Comparison of Two IUDS among Cape Town HIV-positive Women: A Randomized Controlled Trial Assessing Safety of Registered Products in South Africa

NCT01721798

Informed Consent April 28, 2016

INFORMED CONSENT FOR TRIAL ENTRY

Name of Research Study:	Comparison of Two IUDs among Cape Town HIV-positive Women: A Randomized Controlled Trial Assessing Safety of Registered Products in South Africa
Site Principal Investigator:	Prof. Benjamin Landon Myer
FHI 360 Medical Monitor:	Dr. Catherine Todd
Sponsor:	FHI 360, Durham, North Carolina, USA
Funder:	Eunice Kennedy Shriver National Institute of Child Health & Human Development of the National Institutes of Health; Preventive Technologies Agreement, United States Agency for International Development

Introduction

This consent form contains information about the intrauterine device (IUD) trial. The IUD trial is a research study. In order to be sure that you are informed about the research study, we are asking you to read this consent form. If you are unable to read this consent form, a study staff member will read and explain it to you. Someone other than the study staff will be present during this procedure. If you agree to take part in this study, you will be asked to sign this form or make your mark in the presence of a witness.

This consent form might contain some words that are unfamiliar to you. Please ask us to explain anything that you do not understand.

General information about the research

We are from the Desmond Tutu HIV Centre at the University of Cape Town. We are doing a research study to compare two IUDs ("loops") among HIV-positive women. The two IUDs will be the levonorgestrel IUD (LNG IUD) (called Mirena) and the copper IUD. HIV-positive women in Cape Town will be in the trial. We want to find out if the two IUDs are similar in safety and acceptability for HIV-positive women. The IUDs are equally effective at preventing pregnancy.

An IUD (also called a loop) is a small T-shaped flexible device about the length of an egg that is inserted into the womb. The IUD is very good at preventing pregnancy for 5 – 10 years. Both IUDs work mainly by stopping the man's sperm from reaching the woman's egg. The IUD can be removed at any time if a person decides they want to become pregnant. The IUD may change menstrual bleeding patterns after insertion, including causing menstrual bleeding to stop. This is not harmful to you and does not change likelihood of future fertility.

Neither IUD protects against human immunodeficiency virus (HIV) or other sexually transmitted infections. The best way to prevent HIV and other infections is through the use of a barrier method such as the male condom.

You have completed the screening visit for this study and are eligible at this point to take part in the study. This form gives information to help you decide if you want to take part in a research study. The purpose of today's enrollment visit is to explain all the details of the trial to you, review all your test results to confirm that you can take part in the study, obtain your consent to take part, and enroll you.

You can ask any questions to help you decide whether to be a part of the study or not. You may ask questions about the purpose of the research, what will be done during study visits, the possible risks and benefits and anything else about the research or this form that is not clear. When all of your questions are answered, you can decide if you would like to take part in this study or not.

Your part in the research study

288 women will take part in this study. You have successfully completed the medical screening part of this study and are being asked to join the study. Women in the study are 18 to 40 years old with known HIV infection and either a CD4 count greater than the level for antiretroviral therapy (ART) eligibility by Western Cape Province guidelines with no acquired immune deficiency syndrome (AIDS)-defining conditions or taking ART with no HIV virus in blood at the last test. It is important for you to know that you must have a negative pregnancy test before joining this trial and have no plans to get pregnant in the next 2.5 years.

Women in the study will be put into different groups. Each woman will receive one of the IUDs to use for 2 years. The IUD that you get will be chosen by a computer, and half of the women will get an LNG IUD and half of the women will get a copper IUD. Participants will have a 50/50 chance (like tossing a coin) of being placed in one of two groups. But you will not know which kind of IUD you get. This does not mean that one IUD is less effective than the other as both are equally effective at preventing pregnancy. We do not know if there is a difference in safety between the two IUDs, which is why we are doing this study. Which IUD you get will be told to you at the end of the study or sooner if there is a scientific reason to do so.

Taking part in this study will last up to 24 months and will include 5 visits after today. Each visit will last about 2 to 3 hours on 6 separate days, including today.

If you decide to volunteer for this study, the schedule of study visits and the procedures that will be done at each visit are as follows:

Enrollment/ Insertion visit

- At today's visit you should ask any questions about the study and anything you may not understand. Before you sign this consent form, please be sure that you understand what this study is about and what you will be asked to do. You will be asked questions about your understanding of the study. You will sign this consent form or make your mark in front of a witness, if you decide to take part in this study. You will be given a copy of the informed consent form.
- You will give a urine sample for a pregnancy test. If you are pregnant, you cannot take part in the study and will be referred for care.
- You will be randomly assigned by the computer to use one of the IUDs.
- We will ask you to insert a menstrual cup into the vagina to collect cells. The cup will be removed later by the nurse-practitioner during your examination.

- We will ask you personal questions about various areas, including your medical history, your current living and economic situation, your sexual relationships, and your attitudes about birth control and childbearing, within a baseline questionnaire.
- You will have your blood collected to check blood count to check for anemia and HIV viral load.
- You will have an individual risk-reduction counseling session.
- You will have a pelvic exam. A pelvic exam looks at the part of your womb that the doctor can see when looking into the vagina. We will remove the menstrual cup and take several sample of cells from your cervix and vagina, using swabs and a small amount of liquid. We will insert the IUD.
- You will receive counseling on symptoms and warning signs of IUD expulsion and pelvic inflammatory disease.

Follow-up visits

You will return to the clinic for a follow-up visit at 3, 6, 12, 18 and 24 months. You will be called a few days before your appointment as a reminder and, if you are bleeding, you will be asked to delay your visit until bleeding has stopped for at least 2 days. You will be asked to not insert anything in the vagina or have sexual intercourse for three days before each visit. We may call, text message (SMS), or visit you at home if you do not come for an appointment or to remind you of an upcoming appointment.

At each visit:

- You will be asked questions about your health, sexual behavior, and thoughts about using the IUD.
- You will give urine for a pregnancy test.
- You will have your blood collected to test for syphilis and check viral load.
- You will have a pelvic exam to check IUD position and collect cervical and vaginal cells with swabs to test for infections passed through sex. We will give you free treatment for any of the curable infections passed through sex that we find during your exam. We may not be able to do the testing for all infections immediately following your visit and will freeze those samples for possible testing at a later date.
- We will provide you with a disposable menstrual cup and ask you to place it in your vagina at the beginning of your visit. The cup will be removed at the time of examination and the nurse practitioner will take several samples of cells with swabs.
- You will have an individual risk-reduction counseling session.
- You will update your contact information if it changes.

In addition at follow-up visits at 6, 12, 18, and 24 months:

- You will have your blood collected to check blood count, viral load, and, if not on ART, CD4 count. You should always follow up at your home clinic for updated viral load testing.

We will periodically review your medical chart and your other accessible medical records for any new laboratory results, including plasma viral loads if you are using ART, and other information that applies to your safety in this study. We may ask you to bring documents from other clinics if you have received care at other sites.

If you do not want to do any of these procedures or tests, you do not have to take part in this study. Your participation in this study is voluntary. If you choose to take part in this study, you cannot take part in another study that involves a biomedical intervention, like new types of ART medicine. Please discuss your participation in another study with study staff to determine eligibility.

It is very important that you come to each scheduled visit. If you think you cannot keep your scheduled clinic visits over the next two years, please consider not taking part in this study.

If you are not taking ART, if your CD4 count drops below the eligibility level for ART based on local guidelines or you develop AIDS-defining conditions during the study, you will be referred to a clinic for free HIV care and treatment services. If this happens, you will be given a choice about whether you would like to keep your IUD or have it removed. You may remain in this study. If you are taking ART and are found to have increasing HIV levels in your blood based on plasma viral load results, you will be referred to your clinic for medication counseling and possible change. If this happens, you will be given a choice about whether you would like to keep your IUD or have it removed. You may remain in this study.

You can come at any time for an unscheduled visit for IUD removal or for any other medical problem. If you decide to have the IUD removed, you may remain in the study with the same follow-up schedule and may change to a different method of birth control. We may interview you with questions about the IUD and why you chose to have it removed. If you become pregnant after IUD removal, we will refer you for appropriate care in the public sector health system. Obstetric care is not provided through the study.

