University of York: HSRGC/2024/626/E: SCIMITAR-SA
Bangladesh: BMRC/NREC/2025-2027/128
Pakistan: 810/IREF/RMU/2024
IRB-3701/DUHS/2024/39
India: NIMHANS/47th IEC (BEH.SC.DIV.)/2024
F.No P-29010/19/2025-DMCell

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SCIMITAR- South Asia

Feasibility Trial Protocol

Tobacco Cessation Intervention for Individuals with Severe Mental Illness: A Feasibility Randomised Controlled Trial

Sponsor	University of York (UoY), United Kingdom
Protocol authors	<insert>
Funder	NIHR Global Health Research Programme
Grant Reference Number	Research & Innovation for Global Health Transformation (RIGHT) NIHR205601
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	• Leeds City Council, United Kingdom • Valid Research, United Kingdom • Brown University School of Public Health and Alpert School of Medicine, United States of America • University of East Anglia, United Kingdom • Deputy Director of Mental Health, Ministry of Health & Family Welfare, Government of Karnataka, India • University of Nottingham, United Kingdom • London School of Economics, United Kingdom
Ethics Approval Number	**UoY:** HSRGC/2024/626/E: SCIMITAR-SA **Bangladesh:** BMRC/NREC/2025-2027/128 **India:** NIMHANS/47th IEC (BEH.SC.DIV.)/2024 F.No P-29010/19/2025-DMCell **Pakistan:** 4-87/NBCR-1145/24-25/1422 810/IREF/RMU/2024
Trial registration number	<insert>
Version Number and Date	V3.0 , 20-08-2025

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List of Abbreviations Used

AE	Adverse Events
AR	Adverse Reaction
ASTRA	Addressing Smokeless Tobacco Use and Building Research Capacity in South Asia
BCTs	Behaviour Change Techniques
BMRC	Bangladesh Medical Research Council
CEI	Community Engagement and Involvement
CFIR-ERIC	Consolidated Framework for Implementation Research - Expert Recommendations for Implementing Change
CRFs	Case Report Forms
DALYs	Disability Adjusted Life Years
DMEC	Data Monitoring and Ethics Committee
ECT	Electroconvulsive Therapy
ENDS	Electronic Nicotine Delivery Systems
ENNDS	Electronic Non-Nicotine Delivery Systems
FGDs	Focus Group Discussions
GCP	Good Clinical Practice
GHRG	Global Health Research Groups

HMSC	Health Ministry's Screening Committee
HNBs	Heat Not Burn
HRQoL	Health Related Quality of Life
HTPs	Heated Tobacco Products
IAB	Independent Advisory Board
ICMR	Indian Council of Medical Research
IMPACT	Improving Outcomes in Mental and Physical Multimorbidity and Developing Research Capacity
IOP	Institute of Psychiatry
IREF	Institutional Research & Ethics Forum
LMICs	Low- and Middle-Income Countries
MLTCs	Multiple-Long Term Conditions
MOA	Mechanisms of Action
MOHFW	Ministry of Health and Family Welfare
MPSS	Mood and Physical Symptoms Scale
MRC	Medical Research Council
MTQ	Motivation to Quit
NCDs	Non-Communicable Diseases
NCSCT	National Centre for Smoking Cessation and Training
NIHR	National Institute for Health and Care Research

NIMH	National Institute of Mental Health
NIMHANS	National Institute of Mental Health and Neurosciences
NREC	National Research Ethics Committee
NRT	Nicotine Replacement Therapy
ONPs	Oral Nicotine Pouches
PHQ	Patient Health Questionnaire
PMG	Programme Management Group
PTSD	Post Traumatic Stress Disorder
PRC	Patient Record Card
RA	Research Assistant
RMU	Rawalpindi Medical University
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SCIMITAR- SA	Smoking Cessation Intervention for Severe Mental Ill Health - South Asia
SES	Socio-Economic Status
SLT	Smokeless Tobacco
SMI	Severe Mental Illness
SUSAR	Suspected Unexpected Serious Adverse Reaction
TDA	Tobacco Dependence Advisor

TMSS	Thengamara Mohila Sabuj Sangha
UAR	Unexpected Adverse Reaction
UID	Unique ID
UN's SDGs	United Nations' Sustainable Development Goals
VBA	Very Brief Advice
WHO-UMC	WHO Uppsala Monitoring Centre
YLD	Years Lived with Disability

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1. Introduction

Mental disorders are a major contributor to the global disease burden, ranking among the top 10 causes of health loss[1]. Individuals with Severe Mental Illness (SMI) (Schizophrenia, Schizoaffective disorder, Psychosis, Bipolar illness and Severe Depression with psychosis) are among the most vulnerable population groups[2] facing health disparities, increased risk of physical multimorbidity,[3] higher mortality, shorter life expectancy and poor lifestyle choices like smoking, poor diet, drug use, and inactivity [3–5].

Tobacco consumption is a leading modifiable cause of morbidity and mortality. Its use contributed to 8.71 million deaths and 229.77 million DALYs worldwide(2019)[6]. Smoking tobacco accounted for 7·69 million deaths and 200 million DALYs[7]. An analysis from 127 countries reported that 348,798 deaths and 8,691,827 DALYs were lost from Smokeless Tobacco (SLT) use[8]. Globally, the tobacco-attributable deaths are projected to rise to 8.3 million and double (3.4 million to 6.8 million) in Low and Middle-Income Countries (LMICs) by 2030[9]. The combined economic cost of smoking (healthcare expenses and productivity losses) reached USD 1436 billion in 2012. Nearly 40% of this cost occurred in developing countries, underscoring the significant financial burden faced by these nations[10].

Two out of three individuals with severe mental health conditions are current smokers, significantly affecting their health[11]. Reducing smoking among those with mental illness is considered the most impactful step in narrowing the life expectancy gap for this population[12]. Bangladesh, India and Pakistan are LMICs that experience the highest global burden of diseases related to tobacco use, including both smoking and smokeless tobacco [13–15]. Although studies from South Asia are limited, they report smoking prevalence as high as 50% among individuals with SMI [16], and widespread use of

smokeless tobacco in the general population [8]. Despite a decline in tobacco use within the general population over the past 40 years, there has been very little reduction in tobacco consumption among people with SMI [17, 18].

A multi-country survey conducted in Bangladesh, India, and Pakistan among individuals with SMI attending mental health facilities reported higher tobacco use in people with SMI, particularly in men compared with rates reported for the general population in South Asia. However, despite this, only around 38.4% of tobacco users had received advice to quit tobacco [19].

The higher risk of tobacco dependence in individuals with SMI can be attributed to various factors, including genetic predispositions. For instance, research has shown that schizophrenia and smoking behaviour are linked to several common genetic regions[20, 21]. Additionally, socioeconomic status (SES) may play a role, as individuals with lower SES are more likely to experience psychotic disorders and have higher smoking rates compared to those with higher SES [22, 23]. A systematic review and meta analysis reported that tobacco use dependence/ nicotine dependence co-occurred in 33.4 - 65% of people with SMI [24]. Individuals with SMI have high levels of nicotine dependence and heavier patterns of smoking.[25][26]

Despite misconceptions to the contrary, there is evidence that people with SMI are interested in improving their physical health, including quitting tobacco. However, they need additional support compared with the general population to address barriers such as

higher nicotine dependency levels, lower literacy levels and the need to titrate psychotropic medication whilst quitting. The UK-SCIMITAR trial has shown that SMI specific interventions are effective in enabling people with SMI to quit at six [27] and 12 months (longer-term and sustained quitting[28]. This intervention was cost-effective, reducing health utilisation and improving quality of life[29].

Tobacco cessation is crucial for individuals with SMI because it significantly improves their physical health, potentially adding years to their life expectancy[30]. Tobacco cessation support within mental health services offers an opportunity to narrow the gap in life expectancy between SMI and the general population[19]. However, differing patterns of tobacco use, socio-economic challenges, cultural beliefs and practices, health service provision, and regulatory approaches mean that evidence from HICs cannot be directly translated to LMICs. Interventions relevant to South Asian populations need to take into account the high prevalence of both smoking and smokeless tobacco use [31–33]. The cultural perceptions around tobacco use in South Asia differ from Western countries [34] and this issue has emerged as a key barrier in the community consultation panels. There are no clear guidelines to support cessation efforts for non-cigarette (eg. bidi) and smokeless forms of tobacco use. No large-scale trials of tobacco cessation have been conducted among people with SMI in LMICs or identified implementation strategies which could work best in these settings, thus informing practice and policy in this area [35, 36].

The Smoking Cessation Intervention for Severe Mental Ill Health- South Asia (SCIMITAR-SA) programme focuses on including support for exclusive smokeless tobacco users (in addition to individuals who smoke, and those who use smokeless tobacco in conjunction with smoking products). Building on the expertise of the NIHR SCIMITAR and Global Health

Group ASTRA programmes that have pioneered approaches in this area[37, 38] we are developing a tobacco cessation intervention tailored to people with SMI in South Asian LMICs. We now need to test feasibility and refine the proposed intervention before evaluating it in a full scale trial.

This feasibility RCT will establish an evidence base for SCIMITAR-SA, laying the groundwork for a future definitive randomized trial for South Asian individuals with SMI who use tobacco. It will also refine the trial protocol before a full-scale, multi-country study, ensuring feasibility and scalability in real-world settings besides, identifying logistical and methodological challenges across diverse contexts. It will also identify key uncertainties allowing necessary adjustments to strengthen the full trial and optimum utilization of resources [39–41].

2. Trial research questions

We aim to conduct a feasibility randomised controlled trial to inform the design and implementation of a future definitive trial for tobacco cessation in mental health settings in Bangladesh, India and Pakistan. The following research questions will be addressed:

1. Is it feasible to identify individuals with SMI who use tobacco, recruit them to a trial of tobacco cessation and retain them for up to seven months in a trial conducted in mental health facilities?

2. Is it feasible to collect data for the primary (seven months biochemically-verified continuous abstinence) and secondary outcomes of a potential full scale trial and for the economic evaluation?

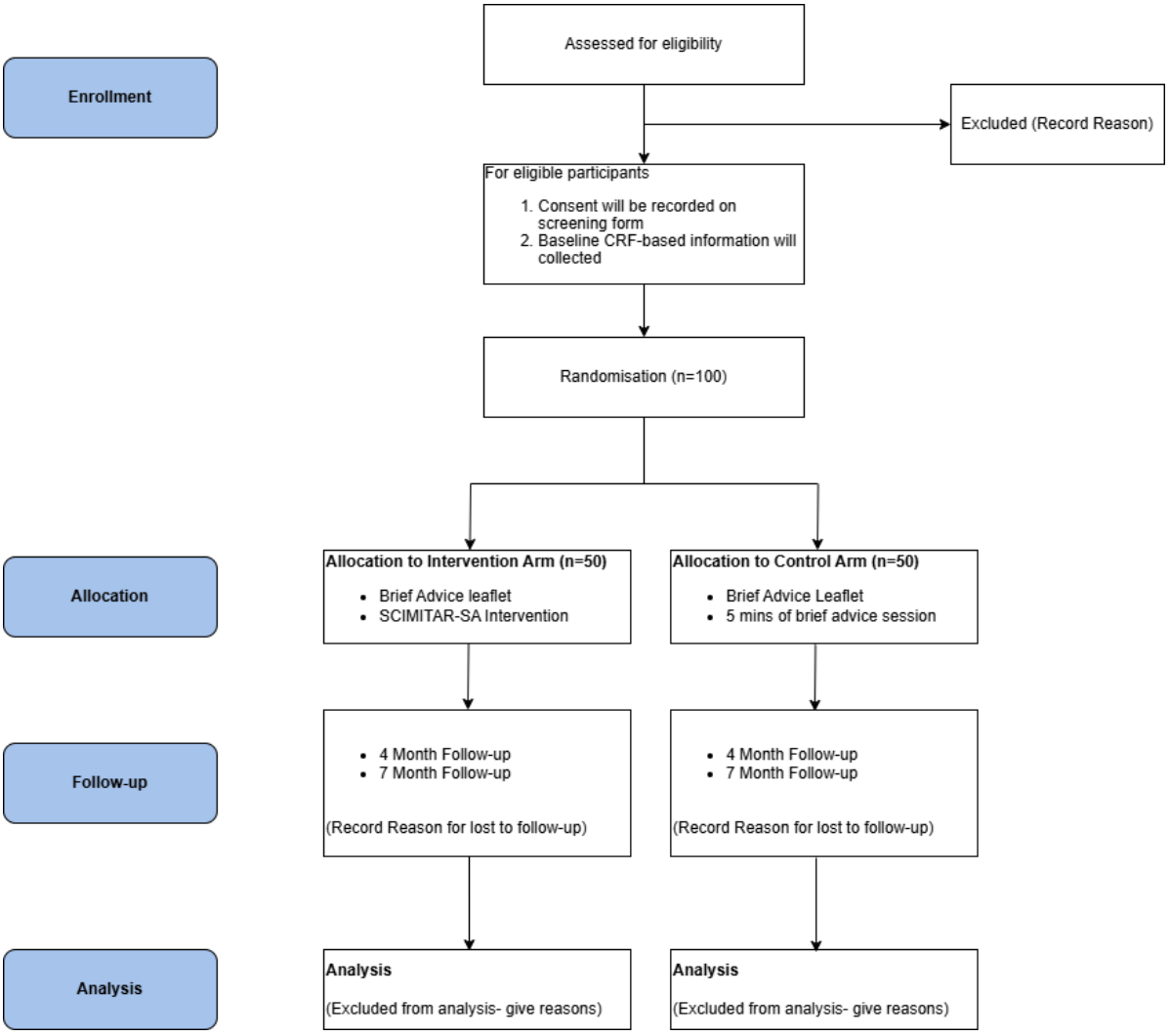
3. Is it feasible to deliver SCIMITAR-SA in mental health facilities?

4. Is SCIMITAR-SA acceptable to participants, and feasible to deliver by tobacco dependence advisors and mental health facility staff?

3. Trial Design

We will conduct a two arm, parallel group, individually randomised, multi-country, multicentre, external pilot trial of the SCIMITAR-SA intervention, with an embedded qualitative process evaluation.

Figure 1: Trial flow diagram



4. Trial outcomes

We will report on the following feasibility outcome measures to address the research

questions for the trial:

i) Recruitment, retention, acceptability

1. Recruitment rates, assessed as the number of participants eligible, consenting and randomised, out of those screened.
2. Reasons for ineligibility/non-participation/non-consent of participants where provided.
3. Retention in the study, assessed as the number of participants randomised who are successfully followed up at four and seven months 4 post randomisation with details of withdrawals and loss to follow-up where available.

ii) Intervention Delivery

1. Retention in intervention reported as the total number of sessions attended out of the total number of sessions offered.
2. Qualitative feedback from research staff, health facility staff and trial participants on trial processes.
3. Qualitative feedback from tobacco dependence advisors, mental health facility staff and trial participants on delivery, implementation and receipt of the SCIMITAR-SA intervention.

iii) Data completion

1. Completeness of data for baseline assessments, outcome measures for the definitive trial and data on health resource use at 4 and 7 months.
2. Data completeness of self-reported and biochemically verified continuous abstinence from all tobacco products at 7 months.

5. Settings and facilities

The feasibility trial will be conducted in selected tertiary care hospitals/mental health facilities providing outpatient and community mental health services in Dhaka and Bogura , Bangladesh; Bangalore , India and Karachi and Rawalpindi, Pakistan. The trial facilities have been selected based on the availability of research infrastructure, mental healthcare staff to deliver the intervention, engagement and support of senior managers, and sufficient patients diagnosed with SMI attending the health facilities. There will be six facilities that will be engaged in the feasibility trial.

1. Department of Psychiatry, Civil Hospital Karachi (CHK), Dow University of Health Sciences
2. Karwan-e-Hayat (KEH), Karachi, Pakistan
3. Institute of Psychiatry (IOP), Benazir Bhutto Hospital, Rawalpindi, Pakistan
4. National Institute of Mental Health (NIMH), Dhaka, Bangladesh
5. Thengamara Mohila Sabuj Sangha (TMSS) Medical College, Bogura, Bangladesh
6. National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India

**These facilities will be reviewed further to progress towards the potential full scale trial.*

5.1 Recruitment sites in Pakistan

In Pakistan, the three recruitment recruitment facilities are based in Rawalpindi City (Punjab province) and Karachi (Sindh province). The Rawalpindi site consists of the Institute of Psychiatry at Benazir Bhutto Hospital, Rawalpindi [43]. This specialised mental health facility offers comprehensive psychiatric care, psychological services, and mental health

training.

There are two recruitment facilities based in Karachi. This includes the Department of Psychiatry, Civil Hospital Karachi, Dow University of Health Sciences and Karwan-e-Hayat Karachi[44]. The Department of Psychiatry at Civil Hospital Karachi[45] provides comprehensive, specialised psychiatric inpatient, outpatient and acute care. It is located in the central part of Karachi and caters to patients from urban and rural areas alike. Karwan-e-Hayat operates one of the largest psychiatric inpatient facilities in Karachi. Its Psychiatric Care and Rehabilitation Centre in Keamari houses a 100-bed inpatient unit offering treatment and rehabilitation services.

Recruitment sites in Bangladesh

In Bangladesh there will be two recruitment facilities located in Dhaka and Bogura. The National Institute of Mental Health and Hospital (NIMH) in Dhaka is a 200-bed tertiary-level psychiatric hospital operated under the Ministry of Health and Family Welfare (MOHFW), situated in the Sher-E-Bangla Nagar area. As the largest teaching-focused psychiatric facility in the country, NIMH offers specialised care for mental health conditions and functions as a center for research, training, and policy development [46, 47].

Thengamara Mohila Sabuj Sangha (TMSS) Medical College, Bogura, Bangladesh - TMSS Medical College and Rafatullah Community Hospital (TMC & RCH) in Bogura is an 850-bed tertiary hospital established to provide affordable, comprehensive medical and surgical services, including specialised care and emergency management, to the rural communities of northern Bangladesh. This institution also supports the clinical education of medical students [48].

5.2 Recruitment sites in India

In India, the National Institute of Mental Health and Neurosciences (NIMHANS), in Bangalore, Karnataka will be the study site for the trial. NIMHANS is a 1098-bed tertiary care institute for patient care, academic pursuit and research in the field of mental health and neurosciences[49].

Each of the above-mentioned facilities is either a direct partner or has strong research collaborations with our country partners in South Asia. Two of the above mentioned facilities (IOP and NIMHANS) have previously delivered the IMPACT 4S intervention[50], thus bringing a rich experience of conducting tobacco cessation trials in real-world settings. The additional facilities in Bangladesh and in Pakistan are similarly well-placed to support our research. Their inclusion will not only ensure wider geographical representation but also feed into plans for capacity building in tobacco cessation in South Asia.

6. Trial participants

The trial aims to recruit adult users of smoked **and/or** smokeless tobacco with a confirmed diagnosis of one or more SMI, who are willing to quit all forms of tobacco use. Participants will be recruited from patients seeking outpatient care at one of the six participating mental health facilities in Bangladesh, India and Pakistan.

6.1. Eligibility

Individuals who meet all of the inclusion criteria will be considered eligible for trial participation. Eligible and consenting patients will be recruited into the trial.

Inclusion criteria

- Adults (≥18 years) receiving outpatient mental healthcare at any of the

aforementioned trial facilities.

- Confirmed diagnosis of one or more SMI (i.e. schizophrenia, schizoaffective disorder, bipolar affective disorder, psychosis, severe depression with or without psychosis) by healthcare staff.
- Self-reported daily users of smoked products (including cigarettes, bidis, waterpipe) and/or users of smokeless forms of tobacco (*such as betel-quid, naswar, gutkha, khaini, zarda, paan, pan-masala, gul, shada pata*) for the last six months (daily or non-daily) and >=25 days in the last month[50].
- Confirmed to be clinically stable* by the healthcare staff at the time of recruitment and able to provide informed consent.
- One member per household is eligible for trial participation (to avoid contamination).
- Willing to quit all forms of tobacco use in the next 30 days and able to attend up to seven face-to-face counselling sessions with trained mental healthcare staff.
- Living within the catchment area for the study facility that is defined by the district/administrative jurisdiction** in respective countries.

**Patients will be considered clinically stable based on the assessment conducted by the treating clinician (Psychiatrist), with less than 25% change in the dosage of the medication and no administration of Electroconvulsive Therapy (ECT) or other neurostimulation treatments within the preceding three months.*

***The trial facilities will maintain a record of patients with their consent, including their addresses and contact information, who will be excluded from the feasibility trial due to residing outside the district or administrative jurisdiction in which the trial facilities are located. This record will be reviewed prior to initiating the main effectiveness trial and will serve as a reference for reassessing and refining the eligibility criteria for inclusion/exclusion moving forward.*

Exclusion criteria

This is a pragmatic trial and therefore criteria for exclusion are minimal.

- Self reported use of Electronic Nicotine Delivery Systems and Electronic Non-Nicotine Delivery Systems (ENDS/ENNDS), Heated Tobacco Products (also known as Heat-Not-Burn products) (HTP/HNBs), noncombustible nicotine products, known as Oral Nicotine Pouches (ONPs) and/or in combination with either smoking and/or smokeless forms of tobacco in the past 30 days.***
- Individuals with comorbid drug or alcohol use disorder (as ascertained by the SCIMITAR-SA research team), personality disorders, eating disorders, autism spectrum disorders, disorders of intellectual development, Post Traumatic Stress Disorder (PTSD) as ascertained clinically by the treating psychiatrist.
- Individuals who have received any pharmacotherapy (including nicotine replacement therapy) or psychosocial intervention except brief advice for tobacco cessation in the past 30 days.
- Dual users who are willing to quit only one form of tobacco use/ product.

****Individuals using e-cigarettes, vapes, or heat-not-burn products may require different cessation*

interventions than those using conventional forms of tobacco (Cigarette, bidis, cigars, khaini zarda, paan masala, etc.) due to the different delivery methods, nicotine dependence, chemical compositions, and psychological aspects associated with each product. These products may be perceived as less harmful, or safer potentially leading to continued use or dual use with cigarettes or other forms of tobacco, making cessation more challenging. Further, social influences such as peer pressure, social norms, and marketing tactics can influence the use of e-cigarettes, and may require specific interventions to address these factors. User experience in terms of the availability of various flavours in e-cigarettes may appeal to different individuals and could be a factor in initiating or maintaining use.

7. Sample Size

We will recruit 100 participants across the six facilities (10 from the two Karachi facilities and 20 from the remaining four) which will allow estimation of recruitment (50%) and retention (80%) to within a 7% and 8% margin of error.

8. Details of intervention and control arms

8.1. Very Brief Advice (Control arm)

We will provide Very Brief Advice (VBA), along with a self-help educational information leaflet on tobacco cessation as usual care. VBA is an evidence-based intervention designed to increase quit attempts among people who smoke[51]. VBA was developed by the National Centre for Smoking Cessation Training (NCSCT) in the United Kingdom (UK) (www.ncsct.co.uk/VBA) and involves three steps:

1. "Ask" patients about their tobacco use,
2. "Advise" them about quitting, and
3. "Act" by supporting them with making a quit attempt using available cessation support.

VBA has been adapted from the ASTRA[52] smokeless tobacco pilot trial where VBA was provided as a standard provision for participants receiving neither of the active intervention (NRT or BISCA). It will include a brief conversation on tobacco use status (smoked and/or smokeless), advice to stop using tobacco, and providing a self-help leaflet[53].

VBA will be delivered by health professionals at recruiting sites in an interaction lasting up to 1 minute to all the patients attending the OPD. Participants will receive a VBA self-help information leaflet with written advice to take home from the health professionals. VBA will fulfil the duty of care responsibility but it is less intense and hence less likely to dilute the SCIMITAR-SA intervention effect. Guidance on VBA will be provided as part of the trial orientation/setup/initiation to all health professionals involved in the treatment and management of SMI patients at the study sites. VBA has been shown to increase the frequency and success of quit attempts when compared to no intervention[51].

8.2. SCIMITAR-SA (Intervention arm)

In addition to VBA, those in the intervention arm will also receive the SCIMITAR-SA intervention. The behavioural support offered in the SCIMITAR-SA intervention will comprise up to seven one-to-one counselling sessions which will range between 20 and 30 minutes each, delivered over a period of 6-7 weeks alongside encouragement/guidance to use Nicotine Replacement Therapy (NRT) where available/ affordable.

The SCIMITAR-SA intervention will allow for two pre-quit sessions, a quit day session and weekly follow up to the 4 week post-quit point (feasibility of the number of sessions and mode of delivery will be informed by the feasibility trial) with trained tobacco dependence advisors (TDA). In line with the findings of (UK) SCIMITAR the sessions may need to be split

into shorter, more frequent interventions if needed to meet the needs of the patients, and delivery could extend beyond the 6-7 weeks if the patient takes a prolonged period of time to set the quit date. (allowing for the 30 day window from first interaction to quit day). The splitting of sessions will most likely be relevant to the 2 x pre quit session. Therefore, we could have a provision of 4 x pre quit sessions of a shorter duration.

The SCIMITAR-SA intervention will be delivered by the TDAs, who are healthcare workers experienced in caring for mental health patients (specialist or non-specialist) and who receive the SCIMITAR-SA training. There will be supervisors to oversee intervention delivery, and to provide the necessary ongoing support for those who deliver SCIMITAR-SA. This will be built in by training of trainers. There will be catch up meetings between the TDAs and the behaviour change experts (who will be delivering the training on SCIMITAR-SA intervention to respective country research teams as well) to discuss any challenges and iron out teething problems.

The participant will be prompted to set a quit date within 30 days of enrollment. Each session is designed to be delivered face-to-face until the quit day session, beyond which the participants would be encouraged to meet face-to-face by the advisor but there would be a fallback option of remote counselling (via platforms such as Call/WhatsApp and/or Zoom) for those patients who are unable to attend face-to-face.

The intervention is designed to be participant centred with the TDA guiding and supporting the process. Participants will be encouraged to articulate their reasons for quitting, set their own quit date, identify situations that could lead to tobacco use and develop coping strategies to manage those situations. The TDA will work with the participant to provide information relevant to the participant, review success and challenges and reinforce key

messages during the sessions. Sessions 1 & 2 are designed as pre-quit that help prepare the participant for their quit attempt; their target quit date will fall within the next two weeks aligning with Session 3 (quit day). Caregiver involvement will be limited to logistic support only, so as to ensure regular follow ups. Caregivers will not actively participate in the intervention but participating patients will be encouraged to seek support from their caregivers as, when and with whichever task they feel appropriate.

Participating patients will be compensated for their travel and time to the study site for research purposes. Each participant will receive a fixed travel allowance BDT 1000 (Bangladesh) /INR 500 (India) / PKR 1500 (Pakistan) per visit.

The SCIMITAR-SA intervention is primarily a behavioural support programme. Cessation aids, such as NRT, will not be provided as part of the trial intervention. However, if a participant specifically requests a cessation aid such as NRT, the TDA will provide appropriate advice and guidance on availability of NRT at the facility (where applicable). This includes guidance on the types of NRT available, recommended usage, dosing (quantity and strength), frequency, and potential side effects.

If a participant obtains NRT through routine care at the facility or purchases it over the counter during the course of the trial, this information will be recorded. Details regarding the use of NRT will be captured via Case Report Forms (CRFs) at the 4-month and 7-month follow-up assessments.

8.2.1. Intervention Materials

The materials used in the SCIMITAR-SA intervention will comprise of the following:

1. ***Tobacco Dependence Advisor Pre-course reading pack***

The TDA Pre-course Reading Pack and a training slide set with notes which align to the flipbooks will serve as a reference for the TDA and will contain an in-depth description about the aim of each session, the content of the session, including the activities, discussion points and the information that will be delivered to the trial participants. Each session component contained in the pre-course reading pack will be referenced to the corresponding slide number from the flipbooks, which are designed to prompt the TDA and ensure consistency with the programme. The pack will also include skills and competencies required/useful at each stage of the patients' quit journey, which will also serve as a reminder of what was covered in the training.

2. Flipbooks

Four patient-facing flipbooks will be developed. This set of four flipbooks will be further tailored for cultural context to include smokeless tobacco cessation and gender (male and female). TDA will be trained on providing behavioural support to SMI patients in their facilities using the flipbooks that will be translated in Bangla/Urdu/Kannada and culturally tailored for Bangladesh/Pakistan/India respectively. The four flipbooks align with four different stages of the patient quit journey, as follows:

- Flipbook 1: Committing to quit
- Flipbook 2: Preparation to quit
- Flipbook 3: Quit day
- Flipbook 4: Life after quitting

The flipbook(s) will be used by the TDA to deliver key messages for quitting tobacco use (smoked/smokeless) through interactive graphics and photo images placed on the front (pages facing the participant), with text on the back to remind tobacco dependence

advisors on the purpose of each slide (pages facing the tobacco dependence advisor).

Patient Record Card (PRC):

The Patient Record Card (PRC) is designed to help the TDA capture key information provided by the participants in the intervention arm; for example, their reasons for stopping tobacco use, what they think will be better for them if they stop using tobacco, usual tobacco use patterns and triggers to use and how they will address these once they stop using tobacco.

The information for the PRC will be collected and completed either during the session or immediately after the session so the TDA can accurately capture the participant's story and be able to refer back to the discussions with the patient with accuracy at subsequent appointments.

VBA educational information leaflets will be handed over to all trial patients.

8.2.2. Intervention adaptation

The SCIMITAR-SA intervention has been adapted from the Standard Treatment Programme offered by the NCSCT[54], and incorporates learning from two trials of tobacco cessation conducted previously in south Asia: IMPACT 4S intervention tested in SMI patients [50] and (ASTRA) tested in people using smokeless tobacco [38]. Further, the SCIMITAR-SA intervention is extended to include support for individuals who use dual forms of tobacco. The intervention adaptation process was further supplemented by the CEI workshops for cultural tailoring and pretesting with SMI people who use tobacco and staff who will be delivering the intervention. A series of stakeholder workshops were held across Bangladesh, India and Pakistan that further informed the tailoring of intervention content,

its delivery, and scheduling to country-specific contexts. Additionally, the SCIMITAR-SA will prioritise a "patient-centred" approach by involving participants in decision-making, tailoring the intervention to their needs (SMI population), preferences, encouraging feedback, and offering autonomy in choosing cessation strategies that align with their lifestyle and cultural values.

8.2.3. Training of SCIMITAR-SA Tobacco Dependence Advisors

The TDAs will be trained using the above adapted intervention package to deliver the SCIMITAR-SA intervention. The recruited staff who will be delivering the intervention will receive an online training to deliver the SCIMITAR-SA intervention. The training process will comprise of the following steps:

1) Pre course reading

2) 3 online taught sessions

3) Practice developing sessions for (fictional) case studies

4) Observed role play delivering sessions

5) Final online presentation of case studies and trainer feedback

The SCIMITAR-SA mental healthcare workers will have experience of working with people with an SMI, similar qualifications, and training to the existing mental health staff in the routine services.

The training sessions will be carried out by behaviour change experts and will cover the sequential steps as described in the above mentioned four flipbooks through interactive

and engaging formats including presentations, roleplays, group discussions and case studies.

The TDAs will be given additional time of seven days post training for gaining familiarity with the pre course reading. TDAs will spend some time reviewing the training to build a comprehensive understanding of the content and delivery of the intervention. During the intervention delivery period, TDAs will also receive ongoing support and supervision from the experienced technical partners.

Some reflective role plays will also be incorporated into the training process. The TDAs could possibly double up for the first few sessions to gain confidence and if needed will also receive some peer observational feedback.

