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PATIENT LABEL

# Participant Information Sheet/Consent Form

**Interventional Study**

| | |
|---|---|
| **Title** | PRECeDe Trial: Prevention of neonatal Respiratory distress with antenatal corticosteroids prior to Elective Caesarean section in women with diabetes – A Randomised Trial |
| **Short Title** | PRECeDe Trial |
| **Protocol Number** | Number 1 Version 3 |
| **Project Sponsor** | The University of Melbourne |
| **Coordinating Principal Investigator** | A/Prof Joanne Said |
| **Principal Investigator** | (add site PI name here) |
| **Associate Investigator(s)** | (add names if required) |
| **Location** (Site) | (add site name) |

## Part 1 What does my participation involve?

### 1 Introduction

You are invited to take part in this research project. This is because you have diabetes and are due to have an elective caesarean section for the birth of your baby. This research project is testing whether giving women 2 injections of betamethasone ('steroid injections') within 7 days before the caesarean section reduces the chances of breathing problems in newborn babies.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the treatments involved. Knowing what is involved will help you decide if you would like to take part in this project.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend, midwife or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:
• Understand what you have read

• Consent to take part in the research project
• Consent to have the treatments that are described
• Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

## 2 What is the purpose of this research?

Diabetes in pregnancy increases the risk of a baby being born with breathing problems (also known as 'respiratory distress'). Caesarean section can also increase this risk compared with vaginal birth. Betamethasone (also known as 'steroid' or 'corticosteroid') is a drug which is often given to women when they are at risk of having a premature baby because betamethasone helps to reduce the risk of breathing problems in premature babies.
Currently, betamethasone is recommended by national guidelines for women who are at risk of giving birth before 35 weeks' gestation (more than 5 weeks early).
Recent studies have also shown that betamethasone might help to reduce the risk of breathing difficulties when babies are born by caesarean section. However, we don't know if betamethasone also works when women have diabetes during pregnancy because women with diabetes weren't included in those studies.

Betamethasone can make the mother's blood sugars a little higher. This could be a problem in women with diabetes and may mean that you need to take more insulin if you are already taking this. Betamethasone might also make the baby's blood sugar lower after birth (hypoglycaemia).

Medications, drugs and devices have to be approved for use by the Australian Federal Government. Betamethasone is approved in Australia to be given to women during pregnancy to reduce the risk of breathing problems in newborn babies when they are born prematurely. We know that it is safe to be given in pregnancy and does not carry any risk of causing birth defects.

This research has been initiated by the study doctor, Associate Professor Joanne Said who is an obstetrician.

This study is a randomised controlled research project. Sometimes we do not know which treatment is best for treating a condition. To find out we need to compare different treatments. We put people into groups and give each group a different treatment. You might receive betamethasone injections, or you might receive placebo injections. A placebo is a medication with no active ingredients. You will not know which group you are in. The doctors, nurses and midwives will not know which group you are in. The results are compared to see if betamethasone is better. To try to make sure the groups are the same, each participant is put into a group by chance (random – like tossing a coin).

## 3 What does participation in this research involve?

To participate in this study, you will need to read this information sheet and sign the consent form. You will also be asked to complete three short questionnaires about your general health and your pregnancy. These questionnaires will take about 10 minutes to complete.
We will also collect some information about your health as well as your height and weight prior randomisation into the study.

The research midwife will then use a computer program to determine if you will receive either betamethasone injections or placebo injections. The computer program will ensure that you have an equal chance of being in either group – just like tossing a coin. The placebo we are using is called 'normal saline' which is lightly salty water and is very safe for both you and your baby.

This is a blinded study. This means that neither you nor your study doctor, nor the midwives or doctors caring for you will know which treatment you are receiving. However, in certain circumstances your study doctor can find out which treatment you are receiving.

Regardless of which group you are in, you will receive 2 injections, approximately 24 hours apart, within 7 days before your caesarean section. The injections are usually given into your thigh or arm muscle. Both injections will be given at your maternity hospital. You will need to return to the hospital for the second injection. An appointment time will be arranged for the second injection. This should take about 15 minutes.

You will be asked to monitor your blood sugars regularly and record these using either a paper blood glucose diary or you can enter these electronically using your mobile phone.To enter the blood glucose result electronically, you will be provided with a QR Code which will allow you to access a short form where you can enter your blood glucose result immediately via your mobile phone. Some blood glucose monitors allow us to download your blood sugar readings directly. If you have a suitable blood glucose monitor, we may also download your blood glucose readings. If your blood sugar goes high, you will need to contact staff at your hospital who will advise on adjustments to your medication, if necessary. The information about who to contact will be provided on the day of your first study injection.

