Newcastle 1000 Pilot Study

Maternal Participant Information and Consent Form

Invitation

You are invited to participate in the Newcastle 1000 Pilot Study. This study is being conducted by Professor Craig Pennell, Chair in Obstetrics and Gynaecology at the University of Newcastle and Professor of Maternal Fetal Medicine at the John Hunter Hospital. Before you decide whether or not you wish to participate in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish.

1. 'What is the purpose of this study?'

We know that the first 1000 days of life is an important time for babies to develop and grow. Our long term aim is to understand how things that happen during pregnancy and a child's first two years of life impact their development and growth. We will need a lot of families to be able to do this, so before we can undertake such a large study we need to do a smaller study (called a pilot study) to make sure families are happy with how we explain the study, how we invite them into the study, and what we are asking them to do.

2. 'Why have I been invited to participate in this study?'

This study is suitable for you if you are pregnant, between 11 – 14 weeks gestation, and plan to have your baby in the Newcastle or surrounding area.

3. 'Are there any reasons why this study may not be suitable for me?"

If you are not planning to stay in the Newcastle or Hunter New England area after the birth of your baby this study may not be suitable for you. Ideally we would like families to be planning to stay in the area so we can contact you to see how you and your baby are going after your birth. If you have an extremely high dependence on medical care including recent Intensive Care Unit admission or a significant life-limiting morbidity this study may not be suitable for you.

4. 'What does this study involve?'

If you agree to participate in this study, you will be asked to sign the Participant Consent Form. At the moment we are asking you to be in the pilot study which involves four visits through out your pregnancy and two check ups with your baby when they are six weeks and six months old. We would like to follow up your child's health and may contact you after the pilot study to ask if you would like to stay in the study and be involved for longer. You do not have to decide this right now as we understand circumstances can change. Joining the study now does not commit someone to stay in the study long-term.

We want to get a good idea of a broad range of things that can impact your health and your babies health and development, so we will ask questions about what you eat and drink, what drugs and medications you may take, your mental and physical health during pregnancy and get your permission

to access your pregnancy records from the hospital. The questionnaires can be done online or we can give you a paper copy if you prefer.

There is also a lot we can learn from your biology, so we will ask to collect biological samples such as blood, saliva, urine, and stool samples (see the list below for each sample and a short description of why we would like to collect it). If you do not want to provide a sample for any reason you can still be part of the study.

We are also planning to do three ultrasounds at 20, 28 and 36 weeks during your pregnancy to measure the growth and development of your baby. As part of routine low-risk care women usually get two ultrasounds around 12 weeks and 20 weeks. We will be requesting two additional ultrasounds at 28 and 36 weeks to monitor your baby's growth. We can do all three ultrasounds (20, 28, 36 weeks) at the Hunter Medical Research Institute, which is the building behind the John Hunter Hospital. A formal report will be created for the routine ultrasound and given to your doctor and/or midwife. Any information from the research scans which is clinically relevant to your care will also be given to your treating doctor and/or midwife.

We will provide you with free parking for the appointments at HMRI where we will perform the scans and collect the samples.

Study Timeline

Time Point	Duration	What will happen	Where	Who is involved
EOI (11-12 weeks)	10mins	A research midwife will discuss the study with you face-to-face and explain the different aspects of the study. You will be given the opportunity to discuss the study with others before consenting.	John Hunter Hospital	You Your partner
14 weeks	45-60mins	A short visit for informed consent, questionnaires, measures and biological sample collection	HMRI	You
20 weeks	90mins	Ultrasound, questionnaires, measures and biological sample collection	HMRI	You Your partner
28 weeks	90mins	Ultrasound, questionnaires, measures and biological sample collection	HMRI	You
36 weeks	90mins	Ultrasound, questionnaire, measures and biological sample collection	HMRI	You
Birth/on ward	30mins	Chart review, questionnaire, baby measures and biological sample collection	John Hunter Hospital	You Baby
6 weeks postpartum	60mins	Questionnaires, measures and biological sample collection Ultrasound on baby's heart	HMRI	You Baby
6 months postpartum	30-60 mins	Questionnaires, measures and biological sample collection	HMRI	You Baby

Clinical Measurements and Biological Samples from You

Weight and body composition

During the study we would like to measure your heart rate, blood pressure, weight, and body composition at each visit. We would also like to measure your waist circumference during the two visits after your baby is born.

Hand Grip and 30 second sit-to-stand test

We will ask you to do two very short (less than a minute each) tests which are commonly used to measure a persons strength and fitness. A grip strength test involves squeezing a hand grip (dynamometer) for about three seconds as hard as you can, while the 30 second sit-to-stand test is a simple count of how many times you can sit and stand up from a chair in 30 seconds. These are done at your first visit at around 14 weeks.

Accelerometer

We may ask you to wear an accelerometer (similar to a watch) on your wrist for one week each visit to track your physical activity throughout your pregnancy.

Ultrasound scans

Ultrasounds will be performed at your 20, 28, and 36 weeks visits during your pregnancy. Ultrasound does not involve any x-ray or other radiation and is safe for you and your baby. We will use these scans to track your baby's growth and development.

Blood samples

We ask your permission to collect blood samples (about 4-6 teaspoons or 20-30mL) at each visit. Blood will be used for several different analyses; we will separate red blood cells, plasma and cells from your immune system to measure circulating markers and immune function and will also ask permission to extract and analyse genetic materials (this is covered in a separate consent form).

Cheek swab and saliva sample

We will take a swab from your mouth during the 20 and 36 week appointments to collect DNA and the natural bacteria from your mouth enzymes (called the microbiome). Your DNA can tell us information about your immune system and how this is related to allergies and disease. The microbiome can be used to study the links between oral microbiome and health outcomes. We will also ask for you to collect two saliva samples at 20 and 36 weeks which can be done at home. We would like you to do these first thing in the morning and we use them to analyse the amount of a stress hormone called cortisol in your body when you first wake up.

Vaginal swab

Self-administered vaginal swabs will be requested at 14, 20, and 36 weeks during pregnancy and before birth to look at the natural bacteria (microbiome) that live in your vagina. As your microbiome changes during pregnancy, and birth, it is important that we get samples early-pregnancy, mid-pregnancy, late-pregnancy, and before birth. We will give you a kit with instructions on how to do the swab. We will also swab the cover used in your internal scan to analyse the microbiome in the upper area of your vagina, as these can be different from the lower area.

Skin swab

We will take a swab from your skin to analyse the natural bacteria (microbiome) that live on your skin. This will be taken from your chest area during pregnancy at 20 and 36 weeks, then just after the birth of your baby and at the six weeks post-partum appointment. We can look at your skin microbiome and see how it effects your baby's skin microbiome.

Hair sample

We will use a sample of your hair, from the 20 week pregnancy appointment, to screen for minerals, environmental toxins and cortisol (a hormone that is associated with stress).

Toenail sample

We will ask for a clipping from your toenails for your 20 week pregnancy appointment to use as a toxicology screen. You can do this at home and bring them into the appointment with you.

Urine sample

We will ask for a sample of your urine at each pregnancy appointment to look at the natural bacteria that live in the urinary tract, measure kidney function and nutrient markers, and screen for toxicology.

Stool sample

A sample of your stool (poo) will be requested at 20 and 36 weeks during your pregnancy. We use an easy swab collection method which you can do at home. These samples will be used to analyse the natural bacteria (gut microbiome) and track how it changes throughout your pregnancy.

Breastmilk and colostrum sample

Once your baby is born we will request a sample of your colostrum and breastmilk. This can provide valuable information on the natural nutrients and compounds in colostrum and breastmilk and the natural bacteria (microbiome) that live on your breast and in the milk.

<u>Clinical Measurement and Biological Samples from Your Baby</u>

Baby measurements

Once your baby is born they have their weight and length measured, and a test in a Peapod machine which uses air to calculate their body composition (the amount of fat and muscle). We will request access to the birth records to obtain information on these and other measures routinely taken after birth (e.g. Apgar scores).

Cord blood sample

After birth, once the umbilical cord is cut and no longer attached to you or your baby we will request some blood from the cord. This will be collected by a Midwife. At the time of collection the cord is no longer connected to the baby so there is no risk to your newborn from taking a cord blood sample.

Placental sample

We will take several small tissue samples from your placenta to look at the blood vessels, structure and growth. This will happen after the umbilical cord has been cut and will not hurt you or your baby.

