PARTICIPANT INFORMATION AND CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

Sponsor / Study Title:	**Brain and Cognition Discovery Foundation / "Randomized, Double-Blinded, Placebo-Controlled Study Evaluating Vortioxetine for Cognitive Deficits in Persons with Post-COVID-19 Condition"**
Protocol Number:	**BCDF002**
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Introduction

You are being asked to take part in a research study. Before agreeing to participate in this study, it is important that you read and understand the following explanation of the proposed study procedures. The following information describes the purpose and procedures of this study. It also describes your right to refuse to participate or withdraw from the study at any time. In order to decide whether you wish to participate in this research study, you should understand enough about its risks and benefits to be able to make an informed decision. This is known as the informed consent process.

Please ask the study team to explain any words you do not understand before signing and dating this consent form. Make sure all your questions have been answered to your satisfaction before signing and dating this document.

An investigator on this study is being paid by Lundbeck, the company supplying the study drug, for activities that are not part of the study. These activities may include, for instance, consulting, serving on advisory boards, or giving speeches. Please speak with your study doctor if you have questions about this.

Background

You have been asked to take part in this research study because you are currently suffering from post-COVID-19 condition.

According to the World Health Organization (WHO), post-COVID-19 condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19, with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue (feeling tired), shortness of breath, and cognitive dysfunction ("brain fog"), but also others, and generally have an impact on everyday functioning. Symptoms may be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms may also fluctuate or relapse over time.

Purpose

The purpose of this study is to evaluate the efficacy of vortioxetine (study drug) in improving cognition among individuals with post-COVID-19 condition. "Cognition" refers to intellectual functions such as thinking, understanding, learning, and remembering.

Vortioxetine is an antidepressant medication approved by Health Canada for the treatment of major depressive disorder (MDD). In addition, vortioxetine has been reported to have a beneficial effect on cognitive areas such as executive function, attention/speed of processing, and memory, that are commonly affected negatively by MDD. Vortioxetine is recognized by Health Authorities in the European Union and many other countries as having a benefit on cognitive dysfunction (loss of intellectual functions) in patients with MDD. The use of vortioxetine in this study is investigational. An investigational use is one that is not approved by Health Canada. Half of the study participants (100 participants) will be randomly chosen (like the flip of a coin) to receive vortioxetine 10 mg/day for the first two weeks of the study treatment period. This dose will be increased to 20 mg/day from Week 2 to 8 in consultation with the study doctor. The other half of the participants (100 participants) will receive placebo (medically inactive substance) for the duration of 8 weeks. Your participation in this study will last approximately 10 weeks.

Participants over 65 years of age will receive vortioxetine 5 mg/day for the first 2 weeks, then transitioned to vortioxetine 10 mg/day for the remaining 6 weeks of the study.

You **should not be enrolled in this study** if you have/are:

1. Current symptoms due to a diagnosis of major depressive disorder or bipolar disorder.

2. Pre-existing conditions that may cause cognitive impairment, or symptoms similar to those seen in post-COVID-19 condition (for example, ADHD [attention-deficit/hyperactivity disorder], major neurocognitive disorder, schizophrenia).
3. Not able to provide written, informed consent.
4. Not able to follow study procedures.
5. Known intolerance to vortioxetine and/or prior use of vortioxetine with demonstrated efficacy.
6. Previous hypersensitivity reaction to vortioxetine or any components of the formulation. Angioedema (swelling of the deeper layers of the skin) has been reported in patients treated with vortioxetine.
7. Currently taking antidepressants or have in the past 4 weeks prior to study start. If you are currently taking antidepressant(s), you will be required to be off the antidepressant(s) for 2-4 weeks prior to the start of the study. In some cases and upon the discretion of the study doctor, you may continue to take your antidepressant(s) during your participation in the study. Combining vortioxetine with another antidepressant would be considered investigational, as the safety and efficacy of this combination is unknown.
8. Current alcohol or substance use disorder.
9. Taking other medications for cognitive dysfunction (for example, psychostimulants).
10. Taking any medication for a general medical disorder that in the opinion of the study doctor may affect cognitive function.
11. Used benzodiazepines within 12 hours of cognitive assessments.
12. Drank alcohol within 8 hours of cognitive assessments.
13. A physical, cognitive, or language impairment that might affect cognitive assessments.
14. A reading disability or dyslexia and clinically significant learning disorder.
15. Had electroconvulsive therapy (ECT) in the last 6 months.
16. A history of moderate or severe head trauma (for example, loss of consciousness for less than 1 hour), other neurological disorders, or medical conditions that in the opinion of the study doctor are likely to affect the central nervous system.
17. Pregnant and/or breastfeeding.
18. Received investigational agents as part of a separate study within 30 days of the screening visit.
19. Actively suicidal/presence of suicidal ideation or evaluated as being a suicide risk.
20. Currently receiving treatment with antidepressants, antibiotics such as linezolid, or intravenous methylene blue.
21. Serotonin syndrome.
22. Abnormal bleeding.
23. Previous history of mania/hypomania.
24. Angle closure glaucoma.
25. Hyponatremia (a condition where sodium levels in the blood are lower than normal).
26. Moderate hepatic (liver) impairment.
27. Active seizure disorder/epilepsy, not controlled by medication.
28. Presence of any unstable medical conditions.

If you are already taking other antidepressants, you may enroll in the study only upon the discretion of the study doctor. It is possible that vortioxetine may augment/enhance the effects of your current antidepressant medication. However, the safety and efficacy of the combination of vortioxetine and other antidepressants has not been well characterized and should be considered investigational.

This study will be sponsored by the Brain and Cognition Discovery Foundation (BCDF). The BCDF is an organization based in Toronto, Ontario, Canada led by Dr. Roger S. McIntyre.

This consent form is for individuals with a diagnosis of post-COVID-19 condition.

Study Design

This is an 8-week, randomized, double-blinded, placebo-controlled study. "Double-blinded" means neither you nor the study team will know if you are getting vortioxetine or placebo. You will be receiving vortioxetine or placebo daily for a period of 8 weeks. You will need to take the study drug daily as prescribed in order to take part in the study.

You will be asked to participate in 5 study visits. As part of this study, your mood, cognition, functioning, overall well-being, as well as lifestyle factors will be assessed. There may be instances when additional visits are required to complete study procedures.

***Due to the ongoing nature of the pandemic, you may choose to participate in ALL study visits remotely. Study visits will be conducted through online platforms (for example, Zoom) and/or telephone. The study drug will be mailed to you, or may be available for pickup at the BCDF office. You will also be mailed/emailed a blood requisition form to complete at your local blood lab. Female participants will be required to complete a home pregnancy test or provide blood/urine sample to the blood lab to confirm they are not pregnant.**

Visits with the study doctor will occur remotely, via the secure online video conference platform or telephone. If necessary/requested by you or study doctor, in-person visits may be scheduled as well.

A total of approximately 200 participants will be enrolled in this study; 100 individuals will receive vortioxetine, and the remaining 100 individuals will receive placebo.

Study Visits and Procedures

Study Doctor Assessment: You will see the study doctor during the same weeks as the study visits with the research team for ongoing monitoring of your care. Some or all visits may be conducted remotely/online through a secure platform. As part of your care, a medical file will be opened for you at CRTCE/KJK Healthplex and the study doctor will document each visit in your

medical file at CRTCE/KJK Healthplex. Your medical records will be protected by the highest standards under Canadian law.

Self-Report Questionnaires: You may choose to complete self-reported questionnaires during your visit with the research team or within 24 hours of the visit. If you choose to complete these questionnaires before/after the visit, you will be emailed a secure and anonymized link to the questionnaire.

Exploratory Blood Analyses: If you are seen in-person, you may volunteer to provide a blood sample for exploratory analyses. The sample will be collected at a local blood lab (Mount Sinai Hospital), followed by processing and storage of the sample at the Biospecimen Repository and Processing Lab (Lunenfeld-Tanenbaum Research Institute, Sinai Health). You may also have blood drawn at the same time for clinical purposes at Mount Sinai Hospital. The clinical blood tubes will be delivered to another local lab (Dynacare, LifeLabs) for analyses. Alternatively, you may also have blood drawn separately for clinical analyses at a local blood lab near you - this will result in two separate blood draws. Blood work is done at baseline and week 8 (endpoint).

Screening Visit (Visit 0)

The following will be completed during this visit:

- Informed consent process will be completed.
- The study team will carry out an interview to confirm your suitability for the study.
- Your demographics and anthropometrics will be documented, including current physical activity levels.
- Medical/psychiatric and medication history will be recorded.
- Your mood, functioning, and overall well-being will be assessed.
- Study doctor assessment.

Reminders:

- Please do not consume any recreational substances (for example, alcohol, marijuana) 8 hours before **any** study visit.
- Some medications may be restricted within 8-10 hours of study visits.
- Please fast (no food or drinks, except for water) for at least 8 hours prior to bloodwork (baseline and end-of-study visits). Only water can be consumed during the fasting period.

Baseline (Visit 1)

The following will be completed during this visit:

- Anthropometrics (for example, weight, hip/waist circumference, height, blood pressure) and physical activity levels will be documented (will be self-reported by participants for remote study visits).
- Adverse events will be recorded.
- Study staff assessments and self-completed questionnaires about cognition, mood, and well-being.

- Fasting (no food or drinks, except for water for a minimum of 8 hours) bloodwork for exploratory and standard clinical analyses. This testing is done for research and clinical purposes. Approximately 20 mL of blood will be drawn in 4-5 blood tubes. You are welcome to request a copy of your clinical results from your study doctor.
- Optional functional magnetic resonance imaging (fMRI) participation for select participants (more information below).
- Receive study treatment (vortioxetine [10 mg] or placebo) after assessment by a study doctor. For participants over 65 years of age, the starting dose is 5 mg for two weeks.
- Pregnancy test (urine or blood).
- The research staff will dispense the study drug to you.

Week 2 (Visit 2)

The following will be completed during this visit:

- Anthropometrics (for example, weight, hip/waist circumference, height, blood pressure) and physical activity levels will be documented (will be self-reported by participants for remote study visits).
- Study staff assessments and self-completed questionnaires about cognition, mood, and well-being.
- Adverse events.
- Study treatment dosage increased to 20 mg by the study doctor. For participants over 65 years of age, the dosage will be increased to 10 mg by the study doctor. The research staff will dispense the study drug to you per the study doctor's recommendations.

Week 4 (Visit 3)

The following will be completed during this visit:

- Anthropometrics (for example, weight, hip/waist circumference, height, blood pressure) and physical activity levels will be documented (will be self-reported by participants for remote study visits).
- Study staff assessments and self-completed questionnaires about cognition, mood, and well-being.
- Adverse events.
- Study doctor assessment.

Week 8 (Visit 4)

The following will be completed during this visit:

- Anthropometrics (for example, weight, hip/waist circumference, height, blood pressure) and physical activity levels will be documented (will be self-reported by participants for remote study visits).
- Study staff assessments and self-completed questionnaires about cognition, mood, and well-being.
- Optional fMRI participation. You will be asked to complete a brief cognitive task during the fMRI imaging.

- Adverse events.
- Fasting (minimum of 8 hours) bloodwork for exploratory and standard biomarker and testing. This testing is done for research and clinical purposes. Approximately 20 mL of blood will be drawn in 4-5 blood tubes. You are welcome to request a copy of your clinical results from your study doctor.
- Study doctor assessment.

fMRI Participation (Optional)

What is an fMRI?

Functional MRI records brain activation signals indirectly from changes in blood flow and oxygenation that arise from activated neurons. You will have your brain scanned while completing a series of neuropsychological tests. The fMRI brain scan will provide a high spatial resolution map of the brain areas activated during task performance and the connection between these activated areas. Additionally, you may be completing these same tasks outside of the fMRI with pen and paper. This will help us ensure that testing done during fMRI is valid. In both cases, a special video camera will record your eye movements to determine where you are looking.

Why is brain imaging used in this study?

Brain imaging is used in this study to better understand the brain measures of anatomy, physiology, and function in people with post-COVID-19 condition. In this study four types of scans will take place: MRI to obtain an anatomical image of your brain, one to measure brain chemistry, another one will measure the electrical connections between neurons, and the fourth will measure blood flow in the small vessels of the brain.

What can I expect if I decide to participate in the fMRI scan?

fMRI scans are completed at an external institution (for example, Sunnybrook Health Sciences Centre, University of Toronto). The research staff will let you know exactly where you are going for the fMRI. You will be asked to participate in two scans at the start of the study (baseline) and at the end of the study (week 8). Please note that only a limited number of participants will be given the opportunity to participate in the fMRI component of the study.

Prior to your *f*MRI scan, you will be trained on how to perform the cognitive test. Before the scan begins, you will be asked to remove any magnetic metals that you may be wearing (for example, watch, jewelry). You will be asked to lie on a padded bed that will be moved into a tunnel-like machine for the fMRI scan of your brain. Because you will be inside the machine during the scan, you may not be able to see the technologist operating the machine or the investigators. However, there is an intercom system that will allow you to talk with them at any time. If you feel uncomfortable during the scan and you wish to discontinue the procedure, you will be taken out of the machine at your request.

We will obtain a series of MRI scans, separated by short breaks, and the entire procedure will take approximately one hour. You should try to remain as still as possible during each scan. Movement will not be dangerous to you in any way, but could blur the picture of your brain. You will hear moderately loud knocking or beeping during the scan when the MRI machine is in operation. Although you may find this to be unsettling, the machine cannot hurt you in any way. You will be provided with earplugs or earphones to drown out the noise, as well as foam pads to make you as comfortable as possible.

In addition, your participation may involve additional procedures and interacting with one or more devices that are being designed to operate inside the MRI scanner. These include:

- wearing a specially-designed plastic “tool” that enables motion of the body to be tracked using a camera;
- wearing a small number of electrodes to measure the electrical conductivity of your skin;
- wearing a small number of electrodes to measure activation of your muscles;
- wearing or using various devices to enable performance of behavioural tasks during fMRI (goggles or glasses to view video, words, or pictures; headphones to hear sounds; transducers to feel vibrations; buttons to make keypress responses; steering wheel and foot pedals for driving tasks; or a tablet to draw or make writing responses);
- wearing virtual reality (VR) equipment (head-mounted display, data glove) to enable behavioural testing to be undertaken in a virtual environment similar to that of the real world;
- recording video of your eye movements to determine where you are looking;
- participating in any of these procedures in a mock, “simulated” MRI scanner, to optimize the experimental study plan prior to working inside the magnet.

Who should NOT participate in fMRI imaging?

You should not participate if you have a cardiac pacemaker or any other metal in your body such as metal implants, aneurysm clips, pieces of shrapnel, wires, body piercings, and metal stitches from surgery. These materials will corrupt the fMRI measurements by producing unwanted signals. Dental fillings are acceptable. We will check all of these issues by having you complete a screening form to ensure that you can undergo MRI measurements safely and to determine whether you are eligible to participate.

What are the risks and harms of participating in an fMRI scan?

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. Please inform the study team immediately about any side effects or study-related injuries that you experience.

While all forms of diagnostic medical procedures involve some risk, the known hazards associated with MRI scanning are negligible. There are no known adverse effects of MRI scanning on biological tissues that are not fully reversed after the end of the investigation. The MRI scanner operates within the US Food and Drug Administration (FDA) limits to ensure that even temporary effects are not severe. Some people may experience claustrophobia (5-10% possibility) because the magnet may feel cramped/confining and makes loud knocking sounds. You will be connected by intercom to an operator who can interrupt and remove you from the scanner at any time. In addition, some MRI scans can cause some people to feel knocking, tapping, or buzzing sensations in their arms or legs. These feelings are completely harmless. You may feel fatigued or sleepy after lying in the magnet.

This MRI study was designed for research, not for medical diagnostics, and cannot rule out the discovery of possible brain abnormalities. There is a small possibility that your research MRI scans might reveal unexpected medical findings. In this case, the study doctor may consult a radiologist. If the radiologist determines that further medical efforts are warranted, the study doctor will inform you and assist you to receive appropriate health care. The radiologist will only be consulted in the case of incidental findings, and will not be reviewing every scan. As these are research MRIs, they may not be reviewed until the end of the study or sometime thereafter.

You will be told about any new information that might reasonably affect your willingness to continue to participate in this study as soon as the information becomes available to the study staff.

<u>Transition to Standard Care Upon Completing the Study</u>

Upon completing the 8-week study, if you benefit from this study drug, you are encouraged to continue the treatment with your most responsible physician (MRP). Please note that your private medical insurance (if any) or the public health insurance plan may not cover the cost of vortioxetine. Should you wish to continue to use this drug post-study where there is no coverage, you will be personally responsible for the costs. Please also note that the study doctor is not able to provide ongoing care beyond the study and is not considered the MRP at any time point.

If you do not experience any improvement upon study completion in mood or cognition, the study drug will be gradually discontinued over a two-week period upon study completion (end of week 8). You will take half of the final dose of vortioxetine during the first week post-study and no study drug during the second week of discontinuation. You will be provided with one week worth of study drug for this discontinuation process but will not be provided any further supply thereafter.

Vortioxetine can be safely discontinued however, you may experience side effects such as:

- Muscle tension
- Rebound depression
- Brain zaps/sensation of an electrical shock
- Depersonalization (feelings of loss of identity)
- Not feeling like yourself
- Dizziness
- Flu-like symptoms
- Nausea and vomiting
- Sweating
- Headaches
- Suicidal thoughts

If you are having suicidal thoughts call the study doctor at the telephone number listed on the first page of this form. If you feel in crisis, you can call 911 and/or a Nationwide Suicide Hotline that is answered 24 hours a day with a skilled, trained counselor. One example is the Canada Suicide Prevention Service at 1-833-456-4566.

If you experience side effects during the study, a study doctor will make a recommendation regarding the discontinuation or dose reduction of the study drug for the remainder of the study.

Please note the study team will not know who received vortioxetine and who received placebo until the study is complete. You may contact the research team once the study is complete to find out whether you received vortioxetine or placebo.

<u>Post-Study Visit (Optional)</u>
You will be seen by the study doctor to monitor safe study drug discontinuation. This visit will consist of the study doctor's assessment of your overall well-being. After one post-study clinical visit two weeks after the end of the study, you will be asked to continue your care with your most responsible physician (MRP). The visit will consist of your overall well-being and management plan with your most responsible physician.

Schedule of Visits

	Screening (V0)	**Baseline** (V1)	**Week 2** (V2)	**Week 4** (V3)	**Week 8** (V4)	**Post-Study Visit** (Optional)
Assessment with Study Staff/Self-Completed Questionnaires	X	X	X	X	X	
Study Doctor Assessment	X		X	X	X	X
Fasting Blood Work		X			X	
Study Drug Receipt		X	X		X*	
fMRI (optional)		X			X	
Approx. Total Time of Visit (hours)**	**2**	**2**	**1.5**	**1**	**2**	

*Applies to participants who will not continue treatment after study. Please see "Transition to Standard Care Upon Completing the Study' for more details.

**Does not include time taken for blood work and optional fMRI scan.

Note:

- You will be expected to take the study drug as prescribed **every day** from the start to the end of the study (end of week 8). Please let the study team know if you have any questions about this.

Risks Related to Being in the Study

Taking part in this study has risks. Some of these risks we know about. There is also a possibility of risks we do not know about and have not been seen in humans to date. Additionally, there may be unknown risks to a pregnancy, embryo, or fetus if you or your female partner become pregnant. Please call the study doctor if you have any side effects even if you do not think it has anything to do with this study.

The known risks associated with vortioxetine are:

Most Common:

- Gastrointestinal adverse events including:
  - Nausea
  - Vomiting

- Constipation
- Diarrhea
- Dry mouth
- Flatulence (gas)
- Dyspepsia (discomfort of the abdomen)
- Abdominal discomfort

These occur most commonly during the first week of study treatment (21-32%)

- Sexual dysfunction (14-34%)

Less Common: (1-10%)

- Dizziness
- Dizziness
- Somnolence (sleepiness)/sedation
- Fatigue
- Insomnia
- Abnormal dreams
- Hyperhidrosis (increase sweating)
- Arthralgia (joint pain)
- Decreased appetite
- Itchy skin
- Nasopharyngitis (common cold)

Rare: (less than 1%)

- Nervous system disorders
- Skin and subcutaneous tissue disorders
- Psychiatric disorders
- Abnormal bleeding
- Clinical worsening or suicide risk

Serotonin Syndrome has been reported with serotonergic antidepressants (SSRIs [selective serotonin reuptake inhibitors], SNRIs [serotonin–norepinephrine reuptake inhibitor], and others), including with vortioxetine both when taken alone, but especially when co-administered with other serotonergic agents (including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, and St. John's Wort). Increased levels of serotonin may cause signs and symptoms that can range from mild (shivering and diarrhea) to severe (muscle rigidity, fever and seizures).

Treatment with serotonergic antidepressants (SSRIs, SNRIs, and others) may increase the risk of abnormal bleeding. There is an increased risk of bleeding when vortioxetine is co-administered with nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin, or other drugs that affect coagulation.

Activation of Mania/Hypomania can occur with antidepressant treatment.

Angle Closure Glaucoma: Angle closure glaucoma has occurred in patients with untreated anatomically narrow angles treated with antidepressants.

Hyponatremia (decreased levels of sodium in the blood) can occur in association with the syndrome of inappropriate antidiuretic hormone secretion (SIADH). This can cause:

- Confusion
- Seizures
- Fatigue
- Low levels of consciousness

Post-Market Adverse Reactions

The following adverse events have been identified during post-approval use of vortioxetine. These events are reported voluntarily from a population of uncertain size, and it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Hyperprolactinaemia (high levels of prolactin [a hormone] in the blood)
- Acute pancreatitis
- Anaphylactic reaction
- Serotonin syndrome, headache
- Agitation, aggression
- Angioedema
- Hemorrhage (bleeding) (including contusion, ecchymosis [bruising], epistaxis [nosebleed], gastrointestinal or vaginal hemorrhage)

As with taking any drug, there is a risk of allergic reaction. If you have a very serious allergic reaction, you may be at risk of death. Some symptoms of allergic reactions are:

- Rash
- Wheezing and difficulty breathing
- Dizziness and fainting
- Swelling around the mouth, throat or eyes
- A fast pulse
- Sweating

Please seek treatment immediately and tell the study doctor and study staff if you have any of these symptoms.

Risk of Blood Sampling:

Blood samples will be drawn from a vein with a sterile needle, usually in the arm. The risks with drawing blood are pain, swelling, bruising, feeling faint, and rarely, infection at the site of the needle stick.

Risks with fMRI

Magnetic Resonance Imaging (MRI) is a test that uses a magnetic field and pulses of radio wave energy to make pictures of organs and structures inside the body. There are few potential risks of having an MRI scan, as it is a non-invasive procedure and does not involve any radiation. The main potential risk comes from loose metal objects, which, if taken near the scanner, could be dangerous. The combination of the noise of the scanner and confined space can also be stressful for people who feel uncomfortable in closed spaces. Please see the section "fMRI Participation (Optional)" for more information.

Risks with Email Communications

BCDF will be using email communications to send you information about the study, schedule appointments, respond to any emails you send and provide any personal health information you may request (for example. copy of blood results). You will also be asked to send a copy of your COVID-19 positive test result (if you have one) via email - this document may contain some of your personal health information.

To minimize risks associated with email communications, BCDF will be using encryption technology to send emails with personal health information. Encryption scrambles the contents of an email so that only those with access to a secret key or password can unscramble and read it. Encryption minimizes the risk of unauthorized collection, use or disclosure of information.

However, please be aware that all electronic communication carries some risk. You may withdraw your consent to communicate with BCDF via email at any time. Please contact BCDF if you do not wish to use this method of communication.

Other Risks

Being in this study may make you feel uncomfortable. You will be asked personal questions about your medical history. You may refuse to answer questions or stop the interview at any time if there is any discomfort. Administering the cognitive testing may sometimes be frustrating particularly if you are not performing as well as you think you should, and may also lead to mild mental and physical fatigue.

If you receive placebo (the inactive substance) as part of this study, your symptoms of post-COVID-19 condition may not improve or may get worse.

Voluntary Participation

Your participation in this study is voluntary. You may decide not to be in this study, or to be in the study now and then change your mind later.

You will be provided in a timely manner with new information that is learned during the study that might affect your decision to stay in the study.

If you decide not to participate, or to withdraw from the study, your medical care or legal rights will not be affected.

The study doctor may also withdraw you from the study if your condition worsens, if you do not follow the study doctor's instructions, if the study doctor feels it is in your best interests to be withdrawn, if the study sponsor discontinues the study, or for administrative reasons. You can be withdrawn without your consent, but the study doctor will tell you why.

You may also withdraw from the study should you become pregnant, have an increase in risk of suicide ideation and any adverse events that, in the opinion of the study doctor, puts you at risk at any point during the study.

You should discuss your birth control methods with the study doctor and ask for guidance about preventing pregnancy.

Alternatives to Participation

Currently, there are no approved alternative treatments for post-COVID-19 condition. This research study is for research purposes only. The only alternative is to not participate in this study.

Please talk to the study doctor about your options before you decide whether or not you will take part in this study.

Confidentiality

Personal Health Information

If you agree to join this study, the study doctor and his study team will collect your personal health information that they need for the study. Personal health information is any information that could be used to identify you and includes your:

- Name
- Address
- Date of Birth
- New or existing medical records, which includes types, dates and results of medical tests or procedures.

The information that is collected for the study will be kept in a locked and secure area by the study doctor for 25 years. Electronically collected data will also be stored on a secured platform for 25 years. Only the study team or the people or groups listed below will be allowed to look at your records.

The blood collected for exploratory biomarker testing will be kept in a locked and secure facility, as would all data related to this information, and will not be shared with any outside sponsor or external vendor. Your blood samples (labelled with your participant ID) will be stored for a maximum of 15 years from the time of collection.

The study team can tell you what information about you will be stored electronically and may be shared outside of the study team.

The following people may look at the study records and at your personal health information to check that the information collected for the study is correct and to make sure the study followed proper laws and guidelines:

- The study sponsor or its representatives/partner/collaboration companies.
- Representatives of Advarra IRB - an independent ethics committee that reviewed the ethical aspects of this study to help protect the rights and welfare of study participants.
- Representatives of Health Canada, or other regulatory bodies (groups of people who oversee research studies), outside of Canada, such as the United States Food and Drug Administration (FDA).

All data that is transferred will be coded to prevent identification of individual participants. The Canadian Data Protection Law will be followed, as a minimum.

Study Information That Does Not Identify You

Some study information will be sent outside of the study team. Any information about you that is sent out will have a code and will not show your name or address, or any information that directly identifies you. The code, with which your data is identifiable, will be stored for a minimum of 25 years.

The information may be shared with the Sponsor's partner companies or with national and international regulatory agencies to help answer the study question, to develop future studies on this product or for research related to this study.

All information collected during this study, including your personal health information, will be kept confidential and will not be shared with anyone outside the study unless required by law.

You will not be named in any reports, publications, or presentations that may come from this study.
If you decide to leave the study, the information about you that was collected before you left the study will still be used. No new information will be collected without your permission.

By signing and dating this information and consent form, you consent to the collection, access, use and disclosure of your information as described above.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site 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.

Rights as a Participant

If you are harmed as a direct result of taking part in this study, all necessary medical treatment will be made available to you at no cost.

By signing and dating this form, you do not give up any of your legal rights nor does this form relieve the study doctor or involved institution from their legal and professional responsibilities.

Benefits of Participation

No direct benefit is guaranteed to you from taking part in this study. Your condition may or may not improve, and could possibly even worsen. The results of this study may help the study team validate an antidepressant for cognitive function in individuals with post-COVID-19 condition.

Costs and Compensation

There is no cost to you, your private medical insurance (if any), or the public health insurance plan, for study procedures. The study drug will be provided at no cost for the duration of the study.

In-Person Participant Compensation:
You will be compensated up to $500 CAD if you complete the study. You may choose to receive your compensation in installments throughout the study (Week 2 - $125, Week 4 - $125, Week 8 - $250) or receive one payment for the full amount at the end of your last visit (Week 8). If you participate in the optional fMRI scans and cognitive tasks, you will receive the amount of money you will receive during the cognitive task, in addition to $500. The additional cognitive task may also be administered as a standalone assessment (outside of fMRI). Participants who complete it will be compensated with what they earn from this task in addition to the $500. This additional amount can vary from approximately $20-80.

You may also receive an additional $50 for completion of exploratory blood work.

Remote Participant Compensation:
You will be compensated up to $250 CAD if you complete the study. You may choose to receive your compensation in installments throughout the study (Week 2 - $31.25, Week 4 - $31.25, Week 8 - $62.50) or receive one payment for the full amount at the end of your last visit (Week 8).

Whom to Contact About This Study

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- By mail:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00055939.

You will receive an electronically signed and dated copy of this consent form via email. If you wish to receive a printed copy of this consent form, please let us know.

Consent

1. I confirm that the information regarding the study has been explained to me, that I have read and understood all pages of the participant information sheet, and that I have had the opportunity to ask questions regarding the study and these have been answered to my satisfaction.
2. I understand the risks and the benefits that may result from taking part in the study.
3. I understand that my participation is voluntary and that I am free to withdraw from the study at any time, without giving a reason, and without my medical care or legal rights being affected.
4. I understand that I may withdraw my consent without giving a reason. The consequences of my withdrawal will be that no new information will be collected, but that already collected data will be used.
5. I understand that I will be randomly assigned vortioxetine or placebo during the 8-week study period.
6. I understand I will have to take one pill every day for 8 weeks.
7. I am currently not pregnant and do not plan to become pregnant during the study. I understand it is my responsibility to use appropriate methods of contraception during the study.
8. I am aware that the combination of vortioxetine and other antidepressants has not been well characterized for safety and efficacy and I understand that such a combination would be considered investigational.
9. I accept that data collected for the study may be disclosed by Brain and Cognition Discovery Foundation to its partners as well as the authorities in and outside of the Canadian territory, including the European Union with the purpose of evaluating safety, efficacy, and cost/effectiveness of vortioxetine. I am aware that an identification number and my date of birth (month and year only) are linked to the data; however, other identifying information will not be transferred.
10. I understand that the study doctor is **not** my most responsible physician (MRP) but will provide care and evaluation in the context of the study during the 8-week active study period and 2-week optional follow-up.
11. I agree to email communications to/from BCDF, which may include personal health information. I understand that electronic communication carries some risk.
12. I will not participate in other studies for the duration of this study.
13. I agree to take part in the above study by signing and dating below.
14. The study doctor has my permission to tell my regular doctor about my being in this study: **YES** or **NO**
15. I agree to participate in the optional fMRI scans: **YES** or **NO**
16. I agree to participate in the optional exploratory blood analyses for future research (only for participants seen in-person) : **YES** or **NO**

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Study Participant's Name	Study Participant's Signature	Date
Name of Person Obtaining Consent	Signature	Date
Name of Study Doctor	Signature	Date