Does mobile phone instructional video demonstrating sputum expectoration improve the sputum sample quality and quantity in presumptive pulmonary TB cases? Protocol for a prospective pragmatic non-randomised controlled trial in Karnataka state, India

Siddharudha Shivalli,1 Amruth Hondappagol,2 Kibballi Madhukeshwar Akshaya,3 Abhay Nirgude,3 Narendra Varun,3 Raveendra Harohally Ramaiah Reddy,4 Burugina Nagaraja Sharath5

ABSTRACT

Introduction Sputum smear microscopy is the cornerstone of tuberculosis (TB) diagnosis under the Revised National Tuberculosis Control Programme (RNTCP) in India. Instructions on how to produce a good sputum sample are a part of RNTCP training manuals, but its assessment is not emphasised. Healthcare provider’s instruction to expectorate a good sputum sample has limitations. Presumptive TB patients often submit inadequate (in quantity and/or quality) sputum samples, which may result in false-negative results. Objectives of the study are, among the selected RNTCP designated microscopy centres in Dakshina Kannada district, Karnataka, India, (a) to assess the effectiveness of mobile phone instructional video demonstrating sputum expectoration on sputum quality and quantity and (b) to explore the mobile phone video implementation challenges as perceived by the healthcare providers.

Methods and analysis This is a pragmatic, prospective, non-randomised controlled trial in two pairs of RNTCP Designated Microscopy Centres (located at secondary and primary healthcare facilities) of Dakshina Kannada district, India. Presumptive pulmonary TB patients aged ≥18 years will be included. We will exclude who are severely ill, blind, hearing impaired, patients who have already brought their sputum for examination, and transported sputum. In the intervention group, participants will watch a mobile phone instructional video demonstrating submission of an adequate sputum sample. The control group will follow the usual ongoing procedure for sputum submission. This study would require 406 participants for each group to achieve a power of 90% for detecting a difference of 15% between the two groups. The participant enrolment started in December 2019.

Ethics and dissemination Yenepoya University Ethics Committee, Mangaluru, India, has approved the study protocol (YEC-1/158/2019). It complies with the Declaration of Helsinki, local laws, and the International Council for Harmonization—good clinical practices. Investigators will present the results in scientific forums, publish in a scientific journal, and share with RNTCP officers.

Trial registration number Clinical Trial Registry of India (CTRI/2019/06/019887).

INTRODUCTION

Tuberculosis (TB) is caused by Mycobacterium tuberculosis and is the leading cause of death from a single infectious agent across the globe.1 To reach the 2030 WHO End TB Strategy milestones, the current global rate of...
decline in TB incidence needs to be accelerated from 2% to 4%–5% annually. Early diagnosis and adequate treatment is one of the key approaches to achieve this.

India is a middle-income country and accounts for 27% of the global TB burden in 2017. By adapting the WHO End TB strategy, India is accelerating its TB control efforts and witnessing a declining trend. The sputum microscopy is one of the mainstays of diagnosis for pulmonary TB (PTB) under the Revised National Tuberculosis Control Programme (RNTCP). In RNTCP, two sputum samples are collected from presumptive PTB patients within a day or two consecutive days. To detect the acid-fast Mycobacteria in sputum, the sample should be expectorated from the lungs after taking a deep breath; good quality sputum contains more of mucus and less of saliva. The sensitivity of the sputum smear microscopy varies from 45% to 75%, and it could be further compromised if sputum samples are inadequate in quantity and quality. These missed patients are most likely to transmit the infection and may lead to delay in diagnosis. An adequate sputum sample is essential for accurate TB diagnosis. However, sputum quantity and quality assessment are usually not emphasised both in high- and low-burden settings. A study from 16 health centres in Indonesia (ranked third in global TB burden and adapted the WHO End TB strategy with sputum microscopy as the mainstay of diagnosis) reported that 45.9% and 46% of the 1168 sputum samples were poor in quantity (<3 mL) and quality (saliva), respectively. An evaluation of 14708 sputum samples in India reported that the sputum positivity, by both smear and culture, increased with improving quality (non-salivary samples) and increasing quantity of the sputum.

There is profound evidence suggesting adequate education of presumptive PTB patients by the healthcare provider improves the sputum quantity and quality, and hence, TB case detection. The RNTCP training manual describes the steps of good sputum sample expectoration from the lungs. However, the method to convey the appropriate information to patients in the right manner is a daunting task. In addition to patient-related factors, healthcare service provider’s experience, motivating skills, attitude and compliance with sputum collection procedure may influence the sputum quantity and quality submitted by presumptive PTB patients. Health education videos have been effectively used as public health intervention tools and had a positive impact on attitudes and behavioural change in populations of different age groups. Mobile phone video demonstrating sputum expectoration could be a feasible and sustainable option to improve the sputum sample quantity and quality. Moreover, it can be incorporated in the existing RNTCP with minimal cost implications, if found effective.

**Objectives**

Among the selected RNTCP designated microscopy centres (DMC) in Dakshina Kannada district, Karnataka, India (a) to assess the effectiveness of mobile phone instructional video demonstrating sputum expectoration on sputum quality and quantity (b) to explore the mobile phone video implementation challenges as perceived by the healthcare providers.

**METHODS AND ANALYSIS**

**Trial design**

Prospective pragmatic non-randomised controlled trial.

**Study setting and groups**

Dakshina Kannada is a coastal district located in the southern part of Karnataka state, India. According to census 2011 data, it has a population of about 2.1 million, with an average literacy rate of 88.6%. The public health infrastructure consists of 1 district hospital, 8 community health centres, 4 first referral units, 65 rural and 12 urban primary health centres. Under the RNTCP, all these public health facilities have a DMC and, TB diagnosis and treatment are offered free of cost. Within the framework of the National Health Mission, Tuberculosis Unit (TU) is the subdistrict level RNTCP supervisory unit covering a population of about 0.25 million. There are seven TUs in Dakshina Kannada district, Karnataka state, India. According to Dakshina Kannada district TB office report, from January to March 2019, a total of 7341 presumptive PTB patients were referred for sputum examination in the public health facilities of Dakshina Kannada district. Of these, 311 patients were positive for TB.

For this study, investigators will use purposive sampling to select two DMCs located at secondary healthcare (SDMC) and two DMCs located at primary healthcare (PDMC) facilities. Purposive selection of DMCs is based on the similarity in the number of sputum sample examinations and slide positivity rate from January to March 2019. All the presumptive PTB patients attending one pair of DMCs (SDMC and PDMC) will receive the intervention, and the other pair (SDMC and PDMC) will follow the ongoing routine procedure for sputum submission.

**Study period**

December 2019 to February 2020

**Participants and methods**

**Inclusion criteria**

A presumptive patient of PTB (any of the symptoms or signs of TB including cough >2 weeks, fever >2 weeks, significant weight loss >5% in last 3 months, haemoptysis or any abnormalities in chest radiography) aged ≥18 years coming to the selected DMC for sputum submission will be included.

**Exclusion criteria**

Severely ill, blind (unable to count the fingers in daylight at a one-metre distance), hearing impaired (who cannot hear the mobile phone audio with or without hearing aid), patients who have already brought their sputum for...
Intervention (mobile phone instruction video)

A team of researchers from Interactive Research and Development (IRD, http://ird.global/), Pakistan developed a sputum submission instructional video to improve the diagnostic quality of sputum samples (‘Good sputum, better diagnosis’, available at http://youtu.be/92dIT_1kbbek). This video demonstrates the step-by-step procedure of submitting a good quality and quantity sputum sample. It is translated into Kannada by Karnataka Health Promotion Trust (KHPT, http://www.khpt.org/), Bangalore, India. The length of the video is approximately 4min. To suit the objectives of this study and nature of the intervention, we will prepare a short video by adapting and further developing the Kannada version of ‘Good sputum, better diagnosis’. We have obtained the necessary permissions from IRD, Pakistan and KHPT, India to modify and adapt the video to the local context. To reach a broad consensus, we will share the adapted video in Kannada with the District TB officer, two independent subject experts, and two communication experts for further validation. We will also pilot the adapted video on five presumptive pulmonary TB patients attending a DMC, who are not part of our study. If necessary, we will further modify the video based on the feasibility and feedback (ease of understanding) from those five presumptive pulmonary TB patients and two laboratory technicians working under RNTCP.

Data collection procedure

Research coordinators for the project shall be placed at all the four study centres. Investigators will train the research coordinators to explain the purpose and details of the study in the local language, obtain written informed consent, assess the quality and quantity of the sputum sample, and record relevant information on a semi-structured questionnaire. Also, two of them, in the intervention arm, will be trained to administer the intervention and obtain feedback from every fifth study participant.

In the intervention group, after assessing the eligibility, the research coordinator will explain the purpose and details of the study. After obtaining written informed consent, presumptive PTB patient will watch the instructional video on mobile, demonstrating the step-by-step procedure of submitting a good quality and quantity sputum. The instructional video will be shown again if the participant says that he/she did not understand the steps of the sputum expectoration procedure. Based on his/her understanding, the participant will collect and submit the sputum in a sputum container provided under RNTCP. The research coordinator will collect relevant information from the participants by using a semi-structured questionnaire. The research coordinator will also collect feedback on the video and sputum submission experience from every fifth study participant. The RNTCP laboratory technician will note the quantity (by comparing it with a premarked standardised empty container) and assess the quality (by comparing it with standard photographs) of the sputum sample.

In the control group, presumptive PTB patients will submit the sputum sample according to the usual ongoing procedure. By using a semi-structured questionnaire, the research coordinator will collect relevant information from the participants. The RNTCP laboratory technician will measure the quantity (by comparing it with a premarked standardised empty container) and assess the quality (by comparing it with standard photographs) of the sputum sample. To minimise the inter-observer variation, we will train the RNTCP laboratory technicians (in both the study groups) to assess the sputum sample quality by comparing it with standard photographs and test the reliability with kappa statistic before the enrolling the participants.

Outcome measures and time points

The primary outcome is the proportional difference in the adequate sputum samples (based on the quantity and quality) between the study groups from December 2019 to February 2020. The sputum sample would be considered as ‘adequate’ if it is at least 2mL and at least half of the sputum is thick/non-salivary (ie, mucoid, purulent, blood-stained or combination of these). Quality of the sputum will be categorised as mucoid (containing mucus, thicker than normal and either yellow or green colour), purulent (containing dead tissue, usually in large amount with foul smell, yellow or green colour), blood-stained (containing varying amounts of blood) or as salivary (transparent and watery specimen with bubbles). To minimise the bias in categorising the sputum quality, RNTCP laboratory technician will use standard photographs for each category to assess the sputum quality.

Secondary outcomes are the proportional differences in the positive sputum smear microscopy and positive Cartridge-Based Nucleic Acid Amplification Test for TB between the study groups from December 2019 to February 2020.

Besides, in the intervention group, investigators will assess the number of times the video played per participant and obtain participant feedback on instructional video regarding ease of understanding, did it help, should it be continued and so on. The investigators will also collect feedback from the RNTCP laboratory technicians on the feasibility and challenges of mobile video implementation within programmatic settings.

Patient and public involvement

No patient involved

Figure 1 shows the proposed flow of the study participants in this trial.

Sample size and power

Based on the reported 39% of the submitted sputum samples by presumptive PTB as salivary, a design effect
Selection of 2 TUs in Dakshina Kannada district, India (Purposive sampling)

Two pairs of SDMC and PDMC

Allocation

Intervention group
(One SDMC & one PDMC)
Consecutive recruitment of presumptive pulmonary TB cases aged ≥18 years

Control group
(One SDMC & one PDMC)
Consecutive recruitment of presumptive pulmonary TB cases aged ≥18 years

Exclude: severely ill, blind, hearing impairment, brought or transported sputum sample

Mobile phone instruction video on sputum expectoration and submission

Ongoing routine way of sputum submission

Analysis

Sputum quantity and quality
Microbiologically confirmed TB

Sputum quantity and quality
Microbiologically confirmed TB

Figure 1 Flow diagram for the trial participants. TB, tuberculosis; TU, tuberculosis unit; SDMC and PDMC, designated microscopic centres located at secondary and DMCs primary healthcare facilities.

of 2 (due to clustering of patients) and after applying continuity correction, this study would require a sample size of 406 for each group (ie, 812 total), to achieve a power of 90% for detecting a difference in proportions of 15% between the two groups at a two-sided p value of 0.05.

Sensitivity analysis of sample size calculation for sputum quantity
Investigators will estimate the power of the study based on the actual number of study participants who complete the study and observed differences in the primary outcome between two study groups.

Masking
Owing to the nature of the intervention and its implementation to all the patients attending the study centres in the intervention group, it is not possible to mask the trial participants and study site coordinators (who administer the intervention). The data analyst will be masked during analysis. Lack of masking is unlikely to affect the study outcomes.

Data collection, management and statistical analysis
A pretested semi-structured questionnaire will be used to collect the data. A blind review of the data will be performed for each trial participant. Data collected in a structured form will be double-entered, validated and analysed using EpiData (V.3.1 for entry and V.2.2.2.183 for analysis; EpiData Association, Odense, Denmark). Statistical analysis will follow the intention-to-treat principle. We will report the baseline participant-level socio-demographic and key clinical characteristics, and test for equivalence between the groups using appropriate parametric or non-parametric tests. Considering the health centre (secondary and primary health facility level) as the primary sampling variable, analyses would be adjusted for the clustering effect. The primary outcome (proportional difference in the adequate sputum samples) measured will be analysed using logistic regression. The primary model will include a variable for the intervention group and will be adjusted for the cluster variable (by adding a random intercept for cluster variable using mixed effect models). The adjusted analysis will also be reported, that is, adjusting for cluster and the other covariates found
to be significant at the baseline level. Similarly, we will perform a cluster and covariate-adjusted analysis for the secondary outcomes. A two-sided p value of <0.05 would be considered significant.

Safety parameters
Intervention does not pose any risk to the participants. However, any adverse event during the trial will be listed and displayed in summary tables. The total number of adverse events, the minimum, maximum and mean number of adverse events per patient will be reported.

Data monitoring committee
This trial does not require an independent data monitoring committee as it involves a health education intervention of very short duration with no risk to the participants.21 22

Study progress
Ethics approval and trial registration number were obtained in June 2019. The participant enrolment started in December 2019.

DISCUSSION
Instructional videos have emerged as novel tools of health education. Owing to its large user base in India,23 mobile phones have caught the attention of public health researchers as effective tools to enhance the impact of public health programme. Mobile phone reminders either by voice call or short message services have been explored to enhance TB treatment adherence and improve the outcomes in India, Thailand, Africa, Pakistan, Malaysia and Cambodia.24–29 Smartphone apps found to be effective in data management, better patient referral and improving treatment adherence and outcome for patients with TB in India and other countries.30–32 Similarly, a study from Tanzania20 assessed the use of instructional video to improve TB patient detection. However, we did not find any such studies to improve the TB diagnosis conducted in India.

The Tanzania study20 used a 4-minute instruction video originally prepared by IRD, Pakistan.19 In a government hospital of Tanzania, 200 presumptive PTB patients were randomly assigned to either intervention (made to watch a sputum expectoration instruction video on a laptop in a designated room) or control group (standard oral instructions to expectorate sputum by healthcare workers of the TB clinic) before sputum submission.20 It did show a significant improvement in sputum volume, quality and sputum smear positivity. However, this study had many limitations. These findings may not be generalisable as it was a single-centre study with individual-level randomisation (high chances of contamination), administration of intervention under more controlled conditions, and on relatively small sample size. Also, the authors used a laptop to deliver the intervention, and the cost of adapting the video to the East African context was US$10,000.30 Hence, the scaling-up of this intervention is not possible in limited-resource settings due to cost implications. Moreover, implementation in remote areas is challenging due to the irregular power supply.

Owing to the lack of data on video-based interventions to improve sputum sample quantity and quality in India, and critical limitations of the previous study,20 this pragmatic trial is designed wherein health centres will be allocated to intervention or control arm. Testing the intervention within the RNTCP framework is a more practical approach to assess the effectiveness and also provides an opportunity to assess the feasibility of the intervention. We have purposefully selected PDMC and SDMC as these report different numbers of sputum sample examinations in each RNTCP quarter. Also, mobile phone instructional video demonstrating sputum submission step-by-step is a feasible and sustainable intervention with minimal cost implications if found effective. This study will also gain participants’ perspectives on the intervention through feedback.

Owing to limited resources, we adapted a non-randomised design for this study, which is a limitation. However, to limit the selection bias, we will select DMCs which have a similar number of sputum sample examinations and slide positivity rate in an RNTCP quarter (January to March 2019). Besides, adjusted analysis is planned for potential observed differences.

Ethics and dissemination
After obtaining the written informed consent, investigators will replace the protected personally identifiable information (PPII) by a research identification code. Face sheets containing PPIIs will be removed from the completed questionnaire. Only one investigator (AH) will have access to master code list. Locked cabinets and password-protected computers and files will be used to securely store the research data and relevant electronic data, respectively. The intervention in this trial (mobile phone instructional video on sputum expectoration) neither poses any additional risk to the participants nor alters the diagnostic and treatment algorithm for pulmonary TB patients under RNTCP. Hence, trial participants will not be eligible for any compensation. Following analysis of the data, investigators will present the results in scientific forums and publish them in a scientific journal. Further, the investigators will share the results with both district and state-level RNTCP officers.

Author affiliations
1Department of Medical Statistics, London School of Hygiene and Tropical Medicine, London, UK
2Department of Public Health, Yenepoya Medical College, Yenepoya (Deemed to be University), Mangaluru, India
3Department of Community Medicine, Yenepoya Medical College, Yenepoya (Deemed to be University), Mangaluru, India
4Department of Community Medicine, Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, India
5Department of Community Medicine, ESIC Medical College and Post Graduate Institute of Medical Sciences and Research, Bengaluru, India
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Contributors SS conceived the study and drafted the protocol. AH, KMA, AN, NV, RRHR and BNS revised the protocol. All the authors evaluated the feasibility of this trial in the study setting and approved this manuscript for publication.

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Competing interests None declared.

Patient and public involvement statement No patient and public involvement

Patient consent for publication Not required.

Ethics approval Yenepoya University Ethics Committee, Mangaluru, India has approved the study protocol (YEC-1/158/2019). Investigators have obtained the necessary permission from the District TB Office, Dakshina Kannada district for data collection in the selected RNTCP DMCs. Trained research coordinators will obtain written informed consent from all the study participants in the local language (Kannada). The study complies with the Declaration of Helsinki, local laws and the International Council for Harmonisation-good clinical practices (ICH-GCP).

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Data availability statement Deidentified participant data will be available upon reasonable request to AH (amrutrh@gmail.com) after obtaining the necessary permission from the funder and Yenepoya University Ethics Committee, India.

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ORCID iD Siddharudha Shivalli http://orcid.org/0000-0003-1454-7114

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