TITLE: TREATING DEPRESSION AMONG HEMODIALYSIS PATIENTS

Introduction

You are being asked to participate in a research study. Before you can decide whether or not to volunteer for this study, you must be given information about the purpose of the research study, how this study may help you, any risks to you, and what is expected of you. This process is called **informed consent.**

You were chosen as a possible participant for this study because you are on hemodialysis and you have been diagnosed with depression. The goal of the study is to compare two strategies for treating depression among hemodialysis patients.

You do not have to participate in this study. You may stop your participation in this study at any time without changing your current or future relations with MetroHealth Medical Center, the Centers for Dialysis Care (CDC), or its medical providers.

If you decide to participate in this study you will be told about any new information learned during the course of the study that might cause you to change your mind about staying in the study. If you decide to withdraw, we will still provide you with information regarding possible impacts to your health status or future health care decisions.

Why is this study being done?

Depression can be difficult to diagnose and treat among dialysis patients. This is due in part to overlap between symptoms of depression (such as poor appetite, trouble sleeping, feeling tired) and symptoms related to kidney failure or dialysis treatment (such as nausea, nighttime cramps, feeling washed out after treatment). This overlap makes it difficult to diagnose and therefore to treat depression. In addition, most dialysis patients already take a number of different medications, and adding another medication for depression will further increase the number of medications they have to take. Moreover, treatments for depression have been less well studied among dialysis patients than among the general population.

The purpose of this study is to compare two strategies for treating depression among hemodialysis patients. One strategy is referring patients to a mental health provider for treatment. The other strategy is taking the antidepressant medication fluoxetine on a weekly basis during dialysis treatment. Fluoxetine is approved by the U. S. Food and Drug Administration (FDA) and has been used for many years in the treatment of depression.

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How many people will take part in the study?

This study will take place at up to 17 Centers for Dialysis Care (CDC) dialysis facilities in Northeast Ohio. A total of about 216 hemodialysis patients will be asked to participate in this study. Participants will not necessarily be MetroHealth Medical Center patients, but rather come from a wide range of other practices and institutions in Northeast Ohio.

What is involved in the study?

You will be asked to read and sign this consent form after all your questions have been answered. A copy of the consent will be provided to you for your records. Your participation in this study is expected to last about 12 weeks. All study tasks will take place during regularly scheduled dialysis treatments. If you choose to participate, you will be randomly selected to be placed into one of two groups. Randomization is like flipping a coin to decide which group you will be in. Neither you nor your doctor(s) can choose the group you will be in. You have an equal chance of being in one or the other group.

All study participants will do the following:

- You will be asked to complete one questionnaire on day 3 and during weeks 1, 2, 4, 6, 8 10 and 12. The questions will be read to you by a study team member. The name of the questionnaire is:
    - **Patient Health Questionnaire (PHQ-9):** there are 9 questions that ask about symptoms related to mood and depression. This takes about 5 minutes to complete.
- You will be asked to complete two additional questionnaires during week 12. The questions will be read to you by a study team member. The names of the questionnaires are:
    - **Kidney Disease and Quality of Life (KDQOL-36):** there are 47 questions that ask about your health and quality of life. This takes about 15 minutes to complete.
    - **Mini International Neuropsychiatric Interview (MINI)**: the MINI is a semi-structured interview that asks about mental health symptoms that are going on now or in the past. This takes about 1 hour to complete.

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If you are randomly selected to be in the referral group:

- You will be given a list of local mental health providers who specialize in treating depression and will be encouraged to seek treatment from one of them.
- If you prefer, you can also ask your nephrologist or primary care physician for treatment or advice.
- We will let your nephrologist or primary care doctor know about your depression diagnosis.

If you are randomly selected to be in the fluoxetine group:

- You will be given a prescription of daily 20 milligram (mg) fluoxetine by a psychiatric nurse practitioner. You will be instructed to take one 20 mg pill once a day for two weeks. A study team member will periodically ask you questions about your adherence to the medication. Your nephrologist or primary care doctor will continue to make decisions about other medications that you are taking.

  You will be asked to keep your fluoxetine pills in a pill box. If you don't have a pill box, we will provide one for you. You will be asked to bring the pill box with you each time you go the dialysis unit. A member of the study team will call you periodically to remind you to take your daily fluoxetine and to bring your pill box to the dialysis unit.

- During week 3, the psychiatric nurse practitioner will instruct you to stop taking the daily 20 mg pills and switch to weekly 90 mg fluoxetine. You will be given a prescription of weekly 90 mg fluoxetine by the psychiatric nurse practitioner.
- You will take each dose of weekly 90 mg fluoxetine at the dialysis unit while a study team member watches you once a week for 10 weeks.
- The psychiatric nurse practitioner will meet with you to monitor side effects and make medication adjustments, if needed, throughout the duration of the study.
- All the fluoxetine pills that you are asked to take during the study will be provided to you at no cost.
    - We will ask you to follow some safety precautions. Fluoxetine must be taken only by you. Keep the fluoxetine in a safe place out of reach of children and other people who cannot read well or understand that they should not take it.

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- At the end of the 12 week study, you will receive a filled 4 week prescription for weekly fluoxetine 90 mg and instructions on how to communicate with your nephrologist and/or primary care physician about how long to continue taking it.

- The psychiatric nurse practitioner will also communicate with your nephrologist and/or primary care physician about the need for further treatment.

What happens if I stop or withdraw from the study?

You are free to withdraw from the study at any time. If you withdraw from the study before its completion, you will not be asked for any further information. Your care at the Centers for Dialysis Care (CDC) or MetroHealth Medical Center will not be affected.

If you are randomly selected to be in the fluoxetine group, you may decide to discontinue fluoxetine. Discontinuation of fluoxetine is usually mild and more tolerable for patients than discontinuation of some other antidepressants. The most common discontinuation symptoms tend to be flu-like symptoms and headache. The onset of discontinuation symptoms can be within a few days of stopping any antidepressant and may take 1 to 2 weeks to resolve. If you are unable to tolerate the discontinuation symptoms of fluoxetine, you will be instructed to contact the study psychiatric nurse practitioner, Kelley Kauffman, by study cell phone (216-339-9244). The nurse practitioner will assess the symptoms with you, and then will consult with the study psychiatrist, Dr. Sajatovic, regarding the appropriate course of action.

What are the risks of this study?

As you complete the questionnaires, some of the questions we ask may be upsetting, or you may feel uncomfortable answering them. If you do not wish to answer a question, you may skip it and go to the next question. If, during the process of being assessed, research staff feel that you are an immediate risk of harm to yourself or others, staff will make efforts to make sure that you are safe. This may include recommending that you go to the emergency room or consulting with our study psychiatrist (Dr. Martha Sajatovic) or your regular doctor or clinician as appropriate.

All antidepressant medications, including fluoxetine, may have side effects. If you are randomly selected to be in the fluoxetine group, the psychiatric nurse practitioner will meet with you to ask questions about any possible side effects of fluoxetine (listed below). If you appear to be having trouble with side effects, the psychiatric nurse practitioner may adjust the dose of your study medication, or in some cases, may instruct you to stop taking fluoxetine. You should call her if you experience serious side effects (listed below) between visits. You are also free to stop participating in the study at any time.

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Common (greater than 10%) possible side effects of fluoxetine:

- Problems falling and staying asleep
- Headache
- Drowsiness
- Anxiety
- Nervousness
- Yawning
- Nausea
- Diarrhea
- Anorexia
- Dryness of mouth
- Tiredness or weakness
- Tremor or shaking
- Sore throat
- Hot flashes

Uncommon (between 1-10%) possible side effects of fluoxetine:

- Chest pain
- High blood pressure
- Dizziness
- Unusual dreams
- Problems concentrating or thinking
- Loss of memory
- Confusion
- Increased sweating
- Skin rash
- Itching
- Weight loss or weight gain
- Stomach pain or discomfort
- Constipation
- Gas
- Vomiting
- Increased or loss of appetite
- Erectile dysfunction (ED)
- Decreased libido
- Vision problems
- Ear pain

- Ringing in the ears
- Flu-like symptoms
- Sinus infection

Rare (1% or less) but Serious possible side effects of fluoxetine (tell the psychiatric nurse practitioner immediately if you experience them):

- Feeling agitated, restless, angry or irritable
- Talking more or faster than what is normal for you
- Hallucinations (seeing something that is not really there)
- Coordination problems or muscle twitching
- Very stiff (rigid) muscles
- High fever
- Fast heartbeat
- Tremors
- Seizure
- Severe allergic reaction: trouble breathing, sore throat, rash, blisters, swelling in your face, tongue, eyes or mouth
- Severe trouble sleeping
- Racing thoughts
- Reckless behavior
- Unusually grand ideas
- Excessive happiness
- Increased bleeding or bruising
- Thoughts about suicide or dying
- Attempts to commit suicide
- Acting on dangerous impulses (urges)
- Acting aggressive or violent
- Worsening of depression
- New or worse anxiety or panic attacks

Confidentiality breach

In any instance where protected health information is collected, there is a risk for a breach of confidentiality. Every effort by study staff will be made to keep your information confidential, including storing documents in locked file cabinets, encrypted laptop computers, and de-identifying information whenever possible. The risk of a confidentiality breach is rare.

Are there benefits to taking part in the study?

It is possible that participating in this study and receiving treatment from a local mental health provider or the study psychiatric nurse practitioner will result in a decrease in your depressive symptoms and improvement in your mood and quality of life. However, you may not respond to treatment and there may be no direct benefit to you in participating in this study. Your participation in this study will help us better understand the best treatments for depression among hemodialysis patients.

What other options are there?

Participation in this research study is voluntary. You do not have to take part in this study to be treated for depression. You can follow-up with your nephrologist or primary care doctor to discuss other treatment options. Other treatment options include a different antidepressant medication, psychotherapy, and electroconvulsive therapy (ECT).

What are the costs?

If you are randomly selected to be in the referral group, the cost of seeing a mental health provider will be the responsibility of you and your health insurance plan.

If you are randomly selected to be in the fluoxetine group, fluoxetine will be provided at no cost to you during the 12 week study duration. Any other health care costs during the 12 week study duration will be the responsibility of you and your health insurance plan. If you decide to continue taking fluoxetine after the end of the study, you and your health insurance plan will be responsible for the cost of fluoxetine.

Will I be paid for participating in this study?

You will receive $20 for completing all questionnaires on day 3 and weeks 1, 2, 4, 6, 8, 10, and 12. Therefore, you could receive a possible total of $160 for the entire study. You will be paid using a ClinCard, which is a re-loadable debit card. You will only be paid for questionnaires that you completed.

What happens if I am injured while participating in this study?

All research involves a chance that something bad might happen to you. This may include the risk of personal injury. If such problems occur during the course of the study, you must contact your study coordinator, Ms. Jacqueline Dolata at (216)-778-1792 or your study doctor, Dr. Ash Sehgal at (216)-778-8484. Necessary medical care will be provided to you by the provider of your choice. This medical care is not free. You and/or your insurance company will be responsible for the costs. However, you can still try to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research, including the hospital.

Health Insurance Portability and Accountability Act (HIPAA)

As part of this study, we are collecting Protected Health Information (PHI) such as: your name, address, date of birth, telephone number, and social security number. This information is being collected in order to provide you with the ClinCard (debit card). All information will be kept on a password-protected secure network, an encrypted laptop computer, or a locked file cabinet in a locked office. Only the primary investigator and study staff will have access to these files. The following individuals, departments or agencies will have access to your PHI: MetroHealth Institutional Review Board or United States Department of Health and Human Services. The investigators will have access to your PHI collected until data analysis is complete. At that time, the PHI will be destroyed. The study file will be kept for 5 years after study completion, at which time it too will be destroyed. You have the right to withdraw your permission/authorization for us to access your PHI at any time except to the extent the PHI already collected by the investigators before your withdrawal has already been acted upon based on your signed Authorization. No new PHI about you will be collected for study purposes unless required by law.

What about confidentiality?

We will make every effort to keep your research records private, but confidentiality cannot be assured. The MetroHealth System has no control over the use of this information once it is released. The information about you that is collected in this study will be shared with the study sponsor and may be combined with information gathered from public sources or other research studies. This information may be used for purposes unrelated to this research and could potentially be used to identify you.

Records that identify you and this consent form may be looked at by a regulatory agency such as:
United States Department of Health and Human Services
MetroHealth Institutional Review Board
National Committee for Quality Assurance

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If the results of the study are published or presented in public, your name will not be used.

What are my rights as a study participant?

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you do not take part in the study, your doctor will still take care of you. You will not lose any benefits or medical care to which you are entitled.

If you chose to take part, you have the right to stop at any time. You will be told of any new findings from this or other studies that may affect your health, welfare, or willingness to stay in this study.

Termination of Participation

Your participation in this study may be ended by the investigator without your consent if they feel it is in your best interest.

Does MetroHealth or any member of the study team have a financial conflict of interest in this study?

This study is being sponsored by a grant from the National Institutes of Health. Portions of Dr. Ash Sehgal's, Dr. Doug Gunzler's, and Dr. Martha Sajatovic's and the study team's salaries are being paid by this grant. There is no other financial conflict of interest among study staff.

Whom do I call if I have questions or problems?

If you have questions about any part of the study now or in the future or if you wish to communicate concerns or a complaint you should contact Ms. Jacqueline Dolata at (216)-778-1792 or Dr. Ash Sehgal at (216)-778-8484. If you have any questions about your rights as a research participant, or if you wish to express any concerns or complaints please contact the MetroHealth Medical Center's Institutional Review Board (which is a group of people who review the research to protect your rights) at (216)-778-2021.

Patient/Subject acknowledgement:

The procedures, purposes, known discomforts and risks, possible benefits to me and to others, and the availability of alternative procedures regarding this research study have been explained to me. I have

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read this consent form or it has been read to me, and I have been given the opportunity to ask questions or request clarifications for anything I do not understand. I voluntarily agree to participate in this study. I have been given a copy of this consent form.

_____ _____ _____
Patient/Subject Signature Date Time

_____ _____ _____
Signature of Person Obtaining Informed Consent Date Time