The 24 hour telephone number with which you can reach the study doctor or another authorized person will be provided to you before you complete the first visit. If you have any problems, please call the 24 hour telephone number and study staff can assist you in making an appointment. If you decide to leave the study before it is completed, you may keep the IUD.

At the end of the study, you will be given the choice to keep your IUD in or have it removed. If you choose to keep it, we will tell you what type of IUD you have and how long it will remain effective for preventing pregnancy. You will need to visit your regular clinic and obtain a new IUD or other form of birth control when the period of effectiveness for your IUD is finished. We may call you after the end of the study visits to follow up on any medical conditions you experience during the study. You may come for care related to these issues at the study clinic after you complete all study visits.

Future use of specimens

We are specifically looking at the IUD in this study. However, the information (data) and samples being collected from all participants may also help answer other questions about HIV, other infections, or safety of other family planning methods. We may want to use your questionnaire information, blood and/or genital tract sample(s) so that other research studies can be done during or after this research study for up to 3 years. Any specimens or information used in future human subjects studies will first be reviewed by a research ethics committee.

The researchers do not plan to contact you or your regular doctor with any results from tests done on your stored samples. Should a rare situation come up where the researchers decide

that a specific test result could help your health, the researchers will try to notify your study doctor. Your study doctor will try to contact you.

Your samples may be shipped to another country for storage and/or testing, because some of the tests may not be available in South Africa. Only approved researchers will have access to the samples and they will not have any information that identifies you.

You can be in the IUD study and not agree to have these samples stored. You can withdraw your consent for the storage of your samples at any time.

There are no additional risks involved in the long-term storage of samples compared to those in IUD study.

Your participation in this research may benefit other women in the future by answering important research questions about HIV infection.

There are no costs to you for agreeing to have your samples stored.

You will not receive any additional compensation if you agree to have your samples stored long-term. Some research using blood or other samples allows the researchers to make medical tests or treatments that may have commercial value. If this happens, there are no plans to pay you for any products or treatments that are made, or for using your samples.

Permission for use of coded specimens:
Please initial below to indicate whether or not you give permission for your data and specimens to be used for research in addition to the core study.

_____ (initial) I agree to have my specimens and data stored for future research by the investigators who are conducting this study or other research collaborators in related areas.

_____ (initial) I do not consent to the use of my blood/genital tract sample for any reason outside of this specific study.

Possible risks
Your participation in this part of the study will involve some risks, which include:

- Possible changes in the chance of HIV transmission to your male sexual partner. We do not know how use of the study IUDs affects the chance of infecting a sex partner with HIV. You should always use condoms during sex, and condoms will be offered to you at each study visit.
- Excessive bleeding with the copper IUD is a risk.
- Possible changes in your HIV disease with the LNG IUD. We know that the copper IUD does not affect HIV disease, but we do not know whether the LNG IUD does affect HIV disease.

Other risks include problems that can happen with IUD insertion, like creating a hole in the uterus, having the IUD ejected from the uterus, pregnancy, and pelvic inflammatory disease. The IUD may also increase or decrease your menstrual bleeding. Heavy bleeding is possible and is a risk of the copper IUD and study staff should be notified with any bleeding similar to the

heaviest day of a normal period for 7 or more days. The risk of these events or conditions is quite low.

Pregnancy with the IUD in place is very rare. If you get pregnant with the IUD in place, an ultrasound will be performed right away to find the location of the IUD and of the pregnancy. Depending on the location of the pregnancy and whether the IUD is still in the uterus, you will be counseled on your options.

With the blood draw, there may be slight pain when a needle is inserted into your arm to get the blood sample. There may be minor bruising or pain that may last for up to 2-3 days at the site of the blood draw. Although rare, you may become lightheaded (feel dizzy) or faint when you have blood drawn, and there is a very small risk of infection at the site from where we take your blood.

We will minimize the risks of bruising or infection by cleaning your skin before using a needle to draw blood. We will use a new needle for each person. We will also apply pressure and a bandage to the site after we are done. These discomforts are usually small. If you get an infection because of the blood draw, we will treat you here.

