Participant Information Sheet – Parent/Guardian

Interventional Study - *Parent/Guardian consenting on behalf of participant*

ANTENATAL (PROSPECTIVE) CONSENT

Title	The Positive End-Expiratory Pressure Levels during Resuscitation of Preterm Infants at Birth Trial
Short Title	The POLAR Trial
Protocol Number	60303
Project Sponsor	Murdoch Children's Research Institute
Principal Investigator	Dr David Quine
Associate Investigator(s)	N/A
Location	Royal Infirmary Edinburgh

1 Introduction

Babies born extremely preterm require that their breathing is supported immediately after delivery. However, we still require evidence about the best way to provide this support. We are inviting you and your baby to take part in this research project, called the **POLAR Trial**, because your baby may be born very early (premature). If your baby is born before 29 weeks of the pregnancy, they could join this research project. This research project compares two ways we may adjust a commonly used treatment, called positive end-expiratory pressure (or PEEP), to help premature babies' lungs in the first few minutes after birth.

This Participant Information Sheet and accompanying Consent Form tells you about 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.

You might also like to view the POLAR trial parent education video which provides a visual summary of what it means for you and your baby to be involved in this research project. The video can be accessed via the homepage of the POLAR Trial website: www.POLARTrial.org.au, or by scanning the following QR code:

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, friend or your baby's local doctor.

Participation in this research is voluntary. If you do not wish your baby to take part, they do not have to. Your baby will receive the best possible care whether or not they take part.

The clinical care team may discuss your involvement in this research project with you, or may ask you to complete a study questionnaire, in person, by telephone or through a digital video-conferencing platform approved for use at Royal Infirmary Edinburgh.

If you decide you want your baby to take part in the research project, you will be asked to initial and sign the consent form. By initialling and 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
- Consent to the use of your personal and health information as described
- Consent to the use of telephone and alternative digital platforms to discuss the study with you remotely, where required.

We will give you a copy of this Participant Information Sheet and Consent Form to keep.

2 What is the purpose of the POLAR Trial (this research)?

Very premature babies almost always need help to breathe immediately after birth. The lungs of preterm baby's will often collapse between each breath. Applying gentle pressure, often by using a mask over their nose and mouth, helps to open their lungs with air and oxygen so that they can start to breath for themselves. This also makes it more comfortable for them to breathe.

To help with this nearly all preterm babies receive a treatment called positive end-expiratory pressure, or PEEP. PEEP applies a gentle pressure to a baby's lungs between breaths that makes it easier for the baby to breath and prevents the lungs from collapsing after each breath.

Currently we do not have enough evidence on the right amount of PEEP to give at birth. As a result, doctors around the world give different amounts (or levels) of PEEP to premature babies at birth. In this study we will compare 2 different approaches to PEEP treatment. At the moment we do not know if one approach is better than the other.

Very premature babies have a greater risk of needing long-term breathing support whilst in hospital and this is called chronic lung disease of prematurity. The longer a premature baby needs breathing support in the NICU, the more likely they are to develop this chronic lung disease. We want to find out whether one approach of opening the baby's lungs at birth results in them needing less breathing support in the NICU and developing less lung disease.

This research has been initiated by a group of doctors from Australia, the Netherlands, and the USA, all who look after premature babies. The overall lead study doctor for the trial is Professor David Tingay. Dr David Quine is leading the study at the neonatal unit at the Royal Infirmary of Edinburgh.

This research is being sponsored and coordinated by the Murdoch Children's Research Institute (MCRI), Melbourne Australia, and will be conducted in up to 30 hospitals that deliver premature babies in Australia, Europe, the United Kingdom, and the USA.

This study will enrol 906 babies from around the world, with 200 babies recruited in the UK. Up to 30 other hospitals will be involved internationally. We are working closely with other researchers and doctors that look after premature babies in the other hospitals as part of a collaboration. For babies who are a part of the POLAR trial, the PEEP groups and treatments are exactly the same in all hospitals.

3 What does participation in the POLAR Trial involve?

These definitions will help you understand the treatments involved in this project.

Abbreviation	Definition
PEEP	**Positive end-expiratory pressure:** This is a treatment where continuous low pressure is given to the air and oxygen mix a baby breathes. PEEP also helps a baby's lungs stay open. PEEP can be given to the lungs when a baby is breathing by themselves (CPAP) or when the medical team need to give extra 'breaths' to support the breathing (PPV).
CPAP	**Continuous positive airway pressure:** CPAP is a way of helping baby's breath that just uses PEEP and oxygen. In this study, all babies will be given PEEP using CPAP at birth. The PEEP is given between each of these extra 'breaths'.
PPV	**Positive pressure ventilation:** This is when the clinical team need to give extra 'breaths' to inflate the lungs using a mask or breathing tube (endotracheal tube) placed in the lungs.

4 What treatment will your baby get?

Your baby will be participating in a randomised controlled research project. When we do not know which treatment is best for treating a condition, we compare different treatments in this way. We put your baby into one of two groups to receive one of two treatments. All the babies in the same group receive the same treatment. The results are later compared to see if one is better.

We are comparing two approaches to PEEP levels given to preterm babies' lungs at birth. We will put your baby into one of two groups, static or dynamic PEEP.

Static PEEP group:
In this group, the PEEP level (the amount given to your baby's lungs) stays the same over time. This is called 'static' PEEP. Static PEEP is used in many countries, including the UK.

Half of the babies in this study will be in this group.

Dynamic PEEP group:
In this group your baby will start at a higher pressure of PEEP for a brief period to help open the lungs at birth. The PEEP level can then be adjusted (up or down) as your baby responds to the treatment. We have information that premature babies may benefit from a brief period of higher PEEP immediately after birth, when the lung is hardest to open and most likely to collapse.

Once the clinical team know your baby's lungs are open, the PEEP pressure is then decreased. This is called 'dynamic PEEP'. In this approach, the PEEP used at birth is higher than used during static PEEP. The clinical team will make changes to the PEEP levels in response to how well your baby is breathing.

Half of the babies in this study will be in this group.

5 How will we decide which group your baby is in?

You do not get to choose which group your baby is put in to. To try to make sure the groups are the same, each baby is put into a group by chance (random). Your baby has an equal (one in two) chance of being in either group. The clinical team will know and will tell you which group your baby is in.

This research project has been designed like this to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors jumping to conclusions.

6 What will happen to your baby while they are on this study?

Apart from the level of PEEP used to help your baby's lungs, the treatment for all babies in both groups is exactly the same and follows a standard pathway for premature babies at the Royal Infirmary of Edinburgh.

During care in the delivery room, the clinical team monitors your baby's response to treatment by assessing their heart rate, how well your baby is breathing and their oxygen levels. If your baby is breathing well, they will just need to keep the mask on their face with CPAP, or if your baby needs more support, short extra 'breaths' are given using 'PPV' breaths.

Babies who do not respond to PPV breaths using a mask will have a breathing tube placed into their windpipe and be connected to a ventilator (breathing) machine to give PPV.

If at any stage the clinical team thinks that your baby is not responding to either treatment, they will follow normal guidelines and give your baby more breathing support. Once your baby is settled, a member of the clinical team will update you on their progress.

7 What do you and your baby have to do?

Babies can join this study if they are born before 29 weeks of pregnancy and need help to start breathing at birth. If you agree, your baby will be in the study from when they are born until they are about 2 years old.

8 Does being in this project cost anything?

There are no additional costs associated with participation in this research project, nor will you or your baby be paid. All medication, tests and medical care required as part of the research project will be provided to your baby free of charge.

9 Does your baby have to take part in the POLAR Trial?

No, 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.

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 Royal Infirmary Edinburgh.

10 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 part of this project, they will have their breathing support at birth with the PEEP levels the clinical team decide to use, this may also include changing the PEEP levels during care in the delivery room.

If you chose not to participate in the POLAR trial, we are asking for your permission to allow us to collect medical record information about your baby's health. We are also asking for your consent to collect your medical record information for this pregnancy. You will be asked to sign a different consent form.

11 What are the possible benefits of taking part?

We cannot guarantee or promise that your baby will receive any benefits from this research. We know that PEEP is essential to help premature babies breathe, but we do not know the best level of PEEP to use or whether there is a difference between the two groups.

We hope that in the future, other babies will benefit from this study because the knowledge learned may go on to improve the way we help premature babies to start to breathe.

12 What are the possible risks and disadvantages of taking part?

Babies born very prematurely are at risk of many complications. Some of them will die, whether they are in this study or not. We believe, based on the information that is available today, that the risks of being in this study are similar to the risks that exist for premature babies having standard medical care immediately after birth.

Premature babies are at risk of a condition called "**pneumothorax**". A pneumothorax happens when air leaks out of the lung into the space between the lung and the rib cage. This trapped air may resolve by itself or if it stops the lung from fully expanding, it can make breathing harder, and babies may become unstable. This may cause a fall in oxygen levels, heart rate or blood pressure until the trapped gas is released.

If this were to happen, a plastic tube may need to be placed between the ribs to release the trapped gas. For some babies, a breathing tube needs to be placed in the windpipe and additional breathing help given with PPV.

Under-developed premature lungs are at higher risk of a pneumothorax, including when receiving CPAP, PPV or support from a breathing machine. This air leak can happen whether a baby is in this study or not and happens in about 1 in 11 babies born very prematurely.

The exact role of PEEP levels in causing a pneumothorax is unknown, with some studies suggesting lower PEEP levels may increase risk and others higher levels. We do not believe there is a higher risk of developing a pneumothorax from being in this study, but it may be possible.

We will also be looking out for side effects of the study treatment. If we find any new risks during the time your baby is in the study, we will tell you when your baby in the care of the neonatal unit or at their next visit. There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell the clinical team or the study doctor Dr David Quine about any new or unusual symptoms that your baby gets. The contact details are at the end of this document. The study doctor will discuss this with you, let you know of available resources and give you information about what to do.

For all large studies like POLAR, a safety committee is set up to monitor the study. The committee is a group of independent doctors and scientists who have reviewed and agreed to the study. They will monitor the study safety issues at all the hospitals involved. If they find unexpected problems, the study will be stopped or changed to reduce any risks to babies.

13 What if new information arises during the POLAR Trial?

Sometimes, during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, a member of the clinical care team will inform you, whilst at the NICU or during the 24-month follow-up visit, discuss the new information with you and discuss whether you want your baby to continue in the research project. If you decide to withdraw your baby, we will ensure their regular care in the NICU continues. If you decide that your baby can continue in the research project, you may be asked to sign an updated consent form. Any new information that arises during the POLAR trial will also be presented on the POLAR trial website.

14 Can your baby have other treatments during the POLAR Trial?

While your baby is participating in this research project, they can have all the regular care they need in the NICU and after.

15 What if you withdraw your baby from the POLAR Trial?

If you decide to withdraw your baby from the project, please notify a member of the clinical team. If you decide to withdraw it will not interfere with your baby's future care.
You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

The data collected up to the time of withdrawal will form part of the research project results. These results will not be identifiable.

16 Could the POLAR Trial be stopped unexpectedly?

This project is expected to end after all the babies have completed their 2-year-old follow up visits, and all information has been collected. This project may also be stopped at any time by the Primary Investigator (Prof Tingay) or the Study Sponsor (Murdoch Children's Research Institute), without your consent because:

- The Primary Investigator feels it is necessary for your baby's health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- The Study Sponsor, the Principal Investigator, or the Safety Committee decides to stop the study.

17 What happens when the POLAR Trial ends?

After completing the POLAR study intervention at birth, your baby will then receive all the standard care given to very preterm babies in your hospital.

After the POLAR trial has finished treating all the babies in the study, the researchers plan to publish the results of this project in scientific/medical journals and present the results at conferences and other professional forums. It may be a number of years before the results of this research are available. Please ask your study doctor if you want to know more about this. When the project is completed, we will display a summary of the results on the POLAR trial website: www.POLARTrial.org.au

18 What information will be collected about your baby?

In this research study, we will use information from the relevant sections of the medical records of you and your baby. We will only use information that we need for the research study. We will let very few people know your name or contact details, and only if they really need it for this study.

If you decide to take part in the study, the personal information and data collected about your baby will be taken from the normal data that the neonatal unit collects about all babies in their care. We are also asking your permission to collect medical information about this pregnancy from your, the baby's mother's, medical history. The information will include:

- your year of birth
- your baby's full date of birth
- your race/ethnicity
- information about you and your pregnancy
- and your baby's health in the Delivery Room and during their stay in the NICU.

We would like to also look at the long-term progress of your child. Therefore, we would like to access information collected on your child's future development that will be routinely assessed through the clinics at Royal Infirmary of Edinburgh when they are about 2 years old, to see how they have grown and developed. We will assess how your child has learned to walk, talk, and play. During this visit the clinical care team will assess if your child suffers any visual or hearing impairment and enquire into any hospital admissions your child may have experienced due to respiratory problems. You may also be asked a series of questions to assist with the clinical care team's assessment of your child. This may include completing a short study questionnaire when your baby reaches two-years of age.

