

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

Study Title for Participants: A Randomized Controlled Trial of Oral Vancomycin for Preventing Recurrent *Clostridium difficile* Infection

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

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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 the use of oral Vancomycin, an antibiotic, for recurrent *Clostridium difficile* infection (CDI). We are inviting you to participate because you have been recently diagnosed with a CDI episode (within the past 90 days) and are currently receiving antibiotics for a non-CDI related infection, or you are willing to participate in the study if you begin new antibiotics in the near future.

The purpose of this consent and authorization form is to give you the information you need to decide whether to be in the study. It also explains how health information will be used for this study, and 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?

The purpose of this research study is to compare the recurrence rate of CDI and the composition of gut microbes (microorganisms that live in the digestive tracts in humans) in individuals undergoing oral treatment with vancomycin versus those given an inactive pill called placebo. We are doing this research because recurrences of CDI are common, difficult to treat, and pose significant threats to public health. Vancomycin is one treatment option for an active CDI episode, but preventive treatment with vancomycin to reduce future episodes of recurrent CDI has not been studied. Because of the high risk of recurrence with antibiotic use and lack of effective therapies available, new approaches to prevent CDI recurrence in patients receiving antibiotics would be a major advance in the field. This is a critical gap that our research group strives to fill.

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, the researchers will ask you to participate in a screening/baseline visit (visit 1), a follow-up visit after taking your last dose of either vancomycin or placebo (visit 2), and a final study visit 8 weeks following your last dose of either vancomycin or placebo (visit 3). If you are still hospitalized during this time, study staff will visit you regularly until you are discharged.

You would be asked to complete a patient diary each day for the duration of the study. On the patient diary, you will track each stool you produce that is consistent with diarrhea, 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.

Visit 1 (will last approximately 90 minutes): Study staff will review the informed consent form with you in detail (both orally and in writing) 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, 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. In addition, if you are a female of child-bearing potential, you will also be asked to undergo a urine pregnancy test. Pregnant women are excluded from this study.

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 current medications. Information on your alcohol use and smoking is being collected because studies have shown that these substances can cause alterations in the types and amounts of different bacteria in your gut, which could affect the results of the 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.

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 daily for the duration of your other antibiotic treatment plus 5 days.

Visit 2 (will last approximately 60 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 60 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 visit (Visit 3).

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.

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.

How long will I be in this study?

You will be part of the study for about 3 months (while you are taking study medication, as well as an 8-week follow-up period).

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.

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.

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 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.

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 \$100 for your participation in this study. You will be paid \$25 for completing visits 1, 2, and 3, and payments will be provided at the end of each study visit. You will receive an additional \$25 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 Indiana University and the Medical College of Wisconsin.

Will information from this study go in my medical record?

- None of the 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 investigators 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 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.
- 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

Signature of Person Obtaining Consent and Authorization

Date

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