9. Screening Process

When a patient visits the outpatient department at a trial facility, the treating mental healthcare clinician (psychiatrists, psychologists and postgraduate psychiatry trainees, consultants or senior residents) will identify patients who are tobacco users and will deliver VBA. Those patients who are diagnosed with a SMI will be referred by the treating clinician to the study research assistant for screening.

9.1 Screening participants for trial eligibility

Before screening, the RA will ask whether the patient is willing to be screened. For those that are willing, the Research Assistant (RA) will assess the eligibility of the patient for the trial using the inclusion/exclusion criteria.

Individuals who meet the eligibility criteria will be invited to participate in the study. They will receive a translated (Bangla/Urdu/Kannada/Hindi) information sheet providing information on study purpose, details of intervention and control arms, frequency and

timing of data collection; the potential benefits and risks of trial participation, information on privacy and confidentiality of the participants' data, and how it will be processed; and participant's rights, including voluntary nature of the trial and the right to discontinue participation at any time in the trial without any consequences. The information sheet will also provide contact details of a research team member in case they wish to seek more information or clarity. In the circumstance that a potential participant cannot read or write, the researcher will provide facilitation by reading out the information sheet to both the participant and the caregiver (if present) and will respond to their queries.

9.2. Informed consent

Participation in the SCIMITAR-SA trial will require written, informed consent from the eligible individual. Informed consent will be obtained before any study specific baseline assessments are carried out. The RA will provide and explain the Participant Information Sheet (PIS) to the eligible patients. Once the participants are familiar with the intent and purposes of the study, and have clarified their queries with the researcher, those willing to participate will be invited by a trained research team member to complete an informed consent form. Those providing informed consent will have baseline data collected before being recruited into the trial.

Consenting individuals will provide their full name and signature or a thumb impression in the presence of an impartial witness (if they are unable to read/write) along with his signature as allowable according to the ethics requirements in Bangladesh, India and Pakistan. A copy of the consent form will be securely stored in a locked filing cabinet at the trial facility(s) in respective countries. Each study participant will get a copy of their signed informed consent form, and the information sheet to take home for their records.

The eligible participants will be allowed a maximum of one week period to provide their informed consent to participate in the trial. If the eligible patient provides informed

consent on the spot or same day and is not exhausted- he/she will be administered the baseline form on the same day. If the baseline data is completely collected, then the patient will be randomised on-the-spot. The RA will call the focal point at the central research office and request randomisation. If the patient is allocated to the intervention arm, then the Trial Coordinator will inform the TDA about the participant's details and scheduling sessions. Thereafter TDA will take over the intervention related procedures.

If the patient wants to discuss with family members or caregiver or wants to take some time before committing, the RA will inform the patient that the trial team is still here and the patient can take up to one week to think, discuss, decide and get back to the trial team with a decision, the RA will give a window of one week for a decision and will also call the patient in between (3 to 4 calls on alternate days and times in a week).

If the patient wishes to consent later (not on the day of screening), the RA will arrange for the patient to visit the clinic again to obtain informed consent and collect baseline information. Meanwhile the RA will make a note of the patient in the screening log (hard copy). Individuals who are eligible but decline to consent will be asked their reason(s) for declining.

Those recruited will be asked to attend the facility at both four months and seven months after randomisation in order to complete follow-up interviews.

9.3 Screening records

Each screened individual will be assigned a unique study ID number. The following anonymised individual information will be collected: age, gender, SMI diagnosis, current tobacco use status, eligibility criteria, and time taken for screening. For those identified as eligible but refuse to participate/ do not consent to participate, reasons will be recorded where available.

All non-identifiable screening data will be collected in the study database (REDCap)[55].

Any personally identifiable information of eligible and consented patients including their name and contact details will be securely stored in site based logs only along with their unique study ID.

11. Randomisation and Trial Arm Allocation

Random allocation will be managed using consecutively-numbered sealed opaque envelopes. A statistician at YTU will generate a random allocation schedule (using Stata v18 or later) using stratified (by site and smoker type [smoked only, smokeless only & dual]) block randomisation with varying block sizes of 2 and 4. Each allocation will be copied onto an individual card and sealed in opaque envelopes (prepared by YTU) labelled sequentially in accordance with the schedule. The envelopes will be transported to the trial sites in advance, where they will be securely stored in a locked cabinet accessible only to authorized staff at a central research office in each country. After completing the baseline data collection the RA with phone a trial coordinator based at a central research office. The coordinator will open the next envelope and will inform the Research Assistant (RA) of the allocation. The RA will record the allocation at the end of the baseline e-CRF(section 11). The trial coordinator will also inform the TDA about the allocated participants in the intervention arm with their details (for example names, contact details which can be taken from RAs hard copy log) so that they can schedule the interventions sessions.

12. Blinding

Given the nature of the intervention, it is not feasible to blind participants or healthcare and research staff from knowing the arm allocation. The RA will phone the central research office and request the trial coordinator for randomisation. The trial coordinator will inform the RA of the allocation. The research assistants (RA) will be aware of the participant's allocation to either intervention or control arm after completing baseline. The RA will

record the allocation on the baseline e-CRF and the trial coordinator will maintain the randomisation log. The RA will inform the patient of their allocation. The trial coordinator will inform the TDA about the participants (along with trial ID and contact details) who are allocated to the intervention arm and request them to schedule theirSCIMITAR-SA intervention sessions.

Please note that although blinding of participants and researchers is not feasible in this trial, we will ensure objective verification of the primary outcome i.e, cessation status, by employing biochemical verification. Saliva samples will be collected and analysed for cotinine levels and anabasine levels (as applicable). Cotinine and anabasine levels are used as reliable biomarkers to assess tobacco use and abstinence. Cotinine, a metabolite of nicotine, is a key indicator of nicotine exposure, while anabasine, a tobacco alkaloid, can help differentiate between tobacco use and nicotine replacement therapy.

13. Baseline and follow-up data collection

Data will be collected from participants with/without the support of caregiver(s), in-person at baseline (after recording consent, and prior to randomisation), and at four and seven months post-randomisation.

Following randomisation, the participants in the intervention arm will be allowed a grace period of 30 days to set their first quit date. Follow-up outcome measures will be assessed four and seven months post randomisation. The data will be collected by trained research assistants using an online survey tool (REDCap)[56] on electronic tablets.

The information to be collected at each follow-up, is summarised in Table 1.

Table 1. Baseline and follow up assessments for the feasibility trial

	Measurement/data collection	Baseline	4 month follow-up	7 month follow-up
1	Socio-demographic and household information	X		
2	History of tobacco use and attempts to quit	X		
3	Quick SCID (module A and B only)	X		
4	BPRS	X		X
5	Self-reported abstinence from tobacco products (past 7-days and since quit date)		X	X
6	Salivary cotinine and anabasine (for biochemical verification)			X
7	Nicotine dependence and urge to use tobacco	X	X	X
8	Quitting intentions, motivations and behaviour	X	X	X
9	Health-related quality of life	X	X	X
10	Mental and physical health	X	X	X
11	Health service utilisation	X	X	X
12	Physical measurements – height and weight,	X	X	X

	waist circumference Vital signs (Blood pressure, heart rate)			
13	Researcher meetings to discuss trial processes	X	X	X
14	Interviews with mental health staff and managers to discuss trial processes and SCIMITAR-SA implementation		x	
15	Focus group discussions with TDAs to discuss SCIMITAR-SA delivery, implementation and administration		x	
16	Interviews with dual users to gather feedback on trial processes and the SCIMITAR-SA intervention		X	

13.1. General Information and psychiatric measures (baseline and seven months)

Data will be collected on diagnosis of severe mental illness (confirmed from Quick SCID[57] (at baseline only), severity of psychiatric symptoms by using Brief Psychiatric Rating Scale[58] (BPRS, at baseline and seven months).

13.2. Sociodemographic data (baseline)

Data will be collected on socio-demographic variables (age, gender, education, occupation, marital status), and on the possession of a number of household items to determine socio-economic status following items from ASTRA trial.[59]

13.3. History of tobacco use and past quit attempts (baseline)

Data will be collected from the trial participants with/without the support of caregiver(s) on history of tobacco use (age of initiation, frequency and duration of use, type of tobacco products used, any quit attempts made in the past, reasons for quit attempts, etc) using items from the ASTRA [59] , Quit4TB Trial and IMPACT 4S Trial[50].

13.4. Tobacco use status (four and seven months)

Self-reported or with/without the support of caregiver(s) tobacco use status since the quit date, and in the past week (7 days) will be assessed at four and seven month follow-ups using the tobacco use questions from ASTRA trial[59]. Also, use of any nicotine products like electronic cigarettes or nicotine pouches will also be recorded.

13.5. Saliva sample (seven months)

Salivary samples will be collected at seven months post randomisation only. For biochemical analysis, a saliva sample with volume 0.5 mL/0.12 mL (optimum/minimum) from the trial participants will be collected using a Salivette. Saliva samples will be taken no earlier than 30 minutes after eating, drinking or taking medication. The participants will be asked to think about their favourite food to help them salivate prior to putting a swab in their mouth. They will be asked to hold the Salivette at the rim of the suspended insert and remove the stopper. Thereafter, place the swab contained within, without using their fingers, under the tongue by tipping up when close to the mouth. Do not swallow and leave the swab until it is 'soggy'. This can take up to five minutes. Return swab directly from the mouth without using your fingers into and close firmly with the stopper. Return the suspended insert into the centrifugation vessel. The research teams will ensure that the details are entered on the label of the Salivette appropriately and each sample collected

will not be labeled with the participant's personal information, but instead the assigned unique ID (unique screening ID) will be used, preventing anyone from directly linking the sample back to the individual it came from. The Salivette will be placed into a padded envelope, cover will be removed to 'sticky tape' and sealed securely. Thereafter, the sample will be posted/couriered to an accredited laboratory within the respective country or biochemical analysis for salivary cotinine or to a specialist laboratory (ACM Global Laboratories, York, UK)[60] as approved by the ethics committee. The salivettes will be procured by University of York from ACM Global Laboratories and thereafter shipped to the partner countries.

We will operationalise the biochemically verified continuous abstinence from all tobacco products using the global Russell Standard of sustained and verified quitting[42]. For those who report using tobacco products on no more than 5 occasions during the cessation period** at the seven-month follow-up, biochemical verification will be carried out through salivary cotinine testing through LC-MS (ACM Global Laboratories, UK for Bangladesh and Pakistan & Laboratory of the Department of Clinical Psychopharmacology and Neurotoxicology for India). Cotinine level <15 ng/ml will be used to identify biochemically verified abstinence), whereas those who self-report continuous abstinence but have cotinine levels above the threshold will be identified as tobacco users. The saliva samples will also be used to detect Anabasine which will be a biomarker for participants reporting quit but using nicotine replacement therapy (NRT).

***Cessation period refers to the duration between the target quit date (for the intervention group) or 30 days post-randomisation (for the control group) and the seven month follow up time point.*

13.5.1. Sample storage, labelling and shipping

Although cotinine has been shown to be stable, these samples are not sterile and therefore will be frozen at -20C or cooled at 4C after collection as samples will not be shipped immediately to ACM Global Laboratories after collection. Human saliva samples should be received 2 months prior to their validated expiry. For cotinine analysis, saliva samples are stable when stored frozen at -20 C for 406 days (13 months) post collection (1.0 - 750 ng/ml). As the lab only has two weeks ambient stability established, it is suggested to freeze the samples and then ship ambiently to save on the costs. All collected samples will be appropriately labelled along with date and time of sample collection. Since the saliva samples will be collected using a Salivette, therefore these will not be frozen during transit. The respective country teams will send suitable declarations of safety and customs forms with the samples. The samples will be described as non hazardous human saliva samples that have no commercial value and will be used for research purposes only. The research teams will use IATA grade large containers and shipping boxes for sending more than a couple of samples. The boxes will be correctly labelled with the UN3373 symbol and as 'Biological substance Category B'.

The trial facilities in Bangladesh and Pakistan will ship the saliva samples to ACM Global Laboratories, York, while the study site in India will undertake the sample analysis within the country as per the ACM, UK guidelines for sample collection and analysis.

Anabasine levels: Anabasine (minor alkaloid) will be used as a biomarker for participants self-reporting quit but using nicotine replacement therapy NRT. It will help us differentiate between active tobacco users and those using NRT, as NRT products typically contain only nicotine and not the minor alkaloids like anabasine. The saliva samples from trial participants will be used to detect anabasine. The ACM labs and Laboratory of the

Department of Clinical Psychopharmacology and Neurotoxicology, NIMHANS in India) will perform this assay on all saliva samples collected from participants who will self-report to have quit tobacco.

13.4.2. Sample analysis

The salivary samples collected from the participants will be analysed to assess salivary cotinine and anabasine levels at the respective labs (ACM Global Labs for Bangladesh and Pakistan and Laboratory of the Department of Clinical Psychopharmacology and Neurotoxicology, NIMHANS in India) using Liquid Chromatography–Tandem Mass Spectrometry (LC-MS/MS).

13.6. Nicotine dependence and urge to use tobacco (baseline, four and seven months)

An adapted version of Heaviness of Smoking Index (HSI) adapted from ASTRA trial[59] , a six point scale, will be used to assess nicotine dependence and urge to use tobacco. The Mood and Physical Symptoms Scale (MPSS)[61] will also be administered. The scale assesses withdrawal symptoms including anxiety, depression, irritability, restlessness, hunger, concentration and sleep.

13.7. Quitting tobacco intentions, motivations and behaviors (baseline, four and seven months)

The motivation to quit (MTQ) questionnaire[62] will be used to measure motivation to quit tobacco use. Questions from the ASTRA trial[59] will also be used to assess tobacco cessation intentions, motivations and behaviours.

13.8. Health Related quality of life (baseline, four and seven months)

The EQ-5D-5L[63] will be used to measure health-related quality of life (HRQoL). EQ-5D is a

standardised measure of health status developed by the EuroQol Group in order to provide a simple, generic measure of health for clinical and economic appraisal, where health is characterised on five dimensions (mobility, self-care, ability to undertake usual activities, pain/discomfort, anxiety/ depression).

13.9. Mental and physical health (baseline, four and seven months)

PHQ-9[64] will be used to measure depressive symptoms. This nine item questionnaire is scored from 0 to 27, and a higher score indicates more severe depressive symptoms. The GAD-7[65] will be used for measuring anxiety. This seven-item instrument is scored from 0 to 21, with a higher score indicating more severe anxiety. The SF-12[66] which consists of two subscales: a physical health component and a mental health component will also be administered. Both components are scored from 0 to 100, with 0 indicating the lowest level of health and 100 the highest level of health measured by the scale.

13.10. Health services use (baseline, four and seven months)

Participant use of health services and other tobacco cessation services outside the study will be assessed. A health service utilisation questionnaire previously used in some of our studies such as the ASTRA trial[59], the POTENTIAL trial[67], and the RESPIRE trial[68] will be adapted to the context of Bangladesh, Pakistan and India and used to collect number and type of contacts with doctors, hospital admissions, pharmacy visits and medication prescriptions for all participants. Information on contact with traditional healers, telephone quitlines or mCessation services, as well as out-of-pocket (OOP) expenditure, will also be recorded.

13.11. Physical body measurements (baseline, four and seven months)

Physical body measurements will include height and weight which will be measured by trained personnel according to the WHO protocol[69]. These will be used to calculate the body mass index.

Process for contacting patients for four months and seven months follow up: There will be a one-week window on either side for the follow-up to still be considered on time. If the follow-up occurs beyond this period, it will be recorded as having exceeded the window. After the feasibility trial, this will be reviewed to assess how often it happens, and adjustments will be made as needed before the main trial.

The RA will be contacting the participant for follow up one week before and for 3 weeks after the due date of follow up. The RA will make three phone calls per week at different times and on different days of the week to schedule the follow up with the participant before being declared as missing. If data is missing for the four month follow-up an attempt will still be made to obtain seven month follow-up data.

14. Measures to enhance participant retention

In order to enhance the retention of participants in the trial, the research team will focus on communication strategies to improve response to questionnaires, active participation of the participant during the intervention sessions/follow up, reimbursement of travel cost borne by the participants to visit the hospital for the consented research purpose. Further, to encourage participants to return to trial facilities for follow-up visits, we will be using multiple strategies for trial participants such as information leaflets, newsletters, careful scheduling of intervention delivery/follow up session(s) in terms of day, date and time to avoid inconvenience and added burden of a hospital visit.

The participants in both study arms will be asked to inform the trial team of any relevant changes, such as plans to relocate or changes in contact details. The RA will maintain regular check-ins with the trial participants of both arms before their due date of follow ups. Participants will be informed about upcoming follow-up activities ahead of time. These follow-up procedures, including communication frequency and method, will be applied consistently across both arms to ensure equal opportunity for reporting changes in status or adverse events. Locally translated information sheets will be provided to ensure participants clearly understand the expectations if they consent to participate in the trial.

15. Withdrawals

The participants will be free to withdraw consent and leave the trial at any time without giving a reason. Written information on who to contact if they wish to withdraw from the trial will be provided to all participants. They will be able to withdraw by letting any member of the research team know that they wish to do so. If a participant withdraws consent to participate, no further data will be collected from them. However, data collected up to the point of withdrawal will be retained and used in the analysis. In the case where removal of data is requested, all personally identifiable data will be destroyed and anonymised data will be retained and used in analysis as per GDPR regulations for research exemptions.

16. Reimbursement

Participants will not be offered any personal incentive for taking part in the trial. However, at every visit, each trial participant will receive reimbursement of actual travel cost and time incurred for each visit (for receiving intervention sessions and follow up(s), as applicable). Each participant will receive a fixed travel allowance BDT 1000 (Bangladesh)

/INR 500 (India) / PKR 1500 (Pakistan) per visit or will be reimbursed based on the receipt or documented proof of travel expense for that visit, such as official receipts or records from online ride-hailing applications (e.g., Careem or InDriver or Uber) as compensation for time spent. In case of the remote sessions after the quit date, participants could be paid the equivalent amount towards their time-costs, excluding the amount generally spent on travel to the institutions. The amount of reimbursement will be reviewed by the local/National Ethics Review Boards as per local prerequisites.

17. Statistical analysis

No formal statistical comparisons will be undertaken. Continuous measures will be reported as means and standard deviations (or medians and interquartile range where there is considerable skew) while categorical data will be reported as counts and percentages. A CONSORT diagram[70] will be constructed to show the flow of participants through the study and detail the number of people: screened, recruited, receiving their allocated treatment, and attending follow-ups.

The number screened, eligible, consenting and recruited will be summarised with reasons for ineligibility and non-consent given where available. For participants in the intervention arm, session attendance will be summarised. The recruitment and retention rates by trial arm will be calculated with 95% confidence intervals (CIs). For each outcome measure, data completion rates will be presented by trial arm at baseline and for each follow-up endpoint. The number of withdrawals from the study and/or the intervention will be given with reasons where available. Adverse events will be summarised descriptively. All statistical analysis will be performed in STATA (final version to be confirmed)[71].

The progression criteria table in section 30 (traffic light system) will be used to assess

progression to the main trial. If all criteria fall into the green category then the main trial will proceed. If at least one of the criteria falls in the red category then a major review will be undertaken; otherwise appropriate amendments will be made in order for the main trial to proceed.

18. Economic and quality of life data analysis

The analysis of health economic data will include a preliminary assessment of the use of healthcare resources and intervention costs. Costing will be undertaken using the national health systems perspective. Costs of delivering the interventions will be estimated by compiling the resources utilised for providing SCIMITAR-SA (including set-up, training, ongoing support and supervision) as well as those for providing the comparator (very brief advice). Relevant resources for providing the SCIMITAR-SA intervention include: human resource, materials/equipment, NRT(wherever applicable), costs for telephone/remote modes (wherever applicable), information-sheets, tobacco dependence advisor's resource for clients' records, flipbooks, and counselling sessions and overheads (if applicable). Relevant resources for the control intervention includes Very Brief Advice information leaflets. Very Brief Advice can be delivered in up to 1 minute[72]. In addition, healthcare resource utilisation of participants will be collected at baseline and follow-ups, using self-reported, comprehensive service-based questionnaires whose performance will be assessed in the external pilot and questionnaires revised in accordance with findings from this component of the study. In a full RCT the unit costs of these items will be derived from national costing sources and literature, however in the feasibility stage of the programme patient cost profiles will not be calculated due to the small numbers of cases.

Intervention costs, healthcare resource utilisation and EQ-5D-5L[63] will be reported

descriptively by trial arm. The overall assessment will include a commentary on the suitability/ feasibility of an economic evaluation alongside a definitive trial.

The purpose of the economic analysis at this stage is to test the feasibility of undertaking a full RCT and thus a full CEA will not be undertaken at this stage due to the small sample size.

19. Process evaluation

A qualitative process evaluation will be embedded within the feasibility trial and will focus on the (1) feasibility of the trial processes, and the (2) delivery of the SCIMITAR-SA intervention and VBA with a particular focus on barriers and drivers to delivery within the mental health facilities, and providing cessation support to dual users (which is a novel component of the intervention). These insights will inform refinements to study processes and strategies to support intervention delivery and implementation in the full trial.

