

Participant Information Sheet

Project Title:

The PEARL study

Invitation:

We invite you to take part in the PEARL study, a research project currently running at the Quadram Institute Bioscience (QIB) in collaboration with Norfolk & Norwich University Hospital (NNUH).

Before you decide whether or not to take part, it is important that you understand why the research is being done and what it will involve. Please take time to read the following information carefully, discuss it with others if you wish, and feel free to ask us if there is anything that is not clear or if you would like more information. It is entirely up to you to decide whether or not to take part and, rest assured, whatever you choose, it will not affect the care you receive.

Taking part in the research is entirely voluntary. You are free to withdraw from the study at any time without giving a reason.

What is the purpose of the study?

All of us have trillions of bacteria and other beneficial microbes in our guts. Collectively they are called the 'microbiome' and they play a critical role in protecting our health, right from the earliest moments of life. They help us with digesting our food and even with programming our immune systems so that we can fight off infections.

Early life, from when a baby is growing in the womb until shortly after birth, is a critical stage in the development of their microbiome and can affect their life-long health. This is when babies first acquire microbes from their mother, and when the microbes colonise and establish in the gut. Anything that affects successful microbiome establishment can have knock-on effects on health in later life, particularly the risk of immune defects, allergies, infections and chronic intestinal disease. Factors influencing this can include antibiotic use, delivery method (vaginal or caesarean) and diet (moving from milk to solids).

The data we collect as part of the PEARL study will enable us to define the microbial community that characterises a 'healthy microbiome'. If we can better understand how a 'healthy microbiome' establishes in early life, and what factors influence it most strongly, then we can identify microbial 'signatures' indicative of future good health.

Results from the PEARL study will provide the critical evidence base necessary to develop safe new therapies for ensuring the establishment of a 'healthy microbiome' in early life, regardless of individual influencing factors. This would be a big step towards providing all babies with the best start in life.

We need your help to achieve this, and sincerely hope that you will consider taking part.

Why have I been chosen?

We are hoping to recruit 250 participants who are under 22 weeks pregnant. This is why you will have received information about the PEARL study.

Inclusion criteria:

To take part in the study you must:
be able to understand the study and provide informed consent
be at least 18 years old
be no more than 22 weeks pregnant
have a planned birth at the Norfolk & Norwich University Hospital (NNUH) (or home birth with maternity care from NNUH)
have a BMI between 18 – 35
be willing to provide samples over a period of 31 months. These samples would be: urine, stool, low vaginal swabs and skin swabs from yourself; and stool and skin swabs from your baby. Breast milk and blood samples will be requested also but these are optional.
be willing to have a small benchtop freezer to store your samples until the end of the study

Exclusion criteria:

Unfortunately, you cannot take part in the study if you:
are acting as a surrogate (planned pregnancy for the purpose of carrying the child on behalf of another woman)
are living with or related to a member of the research study team
are a current smoker
have taken antibiotics, antifungals or antivirals within the last 3 months
have taken steroids within the last 6 months
are taking more than a daily dose (one pot or container) of probiotics
have a history of polyps in your gut
have a long-standing gastrointestinal or liver function abnormality requiring on-going medical management or medication
have a history of cancer apart from squamous or basal cell carcinomas of the skin (skin cancer) that have been medically managed by local excision
have made any major changes to your diet in the last month (e.g. become vegetarian or stopped eating red meat)
have a history of alcohol, drug or substance abuse
have a history of any liver problems (e.g. hepatitis B or hepatitis C)
have any pre-existing medical condition that affects your immune system (e.g. rheumatoid arthritis, type 1 diabetes, multiple sclerosis, asthma, eczema or psoriasis) If you have not had any symptoms of asthma, eczema or psoriasis in the last 5 years, you can still be included in the study.
have had major surgery of the gastrointestinal tract, apart from gall bladder or appendix removal, in the past five years
have had any major bowel surgery at any time
have a history of an inflamed bowel (e.g. ulcerative colitis, Crohn's disease or diverticulitis)
have persistent, infectious gastroenteritis or persistent/ long-term diarrhoea with an unknown cause
have long-term constipation

Do I have to take part?

