Northwell Health

Campus:
Division of General Internal Medicine:
865 Northern Boulevard Office

Medication Consent for Participation in a Research Study

Title: Project ReDUCE (Collaborative Care for Alcohol Use Disorders in the Patient-Centered Medical Home: Phase I & Phase II)

Principal Investigator: Jon Morgenstern, PhD

Sponsor: National Institute on Alcohol Abuse and Alcoholism

Introduction
You already agreed to participate in a research study and have chosen to receive medication.

This consent form will explain:

- the purpose of the overall study
- the purpose of using medication in the study
- information about the medication available to you in this study
- what you will be asked to do if you decide to take medications as part of this study
- the potential risks and benefits of the medications available in this study

It will also explain that you do not have to be in this study or take the study medications to receive medical care. You do not have to agree to take medications to participate in the study. You should ask questions before you decide if you want to take medications as part of this study. You can also ask questions at any time during the study.

Why is this research study being done?
The purpose of this research study is to develop and test a care model to treat problem drinking and alcohol use disorders in the primary care setting. You are being asked to participate in this study because routine screening and assessment conducted at your primary care clinic indicates that you have recently exceeded healthy drinking limits as outlined by the National on Alcohol Abuse and Alcoholism. Medication is available as one treatment option for you, and this consent form will review this option so that you can determine whether you would like to pursue this option. Whether or not you choose to take medication will not affect your participation in the overall study.

How many people will take part in this study?
The overall research study hopes to enroll 85 individuals.

How long will you be in this study?
The study will last for 12 weeks. All of the procedures described in the main study consent form will apply to you. In addition, as part of your initial visit, you will see a medical professional (i.e., a Registered Nurse [RN] supervised by a Medical Doctor [MD], a Nurse Practitioner [NP], or an MD), who will perform a medical exam, review your medical history, and discuss with your primary care team (e.g., your Primary Care Physician) to be sure you are a good candidate for medication.

If you choose to take medication as part of this study, you will be given a prescription for naltrexone during your initial study visit, and you will take the naltrexone daily for 12 weeks as long as you do not experience any side effects.

During the first two weeks, you will meet with the medical professional once per week, so that we can monitor potential side effects. Starting in week three, you will meet with the medical professional every other week, unless you are still experiencing side effects and need to be seen more frequently.

Lab work will be performed prior to enrollment, at your week 4 assessment, and additional times throughout the 12 weeks, IF there is clinical indication that liver enzymes should be assessed an additional time. to make sure that the medication is not affecting your liver. These medication management and lab visits will be part of your treatment visits and will not require you to take part in research surveys, except for your week 4, 8, and 12 appointments where you will have a treatment appointment and research assessment in the same visit, as described in the overall study consent that you already signed.

What will happen in this research study?
You have already provided verbal consent to be screened for risky alcohol use as a standard of care at the 865 Northern Boulevard General Internal Medicine site, and you received a brief counseling session based on your screening results. After that counseling session, you were asked to participate in the overall research study.

After you agreed to participate in the study by signing the main study consent form, you were further assessed and provided medication and behavioral treatment options based on your need. At that time, you chose to pursue medication treatment, and, therefore, undergoing this consent process to learn more about the medication, its side effects, and other relevant information. If you choose to consent, a medical professional will perform a medical exam, review your medical history, and consult with your primary care clinical team to determine if you are appropriate for taking this medication. If you agree to receive medication, the medical professional will write you a prescription.

If you select medication as your treatment options, you will receive 12 weeks of daily naltrexone (50 mg) with medication management appointments. Naltrexone is FDA-approved for the treatment of alcohol problems at 50 mg/day. To minimize any potential side effects, we will

initiate treatment using a 25-mg dosage for the first week, and as long as the medication is well tolerated by you, we will then increase to 50 mg daily.

You will be seen by the medical professional weekly for the first two weeks until the medication dose is stable and then meetings will continue biweekly. At these visits, you will be asked about your drinking and experience with the medication, including compliance and side effects. Additional physician or nurse visits may be scheduled if you experience side effects or do not follow the recommended medication guidelines. We will monitor liver function by doing blood tests to be sure that there is no damage to your liver and to make sure it is functioning properly. Lab work (i.e., 5 cc of blood, the equivalent of one teaspoon) will be performed prior to enrollment, at your week 4 assessment, and additional times throughout the 12 weeks, IF there is clinical indication that liver enzymes should be assessed an additional time

At week 4, your progress in treatment will be assessed by the medical professional and your health coach. You may be offered the below options, if it appears that an alternative may be more suitable than the naltrexone treatment you have been taking the first 4 weeks:

- daily topiramate (200mg) with medication monitoring and management as described as above; **OR**
- behavioral treatment while taking naltrexone.

Decisions regarding additional treatment options will be made by the medical professional, who is part of this study, in consultation with you and this study staff and the primary care clinical team.

Birth Control

The drugs in this study may affect a baby, before or after the baby is born. As a result, women should not be in this study if they are:

- pregnant,
- breast-feeding, or
- trying to become pregnant.

If you are a woman of childbearing age, you should use birth control for the entire time you are in the study and for at least one menstrual cycle after stopping the study. Hormonal methods (birth control pill, etc.), double-barrier methods (condoms with spermicidal, sponge with spermicidal, or diaphragm with spermicidal), or not having sex may be used. Your doctor will discuss these with you.

What are the risks of the research study? What could go wrong?

All the risks reviewed in the main study consent form still apply to you. Using medications in ways other than prescribed by your study doctor (including taking too much or abruptly stopping) can be dangerous. At the end of the study, you will be given a tapering schedule if you do not wish to remain on your study medication (either naltrexone or topiramate) under the care of your own PCP. If you are taking naltrexone, the dose of naltrexone does not need to be tapered at the end of the study but can simply be stopped. If you are taking topiramate, it will be suggested that you decrease your daily dose of topiramate by 50 mg each week until you are off.

Based on studies using topirimate for either seizure or migraine prevention, there is a risk of rebound seizure or headache when the medication is stopped suddenly. It is unknown if the same risk applies when using topiramate to help reduce drinking. To be safe, the same slow decrease in dose should be followed.

Please consult with a member of the study team before abruptly stopping either topiramate or naltrexone.

Naltrexone
There are some potential side effects from taking naltrexone at the dose of 50mg per day. The most common side effects are nausea, vomiting, anxiety, headache, abdominal discomfort, difficulty sleeping, fatigue, irritability, and decreased appetite. Naltrexone has rarely caused serious liver disease; however, persistent nausea/vomiting, severe stomach/abdominal pain, dark urine, yellowing eyes/skin should be reported to your doctor immediately. There are no known effects of naltrexone on liver function that are not reversible upon stopping the medication. Naltrexone can interfere with certain medications, such as opioids.

Naltrexone is an FDA-approved treatment for alcohol use disorder; it is not an experimental drug. We have put several safeguards in place to reduce the risk of serious side effects. For example, you will undergo a medical exam and your medical history will be reviewed by nurses and doctors before you start the medicine. You will meet with a nurse weekly for two weeks and then every other week for the following10 weeks to monitor your self-reported side effects, and the frequency of these visits can be increased if needed. We will monitor liver function monthly to be sure that there is no damage to your liver. We will conduct more frequent medical monitoring as appropriate.

Because naltrexone can interfere with opioids, you will be urged to delay elective procedures, such as dental procedures or elective surgery, requiring opioid treatment until after the study treatment. If you cannot delay such procedure, you will not be eligible to receive naltrexone as a treatment option. If you have a history or evidence of recent opiate use, you will not be eligible to receive naltrexone. In addition, if you have any serious illnesses, including liver disease and/or a known sensitivity to naltrexone, in order to minimize the risk of a serious reaction to study medication, you will not be eligible to receive this medication.

Topiramate
If naltrexone is not working for you, we will be offer topiramate (200 mg per day). Although topiramate is FDA-approved for the treatment of other conditions (i.e., for migraine headaches and prevention of seizures), the use of the drug in this study for the treatment of alcohol use disorders is not FDA-approved and is considered investigational. The target dosage for topiramate will be 200 mg/day and will be increased only if tolerated. It may be reduced if necessary (i.e., patients experiencing side effects will have their dosage decreased gradually to the highest tolerated dosage).

We will start you on a lower dosage and then slowly increase it to make sure you do not have any negative effects. The schedule is as follows:

- Week 1: 25mg once per evening;

- Week 2: 50mg once per evening;
- Week 3: 25mg once per morning + 50 mg once per evening;
- Week 4: 50mg once per morning and once per evening;
- Week 5: 50mg once per morning and 100mg once per evening;
- Week 6-12: 100mg once per morning and evening.

The most common side effect of topiramate is numbness and tingling. The other most common side effects include: change in sense of taste, tiredness/sleepiness, fatigue, dizziness, loss of appetite, nausea, diarrhea, weight decrease, difficulty concentrating, and memory-related difficulties.

Less common side effects include: nervousness, slow thinking, abnormal vision, confusion, anxiety, abdominal pain, dry mouth, involuntary muscle contractions, and language problems. Depression and mood problems have also been reported. Some patients have had suicidal thoughts or actions. Kidney stones and effects on the levels of acid in your blood may occur, though this is less likely.

To safeguard from the above side effects, patients will be informed that, if they feel a change in their mood, feel depressed, or feel they may harm themselves, they should contact the study team. Drinking adequate fluids will be recommended to reduce the risk of kidney stones.

If you have significant suicidal risk, you will not be offered topiramate as part of this study and ongoing monitoring throughout the study will serve to reduce the risk of intentional overdose. If you have cirrhosis and/or significant liver enzyme elevations or histories of significant liver disease, you will not be offered topiramate as part of this study.

The study treatment team physicians will provide guidance for you as you increase your dosage level of medication, if adverse effects occur. A medical professional (i.e., a medical doctor or nurse practitioner) will monitor you closely for side effects weekly for the first two weeks or until your medication dose has been stabilized, and then biweekly for the remainder of the study. We will monitor your liver function monthly by conducting lab work, and we will conduct more frequent medical monitoring as appropriate.

Blood-Drawing

If you choose to take medications as part of this study, you will have blood drawn prior to enrollment, at your week 4 assessment, and additional times throughout the 12 weeks, IF there is clinical indication that liver enzymes should be assessed an additional time. Blood draws will include extracting 5 cc of blood, the equivalent of one teaspoon. Having your blood drawn can be uncomfortable and can sometimes cause a bruise. In some people, it can cause fainting. In very rare cases, and infection can occur. Only trained people will draw your blood. You should discuss any problems with blood draws with the study medial professional, who will be meeting with you.

The study treatment team will meet weekly during the study to ensure that adequate monitoring of your medical stability is being conducted and will communicate closely with your primary

care clinical team. If you develop serious adverse side effects, the medication will be stopped, and you may be offered alternative treatment in the study.

Unknown Side Effects
As with any drug, there might be side effects that are unknown at this time. You will be closely watched for side effects. You should report any unusual events to the study staff.

Women of Childbearing Potential and Pregnant Women
Naltrexone and topiramate may have adverse effects on fertility or a fetus. Both naltrexone and topiramate are excreted in breast milk. For this reason, if you believe you are pregnant or have a chance of becoming pregnant, not take part in the medication arm of the study. During the initial screening appointment, you will be asked if you are pregnant. If you are pregnant, you will not be allowed to participate in the medication arm of the study.

If you do take part in this study and are of childbearing potential, you must use a medically recognized form of birth control for one month before entering the study, while in the study, and for at least one menstrual cycle after stopping the study. If you become pregnant during the study and are receiving medication, you will be immediately withdrawn from the medication arm of the study and closely monitored through your entire pregnancy.

Due to the potential for serious adverse reactions in the nursing infant, you should not take part in the study if you are breastfeeding.

What are the benefits of this research study?
The possible benefits you may experience from the procedures described in this study include a reduction in problem drinking; however, this cannot be guaranteed. We expect that the findings of this research will help your primary care clinical team recognize and treat excessive drinking and alcohol use disorders in primary care settings in the future.

