RANDOMIZATION CONSENT FORM

Title: The Comparison of Outcomes of Antibiotic Drugs and Appendectomy (CODA) Trial

Protocol No.: None
WIRB® Protocol #20161339
1218443

Sponsor: University of Washington

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Emergency Phone (24 hours): Damien Carter, MD: 206-234-6828

Researchers' statement

We are asking you to be in a research study. The purpose of this consent form is to give you the information you will need to help you decide whether to be in the study or not. Please read the form carefully. You may ask questions about the purpose of the research, what we are asking you to do, the possible risks and potential benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions, you can decide if you want to be in the study or not. This process is called "informed consent." We will give you a copy of this form for your records.

University of Washington will be referred to as sponsor throughout this document.

PURPOSE OF THE STUDY

You are being asked to take part in this study because you have appendicitis. Appendicitis is due to inflammation of the appendix, which is a small tube about three inches long that is attached to your intestine and is located in the right lower area of your abdomen. Appendicitis is most likely caused by bacteria that grow and collect in the appendix, causing pain and swelling.

This study is comparing outcomes of two accepted treatments for appendicitis – one that is commonly used in Europe (antibiotics) and one that is commonly used in the United States (appendectomy). The most common treatment for appendicitis in the United States is an appendectomy, a surgical procedure to remove the appendix. During an appendectomy, people are given anesthesia (medication that will put them to sleep), and the doctors remove the appendix. The operation can be done with three small incisions (cuts) on the skin using instruments that are guided by a camera – this is called laparoscopic appendectomy. The operation can also be done with a single incision called an open appendectomy. If you have surgery, the doctor will discuss these two approaches. The operation usually takes about an hour. You may feel groggy in the hours after surgery. Most patients do well and go home the next day, but some people stay longer due to complications of the surgery or because of other reasons. Most people eat and drink shortly after the surgery and return to normal activities after a week or so.

Over the last decade, six studies including more than 1700 people in Europe have found that treatment with antibiotics (medications that kill bacteria) instead of surgery is safe and avoids appendectomy in most patients with appendicitis. Patients taking antibiotics for appendicitis will receive at least one dose of intravenous (through the vein) antibiotics followed by oral (taken by mouth) antibiotics for a total of 10 days. After that first dose of intravenous antibiotics, some people may be able to leave the emergency department and go home for the rest of their antibiotics treatment. Others will be admitted to the hospital for another day of intravenous antibiotics. Whether or not you can go home from the emergency room after your first dose of intravenous antibiotics depends, in part, on how well you feel. You and your doctor will decide whether or not you need to be admitted to the hospital or can go home from the emergency department.

The purpose of this study is to see whether 10 days of antibiotics is just as good as an appendectomy in the treatment of appendicitis. About 2,100 patients will be enrolled in this study. Although appendectomy and antibiotics for appendicitis have both been studied before and found to be safe, this is the first randomized trial to be conducted in the United States to study patient reported outcomes and rates of success with the antibiotic treatment in avoiding appendectomy.

STUDY PROCEDURES

If you decide to volunteer for the study, you will receive either the surgical treatment (appendectomy) or the antibiotics treatment. For patients who are getting the antibiotics treatment, if the signs and symptoms of appendicitis are not improving enough after 48 hours with the antibiotics, then your doctor may recommend surgery to remove the appendix. No matter what treatment you receive, we will control your pain and make sure you can eat and take your medications before you go home.

A computer will randomly assign you to either antibiotics or surgery. You have an equal chance of being assigned to either treatment.

The study involves questions that will be asked about the treatment you received, your current health status, and your quality of life. These questions will be asked at different time points for two years. At the end of the two-year follow-up, we may contact you to ask if you would be willing to participate in a longer-term study with yearly surveys. In addition, we would like to use some of the information collected about you for this study for future research related to understanding the characteristics of surgical patients (across many types of surgeries) and their outcomes.

