ISRCTN43811467 https://doi.org/10.1186/ISRCTN43811467

Tuberculosis (TB) and tobacco

Submission date
23/03/2016

Recruitment status
No longer recruiting

Registration date
31/03/2016

Overall study status
Completed

Last Edited
30/08/2022

Condition category
Other

[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 serious bacterial infection that mainly affects the lungs. Tobacco smoking causes health problems for TB patients. It therefore makes sense to help these patients quit smoking (smoking cessation). There are many effective behavioural interventions and drug treatments available for tobacco cessation, including an inexpensive plant-derived drug called cytisine. However, smoking cessation is generally not offered as part of routine TB care and not integrated within TB programmes even in countries with high TB incidence and high tobacco use. For example, Bangladesh, Nepal, and Pakistan have no such infrastructure to offer cessation support to tobacco users. More evidence is needed of the effectiveness and cost-effectiveness of offering these interventions to TB patients. The aim of this study is to assess the effectiveness and cost-effectiveness of cytisine when added to behavioural support for tobacco cessation in TB patients who smoke.

Who can participate?
Newly diagnosed pulmonary tuberculosis patients aged 15 years (18 years for Bangladesh) and above, who have been smoking tobacco on a daily basis and wish to quit.

What does the study involve?
Participants are randomly allocated to one of the two groups. Those allocated to one group receive cytisine and those allocated to the other group receive a placebo (dummy drug). Behavioural support is delivered by the TB clinical team to all participants using an educational flipbook. Some behavioural support sessions may be audio recorded, but this is optional for the participants. Information on tobacco use, TB outcomes and adverse events is collected at the start of the study, day 5, week 5, 9 and 12 and at months 6 and 12. Breath and urine tests are carried out to confirm the participants' tobacco use at months 6 and 12.

What are the possible benefits and risks of participating?
The results of this study will help to improve the health of TB patients. All participants receive behavioural support which has been proved to be effective and will help some of the participants in quitting smoking. Half of the participants also receive Cytisine, which (although not proven in TB patients) is likely to help them quit too. Cytisine is generally a safe medicine obtained from a plant and has very few side effects. These include nausea, stomach ache, dryness of mouth, sleeplessness, mood changes and headache.

Where is the study run from?
The study will take place at multiple sites in Bangladesh by ARK Foundation and in Pakistan by the NTP/The Initiative, acting as the country coordinating centres.

When is the study starting and how long is it expected to run for?
November 2015 to October 2019

Who is funding the study?
The study has received funding from the European Union's Horizon 2020 research and innovation programme

Who is the main contact?
Dr Omara Dogar

Contact information

Type(s)
Public

Contact name
Dr Omara Dogar

Contact details
Department of Health Sciences
University of York
Room A/TB/220, SRB
Heslington
York
United Kingdom
YO10 5DD

Additional identifiers

Study information

Scientific Title
Tobacco cessation within TB programmes: a ‘real world’ solution for countries with dual burden of disease

Acronym
TB & Tobacco

Study objectives
Primary objective:
To assess the effectiveness and cost-effectiveness of cytisine when added to Behavioural Support for tobacco cessation compared to Behavioural Support alone on tobacco cessation in TB patients who smoke tobacco on a daily basis.

Secondary objectives:
1. To assess the effectiveness and cost-effectiveness of tobacco cessation strategies (cytisine

when added to Behavioural Support) in improving the clinical outcomes of TB patients who smoke tobacco on a daily basis
2. To assess any differences in the effectiveness of these strategies by the form of tobacco used (tobacco smoking only versus a combination of smoking and smokeless tobacco)
3. To assess any differences in the effect across different TB severity groups, high and low socio-economic status (SES), gender and age sub-groups
4. To first translate for use in the target population and then assess psychometric properties (validity and reliability) of the Mood and Physical Symptoms Scale (MPSS) for the assessment of withdrawal symptoms, and the Strength of Urges to Smoke (SUTS) for the assessment of nicotine dependency
5. To assess adverse effects of these strategies in the target population
6. To assess all relevant components of the design and delivery of the smoking cessation programme as part of a process evaluation

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Health Sciences Research Governance Committee (HSRGC) at the University of York, UK, 12/02/2016
2. National Bio-ethics Committee, Pakistan Medical Research Council, 06/06/2016, ref: No.4-87/16/NBC-200 Part-B/RDC/4197
3. National Research Ethics Committee, Bangladesh Medical Research Council, 31/08/2016, Ref: BMRC/NREC/2016-2019/1475)

Primary study design
Interventional

Study design
Double-blind randomised parallel-group placebo-controlled interventional trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Smoking cessation in pulmonary TB patients

Interventions
Arm 1: Cytisine + Behavioural Support
Arm 2: Placebo + Behavioural Support

Cytisine:
Participants allocated to Arm 1 will receive their first five days' cytisine supply on the day of trial enrolment (i.e. Day 0) and will be asked to quit tobacco use on the fifth day. Cytisine is a plant alkaloid and a partial agonist of nicotinic acetylcholine receptors (nAChRs). Cytisine has a short half-life of 4.8 hours, and is rapidly eliminated from the body. Its mechanism of action is similar to the effect of nicotine. It competes with nicotine on the nicotine receptors, which shortens the period of interaction of nicotine with the respective receptors and hence leads to a gradual reduction and elimination of existing psychological nicotine dependence in smokers. For this study hard capsules containing 1.5 mg of cytisine will be used. These capsules have a shelf life of 2 years.

Placebo:
Participants allocated to Arm 2 will receive placebo. By virtue of being a double-blind trial, patients allocated to Arm 2 will be dispensed the placebo in exactly the same manner as cytisine.

Behavioural support:
An adapted version of a pre-developed and proven effective Behavioural Support intervention to help people to quit smoking and smokeless tobacco use will be delivered to all enrolled patients by the clinical team (Health Worker/TB paramedic), irrespective of their treatment arm. This consists of two face-to-face sessions delivered at day 0 and day 5 (+2) and which last 10 and 5 minutes, respectively. The sessions will be structured using an educational flipbook; the session on day 0 will be aimed at encouraging tobacco users to see themselves as non-users, and set a plan for a quit date five days later; with a session on the quit date (day 5) to review progress. Further encouragement and support will be offered at a subsequent visit at week 5.

Intervention Type
Mixed

Primary outcome(s)
Continuous abstinence at six months (self-report of tobacco use not more than five cigarettes /bidis/water pipe sessions/chew after the quit date), which is biochemically verified by Carbon Monoxide (CO) level of <10ppm and cotinine dip-stick level of < 3 in urine (Level 3 =100-200ng /mL cotinine), if using smokeless tobacco as well.

Key secondary outcome(s)
Abstinence, Lapses and Relapses
Based on self-report alone or on the combination of self-report and CO/cotinine levels, these will include:
1. Point abstinence, defined as a self-report of not using tobacco in the previous 7 days at weeks 5 and 12, and verified by a CO level of <10ppm (or cotinine level < 3 for concomitant SLT users), at months 6 and 12.
2. Continuous abstinence at month 12 (only five instances of tobacco use allowed), biochemically verified as for the primary outcome at month 6.
3. Early-lapse, defined by a self-report of tobacco use (even once) after the quit date but having point abstinence at week 5.
4. Late-lapse, defined by a self-report of tobacco use (even once) between week 5 and week 12 but showing point abstinence at week 5 and week 12.
5. Early-relapse, defined by point abstinence at week 5 but a tobacco use status in later assessments.
6. Late-relapse, defined by point abstinence at week 5 and week 12 but a tobacco use status at month 6.

TB outcomes
1. Clinical outcome: an eight-point clinical score (TB score) will be used to assess clinical outcome at baseline, week 5, 9, 12 and months 6 and 12. The score consists of signs and symptoms of TB (cough, chest pain, dyspnoea, anaemic conjunctivae, body mass index (BMI) <18 kg/m2, BMI <16 kg/m2, mid-upper arm circumference (MUAC) <220 mm, and MUAC <200 mm), each contributing one point.
2. Laboratory-based outcome: sputum conversion results at weeks 5, 9 and months 6 and 12, of those that were sputum positive at the time of diagnosis.
3. X-ray-based outcome: patients' chest X-rays taken at baseline, week 9 and months 6 and 12 will be graded according to the National Tuberculosis Association of the USA as normal, minimal,

moderately advanced and far advanced TB
4. Programme outcomes: the proportion of treatment success (including cured and completed treatment), treatment failure, defaulted and died will be recorded from TB register (TB03) at month 6, and relapse will be assessed at month 12 follow-up.

Nicotine Dependency scales
A translated version of the Mood and Physical Symptoms Scale (MPSS) in Bengali, Nepali and Urdu will be administered at baseline, weeks 5, 12, and at months 6 and 12. The frequency and strength of urge to smoke will also be assessed using a translated version of Strength of Urges to Smoke (SUTS) questions that will be administered at baseline, weeks 5, 12, and months 6 and 12. The translated scales will be assessed for their validity and reliability in the study population.

Adverse Events assessment
Adverse events will be classified using Common Terminology Criteria for Adverse Events (CTCAE) and Common Toxicity Criteria (CTC), which will be monitored at each visit (as a part of the CRF), explicitly prompting for symptoms relating to possible Investigational Medicinal Product toxicities.

Completion date
31/10/2019

Eligibility

Key inclusion criteria
Current inclusion criteria as of 04/09/2017:
1. Age at least 15 years (counted as adult TB patients in Pakistan) and 18 years in Bangladesh
2. Able to provide consent
3. Diagnosed with pulmonary tuberculosis (PTB) (smear positive or negative) in the last four weeks
4. Currently smokes tobacco
5. Willing to quit tobacco use

Previous inclusion criteria:
1. Age at least 15 years (counted as adult TB patients in Pakistan and Bangladesh) and at least 18 years in Nepal
2. Able to provide consent
3. Diagnosed with pulmonary tuberculosis (PTB) (smear positive or negative) in the last four weeks
4. Currently smokes tobacco
5. Willing to quit tobacco use

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Other

Lower age limit

15 Years

Sex
All

Total final enrolment
2472

Key exclusion criteria
Patients anticipated to have adverse effects either due to the study treatment or research burden, will be excluded. These will include those who are/have:
1. Retreatment TB, MDR TB, Miliary or Extra-pulmonary TB
2. Currently receiving Streptomycin (Category II anti-TB medication) and/or Para Amino Salicylic Acid (PASA)
3. Currently using any pharmacotherapy for tobacco dependence
4. Pregnant, lactating, or planning to become pregnant
5. Had myocardial infarction, stroke, or an attack of severe angina within the previous two weeks
6. Uncontrolled high blood pressure despite being on medication
7. Severe renal impairment (requiring dialysis)
8. Suffering from schizophrenia or known to be diagnosed with epilepsy

Date of first enrolment
01/06/2017

Date of final enrolment
30/04/2018

Locations

Countries of recruitment
Bangladesh

Pakistan

Study participating centre
Participating Health Centres from various districts of Bangladesh and Pakistan
Bangladesh
-

Sponsor information

Organisation
University of York (UK)

ROR

https://ror.org/04m01e293

Funder(s)

Funder type
Government

Funder Name
European Commission

Alternative Name(s)
European Union, Comisión Europea, Europäische Kommission, EU-Kommissionen, Euroopa Komisjoni, EC, EU

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Individual participant data (IPD) sharing plan
Please contact Professor Kamran Siddiqi (Study Chief Investigator, email: kamran.siddiqi@york.ac.uk) for access to the study datasets.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/11/2020	20/10/2020	Yes	No
Results article	nested study results	08/04/2021	13/04/2021	Yes	No
Results article	Cost-utility results	26/08/2022	30/08/2022	Yes	No
Protocol article	protocol	30/03/2018		Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes