Informed Consent Form for Participation in a Research Study

**Study Title**: **Can**adian Adaptive Platform Trial of **Treat**ments for **COVID** in Community Settings (CanTreatCOVID)

**Sponsor’s Study ID**: [REB application ID once available]

**Study Doctor**: Dr. Andrew Pinto, Upstream Lab, MAP/Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute, Unity Health Toronto, andrew.pinto@utoronto.ca, 416-864-6060 ext. 76148

**Sponsor:** Unity Health Toronto

**Funders:** Canadian Institutes for Health Research (CIHR), Health Canada (HC), the Public Health Agency of Canada (PHAC)

**Emergency Contact Number** (5 am ET – 8 pm ET, Monday-Friday): 1-800-XXX-XXXX\_

INTRODUCTION:

[for Substitute Decision Maker who consents on the patient’s behalf] As 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.

You are being invited to consider participating in a clinical trial (a type of study that involves research). You are invited to participate in this trial because you are infected with COVID-19 and are at a higher risk of developing severe illnesses due to the infection. 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.

The study staff will tell you about the study timelines for making your decision. You will be asked to make your decision within 1-2 days as many COVID-19 drugs are recommended to be taken within the first 5 days after the onset of symptoms in order to be effective. This is necessary because it will take the study team time to review your current medications to make sure they are compatible with the study drugs and ship the medication to you so that you can start taking them within 5 days of your symptoms starting.

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?

*Describe any conflict of interest that exists or may appear to exist as it relates to any of the investigators, study staff or member of their immediate family. A conflict of interest exists if there is a potential benefit to the investigator(s), study staff or member of their immediate family beyond the professional benefit from academic achievement or presentation of the results. Examples include, but are not limited to, speaker’s fees, travel assistance, consultant fees, honoraria, gifts, and intellectual property rights such as patents. A declaration of conflict of interest should include the identity of the person with the conflict of interest, the type of incentive or inducement, and its source. See examples below.*

WHAT IS THE BACKGROUND INFORMATION FOR THIS STUDY?

*Each participating site must ensure that the standard or usual treatment described in below matches the standard of care at that site. Site specific differences must be reflected in the Centre Initial Application and the site-specific consent form.*

Vaccines and public health measures such as masking have reduced the spread of COVID-19 and prevented health systems from being overwhelmed. However, reduced vaccine effectiveness against the continuously evolving virus remains a significant concern. Most antiviral drugs currently approved in Canada need IV infusion thus can only be provided to patients in the hospital or specialized clinics. Yet, more and more patients – including those at a higher risk of becoming severely ill – choose to seek care in the community. Evidence that supports these out-patient drugs is weak. There are no head-to-head comparisons among these drugs, and it is also unclear whether and to what degree these existing drugs are effective in partially or fully vaccinated patients, which includes most of the Canadian population. To date, no drug has been evaluated specifically for its potential in reducing the likelihood of long COVID. Antiviral drugs that are based on strong evidence, that are effective, safe and affordable, and that can be used early on in the community to prevent severe illnesses and reduce hospitalizations are urgently needed.

The study will use a design called an adaptive platform trial. Adaptive platform trials can compare multiple interventions for a single disease at any given time while allowing for new interventions to be added if they become available or removed if they are not effective or better than the other interventions. Adaptive platform trials have helped provide rapid evidence in identifying what does and does not work to treat COVID-19 for in-patients. This study will compare the effectiveness of up to three interventions amongst each other and to the standard of care. Intervention(s) to be added and in what order will be determined by the Canadian COVID-19 Out-Patient Therapeutics Committee, an expert group consisting of study doctors, COVID-19 treatment guideline developers and infectious disease and public health experts, based on most recent evidence available.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to: 1) evaluate the short- and long-term effectiveness of existing and new COVID-19 interventions for non-hospitalized patients using an adaptive platform trial study design and 2) provide rapid evidence to guide clinical, health system, and public health decision making and planning within Canada and internationally.

WHAT OTHER CHOICES ARE THERE?

You do not have to take part in this study in order to receive treatment or care. If you choose not to participate in this study, you will continue to receive standard of care. You may also be enrolled in other studies. Please talk to your usual doctor or the study doctorabout the known benefits and risks of these other options before you decide to take part in this study. Your usual doctoror the study doctor can also discuss with you what will happen if you decide not to undertake any study intervention at this time.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

It is anticipated that about 12,000 patients will take part in this study from research sites located in 6 provinces across Canada. This study will continue on an ongoing basis unless 1) the COVID-19 pandemic is no longer a public health problem; or 2) the effectiveness of all study interventions is known and there is no new intervention to be tested.

WHAT WILL HAPPEN DURING THIS STUDY?

ASSIGNMENT TO A GROUP

If you decide to participate, 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. Depending on the number of intervention groups the study has when you enroll, you will have a 1 in 2 chance of being placed in any group, including the standard of care group. That is, you will have 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. Once randomized, you will be told which group you are in.

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| --- | --- |
| **Study group** | **Number of participants** |
| Standard of care | ~ 3,000 |
| Intervention group #1: Nirmatrelvir/ritonavir (Paxlovid™) | ~ 3,000  |
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Once a certain number of participants have entered the intervention phase of the study from all of the research sites combined, no more participants will be enrolled into the study at any site. For example, if the maximum number of participants have already been enrolled in an intervention group, or the study team makes the decision to stop an intervention group early for safety reasons, you may not be randomized to an intervention group, despite being enrolled in the study. It is possible that you may finish the screening phase and be ready to enter the intervention phase of the study, but not be enrolled into the study.

WHAT IS THE STUDY INTERVENTION?

The study intervention is existing or new drugs for COVID-19 infection for non-hospitalized patients as determined by the Canadian COVID-19 Out-Patient Therapeutics Committee. Please consult the handout you have been provided about the study drugs.

Intervention group #1: If you are randomized to this group, you will be given Paxlovid™. You will take nirmatrelvir 300mg (2 pink tablets) and ritonavir 150mg (1 white tablet) together by mouth twice a day for 5 days.

Standard of care group: If you are randomized to this group, you will receive usual care provided by your usual doctor according to treatment guidelines at the time of your enrollment. You may also be advised to get extra rest, drink plenty of fluids, and try over-the-counter medications for symptom relief.

WHAT ELSE DO I NEED TO KNOW ABOUT THE STUDY INTERVENTION?

If you have side effects while you are on this study, the study doctor may make changes to the intervention.

WHAT ARE THE STUDY PROCEDURES?

Non-Experimental Procedures

You will not be asked to complete any additional diagnostic tests as part of this study. However, your usual doctor may request you to do some tests as part of your routine care.

Experimental Procedures

If you are randomized to one of the intervention groups, the study drug will be couriered to you within 1 - 2 days from randomization. Please make sure that you take the study drug as per the accompanying instructions as soon as you receive the delivery. If you receive your study drug beyond the recommended time window (e.g., more than 5 days after symptom onset) you should NOT take the study drug, but please contact the research staff to arrange a return of the study drug at no cost to you. If you have any concerns about the intervention you receive, please also contact the research staff for help.

Questionnaires

You will be asked to complete 7 surveys in total, 1 before you begin the study (baseline survey) and 1 each at 21 days, 28 days, 90 days, 36 weeks, 12 months and 24 months from randomization. The purpose of the baseline survey is to understand your baseline health and to collect sociodemographic information about you, including your date of birth, sex and gender, race, education level, household income, income source and whether you live in an urban or rural area. We will also collect your health card number, phone number, mailing and email address, postal code, and ask for your permission to use text messaging and contact your study doctor, caregiver/alternative contact person if needed. The purpose of the 21 and 28day surveys is to understand how the study intervention affects your short-term health (e.g. hospitalization and/or death, time to recovery, symptom severity, health services use, and quality of life). The 90-day and 36-week surveys aim to understand how the study intervention affects your long-term health, in particular, the development of long-COVID. The 12-month and 24-month surveys aim to collect your quality of life data. Each survey will take about 30 minutes to complete and can be done online or by telephone with the help of a study staff, if preferred or if you don’t have internet access. If you would like to take a break when doing the survey, you can do so by stepping away from your computer then resuming when possible or asking the research staff to call back at a time convenient for you both.

The information you provide is for research purposes only. Some of the questions are personal. You might feel uncomfortable or upset to disclose your personal information and experiences. You can choose not to answer questions if you wish.

Even though you may have provided information on a survey, these responses will not be reviewed by your health care team or study team - if you wish them to know this information, please bring it to their attention.

Participant Diaries

You will be asked to complete a diary each day for 14 days after randomization. You will be asked to record how you take the study drug if you are in one of the intervention groups, if you stopped taking the study drug early, your symptoms, the severity of your symptoms, and if you visited a primary care provider or specialist, an emergency department, or were admitted to a hospital. The diary can be completed online or by telephone with the help of a study staff if preferred or if you don’t have internet access.

You will receive a call from a study staff if you do not complete your diary for at least 2 consecutive days before Day 7 and Day 14. The staff will try to contact you for 3 times over 3 days before we stop.

WHAT ARE THE RESPONSIBILITIES OF STUDY PARTICIPANTS?

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

* Tell the study doctor/pharmacist about your current medical conditions and vaccination status.
* Tell the study doctor/pharmacist about all prescription and non-prescription medications and supplements, and check with the study doctor/ pharmacist before starting, stopping or changing any of these. This is for your safety as these may interact with the intervention you receive on this study.
* Tell the study doctor/staff if you are planning or become pregnant, or need to nurse (breastfeed) a baby, or father a child.
* Tell the study doctor/staff that you are participating or planning to participate in another COVID-related study.
* Give the study pharmacist permission to contact your usual pharmacy to review your regular medications
* Give the research staff permission to inform your usual doctor of your study participation and any incidental finding related to your health.
* Give the research staff permission to contact you or your caregiver/alternative contact person for follow-up 24 months from your enrollment in the study.
* Give the study doctor permission to access your administrative data on health services use 24 months from your enrollment in the study.
* Complete study procedures (e.g., taking the study drug if you are in an intervention group and completing the surveys and patient diary) on time.
* Return any unused study drug to the study pharmacy in your province.

If you are enrolled in one of the intervention groups, please note that the study drug is for you alone and must not be shared with others. If someone accidentally takes the study drug, they should immediately contact their doctor or go to the nearest emergency department.

HOW LONG WILL PARTICIPANTS BE IN THE STUDY?

The duration of the intervention across study groups is different. For Paxlovid™, the intervention will last for 5 days.

You will be followed up online or by telephone daily for 14 days, then at 21 days, 28 days, 90 days, and 36 weeks from randomization.

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. Your withdrawal from the study will not have any impact on your care. If you choose to withdraw from the study, you are encouraged to contact the study doctor or the 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 or the study staff know. However, this would also mean that you withdraw from the study. In the event that data collected about you has already been aggregated and reported, this will not be possible.

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:

* You are no longer considered eligible for the study
* New information shows that the study intervention is no longer in your best interest
* The study doctor no longer feels this is the best option for you
* You are unable to tolerate the study intervention

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 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 participating 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 daily diary and surveys are monitored closely to see if you have side effects. Additionally, a research staff will contact you 1 and 4 days after you start taking the study drug to ensure there are no immediate and severe concerns. When possible, other medicine will be given to you by your usual doctor to make side effects less serious and more tolerable. Many side effects go away shortly after the study intervention is stopped, but in some cases side effects can be serious, long-lasting, permanent, or may even cause death.

Risks and side effects related to the experimental interventions and the likelihood of having the risks and side effects may be different. New drugs may have serious side effects not yet be discovered, or long term effects that are unknown. It is possible that other drugs (prescription and non-prescription drugs), vitamins, or herbals can interact with the study intervention. This can result in either the intervention not working as expected or result in severe side effects.

Known side effects for Paxlovid™ and likelihood of happening:

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| * Allergic or hypersensitivity reactions: eg, hives, skin rash, swelling of the mouth, lips or face, hoarseness, throat tightness, trouble swallowing or breathing
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| * Altered or impaired sense of taste
 | 6% |
| * Diarrhea
 | 3% |
| * Nausea
 | 1% |
| * Vomiting
 | 1% |
| * Headache
 | 1% |
| * Muscle pain
 | 1% |
| * High blood pressure
 | 1% |

WHAT ARE THE REPRODUCTIVE RISKS?

The effects that some study drugs may have on an unborn baby (fetus) are unknown. You must not become pregnant or father a baby while taking the study drug and for a period of time after the last dose. The study doctor will discuss family planning with you to ensure that you do not become pregnant or father a baby during the study. You should discuss these risks with your sexual partners of the opposite sex.

Women should not breastfeed a baby while taking the drug and for 14 days after the last dose because the drugs used in this study might be present in breast milk and could be harmful to a baby.

Reproductive risks for Paxlovid™:

PaxlovidTM is not recommended in pregnancy because little is known about its effects on the baby. Breastfeeding is also not recommended when taking the drug and before 14 days after the last dose. Paxlovid’sTM effect on fertility in either men or women is also not known.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

If you agree to take part in this study and are randomized to one of the intervention groups, the intervention in that group may or may not be of direct benefit to you. We hope the information learned from this study will help gain scientific knowledge to help other people infected by COVID-19 in the future.

HOW WILL PARTICIPANT INFORMATION BE KEPT CONFIDENTIAL?

***Note:*** *If there will be disclosure of personal identifiers, i.e., disclosed on any research-related information/documents including samples or scans, or as part of the unique identifier, these disclosures must be justified in the REB application and approved. Please ensure that you are aware of institutional and REB policies with respect to the disclosure of personal identifiers.*

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 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. Your name, address, email, or other information that may directly identify you will not be used. The records received by these organizations may contain your disclose identifiers e.g., participant code, sex, and 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 absolutely secure. We do not recommend that you communicate sensitive personal information via e-mail.

This study requires the transfer of identifiable information to the study pharmacist at the study pharmacy for the purposes of conducting a medication review to identify any potential drug-drug interactions and for arranging the courier of the study drug. The following information will be transferred:

* Name
* Date of birth
* Phone number
* Mailing address, including postal code
* Health card number

This study requires the transfer of your health card number to [ICES, PopulationData BC, Alberta Health Services, Manitoba Centre for Health Policy, INESSS, Newfoundland and Labrador Centre for Health Information] for the purposes of understanding the impact of the intervention on your use of health services.

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 conferences and in journals both within Canada and internationally.

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

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

Any information, sent outside of Canadian borders may increase the risk of disclosure of information because the laws in those countries dealing with protection of information may not be as strict as in Canada. However, all study data that are transferred outside of Canada will be coded (this means it will not contain your personal identifying information such as your name, address, medical health number or contact information). Any information will be transferred in compliance with all relevant Canadian privacy laws. By signing this consent form, you are consenting to the disclosure of your coded information to organizations located outside of Canada.

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

Your family doctor/health care provider may be informed that you are taking part in the study or if there is any incidental finding related to your health so that you can be provided with appropriate medical care. **If you do not want your family doctor/health care provider to be informed, please discuss this with the study team**.

WILL information about this study BE available online?

A description of this clinical trial will be available on <http://www.clinicaltrials.gov> and <https://cantreatcovid.org/>. 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. The study drug will be supplied at no charge while you take part in this study. The costs of your medical care will be paid for by your provincial medical plan to the extent that such coverage is available.

ARE STUDY PARTICIPANTS PAID TO BE IN THIS STUDY?

*Each participating site must ensure that the information below matches the compensation/reimbursement provided at that site. Site specific differences must be reflected in the Centre Initial Application and the site-specific consent form.*

If you decide to participate in this study, you will receive $30 each at the beginning baseline survey, and at 21 days, 28 days, 90 days, and 36 weeks after your enrollment as compensation for your time to complete study related activities. Compensation will be provided as a lump sum once you complete the baseline survey.

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

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. The results of this study will 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, 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 participating 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 is in charge of the study at this institution. That person is:

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| --- | --- | --- |
| Andrew Pinto |  | 416-864-6060 ext. 76148 |
| Name |  | Telephone |

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:

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| --- | --- | --- |
| The Chair of the Unity Health Toronto Research Ethics Board |  | 416-864-6060 ext. 2557 |
| Name |  | Telephone |

**Can**adian Adaptive Platform Trial of **Treat**ments for **COVID** in Community Settings (CanTreatCOVID)

SIGNATURES

* All of my questions have been answered,
* I understand the information within this informed consent form,
* I allow access to medical records, administrative data 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 understand that my family doctor/health care provider may be informed of study participation and/or any incidental findings related to my health,
* I understand that my usual pharmacy may be contacted for review of my regular medications
* I agree [or for Substitute Decision Maker: agree to allow the person I am responsible for] to take part in this study.

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| Signature of Participant/ Substitute Decision-Maker |  | PRINTED NAME |  | Date |

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| If consent is provided by Substitute Decision Maker:  |  |
| PRINTED NAME of Participant |

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| 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.

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| PRINT NAME of Interpreter  |  | Signature |  | Date |

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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.

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| PRINT NAME of witness |  | Signature |  | Date |

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Relationship to Participant