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A trial of an electronic pill box with reminders for patients taking treatment for tuberculosis

Submission date
12/04/2016

Recruitment status
No longer recruiting

Registration date
19/05/2016

Overall study status
Completed

Last Edited
25/06/2024

Condition category
Infections and Infestations

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

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. Treatment for TB usually involves taking a combination of antibiotic drugs, usually including rifampicin. After taking medication for a few weeks, many patients begin to feel better and so do not complete their medication course (usually around 6 months). This poor medication adherence can lead to negative consequences, such as the TB infection becoming resistant to the antibiotics. China has the second highest number of TB cases globally and so it is vital to ensure that TB patients adhere to their treatment properly. In a previous study, text message reminders, a medication monitor, or both were compared to standard care alone, to find out if they could improve treatment adherence. The aim of this study is to find out how well a second version of the medication monitor performs and whether improving adherence is related to better recovery of patients.

Who can participate?
Adults who have tested positive for TB which is sensitive to treatment using rifampicin.

What does the study involve?
Twelve communities are randomly allocated to one of two groups. Participants living in communities in the first group are provided with a medication monitoring box, with reminding functions. This box is used to remind patients to take the medication each day and to attend their monthly follow-up visits. The monitor also records the date and time that it is opened, which can be used to record whether patients have been taking their medication properly. Participants in the second group continue to receive standard care only. Participants in both groups are followed up after 6, 12 and 18 months in order to evaluate medication adherence and recovery.

What are the possible benefits and risks of participating?
Patients will benefit from no delay in accessing treatments as their caring physician will receive information early on how well the patient is taking their medication and if the patient has problems then different methods will be started. Additionally, by testing the patient's sputum

for TB at 12 and 18 months and taking a chest x-ray, it is possible to find out if TB has come back and so patients can receive the appropriate treatment faster. There are no notable risks involved with taking part in this study.

Where is the study run from?
The study is run by the China Centre for Disease Control and Prevention and takes place across 24 counties/districts in the provinces of Zhejiang, Jiangxi and Jilin (China)

When is the study starting and how long is it expected to run for?
July 2015 to November 2020

Who is funding the study?
Bill and Melinda Gates Foundation (USA)

Who is the main contact?
Dr Xiaoqui Liu

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
1137180

Study information

Scientific Title
Cluster randomized trial of a medication monitor in the treatment management of patients with pulmonary tuberculosis

Study objectives
A treatment strategy that includes use of a medication monitor for reminding daily drug dosing and monitoring adherence patterns, and targeted intensive management of patients with poor adherence patterns, can reduce a composite poor outcome among adults with drug sensitive pulmonary TB.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Institutional Review Board of China CDC. 09/03/2016, ref: 201603
2. London School of Hygiene and Tropical Medicine Ethics Committee, 04/04/2016, ref: 10665

Study design
Cluster randomized non-blinded controlled trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
This is a cluster randomised non blinded trial. Clusters are defined as a county or district. This is a two armed trial, one intervention arm and one control arm:

Intervention arm: Patients are provided with a medication monitor box with reminding functions. This tool is used to remind patients both to take their tuberculosis medication and to attend their monthly follow-up appointments. It also records drug intake. Doctors collect the drug intake record from medication monitor monthly to assess that how many doses are missed in a month. Based on the missed doses, additional interventions are recommended to be implemented by the patient's doctor such as additional visits from the township/village doctor.

Control arm: Patients are managed based on the current standard of care.

Patients will be followed up for 18 months after the start of tuberculosis treatment.

Intervention Type
Other

Primary outcome(s)

Composite poor outcome* is measured using patient records, laboratory results (culture and smear), chest X-ray results and patient self-report over the 18 month period following enrollment to the study.

*The composite poor outcome is defined as any of: death at any time during the approximately six months of TB treatment (abstracted from patient records); loss to follow-up during the approximately six months of TB treatment i.e. treatment was interrupted for two consecutive months or more (abstracted from patient records); treatment failure i.e sputum smear or culture is positive at month 5 or later during the approximately six months of TB treatment (laboratory results abstracted from patient records); microbiological confirmation of TB, or positive chest X-ray findings in absence of microbiological results, at 12 or 18 months after enrollment to the study (laboratory results, based on smear and culture, and chest X-ray findings); or restarting TB treatment between the end of treatment and 18 months after enrollment to the study (patient records and patient self-report).

Key secondary outcome(s))

Clinical outcomes:
1. Poor outcome at the end of treatment (death, treatment failure or loss to follow-up) is measured using patient records and laboratory results (culture and smear) at the end of approximately six months of TB treatment (definitions of death, treatment failure or loss to follow-up are the same as for the primary outcome)
2. Composite poor outcome is measured using patient records, laboratory results (culture and smear), chest X-ray results and patient self-report over the 12 month period following enrollment to the study. Definition the same as for the primary outcome excluding the microbiological confirmation at 18 months and only assessing for restarting of TB treatment between the end of treatment and 12 months after enrollment to the study.
3. Loss to follow-up during the approximately six months of TB treatment i.e. treatment was interrupted for two consecutive months or more (abstracted from patient records), as per standard TB outcome case definitions

Adherence outcomes:
1. The percentage of months in which the patient missed at least 20% of doses, measured using data from medication monitor box at each of the approximately monthly follow-up visits during the approximately six months of treatment
2. The percentage of doses missed, measured using data from the medication monitor box monthly at each of the approximately monthly follow-up visits during the approximately six months of treatment

Cost-effectiveness outcomes:
1. Mean cost per patient treatment month is measured using financial records, event data from trial CRFs, staff semi-structured interviews and observations, and patient surveys at the end of approximately six months of TB treatment
2. Mean and incremental costs per patient completing treatment is measured using financial records, event data from trial CRFs, staff semi-structured interviews and observations, and patient surveys at the end of approximately six months of TB treatment
3. Mean and incremental costs per death and DALY averted is measured using primary outcomes above, financial records, data from trial CRFs, staff semi-structured interviews and observations, and patient surveys at the end of approximately six months of TB treatment
4. Mean and incremental number of cases experiencing catastrophic costs is measured using data from trial CRFs, and patient surveys at the end of approximately six months of TB treatment

Completion date

17/11/2020

Eligibility

Key inclusion criteria
1. New pulmonary TB case
2. Gene Xpert-positive and rifampicin-sensitive
3. Patient/family member able to use medication monitor after training
4. Likely to be in the study area for next 18 months; or able to attend the 12 and 18 month follow-up visits after the start of treatment
5. Patient agrees to fixed-dose combination (FDC)
6. Patient is receiving treatment from TB designated hospital or TB dispensary at the county (district) level and treatment management in the community health service centers
7. Receiving daily chemotherapy regimen

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Total final enrolment
2686

Key exclusion criteria
1. Aged <18 years
2. Communication impairment
3. Gene Xpert negative or Gene Xpert positive and rifampicin resistant
4. Travel planned during the intensive phase
5. Tuberculous pleuritis
6. Known to be HIV-positive
7. Custody patients (prison and medicine rehabilitation center)
8. Patients who have been hospitalised continuously for the first two months of treatment

Post-enrolment exclusions:
1. Participants whose Gene Xpert result was not known at enrolment and found to either be Gene Xpert-negative or Gene Xpert-positive and rifampicin resistant
2. Participants who stopped taking the Fixed Dose Combination tablets within the first 1 month due to an adverse reaction
3. Participants who permanently stopped the treatment management model within the first 1 month due to, for example, travel, hospitalisation, etc.
4. Participant subsequent found to be HIV-positive

Participants satisfying the exclusion criteria listed above will be withdrawn from the study and not contribute to study outcomes.

Date of first enrolment
01/11/2016

Date of final enrolment
30/06/2019

Locations

Countries of recruitment
China

Study participating centre
China Center for Disease Control and Prevention
Beijing
China
102206

Sponsor information

Organisation
China Center for Disease Control and Prevention

ROR
https://ror.org/04wktzw65

Funder(s)

Funder type
Charity

Funder Name
Bill and Melinda Gates Foundation

Alternative Name(s)
Bill & Melinda Gates Foundation, Gates Foundation, Gates Learning Foundation, William H. Gates Foundation, BMGF, B&MGF, GF

Funding Body Type
Government organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/05/2023	17/04/2023	Yes	No
Protocol article		25/07/2018	25/06/2024	Yes	No
Protocol file	version 3.1	24/06/2020	20/12/2022	No	No
Statistical Analysis Plan	version 8	14/10/2021	20/12/2022	No	No