The Royal's
Institute of Mental Health Research
affiliated with the University of Ottawa

INFORMED CONSENT FORM FOR PARTICIPATION IN A RESEARCH STUDY

Study Title: Adjunctive Methylphenidate extended release in patients with schizophrenia: a single-centre fixed dose cross-over open-label trial to improve functional and cognitive outcomes

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Sponsor: Institute of Mental Health Research

REB Number: 2021025

NCT Number: NCT05414058 (this study is registered on the ClinicalTrials.gov website)

INTRODUCTION

You have been invited to participate in a research study (a clinical trial) examining the effectiveness of a psychostimulant medication in patients with schizophrenia. If you are a Substitute Decision Maker, you are being asked to provide informed consent on behalf of a person who is unable to provide consent for him/herself. If the participant gains the capacity to consent for him/herself, your consent for them will end. Throughout this form, "you" means the person you are representing.

Before agreeing to take part in this project, it is important that you read the information in this research consent form. It includes details we think you need to know in order to decide if you wish to take part in the study. If you have any questions, ask one of the study researchers. You should not sign this form until you are sure you understand the information. 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 can discuss the study with your family doctor, a family member or close friends.

All research is voluntary. You are free to withdraw from the study at any time. Withdrawing from this study will not affect your relationship with any members of the research team or any care providers at Royal Ottawa Mental Health Centre (ROHCG) now or in the future. In addition, withdrawal will not result in any penalty or affect current or future health care.

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?

Psychostimulant medication is commonly used to treat attention deficit hyperactivity disorder (ADHD) and narcolepsy. It has been reported, in general, to help increase the ability to pay attention and stay focused. Psychostimulants have been studied in a few people with schizophrenia and the results seem

promising in improving negative and cognitive symptoms. But most of these studies used high doses of the medication and there is a risk of worsening of psychosis at higher doses. Therefore, it is not clear what benefits psychostimulants can provide for people with schizophrenia.

Health Canada, the regulatory body that oversees the use of medications such as psychostimulants in Canada, has not approved the sale or use of methylphenidate extended release (ER) (the psychostimulant used in this study) for people with schizophrenia. Health Canada has allowed methylphenidate ER to be used in this study.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to obtain information about the use of psychostimulants for people with schizophrenia. Specifically, to assess the use of the psychostimulant methylphenidate ER on functioning and cognitive symptoms in patients with schizophrenia.

WHAT OTHER CHOICES ARE THERE?

You do not have to take part in this study in order to receive treatment or care. You may continue with your standard or usual treatment. If you do not take part in this study, other research studies may be available to you.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Our goal is to recruit 24 participants for this pilot study. This study should take about three years to complete and results should be known after that.

WHAT WILL HAPPEN DURING THIS STUDY?

Should you decide to participate in this study, you will be randomized (i.e., flip of the coin) into one of two arms: 1) you will receive 4 weeks of a psychostimulant called methylphenidate ER, or 2) you will receive 4 weeks of treatment as usual (no additional treatments). After the 4 weeks, you will switch arms for another 4 weeks. So, if you initially received treatment as usual, you will now receive methylphenidate ER and if you were assigned to methylphenidate ER you will continue with treatment as usual. You will have an equal chance of being placed in either group.

The duration of the study is 12 weeks, including 8 weeks of treatment (4 weeks treatment as usual and 4 weeks treatment as usual + methylphenidate ER) and a follow-up visit at 12 weeks (end of study).

STUDY INTERVENTION

Apo-Methylphenidate ER (also called methylphenidate ER):
If you agree to take part in this study, you will be asked to take methylphenidate ER tablets orally, once a day for 4 weeks. The dose of methylphenidate ER will be 36 mg – this is lower than what is usually given to patients for other disorders such as ADHD as there may be a risk for worsening of psychosis at higher doses.

You will be asked to take the methylphenidate ER tablets once a day in the morning. It is recommended that you try to take it at the same time every day.

Treatment as Usual:
For both arms of this study, you can continue with your usual medications, meeting with members of your treatment team, and receiving your current treatments.

STUDY PROCEDURES

If you agree to take part in this study, you will be asked to meet with research staff for a baseline visit to determine if you meet all study requirements. At this baseline visit, we will carry out a physical exam including a pregnancy test, and we will obtain a medical history from you. You will be asked by a research assistant to complete a number of assessments. The assessments focus on cognitive symptoms such as memory and attention, positive and negative symptoms as well as functioning. The research assistant will ask you questions and you will be asked to complete a number of tasks on a tablet/computer. The first task is a tablet-based measure of functioning that assesses activities of daily living in a virtual reality environment. The second task is a tablet-based assessment of cognition.

During the study period, you will continue to be monitored clinically by your treatment team. You will be asked to meet with the research assistant once a week while you are receiving treatment (for 8 weeks), and at a 12-week follow-up visit. During the study visits, you will be asked questions about your consistent use of the medication, your experience of psychiatric symptoms and side effects, and you will have your weight, blood pressure and pulse rate taken. You will be encouraged to ask any questions about the study or the medication, and whether you would like to continue with the study. If any psychiatric or medical concerns are raised in a visit, then one of the on-site investigators of the study will be consulted and if needed, you will be scheduled to see a clinician, an on-site study investigator, or your primary clinician in the Program.

During the study visits, you will be asked to repeat the assessments. The visits for weeks 1, 2, 3, 5, 6, 7 and 12 are shorter check-ins and may take 30 minutes to complete. On weeks 4 and 8, you will also be asked to complete the tablet/computer tasks and these visits may take approximately an hour to complete. 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.

During this study, you will receive methylphenidate ER for a total of 4 weeks and then this medication will be stopped. If you received benefit from the methylphenidate ER medication, you may choose to discuss with your psychiatrist the possibility of adding this medication to your treatment regimen.

For inpatients, the study medication will be administered in the morning by your nurse, alongside your other medications. If you are given a day, overnight and/or weekend pass, the study medication will be provided to you as per standard care, in individual blister packs, along with your other regular medications. As per usual standard practice, you will be asked to return the individual blister packs to your nurse upon returning from the pass. If you are discharged from the inpatient unit during the study trial, you can continue in the study as an outpatient. However, if you are no longer a patient of the Royal and followed elsewhere, you will be withdrawn from the study.

Outpatients will receive the study medication at your weekly visit with the research assistant. The study medication will be provided to you in individual blister packs. In order to monitor compliance, you will be asked to complete a diary while on the study medication. You will also be asked to return the individual blister packs (used and unused) to the research assistant at your weekly visit.

Demographic and other information including chart number, diagnoses, medical and psychiatric history, and your current medications will be collected from your hospital clinical chart. This information will be entered into an electronic database that will be securely stored and maintained by research personnel. The database can only be accessed by people who are involved in this study.

OUTLINE OF EACH VISIT

Initial Appointment		Description of study provided, informed consent obtained
Baseline Visit		Determine eligibility: medical history, physical exam including pregnancy test, provide information about psychiatric symptoms, complete two tablet/computer tasks
Arm 1	Weeks 1-3 (30 min)	Provide information about medication use, psychiatric symptoms, side effects, weight, BP and pulse taken
	Week 4 (60 min)	Provide information about medication use, psychiatric symptoms, side effects, weight, BP and pulse taken, complete two tablet/computer tasks
Arm 2	Weeks 5-7 (30 min)	Provide information about medication use, psychiatric symptoms, side effects, weight, BP and pulse taken
	Week 8 (60 min)	Provide information about medication use, psychiatric symptoms, side effects, weight, BP and pulse taken, complete two tablet/computer tasks
Follow-up Visit	Week 12 (60 min)	Provide information about psychiatric symptoms, side effects, weight, BP and pulse taken, study wrap up

HOW LONG WILL PARTICIPANTS BE IN THE STUDY?

The duration of this study is 12 weeks including 8 weeks of treatment (4 weeks methylphenidate ER and 4 weeks of treatment as usual) and a follow-up visit at 12 weeks. All visits will be held at the ROMHC.

CAN PARTICIPANTS CHOOSE TO LEAVE THE STUDY?

Taking part in this study is voluntary. You can choose to end your participation in this research (called withdrawal) at any time without having to provide a reason. There will be no penalty or consequence if you decide to withdrawal at any point during this study. All data collected will halt at the time of your withdrawal. You will be asked about your willingness to proceed with the study at the start of each visit. This will be documented in your participant file.

CAN PARTICIPATION IN THIS STUDY END EARLY?

Your participation in the study may be stopped early, and without your consent, for reasons such as:

- You are unable to tolerate the study intervention or the study intervention does not work for you
- New information shows that the research is no longer in your best interest
- The research team decides to stop the study

- The research ethics board withdraws permission for this study to be continued
- The study is terminated by Health Canada
- If you plan to or become pregnant

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

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

Psychostimulants are usually well-tolerated, but after taking the methylphenidate ER medication there is the chance that you may experience side effects. The most common side effects include: excitability, energizing/agitated feeling, increased heart rate, headache, nausea, heartburn, dry mouth, loss of appetite, weight loss, blurred vision, sore throat, cough, and sinus pain. Rare side effects include fast or irregular heartbeat, dizziness, feeling lightheaded, muscle twitches or tics, skin rash, facial pain or swelling, bruising, tiredness, weakness, fever or feeling like you have the flu, yellow tinge in the eye or skin, dark-colored urine, persistent or painful erection. There is also the potential risk of relapse or worsening of your psychiatric symptoms such as depressed mood, anxiety, psychosis or mood fluctuations. Please review the Patient Information on Psychostimulants handout for a detailed list of side effects and other relevant information.

To reduce the risk of side effects, we will use a lower dose of methylphenidate ER (half the maximum dose in adults). Higher doses have been associated with increased risk of worsening of psychosis. You will be closely monitored for any signs of side effects. Treatment will be terminated in the event of significant psychiatric or medical symptoms or distress associated with the treatment, and options will be made available for other intervention to target this distress.

As psychostimulants have not been adequately studied in pregnant women, if you are a woman of child bearing potential, you will be asked to use a reliable method of contraception.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

It is anticipated that by participating in this study, you may benefit from an improvement in cognitive symptoms and functioning.

The overall purpose of this study is to learn more about the effectiveness of a psychostimulant, methylphenidate ER, for patients with schizophrenia. We hope the information obtained from this study will help us to better care for and treat patients with schizophrenia and other similar illnesses.

HOW WILL PARTICIPANT INFORMATION BE KEPT CONFIDENTIAL?

If you decide to participate in this study, the research team will only collect the information they need for this study.

Your research records may be reviewed by the Institute of Mental Health Research (IMHR) for quality purposes, and by the Research Ethics Board (REB) and/or Health Canada to check that the study is following proper laws and guidelines. You may be contacted by staff from the REB to answer questions about your experience in the study. This is done to improve the quality of our work.

Records identifying you will be kept confidential, to the extent permitted by applicable law, and will not be disclosed or made publicly available except as described in this consent document. Any personal information will be kept strictly confidential except as required or permitted by law.

The data produced from this study will be stored in locked filing cabinets in a secure office at the ROMHC. Electronic data will be stored in password-protected files on secured computers at the ROHCG. A log linking your name to your anonymous research code will be kept separately from the rest of your data. Only members of the research team will have access to the information. After the study completion, the data will be kept for 15 years after the last publication of this study. They will then be destroyed. You will not be identified in any publication or presentation of this study.

The tablet-based measures will be purchased from a company called VeraSci. As per their license agreement, data collected from these computer tasks such as participant ID, visit number and measure results will be stored on VeraSci servers and VeraSci can use combined data in an anonymous manner. No identifying information from you would be entered or provided to VeraSci. While the study team will take precautions to protect your confidentiality, we cannot completely guarantee the protection of your privacy, as VeraSci is subject to American privacy laws, as well as the Patriot Act.

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

WHAT IS THE COST TO PARTICIPANTS?

Participation in this study will not involve any additional costs to you. The medications will be provided to you as part of the study.

ARE STUDY PARTICIPANTS PAID TO BE IN THIS STUDY?

You will receive $20.00 at every visit that you attend.

STUDY RESULTS

You will receive a copy of the final study results if you provide the required information in the signature pages below. Findings from this study are expected to be reported at scientific conferences and to be published in scientific journals. Your identity will remain confidential. Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated.

COMPENSATION FOR INJURY

If you suffer a physical injury from participating in this study, medical care will be provided to you in the same manner as you would ordinarily obtain any other medical treatment. In no way does signing this form waive your legal rights nor release the study doctors or involved institutions from their legal and professional responsibilities.

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 study is complete. Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected. **A copy of the signed consent form will be provided to you.**

Research Ethics Board Contact
This study has been reviewed and approved by the Royal's Institute of Mental Health Research REB as study #2021015. If you have any ethical concerns about the study, or the way it is conducted, please contact the REB office: tammy.beaudoin@theroyal.ca.

Whom do participants contact for questions?
All study related questions should be directed to:
Dr. Naista Zhand, Tel: (613)722-6521 Ext. 6780

Signature Page

The research project has been explained to me, and my questions have been answered to my satisfaction. I understand the information in this consent form, and the information provided in the Participant Handout. I allow access to my medical records and related personal health information as explained in this consent form.

I have the right not to participate and the right to withdraw without penalty at any time. The potential harms and benefits (if any) of participating in this research study have been explained to me. I have been told that I have not waived my legal rights nor released the investigators or involved institutions from their legal and professional responsibilities. I know that I may ask now, or in the future, any questions I have about the study. I have been told that records relating to me will be kept confidential and that no information will be disclosed without my permission unless required by law. I have been given sufficient time to read the above information. Any personal information that could identify me, such as my name will never be associated with the publication of the data.

☐ I consent to participate in this study. I have been told I will be given a signed copy of this consent form.

☐ I agree that the research coordinator can access my medical file to collect demographic information and other information such as diagnosis, medication, service usage etc

Signature of Participant	Name of Participant	Date

Signature of Person Obtaining Informed Consent	Name of Person Obtaining Informed Consent	Date

Substitute Decision Maker (if applicable):

I was present when _____ (name of participant) read this form and gave his/her signed consent. I have also been informed of the risks and benefits related to this study.

Name of Substitute Decision Maker (please print): _____

Signature of parent/guardian: _____ Date: _____

Request to be informed of final study findings

*I would like to receive summaries of the study findings

_____ Initials of Participant

Participant's email (or postal) address**:** _____