BMJ Paediatrics Open

BMJ Paediatrics Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Paediatrics Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<u>http://bmjpaedsopen.bmj.com</u>).

If you have any questions on BMJ Paediatrics Open's open peer review process please email <u>info.bmjpo@bmj.com</u>

BMJ Paediatrics Open

What CPAP to use in the delivery room? Bench comparison of two methods to provide continuous positive airways pressure in neonates

Journal:	BMJ Paediatrics Open
Manuscript ID	bmjpo-2024-002948
Article Type:	Original research
Date Submitted by the Author:	30-Jul-2024
Complete List of Authors:	Gruber , Viktoria; Medical University of Graz Division of Neonatology, Department of Paediatrics and Adolescent Medicine Morakeas, Stephanie; Westmead Hospital, Neonatal Intensive Care Unit; Sydney University, Biomedical Engineering Hinder, Murray; Westmead Hospital; Sydney University, Department of Paediatrics and Child Health Drevhammar, Thomas; Östersunds sjukhus, Department of Anesthesiology Dronavalli, Mithilesh ; Western Sydney University Tracy, Mark; Westmead Hospital , Newborn Intensive Care Unit; Sydney University, Paediatrics and Child Health
Keywords:	Neonatology, Child Health





I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

for Review Only

What CPAP to use in the delivery room? Bench comparison of two methods to provide continuous positive airways pressure in neonates

Gruber V¹, Morakeas, S^{2,3}, Hinder M^{2,4}, Drevhammar T⁵, Dronavalli M⁶, Tracy M.B.^{2,4}

¹Medical University Graz, Department of Paediatrics and Adolescent Medicine,

Division of Neonatology, Graz, Austria

²Neonatal Intensive Care Unit, Westmead Hospital, Sydney, Australia.

³Faculty of Engineering and Information Technologies, BMET Institute, The University of Sydney, Sydney, Australia.

⁴Department of Paediatrics and Child Health, Sydney University, Sydney, Australia.

⁵Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden.

⁶Translational Health Research Institute, Western Sydney University, Penrith, NSW, Australia

TO REVIEW ONL

Corresponding Author: <u>mark.tracy@syndey.edu.au</u>

ABSTRACT

Background CPAP is a recommended first-line therapy for infants at birth with respiratory distress. Resuscitation devices incorporating CPAP delivery can have significantly different imposed resistances affecting airway pressure stability and work of breathing.

Aim To compare CPAP performance of two resuscitation devices (Neopuff T-Piece resuscitator and rPAP) in a neonatal lung model simulating spontaneous breathing effort at birth.

Methods The parameters assessed were variation in delivered pressures (ΔP), tidal volume (VT), inspiratory effort (model pressure respiratory muscle (PRM)) and work of breathing (WOB). Two data sequences were required with Neopuff and one with rPAP. 1. Set PRM with changes in VT, 2. Constant VT (preterm 6ml, term 22ml) with increased effort. Data were collected at CPAP settings of 5, 7, and 9 cmH₂O using a 1kg preterm (Compliance: 0.5 ml/cmH₂O) and 3.5kg term (1.0 ml/cmH₂O) model.

Results 2298 breaths were analysed (760 rPAP, 795 Neopuff constant VT, 743 Neopuff constant PRM). With CPAP at 9 cmH₂O: Set VT; mean ΔP (cmH₂O) rPAP vs Neopuff, 1.1 vs 5.6 (preterm) and 1.9 vs 13.4 (term), WOB (mJ) 4.6 vs 6.1 (preterm) and 35.3 vs 44.5 (term); Set PRM: the mean VT (ml) were reduced to 6.2 vs 5.2 (preterm) and 22.3 vs 17.5 (term) p<0.001. Similar results were found at pressures of 5 and 7cmH₂O.

Conclusion rPAP had smaller pressure swings than Neopuff at all CPAP levels and was thus more pressure stable. WOB was higher with Neopuff when VT was held constant. VT reduced with Neopuff when respiratory effort was constant.

INTRODUCTION

In recent years, respiratory management in the delivery room has shifted towards a less invasive approach with rising numbers of infants receiving non-invasive respiratory support.¹ Multiple trials have studied the benefits of non-invasive respiratory support for spontaneously breathing preterm infants.²⁻⁴ Systematic reviews and a meta-analysis support the early non-invasive support in preterm infants with findings of reduced incidence of BPD, death, and mechanical ventilation.^{5 6}

The European Consensus Guidelines on the Management of Respiratory Distress Syndrome recommend continuous positive airway pressure (CPAP) as the first line support for the initial stabilization of spontaneously breathing preterm infants with respiratory distress.⁷ The International Liaison Committee on Resuscitation (ILCOR) introduced CPAP as part of neonatal resuscitation to improve lung recruitment in preterm infants in 2010.⁸ Since then the use of CPAP has become increasingly common in late preterm and term infants with laboured breathing or persistent cyanosis without sufficient evidence for ILCOR recommendation.⁹ Term infants treated with non-invasive ventilation in Australasian Newborn Intensive Care Units (NICUs) have approximately doubled within the last few years.¹⁰ The use of T-piece devices with expiratory flow restriction to produce CPAP in the delivery room has been associated with an increase in pneumothorax, especially in infants with increasing gestational age.¹¹⁻¹³

BMJ Paediatrics Open

Since the first use of CPAP as a mode of non-invasive ventilation for preterm infants by Gregory et al. in 1971¹⁴, several devices and methods to generate CPAP have been introduced to clinicians. For resuscitation the number of devices capable of pressure ventilation with PEEP to a non-breathing infant and or providing CPAP to an infant that is breathing is limited. T-piece resuscitator is the most common, but a new alternative is the rPAP.¹⁵ Both have the advantage of easy transition between positive pressure ventilation (PPV) and CPAP but the resistance to breathing and method of generating CPAP is not similar. Previous research has shown differences in the resultant pressure waveforms between CPAP delivery systems ¹⁶⁻¹⁹ and large differences in expiratory resistances.²⁰

In respiratory systems, the work of breathing (WOB) is the product of pressure and volume, with the mechanical work needed for breathing referred to as total or physiological work of breathing. Imposed WOB (iWOB) is the component of work added to the patient by respiratory equipment.^{21 22} CPAP can decrease the total work of breathing in infants with respiratory distress syndrome (RDS) and surfactant deficiency by increasing the functional residual capacity (FRC), splinting airways, and optimizing breathing.^{1 23} However, the WOB may be increased by the added CPAP system resistance from the interface, connectors, and device design. It can be investigated in lung models or real patients but is sensitive to changes in breathing patterns such as VT and minute ventilation.^{21 24}

The infant's effort to breathe causes fluctuations in the pressure waveform around set CPAP levels. Pressure stability refers to the variation in pressures above and below the set mean pressure, the ΔP . Smaller ΔP when comparing CPAP systems with identical respiratory parameters can be described as more pressure stable.¹⁷ In bench tests, rPAP has shown lower imposed resistance and more pressure stability with significantly fewer inspiratory and expiratory pressure fluctuations than the Neopuff TPR.²⁰ In constant-flow CPAP systems, gas flow continues throughout the inspiratory/expiratory cycle resulting in the need for the patient's expiratory effort to overcome the flow and the resistance of the CPAP generating device during expiration, which leads to an increased expiratory work.²⁵

Lung simulators such as the Neonatal Active Lung Model (NALM) are designed to be programmable, dynamic and react to the tested device. They simulate breathing by allowing the user to set airway resistance (R_{aw}), compliance of respiratory system (C_{rs}) and tidal volumes (VT). The muscular effort needed to produce the simulated breath is labelled as the 'pressure of respiratory muscles' (PRM) in NALM.²⁶ PRM is generated with a moving piston within the NALM. Resistance and compliance can be linear or non-linear and in more complex simulations have more than one compartment. The NALM respond with changes in tidal volumes when system pressure and resistance change. Lung model simulators are thus dynamic, but the response is limited as they cannot react actively by changing the respiratory rate or inspiratory-expiratory ratio.

The NALM calculates the total WOB using the area of a pressure-volume loop of a simulated breath.²¹ This includes the simulated effort limited to inspiration with exhalation considered passive. iWOB reflects the added resistance from the CPAP device and is calculated from the pressure-volume loop at the interface. It can be split into an inspiratory and expiratory part. All measurements of work of breathing are directly affected by changes in VT and this makes reporting complicated. To

 standardize the comparison of devices either the pressure or the targeted tidal volume needs to be maintained stable.²⁷

The relationship between simulated effort and VT for resuscitation devices providing CPAP during simulated breathing has not previously been investigated. We aim to compare the delivered CPAP performance of two resuscitation devices with differing imposed resistances in a neonatal lung model simulating spontaneous breathing after birth by examining pressure stability, the effect on delivered tidal volume and simulated WOB.

METHODS

Two CPAP/PPV resuscitation systems were compared; the Inspire rPAP (Inspiration Healthcare) and the Neopuff T-piece resuscitator (Fisher and Paykel Healthcare). Both devices were connected to the Neonatal Active Lung Model (NALM, Schaller Medizintechnik, Germany, V1-4.0) which simulated spontaneous breathing modelling a preterm and term newborn infant with respiratory distress.²⁸⁻³¹ Prior to connection to either CPAP device the NALM was set as per previous researchers for these models ^{16 19 32 33} on 'spontaneous breathing' and is representative of a term 3500 g (C_{rs}:1 ml/cmH₂O, inflation rate 50/min, inspiratory time 0.4sec) and preterm 1000g (C_{rs}:0.5ml/cmH₂O, 70/min, 0.3sec) infant with respiratory distress (supplementary material).¹⁹

Before recording the NALM was equilibrated for 30 minutes and calibrated. The pressure and flow of the tested resuscitation devices were adjusted using a ventilator calibration analyser (Flow Analyser PF-300 IMT Medical, Buchs, Switzerland). The

PEEP was set by adjusting the total flow on Inspire rPAP (7.1L/min for 5.0 cm H₂O, 9.0 L/min for 7 cm H₂O, 10.7L/min for 9.0 cm H₂O), Neopuff was set up with a total flow of 10L/min for all PEEP values. The experiments were conducted without leak, using non-humidified gas at ambient room temperature and with no facemask interface. We found a significant drop in delivered VT comparing to set NALM values when connecting the Neopuff TPR to NALM in both term and preterm models. This did not occur with rPAP. To fairly examine the WOB aspect, changes in PRM were adjusted to maintain a constant VT since in a system with a constant compliance, the WOB is proportional to VT.²⁴ Two data sequences were collected with Neopuff due to examine both states of constant VT and constant PRM. As there was no change in rPAP from set NALM values only one data sequence was collected.

Data analysis

Data were collected from the NALM over 2 minutes for each setting. These data were imported into Stata V.18 MP (StataCorp, College Station, USA). Each respiratory cycle was identified by pressure waveform changes of PRM in Stata. The measured parameters included the mean CPAP pressure, minimum and maximum airway pressures and their difference (Δ P), VT, PRM and WOB (total WOB calculated by NALM). Mean values for those parameters are reported in Table 3. Analysis of variance (ANOVA) for repeated measures was used to determine differences in mean and Coefficient of Variation(CV%) for measured parameters at different set PEEP values and compliance between the two tested devices. Differences between means determined by multiway ANOVA were reported with p

 values adjusted. F test using Box's conservative epsilon; p values <0.05 were considered statistically significant. Bonferroni corrections of estimates were made to adjust for multiple comparisons.

RESULTS

2298 simulated breaths were analysed comprising 760 with rPAP, 795 with Neopuff with constant VT and 743 with Neopuff and constant PRM.

Pressure

Pressure swings were significantly lower with rPAP compared to Neopuff, across all PEEP values in preterm and term models for both settings (VT or PRM constant) Figure 1 and Table 1. The largest ΔP were seen at higher PEEP levels in sequence 2 (constant VT) with a mean of 1.1 vs 5.6 cmH₂O rPAP vs Neopuff, CV% 13% vs 3.5% in the preterm model and 1.9 vs 13.4 cmH₂O rPAP vs. Neopuff CV 7.3% vs 2.6% in the term model. The high CV% observed with rPAP can be attributed to the noisy signal produced by rPAP (Table 1).

A higher PEEP had a greater impact on ΔP with Neopuff compared to rPAP: Mean ΔP 9.4-13.4 cmH₂O Neopuff vs 1.7-1.9 cmH₂O rPAP (ranges for PEEP 5-9, term model). A larger increase in ΔP was recorded in both term and preterm constant VT model with the Neopuff (mean 5.6 preterm vs 13.4 cmH₂O term) compared to rPAP (1.1 preterm vs 1.9 cmH₂O term).

Tidal volume

In simulations with the constant inspiratory effort (PRM), the largest reduction in VT were seen in the term model at PEEP 9 cmH_2O with Neopuff where VT were reduced to a mean of 17.5 ml compared to rPAP of 22.3 ml. Similar findings could be observed

in the preterm model 6.2 vs. 5.2 ml for rPAP vs. Neopuff at highest set PEEP. Showing a VT reduction of 20.5% in the term model and 13.3% in the preterm model (set PEEP 9) with constant inspiratory effort. These findings were less pronounced at lower PEEP levels. (Table 1 and Figure 2)

In the sequence with constant VT, the inspiratory effort (PRM) was adjusted for Neopuff. The highest required PRM were at 9 cm CPAP with a total increase in effort of 2.6 cmH₂O in the preterm and 6.1 cmH₂O in the term model.

Work of breathing

In simulations with constant VT the total WOB was significantly higher with Neopuff. The greatest differences were seen at the highest PEEP level, mean 4.6 vs 6.1 mJ, CV 1.2 vs 1.6% in preterm and 35.3 vs 44.5 mJ, CV 1.6% vs 1.3% in term model rPAP vs Neopuff. A higher increase in WOB between PEEP levels was present with Neopuff (mean 5.2-6.1mJ preterm and 42.7-44.5mJ term) compared to rPAP (4.7-4.6 mJ preterm and 35.2-35.3 mJ term). Examples of pressure-volume loops are presented in Figure 3.

Preterm (1000g) CPAP P min (cm H,Q) P max (cm H,Q) VT (cm H,Q) VT (cm H,Q) Cm H,Q) Imasured (cm H,Q) Effort (cm H,Q) W0B (m (cm H,Q) rPAPI 5 5.0.10% 5.6.1.3% 0.7.13% 6 6.4.9% 12.7.8% 4.7.13% 9 8.9.10% 10.0.10% 1.1.13% 6 6.2.6.7% 12.2.3% 4.6.1.28 NP: VT constant 5 3.5.2.6% 7.2.1.1% 3.9.4.7% 6 6.5.3.33% 1.4.8.3% 6.1.1.48 5.5.1.8% 6 6.6.3.3.3% 1.4.8.3% 6.1.1.48 5.5.0.8% NP: Effort constant 5 3.5.2.6% 7.1.2.7% 3.6.6% NA 5.9.62% 12.2.4.2% 4.3.1.8% 5.1.1.6% NP: Effort constant 5 3.5.2.6% 7.1.2.7% 3.6.9% NA 5.7.34K 12.2.2.2% 4.3.1.8% 5.3.1.6% NP: Effort constant 5 3.5.2.6% 7.1.2.7% 3.6.9% 12.2.2.3.2% 4.2.2.2.2.4.3.2% 4.3.1.8% NP: Effort constant 5 4.1.2%	e 11 of 24			BM.	Paediatrics (Jpen			
CPAP P min [cm H,0] P max [cm H,0] Δ P (cm H,0] VT set [ml] VT measured [ml] Effort (cm H,0] WOB [m (cm H,0] rPAP 5 5.0, 1.0% 5.6, 1.3% 0.7, 1.3% 6 6.4, 9% 127, 8% 4.6, 1.12% 9 8.9, 10% 10.0, 1.0% 1.1, 13% 6 6.2, 6.7% 122, 3% 4.6, 1.24% NP: VT constant 5 3.6, 2% 7.5, 2.1% 3.9, 4.7% 6 6.3, 3.3% 143, 3% 5.8, 1.36% PF: Effort constant 5 3.5, 2.6% 7.1, 2.7% 3.6, 0% NA 5.9, 3.5% 1.48, 3% 5.8, 1.36% P 6, 6, 1.7% 122, 0.9% 5.6, 3.5% 6 6.4, 3.3% 143, 3% 5.8, 1.36% P 9 6.9, 1.9% 4.3, 4.4% NA 5.7, 3.4% 122, 2.9% 8.3, 1.38 P 6 6.9, 1.9% 4.7, 6.8% NA 5.2, 7.8% 124, 6.3% 5.2, 3.5% Term (3500g) 7 6.9, 1.9% 1.7, 2.4% 1.7, 7.3% 22 2.5, 2	Preterm (1000g)								
Image:	(8)	СРАР	P min	P max	ΔΡ	VT set	VT	Effort	WOB [m.
PAPI 5 5.0, 1.0% 5.6, 1.3% 0.7, 13% 6 6.4, 9% 12.7, 8% 4.6, 1.1% 9 8.9, 10% 10.0, 1.0% 1.1, 13% 6 6.3, 5.5% 12.2, 3% 4.6, 1.1% 9 8.9, 10% 10.0, 1.0% 1.1, 13% 6 6.3, 3.3% 13.3, 2.7% 5.0, 3.3% 9 6.6, 1.7% 12.2, 0.9% 5.6, 3.5% 6 6.4, 3.3% 14.3, 3% 5.8, 1.3% 9 6.6, 1.7% 12.2, 0.9% 5.6, 3.5% 6 6.4, 3.3% 14.3, 3% 5.8, 1.3% NP: Effort constant 5 3.5, 2.6% 7.1, 2.7% 3.6, 6% NA 5.7, 8.4% 12.2, 2.9% 4.3, 1.16% Term (3500) 7 6.3, 1.1% 1.1, 0.8% 4.7, 6.3% NA 5.2, 2.3% 2.4, 3.2% 3.5.2, 1.1% PAPI 5 4.4, 2.% 6.1, 2.4% 1.7, 9.4% 22 22.5, 2.3% 24.4, 3.2% 35.2, 1.1% PAPI 7 6.3, 1.1% 10.2, 1.3% 1.7, 9.4% 22 22.5, 2.3%		[cm H ₂ O]	[cm H ₂ O]	[cm H ₂ O]	[cm H₂O]	[ml]	measured [ml]	[cm H ₂ O]	
7 6.8, 1% 7, 7.8 0.9, 10.1% 6 6.3, 5, 5% 122, 3% 4.6, 1.18 9 8.9, 10% 10, 1.0% 1, 1.3% 6 6.2, 6.7% 122, 3% 4.6, 1.28 NP: VT constant 5 3.6, 2% 7.5, 2.1% 3.9, 4.7% 6 6.6, 3.5% 1.3, 3, 7% 5.2, 0% 9 6.6, 1.7% 122, 0.9% 5.6, 3.5% 6 6.4, 3.3% 1.3, 8, 7% 5.3, 0.8% 9 6.5, 1.5% 1.16, 1.8% 4.7, 6.8% NA 5.7, 3.4% 122, 2.9% 4.3, 1.18 9 6.3, 1.9% 11.6, 1.8% 4.7, 6.8% NA 5.7, 3.4% 12.4, 6.2% 4.1, 1.6% 9 6.3, 1.1% 1.9, 6.9% 22 22.5, 2.4% 35.2, 1.1% 9 8.3, 1.1% 10.2, 1.4% 1.7, 9.4% 22 22.5, 2.3% 35.2, 1.1% 9 8.3, 1.1% 10.2, 1.5% 9.4, 2.5% 22 22.3, 3.2% 24.4, 3.2% 35.4, 1.1 9 8.3, 1.1% 10.2, 1.5% 3.4, 2.6%	rPAP ¹	5	5.0, 1.0%	5.6, 1.3%	0.7, 13%	6	6.4, 9%	12.7, 8%	4.7, 1.3%
9 8,9,10% 10.0,10% 1.1,13% 6 6,2,6.7% 12.2,3% 4,6,1.2% NP: VT constant 5 3,6,2% 7,5,2.1% 3,9,4.7% 6 6,5,3,3% 13.2,2% 5,2,0.9% 9 6,6,1.7% 12.2,0.9% 5,6,3.5% 6 6,4,3.3% 12.4,2% 4,5,0.8% NP: Effort constant 5 3,5,2.6% 7,1.2.7% 3,6,6% NA 5,9,6.2% 12,4,2.9% 4,3,1.3% 9 6,9,1.5% 4,3,4.4% NA 5,7,3.4% 12,2,2.9% 4,3,1.3% 9 6,9,1.5% 4,2,6% NA 5,2,7.3% 12,4,2.2% 4,3,1.3% 9 6,9,1.5% 12,4,2.4% 1,7,9.4% 22 22,5,4.7% 24,4,3.2% 35,2,1% 9 6,3,1.1% 10,2,1% 10,7,1.5% 9,7.3% 22 22,5,4.7% 24,4,3.3% 35,3,16 NP: VT constant 5 1,4,8% 10,2,1% 17,9,7.3% 22 22,6,2% 42,5,1.3% NP: Effort constant 5 1		7	6.8, 1%	7.7, 1%	0.9, 10.1%	6	6.3, 5,5%	12.2, 3%	4.6, 1.1%
NP: VT constant \$ 3.6, 2% 7.5, 2, 1% 9.4, 7% 6 6, 3, 3.3% 13.3, 2.7% 5, 2, 0.5% P 5, 1, 1.7% 10, 1.4% 4.9, 4% 6 6, 6, 3, 3.3% 13.3, 2.7% 5, 2, 1.3% P 6, 6, 1.7% 10, 1.4% 4.9, 4% 6 6, 6, 3, 3.3% 14.8, 3% 5, 8, 1.3% P 6, 6, 1.7.5% 7, 2, 2.0% 6, 1.5% 6 6, 4, 3.3% 12, 4.2% 4.5, 0.8% P 5 4, 1.6% 9, 6, 1.5% 4.3, 4.4% NA 5, 7, 3.4% 12, 2.2, 9% 3, 1.3 13, 1.3 13, 1.4% 14, 1.6% 12, 2.2% 4.1, 1.6% Ferm (350g) T 7 6.3, 1.1% 1.1, 1.1% 1.9, 6.3% 22 2.2, 5, 4.7% 2.4, 4.3% 3.5, 3.1% P AB ³ 5 4, 4, 2% 6.1, 2.4% 1.7, 9.4% 22 2.2, 6, 2.4% 2.4, 3.3% 3.5, 3.1% P AB ³ 1, 3% 1.9, 7.3% 22 2.2, 3, 2.2% 2.4, 3.3% 3.5, 3.1% 3.5, 3.1% 3.5, 3.1%		9	8.9, 10%	10.0, 1.0%	1.1, 13%	6	6.2, 6.7%	12.2, 3%	4.6, 1.2%
7 5.1, 1.7% 10, 1.4% 4.9, 4% 6 6.6, 3.5% 14.3, 3% 5.8, 1.3% 9 6.6, 1.7% 12, 2, 0.9% 5.5, 3.5% 6 6.4, 3.3% 1.8, 3% 6.1, 1.6, 1.5% 7 5.4, 1.6% 9.6, 1.5% 4.3, 4.4% NA 5.7, 3.4% 12.2, 4.2% 4.3, 1.3% 9 6.9, 1.9% 11.6, 1.8% 4.7, 6.8% NA 5.2, 7.8% 12.1, 6.2% 4.1, 1.6% 10.6 1.3% 4.7, 6.8% NA 5.2, 7.8% 12.1, 6.2% 4.1, 1.2% 7 6.3, 1.1% 8.1, 1.1% 1.9, 6.9% 22 22.5, 2.8% 24.4, 3.2% 35.3, 1.6 10.7 7 6.3, 1.1% 1.0, 2.1% 1.0, 7.3% 22 22.3, 3% 24.4, 3.2% 35.3, 1.6 NY: VT constant 5 1.0, 3% 10.2, 1.3% 13.4, 1.3% 11.7, 2.5% 22 22.6, 2.9% 24.5, 3.3% 24.5, 2.9% 24.4, 3.3 31.6, 1.2% VT constant 5 1.4, 8.7% 9.8, 2.6% 8.4, 3.7% NA <	NP: VT constant	5	3.6, 2%	7.5, 2.1%	3.9, 4.7%	6	6.3, 3.3%	13.3, 2.7%	5.2, 0.9%
9 6.6, 1.7% 12.2, 0.9% 5.6, 3.5% 6 6.4, 3.3% 14.8, 3% 6.1, 1.6% NP: Effort constant 5 3.5, 2.6% 7, 1, 2.7% 3.6, 6% NA 5.9, 6.2% 12.2, 4.2% 4.5, 0.3% 9 6.9, 1.9% 11.6, 1.8% 4.7, 6.8% NA 5.7, 3.4% 12.2, 2.9% 4.4, 2.4% 4.1, 1.6% Ferm (3500) 7 6.3, 1.1% 1.0, 1.8% 4.7, 6.8% NA 5.2, 7.8% 12.1, 6.2% 4.1, 1.6% Ferm (3500) 7 6.3, 1.1% 10.2, 1% 1.9, 7.3% 22 22.5, 4.7% 24.4, 3.2% 35.2, 1% 9 8.3, 1.1% 10.2, 1% 1.9, 7.3% 22 22.5, 4.7% 24.4, 3.2% 35.3, 1.6 9 3.1, 5.9% 16.5, 1.3% 13.4, 2.6% 22 22.2, 3.2% 24.4, 3.2% 35.3, 1.6 9 3.1, 5.9% 16.5, 1.3% 13.4, 2.6% NA 18.6, 3% 24.5, 3% 29.1, 12 VT with rPAP remained constant t3 set effort. 7 2.6, 6.6% 12.4, 1.3% <t< td=""><td></td><td>7</td><td>5.1, 1.7%</td><td>10, 1.4%</td><td>4,9, 4%</td><td>6</td><td>6.6, 3.5%</td><td>14.3, 3%</td><td>5.8, 1.3%</td></t<>		7	5.1, 1.7%	10, 1.4%	4,9, 4%	6	6.6, 3.5%	14.3, 3%	5.8, 1.3%
NP: Effort constant 5 3.5, 2.6% 7.1, 2.7% 3.6, 6% NA 5.9, 6.2% 12.2, 2.42% 4.5, 0.8% 9 6.9, 1.9% 11.6, 1.8% 4.3, 4.4% NA 5.7, 3.4% 12.2, 2.9% 4.3, 1.3% 10 6.9, 1.9% 11.6, 1.8% 4.7, 6.8% NA 5.2, 7.8% 12.1, 6.2% 4.1, 1.69 Ferm (3500g) 7 6.3, 1.3% 8.1, 1.1% 10.9, 6.9% 22 22.5, 2.8% 24.6, 3% 35.2, 1% 9 8.3, 1.1% 10.2, 1% 1.9, 7.3% 22 22.3, 3.2% 24.4, 3% 35.3, 1.6 NP: VT constant 5 1.10% 10.5, 1.5% 9.4, 2.5% 22 22.3, 3.2% 24.4, 3% 35.3, 1.6 NP: VT constant 5 1.4, 8% 13.4, 1.3% 13.4, 2.6% 22 21.5, 3.3% 29.8, 2.8% 8.4.4, 0.9 9 3.1, 5.9% 16.5, 1.3% 13.4, 2.6% 9.8, 2.6% NA 18.6, 3% 24.5, 3% 29.1, 12 VT with rPAP remained constant at set effort. VT in these simulations reduced and W		9	6.6, 1.7%	12.2, 0.9%	5.6, 3.5%	6	6.4, 3.3%	14.8, 3%	6.1, 1.6%
7 5.4, 1.6% 9.6, 1.5% 4.3, 4.4% NA 5.7, 3.4% 12.2, 2.9% 4.3, 1.3% 9 6.9, 1.9% 11.6, 1.8% 4.7, 6.8% NA 5.2, 7.8% 12.1, 6.2% 4.1, 1.6% PPAP ¹ 5 4.4, 2% 6.1, 2.4% 1.7, 9.4% 22 22.5, 2.8% 24.4, 3% 35.3, 1.6 9 8.3, 1.1% 10.2, 1.5% 1.9, 7.3% 22 22.3, 3.2% 24.4, 3% 35.3, 1.6 NP: VT constant 5 1.0% 10.5, 1.5% 9.4, 2.5% 22 22.6, 2.9% 28.6, 2.9% 42.7, 1.8 9 3.1, 1.9% 10.4, 1.3% 11.7, 2.5% 22 22.3, 3.2% 24.4, 3.0% 35.3, 1.6 NP: VT constant 5 1.4, 8% 13.4, 1.3% 11.7, 2.5% 22 22.3, 3.2% 24.5, 2.9% 4.5, 1.3 NP: Effort constant 5 1.4, 8% 9.8, 2.6% NA 18.6, 3% 24.5, 2.9% 30.4, 1.2 9 3.1, 3.13% 1.1% 1.0% 1.0% 1.0% 1.0% 1.	NP: Effort constant	5	3.5, 2.6%	7.1, 2.7%	3.6, 6%	NA	5.9, 6.2%	12.2, 4.2%	4.5, 0.8%
9 6.9, 1.9% 11.6, 1.8% 4.7, 6.8% NA 5.2, 7.8% 12.1, 6.2% 4.1, 1.6% IPPAP ¹ 5 4.4, 2% 6.1, 2.4% 1.7, 9.4% 22 22.5, 4.7% 24.4, 3.2% 35.2, 1% PPAP ¹ 7 6.3, 1.1% 1.0, 1.3% 1.9, 6.9% 22 22.5, 2.8% 24.4, 3% 35.3, 1.6 9 8.3, 1.1% 10.2, 1% 1.9, 7.3% 22 22.3, 3.2% 24.4, 3% 35.3, 1.6 NP: VT constant 5 1.10% 10.2, 1% 1.9, 7.3% 22 22.3, 3.2% 24.4, 3% 35.3, 1.6 9 8.3, 1.3% 1.3, 4.1% 1.9, 5.3% 22 22.3, 3.3% 29.8, 2.8% 4.4, 0.9% 22 21.5, 3.3% 29.8, 2.6% 1.8, 7.8% 1.3, 1.1% 1.9, 5.3.1% 24.5, 3.9% 29.1, 1.2 9 4.1, 4.3% 1.5, 1.1% 1.0, 9.2.8% NA 18.6, 3% 24.5, 3.9% 29.1, 1.2 VT with rPAP remained constant at set effort. 24.1 1.0% 1.0.9, 2.8% NA 1.7, 5.3.1% 2		7	5.4. 1.6%	9.6. 1.5%	4.3.4.4%	NA	5.7.3.4%	12.2. 2.9%	4.3. 1.3%
Term (3500g) Property 5 4.4, 2% 6.1, 2.4% 1.7, 9.4% 22 22.5, 2.7% 24.4, 3.2% 35.2, 1% 7 6.3, 1.1% 8.1, 1.1% 1.9, 6.9% 22 22.5, 2.8% 24.6, 3% 35.4, 1.1 9 8.3, 1.1% 10.2, 1% 1.9, 7.3% 22 22.3, 3.2% 24.4, 3.8% 35.3, 1.6 NP: VT constant 5 1, 10% 10.5, 1.5% 9.4, 2.5% 22 22.6, 2.9% 28.6, 2.9% 44.4, 0.9 9 3.1, 5.9% 15.5, 1.5% 9.4, 2.5% 22 22.6, 2.9% 28.6, 2.9% 44.5, 1.3% NP: Effort constant 5 1.4, 9% 9.8, 2.6% 8.4, 3.7% NA 19.5, 3.1% 20.6, 2.9% 44.5, 1.3 NP: Effort constant 5 1.4, 9% 9.8, 2.6% NA 17.5, 3.1% 24.5, 3.1% 31.6, 1.2 7 2.6, 4.6% 1.5, 1.3% 1.0, 2.3% NA 17.5, 3.1% 24.5, 3.3% 29.1, 1.2 VT with rPAP remained constant at set effort. 2 2 2.5, 3.3%		9	6.9. 1.9%	11.6. 1.8%	4.7.6.8%	NA	5.2. 7.8%	12.1.6.2%	4.1. 1.6%
Trype 5 4.4, 2% 6.1, 2.4% 1.7, 9.4% 22 22.5, 4.7% 24.4, 3.2% 35.2, 1% P 7 6.3, 1.1% 8.1, 1.1% 1.9, 6.9% 22 22.5, 2.8% 24.6, 3% 35.4, 1.1 9 8.3, 1.1% 10.2, 1% 1.9, 7.3% 22 22.3, 3.2% 24.4, 3% 35.3, 1.6 NP: VT constant 5 1, 10% 105.5, 1.5% 9.4, 2.5% 22 22.6, 2.9% 28.6, 2.9% 44.7, 1.1 7 1.8, 7.8% 13.4, 1.3% 11.7, 2.5% 22 22.6, 2.9% 24.5, 2.9% 44.5, 1.3% 9 3.1, 5.9% 16.5, 1.3% 13.4, 2.6% 22 21.5, 3.1% 30.6, 2.9% 44.5, 1.3% 9 2.6, 4.6% 12.4, 1.3% 9.8, 2.6% NA 17.5, 3.1% 24.5, 2.9% 20.4, 1.2 9 1.4, 4.3% 15, 1.1% 10.9, 2.8% NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant t set effort. VT WOB in preterm and term model at different set PEEP levels.	Term (3500g)		010) 210/0		, e.e.,e		0.2,71070	12.2, 0.2,0	
TM J FA LA LA <thla< th=""> LA <thla< th=""> LA</thla<></thla<>	rDAD ¹	5	11.2%	6124%	1794%	22	225 / 7%	21132%	35 2 1%
J 0.03, 11.% 0.1, 1.% 1.9, 7.3% 22 22.3, 3.2% 24.4, 3.% 35.3, 1.6 NP: VT constant S 1, 10% 10.5, 1.5% 9.4, 2.5% 22 22.3, 3.2% 24.4, 3.% 35.3, 1.6 NP: VT constant S 1, 10% 10.5, 1.5% 9.4, 2.5% 22 22.3, 3.2% 24.4, 3.% 35.3, 1.6 NP: Torstant S 1, 10% 10.5, 1.5% 9.4, 2.5% 22 22.3, 3.2% 24.4, 3.3% 13.4, 2.6% 9 3.1, 5.9% 16.5, 1.3% 13.4, 2.6% A2 21.5, 3.1% 24.5, 3.1% 31.6, 1.2 7 2.6, 4.6% 12.4, 1.3% 19.2, 2.6% NA 18.6, 3% 24.5, 3.3% 29.1, 1.2 VT with rPAP remained constant 4 set effort. NA 10.9, 3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant 4 set effort. NA 18.6, 3% 24.5, 3% 29.1, 1.2 VI with rPAP remained constant 4 set effort. NO NO NO NO NO NO NO NO NO <		7	6 2 1 1%	8 1 1 1%	1.7, 5.4%	22	22.3, 4.7%	24.4, 5.270	25 / 1 1
J O.S. A.1.70 V.2. 170 V.2. 170 <th< td=""><td></td><td>, 9</td><td>Q 2 1 10/</td><td>10.2 10/</td><td>10 7 20/</td><td>22</td><td>22.3, 2.0/0</td><td>24.0, 370</td><td>25 2 1 4</td></th<>		, 9	Q 2 1 10/	10.2 10/	10 7 20/	22	22.3, 2.0/0	24.0, 370	25 2 1 4
Virtue 3 1, 10% 10.3, 13% 3%, 2.3% 122 220, 2.3% 20.6, 2.3% 42.7, 11 9 3.1, 5.9% 16.5, 1.3% 13.4, 2.6% 22 21.5, 3.1% 30.6, 2.9% 44.5, 1.3 NP: Effort constant 5 1.4, 8% 9.8, 2.6% 8.4, 3.7% NA 19.5, 3.1% 24.5, 5.3.1% 31.6, 1.2 7 2.6, 4.6% 12.4, 1.3% 9.8, 2.6% 8.4, 3.7% NA 19.5, 3.1% 24.5, 2.9% 30.4, 1.2 9 4.1, 4.3% 9.8, 2.6% 8.4, 3.7% NA 19.5, 3.1% 24.5, 2.9% 30.4, 1.2 9 4.1, 4.3% 15, 1.1% 10.9, 2.8% NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant at set effort. XT 11.4.8% 10.9, 2.8% NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant at set effort. XT 11.4.8% 10.9, 2.8% NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VIT with rPAP remained constant protocont at set off constant protocont at set off cont at set		5	1 100/	10.2, 170	1.3, 7.3%	22	22.3, 3.270	24.4, 5%	10 7 1 1
Image: Product of the system Image: Product of the system <th< td=""><td></td><td>5</td><td>1, 10%</td><td>10.5, 1.5%</td><td>9.4, 2.5%</td><td>22</td><td>22.0, 2.9%</td><td>20.0, 2.9%</td><td>42.7, 1.1</td></th<>		5	1, 10%	10.5, 1.5%	9.4, 2.5%	22	22.0, 2.9%	20.0, 2.9%	42.7, 1.1
9 3.1, 5.3% 15.1, 1.3% 13.4, 2.0% 22 21.5, 3.1% 30.6, 2.3% V4.5, 1.3 NP: Effort constant 5 1.4, 8% 9.8, 2.6% NA 19.5, 3.1% 24.5, 3.1% 31.6, 1.2 7 2.6, 4.6% 12.4, 1.3% 9.8, 2.6% NA 18.6, 3% 24.5, 3.1% 30.6, 1.2 9 4.1, 4.3% 15, 1.1% 10.9, 2.8% NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant at set effort. VX VX 10.9, 2.8% NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant at set effort. VX VX Inthese simulations reduced and WOB not comparable to constant VT All differences significant p<0.001, ANOVA repeated measurements VT PREAD		/	1.8, 7.8%	13.4, 1.3%	11.7, 2.5%	22	22.3, 3%	29.8, 2.8%	44.4, 0.9
NY: Errort constant 5 1.4, 8% 9.8, 2.6% NA 19.5, 3.1% 24.5, 3.1% 31.6, 1.2 7 2.6, 4.6% 12.4, 1.3% 9.8, 2.6% NA 18.6, 3% 24.5, 2.9% 30.4, 1.2 9 4.1, 4.3% 15, 1.1% 10.9, 2.8% NA 18.6, 3% 24.5, 3.% 20.1, 1.2 VT with rPAP remained constant at set effort. VT NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VT in these simulations reduced and WOB not comparable to constant VT All differences significant p<0.001, ANOVA repeated measurements VT All differences significant p<0.001, ANOVA repeated measurements Table 1 Comparison of rPAP and Neopuff (NP): Mean and Coefficient of Variation% for P, VT, PRM an WOB in preterm and term model at different set PEEP levels. VOB VT VT PRM an WOB		9	3.1, 5.9%	16.5,1.3%	13.4, 2.6%	22	21.5, 3.1%	30.6, 2.9%	44.5, 1.3
Y 2.6, 4.6% 12.4, 1.3% 9.8, 2.6% NA 18.6, 3% 24.5, 2.9% 00.4, 1.2 9 4.1, 4.3% 15, 1.1% 10.9, 2.8% NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant at set effort. VT with rPAP remained constant at set effort. VT in these simulations reduced and WOB not comparable to constant VT All differences significant p<0.001, ANOVA repeated measurements	NP: Effort constant	5	1.4, 8%	9.8, 2.6%	8.4, 3.7%	NA	19.5, 3.1%	24.5, 3.1%	31.6, 1.2
9 4,1,4,3% 15,1,1% 10,9,2.8% NA 17,5,3,1% 24,5,3% 29,1,1,2 VT with rPAP remained constant at set effort. VT in these simulations reduced and WOB not comparable to constant VT All differences significant p<0.001, ANOVA repeated measurements		7	2.6, 4.6%	12.4, 1.3%	9.8, 2.6%	NA	18.6, 3%	24.5, 2.9%	30.4, 1.2
VT with rPAP remained constant at set effort. ² VT in these simulations reduced and WOB not comparable to constant VT All differences significant p<0.001, ANOVA repeated measurements Table 1 Comparison of rPAP and Neopuff (NP): Mean and Coefficient of Variation% for P, VT, PRM an WOB in preterm and term model at different set PEEP levels.		9	4.1, 4.3%	15, 1.1%	10.9, 2.8%	NA	17.5, 3.1%	24.5, 3%	29.1, 1.2
	Table 1 Compar WOB in preterm	ison of rP n and term	AP and Nec n model at	opuff (NP): I different se	Vlean and C t PEEP leve	Coefficien Is.	t of Variatior	1% for P, VT	, PRM an

DISCUSSION

This bench test has confirmed that in both term and preterm NALM models simulating breathing with respiratory distress, the T-piece resuscitator (Neopuff) affects breathing with larger pressure swings around the set CPAP level compared to that measured with rPAP. The increased resistance to breathing was reflected in both ΔP , tidal volumes and the effect on PRM. The overall impact of using Neopuff TRP compared to rPAP to deliver CPAP in our models led to either the tidal volume reducing or a required increase in simulated effort.

Significant differences were also found in WOB levels recorded by the NALM. At a constant compliance the elastic WOB is proportional to the VT.³⁴ Interpreting WOB in our dynamic active model is more complex with the calculations being dependent on the VT and, for total WOB, the simulated effort. Since the added device resistance reduces the VT or requires an increase in simulated effort, this must be accounted for when looking at the absolute values of work of breathing and is a limiting factor in this bench test. Nonetheless, our findings of WOB are consistent with the in-vivo study by Pandit et al. comparing variable to constant flow CPAP devices ²⁵ but could not be confirmed by Courtney et al.³⁵

Fluid clearance in transition to breathing happens quickly ³⁶ with dynamic changes in lung compliance and resistance. This transition is difficult to simulate in current lung simulators. Limitations are 1. The bench testing on fixed respiratory function parameters, which are not representative of these dynamic changes after birth. 2. Our model was intentionally designed to be leak free, 3. The inability to split the work of breathing value of the NALM to an inspiratory and expiratory component. 4. Infants alter respiratory rate more than VT to maintain minute ventilation which cannot be modelled with simulators and the general translation of this bench model to in vivo results needs further investigation.

Infants breathing on identical respiratory support systems with the same settings might have a different iWOB and different inspiratory flow rates.²¹ Increasing the fresh gas flow to Neopuff TPR increased

BMJ Paediatrics Open

pressure stability.²⁰ This has not been investigated in our study. A higher flow on Neopuff might be beneficial in terms of less effort, especially for CPAP use over a longer period. An increased iWOB compared to the WOB of spontaneous breathing is assumed to play a role in CPAP failure.²¹

Whether there are benefits of pressure fluctuations in the initial aeration is uncertain but high resistance might reduce peak flows and tidal volumes. A recent animal study by Kuypers et al. in intubated preterm rabbits receiving PPV using higher expiratory resistance showed reduced deflation rates and increased the accumulation of FRC over time.³⁷ Concerns of adverse effects caused by larger pressure fluctuations such as a higher incidence of pneumothorax have been raised.¹⁸ Use of CPAP for newborn stabilization with a Tpiece system has shown an increased rate of pneumothorax, especially in late preterm and term infants.¹¹ ¹³ This might be associated with faster lung compliance changes in this group. Additionally, high system resistance could increase the risk of inadvertent PEEP due to a shorter expiration time.³⁸

Previous clinical and bench studies report larger VTs and greater changes in lung volume in variable vs continuous flow CPAP.^{25 19 20} Cook et al. found VT drops with a constant inspiratory effort on higher PEEP levels, which were less pronounced in CPAP systems with flow opposition.¹⁶ This is confirmed by the findings in our bench test.

Flow opposition CPAP systems showed an advantage regarding extubation success in preterms.³⁹ A recently performed randomised controlled trial by Donaldsson et al. comparing the more pressure-stable rPAP to the Neopuff TPR reported a reduced delivery room intubation using the dual flow system.⁴⁰ We hypothesize that pressure stability of CPAP systems may be of importance in the early phase during transition to breathing in newborns requiring airway pressure support. In-vivo studies are needed to assess the actual imposed (inspiratory and expiratory) WOB with relation to dynamic changes of lung compliance and resistance during transition.

Prolonged support using resuscitation CPAP systems occurs in many settings whilst awaiting inter-hospital transfer. Our findings of differences in pressure stability and the impact of WOB may be particularly relevant in these clinical scenarios.

CONCLUSION

Our study showed large differences between the two resuscitation systems related to the imposed respiratory resistance of the CPAP devices. rPAP device had smaller pressure swings than Neopuff at all CPAP levels and was more pressure stable. WOB was higher with a greater respiratory effort with Neopuff ιgher pres. Ints, particularly te when VT was held constant, and VT reduced with Neopuff when respiratory effort was constant. This bench test supports the theory that devices with higher pressure stability and lower iWOB might be preferential in the stabilization of newborn infants, particularly term infants.

1	WHAT IS	ALREADY KNOWN ON THIS TOPIC?
2 3 4	-	Lung transition from fetal circulation to independent breathing and lung aeration is
5 6		accompanied by rapid changes in lung compliance with implications for CPAP delivery systems.
7 8 0	-	Resuscitation devices used for CPAP have differences in imposed expiratory resistance with
9 10 11		implications for pressure stability and work of breathing.
12 13		
14 15 16	WHAT TH	IS STUDY ADDS?
17 18 10	-	Increased system resistance for Neopuff led to either the reduction of tidal volume with
20 21		constant effort or increased effort compared to rPAP if the tidal volume was maintained
22 23 24		constant.
24 25 26	-	Airway pressure stability in CPAP systems can significantly affect the work of breathing.
27 28 20		
29 30 31	HOW THI	S STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY?
32 33	-	A required higher effort between different CPAP delivery systems at the same CPAP level might
34 35 36		lead to respiratory exhaustion and CPAP failure.
37 38	-	If CPAP is required for long periods related to interhospital transfer, devices with lower
39 40 41		expiratory resistance and higher pressure stability may be preferable.
42 43		
45 46		
47 48 49		
50 51		
52 53 54		
55 56		
57 58		
59 60		

Figures legend

 Figure 1: Pressure fluctuations around a set mean pressure of 5,7,9 cm H₂O with simulated spontaneous respiration for rPAP (blue) vs. Neopuff (red) with constant tidal volume in term and preterm model. Figure 2: Pressure swings (Δ P in cm H2O) and WOB (mJ) for preterm and term experiments with constant <text> tidal volumes for Neopuff (red) and rPAP (blue) at PEEP 5,7 and 9. Box plots with mean and coefficient of variation percentage (CV%).

Figure 3: Pressure (cmH₂O) - volume (ml) loops for preterm and term model with constant tidal volumes for Neopuff (red) and rPAP (blue).

ว	
2	
3	
4	
5	
6	
0 7	
/	
8	
9	
10	
11	
11	
12	
13	
14	
15	
10	
16	
17	
18	
19	
20	
20	
21	
22	
23	
24	
27	
25	
26	
27	
28	
20	
29	
30	
31	
32	
33	
31	
24	
35	
36	
37	
38	
20	
29	
40	
41	
42	
43	
11	
44	
45	
46	
47	
<u>4</u> 8	
40	
49	
50	
51	
52	
52	
23	
54	
55	
56	
57	
57	
58	
59	

60

- Acknowledgment
- We would like to acknowledge Prof Martin Wald and Dr. Auer-Hackenberg for their great support on
- driving and understanding the Neonatal Active Lung model.

Conflict of interests

- T Drevhammar is one of the inventors of rPAP.
- Contributors Conception: MT and MH
- Design Acquisition of data, analysis and interpretation of data: VG, SM, MT, MD
- Article writing: VG; Revising the article critically for important intellectual content: MH, TD, MT;
- Responsible for the overall content: MT;
- All the authors have read and approved the manuscript.
- Funding: The authors have not declared a specific grant for this research from any j.
 - funding agency in the public, commercial or not-for-profit sectors.

REFERENCES

1 2

3

4 5

6

7

8

- 1. Mahmoud RA. Schmalisch G. Oswal A. et al. Non-invasive ventilatory support in neonates: An evidencebased update. Paediatr Respir Rev 2022;44:11-18. doi: 10.1016/j.prrv.2022.09.001 [published Online First: 20220926]
- 2. Morley CJ, Davis PG, Doyle LW, et al. Nasal CPAP or intubation at birth for very preterm infants. N Engl J Med 2008;358(7):700-8. doi: 10.1056/NEJMoa072788
- 3. Dunn MS, Kaempf J, de Klerk A, et al. Randomized trial comparing 3 approaches to the initial respiratory management of preterm neonates. Pediatrics 2011;128(5):e1069-76. doi: 10.1542/peds.2010-3848 10 [published Online First: 20111024] 11
- 4. Badiee Z, Naseri F, Sadeghnia A. Early versus delayed initiation of nasal continuous positive airway 12 13 pressure for treatment of respiratory distress syndrome in premature newborns: A randomized 14 clinical trial. Adv Biomed Res 2013;2:4. doi: 10.4103/2277-9175.107965 [published Online First: 15 20130306]
- 16 5. Subramaniam P, Ho JJ, Davis PG. Prophylactic or very early initiation of continuous positive airway 17 pressure (CPAP) for preterm infants. Cochrane Database Syst Rev 2021;10(10):CD001243. doi: 18 10.1002/14651858.CD001243.pub4 [published Online First: 20211018] 19
- 6. Schmolzer GM, Kumar M, Pichler G, et al. Non-invasive versus invasive respiratory support in preterm 20 21 infants at birth: systematic review and meta-analysis. BMJ 2013;347:f5980. doi: 10.1136/bmj.f5980 22 [published Online First: 20131017] 23
- 7. Sweet DG, Carnielli VP, Greisen G, et al. European Consensus Guidelines on the Management of 24 Respiratory Distress Syndrome: 2022 Update. Neonatology 2023;120(1):3-23. doi: 25 10.1159/000528914 [published Online First: 20230215] 26
- 8. Wyllie J, Perlman JM, Kattwinkel J, et al. Part 11: Neonatal resuscitation: 2010 International Consensus 27 on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment 28 29 Recommendations. Resuscitation 2010;81 Suppl 1:e260-87. doi: 10.1016/j.resuscitation.2010.08.029
- 30 9. Wyckoff MH, Greif R, Morley PT, et al. 2022 International Consensus on Cardiopulmonary Resuscitation 31 and Emergency Cardiovascular Care Science With Treatment Recommendations: Summary From 32 the Basic Life Support; Advanced Life Support; Pediatric Life Support; Neonatal Life Support; 33 Education, Implementation, and Teams; and First Aid Task Forces. Circulation 2022;146(25):e483-34 e557. doi: doi:10.1161/CIR.00000000000001095 35
- 36 10. Manley BJ, Buckmaster AG, Travadi J, et al. Trends in the use of non-invasive respiratory support for 37 term infants in tertiary neonatal units in Australia and New Zealand. Arch Dis Child Fetal Neonatal 38 Ed 2022;107(6):572-76. doi: 10.1136/archdischild-2021-323581 [published Online First: 20220411]
- 39 11. Smithhart W, Wyckoff MH, Kapadia V, et al. Delivery Room Continuous Positive Airway Pressure and 40 Pneumothorax. Pediatrics 2019;144(3) doi: 10.1542/peds.2019-0756 [published Online First: 41 20190809] 42
- 12. Stocks EF, Jaleel M, Smithhart W, et al. Decreasing delivery room CPAP-associated pneumothorax at 43 44 >/=35-week gestational age. J Perinatol 2022;42(6):761-68. doi: 10.1038/s41372-022-01334-4 45 [published Online First: 20220216]
- 46 13. Hishikawa K, Goishi K, Fujiwara T, et al. Pulmonary air leak associated with CPAP at term birth 47 resuscitation. Arch Dis Child Fetal Neonatal Ed 2015;100(5):F382-7. doi: 10.1136/archdischild-48 2014-307891 [published Online First: 20150408] 49
- 14. Gregory GA, Kitterman JA, Phibbs RH, et al. Treatment of the idiopathic respiratory-distress syndrome 50 51 with continuous positive airway pressure. N Engl J Med 1971;284(24):1333-40. doi: 52 10.1056/nejm197106172842401
- 53 15. Donaldsson S, Drevhammar T, Taittonen L, et al. Initial stabilisation of preterm infants: a new 54 resuscitation system with low imposed work of breathing for use with face mask or nasal prongs. 55 Arch Dis Child Fetal Neonatal Ed 2017;102(3):F203-F07. doi: 10.1136/archdischild-2016-310577 56 [published Online First: 20160823] 57
- 16. Cook SE, Fedor KL, Chatburn RL. Effects of Imposed Resistance on Tidal Volume With 5 Neonatal 58 59 Nasal Continuous Positive Airway Pressure Systems. Respir Care 2010;55(5):544-48.
- 60 17. Drevhammar T, Nilsson K, Zetterstrom H, et al. Comparison of seven infant continuous positive airway pressure systems using simulated neonatal breathing. Pediatr Crit Care Med 2012;13(2):e113-9. doi: 10.1097/PCC.0b013e31822f1b79

1 2	18.	Drevhammar T, Nilsson K, Zetterstrom H, et al. Comparison of nasal continuous positive airway pressure delivered by seven ventilators using simulated neonatal breathing. <i>Pediatr Crit Care Med</i> 2013;14(4):e196-201_doi: 10.1097/PCC.0b013e31827212e4
3 4 5 6	19.	 Auer-Hackenberg L, Stroicz P, Hofstatter E, et al. Breath-dependent pressure fluctuations in various constant- and variable-flow neonatal CPAP devices. <i>Pediatr Pulmonol</i> 2022;57(10):2411-19. doi: 10.1002/ppul.26050 [published Online First: 20220708]
7 8 9	20.	. Kuypers K, Kashyap AJ, Cramer SJE, et al. The effect of imposed resistance in neonatal resuscitators on pressure stability and peak flows: a bench test. <i>Pediatr Res</i> 2023;94(6):1929-34. doi: 10.1038/s41390-023-02715-x [published Online First: 20230717]
10 11 12	21.	French CJ. Work of breathing measurement in the critically ill patient. <i>Anaesth Intensive Care</i> 1999;27(6):561-73. doi: 10.1177/0310057x9902700602
13 14 15	22. 23.	 Banner MJ, Kirby RR, Blanch PB. Differentiating total work of breathing into its component parts. Essential for appropriate interpretation. <i>Chest</i> 1996;109(5):1141-3. doi: 10.1378/chest.109.5.1141 Morley C. Continuous distending pressure. <i>Arch Dis Child Fetal Neonatal Ed</i> 1999;81(2):F152-6. doi:
16 17 18	24.	10.1136/fn.81.2.f152 Natalini G, Tuzzo DM, Comunale G, et al. Work of breathing-tidal volume relationship: analysis on an
19 20		in vitro model and clinical implications. <i>J Clin Monit Comput</i> 1999;15(2):119-23. doi: 10.1023/a:1009912827854
21 22 23 24	25.	. Pandit PB, Courtney SE, Pyon KH, et al. Work of breathing during constant- and variable-flow nasal continuous positive airway pressure in preterm neonates. <i>Pediatrics</i> 2001;108(3):682-5. [published Online First: 2001/09/05]
25 26	26.	. Schaller P. Instruction manual Gina V3.0. 2019; 3. <u>https://www.schaller-mt.de/download/LM_Dt.pdf</u> (accessed 28.05.2024).
27 28 29	27.	. Gherini S, Peters RM, Virgilio RW. Mechanical work on the lungs and work of breathing with positive end-expiratory pressure and continuous positive airway pressure. <i>Chest</i> 1979;76(3):251-6. doi: 10.1378/chest.76.3.251
30 31 32	28.	Anday EK, Godart-Wlodavar A, Delivoria-Papadopoulos M. Sequential pulmonary function measurements in very low-birth weight infants during the first week of life. <i>Pediatr Pulmonol</i> 1987;3(6):392-9. doi: 10.1002/ppul.1950030604
33 34 35 36	29.	Stenson BJ, Glover RM, Wilkie RÅ, et al. Randomised controlled trial of respiratory system compliance measurements in mechanically ventilated neonates. <i>Arch Dis Child Fetal Neonatal Ed</i> 1998;78(1):F15-9 doi: 10.1136/fn.78.1.f15
37 38	30.	Abbasi S, Bhutani VK. Pulmonary mechanics and energetics of normal, non-ventilated low birthweight infants. <i>Pediatr Pulmonol</i> 1990;8(2):89-95. doi: 10.1002/ppul.1950080206
39 40 41	31.	. Estol P, Píriz H, Pintos L, et al. Assessment of pulmonary dynamics in normal newborns: a pneumotachographic method. <i>J Perinat Med</i> 1988;16(3):183-92. doi: 10.1515/jpme.1988.16.3.183
42 43 44	32.	Krieger TJ, Wald M. Volume-Targeted Ventilation in the Neonate: Benchmarking Ventilators on an Active Lung Model. <i>Pediatr Crit Care Med</i> 2017;18(3):241-48. doi: 10.1097/PCC.00000000001088
45 46 47 48	33.	Bordessoule A, Piquilloud L, Lyazidi A, et al. Imposed Work of Breathing During High-Frequency Oscillatory Ventilation in Spontaneously Breathing Neonatal and Pediatric Models. <i>Respir Care</i> 2018;63(9):1085-93. doi: 10.4187/respcare.05703 [published Online First: 20180717]
49 50	34.	. Banner MJ, Jaeger M. J., Kirby R. R. Components of the work of breathing and implications for monitoring ventilator-dependent patients. <i>Crit Care Med</i> 1994;22:515-23.
51 52 53	35.	. Courtney SE, Aghai ZH, Saslow JG, et al. Changes in lung volume and work of breathing: A comparison of two variable-flow nasal continuous positive airway pressure devices in very low birth weight infants. <i>Pediatr Pulmonol</i> 2003;36(3):248-52. doi: 10.1002/ppul.10327
54 55 56 57 58	36.	Blank DA, Rogerson SR, Kamlin COF, et al. Lung ultrasound during the initiation of breathing in healthy term and late preterm infants immediately after birth, a prospective, observational study. <i>Resuscitation</i> 2017;114:59-65. doi: 10.1016/j.resuscitation.2017.02.017 [published Online First: 20170227]
59 60	37.	. Kuypers K, Dekker J, Crossley KJ, et al. Slowing lung deflation by increasing the expiratory resistance enhances FRC in preterm rabbits. <i>Pediatr Res</i> 2024 doi: 10.1038/s41390-024-03388-w [published Online First: 20240708]

- 38. Drevhammar T, Falk M, Donaldsson S, et al. Neonatal Resuscitation With T-Piece Systems: Risk of Inadvertent PEEP Related to Mechanical Properties. *Front Pediatr* 2021;9:663249. doi: 10.3389/fped.2021.663249 [published Online First: 2021/06/25]
- 39. Roukema H, O'Brien K, Nesbitt K, et al. A Crossover Trial of Infant Flow (IF) Continuous Positive Airway Pressure (CPAP) Versus Nasopharyngeal (NP) CPAP in the Extubation of Babies ≤ 1250 Grams Birthweight. *Pediatric Research* 1999;45(7):317-17. doi: 10.1203/00006450-199904020-
- 40. Donaldsson S, Drevhammar T, Li Y, et al. Comparison of Respiratory Support After Delivery in Infants Born Before 28 Weeks' Gestational Age: The CORSAD Randomized Clinical Trial. JAMA Pediatr 2021;175(9):911-18. doi: 10.1001/jamapediatrics.2021.1497 Confidential: For Review Ont



Figure 1: Pressure fluctuations around a set mean pressure of 5,7,9 cm H2O with simulated spontaneous respiration for rPAP (blue) vs. Neopuff (red) with constant tidal volume in term and preterm model.

139x101mm (600 x 600 DPI)

Term

7

7

PEEP cmH₂O

5

5

9





Figure 3: Pressure (cmH2O) - volume (ml) loops for preterm and term model with constant tidal volumes for Neopuff (red) and rPAP (blue).

139x101mm (600 x 600 DPI)

SUPPLEMENTAL MATERIAL NALM

Settings on the Neonatal Active Lung model (NALM).

1000g	
Resistance	Ra1 = 26,51 cmH ₂ O/L/s ¹
Endotracheal tube ¹	5.0 mm
Compliance	0.5 ml/mbar
Respiratory rate	70/min
Inspiratory time	0.3 s
PRM ²	12.2 cmH ₂ O
3500 g	
Resistance	Ra2= 45,89 cmH ₂ O/L/s ¹
Endotracheal tube ¹	5.0 mm
Compliance	1 ml/mbar
Respiratory rate	50/min
Inspiratory time	0.4 s
PRM	24.5 cmH ₂ O

¹ Numeric values of airway resistance according to the manufacturer's manual.

For simulation of spontaneous breathing on non-invasive ventilation (NIV) the maximum endotracheal tube diameter of 5.0mm was used for both models to negate any influence, as recommended in the manufacturer's manual. The PRM was set to yield a VT of approximately 6 ml/kg (22 ml term, 6 ml preterm) during spontaneous breathing, with 12.2 cm H₂O in the preterm and 24.5 cm H₂O in the term model. Random variation of 5% of the presets PRM and T_{ins} were set. ¹⁹

kuta work k
full a kit work k
full a kit watawa k

BMJ Paediatrics Open

What CPAP to use in the delivery room? Bench comparison of two methods to provide continuous positive airways pressure in neonates

Journal:	BMJ Paediatrics Open
Manuscript ID	bmjpo-2024-002948.R1
Article Type:	Original research
Date Submitted by the Author:	27-Sep-2024
Complete List of Authors:	Gruber, Viktoria; Medical University of Graz Division of Neonatology, Department of Paediatrics and Adolescent Medicine, Division of Neonatology Tracy, Mark; Westmead Hospital , Newborn Intensive Care Unit; Sydney University, Paediatrics and Child Health Hinder, Murray; The University of Sydney, Dept Paed & Child Health Morakeas, Stephanie; The University of Sydney Faculty of Engineering, Biomedical Engineering; Westmead Hospital, Neonatal Intensive Care Unit Dronavalli, Mithilesh; Western Sydney University Drevhammar, Thomas; Östersunds sjukhus, Department of Anesthesiology
Keywords:	Neonatology, Child Health, Resuscitation





I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

for Review Only

What CPAP to use in the delivery room? Bench comparison of two methods to provide continuous positive airways pressure in neonates

Gruber V¹, Tracy M.B^{2,4}, , Hinder M^{2,4}, Morakeas, S^{2,3}, Dronavalli M⁶, <u>Drevhammar T⁵</u>.

¹Medical University Graz, Department of Paediatrics and Adolescent Medicine,

Division of Neonatology, Graz, Austria

²Neonatal Intensive Care Unit, Westmead Hospital, Sydney, Australia.

³Faculty of Engineering and Information Technologies, BMET Institute, The University of Sydney, Sydney, Australia.

⁴Department of Paediatrics and Child Health, Sydney University, Sydney, Australia.

⁵Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden.

⁶Translational Health Research Institute, Western Sydney University, Penrith, NSW, Australia

Corresponding Author: thomas.drevhammar@ki.se

ABSTRACT

Background CPAP is a recommended first-line therapy for infants at birth with respiratory distress. Resuscitation devices incorporating CPAP delivery can have significantly different imposed resistances affecting airway pressure stability and work of breathing.

Aim To compare CPAP performance of two resuscitation devices (Neopuff T-Piece resuscitator and rPAP) in a neonatal lung model simulating spontaneous breathing effort at birth.

Methods The parameters assessed were variation in delivered pressures (ΔP), tidal volume (VT), inspiratory effort (model pressure respiratory muscle (PRM)) and work of breathing (WOB). Two data sequences were required with Neopuff and one with rPAP. 1. Set PRM with changes in VT, 2. Constant VT (preterm 6ml, term 22ml) with increased effort. Data were collected at CPAP settings of 5, 7, and 9 cmH₂O using a 1kg preterm (Compliance: 0.5 ml/cmH₂O) and 3.5kg term (1.0 ml/cmH₂O) model.

Results 2298 breaths were analysed (760 rPAP, 795 Neopuff constant VT, 743 Neopuff constant PRM). With CPAP at 9 cmH₂O: Set VT; mean ΔP (cmH₂O) rPAP vs Neopuff, 1.1 vs 5.6 (preterm) and 1.9 vs 13.4 (term), WOB (mJ) 4.6 vs 6.1 (preterm) and 35.3 vs 44.5 (term); Set PRM: the mean VT (ml) were reduced to 6.2 vs 5.2 (preterm) and 22.3 vs 17.5 (term) p<0.001. Similar results were found at pressures of 5 and 7cmH₂O.

Conclusion rPAP had smaller pressure swings than Neopuff at all CPAP levels and was thus more pressure stable. WOB was higher with Neopuff when VT was held constant. VT reduced with Neopuff when respiratory effort was constant.

INTRODUCTION

In recent years, respiratory management in the delivery room has shifted towards a less invasive approach with rising numbers of infants receiving non-invasive respiratory support.¹ Multiple trials have studied the benefits of non-invasive respiratory support for spontaneously breathing preterm infants.²⁻⁴ Systematic reviews and a meta-analysis support the early non-invasive support in preterm infants with findings of reduced incidence of BPD, death, and mechanical ventilation.^{5 6}

The European Consensus Guidelines on the Management of Respiratory Distress Syndrome recommend continuous positive airway pressure (CPAP) as the first line support for the initial stabilization of spontaneously breathing preterm infants with respiratory distress.⁷ The International Liaison Committee on Resuscitation (ILCOR) introduced CPAP as part of neonatal resuscitation to improve lung recruitment in preterm infants in 2010.⁸ Since then the use of CPAP has become increasingly common in late preterm and term infants with laboured breathing or persistent cyanosis without sufficient evidence for ILCOR recommendation.⁹ Term infants treated with non-invasive ventilation in Australasian Newborn Intensive Care Units (NICUs) have approximately doubled within the last few years.¹⁰ The use of T-piece devices with expiratory flow restriction to produce CPAP in the delivery room has been associated with an increase in pneumothorax, especially in infants with increasing gestational age.¹¹⁻¹³

BMJ Paediatrics Open

Since the first use of CPAP as a mode of non-invasive ventilation for preterm infants by Gregory et al. in 1971¹⁴, several devices and methods to generate CPAP have been introduced to clinicians. For resuscitation the number of devices capable of pressure ventilation with PEEP to a non-breathing infant and or providing CPAP to an infant that is breathing is limited. T-piece resuscitator is the most common, but a new alternative is the rPAP.¹⁵ Both have the advantage of easy transition between positive pressure ventilation (PPV) and CPAP but the resistance to breathing and method of generating CPAP is not similar. Previous research has shown differences in the resultant pressure waveforms between CPAP delivery systems ¹⁶⁻¹⁹ and large differences in expiratory resistances.²⁰

In respiratory systems, the work of breathing (WOB) is the product of pressure and volume, with the mechanical work needed for breathing referred to as total or physiological work of breathing. Imposed WOB (iWOB) is the component of work added to the patient by respiratory equipment.^{21 22} CPAP can decrease the total work of breathing in infants with respiratory distress syndrome (RDS) and surfactant deficiency by increasing the functional residual capacity (FRC), splinting airways, and optimizing breathing.^{1 23} However, the WOB may be increased by the added CPAP system resistance from the interface, connectors, and device design. It can be investigated in lung models or real patients but is sensitive to changes in breathing patterns such as VT and minute ventilation.^{21 24}

The infant's effort to breathe causes fluctuations in the pressure waveform around set CPAP levels. Pressure stability refers to the variation in pressures above and below the set mean pressure, the ΔP . Smaller ΔP when comparing CPAP systems with identical respiratory parameters can be described as more pressure stable.¹⁷ In bench tests, rPAP has shown lower imposed resistance and more pressure stability with significantly fewer inspiratory and expiratory pressure fluctuations than the Neopuff TPR.²⁰ In constant-flow CPAP systems, gas flow continues throughout the inspiratory/expiratory cycle resulting in the need for the patient's expiratory effort to overcome the flow and the resistance of the CPAP generating device during expiration, which leads to an increased expiratory work.²⁵

Lung simulators such as the Neonatal Active Lung Model (NALM) are designed to be programmable, dynamic and react to the tested device. They simulate breathing by allowing the user to set airway resistance (R_{aw}), compliance of respiratory system (C_{rs}) and tidal volumes (VT). The muscular effort needed to produce the simulated breath is labelled as the 'pressure of respiratory muscles' (PRM) in NALM.²⁶ PRM is generated with a moving piston within the NALM. Resistance and compliance can be linear or non-linear and in more complex simulations have more than one compartment. The NALM respond with changes in tidal volumes when system pressure and resistance change. Lung model simulators are thus dynamic, but the response is limited as they cannot react actively by changing the respiratory rate or inspiratory-expiratory ratio.

The NALM calculates the total WOB using the area of a pressure-volume loop of a simulated breath.²¹ This includes the simulated effort limited to inspiration with exhalation considered passive. iWOB reflects the added resistance from the CPAP device and is calculated from the pressure-volume loop at the interface. It can be split into an inspiratory and expiratory part. All measurements of work of breathing are directly affected by changes in VT and this makes reporting complicated. To

 standardize the comparison of devices either the pressure or the targeted tidal volume needs to be maintained stable.²⁷

The relationship between simulated effort and VT for resuscitation devices providing CPAP during simulated breathing has not previously been investigated. We aim to compare the delivered CPAP performance of two resuscitation devices with differing imposed resistances in a neonatal lung model simulating spontaneous breathing after birth by examining pressure stability, the effect on delivered tidal volume and simulated WOB.

METHODS

Two CPAP/PPV resuscitation systems were compared; the Inspire rPAP (Inspiration Healthcare) and the Neopuff T-piece resuscitator (Fisher and Paykel Healthcare). Both devices were connected to the Neonatal Active Lung Model (NALM, Schaller Medizintechnik, Germany, V1-4.0) which simulated spontaneous breathing modelling a preterm and term newborn infant with respiratory distress.²⁸⁻³¹ Prior to connection to either CPAP device the NALM was set as per previous researchers for these models ^{16 19 32 33} on 'spontaneous breathing' and is representative of a term 3500 g (C_{rs}:1 ml/cmH₂O, inflation rate 50/min, inspiratory time 0.4sec) and preterm 1000g (C_{rs}:0.5ml/cmH₂O, 70/min, 0.3sec) infant with respiratory distress (supplementary material).¹⁹

Before recording the NALM was equilibrated for 30 minutes and calibrated. The pressure and flow of the tested resuscitation devices were adjusted using a ventilator calibration analyser (Flow Analyser PF-300 IMT Medical, Buchs, Switzerland). The

PEEP was set by adjusting the total flow on Inspire rPAP (7.1L/min for 5.0 cm H₂O, 9.0 L/min for 7 cm H₂O, 10.7L/min for 9.0 cm H₂O), Neopuff was set up with a total flow of 10L/min for all PEEP values. The experiments were conducted without leak, using non-humidified gas at ambient room temperature and with no facemask interface. We found a significant drop in delivered VT comparing to set NALM values when connecting the Neopuff TPR to NALM in both term and preterm models. This did not occur with rPAP. To fairly examine the WOB aspect, changes in PRM were adjusted to maintain a constant VT since in a system with a constant compliance, the WOB is proportional to VT.²⁴ Two data sequences were collected with Neopuff due to examine both states of constant VT and constant PRM. As there was no change in rPAP from set NALM values only one data sequence was collected.

Patient and Public involvement:

This is a bench study of mechanical properties using a computerised lung simulator. There was no patient or animal involvement.

Data analysis

Data were collected from the NALM over 2 minutes for each setting. These data were imported into Stata V.18 MP (StataCorp, College Station, USA). Each respiratory cycle was identified by pressure waveform changes of PRM in Stata. The measured parameters included the mean CPAP pressure, minimum and maximum airway pressures and their difference (Δ P), VT, PRM and WOB (total WOB

calculated by NALM). Mean values for those parameters are reported in Table 1.

 Analysis of variance (ANOVA) for repeated measures was used to determine differences in mean and Coefficient of Variation (CV%) for measured parameters at different set PEEP values and compliance between the two tested devices. Differences between means determined by multiway ANOVA were reported with p values adjusted. F test using Box's conservative epsilon; p values <0.05 were considered statistically significant. Bonferroni corrections of estimates were made to adjust for multiple comparisons.

RESULTS

2298 simulated breaths were analysed comprising 760 with rPAP, 795 with Neopuff with constant VT and 743 with Neopuff and constant PRM.

Pressure

Pressure swings were significantly lower with rPAP compared to Neopuff, across all PEEP values in preterm and term models for both settings (VT or PRM constant) Figure 1 and Table 1. The largest ΔP were seen at higher PEEP levels in sequence 2 (constant VT) with a mean of 1.1 vs 5.6 cmH₂O rPAP vs Neopuff, CV% 13% vs 3.5% in the preterm model and 1.9 vs 13.4 cmH₂O rPAP vs. Neopuff CV 7.3% vs 2.6% in the term model. The high CV% observed with rPAP can be attributed to the noisy signal produced by rPAP (Table 1).

A higher PEEP had a greater impact on ΔP with Neopuff compared to rPAP: Mean ΔP 9.4-13.4 cmH₂O Neopuff vs 1.7-1.9 cmH₂O rPAP (ranges for PEEP 5-9, term model). A larger increase in ΔP was recorded in both term and preterm constant VT model with the Neopuff (mean 5.6 preterm vs 13.4 cmH₂O term) compared to rPAP (1.1 preterm vs 1.9 cmH₂O term).

Tidal volume

In simulations with the constant inspiratory effort (PRM), the largest reduction in VT were seen in the term model at PEEP 9 cmH₂O with Neopuff where VT were reduced to a mean of 17.5 ml compared to rPAP of 22.3 ml. Similar findings could be observed in the preterm model 6.2 vs. 5.2 ml for rPAP vs. Neopuff at highest set PEEP. Showing a VT reduction of 20.5% in the term model and 13.3% in the preterm model (set PEEP 9) with constant inspiratory effort. These findings were less pronounced at lower PEEP levels. (Table 1 and Figure 2)

In the sequence with constant VT, the inspiratory effort (PRM) was adjusted for Neopuff. The highest required PRM were at 9 cm CPAP with a total increase in effort of 2.6 cmH₂O in the preterm and 6.1 cmH₂O in the term model.

Work of breathing

In simulations with constant VT the total WOB was significantly higher with Neopuff. The greatest differences were seen at the highest PEEP level, mean 4.6 vs 6.1 mJ, CV 1.2 vs 1.6% in preterm and 35.3 vs 44.5 mJ, CV 1.6% vs 1.3% in term model rPAP vs Neopuff. A higher increase in WOB between PEEP levels was present with Neopuff (mean 5.2-6.1mJ preterm and 42.7-44.5mJ term) compared to rPAP (4.7-4.6 mJ preterm and 35.2-35.3 mJ term). Examples of pressure-volume loops are presented in Figure 3.

Preterm (1000g) CPAP P min (cm H,Q) P max (cm H,Q) VT (cm H,Q) VT (cm H,Q) Cm H,Q) Imasured (cm H,Q) Effort (cm H,Q) W0B (m (cm H,Q) rPAPI 5 5.0.10% 5.6.1.3% 0.7.13% 6 6.4.9% 12.7.8% 4.7.13% 9 8.9.10% 10.0.10% 1.1.13% 6 6.2.6.7% 12.2.3% 4.6.1.28 NP: VT constant 5 3.5.2.6% 7.2.1.1% 3.9.4.7% 6 6.5.3.33% 1.4.8.3% 6.1.1.48 5.5.1.8% 6 6.6.3.3.3% 1.4.8.3% 6.1.1.48 5.5.0.8% NP: Effort constant 5 3.5.2.6% 7.1.2.7% 3.6.6% NA 5.9.62% 12.2.4.2% 4.3.1.8% 5.1.1.6% NP: Effort constant 5 3.5.2.6% 7.1.2.7% 3.6.9% NA 5.7.34K 12.2.2.2% 4.3.1.8% 5.3.1.6% NP: Effort constant 5 3.5.2.6% 7.1.2.7% 3.6.9% 12.2.2.3.2% 4.2.2.2.2.4.3.2% 4.3.1.8% NP: Effort constant 5 4.1.2%	e 11 of 24			BM.	Paediatrics (Jpen			
CPAP P min [cm H,0] P max [cm H,0] Δ P (cm H,0] VT set [ml] VT measured [ml] Effort (cm H,0] WOB [m (cm H,0] rPAP 5 5.0, 1.0% 5.6, 1.3% 0.7, 1.3% 6 6.4, 9% 127, 8% 4.6, 1.12% 9 8.9, 10% 10.0, 1.0% 1.1, 13% 6 6.2, 6.7% 122, 3% 4.6, 1.24% NP: VT constant 5 3.6, 2% 7.5, 2.1% 3.9, 4.7% 6 6.3, 3.3% 143, 3% 5.8, 1.36% PF: Effort constant 5 3.5, 2.6% 7.1, 2.7% 3.6, 0% NA 5.9, 3.5% 1.48, 3% 5.8, 1.36% P 6, 6, 1.7% 122, 0.9% 5.6, 3.5% 6 6.4, 3.3% 143, 3% 5.8, 1.36% P 9 6.9, 1.9% 4.3, 4.4% NA 5.7, 3.4% 122, 2.9% 8.3, 1.38 P 6 6.9, 1.9% 4.7, 6.8% NA 5.2, 7.8% 124, 6.3% 5.2, 3.5% Term (3500g) 7 6.9, 1.9% 1.7, 2.4% 1.7, 7.3% 22 2.5, 2	Preterm (1000g)								
Image:	(8)	СРАР	P min	P max	ΔΡ	VT set	VT	Effort	WOB [m.
PAPI 5 5.0, 1.0% 5.6, 1.3% 0.7, 13% 6 6.4, 9% 12.7, 8% 4.6, 1.1% 9 8.9, 10% 10.0, 1.0% 1.1, 13% 6 6.3, 5.5% 12.2, 3% 4.6, 1.1% 9 8.9, 10% 10.0, 1.0% 1.1, 13% 6 6.3, 3.3% 13.3, 2.7% 5.0, 3.3% 9 6.6, 1.7% 12.2, 0.9% 5.6, 3.5% 6 6.4, 3.3% 14.3, 3% 5.8, 1.3% 9 6.6, 1.7% 12.2, 0.9% 5.6, 3.5% 6 6.4, 3.3% 14.3, 3% 5.8, 1.3% NP: Effort constant 5 3.5, 2.6% 7.1, 2.7% 3.6, 6% NA 5.7, 8.4% 12.2, 2.9% 4.3, 1.16% Term (3500) 7 6.3, 1.1% 1.1, 0.8% 4.7, 6.3% NA 5.2, 2.3% 2.4, 3.2% 3.5.2, 1.1% PAPI 5 4.4, 2.% 6.1, 2.4% 1.7, 9.4% 22 22.5, 2.3% 24.4, 3.2% 35.2, 1.1% PAPI 7 6.3, 1.1% 10.2, 1.3% 1.7, 9.4% 22 22.5, 2.3%		[cm H ₂ O]	[cm H ₂ O]	[cm H ₂ O]	[cm H₂O]	[ml]	measured [ml]	[cm H ₂ O]	
7 6.8, 1% 7, 7.8 0.9, 10.1% 6 6.3, 5, 5% 122, 3% 4.6, 1.18 9 8.9, 10% 10, 1.0% 1, 1.3% 6 6.2, 6.7% 122, 3% 4.6, 1.28 NP: VT constant 5 3.6, 2% 7.5, 2.1% 3.9, 4.7% 6 6.6, 3.5% 1.3, 3, 7% 5.2, 0% 9 6.6, 1.7% 122, 0.9% 5.6, 3.5% 6 6.4, 3.3% 1.3, 8, 7% 5.3, 0.8% 9 6.5, 1.5% 1.16, 1.8% 4.7, 6.8% NA 5.7, 3.4% 122, 2.9% 4.3, 1.18 9 6.3, 1.9% 11.6, 1.8% 4.7, 6.8% NA 5.7, 3.4% 12.4, 6.2% 4.1, 1.6% 9 6.3, 1.1% 1.9, 6.9% 22 22.5, 2.4% 35.2, 1.1% 9 8.3, 1.1% 10.2, 1.4% 1.7, 9.4% 22 22.5, 2.3% 35.2, 1.1% 9 8.3, 1.1% 10.2, 1.5% 9.4, 2.5% 22 22.3, 3.2% 24.4, 3.2% 35.4, 1.1 9 8.3, 1.1% 10.2, 1.5% 3.4, 2.6%	rPAP ¹	5	5.0, 1.0%	5.6, 1.3%	0.7, 13%	6	6.4, 9%	12.7, 8%	4.7, 1.3%
9 8,9,10% 10.0,10% 1.1,13% 6 6,2,6.7% 12.2,3% 4,6,1.2% NP: VT constant 5 3,6,2% 7,5,2.1% 3,9,4.7% 6 6,5,3,3% 13.2,2% 5,2,0.9% 9 6,6,1.7% 12.2,0.9% 5,6,3.5% 6 6,4,3.3% 12.4,2% 4,5,0.8% NP: Effort constant 5 3,5,2.6% 7,1.2.7% 3,6,6% NA 5,9,6.2% 12,4,2.9% 4,3,1.3% 9 6,9,1.5% 4,3,4.4% NA 5,7,3.4% 12,2,2.9% 4,3,1.3% 9 6,9,1.5% 4,2,6% NA 5,2,7.3% 12,4,2.2% 4,3,1.3% 9 6,9,1.5% 12,4,2.4% 1,7,9.4% 22 22,5,4.7% 24,4,3.2% 35,2,1% 9 6,3,1.1% 10,2,1% 10,7,1.5% 9,7.3% 22 22,5,4.7% 24,4,3.3% 35,3,16 NP: VT constant 5 1,4,8% 10,2,1% 17,9,7.3% 22 22,6,2% 42,5,1.3% NP: Effort constant 5 1		7	6.8, 1%	7.7, 1%	0.9, 10.1%	6	6.3, 5,5%	12.2, 3%	4.6, 1.1%
NP: VT constant \$ 3.6, 2% 7.5, 2, 1% 9.4, 7% 6 6, 3, 3.3% 13.3, 2.7% 5, 2, 0.5% P 5, 1, 1.7% 10, 1.4% 4.9, 4% 6 6, 6, 3, 3.3% 13.3, 2.7% 5, 2, 1.3% P 6, 6, 1.7% 10, 1.4% 4.9, 4% 6 6, 6, 3, 3.3% 14.8, 3% 5, 8, 1.3% P 6, 6, 1.7.5% 7, 2, 2.0% 6, 1.5% 6 6, 4, 3.3% 12, 4.2% 4.5, 0.8% P 5 4, 1.6% 9, 6, 1.5% 4.3, 4.4% NA 5, 7, 3.4% 12, 2.2, 9% 3, 1.3 13, 1.3 13, 1.4% 14, 1.6% 12, 2.2% 4.1, 1.6% Ferm (350g) T 7 6.3, 1.1% 1.1, 1.1% 1.9, 6.3% 22 2.2, 5, 4.7% 2.4, 4.3% 3.5, 3.1% P AB ³ 5 4, 4, 2% 6.1, 2.4% 1.7, 9.4% 22 2.2, 6, 2.4% 2.4, 3.3% 3.5, 3.1% P AB ³ 1, 3% 1.9, 7.3% 22 2.2, 3, 2.2% 2.4, 3.3% 3.5, 3.1% 3.5, 3.1% 3.5, 3.1%		9	8.9, 10%	10.0, 1.0%	1.1, 13%	6	6.2, 6.7%	12.2, 3%	4.6, 1.2%
7 5.1, 1.7% 10, 1.4% 4.9, 4% 6 6.6, 3.5% 14.3, 3% 5.8, 1.3% 9 6.6, 1.7% 12, 2, 0.9% 5.5, 3.5% 6 6.4, 3.3% 1.8, 3% 6.1, 1.6, 1.5% 7 5.4, 1.6% 9.6, 1.5% 4.3, 4.4% NA 5.7, 3.4% 12.2, 4.2% 4.3, 1.3% 9 6.9, 1.9% 11.6, 1.8% 4.7, 6.8% NA 5.2, 7.8% 12.1, 6.2% 4.1, 1.6% 10.6 1.3% 4.7, 6.8% NA 5.2, 7.8% 12.1, 6.2% 4.1, 1.2% 7 6.3, 1.1% 8.1, 1.1% 1.9, 6.9% 22 22.5, 2.8% 24.4, 3.2% 35.3, 1.6 10.7 7 6.3, 1.1% 1.0, 2.1% 1.0, 7.3% 22 22.3, 3% 24.4, 3.2% 35.3, 1.6 NY: VT constant 5 1.0, 3% 10.2, 1.3% 13.4, 1.3% 11.7, 2.5% 22 22.6, 2.9% 24.5, 3.3% 24.5, 2.9% 24.4, 3.3 31.6, 1.2% VT constant 5 1.4, 8.7% 9.8, 2.6% 8.4, 3.7% NA <	NP: VT constant	5	3.6, 2%	7.5, 2.1%	3.9, 4.7%	6	6.3, 3.3%	13.3, 2.7%	5.2, 0.9%
9 6.6, 1.7% 12.2, 0.9% 5.6, 3.5% 6 6.4, 3.3% 14.8, 3% 6.1, 1.6% NP: Effort constant 5 3.5, 2.6% 7, 1, 2.7% 3.6, 6% NA 5.9, 6.2% 12.2, 4.2% 4.5, 0.3% 9 6.9, 1.9% 11.6, 1.8% 4.7, 6.8% NA 5.7, 3.4% 12.2, 2.9% 4.4, 2.4% 4.1, 1.6% Ferm (3500) 7 6.3, 1.1% 1.0, 1.8% 4.7, 6.8% NA 5.2, 7.8% 12.1, 6.2% 4.1, 1.6% Ferm (3500) 7 6.3, 1.1% 10.2, 1% 1.9, 7.3% 22 22.5, 4.7% 24.4, 3.2% 35.2, 1% 9 8.3, 1.1% 10.2, 1% 1.9, 7.3% 22 22.5, 4.7% 24.4, 3.2% 35.3, 1.6 9 3.1, 5.9% 16.5, 1.3% 13.4, 2.6% 22 22.2, 3.2% 24.4, 3.2% 35.3, 1.6 9 3.1, 5.9% 16.5, 1.3% 13.4, 2.6% NA 18.6, 3% 24.5, 3% 29.1, 12 VT with rPAP remained constant t3 set effort. 7 2.6, 6.6% 12.4, 1.3% <t< td=""><td></td><td>7</td><td>5.1, 1.7%</td><td>10, 1.4%</td><td>4,9, 4%</td><td>6</td><td>6.6, 3.5%</td><td>14.3, 3%</td><td>5.8, 1.3%</td></t<>		7	5.1, 1.7%	10, 1.4%	4,9, 4%	6	6.6, 3.5%	14.3, 3%	5.8, 1.3%
NP: Effort constant 5 3.5, 2.6% 7.1, 2.7% 3.6, 6% NA 5.9, 6.2% 12.2, 2.42% 4.5, 0.8% 9 6.9, 1.9% 11.6, 1.8% 4.3, 4.4% NA 5.7, 3.4% 12.2, 2.9% 4.3, 1.3% 10 6.9, 1.9% 11.6, 1.8% 4.7, 6.8% NA 5.2, 7.8% 12.1, 6.2% 4.1, 1.69 Ferm (3500g) 7 6.3, 1.3% 8.1, 1.1% 10.9, 6.9% 22 22.5, 2.8% 24.6, 3% 35.2, 1% 9 8.3, 1.1% 10.2, 1% 1.9, 7.3% 22 22.3, 3.2% 24.4, 3% 35.3, 1.6 NP: VT constant 5 1.10% 10.5, 1.5% 9.4, 2.5% 22 22.3, 3.2% 24.4, 3% 35.3, 1.6 NP: VT constant 5 1.4, 8% 13.4, 1.3% 13.4, 2.6% 22 21.5, 3.3% 29.8, 2.8% 8.4.4, 0.9 9 3.1, 5.9% 16.5, 1.3% 13.4, 2.6% 9.8, 2.6% NA 18.6, 3% 24.5, 3% 29.1, 12 VT with rPAP remained constant at set effort. VT in these simulations reduced and W		9	6.6, 1.7%	12.2, 0.9%	5.6, 3.5%	6	6.4, 3.3%	14.8, 3%	6.1, 1.6%
7 5.4, 1.6% 9.6, 1.5% 4.3, 4.4% NA 5.7, 3.4% 12.2, 2.9% 4.3, 1.3% 9 6.9, 1.9% 11.6, 1.8% 4.7, 6.8% NA 5.2, 7.8% 12.1, 6.2% 4.1, 1.6% PPAP ¹ 5 4.4, 2% 6.1, 2.4% 1.7, 9.4% 22 22.5, 2.8% 24.4, 3% 35.3, 1.6 9 8.3, 1.1% 10.2, 1.5% 1.9, 7.3% 22 22.3, 3.2% 24.4, 3% 35.3, 1.6 NP: VT constant 5 1.0% 10.5, 1.5% 9.4, 2.5% 22 22.6, 2.9% 28.6, 2.9% 42.7, 1.8 9 3.1, 1.9% 10.4, 1.3% 11.7, 2.5% 22 22.3, 3.2% 24.4, 3.0% 35.3, 1.6 NP: VT constant 5 1.4, 8% 13.4, 1.3% 11.7, 2.5% 22 22.3, 3.2% 24.5, 2.9% 4.5, 1.3 NP: Effort constant 5 1.4, 8% 9.8, 2.6% NA 18.6, 3% 24.5, 2.9% 30.4, 1.2 9 3.1, 3.13% 1.1% 1.0% 1.0% 1.0% 1.0% 1.	NP: Effort constant	5	3.5, 2.6%	7.1, 2.7%	3.6, 6%	NA	5.9, 6.2%	12.2, 4.2%	4.5, 0.8%
9 6.9, 1.9% 11.6, 1.8% 4.7, 6.8% NA 5.2, 7.8% 12.1, 6.2% 4.1, 1.6% IPPAP ¹ 5 4.4, 2% 6.1, 2.4% 1.7, 9.4% 22 22.5, 4.7% 24.4, 3.2% 35.2, 1% PPAP ¹ 7 6.3, 1.1% 1.0, 1.3% 1.9, 6.9% 22 22.5, 2.8% 24.4, 3% 35.3, 1.6 9 8.3, 1.1% 10.2, 1% 1.9, 7.3% 22 22.3, 3.2% 24.4, 3% 35.3, 1.6 NP: VT constant 5 1.10% 10.2, 1% 1.9, 7.3% 22 22.3, 3.2% 24.4, 3% 35.3, 1.6 9 8.3, 1.3% 1.3, 4.1% 1.9, 5.3% 22 22.3, 3.3% 29.8, 2.8% 4.4, 0.9% 22 21.5, 3.3% 29.8, 2.6% 1.3 1.6, 1.2% 29 1.16, 1.2% 29 1.16, 1.3% 1.3, 2.6% 8.4, 3.7% NA 1.9, 5.3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant at set effort. 24.1 1.9 24.5 3% 29.1 1.2 VT with rPAP remained constant at se		7	5.4. 1.6%	9.6. 1.5%	4.3.4.4%	NA	5.7.3.4%	12.2. 2.9%	4.3. 1.3%
Term (3500g) Property 5 4.4, 2% 6.1, 2.4% 1.7, 9.4% 22 22.5, 2.7% 24.4, 3.2% 35.2, 1% 7 6.3, 1.1% 8.1, 1.1% 1.9, 6.9% 22 22.5, 2.8% 24.6, 3% 35.4, 1.1 9 8.3, 1.1% 10.2, 1% 1.9, 7.3% 22 22.3, 3.2% 24.4, 3.8% 35.3, 1.6 NP: VT constant 5 1, 10% 10.5, 1.5% 9.4, 2.5% 22 22.6, 2.9% 28.6, 2.9% 44.4, 0.9 9 3.1, 5.9% 15.5, 1.5% 9.4, 2.5% 22 22.6, 2.9% 28.6, 2.9% 44.5, 1.3% NP: Effort constant 5 1.4, 9% 9.8, 2.6% 8.4, 3.7% NA 19.5, 3.1% 20.6, 2.9% 44.5, 1.3 NP: Effort constant 5 1.4, 9% 9.8, 2.6% NA 17.5, 3.1% 24.5, 3.1% 31.6, 1.2 7 2.6, 4.6% 1.5, 1.3% 1.0, 2.3% NA 17.5, 3.1% 24.5, 3.3% 29.1, 1.2 VT with rPAP remained constant at set effort. 2 2 2.5, 3.3%		9	6.9. 1.9%	11.6. 1.8%	4.7.6.8%	NA	5.2. 7.8%	12.1.6.2%	4.1. 1.6%
Trype 5 4.4, 2% 6.1, 2.4% 1.7, 9.4% 22 22.5, 4.7% 24.4, 3.2% 35.2, 1% P 7 6.3, 1.1% 8.1, 1.1% 1.9, 6.9% 22 22.5, 2.8% 24.6, 3% 35.4, 1.1 9 8.3, 1.1% 10.2, 1% 1.9, 7.3% 22 22.3, 3.2% 24.4, 3% 35.3, 1.6 NP: VT constant 5 1, 10% 105.5, 1.5% 9.4, 2.5% 22 22.6, 2.9% 28.6, 2.9% 44.7, 1.1 7 1.8, 7.8% 13.4, 1.3% 11.7, 2.5% 22 22.6, 2.9% 24.5, 2.9% 44.5, 1.3% 9 3.1, 5.9% 16.5, 1.3% 13.4, 2.6% 22 21.5, 3.1% 30.6, 2.9% 44.5, 1.3% 9 2.6, 4.6% 12.4, 1.3% 9.8, 2.6% NA 17.5, 3.1% 24.5, 2.9% 20.4, 1.2 9 1.4, 4.3% 15, 1.1% 10.9, 2.8% NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant t set effort. VT WOB in preterm and term model at different set PEEP levels.	Term (3500g)		010) 210/0		, e.e.,e		0.2,71070	12.2, 0.2,0	
TM J FA LA LA <thla< th=""> LA <thla< th=""> LA</thla<></thla<>	rDAD ¹	5	11.2%	6124%	1794%	22	225 / 7%	21132%	35 2 1%
J 0.03, 11.% 0.1, 1.% 1.9, 7.3% 22 22.3, 3.2% 24.4, 3.% 35.3, 1.6 NP: VT constant S 1, 10% 10.5, 1.5% 9.4, 2.5% 22 22.3, 3.2% 24.4, 3.% 35.3, 1.6 NP: VT constant S 1, 10% 10.5, 1.5% 9.4, 2.5% 22 22.3, 3.2% 24.4, 3.% 35.3, 1.6 NP: Torstant S 1, 10% 10.5, 1.5% 9.4, 2.5% 22 22.3, 3.2% 24.4, 3.3% 13.4, 2.6% 9 3.1, 5.9% 16.5, 1.3% 13.4, 2.6% A2 21.5, 3.1% 24.5, 3.1% 31.6, 1.2 7 2.6, 4.6% 12.4, 1.3% 19.2, 2.6% NA 18.6, 3% 24.5, 3.3% 29.1, 1.2 VT with rPAP remained constant 4 set effort. NA 10.9, 3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant 4 set effort. NA 18.6, 3% 24.5, 3% 29.1, 1.2 VI with rPAP remained constant 4 set effort. NO NO NO NO NO NO NO NO NO <		7	6211%	8 1 1 1%	1.7, 5.4%	22	22.3, 4.7%	24.4, 5.270	25 / 1 1
J O.S. A.1.70 V.2. 170 V.2. 170 <th< td=""><td></td><td>, 9</td><td>Q Q 1 10/</td><td>10.2 10/</td><td>10 7 20/</td><td>22</td><td>22.3, 2.0/0</td><td>24.0, 370</td><td>25 2 1 4</td></th<>		, 9	Q Q 1 10/	10.2 10/	10 7 20/	22	22.3, 2.0/0	24.0, 370	25 2 1 4
Virtue 3 1, 10% 10.3, 13% 3%, 2.3% 122 220, 2.3% 20.6, 2.3% 42.7, 11 9 3.1, 5.9% 16.5, 1.3% 13.4, 2.6% 22 21.5, 3.1% 30.6, 2.9% 44.5, 1.3 NP: Effort constant 5 1.4, 8% 9.8, 2.6% 8.4, 3.7% NA 19.5, 3.1% 24.5, 5.3.1% 31.6, 1.2 7 2.6, 4.6% 12.4, 1.3% 9.8, 2.6% 8.4, 3.7% NA 19.5, 3.1% 24.5, 2.9% 30.4, 1.2 9 4.1, 4.3% 9.8, 2.6% 8.4, 3.7% NA 19.5, 3.1% 24.5, 2.9% 30.4, 1.2 9 4.1, 4.3% 15, 1.1% 10.9, 2.8% NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant at set effort. XT 11.4.8% 10.9, 2.8% NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant at set effort. XT 11.4.8% 10.9, 2.8% NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VIT with rPAP remained constant protocont at set off constant protocont at set off cont at set		5	1 100/	10.2, 170	1.3, 7.3%	22	22.3, 3.270	24.4, 5%	10 7 1 1
Image: Product of the system Image: Product of the system <th< td=""><td></td><td>5</td><td>1, 10%</td><td>10.5, 1.5%</td><td>9.4, 2.5%</td><td>22</td><td>22.0, 2.9%</td><td>20.0, 2.9%</td><td>42.7, 1.1</td></th<>		5	1, 10%	10.5, 1.5%	9.4, 2.5%	22	22.0, 2.9%	20.0, 2.9%	42.7, 1.1
9 3.1, 5.3% 15.1, 1.3% 13.4, 2.0% 22 21.5, 3.1% 30.6, 2.3% V4.5, 1.3 NP: Effort constant 5 1.4, 8% 9.8, 2.6% NA 19.5, 3.1% 24.5, 3.1% 31.6, 1.2 7 2.6, 4.6% 12.4, 1.3% 9.8, 2.6% NA 18.6, 3% 24.5, 3.1% 30.6, 1.2 9 4.1, 4.3% 15, 1.1% 10.9, 2.8% NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant at set effort. VX VX 10.9, 2.8% NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant at set effort. VX VX Inthese simulations reduced and WOB not comparable to constant VT All differences significant p<0.001, ANOVA repeated measurements VT PREAD		/	1.8, 7.8%	13.4, 1.3%	11.7, 2.5%	22	22.3, 3%	29.8, 2.8%	44.4, 0.9
NP: Errort constant 5 1.4, 8% 9.8, 2.6% NA 19.5, 3.1% 24.5, 3.1% 31.6, 1.2 7 2.6, 4.6% 12.4, 1.3% 9.8, 2.6% NA 18.6, 3% 24.5, 2.9% 30.4, 1.2 9 4.1, 4.3% 15, 1.1% 10.9, 2.8% NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant at set effort. VT NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VT in these simulations reduced and WOB not comparable to constant VT All differences significant p<0.001, ANOVA repeated measurements		9	3.1, 5.9%	16.5,1.3%	13.4, 2.6%	22	21.5, 3.1%	30.6, 2.9%	44.5, 1.3
Y 2.6, 4.6% 12.4, 1.3% 9.8, 2.6% NA 18.6, 3% 24.5, 2.9% 00.4, 1.2 9 4.1, 4.3% 15, 1.1% 10.9, 2.8% NA 17.5, 3.1% 24.5, 3% 29.1, 1.2 VT with rPAP remained constant at set effort. VT with rPAP remained constant at set effort. VT in these simulations reduced and WOB not comparable to constant VT All differences significant p<0.001, ANOVA repeated measurements	NP: Effort constant	5	1.4, 8%	9.8, 2.6%	8.4, 3.7%	NA	19.5, 3.1%	24.5, 3.1%	31.6, 1.2
9 4,1,4,3% 15,1,1% 10,9,2.8% NA 17,5,3,1% 24,5,3% 29,1,1,2 VT with rPAP remained constant at set effort. VT in these simulations reduced and WOB not comparable to constant VT All differences significant p<0.001, ANOVA repeated measurements		7	2.6, 4.6%	12.4, 1.3%	9.8, 2.6%	NA	18.6, 3%	24.5, 2.9%	30.4, 1.2
VT with rPAP remained constant at set effort. ² VT in these simulations reduced and WOB not comparable to constant VT All differences significant p<0.001, ANOVA repeated measurements Table 1 Comparison of rPAP and Neopuff (NP): Mean and Coefficient of Variation% for P, VT, PRM an WOB in preterm and term model at different set PEEP levels.		9	4.1, 4.3%	15, 1.1%	10.9, 2.8%	NA	17.5, 3.1%	24.5, 3%	29.1, 1.2
	Table 1 Compar WOB in preterm	ison of rP n and term	AP and Nec n model at	opuff (NP): I different se	Vlean and C t PEEP leve	Coefficien Is.	t of Variatior	1% for P, VT	, PRM an

DISCUSSION

This bench test has confirmed that in both term and preterm NALM models simulating breathing with respiratory distress, the T-piece resuscitator (Neopuff) affects breathing with larger pressure swings around the set CPAP level compared to that measured with rPAP. The increased resistance to breathing was reflected in both ΔP , tidal volumes and the effect on PRM. The overall impact of using Neopuff TRP compared to rPAP to deliver CPAP in our models led to either the tidal volume reducing or a required increase in simulated effort.

Significant differences were also found in WOB levels recorded by the NALM. At a constant compliance the elastic WOB is proportional to the VT.³⁴ Interpreting WOB in our dynamic active model is more complex with the calculations being dependent on the VT and, for total WOB, the simulated effort. Since the added device resistance reduces the VT or requires an increase in simulated effort, this must be accounted for when looking at the absolute values of work of breathing and is a limiting factor in this bench test. Nonetheless, our findings of WOB are consistent with the in-vivo study by Pandit et al. comparing variable to constant flow CPAP devices ²⁵ but could not be confirmed by Courtney et al.³⁵

Fluid clearance in transition to breathing happens quickly ³⁶ with dynamic changes in lung compliance and resistance. This transition is difficult to simulate in current lung simulators. Limitations are 1. The bench testing on fixed respiratory function parameters, which are not representative of these dynamic changes after birth. 2. Our model was intentionally designed to be leak free, 3. The inability to split the work of breathing value of the NALM to an inspiratory and expiratory component. 4. Infants alter respiratory rate more than VT to maintain minute ventilation which cannot be modelled with simulators and the general translation of this bench model to in vivo results needs further investigation.

Infants breathing on identical respiratory support systems with the same settings might have a different iWOB and different inspiratory flow rates.²¹ Increasing the fresh gas flow to Neopuff TPR increased

BMJ Paediatrics Open

pressure stability.²⁰ This has not been investigated in our study. A higher flow on Neopuff might be beneficial in terms of less effort, especially for CPAP use over a longer period. An increased iWOB compared to the WOB of spontaneous breathing is assumed to play a role in CPAP failure.²¹

Whether there are benefits of pressure fluctuations in the initial aeration is uncertain but high resistance might reduce peak flows and tidal volumes. A recent animal study by Kuypers et al. in intubated preterm rabbits receiving PPV using higher expiratory resistance showed reduced deflation rates and increased the accumulation of FRC over time.³⁷ Concerns of adverse effects caused by larger pressure fluctuations such as a higher incidence of pneumothorax have been raised.¹⁸ Use of CPAP for newborn stabilization with a Tpiece system has shown an increased rate of pneumothorax, especially in late preterm and term infants.¹¹ ¹³ This might be associated with faster lung compliance changes in this group. Additionally, high system resistance could increase the risk of inadvertent PEEP due to a shorter expiration time.³⁸

Previous clinical and bench studies report larger VTs and greater changes in lung volume in variable vs continuous flow CPAP.^{25 19 20} Cook et al. found VT drops with a constant inspiratory effort on higher PEEP levels, which were less pronounced in CPAP systems with flow opposition.¹⁶ This is confirmed by the findings in our bench test.

Flow opposition CPAP systems showed an advantage regarding extubation success in preterms.³⁹ A recently performed randomised controlled trial by Donaldsson et al. comparing the more pressure-stable rPAP to the Neopuff TPR reported a reduced delivery room intubation using the dual flow system.⁴⁰ Whether pressure stability of CPAP systems is of importance in the early phase during transition to breathing in newborns requiring airway pressure support needs further investigation. In-vivo studies are required to assess the actual imposed (inspiratory and expiratory) WOB with relation to dynamic changes of lung compliance and resistance during transition.

Prolonged support using resuscitation CPAP systems occurs in many settings whilst awaiting inter-hospital transfer. Our findings of differences in pressure stability and the impact of WOB may be particularly relevant in these clinical scenarios.

CONCLUSION

Our study showed large differences between the two resuscitation systems related to the imposed respiratory resistance of the CPAP devices. rPAP device had smaller pressure swings than Neopuff at all . s hi. . nd lower iWOB in t. CPAP levels and was more pressure stable. WOB was higher with a greater respiratory effort with Neopuff when VT was held constant, and VT reduced with Neopuff when respiratory effort was constant. The clinical impact of higher pressure stability and lower iWOB in the stabilization of newborn infants needs

further investigation in in-vivo studies.

1	WHAT IS	ALREADY KNOWN ON THIS TOPIC?
2 3 4	-	Lung transition from fetal circulation to independent breathing and lung aeration is
5 6		accompanied by rapid changes in lung compliance with implications for CPAP delivery systems.
7 8 0	-	Resuscitation devices used for CPAP have differences in imposed expiratory resistance with
9 10 11		implications for pressure stability and work of breathing.
12 13		
14 15 16	WHAT TH	IS STUDY ADDS?
17 18 10	-	Increased system resistance for Neopuff led to either the reduction of tidal volume with
20 21		constant effort or increased effort compared to rPAP if the tidal volume was maintained
22 23 24		constant.
24 25 26	-	Airway pressure stability in CPAP systems can significantly affect the work of breathing.
27 28 20		
29 30 31	HOW THI	S STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY?
32 33	-	A required higher effort between different CPAP delivery systems at the same CPAP level might
34 35 36		lead to respiratory exhaustion and CPAP failure.
37 38	-	If CPAP is required for long periods related to interhospital transfer, devices with lower
39 40 41		expiratory resistance and higher pressure stability may be preferable.
42 43		
45 46		
47 48 49		
50 51		
52 53 54		
55 56		
57 58		
59 60		

Figures legend

 Figure 1: Pressure fluctuations around a set mean pressure of 5,7,9 cm H₂O with simulated spontaneous respiration for rPAP (blue) vs. Neopuff (red) with constant tidal volume in term and preterm model. Figure 2: Pressure swings (Δ P in cm H2O) and WOB (mJ) for preterm and term experiments with constant <text> tidal volumes for Neopuff (red) and rPAP (blue) at PEEP 5,7 and 9. Box plots with mean and coefficient of variation percentage (CV%).

Figure 3: Pressure (cmH₂O) - volume (ml) loops for preterm and term model with constant tidal volumes for Neopuff (red) and rPAP (blue).