19.1 Feasibility of trial processes

Throughout the feasibility trial, the research teams (research fellows and assistants) in each country will meet to reflect and discuss the trial processes. These meetings will be scheduled (1) when all recruitment is completed - to discuss inviting participants, explaining the study and securing consent, (2) when all intervention delivery is completed - to discuss delivering SCIMITAR-SA and VBA, supporting and monitoring the TDAs with scheduling, and (3) when all follow-up is completed - to discuss data collection including acceptability/feasibility of the tools, scheduling baseline and follow-up visits, reimbursing participants' travel costs for these visits and reflecting on the strategies to encourage retention to the trial. In each meeting, researchers will discuss how these trial processes have been conducted, and any hindering and enabling factors. The meetings will be

audio-recorded and notes taken. At the end of the feasibility trial the research teams from the three countries will come together in an online meeting to systematically discuss each of the trial processes and agree changes for the full trial.

The delivery of VBA and SCIMITAR-SA trial processes that are done by mental health staff (identifying eligible patients, referring them to the research team for further eligibility checks) will be explored within the interviews described in section 20.2.

To gather participants' perspectives on trial processes (e.g. recruitment, consent, scheduling, data collection, expenses) we will include some questions in the interviews with a sub-sample of dual users (described in section 20.2).

19.2. Delivery of the SCIMITAR-SA intervention

Once SCIMITAR-SA delivery is completed, all the TDAs in each participating institution will be asked to take part in a focus group discussion (FGD) (6 FGDs in total) to explore their experiences of (1) intervention delivery including supporting dual users to quit, adopting a participant-centred approach, (2) delivery within mental health outpatient services including time and space considerations and (3) administrative tasks such as scheduling and paying travel expenses for sessions. Further training, support and supervision needs will be identified.

At the end of the intervention period, 1-2 mental health staff member(s) responsible for identifying and referring eligible patients, delivering VBA and/or managerial oversight of the trial in the facility will be interviewed (6-12 in total). This is to gain feedback on these trial processes and/or to reflect on the delivery of the SCIMITAR-SA intervention and VBA within the facility systems including a preliminary review of the bespoke strategies employed to facilitate implementation.

A sub-sample of intervention arm participants who were dual users (2 per site, 12 in total) will be interviewed at 4-month follow-up to explore their experience of the SCIMITAR-SA trial processes and intervention. We are focusing on these participants because providing cessation support for both quitting smoking and smokeless tobacco is a novel component of the SCIMITAR-SA intervention and we need to understand acceptability and feasibility of implementation. Participants will be invited to take part in an interview and provided with an information sheet by the researcher who conducts their 4-month follow-up data collection. They can invite a caregiver to join them in the interview if they choose.

All interviews and FGDs will be conducted in the local language, face-to-face at the mental health facility using topic guides (to be provided as an appendix), digitally audio-recorded. Interviews will be up to 30 minutes duration and FGDs will be 60-90 minutes duration. All interview and FGD participants will provide informed consent prior to data collection commencing.

19.3. Analysis of process evaluation data

Interviews and FGDs will be digitally recorded, transcribed and then translated into English followed by analysis using the Framework Approach[73] which is designed to address applied programme questions. Microsoft Excel will aid data handling and analysis for this data.

20. Data Management

For the feasibility trial there will be two databases, one each at ARK & NIMHANS. The data manager at ARK (managing data for Bangladesh and Pakistan) and NIMHANS (managing data for India) will undertake data quality checks and only the principal investigators,

country investigators, trial coordinators (and/ or Research fellows), and researchers involved in the trial will have access to the identifiable data at any stage of the trial mainly to facilitate participant follow-up. For the purpose of baseline and follow-up data collection and conducting analyses, only the Unique IDs (UIDs) will be used, thereby ensuring anonymity of data.

20.1. Data handling and storage

The trial will follow the data storage archiving guidelines mentioned in the protocol (section 20.2). The researchers will assure that participants' anonymity is protected from unauthorised parties via the use of unique IDs in all data collection forms. Further to this, collected electronic/digital data will be stored separately from signed consent forms Each country site will hold data in accordance with both the General Data Protection Regulation[74], Data Protection Act 2018[75] and any additional country specific requirements.

All baseline and follow-up data will be captured electronically via electronic tablets using REDCap mobile app[55], which are secure electronic data capture systems and compliant with Good Clinical Practice. The ARK Foundation in Bangladesh will develop an electronic database that will be used to enter data by research staff in each participant country. The database will be stored in a secure REDCap server[55] maintained by ARK Foundation (for Bangladesh and Pakistan) and NIMHANS (for India). Data will be shared by ARK and NIMHANS with the University of York for the purposes of statistical analysis and ongoing reporting during the study. ARK and NIMHANS will provide all necessary support in this regard. Respective site teams will have access to their own data only. The Lab data will be

completed in a pre-defined Excel template, which will be password-protected and then submitted to YTU securely.

Qualitative interview and FGD data will be anonymized and linked with the trial ID (for participants) before transcription and translation for analysis. Digital recordings of the interviews and FGDs will be stored in a secure, password-protected folder, erased from recorders as soon as transcription is completed. For all data, a separate file linking names and trial IDs will be kept and password-protected.

The ARK team will develop and set up a dashboard for participant recruitment. Care will be taken to preserve the original datasets, maintain data integrity and security and avoid duplication. If a participant withdraws consent for their data to be used, then in this case the only data that will be deleted will be personally identifiable data as per GDPR. The anonymous study outcome data will be retained. The study information (including consent forms, screening and enrolment data, baseline and follow-up data, audio-recordings of interviews and FGDs and anonymised transcripts) will only be accessed by researchers directly involved in the study or by representatives of the Trial Data Management and Ethics Committee in the event of a study audit and will not be released without written permission, except as necessary for monitoring by study monitors or regulatory bodies.

Encrypted data transfer among ARK, NIMHANS and the University of York will be carried out via secure Drop-off services available through the University of York. The study data will be stored in accordance with UK Good Clinical Practice (GCP) guidelines[76].

20.2. Archiving

In line with the Data Protection Act[75] and the Research Governance Framework for Health and Social Care Research[77], at the end of the programme, all digital records/data

will be securely archived by the University of York. All documents will be retained for a minimum of 10 years and then destroyed according to University of York policy. The University of York will receive data sets that don't contain personal identifiable information. The hard copy logs and information sheets which contain identifiable information of the trial participants will be kept in the locked cabinet as soon as possible. During the study, Site RA will have access to some logs for management and data collection purposes. Once the purpose is fulfilled, the hard copy will be stored at the respective country offices.

20.3. Trial Data Monitoring and Quality Assurance

To monitor trial data and assure data quality, the ARK Foundation team will develop a complete data quality guideline. Study data managers (based at ARK and NIMHANS) along with trial coordinators will routinely monitor data for quality and completeness to ensure consistency across facilities and countries followed by a second check by a statistician at ARK using verification, validation and checking .processes following the ARK's data quality guidelines. Trial statisticians based at York trials unit will also monitor for quality upon each data transfer. An audit trail of data changes will be kept. The data will be remotely uploaded, stored and managed by ARK (Bangladesh and Pakistan) and NIMHANS (India) on the REDCap server.

Access to data (with no personal identifiable information) will be password-protected, with only the data managers, local statisticians (from ARK and NIMHANS) having edit access. Upon study completion, data will be checked for validity and missing entries will be provided where possible. After the dataset is locked, it will remain password protected and only trial investigators will have access to the datasets. The missing data will be pursued

until study ends unless they are data obtained by participant contact and this would cause distress. Data will be reported to the Independent Advisory Board (IAB) as required.

20.4. Ethical Considerations and Regulatory Approvals

The trial will adhere to the fundamental principles of human rights and dignity laid down in the Declaration of Helsinki[78] and follow guidance on good research practice outlined by the Wellcome's Trust and MRC[79], and local legislation governing research in partner LMICs. The trial has been approved by the Health Sciences Research Governance Committee, University of York, National Research and Bioethics Committees in Bangladesh (National Research Ethics Committee (NREC) functioning under Bangladesh Medical Research Council (BMRC)), Health Ministry's Screening Committee (HMSC) operated by the Department of Health Research/Indian Council of Medical Research (ICMR)) and the Screening Committee for Research Proposal (SCRP), Department of Health and Family Welfare, Ministry of Health and Family Welfare, Government of India in India, National Bioethics Committee for Research (NBC-R) at Health Research Institute, National Institutes of Health (NIH)) in Pakistan, as well as institutional ethics committees in India (Ethics Committee (Behavioural Science Division) of NIMHANS, Bengaluru), and Pakistan (Institutional Research & Ethics Forum (IREF), Rawalpindi Medical University (RMU), Rawalpindi and Ethics Review board of Dow University of Health Sciences (DUHS), Karachi). Every possible effort will be made to uphold the principles of autonomy, justice, beneficence and non-maleficence in the design and conduct of the study. Firstly, the eligibility criteria are broad and inclusive to ensure inclusion of groups that may benefit from the trial. Individuals will provide informed consent and will have the right to discontinue participation at any point in the study. During study visits and data collection, efforts to minimize inconvenience and burden to participants will be ensured including

seeking prior appointments for telephonic calls, if these are necessary. Enrolled participants will always be assured of complete confidentiality of their data; UIDs will be used to ensure the anonymity of the participants and the data collected.

21. Other ethical considerations

The SCIMITAR-SA feasibility trial involves patients with SMI, caregivers and healthcare staff. The trial will use sensitive personal and health data, with cross-country data sharing. Key ethical considerations will be around capacity and consent, participant burden, data confidentiality and the need to ensure equitable decision-making between patients/caregivers, healthcare staff and researchers. The Programme Management Group (PMG), Chief investigator, Programme Manager overseen by the Independent Advisory Board (IAB), will regularly review project and data management plans and the risk register.

Capacity to consent will be a requirement for participation in the feasibility trial. Furthermore, individuals with SMI are a vulnerable group, for whom capacity to make decisions about research participation may be affected (and fluctuate) because of illness. We do not anticipate any risks to participants from the intervention itself, which is in effect, part of current best practice. They will be free to withdraw consent and leave the trial at any time without having to cite any reason. Participants will be provided information on who to contact if they wish to withdraw from the trial. All participant rights will be explained to participants and their caregivers at the outset. Participant burden will be mitigated by careful planning and feasibility testing of proposed assessments. We will ensure patient participation is free and without undue inducements. For Community Panel participants, input will be appropriately supported, recognised and reimbursed, in accordance with NIHR guidance on public engagement[80].

In addition, to maintain the quality, integrity and security of data, the trial will follow ARK's data management policies for research data management which covers the collection, use, sharing and storage of research and personal data.

The SCIMITAR-SA feasibility trial will follow University of York's and LMIC partners' policies to ensure safety and security of staff and research participants. Ethics applications and protocols will detail risks monitoring and mitigation. For UK staff travelling to partner countries (Bangladesh, India, Pakistan) risk assessments will be carried out according to University of York policy. For LMIC staff, risks will be assessed by the site lead and mitigations required put in place. We will work within the University of York's Safeguarding Policy and in line with the statement on standards for safeguarding in international development research [81]. The information sheets would also include the contact of an independent ethics committee rep who the participants can access in case of any complaints/ethical considerations related to the study.

