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Truenat molecular testing for the effective diagnosis of tuberculosis

Submission date
22/12/2022

Recruitment status
No longer recruiting

Registration date
13/02/2023

Overall study status
Completed

Last Edited
10/01/2023

Condition category
Infections and Infestations

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Tuberculosis (TB) is a bacterial infection spread through inhaling tiny droplets from the coughs or sneezes of an infected person. In 2020, an estimated 8.4% of the world's 10 million TB cases occurred in Indonesia, making it the country with the third-highest number of cases globally. The Zero TB Yogyakarta Initiative commenced community active TB case finding in 2020 with a pilot in two sub-districts in the province. The Zero TB Initiative Yogyakarta is a collaboration between the Universitas Gadjah Mada, the Burnet Institute (Melbourne), the Yogyakarta TB program and local partners and stakeholders. Active TB case finding is community-based and utilises mobile chest X-ray units deployed in vans. Screening sites are chosen based on the identification of potential 'hotspots' through mapping of reported cases over the past 3 years.
Referral of sputum specimens centrally leads to delays in diagnosis and required extra visits from healthcare workers to follow up and contact patients with TB. The provision of TB molecular testing capacity within the mobile screening service could reduce diagnostic delays, reduce diagnostic loss to follow up and increase community acceptability. Molbio Truenat MTB Plus and MTB-RIF Dx (Truenat) are chip-based point-of-care rapid molecular assays for the detection of tuberculosis. The portability and characteristics of Truenat MTB Plus and MTB-RIF Dx have the potential to enable point-of-care testing for TB, which could support TB diagnosis within primary health care services and within active case finding. This has the potential to reduce diagnostic delays and pre-treatment loss to follow-up. However, the process for running the assay does rely on having trained, dedicated and skilled technicians.
The aim of this study is to assess the operational feasibility and acceptability of the use of Truenat MTB Plus and MTB-RIF Dx testing on the Molbio Truenat platform within a mobile TB active case finding service in Yogyakarta, Indonesia

Who can participate?
1. Laboratory staff and health care workers trained to perform Truenat Mtb Plus and MTB-RIF Dx
2. Healthcare workers and laboratory staff involved in the use of Truenat Mtb Plus and MTB-RIF Dx
3. Participants attending the TB active case-finding service who screen positive for potential TB by symptoms or chest X-ray

What does the study involve?
A nurse will discuss with the participant the potential that they have TB and that they require further testing for TB. They will have the process for sputum sample collection explained and spot sputum samples will be collected under observation following a standard approach for ensuring good quality sputum collection and infection control.
Depending on the diagnostic strategy assigned for the particular screening day (randomly determined by coin toss) the participant will receive either standard of care or decentralised Truenat testing:
For standard of care, participant samples will be sent to a centralised laboratory for GeneXpert testing. The participant will be informed that they will be notified of their results when they become available in 1-3 days. Those with GeneXpert MTB positive results will be informed by telephone to attend the nearest puskesmas for counselling and commencement of TB treatment. Those testing GeneXpert negative for MTB will have their case reviewed by the doctor at the health facility for their catchment to determine if they need further follow-up or not in accordance with the standard ACF protocols.
For decentralised Truenat, two spot sputum samples will be collected and the participant will be informed that their sample will be tested on the day, and will be asked if they prefer to wait for the result or be contacted when the result is available.
Where a patient has a positive result on Truenat MTB Plus, the Truenat MTB-RIF Dx assay will be performed to test for rifampicin resistance. Patients with a positive result on Truenat MTB Plus will be informed of the result and advised to attend the nearest puskesmas or hospital for counselling and commencement of TB treatment, or referral to another facility of their choice for treatment.
Those testing negative for MTB will have their case reviewed by a doctor at the catchment health facility to determine if they need further follow up in accordance with the standard ACF protocols; and taking into consideration the result of the GeneXpert MTB/RIF assay
Due to National Tuberculosis Program requirements, all patients tested with Truenat will also be tested with GeneXpert MTB/RIF using the second spot sputum sample. Treatment will be initiated based on positive Truenat or GeneXpert Mtb/RIF result, with a review by the TB active case-finding service doctor of cases where the result is discordant.
Commencement of TB treatment will be according to standard national TB protocols. Further clinical care and diagnostic investigations will be provided within governmental health care services. If a patient wishes to seek further care at a specific health facility or service of their choosing they will be provided with a referral.

What are the possible benefits and risks of participating?
Some possible specific benefits of participating in the study:
1. Faster diagnosis and treatment initiation
2. Reduced risk of transmission in the community by starting TB patients on treatment earlier.
3. Decreasing the number of people who are lost to follow-up during the diagnostic process
4. Reduced workload for screening staff needing to follow up on lab results and finding and informing patients after they have been screened
The risks of involvement in the study are minimal for participants.

Where is the study run from?
The study is run in Sleman District and Yogyakarta City of Yogyakarta Province (Indonesia)

When is the study starting and how long is it expected to run for?
September 2021 to June 2023

Who is funding the study?
Funding for this study has been provided by FIND. The study will be embedded within the

ongoing community mobile active case-finding program (Zero TB Initiative Yogyakarta) that is funded by the Australian Department of Foreign Affairs and Trade's (DFAT) Centre for Health Security through the PRIME-TB grant.

Who is the main contact?
Dr Rina Triasih, rina_triasih@yahoo.com
Dr Phillip du Cros, philipp.ducros@burnet.edu.au

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
440/22

Study information

Scientific Title

Localised mobile active case finding with Truenat molecular testing for the effective diagnosis of tuberculosis

Acronym
Locate TB

Study objectives
1. Are the MTB Plus and MTB-RIF assays using the Truenat platform feasible and acceptable to implement in decentralised mobile TB active case-finding services in Yogyakarta, Indonesia?
2. Does decentralised testing with Truenat in mobile TB active case finding services reduce the time to result for bacteriologically confirmed TB cases confirmed to centralised GeneXpert testing?
3. Does decentralised testing with Truenat in mobile TB active case-finding services reduce the time to treatment commencement compared to centralised GeneXpert testing?

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 29/08/2022, Alfred Hospital Ethics Committee (55 Commercial Rd, Melbourne, VIC, 3004, Australia; +61 (0)3 9076 8825; research@alfred.org.au), ref: 440/22.
2. Approved 13/10/2022, Universitas Gadjah Mada Ethics Committee (Gedung Radiopoetro Lt 2 Sayap Barat, Jl. Farmako, Sekip Utara, Yogyakarta 55128, Indonesia; +62 (0)811 2666 869; mhrec_fmugm@ugm.ac.id), ref: KE/FK/1297/EC/2022

Study design
Single-centre unblinded interventional study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Community

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

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

Interventions
Participants attending the TB active case-finding service who screen positive for potential TB by symptoms or chest X-ray will be invited to participate in the study. A study team member will

explain the participant information and consent form (PICF) in person and participants who consent to participate will sign and date the PICF. For participants who are illiterate, thumbprint, witness signature and date will be recorded on the PICF. Persons who do not consent to participate in the study will receive standard of care diagnosis (submit a single sputum specimen for central GeneXpert laboratory testing) and their results will not be included in the study. Potential participants have the time between the initial invitation to participate and the cessation of TB screening by the mobile active case finding service on that day to decide whether they wish to participate.

Data on study enrolment will be entered into a study-specific enrolment instrument in the ZTB YY active case finding REDCap database. The instrument will record the person's patient ID as well as their study ID and the details of their consent.

A nurse will discuss with the participant the potential that they have TB and that they require further testing for TB. They will have the process for sputum sample collection explained and spot sputum samples will be collected under observation following a standard approach for ensuring good quality sputum collection and infection control.

Depending on the diagnostic strategy assigned for the particular screening day (randomly determined by coin toss) the participant will receive either standard of care or decentralised Truenat testing:

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Commencement of TB treatment will be according to standard national TB protocols. Further clinical care and diagnostic investigations will be provided within governmental health care services. If a patient wishes to seek further care at a specific health facility or service of their choosing they will be provided with a referral.