Screening and Enrollment

The research coordinator will review your medical record and ask the emergency medicine doctors and surgeons to see if you are eligible to participate in the study. The emergency medicine doctors and surgeons will make this decision based on carefully reviewing the standard tests and procedures that you had when you first came to the emergency room. We will ask you to watch a video or read an informational pamphlet about the treatment options to help you decide whether or not you would like to participate. After you review the study information, you will have the opportunity to ask questions and to further discuss this study with the research coordinator.

In order to be in this study, you must not be pregnant as evidenced by a negative pregnancy test prior to enrollment, and not planning on becoming pregnant within 30 days.

If you are eligible to participate in the study and you decide to take part, you will review and sign this consent form. You will then be randomly assigned to either surgical treatment or antibiotics treatment for your appendicitis.

You will be asked to complete several questionnaires with the research coordinator. These questionnaires will ask you to answer questions about your appendicitis and pain level and intensity. The survey will take about 20 minutes to complete.

Follow-up

There will be additional phone-based, email-based, mailed, or text-message follow-up questions after today, but you will not need to come back to the hospital or clinic to complete this study. You will be paid for your time to complete these studies.

A day or two after you leave the hospital, the study coordinator will contact you to answer any questions you have about the study and to review the follow-up visit schedule. Study staff will also remind you of your follow-up appointment with your medical care team.

The table below describes when you will be contacted for research visits.

	Follow-Up Surveys								
	Year 1							**Year 2**	
	First 4 Weeks			**Month**					
Enrollment Visit	1	2	4	3	6	9	12	18	24
Today	X	X	X	X	X	X	X	X	X

You will be followed up with once a week for two weeks and you will be asked to complete a short questionnaire with the study coordinator on the phone. These questionnaires will ask you to answer questions about your appendicitis symptoms, your medication use, and if you have returned to see a doctor. The surveys for Weeks 1 and 2 will take about 10 minutes to complete.

At the Week 4 follow-up, you will be asked to complete questionnaires about your quality of life and experience as a patient with appendicitis. We will ask you about your pain level and severity, your symptoms, your satisfaction with your treatment, and your ability to return to your work, school, or daily activities. Altogether, the Week 4 survey will take about 20 minutes.

After the first three follow-ups, the next follow-up will be about 3 months from today. You will be contacted every three months from then on for the first year (6-, 9-, and 12-months from today). After the first year of study participation, we will contact you twice more: about 18-months and 24-months from today. Study staff will contact you to complete surveys by phone, by mail, or they may provide you with information on how to answer the survey questions on the internet. The questionnaires will take about 15 minutes to complete. You will be asked to answer questions about the following:

- If you have had any new symptoms related to your appendicitis;
- If you went to see a doctor about your appendicitis;
- How much time and money your medical care cost;
- Your work productivity;

- Your pain level;
- Your satisfaction with your treatment;
- Your gastrointestinal health and your overall quality of life; and
- If you have any new contact information.

During the study, you will be monitored for complications and other illnesses in addition to appendicitis. We would like to record information from your medical records. We will record information about you before and after your treatment date and other information like your age, insurance status, and smoking history. We will also record information that doctors record in your medical record including your medical history, laboratory and imaging tests, medications you are taking, information about your treatments, hospitalizations and any clinical outcomes that occur after your treatment. If you visited another facility for care related to your appendicitis during the study, you may be asked to provide your consent to release those medical records to the study team. While we will only contact you for up to two years to complete surveys, we may continue to collect information from your health records up until the end of the study.

The information that you provide in these follow-up questionnaires is confidential and will not be shared back with your physician unless you report any symptoms suggesting appendicitis-related health concerns.

RISKS, STRESS, OR DISCOMFORT

Participating in this study may have risks. Prior studies have shown that antibiotics treatment of appendicitis without surgery is safe, but on average, previous studies show that 25% or 1 in 4 patients treated this way go on to have an appendectomy in the next year. Surgery, which is the current standard treatment for appendicitis, has risks that include bleeding, wound infection, pain, scarring, and problems from anesthesia (putting you to sleep for surgery). If you will be having surgery for your appendicitis, then the surgeons will explain the possible risks in detail and will get your consent for surgery as they normally would.