22. Adverse Events

The principles of ICH GCP[78, 82] require that both investigators and sponsors follow specific procedures when notifying and reporting adverse events or reactions in clinical trials. This section of the protocol describes the potential adverse events (AEs), adverse event monitoring during the trial, definitions of AEs and reporting procedures. All the specific procedures and guidelines regarding the adverse event assessment, reporting and notifications as given below will be followed:

22.1. Identification of potential adverse events

During research procedures: The SCIMITAR-SA trial involves a behavioural intervention and it may be unlikely that there is a risk of harm caused by the intervention, but presumably the occurrence of AEs is quite likely given the nature of the study population encountered during the trial. However, in some circumstances the information or feedback provided might cause anxiety and distress for participants. There is also a minimal risk to the trial participants from study procedures such as a collection of data using Case Report Forms (CRFs), inquiring about their tobacco use status, administration of scales, collection of saliva samples, anthropometric measures, etc. However, a standard approach to the collection, recording and reporting of adverse and serious adverse events will be followed in order to ensure the safety of trial participants. All our study procedures at the trial facilities in the three countries will be conducted by experienced and appropriately qualified researchers/ TDAs who are trained on privacy and confidentiality. These researchers/TDAs will provide assurance to participants that any information provided will be kept confidential, and study data will only contain their trial ID and not participant names or any other information that might be used to identify the respondents. Whilst answering all questions would really benefit the study to achieve its aims and objectives, there might be questions that the study participants might feel strongly that they do not want to answer. We will advise them to let the researcher/TDAs know so that they do not continue to ask them those specific questions. It is possible that some of the questions might cause distress. The participants will be advised to ask the researcher/TDAs to take a break or stop the interview altogether. The researcher/TDAs will also seek help from clinic staff (e.g. counsellors/psychologists) on the participant's behalf if the participant feels they need such help.

NRT: Some of the side effects from nicotine gum are mouth or throat sores, bad aftertaste, problems with existing dental work, nausea, jaw pain and racing heartbeat. Some of the side effects of nicotine patches are skin irritation, itching, dizziness, headache, racing heartbeat and nausea [83]. We will advise participants about these potential side effects, and to contact the study team as soon as possible if they suffer from any side effects (serious or otherwise), for us to advise them on what to do. If the side effect(s) are serious enough and the participant feels they need immediate medical attention, they will be informed that they should seek medical help in such circumstances and inform the medical team at the facility about their participation in the trial and the form of NRT they are taking as part of their usual care, if any.

22.2. Definition of adverse events

AEs are defined as an untoward clinical development that may occur during a participant's involvement in the trial. This may include:

- An exacerbation of a pre-existing illness.
- An increase in frequency or intensity of a pre-existing episodic event or condition.
- An untoward clinical event for any reason that the participant is seeking or requiring medical treatment.
- Untoward events include any infections, such as Tuberculosis, Dengue or COVID-19.
- Continuous persistent disease or a symptom present at baseline that worsens following administration of the study treatment.
- Any SMI related complications, including suicidal ideation (noted by the research staff/advisor besides the PHQ-9 question; can be detected even in a session of the intervention), relapse of signs and symptoms of SMI and harm to others .
- Any side effects of NRT.

At the point of recruitment into the trial, RAs will explain the definition of adverse events to the patient and ask them or their caregiver to inform the study team of any such events at any time by telephone (using the contact details provided in the trial newsletter) or in-person when routinely visiting the site. Patients or their caregivers may also report adverse events at formal contact times with the study team for the scheduling of SCIMITAR-SA sessions or follow-up sessions through the contact details given in PIS. At four and seven months follow-up, RAs should prompt patients whether any adverse events have occurred including suicidality based on the last question of PHQ-9. Health related events are formally collected using follow-up CRFs at four and seven months. If any of the information provided by patients meets the definition of an adverse event (e.g. a Dengue infection, Stroke/cardiac event), a separate adverse event form will be completed for every event and input into REDCap. Healthcare staff who will be delivering the intervention may identify Severe Mental Illness related adverse events such as suicidal ideation during the intervention delivery phase. AE guidance and definitions will be shared with all facilitators and they are advised to report such events they are made aware of to RAs.

If participants express thoughts of suicide or self-harm whilst attending for clinical consultations, intervention sessions or salivary cotinine test, the clinician, research nurse should explain that they are concerned about the participant's health and safety, and that they would like the participant to be seen by a member of the research team for further assessment. They should contact a study Research Assistant to request further assessment. The Research Assistant will explain to the participant why they are contacting them, and that they would like to ask some questions to explore if the person may need further support.

For identifying and addressing suicidal ideation, we will follow the standard operating procedure adapted from the DiaDeM research programme[84], which include a suicide risk pathway and referral procedure. Each site will identify a named 'Designated Health Professional(s)' for suicide risk assessments. This is a health professional with experience of conducting mental health risk assessments, who will act as the first point of contact for the team following initial risk assessment by anyone implementing the procedures in this protocol. The Designated Health Professional may be a Research Fellow, working as part of the research team, or they may be external to the research team and part of the clinical team. The discussion and advice given by the Designated Health Professional and actions taken by the researcher will be recorded on the 'SCIMITAR-SA Assessing Suicide and Self-Harm Risk (also adapted from the DiaDem Research Programme[84]). An adverse events reporting form will also be completed. If the Designated Health Professional advises further assessment or management is needed, a study Research Fellow will explain this to the participant, and with their consent, arrange an online or in-person appointment at the Outpatients Psychiatry Department with an appropriately trained mental health specialist (e.g. Consultant Psychiatrist or a Postgraduate Trainee, Senior Clinical Psychologist).

22.3. Adverse events exemptions

AEs will not include the following:

- A pre-existing disease or a condition present before inclusion in the study (i.e. a disorder present at the baseline study visit and noted on the baseline medical history/physical examination form/medical notes) that does not worsen.
- Hospitalisations where no untoward or unintended response has occurred, e.g., elective cosmetic surgery, social admissions.

- Medical or surgical procedures; the condition that leads to the procedure is the adverse event.

22.4. Adverse event monitoring

AEs will be assessed at each counselling session irrespective of the mode of delivery (e.g., face-to-face/remote (after setting quit date) and at the face-to-face follow-up visits, to check out for their potential association with study interventions or procedures ascertained. The researchers conducting the counselling session or follow-up visit assessments will record all directly observed AEs (in case of face-to-face session) and all AEs reported by the study participant upon inquiries made during face-to-face or remote sessions. An adverse events review checklist will be developed to be used at each visit / session to explicitly prompt for symptoms relating to possible NRT related side effects. This way we will be able to address any AEs or concerns that the participants might have. In the context of SCIMITAR-SA feasibility trial, it is unlikely that any AEs would be related to the behavioural support within the intervention nor the very brief advice (control) arms as these are behaviour change interventions. The research procedures are also very low risk. Nevertheless, there is a potential for AEs due to the NRT. AEs will be reported on the AE form. Serious adverse events will be defined according to ICH GCP[85], and will be reported to the respective country coordinating centres according to the agreed timelines.

22.5. Identification and reporting of adverse events

Information on adverse events will be collected by researchers as reported by the medical officers at the trial facilities and/or by the trial participants' self-report. This will be done throughout the course of their involvement in the trial. We will include information on the type of adverse events that can be expected, along with information on how to report

adverse events in a quarterly (3-monthly) newsletter in digital format (to both intervention and control arms in order to capture the AE's particularly in the control arm as the intervention group participants can report their AEs, if any during their visits for receiving the intervention) which will be sent to all study participants during the course of the study if the patient consents to receive these newsletters on personal or caregiver's whatsapp mobile numbers. Trial participants who contact the study team to report adverse events will be put in touch with the researcher, who will use a pre-designed data collection form to collect the relevant information. The collected adverse events information will be assessed by a designated member of clinical staff at each study site for expectedness, relatedness and seriousness, and severity. The WHO Uppsala Monitoring Centre (WHO-UMC) scale [86] will be used to identify the relatedness of each unexpected event, which will classify events as certain, probable, possible and unlikely. Seriousness will be assessed on the basis of whether the observed event i) results in death ii) is life-threatening, iii) requires inpatient hospitalisation or prolongation of existing hospitalisation or iv) results in persistent or significant disability or incapacity.

For expected adverse events, a standard reporting procedure will be followed, whereby the information for each recorded event will be reported to the respective country coordinating centre according to the agreed timeline. Adverse events that are classified as serious, unexpected and related to the intervention will require expedited reporting to the Trial Manager and the Principal Investigator who will review the report, and inform the York ethics committee within 7 days of the occurrence. Participants reporting such events will be followed up until the episode has resolved or a final outcome has been reached. Follow-up information, where applicable, will also be sent as soon as it is available. In

addition, each study site staff will follow their institution's procedure for local notification and as per the guidelines of their local Research Ethics Committee Boards.

Table 2: Definitions of AEs used in the trial

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a participant to whom an IMP has been administered including occurrences that are not necessarily caused by or related to that product.
Adverse Reaction (AR)	Any untoward and unintended response to an IMP related to any dose administered.
Unexpected Adverse Reaction (UAR)	An adverse reaction, the nature or severity of which is not consistent with the information about the medicinal product in question set out in the SPC for that product, participant information leaflet, IB or protocol.
Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR) or Suspected Unexpected Serious	Respectively any adverse event, adverse reaction or unexpected adverse reaction that: • Results in death • Is life-threatening* • Requires hospitalisation or prolongation of existing hospitalisation** • Results in persistent or significant disability or incapacity

Adverse Reaction (SUSAR) ***	• Consists of a congenital anomaly or birth defect

The term life-threatening in the definition of a serious event refers to an event in which the participant is at risk of death at the time of the event; it does not refer to an event that hypothetically might cause death if it were more severe, for example, a silent myocardial infarction.

***Hospitalisation is defined as an inpatient admission, regardless of length of stay, even if the hospitalisation is a precautionary measure for continued observation. Hospitalisations for a pre-existing condition that has not worsened or for an elective procedure do not constitute an SAE.*

**** Medical judgement should be exercised in deciding whether an AE or AR is serious in other situations. The following should also be considered serious: important AEs or ARs that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the participant or may require intervention to prevent one or the other outcomes listed in the definition above.*

22.6. Trial facility assessment

Seriousness

When an AE or AR occurs, the clinical team responsible for care of the participant must first assess whether or not the event is serious using the definition given in Table 2. If the event is serious, then an SAE/SUSAR Form must be completed and the country lead or trial manager notified within 24 hours.

