MAIN INFORMED CONSENT FORM: PARTICIPANT

TITLE OF RESEARCH PROJECT: Urine tenofovir point-of-care test to identify patients in need of ART adherence support (UTRA) – Aim 3

PRINCIPAL INVESTIGATOR: Dr Catherine Orrell, Desmond Tutu Health Foundation, University of Cape Town

Introduction

You are being invited to take part in a research study. Before you decide to participate it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. You may ask us for more information or to explain anything that is not clear. Take time to decide whether or not you would like to take part in the study.

Why have I been chosen?

You have been chosen to participate because you are taking antiretroviral therapy (ART) that contains the drug, Tenofovir (also called TDF). You have also previously had a raised viral load at some point during your time on ART. The viral load is the amount of HIV in the blood and is represented by a number.

What is the purpose of the study?

Taking ART every day suppresses (holds down) HIV in the blood, which improves health and lowers the chance of passing the virus on to someone else. Success of ART depends on adherence to ART (how well a person takes their tablets every day). If ART is not taken every day (poor adherence), the virus levels in the blood increase, worsening health and increasing the chance of passing the virus on to sexual partners. Currently, adherence is assessed either by asking patients directly, which is not always accurate, or confirming that the HIV is suppressed by doing a viral load test. These are expensive and are often only done too late, when the viral load is already raised. We therefore need to find a better method to detect problems with adherence early before the viral load rises.

A urine-based test was recently developed, called UTRA (urine tenofovir rapid assay). This test can give clinic staff immediate information about a person's adherence to the antiretroviral medication tenofovir (TDF). In this study we will be trying to find out if using this urine test to identify people with adherence challenges, and giving them adherence counselling, improves their chance of having a low viral load at the end of the study.

Do I have to take part?

It is up to you to decide whether or not to take part. If you decide to take part you will be asked to sign this consent form and given a copy to keep. You will be free to withdraw at any time if you want to. We would like to know your reason for withdrawing but you do not need to give us a reason if you don't want to. Withdrawing from the study will not affect the care you receive at the clinic.

At some point in the study the researchers may decide to withdraw you from the study. This could be because your clinic doctor has decided to switch your ART or if the researcher believes that your ongoing participation is not in your best interest.

What will my participation involve?

For this study, we aim to recruit 200 individuals who are currently receiving ART from the clinic. Each study participant will be randomised into one of two groups. Randomisation is when something is

chosen by chance (like flipping a coin). You will have an equal chance of being in either one of the two groups. The first group is called the **standard of care group**. People assigned to this group will be monitored using their viral load results. If their viral load is raised, they will be referred to adherence support counselling at the clinic. The other group is called the **intervention group**. People assigned to this group will have a UTRA test at each visit. A counsellor or nurse will explain the results of the test to them. If they have no TDF in their urine, they will be referred to adherence counselling as described above.

If you decide to take part in the study we will see you 4 times (approximately every 3 months) over the next year. Where possible, we will try to ensure these study visits take place on the same day as your clinic visit.

At your first visit, you will be asked some questions about yourself, including your age and gender; your history with HIV and ART; and any history of alcohol or drug use. At every visit, we will ask you how often, and how well you take your medication.

We will also take a blood sample from you (about 25ml or 5 teaspoons) at your baseline visit, Month 6 visit and Month 12 visit, which will be used to test for your viral load, haematocrit (the proportion of red blood cells in your blood) and the levels of TDF in your blood. Some of this blood will be stored so that if your viral load is high, we can determine if your treatment is still fighting the HIV in your blood. Throughout the study, we will look at your clinic folder and other health records to find blood results (clinic viral load, CD4 and kidney function) and to see how often you collect your medication.

If you are in the intervention arm, we will take a urine sample from you at each visit, which we will test using the new UTRA test. We will discuss the results of the urine test (UTRA) with you at the end of the visit and will ask you how you feel about having the UTRA test. Once the UTRA test has been done, we will store your urine. The stored urine will be tested to ensure the UTRA test works as it should for people taking ART.

We might also invite you to participate in additional one-on-one interviews about your experiences with HIV and HIV treatment. If we did this, it would mean meeting with us 3-4 times over the course of your participation in the study where we will talk to you about your experiences and record these interviews on an audio device. If at that time, you decide you don't want to discuss your experiences with us, you can tell us and we will not interview you. Choosing to be interviewed or not will not impact your participation in the rest of the study in any way.

If you agree to sign the extra genetic informed consent document, we will ask you to provide an additional 4ml of blood. This blood will be stored and used in the future to investigate factors that may cause antiretrovirals to not work as they should and to test your DNA (genes) to understand how fast your body breaks down antiretrovirals.

What are the side-effects/risks of taking part?

During this study we will not change your medication or the routine care you get from your clinic. Taking the blood samples could result in a small amount of discomfort or bruising. We will ask you personal questions about your health and substance use which may make you uncomfortable. You do not need to answer any questions that make you feel uncomfortable.

What are the possible benefits of taking part?

You may not benefit immediately as a result of taking part in this study, however, the information that we gain from the study will help us improve the standard of care for people taking antiretroviral

treatment. If you are in the intervention arm, you may benefit from additional adherence counselling based on your UTRA results.

How will my participation be kept confidential?

Confidentiality will be maintained at all times. You will be given a unique study number that will be used to identify you and to link the samples and data collected to you during the study. A list matching participant names with study identification numbers will be kept in a locked cupboard. This information will only be available to study staff. No individual will be identifiable from any presentation or publication that results from this research.

What will happen to the results of the research study?

We will combine all the results from the people taking part in the study, and these may be presented at medical conferences or published in medical journals. Results will be communicated with your clinic.

Who is funding the research?

The U.S. National Institute of Health and the South African Medical Research Council funded this study.

Reimbursement

We will reimburse you R120 for your time and expenses for all study visits when additional sample collection or questionnaires are required.

Who can you contact if you have questions or concerns?

This study was approved by the UCT Faculty of Health Science and Human Research Ethics Committee (an independent committee established to help protect the rights of research participants). If you have any questions about your rights as a research participant or concerns about this study, contact the University of Cape Town's Health Science Research Committee on 021 406 6492; they are a group of doctors and researchers whose job it is to make sure research is safe.

For further information about this study please contact: Sr. Zukiswa Nkantsu (Gugulethu Research Office, (021) 007 2275/1930, Gugulethu Scout Hall—adjacent to the Gugulethu Community Health Centre) or the Principal Investigator, Dr. Catherine Orrell (021 406 6958, Catherine.orrell@hiv-research.org.za).

Agreement to participate

My signature demonstrates that:

- The information in the informed consent form was explained to me.
- All of my questions about the study, the possible risks, side effects, and study procedures have been answered to my satisfaction.
- I understand what my participation in the study involves and agree to take part.
- I understand that I am free to withdraw from the study at any point, and do not need to state a reason for this.
- I give permission for the study staff to obtain the required urine and blood samples as described.
- I give permission for study staff to access my medical records, including my clinic folder, pharmacy records and lab results.
- I understand that the study team may call me using the phone numbers I have given them.

Consent to participate in one-on-one interviews:

_____I give permission for the study staff to contact me about participating in one-on-one interviews as described above (please initial).

_____I **DO NOT** give permission for the study staff to contact me about participating in one-on-one interviews as described above (please initial).

Consent to participate in future research:

Please indicate your willingness to be contacted for future research during or after your participation in this study (initial on the line):

_____I give permission for study staff to contact me for future research (please initial).

_____I **DO NOT** give permission for study staff to contact me for future research (please initial).

Study participant:

Name	Signature	Date

Study staff administering consent:

Name	Signature	Date

If the participant is unable to read and/or write, an impartial witness should be present during the informed consent discussion. After the written informed consent form is read and explained to the participant, and after they have orally consented to participation in the study, the participant should provide their fingerprint on the study participant signature line. The witness should sign and personally date the consent form below. By signing the consent form, the witness attests that the information in the consent form was accurately explained to, and apparently understood by, the participant and that informed consent was freely given by the participant.

Person witnessing consent:

Name	Signature	Date

PHARMACOGENETIC INFORMED CONSENT FORM

TITLE OF RESEARCH PROJECT: Urine tenofovir point-of-care test to identify patients in need of ART adherence support (UTRA) – Aim 3

PRINCIPAL INVESTIGATOR: Dr Catherine Orrell, Desmond Tutu Health Foundation

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Introduction

This form should be read in conjunction with main consent.

When you join the UTRA study Aim 3, you will be asked to give permission for having blood samples saved in a repository for future research. A repository is a special laboratory with freezers where specimens of blood that are taken from you during a study are kept. Your name will not be on these specimens, only a study number. This form is to ask your permission to do extra tests on your stored blood samples, if you agree to this part of the study.

Please take some time to read the information presented here which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is **entirely voluntary,** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part initially.

This study has been submitted to and approved by the Health Research Ethics Committee (HREC) of the University of Cape Town. This is a group of scientific and non-scientific people. They review and approve or disapprove research involving patients. The study will be conducted according to the ethical guidelines and principles of the International Declaration of Helsinki (version 2013), South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research. These are policy statements that protect the rights of study participants.

Why have I been chosen?

You have been chosen to participate because you are participating in the UTRA Aim 3 study. You are being asked to participate in a study which is part of UTRA Aim 3 for the investigators to take some of your blood to do future testing. This includes tests that will allow researchers to better understand the factors (called "markers") that can impact on how well antiretrovirals work in the body. This also includes a genetic test (a test of your DNA [genes]) to better understand how fast your body is programmed to metabolise (break down) antiretrovirals in your blood. As part of UTRA we will measure tenofovir in your blood and urine. But we also want to measure your other antiretroviral concentrations in your blood. To make sure you understand this, this additional form explains the process a bit more and you need to sign this form to show you agree to this.

What is genetic research?

Genetic testing is a laboratory test that looks at differences in people's genes. Your body, like all living things, is made up of cells, and cells contain deoxyribonucleic acid, also known as "DNA." DNA is like a string of information put together in a certain order. Parts of the string make up "genes." Genes contain instructions on how to make your body work. Genetic material, also called DNA or RNA, is

usually obtained from a small blood sample. Genes are found in nearly every cell in the human body, including most of the cells that make up your blood. Our genes determine what we look like and sometimes what kind of diseases we may be susceptible to or how we respond to certain medications or how fast we metabolise (break down) medicines.

What is the purpose of the study?

The purpose of this study is to further explore factors that impact on how well antiretrovirals work in the body, to measure your antiretroviral levels in your blood and to do a genetic test to determine how fast you metabolise (break down) your antiretrovirals. We will measure all of this using your blood.

Do I have to take part?

It is up to you to decide whether or not to take part. If you decide to take part you will be asked to sign this consent form and given a copy to keep. You will be free to withdraw at any time and without giving a reason. This will not affect the care you receive at the clinic or your participation in UTRA. If you decide to withdraw from the study, your sample will be removed and destroyed.

What procedures will be involved for the genetic testing as part of this study?

We will take an extra amount of 4 ml (less than 1 tea spoon) of blood during one of the blood draws that are already done as part of the study.

If your blood is to be stored is there a chance that it will be used for other research?

Your blood will only be used for genetic research that is directly related to antiretroviral metabolism and to measure antiretroviral levels. If the researchers wish to use your stored blood for additional research in this field they will be required to apply for permission to do so from the Health Research Ethics Committee at the University of Cape Town. The Health Research Ethics Committee protects the rights of participants.

What are the side-effects/risks of taking part?

Taking the blood samples could result in a small amount of discomfort or bruising. Your name will not be made known. You will not receive any information on your genetic make-up, markers or antiretroviral levels.

What are the possible benefits of taking part?

You are not likely to benefit immediately as a result of taking part in this study, however, the information that we gain from the study may help us improve the standard of care for people taking antiretroviral treatment.

Will you or the researchers benefit financially from this research?

You will not be paid to take part in this study. There will be no financial gain for researchers involved in this study.

How will my participation be kept confidential?

Confidentiality will be maintained at all times. You will be given a unique study number that will be used to identify you and to link the samples and data collected to you during the study. A list matching participant names with study identification numbers will be kept in a locked cupboard. This

information will only be available to study staff. No individual will be identifiable from any presentation or publication that results from this research.

What will happen to the results of the research study?

We will combine all the results from the people taking part in the study, and these may be presented at medical conferences or published in medical journals. Results will be communicated with your clinic.

Who can you contact if you have questions or concerns?

This study was approved by the UCT Faculty of Health Science and Human Research Ethics Committee (an independent committee established to help protect the rights of research participants). If you have any questions about your rights as a research participant or concerns about this study, contact the University of Cape Town's Health Science Research Committee on 021 406 6492; they are a group of doctors and researchers whose job it is to make sure research is safe.

For further information about this study please contact: Sr. Zukiswa Nkantsu (Gugulethu Research Office, (021) 007 2275/6, Gugulethu Scout Hall—adjacent to the Gugulethu Community Health Centre) or the Principal Investigator, Dr. Catherine Orrell (catherine.orrell@hiv-research.org.za).

Agreement to participate

My signature demonstrates that:

- The information in the informed consent form was explained to me.
- All of my questions about the study, the possible risks and study procedures have been answered to my satisfaction.
- I understand what my participation in the study involves and agree to take part.
- I understand that I am free to withdraw from the study at any point, and do not need to state a reason for this.
- I give permission for the study staff to obtain the required blood samples as described.

Study participant:

Name	Signature	Date

Study staff administering consent:

Name	Signature	Date

If the participant is unable to read and/or write, an impartial witness should be present during the informed consent discussion. After the written informed consent form is read and explained to the participant, and after they have orally consented to participation in the study, the participant should provide their fingerprint on the study participant signature line. The witness should sign and personally date the consent form below. By signing the consent form, the witness attests that the information in the consent form was accurately explained to, and apparently understood by, the participant and that informed consent was freely given by the participant.

Person witnessing consent:

Name	Signature	Date

INFORMED CONSENT FORM: KEY INFORMANT INTERVIEW

TITLE OF RESEARCH PROJECT: Urine tenofovir point-of-care test to identify patients in need of ART adherence support (UTRA) – Aim 3

PRINCIPAL INVESTIGATOR: Dr Catherine Orrell, Desmond Tutu Health Foundation

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Introduction

You are being invited to take part in a research study. Before you decide to participate it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. You may ask us for more information or to explain anything that is not clear.

What is the purpose of the study?

ART is given to people living with HIV in order to suppress the virus, resulting in improved health for the individual and decreased transmission of the virus to others. Success of ART is dependent on adherence. Currently, adherence is assessed by asking patients directly and then confirming with a viral load test, which is expensive and is often only done when the viral load is already raised. We therefore need to find a method to detect problems with adherence early before the viral load rises.

A urine-based test was recently developed, called UTRA (urine tenofovir rapid assay). This test can give clinic staff immediate results about a person's adherence to the antiretroviral medication Tenofovir (TDF). In this study we will compare the results of this urine test to drug levels found in blood, self-reported adherence and pharmacy collection records to see if this test can be used as part of routine care in ART clinics. If the test is effective it would allow clinic staff to identify people with adherence difficulties early and give them the necessary support before their viral load rises.

Why have I been chosen?

As part of this study, we would like to conduct some key informant interviews with health care workers in order to better understand how this new point-of-care adherence monitoring tool can best be used at health facilities in the future. You were approached because you have experience providing HIV care and support or because you are knowledgeable about the Department of Health's HIV treatment programmes.

What will my participation involve?

If you agree to participate, you will come to the research office for a face-to-face interview with a trained interviewer. You will be asked to sign this consent form after you have had all your questions answered and you feel comfortable about participating. The interview will be audio-recorded so that we can be sure of what you said later on. The interviewer may also take notes during the interview.

The interview will last approximately 45-60 minutes and can happen at a time that is convenient to you. The interviewer would ask you questions about how you understand patients' adherence challenges and care and support needs, what you think of the new UTRA urine test, and your recommendations for how it can be used at facilities.

What potential benefits are there?

There are no direct benefits to you of participating in these interviews. However, your participation may help the researchers better understand how point-of-care adherence tests can be used at health clinics to help more patients avoid raised viral loads in the future.

What potential risks are there?

Sometimes talking about sensitive subjects causes people to become upset. You will not be pressured to discuss anything personal that you are not comfortable sharing. If there is any reason you think that you would be uncomfortable answering questions about HIV treatment, please feel free not to take part. Note that if a particular question makes you feel uncomfortable, you do not need to answer it.

What can you do if you need support?

It is not expected that you would experience any harm as a result of participating. However, should the conversation cause any emotional discomfort, please contact the researchers to have your concerns addressed. Referrals can be made for counselling, health care or peer-group support, if this would be helpful.

How will confidentiality be ensured?

1. You will not be pressured to discuss any personal details. You may stop at any time during the interview and may refuse to answer any questions that make you feel uncomfortable. The interview will be conducted in a private area.
2. The interview will be digitally recorded and transcribed in order to accurately capture what is said. Your name and other information that could identify you will not be transcribed, to keep your identity anonymous. The audio recordings of the interview will be kept strictly confidential and securely stored on password-protected computers that only study staff can access.
3. You will be identified using the unique study number given to you at the beginning of the study. Your name will not be mentioned during the interview. No participant names will be included in the study write-up, so there will be no way for anyone to connect the findings of the research to you.

What if you change your mind?

You may choose whether or not to participate in this study and are free to withdraw at any point, without experiencing any harm or your employment being affected.

Who can you contact if you have questions or concerns?

This study was approved by the UCT Faculty of Health Science and Human Research Ethics Committee (an independent committee established to help protect the rights of research participants). If you have any questions about your rights as a research participant or concerns about this study, contact the University of Cape Town's Health Science Research Committee on 021 406 6492; they are a group of doctors and researchers whose job it is to make sure research is safe.

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Agreement to participate

My signature demonstrates that:

- The information in the informed consent form was explained to me.
- All of my questions about the study, the possible risks, side effects, and study procedures have been answered to my satisfaction.
- I understand what my participation in the study involves and agree to take part.
- I understand that I am free to withdraw from the study interview at any point, and do not need to state a reason for this.
- I understand that the responses I provide will remain anonymous and no information will be linked to my name at all. I understand that the interview will be audio-recorded and transcribed (without names or any identifying information) and agree to this.
- I have been given the contact information of someone at the Desmond Tutu HIV Foundation who can assist me, should I need any further information or support as a result of the interview.
- I understand that the study team may call me using the phone numbers I have given them

Study participant:

Name	Signature	Date

Study staff administering consent:

Name	Signature	Date