Drug Availability After Completion of Study
At the end of the study, the study doctor will give you a prescription for the medication you have been taking if you would like to continue taking it and you have been taking the medication as directed by the study doctor. If you would like to discontinue the medication, the study doctor will discuss with you how to safely stop taking it.

If you do not want to take part in this research study, what are your other choices?
If you do not choose to participate in the medication portion of this study, you will still be able to participate in the main study. Your alternative treatment options would include behavioral counseling or referral to treatment elsewhere. If you choose to receive a behavioral intervention, a behavioral health specialist will meet with you to undergo a separate consent for those interventions.

Your doctor can also tell you the important risks and benefits associated with the alternative treatment

Are there any costs for being in this research study?

This research study is funded by the National Institute on Alcohol Abuse and Alcoholism. All study related visits will be given to you at no additional cost to you. If you choose to receive medication treatment as a part of this study, your insurance company may be billed for the cost of the medication and potential lab work costs. If you do not have insurance, or do not wish to have your insurance billed, the study will cover the costs of medication and bloodwork during the 12 weeks of the study. In this case, you will have to obtain medications from a specific pharmacy associated with Northwell Health where we will send your prescription at no cost to you.

Will you receive any payments for participating in this research study?
You will receive $20 for each study interview you complete, as discussed in the general consent for the study. Therefore, if you participate in all study sessions, you will be paid up to a total of $80 for your time. Payment will be made at the end of each study assessment or when you end your participation.

If the total payment you receive from Northwell Health, during this year, is equal to $600 or more, the payment is required to be reported to IRS. Although this study does not pay $600, if you participate in other Northwell Health studies, it is possible your payment could end up totaling $600. If this occurs, the payment you receive on this study will be reported to the IRS. In this case, you will be issued a 1099 form and be required to provide your social security number at that time for reporting purposes. You will also be responsible for reporting this income while filing your tax return.

What are your rights as a research participant?
Your participation in this project as well as in receiving medication as part of your treatment is voluntary. The quality of your medical care will be the same, whether you join, refuse to join, or decide to leave the study or to take the medication.

If you do not join the study or do not wish to take the medications, you will not be penalized or lose benefits to which you are entitled. If you join the study you may withdraw at any time or discontinue taking the medications without prejudice to your future care at the Northwell Health System. Follow-up examinations may be needed to assure your well-being.

Could you be taken off the study before it is over?
It is also possible that your participation in taking medication may end without your consent. This decision may be made by a researcher, study sponsor, or the Institutional Review Board (IRB—the committee that oversees research at this institution).

Reasons for withdrawal may include:

- failure to follow instructions,
- failure to show up for study visits,
- side effects from medications
- it is not in your best interest to continue with the medications, or
- the study is stopped.

If you are withdrawn from being able to take medications, any data already collected will continue to be used, and you will be offered alternative treatment in the study or referred to treatment outside of the study. You will still be monitored in the research assessment portion of the study, unless you choose to withdraw, which you are free to do at any time without any effect on your care at Northwell Health.

What happens if new information is learned?
You will be told of any new findings that may change your decision to continue to participate. Your consent to continue to take part in this study may be obtained again.

What information will be collected and used for this study?
If you agree to be in this study, we will collect information about your health and your alcohol use. We may collect the results of questionnaires and interviews. This information may include questions about the amount of alcohol you drink, how often you drink, any problems you have experienced because of drinking, and any reasons why you may have trouble accessing treatment services. If you drop out of treatment, we may ask you why so that we can learn from your experiences. We will only collect information that is needed for the research. This information has been described in this consent form. If you sign this consent form, you are giving us permission to collect, use and share your health information. This permission is called authorization. If you do not want to provide authorization, then you cannot participate in this research study.

Who else will see your information?
Study records that identify you will be kept private. You will not be identified in study records or publications disclosed outside the Northwell Health System, except as detailed below.

