ISRCTN95243114 https://doi.org/10.1186/ISRCTN95243114

Intervening with a Manualised Package to achieve treatment adherence in people with Tuberculosis

Submission date
31/01/2018

Recruitment status
No longer recruiting

Registration date
14/02/2018

Overall study status
Completed

Last Edited
14/11/2022

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Compared to the rest of the UK and Western Europe, England has a big problem with the infectious disease tuberculosis (TB). The large amount of TB in the country has led Public Health England and NHS England to develop a national TB control plan. Treatment for TB lasts a long time (at least six months and even more in people with drug resistant TB). Finding ways to make sure that people are able to take all the doses of their medication is one of the plan's priorities. If people miss doses (described as being 'non-adherent'), their TB can develop resistance to the usual drugs, risking both their health and that of the population. Poor adherence to treatment can occur for a number of reasons. These include someone not knowing much about their disease condition and why they need to take their treatment, side effects from the drugs, or people choosing to stop their treatment as soon as they feel better, rather than taking the entire course. Wider psychological, social, cultural and economic issues, including stigma due to having TB, lack of support from family members or friends, homelessness, drug and alcohol misuse and barriers to good access to NHS services also play a part. At present we don't have good ways of knowing if someone will struggle with their medication. In this study, we will use high quality social and clinical science research methods to find out why taking treatment may be difficult for some people, and how health services can work with them to improve this, or even avoid it happening. The aim of this study is to figure out an approach to enhance identification of at-risk individuals by determining barriers, providing support and increasing the understanding of the reasons why patients don't adhere to medication.

Who can participate?
Adults aged 18 and older who have been starting on treatment for TB.

What does the study involve?
Participants are seen when they start treatment and at 2, 4, 8, 12, 16, 20 and 24 weeks thereafter (the earliest date that treatment can finish). If they need more than 6 months of treatment, they are seen as clinically indicated. At each visit, apart from their usual clinical care, they are assessed for how well they are taking their treatment. If they are being treated at a site that has been randomised to offer the manualised intervention, this is used at each assessment

to identify any difficulties in taking treatment and any measures that could be used to support treatment. The manualised intervention uses narrative aids that helps both the patient and clinical team to understand any problems with taking treatment, how it affects the patient and why it is important to manage this. The agreed measures, which may include an incentive or enabler, social support or referral to another service to manage a specific issue, are sustained throughout the course of treatment.

What are the possible benefits and risks of participating?
Benefits include better monitoring of treatment and the opportunity to have more individualised approaches to support treatment. Participants may experience improved treatment outcomes. There may be additional savings in time and resources with better-supported treatment and the research may result in better treatment support options in the future. There are few risks with participating in this study but there may be cultural or language difficulties and these will be mitigated through the use of translator. In addition, in exploring the difficulties that people may have in taking their TB treatment, patients in particular may discuss difficult, embarrassing or upsetting topics. We will ensure consultations are conducted in a sensitive manner to make these as easy as possible.

Where is the study run from?
1. Royal Free Hospital (UK)
2. The Royal London Hospital (UK)
3. Royal Infirmary of Edinburgh (UK)
4. University Hospital Southampton (UK)

When is the study starting and how long is it expected to run for?
Jan 2018 to May 2022

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

Who is the main contact?
Dr Marc Lipman (Scientific)
marclipman@nhs.net

Contact information

Type(s)
Scientific

Contact name
Dr Marc Lipman

Contact details
University College London
Centre for Respiratory Medicine
The Grove Centre
Royal Free Hospital
Rowland Hill Street
London
United Kingdom
NW3 2AG

+44 20 7317 7560
marclipman@nhs.net

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
16/88/06 (NIHR)

Study information

Scientific Title
Intervening with a Manualised Package to achieve treatment adherence in people with Tuberculosis: the IMPACT study

Acronym
IMPACT

Study objectives
This manualised approach will enhance identification of at-risk individuals by thoroughly determining perceptual and practical barriers, providing intensified risk-based individualised support and increasing our overall understanding of the reasons underlying nonadherence.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 24/12/2018, Camberwell St. Giles Ethics Committee (Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, UK; Tel: +44 (0)207104 8204; Email: NRESCommittee.London-CamberwellStGiles@nhs.net), REC ref: 18/LO/1818

Study design
Mixed-methods work programme

Primary study design
Interventional

Secondary study design
Cluster randomised trial

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Tuberculosis, improving adherence to treatment.

