Informed Consent

Impact of Parasitic Infections on Intestinal Epithelial Barrier and Immune Activation Among Persons Living With HIV in Lilongwe, Malawi

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This consent form should be signed on; between 5 Mar 22 and 5 Oct 2022
Approved by NHSRC, Malawi on 5 Mar 22

University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

Consent Form Version Date: v4.0 dated Feb 2022
UNC IRB Study: 21-2553
NHSRC Study #21/08/2764 UNCPM 22113

Title of Study: UNCPM 22113: Impact of parasitic infections on intestinal epithelial barrier and immune activation among persons living with HIV in Lilongwe, Malawi

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Funding Source and/or Sponsor: National Institutes of Health Fogarty

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CONCISE SUMMARY

The purpose of this research study is to learn more about how parasitic infections affect a person living with HIV. Parasitic infections can cause damage to the intestines, leading to inflammation (irritation) throughout the body, which can weaken the immune system even further in persons living with HIV. We will be using an investigational lab test on your stool sample to identify if you have a parasitic infection.

In order to be a part of the study, we would like to see you for at least 2 visits. During two of these visits, you will have blood drawn (2 teaspoons or 10mL) for tests to evaluate your immune system and the presence of inflammation. In addition, you will provide a stool sample and a urine sample at each visit to test for parasitic infections.

If any of your test results are positive for a parasitic infection, we would like to see you for an additional "treatment visit" to give you antiparasitic medication (pills). The potential benefit of this study is that parasitic infection that you did not know about could be identified and treated. The risks associated with the study include pain or bleeding during blood draws, or an adverse reaction to an antiparasitic medication. These medications are usually very well tolerated.

What are some general things you should know about research studies?
You are being asked to take part in a research study. To join the study is voluntary. You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge that may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies.

Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher or your health care providers. If you are a patient with an illness, you do not have to be in the research study to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study. If you decide that you would like to take part in this study, we will ask you to sign or thumbprint this consent form.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

The purpose of this research study is to learn more about how parasitic infections affect a person living with HIV. Parasitic infections can cause damage to the intestines, leading to inflammation (irritation) throughout the body, which can weaken the immune system even further in persons living with HIV. We will be using an investigational biochemistry test that is not available for clinical use to detect parasitic infections in your stool sample as well as a microscope stool test. The investigational biochemistry test is only available in the research setting. Other studies have shown that this test is able to detect more cases of parasitic infection than the microscope stool test that is used in most laboratories.

Patients with HIV can live longer and lead healthier lives now that antiretroviral therapy is more available. Yet, even patients with HIV that take their antiretroviral therapy regularly seem to have more "inflammation" (irritation) and activation of the immune system. The immune system is the body's defense against infections. Certain infections due to parasites that are common in Malawi can cause damage to the intestines, leading to inflammation (irritation) throughout the body, and weaken the immune system even further in persons living with HIV.
You are invited to take part in a research study because you are a person living with well-controlled HIV, and you live in an area where parasitic infections are common.

Are there any reasons you should not be in this study?

You should not be in this study if:

- you have received antibiotics in the last 60 days (other than trimethoprim-sulfamethoxazole to prevent infection)
- you have received an antiparasitic medication (albendazole, praziquantel) in the last year.
- you are not taking your antiretroviral medication and therefore have a detectable viral load then you can not be a part of the study.
- you have any Inflammatory bowel disease or gastrointestinal tract malignancy

- you have had major intestinal surgery during the last 2 years;
- you are infected with Mycobacterium tuberculosis.
- you are pregnant, planning to become pregnant, or breastfeeding. This is because pregnancy and breastfeeding can affect the markers of inflammation that we are trying to measure.

Additionally, if you have any condition that, in the opinion of the site investigators, would make participation in the study unsafe, complicate the interpretation of study outcome data, or otherwise interfere with achieving the study objectives then you should not be enrolled in the study.

How many people will take part in this study?

If you decide to be in this study, you will be one of about 100 people to participate in this study.

How long will your part in this study last?

Your participation requires 2-3 visits, and the total duration of the study will be less than 12 months. If you do not have a parasitic infection, then it will be a total of 2 visits. If you are found to have a parasitic infection then it will be 3 visits, since we will see you for a treatment visit to give you the antiparasitic medication.

What will happen if you take part in the study?

If you agree and provide consent to participate in this study, there will be two visits which we will try to coordinate to on the same days as your medical visits. During each study visit, you will have blood drawn (2 teaspoons or 10mL) for tests to evaluate your immune system and the presence of inflammation. On the first visit you will also provide a stool and urine sample to test for parasitic infections, and a pregnancy test will be performed on women of childbearing age. On the second visit you will provide a blood and stool sample (no urine sample).

