The Latte Trial

Parent/Caregiver Information Sheet

Caffeine to improve neurodevelopmental outcomes in babies born late preterm: a randomised controlled trial

Your baby/pēpi was born late preterm (4-6 weeks early). While most babies/ pēpi born late preterm have good outcomes, they are at higher risk of having delayed development than term babies/pēpi. We are doing this study to find out if giving late preterm babies/pēpi caffeine every day for 4-6 weeks will improve their development at 2 and a half years of age.

Whether or not you take part is your choice. If you do not want to take part, you don't have to give a reason, and it won't affect the care you or your baby/pēpi receive. If you do want to take part now, but change your mind later, you can withdraw your baby pēpi from the study at any time without giving a reason. This will not affect the future healthcare of your baby/ pēpi.

This Information Sheet will help you decide if you would like to take part. You do not have to decide now, but you will need to decide about taking part in the study before your baby/pēpi is three days old. Before you decide you may want to talk with other people, such as family/ whānau, friends, or healthcare providers.

If you agree for your baby/pēpi to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Parent/Caregiver Information Sheet and the Consent Form to keep.

This document is 8 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

The Health and Disability Ethics Committee has given ethical approval for this study (2022 FULL 13147) and the has been registered on the Australia New Zealand Clinical trial registry, which can be accessed at www.anzctr.org.au (ACTRN12622001344785). The Latte Trail is being run by researchers from the Universities of Auckland and Otago.

What is the purpose of the study?

Most babies/pēpi born late preterm (4-6 weeks early) will have good outcomes. However, compared with term babies/pēpi, they have an increased risk of problems such as cerebral palsy and delayed development. We do not know exactly why late preterm babies/pēpi have this increased risk, but it may relate to more frequent drops in their blood oxygen levels. Frequent drops in blood oxygen levels are more common in children who are born late preterm, and they are also more common in babies/pēpi who later have developmental delay.

Caffeine is a medicine that is commonly used in very preterm babies/pēpi (more than 8 weeks early) to regulate breathing and prevent drops in oxygen levels. Currently, caffeine is not commonly used in late preterm babies/ pēpi (4-6 weeks early) Caffeine treatment is very safe and has been shown to reduce developmental problems in very preterm babies/pēpi, especially cerebral palsy and movement difficulties. Caffeine treatment prevents drops in blood oxygen levels in late preterm babies/pēpi and is well tolerated. Caffeine may also help to improve development in late preterm babies/pēpi, but this has not yet been studied. The purpose of this study is to find out if caffeine improves brain development in babies born 4-6 weeks early.

What will the study involve?

If you agree to your baby/pēpi taking part in the study, your baby/pēpi will be assigned to caffeine or placebo (identical appearing medicine with no caffeine), starting on day three after birth. The groups will be randomly chosen by a computer so that each baby/pēpi has the same chance of being in each study group.

Your baby/pēpi will receive the study medicine (caffeine or placebo) every morning until the date they were expected to have been born (4 to 6 weeks). Neither the study team nor you will know if your baby/pēpi is receiving caffeine or placebo. There will be approximately 500 babies/pēpi in Aotearoa participating in the study.

Study Medicine. Caffeine tastes quite bitter, so to improve the taste the caffeine is given in a syrup commonly used for children's medicines which contains cherry flavouring and sugar. The placebo also contains cherry flavouring and sugar with no caffeine. The study medicine is given by a syringe into your baby's/pēpi mouth each day in the morning. Before you go home, we will teach you how to give the study medicine to your baby. When your baby/pēpi is discharged home, you will be given two bottles of study medicine. When your baby/pēpi is 3 weeks old we will arrange a courier to pick up the first bottle of medicine from your house (this can be left in your letterbox) and ask you to start using the second bottle with a new dose based on your baby's weight.

Your baby/pēpi will have the following tests to determine the effects of the study medicine:

Heart rate. We will measure how fast your baby's heart rate is after your baby/pēpi has been on the study medicine for at least 3 days. If your baby/pēpi has been discharged home before then we will visit you at home to do this. If your baby's/pēpi heart rate is high we will decrease the dose of study medicine and check your baby's/pēpi heart rate again a week later.