On the day of your caesarean section, you will be given a short questionnaire to complete. The questionnaire will collect information about any symptoms you might have noticed since receiving the injections. This should take about 5 minutes. We would also like to collect your blood sugar monitoring book, if you recorded your blood sugars in a paper diary, or download the blood glucose recordings directly from your glucose meter.

After your caesarean section, the research midwife will collect information about your pregnancy and the birth from your medical records. The midwife will also collect information about your baby from your baby's records.

Low blood sugar levels are very common in babies born to women with diabetes. That is why all babies born to mothers with diabetes have their blood sugars monitored so that we can detect low blood sugars, whether or not they are part of this trial. This blood test is usually collected from the baby's heel. The first test is usually collected within 1-2 hours after the baby is born and then the test is repeated every 3-4 hours before each feed for the first 12 hours. If the baby's blood sugar is low, the baby will be offered additional feeds (supplementary milk feeds), dextrose (sugar) gel, or sometimes the baby might need treatment intravenously (through a drip). It is important to understand that monitoring the baby's blood sugars and treating low blood sugars is part of the standard care for babies born to mothers with diabetes. We will collect this information from your baby's records, but it is not a specific part of the research trial.

We will collect information about your medical history, pregnancy, and birth, and you and your baby's/babies' health until six weeks after birth. This information will be collected from your medical records and via questionnaires. To understand if there are any differences on health service utilisation and cost between groups, we will ask your hospital for you and your baby/babies' hospital records during the birth admission. We will ask the Australian Department of Human Services for you and your baby/babies' Medicare records until 2 years weeks after birth to capture the associated health service utilisation and cost out of hospital. We will also ask you about any side effects that occur that may be related to the study medication.

About 4-6 weeks after your baby is born, the research team will contact you to arrange for you to complete some additional questionnaires. These questionnaires will ask about your health since the baby was born and will also ask about your feelings. These questionnaires can be completed 'online' or we can send them to you to complete at home and then send them back to us. It will take about 15 minutes to complete these questionnaires. To thank you for completing and returning the final questionnaires you will receive a $20 gift voucher that will be sent to you on receipt of your completed questionnaires.

After you have completed the questionnaires at about 6 weeks after your baby's birth, there is nothing further you will need to do for this research study. We will, however, ask your permission to keep in contact with you each year as part of the consent process. This contact will take the form of an email message with an annual 'birthday card' sent to your email address as well as an SMS request to update your contact details We would like to keep your updated contact details so that in the future, we can contact you when your child is older to see if you would like to participate in future follow up studies to understand the longer-term effects (if any) of betamethasone on either you or your baby. These studies have not been planned yet, but any future studies will be approved by an Ethics committee before they start. You will be free to decide at the time if you would like to take part in any future studies. Your contact details will be stored securely in a password protected data base located at the University of Melbourne. Your details will be accessible only by the PRECeDe study research team.

There are no additional costs associated with participating in this research project, nor will you be paid. All medication, tests and medical care required as part of the research project will be provided to you free of charge.

## 4 What do I have to do?

While you are participating in this study, it is important that you continue to monitor your blood sugars closely and report any high blood sugar results so that we can adjust your medication. You will need to continue to take your usual medication (if you are taking any) for diabetes. You will also need to continue to attend any scheduled hospital visits for your pregnancy.

If you have any concerns about your health or your baby's health, it is important that you contact the hospital and follow the advice of the doctor's and midwives caring for you. The staff caring for you at the hospital will be aware that you are taking part in this study as we will make a note about this in your medical record. The staff won't know which group you have been allocated to (betamethasone or placebo).

## 5 Other relevant information about the research project

This study is being undertaken in many sites around Australia and New Zealand. In order to properly evaluate the findings of this study, we will need to share the data with researchers around Australia and New Zealand. Although we are sharing this information with the other researchers, we do not share your name or contact details. We keep this information separate and it will only be used to keep in contact with you so that we can let you know about future follow-up studies related to this research.

After this research project has finished, we will not be able to tell you whether you received betamethasone or placebo. This will allow us to continue to do future follow-up studies to determine if there are any long-term differences in mothers or children who received betamethasone compared to those who did not.

## 6 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with (add site name here).

## 7 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this hospital. If you decide not to take part in this study, we do not recommend that women receive betamethasone injections unless they are participating in this study because at this stage we do not know if they are necessary or effective.

## 8 What are the possible benefits of taking part?

We cannot guarantee or promise that you or your baby will receive any benefits from this research; however, possible benefits may include a reduction in the chance that your baby may have breathing problems following their birth or a reduction in the chance that your baby may need to go to the special care nursery following birth. It may also help doctors to understand the best treatments to offer you for future births.

## 9 What are the possible risks and disadvantages of taking part?

Medical treatments can sometimes cause side effects. You may have none, some, or all of the effects listed below, and they may be mild, moderate or severe. If you have any of these side effects, or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms that you get.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment. Your study doctor will discuss the best way of managing any side effects with you.

The side effects that you might experience include:

1. Pain, tenderness or bruising at the place where the injection was given. This is not usually severe and improves within about 24 hours.
2. High blood sugars. This is a very common side effect of betamethasone injections. It is very important that you measure your blood sugar before every meal and 2 hours after every meal. If you get high blood sugars, it doesn't necessarily mean that you have received the betamethasone injection, but you may require some additional insulin to control your blood sugars. You will be provided with a telephone number to contact the staff at your hospital at any time (day or night) during the time between receiving the study injections and your caesarean section. You will also be provided with blood sugar targets and information about what to do if your blood sugars are higher or lower than the recommended target range. High blood sugars may increase the risk of your baby developing neonatal hypoglycaemia.
3. Neonatal hypoglycaemia (low blood sugars in the baby). All babies who are born to women with diabetes have a chance of having low blood sugars which is why we monitor these babies very closely with "heel prick" tests to check their blood sugar. Hypoglycaemia may be a bit more common in babies whose mothers were given betamethasone. This can be easily treated with feeding or sugar treatments when it is recognised and usually resolves quickly. The risk of neonatal hypoglycaemia is greatest in the first 24 hours. If there are no problems by then, then they are unlikely to develop.

When betamethasone is given throughout pregnancy (e.g. every day) it may be associated with longer term problems for the mother (e.g. osteoporosis (thinning of the bones), high blood pressure) or baby (low levels of growth hormone or stress hormones). These problems do not seem to occur when only 2 doses of betamethasone are given as described in this research study.

If you become upset or distressed as a result of your participation in the research, the study doctor will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research project team. This counselling will be provided free of charge.

### 10 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, he/ she will explain the reasons and arrange for your regular health care to continue.

### 11 Can I have other treatments during this research project?

Whilst you are participating in this research project, it is safe for you to take any other medications recommended by your doctors or midwives with the exception of additional corticosteroid drugs. Corticosteroid drugs include Betamethasone, Dexamethasone, Hydrocortisone or Prednisolone. If your doctor recommends any of these medications, please advise them that you are taking part in the PRECeDe Trial so that they can determine whether it is appropriate for you to either continue in the study or take the medication.

### 12 What if I withdraw from this research project?

If you do withdraw your consent during the research project, you will have to option to i) remove all the data that has been collected about you from the study, or ii) allow us to retain the data that has already been collected about you in the study database, but not collect any further data or iii) continue to collect data about you from your hospital records but not contact you to request any further information. If you withdraw from the study after you have received the study medications, we recommend that you continue to test your blood sugars and that we test your baby's blood sugars as this information will be important for you and your baby's health and will help the hospital staff to provide the best possible care for you and your baby.

### 13 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These reasons may include:
- Unacceptable side effects
- Betamethasone being shown not to be effective
- Betamethasone being shown to work and not need further testing

### 14 What happens when the research project ends?

The researchers will analyse the results and will publish the study results in scientific journals and present the findings at scientific meetings. If you wish, the researchers can send you a summary of the results.

## Part 2 How is the research project being conducted?

### 15 What will happen to information about me?

Your health records and any information obtained during the research project are subject to inspection (for the purpose of verifying the procedures and the data) by the relevant authorities

and authorised representatives of the Sponsor, [Name of International and Australian sponsor ], the institution relevant to this Participant Information Sheet, [Name of institution], or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this research project.

Any information obtained in connection with this research project that can identify you will remain confidential. All information will be stored on password protected databases which are located on a secure server at The University of Melbourne in Australia. Any information that can identify you, such as name or email address will be stored on a separate data base and only accessible by PRECeDe study staff. This information is stored separately so that we may contact you annually to update your contact details for follow up contact regarding any future studies, as explained in Section 3 above. All paper copies of information about you will be stored in locked filing cabinets. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified.

Information about your participation in this research project will be recorded in your health records so that the doctors and midwives caring for you are aware that you are participating in this study.

In accordance with relevant Australian and/or (name of state or territory) privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

All information will be stored in accordance with the relevant legislation for a period of 25 years following the completion of the study. After this time, all paper files will be destroyed via secure shredding. All electronic files will be permanently deleted.

## 16 Complaints and compensation

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

## 17 Who is organising and funding the research?

This research project is being conducted by Associate Professor Joanne Said. Funding has been provided by the Australian National Health and Medical Research Council (NHMRC) Clinical Trials and Cohort Studies Grant awarded to A/Prof Joanne Said and the PRECeDe Trial Investigators.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

## 18 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of The Royal Melbourne Hospital. Approval to conduct this research at (add sites name) has been provided by (add Research Governance Committee name).

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research 2007(updated 2018)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

## 19 Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor on (add number) or any of the following people:

**Clinical contact person**

| | |
|---|---|
| Name | |
| Position | |
| Telephone | |
| Email | |

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

**Complaints contact person**

| | |
|---|---|
| Name | |
| Position | |
| Telephone | |
| Email | |

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

**Reviewing HREC approving this research and HREC Executive Officer details**

| | |
|---|---|
| Reviewing HREC name | Royal Melbourne Hospital HREC |
| HREC Executive Officer | Manager HREC |
| Telephone | (03) 9342 8530 |
| Email | research@mh.org.au |

**Local HREC Office contact (Single Site - Research Governance Officer)**

| | |
|---|---|
| Name | |
| Position | |
| Telephone | |
| Email | |

PATIENT LABEL

(Add sites logo here)

# Consent Form

| | |
|---|---|
| **Title** | PRECeDe Trial: Prevention of neonatal Respiratory distress with antenatal corticosteroids prior to Elective Caesarean section in women with diabetes – A Randomised Trial |
| **Short Title** | PRECeDe Trial |
| **Protocol Number** | Number 1 Version 3 |
| **Project Sponsor** | The University of Melbourne |
| **Coordinating Principal Investigator** | A/Prof Joanne Said |
| **Principal Investigator** | (insert sites PI here) |
| **Associate Investigator(s)** | (insert if required) |
| **Location** (site) | (add site name here) |

**Consent Agreement**

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to (insert site details here) concerning my pregnancy and treatment as well as the medical condition and treatment of my baby for the purposes of this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

Follow Up / Future Studies

We would like to contact participants regarding future follow up studies related to this study. Please check the box next to the applicable statement to advise us whether you are willing to be contacted regarding future studies.

☐ I agree to be contacted by the investigators regarding future follow up studies

☐ I do not agree to be contacted by the investigators regarding future follow up studies

**Declaration by Participant – for participants who have read the information**

Name of Participant (please print) _____

Signature _____ Date _____

**Declaration - for participants unable to read the information and consent form**

Witness to the informed consent process
Name (please print) _____

Signature _____ Date _____
* Witness must be 18 years or older.

**Declaration by Study Doctor/Senior Researcher†**

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

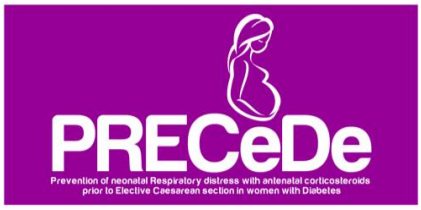
Note: All parties signing the consent section must date their own signature.

A copy of the plain language summary of the findings of this study will be made available to participants. Would you like to receive a copy of the plain language summary at the conclusion of the study? Please include an email address if you wish to receive this.

☐ Yes - Please include an email address below.

☐ No

Email address:_____ _____




(insert site logo here)

PATIENT LABEL

# Form for Withdrawal of Participation

| | |
|---|---|
| **Title** | PRECeDe Trial: Prevention of neonatal Respiratory distress with antenatal corticosteroids prior to Elective Caesarean section in women with diabetes – A Randomised Trial |
| **Short Title** | PRECeDe Trial |
| **Protocol Number** | Number 1 Version 3 |
| **Project Sponsor** | The University of Melbourne |
| **Coordinating Principal Investigator**<br>**Principal Investigator** | A/Prof Joanne Said<br>(add site PI here) |
| **Associate Investigator(s)** | (add if required) |
| **Location** (site) | (add site name here) |

**Declaration by Participant**

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with (insert site details here)

□ Removal of all trial data and full withdrawal from trial procedures (not willing to have any further data collection or follow up)
□ Willing to have data that has already been collected retained but no further data to be collected and no further contact.
□ Willing to continue to have data collected from medical records but no further contact or participation in trial procedures.

I understand that if I have already received the study medication, it will be safest for me to continue to monitor my blood sugars closely and for my baby's blood sugars to be monitored closely. (strike out if not relevant)

Name of Participant (please print) _____

Signature _____ Date _____

*In the event that the participant's decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.*

| |
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| |

**Declaration by Study Doctor/Senior Researcher†**

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of and information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.