You will be given a detailed explanation about how to safely collect your stool sample. We will provide you with a clean plastic container, a pair of gloves and a small plastic bag.

The urine and stool samples that you submit will first be analyzed in the UNC Project Malawi laboratory looking for parasitic infection. The remaining stool sample and the blood sample that will be stored in a freezer at the UNC Project Malawi laboratory. They will be stored at a very cold temperature (-80 C) so that they can be processed weeks or months after they are collected. Only laboratory personnel will have access to the samples while they are stored. Once 100 participants are enrolled in the study, we will ship stool and blood samples to Houston, Texas for further testing. We will use a new test that is able to detect more parasitic infections than the test that is available in Malawi. The blood test will be used to look for parasitic infection, and to measure markers of immune activation. Your samples will be discarded at the close of the study, and will not be used for any future studies.

If either your urine, blood, or your stool sample is positive for a parasitic infection, we will contact you and order an antiparasitic medication (pills) that you can take. If you are a woman of childbearing age, we will perform a pregnancy test before administration of antiparasitic medication. If the pregnancy test is positive, we will follow the recommendations in the medical literature to give you the medication that is safest for you and your baby.

Although the biochemistry stool test that will be performed in Houston, Texas does look for DNA of parasites, it does not sequence your DNA. Thus, this research study does not include "whole genome sequencing" of your DNA.

We would like to see you for a second visit 3-6 months after your first visit and obtain a second blood and stool test.

What are the possible benefits from being in this study?
If you have a parasitic infection that is detected by either the microscope test or the biochemistry test, then you will be notified of this and you can be treated without any cost to you. This could be beneficial for your health and may make you feel better. Outside of this, there is little chance you will benefit from being in this research study, but the information gathered from this study may help researchers better understand the effect of parasitic infections in inflammation and damage of the immune system in patients living with HIV.

What are the possible risks or discomforts involved with being in this study?
If you enroll in this study, there are a few risks or discomforts that you should know about.

Having blood drawn may cause some discomfort, lightheadedness, bleeding, swelling, or bruising where the needle enters the body, and in rare cases, fainting, or infection.

There may be uncommon or previously unknown risks. You should report any problems to the researcher.

Breach of confidentiality is a risk, but measures are taken to ensure this will not happen (see below).

Taking any medication comes with a risk of a reaction, or a side effect, to the medication. The medications that will be given as a part of the study are usually well tolerated, but it is possible that someone taking one of these medications could have nausea, vomiting, diarrhea, bitter or metallic taste, headache, dizziness, abdominal pain, inflammation of the liver, rash. If you are found to have a parasitic infection then we will discuss with you in more details the possible side effects to the medication that we will recommend for you at that time.

If you are a woman and are breastfeeding, pregnant, or planning to be pregnant, you should not be a part of the study. This is because pregnancy and breastfeeding can affect the levels of inflammation that we are trying to measure. If you are found to have a parasitic infection and newly pregnant on repeat testing before administration of antiparasitics, the study team will review the options with you and provide the antiparasitic medication safest for you and the baby, but we will not use your information in the data analysis since pregnancy can affect the markers of inflammation that we are measuring.

Many drugs can get into the mother's breastmilk although usually at low levels. The effects of most antiparasitic medications on the child of a nursing mother are not clear, but because of the possibility of increasing the markers of inflammation that we are studying, we will not be enrolling mothers who are breastfeeding into our study.

If you choose not to be in the study, what other treatment options do you have?
You do not have to be in this research study to receive regular clinical care or treatment for your HIV.

What if we learn about new findings or information during the study?
You will be given any new information gained during the study that might affect your willingness to continue your participation.

Will I receive any other clinical results?
You will receive the results of your diagnostic tests which will show if you are positive or negative for parasitic infection. You will not receive any other clinical information.

How will information about you be protected?
The study team involved in this research have been trained to conduct human subjects research and in confidentiality protection. All forms and samples will be labeled with a code. All data entered into computers from these forms will be encrypted and password protected. This code can be linked back to your signed consent. These signed consent forms will be stored in a locked office and can only be accessed by the lead investigators of the study. The lead investigator at the National School of Tropical Medicine in Houston, Texas will have access to your patient identification code, so that your sample can be matched with your clinical information, but the investigators in Houston will not have access to your name or personal information.

Participants will not be identified in any report or publication about this study. Every effort will be made to keep the information you will share with us confidential to the extent permitted by the law. However, we cannot guarantee confidentiality. You will be identified by a unique study ID number. You will not be personally identified in any publication about this study. Your samples will be discarded after the close of this study. Your samples will not be used in any future studies.

All data that we will collect may be reviewed by the sponsor of the study (National Institutes of Health), the ethical and regulatory committees in Malawi, at the University of North Carolina at Chapel Hill and the office of Human Research Protection. This is for quality control and safety purposes. Your data will not be used or distributed for any future research projects without additional consent from you, even if identifiers are removed. If you are found to be positive for a parasitic infection, a note will be made in your medical chart saying which parasitic infection was detected and the treatment that you were given.

What is a Certificate of Confidentiality?
This NIH funded study has a **Certificate of Confidentiality**, this means that people outside the research team will not see your name on your research information. This includes people who try to get your information using a court order in the United States. One exception is for research projects that have been approved under applicable rules. Other exceptions are for information that is required to be reported under law, such as information about child or disabled persons abuse or neglect or certain harmful diseases that can be spread from one person to another.

Personnel of a government agency sponsoring the study may also be provided information about your involvement in the research study.

Will you receive results from research involving your specimens?
Most research from your specimens are not expected to yield new information that would be meaningful to share with you personally. You will not be compensated for the use of your samples other than what is described in this consent form. There are no plans to compensate you for any future commercial use of these specimens.

What will happen if you are injured by this research?
All research involves a chance that something bad might happen to you. This may include the risk of personal injury. In spite of all safety measures, you might develop a reaction or injury from being in this study. If such problems occur, the researchers will help you get medical care. By signing this form, you do not give up any of your legal rights.

What if you want to stop before your part in the study is complete?
You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped. If you withdraw or are withdrawn from this study all data collected up until the point of withdrawal will be retained, however no additional information will be collected unless you provide additional written permission for further data collection at the time of your withdrawal.

Will you receive anything for being in this study?
If you complete the initial visit with submission of requested samples, you will receive the Malawian Kwacha equivalent of $10 for transportation and for your time. If you test positive for a parasitic infection, the study will provide the recommended antiparasitic medication and will provide the equivalent of an additional $10 for your treatment visit. If you complete the follow up visit with submission of requested samples, you will receive an additional $10.

To summarize, those that test negative for parasitic infection and complete both study visits (baseline visit and follow-up visit) with submission of requested samples will receive the Malawian Kwacha equivalent of a total of $20 USD. Those that test positive for a parasitic infection and complete all three study visits (baseline visit, treatment visit, and follow-up visit), will receive a total of the Malawian Kwacha equivalent of $30 as compensation for your time and transportation to the clinic.

Will it cost you anything to be in this study?
It will not cost you anything to be in this study.

Who is sponsoring this study?
This research is funded by The National Institutes of Health. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If

you have questions about the study, you should contact the researchers listed on the first page of this form.

What if you have questions about your rights as a research participant?
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may, anonymously if you wish, the Head of Secretariat for the Malawi Health Sciences Research Committee Dr. Matias Joshua at 0999 39 79 13.

Title of Study: UNCPM 22113: Impact of parasitic infections on intestinal epithelial barrier and immune activation among persons living with HIV in Lilongwe, Malawi

Key Investigators: Melissa Reimer-McAtee, MD

Participant's Agreement:
If you have read this informed consent, or have had it read and explained to you, and understand the information, and you voluntarily agree to participate in this research study, **please sign your name, make your mark or place your thumbprint** in the signature area at the bottom of this page.

PART A: LITERATE PARTICIPANT

Participant is literate: ☐

Participant Name (print)	Participant Signature	Date
Study Staff Conducting Consent Discussion (print)	Study Staff Signature	Date

Title of Study: UNCPM 22113: Impact of parasitic infections on intestinal epithelial barrier and immune activation among persons living with HIV in Lilongwe, Malawi

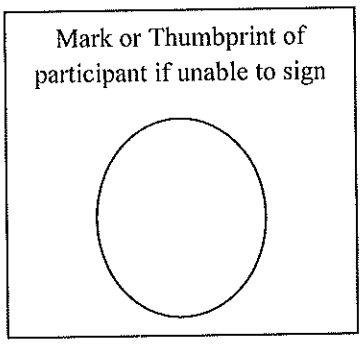
Key Investigators: Melissa Reimer-McAtee, MD

PART B : ILLITERATE PARTICIPANT

Participant is illiterate: ☐

The study staff must complete this section, ONLY if an impartial witness is available.

The **study staff must write participant's name and date of consent below.**



Participant Mark or Thumbprint

_____ _____ _____

Participant Name (print) Date

Participant Name and Date Written By.....on.....

_____ _____ _____

Study Staff Conducting Consent Discussion (print) Study Staff Signature Date

_____ _____ _____

Impartial Witness Name (print) Impartial Witness Signature Date