Study Protocol and Statistical Analysis Plan
Title: Reproductive Life Planning for Women with Mental Illness
Clinical Trials ID: NCT03969589
Document Date: 1/20/22

BACKGROUND:
Many women Veterans are of reproductive age and, of those, a substantial number experience mental health concerns. Women Veterans with mental illness are at greater risk for unplanned pregnancy and adverse pregnancy outcomes due to factors unique to mental illness and mental health treatment. In addition, mental health and mental health-related concerns associated with pregnancy (e.g. impact of pregnancy on mental health, psychiatric medication use during pregnancy) often affect reproductive life decisions and health outcomes. For these reasons, reproductive life planning (RLP), setting personal goals and plans regarding reproductive intentions, that incorporates considerations and addresses concerns specific to mental health conditions is particularly important for women with mental illness. Despite this need, women Veterans with mental illness rarely receive RLP, and current tools do not adequately consider or address the unique reproductive health considerations women with mental illness often experience.

Research on the efficacy of RLP in improving reproductive outcomes in and tailoring for women with mental illness is limited. Use of RLP in routine care and RLP interventions that specifically address the unique needs of women Veterans with mental illness are even more lacking. Both represents significant gaps that hamper the VHA's ability to provide quality comprehensive health care for women Veterans—gaps highlighted by the identification of reproductive mental health as a priority goal in the VHA's Strategic Plan for Enhancing Delivery of Reproductive Health Services and in the Women's Health Research Agenda. The current study attempts to address these gaps by examining the feasibility, acceptability, and potential efficacy of a mental health-informed facilitated RLP/RLP goal setting intervention specifically designed for women Veterans with mental illness (Reproductive Life Plan for Mental Health; RLP-MH).

METHODS:
Overview: We will conduct a pilot feasibility trial of 40 women Veterans of reproductive age with mental illness receiving outpatient mental health services at the VA Maryland Health Care System (VAMHCS). Participants will be randomly assigned to 1) the RLP-MH intervention or 2) control (receipt of the VA's Reproductive Life Planning Quick Guide and other written materials) after completion of the baseline assessment. The purpose of this pilot trial is to establish feasibility and acceptability of the RLP-MH and to explore its potential efficacy.

Participants: Forty participants will be recruited from VAMHCS outpatient mental health and women's health programs (Baltimore & Perry Point VAMCs; CBOCs). Inclusion criteria are: (1) female, 2) between 18 and 40 years of age, (3) chart diagnosis of schizophrenia or schizoaffective disorder, bipolar disorder, major depression, or PTSD, and (4) currently receiving mental health services at the recruitment site. Exclusion criteria are: (1) currently pregnant, or (2) inability to have children (e.g. infertility, hysterectomy, tubal ligation).

Recruitment: Recruitment will take place at outpatient clinics/programs within the VA Maryland Health Care System (VAMHCS). Potential VA participants will be identified by several methods: (1) CPRS chart review and screening via use of a partial HIPAA waiver, (2) VA clinician referrals of participants who meet inclusion criteria and who might be interested in participating, (3) Self referrals by participants who hear about the study and are interested in participating or who have participated in other MIRECC studies and have given permission to be contacted regarding future studies, (4) Self-referral via IRB approved study flyer and other advertisements. Per VA requirements, initial contact with potential veteran participants will be made in person or by letter prior to any telephone contact. Specifically, we will approach individuals before or after their VA appointments.

We may also send out a letter to potential participants to see if they are interested in participating in the study. In this letter, they will be given contact information for the study staff (phone number) as well as a pre-stamped postcard to mail back to indicate their interest or lack of interest in the study. If after a few weeks, we do not hear from them, a follow-up phone call may be made to ensure the potential participant received the mailing. This follow-up phone call is mentioned in the mailing, so that potential participants will not be caught off guard when they receive a call from study staff.

We will use VA email to communicate with potential and current participants in order to send electronic copies of resources, blank worksheets, and/or response cards for them to use at a later time. We will only 1) contact potential veteran participants via VA email at their request after they have provided and given us permission to contact them via email or 2) send study materials at the veteran's request (staff will discuss proper procedures for communication via email with the veterans ahead of time to ensure understanding). The emails will also include a clear statement that no completed forms or personal identifying information should be sent to staff via email correspondence.

