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Can periodically promoting tuberculosis and HIV testing reduce undiagnosed infectious tuberculosis and tuberculosis transmission in communities?

Submission date
03/12/2018

Recruitment status
Stopped

Registration date
07/05/2019

Overall study status
Stopped

Last Edited
07/12/2023

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Tuberculosis (TB) is the leading infectious cause of death, globally, with 1.6 million deaths estimated for 2017. The United Nations have endorsed an ambitious plan to find 40 million undiagnosed TB cases by 2022 as part of the WHO EndTB strategy. Active case finding in the community was a widely used strategy in the 20th Century. However, the broader benefits of active case-finding on underlying TB epidemiology remain unclear and limit the willingness to implement this strategy widely in urban setting such as Blantyre, Malawi, where about 1% of adults have undiagnosed TB and 18% of adults are living with HIV. Patients with TB symptoms have an increased risk of being HIV-positive as well as an increased risk of TB disease.

The broad aims are to investigate whether visiting communities once every 6 months over 13 months to promote testing for TB and HIV (periodic community-wide active case-finding), focused on investigation of chronic cough, leads to reduced undiagnosed infectious TB disease in adults, or any detectable reduction in childhood TB infection in communities.

The key research questions are:
1. Can promoting sputum microscopy for people with symptoms of TB in the community meet the urgent need for reducing undiagnosed infectious TB in urban communities affected by high rates of TB and HIV?
2. Does community-wide active case-finding increase demand for routine facility TB testing services?
3. Does community-wide active case-finding increase the rate at which residents are treated for confirmed TB at hospitals or primary care clinics?
4. Is the offer of HIV self-testing alongside the offer of TB testing acceptable to participants who have TB symptoms and who do not already know their HIV status?

Who can participate?
Participation in the intervention will be offered to all adults aged 18 years or older (estimated

~160 thousand adults in each of 2 study arms) who live within a geographically-defined intervention cluster and who report cough for 2 weeks or longer at any one of 3 outreach visits to the cluster by a team providing door-to-door TB and HIV diagnostic services.

The intervention will be evaluated once completed by surveys for undiagnosed infectious TB in 54 thousand adult cluster residents and for TB infection in 14.5 thousand children aged less than 3 years old who are resident within the study clusters.

What does the study involve?
Participants in the active case-finding intervention will be offered the opportunity to have 2 sputum specimens collected in the community for testing using TB microscopy, and to self-test for HIV if they do not already know their HIV status.

Adults participants in the impact evaluation surveys will be asked questions about TB symptoms and to have a chest X-ray. If they have prolonged cough or abnormal chest X-ray then they will be asked to provide sputum for TB testing.
Parents of guardians of child participants in the skin test surveys will have a small (0.1 ml) injection of TB antigen (tuberculin) in the arm. A large reaction size (a red bump, measured in millimeters) in 2 to 3 days provides evidence of TB infection.

Possible benefits and risks of participating?
Early diagnosis of TB and HIV provide health benefits to the participant themselves, and also reduces (through treatment) infectiousness to others.

With any screening test, there is potential for incorrect results. These risks will be minimized by confirming all positive results before treatment of HIV and TB, and by warning participants that a negative TB test does not fully exclude TB.

A single chest x-ray typically delivers an average effective dose comparable to 10 days of natural radiation, and with less than one in a million chance of causing cancer. The potential benefits of chest x-ray as a TB diagnostic are likely to outweigh this very small risk and are safe in pregnancy. Abdominal shielding will be used for women of child-bearing age.

About one in a thousand participants of the tuberculin skin test survey will have a large reaction, with possible blistering. Other risks are extremely rare, with tuberculin being a widely used product that is currently used in Malawi.

Where is the study run from?
Malawi-Liverpool-Wellcome Clinical Research Programme in Blantyre, Malawi.

When is the study starting and how long is it expected to run for?
Between March 2019 and March 2020

Who is funding the study?
The Wellcome Trust

Who is the main contact?
Professor Liz Corbett (liz.corbett@lshtm.ac.uk)

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
WT200901

Study information

Scientific Title
Sustainable Community-wide Active case finding for Lung hEalth

Acronym
SCALE

Study objectives
1. Can a symptom-then-microscopy screening approach to community-based active case-finding (ACF) meet the urgent need for reducing undiagnosed infectious TB in urban Africa?
2. Does community-wide ACF increase demand for TB testing services?
3. Does community-wide ACF increase the rate of diagnosis of microbiologically-confirmed TB at primary care clinics?
4. Is delivery of HIV self-testing alongside the offer of TB testing acceptable to symptomatic ACF participants of unknown HIV status?

