Patient information leaflet for participants

Pre-eclampsia prevention by timed birth at term 2 (PREVENT-2): A randomised trial

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Chief Investigator: Prof Kypros Nicolaides

PART 1

We'd like to invite you to take part in our research study. Joining the study is entirely up to you. Before you decide, we would like you to understand why the research is being done and what it would involve for you. One of our team will go through this information sheet with you, to help you decide whether or not you would like to take part and answer any questions you may have. We suggest this should take about 15 minutes. Please feel free to talk to others about the study if you wish.

The first part of the Participant Information Sheet tells you the purpose of the study and what will happen to you if you take part.

The second part will give you more detailed information about the conduct of the study. Please ask if anything is unclear.

What is the purpose of the study?

Pre-eclampsia is a medical condition that develops in about 4-5 out of 100 pregnancies. It is characterised by high blood pressure and most commonly, protein in the urine or abnormal blood tests. Pre-eclampsia can lead to serious complications for both the mother and the baby. For the mother, pre-eclampsia can be associated with serious complications affecting the kidney, liver and blood clotting. In rare occasions, it can cause stroke and seizures. Having pre-eclampsia is related to an increased risk of developing high blood pressure later in life. For babies, pre-eclampsia can cause poor growth and increased risk of stillbirth.

At 35-36 weeks of pregnancy, all women in our unit are offered an ultrasound scan of the baby. At this time, women can be given their personal chance of developing pre-eclampsia, by combining information from their medical history, measurement of their blood pressure, and results of a blood test. Previous research from our unit shows that we may be able to prevent 30% of cases of pre-eclampsia through planned birth at term for women at high risk of developing pre-eclampsia. We need to do further research to determine the right time for planned birth at term to take place in women at higher risk of pre-eclampsia, in order to get the best outcomes for both mother and baby. Lastly, we want to understand how the risk of developing pre-eclampsia affects maternal cardiovascular health in the first six months after birth.

We are carrying out a study to determine whether planned birth at 39 weeks in women at high risk of pre-eclampsia can prevent them from developing pre-eclampsia and its' associated complications.

All pregnant women carrying one baby attending for a routine scan at 35-36 weeks are invited to take part in the study.

Do I have to take part in the study?

You are under no obligation to participate. If you agree to participate we will ask you to sign a consent form to show you have agreed to take part. You are free to withdraw your consent at any time, without giving a reason.

What will happen to me if I take part?

If you are agree to take part in the “Pre-eclampsia prevention by timed birth at term 2’’ trial you will be randomly place into one of two groups. This is done by chance, like the tossing of a coin, so you have an equal chance of being allocated into one of the two groups.

- One group of women will be managed with no change to their usual care in pregnancy, with a 35-36 week scan, and routine antenatal visits until they give birth.

- The other group of women will have screening for their risk of developing pre-eclampsia at the time of their 35-36 week scan. If this screening shows a higher risk of pre-eclampsia, we will plan for birth to take place at around 39 weeks.

In both groups, we will take a blood test at the 35-36 week scan. The amount of blood to be taken is 16 ml (about 2 tablespoons). We will also take some measurements of your blood pressure and flow from your arm, neck and leg; we will not tell you or your clinical team the results of these measurements. Finally, we will look at the blood flow in a vessel in your eye by placing an ultrasound probe over your eye for a few seconds.

If you are in the group that has pre-eclampsia screening, we will calculate your risk of developing pre-eclampsia by combining the blood test results and standard blood pressure measurement with information from your medical history. For most women, the risk of pre-eclampsia will be low (a risk less than 1 in 100). In such cases, there is no need for planned delivery at 39 weeks and you would be advised to await for labour naturally or to give birth for another reason if needed. If your risk of pre-eclampsia is high (a risk of 1 in 100 or more), we will plan for birth at around 39 weeks, either through induction of labour or caesarean section, depending on your individual needs and preferences.

If you are found to have a very high risk for pre-eclampsia (1 in 5 or higher), you will have extra monitoring until birth. This will include checking your blood pressure at home each day, attending a weekly in-person appointment for blood pressure checks and having one additional appointment two weeks after the 35-36 week scan to monitor your blood pressure and baby’s growth with another ultrasound scan. At each in-person visit, we will take an additional blood sample for research. You will be given a blood pressure monitor, instructions on how to use it, guidance on what to do with your readings and a diary to record them. The study team will collect this diary from you.

For women in both groups, we will collect information about the outcome of your pregnancy, including the health of your baby until they are discharged (this includes if the baby is admitted to neonatal intensive care). We will get this information from your medical records, and if anything is missing, we may contact your GP to complete the data.

Women in both groups may also be invited to attend an optional follow up visit around six months after birth. This will help us understand how risk of pre-eclampsia affects blood pressure after pregnancy. This is a one-off visit which will involve a blood test, urine sample, measurement of blood pressure and flow from your arm, neck and leg and blood flow in a vessel in your eye by placing an ultrasound probe over your eye for a few seconds. Finally, we will perform a short ultrasound scan of your heart and the surrounding vessels.

What are the possible benefits of taking part?

If you are allocated in the usual care group you will not receive a direct benefit from taking part in this trial.

If you are allocated into the screening for pre-eclampsia group and your risk of developing pre-eclampsia is found to be high, planning birth at around 39 weeks may help to prevent pre-eclampsia and reduce the of related complications for you and your baby. If you are undergoing home blood

pressure monitoring, we might be able to detect and treat high blood pressure at an earlier stage than usual.

What are the possible disadvantages and risks of taking part?

If you are allocated in the usual care group there are no possible disadvantages and risks related to taking part in this trial.
If you are allocated to the screening group and found to be at high risk of pre-eclampsia, a planned birth at around 39 weeks will involve either induction of labour or a planned caesarean section, instead of waiting for labour to start naturally.
Previous research in our unit and other maternity units has shown that having an induction of labour at 39 weeks does not increase the likelihood of needing an emergency caesarean section. Research has also shown that for women who choose a planned caesarean section, having it at 39 weeks does not increase the risk of short-term problems for the baby, such as breathing difficulties after birth. For these reasons, we do not expect you to have a higher risk of complications if you are allocated to the planned delivery group at 39 weeks of pregnancy.

Who is organising and funding this study?

The doctor in charge of this study is Professor Kypros Nicolaides. The study is funded by the Fetal Medicine Foundation, which is a UK registered charity. The study is being sponsored by King's College Hospital NHS Foundation Trust. The Sponsor of this study will pay your study doctor for including you in this study.

How have patients and the public been involved in this study?

We are working with a group of women with a range of experiences of pregnancy events to help inform this study. This group are providing us with feedback on how to improve the study and will help us with communicating the results of this work.

Who has reviewed the study?

Medical research is looked at by an independent group of people called a Research Ethics Committee to make sure that your safety, rights, wellbeing and dignity are protected. This study has been reviewed and given a favorable opinion by the South East Scotland Research Ethics Committee. It has also been approved by the Health Research Authority and King's College Hospital NHS Foundation Trust has also given confirmation that the study can go ahead.

Expenses and Payments

There are no funds available for payments to those participating in this study.

This completes Part 1 of the Information Sheet.

If the Information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

PART 2

What if new information becomes available?

Sometimes we get new information about the intervention being studied. If this happens, your study doctor will tell you and discuss whether you should continue in the study. If you decide not to carry on, your study doctor will make arrangements for your care to continue. If you decide to continue in the study he/she may ask you to sign an agreement outlining the discussion. This new information that becomes available might specifically affect you and your health. If this happens, your study

doctor might consider that you should withdraw from the study. They will explain the reasons for withdrawing from the study and arrange for your care to continue. If the study is stopped for any other reason, we will tell you and arrange for your continuing care.

What will happen if I don't want to carry on with the study?

You are free to withdraw from the study at any time without giving any reason; and if you would like to do so; please speak to a member of the research team or doctor. Your decision to withdraw from the study will not affect the care you receive.

What if there is a problem?

If you have a concern about any aspect of this study, firstly you should ask to speak with the researchers who will do their best to answer your questions (Dr Argyro Syngelaki email: argyro.syngelaki@nhs.net; tel 020 3299 7164). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints procedure by contacting Patient Advice Liaison Service (PALS) office of King's College Hospital by phone on 020 3299 4618 or by email at kings.pals@nhs.net.

Every care will be taken in the course of this study. However, in the unlikely event that you are injured by taking part, compensation may be available. In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against King's College Hospital NHS Foundation Trust but you may have to pay your legal costs.

Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff or about any side effects (adverse events) you may have experienced due to your participation in the study the normal NHS complaints mechanisms are available to you. Please ask your study doctor if you would like more information on this.

Will my taking part in the study be kept confidential?

Yes, we will follow ethical and legal requirements and all information about you will be handled in confidence. It will not be possible your details and study results to be identified outside of the study group. Every participant will be given a unique study number and only those codes will be used for the data analysis. We will not disclose your personal data to any other investigators. Information collected about you will be used to support other research in the future and may be shared anonymously with other researchers.

If you consent to take part in the research, any of the information collected about you may be inspected by the sponsor (including representatives of the sponsor). These inspections are solely for the purposes of the research and analysing the results. Your records may also be looked at by the regulatory authorities or ethics committees to check that the study is being carried out correctly. The organisations listed above will keep information about you confidential and secure. Your name will not be used in any reports about the study and all data is stored in accordance with the principle of the Data Protection Act 2018.

Involvement of the General Practitioner/Family Doctor (GP)

Your GP will not be informed of your involvement in this study. Your GPs may be contacted in case where you do not deliver in this hospital to gather outcome information and that will be done retrospectively, with your permission. This will only be done if necessary.

What will happen to any samples that I give?

As part of this study, we will take a blood sample from you and we will measure serum placental growth factor (PlGF) and soluble fms-like tyrosine kinase receptor 1 (sFlt-1). With your permission we would like to save any remaining of your blood sample for future analysis. The sample will be processed into plasma and serum and the analysis might include biochemical and hematological tests, proteomics, metabolomics and DNA/RNA analysis such as whole-genome sequencing. This sample will be stored for future analysis for the prediction of preeclampsia and other pregnancy complications. The samples will be stored in secure fridges in the UK at the Fetal Medicine Research Institute for 10 years and only authorised personnel will have access to the samples.

What will happen to the results of the research study?

All scientific results will be published in journals and presented at academic meetings. You will not be identified in any of the reports or presentations.

How will we use information about you?

We will need to use information from you and your hospital records for this research project. This information will include your hospital number, full name, date of birth, telephone number and email address held by the hospital for the research. We will use this information either to contact you for the pregnancy outcome in case you don't deliver at King's College Hospital 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.

King's College Hospital NHS Foundation Trust is responsible for looking after your information. We will not share your information related to this research project with other organisations. We will keep all information about you safe and secure by:

- Keeping all documents in locked cabinets in secured rooms within the premises of the Fetal Medicine Unit at King's College Hospital and then will be archived in secure off-site archive facilities. All electronic data will be held securely by individuals authorised to hold the data only. We will keep your anonymised data for 25 years.

International transfers

Your data will not be shared outside the UK.

How will we use information about you after the study ends?

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. We will keep your blood sample data for a maximum of 10 years, and other data for a maximum of 25 years. The study data will then be fully anonymised and securely archived or destroyed.

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.
- If you choose to stop taking part in the study, we would like to continue collecting information about your health from your hospital records regarding pregnancy outcome. If you do not want this to happen, tell us and we will stop.
- You have the right to ask us to access, remove, change or delete data we hold about you for the purposes of the study. You can also object to our processing of your data. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.

- 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.

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

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

- at https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/data-protection-and-information-governance/gdpr-guidance/templates/template-wording-for-generic-information-document/
- our leaflet available entitled 'How we use your data' which you can request from the study team
- by asking one of the research team
- by sending an email to lucy.singh@kcl.ac.uk, or
- by ringing us on 020 3299 7164.
- by contacting our DPO at [KCH: kch-tr.dpo@nhs.net]

Thank you

Thank you for considering taking part and taking the time to read this information sheet. If you decide to take part in the study, we will give you a copy of the information sheet and a signed consent form to keep.

Further information and contact details

Local Contacts:
Your doctor ..... Tel: .....
Your study coordinator..... Tel: .....