Interventions
This study is a mixed-methods work programme comprising of the following:
1. Scoping review of the social sciences and health literature
2. Refinement of a conceptual framework based on qualitative and quantitative service user and health care worker interviews
3. Construction of a manualised intervention package
4. Pilot study
5. Process evaluation of the intervention

Study arm:
Manualised intervention:
The patient's case manager (usually the clinic TB nurse) applies the manual in partnership and consultation with the patient to identify whether personal, sociocultural and/or systems risk factors are present that suggest likely poor adherence with treatment. If these are identified, then the relevant measures outlined in the manualised intervention that may mitigate these are reviewed and implemented with the agreement of the participant. This process is aided by the use of narrative aids (developed during the production of the manualised intervention) that helps both the patient and clinical team to put into context the particular risk factor for non-adherence, how it affects the patient and why it is important to manage this. The agreed measures, which may include an incentive or enabler, social support or referral to another service to manage a specific issue, are sustained throughout the course of treatment. At each subsequent visit, and whether or not risk factors were identified at a previous assessment, the manualised intervention is re-applied to determine if either the risk(s) persist or new risks have arisen. For example a patient who had stable accommodation at the start of treatment may lose this if they are unable to work whilst taking therapy.

In the event that adherence levels deteriorate during treatment, case managers in consultation with the patient, also re-apply the screening tool and re-evaluate the intervention(s) required from the menu.

Study arm:
Standard care for TB:
The national adoption of approaches such as cohort review to TB management means that all patients have case managers, and at the start of treatment are assessed for a set of risk factors felt to be associated with likely non-adherence. These focus generally on areas such as homelessness, drug and alcohol misuse, previous incarceration and mental health issues rather than other psycho-social factors such as what does having TB mean to the person, or do they feel that they really need to take treatment? If a risk factor is identified then the patient will be offered the relevant support available in the clinic. All participants are followed throughout their treatment by their case manager and if concerns regarding adherence are identified, further support measures are implemented in line with clinic practice. Although a process evaluation is performed during the pilot study (see below), the researchers do not intervene to provide advice or to suggest a change in practice in either arm should they identify a problem. The exception to this would be if the Study Steering Committee had concerns about study conduct or outcome and wished to stop the trial.

Study subjects are seen at weeks 0, 2, 4, 8, 12, 16, 20 and 24 (earliest date of treatment completion). Should they require ongoing treatment after 6 months they are seen as clinically indicated. At each review, adherence assessments are performed (see below), and the manualised intervention applied if the patient is within a clinic which has been randomised to the intervention arm.

Most patients who do not have clinically important drug resistant disease receive six months of treatment. To allow for treatment interruptions, patients within the pilot study are followed to either treatment completion or for a total of 9 months from starting anti-TB therapy. Although this means that depending on when they enter the study, patients with extensive or drug resistant disease (who can require therapy for anything between nine and 20 months) may not have all of their treatment captured within the pilot, the maximal time of 18 months that a participant could be within the study allows us to obtain good data on the majority of patients with complex TB.

Intervention Type
Mixed

Primary outcome measure
Adherence is measured using:
1.1. Pill counts, assessed at every visit for the duration of treatment
1.2. Patient-reported drug administration, timely clinic attendance as planned
1.3. Urine tests for anti-TB drug metabolites and
1.4. If the patient is receiving either DOT or VOT, objective evidence of taking medication.

These are validated against the other adherence measures and the quality of each assessed.

Secondary outcome measures
1. The number of patients who give consent as a proportion of those who were approached and asked if they would participate are assessed using consent logs and consent rate at the end of recruitment.
2. Completeness of data for measures of adherence and treatment completion is measured as the proportion of patients who have pill counts entered at each visit and the proportion of patient visits with a recorded pill count. These measures of completeness will be monitored throughout the study and finally determined at the end of the study.
3. The number and proportion of patients who were identified by the application of the manual as likely to benefit from at least one of the menu of interventions available to support adherence at any point during their treatment. It will be assessed at 6 months after treatment commences.
4. The number and proportion of patients who were offered and the number and proportion of patients accepting at least one of the menu of interventions available to support adherence at any point during their treatment. It will be assessed at 6 months after treatment commences.
5. Adherence and treatment completion rates:
5.1. Proportion of patients completing treatment
5.2. Proportion of patients still on treatment after 9 months

Overall study start date
01/01/2018

Completion date

01/05/2022

Eligibility

Key inclusion criteria
1. Individuals aged over 18 being started on treatment for TB affecting any site.
2. Migrants newly arrived in the UK
3. People whose first language is not English
4. Woman who are pregnant
5. People with a mental health disorder
6. People taking immunosuppressive therapy or known to have immunodeficiency
7. Those with a previous history of treatment for TB or non-adherence with anti-TB medication
8. People with a current or previous history of drug or alcohol misuse

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
80, 4 clusters, 20 per site.

Total final enrolment
79

Key exclusion criteria
1. Patients already on treatment for TB at the point they attend the TB services in the study
2. If the patient is not expected to live for the duration of treatment (that is a minimum of six months from starting treatment)
3. Age under 16

Date of first enrolment
01/04/2019

Date of final enrolment
29/08/2021

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
Royal Free Hospital
Royal Free London NHS Foundation Trust
London
United Kingdom
NW3 2QG

Study participating centre
The Royal London Hospital
Barts Health NHS Trust
Whitechapel Road
Whitechapel
London
United Kingdom
E1 1BB

Study participating centre
Royal Infirmary of Edinburgh
Department of Respiratory Medicine
51 Little France Crescent, Old Dalkeith Road
Edinburgh
United Kingdom
EH16 4SA

Study participating centre
University Hospital Southampton
University Hospital Southampton NHS Foundation Trust
Tremona Road
Hampshire
Southampton
United Kingdom
SO16 6YD

Study participating centre
Whittington Health NHS Trust
The Whittington Hospital
Magdala Avenue

London
United Kingdom
N19 5NF

Sponsor information

Organisation
Joint Research Office

Sponsor details
UCL Hospitals NHS Foundation Trust and Royal free Hospitals NHS Foundation Trust
1st Floor of Maple House
149 Tottenham Court Road
London
England
United Kingdom
W1T 7DN
+44 20 3447 5557
r.sidhu@nhs.net

Sponsor type
University/education

Website
http://www.ucl.ac.uk/jro/index

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Not defined

Funder Name
National Institute for Health Research Health Technology Assessment Programme

Results and Publications

Publication and dissemination plan
We will disseminate the findings of this study widely to ensure immediate translation of results to policy and uptake of the intervention across the NHS through engagement with the following

groups:
Patient and civil society: via our health care, policy and patient groups, the project will benefit from key stakeholder input. Utilising the expertise of our PPI representatives, we will also produce lay summaries of the study results to share with patient groups, the TB civil society community and the public (through local clinical networks, community-based programmes working with at-risk for tuberculosis populations and voluntary sector agencies). We will also ensure that the All Party Parliamentary Group on TB are aware of our research findings, and use it to promote good working practice.

Professional bodies or entities: The manualised intervention will be co-produced with input from the TB Nurses Network. We will enlist support from the British Thoracic Society Joint Tuberculosis Committee (BTS), the British HIV Association and the National Clinical MDR-TB Advice Service, with whom we have strong links. A report of the trial results will be published in the respective newsletters and discussion documents ensuring wider dissemination to individual members. We will present our results at national and international meetings (including the BTS and Public Health England events).

Engagement with policy makers: We will produce a full project report, which will be shared with Public Health England, NHS England,
and local commissioners via TB Control Boards after peer review by the HTA. This will include recommendations regarding the
manualised intervention and any subsequent evaluation required. The report will summarise findings particularly relevant to UK
tuberculosis control policy.

Journals and conferences: Peer reviewed journal articles and conference presentations on all key elements of the study will be published with appropriate media engagement through a press release.

We envisage that each of the objectives will result in a publishable manuscript.

The study protocol, patient information sheets and consent forms will be made available on the study website once this has been set up.

Intention to publish date
30/04/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request. Documents will be retained for at least 15 years after the conclusion of the trial in accordance with legislation governing the retention of trial records (European Directive 2003/63 /EC). Data for the pilot study trial will be stored in locked offices of the clinical or research teams in University College London. Only members of the clinical / immediate research team will have access to any identifiable information. After 5 years, the data will be anonymised and archived by Iron Mountain Services. Data will be available following permission from NIHR and after publication of study outcomes. If there is a further study following on from this then it will be with the consent of the Steering Group. Requests for data should be directed to Dr Marc Liplman at marclipman@nhs.net.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	17/12/2019	12/11/2020	Yes	No
Interim results article	Qualitative study	29/03/2021	14/11/2022	Yes	No
Other publications	Scoping review	01/06/2021	14/11/2022	Yes	No
Other publications	Scoping review	21/09/2021	14/11/2022	Yes	No
HRA research summary			28/06/2023	No	No