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Community and universal testing for tuberculosis among contacts

Submission date	Recruitment status	[X] Prospectively registered
11/12/2020	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
22/12/2020	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
12/08/2025	Infections and Infestations	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Tuberculosis (TB) is a disease which is caused by a bacteria called Mycobacterium tuberculosis. The bacteria spreads from person to person through the air when a person with TB disease coughs, sneezes or speaks. The bacteria commonly attacks the lungs but it can also spread to other parts of the body, like the brain and spine. Once infected with TB, people often develop latent TB (TB that is "sleeping") or active TB (TB that is awake and attacking the body). People with latent TB have TB germs in their bodies but they are not sick because the germs are not active, and they cannot spread the germs to others. The germs may become active in the future and people often develop disease and present with the following symptoms: a persistent cough that lasts more than 3 weeks, chest pain, coughing up blood, feeling tired all the time, night sweats, chills, fever, loss of appetite, and weight loss. TB is an important health problem in sub-Saharan Africa and is a particularly serious problem among people staying or working with a person who has TB. That is why when someone has TB, it is important for household members or community contacts to be checked for TB using symptom screening tools. However, these symptom screening tools sometimes fail to detect if TB contacts have active or sleeping TB. The aim of this study is to evaluate the Test-and-Treat strategy and universal TB testing of all household and community contacts regardless of symptoms. The researchers are hoping to find more people who have TB by testing everyone among household and community contacts instead of just checking symptoms and testing only people who are symptomatic (screening and test).

Who can participate?
Any adult (aged over 18) who is the first person to be diagnosed with TB within their household can participate in the study. The adult must have laboratory results that are not older than 2 weeks and must at least stay with at least one person.

What does the study involve?
The study involves evaluating the Test-and-Treat strategy and universal TB testing of all household and community contacts regardless of symptoms. Consenting TB index patients from health facilities will be requested to provide a list of their household and community contacts. Then TB index patients and their household contacts will be randomly allocated into either standard TB screening or universal testing arms. Index patients will receive routine TB treatment

but will be requested to provide a sputum sample for culture and future genome sequencing. Standard TB screening will involve TB screening using WHO four-symptom screen questions; investigation of symptomatic patients with the Xpert Ultra test; and referral of TB-positive patients for TB treatment at their chosen or nearest health facility. Those who don't have symptoms or test negative on Xpert Ultra will be referred for TB preventive therapy. Universal testing will involve universal testing of all household contacts (regardless of TB symptoms) with Xpert Ultra and referral of TB-positive patients for TB treatment at their chosen or nearest health facility. Those who test negative on Ultra will be referred for TB preventive therapy.

Summary of Phase I and II and study arms
Phase I: Before delivery of the pragmatic CRT, 100 TB source cases will be enrolled and requested to identify contacts that can provide sputum for testing with Xpert Ultra and will have LTBI tested using QuantiFERON-TB-Gold-Plus. If the proportion of contacts eligible for LTBI treatment (i.e. HIV positivity on history, <5 years or LTBI positivity), in each country is lower than 80%, we will consider LTBI testing in the main trial. We are not planning to follow up with the study participants, except to report positive TB cases and those with LTBI if guidelines warrant treatment for LTBI and ensure linkage to care for those individuals.
In Phase II, we will conduct a CRT with randomisation at the household level of the TB source case (index patient). In Lesotho and Tanzania, the intervention will be the Universal TB Testing arm which will be compared with Standard TB Screening arm, herein referred to as standard of care. Since universal testing has become standard of care in South Africa, our intervention will be Enhanced Universal TB Testing which will be compared with the Standard Universal TB Testing arm as described below:

Phase II in Lesotho and Tanzania: as shown in Figure 1, we will conduct a CRT with randomization at the household level of the TB index patient in Lesotho and Tanzania. At enrolment, TB index patients and their household contacts will be randomized into either 'Standard TB Screening' or 'Universal TB Testing' arms. HIV counselling and testing will be offered to all participants regardless of study arm. We will enrol 600 TB source patients in each country. Then, 300 TB index patients and their household contacts will be randomly assigned into either 'Standard TB Screening' or 'Universal TB Testing' arms.
•Standard TB Screening: TB screening using WHO four-symptom screen questions (cough>2 weeks, fever, night sweats or unintentional weight-loss); investigation of symptomatic patients with Xpert Ultra and referral of TB positive patients for TB treatment at their chosen or nearest health facility. Participants that do not report TB symptoms or test negative on Xpert Ultra will be referred for TPT.
•Universal TB Testing: Universal TB testing of all household contacts (regardless of TB symptoms) with Xpert Ultra and referral of TB positive patients for TB treatment at their chosen or nearest health facility. Symptom screening will be done after sputum is collected. Those that test negative on Ultra will be referred for TPT.

Phase II South Africa: In South Africa, we will also conduct a CRT with randomization at the household level of the TB index patient as shown in Figure 2. At enrolment, TB index patients and their household contacts will be randomized into either 'Standard Universal TB Testing' or 'Enhanced Universal TB Testing' arms. HIV counselling and testing will be offered to all participants regardless of study arm. We will conduct a CRT and enrol 400 TB source patients and their household contacts. Then, 200 TB index patients and their household contacts will be randomly assigned either to Standard Universal Screening or Enhanced Universal TB Screening (lung flute for sputum collection and eCase Manager/mHealth intervention to ensure linkage to care).
•Standard Universal TB Screening: This will involve universal testing of all household contacts (regardless of TB symptoms) with Xpert Ultra and referral of TB positive patients for TB

treatment at their chosen or nearest health facility. Symptom screening will be done after sputum is collected. Those that test negative on Ultra will be referred for TPT.
•Enhanced Universal testing: All contacts aged ≥5 years will be asked to use a lung flute to improve sputum quality for Xpert Ultra testing. Contacts will also receive theory of informed communication to influence their behavioural intention to link to care. In addition, they are enrolled into an eCase Manager, a WhatsApp-based mHealth technology that will be designed to improve linkage to care and referral pathways for TB and TPT initiation and completion.

What are the possible benefits and risks of participating?
TB contacts may potentially benefit from access to improved TB diagnostic technologies, including diagnosis of sub-clinical TB, as well as access to rapid testing for drug-resistant TB to improve case detection in all patients with suspected drug-resistant TB. They may also benefit from decreased diagnostic and treatment initiation time and close follow-up from the study staff in addition to the standard clinic care. The possible risks of participating in the study among contacts may be related to the blood draw. Drawing of blood is normally done as part of routine medical care but may present a slight risk of discomfort, and in some cases, may result in faintness, inflammation of the vein, pain, bruising or bleeding at the puncture site. There is also a slight possibility of infection. Trained study staff will apply the greatest possible caution to prevent any injury (such as bruises or local infection) during the blood draw.

Where is the study run from?
The multidisciplinary team of African and European researchers is made up of three African partners and three European partners. The Aurum Institute (Aurum) will co-ordinate the project overall and will implement the project in Ekurhuleni district in South Africa. NIMR-Mbeya Medical Research Centre (NIMR-MMRC) will implement the project in the Mbeya and Rungwe districts in Tanzania. Jhpiego will implement in the Thaba-Tseka and Butha-Buthe districts in Lesotho. The three research sites will be supported by University College London (UCL) from the United Kingdom, Karolinska Institutet from Sweden, and DZIF-Borstel Research Center (FZB) from Germany.

When is the study starting and how long is it expected to run for?
October 2020 to July 2025

Who is funding the study?
The European & Developing Countries Clinical Trials Partnership (Netherlands)

Who is the main contact?
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Cluster-randomized trial to increase tuberculosis yield through universal testing compared to standard TB screening among household contacts

Acronym
CUT-TB

Study objectives
Universal TB testing increases TB yield among household and community contacts when compared to standard TB screening.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 09/03/2021, Wits Human Research Ethics Committee (Suite 189, Private Bag x2600, Houghton, 2041, South Africa; +27 (0)11 274 9200; ; jpalmer@witshealth.co.za), ref: 210107

Study design
Multicenter interventional cluster-randomized pragmatic trial

Primary study design
Interventional

Study type(s)
Screening

Health condition(s) or problem(s) studied
Tuberculosis

Interventions
Randomization will be at the household level and will be simple randomization. At enrolment, TB index patients and their household and community contacts will be randomized into either ‘standard TB screening’ or ‘universal testing’ arms. The primary outcome of the trial is TB yield among household contacts. Standard TB screening will involve TB screening using WHO four-symptom screen questions; investigation of symptomatic patients with Xpert Ultra and referral of TB positive patients for TB treatment at their chosen or nearest health facility. Those that don’t have symptoms or test negative on Xpert Ultra will be referred for TB Preventive Therapy. Universal testing will involve universal testing of all household contacts (regardless of TB symptoms) with Xpert Ultra and referral of TB positive patients for TB treatment at their chosen or nearest health facility. Those that test negative on Ultra will be referred for TB Preventive Therapy. The intervention is a once-off intervention made up of a maximum of 2-3 visits for each patient. There is no follow-up period.

Intervention Type
Mixed

Primary outcome(s)
TB yield among household contacts (defined as the proportion of new microbiologically-confirmed contacts with TB) measured using the Xpert Ultra test at baseline

Key secondary outcome(s))
1. The prevalence of latent TB infection (LTBI) in TB contacts measured using QuantiFERON-TB Gold Plus test at baseline
2. The proportion of household contacts (adults or children) started on TB preventive therapy in accordance with national guidelines, measured using a questionnaire and medical records within 1 month of the household visit
3. The proportion of household contacts (adults or children) diagnosed with TB started on TB treatment in accordance with national guidelines, measured using a questionnaire and medical records within 1 month of the household visit
4. Cost-effectiveness in terms of incremental cost per additional case detected through a universal test and treat strategy using GeneXpert ultra vs the standard TB screening using symptom screen at baseline
5. TB transmission dynamics measured using Next-Generation Whole Genome Sequencing (NG-WGS) at baseline

Completion date
30/07/2025

Eligibility

Key inclusion criteria
1. Fulfilling definition for an index patient: diagnosed with new or recurrent TB disease
2. Diagnosed ≤2 weeks at enrolment
3. Microbiologically confirmed TB disease (drug-sensitive or drug-resistant)
4. Adult aged 18 years and above
5. Have at least one household contact
6. Willing and able to provide written informed consent
7. Willingness to be randomized
8. Patients living within the study catchment area and willing to inform the study team of any change of address during the treatment and follow-up period

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
5028

Key exclusion criteria
1. Not willing to give written informed consent
2. Not fluent in any language in which informed consent is provided, or in which researchers are able to communicate
3. Participating in other investigational product/device trials related to TB and/or lung diseases
4. Having another member of the household enrolled in this study

Date of first enrolment
01/05/2021

Date of final enrolment
28/02/2025

Locations

Countries of recruitment
Lesotho

South Africa

Tanzania

Study participating centre
The Aurum Institute
29 Queens Road
Parktown
Johannesburg
South Africa
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Study participating centre
Jhpiego
23 Motsoene Road, 2nd Floor Dolphin House
Industrial Area, 100
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Study participating centre
National Institute for Medical Research
NIMR-Mbeya Medical Research Centre
PO Box 2410
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Sponsor information

Organisation
Aurum Institute

ROR
https://ror.org/01tcy5w98

Funder(s)

Funder type
Research organisation

Funder Name
European and Developing Countries Clinical Trials Partnership

Alternative Name(s)
Le partenariat Europe-Pays en développement pour les essais cliniques, A Parceria entre a Europa e os Países em Desenvolvimento para a Realização de Ensaios Clínicos, The European & Developing Countries Clinical Trials Partnership, European and Developing Countries Clinical Trials, EDCTP

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
Netherlands

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication. Participant-level data or raw data will be anonymized and de-identified to ensure that all participants are not identified in any way

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		11/08/2025	12/08/2025	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes