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Research to improve the detection and treatment of latent tuberculosis infection: diagnostics

Submission date
21/07/2021

Recruitment status
No longer recruiting

Registration date
28/07/2021

Overall study status
Completed

Last Edited
01/08/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
People who have been infected with the bacteria that cause tuberculosis (TB) but who do not have any symptoms and are not yet ill are said to have latent TB. Although latent TB does not make people unwell, the bacteria could become 'active' at any time, causing them to become ill with TB. Once ill they become symptomatic and contagious and can also pass TB on to other people. Latent TB can be treated to help prevent active TB from developing. The treatment for latent TB is usually shorter than treatment for active TB and uses fewer drugs. The RID-TB:Dx study will investigate whether a new latent TB skin test, called C-Tb, can be offered as an alternative to the standard interferon gamma release assay (IGRA) blood test to diagnose LTBI.

Who can participate?
Patients aged 16-65 years attending a RID-TB clinic who are eligible for latent TB infection testing according to UK guidance

What does the study involve?
Participants will be randomly allocated 2:1 to either the intervention group (C-Tb skin test) or the control group (IGRA blood test. Although the study is a randomised controlled trial (RCT), enrolled participants will have an IGRA test if they would prefer not to have the C-Tb test, or if they are not eligible to receive the C-Tb test.
The C-Tb skin test involves an injection under the skin of the forearm, which will become raised and red if the person has been exposed to TB bacteria. This reaction will be checked at the clinic after 2-3 days in order to make a diagnosis. A small pilot study will explore whether it is possible for the C-Tb skin test to be read remotely, using a supported participant-led self C-Tb read. If these self-reads are as accurate as the skin test being read in the clinic, then the option to have a remote appointment, rather than attending the clinic in person, will be offered for the remainder of the study.
We will also look at how people feel about LTBI, including how they feel about the C-Tb test and whether they decide to receive the test if it is offered to them, in an optional behavioural sub-study. Some people may also be invited to a short (15-20 minute) recorded interview, to talk in more depth about their views on the LTBI tests.

We are also analysing how much it costs people to come to the clinic for the appointments alongside other health service use data, using an optional health economics sub-study that will allow us to see if the C-Tb test offers value for money for the NHS.
Any participants who are found to have a positive result for latent TB, either from the C-Tb skin test or the IGRA blood test, will be offered treatment as per their clinic's local policy. Routine blood tests will be carried out as per local guidelines.

Active study involvement is up to Week 4 post-randomisation. Follow up information will then be collected 3 months after enrolment; this may be by telephone, a clinic visit or review of clinic notes and registries.

What are the possible benefits and risks of participating?
There are no direct benefits to participants but they will help improve diagnosis and care for other people who may be at risk from latent TB. Participants allocated to the C-Tb group will be asked to come to the clinic once more time than they would just for the standard of care IGRA blood test. There is a risk of mild, localised side effects from the new C-Tb test. These include swelling, rash, itching and discomfort. People may also experience bruising, pain and discomfort at the injection site for the IGRA blood test.

A £15 voucher will be given to all randomised participants to thank them for their time. Additional vouchers will be given to participants who take complete the C-Tb self-read pilot study (£15) and the behavioural interviews (£5).

Where is the study run from?
University College London (UK)

When is the study starting and how long is it expected to run for?
October 2018 to December 2024

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

Who is the main contact?
RID-TB Trial Manager
mrcctu.rid-tb@ucl.ac.uk

Contact information

Type(s)
Public

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2019-002592-34

Integrated Research Application System (IRAS)
269485

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
RID-TB:Dx, IRAS 269485, CPMS 43562

Study information

Scientific Title
A randomised controlled trial to evaluate a RD-1 based C-Tb skin test diagnostic strategy for detection of latent TB infection and initiation of TB preventive treatment in the UK

Acronym
RID-TB:Dx

Study objectives
Current study hypothesis:
It is acceptable and feasible to offer C-Tb skin test diagnostic strategy as an alternative to IGRA for the management of LTBI in the UK?

Previous study hypothesis:
Using the C-Tb skin test for the management of latent TB infection (LTBI) will be as good as (non-inferior to) the current standard-of-care based on Interferon Gamma Release Assay (IGRA) testing.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/01/2020, London Harrow Research Ethics Committee (Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, UK; +44 (0)207 104 8306; nrescommittee.london-harrow@nhs.net), ref: 19/LO/1624

Study design
A multi-centre parallel 2-arm open-label randomised controlled trial

Primary study design
Interventional

Study type(s)
Diagnostic, Prevention

Health condition(s) or problem(s) studied
Latent tuberculosis infection (LTBI)

Interventions
Current interventions as of 30/07/2024:

Participants will be randomised 2:1 into either the intervention arm (C-Tb skin test) or control arm (standard of care IGRA blood test)
Method of randomisation: minimisation with a random element, over a number of clinically important factors (including centre and age group).

The C-Tb skin test will be administered at baseline to participants in the intervention arm, who will be asked to return to the clinic 2-3 days later to have the result (induration) read.

Both arms will have the standard of care IGRA blood test to test for latent TB infection, results of which will be available 2-4 weeks after baseline. Routine blood tests will be done as per standard of care.

Participants testing positive for latent TB infection will be offered treatment as per standard of care (not part of the trial protocol).

Behavioural questionnaires relating to testing and beliefs in medicines will be completed by selected participants. Additional consent will also be sought for the completion of a health economics questionnaire and blood sample storage for future tests, including genetics. Outcome data relating to the primary and secondary outcomes will be collected at week 24.

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Previous interventions:

Participants will be randomised into either the control arm (standard of care IGRA blood test) or intervention arm (C-Tb skin test plus IGRA blood test).

Method of randomisation: minimisation with a random element, over a number of clinically important factors (including centre and age group).

The C-Tb skin test will be administered at baseline to participants in the intervention arm, who will be asked to return to the clinic 2-3 days later to have the result (induration) read.

Both arms will have the standard of care IGRA blood test to test for latent TB infection, results of which will be available 2-4 weeks after baseline. Routine blood tests will be done as per standard of care.

Participants testing positive for latent TB infection will be offered treatment as per standard of care (not part of the trial protocol).

Behavioural questionnaires relating to testing and beliefs in medicines will be completed by selected participants. Additional consent will also be sought for the completion of a health economics questionnaire and blood sample storage for future tests, including genetics. Outcome data relating to the primary and secondary outcomes will be collected at week 24.

Intervention Type
Other

Primary outcome(s)
Current primary outcome measure as of 30/07/2024:

Initiation of LTBI treatment within 12 weeks (following a positive result), as determined by confirmation of LTBI treatment medications issued by pharmacy.

Previous primary outcome measure:

Initiation of LTBI treatment (within a defined 24 ± 4 week follow-up period) based on a positive result of the randomised test. The treatment initiation is based on pharmacy records that confirm the issuance of medications for LTBI treatment within a defined 24±4 week follow-up period.

Key secondary outcome(s))
Current secondary outcome measures as of 30/07/2024:

1. Related to patient and process outcomes (impact) on the LTBI pathway process outcomes:
• Acceptance of C-Tb testing
• Failure to have C-Tb test read within 2-3 days among participants receiving C-Tb test
• Positive test result among participants receiving the randomised test
• Initiating treatment among participants receiving C-Tb test
• Initiating treatment among participants testing C-Tb positive
• Acceptance of LTBI treatment among participants, determined by verbal agreements.
• Losses to follow up (default rate) between diagnosis with LTBI and starting treatment
• Time from testing to starting preventative therapy

2. Safety
• Local reactions
• Systemic reactions
i. Serious adverse events at least possibly related to the diagnostic test received
ii.Pre-defined adverse events

Previous secondary outcome measures:

1. Safety:
1.1. Local and systemic reactions in participants randomised to the C-Tb test assessed by clinicians using a standard checklist at follow-up visits
2. Process outcomes related to impact on the LTBI pathway:
2.1. For participants randomised to C-Tb, failure to return for C Tb reading within 2-3 days as

recommended by the manufacturer will be documented on the CRF at the scheduled follow-up visit for reading C-Tb results
2.2. Acceptance of LTBI treatment among participants with a positive result of the randomised test, as determined by verbal agreement, will be recorded on the CRF at each follow-up visit
2.3. Initiation of LTBI treatment among those with a positive result of the randomised test will be assessed based on confirmation of LTBI treatment medications issued by the pharmacy within a defined 24±4 week follow-up period
2.4. Losses to follow-up between diagnosis with LTBI and starting LTBI treatment. Participants will be deemed lost to follow-up if they fail to attend any of the scheduled visits/appointments and are still not contactable at the end of the diagnostic follow-up period (Week 24 (±4 weeks)). The information will be documented on the CRF at each follow-up visit and also collected using patient records.
2.5. Time (days) from testing to starting preventative therapy measured based on the date of starting preventive treatment and testing recorded on the CRF
2.6. Completion of LTBI treatment within a 24 ± 4 week period from starting treatment is collected using patient records

Completion date
20/12/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 30/07/2024:

1. Aged 16 – 65 years
2. Eligible for LTBI testing with IGRA and treatment for LTBI according to UK guidance
3. Willing and able to provide written informed consent
4. Willing and able to comply with the trial

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Previous inclusion criteria:

1. Aged 16 – 65 years
2. Eligible for LTBI testing with IGRA and treatment for LTBI according to UK guidance
3. Willing and able to provide written informed consent
4. Willing and able to comply with the trial, including the randomised test(s) and adherence to follow up visits

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
16 years

Upper age limit
65 years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 30/07/2024:
1. Displaying any symptoms or signs of active TB disease

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Previous exclusion criteria:

1. Allergy to C-Tb product or any of its constituents
2. Displaying any symptoms or signs of active TB disease
2.1. Unexplained fever
2.2. Cough (more than 3 weeks)
2.3. Haemoptysis
2.4. Blood in sputum
2.5. Unexplained weight loss
2.6. Drenching night sweats
2.7. Lymph node swelling
3. Women who are breastfeeding, pregnant or plan to become pregnant during the study
4. Women of childbearing potential not using contraception

Date of first enrolment
10/08/2021

Date of final enrolment
20/12/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Whittington Hospital
Magdala Avenue
London
United Kingdom
N19 5NF

Study participating centre
Whipps Cross University Hospital
Whipps Cross Road
Leytonstone
London
United Kingdom
E11 1NR

Study participating centre
Mile End Hospital
Bancroft Road
Bethnal Green
London
United Kingdom
N1 4DG

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

Study participating centre
Newham Transitional Practice
30 Church Road
Manor Park
London
United Kingdom
E12 6AQ

Study participating centre
The Shrewsbury Centre (Newham Chest Clinic)
Shrewsbury Road
Forest Gate
London
United Kingdom
E7 8QP

Study participating centre

North Middlesex Hospital
Sterling Way
London
United Kingdom
N18 1QX

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
The trial data are held at the MRC Clinical Trials Unit at UCL which encourages optimal use of data by employing a controlled access approach to data sharing. Requests for data can be made

via application to the Programme Steering Committee. Further information on both the approach and the application process can be found here: http://www.ctu.mrc.ac.uk/our_research/datasharing/

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		30/12/2021	30/07/2024	Yes	No
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes