moreRESPECT: A Randomised controlled trial of a sexual health promotion intervention for people with severe mental illness delivered in community mental health settings

PROTOCOL Version 1.5_08.08.2024

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Institutions:

Glasgow Caledonian University

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Leeds and York Partnership NHS Foundation Trust

Guy's and St Thomas' NHS Foundation Trust

East London NHS Foundation Trust

Sponsor:

Glasgow Caledonian University

Funder:

National Institute for Health and Care Research (NIHR)

Reference number: NIHR133865

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the ethical principles outlined by Good Clinical Practice (GCP) and in the Declaration of Helsinki, the Sponsor's/delegated Standard Operating Procedures (SOPs), and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:	
Signature:	Date: 22/08/2024
Name (please print): Professor Sharron Dolan	
Position: Associate Dean Research, School of Health and Life Sciences	
Chief Investigator:	
Signature: 	Date: 08/08/2024
Name: (please print): Professor Elizabeth Hughes	

STUDY SUMMARY

TITLE	A Randomised controlled trial of a sexual health promotion intervention for people with severe mental illness delivered in community mental health settings.
Acronym	moreRESPECT
Protocol Version **Date** **ISRCTN**	Version 1.5 08/08/2024 ISRCTN36391109
Study design	A two-arm, individually randomised controlled trial with internal pilot, embedded process evaluation and cost-effectiveness analysis
Study type and phase	Non-CTIMP. Phase III
Funder	National Institute for Health and Care Research Health Technology Assessment programme NIHR133865
Sponsor	Glasgow Caledonian University
Study Duration	49 months
Start date:	01/07/2023
Anticipated finish date:	30/06/2026
Study Centres	NHS community mental health services in England and Scotland
Objectives	To undertake a randomised controlled trial to determine whether a bespoke sexual health intervention is effective and cost-effective in reducing unprotected sexual acts, increasing knowledge about sexually transmitted diseases, motivation to engage in safer sex and condom use.
Study population	People with severe mental illness under the care of community mental health services
Target number of participants	400

Study groups	Control and intervention Control: Will continue to receive usual care for sexual health, a localised sexual health services leaflet and a sample pack of condoms. Intervention: Will continue to receive usual care for sexual health, a localised sexual health services leaflet, a sample pack of condoms and be offered 3x one-hour 1:1 manualized, theory driven sessions (either face to face or online via videoconferencing) with a health professional promoting sexual health.
Main Inclusion Criteria	People aged 16 or over currently in treatment with the community mental health services diagnosed with a severe mental illness. Willing and able to give informed consent (i.e., has capacity to consent). Exclusion: Lacking capacity to give informed consent; poses a risk to others (including risk of sexual/physical violence); a co-existing learning disability of other significant cognitive impairment; those on sex offenders register
Primary outcome measure(s)	Number of unprotected sex acts (anal, vaginal, oral) recorded every three months (at 3, 6, 9 and 12 months) over the 12-month follow-up using the Sexual Risk Behaviour Assessment Schedule (SERBAS).
Secondary outcome measure(s)	Knowledge about human immunodeficiency virus (HIV) and sexually transmitted infections using the HIV Knowledge Questionnaire (HIV-KQ), Motivation to Engage in Safer Sex, Condom use Self-Efficacy Scale, Behavioural Intentions for Safer Sex, Quality of life (Qol) using the EQ-5D-5L and Recovery QoL (ReQol) measures, General questions about sexual health (items adapted from the National Surveys of Sexual Attitudes and Lifestyles (NATSAL), and health care resource use
Other outcome measure(s)	A process evaluation will be conducted with a small group of participants to find out how they found the support package and whether it worked better for some than others and in what circumstances. An economic evaluation will be undertaken from the perspective of the NHS and personal social services.

PLAIN ENGLISH SUMMARY

People with severe mental illness (SMI) have significant needs in terms of physical health compared to the general population. Initiatives have commenced to address this; however, sexual health has been missed off the agenda. Like everyone else, positive sexual relationships are important for people with SMI, but this is rarely discussed in routine mental health care. Therefore, they can be unaware of important information such as where to get sexual health advice, how to reduce risk of sexually transmitted infections, contraceptive choices and finding relationships that are mutually respectful, not violent or abusive.

In a National Institute for Health and Care Research (NIHR)-funded feasibility study, this research team developed a 3-session support package that helped people with SMI to think about their own sexual health and provided useful information about how to improve their sexual health. Following the success of the feasibility study, this full trial will examine the effectiveness and cost-effectiveness of the intervention by recruiting 400 people with SMI from National Health Service (NHS) community mental health teams across England and Scotland.

People who agree to take part will be randomly allocated to either usual care (control arm) or usual care plus the moreRESPECT intervention (intervention arm). Data will be collected at baseline and then at 3-, 6-, 9- and 12 months post-randomisation. As part of a nested process evaluation, interviews with a small group of participants will also be conducted at 6 months post randomisation to find out how they found the support package and whether it worked better for some than others and in what circumstances.

PROTOCOL AMENDMENT HISTORY

Protocol version and date	Amendment number and ethics approval date	Details of changes made
1.1 16/06/2023	N/A – Amendments made in response to REC / HRA and other minor updates after initial IRAS submission Approved by REC / HRA on 05/07/2023	• Combined participant identification routes '3) Direct route to moreRESPECT study team' and '4) Direct approach in clinics' since they use the same principles of study promotion. It is now referred to as '3) Study promotion and self-referral to moreRESPECT study team (pg 19-20). It has also been made clear that the MR researcher or members of the NHS sites R&D research team will only only directly approach if the potential participant has given verbal consent for a researcher to talk to them about the study (pg 20). • Updated the wording of the responsibilities of the MR researcher and R&D staff based on the above update (pg 12). • Added that audio files will be deleted after transcription has been checked for accuracy and any typos corrected (pg 33). • The organisation of co-applicant Ms Elana Covshoff was corrected from 'Kings College Hospital NHS Foundation Trust' to 'Guy's and St Thomas NHS Foundation Trust (pg 11).
1.2 21/09/2023	Non-Substantial Amendment 4 - Updates to trial documents: Approved by HRA on 03/10/2023 Substantial Amendment 1 - Change in Sponsor name: Approved by REC / HRA on 13/10/2023	• Change of Sponsor and CI/Intervention Lead place of work: Replaced Edinburgh Napier University logo/details with Glasgow Caledonian University logo/details.
1.3 06/06/2024	Non-Substantial Amendment 8 Approved by HRA on 20/06/2024	• Timing of intervention delivery added to be delivered before the 3 month follow up. • The inclusion criteria has been revised to allow the recruitment of participants from inpatient units if they are due for discharge but remain in inpatient care due to the unavailability of suitable community placements. • Added clarification to confirm that the inclusion criteria 'Willing and able to give informed consent to participate' is about capacity, not consent. • Added clarification on what will be accepted as a valid consent form.
1.4 10/07/2024	Non-Substantial Amendment 9 Approved by HRA on 18/07/2024	• To support remote data collection the interview version of the EQ-5D-5L has been added to the researcher CRF at baseline and all follow ups. The self-complete version of the EQ-5D has been removed from the participant completed baseline CRF and all follow ups. • The protocol has been updated to reflect this.
1.5 08/08/2024	Non-Substantial Amendment 11	• Added clarification of how consent, baseline data collection and follow-up data collection can be conducted, which includes face to face or remote (online videoconferencing/telephone) methods.

LIST OF COMMON ABBREVIATIONS

AE	Adverse event
AUC	Area under the curve
CEACs	Cost effectiveness acceptability curves
CI	Chief Investigator
CRF	Case report form
CRN	Clinical Research Network
DMC	Data Monitoring Committee
GCP	Good Clinical Practice
HEAP	Health economics analysis plan
HIV	Human Immunodeficiency Virus
HIV-KQ	Human Immunodeficiency Virus Knowledge Questionnaire
HPV	Human Papilloma Virus
HRA	Health Research Authority
LEAG	Lived Experience Advisory Group
LGBTQ	Lesbian, Gay, Bisexual, Transgender, Queer
MRC	Medical Research Council
NATSAL	National Surveys of Sexual Attitudes and Lifestyles
NHS	National Health Service
NIHR	National Institute for Health and Care Research
PIS	Participant information sheet
PPI	Patient and public involvement
PSSRU	Personal Social Services Research Unit

PWLE	People with lived experience
QALYs	Quality adjusted life years
QR	Quick response
RCT	Randomised controlled trial
REC	Research Ethics Committee
ReQoL	Recovering Quality of Life
R&D	Research and Development
SAE	Serious Adverse Event
SERBAS	Sexual Risk Behaviour Assessment Schedule
SMI	Severe mental illness
SOP	Standard operating procedure
TA	Thematic Analysis
TMG	Trial Management Group
TSC	Trial Steering Committee
YTU	York Trials Unit

CONTENTS

1. Roles and responsibilities

1.1 Chief Investigator

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1.2 Co-applicants

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Mrs Ceri Dare — Individual PPI member

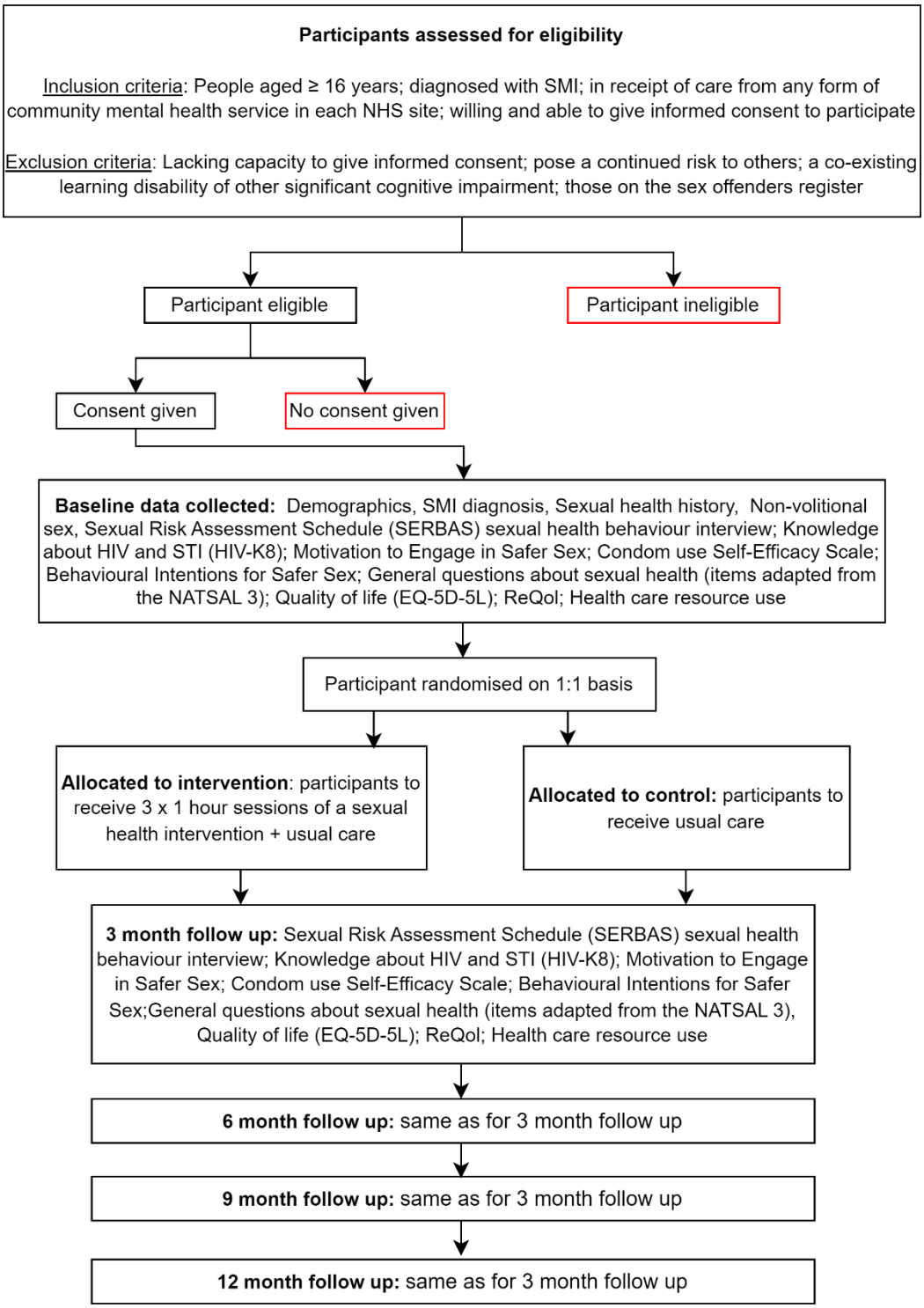
Mrs Charlotte Walker — Individual PPI member

1.3 Researcher titles, roles and responsibilities

Researcher title:	Based at:	Responsibility:	Access to data:	Blinded to participant allocation:
moreRESPECT researcher	Site or University employed	- Promote study in public areas of NHS sites such as waiting rooms, communal areas, with prior permission of clinical team - Speak to potential participants patients who have given consent to be contacted, - Obtain informed consent - Conduct baseline and follow-up assessments - Conduct randomisations - Complete the MR Researcher interview CRF including the SERBAS questionnaire - (if in clinic) confirm completion of the Participant self-completed CRF - Post completed CRFs to YTU - Conduct reminder telephone calls with participants who have not completed their CRF - Complete change of status and AE forms and notify YTU	- Consent form and consent to contact forms - Participant CRFs - Patient identifiable data	Yes
R&D staff	Site	- Promote study in public areas of NHS sites such as waiting rooms, communal areas, with prior permission of clinical team Maintain and update a record sheet of patients enrolled at site - Post completed CRFs to YTU - Maintain a file of essential trial documentation	- Participant allocation - Consent form and consent to contact forms - Participant CRFs - Patient identifiable data	No
YTU staff	YTU	- Conduct randomisations - Inform participant, sites, MR researcher, lead interventionist (if applicable), participants GP and participants NHS care provider of participant randomisation - Support day to day trial management and monitoring activities - Conduct site set-up	- Participant allocation - Consent form and consent to contact forms - Participant CRFs - Patient identifiable data	No

		- Provide trial Standard Operating Procedures - File, process and analyse patient and researcher data		
Intervention lead	Glasgow Caledonian University	- Work with sites to provide training and supervision for interventionists - Coordinate the allocation of an interventionist to a participant - Confirm interventionist and participant pairings to YTU - Deliver monthly supervision groups online with interventionists	- Participant allocation - Patient identifiable data	No
Interventionist	Site	- Complete intervention training - Conduct intervention - Send reminders.to participants regarding future sessions - Attend monthly supervision with intervention lead	- Participant allocation - Patient identifiable data	No

2. Study flow diagram



3. Background and rationale

Sexual health is a broad term defined by the World Health Organisation as "a state of physical, emotional, mental and social well-being in relation to sexuality" ([1]). Sexual health is about having positive and respectful sexual relationships, being able to express one's own sexuality, and being free from control, coercion and violence. People who live with severe mental illness (SMI) such as psychosis, bipolar affective disorders who require the services of secondary mental health care, value intimate partner relationships (like everyone else) and see them as a positive part of their lives ([2]). However, people with SMI struggle to find relationships for reasons that include mental health stigma ([3]) as well as limited social opportunities and loneliness ([4]). The sexual health of this group has been largely ignored by mental health services ([5],[6],[7],[8]) despite the increased focus on improving physical health for people with SMI ([9]). People with SMI experience significant disparities in sexual health ([10]) across several domains including:

1) increased risk of exploitation, sexual violence and intimate partner violence ([11]),

2) higher rates of sexually transmitted infections and blood borne viruses ([12]), and

3) reproductive health (e.g., unintended pregnancy, access to contraception) ([13]).

The domains above are interconnected; for instance, violent and/or psychologically abusive relationships are associated with poor sexual health ([14]). Therefore, addressing sexual health should also include a focus on relationships.

In order to address the sexual health of a population, three areas need to be considered: prevention of infection, early detection and treatment, and reducing onward transmission. Untreated sexually transmitted infections can lead to significant health problems; Human Papilloma Virus (HPV) can lead to cervical cancer; other HPV can result in infertility; and blood borne viruses such as Hepatitis B and C can result in premature death. Co-morbidity of Human Immunodeficiency Virus (HIV) and a severe mental illness such as schizophrenia poses particular challenges for both users and services; in particular engagement with services and treatment adherence, as well as the psychiatric and neurological consequences compounding a pre-existing mental health problem ([15]).

There is limited, but promising, evidence regarding effective interventions to promote sexual health in this population ([16],[17]). The NIHR commissioned a feasibility trial ([18]) of a sexual health intervention for people with SMI (undertaken by this research team), which established the safety, feasibility, and acceptability of undertaking a randomised controlled trial of this intervention in this population. The lessons learnt and experience from conducting the feasibility study have informed and shaped this full trial.

4. The research question

Is an intervention designed to promote sexual health for people with severe mental illness clinically and cost effective?

5. Research aims and objectives

5.1 Aim

The Randomised Evaluation of Sexual health Promotion Effectiveness informing Care and Treatment (moreRESPECT) trial aims to assess whether a bespoke sexual health intervention designed for people with severe mental illness reduces unprotected sexual acts and is cost-effective.

5.2 Objectives

1) Undertake an eight-month internal pilot phase to confirm feasibility of the trial in terms of recruitment rate, retention rate, data completeness and intervention uptake.
2) Undertake a randomised controlled trial to determine whether a bespoke sexual health intervention reduces unprotected sexual acts.
3) Undertake an analysis of secondary outcomes including knowledge about sexually transmitted diseases, motivation to engage in safer sex, and condom use.
4) Assess the cost-effectiveness of the intervention compared to usual care and describe the implications for NHS resource management.
5) Undertake a process evaluation to identify what worked (and what didn't work), for whom, why, how and in what circumstances.

6. Study design

The moreRESPECT trial is a multi-centre, pragmatic, two-arm, individually randomised controlled trial of the intervention plus usual care versus usual care only in patients with SMI including an internal pilot, embedded process evaluation and cost-effectiveness analysis. We will randomise people currently in treatment with the community mental health services diagnosed with a SMI and aged 16 or over to receive either:

Intervention: Participants will be offered three, 60-minute sessions of a manualized, theory driven sexual health intervention (either face to face or online via videoconferencing), plus their usual care; or

Control: Participants will receive their usual care; this would include the local primary care and/or specialist sexual health services as part of usual sexual health care (including contraception) as well as referral/sign-posting through mental health services

6.1 Setting

Any NHS community mental health care in England and Scotland. This includes but is not limited to services such as Community Mental Health Recovery Teams, Assertive Outreach Teams, Psychiatric Outpatient Clinics, and Early Intervention for Psychosis.

6.2 Sites

For the purposes of recruitment, the definition of sites are geographical localities within an NHS organisation (Trust or Health Board (Scotland)). The aim is to have 12 localities actively recruiting throughout the recruitment period (equivalent to 3-4 NHS organisations recruiting at any given time) although additional NHS organisations will be brought on board if necessary.

7. Study Population

All individuals will be considered for inclusion in this study regardless of their age, disability, gender, marriage and civil partnership status, pregnancy and maternity, race, ethnicity, religion and beliefs, and sexual orientation except where the study inclusion and exclusion criteria explicitly states otherwise.

7.1 Inclusion criteria

- Aged ≥16 years;
- Diagnosed with a severe mental illness*;
- In receipt of care from any form of community mental health service in each NHS site; (outpatient clinics, day care, on caseload of community mental health team including assertive outreach; forensic, early intervention for psychosis, recovery colleges, depot clinics), or on inpatient mental health units if they are awaiting discharge, but remain in inpatient care due to the unavailability of suitable community placement.
- Willing and able to give informed consent to participate (i.e., has capacity to consent).

*There is no agreed definition of SMI, so we will adopt a pragmatic and inclusive definition: a Psychiatrist assessed and documented (care record) primary diagnosis of schizophrenia schizoaffective disorder, or delusional/psychotic illness, or bipolar disorder, or major depression (with or without psychotic features), or severe anxiety, or personality disorder.

7.2 Exclusion criteria

- Pose a current risk to others (e.g. research staff) including risks of sexual and/or physical violence;
- A learning disability or other significant cognitive impairment;
- Those known to be on the sex offenders register.

8. Recruitment

8.1 Source

From the work conducted in the feasibility study, it was found that having multiple routes into the study is important. Potential participants will be identified via three main routes.

1) **Caseload screening and promotion within the community mental health teams**: People will be identified via screening of caseload records by a person designated to this task within the NHS organisation. They will work with the clinically facing NHS staff in community teams to promote the study and undertake caseload screening for potentially eligible participants using the eligibility criteria outlined above. Once someone has been

identified as potentially eligible, clinically facing NHS staff will be asked to distribute information to them. This initial information will consist of an emailed PDF or printed version of the study leaflet which will include the study teams contact details and a quick response (QR) code for linking to the study website. The website has been designed to provide detailed information about the study for both staff and potential participants, as well as other interested parties. The website will contain information in a user-friendly format and this will have an in-built translation software tool so that all the information about the study including a web-based PIS and Consent Form can be translated into any language. A potential participant can directly contact the study team via email by completing a form on the website. If the patient expresses an interest in finding out more about the study, they will be provided with an information pack (invitation letter, patient information sheet (PIS) and consent to contact form). This pack can be either accessed directly from the study website, face to face by their NHS care provider, the sites NHS R&D staff or the moreRESPECT researcher (MR researcher), or posted to their home address from their NHS care provider. If after reading the materials they are interested in hearing more, they will be asked to give consent to be contacted for a further discussion. This consent to contact can be done via the study website "contact us" section; returning a completed form (by post or email) or verbally (and documented by site NHS staff). The MR researcher then will make contact with the potential participant to discuss the study and obtain informed consent.

2) **Permission to be contacted about research:**

In some NHS organisations there is a "permission to be contacted about research" field on people's care records; this will be utilised to identify people to send the study information to. And subsequently to this, then procedure will follow as in route 1.

3) **Study promotion and self-referral to moreRESPECT study team**:

Self-referral will be possible via the study website, which will be promoted online via social media and also in areas where potential participants congregate at NHS services, such as communal areas, waiting rooms, local service user groups, clozapine clinics or local voluntary sector organisations through posters and leaflets. Prior permission will be obtained from the clinical team in clinics/wards for the MR researcher or members of the

NHS sites R&D research team to display study posters and offer the study leaflet in person. If a patient who is attending a clinic wishes to ask any questions, then they will be able to discuss the study informally face to face with the MR Researcher or R&D research team member who is present. They will only directly approach a potential participant if they have given verbal consent for a researcher to talk to them about the study. Potential participants will not be under any obligation to decide to participate at this time. This approach was used for recruitment in the RESPECT Feasibility study and was effective as well as being acceptable to potential participants. Our Lived Experience Group also advocated for this approach as an acceptable way of promoting the study.

The study poster and leaflet will contain details of how to get in touch with the study team as well as a link (QR code) to the website which has more information about the study including the PIS. A potential participant can directly contact the study team via email by completing a form on the website. All self-referrals will be informed that the MR researcher will pass on their name to their NHS care provider to complete an eligibility check and once this is confirmed, the MR researcher will make contact with the potential participant to discuss the study and obtain informed consent. The MR researcher will be responsible for ensuring that the potential participant has accessed the digital versions of the PIS online, and if not, will be able to email this document. Self-referring participants will be unable to participate in the study without an eligibility check that has been completed by their NHS care provider.

8.2 Informed consent

All potential participants will have received a PIS and this will be checked by the MR researcher. At the consent meeting, which will be conducted face to face or remotely (online videoconferencing / telephone) the MR researcher will fully explain the study verbally, and give the patient the opportunity to ask questions. Potential participants will be assured of confidentiality, what to expect after the study ceases and given contact details in case of complaint or need for further information. They will be informed that participation is not compulsory and that they can withdraw from the study at any time without affecting their care. They will also be informed that, if randomly allocated to the sexual health intervention, they can withdraw from the intervention at

any point but still have the option of staying in the study for the purposes of follow-up data collection. The PIS will clearly present the potential positives and negatives associated with taking part in the trial. If the person is willing, then the MR researcher will invite the patient to participate and written informed consent will be sought.

If the person is accessing the study by remote access (online videoconferencing /telephone) then the person will be asked to provide their verbal consent to participate in the study. This will involve the individual confirming to the MR researcher that they have received the study information, have had the opportunity to ask questions, that they agree to the consent statements on the example consent form (included in the study information pack they will have received) and that they agree to participate in the study. The MR Researcher will document this verbal consent to participate in the study to include name and researcher signature and date of participant verbal consent to participate using the verbal consent form. A copy of this verbal consent will be provided to recruited participants. Consent will be re-checked verbally (and documented) at every subsequent data point and at each intervention session (if allocated to that arm).

Consent forms will be accepted as valid if participants (or MR researchers for verbal consent) place a tick/cross (rather than their initials) in the consent statement boxes, provided that they have printed their name, and signed and dated the form.

8.3 Baseline assessment

Baseline data will be collected during a one-to-one meeting which will be conducted face to face or remotely (online videoconferencing). In addition, in rare circumstances where face to face or videocalls are not possible, then the data can be collected by telephone.

There will be two baseline case report forms (CRFs) completed. In the first CRF the MR researcher will ask the questions as an interview and add responses onto a paper form. In the second CRF, there will be a set of questionnaires that the participant can self-complete via a paper form that can be handed back to the MR researcher on the day (if meeting face to face). If the data is being collected using online videoconferencing or telephone methods then both CRFs are administered by the researcher as an interview. A stamped addressed envelope will be provided to sites for return of the CRFs to York Trials Unit (YTU).

8.4 Randomisation and blinding

Randomisation will be undertaken by a MR researcher (who will be blinded to allocation) or member of staff at YTU working on the study via a trial management system built by YTU. The allocation sequence will be generated by an independent statistician at YTU who is not involved in the recruitment of participants. Participants will be randomised on a 1:1 basis to either usual care or intervention plus usual care. Stratified block randomisation will be used, with the NHS site as the stratifying variable, and randomly varying block sizes, to ensure even allocation to intervention across sites.

The following information will be collected for each participant at baseline, prior to randomisation:

- Site the participant belongs to;
- NHS community mental health service that provides the participants care;
- Participants details including full name, date of birth, full postal address, contact telephone number(s) and email address;
- Participants GP details including practice name, postal address and where possible contact telephone number(s) and email address
- Participants NHS Care provider details including full name, postal address and where possible contact telephone number(s) and email address
- Both the MR researcher interview and participant self-completed baseline CRFs completed and returned to YTU (*see section 10.4 Data collection schedule*)
- Confirmation that patient meets all the eligibility criteria
- Confirmation that informed consent has been obtained
- Confirmation if they can be contacted for qualitative interviews
- Confirmation if they would like to be sent a plain English summary of results
- Confirmation if they can be contacted for future studies.

To keep the MR researcher blinded to the allocation, the YTU will inform the participant of their allocation, and arrangements for the intervention delivery if allocated to this, via letter generated from the trial management system. YTU will alert the intervention coordinator/lead that there is a new participant and securely pass on the name and contact details either via

telephone call, the University of York's secure Drop-off system or via providing access to the secure Trial Management System. The intervention coordinator/lead will assign an interventionist to the participant and will confirm to YTU who this is; YTU can then add this information to the participants details. The interventionist will keep a record of intervention appointments and attendance by ID number. This will be stored securely until the intervention is completed, and then it will be transferred to the YTU.

The MR researchers who will be collecting follow-up data will be blinded to the participants' allocation. Participants will be asked not to reveal if they had the intervention or not and any accidental revelation of the trial arm will be recorded by the MR researcher as unblinded. Those who deliver the intervention will know the allocation but will not communicate this to the MR researchers working on the study. The trial statisticians and the health economist will not be blinded to allocation.

The participants GP and NHS Care Provider will be informed about their patients' study participation via letter generated from the trial management system; however, they will not be informed about allocation status, reducing the risk of inducing behaviour change based on this knowledge. However, allocation may be revealed to a participant's GP and NHS Care Provider in response to an adverse health event if necessary.

9. Sample size

The primary outcome for this trial will be the number of unprotected sex acts (vaginal, oral, and anal). In the RESPECT feasibility trial ([19]), we observed an excess of zeroes in this outcome at baseline - from both people who always used protection, and those who had not engaged in any acts at all. Therefore, to calculate the sample size we followed the method outlined for a zero-inflated Poisson analysis by Wang & Fan ([20]). In the feasibility trial, at baseline, participants had undertaken an average of 9 unprotected sex acts in the previous three months. Extrapolating this across 12 months, we might expect to observe an average of approximately 40 unprotected sex acts a year in the control group. Assuming a 0.35 zero-inflated probability in both groups, we would have 90% power, with a 5% two-sided significance, to detect a 25% reduction in the intervention group in the number of unprotected sex acts (40 to 30 acts) over a 12-month period, with 296 participants. Inflating for 20% attrition, we would require 370 participants to be randomised. To

allow for some flexibility in the parameters, as they are based on the feasibility trial, we shall aim to recruit 400 participants.

10. Outcome Measures

10.1 Primary outcome

Number of unprotected sex acts (anal, vaginal, oral) recorded every three months (at 3, 6, 9 and 12 months) over the 12-month follow-up using the Sexual Risk Assessment Schedule (SERBAS). This is a validated HIV risk behaviour measure which was developed in the USA and has been validated for use with populations who have SMI ([21],[22]).

This is a semi-structured interview, carried out by a trained researcher, that uses gender-specific (gender self-identified) questions to obtain information regarding sexual practices and related behaviours in the past 3 months, including the number, gender, and type of sex partner (steady, casual, or exchange); the types of sexual acts performed during each sex occasion; whether sexual acts were protected by condoms (male or female); whether sex was preceded by substance use (e.g., alcohol/drugs); whether sex was bought or sold (e.g., exchange sex); and the participant's self-reported history of HIV testing and status and knowledge of his/her partner(s)' HIV testing history and status. This measure has been used in sexual health promotion trials in the USA ([23]) and Brazil ([22]) as well as the RESPECT feasibility study ([19]). Completion of the SERBAS via semi-structured interview will be recorded in the Researcher CRF at baseline and follow-up.

10.2 Secondary outcomes

Includes a set of questionnaires that assess knowledge, motivation and behavioural intention to adopt safer sexual behaviour will be used and captured through participant CRFs at baseline and follow-up. These have been developed by Carey et al (2004) ([24]) and used in trials of sexual health promotion for people with SMI as well as in the RESPECT study ([19]):

- **Knowledge about human immunodeficiency virus and sexually transmitted infections – HIV- Knowledge Questionnaire (HIV-KQ)** ([24]): a 17-item measure that assesses knowledge about HIV. This originally comprised 18 items but we removed one question about lamb-skin condoms as this is now outdated.

