University of Wisconsin-Madison
Consent to Participate in Research
and
Authorization to Use Protected Health Information for Research

Study Title for Participants: Preventing Recurrent *Clostridium difficile* Infections

Formal Study Title: Efficacy of oral vancomycin prophylaxis for prevention of recurrent *C. difficile*

Lead Researcher: Nasia Safdar, MD, PhD, ns2@medicine.wisc.edu

Where Lead Researcher works: University of Wisconsin-Madison, Division of Infectious Disease, UW Medical Foundation Centennial Building, 1685 Highland Ave, Madison, WI, 53705

Invitation

We invite you to take part in a research study about preventing recurrent *Clostridium difficile* infections (CDI). We are asking you to join because you were diagnosed with a CDI within the past 180 days and are (or will be) getting antibiotics for a reason other than CDI.

The purpose of this form is to give you the information you need to decide whether you want to be in this study. It also explains how health information will be used for this study, for other research in the future, and requests your authorization (permission) to use your health information. Ask questions about anything in this form that is not clear. If you want to talk to your family and friends before making your decision, you can. Once we have answered all your questions, you can decide if you want to be in the study. This process is called "informed consent."

Why are researchers doing this study?

A portion of people who get one CDI will have a CDI happen again. This is called a recurrent infection. We are doing this research because recurrences of CDI are common, difficult to treat, and can be passed from person to person. These recurrent infections usually occur when people use antibiotics for reasons other than to treat a CDI, like for a urinary tract infection or to prevent infections during surgical procedures. We do not have well studied ways of preventing recurrent CDIs and are trying to change that.

The purpose of this research study is to see if oral vancomycin can reduce the number of patients who have CDI happen again. Vancomycin is an antibiotic used to treat active CDI episodes and we believe it may be able to prevent recurrent CDI.

We are also studying how vancomycin changes the types of gut microbes (microorganisms that live in the digestive tracts in humans) in people who take oral vancomycin.

Where is this study being conducted, and how many people will join?

This study is being done at the University of Wisconsin-Madison (UW-Madison) and other sites around the US. A total of about 150 people will participate in this study.

Funding for this study is provided by the Agency for Healthcare Research and Quality (AHRQ).

What will happen in this study?

If you decide to participate in this research study, you will participate in a screening/baseline visit (visit 1), a follow-up visit after taking your last study pill (visit 2), and a final study visit 8 weeks following your last study pill (visit 3).

You would be asked to complete a patient diary each day between visit 1 and visit 3. On the diary you will track each stool you produce, any symptoms you may experience after you began taking the study medication, such as constipation, diarrhea, and fever. You will also record each time you take the study medication. Additionally, you would be asked to have an unscheduled study visit if you develop a CDI infection during the course of the study.

You will also be asked to have a weekly phone call with study staff regarding the information you record in your study diary. After Visit 3, the study team will call you once more, about three months later. If you are hospitalized during this time, study staff will visit you regularly until you are discharged.

If you have caregivers we may ask them to help you complete any study activities listed here that you may need assistance with.
If you are unable to travel to UW Health for study visits they may be done via phone call. We will then ask you to accept and send study related items such as study pills, diaries and stool samples through a shipping service. All items sent will be prepaid by the study and there will be no cost to you. You may need to sign delivery confirmations when packages arrive.

Visit 1 (will last approximately 90 minutes): Study staff will review the informed consent form with you in detail and ask you to sign at the bottom. Then you will be asked to undergo a detailed clinical assessment, which will include undergoing a physical exam if you report symptoms that need further exploration, obtaining vital signs (temperature, height, weight, blood pressure, and pulse rate or how fast your heart beats), and answer a variety of health and personal questions.

Health questions will include date of birth and where you live, race, ethnicity, medical history, social history (including history of alcohol and smoking), dietary information, travel history and review current medications. If you are currently taking oral vancomycin prophylaxis you will be required to stop in order to participate in this study. Information on your alcohol use and smoking is being collected because studies have shown that these substances can change the types and amounts of different bacteria in your gut, which could affect the results of the study.

If you are a woman of child-bearing potential, you will also be asked to undergo a urine or blood pregnancy test unless you have a recent negative pregnancy test as part of your clinical care (within last 7 days). Pregnant women are excluded from this study.

You will then be asked to provide a stool sample. To obtain each study sample, you will be given a stool collection kit/hat to collect the stool at home or at the hospital/clinic, or perirectal swabs will be obtained during the study visit. You may be given the stool collection kit to submit the sample before signing this consent if you will begin antibiotics in the near future. If you have diarrhea at Visit 1, your stool sample results will need to be negative for *C.diff* for you to participate.

Following this assessment and collection of your stool sample, you will be placed into one of two groups: (1) vancomycin treatment group, or (2) placebo group. A placebo is a material that looks like the study drug but has no medicine. A method called randomization (done by computer and selected by chance; like flipping a coin) will determine which group you will be in. You will have a 1:1 (50%)

chance of receiving placebo and a 1:1 (50%) chance of receiving vancomycin. You and study staff will be "blinded" to the group you are randomized to, meaning you won't know which group you are in. In both cases, you would be asked to take either the placebo or vancomycin once a day while you are taking your other antibiotic treatment and for five days after you complete your other antibiotic treatment.

Visit 2 (will last approximately 30 minutes): Visit 2 would occur when you are finished with both treatment courses. At this visit, the study team would ask you questions about your health as related to the study, ask you about possible symptoms of adverse reactions to the study medication, such as constipation, abdominal pain, or nausea, and collect vital signs including temperature, blood pressure, heart rate, and weight. You would also be asked to provide a stool sample at this visit and return your stool diary.

Visit 3 (will last approximately 30 minutes): The final study visit would occur 8 weeks after you finish taking the study medication. At this visit, the study team would ask you questions about your health as related to the study and collect vital signs including temperature, blood pressure, heart rate, and weight. You would also be asked to provide a stool sample at this visit and return your stool diary.

If you have a health condition that began after you started taking study pills, the study physician may ask to follow you until the condition resolves, even if it is after your final scheduled study call.

Unscheduled Visit (will last approximately 30 minutes): If you develop a CDI during the course of the study, you will be asked to complete an unscheduled visit. At this visit, you would be asked to provide an additional stool sample. A study team member would also assess your vital signs and overall health status. In addition, if you develop an infection with any multi-drug-resistant organism (including VRE or MRSA) during the course of the study, the study team will review your medical record to collect data on your diagnosis, treatment, and treatment progress until it has resolved.

Follow-Up Phone Call (will last approximately 15 minutes): A member of the study team will call you about 3 months after Visit 3 to ask if you have had a CDI since your last visit. We will also regularly review your medical record to check for CDI while you are on the study. If you do have CDI during this time, please contact the study team. You may be asked for another stool sample if you report that you had CDI anytime during the study

How we will use your protected health information (PHI)

Protected health information, also called PHI, is information about your physical or mental health that includes your name or other information that can identify you, like your date of birth or medical record number. To do this study, we will use the following kinds of PHI:

- Results of tests or procedures done as part of the study
- Things you tell the researchers about your health
- Information currently in your medical records as well as information added to your medical records during the course of this study. This information could include your medical history, your diagnosis, and lab test results. We will get this information from your UW health care records.
- If you get care from a facility outside UW Health we may ask to contact your provider to get information about your health in limited situations that specifically relate to study, like C. diff stool test results. You would be asked to sign a medical release form giving us permission to obtain these records.

How long will I be in this study?

You will be part of the study for about 6 months – 3 months of active participation (while you are taking study medication, as well as an 8-week follow-up period) and a phone call 3 months later. The researchers may take you out of the study, even if you want to continue, if

- Your health changes and the study is no longer in your best interest
- You do not follow the study rules or no longer meet the requirements to be in the study
- The study is stopped by the sponsor or researchers

How is being in this study different from my regular health care?

People being treated for infections not related to CDI usually receive an antibiotic to treat their infection. They do not usually receive additional treatments as a result of their past CDI.

As part of this study, half the people enrolled will get an additional treatment with vancomycin to take with their prescribed antibiotic, while the other half of people will get a placebo pill to take.

Do I have to be in the study? What if I say "yes" now and change my mind later?

No, you do not have to be in this study. Taking part in research is voluntary. This means that you decide if you want to be in the study. If you decide now to take part, you can choose to leave the study at any time. Let the researchers know if you choose to leave the study. We will ask you to come in for a final study visit to check your health status.

If you decide to be in the study, the researchers will tell you about new information or changes in the study that may affect your willingness to continue in the study.

If you decide not to take part in the study, or if you choose to leave the study, your choice will not affect any treatment relationship you have with healthcare providers at UW-Madison, UW Health or any affiliated organizations, or any services you receive from them. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

Your authorization for researchers to use your protected health information (PHI) will last until the research study is done. However:

- You can choose to take back your authorization for researchers to use your health information. You can do this at any time before or during your participation in the research.
- If you take back your authorization, information that was already collected may still be used and shared with others, but the researchers will no longer be able to collect NEW information about you.
- If you take back your authorization, you will not be able to take part in the research study.
- To take back your authorization, you will need to tell the researchers by writing to the Lead Researcher, Nasia Safdar at University of Wisconsin-Madison, Department of Infectious Diseases, UW Medical Foundation Centennial Building, 1685 Highland Ave, Madison, WI, 53705.

Will being in this study help me in any way?

We do not expect that you will directly benefit from participating in this study. Your participation in the study may benefit other people in the future by helping us learn more about how to treat recurrent CDI.

This study is not a substitute for your regular medical care. You should continue to see your regular medical providers.

What are the risks?

Known side effects from oral vancomycin range from mild to severe, and include hearing loss, constipation, nausea, abdominal pain, and kidney problems including swelling, rapid weight gain, and reduced urination.

For both vancomycin and placebo, there is a risk for choking on the pill and/or experiencing an allergic reaction. Allergic reactions can be mild or more serious, and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you think you are having an allergic reaction, let the study doctor know right away. If you are away from the hospital and think you are having an allergic reaction, especially if you have swelling of your throat or trouble breathing, call 911 immediately and get medical assistance.

There is also risk that your information could become known to someone not involved in this study. The study team has taken precautions to minimize these risks by keeping the number of team members to only those needed to complete the study, storing all electronic data on password-protected servers, and storing all paper copies in locked filing cabinets.

There may be risks to you, or to an embryo or fetus, if you are pregnant or father a child that are currently unforeseeable while taking study pills. Because of unknown fetal risk, women of childbearing potential in sexual relationships with men must use an acceptable method of contraception from enrollment until 4 weeks after completing the study. Acceptable methods include, but are not limited to barrier with spermicidal foam or jelly, intrauterine device, hormonal contraception, intercourse with men who underwent vasectomy.

If you are asked to provide a blood sample for pregnancy testing, venipuncture complications are rare, but can include fainting, dizziness, and bruising or swelling at the puncture site (known as a hematoma).

Will being in this study cost me anything?

There will be no cost to you for any of the study activities or procedures.

Will I be paid or receive anything for being in this study?

You will be paid up to $300 for your participation in this study. You will be paid $150 for completing visit 1, $50 each for completing visits 2, and 3, and payments will be provided at the end of each study visit. You will receive an additional $50 for completing all of the patient diaries and returning them to study staff. If you choose to withdraw or we take you off the study before you complete the study, you will be paid for the activities that you have completed

What happens if I am injured or get sick because of this study?

If you are injured or get sick because of this study, medical care is available to you through UW Health, your local provider, or emergency services, as it is to all sick or injured people.

- If it is an emergency, call 911 right away or go to the emergency room.
- For non-emergency medical problems contact your regular health care provider.
- Call the Lead Researcher, Nasia Safdar, at (608) 213-4075 to report your sickness or injury.

Here are some things you need to know if you get sick or are injured because of this research:

- If the sickness or injury requires medical care, the costs for the care will be billed to you or your insurance, just like any other medical costs.
- Your health insurance company may or may not pay for this care.
- No other compensation (such as lost wages or damages) is usually available.
- UW-Madison and UW Health do not have a program to pay you if you get sick or are injured because of this study.
- By signing this consent form and taking part in this study, you are not giving up any legal rights you may have. You keep your legal rights to seek payment for care required because of a sickness or injury resulting from this study.

How will the researchers keep my research information confidential?

We have strict rules to protect your personal information and protected health information (PHI). We will limit who has access to your name, address, phone number, and other information that can identify you. We will also store this information securely. We may publish and present what we learn from this study, but none of this information will identify you directly without your permission.

However, we cannot promise complete confidentiality. Federal or state laws may permit or require us to show information to university or government officials responsible for monitoring this study. This includes access to your medical records so that study monitors, auditors, the Institutional Review Board and regulatory authorities can verify study procedures and/or data. These groups will maintain your confidentiality. By signing this consent form, you are authorizing this access to your records.

Who at UW-Madison can use my information?

- Members of the research team
- Offices and committees responsible for the oversight of research
- Personnel who schedule or perform medical tests or procedures, handle accounting and billing, or do other tasks related to this study

Who outside the UW-Madison may receive my information?

