Written Informed Consent

Full Title: Options for Delivering Isoniazid-Rifapentine (3HP) for TB Prevention (3HP Options Implementation Trial)
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INFECTIOUS DISEASES RESEARCH COLLABORATION

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: Options for Delivering Isoniazid-Rifapentine (3HP) for TB Prevention (3HP Options Implementation Trial)

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Introduction: We are inviting you to take part in a research study to evaluate how best to deliver short-course preventive therapy for tuberculosis (TB) in the context of routine HIV/AIDS care. The treatment, called 3HP, involves taking two types of medicine, isoniazid (INH) and rifapentine (RPT) once a week for 3 months. We are asking you to participate because you access HIV care at Mulago Immune Suppression Syndrome (ISS) Clinic. You can choose whether or not you want to participate in this study. Take your time when making your decision about participating. You may discuss your decision with your family and friends, if you wish. If you have any questions, you may ask your colleagues or research staff at any time. You can ask questions any time. You can ask now. You can ask later. You can talk to me or you can talk to someone else.

Sponsor: This study is sponsored by the University of California, San Francisco (UCSF) and the Infectious Diseases Research Collaboration (IDRC).

Funding: This study is funded by the United States National Institutes of Health.

Purpose: TB is a common disease in Africa and is very dangerous. Preventive therapy can reduce your risk of developing TB, and of dying or becoming severely ill due to TB. For this reason, TB preventive therapy is recommended for all people living with HIV (PLHIV) in settings such as Uganda where TB is common. Fortunately, there is now a treatment regimen called 3HP that is shorter, safer and just as effective in preventing TB as taking INH every day for 9 months, which has until recently been the standard-of-care. We are doing this research study to find out how we can best deliver this shorter treatment regimen to PLHIV engaged in HIV/AIDS care. We will do this by randomly assigning patients to 1) come to the clinic weekly to take 3HP (also called directly observed therapy or DOT), 2) take 3HP weekly on their

own at home or work (also called self-administered therapy or SAT), or 3) have a health worker help patients choose whether to receive 3HP by DOT or SAT. In all three delivery strategies, patients will receive standardized counseling, will have streamlined clinic visits, be reimbursed a standard amount to cater for transport costs for 3HP-related clinic visits, and receive SMS messages or interactive voice response messages from the clinic to support completion of treatment.

Your rights: Taking part in this study is your choice. You may choose to take part or not take part. If you decide to take part, you may leave the study at any time. If you decide not to take part, there will be no penalty to you, and you will not lose any of your regular benefits. We may also terminate your enrollment in the study at any time, even without your consent. Leaving the study will not affect your medical care at the Mulago ISS Clinic. You will not be charged for taking part in this study, nor will you be paid for being in the study. We will tell you about new information or changes that may affect your health or willingness to continue in the study. Although this study poses minimal risk to participants, if any participant is injured as a result of being in this study, treatment available at Mulago Hospital will be provided at the expense of the study. No other form of compensation for injury will be provided.

Procedures: We will enroll 1,656 participants into this study from the Mulago ISS Clinic.

The following procedures will be done to determine whether you are eligible for the study:

- **Screening survey and review of your medical records:** We will ask you some questions and review your medical record to look for any reasons you should not take 3HP or participate in the study.
- **Evaluation for active tuberculosis:** We will check you for symptoms, and if necessary, we will prick your finger for 1-2 drops of blood to determine whether you might currently have TB.
- **Urine/Blood collection:** If you are a woman of childbearing age and have not completed a pregnancy test within the last 14 days, we will ask you to provide a urine or blood sample to confirm that you are not pregnant. These urine/blood samples will not be stored for future use.

If you are eligible for the study and agree to participate, we will randomly assign you to one of the three delivery strategies and then ask you to participate in the following activities on the day of enrollment:

- **Pre-treatment counseling:** A research nurse will provide you with standardized counseling and review a handout containing information about TB, the benefits/risks of preventive therapy with 3HP, and the details of the 3HP delivery strategy to which you have been randomly assigned. If you are randomly assigned to the choice arm, the research nurse will use a standardized decision aid to review the two options for 3HP delivery and help you choose between them. After addressing any questions, the research nurse will ask if you are willing to initiate 3HP treatment. It will be your choice whether or not to initiate treatment. Even if you choose not to initiate treatment, we will ask you to complete the other study procedures below.
- **Demographic/Clinical Survey and review of your medical record:** We will ask you some questions about your background and about your medical conditions. You may refuse to answer certain questions (if the questions make you feel uncomfortable) and still participate. We will review your medical record for information about your medical conditions and for lab tests.
- **Counseling Survey:** We will ask you some questions to assess uptake of some key messages included in our standardized counseling and the costs you face in coming to the clinic.
- **Medication ingestion:** If you agree to initiate 3HP treatment, we will ask you to take two types of medicine, INH and RPT, to prevent TB and Vitamin B6 to help prevent side effects once a week for 12 weeks. If you are taking 3HP by SAT, we will ask you to come back to the clinic for refill visit/check-up visits 5 weeks after you begin and at the end of treatment (12 weeks). If you are taking 3HP by DOT, we will ask you to come back to the clinic each week for 12 weeks.
- **Weekly reminders:** As a part of this study, you will receive a message via Short Message Service (SMS) or phone call weekly 1) to remind you to take medicines and check-in about side effects if you are taking 3HP by SAT or 2) to remind you to come to the clinic to take medicines if you are taking 3HP by DOT.

We will ask you to participate in the following activities after you stop taking 3HP:

- **Care Experience Survey:** After 3HP treatment is completed, we will ask you some questions to document your experience with TB preventive care.
- **Sputum collection:** After 3HP treatment is completed, we will ask your clinic doctors to check in with you at your routine clinic visits every 2-3 months to ask you about TB symptoms and collect sputum for TB testing if you are symptomatic. If needed, we may ask you to breathe salt water mist in order to produce sputum. These sputum samples will not be stored for future use.

We may also ask you to participate in the following activities:

- **Choice survey:** If you are randomly assigned to the patient choice arm, we will ask you some questions to assess the reasons why you chose DOT or SAT.
- **Cost Survey:** We will select approximately one-quarter of participants who initiate 3HP treatment to participate in the cost survey once they stop taking treatment. The survey will ask you some questions to assess the costs you faced in taking 3HP treatment.
- **Time-and-motion studies:** We will select approximately one-quarter of participants who initiate 3HP treatment to participate in time-and-motion studies while they are taking treatment. This will involve you recording the amount of time you spend to complete each activity related to 3HP treatment during one of your clinic visits.
- **In-depth Interviews:** We will select up to 24 participants from each study arm who have undergone 3HP treatment to participate in these interviews. If you are selected for this interview, we will ask you to tell us your experiences while taking 3HP. This interview may be conducted over the phone.

Duration of study: If you choose to participate, completing the baseline survey will take about 30-45 minutes. Participation in other Day 1 procedures mentioned above will take about 50 minutes. If you are taking 3HP by SAT, we will ask you to return to the ISS Clinic in approximately 5 weeks for your medication refill and follow up appointment and at the end of treatment (12 weeks). If you are taking 3HP by DOT, we will ask you to return to the ISS Clinic every week for 12 weeks. In approximately 15-16 months, we will ask you to submit sputum for assessment if you have TB symptoms. If chosen to participate, completing the cost survey will take about 30-45 minutes, time-and-motion activities will take about 10 minutes and In-depth interviews will take about 30-45minutes. Your participation will end after your last study visit.

Risks and side effects:

- **Baseline survey and review of your medical record:** Providing us with personal information may be uncomfortable or lead to loss of privacy. We will take precautions to prevent you from being uncomfortable and to prevent revealing your medical information. For example, we will not keep track of your name but for our records we will keep track of the date.
- **Finger prick:** You may feel some pain from the needle puncturing your skin. There may be some darkening at the site after, but if you have prolonged pain, warmth, or tenderness, tell your doctor.
- **Side effects from medication:** Although the medication being used in this study has a lower rate of side effects than the most commonly used preventive TB regimen and very few side effects/adverse events have occurred in previous studies using 3HP, you may experience some side effects or adverse events as a result of taking study medication. This can include hypersensitivity reactions (e.g. fever, chills, headaches, dizziness, muscle, joint or bone pain), shortness of breath or other signs and symptoms including wheezing, skin rash, and feeling light headed or having low blood pressure. Other side effects, including yellowing of eyes, abdominal pain or nausea due to liver injury, are uncommon with once-weekly dosing but will also be assessed at every clinic visit or by weekly SMS check-in. 3HP reduces the effectiveness of hormonal birth control including both oral and injectable contraceptives, which increases the risk of pregnancy. While taking 3HP, barrier methods of contraception are required to prevent pregnancy.

- **Sputum induction:** Breathing the salt water mist will make you cough and produce sputum. You may feel short of breath or experience mild chest pain from coughing during this test. Please tell us if you have side effects during the study.

- **Injuries:** If you are injured as a result of being in this study, you will receive immediate treatment for your injuries. You must tell the study team if you feel that you have been injured. You can tell any of them in person or call them at the telephone numbers listed on this consent form. The usual treatments offered at Mulago Hospital will be available. Care will be provided free of charge, if possible, for protocol-related injuries using available funds. Makerere University and the study sponsor do not normally provide any other form of compensation for injury.

If you are a woman of childbearing age additional risks or discomfort associated with pregnancy testing include:

- **Urine collection:** You may feel uncomfortable urinating into a specimen cup, but it is unlikely that you will feel discomfort or experience any side effects from this procedure. If you experience burning when you urinate, please tell us as this may be a sign that you have a urinary tract infection.
- **Blood collection:** You may feel some pain from the needle going through your skin. There may be some darkening at the site after, but if you have prolonged pain, warmth, or tenderness, tell your doctor. If your blood count is low, you may feel weak after the procedure. We will check your blood count if your blood count appears low to try to avoid this.

Benefits: Participating in this study might lower your risk of developing TB if you complete treatment with 3HP. In addition, you will help to provide more information about how best to deliver 3HP to people living with HIV.

Confidentiality: If you agree to join this study, we will collect some personal information from you, but only the people working on the study will see it. We will assign a code to your information. The key to the code will be stored in a safe place. Your name will not be used in any published reports from research using your health information. Research staff will have access to information about you, but they will not keep or release any identifying information about you to others. If you are found to have active TB, research staff will access your personal information (name, telephone number, clinic records) and contact you immediately to inform you of your TB diagnosis and arrange immediate referral to HIV/TB clinicians so that you may begin life-saving TB treatment. To make sure the project follows good research practices, the Makerere University School of Public Health Higher Degrees Research and Ethics Committee, the UCSF Institutional Review Board, the Ugandan National Council for Science and Technology, or the U.S. National Institutes of Health may look at or copy records that show your study number. We will comply with all laws that protect your confidentiality.

Trial Registration: 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.

Voluntary participation: Participating in this study is voluntary. It is your choice whether to participate or not. You may leave the study at any time. You may refuse to answer any questions you do not want to answer. Participation in the study has no impact on your employment. You may change your mind later and stop participating even if you agreed earlier. If you decide after the study that you do not wish to be in the study, you can contact the study staff and you will be removed from the study. We will tell you about any new information or changes in the study that may affect your willingness to continue in the study. The study staff may also stop you from taking part in this study at any time if the study is stopped, or if they believe that it is in your best interest.

Alternatives: You may undergo standard treatment to prevent TB, which involves taking INH daily for 9 months, or choose to continue your routine care without being in this study. You may ask your doctor about your choices before deciding whether to participate in this study.

Costs: You will not be charged for any of the study activities.

Payment: To reimburse costs associated with coming to the clinic, you will be given 15,000 Uganda Shillings (USh) after completing each clinic visit scheduled during 3HP treatment (11 visits if taking 3HP by DOT and 2 visits if taking 3HP by SAT), and after completing the end-of-study clinic visit. During periods when local transportation costs are increased (such as due to the current COVID-19 pandemic), the reimbursement amount per visit may be increased up to 30,000 USh.

Questions: You can talk to the study staff about any questions, concerns, or complaints you have about this study. You can also contact Dr. Fred Semitala, the Principal investigator by calling 256-755-553-004. If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers, or if you wish to voice any problems or concerns you may have about the study, please call Dr. Susanne Kiwanuka, 256-701 888 163/ 256-312 291 397 or Dr. John Ssempebwa, 256-772-963-074, chairperson of Makerere University, School of Public Health Higher Degrees Research and Ethics Committee.

You can ask questions any time. You can ask now. You can ask later. You can talk to me or you can talk to someone else.

PARTICIPANT

You have been given a copy of this consent form to keep. PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled. If you wish to participate in this study, please sign below.

_____	_____	_____
Date	Name of participant	Participant's Signature or Mark

(Do not date here if participant cannot read and write)

WITNESS – ONLY IF NEEDED

(Only for adult participants who cannot read and write but can communicate)

_____	_____	_____
Date	Name of witness attending consent	Signature of Witness Attending Consent

RESEARCH STAFF

_____	_____	_____
Date	Name of person Obtaining Consent	Signature of Person Obtaining Consent