
# Upright Newborn Bag-Mask Resuscitator Comprehensive Document

March 2018

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## March Update Summary

There are several updates since the last version of this document was released.

- Dr. Monica Thallinger has published the results of her clinical study with Upright in Tanzania in Resuscitation in a publication titled “Born not breathing: A randomized trial comparing two self-inflating bag-masks during newborn resuscitation in Tanzania”.
- Dr. Indira Narayanan has published a paper titled “Evaluation of Simulated Ventilation Techniques with the Upright and Conventional Self-Inflating Neonatal Resuscitators”.
- Dr. Jorgen Linde has released two new publications around heart rate and asphyxia titled “Feasibility of a prototype newborn resuscitation monitor to study transition at birth, measuring heart rate and ventilator parameters, an animal experimental study” and “The relation between given volume and heart rate during newborn resuscitation”.
- PATH has published a set of reprocessing guidelines for neonatal equipment in low-resource settings.
- Upright with PEEP Newborn Bag-Mask has been released.
- US FDA approval is being sought for both Upright and Upright with PEEP.
- The Laerdal Newborn Mask has received FDA Class I approval and is available for sale as an individual product.

## Executive Summary

The Upright Newborn Bag-Mask was developed as the result of lessons learned through the implementation of Helping Babies Breathe as a way to address some of the primary shortcomings with bag-masks on the market and to facilitate easy ventilation to newborns.

Compared to other newborn bag-masks on the market, Upright has demonstrated better mask seal, easier reprocessing, and acceptability by healthcare workers. Upright is CE marked and is seeking US FDA approval, and is reprocessable by boiling, autoclaving, and glutaraldehyde. Upright is available as an individual product, included with the NeoNatalie Newborn Simulator, or with a PEEP valve.

Upright has received several awards and was chosen to be included in WHO's compendium of innovative health technologies for low-resource settings. Since it's launch, over 14,000 Upright are being used in around 60 countries, including several country-wide implementation projects.

Upright has been used in several trials and publications, with more trials ongoing. Clinical research with Upright has demonstrated that Upright gives higher early expired $CO_2$, indicating more effective ventilation, and that Upright gives higher median expiratory tidal volume (8.6 ml/kg NNR vs 10 ml/kg UR, p=0.014). Research on manikins has also demonstrated fewer inadequate ventilations, significantly less mask leakage, and preference for the Upright compared to conventional bag-masks.

## The History

The Helping Babies Breathe Alliance started to roll out the Helping Babies Breathe training in 2010. This simplified, hands-on newborn resuscitation training quickly spread across the world. By mid-2015, HBB training has reached over 300,000 birth attendants in over 75 low resource countries[1]. Throughout the implementation of the training, alliance partners and trainers got important insight into how to improve the training program and together they identified several key issues with current resuscitation equipment, particularly related to the design and use of the bag mask resuscitator.

1. Poor mask seal: Creating a good mask seal is a difficult skill, even after HBB training. Research has shown that with available bag-masks, facemask leakage varied from 24% to 59%[2] (Schilleman et al, 2013 & Schmölzer et al, 2011). Although this leakage is always not a problem due to large bag volumes, it may prevent adequate ventilation in cases of fluid filled lungs and newborns with low lung compliance.
2. Mask design: The HBB training is teaching the "C-grip" with the thumb and index fingers creating a C on top of the mask. But the existing mask design is not optimal for this grip. It has a very small surface on top with large inviting sides that make users, even after training, incorrectly put their fingers on the side and press the mask together, which creates openings on the sides of the mask and the seal is broken. Also, as the top is soft, even with a correct C-grip, if the weight is not distributed evenly between the two fingers on top, it's difficult to create a seal.
3. Masks falling out during a resuscitation: An existing problem in the market is that masks are difficult to correctly push into the bag's connector and can easily fall off during a resuscitation, taking away essential time that should be used to help the baby breathe.
4. Positioning causes leakage: The traditional design can be counterproductive to ventilations as the weight of one's hand can tilt the bag-mask downwards, leading to increased leakage. When ventilating manikins, there were less mask leakage with Upright compared to the standard BVM, although the same mask was used.[3]
5. Inadequate cleaning and decontamination: Even if a traditional bag-mask can be taken apart to be cleaned, it was clear to the HBB alliance that the cleaning process lacked focus, and that it was difficult for many providers to reassemble them correctly. Reusable bag-masks on the market contain nine to twelve parts. With every added part, users are more likely to made mistakes during disassembly and reassembly procedures. Some of these assembly mistakes can lead to poor patient outcomes.[4]

This feedback was shared with Laerdal Global Health, who worked very closely with the alliance partners and global experts to address the issues in a new upright version of the bag-mask:

1. Improving mask sealing, by
   - The upright design: The dominant hand holds the bag, and helps the user provide an even, downward pressure onto the mask.

[1] Helping Babies Breathe: Lessons learned guiding the way forward. A 5-year report from the HBB Global Development Alliance.
[2] The Schilleman study was conducted in the Netherlands and the Schmölzer study was conducted in Australia
[3] Thallinger, M et al. Randomized comparison of two neonatal resuscitation bags in manikin ventilation. *Arch Dis Child Fetal NeoNatal*. 2015.
[4] Schmölzer GM: Assessment of tidal volume and gas leakage during mask ventilation of preterm infatns in the delivery room. Archives of disease and childhood fetal and neonatal edition 2008, 93(3):F393-7.

- **The new "Laerdal Newborn Mask":** The mask[5] has a thicker and broader top surface than most other facemasks, and a more pliable bottom cuff part. This design makes it easier to hold the mask correctly, which in manikins has been shown to deliver a higher tidal volume.[6] The stiffer top distributes the grip more evenly than before, and it's almost impossible to place fingers incorrectly on the side of the mask, as it's too small and soft to accommodate the fingers. The Newborn Mask is also designed to give a snap fit with Upright bag and NeoNatalie Resuscitator, to prevent the mask from disconnecting from the bag during use.[7]

2. Easier to disassemble and reassemble correctly for cleaning and disinfection
   - Upright has fewer parts (total 6) compared to other resuscitators (typically 9 - 12), making Upright significantly easier to disassemble and reassemble correctly. Extensive time has also been spent on developing solutions that will make it easier for the user to take the bag apart and put it back together, for example adding a pull strap to the large soft part of the bag.
   - A highly visible label around the neck coupling is a reminder on how the parts are reassembled after cleaning.
   - The product comes with a pictorial poster that shows assembly, disassembly, disinfection and testing steps. See Upright DFU.
3. Larger bag volume
   - The volume of the bag has been increased to 320 ml (from typically 220-250 ml on other resuscitators), to help compensate for mask leakage and for the air that is released through the pop-off safety valve when the user is ventilating too vigorously.
4. Even more convenient to store and transport
   - The silicone bag can be folded for reduced volume during transportation. The length of the bag is shortened by 73 mm when folded.
   - The product can stand upright or hang from an integrated strap, to help reduce risk of soiling of the product before use.
5. Can be high-level disinfected in low-resource settings
   - Upright has been independently validated to achieve high-level disinfection with boiling in clean water, when specified reprocessing procedures are followed. It can be high level disinfected with glutaraldehyde (following manufacturer's recommendation). It can also be sterilized by autoclaving.

The process of developing Upright took over 3 years. Global newborn resuscitation experts within the Helping Babies Breathe Global Alliance worked closely with Laerdal Global Health to create an affordable improved newborn bag mask of quality and standard. This design resulted in a product that is durable, CE marked (hence tested and approved to be used in Western hospital settings) and long-lasting but affordable.

[5] The Laerdal Newborn Mask comes in two sizes: 1 and 0.

[6] Narayanan, I et al. Evaluation of simulated ventilation techniques with the Upright and conventional self-inflating neonatal resuscitators. Respiratory Care. 2017.

[7] The Laerdal Newborn Mask is also compatible with NeoNatalie Resuscitator and other Laerdal resuscitators

## Purchasing Options

Upright can be purchased either as a stand-alone model or as part of the NeoNatalie Complete kit at www.laerdalglobalhealth.com.

| Product | Price* | Price (Valid Feb 2018) |
|---|---|---|
| Upright Newborn Bag-Mask | $20 | $21 |
| Upright with PEEP Newborn Bag-Mask | $25 | $26 |
| Upright bag-mask with oxygen kit | $24 | $25 |
| Upright bag-mask with NeoNatalie and accessories | $83 | $86 |
| Laerdal Newborn Mask (Qty 10) | - | $35 |

* This does not include shipping and custom clearance etc. Price is in USD and is only applicable to qualifying countries.

Upright's Oxygen Kit can be easily attached or detached for settings that require oxygen.

