PARTICIPANT INFORMATION SHEET AND
GENERAL INFORMED CONSENT FORM FOR ADULTS & CHILDREN
AIM 1

Title of Project: Project TRUST

The Impact of Alcohol Consumption on TB Treatment Outcomes

NCT02840877

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Background

You are being asked to take part in this research study because you have tuberculosis (TB) disease. This study is funded by the United States National Institutes of Health (NIH) and led by Dr. Tara Carney from the South African Medical Research Council (SAMRC), and Dr. Karen Jacobson from Boston Medical Center (BMC). Before you decide if you want to take part, we want you to know more about the study.

This is a consent form. It gives you information about this study. The study staff will talk with you about this information. You are free to ask questions at any time. If you agree to take part in this study, you will be asked to sign this consent form. You will get a copy to keep.

Purpose

The main purpose of this study is to understand why some people do better on TB treatment than others. We want to know if alcohol, tobacco, drug use, food insecurity, or depression affect response to treatment. We want to learn if alcohol use affects levels of TB medications in the body and/or how well blood cells fight TB during treatment. We also want to know how TB bacteria changes and is associated with response to treatment.

What Happens In This Research Study

If you agree, you will be one of up to 450 patients participating in this study. In this study, you will not get special treatment for your TB. You will still receive all of your TB treatment and monitoring at your usual clinic. If you have any health problems during your TB treatment, you should seek medical care from your doctor or nurse at your usual clinic. The following will be the additions from this study:

If you choose to be part of this study, you will be asked to attend monthly study visits at the CDC while you are getting TB treatment, receive daily visits from a DOT worker who will observe you taking your TB medicine, and complete interviews every three months for up to a year after you finish treatment (four interviews in total). Interviews will take place at the clinic, unless you are unable to attend, in which case the interview may be conducted in a private space of your choosing. You may also be selected for the second part of this study, for which you will be asked

to spend a day at Brewelskloof Hospital where blood will be drawn to test for TB medicine levels. You will sign a separate consent form if you are selected for this part of the study.

Screening visit

After you have read and signed the consent form, we will confirm if you are eligible to take part in the study by using health information provided by you and your medical records. If you have not been tested for HIV in the last 6 months, you will need to be tested to take part in the study.

If you are a woman aged 50 years or younger, you will be asked to provide a urine sample for pregnancy testing. If you are pregnant, you will not be allowed to take part in the study. After you sign this consent form, if you decide not to take part or you are not eligible, we will still use some of your information to understand why some people do not join our study.

Enrollment Visit

This visit will take place at the CDC, ideally on the same day you are screened. The study procedures will last up to 3 hours, including time for chest x-ray. At this visit, we will ask you to:

- Provide information on how to contact and find you.
- Answer questions about yourself, your medical conditions, and your alcohol, tobacco, and drug use.
- Provide 30 ml (2 tbsp) of blood to test for blood counts, liver function, kidney function, diabetes, and at a later time, recent alcohol use. You may be selected to also be tested to check for differences in how your immune cells function during TB treatment and whether you were ever exposed to COVID-19. You will not be given the results of this testing. The COVID-19 test will tell us if you were ever exposed to COVID-19. This is not a test to determine you are infected with the COVID-19 virus.
- Provide a urine sample that will be used to test for recent drug use.
- Provide sputum to do a test for TB. Your sputum will also be used to test your TB bacteria. You may be asked to provide a second sputum sample for these tests.
- Go to Mediclinic to have a chest x-ray performed.

Follow-up Study Visits

Everyone enrolled in this study will have monthly follow-up visits at the CDC while they are receiving TB treatment. If possible, these visits will happen on the same day as your TB clinic visits and will take about 30 minutes. We may collect additional information on your health, treatment progress, and recent clinic visits from your medical records. At this visit, we will ask you to:

- Answer questions about how you are feeling and alcohol use during the past month.
- Provide sputum to do a test for TB again after 5 months of treatment. This sputum may also be used for additional TB bacteria testing.
- We may also collect some of your sputum that you gave to the clinic after 5 months of treatment if TB was found.
- If you have any symptoms of TB medication side effects, provide about 10 ml (2 tsp) of blood to check your blood counts and liver function.
- You may be selected to provide about 3 ml (1 tsp) of blood once you have finished two weeks of TB treatment and again when you finish your treatment to see if there are differences in how your immune cells function during TB treatment.

- You may be selected to provide about 5 ml (1 tsp) of blood once you have finished three months of TB treatment and again when you finish your treatment to look for recent alcohol use.
- Go to Mediclinic to have a second chest x-ray performed.

DOT worker home visits

Everyone enrolled in this study will be assigned a DOT worker. The DOT worker will watch and record you taking your pills at a location you choose Monday through Friday. On Mondays, they will also ask you if you took your pills over the weekend. This will happen for the full 6 months of treatment. During the first 12 weeks of treatment, the DOT worker will also give you a specimen cup each week to provide a sputum specimen first thing in the morning before your DOT visit.

Follow-up Interviews

You will be interviewed 3, 6, 9, and 12 months after you complete treatment. At the visit, we will ask you to:

- Answer questions about yourself, how you are feeling, and your alcohol, tobacco, and drug use.
- If the clinic determines that your TB disease has come back or you tell us you have symptoms that could be from TB again, provide an additional sputum sample to see whether you have a new type of TB infection. We may also collect some of the specimen you gave to the clinic if it does show evidence of TB again.
- If your TB disease has come back or if you are diagnosed with COVID-19 at any time during the study, we will also access information about your diagnoses, the treatment you were given, and the outcome of your illness from your medical record and/or the South Africa National Health Laboratory Services (NHLS) or the University of Cape Town Provincial Health Data Centre. As a reminder, this study will not provide a test to determine if you are infected with the COVID-19 virus.
- You may be selected to provide about 5 ml (1 tsp) of blood at your final follow-up visit (12 months after you complete your TB treatment) to look for recent alcohol use.
- You may be selected to provide up to 30 mL (2 tbsp) of blood at one of your final follow-up visits (9 or 12 months after you complete your TB treatment) to test blood sugar levels, and markers of stress and inflammation. If you are interested in allowing some of your blood sample to be used to test genes that may be associated with your body's response to tuberculosis (TB) infection, HIV infection, and response to treatment, you will be asked to sign a separate consent form.

Risks and Discomforts

Participation in this study is voluntary. There are a few risks with participating in this study:

- The urine test for drug use or pregnancy may cause some embarrassment. If you feel distressed by the results, we will ensure that you access services to help you cope.
- Blood draws may cause mild pain, bruising, bleeding, and sometimes fainting. Our study nurses are properly trained to minimize such happenings.
- There is a small chance of stigma. People may treat you differently if they know you are someone with TB. The study team will do its best to keep your participation confidential.

- The risk of radiation exposure from each chest X-ray is very small. X-rays can damage cells, but your body can typically repair cells after low doses. The radiation exposure that you will receive from each chest X-ray (if you choose to get the optional second chest X-ray) is about the amount of radiation you would receive from natural sources like the soil and the air over 10 years. If you are found to be pregnant, you will not be able to participate in the study due to additional risk from chest X-ray. If you are asked to get a second chest X-ray, we will confirm that you are not pregnant beforehand.
- You may feel embarrassed by the personal nature of the questions we will ask you.
- We may provide specific information back to the CDC or your local clinic, which they may use to better treat your TB disease. We will inform the clinic of your blood test results and if we find that your TB is resistant to isoniazid, one of your TB drugs. We will inform the clinic if you are having challenges taking your TB drugs so that they can reach out to you. We will not provide the clinic with any other information that you share with us.

If you feel stress from this study, you should tell our study staff. We will update you in a timely way on any new information that may affect your health, welfare, or decision to stay in this study.

Potential Benefits

You may benefit from participating in this study because you will receive close monitoring during your TB treatment. If you miss doses of your TB medicine, we will reach out to help you stay in care. Participation may help you take all of your TB medications and increase your awareness of TB-related issues. After you finish treatment, we may help you identify if your TB has come back again so you get back on treatment earlier and minimize your risk of infecting others. However, you may not receive any benefit from participating.

Alternatives

Your alternative is to not participate in the study. You can still receive standard care from your usual clinic.

Costs and Reimbursement

There is no cost to you to participate in this study. You will receive reimbursement in the form of grocery store vouchers at each visit to help cover your time, inconvenience, and expenses.
You will receive a voucher of R200 for the screening/enrollment visit and a voucher of R150 for the completion of each study visit from months 1-5. You will receive an extra R50 voucher for completing 80% or more of your scheduled DOTS visits in months 1-3. If, at the end of the second week of treatment, you are selected for the phase of the study that examines how your immune cells respond to TB treatment, you will receive a voucher of R50 to cover the additional time and inconvenience. You will receive a voucher of R200 for completing your month 6 visit. You will receive a voucher of R150 each time you come to a post-treatment visit, there are 4 of these in total. You will also receive a voucher of R100 for completing a second chest x-ray during one of your follow-up/post-treatment visits. If you are asked to provide additional blood at one of your final post-treatment visits you will receive a voucher of R100. If the study team ends your participation in the study because your TB disease comes back during the follow-up period and you completed at least one post-treatment follow-up visit, you will be reimbursed a R50 voucher.

Confidentiality

Information from this study and from your medical record may be reviewed by the SAMRC, University of Cape Town (UCT), and Stellenbosch University's (SU) Research Ethics Committees and U.S. regulatory agencies such as the Office of Human Research Protection, the Institutional Review Board (IRB) of BMC, and the NIH. Your contact information will be kept confidential and will be destroyed one year after the end of the study. Information from this study and from your medical record may be used for research purposes and may be published. Your name will not be used in any publications.

To protect your privacy, information we collect from you will be stored with code numbers, rather than your name. A log that links your name to the code will be stored securely and will not be shared unless required by law. The laboratories processing your biologic samples will never have access to your name. Your samples will be stored at SU for future research and training, and the link to your information will be destroyed after five years. TB bacteria may be extracted from your samples and shipped to the United States of America and/or Germany for further testing. The blood samples you provide two weeks after you start treatment, and at the end of your treatment, will be stored at SU until they are shipped to the Ragon Institute in Boston, MA, USA for analyzing. These samples will be stored in the USA and destroyed after the study and quality assurance is complete, which may be up to 5 years after the end of the study. We might use your research data/samples in future studies to help us understand more about tuberculosis and/or alcohol use. These future studies might be done by us or by other investigators but will never be for commercial purposes. Before we use your data/samples, we will remove any information that shows your identity. If you have concerns or questions about your stored specimens, you can contact the SU Health Research Ethics Committee at 021 938 9207.

This study is covered by a Certificate of Confidentiality (CoC) from the National Institutes of Health. All studies funded by the National Institutes of Health that involve identifiable information or biological samples are covered by a CoC. The CoC provides how we can share research information or biological samples. Because we have a CoC, we cannot give out research information or biological samples that may identify you to anyone that is not involved in the research except as we describe below. Even if someone tries to get your information or biological samples in connection with a legal proceeding, we cannot give it to them. The CoC covers **only** data and specimens stored in the United States of America. The CoC does not prevent you from sharing your own research information. Once the information we give back to the clinic (described above) has been put into your clinic medical records, it is not covered by the CoC. However, information in your medical records is protected in other ways. Please ask us if you have any questions about what information will be included in your clinic medical records. Data and specimens stored locally in South Africa, are also not covered by the CoC, but are protected in other ways. We cannot give your locally stored data biological samples in connection with a legal proceeding unless there is a court order or if so required by a specific law.

Your information will only be disclosed as required by law in two instances: 1) If you tell us that you are about to hurt yourself or someone else, or 2) if you are involved in the neglect and/or abuse of a child. In either case, we will report that information to the appropriate authorities.

The information collected for this study, excluding your name and other contact information, will be stored at the SAMRC for at least fifteen years after the end of the study.

Who to Contact with Questions

This study has been approved by the SAMRC, UCT, and SU Ethics Committees, and the Institutional Review Board (IRB) of BMC. It will be conducted according to the ethical guidelines and principles of the International Declaration of Helsinki and the South African Guidelines for Good Clinical Practice. If you have any questions or concerns about the research, please contact Dr. Tara Carney(South African Principal Investigator) at 021 938 0326 or write to tara.carney@mrc.ac.za, or Medical Research Council (MRC) P.O. Box 19070, Tygerberg 7505, South Africa.

Your Rights and Right to Refuse or Withdraw

By consenting to participate in this study, you do not give up any of your legal rights. Giving consent means that you have heard or read the information about this study and that you agree to participate in all outlined activities. Taking part in this study is voluntary. You have the right to refuse to take part in this study or to withdraw at any time. Your participation is completely up to you. If at any time you choose to withdraw, you will not suffer any penalty or lose any benefits to which you are entitled, including your access to health care.

The investigator may decide to discontinue your participation without your permission because he/she may decide that staying in the study will be bad for you or that you are no longer eligible, or the sponsor may stop the study.

If you have any questions about your rights as a participant, you may contact the chairperson of the MRC ethics committee, Prof Danie du Toit at 021 938 0687 or email adri.labuschagne@mrc.ac.za

Indicating Consent

Please let us know if you have any questions before signing this consent form. Please initial next to each item to show that you agree to what is required:

	Agree	What We're Asking of You
1		I agree to continue in the study, which has been fully described to me
2		I agree to provide contact information.
3		I agree to allow study staff to access my medical records, including for unplanned visits to health providers
4		I agree to answer questions about myself today
5		I agree to be tested for HIV if I have not been tested in the past 6 months
6		If eligible, I agree to provide urine for drug and pregnancy testing and provide blood for biological testing, including testing for associations between your immune cells and your response to TB treatment.
7		I agree that some of my blood may be shipped to the United States of America, where it will be tested for associations between my immune cells and how I

		respond to TB treatment, and that my blood may be stored in the United States of America for up to 5 years after the end of the study and then destroyed.
8		I agree to return for study appointments during each month of TB treatment.
9		I agree to allow DOTS workers to observe me taking my medication five days per week.
10		I agree to provide a sputum sample each week for the first 12 weeks of my treatment, once more at the fifth month of treatment, at the six month visit if the fifth month sputum sample was positive, and once more if the clinic or the research program thinks that I may have TB again after I have finished treatment
11		I agree that the TB bacteria from my sputum may be shipped to the United States of America and/or Germany, where the TB bacteria will be tested, and that the TB bacteria from my sputum may be stored in the United States of America and/or Germany for up to 5 years after the end of the study and then destroyed.
12		I agree to come to the clinic for four follow up interviews after my TB treatment has been completed
13		I agree that I may have up to a total of 14 study visits during my entire time enrolled in this research study

Future Use of Samples

Please check **one** of the options below (and initial):

_____ (Participant initials) — I agree that my samples may be stored for up to 10 years after the study for use by the investigators on this study or other studies who are interested in learning more about tuberculosis and/ or substance use. Any future use of samples will first be approved by a research ethics committee.

_____ (Participant initials) — I do not agree to have my samples stored for use after the end of this study.

Access to Treatment Outcome

Please check **one** of the options below (and initial):

_____ (Participant initials) — I agree that if I un-enrol from the TRUST study before completing TB treatment (either by choice or by the choice of the study team), TRUST study staff may check with the sisters at the TB Clinic at Worcester Community Day Clinic (CDC) and in my medical record to see what my treatment outcome was.

_____ (Participant initials)

I do not agree to allow TRUST staff to see what my treatment outcome was if I un-enrol from the study before completing TB treatment.

Future Contact

Please check **one** of the options below (and initial):

_____ (Participant initials)

I agree to be contacted after my time in the study by the investigators about matters related to this study or other potential studies I may be eligible for.

_____ (Participant initials)

I do not agree to be contacted after the study by investigators about matters related to this study or other potential studies I may be eligible for.

Blood Sample DNA Analyses

Please check **one** of the options below (and initial):

_____ (Participant initials)

I agree to learn more about how my blood samples could be used for additional research to test genes that may be associated with my body's response to tuberculosis (TB) infection, HIV infection, and response to treatment.

_____ (Participant initials)

I do not agree for my blood samples to be used for additional DNA analyses, and I do not wish to learn more about these procedures.

Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

_____

Participant (Signature and Printed Name) Date

_____

Person Obtaining Consent (Signature and Printed Name) Date

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Witness (Signature and Printed Name) **Date**

**A witness is required if the research patient or legal representative cannot read (e.g. blind or illiterate) or if it is required by the study plan. The witness should participate in all of the discussions with regards to the participant research during the consent process. By signing this consent term, the witness guarantees that all the information within the consent has been explained to the participant, and that the consent seemed to have been understood and given by free will.*