Protocol for a randomised controlled trial comparing two CPAP levels to prevent extubation failure in extremely preterm infants

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INTRODUCTION
Respiratory distress syndrome (RDS) is a complication of prematurity and extremely preterm infants born before 28 weeks’ gestation and often require endotracheal intubation and mechanical ventilation. In this high-risk population, mechanical ventilation is associated with lung injury and contributes to bronchopulmonary dysplasia. Therefore, clinicians attempt to extubate infants as quickly and use non-invasive respiratory support such as nasal continuous positive airway pressure (CPAP) to facilitate the transition. However, approximately 60% of extremely preterm infants experience ‘extubation failure’ and require reintubation. While CPAP pressures of 5–8 cm H2O are commonly used, the optimal CPAP pressure is unknown, and higher pressures may be beneficial in avoiding extubation failure. Our trial is the Extubation CPAP Level Assessment Trial (ÉCLAT). The aim of this trial is to compare higher CPAP pressures to lower CPAP pressures to determine which pressure is more effective at preventing extubation failure in extremely preterm infants. The optimal way to provide respiratory support to extremely preterm infants after mechanical ventilation remains under investigation, and the transition from mechanical ventilation to non-invasive respiratory support remains a poorly understood process. There is a paucity of data on the optimal timing of extubation, criteria for readiness for extubation, and the best strategy to use when providing post-extubation respiratory support. The extubation failure rate in extremely preterm infants is high, and reducing this outcome must be a focus of research.

Nasal continuous positive airway pressure (CPAP) is the most frequently used mode of ventilation, particularly if prolonged, injures the lungs and contributes to bronchopulmonary dysplasia (BPD), the chronic lung disease of prematurity, is a major morbidity following RDS and its treatment. Many extremely preterm infants require endotracheal intubation and mechanical ventilation. Mechanical ventilation remains a poorly understood process. There is a paucity of data on the optimal timing of extubation, criteria for readiness for extubation, and the best strategy to use when providing post-extubation respiratory support. The extubation failure rate in extremely preterm infants is high, and reducing this outcome must be a focus of research.

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ABSTRACT

Introduction Respiratory distress syndrome is a complication of prematurity and extremely preterm infants born before 28 weeks’ gestation often require endotracheal intubation and mechanical ventilation. In this high-risk population, mechanical ventilation is associated with lung injury and contributes to bronchopulmonary dysplasia. Therefore, clinicians attempt to extubate infants as quickly and use non-invasive respiratory support such as nasal continuous positive airway pressure (CPAP) to facilitate the transition. However, approximately 60% of extremely preterm infants experience ‘extubation failure’ and require reintubation. While CPAP pressures of 5–8 cm H2O are commonly used, the optimal CPAP pressure is unknown, and higher pressures may be beneficial in avoiding extubation failure. Our trial is the Extubation CPAP Level Assessment Trial (ÉCLAT). The aim of this trial is to compare higher CPAP pressures to lower CPAP pressures to determine which pressure is more effective at preventing extubation failure in extremely preterm infants.

Methods and analysis 200 extremely preterm infants will be recruited prior to their first extubation from mechanical ventilation to CPAP. This is a parallel group randomised controlled trial. Infants will be randomised to one of two set CPAP pressures: CPAP 10 cmH2O (intervention) or CPAP 7 cmH2O (control). The primary outcome will be extubation failure (reintubation) within 7 days. Statistical analysis will follow standard methods for randomised trials on an intention to treat basis. For the primary outcome, this will be by intention to treat, adjusted for the prerandomisation strata (GA and centre). We will use the appropriate parametric and non-parametric statistical tests.

Ethics and dissemination Ethics approval has been granted by the Monash Health Human Research Ethics Committees. Amendments to the trial protocol will be submitted for approval. The findings of this study will be written into a clinical trial report manuscript and disseminated via peer-reviewed journals (on-line or in press) and presented at national and international conferences.

Trial registration number ACTRN12618001638224; pre-results.

INTRODUCTION
Respiratory distress syndrome (RDS) is common in preterm infants, and almost universal in extremely preterm infants born <28 weeks’ gestation. In this high-risk population, bronchopulmonary dysplasia (BPD), the chronic lung disease of prematurity, is a major morbidity following RDS and its treatment. Many extremely preterm infants require endotracheal intubation and mechanical ventilation. Mechanical ventilation remains a poorly understood process. There is a paucity of data on the optimal timing of extubation, criteria for readiness for extubation, and the best strategy to use when providing post-extubation respiratory support. The extubation failure rate in extremely preterm infants is high, and reducing this outcome must be a focus of research.

Nasal continuous positive airway pressure (CPAP) is the most frequently used mode of
non-invasive support used after extubation of extremely preterm infants. The reasons for extubation failure during CPAP are multifactorial. Variables such as infant weight (birth weight <750 g), immaturity (<26 weeks' gestation) and the severity of RDS (alveolar-arterial gradient >180 mm Hg) are weakly predictive of early CPAP failure in very preterm infants.9 The use of a set CPAP pressure sufficient to maintain functional residual capacity is likely to be important.6 The optimal CPAP pressure to use after extubation is unknown, although a meta-analysis of studies suggests that pressures of at least 5 cm H2O are needed.6 Many infants are reintubated following extubation for increased oxygen requirement and work of breathing suggesting that a low end-expiratory lung volume may contribute to extubation failure.5

Utilising higher CPAP pressures post-extubation may prevent alveolar collapse, improve lung function and reduce extubation failure.7,8 Kitsommart et al compared CPAP 7–9 cm water (H2O) with CPAP 4–6 cm H2O after extubation of infants with birth weight <1250 g and demonstrated no difference in extubation failure within 72 hours.7 In a second trial, Buzzella et al randomised very preterm infants born 25–30 weeks' gestation with RDS to receive either CPAP 7–9 cm H2O or CPAP 4–6 cm H2O after extubation.8 Rates of extubation failure within 96 hours were significantly lower in the group randomised to the higher range of CPAP pressures.8 Current CPAP pressure recommendations are wide and varied.6 Most clinicians report pressures of 5–8 cm H2O, however, use of CPAP pressures up to 12 cm H2O have been reported and have not been associated with adverse effects.9

In extremely preterm infants, extubation failure is associated with significant morbidities, including BPD, pulmonary vascular disease, airway trauma, poor feeding and oral aversion, adverse neurodevelopmental outcomes and delayed family unit bonding.10 Thus, improving rates of successful extubation in this high-risk population of preterm infants is a clinical priority.5,6–11 The ÉCLAT trial will investigate the CPAP pressure range of 6–8 cm H2O, routinely used in our clinical practice, with a higher-pressure range of 9–11 cm H2O. We hypothesise that the higher-pressure range will result in less atelectatic pulmonary failure and extubation failure.

Methods and analysis

Study design and aim
We used the Standard Protocol Items: Recommendations for Interventional Trials checklist when writing our report.15 This is a multicentre, unblinded, randomised controlled trial. The aim of the ÉCLAT study is to determine, in extremely preterm infants born <28 weeks' gestation who are undergoing their first extubation, whether extubation to a higher CPAP pressure (10 cm H2O, range 9–11 cm H2O), compared with a standard CPAP pressure (7 cm H2O, range 6–8 cm H2O) decreases extubation failure within 7 days.

Sample size
The rates of extubation failure within 7 days in extremely preterm infants at the participating centres is estimated at 55%. To detect a reduction in extubation failure from 55% to 35% (absolute risk reduction 20%, relative risk reduction 40%) with 80% power and a two-tailed alpha error of 0.05, a sample size of 95 infants in each arm (total 186 infants) is required.

Patient population
Infants born extremely preterm (<28 weeks' gestation) who are intubated and mechanically ventilated and being extubated for the first time are eligible for participation in the ÉCLAT trial. The timing of the extubation is determined by the clinical team caring for the infant, and there is no postnatal age limit for participation.

Inclusion criteria
Infants are eligible if they
► Were born <28 completed weeks' gestation.
► Are being extubated for the first time from mechanical ventilation to nasal CPAP.
► Have received enteral or intravenous caffeine (as prophylaxis for apnoea of prematurity) <24 hours prior to the planned extubation.
► Have received exogenous surfactant treatment.

Exclusion criteria
Infants are excluded if they
► Are being extubated to any other mode of non-invasive respiratory support other than nasal CPAP, or to no respiratory support.
► Have a major congenital anomaly or condition that might adversely affect breathing or ventilation: for example, known upper airway obstruction or major airway abnormality, or major congenital heart disease.
► Are not receiving full intensive care after extubation.

Randomisation
Enrolled infants are randomised using Research Electronic Data Capture (REDCap) electronic data capture tools,16 hosted at the Murdoch Children’s Research Institute, Melbourne, Australia. REDCap is a secure, password-encrypted, web-based application designed to support data capture and randomisation for research studies. Only the infant’s first extubation is randomised. Multiple births are randomised individually. Randomisation occurs after the clinical decision to extubate has been made and shortly before extubation using a computer or smartphone. Stratification is by centre and gestational age at birth (<26 weeks; ≥26 weeks).

Clinical management
Higher CPAP pressure (intervention)
Infants are extubated to a set CPAP pressure of 10 cm H2O. While receiving CPAP, infants will remain within a set CPAP pressure range of 9 cm H2O–11 cm H2O for at least 24 hours, with changes within this range at the discretion of the treating team. After 24 hours, infants

may have their set CPAP pressure weaned at the discretion of the treating team but must remain within a set CPAP pressure range 5 cm H₂O–11 cm H₂O for at least 7 days after extubation if receiving CPAP. Infants are reintubated if they satisfy the extubation failure criteria described below within 7 days after extubation. The fraction of inspired oxygen (FiO₂) is titrated to keep oxygen saturations (SpO₂) in the standard target ranges of the participating unit. If extubation failure occurs, management following reintubation will be at the discretion of the treating team. For subsequent extubations, clinicians will be encouraged to use the assigned set CPAP pressure range (see figure 1).

Standard CPAP pressure (control)

Infants are extubated to a set CPAP pressure of 7 cm H₂O. While receiving CPAP, infants will remain within a set CPAP pressure range of 6 cm H₂O–8 cm H₂O for at least 24 hours, with changes to the set CPAP pressure within this range at the discretion of the treating team. After 24 hours, infants may have their set CPAP pressure weaned at the discretion of the treating team but must remain within a set CPAP pressure range 5 cm H₂O–8 cm H₂O for at least 7 days after extubation if receiving CPAP. Infants are reintubated if they satisfy the extubation failure criteria described below within 7 days after extubation. The FiO₂ is titrated to keep SpO₂ in the standard target ranges of the participating unit. If extubation failure occurs, management following re-intubation will be at the discretion of the treating team. For subsequent extubations, clinicians will be encouraged to use the assigned set CPAP pressure range (see figure 1).

**Device**

In both groups, infants will be extubated to continuous-flow nasal CPAP, via a mechanical ventilator (either the Dräger VN500, Dräger Medical, Lübeck, Germany, or the SLE 5000, SLE, Croydon, UK) operating in CPAP mode. After 24 hours the infant may be transitioned to ‘bubble’ nasal CPAP (Fisher & Paykel bubble CPAP circuit, Fisher & Paykel Healthcare, Auckland, New Zealand) but only if receiving a CPAP ≤ 10 cm H₂O given the pressure limitations of the ‘bubble’ CPAP device. Nasal CPAP may be delivered via any binasal CPAP prongs or mask, according to the participating unit’s protocol. Nasal prongs should be sized as per the manufactures guidelines to the largest size to occlude the infant’s nares.