Intervention Type
Other

Primary outcome measure
1. Operational performance will be assessed through laboratory staff and health care worker Truenat proficiency assessments after initial training, and by measurement of platform error rates during the study.
2. Views on the acceptability and operational challenges of Truenat will be assessed by a survey of laboratory staff and health care workers (HCW) within the program at 21 days
3. Individual in-depth qualitative interviews will be conducted with a purposive sample of screening participants to obtain their views on the acceptability and suitability of decentralised testing using Truenat at 21 days

Secondary outcome measures
1. Time to result for those tested with Truenat MTB Plus and MTB-RIF Dx, defined as the time from initial assessment to time of TB laboratory report completion at Zero TB mobile active case finding laboratory
2. For those with a positive result on Truenat MTB Plus or GeneXpert (standard of care) the median time from initial assessment to TB treatment initiation, defined as the initiation of the first dose of anti-TB treatment at a registered TB treatment facility

Overall study start date
01/09/2021

Completion date
30/06/2023

Eligibility

Key inclusion criteria
Eligibility criteria for randomised comparison:
1. People aged 12 years old or above presenting to mobile CXR-based screening in Sleman district and Yogyakarta City
2. Able and willing to consent. For adolescents aged 12-17, verbal consent as well as parental /guardian informed consent will be required

Eligibility criteria operational feasibility and acceptability assessments:
1. Post-Training Assessment (Objective 1a): All laboratory staff and health care workers trained in performance of Truenat assays who consent to participate
2. Feasibility and HCW acceptability (Objective 1c): All HCWs involved in the mobile screening service who consent to participate
3. Screening participant acceptability (Objective 1d): Adults 18 years of age or older who screened positive for presumptive TB in the active case finding program within the preceding 1

week and provide informed consent; and parents and legal guardians who have a child aged 12 to 17 years that screened positive for presumptive TB in the active case finding program within the preceding 1 week and provide informed consent.

Participant type(s)
Mixed

Age group
Mixed

Lower age limit
12 Years

Sex
Both

Target number of participants
Post-Training Assessment = 10 people; Feasibility and Health Care Workers' acceptability = 30 people; Screening participant acceptability = 30 people; 5.9.2 Objectives 2 and 3: Randomised comparison of decentralised Truenat MTB Plus and MTB-RIF Dx to standard of care = 3000 people

Key exclusion criteria
1. Unable to provide sputum
2. Currently receiving anti-TB therapy
3. Patients who are seriously ill and need to be admitted to hospital
4. Patients with potential COVID-19 referred for further assessment

Date of first enrolment
01/01/2023

Date of final enrolment
30/06/2023

Locations

Countries of recruitment
Indonesia

Study participating centre
Universitas Gadjah Mada – Pusat Kedokteran Tropis
Fakultas Kedokteran, Kesehatan Masyarakat dan Keperawatan UGM
Gedung Penelitian dan Pengembangan FK-KMK UGM, Sayap Utara Lantai 2
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Sponsor information

Organisation
FIND

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-
info@finddx.org

Sponsor type
Charity

Website
https://www.finddx.org/

Funder(s)

Funder type
Charity

Funder Name
FIND

Results and Publications

Publication and dissemination plan
Study results will be disseminated among the stakeholders, health care workers, and implementers in the study sites. Manuscript will be written and published in a scientific journal after the completion of data analysis.

Intention to publish date
01/01/2024

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are available from the corresponding author Dr Rina Triasih (rina_triasih@yahoo.com) on reasonable request.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	diagnostic_testing version 1.2	16/08/2022	03/01/2023	No	Yes
Participant information sheet	diagnostic_testing_for parents and guardian of a child version 1.1	08/10/2022	03/01/2023	No	Yes
Participant information sheet	phone_interview_consent_script_patient_acceptability version 1.1	03/08/2022	03/01/2023	No	Yes
Participant information sheet	phone_interview_consent_script_patient_acceptability_for parents or guardian of a child version 1.1	04/10/2022	03/01/2023	No	Yes
Participant information sheet	proficiency assessment version 1.2	16/08/2022	03/01/2023	No	Yes
Participant information sheet	user_feasability_acceptability_survey version 1.2	16/08/2022	03/01/2023	No	Yes
Protocol file	version 1.2	12/12/2022	03/01/2023	No	No