Work package 1b&c and 2b

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF RESEARCH PROJECT:	
Post-TB CARE (Centre for Assessment and Research Excellence)	
DETAILS OF PRINCIPAL INVESTIGATOR (PI)/RESEARCHER(S):	
Prof Brian Allwood Prof Rein Houben	**Ethics reference number:** **N24/11/153**
Full postal address: Division of Pulmonology, Department of Medicine, 3rd Floor Clinical Building, Tygerberg Campus Stellenbosch University Francie van Zijl Drive Parow Valley	**PI Contact number: 0219389464**

We would like to invite you to take part in our research project about improving the lives of people after they've had TB. We are interested in how people's lives change after having TB and how we can support them. We are a team of researchers and clinicians based at Stellenbosch University, led by Professor Brian Allwood. We are working closely with two non-government organisations (NGOs) that represent TB survivors, TB Proof and KHANA. TB Proof is an NGO started by health workers in 2012, that advocates for access to high quality TB diagnostic tests and treatment, developing stigma interventions and improving support to people affected by TB. We are also working with an NGO in Cambodia, called KHANA. KHANA was established in 1996, and advocates for TB survivors' rights, and helps plan future policies to support them.

Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff any questions about any part of this project that you do not fully understand. It is very important that you are completely 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. In other words, you may choose to take part, or you may choose not to take part. Nothing bad will come of it if you say no: it will not affect you negatively in any way whatsoever. Refusal to participate will involve no penalty or loss of benefits or reduction in the level of care to which you are otherwise entitled. You are also free to withdraw from the study at any point, even if you do agree to take part initially.

The Health Research Ethics Committee at Stellenbosch University has approved this study**.** The study will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, the South African Guidelines for Good Clinical Practice (2006), the Medical Research Council (MRC) Ethical Guidelines for Research (2002), and the Department of Health Ethics in Health Research: Principles, Processes and Studies (2015).

What is this research study all about?

The purpose of this study is to find out more about who is more likely to experience severe problems from having TB. We know that TB has lasting impacts on people's lives. What we don't know is who is more likely to experience worse post-TB health outcomes. We are inviting TB survivors, like yourself, to participate in the project with us. Altogether we want to include 250 TB survivors in South Africa, and 50 TB survivors in Cambodia. We plan to recruit people who have completed TB treatment within the past 6 weeks (about 125 people) and people who have had TB more than six months ago but are now seeking help for problems because of their

previous TB (about 125 people). The purpose of the Post-TB CARE project is to find the best way to assess the impact of TB on different people over time.

Why are you invited to participate?
We're inviting you to participate in a study because you have completed treatment for tuberculosis (TB) within the past 6 weeks or have health problem related to TB which you had more than 6 months ago.

What will your responsibilities be?
If you decide to participate in the study, you will be expected to visit the study team to have the following tests done. We will **split the tests over two days**, so you don't get too tired doing them. You will have these tests done the **first time** we see you and then again **12 months later**. We would also like permission to access your medical history, including all previous TB episodes, through the single patient viewer and the national health laboratory service.
The tests that we will be doing as part of the study are described below.

We will be doing some tests to measure your lungs called **lung function tests**. This is done to look at how well your lungs are working. During these tests you will sit and breathe into a machine, and it records many aspects of how your lungs are working. These tests should take approximately 30-45 minutes.

You will also be asked to undergo a **Cardiopulmonary Exercise Test (CPET)** to assess how your heart, lungs, and muscles respond to physical exercise and assess how efficiently your body uses oxygen while you are moving. During the test, you will be asked to walk on a treadmill or cycle on a stationary bike, starting at a low intensity that gradually increases. While you exercise, your heart rate, blood pressure, oxygen levels, and breathing will be monitored. You will wear a face mask to measure the amount of oxygen you are breathing in and the carbon dioxide you are breathing out. The test may last anywhere from 8 to 15 minutes, depending on your ability to exercise.

You will also do some **functional exercise tests**. These consists of **walking tests and muscle strength tests**. In these tests we will ask you to walk as fast or far as possible in a given time. We will measure your heart rate, respiratory rate, how tired you are and how much oxygen is in your blood (using a finger probe). We will also ask you to breath or push your leg against resistance to measure how strong your muscles are. All these tests will take between 1 to 2 hours. You will be given chances to rest between tests and if you get tired.

You will have a test called a heart sonar also known as an **echocardiogram or ECHO**. It is not painful or dangerous. We place a blob of jelly on your chest before moving the sonar probe, a device as big as a cellphone, over your chest. The test will take approximately 30 – 40 minutes in total. The study will be done in a private area so that no one else can see you while this test is being done.

Using a similar sonar probe, we will also take an **ultrasound image** of your thigh muscle to see how much muscle you have. It is not painful or dangerous. The test will take approximately 15 minutes in total. The study will be done in a private area so that no one else can see you while this test is being done.

We will use a device called the **InBody S10** to measure your **body composition**. This device tells us important information about your body, like how much muscle, fat, and water you have. It does this by sending a very safe, low electrical signal through different parts of your body. You will not feel the electrical signal. We all ask you to lie still, and we will place electrodes (stickers) on each arm, each leg, and your trunk (tummy). This should not take longer than 10-15 minutes.

Indirect calorimetry is a test that helps us figure out how many calories your body uses when you are resting. It gives us an idea of how much energy your body needs just to keep basic functions going, like breathing and keeping your heart beating. This is called your **resting energy expenditure (REE)** or **basal metabolic rate (BMR)**. When you breathe, your body uses oxygen and produces carbon dioxide. Indirect calorimetry measures the amount of oxygen you use and the amount of carbon dioxide you breathe out. By analysing these, we can calculate how many calories your body is burning. You will lie down and relax while breathing into a special mask or mouthpiece. There is no pain or discomfort with this test. You will need to lie still for about 30 minutes.

We will take some **blood** from you to look at measures of levels of inflammation and infection in your body. We will also ask you to provide a blood sample to assess various markers in your body to see how some of the organs are functioning. These tests will help evaluate levels substances (e.g., your kidney function or haemoglobin) and identify any abnormality that could be corrected. We will also test for HIV in patients who are not on treatment for HIV. Your **blood** will be used to look for indicators of disease, found in the blood of people with post TB lung disease, known as biological markers (or **Biomarkers**) to see if they are different from people without post TB lung disease. These are highly specialized tests, and we will use these results to try to work out why some people develop this condition after completing TB treatment, and how better to identify people who will need additional medical help after completing TB treatment.

We will not take more than 60ml of blood, (which equals about 2 and a half table spoons and which is perfectly safe to donate).

You will submit a **sputum sample** at baseline. Additionally, if you get ill or admitted to the hospital in the year between your first visits and the follow up visit, we will ask you to come in so we will also collect **sputum and nasopharyngeal swab** samples. This will help us to identify the causes of any possible chest infections that could be the cause of your symptoms or potentially make your symptoms worse. These will include testing for new TB infection as well as other bacterial and viral infections. These samples are to see if you have any new infections that could be treated. Some of your sputum will be stored to test later for other organisms, e.g. Aspergillus, that are associated with post TB lung disease.

We will also collect **stool samples** to study the relationship between the bacteria in your gut and your immune system. It will allow us to understand if the bacteria in your gut contributes to how you recover after you have had TB. Some of your **stool** samples will be stored in long-term storage in freezers, without your name or any personal identifying details for later processing to look at bacteria and organisms in more detail.

We will collect a **urine sample** to look for certain signs in your body that may show how your immune system, overall health, or metabolism are changing as you recover from TB.

Some of your specimens will be stored for g**enetic testing**: this is looking at your DNA and genes. This is explained in a **separate consent** and will only be done if you are willing to participate.
Some of your samples will be processed immediately and some will be stored in long-term storage in freezers. They will be stored without your name or any personal identifying details. We will only be able to link your name to the samples through number codes, which will only be available to authorized study personnel. Only authorized personnel will be allowed to work with your samples in the future.

Some imaging of the chest and heart, such as **chest x-ray and CT scan**, will also be done to assess the severity of the disease and look for any complications from post TB lung infection. Both a HRCT (High-Resolution CT) scan and a CTPA (CT Pulmonary Angiography) will be done. An HRCT is a detailed lung imaging test that uses X-rays to produce clear pictures of the lungs, helping doctors detect lung diseases or damage. It is not painful or harmful. A CTPA is a specialized scan that uses X-rays and contrast dye to create detailed images of the lung's blood vessels, commonly used to check for blood clots in the lungs and the heart. It is not painful or harmful.

During each visit, we will also ask you to fill out a number of forms with our help. These forms will ask about your **mental (emotional) health, physical (how your body works/feels) health, social life, relationships, and economic and financial situation**. We want to get to know you better so we can understand how people who have had TB are doing.

You should plan to spend about **6 - 8 hours** at our clinic each time you visit.

As part of participating in this study, you will be given the option to come to our clinic to participate in a **lung exercise or lung rehabilitation program**. This is **not part of the study but is offered as standard of care**. By saying yes to this program, you will also be allowing us to make use of the findings for possible publication of the data and similar research.

This program will require you to come to our clinic for **up to 12 visits**. The first time will be one week from today, and it will be the initial assessment. This will be followed by **weekly reviews**, which should consist of a **2-hour**

rehabilitation session. At your **12 months visit** we will see you for the last review for the study where we will check your health with some of the rehab tests.

During the year between your first visits and the follow up visits, a member of the study team will **phone** you every **3 months**, or so, to assess how you have been. They will ask questions to see if you have been feeling better or worse, as well as if you have gone to the clinic or hospital.

There may be some **additional tests** that we will ask you to do, however you do not need to say yes to these. At the end of this consent form you will indicate if you are willing to have these extra assessments done. If you decide that you do not want to do the additional tests, you can still take part in the other parts of the study.

The additional assessments/tests that may be done are listed below:
Additional imaging: Participants will be selected at random to have additional imaging of their lungs and heart, and you will be given the opportunity to have the imaging done, or not. The additional imaging is explained below.

Will you benefit from taking part in this research?
This is a research project. However, if we see or find anything through the tests that we think might harm you, we will tell you and help you access the care you need.

As a participant in this study, you will be given the opportunity to participate in the lung exercise or rehabilitation program, if you choose. This service is not usually offered to patients within the state healthcare system.

Additionally, we are doing many tests that are not routinely offered to patients, unless they show symptoms or require treatment. This means that we may pick up symptoms much earlier than you would normally and if this happens, we will help you to access the appropriate

There is no cost for the study-related clinic visits, study antibodies, examinations, and laboratory tests in this study.
You will be compensated for taking part in the study at every study visit for transport expenses, time spent in the research unit and inconvenience. The amount you will get is based on the SAHPRA guidelines. This will be a minimum of R400 per visit. You will get the money through a Standard Bank PIN code and voucher number that will be sent to your cell phone via SMS. You can then draw cash at any Standard Bank ATM or at certain shops (we will give you a list of these shops).

Are there any risks involved in your taking part in this research?
Lung function testing is performed routinely. However, if you have had surgery in the last 6 weeks, are pregnant or have any condition where the investigators feel it will not be safe, we may choose not to perform this test.

The only risk from the blood test is minor discomfort at the site of the blood draw. Occasionally people may have a bruise at the site of blood draw for a few days afterwards. These are minimized by having experienced personnel perform the procedure to ensure initial success and minimize potential complications which are very uncommon.

CPET testing is safe, however you may feel some discomfort or dizziness due to the excess exertion. You may feel a little discomfort due to the leads that are placed on your body to monitor your heart, the blood pressure cuff on your arm to monitor your BP or the face mask placed to monitor your oxygen and carbon dioxide levels. Other potential risks will include shortness of breath, chest pain and infrequently coughing up blood or vomiting from the exercising. These complications do not occur very often and if they do, you will be attended to immediately by a trained medical professional that will assist you.

An echocardiogram is safe and carries no risk to you.

All tests are administered by trained healthcare professionals, and you will be closely monitored, and you will be asked to stop if you experience significant discomfort or any concerning symptoms.

There is also a risk that you will be recognised by other people when coming to our clinic. There will be a few people at our clinic each time. Although we cannot guarantee that other people won't recognise you or tell others that they saw you at our clinic, we will ask everyone who comes to our clinic not to repeat what they hear or see. By being part of this study, you agree to keep who you see and what you hear about other private and not share the personal information or comments of others outside of the listening group sessions.

The imaging tests are routinely performed tests every day in South Africa and around the world, and are done in a safe manner. The imagining by its nature, involves small doses of exposure to radiation. However, the testing machines will be programmed to give the least amount of radiation needed for each test, and people who are likely to be at higher risk based on the specific test (e.g. pregnant women) will be excluded for that specific test.

The lung function testing, CPET and some radiological imaging (e.g. CT scan, chest x-ray) are not safe to do in pregnant individuals. For this reason, if you are pregnant at the start of the study you will not be included in the study. If you become pregnant while on the study, you will not have the tests mentioned above. We will also perform a pregnancy test on all returning female participants prior to any test.

Another potential risk is being seen with Stellenbosch University staff might lead other people to make assumptions about you. Stellenbosch University is well-known in communities around the country for being involved in TB treatment and prevention projects. However, some people might still make the wrong assumptions about you and your interactions with us. Please inform us if you ever feel that this is the case, so that we can make alternate arrangements to support your participation. For example, we might pick you up from a different location where you won't be easily recognised.

If you do not agree to take part, what alternatives do you have?
The research study is an opportunity for us to learn from you. If you decide not to participate in this study but would like to receive more information about your health concerns like TB, or you would like to access TB tests and other services, please visit your local health facility.

Who will have access to your medical records?
Confidentiality means we as the research team will protect your identity and take steps to make sure that your information and other identifying recordings are separated from your identity as a person. We do this so that no one will be able to identify you through the information we gather from you. We keep this confidentiality in everything that we do and in several ways. For example, we will give every person in our study a number, and use that number in the way that we save your information, so that your name and your data are never together. We store all the data in a safe and secure way, only study staff have access to it. All your personal information (name, address, phone number) will be protected by the study staff (the facilitators and research assistants). This information will not be used in any publication of information about this study.

There are some people who may review the records of your data. They do this to check that we, the staff, are treating you in the correct way and otherwise adhering to guidelines for good scientific practice. The people who may review your records including Stellenbosch University Health Research Ethics Committee, local regulatory agencies, study staff, and study monitors. Institutional Review Boards (IRBs) or Ethics Committees (ECs) are committees that watch over the safety and rights of research participants.

As with all studies, we are obligated legally to address any life- threatening or potential harmful matters that may arise during the study. For example, if we observe child abuse, we will need to report this to the Ethics Committee immediately and this matter will be referred to appropriate services.

Even though it is unlikely, what will happen if you get injured somehow because you took part in this research study?
If you are injured while participating in this study, immediate treatment is more important than the research study. This care will be the normal care available from the local Department of Health facilities. Participation in this study does not give you access to any extra care or support. There is no program for compensation either through the project or through the University of Stellenbosch. At the same time, you will not be giving up any of your legal rights to care by signing this Informed Consent Form.

By agreeing to participate in this study, you understand the possible, though minimal, risks involved in the discussions and/or the learning groups. Stellenbosch University will provide comprehensive no-fault insurance and will pay for any medical costs that came about because participants took part in the research (either because the participant used the medicine in this study or took part in another way). The participant will not need to prove that the sponsor was at fault.

Are there any costs involved if I decide to participate/take part?
You will be compensated for your time in taking part in the study and your expenses will be reimbursed for each study visit. You will not have to pay for anything related to the research if you do take part.

What are some reasons why the researchers may withdraw your participation in the study?
You may be withdrawn from the study without your consent for the following reasons:

- The research study, or this part of the study, is stopped or cancelled.
- The study staff feels that completing the study would be harmful to you or others.
- The scientific goals for the research have already been met and continuing would be of no further scientific benefit.
- If you as participant would not be able to or would be unwilling to participate in the study in such a way that is in accordance with the needed study procedures.

Persons to Contact for Problems or Questions
If you have any questions about your participation in this research study or your rights as a research participant, contact.

Principal Investigator: Prof Brian Allwood, Division of Pulmonology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa.
Telephone: +27 21 938 9247
Email: brianallwood@sun.ac.za

If you have any questions or concerns about your rights as a research participant or want to discuss a problem, get information, or offer input, you may contact:

Independent Review Board/Ethics Committee: Stellenbosch University Health Research Ethics Committee, Tygerberg Campus.
Telephone: 021 938 9819.

Declaration by participant
By signing below, I …….…… agree to take part in a research study entitled Post-TB CARE (Centre for Assessment and Research Excellence): Public Engagement.

☐ I acknowledge that in consenting to participating in this study that I will be required to doing the following procedures, tests and questionnaires:

- Full lung function testing that includes spirometry, plethysmography, diffusion capacity and 6 minute walking distance
- Cardiopulmonary Exercise Test
- Functional Exercise Tests
- Echocardiogram (ECHO) and ECG
- Questionnaires regarding your mental (emotional) health, physical (how your body works/feels) health, social life, relationships, and economic and financial situation
- Chest x-ray and CT scan
- Biological samples including blood, sputum, urine and stool, some of which will be stored.

☐ I acknowledge that details of my medical and treatment history may be accessed using the Single Patient Viewer (SPV)

I declare that:

- I have read this information and consent form, or it was read to me, and it is written in a language in which I am fluent and with which I am comfortable.

- I have had a chance to ask questions, and I am satisfied that all my questions have been answered.
- I understand that taking part in this study is **voluntary,** and I have not been pressurised to take part.
- I may choose to leave the study at any time and nothing bad will come of it – I will not be penalised or prejudiced in any way.
- I may be asked to leave the study before it has finished, if the study staff or researcher feels it is in my best interests, or if I do not follow the study plan that we have agreed on.

Signed at (*place*) ..... on (*date*) …….. 202….

Signature of participant **Signature of witness**

Declaration by investigator

I *(name)* ……..…… declare that:

- I explained the information in this document in a simple and clear manner to ……..
- I encouraged him/her to ask questions and took enough time to answer them.
- I am satisfied that he/she completely understands all aspects of the research, as discussed above.
- I did/did not use an interpreter. (*If an interpreter is used then the interpreter must sign the declaration below.)*

Signed at (*place*) ..... on (*date*) …….. 202….

Signature of investigator Signature of witness

Please carefully read the statements below (or have them read to you) and think about your choice. No matter what you decide, it will not affect whether you can be in the research study, or your routine health care

I would like to participate in the lung exercise or lung rehabilitation program and allow the study team to make use of the findings for possible publication of the data.

☐ Signature_____

Please indicate, by ticking below, if you would be interested in any additional imaging tests as described briefly below

☐ Cardiac MRI

Cardiac MRI is a detailed heart scan that uses powerful magnets and radio waves to create clear images, helping doctors check for heart problems without surgery. It is not painful or harmful.

☐ VQ Scan

A VQ scan is a lung test that uses small amounts of radioactive material to see how well air and blood flow through the lungs, often used to check for blood clots, and to see how the air and bood flows in your lungs. It commonly performed at Tygerberg and around the world, is not painful or harmful, and is safe even in pregnant women.

☐ PET-CT

A PET-CT scan combines two imaging techniques—PET (Positron Emission Tomography) and CT (Computed Tomography)—to provide detailed pictures of the body, helping doctors detect inflammation, infections, and other conditions by showing both structure and activity in tissues. It is not painful or harmful.

☐ MIGET

MIGET (Multiple Inert Gas Elimination Technique) is a specialized test that measures how well the lungs are transferring gases like oxygen and carbon dioxide, helping doctors assess ventilation and blood flow issues in the lungs. It is done by breathing different gases and measuring their concentrations in the blood. It is not painful but requires blood sampling.

Please provide your signature for the selected additional imaging tests Signature _____

Permission to have all anonymous data shared with journals:
When this study is finished, we would like to publish results of the study in journals. Most journals require us to share your anonymous data with them before they publish the results. Therefore, we would like to obtain your permission to have your anonymous data shared with journals. In accordance with the POPI Act, the researchers will take care to ensure that you are not identifiable (all personal information is not linked to the data shared.

Tick the Option you choose for anonymous data sharing with journals:
I agree to have my anonymous data shared with journals during publication of results of this study

☐ Signature_____

OR
I do not agree to have my anonymous data shared with journals during publication of results of this study

☐ Signature_____

Permission for sharing samples and/or information with other investigators:
In order to do the *research* we have discussed, we must collect and store the blood, sputum, urine and stool samples and health information from people like you with Post TB lung disease. We will do some of the tests right away. Other tests may be done in the future. Once we have done the research that we are planning for this research project, we would like to store your sample and/or information. Other investigators from all over the world can ask to use this data in future research. All the data, will however, remain in the possession of our team in South Africa, and no one will have access to your information without first applying and been granted permission. To protect your privacy, we will replace your name with a unique study number. We will only use this code for your data. We will do our best to keep the code private. It is however always possible that someone could find out about your name but this is very unlikely to happen. Therefore, we would like to ask for your permission to share your data with other investigators.

Tick the Option you choose for sharing samples and/or information with other investigators:
I do not want my sample and/or information to be shared with other investigators

☐ Signature_____

OR
My sample and/or information may be shared with other investigators who are able to conduct further analysis in Post TB lung disease research

☐ Signature_____

Permission to store samples and/or information for future studies:
As researchers learn more about illnesses or diseases, new research is possible using existing data, instead of returning to participants to ask for additional samples.
Any future studies or reuse of your data will need to be approved by the Stellenbosch University Health Research Ethics Committee.

Tick the Option you choose for storage and reuse of samples/data for studies in the future:
I do not want my sample(s) and/or information (data) to be stored for reuse for future studies

☐ Signature_____

OR
I hereby agree that my sample(s) and/or information (data) may be stored for future research in a field related to Post TB.

☐ Signature_____

Agreement to be contacted for future research studies:
I agree to be contacted for future studies that are relevant to me

☐ Signature_____

OR

I do not agree to be contacted for future studies

☐ Signature_____