Severity or Grading of Adverse Events

This relates to the intensity or severity of the event experienced by the participant. The severity of all AEs and/or ARs (serious and non-serious) in this trial should be based on the

clinical team's (supported by the country lead or trial manager if needed) judgement using the following definitions:

Mild: An event that is easily tolerated by the participant, causing minimal discomfort and not interfering with everyday activities.

Moderate: An event that is sufficiently discomforting to interfere with normal everyday activities.

Severe: An event that prevents normal everyday activities.

**Please note that the severity should not be confused with the seriousness of the event which relates to the participant or event outcome.*

22.7. Causality

The respective country lead(s) or mental health care team(s) must assess the causality of all serious events or reactions in relation to the trial therapy using the definitions in Table 3. Alternative causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors etc. should be considered. There are five categories: unrelated, unlikely, possible, probable, and definitely related. If the causality assessment is unrelated or unlikely to be related, the event is classified as an SAE. If the causality is assessed as possible, probable or definitely related, then the event is classified as an SAR.

Table 3 : Assigning Type of SAE through Causality

Relationship	Description	SAE type

Unrelated	There is no evidence of any causal relationship	Unrelated SAE
Unlikely	There is little evidence to suggest that there is a causal relationship (for example, the event did not occur within a reasonable time after administration of the trial medication). There is another reasonable explanation for the event (for example, the participant's clinical condition, other concomitant treatment).	Unrelated SAE
Possible	There is some evidence to suggest a causal relationship (for example, because the event occurs within a reasonable time after administration of the trial medication). However, the influence of other factors may have contributed to the event (for example, the participant's clinical condition, other concomitant treatments).	SAR
Probable	There is evidence to suggest a causal relationship and the influence of other factors is unlikely.	SAR
Definitely	There is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out.	SAR

22.8. *Expectedness*

If there is at least a possible involvement of the trial treatment, the respective country lead(s) or mental health care team(s) must assess the expectedness of the event. An unexpected adverse reaction is one not previously reported in the current Summary of Characteristics or one that is more frequent or more severe than previously reported. The definition of an unexpected adverse reaction (UAR) is given in Table 2. The 'Adverse Event and Serious Adverse Event Reporting' SOP will contain a list of expected side effects associated with the NRT (if the participant is receiving NRT from their facility). If a SAR is assessed as being unexpected, it becomes a SUSAR.

22.9 Notification

The country lead(s) or trial manager should be notified of all SAEs **within 24 hours** of becoming aware of the event by the site's mental health care team(s) or researcher. The mental health care team(s) should notify the country lead(s) or trial manager and the country lead(s) should notify the University of York research team of all SAEs occurring from the time of randomisation until 30 days after the last protocol treatment administration using the SAE/SUSAR form. SARs and SUSARs must be notified to the country trial managers or country lead(s) and University of York research team until trial closure.

Notification procedure

- The SAE/SUSAR form must be completed by the site clinician (who is responsible for the participant's care), with due care being paid to the grading, causality and expectedness of the event as outlined above. In the absence of the responsible

clinician, the form should be completed and signed by a suitably qualified member of the mental health care team or the trial researcher and sent to the country office as appropriate. The responsible clinician should subsequently check the SAE/SUSAR form; make changes as appropriate, sign and then re-send to the respective country coordinating centre as soon as possible. The initial report must be followed by detailed, written reports as appropriate.

- The minimum criteria required for reporting an SAE are the trial ID and age, name of clinician reporting, the event, and why it is considered serious.
- The SAE/SUSAR form must be sent as a scanned copy by email to the respective country coordinating centre:

SAE REPORTING

Within 24 hours of becoming aware of an SAE, please email a completed SAE form to the respective country office on:

India: email: pratimamurthy@gmail.com

Pakistan: email:uroosa.talib@pill.org.pk ; administrator_rgmo@rmur.edu.pk

Bangladesh: email: info@arkfoundationbd.org

- Follow-up: The participants must be followed up until clinical recovery is complete (including laboratory results returning to normal or baseline if relevant), or until the event has stabilised. Follow-up should continue after completion of protocol treatment if necessary. A further SAE/SUSAR form, by indicating a 'Follow-up report' should be completed and emailed to the country coordinating centre as information

becomes available. Extra, annotated information and/or copies of test results may be provided separately. The participant must be identified by trial ID, age and initials only. The participant's name should not be used on any correspondence and should be deleted from any test results.

- The staff should follow their institution's procedure for local notification (for e.g. to Research Ethics Committees (REC)/ Institutional Review Boards (IRB)) requirements as applicable.

22.10. Country PI/ lead responsibilities

Medically-qualified staff at the country coordinating centre (the respective country trial manager or lead(s)) will review all SAE reports received. The events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA)[87]. The causality assessment given by the mental health care team at the mental health facility cannot be overruled; in the case of disagreement, both opinions will be provided in any subsequent reports.

The country lead(s) are responsible for reporting the SAEs to the competent authorities (REC/IRB) as per the guidelines of their local Research Ethics Committees Boards in their respective countries and to the University of York research team in the UK. Fatal and life-threatening SUSARs must be reported to the competent authorities (REC/IRB) within 7 days of the country coordinating centre being notified of the event and follow-up information within a further 8 days; other SUSARs must be reported within 15 days.

23. Responsibilities of University of York research team

The University of York research team is undertaking the duties of trial sponsor and must ensure the reporting of SUSARs and other SARs, by the country leads, to the local

competent authorities of the countries in which the trial is taking place and the REC/IRB, has been done appropriately. The University of York research team will also keep all country lead(s) informed of any safety issues that arise during the course of the trial.

24. Annual safety reports

The University of York research team, as delegated by the funder / Sponsor, will submit Annual Safety Reports in the required format to the main ethics committee (Health Sciences Research Governance Committee(HSRGC)[88] which gave the favourable opinion 12 months after the date on which the favourable opinion was given and thereafter until the end of the study. This report will be provided to the country leads to submit to their national competent authorities.

25. Urgent safety measures

The country lead(s) or trial managers may take appropriate urgent safety measures in order to protect research participants against any immediate hazard to their health or safety. These safety measures should be taken immediately and may be taken without prior authorization from the HSRGC or local competent authorities. The country lead(s) or trial managers must alert the University of York research team who must alert the funder /Sponsor, as soon as possible of the urgent measures.

26. Guidance for stopping the trial

The study will be stopped, as guided by the Independent Advisory Board (IAB) if new literature indicates findings that can be applied to this question in terms of benefit or side

effects. However, early evidence of clear benefit would not be a reason to halt recruitment in the trial.

27. Incidental findings

Our trial procedures present the potential of a number of incidental findings:

At the time of screening: We will be administering the AUDIT for alcohol use[89] and the ASSIST Lite for psychoactive substance use[90] as a part of our screening form. We are using these tools to confirm alcohol and the psychoactive substance use as we are also using the standardised diagnostic tools to confirm the diagnosis of SMI. This will help the research team to screen the right participants for the trial. Some individuals may be identified as at-risk drinkers, having alcohol problems, or problematic substance use. Our country-level teams are experienced in managing these issues and collaborate closely with addiction services. Participants will receive brief feedback on the results on these tools, with a clear explanation that this is not a formal diagnosis, along with information on the risks of unhealthy drinking. They will also be given a leaflet commonly used by local addiction services. If necessary, participants will be referred to appropriate addiction or support services for further assessment and care.

During the course of trial: Hospitalisation, relapse of symptoms, physical health complications, any additional treatments prescribed during the course for example suicidality necessitating electroconvulsive therapy. These things may be anticipated and need to be captured and documented in the AE form.

28. Trial Management Structure

(1) Programme Management Group (PMG)

The Programme Management Group (PMG) will oversee delivery of the project, guide the Research Fellows and other researchers involved in study implementation, and contribute to the write up and dissemination of findings. The PMG will consist of all of the study investigators and will meet once every month.

(2) Independent Advisory Board (IAB)

The Independent Advisory Board (IAB) will independently oversee the SCIMITAR-SA programme, track its progress, advise on potential changes to achieve goals, and highlight relevant new evidence. IAB will be led by an independent Chair, and include members with global health expertise (tobacco control, mental health policy and trials) and will meet twice in the first year and then annually to monitor progress against milestones of the SCIMITAR-SA programme. For quoracy of at least 2 independent members must be in attendance.

29. Checkpoint on progress to full trial

The following criteria given in table 4 below will be used by the SCIMITAR-SA Independent Advisory Board (IAB) to determine the approach for the full trial:

Table 4: Checkpoints on progress to full trial

	GREEN: **Proceed as planned**	**AMBER:** **Proceed with amendments to intervention and/or trial procedures and outcomes**	**RED:** **Major review of intervention and /or trial procedures and outcomes**
Recruitment	≥80% of sample size recruited in allocated time period	50-79% of sample size recruited in allocated time period	Less than 50% of the sample size recruited during allocated time period
Retention at 7 months	≥80% of the number recruited retained in each trial arm, with the absolute difference in retention rates between arms no greater than 10%	Any scenario which satisfies neither Green nor Red criteria.	Either less than 50% retention of the overall number recruited, or an absolute difference in retention rates between trial arms of greater than 16%
Data on primary trial outcome	>80% providing a self-reported	Primary outcome data availability falls	<50% providing a self-reported

	smoking status at 7 months AND >80% of lab results available.	into neither the GREEN nor the RED category.	smoking status at 7 months OR <50% lab results not available.
Acceptability of trial procedures	Acceptability judged strongly acceptable by qualitative data from research teams, participants, TDAs and mental health staff	Acceptability judged acceptable by qualitative data from research teams, participants, TDAs and mental health staff	Acceptability judged possibly acceptable by qualitative data from research teams, participants, TDAs and mental health staff
Intervention delivery	**Number of sessions offered:** At least one of each pre-quit, quit and post-quit sessions (total three) offered/scheduled for >80% of participants **Number of sessions attended:** at least one of each	**Number of sessions offered:** At least one of each pre-quit, quit and post-quit sessions (total three) offered/scheduled for 50-79% of participants **Number of sessions attended:** at least one of each	**Number of sessions offered:** <50% of participants are offered at least one of each pre-quit, quit and post-quit sessions (total three) **Number of sessions attended:** at least one of each pre-quit, quit and

	pre-quit, quit and post-quit sessions attended by >80% of participants	pre-quit, quit and post-quit sessions attended by 50-79% of participants	post-quit sessions attended by <50% of participants
Acceptability of intervention	Acceptability judged strongly acceptable by qualitative data from participants, TDAs and mental health staff.	Acceptability judged as acceptable by qualitative data from participants, TDAs and mental health staff.	Acceptability judged as possibly acceptable by qualitative data from participants, TDAs and mental health staff.

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