Participant Information Sheet

Healthy Brains, Healthy Futures:
A Children Growing Up in Liverpool (C-GULL) Sub-Study

You are invited to take part in a new study about children's brains, minds and immune systems. This study is part of the C-GULL project that you are already involved in.

It's important you understand why we're doing this research and what taking part would involve. Please read this information carefully and feel free to talk it through with others. A member of the research team will go through it with you and answer any questions. Take as much time as you need to decide.

Thank you for your time

Why are we doing the study?
As children grow, their brains, minds and immune systems are shaped by many different factors including the genetic information a child inherits from their parents, and the environment they grow up in. We're also learning that these systems – brain, mind and immune – affect each other in complex ways, but our understanding is limited because researchers don't often have all the information they need to study these systems together.

This new study adds to the C-GULL project by collecting extra information about how the body, brain and mind interact during development. We will collect information about your child's immune system (taken from blood samples), and their brain (using brain scans). This will allow researchers in the future to explore important questions, like how genes linked to mental health shape our immune systems, even very early in life – or how early changes in our immune systems can influence how the brain develops.

Why is this study important, and who should take part?
We hope to better understand why some children experience poor mental health later in life while others do not. We are inviting all current eligible participants of the C-GULL study to take part in this study.

Do I have to take part?
No — taking part is entirely voluntary. If you choose not to take part, it will not affect your healthcare or your involvement in the main C-GULL study. Even if you agree now, you can change your mind and withdraw from the 'Healthy Brains, Healthy Futures' sub-study at any time, without giving a reason.

What should I do if I want to take part?
If you would like to take part, speak to the C-GULL research team when you are next visiting Liverpool Women's Hospital for your antenatal care. A member of the clinical research team will approach you during one of your scheduled appointments and provide information about this part of the study. They will explain what taking part involves and answer any questions you may have. If you are happy to be involved, you will be asked to complete and sign the first of two consent forms. This first consent form allows the C-GULL research team to contact you shortly after the birth of your child. At that point, we will arrange a convenient time to speak with you further about the study and, if you wish to proceed, set up a visit for you and your baby at Alder Hey

Children's Hospital for the first study assessment. When you attend your visit at Alder Hey, you will meet with a research nurse who will go through everything with you again and answer any further questions. If you are still happy to take part, you will be asked to complete the second consent form. This full consent is required before we can carry out any study assessments or collect samples. It ensures that you have had time to consider your involvement and fully understand what the visit will include. You can take as much time as you need at any stage and the research team will support you.

What will happen to me if I take part?
If you decide to take part, here's what the study will involve:

1. **Scans of Your Child's Brain**: We will contact you to arrange two MRI scans of your child's brain—one when they are around 6-12 weeks and another when they are 5 years old.
2. **Blood Sample**: We will also ask for two samples of your child's blood, one at age 6-12 weeks, which we aim to take when you visit for the MRI scan, and another when they are aged 2 years, which will be taken at their routine C-GULL follow up assessment. For the first sample at 6-12 weeks, we will collect no more than 4ml (less than a teaspoon) of blood from your child and at age 2 years we will collect no more than 10ml (two teaspoons). These samples will be collected by qualified clinical researchers who are experienced in collecting blood from small children. These procedures will cause no harm to your child and special creams can also be used that ensure it is also pain-free.
3. **Questionnaires:** We will ask you about any recent infections or vaccinations, as these can affect the blood results. Even if you're unsure, any information helps. If possible, please bring your child's red book to the visit.

What happens during the MRI scan and is it safe?
MRI scans are a very important part of this study and allow us to look at how your child's brain is developing.

- **Safe and Non-invasive**: MRI is a safe, non-invasive technique that uses magnets and radio waves to take detailed pictures of the brain. It does not involve any radiation and there are no known risks or side effects. MRI scans are widely used in healthcare and research, including with newborn babies, and are considered one of the safest ways to study the brain.
- **Comfort First**: We understand that the idea of your child having a scan might be worrying. Please be assured that we will do everything we can to make the experience calm and comfortable. Most babies sleep through the scan. Children aged 5 years often enjoy the experience, especially when they get to see a picture of their own brain.
- **During the Scan**: During the scan, your child will lie on a special bed that gently moves into the MRI scanner. You can stay with them throughout to help keep them settled. The scanner can be a little noisy, so we will provide ear protection. All scans will be carried out by specially trained professionals who are experienced in working with babies and young children. Our team will guide you through each step and will be there to answer any questions.

How will we use personal information about you?
To carry out this research, we will need to use some personal information from you and your child's medical records. This includes identifiable details such as your name, date of birth, NHS number, contact information (telephone number, email address, home address and postcode) and your child's health information. This information is already collected as part of the main C-GULL study and will be securely linked to this sub-study. Only authorised members of the research team will have access to your personal details and only where needed — for example, to contact you or check medical records to ensure the study is being done properly. All other researchers working on the study will only use fully anonymised data. This means they will not know who you are and will not have access to your name or contact details.

We will handle all personal data in line with the UK General Data Protection Regulation (UK GDPR) and the Data Protection Act 2018. Your information will be kept secure, treated in confidence and used only for the purposes of this research.

How will my child's samples be used, and where will they go?
As part of this sub-study, we will collect a small blood sample from your child. These samples will be analysed to understand how the brain, immune system, and genetics interact in early childhood.

We will carry out a range of tests on your child's blood sample to help us understand how their body and immune system are working. These tests will include ways of:

- Looking at your child's genetic information (DNA) to understand if certain genetic factors they inherit (are born with) or acquire might be linked to brain development and mental health.
- Examining how the body is working by looking at the types and functions of cells in your child's blood, including how genes, proteins, and molecules are being used in different blood cells and in the fluid surrounding the cells (plasma).
- Studying how the environment (like stress or infections) might affect how their immune system develops.
- Checking for markers of inflammation or infection, or how your child's body is responding to infections.

These tests will be carried out by expert research teams at the University of Cambridge and the Wellcome Sanger Institute (Cambridge). Some tests may also be carried out by approved laboratories elsewhere in the UK or internationally, including specialist commercial laboratories, if they offer the most appropriate and high-quality services. In these cases, samples will be fully anonymised so that your child cannot be identified, and we will ensure that all transfers comply with UK data protection and research ethics regulations.

Once testing is complete, any remaining samples will be returned to Liverpool, where they will be securely stored as part of the C-GULL biobank for future research related to the C-GULL programme only. Some of the tests involve extracting and analysing DNA and RNA from your child's blood. We will ask for your specific permission for this when you sign the full (second) consent form at your visit to Alder Hey.

What will happen to the data collected for this sub-study, is it safe?
All data collected for this sub-study, including MRI scans, blood test results, and questionnaires, will be used to create a research dataset under managed access. This means researchers from the original team and other approved researchers from around the world can apply to use the data for studies that are appropriate, safe, and in the public interest. To help make the most of this valuable dataset, the information from this sub-study will be combined with data already collected through the main C-GULL study. Data will be stored securely at the University of Liverpool, University of Cambridge and Wellcome Sanger Institute, and anonymised RNA sequencing data will be stored on the European Genome phenome Archive (EGA). Researchers will only be granted access after providing clear plans for how they will use the data. You and your child will not be identifiable, as all samples and data are coded using a study number. Any identifiable information will be stored securely and separately and kept for at least ten years after the study ends. Your child's samples and data will be given a code and stored separately from personal information to protect their identity. We use strict security measures – including encryption, password-protected systems, key card access and locked storage – to keep all information safe.

What are the possible benefits of taking part?
There may not be a direct benefit to you or your child, but the information we collect could help other families in the future. Taking part may help us better understand child development and improve mental health care for children.

Travel costs and other reasonable costs will be reimbursed.

What are the possible risks of taking part?
Your and your child's safety is our top priority and the study has been carefully checked to make sure it is safe. The assessments and samples we have chosen have been used with children before and are not known to carry any risks. The questions you are asked should not cause discomfort and you can choose not to answer any you are unsure about. If you or your child feel uncomfortable at any point, please let a member of the research team know straight away.

What if I no longer want to take part?
You can withdraw from the study at any time without giving a reason. This will not affect the care you or your child receive in any way. If you withdraw, we will stop collecting any new samples or data, but we will keep and use anything already provided, with your personal details removed. If you cannot attend the MRI appointment, please let us know on 0151 795 6700 so we can offer the slot to another participant.

Will I get the results from the tests on my child's samples?
No. The tests are for research only and not designed to give medical results. We won't be able to share individual results, but we will share overall study findings with participants in the future. However, if an undiagnosed medical disorder is picked up, research staff will be able to provide referral information, which could help you to receive appropriate treatment and local services in the future.

Where can I find out more about how my information is used?
You can find out more by:

- Visiting: www.hra.nhs.uk/information-about-patients
- Reading the leaflet at: www.hra.nhs.uk/patientdataandresearch
- Asking a member of the research team
- Emailing: legalservices@liverpool.ac.uk
- Calling: 0151 795 0523

Where can I get further information or discuss any problems?
If you have any questions or concerns about any aspect of this study, please contact a member of the C-GULL Study research team on 0151 795 6700. If your concerns are not resolved, you can contact the Patient Advisory Liaison Services (PALS) at Liverpool Women's Hospital on 0151 702 4353 and at Alder Hey Children's Hospital on 0151 252 5161. You can also visit PALS by asking at the Liverpool Women's Hospital and Alder Hey Children's Hospital main reception areas.

Who is organising and funding the research?
This study is a collaboration between the Universities of Cambridge and Liverpool as well as Alder Hey Children's NHS Trust and Liverpool Women's NHS Foundation Trust, with input from experts in mental health and lived experience.

Healthy Brains, Healthy Futures is part of the larger C-GULL project, a long-term study following families to understand the development of health and well-being. Wellcome Trust is funding this sub-study (Reference: 309245/Z/24/Z) - Professor Duncan Astle is the Chief Investigator and Professor Melissa Gladstone is the C-GULL Lead Investigator. Professor Louise Kenny is the Chief Investigator of the C-GULL study (Reference: 217067/Z/19/Z). The study is sponsored by the University of Liverpool and managed by the Harris Research Centre, University of Liverpool.

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed for ethical considerations and given a favourable opinion by members of the North East – Newcastle & North Tyneside 1 Research Ethics Committee.

Where can I find further information?
Should you need any further information about the study, please contact us on cgullstudy@liverpool.ac.uk or 0151 795 6700. You can also visit our website www.cgullstudy.com or follow us on social media @cgullstudy.

Thank you for taking the time to read and consider this information sheet. Should you decide to take part in the study, you will be given a copy of the information sheet and the signed consent forms to keep.