Investigators will share de-identified information collected from this research study with:

- study sponsor and/or its agents,
- data safety monitoring board,
- clinical staff not involved in the study who may be involved in the participant's treatment

The following reviewers may access your study and medical records to make sure that this study is being done properly:

- Representatives from federal and state government oversight agencies, such as National Institutes of Health, US Department of Health and Human Services (DHHS), or the New York State Department of Health. Representatives from the Northwell Health System Human Research Protection Program (a group of people that oversee research at this institution)

We will do our best to protect the privacy of your records, but it is possible that once information is shared with people listed on this form that it may be released to others. If this happens, your information may no longer be protected by the federal law.

In the future, we may publish results of this study in scientific journals and may present it at scientific meetings. If we do, we will not identify you.

If the researchers learn about potential serious harm to you or someone else or other public health concerns, it will be shared with the appropriate authorities.

Will you be able to access your records?
If your research records are used for decisions related to your clinical care, then you have the right to review this information and request changes. This is limited to information about your treatment and does not include information related to procedures or tests that are for research purposes only. You may access this information only after the study analysis is complete. You have the right to know who has and who will see your records. To request this information, please call the Human Research Protection Program at 516-321-2100.

How long will your health information be kept?
There is no limit on the length of time we will keep your information for this research because it may be analyzed for many years. We will keep it as long as it is useful, unless you decide you no longer want to take part or we close the study. You are allowing access to this information indefinitely.

Can you change your mind?
If you change your mind about being in the study or about taking medications, you may withdraw at any time or discuss alternative treatment options with study staff. If you want us to stop collecting your health information, you can send a letter to the researcher at the following address:

Dr. Jon Morgenstern.
1010 Northern Blvd. Suite 311
Great Neck, N.Y., 11021

Your letter needs say that you have changed your mind and do not want the researcher to collect and share your health information. You may also need to leave the research study if we cannot collect any more health information. We may still use the information we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it.

Will information about this study be available to the public?
We may write about this study and publish it in a scientific journal; however, you will not be named and all participants' data will be combined such that no one participant is written about. Also, a description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most the website will include a summary of the results. You can serach this website at any time.

Does the investigator of this study receive money if you take part?
Funding for this research study is provided by the National Institute on Alcohol Abuse and Alcoholism. The investigators on this study receive money to conduct the study but do not financially benefit from your participation. The money they receive is to pay them back for the

costs of conducting the research study. If your doctor is an investigator for this study s/he is interested in both your healthcare and the conduct of this research. You do not have to take part in a research study conducted by your doctor.

Who can answer your questions about this study?
If you have any questions about the study, you may call Dr. Jon Morgenstern at (516) 837-1694. If you have questions about side effects or injury caused by research you should call Dr. Jon Morgenstern at (516) 837-1694. If you need emergency care, dial 911 or go to the nearest Emergency Room. If you have questions about your rights as a research participant, concerns about being in the study, or would like to offer input, you may contact the Office of the Institutional Review Board (the committee that oversees research at this institution) at (516) 321-2100.

A signed copy of this consent form will be given to you.

Research Review Questionnaire

After reviewing the consent form for this study please answer the following questions by circling "True" or "False". The researchers doing this study want to be sure that you know what is involved in being in this research study. This questionnaire will help them make that decision. You may ask questions of the researcher and review the consent form again at any time.

You do not have to be in this study or take the study medications to receive medical care.	True	False
Naltrexone can interfere with certain medications, such as opioids.	True	False
I can withdraw from participating in this study at any time.	True	False
There are no risks to me from participation in this study.	True	False

[Signature Page Follows]

Summation/Signature

You have read the above description of the research study. You have been told of the risks and benefits involved and all your questions have been answered to your satisfaction. A member of the research team will answer any future questions you may have. You voluntarily agree to join this study and know that you can withdraw from the study at any time without penalty. By signing this form, you have not given up any of your legal rights.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

_____ _____ _____
Witness's Printed Name Witness's Signature Date
(Note: A witness can be a member of the research team, but cannot be the same person signing consent as the investigator)

Investigator's Statement
In addition to advising the above participant of other forms of treatment and therapy which are appropriate, I have offered an opportunity for further explanation of the risks and discomforts which are, or may be associated with this study and to answer any further questions relating to it.

_____ _____
Investigator's signature **Date**

_____
Investigator's printed name