No. It is entirely up to you to decide whether or not to take part. If you do, you will be asked to sign a consent form and be provided with all the information you need to take part. You are free to withdraw at any time and without giving a reason. If you decide to withdraw from the study, we will give you the option to fully withdraw from the study, or partially withdraw. A partial withdrawal from the study would mean you would no longer wish to provide samples or answer any questionnaires, but you would be happy for us to continue to collect the data from your health records for the duration of the study. You would not need to do anything; the research team would collect this information from your medical records/ health visitors. A decision to withdraw or not to take part will not affect the standard of care you receive. An expression of interest does not mean you are committed to participating in the study.

What will I have to do if I take part?

Consenting

To take part in the PEARL study, we first need you to sign a consent form. You can do this by speaking to the research midwife/ a member of the research team by video/telephone call (we are happy to use your preference of platform e.g. a call with video, without video, phone, Teams, Zoom, etc.); or we can make an appointment to meet you at the Quadram Institute Clinical Research Facility at a time that is convenient to you. On any of these occasions we will explain what taking part in the study entails, exactly how to collect the samples, and check you are eligible to take part; it also gives you the chance to ask any questions you might have and make an informed choice about whether to continue.

If you decide to continue, we will ask you to complete two separate consent forms confirming your participation in the study and your permission to store your samples in the tissue bank (Norwich Research Park Biorepository) for research purposes. If you are consenting digitally/via phone we will ask you to provide your consent in an email after going through the consent forms with you digitally/via phone, or alternatively, we can send you a copy in the post to sign and return. We will also give you your first sample collection packs. A copy of your consent forms will be sent to your GP and to the NNUH with a copy of this PEARL study participant information sheet to be inserted into your personal medical records. You will also be given a copy of the consent forms to keep.

Once you have consented and are enrolled, we will take the opportunity to collect some basic information from you, such as your due date and whether you are expecting twins. We will also put a sticker into your maternity booklet so that your caregivers at birth are aware that you are taking part in the PEARL study. If you are consenting via video call, we will provide this sticker in your first collection packs. Our team will also introduce a new study, called PEARL-AGE, that is linked with our research. The PEARL study is investigating the transfer of microbes between mother and baby. The PEARL-AGE study will expand this to look at the transfer of microbes amongst the wider family. You would not need to do anything additional, only to pass on the research information to your family if you think they might be interested to take part.

Collecting samples

Sample collection has been designed to be as easy as possible for you during this busy time, including sample pick up from your home by our research team so you don't have to go anywhere to drop off your samples. You can ask for help from friends and family to collect any of these samples.

Once you are enrolled, we will ask you to collect samples from yourself and your baby during pregnancy and the first 2 years after your baby is born. There are 12 timepoints in total when we would like you to collect samples. The details of which samples are requested at each timepoint, are shown in the table below. As you will see, not all the samples are compulsory. We will also ask you to complete questionnaires at some of these timepoints and further information about these are provided later in this document.

We will provide you with your collection packs before your samples are due. This will contain everything you need to take your samples, including clear instructions. It is fine for samples to be taken within a 7-day period of the date they are due and we will text you beforehand to help you remember.

		Samples collected from participants' homes by research team at these 4 timepoints											
		Phase 1 (pregnancy)			Phase 2 (birth)			Phase 3 (following birth)					
		Trimester 1 (week 12)	Trimester 2 (week 23)	Trimester 3 (week 30)	At birth	Week 1	Week 3	Month 4	Month 8	Month 12	Month 16	Month 20	Month 24
Mother's samples	Urine	✓											
	Stool		✓										
	Low vaginal swab			✓									
	Skin swab												
	CDCP questionnaire			✓									
	Health questionnaire			✓									✓
Baby's samples	Dietary questionnaire (optional)			✓						✓			
	Colostrum/ breast milk (optional)					✓	✓	✓	✓				
	Blood samples (optional)	Please provide samples at 12, 16, 20 and 28 weeks if you can											
	Stool, meconium and skin swabs				✓	✓	✓	✓	✓	✓	✓	✓	✓
	CDCP questionnaire					✓	✓	✓	✓	✓	✓	✓	✓
	Cord blood (optional)				✓								

¹Centre for Disease Control & Prevention ²Participant Dietary Preferences and Perceptions Questionnaire ³Data collected from Primary and Secondary Care records by GP Data Manager and Study Researcher

We will collect the samples from you, at home, at a time that is convenient for you at 4 points throughout the study, once you have let us know they are ready for collection (via text message). This will be after phase 1, after phase 2, and twice during phase 3 (see table above). If you collect any samples at the hospital either at birth or after your baby is born, you can give your samples to your midwife/nurse and we will collect from them.

Please inform the research team if you will need assistance at the time of the freezer delivery to move the freezer into your home during this time as the delivery team may not be able to assist.

To make storage easier, we will provide you with a small benchtop freezer to store your samples at home until the research team can collect them from you. At the end of the study, you are welcome to keep the freezer if you wish, or we will collect it from you. The freezer is approximately 15.5kg in weight and 51 x 44 x 47.5 cm (H x W x D) in size.

If possible, we ask that you collect your 'at birth' low vaginal swab during labour and before you give birth but we do understand that not everyone will want/ be able to do so. However, if this is not possible, it is fine if you collect this sample in the days following birth.

CORONAVIRUS UPDATE: While the UK government recommend social distancing measures to prevent the spread of coronavirus, we will be implementing a few changes in the way we run the PEARL study. We will not collect samples from participants homes until we are assured that it is safe to do so. We will send sample collection packs to participants in the post, and we ask that participants continue to collect their samples and freeze them until the research team are able to arrange a collection once the social distancing measures are relaxed. We will continue to send text reminders when your samples are due to be taken. We apologise for any inconvenience this may call while we are working in these unprecedented circumstances.

Please do not collect any samples and inform the study team if you or anyone in your household has:

- symptoms of coronavirus (COVID-19) infection or are currently awaiting a test result.
- tested positive for coronavirus (COVID-19) – *please contact the research team to discuss when you can start taking samples again after a positive test.*
- had recent contact with someone who has coronavirus – ensuring you self-isolate if the NHS test and trace service advises you to do so. *You can collect samples again once you are advised you no longer need to self-isolate.*

Why are we asking for these particular samples?

Each of these samples helps us identify which microbes you pass onto your baby and what factors, e.g. antibiotics, affect them most.

Microbes also produce compounds that we can detect in your samples, some are linked to important processes in you and your baby's bodies, so it is important to identify whether they are present.

Additionally, your own genetics influence the microbes that you have. We will evaluate this factor in your samples to better understand how the genes that you and your baby have might influence the type of microbes that you have in your gut and on your skin.

What is the purpose of the questionnaires?

The questionnaires we are asking you to complete will provide us with information about your general health, lifestyle, and dietary preferences. This allows us to determine whether these factors affect your gut microbiome. Not all of them are compulsory. They each take about 5-10 minutes each to complete. We will send you these questionnaires via a digital link when they are due to be completed.

Other data we will collect

In addition to the samples/questionnaires already described, we will collect your general health information data collected routinely during pregnancy, from health visitor checks and if you should visit your GP or hospital throughout the duration of the study. You would not need to do anything to provide this information.

During the study, you may be invited to provide an audio/video recording of your experience of taking part in the study. This material will be used to promote public awareness of the study. We may also ask you to provide anonymised quotes for use in research reports and publications. This is completely optional.

Are there any benefits to taking part?

There are no direct benefits to taking part in the study, but by taking part you would be contributing important information that will help us better understand how the transfer of a mother's gut microbiome to her baby might influence that baby's health as they develop during pregnancy and early life.

Will my GP be informed?

Yes, it is standard practice to inform your GP that you are participating in a research study at the QIB. This is one of the things that you will be agreeing to when you sign the consent form to take part in the study.

Are there any risks or side effects from participating in this study?

There are no known risks to you taking any of the samples for this study. Some people find a small amount of discomfort associated with taking blood.

Do I get paid for doing this?

Participating in this study is entirely voluntary. However, we do recognise that taking part may cause you some inconvenience. As a thank you for participating in the study, a 'Love-To-Shop' voucher to the value of £20 will be posted to your home address at the end of the study as a contribution towards your time and any inconvenience.

What happens when the research study ends?

Findings of this study will be reported in the scientific literature. No individual's data will be identifiable.

What will happen to my samples?

