UNIVERSITY OF ALBERTA

Faculty of Kinesiology, Sport, and Recreation

1-052 Li Ka Shing Center
Edmonton, AB, Canada
T6G2H9

margie.davenport@ualberta.ca
craig.steinback@ualberta.ca

Tel: 780.492.0642
780.492.5553

PARTICIPANT CONSENT FORM

Title of Research Study: **Impact of exercise on vascular health during pregnancy.**

Principal Investigators: **Dr. Margie Davenport. PhD** **margie.davenport@ualberta.ca**
Dr. Craig Steinback, PhD **craig.steinback@ualberta.ca**

Before you make a decision one of the researchers will go over this form with you. You are encouraged to ask questions if you feel anything needs to be made clearer. You will be given a copy of this form for your records.

Introduction:

The purpose of this letter is to provide you with the information you require to make an informed decision as to whether or not you wish to take part in our study.

Pregnancy is a unique period of time where the body undergoes major changes (for example, increase in weight, heart rate, the amount of blood the heart pumps). We also know that the sympathetic nervous system, which is a major factor controlling cardiovascular function and blood pressure, is more active during pregnancy than before becoming pregnant. However, it is possible, if sympathetic nervous system activity increases too much, increases in blood pressure may develop. Increased sympathetic nervous system activity is observed in hypertension and hypertensive pregnancy disorders (i.e. pre-eclampsia). Exercise may be one way to control the increase in sympathetic nervous system activity and or its effect on blood pressure during pregnancy.

You are being asked to participate in a research study that examines the effect of exercise during pregnancy on your cardiovascular and sympathetic nervous system health. We think that one of the reasons that sympathetic nervous system activity in women is increased is because the blood vessels become less sensitive to this activity. However, we also know that exercise can play an important role in this process.

We are currently recruiting one hundred women without contraindication to exercise (meaning that there is no reason for you not to exercise during pregnancy) to be randomized into 1) a group who follows an aerobic exercise program during pregnancy, or 2) continues with their normal level of activity during pregnancy. If you agree to participate, you will be tested between 16 to 20 weeks and at 34-36 weeks of pregnancy.

Requirements: In order to participate you must be at least 18 years of age, be a non-smoker for at least one year and be pregnant with a single baby. You will be asked what medications you are taking. If you are on any medications prescribed by your doctor you will continue taking these throughout the study.

Before starting the exercise program, we ask that your health care professional complete the PARmed-X for Pregnancy which is a medical pre-screening tool to make sure that there is no reason that you shouldn't exercise during pregnancy. This form should not cost you anything to have filled out by your health care professional. If you do incur any costs associated with obtaining this form you will be reimbursed (a receipt will be required).

You will be most comfortable if you wear loose fitting shorts and a tank top or short sleeve top that is loose fitting. Once in the lab, it is important that you are comfortable and relaxed and tell us if anything is wrong or uncomfortable.

Procedures: You will be asked to come into the Physical Activity and Diabetes Laboratory for testing on four occasions; two times in early pregnancy, two times late in pregnancy, and once at 2 months postpartum.

The location of the lab is at the University of Alberta Li Ka Shing building on the corner of 112St and 87Ave NW. It is accessible by city transit and near two train stations (University or Health Sciences/Jubilee). We will need you to stay here for between one and three hours each visit.

TESTING SESSIONS
The testing sessions (2 days) will occur between 16-20 weeks gestation and repeated at 34-36 weeks gestation.

Day 1 (Approximately 3.5 hours):
When you come to the laboratory for your test we ask that you not have any food or drink, except water, for 12 hours (overnight) before your visit. We also ask you not have any coffee or over-the-counter pain medication (i.e., Tylenol, advil, aleve, asprin etc.) that morning or alcohol the night before. Finally, please do not go the gym or do any physical activity more than normal walking/stair climbing the morning of your visit. Once in the lab we will measure your weight and height. We will also take a fasted blood draw to measure blood markers related to your overall health and cardiovascular function. We will check your blood glucose level (a single drop of blood from a finger poke is measured on a small machine called a glucometer). We will also measure blood gases and metabolites from a small amount of blood from the same finger poke. We will then give you a standard breakfast. Following breakfast we will ask you to complete an assessment of your cardiovascular function and sympathetic nerve activity. After lying in a reclined position in a comfortable chair we will then connect you to a number of instruments designed to measure your general cardiovascular function.

- We will measure your heart rate using self-adhesive electrodes placed on your chest
- We will measure your blood pressure with every heart-beat using a small cuff placed on your middle finger.
- We will periodically measure your blood pressure in the same manner as your physician using a cuff placed on your upper arm.

- We will detect your pulse in you your toe using a small cuff wrapped around your big toe

- We will monitor the amount of oxygen in your blood using a small sensor which will clip to your index finger.

- We will measure your breathing rate and oxygen and carbon dioxide levels in your breath using a mouthpiece (similar to a snorkel) and a nose clip.

The blood samples taken (approximately 50mls (~3 tbsp or ~1/12th of a blood donation) will be used to analyze blood sugar, lipids (fat), cytokines (proteins), markers of inflammation, insulin (a hormone that responds to blood sugar), markers of bone health, blood volume and hormones.

The function of your blood vessels will be measured using two specialized devices, applanation tonometry and Doppler ultrasound.

Applanation tonometry involves detecting your pulse by placing a small pen like sensor against your skin over one of your arteries.

Ultrasound involves using a small probe that emits ultrasound waves that will be held against your skin over one of your arteries. A similar device was used to image your baby by your health care professional earlier in your pregnancy. We will hold this probe over one of the arteries in your upper thigh (the femoral artery), over your belly (uterine artery), over your neck (the carotid artery) and over your upper arm (the brachial artery).This probe will take pictures of your artery and detect how fast the blood is moving through them.

Once all of the above equipment has been put in place, we will set-up the equipment required to record the activity of your sympathetic nervous system. This procedure involves using two very small needles, similar to acupuncture needles. A trained researcher will insert the first of these needles just under your skin below the knee. The same trained researcher will then insert the second needle into a nerve located just below the knee.

Identifying the right location to obtain a useable nerve activity signal may take some time. We will not do this in any one spot for more than ten minutes and we will not search for an appropriate signal for longer than 45 min in total. These are standard practices. Once the nerve recording is obtained, we will require you to sit very still.

If we do not obtain a useable signal after 45 min, we will remove both needles and begin the protocol without this measurement. In addition, if you feel uncomfortable with this procedure, for whatever reason, you may stop at any time. We will then proceed with the remainder of the protocol without this measurement.

Once the equipment has been setup you will sit quietly for 10 min. Next, we will assess the function of your blood vessels by placing the ultrasound on your right carotid artery (at the side of the neck) and tonometer on your left carotid artery for approximately 2 minutes to measure blood flow. This will be repeated on your femoral artery (upper thigh). In addition, a picture of each of the blood vessels will be taken using the ultrasound.

We will then have you perform 3 short and simple experiments. We will measure the blood flow in your femoral artery (upper thigh), and the pulse at your carotid artery (neck) throughout each test.

For the first experiment, you will submerse your hand in ice water for 3 min. This will increase the activity of your sympathetic nervous system. This will allow us to determine how your blood vessels respond to changes in the activity of your sympathetic nervous system. Once you remove your hand from the ice water we will use a heating pad and blanket to dry and rewarm your hand.

For the second experiment, the ability of your one of the blood vessels in your arm (your brachial artery) to dilate will be assessed using a technique called flow mediated dilation. The diameter and blood flow in your brachial artery will be assessed at rest for 1-2 minutes using the ultrasound. Then, a standard blood pressure cuff will then be inflated around your forearm for 5 min. The inflated blood pressure cuff will temporarily squash the artery to prevent blood from entering your forearm. When the cuff is released, the rush of returning blood causes the artery to dilate. This dilation will be measured for 5 min following deflation of the cuff.

