**Study C:**

**The effectiveness of a self-stigma and shame reduction intervention upon stigma measures for patients with TB and MDR-TB in Vietnam: a randomised controlled trial**

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**Glossary**

|  |  |  |
| --- | --- | --- |
| **Treatment outcomes** | |  |
| **For patients with new TB (new TB)** | | Patients are presumed to have drug-susceptible tuberculosis, where they have not been diagnosed with any form of drug resistance and have not previously been treated for TB1 |
|  | *Cured***:** | Bacteriologically confirmed TB at the beginning of treatment which was smear- or culture-negative in the last month of treatment, and on at least one previous occasion during treatment1 |
|  | *Treatment completed:* | Completed treatment, without evidence of failure, BUT with no record to show that sputum smear or culture results in the last month of treatment, and on at least one previous occasion, were negative (either because tests were not done or because results are unavailable)1 |
|  | *Treatment failed:* | Sputum smear or culture is positive at month five of treatment, or later during treatment1 |
| **For patients with RR/MDR-TB** | | For this study, patients with RR/MDR-TB (or Rifampicin-resistant TB) will include patients who have TB that is resistant to rifampicin and isoniazid (or rifampicin only). Rifampicin resistance is typically detected using GeneXpert MTB/RIF or phenotypic drug susceptibility testing. |
|  | *Cured*: | Treatment completed as recommended by the national policy without evidence of failure AND three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase1 |
|  | *Treatment completed:* | Treatment completed as recommended by the national policy without evidence of failure, BUT no record of cure1 |
|  | *Treatment failed*: | Treatment terminated or need for permanent regimen change of at least two anti-TB drugs on account of:   * Lack of smear or culture conversion by the end of the intensive phase, or * Bacteriological reversion in the continuation phase after conversion to negative, or * Evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs, or * Adverse drug reactions (ADRs) 1 |
| **Died** | | A patient who dies for any reason during treatment1 |
| **Not evaluated** | | No treatment outcome is assigned. (This includes cases “transferred out” to another treatment unit and whose treatment outcome is unknown) 1 |
| **Treatment success:** | | The sum of cured and treatment completed1 |
| **Lost to follow-up** | | Not starting treatment or whose treatment was interrupted for two consecutive months or more1 |
| **Likert scale** | | A widely used scale to assess participant responses. When responding to a Likert questionnaire item, respondents specify their level of agreement to a statement, typically over a four or five-point range. |
| **Self-stigma** | | Refers to the internalisation of public stigma by a person2. This internalisation can lead to denial of symptoms and rejection of treatment and contribute to the isolation of people from valuable social supports3 |

**Summary**

*Significance:* Self-stigma harms patients’ psychosocial wellbeing, creating barriers to their effective treatment and recovery from disease. Despite multiple studies aimed at measuring self-stigma in patients with TB and MDR-TB and the existence of one or more interventions to reduce it, there remains a lack of quantifiable evidence to support their effectiveness and facilitate their implementation.

*Objectives:* This study aims to evaluate the effectiveness of a self-stigma and shame reduction intervention upon stigma, treatment outcomes, psychological wellbeing, depression, self-efficacy and self-compassion for patients with new TB and RR/MDR-TB in Vietnam.

*Methods*: We will perform an open-label randomised controlled trial of a stigma-reduction intervention in Hanoi province of Vietnam. Patients with RR/MDR-TB and new TB and receiving treatment will be randomly allocated to the intervention or control arm. The intervention group will participate in a self-stigma and shame workshop titled ‘From the inside out’. The workshop consists of eight modules run across four days. Before commencement, the intervention will be pilot tested to make it culturally and linguistically appropriate for Vietnam. Trained Vietnamese researchers will facilitate the workshops and coordinate the study. The control arm will receive usual care. Participants in both groups will receive standardised treatment through the Vietnam National TB Program. The study participants will self-administer a questionnaire at baseline, after two months and after four months. The questionnaire will comprise validated scales to measure stigma, treatment adherence, psychological wellbeing, depression and self-efficacy. Data from the programmatic outcome data from the National TB program will be used to collect treatment outcome data for the study participants.

*Analysis*:The hypothesis is a reduction of self-stigma in the intervention arm by ≥10% when compared to the control arm. The mean scores for the included scales will be compared between the control and intervention groups.

**Background**

**Tuberculosis**

Tuberculosis (TB) is the world’s deadliest infectious disease, killing 1.6 million people annually4. It is one of the top 10 causes of death worldwide and the leading cause of death in people living with HIV. TB is caused by the bacterium *Mycobacterium tuberculosis* and primarily affects the lungs. Drug-susceptible TB can be treated effectively with a course of four antibiotics over six months. However, the causative bacteria have become resistant to one or more of the antibiotics used to treat it. Resistance to the two most effective TB medications, isoniazid and rifampicin, is referred to as multidrug-resistant tuberculosis (MDR-TB). The treatment for patients with RR/MDR-TB is at least five antibiotics for a minimum of 9 months, depending upon response to therapy, availability of drugs and drug resistance profile. The antibiotics are second-line tuberculosis drugs and vary depending on the type of resistance.