All data and samples will be anonymised. Samples will be stored securely at QIB or, if you provide your consent, we will store your samples securely in the Norwich Research Park Biorepository where your samples may be used for future ethically-approved research after the PEARL study has finished.

What if relevant new information becomes available or changes to the study are made?

If this happens, we will tell you. If changes to the study are necessary we may need to ask you to sign another consent form.

Will I be told the results of the study?

At the end of the study, we will provide you with feedback about what we have found as a result of your help and what it may mean for future research. We will regularly update our websites to fill you in on all the exciting research that we have done using your samples.

The results of the study will also be published in scientific journals and presented at national and international scientific meetings. We are unable to tell you any of your individual results since it is only possible to draw conclusions from the group as a whole.

What if there is a problem, or I would like to make a complaint?

If you have a concern about any aspect of the study, you should ask to speak to a member of the research team by calling 07876182564 or via email on pearl@quadram.ac.uk. If you remain unhappy and wish to complain formally, you can do this through Dr Antonietta Hayhoe, the chairperson of the Human Research Governance Committee (HRGC) at QIB: antonietta.Hayhoe@quadram.ac.uk; 01603 255030.

If you wish to complain or have any concerns about the way you have been treated whilst taking part in this study at the NNUH clinics, there will be a local hospital complaints procedure that you can follow. The PALS (Patient Advice and Liaison Service) is a confidential service designed to support patients, relatives and carers. Their website is pals@nnuh.nhs.uk and the office has an answerphone which is available 24 hours a day: 01603 289036 or 01603 289045.

We are always looking for ways to improve the participant experience in these studies. If you wish to provide any anonymous feedback to the study team you can do so by using this link <https://www.surveymonkey.co.uk/r/PEARLcomments>. The research team will not be able to see who posted these comments so will not be able to respond directly but will certainly take your thoughts on board.

If something happens to me, will I receive compensation?

QIB accepts responsibility for completing trials and, as such, will consider claims from participants for any harm suffered by them as a result of participating in the trial, with the exception of those claims arising from negligence by the participant. QIB has liability insurance in respect of research work involving human participants.

However, if you are harmed as a result of taking part in this research project there are no special compensation arrangements. If you are harmed due to someone's negligence, you may have grounds for legal action, but you may have to pay for it. Please note that QIB will not fund any legal costs arising from any action unless awarded by a court.

How will we use information about you?

We will need to use information from you, from your medical records and your GP for this research project.

This information will include your (and your baby's):

- Name/initials
- Contact details
- Date of birth

- Clinical data and measurements taken as part of routine care collected from GP and hospital records (including routine pregnancy scans and tests).
- General health, lifestyle and dietary information. This will be gathered from your answers to the questionnaires we will ask you to complete as part of the study.
- Data we will produce from the samples that you provide us

People will use this information to do the research or to check your records to make sure that the research is being done properly.

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 code number instead.

We will keep all information about you safe and secure.

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.

What are your choices about how your information is used?

- 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.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.
- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study by providing your consent to store your samples in the NRP Biorepository.

Where can you find out more about how your information is used?

You can find out more about how we use your information:

- at www.hra.nhs.uk/information-about-patients/
- our leaflet available from www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team
- by sending an email to our data protection advisor: dpa@nbi.ac.uk, or
- by ringing us on 07876182564.

Who has reviewed this study?

To protect your safety, rights, wellbeing and dignity the study has been reviewed and agreed by the QIB Human Research Governance Committee (HRGC) and an independent group called the London-Dulwich Research Ethics Committee (REC) which is made up of expert and lay members. RECs review research proposals and give an opinion about whether the research is ethical. They also look at issues such as participant involvement in the research. The committees are entirely independent of research sponsors (the organisations responsible for the management and conduct of the research), funders and the researchers themselves. This enables them to put participants at the centre of their review.

What should I do now?

If you are interested in taking part in the study and would like to know more, you can speak to the research nurse/midwife at your 12/20 week antenatal scan at NNUH, contact the research team on 07876182564/pearl@quadram.ac.uk, or go to the study website <https://quadram.ac.uk/pearlstudy/> and complete the expression of interest form.

If you are not interested in taking part in the study or you are not eligible, you need not do anything. No one will contact you further about the study.

Thank you for taking the time to read this information.