Research staff will email or mail potential Veteran participants a copy of the informed consent form and then meet with the potential Veteran participants by phone or via telehealth. We will use the following procedures outlined below to review to consent document and ensure that the participant is fully informed prior to providing verbal consent (we will not collect informed consent forms signed by the participant).

The study interviewer will provide an overview of the project, and invite him/her to participate. Interested participants are provided an informed consent form. After the consent form has been summarized in detail and all questions answered, the staff confirms that the participant is still interested in participating by soliciting a verbal response. Those who express willingness to provide consent must complete a brief questionnaire to assess competency and understanding of the consent form. If the participant is unable to answer the questions correctly, staff re-reviews the aspects of the study that the participant did not understand. The staff member asks the questions a second time. If the participant cannot answer all questions correctly, he/she will not be enrolled in the study. Participants will also receive a Health Insurance Portability and Accountability Act Authorization to Obtain, Use and Disclose Protected Health Information for Research (HIPPA) that will be reviewed with them. Staff will ask participants if they have any questions once the document has been read.

Procedures:
Baseline Assessment: Women Veterans who consent to participate will complete a baseline assessment. Research assistants conducting the baseline interviews will be blind to the participant's condition. After the assessment is completed (~45-60 min), the Veteran will be randomized to one of the two study conditions by the study interventionist 1) the RLP-MH intervention (a RLP-MH session and 1-month follow-up phone session) or 2) the control (written materials on reproductive life planning).

Study Interventions:
RLP-MH condition:
RLP-MH session: Those who are assigned to the RLP-MH intervention condition will complete the RLP-MH session after baseline. Sessions will be completed using telehealth. During this session, participants will meet with the RLP facilitator to complete the RLP-MH tool and develop a reproductive life plan. This will involve discussing whether the participant wants to have children, number and timing of pregnancies, physical and mental health conditions and

behaviors that may impact pregnancy, planned method of contraception if the participant does not want to get pregnant immediately, and potential action steps related to the reproductive life plan. Once all relevant components of the RLP-MH are completed, the facilitator and participant will develop a brief personal RLP summary (~4-5 sentences long) that summarizes the individual's reproductive life plans and goals. The final RLP summary, action steps, and obstacle-minimizing strategies will be recorded on the RLP Goals Worksheet and a copy given to the participant either in person or via mail if being completed via telehealth. Their RLP summary and goals will also be entered into a chart note with providers chosen by the participant included as co-signers. This session will take approximately 45-60 min to complete. Immediately after completing their RLP summary and goals, participants will be asked to complete a brief post-treatment assessment (~15 minutes; RLP-MH condition participants only). For appointments conducted over telehealth, participants will be sent a link to the questionnaires via by email or text.

One-month Follow-Up Session: The RLP-MH facilitator will conduct a brief follow-up session in-person or by phone (depending on the individual's preference) ~ one month after completing the RLP-MH session to discuss progress in addressing RLP goals and problem-solve around any obstacles to addressing goals. This session will last ~ 15 minutes.

Control Condition: Those that are assigned to the control condition will received written materials on reproductive life planning and information on VA resources for women Veterans. The facilitator will briefly review these materials with the participant, including a brief description, potential purpose/benefit, how they might be used, and how a RLP can be shared with provider(s). Review of these materials will take approximately 15 minutes. This intervention can be done via telehealth, or over the phone, depending on the participant's availability following randomization. Participants will either be emailed or mailed the corresponding materials, depending on their preferences, prior to reviewing the materials.

2-month Follow-up Assessment:
Research staff will attempt to contact participants by phone and/or by letter in order to schedule the 2-month post-treatment assessment. Follow-up interviews will be completed either in person or via telephone and will last approximately 45-60 min.

STATISTICAL ANALYSIS PLAN:
Overview: Consistent with the objectives of this small pilot randomized controlled trial (RCT), our primary data analysis approach will be to estimate means, proportions, and group differences with point and interval estimation (i.e. 95% confidence intervals). In the face of sample variation, a confidence interval provides a range for the "true" population value of a parameter consistent with the observed data. Further, estimates of recruitment, completion, and attrition percentages will be used to plan for a larger trial if warranted. We will estimate difference of means (and effect sizes) and proportions on outcomes to evaluate potential for efficacy as another input to the decision whether the RLP-MH intervention merits further testing. The trial will be conducted according to the "intent-to-treat" principle in that outcomes will be assessed regardless of RLP-MH attendance.

Aim 1 - Feasibility: We will calculate point and interval estimates of the overall recruitment percentage and the RLP-MH intervention completion percentage (defined as attending baseline visit and the one-month follow-up visit). The point estimate for overall recruitment percentage = number consented / number approached to participate in the trial. Interval estimation will be by 95% confidence intervals. The point estimate for the RLP-MH completion percentage = number completed / number randomized to the intervention. The overall and group attrition percentages

will also be estimated, = number without the 2-month assessment / number consented and randomized. Interval estimation will be by 95% confidence intervals. In addition to assessing feasibility, these estimates will also inform the planning of a subsequent confirmatory trial if warranted. Point and interval estimates will be calculated to estimate mean fidelity score to further assess feasibility.
Aim 2 – Acceptability: Acceptability of the RLP-MH intervention will be assessed quantitatively and qualitatively. Quantitatively, we will calculate point and interval estimates of our satisfaction questionnaire. Responses to open-ended acceptability questions at the post-treatment assessment will be compiled and examined for common themes.
Aim 3 – Explore Potential Efficacy: Preliminary. Before we perform analyses, we will first check variable distributions and missing data. Despite randomization, with a smaller sample size it is possible for covariate imbalance to occur by chance. As a sensitivity analysis, when making group comparisons, if a clinically relevant covariate (e.g. age, race) significantly differs across the two conditions we will repeat the primary analysis adjusting for the covariate to assess its impact on outcome effects as a secondary analysis.
3a: For the three outcomes for this sub-aim, the Decisional Self-Efficacy, Attitudes Towards RLP, and RLP Behavioral Intentions scales we will estimate the difference in mean change from baseline to the 2-month follow-up between the RLP-MH and control groups using a simple random intercept linear mixed model. This will allow inclusion of all observed outcome data. Between-group effect sizes will be calculated as the model-estimated difference in mean change divided by baseline pooled (across interventions) raw standard deviation. A bootstrap procedure will be used for effect size interval estimation. In addition to the comparisons between groups above, we will estimate the mean change in the RLP-MH condition on the RLP Behavioral Intentions and Decisional Self-Efficacy Scales from baseline to post-intervention using a mixed model.
3b: The RLP behaviors that will be quantitatively analyzed are generally Yes/No self-report questionnaire items that will be assessed at the 2-month follow-up in both arms of the trial. For example, questions ask: (1) if they've had any patient-provider reproductive health discussions, (2) if they've sought after reproductive health information, and (3) if they've taken any steps to address they're reproductive needs or goals. We will estimate the group difference in the proportion of 'Yes' responses with point and interval estimates using normal approximation. To adjust for a potential out-of-balance covariate (e.g. race) we will use logistic regression.

Sample size considerations: With an interval estimation approach, sample size is reflected in the precision of these estimates (i.e. the larger the sample the smaller the confidence interval widths). For example, for feasibility (Aim 1), with the proposed sample size of 20 randomized per study arm, observed intervention completion proportions in the RLP-MH group of .60, .75, and .90 would have 95% confidence intervals of (.39,.81), (.56,.94), and (.77,1.00). For potential efficacy assessed at the 2-month follow-up (Aim 3b), one assessed health behavior outcome will be "Any conversations with health provider regarding RLP or reproductive health? Yes/No". If the proportions of Yes responses to this question in the RLP-MH and control condition are, respectively, .25 and .10, .50 and .20, or .60 and .20, then the point estimates for the difference would be .15, .30, and .40, favoring RLP-MH, and the 95% confidence intervals for the differences would be (-.08,.38), (.02,.58), and (.12,.68). These calculations account for attrition equal to 15%.