1	Acknowledgment
2 3	We would like to acknowledge Prof Martin Wald and Dr. Auer-Hackenberg for their great support on
4 5 6 7	driving and understanding the Neonatal Active Lung model.
8 9 10	Conflict of interests
11 12 13 14	T Drevhammar is one of the inventors of rPAP.
15 16 17	Contribution statement
18 19	Contributors Conception: MT and MH, MT is the guarantor.
20 21 22	Design Acquisition of data, analysis and interpretation of data: VG, SM, MT, MD
23 24	Article writing: VG; Revising the article critically for important intellectual content: MH, TD, MT;
25 26 27	Responsible for the overall content: MT;
27 28 29	All the authors have read and approved the manuscript.
30 31	Funding: The authors have not declared a specific grant for this research from any
32 33 34	funding agency in the public, commercial or not-for-profit sectors.
35 36	Ethical approval statement:
37 38 39	Not required as this is a bench study and no human or animal subjects were involved.
40 41	
42 43 44	
45 46	
47 48 49	
50 51	
52 53	
54 55 56	
57 58	
59 60	

REFERENCES

1 2

3 4

5

6

7

8

- 1. Mahmoud RA, Schmalisch G, Oswal A, et al. Non-invasive ventilatory support in neonates: An evidencebased update. Paediatr Respir Rev 2022;44:11-18. doi: 10.1016/j.prrv.2022.09.001 [published Online First: 20220926]
- 2. Morley CJ, Davis PG, Doyle LW, et al. Nasal CPAP or intubation at birth for very preterm infants. N Engl J Med 2008;358(7):700-8. doi: 10.1056/NEJMoa072788
- 3. Dunn MS, Kaempf J, de Klerk A, et al. Randomized trial comparing 3 approaches to the initial respiratory 10 management of preterm neonates. Pediatrics 2011;128(5):e1069-76. doi: 10.1542/peds.2010-3848 11 [published Online First: 20111024]
- 12 4. Badiee Z, Naseri F, Sadeghnia A. Early versus delayed initiation of nasal continuous positive airway 13 pressure for treatment of respiratory distress syndrome in premature newborns: A randomized 14 15 clinical trial. Adv Biomed Res 2013;2:4. doi: 10.4103/2277-9175.107965 [published Online First: 16 20130306]
- 17 5. Subramaniam P, Ho JJ, Davis PG. Prophylactic or very early initiation of continuous positive airway 18 pressure (CPAP) for preterm infants. Cochrane Database Syst Rev 2021;10(10):CD001243. doi: 19 10.1002/14651858.CD001243.pub4 [published Online First: 20211018] 20
- 21 6. Schmolzer GM, Kumar M, Pichler G, et al. Non-invasive versus invasive respiratory support in preterm 22 infants at birth: systematic review and meta-analysis. BMJ 2013;347:f5980. doi: 10.1136/bmj.f5980 23 [published Online First: 20131017] 24
- 7. Sweet DG, Carnielli VP, Greisen G, et al. European Consensus Guidelines on the Management of 25 Respiratory Distress Syndrome: 2022 Update. Neonatology 2023;120(1):3-23. doi: 26 27 10.1159/000528914 [published Online First: 20230215]
- 28 8. Wyllie J, Perlman JM, Kattwinkel J, et al. Part 11: Neonatal resuscitation: 2010 International Consensus 29 on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment 30 Recommendations. Resuscitation 2010;81 Suppl 1:e260-87. doi: 31 32 10.1016/j.resuscitation.2010.08.029
- 33 9. Wyckoff MH, Greif R, Morley PT, et al. 2022 International Consensus on Cardiopulmonary Resuscitation 34 and Emergency Cardiovascular Care Science With Treatment Recommendations: Summary From 35 the Basic Life Support; Advanced Life Support; Pediatric Life Support; Neonatal Life Support; 36 37 Education, Implementation, and Teams; and First Aid Task Forces. Circulation 2022;146(25):e483-38 e557. doi: doi:10.1161/CIR.00000000000001095
- 39 10. Manley BJ, Buckmaster AG, Travadi J, et al. Trends in the use of non-invasive respiratory support for 40 term infants in tertiary neonatal units in Australia and New Zealand. Arch Dis Child Fetal Neonatal 41 Ed 2022;107(6):572-76. doi: 10.1136/archdischild-2021-323581 [published Online First: 20220411] 42
- 43 11. Smithhart W, Wyckoff MH, Kapadia V, et al. Delivery Room Continuous Positive Airway Pressure and 44 Pneumothorax. Pediatrics 2019;144(3) doi: 10.1542/peds.2019-0756 [published Online First: 45 20190809] 46
- 12. Stocks EF, Jaleel M, Smithhart W, et al. Decreasing delivery room CPAP-associated pneumothorax at 47 >/=35-week gestational age. J Perinatol 2022;42(6):761-68. doi: 10.1038/s41372-022-01334-4 48 49 [published Online First: 20220216]
- 50 13. Hishikawa K, Goishi K, Fujiwara T, et al. Pulmonary air leak associated with CPAP at term birth 51 resuscitation. Arch Dis Child Fetal Neonatal Ed 2015;100(5):F382-7. doi: 10.1136/archdischild-2014-52 307891 [published Online First: 20150408] 53
- 54 14. Gregory GA, Kitterman JA, Phibbs RH, et al. Treatment of the idiopathic respiratory-distress syndrome 55 with continuous positive airway pressure. N Engl J Med 1971;284(24):1333-40. doi: 56 10.1056/nejm197106172842401 57
- 15. Donaldsson S, Drevhammar T, Taittonen L, et al. Initial stabilisation of preterm infants: a new 58 resuscitation system with low imposed work of breathing for use with face mask or nasal prongs. 59 60 Arch Dis Child Fetal Neonatal Ed 2017;102(3):F203-F07. doi: 10.1136/archdischild-2016-310577 [published Online First: 20160823]

Page 19 of 24

1	16. Cook SE, Fedor KL, Chatburn RL. Effects of Imposed Resistance on Tidal Volume With 5 Neonatal Nasal
2	Continuous Positive Airway Pressure Systems. Respir Care 2010;55(5):544-48.
3	17. Drevhammar T, Nilsson K, Zetterstrom H, et al. Comparison of seven infant continuous positive airway
4	pressure systems using simulated neonatal breathing. <i>Pediatr Crit Care Med</i> 2012:13(2):e113-9.
5	doi: 10.1097/PCC.0b013e31822f1b79
6	18 Dreyhammar T. Nilsson K. Zetterstrom H. et al. Comparison of pasal continuous positive airway
7	10. Dievinammar 1, Misson K, Zetterström 1, et al. comparison of hasar continuous positive all way
8	pressure derivered by seven ventriators using simulated neonatal breathing. Pedidir Chi Cure Med
9	2013;14(4):e196-201. doi: 10.1097/PCC.0b013e31827212e4
10 11	19. Auer-Hackenberg L, Stroicz P, Hofstatter E, et al. Breath-dependent pressure fluctuations in various
17	constant- and variable-flow neonatal CPAP devices. <i>Pediatr Pulmonol</i> 2022;57(10):2411-19. doi:
13	10.1002/ppul.26050 [published Online First: 20220708]
14	20. Kuypers K, Kashyap AJ, Cramer SJE, et al. The effect of imposed resistance in neonatal resuscitators on
15	pressure stability and peak flows: a bench test. <i>Pediatr Res</i> 2023;94(6):1929-34. doi:
16	10.1038/s41390-023-02715-x [published Online First: 20230717]
17	21. French CI. Work of breathing measurement in the critically ill patient. Angesth Intensive Care
18	1999.27(6).561-73 doi: 10.1177/0310057x9902700602
19	22 Papper MI Kirby PP. Planch PP. Differentiating total work of breathing into its component parts
20	22. Bailler WJ, Kirby KK, Blanch PB. Differentiating total work of breathing into its component parts.
21	Essential for appropriate interpretation. <i>Chest</i> 1996;109(5):1141-3. doi: 10.1378/chest.109.5.1141
23	23. Morley C. Continuous distending pressure. Arch Dis Child Fetal Neonatal Ed 1999;81(2):F152-6. doi:
24	10.1136/fn.81.2.f152
25	24. Natalini G, Tuzzo DM, Comunale G, et al. Work of breathing-tidal volume relationship: analysis on an in
26	vitro model and clinical implications. J Clin Monit Comput 1999;15(2):119-23. doi:
27	10.1023/a:1009912827854
28	25. Pandit PB, Courtney SE, Pyon KH, et al. Work of breathing during constant- and variable-flow nasal
29	continuous positive airway pressure in preterm neonates. <i>Pediatrics</i> 2001:108(3):682-5. [published
30 31	Online First: 2001/09/05]
32	26 Schaller P. Instruction manual Gina V3.0. 2019: 3 https://www.schaller-mt.de/download/LM. Dt.ndf
33	(accessed 28.05.2024)
34	(accessed 20.03.2024).
35	27. Gherini S, Peters Rivi, Virgilio RW. Mechanical work on the lungs and work of breatning with positive
36	end-expiratory pressure and continuous positive airway pressure. Chest 1979;76(3):251-6. doi:
37	10.1378/chest.76.3.251
38	28. Anday EK, Godart-Wlodavar A, Delivoria-Papadopoulos M. Sequential pulmonary function
39 40	measurements in very low-birth weight infants during the first week of life. <i>Pediatr Pulmonol</i>
41	1987;3(6):392-9. doi: 10.1002/ppul.1950030604
42	29. Stenson BJ, Glover RM, Wilkie RA, et al. Randomised controlled trial of respiratory system compliance
43	measurements in mechanically ventilated neonates. Arch Dis Child Fetal Neonatal Ed
44	1998:78(1):F15-9. doi: 10.1136/fn.78.1.f15
45	30 Abhasi S Bhutani VK Pulmonary mechanics and energetics of normal non-ventilated low hirthweight
46	infants. Dediatr Pulmonol 1990;9(2):99, 95, doi: 10.1002/ppul 1950090206
47	21 Ected D. Diviz H. Dintoc L. et al. Accordment of nulmonary dynamics in normal navyborney a
48 40	31. ESTOLP, PIRZ H, PIRTOS L, et al. Assessment of pulmonary dynamics in normal newborns: a
49 50	pneumotachographic method. J Perinat Med 1988;16(3):183-92. doi: 10.1515/jpme.1988.16.3.183
51	32. Krieger TJ, Wald M. Volume-Targeted Ventilation in the Neonate: Benchmarking Ventilators on an
52	Active Lung Model. <i>Pediatr Crit Care Med</i> 2017;18(3):241-48. doi: 10.1097/PCC.0000000000001088
53	33. Bordessoule A, Piquilloud L, Lyazidi A, et al. Imposed Work of Breathing During High-Frequency
54	Oscillatory Ventilation in Spontaneously Breathing Neonatal and Pediatric Models. Respir Care
55	2018;63(9):1085-93. doi: 10.4187/respcare.05703 [published Online First: 20180717]
56	34. Banner MJ, Jaeger M. J., Kirby R. R. Components of the work of breathing and implications for
5/ 50	monitoring ventilator-dependent patients. Crit Care Med 1994:22:515-23.
50 59	35. Courtney SE, Aghai 7H, Saslow IG, et al. Changes in lung volume and work of hreathing: A comparison
60	of two variable-flow nasal continuous nositive airway pressure devices in very low hirth woight
	infante Dediate Dulmonal 2002;26(2):248 F2 dai: 10.1002/mail 10227
	mants. <i>Pediatr Palmonol</i> 2005,30(3):248-52. doi: 10.1002/ppui.1032/

- 36. Blank DA, Rogerson SR, Kamlin COF, et al. Lung ultrasound during the initiation of breathing in healthy term and late preterm infants immediately after birth, a prospective, observational study. Resuscitation 2017;114:59-65. doi: 10.1016/j.resuscitation.2017.02.017 [published Online First: 20170227]
- 37. Kuypers K, Dekker J, Crossley KJ, et al. Slowing lung deflation by increasing the expiratory resistance enhances FRC in preterm rabbits. Pediatr Res 2024 doi: 10.1038/s41390-024-03388-w [published Online First: 20240708]
- 38. Drevhammar T, Falk M, Donaldsson S, et al. Neonatal Resuscitation With T-Piece Systems: Risk of Inadvertent PEEP Related to Mechanical Properties. Front Pediatr 2021;9:663249. doi: 10.3389/fped.2021.663249 [published Online First: 2021/06/25]
- 39. Roukema H, O'Brien K, Nesbitt K, et al. A Crossover Trial of Infant Flow (IF) Continuous Positive Airway Pressure (CPAP) Versus Nasopharyngeal (NP) CPAP in the Extubation of Babies ≤ 1250 Grams Birthweight. Pediatric Research 1999;45(7):317-17. doi: 10.1203/00006450-199904020-01889
- .d.O. A Cross. ryngeal (NP, r 1999;45(7):31. r, et al. Compariso stational Age: The CORS r: 10.1001/jamapediatrics.2L 40. Donaldsson S, Drevhammar T, Li Y, et al. Comparison of Respiratory Support After Delivery in Infants Born Before 28 Weeks' Gestational Age: The CORSAD Randomized Clinical Trial. JAMA Pediatr 2021;175(9):911-18. doi: 10.1001/jamapediatrics.2021.1497



Figure 1: Pressure fluctuations around a set mean pressure of 5,7,9 cm H2O with simulated spontaneous respiration for rPAP (blue) vs. Neopuff (red) with constant tidal volume in term and preterm model.

139x101mm (600 x 600 DPI)





Figure 2: Pressure swings (Δ P in cm H2O) and WOB (mJ) for preterm and term experiments with constant tidal volumes for Neopuff (red) and rPAP (blue) at PEEP 5,7 and 9. Box plots with mean and coefficient of variation percentage (CV%).

99x98mm (300 x 300 DPI)



Figure 3: Pressure (cmH2O) - volume (ml) loops for preterm and term model with constant tidal volumes for Neopuff (red) and rPAP (blue).

139x101mm (600 x 600 DPI)

SUPPLEMENTAL MATERIAL NALM

Settings on the Neonatal Active Lung model (NALM).

1000g	
Resistance	Ra1 = 26,51 cmH ₂ O/L/s ¹
Endotracheal tube ¹	5.0 mm
Compliance	0.5 ml/mbar
Respiratory rate	70/min
Inspiratory time	0.3 s
PRM ²	12.2 cmH ₂ O
3500 g	
Resistance	Ra2= 45,89 cmH ₂ O/L/s ¹
Endotracheal tube ¹	5.0 mm
Compliance	1 ml/mbar
Respiratory rate	50/min
Inspiratory time	0.4 s
PRM	24.5 cmH ₂ O

¹ Numeric values of airway resistance according to the manufacturer's manual.

For simulation of spontaneous breathing on non-invasive ventilation (NIV) the maximum endotracheal tube diameter of 5.0mm was used for both models to negate any influence, as recommended in the manufacturer's manual. The PRM was set to yield a VT of approximately 6 ml/kg (22 ml term, 6 ml preterm) during spontaneous breathing, with 12.2 cm H₂O in the preterm and 24.5 cm H₂O in the term model. Random variation of 5% of the presets PRM and T_{ins} were set. ¹⁹

 The NALM displays the total work of breathing based on formula:

 $W_{tot} = \int insp (Py - Prm) * dV$, with Py referring to airway pressure in NALM.²⁶

Data were outputted in National Instruments Technical Data Management Streaming

(TMDS) file format at a sample frequency of 5ms.