INSIGHT-2: Participant Information Sheet

You are invited to take part in the INSIGHT-2 research study. Before you decide, it is important for you to understand the purpose of the research and what it will involve. Please take time to read the following information carefully and discuss it with friends and family if you wish. Please ask the study team if anything is not clear or if you would like more information. Take time to decide whether you wish to take part.

Please note that throughout this leaflet, the terms "baby", “infant” and “child” are used to refer to an individual offspring in the case of a singleton pregnancy. However, in the context of multiple pregnancies (e.g., twins, triplets), these terms should be understood to encompass all individual offspring within the specified multiple pregnancy (i.e., “babies”, “infants” and “children”).

1. Background

Some women develop complications during pregnancy which can affect their and their babies’ health, such as high blood pressure, diabetes, or babies being born small or too early. We would like to investigate biomarkers in the blood which might help us to predict which women are at risk of pregnancy complications. We are also trying to understand how pregnancy complications affect the baby’s developing immune system. To do this, we can take blood from the baby’s umbilical cord after they are born. Sometimes, we can also take a sample from the placenta. To understand how thebaby’s immune system changes after birth, we can take blood samples when the baby is one and three months old.

2. Why have I been chosen?

You have been asked to take part because you are pregnant. You may have a medical condition which might put you at higher risk of some pregnancy complications.

3. What do I have to do if I take part?

You will be seen by a member of the research team who will answer any questions you may have. Once you have agreed to take part you will be asked to sign a consent form and given a copy of this to keep. The research team member will ask you about basic demographics (age, lifestyle, education, employment etc…) and about your medical and obstetric history, and collect relevant information from your clinical record. We will find out what happened to you during your pregnancy, and to your baby and childthrough regular contact and both of your medical records. This is the list of samples you can choose to give:

Maternal blood	We will take a blood sample from you at different times throughout your pregnancy. If you are already having a blood test, we will do both at the same time.
Umbilical cord blood	When your baby is born, your doctor or midwife can take a blood sample from the baby’s umbilical cord after it has been clamped and cut. This does not prevent delayed cord clamping.
Placental	You may allow us to collect a sample of the placenta.
Placental image	You may allow us to take an image of the placenta.
Neonatal blood	You may allow us to take a small heel prick blood sample from your baby as a newborn.
Child blood (1 & 3 months)	You may allow us to take a small blood sample (venous or heel prick) from your baby at 1 & 3 months of age. This will involve a visit to the children’s blood test department at St Thomas’ Hospital. You will be given a gift card to thank you for your time.
Questionnaires	We will give you a link to short questionnaires to assess your diet, mental well-being, and infant feeding intentions. If you are feeling distressed or worried about your mental health, please tell us in person or speak to your midwife or doctor.

Tick if this page is not applicable: ☐

Additional Information for the PTB Risk Sub-Cohort:

1.A. Background

Spontaneous preterm birth is when a baby is born before 37 weeks. Tests such as ultrasound scans of the cervix (neck of the womb) and vaginal swabs for fetal fibronectin (a common clinical test to predict the chance of preterm birth) help to detect some women who are at high risk of preterm birth. However, doctors are not always able to predict which women will have their babies early.

We would like to investigate biomarkers which might help us to predict which women are at higher risk of preterm birth and other pregnancy complications. They are found in saliva, blood, and vaginal fluid. Additionally, we would like to measure the firmness of your cervix.

2.A. Why have I been chosen?

You have been asked to take part because you are pregnant. You may also have risk factors for having a preterm baby (e.g., a previous preterm baby, a previous operation on your cervix, or other risk factors).

3.A. What do I have to do if I take part?

In addition to what mentioned in section 3 page 1, we will ask you to consent for the following samples to be collected:

Cervicovaginal	We will collect cervical/vaginal swabs via a speculum exam (like a smear test).
Cervical stiffness measurement	At the same time, we can test the firmness of your cervix with a painless Pregnolia device. This is a safe procedure which takes about 30 seconds.
Maternal saliva	You will be provided with a universal specimen container to take home. You will take the sample immediately upon waking after rinsing their mouth with water. You will then be asked to keep the sample cold until it has been delivered to the study team. You will be asked to collect the sample on a day where they have a pre-existing appointment.
Infant saliva	Infant saliva will be collected through a specially designed buccal swab. This is a pain-free procedure.

Tick if this page is not applicable: ☐

Additional Information for the PISA Sub-Cohort:

1.B. Background:

Type 1 diabetes mellitus (T1D) is an autoimmune disease affecting 1:500 children aged under 15 years in the UK. As childhood onset of T1D becomes more prevalent, there is an increasing need to understand how early life exposures could influence the development of the child and predispose to the development of autoimmunity. INSIGHT-2 PISA will test the idea that different exposures in pregnancy may influence fetal development to increase the risk of childhood autoimmunity, in those infants already at higher risk. Infants born to mothers/fathers with T1D, to mothers with first-degree relatives with T1D or mothers at risk of preterm birth have a slightly higher risk of developing autoimmune diseases when young.

We would like to monitor maternal exposures to infections and other environmental factors and monitor the development of the immune system in infants by looking at cells and mediators in blood. Additionally, we would like to perform testing of autoantibodies that are linked to potential development of T1D. Similar tests are used clinically to help diagnose the risk of developing autoimmune diseases. This research will give important insights into the mechanisms of autoimmune disease development in children and how we can potentially predict its onset.

2.B. Why have I been invited to take part?

You have been invited to take part because:

- you are pregnant and have T1D or
- you are pregnant and have a first-degree relative with T1D or
- you are pregnant and the father of the baby has T1D or
- you are pregnant and are at high or low risk of preterm birth or
- you were enrolled in this study before or in the INSIGHT Study (13/LO/0393).

3.B. What do I have to do to take part?

In addition to what mentioned in section 3 page 1, we will ask you to consent for the following samples to be collected:

Child blood (12 & 24 months)	You may allow us to take a small venous blood sample from your baby at 12 and 24 months of age. This will involve a visit to the children's blood test department at St Thomas' Hospital.
Child blood (18 months)	This may be collected the same way as above (at 12 and 24 months of age), or you may agree to use a home sampling kit to take a small prick blood sample from your child at around 18 months of age and send this back for antibody measurement.

As part of this study we will perform, on your child's samples, a test which looks at several antibodies linked to the potential development of T1D. This test is not normally performed in children without symptoms. A positive test result does not mean that your child has T1D but indicates that their risk of developing T1D in the future is higher. A member of the study team will contact you by telephone and email to explain the result and discuss the next steps. If more than one autoantibody is identified, the likelihood of developing T1D is higher. With your consent, we would inform your child's GP of any positive results by letter so that your child's risk status can be recorded in NHS clinical systems and appropriate follow-up support can be arranged. This may include referral to a paediatric diabetes team. If the test is positive for two or more autoantibodies, we will offer you to repeat testing after three months as part of our research study, to confirm the result. If additional research samples are due as part of the study schedule, we will continue to perform autoantibody testing on those samples.

4. What will happen to my samples?

Samples will be stored and analysed at St Thomas' Hospital London, King's College London and other INSIGHT-2 study centres and research partners. No one will be able to identify you from the samples. We will use the samples to identify biomarkers associated with pregnancy complications, markers of infection and inflammation, and look at how your and your baby's cells respond to the pregnancy environment. We will look at how mother's and baby's genetic background may protect or predispose them to pregnancy complications by studying anonymised DNA and RNA. Analyses will be undertaken by KCL researchers, commercial partners, and academic collaborators. Your usual antenatal care will continue, and you will be seen by your normal doctors and midwives.

5. Who will have access to my information?

King's College London and Guy's and St Thomas' NHS Foundation Trust co-sponsor this UK-based study. We will be using information from you and from your medical records to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways for the research to be reliable and accurate. To safeguard your rights, we will use the minimum personally identifiable information possible. You can find out more about how we use your information by contacting us below.

For research purposes, we will document your and your baby's experiences by speaking with you and reviewing your hospital medical records/hand-held notes. We will also ask for your consent to use your NHS number, as well as your baby's, to connect the findings of our study to your and your child's future health, social, and educational data (up to 16 years of age). This information will only be accessible to authorised study personnel.

The sample(s) you give us will be given a unique number so you cannot be identified by laboratory staff. In addition to storing and using samples for the current study, any remaining samples at the end of the study will revert to the KCL HRA research tissue bank. They may then be used by another study with appropriate ethical and regulatory approvals to answer a different research question. Our current research and future studies may involve teamworking with other research departments in the wider academic network both in the UK and elsewhere, and with commercial partners. As part of this study, some of your anonymous data and sample information may be shared with approved academic or commercial research partners. Any sharing will only occur under strict data-sharing agreements and for research purposes that align with this study. We will not share any information that can identify you or your baby with external partners.

We may share or provide access to data about you outside the UK for research related purposes to:

- To collaborate with other institutions to assist in answering research questions aligning with the goals of this study.
- To process samples or information together with other researchers or institutions, or where we are unable to complete this without collaboration.