The visit will involve collecting cells inside the vagina with a swab and possibly with a liquid. This process may feel uncomfortable and you may experience a bit of spotting afterward.

There is no known risk associated with menstrual cups. There may be slight discomfort if the cup is not inserted correctly. You will be provided with clear instructions on how to insert the cup.

Some of the questions we ask will be of a personal nature, which may make you uncomfortable.

There may be other risks of taking part in this research study that we don't know about. If we learn about other risks, we will let you know what they are so that you can decide whether or not you want to continue to be in the study. If there are any future findings regarding the safety or acceptability of the IUDs we are investigating for HIV-positive women, we will also notify you.

Possible benefits

You will not have to pay for the LNG IUD, if you receive this IUD by chance, in this study, or for any tests that we do.

You will receive free condoms. We will demonstrate how to use them.

You will receive individual risk-reduction counseling with trained staff about the need for condom use for sexually transmitted infection and HIV transmission prevention, tips for negotiating condom use, and we will give you male and/or female condoms, if you wish.

We will give you free treatment for any of the curable infections passed through sex that we find by nurse diagnosis or, where possible, infection tests, during your exams.

There are no other direct benefits to being in the study. If you need referral for more care somewhere else, we will assist with this, but you may have to pay for care at other clinics. We

will not provide payment for injuries or complications resulting from being in the study but will provide or refer for appropriate care. Your participation in this research may benefit other women in the future by helping us understand IUD safety and acceptability in HIV positive women.

Choosing to be in this study
You do not have to take part in this study to get treatment for your condition. You may continue with routine HIV care and receive family planning methods at the Desmond Tutu HIV Center and/or Gugulethu Community Health Centre with no penalty. Whether or not you decide to join this study will not affect your treatment and care at this clinic or any other clinic.

Confidentiality
Any information collected during this study that can identify you by name will be kept confidential. We will do everything we can to keep your data secure, but complete confidentiality cannot be promised. Your name will not appear in any study reports or on any blood samples. Despite all of our efforts, unanticipated problems such as a stolen computer may occur, although it is highly unlikely. Your specimens and questionnaires will be assigned a code number, and separated from your name or any other information that could identify you.

The following individuals and/or agencies will be able to look at and copy your research records (such as this consent form, completed questionnaires, lab results, etc.):

- The investigator, study staff and other medical professionals who may be evaluating the study;
- Authorities from the University of Cape Town, including the Institutional Review Board (IRB);
- Authorities from FHI 360, including the Protection of Human Subjects Committee (PHSC);
- The United States Food and Drug Administration ('FDA') and/or the Office of Human Research Protections ('OHRP');
- The sponsors of this study, NIH, USAID, including persons or organizations working with or owned by the sponsor;
- Other South African government regulatory agencies.

Study staff may request copies of your medical records if you receive any treatment at any other facility. We will request your permission to look at these records.

Compensation
You will receive compensation valued at 150 Rand at this visit. You will receive compensation valued at 150 Rand at each study visit. This is for your time and travel costs. There is no compensation for missed visits.

WHAT ABOUT INSURANCE?
There are no experimental medicines being used in this study. Therefore no insurance has been obtained. However you will be protected in terms of the study staffs' personal malpractice insurance or that of the university's insurance cover in the event of injury or illness that is caused by you taking part in this study (details of this insurance cover are attached in appendix at the end of this document).

Leaving the Research
You may leave this research study at any time. If you decide to stop taking part, please tell the study staff why you wish to leave.

Also, you may be asked to leave the research if:

- The research doctor or study staff feel it is best for you, or
- You are not able to follow the study procedures, or
- The research is stopped. If the research is stopped, you may be asked additional questions about your participation in the study. You may choose not to answer these questions if you wish.

We will tell you if we learn something new about the IUD that could affect your choice to stay in the study. When you are no longer in the research, you will still be able to receive care at this clinic.

If there is anything that is unclear or if you need further information, please ask us and we will provide it. Do you have any questions?

Contacts for more information
If you have any questions after you leave the clinic, or if you are hurt while taking part in this research study, you should contact:

Dr. B. Landon Myer
School of Public Health and Family Medicine,
Faculty of Health Sciences, University of Cape Town (UCT)
Tel: +27 21 406 6661 or the study clinic at 074-931-6740
Email: Landon.Myer@uct.ac.za

If you are sick or have a health problem due to taking part in the study, you will not have to pay to see study staff. If you need more help, we will refer you to other clinics, where you may have to pay.

Your Rights as a Participant
Before a research study can be carried out, it must be approved by an ethics committee. An ethics committee is a group of people who review details of a proposed research study and determine whether the research may be conducted. Their main goal is to help protect participants.

This protocol has been approved by the ethics committees of:
- The University of Cape Town and
- FHI 360 (Protection of Human Subjects Committee).

If you have any questions about how you are being treated by the study your rights as a research participant, you may contact:
UCT Ethics Committee
Prof Marc Blockman

Chair, Human Research Ethics Committee
Faculty of Health Sciences, University of Cape Town
Tel: +27 21 406 6338

You may also contact:
FHI 360 Protection of Human Subject Committee
P. O. Box 21059
Durham, NC 27703, USA
Tel: +1 919 405 1445
Email: phsc@fhi360.org

If you have questions about this trial you should first discuss them with your doctor or the ethics committee (contact details as provided on this form). After you have consulted your doctor or the ethics committee and if they have not provided you with answers to your satisfaction, you should write to the South African Medicines Control Council (MCC) at:

The Registrar of Medicines
Medicines Control Council
Department of Health
Private Bag X828
PRETORIA
0001

Fax: (012) 395 9201

e-mail: mogobm@health.gov.za

VOLUNTEER AGREEMENT

I understand that the purpose of the research study titled "Comparison of Two IUDs among Cape Town HIV-positive Women," is to compare the safety of two IUDs among HIV-positive women.

I have read the information in the informed consent form, or it has been read to me. I have had the opportunity to ask questions about it, and the questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate in this study. I understand that I have the right to withdraw from the study at any time without affecting the care that I can get at this clinic or other clinics.

_____ _____

Printed Name of Volunteer **Date**

_____ _____

Signature (or mark) of Volunteer **Date**

If a volunteer cannot read the form for herself, a witness must sign here:

I was present while all information in this consent form, including the benefits, risks and procedures were read to the volunteer. All questions were answered and the volunteer has agreed to take part in the research.

_____ _____

Printed Name of Witness **Date**

_____ _____

Signature of Witness **Date**

I certify that all information in this consent form, including the nature and purpose, the potential benefits, and possible risks associated with participating in this study have been explained to the volunteer.

_____ _____

Printed Name of Person Who Obtained Consent **Date**

_____ _____

Signature of Person Who Obtained Consent **Date**

A signed copy of this consent form was offered to the participant.

_____ _____

Initials of Person Who Obtained Consent **Date**

Details of UCT's no-fault insurance

What if Something Goes Wrong?

The University of Cape Town (UCT) has insurance cover for the event that research-related injury or harm results from your participation in the study. The insurer will pay all reasonable medical expenses in accordance with the South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI) in the event of an injury or side effect resulting directly from your participation in the study. You will not be required to prove fault on the part of the University.

The University will not be liable for any loss, injuries and/or harm that you may sustain where the loss is caused by

- The use of unauthorised medicine or substances during the study

- Any injury that results from you not following the protocol requirements or the instructions that the study doctor may give you

- Any injury that arises from inadequate action or lack of action to deal adequately with a side effect or reaction to the study medication

- An injury that results from negligence on your part

By agreeing to participate in this study, you do not give up your right to claim compensation for injury where you can prove negligence, in separate litigation. In particular, your right to pursue such a claim in a South African court in terms of South African law must be ensured. Note, however, that you will usually be requested to accept that payment made by the University under the SA GCP guideline 4.11 is in full settlement of the claim relating to the medical expenses.

An injury is considered trial-related if, and to the extent that, it is caused by study activities. You must notify the study doctor immediately of any side effects and/or injuries during the trial, whether they are research-related or other related complications.

UCT reserves the right not to provide compensation if, and to the extent that, your injury came about because you chose not to follow the instructions that you were given while you were taking part in the study. Your right in law to claim compensation for injury where you prove negligence is not affected. Copies of these guidelines are available on request.