MANCHESTER 1824
The University of Manchester

MIMICH Trial Patient Information Sheet

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Metformin Impact on Maternal and Infant Cardiometabolic Health

We would like to invite you to take part in a study in which we wish to investigate the effects of a drug called metformin on your health and the health of your baby.

Before you decide whether you wish to take part, please take the time to carefully read through the information provided in this leaflet. It will help to explain why the research is being done and what it will involve. To help you make an informed decision about participating in the study, please ask the research team as many questions as you wish and talk it through with others. Taking part in the study is completely voluntary.

About the research

- **Who will conduct the research?**

This research is being funded by the European Commission and is led by researchers working for the University of Manchester. Other healthcare professionals and research staff working on the study are from the Maternal and Fetal Health Research Group at Saint Mary's Hospital. The day to day organisation is coordinated by the Clinical Trials Unit at the University of Manchester.

Who has reviewed the study?

- **What is the purpose of the research?**

Diabetes in pregnancy is associated with an increased risk of growth problems for the baby. The most common problem for women with diabetes is that the baby gains weight/grows too quickly over the pregnancy. In these pregnancies, the baby is born weighing more than we would expect (called 'large for gestational age'). Increased growth in the baby is related to the mum's blood glucose (sugar) levels. For this reason, in pregnancy we recommend close monitoring of the blood glucose levels and we often offer a tablet treatment called metformin if the blood glucose levels are above target after diet and lifestyle changes.

Metformin is recommended by the National Institute of Clinical Excellence (NICE) as the first line treatment for diabetes in pregnancy and is given to lower blood glucose levels with the aim of helping to keep the baby's growth within the normal range. It is considered safe in pregnancy and is routinely prescribed to women with diabetes.

In **some** women with diabetes, there can also be reasons why the baby might be at an increased risk of not gaining weight/growing quickly enough during the pregnancy. In these pregnancies, there is a risk that the baby may be born at a birthweight lower that we would expect (called 'small for gestational age'). The risk factors for a smaller baby include a history of high blood pressure, older maternal age, previous babies born small for gestational age and/or abnormal blood flow measurements in the blood vessels which connect to the womb (uterine arteries).

In this study, we aim to understand what impact metformin has on the growth and long term health of the baby when a woman has diabetes in conjunction with other risk factors which might affect the baby's growth.

- **Will the outcomes of the research be published?**

The results from this project will be published as research papers in medical journals. No data will be published that will allow women or their babies to be identified. All participants will be provided with research team contact details and if you wish to access the results of this study, you are welcome to contact any of the named persons.

At the end of the study, data collected will be stored in a secure, electronic database, identified only by your study number (so it will not be possible to identify participants from the database) and retained within the Maternal & Fetal Health Research Centre for 15 years, in line with current guidelines.

- **Who has reviewed the research project?**

This study has been reviewed and approved by a Research Ethics Committee. The Research Ethics Committee is an independent group of people including medically trained and lay people, who assess the study and check that full information is given to participants and to protect your safety, risks, wellbeing and dignity.

- **Who is funding the research project?**

European Research Council.

What would my involvement be?

- **What would I be asked to do if I took part?**

For this study, we are asking women who have type 2 diabetes or who have been diagnosed with diabetes during their pregnancy to take part. As part of your routine care you will be asked to monitor your blood glucose levels at home. You will also be provided with diet and lifestyle advice to help improve your glucose levels. If your levels remain above the targets set for you, we will discuss with you the need for treatment with metformin tablets.

If you meet the criteria to enter the study, then we will offer you an appointment in the research clinic for an additional scan and review.

If we recommend treatment for your blood glucose levels based on your home monitoring, but you have other risk factors which could potentially affect the growth of your baby then you will be considered eligible to take part in the study.

The impact of taking part in the study for you and your baby

- You will be randomly allocated to treatment with diet & lifestyle (and insulin if required) or diet & lifestyle, metformin (and insulin if required)
- You will be asked to have an appointment and ultrasound scan (including 3D thigh volume measurements) every 4 weeks during your pregnancy

- We will ask to record your weight and take skinfold measurements and blood samples (2 teaspoons) from you at each hospital visit as part of the research
- We will ask to collect your placenta and some blood samples from the baby's umbilical cord after birth
- We will record information regarding you, your pregnancy and your baby's birth details which will be stored on our protected research database
- We will ask to take some measurements from baby after he/she is born which use a tape measure and skin callipers used to measure your baby's skinfold thickness
- We will ask you to visit the clinic with your baby at 3-6 and 12 months of age for further measurements of weight and growth. At these visit we will ask to take blood samples from you and measure your height, weight and skinfold thickness.

Study enrolment (visit 1; approximately 1 hour visit)

Before you are enrolled in the study, we will perform an ultrasound scan (if you are more than 16 weeks pregnant) and assess your medical history. You will then be asked to sign a consent form and have some initial measurements recorded. These will include:

- Blood pressure
- Three blood samples (approximately 15 mL, around 3 teaspoons for measurement of blood markers related to L-citrulline)
- Measurement of blood vessel stiffness ('pulse-wave velocity') – a non-invasive measurement that provides information about the health of your blood vessels.

Your allocation within the study will be explained and we will ask you to continue monitoring your blood glucose levels. We will discuss your results over the phone or by email (as you prefer) every 1-2 weeks between hospital visits.

Follow up visits (approximately 30 minutes visit)

We will ask you attend the hospital every 4 weeks for assessment of your health and the baby's growth. You will have an ultrasound at each visit. These visits will replace your usual appointments so there will be no additional hospital visits as part of the study. Towards the end of your pregnancy you may wish to have some appointments with your community midwife team and we can help to arrange these.

At birth

When your baby is born we will ask if we can collect your placenta and some blood samples from the baby's umbilical cord. This will not interfere with the birth of your baby. In addition to recording the weight of you baby at birth, we will also ask your permission to take some measurements from your baby after he/she is born. Further information will be provided regarding this aspect of the study after your baby is born.

Are there disadvantages or risks in taking part?

The major potential disadvantage of taking part is that for women allocated to the 'no metformin' part of the study, insulin injections to control blood glucose levels may be required sooner than if metformin had been prescribed. However, we know that insulin is safe in pregnancy and is used in many hospitals as the first line treatment for diabetes in pregnancy. Unlike metformin, insulin does not cross the placenta and does therefore not affect the function of the placenta. It is possible that

metformin could affect the function of the placenta and therefore the growth of the baby. This is unproven – we will be able to answer this question after this study.

The other disadvantages of taking part are that you will be asked to attend hospital research clinic appointments every 4 weeks. It is normal to have 4 weekly appointments at the hospital when you have diabetes; there won't therefore be extra appointments if you take part. We will however ask you to return to the clinic twice after your baby is born. These are additional visits. Where possible we will compensate your travel expenses for these visits.

What are the possible benefits of taking part?

The possible benefits include appointments in the research clinic with the same clinical team during your pregnancy. By participating in the study, you will help us to collect information about the effects of metformin on the health of women and their babies so that we can discuss much more accurately the potential advantages and disadvantages of metformin treatment with women in the future.

- **Will I be compensated for taking part?**

Reimbursement of travel expenses and parking charges are available on request.

- **What happens if I do not want to take part or if I change my mind?**

It is up to you to decide whether or not to take part. If you choose to take part we will arrange an appointment for you in the research clinic at St Mary's Hospital. If you do decide to take part you will be given this information sheet to keep and you will be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time without giving a reason and without detriment to yourself. However, it will not be possible to remove your data from the project once it has been anonymised as we will not be able to identify your specific data. This does not affect your data protection rights. If you decide not to take part you do not need to do anything further. Your decision will NOT affect the standard or type of care you receive from the hospital or doctor now or in the future.

Data Protection and Confidentiality

- **What information will you collect about me?**

In order to participate in this research project we will need to collect information that could identify you, called "personal identifiable information". Specific information will include:

- Your full name
- Date of birth
- Address and postcode
- Contact details (phone number and/or email)

All paperwork relating to your taking part in the trial will be identified by your study number and initials. Only your consent form and the enrolment log will include your name, hospital number and date of birth, this information will be stored in a secure, locked office within the research centre and

can only be accessed by members of the research team (the research centre is a restricted area). Your personal data will not be shared with anyone beyond the clinical research team.

Information about your pregnancy will be entered onto our secure web-based database (only accessible by members of the research team). Your baby's measurements will be entered under your study number and only their date of birth and sex will be recorded within the research database.

- **Under what legal basis are you collecting this information?**

We are collecting and storing this personal identifiable information in accordance with data protection law which protect your rights. These state that we must have a legal basis (specific reason) for collecting your data. For this study, the specific reason is that it is "a public interest task" and "a process necessary for research purposes".

- **What are my rights in relation to the information you will collect about me?**

You have a number of rights under data protection law regarding your personal information. For example you can request a copy of the information we hold about you.

If you would like to know more about your different rights or the way we use your personal information to ensure we follow the law, please consult our Privacy Notice for Research. https://documents.manchester.ac.uk/display.aspx?DocID=37095

- **Will my participation in the study be confidential and my personal identifiable information be protected?**

In accordance with data protection law, The University of Manchester is the Data Controller for this project. This means that we are responsible for making sure your personal information is kept secure, confidential and used only in the way you have been told it will be used. All researchers are trained with this in mind, and your data will be looked after in the following way:

Only the study team at The University of Manchester will have access to your personal information, but they will anonymise it as soon as possible. Your name and any other identifying information will be removed and replaced with a random ID number. Only the research team will have access to the key that links this ID number to your personal information. Your consent form and contact details will be retained for X years (describe where, why and how).

At the end of the study, if you agree to donate any of your spare blood samples or placental tissue for future research within the Maternal and Fetal Health Research Centre, these will be held under your study number in an ethically approved tissue bank to be used in future ethically approved research. These samples can only be used and linked to your pregnancy information following permission granted by the Data Protection Officer within the research centre (Professor Edward Johnstone). Scientists involved in the processing, storage and analysis of your samples will not be able to identify you and will not have access to your personal data. Your samples will be considered as a gift and will be kept for a minimum of ten years. You can choose not to donate your samples to the biobank if you wish.

As part of this research study, we will ask your permission to contact you in the future regarding follow up research regarding the health of you and your baby. Participation in future research is voluntary and you will have the option to opt out at any time. If we are unable to contact you after two attempts within five years we will remove your contact details from our study register.

Please also note that individuals from The University of Manchester or regulatory authorities may need to look at the data collected for this study to make sure the project is being carried out as planned. This may involve looking at identifiable data. All individuals involved in auditing and monitoring the study will have a strict duty of confidentiality to you as a research participant.

What if I have a complaint?

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. If they are unable to resolve your concern or you wish to make a complaint regarding the study, the normal National Health Service complaints mechanisms will still be available to you and your local Patient Information and Liaison Service are available to advise you.

- **Contact details for complaints**

If you have a complaint that you wish to direct to members of the research team, please contact:
PROFESSOR JENNY MYERS
Maternal & Fetal Health Research Centre
St Mary's Hospital
Hathersage Rd
Manchester
M13 9WL
+44 161 7016963
Jenny.myers@manchester.ac.uk

If you wish to make a formal complaint to someone independent of the research team or if you are not satisfied with the response you have gained from the researchers in the first instance then please contact

The Research Ethics Manager, Research Office, Christie Building, The University of Manchester, Oxford Road, Manchester, M13 9PL, by emailing: research.complaints@manchester.ac.uk or by telephoning 0161 306 8089.

If you wish to contact us about your data protection rights, please email dataprotection@manchester.ac.uk or write to The Information Governance Office, Christie Building, The University of Manchester, Oxford Road, M13 9PL at the University and we will guide you through the process of exercising your rights.

You also have a right to complain to the Information Commissioner's Office about complaints relating to your personal identifiable information Tel 0303 123 1113

If using a hard copy version of the PIS with participants, you must ensure the full URL of the ICO's complaints procedure is listed here or a hard copy is printed and appended with the information sheet.

Contact Details

If you have any queries about the study or if you are interested in taking part then please contact the researcher(s)

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