If this happens, we will only share the data that is needed. We will also make sure you can't be identified from the data that is shared where possible. This may not be possible under certain circumstances – for instance, if you have a rare illness, it may still be possible to identify you. If your data is shared outside the UK, it will be with the following sorts of organisations:

- Universities and institutions investigating studies where their research questions align with this study
- Commercial collaborators for future research and product development

We will make sure your data is protected. Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law. We will make sure your data is safe outside the UK by doing the following:

- we use specific contracts approved for use in the UK which give personal data the same level of protection it has in the UK. For further details visit the Information Commissioner's Office (ICO) website: https://ico.org.uk/for-organisations/uk-gdpr-guidance-and-resources/international-transfers/
- we do not allow those who access your data outside the UK to use it for anything other than what our written contract with them says
- we need other organisations to have appropriate security measures to protect your data which are consistent with the data security and confidentiality obligations we have. This includes having appropriate measures to protect your data against accidental loss and unauthorised access, use, changes or sharing
- we have procedures in place to deal with any suspected personal data breach. We will tell you and applicable regulators when there has been a breach of your personal data when this is legally required. For further details about UK breach reporting rules visit the Information Commissioner's Office (ICO) website: https://ico.org.uk/for-organisations/report-a-breach

6. What will happen to my information?

Your name, date of birth and contact details will be kept confidential, and only used by the research team as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. The people who analyse the information will not be able to identify you and will not be able to find out your name, date of birth or contact details. King's College London/Guy's and St Thomas' NHS Foundation Trust will keep identifiable information about you from this study for 25 years after the study has finished, in line with NHS and Department of Health and Social Care rules governing maternity records.

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

You can find out more about how we use your information, including the specific mechanism used by us when transferring your personal data out of the UK:

- HRA leaflet: www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team✉ gstt.insight-2@nhs.net ☎ 077 2110 9201

8. Do I have to take part?

Whether you decide to take part or not is entirely up to you. Your decision will not affect the care you receive in any way. If you agree to take part, you will be able to review your consent form at every follow-up visit and confirm whether it is correct or if you would like to change your preferences and re-consent. You are also free to withdraw at any point, without giving a reason. In that case, we would ask you to specify what type of consent you would like to remove. This could include one to all of the following:

- Future sample collection.
- Future access to medical records by the research team for data collection (e.g., delivery outcome details).
- Use of previously collected samples and data for future research analysis.
- Use of NHS/hospital number for data linkage with future health, social and educational data.
- Use of their baby's NHS/hospital number for data linkage with future health, social and educational data.

9. What are the benefits of taking part?

You may not benefit personally from taking part, but you may help us develop a screening test that helps women and their families in the future.

10. Are there any potential side-effects to taking part?

Blood samples will be taken that are not related to your or your baby's routine care. They are associated with momentary discomfort and occasionally bruising. Some women can find high vaginal swabs uncomfortable. Furthermore, taking part may increase the time you need to spend in the clinic.

11. What happens if anything goes wrong?

If something does go wrong and you are harmed during the research, you may have grounds for legal action for compensation against Guy's and St Thomas' NHS Foundation Trust and/or King's College London but you may have to pay your legal costs. In the unlikely event that an incidental finding not already diagnosed by the clinical team will be found by the research team, the relevant clinical team would be informed as soon as possible, to make sure that you will receive the necessary care. In the event of any unforeseen events around the birth, the researcher team will only obtain post-partum samples/data if deemed appropriate by the Chief Investigator.

12. What drug is being tested?

No drug is being tested.

13. What will happen to the results of the study?

The results will be published in medical journals and associated repositories. You will not be identified in any report/publication.

14. Who is paying for this research?

The Borne Foundation and the Leona M. and Harry B. Helmsley Charitable Trust have both funded this study.

15. Who has reviewed this study?

This study was reviewed by the Guy's and St Thomas' NHS Foundation Trust and King's College London Research and Development (R&D), and the West of Scotland Research Ethics Committee 5.

16. What if there is a problem?

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 (see contact information below). If you remain unhappy and wish to complain formally, you can do this through the Guy's and St Thomas' Patients Advice and Liaison Service (PALS) on 020 7188 8801, gstt.pals-gstt@nhs.net. The PALS team are based in the main entrance on the ground floor at St Thomas' Hospital and on the ground floor at Guy's Hospital in the Tower Wing.

If at any time you have any unanswered questions, concerns, or a complaint about the study, please contact:

INSIGHT-2 Research Team: ✉ gstt.insight-2@nhs.net ☎ 077 2110 9201

Thank you for taking the time to read this leaflet and considering taking part in this study.
You will be given a copy of this leaflet and signed consent form to keep if you choose to participate.