**OUTCOMES**

**Extubation failure**

The primary outcome is extubation failure within 7 days, defined as receiving the maximum CPAP level (11 cm H₂O in the intervention group; 8 cm H₂O in the control group) and having at least one of:

- FiO₂ requirement > 0.20 above the pre-extubation FiO₂
- Two or more apnoeic episodes within any 24-hour period requiring intermittent positive pressure ventilation, or six or more apnoeic events requiring stimulation in any 6-hour period.
- Respiratory acidosis with pH < 7.2 and pCO₂ > 60 mm Hg.
- Require urgent intubation for an acute deterioration (at clinical discretion) with the reason for reintubation documented.
Treatment failure
Should infants not be immediately reintubated and instead managed with non-invasive positive pressure ventilation or escalated to a higher CPAP pressure than their assigned range they will be documented as an extubation failure and reported as a protocol violation.

SECONDARY OUTCOMES
- Incidence of reintubation within 72 hours, and within 96 hours.
- Failure in hours after extubation.
- Reason(s) for extubation failure.
- Kaplan-Meier Survival curve between both groups.
- Death before hospital discharge.
- Duration of mechanical ventilation in days after randomisation in survivors.
- Total duration of hospitalisation in days in survivors.
- Postmenstrual age at last supplemental oxygen, and at last positive pressure ventilation (mechanical ventilation, CPAP (or variants) or nasal high-flow >2 Litres per minute) in survivors.
- Incidence of treatment with systemic postnatal corticosteroids for lung disease after randomisation.
- Incidence of new pneumothorax requiring drainage with thoracocentesis or intercostal catheter insertion after randomisation.
- Incidence of new, radiologically diagnosed pulmonary interstitial emphysema after randomisation.
- Incidence of BPD, defined as a requirement for supplemental oxygen and/or respiratory support (mechanical ventilation, CPAP (or variants) or nasal high-flow >2 Litres per minute) at 36 weeks’ postmenstrual age.
- Incidence of necrotising enterocolitis Bell’s stage 2 or above after randomisation.¹⁷
- Incidence of spontaneous intestinal perforation after randomisation.
- Incidence of retinopathy of prematurity requiring treatment with laser therapy or intraocular medication in one or both eyes after randomisation.
- Incidence of new diagnosis of grade 3 or 4 intraventricular haemorrhage after randomisation.

OTHER DATA
Data collected will include
- Maternal and infant demographics: maternal parity, infant sex, gestational age at birth, birth weight in grams, mode of delivery, exposure to any antenatal corticosteroids, duration of ruptured membranes prior to delivery in days, presence of histologically diagnosed chorioamnionitis.
- Postnatal age at extubation in days, last weight prior to extubation in grams, age at first intubation in hours.
- Previous dose of exogenous surfactant received in milligrams/kilogram, prior treatment for a patent ductus arteriosus (pharmacological or surgical), prior systemic postnatal corticosteroids for lung disease.
- Mechanical ventilator settings immediately prior to extubation (mode, mean airway pressure in mm Hg, \(\text{FiO}_2\), tidal volumes (set and achieved), peak pressures (set and achieved) and end expiratory pressure.
- Blood gas analysis results within 24 hours prior to extubation (if applicable): lowest pH, highest pCO₂, lowest base excess.

DATA ANALYSIS PLAN
Statistical analysis will follow standard methods for randomised trials. For the primary outcome, the analysis will be by intention to treat and be adjusted for the prerandomisation strata (gestational age (GA) and centre). For dichotomous outcomes, including the primary outcome, the two treatment groups will be compared using risk difference with 95% CI, both overall, and within the prespecified subgroups (gestational age at birth <26 weeks, ≥26 weeks). For dichotomous secondary outcomes, analysis will be limited to the two treatment groups, using risk difference with 95% CI. For continuous outcomes, the two treatment groups will be compared using difference of means, together with 95% CI, for outcome variables which are normally distributed; for outcome variables, which are not normally distributed, the comparison will be difference of medians, with 95% CI. All comparisons (risk difference, difference of means, difference of medians) will be estimated using regression models with the randomisation strata as covariates, and with SEs adjusted to take into account the clustering due to multiple births. Reporting of findings will be done in accordance with Consolidated Standards of Reporting Trials guidelines.

Adverse events
Adverse events (AEs) are recorded within 7 days after the randomised extubation. They are recorded as part of the study design and secondary outcomes of ÉCLAT. The site investigators are responsible for recording all AEs regardless of their relationship to the intervention. The following outcome are designated as AEs:
- Necrotising enterocolitis (Bell’s stage III or IV).¹⁷
- Intraventricular haemorrhage (grade III or IV).

Serious AEs
Serious AEs (SAEs) are recorded within 7 days after the randomised extubation. All are prespecified secondary outcomes of ÉCLAT. The investigators are responsible for recording all events regardless of their relationship to the intervention. All SAEs are reported to an independent data safety monitoring committee (DSMC) and the local ethics committee within 72 hours of the principle investigator being notified. The following outcomes are designated as SAEs:
- Death.
- Spontaneous intestinal perforation.
- Pneumothorax.
- Pulmonary interstitial emphysema.
Study oversight
The independent DMSC established for the ÉCLAT trial have their roles and responsibilities detailed in a separate DSMC Charter. The DSMC includes two independent, experienced neonatologists and a senior statistician. The terms of reference for the DSMC include performance of interim safety analyses, periodic examination of relevant emerging external evidence, monitoring of AEs, compliance with the trial protocol, and progress of recruitment. Safety analyses by the DMSC are planned after the primary outcome is known for the first 50 and 100 infants and will occur blinded to group allocation. If required, an additional safety analysis will be performed at 150 infants. No interim analyses of the primary outcome are planned.

Clinical significance
Exubation failure is common in extremely preterm infants and associated with important neonatal morbidities. CPAP is the most commonly used form of non-invasive ventilation used postextubation but the optimal pressure to use for this indication remains uncertain. The ÉCLAT study will reveal novel information regarding CPAP pressures in extremely preterm infants. The ÉCLAT study is the largest trial comparing and researching CPAP pressures >8 cm H₂O. Results from ÉCLAT will inform clinical practice and support clinicians in understanding and optimising CPAP pressures for extremely preterm infants. Results from this study will be disseminated via peer-reviewed journals and presented at national and international scientific conferences.

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RB, AM and AMK developed the concept and RB and AMK wrote the protocol. RB, BJM, RAB, AM and PGD gave input into the protocol and revised the manuscript. SMD designed the statistical analysis and revised the manuscript. All authors have read and approved the final manuscript and are accountable for its accuracy.

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None declared.

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Supplemental material
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REFERENCES
Master Participant Information Sheet/Consent Form – Parent/Guardian
Interventional Study - Parent/Guardian consenting on behalf of participant

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Part 1 What does your baby’s participation involve?

1. Introduction
This is an invitation for your baby in your care to take part in this research project because they are currently intubated with an endotracheal tube. The research project is testing the use of different air pressures on an existing type of respiratory support *Continuous Positive Airway Pressure* (CPAP) after the endotracheal tube is removed.

This Participant Information Sheet/Consent Form informs you of the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want your baby to take part in the research.

Please read this information carefully. Ask questions about anything that you don’t understand or want to know more about. Before deciding whether or not your baby can take part, you might want to talk about it with a relative or friend.

Participation in this research is voluntary. If you do not wish your baby to take part, they do not have to. Your baby will still receive the best possible care whether or not they take part. They will still receive the same CPAP care as those babies in the trial. The only difference will be your baby’s data will not be recorded and used to further develop the extubation process.

If you decide you want your baby to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:
- Understand what you have read
- Consent to your baby taking part in the research project
- Consent for your baby to have the tests and treatments that are described
- Consent to the use of your baby’s personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2. What is the purpose of this research?
Your premature baby is currently intubated with an endotracheal tube to help them breathe because they are requiring extra support. Soon the treating team will want to remove this tube to let your baby breathe on his/her own (extubate). Most often extremely premature infants will still require a form of non-invasive breathing support after the tube is removed to help hold their lungs open for a period of time.

Neonatal intensive care units are currently using Continuous Positive Airway Pressure (CPAP) as this support. CPAP involves short soft prongs that sit in your baby’s nose connected to a circuit that delivers a continuous amount of distending pressure (and or oxygen) into your baby’s lungs. This amount of pressure is measured in cm H\textsubscript{2}O and can range from 4-12.

At the moment most babies, once extubated are prescribed a level of 7 cm H\textsubscript{2}O. Sometimes a baby is not ready to have the breathing tube removed and so needs to be re-intubated. The aim of our study is to compare the current practice of 7 cm H\textsubscript{2}O to using higher pressures of 10 cm H\textsubscript{2}O and to investigate whether the higher pressures of CPAP reduce re-intubation.

The results of this research will be used by Miss Anna Kidman to obtain a Doctor of Philosophy degree at the University of Melbourne.

3. **What does participation in this research involve?**

Your baby’s participation in this study will involve the signing of witnessed, informed consent after he/she is screened for eligibility prior to him/her having their breathing tube removed.

When the doctors decide your baby is ready to try breathing by themselves, participation in the ÉCLAT study will involve your baby receiving a CPAP of 7 cm H\textsubscript{2}O or 10 cm H\textsubscript{2}O after his/her breathing tube is removed. Your baby will be participating in a randomised controlled research project. You will not be able to choose which CPAP level your baby will receive. To determine which level results in the better outcomes we need to compare different treatments. We put babies into groups and give each group a different treatment. The results are compared to see if one is better. To try to make sure the groups are the same, each baby is put into a group by chance (random).

Regardless of which group your baby is allocated to, they will continue to receive routine care from the doctors and nurses as they would without this trial. They will only have specific guidelines for how their breathing support will be managed.

If you choose to allow your baby to participate in the ÉCLAT study, they should not require any extra blood tests, procedures or investigations. There may be extra observations documented by medical and nursing staff however this will not disturb your baby in any way. If your baby has a change in condition the medical staff will escalate care appropriately regardless of what CPAP treatment your baby is receiving.

Your baby will remain in the study until discharge. Data will be collected from your baby’s medical chart and there will be no follow up required after you are discharged from hospital.

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids investigators or participants jumping to conclusions. There are no additional costs associated with participation in this research project, nor will you or the your baby be paid. The CPAP used is currently used for all babies in this unit.
4. **What does your baby have to do?**
To participate in the ÉCLAT study you or your baby will not have to do anything different that you usually would.

5. **Other relevant information about the research project**
The ÉCLAT will aim to recruit 200 babies over 2 years. Other hospitals may be invited to be involved. The project involves researchers from Monash Newborn, The Royal Women’s Hospital and the University of Melbourne.

6. **Does your baby have to take part in this research project?**
Participation in any research project is voluntary. If you do not wish for your baby to take part, they do not have to. If you decide that they can take part and later change your mind, you are free to withdraw your baby from the project at any stage.

If you do decide that your baby can take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision that your baby can or cannot take part, or that they can take part and then be withdrawn, will not affect their routine treatment, relationship with those treating them, or their relationship with The Site.

7. **What are the alternatives to participation?**
Your baby does not have to take part in this research project to receive treatment at this hospital. If your baby is not in the study they will receive routine care as per normal.

8. **What are the possible benefits of taking part?**
We cannot guarantee or promise that your baby will receive any benefits from this research. The results of the study will be important in helping us to look after premature babies in the future, and may change the way we provide breathing support to these babies.

9. **What are the possible risks and disadvantages of taking part?**
Medical treatments can cause side effects. your baby may have none, some or all of the effects listed below, and they may be mild, moderate or severe. If your baby has any of these side effects, or you are worried about them, talk with your baby’s bedside nurse to contact the study investigators or the treating doctor. The investigator will also be looking out for side effects including; Air leak syndromes causing difficulty to breath, injury to the skin/septum around the nose and the usual discomfort some babies find from having prongs in their nose.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell the principle investigator/ study doctor/ treating team or bedside nurse immediately about any new or unusual symptoms that your baby gets.

10. **What will happen to your baby’s test samples?**
No physical data/tissue samples will be collected for this study.

11. **What if new information arises during this research project?**
Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, the investigator will tell you about it and discuss with you whether you want your baby to continue in the research project. If you decide to withdraw your
baby, clinical care as usual will continue. If you decide that your baby can continue in the research project, you will be asked to sign an updated consent form. Also, on receiving new information, the investigator might consider it to be in your baby best interests to withdraw them from the research project. If this happens, the investigator will explain the reasons and arrange for your baby regular health care to continue.

12. **Can your baby have other treatments during this research project?**
This study will not affect any other treatments/ potential treatments your baby will receive.

13. **What if I withdraw my baby from this research project?**
If you decide to withdraw your baby from the project, please notify a member of the research team before you withdraw them. This notice will allow that person or the research supervisor to further discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your baby during the research project, the study doctor and relevant study staff will not collect additional personal information, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the sponsor up to the time of withdrawal will form part of the research project results. If you do not want them to do this, you must tell them before your baby joins the research project.

14. **Could this research project be stopped unexpectedly?**
This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:
- Unacceptable side effects
- The drug/treatment/device being shown not to be effective
- The drug/treatment/device being shown to work and not need further testing
- Decisions made in the commercial interests of the sponsor or by local regulatory/health authorities.

15. **What happens when the research project ends?**
The results of this research project will be submitted for publication in a medical journal, and also used as part of a thesis towards a postgraduate degree. Both of these formats are made available to the public. A plain language summary of group results will also be made available to you at the end of the trial if you request it.

**Part 2 How is the research project being conducted?**

16. **What will happen to information about your baby?**
By signing the consent form you consent to the principle investigator and relevant research staff collecting and using personal information about your baby for the research project. Any information obtained in connection with this research project that can identify your baby will remain confidential. All data and information collected will be stored under a de-identified number only accessible by the research team. The information will be kept for 25 years than destroyed. Only the research team can access this data during this time.

Your baby’s information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

Information about your baby may be obtained from their health records held at this and other health services, for the purpose of this research. By signing the consent form, you agree to the study team accessing health records if they are relevant to your baby’s participation in this research project.
It is anticipated that the results of this research project will be published and or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that your baby cannot be identified, except with your permission. All individual results will be grouped into their treatment stream, de-identified and not discussed on an individual level.

Information about your baby’s participation in this research project will be recorded in their health records.

In accordance with relevant Australian and or Victorian state privacy and other relevant laws, you have the right to request access to your baby’s information collected and stored by the study team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your baby’s information.

Any information obtained for the purpose of this research project that can identify the participant will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

17. Complaints and Compensation
If your baby suffers any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment for your baby. If your baby is eligible for Medicare, they can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

18. Who is organising and funding the research?
This research project is being conducted by Anna Kidman for her Doctor of Philosophy degree. No member of the research team will receive a personal financial benefit from your baby’s involvement in this research project (other than their ordinary wages).

19. Who has reviewed the research project?
All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of Monash Children’s Hospital/ The Site Melbourne, Australia.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

20. Further information and who to contact
The person you may need to contact will depend on the nature of your query. If you want any further information concerning this project or if your baby has any medical problems which may be related to their involvement in the project (for example, any side effects), you can contact the principal study investigator.

Anna Kidman
Monash Newborn
Level 5, Monash Children’s Hospital
246 Clayton Road

Dr Risha Bhatia
Monash Newborn
Level 5, Monash Children’s Hospital
246 Clayton Road
Clinical contact person
If you have any clinical concerns about your baby at any time, you can always speak to your baby’s doctor or bedside nurse.

For matters relating to research at the site at which your baby is participating, the details of the local site complaints person are:

Complaints contact person

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<th>Name</th>
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<tbody>
<tr>
<td>Position</td>
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<td>Telephone</td>
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<td>Email</td>
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If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC approving this research and HREC Executive Officer details

<table>
<thead>
<tr>
<th>Reviewing HREC name</th>
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<tr>
<td>HREC Executive Officer</td>
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<td>Telephone</td>
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<td>Email</td>
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</table>
Consent Form – Parent/Guardian

Title  
*Extubation CPAP Level Assessment Trial*

Short Title  
*ÉCLAT*

Protocol Number  
1

Project Sponsor  
*Anna Kidman – PhD study*

Coordinating Principal Investigator/Principal Investigator  
*Anna Kidman & Dr Risha Bhatia (Monash Health)*

Associate Investigator(s)  
*Dr Brett Manley (Royal Women’s Hospital)*
*Dr Rose Boland (Royal Women’s Hospital)*
*Professor Peter Davis (Royal Women’s Hospital)*

Location  
*Monash Newborn*

Consent Agreement

I have read the Participant Information Sheet, or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to my baby participating in this research project as described and understand that I am free to withdraw them at any time during the research project without affecting their future health care.

I understand that I will be given a signed copy of this document to keep.

Declaration by Parent/Guardian – for Parent/Guardian who has read the information

<table>
<thead>
<tr>
<th>Name of Baby (please)</th>
<th>............................................</th>
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<tbody>
<tr>
<td>Name of Parent/Guardian (please)</td>
<td>............................................</td>
</tr>
<tr>
<td>Signature of Parent/Guardian</td>
<td>............................................ Date</td>
</tr>
</tbody>
</table>
**Declaration - for Parent/Guardian unable to read the information and consent form**

Witness to the informed consent process

Name (please print) __________________________________________________________
Signature _______________________________ Date ______________________________

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

**Declaration by Study Doctor/Senior Researcher†**

I have given a verbal explanation of the research project, its procedures and risks and I believe that the parent/guardian has understood that explanation.

Name of Investigator/
Senior Researcher† (please print) ____________________________________________
Signature _______________________________ Date ______________________________

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.
Form for Withdrawal of Participation – Parent/Guardian

Title
Extubation CPAP Level Assessment Trial

Short Title
ÉCLAT

Protocol Number
1

Project Sponsor
Anna Kidman – PhD study

Coordinating Principal Investigator/Principal Investigator
Anna Kidman & Dr Risha Bhatia (Monash Health)

Associate Investigator(s)
Dr Brett Manley (Royal Women’s Hospital)
Dr Rose Boland (Royal Women’s Hospital)
Professor Peter Davis (Royal Women’s Hospital)

Location
Monash Newborn

Declaration by Parent/Guardian
I wish to withdraw my baby from participation in the above research project and understand that such withdrawal will not affect their routine treatment, relationships with those treating them or the relationship with Monash Children’s Hospital – The Site.

Name of Baby (please print)

Name of Parent/Guardian (please print)

Signature of Parent/Guardian

Date

Declaration by Investigator/Senior Researcher†
I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the parent/guardian has understood that explanation.

Name of Investigator
Senior Researcher† (please print)

Signature

Date

† A senior member of the research team must provide the explanation of, and information concerning, withdrawal from the research project. Note: All parties signing the consent section must date their own signature.