## Awards and Recognition

- *WHO 2014 Compendium*
  Upright was selected to be in the WHO's Compendium of Innovative Health Technologies for Low-Resource Settings. See more at http://www.who.int/medical_devices/innovation/en/.
- *PATH's Innovation Countdown 2030 Report*[8]
  In June 2015, Upright was chosen as one of 30 high-impact innovations to save lives. Read the report at http://ic2030.org/.
- *Norsk Design - Award of Design Excellence*
  Norway Design awarded Upright the award of design excellence in April 2015. In its verdict, the Award of Design Excellence Jury wrote: "The bag has clear functional advantages thanks to its vertical product architecture. The changed angle makes it easier to use and gives close contact with the child. The mask is intuitive and has a design that minimizes the mask leak. Upright can be folded, so that is small and compact. It is easy to assemble and disassemble and facilitates good cleaning practices. With only seven mechanical components, this cost-effective bag will save lives. The product has a robust and credible expression with clear universal qualities. In a remarkable way, Laerdal Global Health have solved the challenges they have been facing. Upright is a textbook example of successful use of design." Read about the award of design excellence here.
- *Core 77 Design Awards*
  Upright was selected by the Core77 Design Awards, an internationally recognized design competition, as a notable submission in the design for social impact competition in June 2015. Read more about this competition here.
- *NPR features Upright as Top 5 Innovations*
  In July 2015, NPR and PATH narrowed down their countdown 2030 report and featured five top innovations that are already in use and show great promise. Read the entire article here.

[8] PATH. Reimagining Global Health, The 2030 Countdown Report: http://ic2030.org/report/

## Locations where Upright is Being Used

Since Upright was launched, over 14,000 Uprights are now in use in around 60 countries. An up-to-date list of current users is available on request. Partners such as UNFPA, UNICEF, Save the Children, ICM, MSF and Red Cross are using Upright in HBB training.

| Country | Amount | Country | Amount |
|---|---|---|---|
| Australia | 86 | Israel | 12 |
| Bangladesh | 170 | Japan | 1 |
| Belgium | 77 | Kenya | 57 |
| Benin | 15 | Korea | 3 |
| Burkina Faso | 1354 | Liberia | 108 |
| Burundi | 25 | Madagascar | 707 |
| Cambodia | 53 | Malawi | 255 |
| Cameroon | 14 | Mali | 435 |
| Canada | 32 | Myanmar | 1094 |
| China | 4 | Nepal | 228 |
| Comoros | 18 | Netherlands | 253 |
| Congo | 60 | Niger | 60 |
| Cote D'Ivoire | 18 | Nigeria | 2274 |
| Cuba | 25 | Norway | 43 |
| DRC | 154 | Pakistan | 53 |
| Dominican Republic | 13 | Papua New Guinea | 42 |
| Ethiopia | 1474 | Rwanda | 12 |
| France | 129 | Senegal | 58 |
| Gambia | 13 | South Africa | 25 |
| Germany | 22 | Switzerland | 23 |
| Ghana | 9 | Tanzania | 385 |
| Greece | 17 | Thailand | 42 |
| Guatemala | 614 | Togo | 50 |
| Guinea | 914 | Uganda | 158 |
| Haiti | 602 | United Kingdom | 403 |
| Hong Kong | 2 | United States[9] | 2 |
| India | 565 | Vietnam | 176 |
| Ireland | 1 | Zambia | 824 |

[9] Not for clinical use.

*Additional information:*

The Ministry of Health in Ethiopia with the Ethiopian Pediatrics Society has decided to use Upright for the Helping 100,000 Babies Survive & Thrive project, which has been rolled out in all 180 hospitals in Ethiopia.

The Federal Ministry of Health in Nigeria, in collaboration with the Paediatric Association of Nigeria (PAN), and the Nigerian Society of Neonatal Medicine (NISONM), have also decided to use Upright for the Helping 100,000 Babies Survive & Thrive project in Nigeria.

## International Regulatory Approval for Clinical Use

Upright is CE marked, and therefore is approved for clinical use and sale in all countries that accept CE marking. Currently a limited number of languages are provided (EN, N, NL, FR, D).

Laerdal is in the process seeking US FDA approval of Upright, along with Upright with PEEP and the Newborn Mask.

Proper CE-marking indicates that ISO 10651-4 has been met. ISO 10651-4 is the recognized standard for manual self-expanding resuscitators. Regulatory bodies of Europe (CE-marking), USA (FDA), Canada, Australia, Japan, etc, all require that ISO 10651-4 is met for sales in their countries. Upright has been rigorously tested both internally and through external labs for safety and efficacy.

Therefore, only countries that require specific regulatory approval separate from CE marking (like the US) are not using Upright for clinical use in their countries. This does not apply to most low-resource countries. Therefore, since our current focus is the 95 countries which have not met SDG 3.1 and 3.2, which do not require FDA approved devices, 510(k) approval is not necessarily required for Upright to be adopted. In addition, it took over 2 years to get NeoNatalie Resuscitator FDA approved and the process was very cost prohibitive.

Regarding cleaning, disinfection and sterilization of reusable medical devices, the AAMI TIR12 and TIR30 standards are to our experience equally acceptable for both FDA 510(k) approval and CE-marking. Regarding sterilization by steam autoclaving, there are some different standards and expectations between Europe and the US.

## Upright Validation & Verification

Upright meets ISO 10651-4:2002/EN ISO 10651-4:2009, Lung ventilators – Particular requirements for operator–powered resuscitators, for newborns and infants with up to 10 kg body mass. Upright underwent extensive testing to verify values for tidal volume, expiratory and inspiratory resistance, patient valve malfunction, pressure limitation (pop off) and dead space. The accessory oxygen kit complies with requirements for oxygen concentration. Upright also underwent environmental challenges, such as extreme operating (-18 °C to 50 °C) and storage (-40 °C to 60 °C) temperatures, contamination with simulated vomitus, immersion in water, and 1-meter high drop testing, to ensure that it operates safely under all conditions.

## Reprocessing & Disinfection Testing

Manual Cleaning Effectiveness Study, performed by NAMSA and Nelson Labs*:

- Requirements: Based on guidelines in AAMI TIR12 and TIR30. The cleaning process ensures that disinfection/sterilization process can be effective.
- Testing: Device is soiled with worst-case contaminants regarding cleaning (i.e. blood and proteins), allowed to dry for 1 hour, and then cleaned in accordance with the User Guide. This is repeated 5 times. The cleaned products are extracted for remaining contaminants, and the extract is subjected to a protein analysis and hemoglobin analysis, with positive and negative controls.
- Results: The acceptance criteria are < 6.4 µg/cm2 of protein and < 2.2 µg/cm2 of hemoglobin. These criteria were met and both Upright and Upright with PEEP passed the test.

Steam Sterilization Efficacy Study, performed by NAMSA and Nelson Labs:

- Requirements: In accordance with ANSI/AAMI/ISO 17665, AAMI TIR12, and ANSI/AAMI ST79.
- Specification: Sterilization procedure in the User Guide: Steam autoclaving at 132 °C, 10 minutes, unwrapped, gravity cycle configuration.
- Testing: The study was done as a half-cycle (5 minutes), which is worst case to 10 minutes.
- Results: Sterilization of biological indicators (*Geobacillius stearothermophilus* spores), which Upright and Upright with PEEP passed.

High-level disinfection; Cleaning and Boiling validation, performed by NAMSA, and boiling validation performed by Nelson Labs: Standard was updated in 2010.

- Requirements: In accordance with AAMI TIR12
- Specification: Boiling at 100 °C for 10 minutes
- Testing: Contaminated with a bacteria strain. Devices soiled internally into the patient port and externally from soiled gloved hands.
- Results: Acceptance criteria is > 6 log reduction, which Upright and Upright with PEEP passed.

High-level disinfection; Cleaning and Glutaraldehyde validation, performed by NAMSA: Standard was updated in 2010.

- Requirements: Specified for immersion in activated glutaraldehyde solution for 60 minutes
- Testing: Contaminated with bacteria. Devices soiled internally into the patient port and externally from soiled gloved hands.
- Results: Acceptance criteria is > 6 log reduction, which Upright passed.

In addition, material compatibility tests are performed for each specified disinfection process. Typically, 100 complete reprocessing cycles are performed. No significant performance change or visual degradation has been seen.

*NAMSA and Nelson Laboratories are both well-known medical device contract research organizations with several decades of experience with medical device product testing. They follow the standards set by the device industry and conduct tests for regulatory bodies (i.e. CE and FDA testing). NAMSA was used for Upright testing and Nelson Labs for Upright with PEEP testing.

