ISRCTN77241966 https://doi.org/10.1186/ISRCTN77241966

Evaluation of GeneXpert Ultra and digital chest radiography for diagnosing tuberculosis

Submission date
03/07/2019

Recruitment status
No longer recruiting

Registration date
02/09/2019

Overall study status
Completed

Last Edited
09/09/2022

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Tuberculosis (TB) is a major cause of morbidity and mortality worldwide and early diagnosis is key to reducing this high disease burden. The Xpert MTB/RIF assay (GeneXpert) is a rapid test for diagnosing TB which was endorsed by WHO in 2010. An improved version of the Xpert MTB/RIF, the Xpert MTB/RIF Ultra (Xpert Ultra), is now available. However, little evidence exists for the impact of Xpert Ultra on clinical outcomes among ambulatory patients in high HIV and TB burden settings. Digital radiography machines designed as portable systems with better image quality are now available. Their availability has led to renewed interest in their inclusion in the TB diagnostic pathway. The aim of this study is to find out whether the use of Xpert Ultra in HIV-positive patients attending antiretroviral (ART) clinics can increase diagnostic yield and treatment initiation, and potentially reduce the number of deaths.

Who can participate?
Patients aged 18 and over attending antiretroviral therapy (ART) clinics at Bangwe health centre and Queen Elizabeth Central Hospital (QECH) and presenting with symptoms of TB

What does the study involve?
Participants are randomly allocated to one of four groups. Participants are requested to submit two sputum samples and depending on their group, the samples are analysed with Xpert Ultra or available standard of care test (GeneXpert or microscopy). Participants are also requested to undergo chest radiography depending on their group. All participants are followed up after 28 and 56 days for TB treatment initiation and vital status.

What are the possible benefits and risks of participating?
The benefit of this study is that participants will find out whether they have TB or not and have the opportunity to start TB treatment. The study is also beneficial to healthcare providers because it will show how effective these new TB diagnostic tests are.

Where is the study run from?
1. Queen Elizabeth Central Hospital (Malawi)
2. Bangwe Health Centre (Malawi)

When is the study starting and how long is it expected to run for?
June 2018 to August 2021

Who is funding the study?
1. Helse Nord Tuberculosis Initiative
2. Foundation for Innovative New Diagnostics (FIND)

Who is the main contact?
1. Dr Marriot Nliwasa
mnliwasa@medcol.mw
2. Dr Madalo Mukoka
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Utility of the Xpert® MTB/RIF Ultra assay with the GeneXpert®Omni System and digital chest radiography for diagnosis of tuberculosis in high HIV prevalence settings: protocol for a randomised control trial

Acronym
FIND EXACT-TB

Study objectives
The use of Xpert Ultra in HIV-positive patients attending antiretroviral (ART) clinics can increase diagnostic yield and treatment initiation, and could potentially reduce mortality.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/07/2019, College of Medicine Research Ethics Committee (COMREC) (College of Medicine, Private Bag 360, Blantyre, Malawi, Email: comrec@medcol.mw), ref: P.05/17/2175

Study design
Pragmatic multi-site individually-randomized controlled trial with a 2 by 2 factorial design

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format

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

Interventions
A random allocation sequence will be generated in advance using computer-generated random numbers. This will be done by the study statistician. Randomisation will be 1:1 to the four arms of the trial and block randomised with a variable block size. Paper slips with a randomisation number will be printed and inserted and sealed in an opaque envelope. The envelopes will be kept by the study statistician and distributed consecutively to the research assistants on the enrolment of the participant. The envelope will only contain information of allocation to chest radiography. That is to say research assistants and clinicians will know if participants will have to be referred for a chest x-ray or not. As specified in each arm, chest radiography results will be offered to the responsible clinicians to help guide TB treatment. Randomisation to Xpert Ultra will only be known by the laboratory technicians (the research team and responsible clinicians will be masked to the sputum screening arm allocation).

Participants will be requested to submit two sputum samples and depending on study arm, the samples will be analysed with Xpert Ultra or available standard of care test (GeneXpert or microscopy). Participants will also be requested to undergo chest radiography depending on study arm. All participants will be followed up at 28 days and 56 days for TB treatment initiation and vital status.

Intervention Type
Other

Primary outcome measure
Proportion of patients initiating TB treatment within 28 days of enrolment compared between standard of care Xpert and Xpert Ultra arms

Secondary outcome measures
1. Proportion of patients diagnosed with TB initiating TB treatment within 28 days of enrolment between Standard Of Care and Xpert Ultra arms
2. Time from enrolment to TB treatment initiation between Standard Of Care and Xpert Ultra arms
3. All-cause mortality risk between Standard Of Care and Xpert Ultra arms
4. Proportion of patients diagnosed with bacteriologically-confirmed TB initiating TB treatment within 28 days of enrolment between chest radiography and no chest radiography arms

Overall study start date
01/06/2018

Completion date
01/08/2021

Eligibility

Key inclusion criteria
1. Aged ≥ 18 years
2. Having TB symptoms (cough of any duration, fever, night sweats or weight loss)
3. Able to submit sputum
4. Willing and able to provide informed consent

Participant type(s)

Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
1252

Total final enrolment
640

Key exclusion criteria
1, Presence of clinical danger signs (unable to walk unaided, confused or agitated, breathless when speaking or at rest)
2. Already taking TB treatment, or taken TB treatment within the last 60 days
3. Unable to submit sputum and refuses offer of sputum induction
4. Previously been enrolled in the trial

Date of first enrolment
02/09/2019

Date of final enrolment
31/01/2021

Locations

Countries of recruitment
Malawi

Study participating centre
Queen Elizabeth Central Hospital
PO Box 95
Blantyre
Malawi
PO Box 95

Study participating centre
Bangwe Health Centre
Private Bag 66

Blantyre
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Sponsor information

Organisation
London School of Hygiene and Tropical Medicine

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Sponsor type
University/education

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ROR
https://ror.org/00a0jsq62

Funder(s)

Funder type
Research organisation

Funder Name
Helse Nord Tuberculosis Initiative

Funder Name
Foundation for Innovative New Diagnostics (FIND)

Results and Publications

Publication and dissemination plan
The results of this trial will be disseminated to relevant local and international conferences. The main local conference is the annual Malawi College of Medicine research dissemination conference and the target international conference is the annual Union World Conference on Lung Health. The results of this trial will be submitted for publication in open access, medical journals. The researchers will give frequent updates to the consultants working in the medical department at the Queen Elizabeth Central Hospital.

Intention to publish date
01/05/2021

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Marriot Nliwasa (mnliwasa@medcol.mw) and Dr Madalo Mukoka-mmukoka@medcol.mw. Individual-level data will be available at the time of publishing and will be shared together with the publication. The researchers will make a GitHub repository which allows access to the datasets and allows replication of the analyses. Consent will be sought from the patients and all data will be anonymized. There are no ethical or legal restrictions.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		13/08/2022	09/09/2022	Yes	No