In the third experiment, you will sit for 3 min. Without changing how you are breathing, we will then ask you to hold your breath at the end of a normal breath out (end-expiration). This will activate briefly the sympathetic nervous system to near maximal levels. This will last on average for 15s and can be stopped at any time. This will tell us if the maximal ability of your sympathetic nervous system to increase its activity has changed during pregnancy.

Day 2 (approximately 1.5 hours):

On day 2 you will come into the lab to perform an exercise test until you feel too tired to continue exercising (peak exercise test). In preparation for this test, we ask that you eat normally, but that you abstain from the ingestion of caffeine (tea, coffee, chocolate, cola drinks, etc.) for at least 12 hours prior to the visit, and no alcohol or strenuous exercise the day of the test.

The exercise test is conducted on a recumbent bike. During testing, we will ask you to put on a nose clip and to breathe through a mouth-piece. This will be similar to breathing through a snorkel. Breathing through the mouthpiece will allow us to measure the rate and depth that you breathe as well as the amount of oxygen and carbon dioxide you inhale and exhale. Throughout the test we will measure your heart rate and blood pressure as described above. We will also measure the blood flow in one of the blood vessels in your brain during this test using ultrasound. This ultrasound is similar to the one used at the by your health care professional to image your baby, but sits on the side of your head over your temple. This probe is held in place using a head-piece placed over your head (similar to the band of a ball cap). We use this probe to measure the speed of blood within the arteries in your brain. You may stop this test at any time.

Prior to beginning the exercise protocol we will have you perform a breathing maneuver to determine your lung function. This will consist of a large (maximal) breath in and a rapid full breath out. We will repeat this maneuver three times. We will then have you sit and rest quietly for 5 minutes breathing normally followed by three minutes of standing where we will measure how your brain blood flow responds to a change in body position.

During the exercise test on a recumbant bike, we will have you warm up at 25 watts (constant speed of 50 rpm) for 5 minutes. At the end of the warm up we will increase the resistance (increase by 25 watts) every minute until you do not want to continue (volitional fatigue). We will then do a cool down at 25 watts.

Following the cool down, we will have you sit for five minutes of rest and stand up for three minutes to test your brain blood flow responses to a change in body position after exercise.

For either protocol, we will continuously monitor your heart rate and blood pressure during the test and will ask you to rate how hard you feel you are working every 2 minutes by pointing to a 10 point scale. The 10 point scale ranges from the lowest rating of "0 – nothing at all" (meaning the work load is very easy), a medium rating of "3 – moderate", to a very high work rating "10 – very, very strong". You may stop the test at any time.

After delivery, we will contact you to ask you about your baby's weight and length at birth, as well as whether you had a cesarean or vaginal delivery and any complications you or baby may have had.

QUESTIONNAIRES (16-20 weeks, 26-28 weeks, 34-36 weeks, 2 months postpartum):

Throughout your pregnancy and during the postpartum we will ask you to fill in a set of questionnaires. This will occur at the beginning of the study, during your second trimester, and at the end of the study. Each time, you will be provided five questionnaires which are returned to us in an envelope with pre-paid postage: 1) Health History Questionnaire which asks about the medical history of you and your family (some questions will be updated at 34-36 weeks); 2) Pregnancy Physical Activity Questionnaire which asks about your physical activity levels over the past 2 months); 3) the Pittsburg Sleep Quality Index, 4) a questionnaire asking about your thoughts regarding exercise during pregnancy, and 5) a pregnancy depression questionnaire. All of these questionnaires can be filled in online (through a secure link) or using pen and paper. In addition, you will be asked to record everything you eat and drink for 3 consecutive days (including 1 weekend day) using a website. You will receive a special login that is linked to your study ID (your name will not be linked to the account) which can be accessed by your computer or smartphone. If you prefer, we can provide a paper copy of the 3 day food intake record which can be returned to us by mail. You are under no obligation to complete the questionnaires and you may refuse to answer any or all of the questions. At this time you will also be given an accelerometer to measure your level of activity for 7 consecutive days and levels of sleep of 7 consecutive nights. An accelerometer is about the size of a small box of matches and is worn on your belt or as a watch. It will record your movements over the course of the day but shouldn't interfere with your daily activities.

EXERCISE RANDOMIZATION:

At the end of the second day of testing, you will be assigned at random; that is, by a method of chance (like the flip of a coin), into one of two groups. You will be given a sealed, opaque envelope which will tell you which group you have been randomized to (the researchers will not know which group you have been assigned to until after you open the envelope):

Exercise – You will be advised to walk at a target heart rate equivalent to 50-70% of peak oxygen consumption (as determined from your peak exercise test. This is a moderate intensity of walking similar to a fast walking pace), gradually increasing the time from 25 to 40 minutes per day 3-4 times a week. You will receive all exercise instructions from a qualified exercise physiologist.

Control – You will be advised to not increase your activity during pregnancy over your current levels.

Controlled Walking Program:

You will be invited to take part in supervised exercise sessions in our dedicated research gym. After the first exercise session you have the option of using aerobic exercise equipment (eg. Treadmill or bike) in the lab, in your own gym, walking on an outdoor trail (weather permitting), or in your neighbourhood. We do, however, want you to exercise in the lab at least once a week so that we can monitor your progress (weight, blood pressure, and blood glucose) and address any concerns that you may have. We will provide you with a heart rate monitor (i.e. watch or handles on treadmill at the gym) or you can use your own. We will ask you to monitor your heart rate during exercise sessions not performed in the lab.

During your initial session we will orient you with various aerobic training equipment available including recumbent bikes and treadmills. We will also check your resting heart rate and blood pressure, and then show you how to monitor your blood glucose level (a single drop of blood from a finger poke is measured on a small machine called a glucometer). We will attach a halter-type monitor to your chest, which will record your heart rate as you exercise. By working at, or close to, a recommended heart rate (target heart rate) we can be sure that you are working at the appropriate intensity.

The walking program continues from 16-20 weeks to 34-36 weeks gestation. The total time involved for each exercise session will be approximately ½ - 1 hour. We ask that you complete 3 to 4 exercise sessions per week until weeks 34-36 of your pregnancy, when you will be tested again. You will be exercising at 50-70% of your peak oxygen consumption (based on a pre-determined target heart rate) based upon the fitness assessment that you completed in Visit 2. This represents a brisk walking pace that is easy for you to maintain without you becoming breathless.

2 month postpartum follow up (1.5 hours – childcare available with notice):

We will test your blood vessel health at two months postpartum. For this test, we will ask you to not have any food or drink, except water, for 12 hours (overnight) before your visit. We also ask you not have any coffee or over-the-counter pain medication (i.e., Tylenol, advil, aleve, asprin etc.) that morning or alcohol the night before. Finally, please do not go the gym or do any physical activity more than normal walking/stair climbing the morning of your visit. Once in the lab we will measure your weight. We will also take a fasted blood draw to measure blood markers related to your overall health and cardiovascular function. We will check your blood glucose level (a single drop of blood from a finger poke is measured on a small machine called a glucometer). We will also measure blood gases and metabolites from a small amount of blood from the same finger poke. We will then give you a standard breakfast. Following breakfast we will ask you to complete an assessment of your blood vessel function.

First, we will assess the function of your blood vessels by placing the ultrasound on your right carotid artery (at the side of the neck) and tonometer on your left carotid artery for approximately 2 minutes to measure blood flow. This will be repeated on your femoral artery (upper thigh). In addition, a picture of each of the blood vessels will be taken using the ultrasound.

Then we will assess the ability of your one of the blood vessels in your arm (your brachial artery) to dilate will be assessed using a technique called flow mediated dilation. The diameter and blood flow in your brachial artery will be assessed at rest for 1-2 minutes using the ultrasound. Then, a standard blood pressure cuff will then be inflated around your forearm for 5 min. The inflated blood pressure cuff will temporarily squash the artery to prevent blood from entering your forearm. When the cuff is released, the rush of returning blood causes the artery to dilate. This dilation will be measured for 5 min following deflation of the cuff.

At the postpartum follow up, we will have you fill out all of the same questionnaires as you did during your pregnancy. You will also wear the accelerometer for one week again. During this appointment, we will also have you fill in three additional questionnaires regarding your infants behavior, sleep and activity.

If you have any questions or concerns at any point during the study please ask a member of the study team.

Possible Benefit: You are not expected to benefit directly from being in this research study. However, the results of this study may help other pregnant women in the future.

Possible Risks:

All of these procedures have previously been done in pregnant women and are considered safe for both the mother and baby.

***Cold stress protocol*:** There are no risks associated with exposure to ice water for the duration used in this study (3 min). Cold stress is a familiar experience to most people (handling frozen foods, making snowballs, etc.). This exposure is meant to cause a minimal amount of discomfort (stress). This may be experienced as a sharp sensation on the skin, tingling, or numbness. You are encouraged to keep your hand in the ice water for the full 3 minutes, but this is voluntary and you may remove your hand at any point. Any discomfort or sensations will go away quickly once your hand is removed from the ice water and a heating pad will be used to rewarm your hand.

***Blood Samples*:** With any procedure using needles, there is minimal risk of infection. Aseptic technique will be used and only a certified technician will take blood samples. This procedure may result in some discomfort, minimal pain upon insertion, swelling, redness or bruising. As you will not have eaten for at least twelve hours, you may feel hungry. We will feed you immediately after the blood draw, prior to the protocol.

***Ultrasound*:**

The ultrasound used in the neurovascular assessment day has no known risks involved with it. The ultrasound used on the exercising day (brain blood flow) may be uncomfortable. The head-piece used to keep the probes in place for measuring brain blood flow must fit snugly. This may result in a mild headache if worn for an extended period of time. This should go away quickly when the head-piece is taken off.

***Blood Pressure Monitors*:** The cuffs for measuring blood pressure may cause some discomfort including numbness, tingling, or discoloration in the finger or arm. These will return to normal soon after the cuff is removed.

***Nerve Activity Recording*:** As we search for a suitable location to record sympathetic nervous system activity from you may feel odd or new sensations. This may include change in temperature, tingling, mild cramping, or pressure in your lower leg. These are all normal and may help us to know if we are recording from the right location within the nerve. These sensations occur only briefly and go away quickly if searching is paused or if the needle is pulled back from the spot that caused the sensation. You will be asked to indicate the presence of any of these feelings to the person looking for the signal.

Following the experiment there is a minimal risk that you may experience lasting effects of the procedure. These may include mild tenderness, numbness, increased sensitivity, and redness around the location of the needles, or in the lower leg. In extremely rare circumstances (<1/1000) there is also the risk of permanent muscle weakness (foot drop) in the lower leg. To minimize any persistent effects, we limit the amount of time for which we search for a suitable signal (10 min in one spot and no more that 45 min in total). We also recommend that you do not take part in any physical activity greater than walking in the 24 hours after the protocol is complete to help reduce any inflammation that may result.

With any procedure using needles, there is a minimal risk of infection; however we follow all appropriate steps to sterilize both the skin and the needles to help minimize this risk. This includes washing hands thoroughly, using alcohol wipes on the skin where the needles will be inserted and sterilizing the needles using the same technique used for surgical equipment (autoclaving).

Exercise testing: This test should cause no risk to you but you may feel a little stiff and have minor soreness in your legs for the next few days. We will check your resting blood pressure before and after exercise using the same blood pressure cuff technique that your doctor uses. You will feel a slight pressure on your arm when the cuff is inflated. While unlikely, slight bruising may occur.

***Other*:** If we find out anything new during the course of this research which may change your willingness to be in the study, we will tell you about these findings.

Voluntary Participation: Your participation is completely voluntary. You are free to withdraw from this study at any time for any reason. You can do this by contacting the investigators. If after participating in the study you wish to remove your data (including blood samples) from the study, you have until December 31, 2019 to do so, after this time all data collected will be used. We may request that you withdraw from the study during the protocol if we are at all worried about your general health (i.e. high blood pressure, irregular heart rhythm etc.) and we will notify you as to our reason should that situation occur.

Confidentiality: We will keep any personal information relating to this study confidential. Any data collected will be kept in a locked cabinet. Digital data will be stored in a password protected and encrypted computer. Only study investigators have access to these data. Your name will be excluded. We will only use the data collected for research purposes. Any research data published as a result of this study will be presented as group data and will not identify you as a participant. The University of Alberta auditors or Health Research Ethics Board may review the study records in order to monitor the research. We will keep your personal information (name, consent form) for 5 years after the end of the study and then it will be destroyed.

Blood Samples for Future Research: Your blood samples collected for this study will be kept until analysis for tests described above. If any blood samples are left over after testing, they will be stored indefinitely and may be used for future research examining metabolic and/or cardiovascular health. The left over samples will not be labeled with your name, and will be stored securely at the University of

Alberta. You can ask for your left over samples to be destroyed at any time, however since your personal information will be destroyed after a 5 year storage period we will no longer be able to match the sample to you after this time.

Reimbursement for Expenses: You will not be paid for participation in this study, nor should you incur any expenses related to this study. We will provide parking free of charge (in our reserved parking spot) or public transit related to your testing visits. We will accommodate free parking in the reserved parking spots during the exercise intervention, when possible. In addition, upon completing the pregnancy component of the study, we will provide you with a "Baby Gift Basket" including a box of diapers, wipes, baby book etc. Women in the control group who complete the study will also be offered the option of either 6 months access to our gym free of charge, or 6 group exercise sessions with a fitness instructor in the postpartum period. Women who complete the 2 month postpartum follow up testing will receive an additional box of diapers as a thank you.

Compensation for Injury: If you become ill or injured as a result of being in this study, you will receive necessary medical treatment, at no additional cost to you. By signing this consent form you are not releasing the investigator(s), and/or institution(s) from their legal and professional responsibilities. If you suffer a research-related injury, please call either Dr. Margie Davenport at 780-492-0642 or Dr. Craig Steinback at 780-492-5553. Should you need urgent medical care, go to the hospital.

Questions: If you have any questions about the research now or later, please contact either Dr. Margie Davenport at 780-492-0642 or Dr. Craig Steinback at 780-492-5553. If your question is occurring outside normal business hours you may email Dr. Davenport at margie.davenport@ualberta.ca or Dr. Steinback at craig.steinback@ualberta.ca and we will respond as soon as we can.

If you have any questions regarding your rights as a research participant, you may contact the Health Research Ethics Board at 780-492-2615. This office has no affiliation with the study investigators.

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CONSENT FORM

Title of Study: Impact of exercise on vascular health during pregnancy.

Investigators **Dr. Craig Steinback. PhD** **Phone Number: 780-492-5553**
Dr. Margie Davenport **Phone Number: 780-492-0642**

	Yes	No
Do you understand that you have been asked to be in a research study?	☐	☐
Have you read and received a copy of the attached Information Sheet?	☐	☐
Do you understand the benefits and risks involved in taking part in this research study?	☐	☐
Have you had an opportunity to ask questions and discuss this study?	☐	☐
Do you understand that you are free to leave the study at any time without having to give a reason and without affecting your future medical care?	☐	☐
Has the issue of confidentiality been explained to you?	☐	☐
Do you understand who will have access to your records, including personally identifiable health information?	☐	☐
Do you want the investigator(s) to inform your family doctor that you are participating in this research study? If so, give his/her name _____	☐	☐
Do you consent to be contacted in the future for other similar or related research study(s)?	☐	☐

Who explained this study to you? _____

I agree to take part in this study:

Signature of Research Participant: _____

Printed Name: _____

Date: _____

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

Signature of Investigator or Designee: _____
Date: _____

THE INFORMATION SHEET MUST BE ATTACHED TO THIS CONSENT FORM AND A COPY GIVEN TO THE RESEARCH PARTICIPANT