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 19/03/2019, College of Medicine Research Ethics (University of Malawi), ref: 16228.
2. Approved 07/03/2019, the London School of Hygiene and Tropical Medicine Research Ethics Committee, ref: 16228.

Study design
Single-centre cluster-randomised interventional trial

Primary study design
Interventional

Study type(s)
Screening

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

Interventions
Active Case-Finding (ACF) intervention: All symptomatic household members identified on brief door-to-door enquiry for chronic cough will be left information leaflets, sputum collection pots, with sputum specimens collected the following day for microscopy. Results will be reported within 2 to 4 days. ACF participants will also be offered an oral HIV self-testing kit with instructions on use if HIV status is unknown and, if newly diagnosed HIV positive, will be offered confirmatory testing and a urine test for disseminated TB. Each intervention cluster will receive 3 rounds of ACF, spaced approximately 6 months apart.

Prevalence Surveys: TB screening will be based on digital chest x-ray read by an experienced radiographer assisted by computer assisted diagnostics. Patients reporting chronic cough or with abnormal chest x-ray will be asked to submit 2 sputum specimens for TB testing with Xpert (automated nucleic acid amplification test), microscopy and culture. Oral HIV testing will be offered to all participants in the pre-intervention survey, and to patients requiring sputum examination in the post intervention survey. Finger prick rapid HIV diagnostic tests will be used to confirm positive results, and in the pre-intervention survey will be offered to all participants.

Skin test surveys: children will have 0.1 mls of skin test reagent (tuberculin or c-TB, if available) placed by intradermal injection in the forearm, with return for reading at 48 to 72 hours.

Intervention Type
Other

Primary outcome(s)
The prevalence of undiagnosed infectious tuberculosis among adult cluster residents (per 1000 population surveyed) post-intervention will be measured using digital chest x-rays read by an experienced radiographer assisted by computer assisted diagnostics. Participants reporting chronic cough or with abnormal chest x-ray will be asked to submit 2 sputum specimens for TB testing with Xpert (automated nucleic acid amplification test), microscopy and culture.

Key secondary outcome(s))
1. Post-intervention prevalence of latent TB infection in children aged<36 months. Children who are cluster residents will have 0.1 mls of skin test reagent placed by intradermal injection in the forearm, with return for reading at 48 to 72 hours.
2. Rate of treatment (per 1000 adult cluster residents per year) during the ACF intervention period, defined by entry into the District Health Office TB Treatment Register.
3. Post-intervention prevalence (per 1000 adult cluster residents) of having tested for TB (by self-report) by chest radiograph or sputum testing at facility-level, during the (actual/nominal) ACF intervention period.

Completion date
31/03/2020

Reason abandoned (if study stopped)
Study was suspended in March 2020 due to the COVID-19 pandemic and due to logistical and funding restrictions did not re-start

Eligibility

Key inclusion criteria
For the ACF intervention:
1. Aged 18 years or older
2. Resident of an intervention cluster
3. Reported cough for 2 weeks or longer
4. Willing to provide sputum for TB testing following information provided in lieu of informed consent.

For the post-intervention TB disease prevalence surveys:
1. Aged 18 years or older
2. Resident of an intervention or non-intervention cluster
3. Intending to remain within Blantyre City for at least the next 8 weeks
4. Willing to have radiological screening for TB (with abdominal screening for women of child bearing age)

For the post-intervention Skin Test Survey:
1. Aged less than 3 years
2. Resident of an intervention or non-intervention cluster
3. Available for reading of results 48 to 72 hours after skin test placement

Participant type(s)
Mixed

Healthy volunteers allowed

No

Age group
Mixed

Lower age limit
18 years

Sex
All

Key exclusion criteria
ACF participants:
1. Not currently on TB treatment

Date of first enrolment
25/03/2019

Date of final enrolment
13/03/2020

Locations

Countries of recruitment
United Kingdom

Malawi

Study participating centre
Malawi-Liverpool-Wellcome Trust Clinical Research Programme (MLW)
Queen Elizabeth Central Hospital
Chipatala Avenue
Chichiri
Blantyre3,
Republic of Malawi
Blantyre
United Kingdom
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Sponsor information

Organisation
London School of Hygiene & Tropical Medicine

ROR

https://ror.org/00a0jsq62

Funder(s)

Funder type
Research organisation

Funder Name
Wellcome Trust

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		05/12/2023	07/12/2023	Yes	No