People will use this information to do the research or to check you and your baby's records to make sure that the research is being done properly, they can include individuals from the research team, from regulatory authorities or from the NHS Trust, where it is relevant to them taking part in this research.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a unique ID number instead.

We will keep all information about you safe and secure.

Some of your information will be sent to Australia as the research is being led by the Murdoch Children's Research Institute and may be held on servers in the EU. They must follow our UK rules about keeping your information safe.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study. The Sponsor, the Murdoch Children's Research Institute, will keep the identifiable information for a period of 25 years or until the 25th birthday of the youngest participant, whichever is later, after the study has finished.

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

For more information on how we process and protect you and your baby's data please see the POLAR Privacy Notice and the Privacy Notice of the Murdoch Children's Research Institute which can be found via this link: https://www.mcri.edu.au/privacy-policy or on each footer of the POLAR trial web-site: https://www.polartrial.org.au/

If you have any questions about your rights, please contact the Privacy Officer of the Sponsor: Murdoch Children's Research Institute:
Email: notices@mcri.edu.au
P: +61 3 9936 6337

19 Who is involved in the POLAR Trial?

The POLAR trial is being led by the Murdoch Children's Research Institute, Australia. The trial is also being supported by local Coordinating Centers in Europe, the USA, and the UK. The UK Coordinating Centre, the National Perinatal Epidemiology Unit Clinical Trials Unit (NPEU CTU) is based at the University of Oxford. NPEU CTU is responsible for obtaining ethical and other approvals from regulatory authorities and NHS Foundation Trusts to ensure the POLAR trial is safe for all UK based participants.

The Murdoch Children's Research Institute has also engaged with software provider Florence Healthcare, who are providing a safe and compliant filing system required by all clinical trials to manage study-related documents. In doing so, some limited personal information such as your and your babies' name, initials and date of birth may be securely stored off site within this platform.

The platform is hosted in Europe and has been carefully chosen by the Murdoch Children's Research Institute so that your personal information will be stored securely and processed only in accordance with applicable data protection and privacy laws and regulations including the European General Data Protection Regulation (GDPR). The vendor of the platform is required to comply with strict confidentiality obligations and is not permitted to share your personal information with any third parties whatsoever.

20 Registration of the Study

A description of this clinical trial is available on https://www.clinicaltrials.gov (#NCT04372953). This website will not include information that can identify you or your baby or that can be traced back to you. You can search this website at any time. After the study concludes, the website may show a summary of the results of this investigation.

21 Complaints and Compensation

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions - please raise your concerns in the first instance with Dr David Quine, his contact details are – david.quine@nhslothian.scot.nhs.uk, or telephone 0131 2422577 or 0131 2422601.

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. In the event of injury or harm arising from routine clinical treatment or clinical negligence then NHS indemnity arrangements apply. In the event of injury or harm arising from the design and/or management of the research, the Murdoch Children's Research Institute insurance applies.

For any complaints or queries arising from your experience as a patient of the NHS please contacts the PALS service contact (Tel: 0131 536 3370 (9am – 2pm), Email: feedback@nhslothian.scot.nhs.uk). Or Patient Advice and support service, PASS | Patient Advice and Support Service Scotland (pass-scotland.org.uk)

You will not lose any legal rights by signing this form.

22 Who is organising and funding the POLAR Trial?

This research project is being conducted by the POLAR Trial group, headed by Prof David Tingay at the Murdoch Children's Research Institute, Melbourne, Australia. This research has been funded by the Medical Research Future Fund (Australian Government) International Clinical Trials Collaborations Grant #1170957. There is no commercial sponsorship or funding for the POLAR Trial.

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).

23 Who has reviewed the POLAR Trial?

All research in the UK involving humans is reviewed by an independent group of people called a Research Ethics Committee (REC). This trial has been reviewed and given favourable opinion by NHS/HSC REC.

24 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 one of the local study doctors named below:

Clinical contact person

Name	**Dr David Quine**
Position	Neonatal Consultant
Telephone	*0131 2422577 or 0131 2422602*
Email	david.quine@nhslothian.scot.nhs.uk

24 Signing of Informed Consent Form

After you have had sufficient reflection time, you will be asked to decide whether you wish to participate in this study. If you give permission, we will ask you to confirm this in writing on the accompanying consent form. By giving your written consent, you indicate that you understand the information and freely agree to participate in the study. Both you and the researcher will receive a signed copy. A copy will also be filed in your medical records.