|  |
| --- |
| protocol  **RFM in simulated neonatal ventilation** |
| A randomised controlled trial of the use of a respiratory function monitor to teach neonatal mask ventilation to healthcare professionals in a simulation setting. |
| Protocol Number (if applicable): HREC 36031  Protocol Version # and date: version 3 21.03.2016  **Revision Chronology:**   | **Date of change** | **Summary of changes** | | --- | --- | | **8/02/2016** | **MT edits** | | **9/02/2016** | **PD edits** | | **17/02/2016** | **LM/COD edits** | | **21/03/2016** | **LH (peer review) edits** | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  | |  |  | |
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# PROTOCOL SYNOPSIS

|  |  |
| --- | --- |
| ***Title*** | A randomised controlled trial of the use of a respiratory function monitor to teach neonatal mask ventilation to healthcare professionals in a simulation setting. |
| ***Objectives*** | The primary objective is to compare the leak from mask ventilation performed by a healthcare professional on a mannequin, after learning mask ventilation using a respiratory function monitor and after learning mask ventilation without using a respiratory function monitor. |
| ***Design*** | Single centre, randomised controlled trial. The participant will be randomised to either the intervention group (neonatal mask ventilation taught with a respiratory function monitor) or control (standard teaching of neonatal mask ventilation). No crossover to the alternative learning method will be permitted. |
| ***Outcomes*** | *Primary outcome*  Difference in leak measured after neonatal mask ventilation training between the control and intervention groups.  *Secondary Outcomes*   1. Difference in expired tidal volume 2. Stability of tidal volume achieved i.e. consistency of tidal volumes in consecutive breaths 3. Percentage of obstructed inflations |
| ***Study Duration*** | 2 years 3 months |
| ***Interventions*** | Training in mask ventilation conducted according to the Victorian Newborn Resuscitation (NeoResus) program with or without the addition of continuous mask leak feedback via a respiratory function monitor attached to the t-piece device (Neopuff). |
| ***Number of participants*** | 382 (191 in each arm) |
| ***Population*** | Adult health care professionals attending the Victorian Neonatal Resuscitation training program (a structured simulation training program, *NeoResus*) in the Royal Children’s Hospital during the study period. Doctors from any specialty, midwives, nurses, physiotherapists, occupational therapists, paramedics, medical students, midwifery and nursing students will be included. |

# GLOSSARY OF ABBREVIATIONS

|  |  |
| --- | --- |
| **ABBREVIATION** | **TERM** |
| AE | Adverse Event |
| ANOVA | Analysis of Variance |
| CRF | Case Report Form |
| HREC | Human Research Ethics Committee |
| ITT | Intention To Treat |
| MCRI | Murdoch Children’s Research Institute |
| NHMRC | National Health and Medical Research Council |
| RCH | Royal Children’s Hospital |
| RWH | Royal Women’s Hospital |
| PI | Principal Investigator |
| RFM | Respiratory Function Monitor |

# ADMINISTRATIVE INFORMATION

# Trial registration

Intended registry is clinicaltrials.gov

# Sponsor

| Study Sponsor | Newborn Research Centre, Royal Women’s Hospital |
| --- | --- |
| Contact name | Prof Peter Davis |
| Address | Parkville, VIC 3052 |

The PI, Eoin O ‘Currain will administer the study from the Newborn Research Centre, RWH. The investigators (Director Prof Peter Davis & Marta Thio) are sponsoring the study and are responsible for supervising the PI in study design, data collection, analysis and interpretation, report and publication writing and submission and have ultimate authority over these activities.

# Expected duration of study

The recruitment period is projected to be 18 months. The intervention period lasts for 1 hour 25 minutes and the follow-up period is 3 -6 hours (duration of the course).

# Contributorship

| **Name** | **Summary of contribution** |
| --- | --- |
| Dr Eoin O’Currain, Royal Women’s Hospital | Study design, protocol author |
| Dr Marta Thio, Royal Women’s Hospital | Concept, Study design, protocol review |
| Dr Colm O’Donnell, National Maternity Hospital, Dublin, Ireland. | Protocol review, study design, experimental model |
| Dr Lisa McCarthy, National Maternity Hospital, Dublin, Ireland. | Protocol review, study design |
| Dr Jennifer Dawson, Royal Women’s Hospital | Protocol review, study design |
| Dr Rosemary Boland, Royal Women’s Hospital | Protocol review |
| Dr Michael Stewart, Royal Children’s Hospital | Protocol review |
| Prof Colin Morley, Royal Women’s Hospital | Protocol review, study design |
| A/Prof Susan Donath, The University of Melbourne | Protocol review, randomisation, stratification and sample size estimation |
| Prof Peter Davis, Royal Women’s Hospital | Concept, study design, protocol review |

# 

# INTRODUCTION AND BACKGROUND

# Background and rationale

Preterm birth and newborn birth asphyxia are responsible for 1.7million of the 2.9 million neonatal deaths that occur worldwide each year (1 million and 0.7 million respectively). Complications of labour and delivery also represent the highest risk of disability and developmental impairment in survivors. (1) Despite this high burden of disease there is a surprising lack of evidence in how best to train critical newborn resuscitation skills. (2) Approximately 10% of newborn infants require some assistance at birth. The latest report (2013) on Australian mothers and babies’ outcomes showed that >68,000 babies needed assistance after birth with 7.9% requiring respiratory ventilation. (3) Establishing effective ventilation in the first minutes after birth is the first critical intervention in newborn resuscitation. (4) This is an opportunity to make a difference by saving newborn lives and reducing poor neurodevelopmental outcomes but the skills are difficult to master and maintain. To this end, all healthcare professionals that care for newborns require ongoing resuscitation training. (2) Teaching resuscitation skills allows us to translate research advances into real improvements in the care of sick newborns. This randomised controlled clinical trial aims to improve health outcomes for newborns by investigating a new method of teaching neonatal mask ventilation.

Very little is known about specific ways to improve the teaching of resuscitation skills. (5) Training methods have the potential to improve the standard of neonatal care, particularly in inexperienced or infrequent resuscitators. (6) The effectiveness of mask ventilation may be compromised by a large or variable leak around the mask or airway obstruction. (7) (8) (9) Mask leak is reported as being between 14-65% in neonatal mannequin studies and 29% in preterm infants (interquartile range 16-63%). (7) (10-12) Currently, there is limited evidence on methods to objectively assess a candidate’s proficiency at this skill and to provide feedback during training.

Some research has demonstrated improvements in psychomotor performance after neonatal resuscitation training. (6) Previous publications in this field report variability in both the educational interventions and outcomes. Outcomes were mostly based on checklist or knowledge-based assessments. Nadel demonstrated an improvement in simulated completion of airway and resuscitation skills after a 2 day paediatric resuscitation training program, as compared to no formal training. (13) Ernst found that weekly or daily intubation training improved medical students simulated intubation success rate. (14) In a mannequin study of neonatal bag mask ventilation, Pearlman found that participants of varying skill levels delivered inadequate tidal volumes and using chest wall movement as a feedback mechanism resulted in the lowest volumes. (15) Several mannequin studies have suggested that respiratory monitoring adjuncts may improve neonatal mask ventilation by reducing mask leak and percentage of obstructed breaths. (16-19)

Respiratory Function Monitors (RFMs) may be used to monitor the effectiveness of newborn ventilation. (19) Their role in training has not yet been explored in a randomised controlled trial. This trial will address two knowledge gaps identified in the 2015 International Liaison Committee on Resuscitation (ILCOR) guidelines, to determine what educational techniques are useful for teaching and maintaining resuscitation skills. Specifically,

“There is a need for further research to determine whether routine use of flow and volume monitoring for task training in newborn resuscitation improves training or clinical outcomes” and

“There is a need for well-designed and well-powered clinical trials, possibly cluster randomised, that answer key questions with critical outcomes: How frequently should learning occur? What type of intervention is most effective? What validated tools are available to measure educational outcomes?”. (6)

More than 200 multidisciplinary health care professionals attended the Victorian Neonatal Resuscitation training program in 2015. 14 courses are planned for 2016 with 18-24 participants per course. This structured simulation environment provides an excellent opportunity to study methods to improve training techniques.

**Research Question**

**P**opulation: In healthcare professionals with different levels of mask ventilation experience undergoing resuscitation training in a simulation setting in Victoria

**I**ntervention: does using a respiratory function monitor while learning neonatal mask ventilation on a mannequin compared to

**C**ontrol: standard mask ventilation learning reduce

**O**utcome: leak between the mannequin and the t-piece resuscitation device (Neopuff).

# Aim(s)

The aim of this study is to assess the effectiveness of a respiratory function monitor to teach neonatal mask ventilation.

# STUDY OBJECTIVES

# Primary objective

The primary objective of this study is to compare the leak from mask ventilation performed by a healthcare professional on a mannequin after learning mask ventilation using a respiratory function monitor and after learning mask ventilation without using a respiratory function monitor.

# Secondary objectives

1. Difference in expired tidal volume
2. Stability of tidal volume achieved i.e. consistency of tidal volumes in consecutive breaths
3. Percentage of obstructed inflations

# STUDY DESIGN

# Type of Study

This is a single centre, outcome-assessor blinded, randomised controlled superiority trial. The participant will be randomised to either the intervention or control (standard teaching) group. No crossover to the alternative learning method will be permitted.

# Study Setting

The study setting will be the Health Education and Learning Precinct, RCH during the Victorian Neonatal Resuscitation training program (a structured simulation training program, *NeoResus*).

# PARTICIPANTS AND RECRUITMENT



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# Number of Participants

The expected number of participants in the study is 382. 336 course attendees per year will be eligible for participation. 14 neonatal resuscitation courses are planned in the Royal Children’s Hospital, Melbourne in 2016 with 24 participants per course.

# Eligibility Criteria

Course participants will be randomised to the intervention or control group only if they fulfil all inclusion criteria and none of the exclusion criteria.

# Inclusion criteria

Each participant must meet the following criteria to be enrolled in the study:

* Over 18 years of age
* One of the following healthcare professionals: Doctors from any specialty, midwives, nurses, physiotherapists, occupational therapists, paramedics, or a medical, nursing or midwifery student
* Attending the Victorian Neonatal Resuscitation training program. Attendees of both the first response program (3 hours’ duration) and the Advanced Resuscitation (7 hours’ duration) are eligible.

# Exclusion criteria

Participants meeting any of the following criteria will be excluded from the study:

* Unable or unwilling to provide written informed consent
* Attendees who are not one of the healthcare professional groups or student groups listed above will not be included

# Recruitment and identification of potential participants

A list of confirmed course participants will be obtained from the PIPER nursing educators one week before each course. All planned course participants will be contacted via email. A brief introduction of the PI and the rationale of the study will be provided. The participant information leaflet and consent form will be included. Participants will be asked to respond to the email if they wish to participate and they will be asked to sign the consent form on the morning of the course. They will then be screened for eligibility. Recruitment will be performed by one of the researchers.

# Consent

Signed, written consent will be obtained prior to eligibility screening. The consent form will describe the study rationale and aim, the participant procedure and any risks and benefits to the participants. The investigator will conduct the informed consent procedure, which will take the form of a short 5-minute presentation to the group. It will be emphasised that consent will be voluntary and free from coercion. It will also be emphasised that the learning and educational experience of the participants will not be in anyway affected should they decline to consent. If they do so decline, they will receive standard NeoResus education. The investigator that performs the informed consent procedure will also sign the consent form. A copy of the signed consent form will be provided to the participant. When eligibility status is confirmed and the inclusion/exclusion criteria have been assessed, the participants will be assigned to a randomisation intervention in the study.

A record of ineligible and non-participating course attendees will be maintained. This will record their professional role, exclusion criteria or whether they declined consent.

# INTERVENTION

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# Intervention arms

*Intervention*

Training in mask ventilation will be conducted according to the Newborn Resuscitation (NeoResus) program with the addition of a respiratory function monitor attached to the t- piece device (Neopuff). This will provide continuous real time feedback on mask leak. Participants will perform the mask ventilation skill station in groups of six. Neonatal mask ventilation training will last for 1 hour and 25 minutes in total. During this time period each participant will perform two episodes of mask ventilation, each lasting 90 seconds. The first episode will consist of the participant performing mask ventilation as a standalone skill. The second episode will consist of the participant performing mask ventilation as part of a simulated resuscitation scenario. Participants will be instructed on mask ventilation and on interpretation of the RFM. When performing mask ventilation, the participants will be instructed to achieve:

1. Minimal (0-10%) mask leak, and

2. Mannequin chest rise

Both the participants and trainers will observe leak and chest rise during ventilation. Participants will adjust their technique to minimise the leak by making the following changes:

1. Reposition airway to the neutral position, avoid neck flexion or overextension

2. Mask adjustment: adjust face mask hold, ensure face mask is covering nose and mouth, ensure mask is pressed against mannequin face, adjust face mask position on face, reapply face mask

Participants will be advised of additional manoeuvers (suction mouth and nose, open mouth, increase pressure, consider an alternative airway) to attempt if they are unable to obtain chest rise and improvement in heart rate/colour and saturations in the simulation setting.

*Control*

Training in mask ventilation will be conducted according to the Newborn Resuscitation (NeoResus) program with a T-piece device (Neopuff). Participants will perform the mask ventilation skill station in groups of six. Neonatal mask ventilation training will last for 1 hour and 25 minutes in total. During this time period each participant will perform two episodes of mask ventilation, each lasting 90 seconds. The first episode will consist of the participant performing mask ventilation as a standalone skill. The second episode will consist of the participant performing mask ventilation as part of a simulated resuscitation scenario.

Participants will be instructed on mask ventilation. When performing mask ventilation, the participants will be instructed to achieve adequate mannequin chest rise. Both the participants and trainers will observe chest rise during ventilation.

Participants will adjust their technique to improve chest rise by making the following changes:

1. Reposition airway to the neutral position, avoid neck flexion or overextension

2. Mask adjustment: adjust face mask hold, ensure face mask is covering nose and mouth, ensure mask is pressed against mannequin face, adjust face mask position on face, reapply face mask

Participants will be advised of additional manoeuvers (suction mouth and nose, open mouth, increase pressure, consider an alternative airway) to attempt if they are unable to obtain chest rise and improvement in heart rate/colour and saturations in the clinical setting. (17)

# Intervention(s)

The intervention and control groups will be taught in separate rooms by separate instructors. The following timetables indicate the timings and duration of the interventions. The facilitators will first demonstrate the technique of mask ventilation. To ensure standardisation of training in both arms all facilitators will be provided with a checklist, detailing the instructions that they will give the participants. The participants will then perform mask ventilation under supervision and will receive instruction as detailed, in the order specified.

Advanced Resuscitation program: Mask ventilation station 10:45 – 12:10

**Intervention group**: RFM visible

|  |  |  |
| --- | --- | --- |
| **Time** | **Training Component** | **Training Format** |
| 10:45-11:00 | Equipment: Resuscitaire, power source, oxygen supply, height adjustment, Apgar clock, heat source, suctioning, Neopuff set-up, Bag and mask check, troubleshooting | Demonstration by facilitator.  Group questions |
| 11:00-11:05 | **Baseline leak assessment** (RFM covered)  Each participant performs 30 seconds of mask ventilation and baseline leak is recorded | Leak recorded by researcher. Trainer and participant blinded to leak. |
| 11:05 – 11:20 | **Intervention:**  Each participant performs neonatal ventilation with the Neopuff and with the BMV + **RFM (visible)** for 90 seconds (1.5 mins x 6) | Participant practice with instruction |
| 11:20 – 11:25 | Chest compression demonstration and practice | Participant practice with instruction |
| 11:25 – 12:00 | Neonatal simulated scenarios x 2  All six participants perform neonatal ventilation with the Neopuff + **RFM (visible)** for 90 seconds  (1.5 mins x 6) | Participant practice with instruction |
| 12:00 – 12:10 | **Post-training leak assessment.** Each participant performs Neopuff (RFM covered) for 90 seconds  (1.5 mins x 6) | Participant practice with instruction |

Advanced Resuscitation program: Mask ventilation station 10:45 – 12:10

**Control group:** RFM covered

|  |  |  |
| --- | --- | --- |
| **Time** | **Training Component** | **Training Format** |
| 10:45-11:00 | Equipment: Resuscitaire, power source, oxygen supply, height adjustment, Apgar clock, heat source, suctioning, Neopuff set-up, Bag and mask check, troubleshooting, Demonstrate neonatal ventilation | Demonstration by facilitator.  Group questions |
| 11:00-11:05 | **Baseline leak assessment** (RFM covered). Each participant performs 30 seconds of mask ventilation and baseline leak is recorded | Leak recorded by researcher. Trainer and participant blinded to leak. |
| 11:05 – 11:20 | **Control**  Each participant performs neonatal ventilation with the Neopuff and with the BMV + **RFM (covered)** for 90 seconds (1.5 mins x 6) | Participant practice with instruction |
| 11:20 – 11:25 | Chest compression demonstration and practice | Participant practice with instruction |
| 11:25 – 12:00 | Neonatal simulated scenarios x 2  All six participants perform neonatal ventilation  with the Neopuff + **RFM (covered**) for 90 seconds  (1.5 mins x 6) | Participant practice with instruction |
| 12:00 – 12:10 | **Post-training leak assessment.** Each participant performs Neopuff (RFM covered) for 90 seconds  (1.5 mins x 6) | Participant practice with instruction |

Neonatal mask ventilation training: facilitator checklist

Instructions given by the facilitator while participants perform ventilation**: RFM visible**

**Intervention Group**

|  |  |  |  |
| --- | --- | --- | --- |
| **Time** | **Training component** | **Instruction** | **√** |
| 10:55 – 11:00 | Demonstration of neonatal ventilation | Position the head and neck in the midline.  Position the airway in the neutral position.  Do not use a head roll (advise that it may be used in the clinical situation)  Perform the two finger mask hold  Administer breaths at a rate of 1 per second |  |
| 11:05 – 11:55 | Participant performs neonatal mask ventilation (with Neopuff) + **RFM visible** | Advise to target   1. Leak <10% 2. Visible chest rise   Advise to also target HR improvement, saturation, and colour in the clinical situation |  |
|  | 1. Poor chest rise or and/or leak >10% | Advise in the following order:  1. Reposition airway to the neutral position, avoid neck flexion or overextension, avoid obstructing the airway with the finger |  |
|  |  | 2. Mask adjustment: adjust face mask hold, ensure face mask is covering nose and mouth, ensure mask is pressed against mannequin face, adjust face mask position on face, reapply face mask |  |
|  |  | Advise additional manoeuvers (suction mouth and nose, open mouth, increase pressure, consider an alternative airway) to attempt if they are unable to obtain chest rise and improvement in heart rate/colour and saturations in the clinical setting |  |
|  | 1. Adequate chest rise and leak <10% | Advise of interventions (as above) if chest did not rise and HR did not improve in a clinical setting |  |

Neonatal mask ventilation training: facilitator checklist

Instructions given by the facilitator while participants perform ventilation: **RFM covered**

**Control Group**

|  |  |  |  |
| --- | --- | --- | --- |
| **Time** | **Training component** | **Instruction** | **√** |
| 10:55 – 11:00 | Demonstration of neonatal ventilation | Position the head and neck in the midline.  Position the airway in the neutral position.  Do not use a head roll (advise that it may be used in the clinical situation)  Perform the two finger mask hold  Administer breaths at a rate of 1 per second |  |
| 11:05 – 11:15 | Participant performs neonatal mask ventilation (with Neopuff) + **RFM covered** | Advise to target   1. Visible chest rise   Advise to also target HR improvement, saturation, and colour in the clinical situation |  |
|  | 1. Poor chest rise | Advise in the following order:  1. Reposition airway to the neutral position, avoid neck flexion or overextension, avoid obstructing the airway with the finger |  |
|  |  | 2. Mask adjustment: adjust face mask hold, ensure face mask is covering nose and mouth, ensure mask is pressed against mannequin face, adjust face mask position on face, reapply face mask |  |
|  |  | Advised additional manoeuvers (suction mouth and nose, open mouth, increase pressure, consider an alternative airway) to attempt if they are unable to obtain chest rise and improvement in heart rate/colour and saturations in the clinical setting |  |
|  | 1. Adequate chest rise | Advise of interventions (as above) if chest did not rise and HR did not improve in a clinical setting |  |

# Modification

Modification to the intervention protocol will not be permitted. Should participants decline to participate in the mask ventilation scenarios they will be recorded as a withdrawal from the study. See 13.2.1 for intention-to-treat analysis and 13.2.2 for the data analysis plan for withdrawals.

# Measurement of participant compliance

Compliance with the standardisation of training and instruction will be ensured by facilitator instruction pre-course, assessment of facilitators, the use of checklists to assist facilitators, intermittent reassessment of each facilitator (6 monthly) and the presence of an independent researcher at each station, who is responsible for compliance with the study protocol i.e. timing of intervention, clarity and order of instruction. Compliance with the protocol will be recorded in each participant CRF.

Significant non-compliance is defined as a participant failing to perform two episodes of mask ventilation or performed mask ventilation for under 50% of the allocated time. Facilitators and researchers will be advised to report each incidence of significant non-compliance to the PI. A high number of non-compliance incidents will trigger a protocol review.

# Exclusion

During the training session, equipment, team formation and allocation of roles, communication and resuscitation skills are taught and practiced. These occur simultaneously during the scenarios performed by participants and are permitted to occur concurrently.

# RANDOMISATION AND BLINDING

*Stratification and randomisation*

Each participant will be randomised to control or intervention teaching using a random number table. Randomisation lists will be stratified according to professional role into three groups: 1. Doctor 2. Midwife 3. Nurse/other healthcare professional/student.  Variable block randomisation will be used within each stratification to ensure balance is achieved over the recruiting period.

Randomised participants will be assigned into groups up to or equaling 6 participants. In each group there will be a minimum of one participant from each stratum (professional group) to allow the formation of multidisciplinary resuscitation teams. Each group will be taught neonatal mask ventilation by a single instructor. Participants in each group will all receive the same teaching, intervention or control.

*Blinding*

Trial participants will not be blinded as both arms will be aware of the use or not of the respiratory function monitor during training. During pre- and post-teaching assessment, the participants and instructors will be blinded to the measurement of the primary outcome i.e. mask leak after training. During data analysis, the outcome assessor who determines the leak from the data obtained will be blinded to the group assignment.

# Concealment mechanism

Allocation concealment will be achieved using sequentially numbered, sealed opaque envelopes. Study envelopes will be kept in the Paediatric Infant Perinatal Emergency Retrieval (PIPER) Education office, Second floor, Royal Children’s Hospital, Parkville, VIC 3052, Australia.

# Breaking of the Study Blind

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# During study

**N/A participants are unblinded.**

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# On completion of the study

Each individual will have a single study number linked to a CRF and a randomisation code. During data analysis the outcome assessor who determines the leak from the data obtained will not have access to the randomisation codes. The participant CRF data will be entered into a trial database. The leak will then be calculated for each participant and entered. When finalised, the trial randomization codes will then be entered, ensuring that the outcome assessor is blinded to the group assignment.

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# STUDY VISITS AND PROCEDURES

# 8.1 Schedule of Assessments

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **STUDY PERIOD** | | | | | |
|  | **Enrolment** | **Allocation** | **Post-allocation** | | **Close-out** |
| **TIME POINT\*\*** | ***Pre-course***  ***Emailed >1 week in advance*** | **Morning of course before ventilation skill station 9:00-10:45** | ***11:00*** | ***11:05 – 11:55*** | ***12:10*** |
| **ENROLMENT:** |  |  |  |  |  |
| **Eligibility screen** | X |  |  |  |  |
| **Informed consent** | X | X |  |  |  |
| **Allocation** |  | X |  |  |  |
| **INTERVENTIONS:** |  |  |  |  |  |
| ***Intervention: ventilation + RFM visible*** |  |  |  | X |  |
| ***Control: ventilation + RFM covered*** |  |  |  | X |  |
| **ASSESSMENTS:** |  |  |  |  |  |
| ***Baseline leak assessment*** |  |  | X |  |  |
| ***Primary outcome: leak post- training*** |  |  |  |  | X |
| *Secondary outcomes:*   * *Difference in expired tidal volume* * *Stability of tidal volume achieved* * *Percentage of obstructed inflations* |  |  |  |  | X |

* 1. Study Timeline

# Screening

Screening session: occurs morning of course

* Review email responses, obtain and document consent on morning of course
* Review participant information to assess eligibility
* Enrol participant

# Baseline assessment

* Leak between the mask and the mannequin face will be measured. Mask ventilation will initially be performed for 30 seconds at the beginning of the skill station and baseline leak will be recorded.
* A Florian Respiratory Function monitor (Acutronic Medical Systems, Zug, Switzerland) will be used to measure inflating pressures and gas flow. The monitor measures flow directly through a line connected at the T-piece. Gas flow is measured using a flow sensor placed between the mask and the Neopuff. The monitor integrates the flow signal to determine the tidal volume of gas passing through the sensor. The expiratory leak will be calculated from the volume of gas that does not return back through the flow sensor on expiration, expressed as a percentage of the inspired volume.
  + - Leak (%) = inflating tidal volume - expired tidal volume     x100

inflating tidal volume

* Demographic data will be obtained including: participant’s professional role, years of experience in neonatology, number of times positive pressure ventilation via a Neopuff or Bag-mask valve was performed in the preceding year.

# Post-intervention assessment

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After the skill session, participants will be reassessed and mask leak will be recorded for 90 seconds of mask ventilation. This timeframe was chosen because international guidelines recommend operators re-assess the airway every 30 seconds and we wish to capture at least 2 reassessment episodes. Mask leak will be recorded during 90 seconds of ventilation.

# Participant Withdrawal

# Reasons for withdrawal

The investigator may withdraw a subject from the trial prematurely if the following criteria are met:

* Equipment failure i.e. RFM not functioning in intervention group
* Participant request: Participants are free to withdraw from the intervention or control groups at any point on request. If this occurs, the participant will be moved to a teaching group that is not part of the study and will receive the standard teaching. Continuation of follow up will be requested e.g. if a participant is in the intervention group using the RFM and requests to leave the study he/she will be moved to a standard teaching group outside the study to receive their training. The participant will be asked if they would like to participate in the outcome measure i.e. repeat leak assessment.

# Handling of withdrawals and losses to follow-up

If a participant ceases participation in the trial prematurely, the reasons for cessation will be recorded on the CRF. The participant will be recorded as “WITHDRAWAL”. One of the study investigators present at the course will ask the participant to allow assessment of the outcome measure. If this is declined the participant’s outcome measure will be recorded as “MISSING DATA” and data analysis will be performed as per point 13.2.1 intention-to-treat analysis and 13.2.2 handling of missing data.

# Replacements

Participants who withdraw during a course will not be replaced during the same course. To maintain sample size, additional participants may be recruited at subsequent courses.

# Trial Closure

The principal investigate (EOC), associate investigator (MT) and Head of Department (PD) may make decisions about whether to extend or terminate the study.

# Continuation of intervention

After completion of the outcome assessment all course attendees will be offered an opportunity for self-assessment using the RFM. This will be offered from 12:30-13:30hrs on completion of the morning session of the course. All course attendees will be given an opportunity to perform mask ventilation with the mannequin and to assess their leak.

# OUTCOMES

# Primary outcome

The primary outcome is difference in leak measured after neonatal mask ventilation training between the control and intervention groups. Leak between the mask and the mannequin face will be measured.

* The expiratory leak will be calculated from the volume of gas that does not return back through the flow sensor on expiration, expressed as a percentage of the inspired volume.

Leak (%) = inflating tidal volume - expired tidal volume     x100

           inflating tidal volume

# Secondary outcome(s)

* Difference in expired tidal volume
* Stability of tidal volume achieved i.e. consistency of tidal volumes in consecutive breaths
* Percentage of obstructed inflations

# ADVERSE EVENTS AND RISKS

The potential for adverse events is felt to be negligible given the nature of the intervention. However, the following definitions of unanticipated and adverse events will be applied.

# Definitions

Unanticipated Problems:

Unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets all of the following criteria:

* unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, and (b) the characteristics of the participant population being studied;
* related or possibly related to participation in the research; and
* suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognised.

Adverse Event (AE): Any untoward medical occurrence in a participant enrolled into this study regardless of its causal relationship to study/interventions.

Serious Adverse Event (SAE)

Adverse events are classified as serious or non-serious.

An SAE is defined as any AE that:

* results in death; or is immediately life threatening; or
* requires inpatient hospitalisation; or
* requires prolongation of existing hospitalisation; or
* results in persistent or significant disability/incapacity

# Assessment and documentation of adverse events

The investigator is responsible for recoding all adverse events, regardless of their relationship to the study intervention.

The description of each AE on the CRF will include:

* A description of the AE
* The onset date, duration, date of resolution
* Severity (mild, moderate or severe)
* Seriousness (i.e. is it an SAE?)
* Any action taken
* The outcome
* The likelihood of the relationship of the AE to the study intervention (Unrelated, Possible, Probable, Definite)

# Eliciting adverse event information

Unintended or unexpected adverse effects will be monitored via the course attendee’s feedback form at the end of the course day and via any alternative communication (verbal conversations, phone calls, emails) regarding the study from attendees to course facilitators. When briefing the course facilitators on the study, the facilitators will be asked to report any feedback regarding the study to the PI (EOC).

# Serious adverse event reporting

Any feedback found to be consistent with an adverse event will be recorded on the participant CRF and in a database called “adverse effect log”. The PI will follow up on any adverse events with an email or phone call to the course attendee, and further interventions/follow-up will be organised if necessary. The PI EOC will be responsible for detecting SAEs and reporting them to the ethics committee and/or regulatory agencies.

# SAEs

Any SAE occurring in a study participant will be reported to the HREC within 24-72 hours of occurrence, in accordance with the safety reporting policy of the HREC. The HREC safety reporting form will be completed, signed and submitted by an investigator.

# DATA MANAGEMENT



# Data Collection

Case report forms (CRFs) will be completed on the day of the course. The study investigators will be responsible for the accurate collection of neat, legible data in the CRFs.

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# Source Data

A case report form (CRF) will be completed for each participant to record training interventions, ventilation interventions and participant demographic data (profession, neonatal resuscitation experience, normal clinical environment). Recorded respiratory data (tidal volumes, pressures) will be analysed and leak will be calculated by a reviewer blinded to the group of assignment. These CRFs will be kept in the Research Fellow Office, Newborn Research Centre, 7th Floor, Royal Women’s Hospital, accessible to EOC, MT and PD.

# Data Capture Methods

Data will be recorded on paper CRFs on the day of the study. They will be entered into an electronic database on a password-protected computer in the Research Fellow Office, Newborn Research Centre, 7th Floor, Royal Women’s Hospital, accessible to EOC, MT and PD. Data will be entered in a timely fashion.

# Data Storage

The database will be stored on a password-protected computer in the Research Fellow Office, Newborn Research Centre, 7th Floor, Royal Women’s Hospital, accessible to EOC, MT and PD.

# Record Retention

Records will be maintained for at least 15 years post completion of the trial.

# STUDY OVERSIGHT

# Governance structure

The PI and AIs MT and PD will have weekly meetings (Tuesday 15:30 RWH 1 hour) to discuss planning and progress of the study. This meeting may occur fortnightly once the study is established and progressing well. The PI will attend monthly Neonatal Resuscitation and Respiratory Group meetings in the Newborn Research Department in RWH. This committee consists of the PI EOC, AIs MT, JD & PD, and staff members of the Newborn Research Department. Ongoing supervision of this trial will be included in the Terms of Reference of the committee. An update on trial recruitment, protocol compliance and adverse events will be provided by the PI EOC at each meeting.

# Quality Control and Quality Assurance

* The PI EOC will be responsible for quality control and assurance. This will be ensured by adherence to a quality management plan as detailed:
  + Data will be evaluated for compliance with the protocol by bi-monthly reviews of the source documents (CRFs and data recordings) by the PI EOC
  + EOC in conjunction with the AIs (MT and PD) will be responsible for addressing quality assurance issues (correcting procedures that are not in compliance with protocol) and quality control issues (correcting errors in data entry)
  + Staff training will occur before commencement of the study. This will take the form of a two-hour training session on data collection methods and standardised ventilation training. A training checklist will be provided as detailed in point 6.2.
  + These training checklists will be checked on a three-monthly basis to ensure adherence to the trial protocol. Training updates will be scheduled every 6 months.

# STATISTICAL METHODS



# Sample Size Estimation

Mask leak has been reported between 14-65% in neonatal mannequin studies and 29% (interquartile range 16-63%) in preterm infant resuscitation studies. (4) (7) (6) (8) (9) Assuming a median leak of 50% in the control group and a standard deviation of 30% a sample size of 382 (191 in each arm) would give a power of 90% to detect a 10% absolute difference in leak (50% leak versus 40% leak). Fourteen neonatal resuscitation courses are planned in the Royal Children’s Hospital, Melbourne in 2016 with 24 participants per course. We estimate that consent, equipment and availability of researchers will allow for 12 participants per course to be enrolled. We therefore expect to be able to complete recruitment in 27 months.

# Statistical Analysis Plan

# Population to be analysed

Analysis will be performed on an intention-to-treat basis.

# Handling of missing data

Analysis will include data from all participants randomised including participants defined as protocol non-adherent. Protocol non-adherence is defined as: when participants do not complete the baseline assessment and/or the intervention and/or the outcome assessment.

Describing the extent and nature of missing data: to address the risk of generalisability and causal validity bias, a clear and accurate account of the extent and nature of missing data will be obtained. A CONSORT diagram (Campbell 2012) will be created that outlines the numbers assessed for eligibility, excluded (including declined consent), randomised, allocated to intervention or control, missing outcome measures and reasons, and number analysed. The study retention rate will be analysed by creating a table as per the attached example.

|  |  |  |  |
| --- | --- | --- | --- |
|  | *All participants* | *Intervention* | *Control* |
| *Number of participants randomised (1)* |  |  |  |
| *Number of participants with protocol adherence and complete outcome data (2)* |  |  |  |
| *Study retention rate (2/1)* |  |  |  |

To address the risk of generalisability bias by allowing the comparison of participants who adhere and those with non-adherence, baseline characteristics of all eligible participants will be recoded as per the following table.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Characteristic | All participants who were randomised | | All participants who were not missing outcome data (analytic sample) | |
| Not missing outcome data | Missing outcome data | Control | Intervention |
| Sex |  |  |  |  |
| Experience (years) |  |  |  |  |
| Profession |  |  |  |  |

A data analysis will be performed to assess the missing data rate and to assess if the baseline characteristics of the missing and non-missing data groups are similar. It is anticipated that there will be little or no missing outcome data. In this case a complete case analysis with regression adjustment for baseline covariates will be performed.

# Methods of analysis

Data will be analysed using Stata software (Intercooled 10, Stata Corp, College Station, Texas, USA). The data will be presented as mean (standard deviation) for normally distributed variables and median (interquartile range) when the distribution is skewed. The clinical characteristics and outcome variables will be analysed by using the Student t test for parametric and Mann-Whitney U test for nonparametric comparisons of continuous variables and Chi squared for categorical variables. Data will be clustered by operator. P values will be 2-sided and P values of less than 0.05 will be considered statistically significant

# Interim Analyses

An interim analysis will not be performed.

# ETHICS AND DISSEMINATION

# Research Ethics Approval

This study protocol, the informed consent documentation and any protocol modifications will be submitted for review and approval by the RCH Human Research Ethics Committee (HREC). The project will not commence until a letter of protocol and associated study document approval has been obtained from this body.

# Modifications to the protocol

This project will be conducted in adherence to the current version of the study protocol. An amendment will be defined as any change to the protocol or informed consent form that alters the scientific intent, study design, participant safety or participant withdrawal. All protocol amendments will be written and submitted to the RCH HREC for approval prior to becoming effective.

# Protocol Deviations

Protocol deviations will be recorded on the CRF and must be reported to the PI. Their significance will then be assessed by the PI. A significant deviation will be defined as one that has a potential impact on the integrity of the study results, patient safety or ethical acceptability of the trial will be reported to HREC in a timely manner. If significant deviations trigger a protocol review the protocol will be amended as per section 14.2.

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# Confidentiality

The participating investigator, research staff, sponsoring institution and their agents will hold participant confidentiality in strict trust. This confidentiality includes all participant demographic and educational information. The study protocol, documentation, data and all other information generated relating to the study will be held in confidence. No information concerning the study will be released to any unauthorized third party without prior written approval from the sponsoring institution. Authorised representatives of the sponsoring institution may inspect all documents and records required to be maintained by the PI including CRFs, consent forms and data retained regarding the participants in the study. The clinical study site will permit access to these records. All records that leave the site will be identified only by a study identification number to protect the participant’s confidentiality. Participant information will not be released without the written permission of the participant, except as necessary by HREC or regulatory agencies

# Participant Reimbursement

There will be no participant reimbursement.

# Financial Disclosure and Conflicts of Interest

The investigators state that they have no financial or other conflicts of interest for the trial.

# Dissemination and translation plan

The trial results will be disseminated via peer review publication. The principal investigator holds primary responsibility for publication of the results of the study.

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# APPENDICES

# Informed consent materials

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See attached

# Causality and Assessment of Severity – Adverse Events

Adverse Events will be defined as follows:

* **Mild**: Events that require minimal or no treatment and do not interfere with the participant’s daily activities or work related performance.
* **Moderate**: Events that cause sufficient discomfort to interfere with daily activity.
* **Severe**: Events that prevent usual daily activity or require complex intervention.

The relationship of the event to the study intervention will be assessed as follows:

* **Unrelated:** There is no association between the study intervention and the reported event. AEs in this category do not have a reasonable temporal relationship to exposure to the test product, or can be explained by a commonly occurring alternative aetiology.
* **Possible:** The study intervention could have cause or contributed to the AE. AEs in this category follow a reasonable temporal sequence from the time of exposure to the intervention and/or follow a known response pattern to the test article, but could also have been produced by other factors.
* **Probable:** The association of the event with the study intervention seems likely. AEs in this category follow a reasonable temporal sequence from the time of exposure to the intervention and are consistent with the effects of the intervention.
* **Definite:** The AE is a consequence of exposure to the intervention. AEs in the category cannot be explained by other causes. Such events may be widely documented as having an association with the intervention or that they occur after re challenge.