ISRCTN17706019 https://doi.org/10.1186/ISRCTN17706019

Four-country evaluation of digital adherence technologies linked to a web-based platform to support adherence to TB treatment

Submission date
05/11/2020

Recruitment status
No longer recruiting

Registration date
18/11/2020

Overall study status
Completed

Last Edited
18/03/2025

Condition category
Infections and Infestations

[X] 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. In 2017, an estimated 10 million people fell ill with TB. Not adhering to treatment leads to unfavourable outcomes, relapse, drug resistance, disease transmission and increased health system costs. Innovations are therefore needed to improve TB treatment adherence. Digital adherence technologies (DAT) may be a major step forward. The aim of this study is to measure the impact of DATs for daily monitoring of adherence for adult TB patients in the Philippines, Tanzania, South Africa and Ukraine.

Who can participate?
All adults (according to country definition) receiving treatment for TB in participating health facilities.

What does the study involve?
Facilities in each country will be randomly allocated to employ either a DAT intervention or the standard of care. At intervention facilities, health care providers will enrol patients receiving treatment for drug-sensitive TB who are willing to use the DATs. Patients who decline will be offered the standard of care. Over the course of the participant’s treatment at these facilities, TB healthcare providers will monitor a patient's adherence pattern generated from the DAT using a web-based platform. This will enable daily monitoring and give healthcare providers the ability to provide a tailored response to those patients requiring more treatment support, including the use of messaging and reminders supported by the platform and possibly home visits. The study will evaluate the treatment outcome of patients, comparing the intervention facilities to standard of care facilities. In addition, several sub-studies will assess how the intervention may work in patients receiving treatment for both drug-sensitive and drug-resistant-TB.

What are the possible benefits and risks of participating?
By participating patients who need it may receive more support to complete their treatment for TB as intended while allowing patients demonstrating good adherence, greater autonomy and

freedom to self-manage their own care. This may include a decrease in the burden of visits to the health facility compared to those receiving the standard of care. This may benefit both those on TB treatment as well as their healthcare providers. Possible risks to participants include inadvertent disclosure of TB status, and possibly inferred HIV status in some settings by use or possession of tools (smart pill boxes or medication sleeves) associated with TB.

Where is the study run from?
KNCV Tuberculosis Foundation (Netherlands) with support from the London School of Hygiene and Tropical Medicine (UK)

When is the study starting and how long is it expected to run for?
November 2020 to December 2022

Who is funding the study?
Unitaid (Switzerland)

Who is the main contact?
Degu Jerene Dare, MD, PhD, MBA
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Study website
https://www.kncvtbc.org/en/ascent/

Contact information

Type(s)
Public, Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
2020-0001

Study information

Scientific Title
Adherence Support Coalition to End TB (ASCENT): four-country evaluation of digital adherence technologies for TB treatment

Acronym
ASCENT

Study objectives
It is hypothesized that implementing digital adherence technologies (DATs) with daily monitoring using a web-based platform and a differentiated response to patient adherence among adult patients receiving drug-sensitive TB therapy will decrease poor end of treatment outcomes relative to the standard of care.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. South Africa: Approved 23/04/2020, University of Witwatersand (Johannesburg Secretariate, Suite 189 Private bag x2600, Houghton 20141, South Africa +27 (0)11 274 9200; email: not available), ref 2001102
2. Ukraine: Approved 04/09/2020, Public Health Center MoH of Ukraine (41 Yaroslavska Street, Kyiv, 04071, Ukraine; tel: not available; irb@phc.org.ua), ref IRB2019-33
3. Tanzania: Approved 10/06/2020, The United Republic of Tanzania (3 Barack Obama Drive, PO Box 9653, 11101 Dar es Salaam, Tanzania; +255 (0)22 2121400; nimrethics@gmail.com), ref NIMR /HQ/R.8a/Vol. IX/3431
4. Philippines: Approved 03/07/2020, Republic of the Philippines Department of Health Single Joint Research Ethics Board (contact details not available), ref: SJREB-2019-57

Study design
Multicountry multicenter interventional open health-facility-based cluster randomized trial

Primary study design
Interventional

Secondary study design
Cluster randomised trial

Study setting(s)
Other

Study type(s)
Treatment

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

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

Interventions
Randomization of the clusters, health facilities or rayons (in Ukraine), to the intervention arm or the standard of care arm in a ratio of 1:1, will be conducted using stratification and restriction in order to reduce the intra-cluster correlation (former) and help ensure a balance between study arms. One row of a sample frame of 10,000 randomly selected possible allocations of facilities /rayons to the treatment or control arms after restriction will be randomly selected by an NTP official. In facilities randomized to the intervention, TB medication adherence monitoring will be done using digital adherence technologies (DATs) linked to a web-based adherence monitoring platform. Control facilities will use adherence monitoring employing the standard of care.

In facilities randomized to the intervention, TB medication adherence monitoring will be done using digital adherence technologies (DATs) - either 99DOTS medication sleeves or Evrimed smart pill boxes - linked to a web-based adherence monitoring platform. Control facilities will use adherence monitoring employing the standard of care. In three countries intervention facilities will themselves be randomized to receive either the 99DOTS or smart pill box. In Ukraine, only the smart pill boxes will be employed.

Facilities in each country will be randomized to employ either a DAT intervention or the standard of care in a ratio of one to one. At intervention facilities, health care providers will enroll patients receiving treatment for drug-sensitive TB who are willing to consent to use the DATs. Patients who decline will be offered the standard of care. Over the course of the participant’s treatment at these facilities, TB health care providers will use a single user interface on tablets to view a patient's adherence pattern generated from the DAT via a web-based platform. This will enable daily monitoring and give healthcare providers the ability to provide a step-wise differentiated response to those patients requiring more treatment support, including the use of messaging and reminders supported by the platform and possibly home visits. The particular differentiated care algorithm in each country will be worked out during the study preparatory phase.

The intervention will be employed over the course of their participant’s treatment at these facilities (approximately 6 months). The follow-up is limited to the duration of their treatment. The study will evaluate the treatment outcome of patients, comparing that in the intervention facilities relative to the standard of care facilities in an intent-to-treat analysis. In addition, several sub-studies will include process evaluation components in order to provide an understanding of how the intervention may work in patients receiving treatment for both drug-sensitive and drug-resistant-TB.

Intervention Type
Device

Pharmaceutical study type(s)
Not Applicable

Phase

Not Applicable

Drug/device/biological/vaccine name(s)
99DOTS medication sleeves, Evrimed smart pill boxes

Primary outcome measure
The proportion of adult DS-TB patients with poor end of treatment outcome, defined as having documented treatment failure, lost to follow-up or death as reported in the facility/rayon TB register upon completion of treatment (approximately 6 months)

Secondary outcome measures
1. The proportion of adult DS-TB patients who are lost to follow-up during treatment as reported in the facility/rayon TB register 6 months after the initiation of therapy
2. Time to treatment completion among DS-TB patients calculated from start and completion date as reported in the facility/rayon TB register upon completion of therapy
3. The proportion of adult DS-TB patients with poor treatment outcomes, as reported in the facility/rayon TB register upon completion of therapy

Intervention arm only:
4. Patterns of longitudinal technology engagement in the intensive and continuation phase, to be characterized, at a minimum, as the proportion of days upon completion of a patients treatment phase (intensive and continuation) with a dose being reported (adherence) to the platform
5. The proportion of patient events upon completion of treatment who had a differentiated response (either reminder SMS, home visit or facility visits) due to non-adherence as reported on the platform, among all patients and among non-adherent patients
6. The proportion of patients who received phone calls, home visits, and motivational counselling due to a non-adherence event as reported on the platform over the course of a patients treatment

Impact modelling:
7. The change in the number of adult DS-TB patients with poor treatment outcome at the time of treatment completion compared to the current standard of care if the intervention were to be scaled up nationally, projected using simple cohort model using study data
8. The cost-effectiveness of DAT compared to standard of care from health system and societal perspectives, relative to country-specific cost-effectiveness thresholds

DR-TB patients:
9. Patterns of longitudinal technology engagement in the intensive and continuation phase to be characterized, at the minimum, as the proportion of days through the end of treatment with a dose being reported (adherence) to the platform
10. The proportion of adult DR-TB patients with poor treatment outcomes as reported in the facility/rayon TB register at the interim (6 months) or completion of DR-TB treatment

Overall study start date
04/11/2020

Completion date
31/12/2022

Eligibility

Key inclusion criteria
Adult (based on country) pulmonary DS-TB patients initiated on TB treatment

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Tanzania: 72 facility and 8,136 patients; South Africa: 58 facilities and 14,674 patients; Philippines: 62 facilities and 21,700 patients; Ukraine: 11 facilities and 1936 patients

Total final enrolment
25606

Key exclusion criteria
Does not meet inclusion criteria

Date of first enrolment
01/01/2021

Date of final enrolment
30/06/2022

Locations

Countries of recruitment
Philippines

South Africa

Tanzania

Ukraine

Study participating centre
Public Health Center of the Ministry of Health of Ukraine
41, Yaroslavska St
Kyiv
Ukraine
04071

Study participating centre
Oblast Clinical TB Dispensary
10, Kyrylkina St., Kramatorsk
Donetska Oblast
Ukraine
84333

Study participating centre
Mykolaiv Regional Physiology and Pulmonology Medical Center of Mykolaivska Oblast Council
4, Veselynivska St., Nadbuzke, Mykolaivskyi rayon
Mykolaivska oblast
Ukraine
57130

Study participating centre
Lviv Regional Physiology and Pulmonology Clinical Treatment and Prevention Center of Lvivska Oblast Council
477, Zelena St.,
Lviv, Lvivska oblast
Ukraine
79000

Study participating centre
Odeska Oblast Center of Socially Significant Diseases of Odeska Oblast Council
9/1 Leontovycha St.
Odesa, Odeska oblast
Ukraine
65014

Study participating centre
Oblast Clinical Physiology and Pulmonology Treatment and Prevention Center of Zakarpatska Oblast Council
4, Nakhimova St.
Uzhhorod, Zakarpatska oblast
Ukraine
88000

Study participating centre
The Provincial Health Office (PHO) - Bulacan
Provincial Capitol Building
Malolas City, Bulacan

Philippines
3000

Study participating centre
The Provincial Health Office (PHO) - Pampanga
Pampanga Provincial Capitol
San Fernando, Pampanga
Philippines
2000

Study participating centre
Ministry of Health, Community Development, Gender, Elderly and Children
PO BOX 119
Mwanza
Tanzania
-

Study participating centre
Ministry of Health, Community Development, Gender, Elderly and Children
PO BOX 315
Geita
Tanzania
-

Study participating centre
Ministry of Health, Community Development, Gender, Elderly and Children
PO BOX 3092
Arusha
Tanzania
-

Study participating centre
Ministry of Health, Community Envelopment, Gender, Elderly and Children - Manyara
PO BOX 577
Manyara
Tanzania
-

Study participating centre

Gauteng Department of Health
45 Commissioner Street
Johannesburg
South Africa
2001

Study participating centre
Cape Town Department of Health
20th Floor, 4 Dorp Street
Cape Town
South Africa
8000

Sponsor information

Organisation
KNCV TB Foundation

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Sponsor type
Research organisation

Website
https://www.kncvtbc.org/

Funder(s)

Funder type
Research organisation

Funder Name
Unitaid

Results and Publications

Publication and dissemination plan

The protocol will be made available on ASCENT website (https://www.digitaladherence.org/) from 15/11/2020 onwards.

The research findings will be presented first to national stakeholders, and disseminated to the Community Advisory Board, stakeholders and participants in each country by means of local meetings, and presented at national and international conferences. The results will be written as country-specific articles for submission to suitable scientific journals.

Intention to publish date

01/01/2023

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a publicly available repository. The researchers will provide a participant level (de-identified and anonymized) dataset on OpenTrials (https://explorer.opentrials.net/) sufficient to reproduce analysis upon publication of the principal findings related to the primary objective. Consent from participants is available for the adherence data only. Outcome data will be available for those patients who did not opt-out.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		14/03/2023	15/03/2023	Yes	No
Other publications	A cross-sectional survey among adults with drug-sensitive tuberculosis (DS-TB), participating in pragmatic cluster-randomized trials, including this study	20/02/2024	11/03/2024	Yes	No
Results article	Adherence	11/03/2025	18/03/2025	Yes	No