- U.S. Office for Human Research Protections
- The Agency for Healthcare Research and Quality (AHRQ), which sponsors the study.
- The U.S. Food and Drug Administration (FDA)
- Collaborating researchers outside UW-Madison, including researchers at the Medical College of Wisconsin.

Will information from this study go in my medical record?

- If we collect a blood sample for a pregnancy test as part of the study, the result of this test will be recorded in your medical record.
- No other data we collect for this study will be put in your medical record.

Authorizing the research team to use your PHI means that we can release it only to the people or groups listed above, and only for the purposes described in this form. However, once your health information is released outside UW-Madison or UW Health it may not be protected by privacy laws and might be shared with others.

Also, if ALL information that can identify you is removed from the health information collected in this study, then it is no longer PHI and this authorization will no longer limit how the remaining information

can be used. This means the information could be used or shared for reasons other than the ones described in this form, such as a research study about another kind of disease. It also means that the information could be shared with researchers working at institutions that are not listed above.

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 search this website at any time.

E-mail contact

If you prefer e-mail over phone calls, we are able to communicate with you via e-mail about study visit appointments and reminders for home stool collection and dosing. You do not have to provide your e-mail address to participate in this study. E-mail is generally not a secure way to communicate about your health as there are many ways for unauthorized users to access e-mail. You should avoid sending sensitive, detailed personal information by e-mail. E-mail should not be used to reach someone immediately; if you need urgent assistance please call Dr. Nasia Safdar at (608) 213-4075

____No, I do not want to be contacted via e-mail.

____Yes, you may use e-mail to contact me for this study. My e-mail is:_____

Optional Sample Banking

You will be asked to indicate below whether you consent to allow any leftover stool samples collected for this study to be stored at UW-Madison to be used for future research in order to learn more about fecal microbiota. Your specimens would be labeled with a code, linked to information collected during this study, such as your medical history. However, any information that could identify you will be stored separately from your samples for purposes of the banking.

These samples and data will be kept indefinitely, meaning there are no plans to destroy them. You can decide if you want your sample to be used for future research or have them destroyed at the end of the study. Your decision can be changed at any time, even after the study ends by notifying the study team. However, if you consent to future use and some of your stool has already been used for research purposes, the information from that research may still be used.

Samples may be shared with other researchers at other institutions outside UW-Madison with their consent. Each sample will be coded (labeled) only with a barcode and a unique tracking number to protect your confidentiality. Research using stored samples and data may be conducted by other institutions. Any samples provided to the receiving-institution will be coded. In no case will either individual personal identifiers or the key linking coded data to individuals be released to the other (receiving) institution.

Please initial below indicating your preference. Your decision to allow us to store these samples is optional and does not affect your participation in the study. We will only store leftover samples and no additional stool samples will be collected.

_____ My initials here give permission to have my leftover stool samples stored for possible future research testing. I understand I will not be contacted prior to these samples being used or to inform me of how they will be tested. If I agree to the storage of the samples, I can decline the use of the samples at any time in the future if I change my mind.

_____ My initials here indicate I do NOT want my stool samples stored for possible future research testing. My samples will be destroyed at the end of study.

What if I have questions?

If you have questions about this research, please contact the Lead Researcher, Nasia Safdar, at (608) 213-4075. If you have any questions about your rights as a research subject or have complaints about the research study or study team, contact UW Health Patient Relations at 608-263-8009. The Patient Relations Representatives work with research subjects to address concerns about research participation and assist in resolving problems.

Agreement to participate in the research study

You do not have to sign this form. If you refuse to sign, however, you cannot take part in this research study. If you are a Legally Authorized Representative (LAR) for the person being invited to take part in this study, you are deciding whether the person can be in this research study.

If you sign the line below, it means that:

- You have read this consent and authorization form.
- You have had a chance to ask questions about the research study, and the researchers have answered your questions.
- You want to be in this study, or if you are a LAR you believe the person wants, or would want to be in the study. If you cannot find out if the person wants to take part, you believe that participating in the study is in the person's best interest
- You give authorization for your protected health information to be used and shared as described in this form.

Printed Name of [Subject/Participant]

Signature of Research [Subject/Participant] Date

Printed Name of Legally Authorized Representative, if applicable

Signature of Legally Authorized Representative, if applicable Date

Signature of Person Obtaining Consent and Authorization Date

****You will receive a copy of this form****