Antibiotics are also given routinely for appendicitis, even when it is treated with surgery. Risks of antibiotics include allergic reactions (sometimes severe) and diarrhea. The antibiotics used in this study have risks that are similar to the antibiotics you would be receiving even if you do not participate in the study. Your specific medication regimen and its side effects will be discussed with you by your treating physician.

In prior studies of antibiotics treatment of appendicitis, there was no higher rate of a ruptured (“burst”) appendix in patients who had antibiotics only and complications did not happen more often when compared to the surgery patients. Because of small numbers of patients in these studies, we cannot say for sure whether the risk is greater or not in one group or the other. One study found a slightly greater rate of infection in the abdomen with antibiotics treatment, but the difference was not considered significant. An analysis of all studies of antibiotics vs. surgery for appendicitis found that patients treated with antibiotics alone had nearly half the complications of the surgery group as well as less pain and faster recovery time than the surgery group.

One advantage of surgery is that very rarely when surgeons look inside your abdomen they find unrelated problems in your internal organs. This might mean that your surgeon identifies a mass or cancer in another organ (e.g., liver) or even in the appendix itself (~1 in 200 appendix removals identify some mass of the appendix). If we treat patients with antibiotics only (without surgery), we might “miss” the opportunity to see another problem that we did not expect to find (such as a small mass that cannot be seen in the computed tomography (CT) scan or ultrasound test you had in the diagnosis of appendicitis).

It is expected that some patients who are selected to be treated with antibiotics alone may still need surgery. In other studies, most of these surgeries occurred in the first few weeks after the antibiotics treatment was started. Some patients had surgery because the appendicitis did not get better with antibiotics alone, and some got better but had symptoms of appendicitis again later.

We will ask you to complete a number of surveys over the next two years, which will help us understand how your treatment has worked for you. There are some personal questions. You may feel discomfort when completing the survey questions. You are free to skip any questions that you do not want to answer. There is also a possibility that there could be a loss of confidentiality. Some people do not want information from their medical records used for research. Every effort will be made to ensure your confidentiality is protected throughout the duration of the study. We have addressed concerns about confidentiality below.

This study may pose risks that we do not currently know about. You may also receive the same treatment even if you choose not to enroll in the study.

ALTERNATIVES TO TAKING PART IN THIS STUDY

If you choose not to participate, you and your doctor will discuss the best way to treat your appendicitis. If you choose not to participate in randomization, we may also talk to you about other ways you can participate in this research. The alternative to participation in the clinical trial is receipt of usual care, which currently most often involves urgent surgical appendectomy with peri-operative antibiotics.

BENEFITS OF THE STUDY

Although it is possible that you may not receive any direct benefit from your participation in this study, you will contribute to medical knowledge that may help improve future patient choices in their treatment decisions about appendicitis.

SOURCE OF FUNDING

The study team and/or the University of Washington is receiving financial support from the Patient-Centered Outcomes Research Institute (PCORI).

CONFIDENTIALITY OF RESEARCH INFORMATION

The researchers will keep your study information confidential. We will assign a unique study code to your study information. Information that identifies you will be kept in a secure location. We will destroy any link between you and the study information once the study has ended. If the results of this study are published, we will not use any information that identifies you.

- Government regulators, such as the U.S. Food and Drug Administration (FDA), university staff, and agents for the sponsor; agents for the study doctor, and Western Institutional Review Board ® (WIRB®) review studies such as this one to make sure they are being done safely and legally. If a review of this study takes place, your study information or research records may be examined. The reviewers will protect your privacy. Your study information or research record will not be used to put you at legal risk of harm.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Your coded research information will be combined with information from other sites at the Data Coordinating Center located at the University of Washington. The Data Coordinating Center will store information that can identify you in a separate location.

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information may be used and given to others?
The study doctor will get your personal and medical information. For example:
- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits.

