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Intensified household contact tracing, prevention and treatment support versus enhanced standard of care for index tuberculosis cases in South Africa

Submission date
12/01/2017

Recruitment status
No longer recruiting

Registration date
01/02/2017

Overall study status
Completed

Last Edited
04/06/2024

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Tuberculosis (TB) is a bacterial infection that mainly affects the lungs. It is now the leading cause of death from infectious disease worldwide, and in South Africa, HIV has led to very high TB rates, as the HIV virus weakens the body's ability to fight infections. People who live in the same house as individuals with TB have a high chance of also being infected with TB and HIV, but often don't get the care they need. This study sets out to test two strategies that could improve the rates of diagnosis of TB and HIV among people who have lived with a person recently diagnosed with TB.

Who can participate?
People of any age who have recently been diagnosed with TB in two districts of South Africa, and their household members

What does the study involve?
Participants are randomly allocated to one of two groups. Participants in the first group receive a letter with instructions about how to access TB and HIV testing and treatment, followed up by a phone call. Participants in the second group receive a home visit, where a nurse tests everyone in the house for TB and HIV, and supports them to access the treatment that they need. After 15 months all participants received a home visit to test everyone for TB and HIV.

What are the possible benefits and risks of participating?
Participants should be able to receive more rapid TB and HIV diagnosis and quicker access to treatment by participating in the study, and this could reduce their chances of developing disease, having severe disease, or dying. The risks of participating are felt to be low, but might include accidental sharing of TB or HIV status to household members.

Where is the study run from?
Chris Hani Baragwanath Academic Hospital (South Africa)

When is the study starting and how long is it expected to run for?
February 2016 to July 2020

Who is funding the study?
MRC UK/South Africa Newton Fund

Who is the main contact?
1. Ms Charity Leeuw
2. Dr Neil Martinson

Contact information

Type(s)
Public

Contact name
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Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
1.0

Study information

Scientific Title
Intensified household contact tracing, prevention and treatment support versus enhanced standard of care for index tuberculosis cases in South Africa: a cluster-randomised trial

Acronym
The HomeACF Study

Study objectives
A intensified TB/HIV household contact tracing, screening, treatment, prevention and support intervention will improve TB free survival among household contacts and will decrease the prevalence of new TB infection among children.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Human Research Ethics Committee (Medical), University of Witwatersrand, 29/08/2016, ref: 106414
2. Committee on Research Ethics, University of Liverpool, 28/11/2016, ref: 0788
3. Research Ethics Committee, London School of Hygiene and Tropical Medicine, 13/12/2016, ref: 11644

Study design
Open multi-site household cluster randomised trial, conducted in two districts of South Africa (Capricorn and Mangaung)

Primary study design
Interventional

Secondary study design
Cluster randomised trial

Study setting(s)
Home

Study type(s)
Other

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

Health condition(s) or problem(s) studied
Tuberculosis and human immunodeficiency virus infection

Interventions
Index TB cases (defined as any patient, living or recently deceased who is a permanent resident of one of the study districts and who has been diagnosed with TB [if older than 5 years:

bacteriologically-confirmed pulmonary TB only; if five years or younger: clinically diagnosed by a doctor, or bacteriologically-confirmed TB of any organ] at any health facility in the study districts in the six weeks prior to recruitment) will be recruited to the trial.

Household members of TB case participants (defined as all individuals who either slept overnight at least once, or shared at least two meals in the same household as the index case in the 14 days prior to the index case's diagnosis of TB.) will be allocated in a 1:1 ratio to receive either
1. Intensified household contact tracing and treatment support, or
2. Enhanced standard of care
The unit of randomization will be households of recruited index TB cases. Random allocation will use a computer-generated allocation sequence stratified by district and with a block size of 10. For each index case, the allocation will be accessed through a central study telephone line, staffed by a data manager who is otherwise independent of the study. Randomisation will occur after consent procedures and immediately after all eligibility criteria have been satisfied.

Intensified household contact tracing and treatment support group:
Household members allocated to the intensified household contact tracing and treatment support group will receive:
1. A home visit within 14 days by a research team comprising of an enrolled nurse and counsellors who will seek consent to participate from all household members, and administer a brief questionnaire
2. Offer confidential HIV testing and counselling to all household members in accordance with South African national guidelines, or anonymised HIV testing for study purposes
3. Collection of one spot sputum sample from all household members capable of producing a sputum sample (and irrespective of symptoms), which will be transported to laboratories and tested using the GeneXpert MTB/Rif platform and cultured using the liquid MGIT platform
4. Offer of tuberculin skin testing to all household members, with provision of the first month of isoniazid preventive therapy for household members who test HIV-positive and whose sputum tests are negative for TB, or who are HIV-negative and whose tuberculin skin test is positive (≥10 mm)
5. A second home visit after 1-week to provide results of TB and HIV testing in confidence, and support linkage to treatment and prevention services by referral to local primary care clinics
6. A follow-up visit at 3 months after recruitment to support access to treatment where required

Enhanced standard of care group:
Each recruited index case allocated to the enhanced standard of care group will be provided with a referral letter and information materials for every household member they identify, and will be requested to give the pre-printed referral letter and materials to each person in their household. The household member materials will contain information about tuberculosis and HIV, will recommend screening for TB and HIV, and will provide details of local health facilities where screening and further care (if required) may be accessed. Additionally, the referral letter will contain instructions for health providers, including recommendations that TB screening, HIV testing and further care and prevention services (including ART and TB preventive therapy as required) should be offered as per national guidelines because the individual was exposed to a likely infectious case of TB.

A week after recruitment, study research assistants will make a follow-up telephone call to the index case or the caregiver of the index paediatric case to assess if the referral letters were given to household members, and to confirm that any ill household members have accessed their local health facility. If they have been unable to do this, advice on locations of clinics, and other assistance will be provided by telephone.

Outcome assessment
An outcome household visit to all households will be conducted, irrespective of their study allocation at 15 months after the recruitment of the index case. At this visit, research assistants blinded to the original allocation of the household, will:
1. Trace all household participants, ascertain vital status and perform verbal autopsies for those who have died
2. Record episodes of TB and HIV diagnosis, treatment and other hospitalizations from verbal report and inspection of patient-held records
3. Investigate participants with symptoms of TB (any of: cough, fever, weight loss, night sweats) by collecting sputum for smear microscopy, sputum culture for M. tuberculosis and Xpert
4. Offer repeat HIV testing to participants negative or not previously tested at baseline
5. Conduct a prevalence survey for latent TB infection by testing all children under 14 years old with the tuberculin skin test.

Intervention Type
Mixed

Primary outcome measure
TB-free survival from randomisation to the final ascertainment visit (a total follow-up time of 15 months). This is a composite outcome: the follow-up time for those reaching the endpoint will be the time from randomisation or date of becoming a permanent household member to date of loss to follow-up or the date of the 15-month outcome ascertainment visit; the follow-up time for those not reaching the endpoint will be the time from randomisation or date of becoming a permanent household member to date of tuberculosis diagnosis or to date of death (or if both occur during the follow-up, the earliest of these). All analyses will be done using two different definitions of TB: (1) including all cases where TB was diagnosed or multi-drug TB treatment started, irrespective of the diagnostic method; (2) including only those with a hard copy of a laboratory confirmation of TB.

Secondary outcome measures
1. Prevalence of TB infection, measured by tuberculin skin test reactivity >10mm at month 15 among household children who are aged under 14 years of age at outcome assessment
2. Time between onset of symptoms and initiation of anti-tuberculosis treatment, among household members diagnosed with TB between baseline and month 15
3. Prevalence of previously undiagnosed or untreated HIV infection (reported as a percentage of those tested at 15 months)
4. Cumulative incidence of all-cause mortality at 15 months
5. Community HIV load, defined as the prevalence of detectable viraemia within each trial arm
6. Estimation of the cost-effectiveness of the intensified household contact tracing and treatment support intervention compared to the enhanced standard of care from a societal perspective

Overall study start date
01/02/2016

Completion date
01/07/2020

Eligibility

Key inclusion criteria
Index TB cases eligible to participate in the study will be:
1. Patient (living or recently deceased), diagnosed with TB within six weeks before recruitment (recently deceased is defined as within the 6 weeks before recruitment)
2. Permanent resident in study District and living with at least one other household member for at least 3 months in the last 6 months before recruitment
3. No plan of relocation to another municipality or health district during the 15 months follow-up period
4. If older than 7 years of age: laboratory confirmation of pulmonary TB (either a positive sputum result for acid fast bacilli, or a positive sputum Xpert MTB/Rif test result; or a positive sputum culture for M. tuberculosis)
5. If 7 years old or younger: a child with signs and symptoms suggestive of TB recorded in clinic or hospital record, and a recorded diagnosis of TB in a clinic or hospital record, and the prescription of TB treatment by a doctor

Participant type(s)
Mixed

Age group
All

Sex
Both

Target number of participants
2400 index cases

Key exclusion criteria
1. Unwilling to provide informed consent or assent
2. Unable to obtain informed consent from the parents/legal guardian for those younger than 18 years
3. Unable to obtain informed consent from close next of kin of adult patients who are too ill to provide their own consent or have died
4. Patient with TB who appears to have developed or contracted TB while institutionalized or imprisoned
5. Imprisoned or institutionalized at the time of diagnosis

Date of first enrolment
01/12/2016

Date of final enrolment
01/03/2019

Locations

Countries of recruitment
South Africa

Study participating centre

Chris Hani Baragwanath Academic Hospital
Perinatal HIV Research Unit
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Sponsor information

Organisation
Chris Hani Baragwanath Hospital

Sponsor details
Perinatal HIV Research Unit
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Sponsor type
Research organisation

Website
http://www.phru.co.za

ROR
https://ror.org/02g48bh60

Funder(s)

Funder type
Research council

Funder Name
MRC UK/South Africa Newton Fund

Results and Publications

Publication and dissemination plan
The trialists plan to publish the study results in a high impact peer-reviewed journal within 1 year of trial completion. The trialists also plan to report the study results at international conferences focused on TB and HIV.

Intention to publish date

01/12/2020

Individual participant data (IPD) sharing plan

The current 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?
Protocol article	protocol	12/10/2019	06/01/2021	Yes	No
Results article		24/12/2021	04/08/2022	Yes	No
Other publications	Baseline data analysis of latent TB infection among household contacts of index cases	17/03/2020	04/06/2024	Yes	No