**Self-stigma**

Goffman et al. first described stigma as “an undesirable or discrediting attribute that an individual possesses, thus reducing that individual’s status in the eyes of society” 5. Self-stigma occurs when the individual believes these views, and that they are weak or damaged because of the attribute (disease). Corrigan's theoretical model is useful to explore this process of self-stigma in patients with TB. Despite being initially developed for people with mental illness in 2007, the common stereotypes surrounding mental illness are comparable to those for patients with TB (dangerous, to blame and incompetent) and it is relevant for other stigmatising attributes such as smoking and alcohol abuse6–8. The model has three stages, commencing with stereotype awareness, where people with the attribute are aware of the community’s beliefs surrounding their attribute. The second stage is an agreement with these stereotypes. The third stage is an association of these beliefs with themselves (see figure 1). An example of this thought process in a person with TB could include:

1) Stereotype awareness: Others believe that it is people with TB's fault for getting TB

2) Stereotype agreement: I believe it is people with TBs fault for getting sick

3) Stereotype adaption: It is my fault for getting TB

A systematic review of self-stigma in people who smoke using this model found that this thought process did not occur in everyone7. A few people rejected the stereotypes and can cope well with the pervasive stigma or find strength with other smokers7. Stigma and self-stigma have many facets that require careful measurement and analytical considerations by researchers. These will be discussed below and include, but are not limited to drivers, consequences, confounders and correlates of self-stigma.

Self-stigma is just one of the psychological characteristics of TB and MDR-TB. Other characteristics include social stigma, discrimination, feelings of hopelessness, dependence on others, fear, loss of identity, low self-esteem, guilt, isolation, anxiety and depression9–13. Furthermore, treatment side-effects also account for some of the substantial physical and psychological disability inflicted on patients with TB and MDR-TB12. The combined effects of stigma, treatment side effects and illness from TB often prevent patients from working, and negatively affects the financial capacity of the household. These factors lead to further stress and anxiety, exacerbating patients’ already fragile mental health state11–13.

This demonstrates that self-stigma rarely manifests alone. It interacts with numerous other factors. Self-stigma is just one of the factors that have significant impacts on the emotional and physical wellbeing of patients with TB and MDR-TB9. Figure 1 adapted from the Corrigan theoretical model displays some of the known factors that interact with self-stigma in patients with TB and MDR-TB. There are arrows from the drivers directly to the consequences, as this relationship can exist without stigma. For example, a cross-sectional study identified that patients with MDR-TB have significantly (P < 0.01) lower quality of life (QOL) and psychological wellbeing when compared to patients with TB and people with no TB14. These direct relationships do not diminish the importance of self-stigma. It highlights that some consequences and drivers are interchangeable, cyclical and can be affected by many factors. Studies that evaluate the behavioural and emotional consequences of TB for patients often identify self-stigma as important a contributing factor. Hence, reducing self-stigma may also have secondary effects on these interrelated factors.

Figure 1: Adaptation of Corrigan et al. theoretical model for self-stigma in people with TB6

**Emotional consequences**

**Depression**

**Anxiety**

Reduced

- Self-esteem

- Self-efficacy

- QOL

- Psychological

Wellbeing

Blame

Guilt

Shame

External drivers

* TB context
* Community stigma
* Enacted stigma
* Perceived stigma

**Self-stigma**

Stereotype Awareness

Poor treatment adherence

Treatment

drop out

Isolation

Why try?

Hopelessness

**Develop MDR-TB**

**TB relapse**

**Death**

**Behavioural consequences**

Internal drivers

* Co-morbidities
* Stage of treatment
* Other stigmatised attributes
* Past experiences
* Poor social support
* Treatment side-effects
* Gender

Stereotype Agreement

Self-Concurrence

## 

## Drivers and consequences of self-stigma

Self-stigma is a significant challenge and can devastate the lives of patients with TB and MDR-TB in the short term and long term. Self-stigma can develop from, and be compounded by, external stigma from family members, their communities and health care providers9. Patients with TB are often held responsible for their illness and blamed for not adhering to treatment by their communities13. The considerable morbidity associated with MDR-TB translates explicitly into an increased level of stigma and more severe consequences15. Self-stigma manifests itself in feelings of shame, guilt and disgust16. These then overcome the mind creating the emotional consequences of reduced self-esteem, efficacy, QOL and overall psychological wellbeing (see figure 1)14. These changes contribute to the development of anxiety and depression11,15. In 2014, Corrigan et al. adapted the model to include another consequence of self-stigma dubbed the ‘why try’ effect2. They defined it as “as a sense of futility in which people believe they are unworthy or incapable of achieving personal goals because they apply the stereotypes…to themselves”2. This is the shifting point in ones-self where one is overcome by their self-stigma and emotional state that they are unable to function at their pre-stigma state. This effect expands to behavioural consequences such as poor treatment adherence, treatment dropout, isolation (see figure 1).

**Stigma reduction interventions**

Despite multiple studies evaluating self-stigma reduction interventions across multiple areas, there is a lack of reliable and measurable data to support their implementation and guide their delivery in patients with TB and MDR-TB 17. A systematic literature review of stigma interventions for TB identified seven studies, four qualitative and three quantitative17. Three of the studies were interventions with health care workers, and four of the studies focused on an intervention with patients with TB or MDR-TB. The interventions included patient education, support groups, TB-clubs and counselling. Despite all of these studies reporting favourable outcomes, three were qualitative studies, which could not quantify the impact of the intervention17. Macq et al. 2008 was the only study identified that used a validated TB stigma scale to measure the effect of the intervention. They conducted a quasi-experimental study that measured the effect of TB clubs and home visits after 15 days and 2 months of treatment using a validated internalised stigma scale18. The results showed a statistically significant reduction in internalised stigma after two months. The main limitations of this study include quality and study design. The paper scored 11/27 on the Downs and Black assessment tool for quality. The study design did not randomly allocate study participants, which reduced internal validity, did not account for confounders and could introduce selection bias. All of which limits the generalisability of the results17.

**Overview of study/intervention and hypothesis**

We will undertake a randomised controlled trial to evaluate the effectiveness of a stigma-reduction intervention in Vietnam. The study aims to fill this gap by providing a rigorous evaluation of ‘from the inside out’ a 4-day workshop aimed at reducing self-stigma and shame in patients with TB and RR/MDR-TB which was developed by KNCV Tuberculosis Foundation and the Work For Change.

# Study Objectives

Co-primary Objectives are to:

1. Evaluate the effect of a self-stigma and shame workshop (the intervention) upon the self-stigma of patients with RR/MDR-TB, measured according to a validated self-stigma scale (the Redwood self-stigma subscale).
2. Evaluate the effect of the intervention upon the measured stigma of patients with new TB, measured according to a validated self-stigma scale (the Redwood self-stigma subscale).

Secondary Objectives are to:

1. Evaluate the effect of the intervention upon stigma, according to the Redwood MDR-TB for patients with RR/MDR-TB.
2. Evaluate the effect of the intervention on stigma, according to the Van Rie TB stigma scale, among patients with TB.
3. Evaluate the effect of the intervention upon treatment success (treatment cure and treatment completion) according to the programmatic outcome data from the national TB program.
4. Evaluate the effect of the intervention upon depression, using the Patient Health Questionnaire (PHQ-9).
5. Evaluate the effect of the intervention upon self-efficacy, according to Patient Activation Measure (PAM-13).
6. Evaluate the effect of the intervention upon self-compassion, according to Neff self-compassion scale – short version (12 items).
7. Evaluate the effect of the intervention upon psychological wellbeing, according to Ryff Psychological Wellbeing Scale.

All objectives will be measured at baseline, 2 months and 4 months. Secondary objective 3 will be measured when the patient is due to complete treatment.

# Study design and implementation

This study is an unblinded parallel-randomised controlled trial. The intervention will be preceded by the localisation of the intervention to the Vietnamese context. The intervention is “From the Inside out” a four-day workshop on self-stigma and shame to be run with the patients. It was developed by KNCV and the Work for Change who designed it specifically for patients with TB and MDR-TB19.

The study will follow three stages. Stage 1 will be the ‘training of trainers’. Stage 2 will adapt the intervention to the local context, and stage 3 will be the randomised controlled trial to implement the intervention.

## Stage 1: Pre-intervention training of Vietnamese trainers

Trainers of the workshop will be Vietnamese researchers. The training will be conducted over three consecutive days. Two experienced international facilitators who created the workshop will train the trainers by going through each module with the trainers so they can experience the workshop first hand. They will then train them in the delivery of the workshops.

## Stage 2: Adaptation workshop (pilot) to adapt the intervention to the Vietnamese context

The pilot will run over four consecutive days, within one month of the training. The newly trained Vietnamese researchers will facilitate it, with assistance from the international facilitators. This stage has two objectives. It will allow the Vietnamese trainers to practice implementing the intervention and it will allow the intervention to be adapted to the Vietnamese context with the assistance of the international facilitators. The international facilitators have experience adapting the workshop in Indonesia, the Philippines and Kazakhstan. The participants of this workshop will include10-20 people with a history of TB or RR/MDR-TB. At the end of the pilot, the participants will be asked to evaluate it. They will be asked to complete a survey including which aspects they liked the most, which part they did not understand, how it could be improved and how well the trainers ran the workshop. The facilitators and Vietnamese trainers will use this information and work in collaboration to alter the workshop for the context and make it appropriate for the study population (patients with TB and RR/MDR-TB) including:

Translation of materials.

Adaptation of scenarios and activities.

Context-specific warm-up exercises.

It is expected to take one week to finalise the information gathered in the pilot and adapted the workshop to create the final version for the RCT.

## Eligibility for participation in the pilot

People with a history of bacteriologically confirmed pulmonary TB or RR/MDR-TB and who have completed treatment by the National Tuberculosis Program (NTP) in Hanoi will be eligible to participate. Participants will be identified through the Hanoi Lung Hospital patient records and be contacted by phone by the Vietnamese researchers asking if they would like to participate. From the records, we will recruit a range of ages and genders to gain various input from the participants for the evaluation of the pilot. Table 1 summarises the eligibility criteria for this workshop.

Table 1: Inclusion and exclusion criteria for participants in the pilot

|  |  |
| --- | --- |
| **Inclusion criteria for participants** | **Exclusion criteria for participants** |
| * 18 years or older * Documented treatment completion for pulmonary TB or pulmonary RR/MDR-TB within the last three years in Hanoi | * Unwilling or unable to provide informed written consent * People that are currently incarcerated |

# Stage 3: Randomised controlled trial

## Study sites

The study will be conducted in the capital, Hanoi in northern Vietnam. This site was chosen because it has a high number of notified cases of people with RR/MDR-TB. The Woolcock Institute of Medical Research (WIMR), an Australian research institute affiliated with the University of Sydney, has a local representative office in Vietnam and established collaborations with the health care facilities20. Patients with RR/MDR-TB will be identified through the Hanoi Lung Hospital. The patients with new TB will be identified through the Hanoi Lung Hospital and TB clinics within five kilometres from the Hanoi Lung Hospital. This study site is an urban area.

## Eligibility of patients for the randomised controlled trial

*Patients with RR/MDR-TB*

Patients with bacteriologically proven pulmonary RR/MDR-TB and undertaking treatment for RR/MDR-TB within the NTP at the participating health facilities will be eligible to participate, see table 2.

Table 2: Inclusion and exclusion criteria for patients with RR/MDR-TB

|  |  |
| --- | --- |
| **Inclusion criteria for patients with RR/MDR-TB** | **Exclusion criteria for patients with RR/MDR-TB** |
| * 18 years or older * A diagnosis of bacteriologically proven pulmonary RR/MDR-TB\* * Commenced on treatment for RR/MDR-TB by the NTP within the prior six months, * Be considered non-infectious:   1. Reduction in symptoms following treatment commencement, AND   2. One of either:      + Reduction in smear grade (e.g. from 3+ to 1+) OR      + Culture-negative for at least 4 weeks on the most recent sample; OR      + Unable to produce sputum AND   3. Completed at least 6 weeks of treatment * Available to participate in the intervention | * Unwilling or unable to provide informed written consent * Usual residence is outside of the Provinces participating in the study * Patients that are currently incarcerated |

\*See glossary

*Patients with new TB*

Patients with bacteriologically proven pulmonary TB and undertaking treatment for TB within NTP at the participating health facilities will be eligible to participate. Table 3 summarises the eligibility criteria for these patients.

Table 3: Inclusion and exclusion criteria for patients with new TB

|  |  |
| --- | --- |
| **Inclusion criteria for patients with new TB** | **Exclusion criteria for patients with new TB** |
| * 18 years or older * A diagnosis of bacteriologically proven pulmonary TB \* * Commenced on treatment for TB by the NTP within the last eight weeks * Be considered non-infectious   1. Reduction in symptoms   2. One of either:      + Reduction in smear grade (e.g from 3+ to 1+) OR      + Culture-negative for at least 4 weeks on the most recent sample; OR      + Unable to produce sputum AND   3. Completed at least 2 weeks of treatment * Reports never having previously received treatment for TB before the current diagnosis * Available to participate in the intervention | * Unwilling or unable to provide informed written consent * Usual residence is outside of the Provinces participating in the study * Patients that are currently incarcerated |

\*See glossary

## Participant Recruitment

The processes for making contact with study participants (both patients with TB and with RR/MDR-TB) will involve the following steps (see figure 1).

1. Agreement with the Director of the facility, or his/her delegate, and from the head of the outpatient facilities to undertake the study and recruit patients from their hospital/facility/ward.
2. The Vietnamese researchers will inform the health care staff at the participating facilities of the study and patient eligibility verbally and on paper.
3. The Vietnamese researchers will use the patient registers and referrals from the health care workers to invite eligible participants to participate in the study.
4. If the patient agrees to participate, the Vietnamese researcher will them, answer any questions that they have, confirm eligibility and give them the approved participant information statement.
5. The Vietnamese Researcher will confirm the participant's eligibility before consent is signed.
6. Participants who agree to participate will provide written informed consent with a Participant Consent Form.
7. The age, gender and treatment length of patients that do not participate wish to participate in the study will be recorded.

Figure 1: Flowchart showing recruitment procedure for study participants

Identification of Patients

Confirm eligibility

Informed consent gained

No

Yes

Randomisation

## Intervention

#### “From the inside out” training

A team of experts from KNCV and The Work for Change who have extensive experience in international health and stigma in multiple contexts developed a self-stigma package for patients with TB and MDR-TB. This intervention has been designed based on evidence-based research of self-stigma as it relates to various health issues such as TB, HIV and cancer. Interventions must target cognitive, affective, and behavioural levels. The intervention was made available in September 2018 and has been piloted with TB and MDR-TB survivors in Kazakhstan and Indonesia to adapt it to the context19. The intervention consists of eight modules that can be covered over four 7-hour days. The modules include (see figure 2):

* Module 1: What is self-stigma?
* Module 2: Dealing with self-stigma and shame
* Module 3: Drug-Resistant TB and self-stigma
* Module 4: Transmission control and self-stigma
* Module 5: Health rights, TB and self-stigma
* Module 6: TB treatment and self-stigma
* Module 7: Planning for the future – TB free! Now what?
* Module 8: Monitoring & evaluation of this intervention

Figure 2: ‘From the Inside out’ module overview



(This image was taken from “from the inside out” self-stigma and shame workshop book19)

The modules include a mix of interactive games, exercises and brief PowerPoint slides.

The goal of the intervention is to help individuals identify, understand, and address self-stigma and anticipated stigma. It provides a framework and tools to reduce self-stigma in people with TB. In particular, the package aims to challenge and overcome self-stigmatising beliefs to improve well-being and ensure affected people can lead productive lives that are free of self-judgment. The primary rationale is that the participants who go through the whole intervention will come out with increased knowledge of TB, recognition and management of self-stigma and enhanced self-efficacy.

#### *Intervention design (fidelity, dosage and coverage)*

The intervention will be delivered one day per week, over four weeks for all study participants (figures 4&5 and table 8). Two trainers will facilitate each workshop. The local researchers, chief investigator and international facilitators will approve a final Vietnamese version of the workshop to ensure that the intervention is delivered as intended. There will be an agreed timeline of the workshop and strict timing of what will be included each day, see table 4. The local researchers are required to follow this and to sign the timetable for the workshop after each section is completed.

Table 4: Sample agenda for day one of the workshop19

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Day one** | **Activity** | **Topic** | **Sign (2 people)** | |
| 8:15-8:30 am | Registration |  |  |  |
| 8:30-9:15 am | Introductions and Expectations |  |  |  |
| 9:15-10:45 am | Module 1 [exercises 1.1, 1.2 or 1.3] | What is self-stigma? |  |  |
| 10:45-11:00 am | BREAK |  |  |  |
| 11:00-12:00 pm | Module 2 [exercises 2.1 and 2.2] | Dealing with self-stigma and shame |  |  |
| 12:00-1:15 pm | LUNCH |  |  |  |
| 1:15-1:45 pm | Module 2 [exercise 2.3] |  |  |  |
| 1:45-3:15 pm | Module 2 [exercise 2.4] |  |  |  |
| 3:15-3:30 pm | BREAK |  |  |  |
| 3:30-4:30 pm | Module 2 [exercise 2.6] |  |  |  |
| 4:30 pm | Finish |  |  |  |

Note: adapted from the Self-stigma and shame workbook

After each workshop, the participants will be asked several questions to evaluate the workshop, and the facilitators will complete a self-reflection questionnaire. The facilitators are required to have a core set of skills to deliver this workshop. Examples of core skills required include:

* Good listener and refrains from giving advice
* Knowledgeable and able to answer questions
* Approachable and friendly
* Can connect well with people

These mini evaluations are integrated into module 8 of the workshop and will provide feedback on their ability to perform these skills.

Coverage will be recorded by the researchers using an attendance sheet for the participants at the start of the day and after lunch. At the end of the workshop, the participants will have a score ranging from 1-8 for attendance, where 1 would indicate a half day. If they do not attend, the researcher will contact them to ask them to join another session. Participation will be recorded twice a day. Together, the two researchers will discuss the extent of each participant's participation in the workshop. They will give them a score from 0-1, where 0 would indicate did not participate at all, did not contribute to the discussion or join activities, 0.5 half participates, sometimes joined in, sometimes did not 1 would indicate full participation, they were involved in all activities and completed all tasks required. Both attendance and participation scores will be added up over the four days to give a total score ranging from 0 to 8 each. Where ≥6 would indicate excellent participation and attendance, <6 (<75%) is not acceptable attendance. For participation, 4-6 is good, 2-4 is poor, and ≤2 would indicate no participation. See examples below:

Example of day 1 record of attendance and participation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Day 1 | | | |
| Name | Morning | | Afternoon | |
|  | Attendance\* | Participation\*\* | Attendance\* | Participation\*\* |
| Steve | 1 | 1 | 1 | 0.5 |
| Mary | 0 | 0 | 1 | 1 |
| Jo | 0 | 0 | 1 | 1 |

\* 1=attended session, 0=did not attend the session. \*\* 1=full participation, 0.5=half participation, 0=did not participate

## Control

The control participants will not receive an intervention. They will be asked in the follow-up questionnaires if they have received any possible confounding interventions such as counselling. At the time of writing, there is no formal psychosocial support offered to patients with TB or RR/MDR-TB in Vietnam.

## Randomisation

Participants will be randomised individually to either the intervention or control group using permuted block randomisation. This will ensure balance across groups, while also ensuring those recruiting participants cannot predict the group allocation of the next participant. A person independent of the researchers recruiting the study participants will create and manage the randomisation spreadsheet that will contain the randomisation list.

How randomisation will be implemented

1. The new study participant is recruited and the consent form signed
2. The Vietnamese researcher will contact the study coordinator to find the participant’s allocation
3. The study participant will complete the baseline questionnaire
4. The study participant will be informed of their allocation

The staff recruiting the study participants will not be aware of the allocation of the participants before this time. A date will be set for the workshop when either (a) after 10 participants have been recruited or (b) after one month since the first recruited participant who has not yet been allocated to a workshop.

## Data Collection

The Vietnamese researchers who conduct the intervention will also collect the data. All surveys will be self-administered using a tablet computer. Self-administered surveys are less likely to be affected by social desirability bias, which can be present when sensitive topics such as stigma and tuberculosis. The researchers will remain nearby to assist the participant when necessary. These will be completed in a quiet area to ensure privacy. Data will be collected at baseline, after 2 months and after 4 months, see figure 3 and figure 4. Treatment completion data will be collected from the programmatic outcome data from the National TB Program.

Figure 3: Consort diagram

Assessed for Eligibility (n= )

Enrolment

Excluded (n= )

(with reasons)

Randomised (n= )

Allocated to control (n= )

Allocated to intervention (n= )

Baseline

Lost to follow-up (n= )

Received some psychosocial intervention (n=)

Received full intervention (n=)

Missed 1 or more day (n=)

Did not receive intervention (n=)

Lost to follow-up (n= )

2-month follow-up

Lost to follow-up (n= )

(with reasons)

Lost to follow up (n= )

(with reasons)

4-month follow-up uop

Cured (n= )

Treatment completed (n=)

Treatment fail (n=)

Relapse (n=)

Drop out (n=) (with reasons)

Cured (n= )

Treatment completed (n=)

Treatment fail (n=)

Relapse (n=)

Drop out (n=) (with reasons)

End of treatment

Analysed (n= )

Excluded from analysis (n=) (with reasons)

Analysed (n= )

Excluded from analysis (n=) (with reasons)

Analysis

*Data to be collected*

Table 5: Data to be collected

|  |  |
| --- | --- |
| **Questionnaire data** | **Reason for collection** |
| Participant ID | A unique identifier for each patient |
| Clinical characteristics of TB | To assess eligibility |
| Sociodemographic information | To characterise the cohort |
| Arm allocation | To compare the two groups |
| Self-stigma subscale | To address primary objectives 1&2 |
| MDR-TB stigma scale | To address secondary objective 1 |
| TB stigma scale | To address secondary objective 2 |
| Treatment completion | To address secondary objective 3 |
| Depression scale | To address secondary objective 4 |
| “why try” effect scale | To analyse how these indicators interrelate |
| Self-efficacy scale | To address secondary objective 5 |
| Self-compassion scale | To address secondary objective 6 |
| Psychological wellbeing | To address secondary objective 7 |
| Participation in other programs | To assess potential confounding |
| Workshop evaluation form | To evaluate participant opinion about the workshop, and improve the use of the toolkit (intervention arm only) |

*Self-stigma sub-scale*

This subscale exists as part of the Redwood MDR-TB stigma scale. It is currently being developed and validated in Vietnam. It will consist of approximately six items. Each question will be measured using a 7-point Likert scale. This sub-scale will be used for both participants with MDR-TB and TB.

*MDR-TB Stigma scale*

The Redwood MDR-TB stigma scale is currently being developed and validated in Vietnam. It will consist of 10-15 items across the three facets of stigma (enacted, anticipated and self). Each question will be measured using a 7-point Likert scale.

*TB Stigma Scale*

The Van Rie TB stigma scale was developed and validated in Thailand in 200821. The PhD candidate has revalidated the scale in the Vietnamese context; the manuscript is currently being written. It has a Cronbach alpha of 0.85, a score of >0.7 is considered as acceptable. The adapted version consisted of 10 items and will use a 7-point Likert scale.

*Tuberculosis Medication Adherence Scale (TBMAS)*

The TBMAS was validated with 438 patients with TB in China in 201222. The Cronbach alpha for the scale is 0.88. The test-retest reliability was 0.85, a score of >0.7 is considered as acceptable. The authors compared the scale scores to the continuous medication gap of pharmacy refill records over 15 weeks. The TBMAS had a positive predictive value of 65.5% and sensitivity of 82.9% in identifying non-adherents. The ROC curve was 0.82, and the cut-off point for labelling as non-adherent was identified where the total TBMAS score is at 113. The scale consists of 30 questions, which address nine factors including communication with healthcare providers, personal traits, confidence in curing TB, social support, mood disorders, living habits, active coping behaviours, forgetfulness and access to healthcare.

*Depression scale*

The Patient Health Questionnaire (PHQ-9) is a scale used to measure depression consisting of nine items. The items are scored on a 4-point Likert frequency scale including: not at all (0), several days (1) more than half of the days (3) and nearly every day (3). It incorporates DSM-IV depressive diagnostic criteria. The diagnostic validity was established in eight primary care clinics and seven obstetrical clinics. PHQ score of greater than or equal to 10 has a sensitivity of 88% and a specificity of 88% for significant depression23.

*Self-efficacy scale*

The Patient Activation Measure (PAM-13) is a shortened version of the PAM-22. The shortened version was developed and validated in 2005 by Hibbard et al. in the United States24.

*Self-compassion scale (SCS)*

Neff et al. created and validated the original self-compassion scale in 200325. A short version containing 12 items was created in 2011. This version demonstrates a near perfect correlation of r = 0.98 with the long SCS total score26.

*Ryff psychological wellbeing scale*

Developed by psychologist Carol D. Ryff, the Psychological Wellbeing (PWB) Scale contains 42-item that measures six aspects of wellbeing and happiness including autonomy, environmental mastery, personal growth, positive relations with others, purpose in life, and self-acceptance. It was redeveloped in 1995 into a shorter, 18 item scale containing the same six aspects27. This study will use the shorter versions to minimise the time needed for the participant’s to complete it.

*“Why try” stigma scale*

The why try stigma scale WTSS has two forms, the original version which contains 12 items and a short version containing 6 items. The 6 item version demonstrates a good fit with the original version28.

*Potential confounders and covariates*

When evaluating the effect of an intervention upon stigma is it essential to measure other possible confounders that may explain the association. However, as this study is an RCT, it is unlikely there will be an imbalance in measured or unmeasured confounders between the two arms. For this study, we will collect information regarding three main stigmatising attributes in Vietnam relating to TB, and evaluate their distribution between groups.

Where the scale has not already been used in Vietnam, it will be piloted on stage 2, with the TB and MDR-TB survivors to ensure the translation is correct and it is understandable.

*Data handling and record keeping*

The procedure for data storage is described in a detailed Research Data Management Plan (RDMP). All data will be stored on Cloudstor or an equivalent online Research Data storage site approved by the University of Sydney. The data will be collected using Open Data Kit and Ona. The Woolcock Institute of Medical Research (WIMR) have used these tools to conduct other research. They have also proven to be more appropriate for data collection in this setting. These tools comply with the University of Sydney’s Research Data Management Policy 2014. A Research Data Management Plan has been created and approved by the University of Sydney. The data collected from this study may be posted as a publicly accessible dataset, with no personally identifiable information available. Data will be kept for fifteen years post study as per the Universities Data Management Policy (2014). Completed written informed consent forms will be stored at the WIMR in Vietnam in a locked cabinet for the required period. All data will be stored on the secure online platforms outlined above to protect the privacy of the participants.

Figure 4: Timeline of the study participant’s involvement in the intervention arm of the study.

1 month

0\*\*\* 1 2 3 4 5 6…

Months

Intervention\*

Recruitment

\*The intervention will commence within one month of recruitment and will take one month to complete. It will be completed before the 2 months survey. \*\*Surveys will be given to participants on recruitment, at 2 and 4 months after the baseline survey. \*\*\*Recruited when non-infectious (See table 2 and table 3). Note: the control arm will be the same without the orange intervention line.

Surveys\*\*

Outcome data collected at treatment completion

**Data Analysis**

Data will be analysed using the intention to treat analysis on SPSS 22 or similar (table 6). The scales used in the questionnaire will be compared pre and post intervention and between the intervention and control arm for both DS-TB and RR/MDR-TB participants. RR/MDR-TB and new TB participants will be compared to evaluate the effect of the intervention on the population groups. We will review the potential confounding factors to ensure they are balanced between the groups.

Table 6: How to manage study participant withdrawal and non-participation

|  |  |  |
| --- | --- | --- |
| Ask not to participate in further components of the study: | | Actions |
| Arm | Time |
|  | Before randomisation | Recruit another participant  Record the reason for withdrawal\* |
| Intervention | 1. Request not to participate in the workshops, but remain in follow-up | Keep baseline data  Follow-up for surveys  Include in analysis  Record the reason for non-participation\* |
|  | 1. Withdraw from the study | Keep data already collected  Include in analysis  Record the reason for withdrawal\* |
| Control | 1. Request not to participate in the workshops, but remain in follow-up | Keep baseline data  Follow-up for surveys  Include in analysis  Record the reason for non-participation\* |
|  | 1. Withdraw from the study | Keep data already collected  Include in analysis  Record the reason for withdrawal\* |

\*participant recruitment information will be recorded in a logbook (C\_Stigma\_MDR-TB patient log\_V1)

## Sample size calculation

A previous study demonstrated that a psychosocial stigma intervention reduced the average TB stigma score by 4.3 points using a 10 item scale with a 5-point Likert scale29. The control group in the same study also showed a reduction of 1.5 points. Based on the maximum range possible of 40, there was a change of 14.25% between the control and intervention cohorts. Using a conservative approach, we hypothesise a minimum difference of 10% between the control and the intervention group29. The increase will also allow for stigma fluctuation in the control group. Stigma in patients with RR/MDR-TB is expected to be higher than TB due to increased fear around transmission, extended treatment period and a more substantial burden of diseases. We found the data from the stigma scales to be normally distributed from studies A and B of this stigma series. The following data were extracted from these studies:

|  |  |  |  |
| --- | --- | --- | --- |
| **Data** |  | **Patients with MDR-TB** | **Patients with TB** |
| Range |  | (69-153)/180 | (13-47)/48 |
| Difference (10%) | δ1 | 8.4 | 3.4 |
| Standard Deviation | σ | 14.5577 | 7.291 |
| Mean |  | 113.1 | 26.9 |
| Significance | Z2α | 1.96 | 1.96 |
| Power |  | 80% | 80% |
| Power | Z2β | 0.842 | 0.842 |

Using the two-sample t-test, as we want to analyse the difference between two normally distributed continuous variables30:

Patients with RR/MDR-TB, the sample size in each group, is calculated as:

Patients with TB, the sample size in each group, is calculated as:

Therefore the sample size required is:

|  |  |  |
| --- | --- | --- |
|  | Patients with RR/MDR-TB | Patients with TB |
| Each group | 48 | 73 |
| Total | 96 | 146 |
| +10% to account for loss to follow up (each group) | 106 (53) | 162 (81) |

*Withdrawal/dropout of subjects*

If a participant requests to withdraw from the study before randomisation or the intervention commences, a new participant will be recruited. If a participant request to withdraw from the study after the intervention has commenced, their data will be included in the final analysis (see table 6). The Vietnamese researchers will record two phone numbers of all participants. The patient information statement informs the study participants of the withdrawal process. The participant will not be penalised in any way. If a participant is unable to be contacted for follow-up interviews or workshop attendance, they will be classified as missing after three attempts. Their data will remain in the study for final analysis. The sample size has been increased by 10% to account for missing data.

# Ethical considerations

Ethics approval will be obtained from the National Lung Hospital in Hanoi, Vietnam and the Human Research Ethics Committee at the University of Sydney. All participation within this study is voluntary, and written consent is required for all participants to meet inclusion criteria. Study participants will receive approximately 50,000VND (~$3AUD) per questionnaire completed and100,000VND (~$9AUD) per day for attending the workshop, with a bonus of 100,000VND if they attend all four days, totaling 500,000VND for full attendance. Lunch and snacks will be provided for the days that the participants attend the workshop.

# Reporting and dissemination

The results of this study will be submitted for publication in a peer-reviewed Journal. The data will be open source with all personally identifiable information removed. It is likely that this study will be able to be presented at conferences. The study participants will be asked if they wish to receive a summary of the study findings. If they indicate yes, their details will be recorded on the consent form, and a 1-page summary will be given to them after the analysis.

# Timeline

The total study period will be 14 months for the 4 month follow up objectives. The treatment outcomes objective will take an additional 18 months.

Table 7: Summary of the timeline

|  |  |  |
| --- | --- | --- |
| Step | Duration | Month |
| **Study Preparation**   * Obtain Australian and Vietnamese ethics approval * Hire Vietnamese staff * Translate workshop materials to Vietnamese * Obtain approval from the participating provinces lung hospitals and TB Clinics * Secure a room at the hospital/clinic to run the workshop * Train new staff on the study | 3 Months | February-April 2019 |
| **Stage 1: Training the Trainers**   * The expert facilitators will train the new staff on how to conduct the workshop | 3 days | 9-11 of May 2019 |
| **Stage 2: Pilot the toolkit to the Vietnamese context**   * Pilot the intervention with TB and RR/MDR-TB survivors * Modify the workbook and workshop * Feedback on workshop delivery * Analyse the scales translation into Vietnamese | 2 weeks | 13-16 of May 2019 |
| **Stage 3: Evaluation (RCT)**   * Recruit study participants (initial) * Run the intervention * Final follow up interviews | 10 months   * 1 month * 6 months * 2 months | June 2019-March 2020   * June 2019 * July-December 2019 * January-February 2020 |
| **Data analysis** | 2 month | February-March 2020 |
| **Write PhD manuscript/thesis** | 1 month | April 2020 |
| **Treatment outcomes follow-up** | 18 months | October 2021 |
| **Data analysis and manuscript preparation** | 1 month | November 2021 |

It is estimated that the intervention will take five months to complete, see table 8. The average number of participants in each workshop will be between 10-16

Table 8: Estimation of intervention delivery timeframe

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Month | Number of Patients with RR/MDR-TB who completed the intervention | Number of Patients with TB who completed the intervention | Number of Patients with TB who completed the intervention | Cumulative total (completed) |
| 1/ June | Recruit | Recruit | Recruit |  |
| 2/ July | 10 | 10 | 10 | 30 |
| 3/ August | 10 | 10 | 10 | 60 |
| 4/ September | 10 | 10 | 10 | 90 |
| 5/ October | 10 | 10 | 10 | 120 |
| 6/ November | 10 | 10 | 10 | 150 |
| 7/ December | Extra month allowance for recruitment difficulties | | |  |
| Total: | 50 | 50 | 50 | 150 |

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