ISRCTN11432500 https://doi.org/10.1186/ISRCTN11432500

Promoting rapid diagnosis of tuberculosis

Submission date
18/05/2016

Recruitment status
No longer recruiting

Registration date
04/08/2016

Overall study status
Completed

Last Edited
12/10/2017

Condition category
Respiratory

[ ] Prospectively registered
[ ] 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 common, infectious condition caused by a bacterial infection. It is generally spread by breathing in tiny droplets released into the air by an infected person coughing or sneezing. TB usually affects the lungs (pulmonary TB), but it can also affect other areas of the body such as the bones, brain and kidneys. Controlling the spread of TB is founded on the basis of early diagnosis (confirmed under a microscope) and treatment and ensuring patients complete the full course of treatment needed to cure the disease. Often the first way of testing for TB is to take a sample of sputum (mixture of saliva and mucous that has been coughed up) and examining it under a microscope for signs of TB bacteria (smear microscopy). This is around 50-60% accurate however, and so further tests are needed to confirm diagnosis and start treatment. Experience of TB screening among hard to reach groups and other TB patients by the pan London Find&Treat TB outreach service has shown that the current service offered in the UK rarely achieves same day diagnosis in patients who have a positive TB smear. This could mean that many patients who need follow up can do not receive it, especially amongst hard to reach groups, and the risk of an outbreak increases. Patients with negative smears often have to wait several weeks for their results before starting treatment, and there is further delay in the availability of drug sensitivity tests (tests to show how effective a particular treatment will be on the TB bacteria) to inform clinical management. The use of PCR based molecular technologies allows a high proportion of smear negative cases (later confirmed by culture) to be diagnosed within 48 hours. In addition these technologies enable identification of mutations specific to rifampicin drug resistance (a key marker of multidrug resistance). The study aims to determine the effects of a rapid diagnostic service alongside the pan London mobile X-ray screening (MXU) for TB in best possible management of suspected TB cases in hard to reach groups.

Who can participate?
Patients aged 16 years and over who have a chest x-ray result suggesting they have pulmonary TB identified through MXU screening at hostels for homeless people and drug and alcohol services across London.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group provide a sputum sample for immediate analysis using by staff working on the MXU. An additional sample is also submitted for routine smear microscopy and culture (growing in a petri-dish) in the local hospital laboratory. Patients with a positive test result are referred immediately to a local

hospital for clinical assessment, isolation and to start TB treatment. Patients with a negative test result but who still show signs of TB are also referred. Patients with a negative test result without these symptoms are followed up in the community with two further sputum samples (including 1 early morning specimen for microscopy and culture) and clinic referral if these tests are positive. Patients with three negative microscopy and culture results are offered a repeat chest X-ray on the MXU three months from the initial X-ray and travel expenses are provided as necessary. Those in the second group are managed as per standard practice. This involves being accompanied directly to a hospital and a sputum sample will be collected for routine analysis in a hospital laboratory. Further investigations at the clinic will include collection of additional samples for microscopy and culture.

What are the possible benefits and risks of participating?
Participants may benefit from early detection of TB, meaning that treatment can be started earlier and the risk of spreading TB to others is reduced. There are no notable risks involved with participating.

Where is the study run from?
Royal Free Hospital (London)

When is the study starting and how long is it expected to run for?
March 2012 to December 2016

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Professor Andrew Hayward
a.hayward@ucl.ac.uk

Contact information

Type(s)
Public

Contact name
Prof Andrew Hayward

Contact details
Farr Institute of Health Informatics
Research Department of Infectious Disease Informatics
University College London
222 Euston Road
London
United Kingdom
NW1 2DA
+44 (0)20 7794 0500
a.hayward@ucl.ac.uk

Additional identifiers

Protocol serial number

14469

Study information

Scientific Title
TB Reach 4 - Randomised controlled trial of rapid diagnosis of tuberculosis on the mobile X-ray unit (MXU) using Cepheid PCR system

Acronym
TB Reach 4

Study objectives
The aim of this study is to determine the impact of a rapid diagnostic service alongside the pan London mobile X-ray screening (MXU) for TB on optimal management of suspected TB cases in hard to reach groups.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee East of England - Essex, Research Ethics, 20/03/2012, ref: 10/H0302/51 AM01

Study design
Randomised; Interventional; Design type: Not Specified, Not Specified

Primary study design
Interventional

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Specialty: Respiratory disorders, Primary sub-specialty: Respiratory disorders

Interventions
Those who have consented to participating in the study will be randomised using a text messaging randomisation service provided by Sealed Envelope (http://www.sealedenvelope.com). A stratified randomisation method balanced by the presence and absence of cavitation on the chest X-ray will be used. Participant's unique study number, initials, date of birth, as well the presence or absence of cavitation will be collected at randomisation and sent to Sealed Envelope via text to generate an instant text message with the group allocation.

Intervention arm: Participants will be asked to produce a sputum sample for immediate analysis using the Cepheid Xpert® MTB/RIF test by staff working on the MXU with result in 90 minutes. An additional sample will also be submitted for routine sputum microscopy and culture in the local hospital laboratory. Patients with a positive point of care Cepheid Xpert® MTB/RIF test result will be referred immediately to a local hospital for clinical assessment, isolation and to commence TB treatment. Patients with a negative test result, but with any of the following clinical symptoms haemoptysis, night sweats and weight loss will also be referred as above. Intervention arm participants who are negative according to Cepheid Xpert® MTB/RIF and who

do not have the symptoms described above will be followed up in the community with two further sputum samples (including 1 early morning specimen for microscopy and culture) within the next two days and clinic referral if these subsequent tests are positive. Patients with three negative microscopy and culture results will be offered a repeat chest X-ray on the MXU three months from the initial X-ray with onward referral if needed, and travel expenses will be provided as necessary.

Control arm: Participants will be managed according to standard practice i.e. patients will be accompanied directly to a hospital and a sputum sample will be collected for routine analysis in a hospital laboratory. Further investigations at the clinic will include collection of additional samples for microscopy and culture, as well as clinical assessment to determine if isolation and treatment is required.

Intervention Type
Other

Primary outcome(s)
Number of clinic visits needed for exclusion or confirmation of tuberculosis diagnosis is determined by checking TB clinic notes at 3 months post referral.

Key secondary outcome(s))
1. Time to diagnostic conclusion through smear microscopy and culture investigations is determined by checking TB clinic notes at 3 months post referral.
2. Time to onset of appropriate treatment is determined by checking TB clinic notes at 3 months post referral
3. Time to isolation for infectious cases is determined by checking hospital in-patient records at 3 months
4. Number of participants who develop active TB from the initial X-ray on the MXU is determined by checking surveillance record at 12 months post referral

Completion date
31/12/2016

Eligibility

Key inclusion criteria
Any hard to reach patient, 16 years of age or older with an abnormal chest X-ray suggestive of active pulmonary TB identified through MXU screening.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
Persons who refuse to participate.

Date of first enrolment
01/09/2013

Date of final enrolment
31/10/2016

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration