Sinai Health | Mount Sinai Hospital
Joseph & Wolf Lebovic Health Complex

Informed Consent Form for Participation in a Research Study

Study Title: A pilot study assessing the feasibility of a randomized controlled trial evaluating aspirin in postpartum women at risk of developing venous thromboembolism.

Study CTO ID: 2099

Study Doctor: Dr. Ann Kinga Malinowski, Department of Obstetrics and Gynaecology, Mount Sinai Hospital, 416-586-4800 x5127

Sponsor: University of Calgary

Funder: Canadian Institutes of Health Research (CIHR)

In case of emergency: Please present to your local emergency department. Please bring wallet card identifying study and notify the Study Team when possible within 24 hours.

INTRODUCTION

You are being invited to take part in a clinical trial (a type of study that involves research). You are invited to participate in this trial because you are pregnant or have just given birth and have known risk factors for blood clots. This consent form provides you with information to help you make an informed choice. Please read this document carefully and ask any questions you may have. All your questions should be answered to your satisfaction before you decide whether to take part in this research study.

The research study staff will tell you about the study timelines for making your decision.

Taking part in this study is voluntary. You have the choice to not take part at all or you may choose to leave the study at any time. Whatever you choose, it will not affect the usual medical care that you receive outside the study.

IS THERE A CONFLICT OF INTEREST?

There are no conflicts of interest to declare related to this study.

WHAT IS THE BACKGROUND INFORMATION FOR THIS STUDY?

Some women are at risk for developing blood clots in the legs or lungs (thrombosis) after they deliver a baby (postpartum). A blood clot can form in the lungs, which can be serious. The risk of blood clots is highest in the first 6 weeks following delivery. While we know what the risk factors are for getting a blood clot after delivery, we still do not know what the best way is to prevent blood clots.

Earlier research studies (trials) tried to see if using daily injectable blood thinners after delivery could prevent blood clots. These trials were not successful because taking daily injectable blood thinners at home was not desirable. Women were not comfortable giving themselves or having daily blood thinner injections. Many women who deliver babies and have modest risk factors for blood clots may be given injectable blood thinners while they are in hospital, but they usually do not go home on injectable blood thinners.

The PARTUM trial asks if aspirin is a safe and effective option for preventing blood clots in women who have risk factors for blood clots after delivery. Aspirin helps to prevent blood clots in people after hip and knee surgery. It is an attractive choice after delivery because it is safe with breastfeeding. We are studying whether low dose aspirin will help to prevent blood clots in postpartum women who have risk factors for blood clots.

Health Canada, the regulatory body that oversees the use of drugs in Canada, has not approved the sale or use of Aspirin for preventing blood clots specifically in women after delivery. Health Canada has approved the use of Aspirin in this study.

WHY IS THIS STUDY BEING DONE?

The purpose of this pilot study is to test the feasibility to run a larger international trial. Our primary objective is to assess the average recruitment rate in each study site each month over 6 months, consent rate, compliance rate of the patient using the study tablet and obtain an estimate of venous thromboembolic events and bleeding events. This type of study involves a small number of participants and so it is not expected to prove information on safety or effectiveness. The results may be used as a guide for larger studies, although there is no guarantee that they will be conducted. Participation in a pilot study does not mean that you will be eligible to take part in a future larger study.

If the results of this trial show that it is feasible, the information collected during your participation may be used in a larger trial. Our larger trial will be able to answer if aspirin does safely prevent blood clots in postpartum women. This will allow us to better care for postpartum women who are at risk of blood clots.

WHAT OTHER CHOICES ARE THERE?

You do not have to take part in this study in order to receive treatment or care. Other options (in addition to the standard or usual treatment described above) may include, but are not limited to:

- no therapy at this time
- other research studies may be available if you do not take part in this study

Please talk to your usual doctor or the study doctor about the known benefits and risks of these other options before you decide to take part in this study. Your usual doctor or the study doctor can also discuss with you what will happen if you decide not to undertake any treatment at this time.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

It is expected that about three hundred and eighty-four (384) participants will take part in this study, from research sites across Canada and in Europe.

This study should be complete with results and analysis known within two years.

WHAT WILL HAPPEN DURING THIS STUDY?

ASSIGNMENT TO A GROUP

If you decide to take part in this study you will be "randomized" into one of the two groups described below after the birth of your baby. Randomization means that you are put into a group by chance (like flipping a coin). There is no way to predict which group you will be assigned to. You will have an equal chance of being placed in either group. Neither you, the study staff, nor the study doctors can choose what group you will be in nor will they know which group you are in.

Your group assignment can be identified if medically necessary. Requests to reveal your assignment for your information or participation in other research studies will not be considered until this pilot study and the possible larger trial has been completed and the results are known.

WHAT IS THE STUDY INTERVENTION?

A computer system is used to randomly put each participant into one of the following two groups:

Group 1 (Experimental Intervention): Aspirin (81mg)-low dose aspirin

Group 2 (Non-Experimental Intervention): Placebo (a substance that looks like the study drug but does not have any active or medicinal ingredients)

The dose for both groups will be one tablet taken daily for six (6) weeks.

WHAT ARE THE STUDY PROCEDURES?

Non-experimental procedures:

Screening Visit

You will be screened for eligibility and detailed study information will be provided to you. You will meet with a member of the research team during your pregnancy, prior to delivery or within forty-eight (48) hours postpartum (after delivery) to discuss participation in this research study. Consented participants will have their eligibility and consent confirmed after delivery up until forty-eight (48) hours postpartum.

Baseline Visit and Randomization

If you consent to take part in the study a study team member will complete a baseline assessment including collection of information about your medical history, pregnancy history, labor, delivery, early postpartum and preventative blood thinners used in hospital. If any results show that you are not able to continue to take part the study doctor or research team will let you know.

Randomization is completed and the first dose of study tablet will be given between 6 and 48 hours after delivery. You will be provided with a bottle of the study tablet prior to leaving the hospital. You will be instructed about study tablet administration, symptoms of blood clots in the legs or lungs, bleeding and potential side effects.

A study diary will be provided to record taking the study tablet daily and any nonsteroidal anti-inflammatory drug (NSAID) use.

Follow-up Six (6) Weeks post Randomization

At six (6) weeks after randomization participants will have an in-person visit to assess for symptoms of blood clots, bleeding, possible side effects, and how your baby is doing. We will also collect the study medication bottle and drug diary. If an in-person visit is not possible, a telephone or video visit will be conducted. A pre-paid envelope package will be supplied to return the diary and study tablet bottle to the research team. This visit will take fifteen (15) minutes or less.

Follow-up Three (3) Months post Randomization

The final visit will be conducted by telephone to assess for symptoms of blood clots, bleeding, and possible side effects. This visit will take fifteen (15) minutes or less.

WHAT ARE THE RESPONSIBILITIES OF STUDY PARTICIPANTS?

If you choose to take part in this study, you will be expected to:

- Tell the study doctor or study staff about all prescription and non-prescription medications and supplements, including vitamins and herbals, and check with the study doctor or study staff before starting, stopping, or changing any of these. This is for your safety as these may interact with the intervention you receive in this study.
- Contact the study doctor or study staff if you would like to stop taking part in this study.
- Tell the study doctor or study staff if you are thinking about taking part in another research study.
- Return any unused study tablets.
- Return the study diary that you take home to complete.

HOW LONG WILL PARTICIPANTS BE IN THE STUDY?

The study intervention lasts for about six (6) weeks.

There are two follow up visits:

- Follow-up visit at six (6) weeks (attend in person at the same time as your postpartum visit, over the phone, or video)
- Follow-up visit at three (3) months (over the phone)

You may be seen more often if the study doctor decides that this is necessary.

CAN PARTICIPANTS CHOOSE TO LEAVE THE STUDY?

You can choose to end your participation in this research (called withdrawal) at any time without having to supply a reason. If you choose to withdraw from the study, you are encouraged to contact the study doctor or study staff.

Information that was recorded before you withdrew will be used by the researchers for the purposes of the study, but no information will be collected or sent to the sponsor after you withdraw your permission.

CAN PARTICIPATION IN THIS STUDY END EARLY?

The study doctor may stop your participation in the study early, and without your consent, for reasons such as:

- New information shows that the study intervention is no longer in your best interest
- The study doctor no longer feels this is the best choice for you
- The Sponsor, University of Calgary, decides to stop the study
- The Regulatory Authorities (for example, Health Canada) or research ethics board withdraw permission for this study to continue
- Your group assignment becomes known to you or others (like the study doctor or study staff)
- The funder, Canadian Institute for Health Research (CIHR), decided to stop funding the study.

If this happens, it may mean that you would not receive the study intervention for the full period described in this consent form.

If you are removed from this study, the study doctor or study staff will discuss the reasons with you and plans will be made for your continued care outside of the study.

WHAT ARE THE RISKS OR HARMS OF PARTICIPATING IN THIS STUDY?

You may experience side effects from taking part in this study. Some side effects are known and are listed below, but there may be other side effects that are not expected. You should discuss these with the study doctor. The study team will watch you closely to see if you have side effects.

Low Dose Aspirin (81mg)

Low dose aspirin is well tolerated. Side effects of low dose aspirin include nausea, stomach upset and a small increased risk of bruising or bleeding, including gastrointestinal (stomach and intestines) bleeding. There is the potential that aspirin could make your lochia (vaginal bleeding after birth) heavier.

Aspirin can trigger asthma, bronchospasm (tightening of the muscles that line the airways) or allergic reactions, especially in those already at risk (people who have asthma, hay fever, nasal polyps, or chronic lung disease).

Breast Feeding

Expert guidelines recommend that low doses of aspirin can safely be taken daily during breastfeeding, but that higher doses of aspirin should be avoided. Your study medication will either be a low dose aspirin (81mg) or placebo (inactive substance) and we will instruct you to take only one pill of the study medication a day. Low dose aspirin (81mg) is safe for babies who are being breastfed.

In a research trial of women who took low dose aspirin (81mg) daily, there was no aspirin detected in breast milk. Only a small amount of the break-down products of aspirin was detected in breast milk and that amount was below the level considered safe for breast fed infants. In a research trial of postpartum women who were taking low doses of aspirin, there were no negative effects seen in their breastfed babies.

If you experience serious side effects that require treatment between regular clinic/hospital visits, it is important that you make every effort to return to the clinic/hospital where the study medication was given. If you need immediate treatment and are unable to return to the clinic/hospital, the study doctor or study staff should be contacted as soon as possible.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

If you agree to take part in this study, the intervention may or may not be of direct benefit to you. You will not benefit from the placebo used in this study. Your chance of developing a blood clot after delivery of your baby may improve during the trial but there is no guarantee that this research will help you.

We hope the information learned from this study will help us supply better treatments in the future for women at risk of blood clots after delivering a baby.

HOW WILL PARTICIPANT INFORMATION BE KEPT CONFIDENTIAL?

If you decide to take part in this study, the study doctors and study staff will only collect the information they need for this study.

Records identifying you at this hospital will be kept confidential and, to the extent allowed by the applicable laws, will not be disclosed or made publicly available, except as described in this consent form.

Authorized representatives of the following organizations may look at your original (identifiable) medical/clinical study records at the site where these records are held, to check that the information collected for the study is correct and follows proper laws and guidelines.

- University of Calgary, the Sponsor of this study
- The research ethics board who oversees the ethical conduct of this study in Ontario
- This institution and affiliated sites, to oversee the conduct of research at this location
- Health Canada (because they oversee the use of natural health products/drugs/devices in Canada)

Information that is collected about you for the study (called study data) may also be sent to the organizations listed above. Representatives of Clinical Trials Ontario, a not-for-profit organization, may see study data that is sent to the research ethics board for this study. Your name, address, email, or other information that may directly identify you will not be used. The records received by these organizations may have your sex, partial date of birth.

Studies involving humans sometimes collect information on race and ethnicity as well as other characteristics of individuals because these characteristics may influence how people respond to different interventions. Providing information on your race or ethnic origin is voluntary.

Communication via e-mail is not secure. We do not recommend that you communicate sensitive personal information via e-mail.

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during this study will be used in analyses and will be published/ presented to the scientific community at meetings and in journals.

The study data will be held in a secure database for future use for the larger PARTUM research trial. Your PARTUM data may be linked to Ontario administrative databases (including registries or entities) to evaluate longer term outcomes related to the health of you and your baby. Any future use of this research data must undergo review by a Research Ethics Board.

Even though the likelihood that someone may name you from the study data is very unlikely, it can never be eliminated.

A copy of the consent form that you sign to enter the study may be included in your health record/hospital chart.

WILL FAMILY DOCTORS/HEALTH CARE PROVIDERS KNOW WHO IS PARTICIPATING IN THIS STUDY?

Your family doctor/health care provider will not be informed by the study team that you are taking part in the study. You can choose to let your family doctor/health care provider know that

you are taking part in a research study.

WILL INFORMATION ABOUT THIS STUDY BE AVAILABLE ONLINE?

A description of this clinical trial will be available on www.clinicaltrials.gov. This web site will not include information that can name you. You can search this web site at any time by using the clinical trial registration number NCT04153760.

WHAT IS THE COST TO PARTICIPANTS?

The study tablet will be supplied at no charge while you take part in this study.

Participation in this study will not involve any added costs to you or your private health care insurance.

ARE STUDY PARTICIPANTS PAID TO BE IN THIS STUDY?

You will not be paid for taking part in this study.

If you decide to take part in this study, you will be given a $10 gift certificate to Second Cup, if you choose to attend the six week visit in person or once your study bottle, remaining tablets, and diary are received.

In the case of research-related side effects or injury, medical care will be provided by your doctor or you will be referred for proper medical care.

WHAT ARE THE RIGHTS OF PARTICIPANTS IN A RESEARCH STUDY?

You will be told, promptly, about new information that may be relevant to your willingness to stay in this study.

You have the right to be informed of the results of this study once the entire study is complete. The results of this study will be available on the clinical trial registry or you can contact the study team.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form, you do not give up any of your legal rights against the study doctor, sponsor or involved institutions for compensation, nor does this form relieve the study doctor, sponsor, or their agents of their legal and professional responsibilities.

You will be given a copy of this signed and dated consent form prior to taking part in this study.

WHOM DO PARTICIPANTS CONTACT FOR QUESTIONS?

If you have questions about taking part in this study, or if you suffer a research-related injury, you can talk to your study doctor, or the doctor who oversees the study at this institution. That person is:

Dr. Ann Kinga Malinowski	416-586-4800 x5127 PARTUMTrial@sinaihealth.ca

If you have questions about your rights as a participant or about ethical issues related to this study, you can talk to someone who is not involved in the study at all. That person is:

OHSN-REB, Chairperson	613-798-5555, Ext 16719

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SIGNATURES

- My questions have been answered,
- I understand the information within this informed consent form,
- I allow access to medical records, and related personal health information as explained in this consent form,
- I do not give up any legal rights by signing this consent form.
- I agree to take part in this study.

Signature of Participant	PRINTED NAME	Date
Signature of Person Conducting the Consent Discussion	PRINTED NAME & ROLE	Date

The following attestation must be provided if the participant is unable to read or requires an oral translation:

If the participant is assisted during the consent process, please check the relevant box and complete the signature space below:

☐ The person signing below acted as an interpreter, and attests that the study as set out in the consent form was accurately sight translated and/or interpreted, and that interpretation was provided on questions, responses and additional discussion arising from this process.

PRINT NAME of Interpreter	Signature	Date

Language

☐ The consent form was read to the participant. The person signing below attests that the study as set out in this form was accurately explained to the participant, and any questions have been answered.

PRINT NAME of witness	Signature	Date

Relationship to Participant