

PARTICIPANT INFORMATION SHEET AND CONSENT FORM: MAIN STUDY

STUDY TITLE: XPHACTOR: Xpert MTB/RIF for People Attending HIV Care – An Interventional Cohort Study to Guide Rational Implementation

The investigators doing this study are:

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Collaborators:

- *National Department of Health:* Dr David Mametja, Dr Lindiwe Mvusi, Dr Norbert Ndjeka, Dr Kgomotso Vilakazi

INTRODUCTION

Good day, my name is [*name of researcher*] _____, and I am a researcher with the XPHACTOR study team. We would like to invite you to take part in a research study about a new laboratory test for tuberculosis (TB). Research is the process to learn the answer to a question and this information sheet explains our study. You are free to decide whether you wish to participate, and before you decide, it is important that you understand why the research is being done and what it will involve. Please ask me if there is anything which is not clear. If you decide to take part, to show that you understand the study and agree to take part, we will ask you to sign or make your mark or thumbprint on a consent form. It is your right to withdraw from the study at any time. Your decision to take part or not will not affect your health care in any way.

WHY ARE WE DOING THIS STUDY?

TB is a major health problem in South Africa, especially among people with HIV infection, in whom it can be more difficult to diagnose: but TB can be cured. One reason it has been difficult to control TB in countries like South Africa is that the traditional test, which looks for the TB germ in sputum (spit from the chest) with a microscope, does not detect every case of TB first time. A new sputum test called Xpert MTB/RIF is being introduced across labs in South Africa. This test picks up more cases of TB, although it is not perfect, and it is more expensive than the traditional test.

Experts recommend that patients with HIV are checked for TB every time they attend a clinic, and a spit test sent if they have any TB symptoms (cough, fever, night sweats or weight loss). We know that although many patients will have these symptoms, most will not have TB.

In our study we want to find out:

1. The best way of using the new Xpert TB test in patients with HIV, so those with TB can start correct treatment faster, and those without TB do not have unnecessary tests.
2. The best way to diagnose TB if it is not picked up in the first spit test.
3. Among patients who have symptoms suggesting TB, but tests do not find TB, what illness they have; and if no other illness is found, how long the symptoms last.
4. How much it costs the health department to do all these tests.

This study will include about 3750 people in total, from about 3 clinics across South Africa, and will take about two years to complete. It is funded by the Bill and Melinda Gates Foundation.

IF I TAKE PART IN THIS STUDY, WHAT WILL HAPPEN?

If you agree to take part in this study, with your permission and in a private space we will:

Today:

- Ask you some questions about yourself (such as your age, address, your education, the sort of house you live in, and how much it costs you to come to clinic).
- Ask about your health, including symptoms you have at the moment (in particular symptoms which might indicate that you are sick with TB) and when they started.
- Check your clinic records to find the most recent CD4 count result.
- Measure your height and weight.
- Ask about any treatments you are taking, and whether you have been treated for TB in the past.
- Ask you to give us a sputum sample (spit from the chest).
 - If our assessment suggests it is likely that you might have TB, we will send your sputum for testing today, using the new TB test.
 - Otherwise we will freeze your sputum and check it for TB with the new test at the end of the study.
- If we check your sputum for TB today, we will ask you to come back after *[time period appropriate to the clinic]* for the result.
 - If TB is found, you will be started on TB treatment by the clinic in the normal way, according to South African guidelines. TB can be cured by the correct treatment.
 - If TB is not found on this first test, we may arrange further tests (sputum and chest X-ray) as recommended by South African guidelines; and we may phone you to see how you are. We may also ask you for another sputum sample to freeze. At the end of the study, we will check the sample using the new TB test. If you need a chest x-ray and this clinic does not provide x-rays, we will reimburse you for travel to a clinic that does *[cost of return travel to x-ray facility closest to clinic]*.
- *[FOR PARTICIPANTS NOT ON ART, OR WITH CD4<200 ONLY: Ask you to give us a urine sample which we may test for TB. These tests would be only for our study, and we will not give the results back to the clinic]*
- *[FOR PARTICIPANTS SELECTED FOR HEALTH ECONOMICS STUDY ONLY: To help us understand how much it costs you to come to clinic when you are sick, and the effect on your family, we would like to ask you some more detailed questions about your household income, and things you pay for or have in your home; how much it has cost you in money and time to attend pharmacies, clinics and healers about this illness, and how much any tests and treatment have cost you so far; also about any income you have lost if you needed to take time off work because of this illness, or to seek care; or if family members have needed to take time off to look after you or others because of this illness. These questions will take about 20 minutes. We would be very grateful if you are able to take the time to help us by answering these questions.]*

For the next 3 months (all participants):

- *[ON-ART, "LOW PRIORITY" AT ENROLMENT: If today we assess it is highly unlikely you have TB, we will see you at the clinic for your 3-month visit, and phone you around once a month before this to keep in touch with you and check your contact details. Each time we confirm any changes to your contact details we will give you cell phone airtime, around ZAR12.50 (depending on your network).]*
- *[ALL OTHER PARTICIPANTS we will see you once a month at the clinic (3 more visits), to check if you have TB symptoms. If you are unable to come to the clinic, we may phone you, and ask you the same questions by phone. If, at any visit, our assessment suggests it is likely that you might have TB, we will send your sputum for testing, using the new TB test. We will ask you to come back for the results to start treatment if TB is found. If TB is not found, we will review you, which may be by phone, and we may arrange further tests if necessary, as above.]*
- At your 3-month visit we will ask you for a sputum sample to test for TB using the traditional test, and a blood sample to test for TB as sometimes TB is only found in the blood. If you are not able to produce a sputum sample, we will ask you to breathe in some mist through a mask (called a nebuliser) to help you cough up sputum. If you cannot attend the clinic for the 3-month visit, we may ask your permission to visit you at home to do all of these procedures, except the nebuliser.
- If by the 3-month visit we have found that you have TB, to help us understand how much it costs you to come to clinic for tests and treatment, and the effect on your family, we would like to ask you some more detailed questions about your household income, and things you pay for or have in your home; how much it has cost you in money and time to attend pharmacies, clinics and healers about this illness, and how much any tests and treatment have cost you so far; also about any income you have lost if you needed to take time off work because

of this illness, or to seek care; or if family members have needed to take time off to look after you or others because of this illness. These questions will take about 45 minutes. We would be very grateful if you are able to take the time to help us by answering these questions.

- [FOR PARTICIPANTS SELECTED FOR HEALTH ECONOMICS STUDY ONLY: At each visit, we would like to ask you more questions about how often you have come to the clinic and any money that you have to pay to get to the clinic. These questions will take about 20 minutes.]

If possible, we will arrange these visits which are part of the study to be at the same time as your routine appointments at the clinic. We will give you ZAR50 at the visits after one and two months, or if we ask you to come back for further tests or results, and ZAR100 at the 3-month visit, so for most people who pay about ZAR20 for travel, you will get about ZAR30 for your time at the one- and two-month visits, and ZAR70 at the 3-month visit.

After 3 months if you still have TB symptoms but we have not picked up TB on any tests:

We will ask a smaller group of patients (around 250 in total) who still have TB symptoms at 3 months to continue in the study for three more months, up to six months in total. If you are chosen for this group:

- We may discuss with your clinic doctor to arrange further tests to try to find out what is causing your symptoms.
- We will ask you to continue to come for study visits every month for 3 more months, to see if you are diagnosed with any other illness, or if your symptoms get better. If you are unable to come to the clinic, we may phone you, and ask you the same questions by phone. If, at any visit, our assessment suggests it is likely that you might have TB, we will send your sputum for testing, using the new TB test. We will ask you to come back for the results to start treatment if TB is found, or to check you again (in person or by phone) if TB is not found.
- At the 6-month visit, we would like to ask you some questions about how much it costs you to get health care, how often you have come to clinic, and other costs such as transport. These questions will take about 20 minutes.

These further visits (after months 4, 5 and 6) may coincide with your routine appointments at the clinic. We will give you ZAR50 at the visits after four and five months, or if we ask you to come back for further tests or results, and ZAR100 at the 6-month visit, to cover your travel and time as detailed above.

We will also check your medical records from time to time over the next 12 months to check your health, the results of any further tests your doctor requests at the clinic as part of your HIV care, and treatment given.

We would also like your permission to use the sputum and urine sample(s) you give us and the information we collect from this study for other research studies to help us understand HIV and TB better. We would only do this if the ethics committees, who are there to protect the interests of people taking part in our studies, first approved these further research studies.

It is very important for this study that we have a reliable way to contact you. This is, first, because if we get a positive test result, we need to be sure you know about it and are on the correct treatment. Second, it is very important that we find out how you are at the end of the study. So we can do this, we will ask you to give us the best phone number to reach you, and the phone numbers of two close friends or family members, as well as details about where you live. If we need to contact you, we will first try to contact you directly, using the phone number you give us, taking care to be sure we are talking to you in person before we ask any questions about your health. If you do not have a phone we will discuss with you today and agree how best to contact you. If we cannot contact you directly, we would then contact your friend or relative, using the numbers you give us, to ask your friend / relative if they know where you are and can help us contact you, taking care not to give away any information about your health. If you would prefer not to give contact details of a friend or relative, it is still ok for you to take part in the study. If we cannot trace you at the end of the study, we may approach the Department of Home Affairs to check their registers so we can be sure you did not pass away.

This study will take about 40 minutes of your time today [60 minutes if participating in the health economics study]. The visits after one and two months should take about 20 minutes of your time [35 minutes if participating in the health economics study]. The visit after 3 months may take about 45 minutes [an hour if participating in the health economics study].

For people asked to continue in the study to 6 months, the visits after four and five months should take about 35 minutes each, and the visit after 6 months may take about an hour.

WHAT ARE THE RISKS AND BENEFITS OF TAKING PART IN THIS STUDY?

Although it is recommended that people with HIV who have any symptom of TB are tested for TB straight away, in most clinics (including this one) this is not done, because it would mean doing very many TB tests when most people do not actually have TB. In this study, we aim to identify those people at highest risk from TB and make sure they get tested straight away. People at lower risk will not be tested straight away, but will be reviewed after a month and checked to see if they need a TB test at that point. If you are selected for telephone contact only, but you report feeling unwell during this contact, we will ask you to see clinic staff as soon as possible, so you can be tested for TB and other illnesses. As we are only testing patients who are most likely to have TB with new TB test, it is important that you return to the clinic as soon as possible if you feel unwell in between your clinic appointments, so you can be tested for TB and other illnesses.

If the questions about your health, or the results of the tests, suggest you might have TB, and this is confirmed by further tests, this will benefit your health, because you will start on TB treatment quickly, which will reduce any risk that your body will be damaged by TB. However, the results of the study will help us know how best to use this new test for TB, and so it will help people like you in the future.

WHAT HAPPENS IF I DO NOT AGREE TO TAKE PART IN THIS STUDY?

You do not have to take part in this study: if you do not take part, this will not affect the medical care that you receive. You can stop taking part in the study at any time, without giving a reason.

HOW WILL THE INFORMATION COLLECTED DURING THIS STUDY BE KEPT CONFIDENTIAL?

All information collected on paper during the course of this study will be kept securely and confidentially in a locked cabinet: Dr Hanifa is responsible for this. The only exception to this is if we find TB in any of your samples: we are required by law to inform the health service of positive TB results, so that you can receive correct treatment. In order to access your medical records we need to record your name and identifying details. This information will only be available to study staff and will be stored securely, separately from the other information about your health. The rest of the information we collect will be identified on forms and computer files only by a study number, not your name. When we enter your information into a computer, we will keep your identifying details separately, protected by a password, and only restricted study staff will have access. The rest of the information will be entered into another database, identified only by your study number, and we will use only this database to find the answers to our study questions. Only restricted study staff can link your identifying details with the rest of your information on the computer databases, ensuring that your information remains confidential.

Study information may be reviewed by the Ethics Committee, and independent monitors, to check that the study procedures were done correctly and the information is correct. Your information will remain confidential, unless we are required by law to release information. Reports about the study and results that may be published in scientific journals will not include any information which allows you to be identified.

WHAT IF I HAVE QUESTIONS ABOUT THIS STUDY?

If you have any questions about this study, please feel free to ask me now. If you have questions later you can ask study staff here at the clinic, or telephone Dr Hanifa on 010 590 1300.

The committees reviewing this study are the University of the Witwatersrand Human Research Ethics Committee, and the Research Ethics Committees of the University of Cape Town and the London School of Hygiene & Tropical Medicine, UK. If you have any questions or concerns about your rights as a person taking part in a research study, or if you wish to make a complaint about the study, you may contact Prof Cleaton-Jones, Chairperson of the University of the Witwatersrand, Human Research Ethics Committee, an independent committee established to help protect the rights of research participants, at 011 717 2301.

We will give you a copy of this sheet which explains the study to take away with you.

If you would like a copy of a report on this study, and you give us an email or postal address, we will send you a report. The final results may not be available until 2-3 years from now.