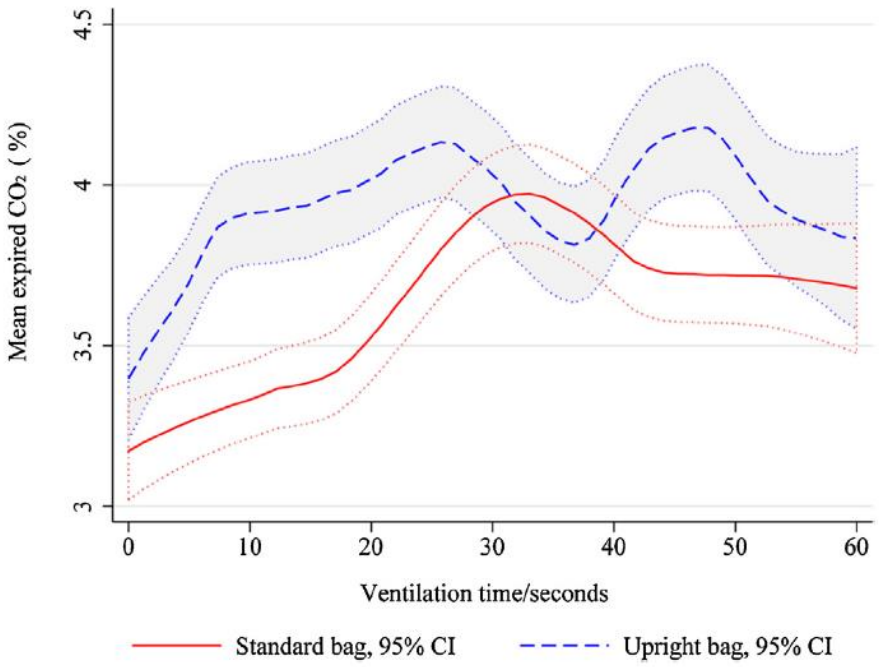
PATH has published new guidelines and job aids for reprocessing of newborn resuscitation equipment: Reprocessing Guidelines for Basic Neonatal Resuscitation Equipment in Resource-Limited Settings. These guidelines and supporting documents are available in English, French and Spanish.

## Completed Studies

**Location:** Tanzania

**Collaborator:** Safer Births, Dr. Monica Thallinger

- Published in *Resuscitation* in April 2017
- Research Question:
  - Does Upright bag-mask provide more effective ventilation than the standard bag-mask?
- Methods:
  - Newborns were resuscitated with either with the Upright bag or the NeoNatalie resuscitator (192 and 136 newborns respectively).
  - A monitor collected ventilation data through a flow sensor and heart rate with ECG electrodes.
  - The primary outcome was expiratory tidal volume per birth weight.
- Results:
  - Upright (UR) gave higher median expiratory tidal volume (8.6 ml/kg NNR vs 10 ml/kg UR, p=0.014).
  - Upright had increased mean airway and peak inspiratory pressures.
  - Upright had higher early expired $CO_2$ (median at 20 seconds was 4.2% vs 3.2%, p=0.0099), indicating more effective ventilation.
  - Clinical outcome 30 minutes post-delivery was normal in 44% with NNR versus 57% with UR (p=0.016), but similar at 24 hours.
- Publication- Born Not Breathing: A randomized trial comparing two self-inflating bag-masks during newborn resuscitation in Tanzania



**Location:** Seattle, USA

**Collaborator:** PATH & George Washington University

- Published August 2017
- Research Question:
    - Was there a difference between the delivered tidal volume and pressure of Upright versus a conventional self-inflating neonatal bag-mask on manikins?
- Methods: Videos were analyzed of users ventilatory performance with a newborn simulator and a test lung, for normal and low lung compliance scenarios.
- Results:
    - Delivered tidal volume and peak inspiratory pressures (PIP) values were higher when using the Upright than when using the conventional bag-mask
    - With low compliance, PIP was significantly higher when using the upright with the "OK" hold (upright, 36.3 ± 4.4 mL, vs conventional, 30.3 ± 6.6 mL, P =.009) and when the bag was squeezed by more than half (P = .046).
    - With normal compliance, delivered volume was high with both bag masks and was significantly higher with upright resuscitator with the "OK" hold (P < .001), and when the bag was squeezed using more than 2 fingers (P =.01) and by more than half (P=.004).
    - With normal compliance, PIP was significantly higher when using the upright with the OK hold (P <.001) and when the bag was squeezed using more than 2 fingers (P= .005), and by more than half (P= .001).
- Conclusion: On manikins, high tidal volumes were observed with both types of self-inflating BVMs, but more so with Upright with normal compliance. The study highlights the lack of recognition of changes in compliance and the need for training around better ventilation technique.
- Publication- Evaluation of Simulated Ventilation Techniques with the Upright and Conventional Self-Inflating Neonatal Resuscitators

**Location:** Seattle, USA

**Collaborator:** PATH

- Research done between March 2011 through December 2012
- Published March 2013 (User Evaluation of Simplified Neonatal Resuscitators)
- Research Question:
    - Is Upright easier to use/more acceptable than the NeoNatalie Resuscitator?
    - Is Upright easier to assemble and disassemble compared with NeoNatalie Resuscitator?
    - Does Upright have decreased mask leak?
- Methods: Each of the devices was tested for user ventilatory performance with newborn simulator and an Ingmar Medical ASL-5000 test lung, for two newborn patient-condition scenarios:
    - Low-compliance lung expansion (0.5 mL/cm$H_2O$), simulating newborns with fluid-filled lungs.

- Normal-compliance lung expansion (2.0 ml/cm$H_2O$), simulating infants with fully developed lungs.

- Results:
  - Improved ventilation: The percentage of inadequate ventilations is significantly lower for Upright device than for NeoNatalie Resuscitator (8.31% vs. 19.01%, respectively; p<0.001) on the low-compliance setting and (1.05% vs. 8.64%, respectively; p< 0.001) on the normal-compliance setting.
  - The majority (68%) of participants stated that they preferred Upright resuscitator.
  - Disassembly of NeoNatalie Resuscitator took longer (87.94 +/- 44.22 seconds) as compared to Upright device (64.27 +/ - 39.05 seconds) (p=0.0245). Participants were able to correctly assemble all component parts of NeoNatalie Resuscitator less often than those of Upright device (summary index score of 13% vs. 53%, respectively).
  - Decreased mask leak: In low-compliance settings, the leak through the mask-face interface was significantly less for Upright device than for NeoNatalie Resuscitator (8.83 vs. 12.41 ml/s)
- Publication

**Location:** Tanzania & Norway

**Collaborator:** Safer Births, Dr. Monica Thallinger

**Details:**

- Research Question: Is Upright or the standard bag-mask easier to use and which do students prefer?
- Method:
  - 41 nursing and medical students without any knowledge of newborn resuscitation were trained in basic bag-mask ventilation and ventilated with the two devices; a new Upright resuscitator and a standard newborn resuscitator (Laerdal Medical, Stavanger) on a NeoNatalie manikin in random order. Ventilation data was collected with the Newborn Resuscitation Monitor. The students answered questions grading mask seal (1) and ease of air entry (2) from 1 (difficult) to 4 (easy) and finally which device they preferred.
- Results:
  - Less mask leak: Mean mask leakage for Upright was 46% and standard 60% (paired sample test p<0.001, which indicates a significant difference in mask leakage between the products)
  - Easier to ventilate: Mean score of 3.5 for Upright and 3.2 for standard (where 4 is easy and 1 is difficult)
  - 31 of 41 (76%) students preferred Upright resuscitator
  - Mean expired lung volume was 15.5 ml for Upright and 13.8 for standard resuscitator with mean difference 1.7 ml (one sample t-test for paired observations p=0.03, which indicates a significant difference in the amount of air delivered into the lungs of the manikin).
- Abstract

**Location:** Uttar Pradesh, India

**Collaborator:** PATH, Save the Children, Aligarh Muslim University

**Details:**

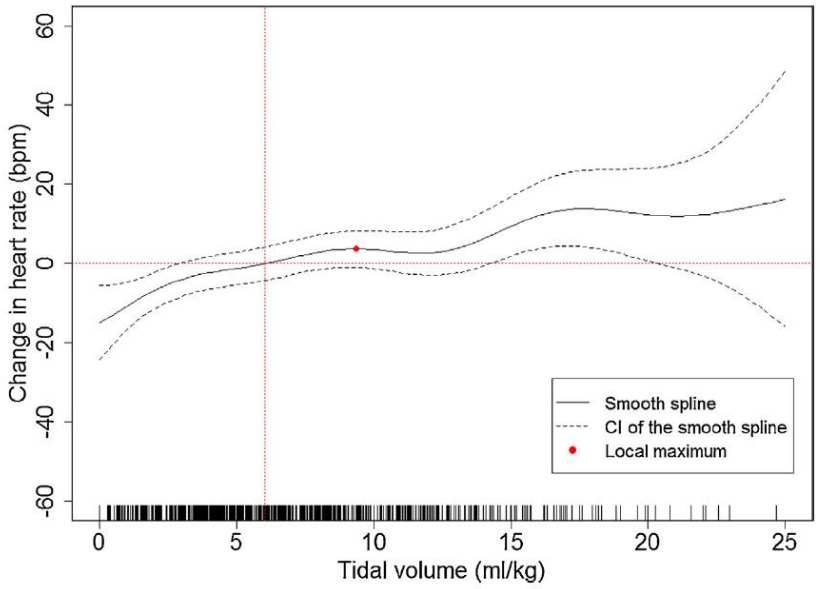
- Research question: Is Upright when compared with the Laerdal 500 ml resuscitator more effective in delivering adequate ventilation on manikins, and is it easier to use?
- Method:
    - Tests were conducted using NeoNatalie manikin, Laerdal Silicone 500ml bag and mask resuscitator and Upright resuscitator.
    - 60 participants were stratified by professional experience and hand size.
    - Quantitative: Measure proportion of adequate ventilations achieved when using each resuscitator
    - Qualitative: Evaluating preference and ergonomics.
- Results:
    - In low compliance, mean tidal volume, mean PIP, and excessive ventilations (defined as greater than 15 mL/kg) were statistically significantly higher for Upright.
    - In normal compliance, the mean ventilation rate was significantly lower for Upright.
    - There were no statistically significantly differences in performance between resuscitators across all variables.
    - 85% of participants preferred Upright and inexperienced users were more likely to prefer Upright.
    - There was no observed variation in mask hold positions and ventilation techniques between the resuscitators.
- Conclusions:
    - The Upright was easier to user than the pediatric 500-mL BVM.
    - Both products are capable of delivering the minimum required tidal volumes to newborns.
    - The usefulness of chest rise as a subjective measure of device performance should be explored further.
    - Participants were not able to recognize changes in lung compliance.
- Publication: Manuscript submitted- *A PATH Report: User Evaluation of Simplified Neonatal Resuscitators in Uttar Pradesh, India*. Poster presented to WHO at the Third WHO Global Forum on Medical Devices in May 2017.

**Location:** Haydom, Tanzania

**Collaborator:** Safer Births, Dr. Jorgen E. Linde

**Details:**

- Published August 2017 in *Resuscitation*.
- Research question: The study objectives were to determine the following:
    - The relationship between a given tidal volume during initial ventilation and heart rate responses of depressed newborns.
    - The optimal delivered tidal volume associated with a rapid increase in heart rate.
- Methods: In a Tanzanian rural hospital, ventilation and ECG signals were recorded during neonatal resuscitation and stored in neonatal resuscitation monitors. Newborn bag-masks without positive end-expiratory pressure were used for positive pressure ventilation (PPV). Perinatal events (n=215) were observed and recorded by research assistants.
- Results:
    - There was a non-linear relationship between delivered tidal volume (TV) and heartrate (HR) increase.
    - TV of 9.3 ml/kg produced the largest increase in HR during PPV.
    - Frequent interruptions of PPV to provide stimulation/suctioning occurred in all cases and were associated with further HR increases, especially for newborns with initial HR < 100 beats/minute. This suggests that most newborns were in primary rather than secondary apnea.
    - There was a consistent positive relationship between HR increase and delivered TV.
- Conclusion: Tidal volumes below 6 mL/kg will not give an increase in heart rate, and a tidal volume of 9.3 ml/kg resulted in the largest increase in HR.
- Publication- The relation between given volume and heart rate during newborn resuscitation.



**Location:** Tanzania & Norway

**Collaborator:** Safer Births, Dr. Monica Thallinger

**Details:**

- Research Question: Is Upright or the standard bag-mask easier to use and which do students prefer?
- Method:
    - 83 nursing and medical students from Tanzania and Norway without any knowledge of newborn resuscitation were trained in basic bag-mask ventilation. They ventilated with two new devices, Upright resuscitator and a standard newborn resuscitator, on a NeoNatalie manikin in a random order. Ventilation data was collected with the Newborn Resuscitation Monitor and analyzed for all students. The students answered questions grading mask seal (1) and ease of air entry (2) from 1 (difficult) to 4 (easy) and finally which device they preferred.
- Results:
    - Less mask leak: Mean mask leakage for standard was 57% and Upright 48%.
    - 68% of the students preferred Upright resuscitator.
    - Mean expired lung volume was 15.9 ml for Upright and 14.6 for standard resuscitator with mean difference 1.4 ml. This indicates that Upright's improved mask seal led to a higher amount of air delivered.
    - For "mask seal" mean score was 2.7 for standard and 3.2 for Upright (one sample binomial test p= < 0.01, indicating significantly better perception of mask seal), and for "ease of air entry" 3.0 for standard and 3.4 for Upright (p= <0.01, indicating a significantly better perception of ease of air entry for the students)
- Abstract, Published Paper

**Location:** Tanzania

**Collaborator:** Safer Births, Dr. Monica Thallinger

**Details:**

- Research Question: Can inexperienced providers generate PEEP during simulated neonatal ventilation, using two novel prototype PEEP valves, on Upright?
- Method:
    - Tanzanian nursing students (n=46) were trained in ventilation using Upright on a manikin with a newborn resuscitation monitor.
    - Ventilation was studied with and without PEEP on low and normal compliant lungs. One PEEP valve had PEEP of 4-5 $cmH_2O$, and one had 9-10 $cmH_2O$.
- Results:
    - PEEP was generated even when high mask leak was present. Mean mask leak was similar with and without PEEP.
    - Mean PEEP with PEEP1 was 4.4 $cmH_2O$ and with PEEP2 was 4.9 $cmH_2O$.
    - PEEP ≥4 $cmH_2O$ was generated with 70% of inflations with PEEP1 and 65% with PEEP2.

- Mean airway pressure was 16.3 $cmH_2O$ with both PEEP valves compared with 14.2 without PEEP ($p<0.001$).
- Findings with normal and low compliance were similar.

- Conclusion: PEEP between 4 $cmH_2O$ and 5 $cmH_2O$ was achieved when ventilating a neonatal manikin using a self-inflating bag and novel PEEP valves. Valves that can generate PEEP without external gas sources may aid resuscitation in resource-limited settings.
- Publication-Neonatal ventilation with a manikin model and two novel PEEP valves without an external gas source. *Arch Dis Child Fetal Neonatal Ed.* 2016

## Ongoing Studies

**Location:** Tanzania

**Collaborator:** Safer Births, Dr. Kari Holte & Dr. Hussein Kidanto

**Details:**

- A randomized controlled trial comparing Upright with Upright with PEEP.
- The aim is to study whether lung aeration can be improved by adding a device for positive end expiratory pressure (PEEP) to better distend the airways in neonates more than 28 weeks gestation.
- The estimated enrollment is 330 participants.
- Study start date: September 2016
- Estimated study completion date: April 2018
- Primary outcome: Heart rate during ventilation
- Secondary outcomes:
  - Neonatal deaths at 24 hours
  - Time of ventilation
  - Time to hear rate above 140 beats/minute
  - Mean airway pressure
  - Time to detection of exhaled $CO_2$ above 1% and 4%
- More information can be found on the registered clinical trial: https://clinicaltrials.gov/ct2/show/NCT02971553

**Location:** Uganda

**Collaborator:** Mbarara University, MIT, Massachusetts General Hospital, Harvard University

**Details:**

- The Augmented Infant Resuscitator (AIR) project will be using Upright bag-mask in their tests.
- This project has received three USAID Saving Lives at Birth grants.
- For more information, visit the SLAB website: https://savinglivesatbirth.net/summaries/2017/549

## Upright with Newborn PEEP


Positive End-Expiratory Pressure (PEEP) retains a volume of air in the lungs between each ventilation. For newborns with fluid-filled or immature lungs, PEEP during first and subsequent ventilations helps clear fluid from the lungs, reduces airways resistance, recruits lung volume and reduces damage to the newborn's lung tissue from repeated lung alveolar collapse.

Upright with Newborn PEEP was released in 2016. Upright with Newborn PEEP includes a PEEP valve intended for preterm and term newborns and infants up to 10 kg body mass who require respiratory support. This PEEP replaces Upright's patient port connector. Upright is used as normal when Newborn PEEP is attached.

Research conducted by Dr. Monica Thallinger also show that students were able to provide acceptable levels of PEEP using Upright with Newborn PEEP even with high rates of mask leakage (see more information on study and publication on page 16).

## WHO Technical Specifications for Neonatal Resuscitation Devices

WHO, as part of the United Nations Commission on Life-Saving Commodities for Women and Children, published technical specifications on basic newborn resuscitation in 2016, which provides a guideline for procuring neonatal resuscitation equipment in low resource settings to decrease infant mortality rate. This document can be download at this link.

These specifications are the result of a collaboration of experts from different backgrounds and organizations, including WHO, UNICEF, CHAI, PATH and Save the Children, and Upright is accepted under their specifications for a self-inflating neonatal resuscitation bag with mask.

## Interesting Research Questions Currently Not Addressed in Any Ongoing Studies

- Can people who have been trained with an Upright use a traditional bag-mask safely/correctly?
- Can Upright be used as a transition product for practitioners who are using the 500 mL bags?
- Can you have a conventional bag-mask and an Upright bag present in a facility or do you only need to have an Upright present?
- Is there a difference in outcomes between preterm and term babies?
- If a provider who has experience only with "traditional" bag-mask resuscitators on children or adults is given Upright, will they be able to use the skills they have on adults/children with Upright on newborns?

## Contact Information

In case of further questions or concerns, please contact:

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