- **Motivation to Engage in Safer Sex** ([24]): a four-item scale to assess people's own perception of their risk of infection with a STI.
- **Condom use Self-Efficacy Scale** ([24]): an 18-item Likert scale to assess attitudes towards the use of condoms as well as questions on self-efficacy in the use and negotiation of use.
- **Behavioural Intentions for Safer Sex** ([24]): an eight-item measure in which patients are presented with a scenario describing a possible sexual encounter and asked to rate how likely it was that they would engage in six risky or protective behaviours (e.g. 'I will tell the person I don't want to have sex without a condom'). Patients respond to each behaviour using a six-point scale (ranging from 0 'definitely will not do' to 5 'definitely will do'.
- **General questions about sexual health:** items adapted from the National Survey of Sexual Attitudes and Lifestyle (NATSAL)
- **Quality of life – EQ-5D-5L**: standardised instrument for use as a measure of health outcome that is applicable to a wide range of health conditions and treatments ([25]).
- **Recovering Quality of Life (ReQoL):** 20-item patient-reported outcome measure that has been developed to assess the quality of life for people with different mental health conditions ([26])
- **Health care resource use:** a bespoke resource use questionnaire will be used to capture all health care use, including medications.

Demographics and other relevant information will also be collected in the baseline CRFs: age, SMI diagnosis, sexual health history, non-volitional sex, relationship status, socio-economic data, gender identity, sexual identity, ethnicity.

10.3 Follow-up Data

Participants will be followed-up for a total of 12 months. Follow up data collection will be collected at 3 months, 6 months, 9 months and 12 months post-randomisation for both groups, which will be conducted as per baseline assessment. Participants will be actively contacted via telephone call by the MR researcher for up to 3 weeks post-data collection appointment schedule to complete the follow-up data collection. Participants will be contacted a maximum of 3 times over the 3 week period, with voicemails being left providing a contact number should the participant wish to discuss the trial or CRF. The MR researchers will record missed

appointments, as well as how many times they have been contacted (by text, telephone or via case provider) to arrange follow-ups.

10.4 Data collection schedule

Data	Time point collected				
	Baseline	Month 3	Month 6	Month 9	Month 12
Eligibility form (includes SMI diagnosis)	x				
Contact details	x				
Consent	x				
Demographic details and sexual health history **	x				
Non-volitional sex *	x				
SERBAS *	x	x	x	x	x
HIV-KQ **	x	x	x	x	x
Motivation to Engage in Safer Sex **	x	x	x	x	x
Condom use Self-Efficacy Scale **	x	x	x	x	x
Behavioural Intentions for Safer Sex **	x	x	x	x	x
General questions about sexual health: items adapted from NATSAL 3**	x	x	x	x	x
ED-5D-5L *	x	x	x	x	x
ReQol **	x	x	x	x	x
Health care resource use *	x	x	x	x	x
Qualitative interview			x		
Adverse event reporting	Ongoing				
Change of status reporting	Ongoing				

* Collected as part of the MR researcher interview CRF. The primary outcome (SERBAS) will be the first measure collected in this CRF.
**Collected as part of the participant self-completed CRF

11. Study treatments

Participants will be randomised to either receive the intervention plus usual care or usual care only.

11.1 Sexual Health Intervention

The sexual health intervention was designed and developed during the RESPECT feasibility study [18]. It comprises of three components:

1) Raising awareness of issues related to sexual health such as contraception choices, how to engage in sex acts safely, positive intimate relationships (Information)

2) Facilitating dialogue and reflection on own (and sexual partners) sexual health and unmet needs for advice, treatment, testing, contraception, skills (Motivation)

3) Behavioural skills (such as how to use a condom correctly), negotiate safer sex and/or communicate preferences or boundaries effectively (Behaviour)

The intervention manual is divided into sections on a variety of topics and includes interactive exercises rather than didactic presentation of information. There is flexibility to focus on people's specific needs and interests, sexuality and gender identity.

Timing: It will be delivered over 3 x one-hour 1:1 sessions by a person from the local NHS service (interventionist) who has received specific training from the study team. The three intervention sessions should be delivered as soon as practical after randomisation but must be completed before the 3-month follow-up data collection time point.

Location: It is designed to be delivered face to face or using remote videoconferencing sessions. In the feasibility study it was delivered in a person's home or using an office in a local service, and this was found to be acceptable to participants. The intervention can also be delivered on inpatient mental health units if a patient is awaiting discharge but remain in inpatient care due to the unavailability of suitable community placement.

Interventionist: An Intervention lead will work with the NHS sites to provide training and supervision for those who will be delivering the intervention. The criteria for the interventionists are broad:

- Experience of working with people who live with SMI
- Comfortable talking about sexual health and sexual practices
- Ability to work in a non-judgemental way, using core skills of engagement, empathy, listening, reflecting and summarising. Each recruiting site will be required to provide interventionists with protected time to deliver the intervention to participants in the NHS organisation (3 x one-hour sessions per participant).

The person does not require prior expertise of working in sexual health.

Fidelity to the manual: This will be assessed by a brief checklist at the end of each session completed by the interventionist. The interventionist will check off which of the session's components have been completed, which were omitted and why, and note any specific issues or needs that arose and if they were addressed in the session. The interventionist will also record the date and timing of each session and whether there were any cancellations and rearrangements. This data will be sent to the YTU for storage.

Engagement: Reminders will be sent by the interventionist via the participant's preferred communication method (e.g. such as text or telephone calls)**.**

Training and supervision: Intervention training will be provided by the Intervention Lead based at Glasgow Caledonian University, along with the Lived Experience Advisory Group (LEAG) and will introduce staff to the key-concepts and procedures involved in the intervention and research. The training will follow a similar format to the RESPECT feasibility study and will comprise of the following:

1) Introduction to the study including learning from the feasibility study.

2) Overview of the diverse sexual health needs that people with SMI experience.

3) Induction to the intervention. Each component of the manual will be presented as well as discussions about how to deliver the content to a range of people. Interventionists will practise using the materials to build confidence.

All interventionists will have access to additional resources should they be required - e.g., specific needs of people who identify as Lesbian, Gay, Bisexual, Transgender, Queer (LGBTQ).

Suitable interventionists from each NHS organisation will be identified in the months before the trial opens to recruitment and will be required to complete the one day of intervention training. This will be delivered online. This will be a rolling programme (repeated approximately every 2 months) to ensure that the intervention pool can be refreshed should sites lose interventionists,

and to allow for the staggered opening of sites. During the intervention delivery period the interventionists will have access to online monthly supervision sessions with the intervention lead.

11.2 Usual Care

There is no specific service for people with SMI in terms of their sexual health. All participants (irrespective of allocation) will continue to receive usual care for mental health and sexual health. All participants will all be given a localised sexual health services leaflet developed for the study (containing names and contact details of local sexual health, family planning and domestic violence support services) and sample pack of condoms.

12. Internal pilot

The first eight months will be run as an internal pilot with three progress measures used to determine the continuation of the trial: recruitment, attendance at sessions, and response rate at 3 months.

	GREEN {progress without any major modifications}	**AMBER {progression may be possible with modifications}**	**RED {consider stopping the trial}**
Pilot target recruitment	100% or more (n>=80 participants)	Between 75% and 99% (n=60-79 participants)	<75% (n<60 participants)
Attendance at intervention (sessions attended)	Average of 75-100% attendance	Average of 50-74% attendance	Average of <50% attendance
Questionnaire response rate at 3 months	75-100%	50-74%	<50%

13. Participant incentives

In acknowledgment of the time involved and as a thank you, each participant will receive a £10 voucher each time they complete and return a self-completed questionnaire (baseline, 3, 6, 9 and 12 months) up to a maximum of five vouchers in total, per participant.

14. Completeness of data

The primary outcome will be collected via meetings with the MR researcher (face to face or remotely) and therefore we expected minimal missing data, with the exception of those participants who do not attend/engage with appointments or whom MR researchers are unable to locate. Furthermore, the return of data is incentivised with a voucher, and therefore we believe participants will be motivated to complete and return data. We also know that there was good completeness of data in the RESPECT feasibility study with excellent engagement with data collection appointments by both intervention and control group. In addition, the participants reported that they found the data collection comfortable and interesting and appreciated receiving a Love to Shop Voucher [19].

15. Data handling, management and storage

Information with regards to the study participants will be kept confidential and managed in accordance with the Data Protection Act, NHS Caldicott Guardian, UK Policy Framework for Health and Social Care Research and the Health Research Authority.

Data management will ensure that each site and study participant is assigned a unique trial identification number at the start of data collection; all data (paper and electronic) will use this unique trial identification number. A record sheet linking patient identity, contact details and trial identification number for all participants will be kept at each site. This will be placed securely in a locked filling cabinet, separate from datasheets.

Identifiable data of consenting participants will be stored on paper and on a secure password protected electronic server at the University of York, for the purposes of assisting in follow-ups during the study. Personal data will be stored separately to the trial data. Study data will be collected using anonymous paper CRFs, which will be completed by both the MR researcher and the participant and returned to YTU via post. Paper CRFs collected from participants will be kept in a safe, secure environment (locked drawer in a locked office) by the MR researchers and posted as soon as possible to the YTU. Analytical datasets will not contain any identifiable information. The data management system, CRFs, identifiable data and non-identifiable data will be stored securely for up to 10 years after the end of the trial and then destroyed securely in accordance with the current YTU Standard Operating Procedures. Consent forms will be stored up to 6 years after the end of the trial and then destroyed, as allowed by the Prescriptions and Limitations Act.

All data will be kept secure at all times, maintained in accordance with the requirements of GDPR and archived according to Good Clinical Practice (GCP) regulations. Paper data collection forms transferred to or from the YTU will be coded with a participant ID. Data will be held securely on paper and electronically at YTU and appropriate processes put in place for the transfer, storage, restricted access, and disposal of personal information. Relevant Standard Operating Procedures (SOPs), guidelines, and work instructions in relation to data management, processing, and analysis of data will be followed.

Participating sites will be expected to maintain a file of essential trial documentation (Investigator Site File), which will be provided by YTU, and keep copies of all completed paper assessment packs and consent forms for the trial securely (until these are returned to YTU).

In terms of the qualitative data, this will be collected using Microsoft Teams at Glasgow Caledonian University. Interviews will be conducted with participants and recorded in Teams. This generates a transcript and an MP4 file. This will be stored in a secure drive at Glasgow Caledonian University. The transcript will be cleaned and de-identified and the names removed and the participant will only be identified by their unique trial ID number. Any personal information required will also be coded with this identification number and kept in a password protected electronic file or separate filing cabinet which will be locked at all times. Any quotes published will be anonymous further protecting participant confidentiality. All qualitative data will be stored and analysed using a secure drive at Glasgow Caledonian University. The qualitative data will be stored for 10 years.

All data from the trial will be collected using paper-based CRFs. These will be filled in by both the researchers and the participants themselves. MR researchers and clinicians will be responsible for ensuring the completeness and reliability of the data from their site, and then for securely transferring this data to YTU. Once the paper forms have been returned to YTU, this data will be entered into a master database for the trial using either optical scanning techniques or will be entered manually.

16. Qualitative research

16.1 Interview format

The aim of the qualitative interviews is to gather richer data about what works for whom under what circumstances with regards to sexual health in this group (realist evaluation). We will purposively sample people from those who consented to participate in the trial and consented to be considered for the qualitative interviews at 6 months post randomisation. The sampling framework will ensure there is representation across a range of diversity characteristics including location, sexuality, gender, ethnicity, age, and type of mental health condition.

Sample Size: In qualitative research, the sample size is not precise, and it is more important to achieve a range of diverse participants. We will aim to interview up to 40 people via videoconferencing (MS Teams) or telephone. The interviews will be conducted by peer researchers who are part of the LEAG, and the MR researcher based at Glasgow Caledonian University. The peer researchers will be employed as casual workers at Glasgow Caledonian University, receive supervision and training from the chief investigator (CI) (who is experienced in realist interviews and evaluation). All have conducted GCP training, and will have letters of access from relevant NHS sites. In addition, the peer researchers will co-produce the topic guide and will receive training and practice in undertaking the realist interview.

The interviews will take approximately 40-60 minutes. It will be based on realist evaluation and will seek to test and refine a set of programme theories about what works in terms of addressing sexual health needs for people with severe mental illness.

The data obtained will complement the trial data and identify the contexts, mechanisms that lead to positive outcomes in the trial by comparing those who had participated in the intervention as well as those in the control group, as well as across different sites and locations.

16.2 Transcription and analysis of data

The data will be collected using Microsoft Teams video/audio call within Glasgow Caledonian University Teams account. The interview will be recorded and transcription is automatically generated. This is then checked for accuracy and any typos corrected. Audio files will then be deleted. A realist approach to Thematic Analysis (TA) will be adopted in order to develop three types of themes ([27]).

The stages of Braun and Clarke TA will be followed using familiarisation, generating codes, constructing themes, reviewing themes and producing the findings. Using a realist approach will identify the contexts and mechanisms required to produce the desired outcomes. This is particularly important in a large trial being delivered in several organisations and geographical locations. This will enable better understanding of how the intervention worked (or not) in order to assist with translation of sexual health promotion into routine care ([28]).

17. Economic Evaluation

An economic evaluation will be undertaken to determine the cost-effectiveness of the moreRESPECT sexual health promotion intervention. The analysis will be conducted from the perspective of the NHS and personal social services and will assess the relative cost-effectiveness of moreRESPECT compared with usual care. We will measure relevant costs and calculate quality adjusted life years (QALYs) to estimate the incremental cost-effectiveness ratio. We will record the costs of delivering the intervention, including training costs. A bespoke resource use questionnaire was developed during the RESPECT feasibility trial [(19)]. This has been adapted for the present trial based on lessons learnt during the feasibility study and will collect health care usage.

The intention-to-treat population will be used for all analyses and the time horizon will be one year as per the duration of follow-up. Costs and outcome data for the economic analysis will be collected prospectively during the trial using questionnaires following the same timeline as the clinical outcomes, specifically, baseline, 3, 6 and 12 months.

18. Statistical Analysis

A detailed statistical analysis plan will be developed prior to completion of data collection and agreed with the DMC and TSC. All analyses will be undertaken on an intention to treat basis, where participants are analysed as randomised, regardless of whether they complied to their allocation or not. The analyses will be conducted at a 5% significance level using two-sided statistical tests, unless otherwise specified. The flow of participants through the trial will be detailed using a CONSORT flow diagram ([29]). Baseline and outcome data will be summarised descriptively, overall and by arm, with continuous measures using means and standard deviation, and categorical variables by counts and percentages. All assumptions related to the analyses detailed below will be checked.

18.1 Primary analysis

A zero-inflated Poisson regression model will be used to compare the number of unprotected acts between the two groups. The model will be adjusted for relevant baseline covariates as well as site as a random effect. The length of follow-up will be accounted for in the model. Should model assumptions not be met, or there is evidence of overdispersion, other appropriate models will be considered, such as a negative binomial regression model. The incidence rate ratio will be extracted as the point estimate of treatment effect and reported with the 95% confidence interval and p-value.

A compiler average causal effect analysis may be undertaken as a sensitivity analysis of the primary outcome, to account for non-compliance with the intervention.

18.2 Secondary analysis

The secondary outcomes will be analysed using appropriate regression models, adjusted in the same way as the primary analysis, but including a random effect for participant to account for the repeated measures. HIV-KQ, Condom use Self-Efficacy Scale, and Behavioural Intentions for Safer Sex are continuous outcomes, and a mixed-effects linear regression model will be used. As there is no scoring for the 4-item Motivation to Engage in Safer Sex measure, the responses to each question will be compared between the two groups using a multinomial logistical regression.

18.3 Analysis of economic and quality of life data

The within-trial cost-utility analysis will be conducted from an NHS and personal social services research unit (PSSRU) perspective to assess the cost-effectiveness of the moreRESPECT intervention compared with usual care. In the primary analysis, utility will be measured using the EQ-5D-5L, the preferred instrument by NICE for measuring quality of life ([30]). The ReQoL will also be used as a secondary measure of quality of life as this instrument is specifically designed for users of mental health services. The domains of the EQ-5D-5L and the ReQoL will be valued using UK population tariffs to provide utility scores at each time point to derive QALYs for each participant using the area under the curve (AUC) method.

Health care resource use will be presented for both arms in terms of mean value, standard deviation, and mean difference (with 95% CI) between the groups. The cost of the intervention will be estimated according to treatment and resource use costs. Costs will be derived from established national costing sources such as NHS Reference Costs ([31]) and PSSRU costs ([32]) of health and social care. Unit costs will be multiplied by resource use to obtain a total cost for each patient.

The cost of delivering moreRESPECT will be estimated taking a bottom-up approach to identify and place a value on the constituent parts of the intervention delivery, e.g. staff and training costs, to estimate its total cost in monetary terms.

Multiple imputation methods will be used to deal with missing data if appropriate ([33]). Uncertainty will be described using confidence intervals and cost effectiveness acceptability curves (CEACs). A range of sensitivity analysis will be conducted to test the robustness of the results under different scenarios.

The economic analyses will adhere to the NICE Guide to the Methods of Technology Appraisal ([30]) and will be detailed separately to this protocol in a trial-specific Health Economics Analysis Plan (HEAP).

19. Compliance and withdrawal

19.1 Participant compliance

Participants will not be withdrawn on the basis of non-compliance with the intervention.

19.2 Loss to follow up

The moreRESPECT team will contact the participant's NHS case provider or GP to identify any new contact details for a participant who we have lost contact with.

19.3 Withdrawal/ dropout of participants

Participants may withdraw from the study at any time without influencing their future care or treatment. Withdrawal may refer to the following situations:

- '*Withdrawal from intervention':* where a participant wishes to withdraw from the study intervention, but is prepared to continue completing follow-up questionnaires (i.e. no intervention sessions are attended but the data is still collected). This is pertinent only to the sexual health intervention arm of the study.
- '*Withdrawal from follow-up':* where a participant wishes to withdraw from completing any further follow-up interviews after completing their intervention sessions or after baseline data collection if in the control group.
- '*Full withdrawal': w*here a participant wishes to withdraw from both the study intervention (if applicable) AND from completing any further follow-up interviews. Where full withdrawal is requested this will be termed trial exit, where a participant leaves the trial and no further data are collected from them.

A participant can be withdrawn without their consent from the intervention and/or the trial for reasons of risk or harm to self and/or others. This would only be actioned with evidence of serious and significant risk. In these instances, a safeguarding protocol developed for the trial will guide the interventionist and/or researcher in the appropriate action to be taken in conjunction with the lead research clinician and the duty worker in the organisation. Where possible this would include discussion with the participant so that they understood the reason for discontinuing their participation, however would not be an essential requirement.

Where participants lose capacity to consent during their time in the study, they will be withdrawn from further follow up; however, data collected until this point will be retained for use. No further data would be collected or any other research procedures conducted in relation to the participant.

We will ensure that the moreRESPECT researchers are aware of the differences in types of withdrawal, and that they are explicit about whether participants wish to withdraw from the intervention, follow up, or both. In any event, a change of status form will be completed and YTU will be informed.

20. Data Monitoring

The CI will ensure that the study is appropriately monitored by ensuring that: all rights of the trial participants are adequately protected; that written informed consent is obtained; the trial data are accurate and complete; and that the conduct of the trial complies with the protocol and its subsequent amendments, with GCP and applicable regulatory requirements.

Monitoring and source data verification will be conducted by YTU on behalf of the Sponsor according to a study monitoring plan. The extent and nature of monitoring will be determined by the study objectives, purpose, design, complexity, masking, number of patients and sites, and endpoints.

The Sponsor may suspend or prematurely terminate either the entire study, or the study at an individual site, for significant reasons that must be documented (e.g. an unacceptable risk to participants or serious repeated deviations from the protocol/ regulations). If this occurs the Sponsor shall justify its decision in writing and will promptly inform any relevant parties (i.e. participants, investigators, participating sites, REC, regulatory bodies).

21. Ethical and Regulatory considerations

21.1 Assessment and Management of Risk

No formal monitoring visits will be planned for this study. A monitoring plan will however be generated for the study, to outline the range of centralised monitoring activities (e.g. eligibility, consent, safety checks), which will be undertaken in this study.

21.2 Peer Review

This study has been peer reviewed as part of the NIHR Health Technology Assessment application process.

21.3 Research Ethics Committee (REC) & Regulatory Considerations

The moreRESPECT trial will be subject to approval from the REC and the Health Research Authority prior to trial activity commencing. The study will be conducted in accordance with the UK Policy Framework for Health and Social Care Research ([34]) and Medical Research Council (MRC) GCP Guidance ([35]).

Before any sites can enrol a participant into the trial, confirmation of capacity must be sought from the site's Research and Development (R&D) department. In addition, for any amendment that will potentially affect the site's permission, the research team must confirm with the site's R&D department that permission is ongoing.

21.4 Informed consent

All eligible people will be provided with a detailed PIS prior to giving consent and provided the opportunity to ask any questions regarding the study. The PIS will outline fully the potential benefits and risks of being involved in the trial and will meet all the requirements of the Health Research Authority (HRA). It will state explicitly that quality of care will not be compromised if the participant decides to a) not enter the trial or b) withdraw their consent. We will make it clear that there is no obligation to participate.

Maintenance of confidentiality and compliance with the UK Data Protection Acts will be emphasised to all study participants. Participation in the study will be entirely voluntary and written consent will be sought. All data will be treated with the strictest confidence. Potential participants will be excluded from participating in the trial if it is felt they are lacking in capacity to consent as guided by the Mental Capacity Act.

21.5 Risks and anticipated benefits for trial participants and society

Individual participants may not benefit directly from this research. Risks and burdens to patients have been considered during the study design process. Burdens include time to fill in the questionnaires and, if in the intervention group, meeting with the interventionist three times. The main risk from participating in the study is embarrassment regarding collecting data about sexual behaviour, and if receiving the intervention, discussing sexual health and relationships. Some of the questions may also trigger upsetting memories (see 'Distress management section). These aspects are clearly explained in

the PIS and patients are given as much time as they need to decide whether or not they would like to take part. The research will be undertaken in a sensitive way, maintaining awareness of the vulnerability of many of the participants. MR Researchers will be briefed in and have a copy of the safeguarding protocol which will cover all aspects of risk, including disclosures.

In terms of benefits to society, should this intervention prove clinically and cost effective and be widely implemented, it would have a significant impact on the sexual health of people diagnosed with SMI.

21.6 Protocol Compliance

The CI is responsible for ensuring that the study is conducted in accordance with the procedures described in this protocol. Prospective, planned deviations and/or waivers to the protocol are not acceptable. Accidental protocol deviations may happen and as such these must be reported according to the YTU SOP. Deviations from the protocol which are found to frequently recur are not acceptable, and will require immediate action. Where events are repeated this may constitute a serious breach.

21.7 Notification of Serious Breaches to GCP and/or the Protocol

A “serious breach” is a departure from the protocol, agreed procedures (i.e. SOPs), or regulatory requirements which is likely to effect to a significant degree:

(a) The safety or physical or mental integrity of the subjects of the study; or
(b) The scientific value of the study.

If a serious breach is identified YTU should be notified immediately (i.e. within 1 working day) using the appropriate form. The report will then be reviewed by the Sponsor and CI, and where appropriate, the Sponsor will notify the REC within 7 calendar days of being made aware of the breach.

22. Safety and Adverse events

22.1 Definition of adverse events

The moreRESPECT trial intervention is a psychosocial intervention not a medicinal product and as such does not have medical/physical health adverse events associated with it. However, there is a low risk that conversations around sexual health could trigger distressing emotions and thoughts and for people with severe mental illness, and this could then trigger a relapse of their mental health issues. Any study involving people who are vulnerable should be vigilant for the impact of the study on mental well-being and psychological safety.

For the purposes of the moreRESPECT trial, adverse events (AEs) are defined as any untoward medical occurrence (i.e. any unfavourable and unintended sign, symptom or disease), experienced by a trial participant and which is temporally associated with trial treatment (intervention or control).

Adverse events, which might be expected include:

Attempted or completed suicide, serious assault of others, victim or perpetrator of a serious sexual assault or sexual harassment.

AEs which would not require reporting include:

Medical conditions such as stroke, heart attack, accidents, infections etc that required emergency treatment or admission to general medical services.

22.2 Serious Adverse Events

To ensure no confusion or misunderstanding of the difference between the terms "serious" and "severe", which are not synonymous, the following note of clarification is provided:

> *The term "severe" is often used to describe the intensity (severity) of a specific event (as in mild, moderate, or severe myocardial infarction); the event itself, however, may be of relatively minor medical significance (such as severe headache). This is not the same as "serious," which is based on patient/event outcome or action criteria usually associated with events that pose a threat to a participant's life or functioning. Seriousness (not severity) serves as a guide for defining reporting obligations.*

Serious adverse events (SAE) are defined as any untoward medical occurrence that:

a) Results in death;
b) Is life threatening;

   NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if it were more severe.

c) Requires inpatient hospitalisation (unplanned or prolongation of existing inpatients' hospitalisation);
d) Results in persistent or significant disability or incapacity;
e) Is a congenital anomaly or birth defect;
f) Any other important medical condition that, although not included in the above, may require medical or surgical intervention to prevent one of the outcomes listed.

22.3 Reporting Procedures for Adverse and Serious Adverse Events

Adverse events that are deemed related to participation in this study should be entered onto the Adverse Event reporting form and reported to YTU within 5 days of discovery or notification of the event.

SAEs are reported to the CI and YTU within 24 hours of discovery or notification of the event. Once received, causality and expectedness of SAE will be confirmed by the CI or another clinical member if the CI is unavailable. Any serious adverse events deemed as 'related and unexpected' to trial intervention will be reported to the Research Ethics Committee and Sponsor within 15 days. All such events will be reported to the Trial Steering Committee (TSC) and Data Monitoring Committee (DMC) at their next meetings.

All AEs [serious and non-serious] will be reported to the CI and reviewed by CI and a senior member of the YTU according to a SOP specific to this study. We are aware that judgements regarding relatedness can be difficult in this type of study, and therefore all SAEs will be forwarded to the DMC within 48 hours of the CI becoming aware of the event. Any event deemed by the team and the DMC as 'related' to study treatment will be reported to the sponsor, ethics committee and TSC. Any non-serious AEs considered as 'related' to study treatment will also be forwarded to the DMC.

22.4 Distress management

The research team are aware that some people who have experienced sexual abuse and exploitation may find participating in this study distressing and may trigger difficult feelings. The participant information sheet will be clear about the nature of the study and the potential for it to be distressing. If a participant expresses any signs or reports any distress during any study related activity (e.g. meeting with a member of the research team or during intervention delivery) an immediate halt will be implemented to the activity. Study specific guidance will be used to guide the researcher or interventionist for the management of this situation. Incidences of low-level distress will be reviewed during the researcher's own scheduled supervision meetings. If a participant is referred to the local mental health team for management of their distress the CI (or delegated research clinician) will be informed within 24 hours. This could be a potential AE and the severity will be assessed at the time in conjunction with the CI. If it is deemed to be an AE, the AE procedure will be followed.

23. Definition for the End of Trial

End of study will be defined as the date at which the last participant has completed their final study process.

24. Project management

24.1 Trial Sponsor

The trial will be sponsored by Glasgow Caledonian University.

24.2 Trial Management

YTU at the University of York is responsible for trial management. The day-to-day management of the trial will be the responsibility of the Trial Coordinator and the Trial Manager, supported by other relevant members of trials unit staff. The Trial Coordinator, on behalf of the CI, will submit and, where necessary, obtain approval from all relevant parties for all substantial amendments to the original

approved documents. Regular progress reports will be submitted as required to the funding body and regulatory authorities.

24.3 Trial Management Group (TMG)

A Trial Management Group (TMG) will monitor the day-to-day management of the trial including the detailed design, set up, initiation and supervision of the study. Regular meetings of the TMG will take place to oversee the progress of the trial and review recruitment. This group will include the CI, co-applicants, collaborators, local principal investigators, representatives from the data management staff, trial statisticians and research staff. A representative of the Sponsor will also be invited to attend. The group will meet every two months as an online or hybrid group.

24.4 Trial Steering Committee (TSC)

The committee will consist of an independent chair and at least two other independent members including a statistician and someone from a relevant discipline/ profession, and an independent person with lived experience, along with the CI and the Trial Coordinator/Trial Manager. Other study collaborators may also attend the meeting at the discretion of the Chair. The TSC will meet at least twice a year to discuss progress of the trial, or more often as appropriate. The role of this committee will also include the review of all serious adverse events, and the AEs which are thought to be treatment related and unexpected.

24.5 Data Monitoring Committee (DMC)

The committee will consist of independent experts (including independent statistician and mental health professionals), who are independent of the CI and the study team. Its remit will be to monitor the trial data in particular quality control and quality assurance of the data collected and progress of the trial including adherence to the trial protocol. The committee will also examine and ensure that the dignity, rights, safety and wellbeing of all study participants are maintained at all stages of the trial. Data reports will be supplied, including any adverse events, and the committee will have access to summary data and documentation. The Chair of the DMC will be informed of any AEs that arise from the study or regarding participants during the study period, and they will

be in a position to recommend suspension or ending the trial depending on the severity of the adverse event. The DMC will report to the TSC as necessary.

25. Patient and Public Involvement

Active involvement of People with Lived Experience (PWLE) of SMI is essential for this trial. Development of an acceptable and feasible complex intervention requires co production with service users and clinicians as well as researchers (MRC, 2008) and PWLE were integral to all stages of the original RESPECT feasibility study. In this present study, we will continue to have PWLE representation on the Trial Management Group as co-applicants.

There is a LEAG comprising of 6 people who have all experienced mental health issues as well as having an interest in promoting sexual health. The LEAG meet monthly to discuss the study and progress. Two of the LEAG are also co-investigators on the moreRESPECT team. The LEAG are involved in recruitment strategy, creating promotional materials, informing the protocol, and refreshing the manual for the intervention. They also advise on how to increase accessibility for people to participate. Members of the LEAG will be involved in the qualitative process evaluation and will undertake qualitative interviews and analysis of the data. All LEAG members will be involved in the report and paper writing outputs as well as lay outputs such as blogs.

26. Financing and insurance

This study is conducted by staff from Glasgow Caledonian University, YTU (University of York), University College, London, Leeds and York Partnership NHS Foundation Trust, Guy's and St Thomas' NHS Foundation Trust and East London NHS Foundation Trust. The research has been funded by the National Institute of Health Research Health Technology Research Programme.

NHS Indemnity will apply for patients treated within NHS sites. Glasgow Caledonian University, University College, London and the University of York will provide legal liability cover for their employed staff. Non-negligent harm will not be covered.

27. Reporting and dissemination

Results from this study will be written up and submitted to peer-reviewed journals, irrespective of the feasibility outcome. A publications policy will be generated in advance to detail authorship, acknowledgements and review processes for any publications arising from the moreRESPECT study.

The findings will be presented at relevant national and international conferences.

A summary of the trial results will be produced and made available to participants via a lay summary or blog that will be sent to every site to be distributed to those who participated. Service users involved in the LEAG will be asked to actively participate in the generation of this to ensure the results are easily accessible to patients.

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