Growth. We will ask you to tell us how your baby/pēpi is growing (weight, length and head circumference) from measurements taken by your midwife or doctor and written in your baby's Well Child book at 3 weeks and when the baby was expected to be born. We will also ask if your baby/pēpi is breastfeeding.

For mothers, we will ask you to fill in a short questionnaire about you (contact details, age, height and weight, smoking history and the ethnicity of yourself and your baby/pēpi).

We will collect general health information about your pregnancy and birth from your health records.

Development and growth*.* When your baby/pēpi is 2.5 years old we will arrange to see you and your child to assess your child's growth and development. Your child will see a developmental assessor at this visit. The assessment includes several games to assess development and growth, each of which are often used with children of this age. We will also ask you to fill out questionnaires about the health and development of your child/tamariki. The visit will take 1.5 hours, including breaks for kai and rest. The assessment will either be done at your home or a local clinic depending on your choice.

Healthcare. We will ask your permission to obtain information from the Ministry of Health Manatū Hauora on the number of times and the reason your child has been admitted to hospital, seen in the emergency department or had an outpatient visit from the time that they went home from hospital after being born until they were 2.5 years of age. This information will only be available to the members of the research team and will be used to determine if caffeine reduces healthcare costs of babies/pēpi born late preterm.

Recruitment. Māori pēpi are at higher risk of being born preterm and it is important that they are included in this study. To support recruitment of Māori, Māori whānau who have taken part in the Latte Trial are invited to suggest ways in which recruitment of Māori whanau to the study might be improved. If you are happy for the research team to contact you to discuss this, please tick the box on the consent form.

Heart and Mind Sub-Study (Optional). Auckland participants in The Latte Trial will have the opportunity to take part in additional assessments to assess the heart and brain effects of the study medicine. Caffeine improves blood oxygen levels, and this sub-study will help us understand whether caffeine improves brain oxygen levels and blood flow too. We will assess heart function and blood flow to the brain with a brief ultrasound before the study medication, 2 hours after the first dose and at the 5th dose. We will also record the oxygen level in blood and the brain using small skin sensors on the foot and forehead. These recordings will last for around 6 hours at the first and 5th dose. Several blood pressures will be taken during this time. These are routine assessments that are very safe and are regularly used for continuously monitoring babies. You can continue to feed your baby as normal even when the skin sensors are on. With your permission we will collect a small amount of blood (less than a 10th of a teaspoon) after the first and 5th doses to measure the breathing gases in blood, which will be timed with any other routine blood tests that your baby needs. We will tell you the results of the heart scan and other measurements, and many parents find this information reassuring. You can still take part in Latte without having these extra assessments. If your baby/pēpi is discharged home before the 5th dose assessment, a partial assessment can be performed at home. Heart scans will stored on the hospital system and any abnormal findings will be communicated to your family doctor. .

What are the possible benefits and risks of this study?

As caffeine is a standard treatment for all very preterm babies (more than 8 weeks' early) throughout Aotearoa New Zealand, and has been shown to be safe, we do not expect any significant risks for your baby/pēpi. Occasionally babies/pēpi on caffeine may develop a faster heart rate. We will monitor your baby's/pēpi heart rate, and if it is too fast, we will reduce the dose of the study drug.

We will ask you to fill out a questionnaire about your child's quality of life, including questions about your child's growth and development, physical functioning, behaviour, and getting along with other people. If you are concerned about any of these questions you will be able to talk with the research team member assessing your child about a referral to your child's doctor.

This study may benefit your baby/pēpi if caffeine treatment in late preterm babies turns out to improve brain development, but this is not yet known. When your child is 2.5 years old, we will send you a summary of your child's growth and development (many parents find this information helpful). If we discover any areas of concern, we will discuss this with you and help you decide if any further action is needed. With your permission, we can give this information to your family doctor, which can help with your child's ongoing care and development.

Who pays for the study?

This study is funded by the Health Research Council of New Zealand, the government agency for health research funding. There are no financial costs associated with participation in this study. You will receive a koha (gift) at enrolment into the study (a muslin wrap for your baby/pēpi) and at the 2.5-year assessment (kai (food) and a $50 voucher), and if you have to travel to attend the assessment, we will reimburse the cost of your travel.

What if something goes wrong?

In the unlikely event that you or your baby/pēpi were injured in this study, you would be eligible **to apply** for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

What are my rights?

Participation in this study is voluntary. If you join the study but change your mind you can withdraw your baby at any time and your baby's usual medical care will not be affected. With your consent, data collected prior to your withdrawal will be used in study analysis.

All information collected from you or about your child/tamariki as part of the study will be kept securely in locked cabinets and electronically on a secure University of Auckland server until your child is 26 years old. To protect confidentiality, their personal information will be kept separately from all the other information collected, which is identifiable only by a study number. Information can only be accessed by members of the research team with specific permission.

What will happen to my information?

During this study the study researchers will record information about you and your child/tamariki. This includes the results of the study assessments and data from the hospital records when your child/tamariki was born. You cannot take part in this study if you do not consent to the collection of this information.

Your child's treatment and outcome information will be stored using a deidentified code. Only researchers will be able to use this code to link the study record to your child. Only researchers will have access to your contact information. This will not be released to any third party. Publications and presentations of study results will not identify you or your child.

Study information will be stored on secure electronic databases at the University of Auckland. Only researchers will have access to this information, and this will be carefully controlled. All storage will comply with local and/or international data security guidelines.

<u>Future Research Using Your Information</u>

Researchers from other teams, including overseas, may request anonymised information (deidentified information without the identifying code) about children in the study. They would need to have appropriate ethical approval to be given the information and a Māori member of the research team will directly oversee the use of the information to ensure it is used appropriately and respected as taonga (treasure). There would be no information that could be identified as belonging to your child sent to other researchers. Results of this future research would be made available to you and your child. It is optional to provide for consent for other researchers to have access to your child's information. You may choose not to allow other researchers to have access to your child's information, and this does not affect your child taking part in the Latte trial.

Māori Data Sovereignty

Māori data sovereignty is about protecting information or knowledge that is about (or comes from) Māori people. We recognise the taonga (treasure) of the data collected for this study. To help protect this taonga:

We have consulted with the On Track network Te Awhi Rito clinical trial workshop Māori advisory group about the collection, ownership, and use of study data.

Data collaborations with other researchers will only be considered if certain principles are met:

- Rightsholders and stakeholders in the study, especially Māori, are consulted and engaged in the use and interpretation of study data
- The use of study data upholds and is respectful of Māori knowledge, worldviews and self-determination
- Patients are likely to derive benefit from the use of study data, including promotion of equitable outcomes
- Communities are not stigmatized or portrayed in terms of deficits and a strengths-based lens is applied
- The use of study data aligns with Aotearoa New Zealand ethical and Māori data sovereignty frameworks and standards

Security and Storage of Your Information.

Risks

Although efforts will be made to protect your privacy, absolute confidentiality of your information cannot be guaranteed. Even with coded and anonymised information, there is no guarantee that you cannot be identified. The risk of people accessing and misusing your information (e.g., making it harder for you or your child to get or keep a job or health insurance) is currently very small but may increase in the future as people find new ways of tracing information.

Rights to Access Your Information

You have the right to request access to you and your child's information held by the research team. You also have the right to request that any information you disagree with is corrected. If you have any questions about the collection and use of information about you and your child, you should ask the Study Doctor.

Rights to Withdraw Your Information

You may withdraw your consent for the collection and use of you and your child's information at any time, by informing your Study Doctor. If you withdraw your consent, your study participation will end, and the study team will stop collecting information from you. We will ask permission to continue to use data that we have already collected from you. If you agree, information collected up until your withdrawal from the study will continue to be used and included in the study. You may ask for it to be deleted when you withdraw, unless you withdraw after the study analyses have been undertaken.

What happens after the study?

You may change your mind about you and your child taking part at any time.

The results of your child's assessment will be discussed with you and a summary of the results will be sent to you and to your child's family doctor, if you agree. The results from the completed study will be published in a scientific journal. The information will be presented in such a way that neither you nor your child can be identified in any way.

If you agree, you will be sent a summary of the study results. This is not likely to be before 2028.

Who has approved the study?

This study has been approved by an independent group of people called a Health and Disability Ethics Committee (HDEC), who check that studies meet established ethical standards. The Northern B Health and Disability Committee has approved this study. The scientific aspects of this study have been approved by the Standing Committee on Therapeutic Trials (SCOTT), which is part of Medsafe.

Who do I contact for more information or if I have concerns?

If you have any questions, concerns or complaints about the study at any stage, you can talk to the nurse or doctor looking after your baby or contact one of the researchers.

Principal Investigator:
Assoc Prof Jane Alsweiler
Neonatal Paediatrician
Email: j.alsweiler@auckland.ac.nz
Phone: 021 52 6363

Site Principal Investigator:
Assoc Prof Chris McKinlay
Neonatal Paediatrician
Email: c.mckinlay@auckland.ac.nz
Phone: 0274725099

If you want to talk to someone who isn't involved with the study, you can contact the following:

Health and Disability Advocate:

Phone: 0800 555 050

Fax 0800 2 SUPPORT (0800 2787 7678)

Email: advocacy@advocacy.org.nz

Health and Disability Ethics Committee:

Phone: 0800 400 569 (MOH general enquiries)

Email: hdecs@health.govt.nz
Reference number: 2022 FULL 13147

Māori Health Support

If you require Māori cultural support talk to your whānau in the first instance. Alternatively you may contact the administrator for He Kamaka Waiora (Māori Health Team) by telephoning +64 9 486 8324 ext 2324. If you have any questions or complaints about the study you may contact the Auckland and Waitematā District Health Boards Māori Research Advisory Committee by telephoning

+64 9 486 8920 ext 3204.

Consent Form: The Latte Trial

Interpreters are available on request

Parent / Caregiver Statement:

I have read or have had read to me in my first language, and I understand the Participant Information Sheet.			
I have been given sufficient time to consider whether or not to participate in this study.			
I have had the opportunity to use a legal representative, whānau/ family support or a friend to help me ask questions and understand the study.			
I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.			
I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.			
I consent to the research staff accessing my medical records relevant to this pregnancy and my baby's/pēpi medical records.			
I agree to an approved auditor appointed by the New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.			
I understand that my participation in this study is confidential and that no material, which could identify me or my baby/pēpi personally, will be used in any reports on this study.			
I understand the compensation provisions in case of injury during the study.			
I know who to contact if I have any questions about the study in general.			
I understand my responsibilities as a study participant.			
I consent to the research staff contacting me again when my baby is older.			
I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study			
I consent to my baby/pēpi participating in the Heart and Mind part of the study	Yes ☐	No ☐	NA ☐
I consent to the researchers collecting information including the number of times and the reason why my child has been admitted to hospital, seen in emergency department or had an outpatient visit from the Ministry of Health's National Data Collections.	Yes ☐	No ☐	
If I decide to withdraw from the study, I agree that the information collected about me and my child up to the point when I withdraw may continue to be processed.	Yes ☐	No ☐	
I wish to receive a summary of the results from the study.	Yes ☐	No ☐	
I agree to being approached for suggestions on how recruitment of Māori to the trial might be improved (Māori whānau only).	Yes ☐	No ☐	NA ☐

Declaration by participant:

I hereby consent for my baby and myself to take part in this study.	
Parent/guardian name:	Baby name:
Signature:	Date:

If you are willing for anonymised study data to be shared with other approved researchers, including outside of Aotearoa New Zealand, please also sign below. You can still participate in the study if you don't agree to this.

Parent/guardian name:	
Signature:	Date:

Declaration by member of research team:

I have given a verbal explanation of the research project to the participant and have answered the participant's questions about it. I believe that the participant understands the study and has given informed consent to participate.

Researcher's name:

Signature: Date: