infant born before 37 weeks gestation regardless of their weight. Usually the preterm infant are found in the NICU of the hospital on some form of respiratory support. They can be further divided into -
- Moderate to late preterm
  32 to <37 weeks gestation.
- Very preterm
  28 to <32 weeks gestation.
- Extremely preterm
  <28 weeks gestation.

RESPIRATORY DISTRESS SYNDROME (RDS)
A lung disease of the newborn, most frequently occurring in premature infants, that is caused by abnormally high alveolar surface tension as a result of a deficiency in lung surfactant; also called hyaline membrane disease.

RELATIVE HUMIDITY (RH)
The maximum amount of water a gas can hold at a given temperature.

SELF INFLATING BAG (SIB)
A hand-held resuscitation device that fills spontaneously with gas after it has been squeezed.

SURFACTANT
A substance produced in the lungs that tends to reduce the surface tension of the fluid in the lungs and helps make the small air sacs in the lung (alveoli) more stable.

SUSTAINED LUNG INFLATION (SLI)
Prolonged inflation of the lung.

T-PIECE RESUSCITATOR (TRP)
A resuscitation device that provides flow-controlled and pressure limited breaths, using gas from a compressed flow source.

TIDAL VOLUME (VT)
Volume of air inspired or expired with each normal breath. The amount of gas delivered to a patient in one breath.

WORK OF BREATHING (WOB)
The force required to expand the lung against its elastic properties.