Who may use and give out information about you?
The study doctor and the study staff.

Who might get this information?
The sponsor of this research. "Sponsor" means any persons or companies that are:
- working for or with the sponsor, or
- owned by the sponsor.

Your information <u>may</u> be given to:
- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies in other countries,
- Governmental agencies to whom certain diseases (reportable diseases) must be reported, and
- Western Institutional Review Board® (WIRB®)
- Employees of Maine Medical Center Office of Research compliance

Why will this information be used and/or given to others?
- to do the research,
- to study the results, and
- to make sure that the research was done right.

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?
Yes, but this permission will not stop automatically.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
There is a risk that your information will be given to others without your permission.

Will the information collected as part of this study be destroyed when it is no longer needed?
It is difficult for sponsor or investigator to know how long your information will be kept. Your information will be kept at least until the data are sent to FDA/data collection center/sponsor, but most likely it will be kept on the database at sponsor for an indefinite length of time. We do not know when your information will no longer be used, and there is no expiration date after which it will be discarded.

OTHER INFORMATION

Your participation in this study is completely voluntary. You may refuse to participate and you are free to withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled. If you choose to withdraw, the study doctor will still be able to use the information collected about you prior to your withdrawal from the study. Information that has already been sent to the study sponsor may not be able to be withdrawn.

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent for any reason.

You will be told about any new information that might change your decision to be in this study.

You are responsible for the cost of your clinical care that includes, but is not limited to, the costs for surgery and/or antibiotics. There may be a difference in costs between the two treatments. These treatments are considered routine treatments for appendicitis. All medications, laboratory fees, physician fees, and hospital costs will be charged to you in the same way as if you were not a part of this study. You are responsible for either paying for or having your insurance pay for all the clinical care you receive during the study. If you have a complication from your assigned appendicitis treatment, you are responsible for the cost of follow-up care in the same way as if you were not part of this study.

You will receive a total of $125 for completing the surveys related to the study. You will receive $20 for completing the baseline questionnaires today. You will receive $10 for both the Week 1 and Week 2 follow-up surveys and $20 for the Week 4 survey for a total of $40. You will receive $10 for each of the quarterly follow-up surveys (3-, 6-, 9-, and 12-months) for a total of $40. You will receive $10 for the 18-month survey and $15 for the final 24-month survey.

RESEARCH-RELATED INJURY

If you become sick or injured during your participation in this study, Damien Carter, MD will arrange or provide medical care. Medical treatment is available and will be provided at the usual charge.

The sponsor of this research is a part of the federal government/foundation. It is University of Washington policy, that if you are injured or become ill as a result of research procedures, medical treatment will be provided to you but University of Washington will not pay for this treatment. If any research activity resulted in an injury, treatment will be available, including first aid, emergency treatment and follow up care as needed. Care for such injuries will be billed in the ordinary manner to you or your insurance company.

However, this does not take away your rights to seek or collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research, including the hospital.

You or your insurance company will be responsible for any costs resulting from underlying disease or treatments provided to you outside of this research study.

If you think that you have suffered a research related injury, let the study physicians know right away. If you have any questions or concerns about the legal responsibility of University of Washington please call Damien Carter, MD at 206-234-6828 at Maine Medical Center.

Subject's statement

This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions, concerns, or complaints later about the research, or if I have been harmed by participating in this study, I can contact one of the researchers listed on the first page of this consent form. If I have questions about my rights as a research subject, or questions, concerns, or complaints about the research, I can contact:

Western Institutional Review Board® (WIRB®)
1019 39th Avenue SE Suite 120
Puyallup, Washington 98374-2115
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com.

WIRB is a group of people who perform independent review of research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, I may contact WIRB if the research staff cannot be reached or if I wish to talk to someone other than the research staff.

I give permission to the researchers to use my medical records as described in this consent form. I will receive a copy of this consent form.

Printed name of subject	Signature of subject	Date

Printed name of study staff obtaining consent	Signature	Date

Copies to: Researcher
Subject