Informed Consent Form for Participation in a Research Study

Study Title: PREPARE Trial: a parallel arm multicenter randomized trial of frailty-focused PRerative Exercise to decrease Postoperative complication Rates and disability scorEs

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Sponsor: The Ottawa Hospital Research Institute

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Clinical Trial Registration Number: NCT04221295

INTRODUCTION
You are being invited to participate in a clinical trial (a type of study that involves research). You are invited to participate in this trial because you are at least 60 years of age and you are or are soon to be scheduled for elective surgery. 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 participate in this research study.

Please take your time in making your decision. You may find it helpful to discuss it with your friends and family. The study staff will tell you about timelines for making your decision.

Taking part in this study is voluntary. You have the option to not participate 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?
More than 200,000 older Canadians have major surgery each year. 40% of these patients live with frailty. This is important for a number of reasons. First, older people represent well over half of all people having major surgery in Canada. Second, older people with frailty face a greater than two times higher risk of having a major complication, developing a new disability, or dying after surgery than older people without frailty. Strategies and treatments to decrease the risks faced by older people with frailty having surgery are urgently needed but have not been widely developed or studied. The strongest findings suggest that exercise before surgery may improve older people’s ability to walk and stand after surgery and lower rates of complications. Unfortunately, these findings are currently limited.
Therefore, to help improve outcomes after surgery in a meaningful way for the growing number of older Canadians with frailty, we propose to study the effectiveness of a home-based exercise program compared to the standard care that people usually receive.

WHY IS THIS STUDY BEING DONE?
The purpose of this study is to obtain additional information about the effectiveness of a home-based preoperative exercise program (exercise prehabilitation) in lowering patient-reported disability and postoperative complications in older people with frailty having major surgery.

People aged 60 years and older are the fastest growing part of the population and undergo surgery at a higher rate than any other age group. This is of particular concern as frailty becomes more common with advancing age. Frailty is a condition that describes the build-up of weakness across multiple body systems and is a known risk factor for unfavorable outcomes after surgery.

Given the high rate of frailty, and the strong link between frailty and patient recovery after surgery, the care of older patients with frailty has been identified as a key area of focus to improve the quality of care for people having surgery. Specifically, the role of exercise before surgery (prehabilitation) is a priority for patients, clinicians, and the healthcare system. Our plan is to explore the usefulness of a home-based prehabilitation program.

To answer these questions, the Departments of Anesthesiology, Surgery, and Geriatrics at The Ottawa Hospital with the assistance of the Faculty of Health Sciences (alongside 11 additional Canadian hospitals), will be doing a study of patients before and after surgery. We will compare the results between those who participate in a home-based prehabilitation program before surgery to those who do not.

WHAT OTHER CHOICES ARE THERE?
You do not have to take part in this study.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
It is anticipated that about 750 people will take part in this study, from research sites located in Ontario, Manitoba, Alberta, and British Columbia.

This study should take approximately 3.5 years to complete and the results should be known in about 4 years.

WHAT WILL HAPPEN DURING THIS STUDY?

ASSIGNMENT TO A GROUP
If you decide to participate then you will be “randomized” into one of the groups described below. 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. You will be told which group you are in.

WHAT IS THE STUDY INTERVENTION?
Before Your Surgery

On or near the date of your pre-operative visit with your surgeon, if you agree to take part in this study, you will be asked to complete a standardized set of questionnaires to document your own report of your health status and answer demographic questions. In total, there will be eight questionnaires to complete. These questionnaires will be administered electronically by a research staff member using an iPad or a computer. We will measure your physical function with a 5 Times Sit to Stand (5TSTS) Test. Altogether, this should take approximately 30 minutes of your time.

If you are randomized to the interventional group (the prehabilitation program which is a minimum of 3 weeks, depending on date of surgery); you will be asked to complete 1-hour exercise sessions a minimum of 3 times per week. The exercise sessions include cardio (aerobic exercise videos, walking, swimming, biking), as well as strength and flexibility training. You will be provided with a pedometer to track your walking and an elastic resistance band for the strength and exercise training. You will receive an instructional booklet, an exercise tip sheet and two exercise videos that you may watch in your home – one for strength and flexibility training and one for cardio exercises (seated and standing options). Should you have any questions or concerns about the materials or videos, the research assistant will address these with you over the telephone. You will be asked to complete a calendar that is intended to track your exercise. You will also be given a nutrition pamphlet, including recommendations for consumption, and coupons for oral nutrition supplements that you may take if you wish while exercising. A research team member from the coordinating site (The Ottawa Hospital) will phone you once a week to ask you how you are doing with the program, what exercises you have completed, if you have watched the videos, and if you have experienced any discomfo ts or challenges with the program. During the last weekly phone call before your surgery, you will be asked to answer a few additional questions to better understand your experience with the program. This will take about 10 additional minutes of your time.

The control group will be provided with A Guide to Healthy Eating for Older Adults, the World Health Organization’s Global Recommendations on Physical Activity for Health – 65 years and above and a pedometer and log to track steps for 30 days after surgery. Intervention and control group participants will receive a phone call the day before surgery to self-report their activity levels for the previous 4 weeks, as well as inform the study team of any falls they had during the time of enrollment and day before surgery.

Regardless of your group assignment, all of your in-hospital care around the time of surgery will be in accordance with hospital standards as prescribed by your surgeon and anesthesiologist.

Day of Your Surgery

All aspects of your medical, surgical, and anesthetic care will be routine and will not be affected in any way by your participation in this study.

After your Surgery
Regardless of group assignment, a research assistant will meet with you in the hospital 3, 5, and 7 days after your surgery (provided you are in the hospital on these days) as well as on the day of your discharge. If you are discharged earlier than 3 days after your surgery, they will only meet you on your day of discharge. If you remain in hospital longer than 30 days, the last possible date the research assistant will meet with you is on day 30. During each of these visits with the research assistant, you will be asked to complete some standardized questionnaires. On your date of discharge, you will be asked to complete the same questionnaires, as well as the same 5 Times Sit to Stand (5TSTS) Test that you completed before your surgery. If in-person visits are not feasible due to hospital restrictions, a research assistant will contact you via telephone while in hospital, or at home after you have been discharged.

The research assistant from the study coordinating site (The Ottawa Hospital) will call you 30 days, 90 days and one-year after surgery to ask you a few questions over the phone and to see how you have been feeling since your surgery. These will be the same set of questions that you answered at the clinic before your surgery.

If you are in hospital at the time of the 30 day, 90 day, and one year calls, the research assistant will call you in hospital or a research assistant from this site will meet with you in person to ask you these questions.

If you do not have a scheduled surgery within 12 weeks from the date of your enrollment, we will continue with the after-surgery study procedures as though you had surgery (this helps with something called 'sensitivity analysis'). If your surgery takes place within one month of beginning the after-surgery study procedures (within 16 weeks of enrollment), we will collect the in-hospital data and will phone you 30 days after your surgery for the planned data collection.

**Questionnaires**

You will be provided with questionnaires before you begin the study, during a telephone call the day before your surgery and again at 30 days, 90 days, and one year following your surgery. The purpose of the questionnaires is to understand how the study intervention affects your function, quality of life, complications, as well as obtain your feedback on the prehabilitation program. Each set of questionnaires will take approximately 10 minutes to complete. All in-person questionnaires (those not completed over the telephone) will be completed by a research staff member on an iPad or a computer. The information you provide is for research purposes only. Some of the questions are personal. You can choose not to answer questions if you wish.

In the event that you are unable to complete the study questionnaires on your own, you may provide your permission for the study team to contact a family member, caregiver or friend (proxy) to answer the questions on your behalf. You can choose to not provide this permission if you wish.

**Participant Logs**

If you are randomized to the intervention group, you will be asked to keep track of when you engage in your exercises on a calendar that you will be provided. Using the calendar, you will be asked to record the frequency and type of exercise you engage in. When you are finished, you will be asked to return your calendar by mail using a pre-stamped and pre-addressed
Participants in both the intervention and control groups will be given a Step Count Log to track their steps for 30 days after surgery. You will be given a pre-stamped and pre-addressed envelope in order to mail your Step Log back after the 30 days is complete.

WHAT ARE THE RESPONSIBILITIES OF STUDY PARTICIPANTS?
If you choose to participate in this study, you will be expected to:

- Inform the study doctor if you are thinking about participating in another research study.
- Engage in the prescribed exercises and record these in the provided calendar (intervention group).
- Provide the research assistant from the coordinating site (The Ottawa Hospital) with an update on how your exercise program is going during weekly calls (from enrollment to surgery for intervention group participants).
- Return your calendar by mail following completion of your exercise program (intervention group participants).
- Complete the necessary questionnaires on date of enrollment and postoperative days 3, 5, 7 and discharge, as well as a 5 Times Sit to Stand (5TSTS) on the date of discharge from hospital. Questionnaires only during the phone call the day before surgery, 30 day, 90 day and one-year follow-up calls.
- Wear the pedometer provided for 30 days after surgery (control group) OR from date of enrollment to 30 days post-surgery (intervention group).
- Return your Step Count Log using the pre-stamped, pre-addressed envelope provided to you at enrollment.

HOW LONG WILL PARTICIPANTS BE IN THE STUDY?
Your participation will begin at the time of your routine surgical consultation and will conclude one year after your surgery.

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 provide a reason. If you choose to withdraw from the study, you are encouraged to contact the study doctor or study staff. You may withdraw your permission to use information that was collected about you for this study at any time by letting the study doctor know. However, this would also mean that you withdraw from the study. If you decide to leave the study, you can ask that the information that was collected about you not be used for the study. Let the study doctor know if you choose this.

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:

- The study intervention does not work for you
- You are unable to tolerate the study intervention
- The study doctor no longer feels this is the best option for you
- The research ethics board withdraws permission for this study to continue
• The sponsor decides to stop the study

If you are removed from this study, the study doctor will discuss the reasons with you.

WHAT ARE THE RISKS OR HARMS OF PARTICIPATING IN THIS STUDY?
The risks and side effects of the standard or usual treatment will be explained to you as part of your standard care. These risks are not included in this consent form.

There is no added risk related to your participation in this study. The exercise program has been developed for older adults with frailty. There are different levels of exercise that you may complete. Ensure you choose the level that is appropriate for you. The questionnaires and function test will take some added time during your visits with the research assistant. You are able to skip any questions and any aspects of the function test that you do not feel comfortable with.

In order to be cleared for surgery, you had to pass a pre-operative functional status evaluation. The exercises in the prehabilitation program are associated with much less risk than surgery, suggesting that you are also qualified to participate in the prehabilitation program. However, exercise can be associated with heart and breathing problems, especially if you haven't exercised regularly and start out with exercises that are too intense. For this reason, our recommended activities allow you to gradually increase your intensity over time.

However, if you ever experience chest pain or have serious shortness of breath during or after exercising, you should seek emergency medical help. If you are randomized to the control group, there are no foreseeable risks involved for not participating in the prehabilitation program, as you will receive the same care that you would get if you were not in the study.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?
There are no medical benefits to you for taking part in this study. However, we are encouraged by the previous research to date which suggests the usefulness of prehabilitation before surgery. Therefore, if you are randomized to the intervention group, you may benefit in terms of how well you do after surgery, though this is not yet conclusive.

HOW WILL PARTICIPANT INFORMATION BE KEPT CONFIDENTIAL?
If you decide to participate in this study, the study doctors and study staff will only collect the information they need for this study.

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

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.

• 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
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. Information that may directly identify you including your name, telephone number, address, email, will be securely shared with the coordinating site only. Should you name a proxy, their name and telephone number will also be shared with the coordinating site. The records received by the organizations listed above may contain your participant code, sex, date of birth, surgery, admission and discharge dates.

Your provincial health card number will be linked with the Institute for Clinical Evaluative Sciences (ICES) to collect health administrative data for health system and resource use outcomes. ICES will remove all personal identifiers and assign you a personal identification code, therefore the likelihood that your identify becomes known is very low. ICES is governed by policies and procedures that comply with the requirements of the Ontario privacy commission. This database is responsible for ensuring that necessary infrastructure (i.e. privacy office, data linkage and security measures, data sharing agreements) are in place to comply with these policies and to maintain a secure data platform.

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

- All information collected during your participation in this study will be identified with a unique study number, and will not contain information that identifies you, such as your name, address, etc.
- The link between your unique study number and your name and contact information will be stored securely. Your contact information will be shared with the coordinating site (The Ottawa Hospital) as they will be following up with you throughout the duration of the study.
- Any documents leaving this site will contain only your unique study number (with the exception of select identifying information, which will be shared securely with the coordinating site for follow-up purposes). This includes publications or presentations resulting from this study.
- Information that identifies you will be released only if it is required by law.
- For audit purposes only, your original medical records and study records may be reviewed under the supervision of Dr. McIsaac’s staff by representatives from:
  o the Ottawa Health Science Network Research Ethics Board (OHSN-REB),
  o the Ottawa Hospital Research Institute
- Research records will be kept for 10 years, after this time they will be destroyed.

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, if you like.

WILL INFORMATION ABOUT THIS STUDY BE AVAILABLE ONLINE?
A description of this clinical trial will be available on [http://www.ClinicalTrials.gov](http://www.ClinicalTrials.gov). This website will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

A description of this clinical trial will also be available on [www.preparetrial.ca](http://www.preparetrial.ca). This website will not include information that can identify you. You can search this website at any time.

**WHAT IS THE COST TO PARTICIPANTS?**
Participation in this study will not involve any additional costs to you or your private health care insurance. If you are randomized into the intervention group, the materials that you require to complete the prehabilitation program will be provided to you.

**ARE STUDY PARTICIPANTS PAID TO BE IN THIS STUDY?**
You will not be paid for participating in this study.

**WHAT ARE THE RIGHTS OF PARTICIPANTS IN A RESEARCH STUDY?**
You will be told, in a timely manner, 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. If you would like to be informed of the results of this study, please let the study doctor know. The results of this study will also be available on the clinical trial registry (see the “Will information about this study be available online” section for more details).

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 or involved institutions for compensation, nor does this form relieve the study doctor or their agents of their legal and professional responsibilities.

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

**WHOM DO PARTICIPANTS CONTACT FOR QUESTIONS?**
If you have questions about taking part in the study, or if you feel that you suffered a research-related injury, you can talk to your study doctor, or the doctor who is in charge of the study at this institution. That person is:

**Daniel I McIsaac, MD, MPH, FRCPC**
The Ottawa Hospital, Monday to Friday, 9:00 a.m. to 5:00 p.m.
613-761-4940

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:

**Ottawa Health Sciences Research Ethics Board (OHSN-REB)**
613-798-5555 ext. 16719