Newborn Screening Card

After birth it is highly recommended that your baby has a Newborn Screening Test (sometimes called a heel prick test) which is usually done 48-72 hours after birth to screen for rare but serious disorders. If you are on the postnatal ward and have given permission for this test a hospital midwife will collect a few drops of your baby's blood onto a screening card (sometimes called a Guthrie card) by pricking the baby's heel. We request that, at the same time, a second card be taken for research purposes.

Bilirubin Test

Sometimes the hospital staff may request a small amount of blood from your baby to test for a pigment called bilirubin in the blood which is a sign of jaundice. While most cases of jaundice resolve within a couple of weeks it is important to check the bilirubin levels and this test is usually done on the postnatal ward. If your baby is having a bilirubin test we request that a very small amount (1-2ml) of blood be taken at the same time for research purposes.

Biological samples

After your baby is born we will request a urine and stool (poo) sample, a cheek swab and a skin swab. One of our friendly and gentle Research Midwives will take these samples. We would also like to collect these same samples at six weeks after birth, as well as a toenail and hair sample if possible.

Ultrasound for aortic intima media thickness

At six weeks we would like to see you and your baby and do a short ultrasound to look at your baby's heart. We will check the aorta, the largest blood vessel in the human body which carries blood away from the heart to the rest of the body. This will be done at HMRI.

Lung Function

At six weeks we would like to look at you baby's lung health. We do this while they are asleep and wearing a special mask which helps to measure their breathing. The lung function test will be done by Paediatric researchers who specialise in infant and child respiratory health.

5. 'What if I don't want to take part in this study, or if I want to withdraw later?'

Participation in this study is completely voluntary. It is up to you whether or not you participate. If you decide not to participate, it will not affect any treatment you receive now or in the future. Whatever your decision, it will not affect your relationship with the staff caring for you.

If you decide to withdraw from the study, you have the option of withdrawing all information relating to you and have any biological samples that have been taken destroyed. An exception to this is in the case of an adverse event, or a serious adverse event, where the information needs to be retained for regulatory reporting.

If you wish to withdraw from the study once it has started, you can do so at any time without having to give a reason.

6. How Many Visits?
We will book four visits throughout your pregnancy at HMRI to do ultrasounds, collect biological samples and help you with your questionnaires if you need assistance. Each visit will take between one to one and a half hours. We will also ask you to come in for a six week and six month visit once your baby is born.

7. 'How is this study being paid for?'
The study is supported through philanthropy and the Mothers and Babies Research Centre at Hunter Medical Research Centre.

8. 'Are there risks to me in taking part in this study?'
The side effects of having blood collected may include bleeding or bruising at the injection site and possible dizziness and/or possible fainting. We have trained, experienced staff to take the samples to minimise any discomfort. Please advise the research team if you normally feel dizzy or faint when you have blood collected.

After birth, once the umbilical cord has been cut, remaining blood that is in the umbilical cord will be collected in a tube. Therefore, there is no risk to mother or baby when we take blood from the umbilical cord.

Your emotional and mental health is an important part of your overall health. We will ask some questions about how you are feeling and if you have experienced any stressful events. If you feel upset or uncomfortable about answering these questions, or they bring up unwanted feelings please let the research staff or your treating obstetrician know and we can refer you to get support.

9. 'Will the study cost me anything??'
As participation is voluntary you will not be paid for the study, however we will provide parking for all of your research related visits.

10. 'Will I benefit from the study?'
You, your partner and your baby are not likely to benefit directly from this study, however the results may have a positive impact on the way we research and deliver pregnancy and child health care. The on-on-one midwifery contact and regular ultrasounds which allow you to see how your baby is growing might be something you enjoy as part of the study.

11. 'How will my privacy be protected?'
Only the researchers on the study, and the hospital midwives who are on the birthing suite, will know whether or not you are participating in this study. The hospital midwives are notified of your participation in a study so they can call a research team member to collect samples such as the placenta and cord blood but they do not have access to your research data. Any identifiable information that is

collected about you in connection with this study will remain confidential and will be disclosed only with your permission, or except as required by law. The study results may be presented at a medical conference or in a scientific publication, but individual participants will not be identifiable in such presentations.

Your personal information will be accessed, used and stored in accordance with Commonwealth Privacy Laws and the NSW Health Records and Information Privacy Act 2002. All information will be stored on a password protected HMRI Database (REDCap) which is both physically and virtually secure.

If you decide to withdraw from the study, you can request any data collected be withdrawn and destroyed. In some cases, your information may already be included in data analysis that has already been published in scientific publications or presented at a conference. In these cases, it may not be possible to withdraw your individual information from these presented data. Please be assured, any information used for publication or presentation will not be traceable back to your identity.

12. 'What happens with the biological samples?'

At all times your privacy will be maintained; your biological samples will be stored in a secure laboratory with an anonymous code before they can be analysed. We will store the codes and names in a secure locked file that can only be accessed by the research team.

With your permission, we will use blood samples from you and your baby to perform genomic testing. Genomic testing involves studying genes and their links to health and disease. The type of genomic testing we will perform on your blood samples will not provide any information about your health, or risk of disease for you, your baby or your family. On the extremely rare occasion that information is obtained about the health of you, your baby or family is found, we will inform your treating team, who will discuss these results with you. A separate consent form covers this type of analysis.

Samples collected from this study may be stored and used for future studies in pregnancy by researchers in our department and/or national/international collaborators. Any future proposed research study in which your samples are used will be reviewed by the Hunter New England Research Ethics Committee and The University of Newcastle Human Ethics Committee prior to commencement.

Although the biological samples will be stored in a biobank facility they will remain your property, as such if you have a clinical reason to access them, or the data and test results from any of the analyses we have performed you can request this through the Study Manager. If you wish to withdraw any or all of your samples at any time you can contact the study manager or one of the Research Midwives via phone (02 4042 0345) or email (new1000@newcastle.edu.au).

13. 'What happens with the results?'

We plan to publish the results of the study in peer reviewed journals. Results of the study will be presented to researchers and clinicians via presentations at national and international conferences, and publication in peer reviewed journal articles. Your privacy will be protected as the information will be de-identified (for more information on protecting your privacy see section 11).

14. 'What should I do if I want to discuss this study further before I decide?'

When you have read this information, one of the researchers will discuss it and any queries you may have with you. If you would like to know more at any stage, please do not hesitate to contact Professor Craig Pennell or Dr Tegan Grace on the numbers listed below. If you want to discuss the study with family members or your baby's other parent, you are welcome to take the time to do so before you decide whether to participate in the study.

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13. 'Who should I contact if I have concerns about the conduct of this study?'

Ethics: This research has been approved by the Hunter New England Human Research Ethics Committee of Hunter New England Local Health District, Reference 2020/ETH02219.

Governance: The conduct of this research has been authorised by the Hunter New England Local Health District to be conducted at the John Hunter Hospital site.

Should you have concerns about your rights as a participant in this research, or you have a complaint about the manner in which the research is conducted, it may be given to the researcher, or, if an independent person is preferred, please contact the HNE Research Office, Hunter New England Local Health District, Level 3, POD, HMRI, Lot 1 Kookaburra Circuit, New Lambton Heights NSW 2305. Telephone: 02 4921 4140. Email: HNELHD-ResearchOffice@health.nsw.gov.au and quote the reference number 2020/ETH02219

Thank you for taking the time to consider this study.
If you wish to take part in it, please sign the attached consent form.
This information sheet is for you to keep.

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PARTICIPANT CONSENT FORM MATERNAL

I, ... (participant name),

of ……..... (participant's address),

have read and understand that the study will be conducted as described in the Information Statement, a copy of which I have retained.

I have been made aware of the procedures involved in the study, including any known or expected inconvenience, risk, discomfort or potential side effect and of their implications as far as they are currently known by the researchers.

I understand that my participation in this study will allow the researchers and others, as described in the Information Statement, to have access to my medical record, and I agree to this.

I agree to participate in this study and understand that I can withdraw at any time without providing a reason.

I understand that my personal information will remain confidential to the researchers.

I have had the opportunity to have questions answered to my satisfaction.

I hereby agree to participate in this research study.

Name of participant: .....

Signature of participant: .....

Date: .....

Declaration by person conducting the consent process

I, the undersigned, have fully explained this research to the participant named above.

Name: .....

Signature: .....

Date: .....