RESEARCH PROTOCOL

Behavioral Activation and Medication Optimization For Improving Perioperative Mental Health In Older Adults Undergoing Cardiac Procedures

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1. SYNOPSIS

Study Title	Behavioral activation and medication optimization for perioperative mental health in cardiac procedures
Abbreviated title	CPMH Cardiac R34 RCT
Objective	Using a Hybrid Type 1 Effectiveness-Implementation RCT design, we will test the effectiveness of a bundled behavioral activation and medication optimization in reducing symptoms of depression and anxiety in older adults undergoing cardiac surgery (compared with usual care), while examining implementation outcomes.
Study Period	Planned enrollment duration: 12-15 weeks (an initial visit; follow-up survey at 1 and 3 months) Planned study duration: 2 years
Number of Patients	100
Study Treatment	Behavioral activation and medication optimization
Study Design	Hybrid Type 1 Effectiveness-Implementation prospective randomized controlled trial design.
Inclusion and Exclusion Criteria	Inclusion criteria: • Adults ≥ 60 years • Scheduled major cardiac procedure • PHQ-ADS ≥ 10, indicating clinically significant depression or anxiety symptoms Exclusion criteria: • Barrier to communication (Unable to read, speak, and understand English) • Severe cognitive impairment screened by the SBT (Short Blessed Test) >10 • Acutely suicidal

	• Previous participation in this study or another CPMH study of the intervention bundle or its feasibility.
Measurements	<u>Baseline</u> PHQ-ADS Quality of Life (CDC HRQOL-14) Short Blessed Test (SBT) Presence and intensity of preoperative pain <u>In-Hospital</u> Delirium (extracted from electronic health record retrospectively) Medications of interest <u>Postoperative</u> PHQ-ADS Quality of life Rehospitalization Falls Presence and intensity of Persistent post-surgical pain (PPSP) Pain interference, using modified Brief Pain Inventory (BPI) Medications of interest
Statistical Methodology	The study will use a modified Intent To Treat (mITT) approach where randomized patients who did not have the surgery or procedure will not be included in the analyses. We will compare the intra-group PHQ-ADS change scores from baseline to 3 months after surgery as the primary outcome. As exploratory outcomes, we will compare each the following outcomes between the groups: (occurrence, or change from baseline to 1-month, and 3-month follow-ups, as appropriate): • Quality of life (CDC HRQOL-14) • Length of stay (ICU & hospital) • Delirium • Rehospitalization • Falls • Persistent post-surgical pain presence and pain interference • Medications of interest The following measures will be collected from patients allocated to the intervention arm for implementation assessment: • Reach • Implementation potential (i.e., Acceptability of intervention; Appropriateness of intervention; Feasibility of intervention)

	• Patient satisfaction and experiences with overall surgical experience and intervention bundle A combined measure including modified versions of the following scales will be collected only from patients allocated to the intervention arm to assess engagement with our intervention bundle approximately 2 months after surgery: • Sinclair Compassion Questionnaire-Short Form (SCQ-SF) • Behavioral Activation for Depression Scale (BADS) Activation subscale • MiPrep survey

2. STUDY PROTOCOL

2.1 Background and Significance

Inadequate management of preoperative mental health disorders often contributes to poor postoperative outcomes [1], including increased rates of readmission, delirium, falls, and mortality [2-5]. However, very little work has been done to improve perioperative mental health. In particular, there have not been any systematic efforts to identify evidence-based behavioral interventions that were originally developed for depression and anxiety in otherwise medically well psychiatric patients, adapt them for use in surgical populations, test their effectiveness in these patient populations, and study implementation strategies.

Consequently, we currently lack conclusive evidence on effectiveness of interventions specifically focused on the delivery of perioperative mental health care in older surgical patients. To address this understudied research area, the proposed study will focus on comparing a bundled intervention of Behavioral Activation (BA) and Medication Optimization (MO) (compared to usual care) among older adults undergoing cardiac procedures with anesthesia.

The mental health intervention bundle, (Surgical Wellness Program) composed of BA and MO, can mitigate anxiety and depression symptoms during the perioperative period [6]. Towards this end, we propose to test the effectiveness as well as the implementation potential of the intervention bundle in a Hybrid Type 1 Effectiveness-Implementation RCT Design.

2.1.1 Preliminary Data

In an IRB-approved study (IRB # 202101103), we enrolled 8 patients undergoing cardiac surgery to an open-label feasibility phase of the study, to establish recruitment feasibility, and finalize the details pertaining to the study protocol, participant screening, informed consent process, recruitment and follow-up, as well as finalize the workflow for medication optimization and behavioral activation.

Given that these objectives were attained, and reflected in the finalized methodology proposed in this study protocol, we are ready to launch our clinical trial to evaluate the effectiveness and implementation-potential of our intervention bundle using a Hybrid Type 1 Effectiveness-Implementation RCT design.

2.2 Objective

We will test the effectiveness of a bundled intervention comprised of behavioral activation and medication optimization in reducing symptoms of depression and anxiety in older adults undergoing cardiac surgery (compared with usual care), while examining implementation outcomes. The study will be conducted by the members of the newly established Center for Perioperative Mental Health (CPMH), supported by National Institute of Mental Health (NIMH).

2.3 Patient Selection

The study coordinators will screen the Cardiac and Cardiology clinics and procedure schedules, as well as the schedule for the Center for Preoperative Assessment and Planning (CPAP) at Barnes-Jewish

Hospital for patients undergoing cardiac procedures. Prospective patients will also be identified by Epic workbench reports customized to limit results to those at least 60 years of age with an eligible procedure scheduled at BJH/WUSM. Additionally, patients under the care of WashU Anesthesiology providers with eligible procedures scheduled at BJH and Missouri Baptist Medical Center (MBMC) will be included. Study collaborators in both Anesthesiology as well as in cardiac surgery (Drs. Masood and Kotkar, along with cardiac surgery research support team) will refer patients from their clinics who meet the inclusion criteria sought from the EHR. Flyers will be available in clinical areas for potentially eligible patients at both BJH and MBMC, so interested patients may reach out to the study team for screening.

A member of the study team will obtain the patient's phone number, age and sex, as well as type of procedure, the provider's name and planned surgery date through Epic. A member of the study team will contact potentially eligible patients to screen for inclusion criteria.

2.3.1 Inclusion Criteria

Pre-screening:

To be considered for participation, patients will be screened using PHQ-4 questionnaire. Scores ≥3 will indicate positive pre-screen (i.e. can be considered for participation and formal screening). Scores < 3 will indicate negative screen (i.e. patient not considered for formal screening due to low risk for anxiety or depression).

Screening:

Each participant must meet all of the following criteria:

Inclusion

- Adults age≥60 years
- Scheduled major cardiac procedure
- PHQ-ADS (Patient Health Questionnaire Anxiety and Depression Scale) ≥10 indicating clinically significant depression or anxiety symptoms.[7]

2.3.2 Exclusion Criteria

Participants will not be enrolled if any of the following criteria exist:

Exclusion

- Barrier to communication (Unable to read, speak, and understand English)
- Severe cognitive impairment screened by the SBT (Short Blessed Test) >10
- Acutely suicidal
- Considered ineligible per the discretion of the cardiac surgeon or study PI
- Previous participation in this study or another CPMH study of the intervention bundle or its feasibility.

2.4. Study Design

All eligible and consenting patients will be randomized in 1:1 ratio (with no stratifications) to receive either the intervention bundle or usual care.

Consenting participants (in both arms) will undergo a standard battery of assessments at baseline (prior to the intervention in the intervention group) and will be followed until approximately 3 months postoperatively. In conjunction with the effectiveness outcomes data, implementation outcomes related to reach, and implementation feasibility, acceptability, and appropriateness of the intervention bundle will be collected.

2.4.1 Study Procedures

Consented subjects will be asked to participate in the study for approximately 3 months after surgery. All participants must sign a consent document (e-consent or paper), indicating their consent, approved by the Washington University School of Medicine Institutional Review Board, before they can participate in the study.

All participants will be asked to complete the following questionnaires at baseline (in person, remotely via a web-based survey, or via telephone):

- CDC HRQOL-14 Quality of Life survey
- PHQ-ADS (Patient Health Questionnaire Anxiety and Depression Scale)
- SBT (Short Blessed Test)
- Presence and intensity of preoperative pain
- Demographics survey
- Patient-reported falls

All participants will be followed for up to approximately 3 months after their scheduled procedure. They will complete follow-up surveys at approximately 1 month and 3 months after surgery by either web-based survey, mail, or via a telephone interview.

At the end of the study, all participants in the intervention arm will be invited to take part in a semi-structured telephone interview conducted by a research team member experienced in qualitative research. The interviews will explore the participants' perceptions, attitudes, and experiences of the intervention bundle.

2.4.2 Minimization of Bias

Enrollment will not be based on sex or ethnic background. Standard of care will not be affected for any of the participants due to study participation. Completion of the outcomes will be entirely patient-reported, to minimize assessor's bias in interpreting patient responses.

2.4.3 Pre-Study Period

Patients who are ≥ 60 years of age undergoing cardiac procedures will be approached for consent to this study. Eligible patients will be invited to participate in the study, which will be conducted remotely and in-person. Potential candidates for the study will be provided a written and oral description of the study procedures, benefits, and potential risks as well as the opportunity to ask questions regarding the study. Participants are informed that their participation is voluntary and that they may refuse to participate or withdraw from the study at any time without penalty. Patients will be required to give

informed consent prior to participation. A study team member who is experienced with cognitive testing will recruit the subjects to the study, and perform the SBT assessment.

Each subject who qualifies for entry into the study on the basis of inclusion/exclusion criteria and completion of informed consent will be assigned the next available patient number. This indicates enrollment in the study. Patients who are eligible but decline participation will be invited to complete an optional survey indicating reasons for decline.

2.4.4. Randomization

The randomization table will be generated by the study biostatistician, using a variable block sequence. The assignment of the treatment condition for each individual participant will be done by the REDCap randomization module after they have been determined to be eligible for the trial.

2.4.5. Blinding

Study staff responsible for administering ratings throughout the study are blinded. This blinding is kept throughout the study until data collection is complete. At the end of the follow-up, the study coordinator will complete a blinding question to try to guess the arm to which each participant was allocated. This will allow to determine whether the blinding procedures in the study were effective [8].

2.4.6 Study Period

Baseline Characterization of Participants: At enrollment, a battery of assessments will characterize participants. *Anxiety and depression* assessment will use the PHQ-ADS, as described above. The use of this tool for this population is supported by a recent meta-analysis suggesting that the PHQ9 (on which this tool is based) has good sensitivity and specificity in the diagnosis of depression in older adults [9]. *Quality of Life* (QoL) will be assessed using the CDC HRQOL-14 survey) [10]. The questions in this patient-reported survey correspond to the QoL domains of Healthy days (physical and mental), Activity Limitations, and Healthy Days Symptoms. *Cognitive function* assessment will be performed using the Short Blessed Test (SBT). SBT is a reliable test, with high inter-rater agreement, which is beneficial for characterizing cognitive functioning in the perioperative setting [11, 12]. Recognizing the uncertainty associated with face-to-face data collection due to the COVID-19 pandemic, we selected tools such as the SBT because it can be delivered remotely [13].

All patients in both arms will receive resources (see Handouts for CPMH RCT SOC Group and Handouts for CPMH RCT Intervention Group) either by mail or email if they prefer. The resources include options for exploring brain health, supporting sleep and mental health, and introducing community resources for older adults.

Intervention Bundle: This will be initiated prior to or soon after the surgery and will be continued until approximately 3 months postoperatively.

The basic premise of *behavioral activation* is to help people with mental health problems to engage in activities that are reinforcing or meaningful and guided by their personal values [14]. Patients will

be asked to check with their physicians if there is any question about the safety of any physical activities that are included in the behavioral activation plan. Behavioral activation as the core intervention allows for uniformity across participants from each cohort, yet enough flexibility for the actual components of behavioral activation to be individually adapted based on patient preferences. In a recent meta-analysis, behavioral activation programs improved depression and anxiety [15], as well as disability in older adults [16]. In addition, behavioral activation delivered by telehealth to older adults was cost-effective and lowered health care utilization costs over 1 year [17]. In addition to the core intervention of behavioral activation, study participants will tailor the intervention by choosing activities, per their preference, with demonstrated benefit in improving depression and anxiety symptoms in older adults [18, 19]. Behavioral activation will generally begin pre-operatively, with sessions approximately every two weeks. After discharge, the behavioral intervention will continue, for 10-12 sessions, or out to approximately 3 months postoperatively. Patients in the intervention arm will receive information (Handouts for CPMH RCT Intervention Group) by mail or email if they prefer. The handouts include tools to support behavioral activation and optional activities.

Medications will be *reviewed and optimized*, as appropriate. In several clinical trials including thousands of older adults, we have developed and refined a process for this review and medication optimization, including adjusting suboptimal dosing for anti-depressants and discontinuing medications that are harmful for brain health (such as anticholinergics [20]). Medication optimization consists of a simple set of principles: reconcile patient's medications, identify the patient's likely need for, and interest in, a medication adjustment, make the adjustment, and assess the response to that adjustment. Benzodiazepines, and strong centrally acting anticholinergics and antihistamines, are the focus of *deprescribing*, as they increase the risk for falls and delirium. We will follow the principles of shared decision-making with patients for medication changes. While the participant is an inpatient, the study pharmacy team will coordinate with the inpatient team to ensure that medication changes that were introduced preoperatively are maintained in-house and that no new inappropriate medications are initiated. After discharge, and up to approximately 3 months postoperatively, the interventionist (also referred to as a perioperative wellness partner) and pharmacy team will ensure that targeted medication changes are reconciled during transitions of care.

Methods

2.4.6 Observations and Measurements

2.4.6.3 Primary Outcome Measures

Effectiveness outcomes will include the primary outcome measure of PHQ-ADS, a validated composite scale of depression and anxiety symptoms [7], measured at 1 and 3 months after surgery. Three months post-operatively is the primary endpoint.

Process measure for target engagement

As a process measure of target engagement at approximately 2 months after surgery, we will use a combined measure including modified versions of the Sinclair Compassion Questionnaire-Short Form (SCQ-SF) [21], Behavioral Activation for Depression Scale (BADS) Activation subscale [22, 23], the MiPrep survey [24], four questions specific to our Wellness Program, and one question to

assess participants' understanding of how the study's target medications can affect their mental health, if applicable.. The target engagement measure will be collected by survey, which participants in the intervention group can complete either online via REDCap link or by phone if they prefer, with an unblinded member of the study team.

2.4.6.4 Exploratory Outcome Measures

The exploratory outcomes will include QoL measured via the CDC HRQOL-14 survey, and other perioperative outcomes of interest, nominated by our stakeholders as key outcomes of interest, including:

(1) In-hospital: (i) Delirium incidence,[20], (ii) Length of Stay (hospital and ICU), (iii) information on the use of common medications for chronic pain, such as opioids, gabapentin and pregabalin.

(2) Post-discharge: (i) Falls, (ii) All-cause rehospitalization out to 90 days postoperative. (iii) persistent post-surgical pain (PPSP), (iv) information on the use of common medications for chronic pain, such as opioids, gabapentin and pregabalin.

(3) Process outcomes: For patients on the intervention arm, CAHPS modified survey will be administered after the intervention is complete.

(4) Implementation-potential surveys: Acceptability of Intervention Measure, Intervention Appropriateness Measure, Feasibility of Intervention Measure.

Table 2. Details on Study Outcomes

Effectiveness Outcomes		**Data Source**	**Description**	**Data Collection Mechanism**	**Time points (Baseline, 1, 2, 3 month-post-op or EOS)**
Primary ***(Clinical)***	Anxiety and Depression	Patient Health Questionnaire Anxiety and Depression Scale (PHQ-ADS)	A validated composite of symptoms of depression and anxiety	Patient Self-Report	Baseline; 1 mo and 3 mo
Exploratory (Clinical)	Quality of Life	The Health-Related Quality of Life CDC HRQOL-14 survey [10]	A patient-reported global health measure. The questions in this survey correspond to the QOL domains of Healthy days (physical and mental), Activity Limitations, and Healthy Days Symptoms	Patient Self-Report	Baseline; 1 mo and 3 mo

	In-hospital delirium incidence	Retrospective EHR chart review	.	EHR report, and Research Team Member review EHR for delirium-related information from the time of post-op inpatient stay.	In-hospital: at ICU and hospital floor
	Post-discharge falls	Patient Reported Falls	A Patent Reported Falls survey will be collected at 1 month and 3 months either by phone or REDCap link, at follow-up clinic appointments.	Patient Self-Report	Baseline; 1mo and 3mo
	Pain	Pain presence and severity at the site of surgery, and Brief Pain Inventory (BPI) pain interference scale	BPI is a well validated measure of pain severity and pain interference items.	Patient self-report	Baseline, 1 mo, 3 mo
	Medications of Interest	EHR	Review of CPMH targeted medicationsand common medications for chronic pain, such as opioids, gabapentin and pregabalin	Patient Self-Report/ study team member verifies targeted meds and/or EHR review	Baseline, at transitions of care, and up to 3mo post-op
	Length of stay (both hospital and ICU)	Research Data Core	Standardized reports on RDC warehouse will generate statistics of enrolled patients regarding the length of stay, rehospitalization, and related clinical metrics.	EHR report	In-hospital: at ICU and hospital discharge
	All-cause rehospitalization	EHR and patient		EHR, patient	Post-op: 1 mo and 3 mo
Implementation and Process Outcomes		**Data Source**	**Description**	**Data Collection Mechanism**	**Time points**
Reach		Enrollment Log	Reach of the study: patients who agreed to participate in the study out of total eligible to participate	Electronic Health Record	End of Study

		Reach of the intervention bundle: patients who completed the interventions out of patients who agreed to participate		
Implementation-Potential (I)	Acceptability of Intervention Measure, Intervention Appropriateness Measure, Feasibility of Intervention Measure	Acceptability, Feasibility and Appropriateness 4-item Likert scale survey	Patient Self-Report	Post-EOS
Patient satisfaction and experience	Modified-Consumer Assessment of Healthcare Providers and Systems (CAHPS)[26]	The modified CAHPS asks patients about their experience with the intervention bundle before surgery, during surgery, and after surgery.	Patient Self-Report	Post-EOS
Process measure for target engagement	**Data Source**	**Description**	**Data Collection Mechanism**	**Time points**
Target engagement measure	Combined measure of modified versions of the following scales: Sinclair Compassion Questionnaire-Short Form (SCQ-SF)[21], Behavioral Activation for Depression Scale (BADS) Activation subscale [22], the MiPrep survey[24]	The SCQ-SF is a 5-item patient-reported measure modified to assess compassion of the Wellness Provider; the BADS Activation Subscale (7 items) measures target engagement of BA in studies of geriatric depression [23]; and the MiPrep survey (3 items) assesses patients' preparation for medical interventions.	Patient Self-Report	approximately 2 mo post-op

In addition to these outcomes, we will assess fidelity to our intervention bundle to ascertain the extent to which an intervention bundle is carried out, as intended and consistently across different settings, and patients. If the patient agrees to audio/video recording, the intervention sessions will be audio recorded (or audio/video if the patient prefers to meet by Zoom teleconference). To track this, we will use the recordings of these discussions between the patient and the perioperative wellness partner during the behavioral intervention and medication optimization sessions. We will capture data on patient interactions with the wellness partner, their delivery of the intervention bundle, any observed barriers and facilitators to the intervention adherence, acceptance and fit within the perioperative

workflow. 10% of these sessions of patients and their wellness partners will be selected based on a convenience sample for evaluating fidelity of the bundle.

Lastly, we will also obtain stakeholder perspectives on the intervention bundle after the intervention period has been completed using semi-structured interviews. We will conduct interviews with patients who participated in the intervention, and the topics of discussions will be guided by an implementation science framework referred to as CFIR (Consolidated Framework of Implementation Research). The interviews will explore the participants' perceptions, attitudes, and experiences with the intervention bundle, intervention bundle acceptability and detailed accounts of participants' experiences after the intervention has been stopped with regards to intervention sustainability and maintenance. Interviews will be conducted via Zoom or telephone and will be digitally recorded and transcribed verbatim.

Study Calendar

	Time 0	Baseline/ Time 1	1 mo follow up	2 mo follow up	3 mo follow up	Post-EOS
Patient Consent	X					
Patient Screening	X					
Patient Baseline Surveys		X				
Patient Follow-up 1 & 3 mo Surveys			X		X	
For Patients on the Intervention Arm: Process Target Engagement Measure				X		
For Patients on the Intervention Arm: Intervention-Patient Interviews and Implementation, Patient Satisfaction and Experience surveys						X
For Patients on the Intervention Arm: Behavioral Activation and Medication Review Intervention Sessions			Approximately 8-12 sessions as needed (per Pt preference) after Baseline, continuing for up to approximately 3 months post-op.			

2.4.6.5 Statistical Methods

Primary Outcome Analysis: The primary outcome for the R34 is the change in PHQ-ADS from baseline to 3-month visit. The primary statistical model will be a mixed model repeated measures ANOVA with a treatment group by time point design. This model is ideal because it uses all available data and is robust even with some expected missing follow-up data. The primary statistical test is a contrast which compares the change in the treatment group to the change in the control group. The population used for the modified Intent to Treat analysis consists of those randomized patients who actually received the procedure or surgery.

Analysis of Exploratory Endpoints: For exploratory endpoints which are measured on the same schedule as the PHQ-ADS, they will be analyzed utilizing the same mixed model. For the outcomes of length of stay (ICU & hospital), a simple analysis of covariance will compare the two groups where we will identify the relevant covariates during the planning phase. For the presence of delirium and rehospitalization we will use a corresponding generalized linear model with a logistic link

function and appropriate covariates. For the presence of falls we will use the extension of the Cox model when there may be multiple events with appropriate covariates. [27] For all analyses, we will examine the potential moderating effect of sex.

Descriptive data will be presented from the semi-structured interviews. The interviews will be conducted using an interview guide developed by study team members. These will either be audio-recorded and transcribed verbatim or notes will be taken by a second researcher to capture the data.

The transcriptions will be analyzed thematically using a pre-determined framework derived from the interview schedule and adapted and revised based on participant responses [45]. Semi-structured interviews will provide data on the acceptability of the intervention and detailed accounts of participants' experience after the intervention has been provided.

2.4.6.6 Sample Size and Power of Primary Analysis:

In order to estimate the power of the primary outcome analysis we examined the manuscript which provided the original validity and reliability studies for the PHQ-ADS [28] and one of the trials which provided data for that study (SCOPE) [29, 30]. At 3 months they observed a change from baseline divided by the standard deviation of the change of 0.43 which corresponds to a change of 3 points on the PHQ-ADS. The PHQ-ADS authors estimate the minimal important clinical difference (MICD) from the standard error of measure (SEM) as 3-4 points. If we postulate a difference in the change scores of 2 points between the two groups, then with a power of 0.80 we would need 36 in each group. Since the SCOPE trial was a pain relief study without a requirement of anxiety or depression, we consider these estimates rough estimates. This trial will target having 100 mITT patients (50 per arm). In order to account for any incomplete data among recruited patients, recruitment will continue until 100 randomized patients have had their procedure or surgery.

2.5 Management of Intercurrent Events

2.5.1 Adverse Experiences

Based on the nature of this study, which involves surveys, a cognitive test, and a behavioral intervention, study related adverse events are exceedingly unlikely.

2.5.2 Premature Withdrawal

Subjects will be withdrawn if the investigator decides that discontinuation is in the best interest of the subject, or the subject requests withdrawal from the study. Additionally at PI discretion, they may be withdrawn if their surgery is cancelled or postponed (for clinical or non-clinical reasons) for more than approximately 3 months after baseline.

Participants who choose to end study participation early, may be asked to complete early termination assessments. Additionally, those in the intervention arm may choose to withdraw from that at any time, but will be allowed to continue with data collection follow-ups if they still want to participate.

2.5.3 Potential Risks

This study involves minimal risk to subjects. Unlikely but potential risks include increased risk of depression or anxiety, errors in medication recommendations or medication withdrawal symptoms, and breach of confidentiality. The risk of medication withdrawal (i.e., from benzodiazepines) is mitigated by slowly tapering rather than stopping these medications. Patients who are identified as being acutely suicidal will be excluded from the study. Nevertheless, since the rate of completed suicide in the USA remains high (i.e., about twice the rate of homicide) and most Americans who commit suicide suffer from depression, all participants eligible to participate in this study are statistically at a relatively higher risk for suicide than the general population. However, the participants' absolute risk for completing suicide during this brief study remains very low (i.e., about 1 in 3,000 to 10,000) and participation in the study does not create or increase the risk of completed suicide; rather, most experts believe that one of the most efficient ways to decrease suicidal risk in older depressed individuals is to treat their depression. Furthermore, all participants will be formally assessed frequently throughout the study. If the study personnel identify that a participant has become acutely suicidal, this participant will be referred to a mental health professional for further evaluation and treatment (see section: Procedures to Minimize Risks). This may lead to a clinical intervention that is lifesaving and may not have occurred had the participant not been participating in the study.

2.5.4 Procedures to Minimize Potential Risks

Medication Error Risk: Dr. Eric Lenze will supervise careful training and oversite of the intervention pharmacists making medication optimization recommendations to reduce the risk of medication error or medication withdrawal symptoms. Algorithms for tapering medications that should not be abruptly discontinued will be employed. We have carried out this deprescribing protocol in several large RCTs and have not seen any problems occur.

Suicide risk management: As discussed above, at each assessment point, the research staff will assess for passive death wish, and suicidal ideation, intent or plan when they administer the PHQ-ADS. If a participant endorses suicidal ideation, intent, or plan, the rater will be trained to follow an operationalized protocol that has been developed to manage high-risk participants in other studies of depressed participants potentially at risk for suicide. This protocol has already been used successfully by Dr. Lenze's team to manage acutely suicidal patients. Briefly, the protocol entails a specific determination of the suicidal risk and prescribes a set of actions. For instance, when a participant is determined to be at high and immediate risks, the rater is instructed to stay with the participant until he or she has contacted a study psychiatrist (Dr. Lenze) to discuss the situation and to devise a plan. For this reason, raters will have cell phones and Dr. Lenze will be reachable via email and cell phone. In case of extreme emergency, raters are instructed to call their hospital security team or 911 for immediate help and to initiate commitment proceedings.

Patients will be asked to check with their clinician if there is any question about the safety of any physical activities that are included in the behavioral activation plan.

The risk of breach of confidentiality will be minimized by ensuring that protected health information will only be shared with members of the research team. Only data necessary to complete the study will be collected. Electronic data will be kept in a password-protected electronic database only

assessable via password protected departmental computers. Patients may choose to not participate in the study or withdraw at any time with no penalty in terms of the care they receive.

2.5.5 Data and Safety Monitoring Plan

The specific monitoring plan for this investigation is commensurate with the risks and the size and complexity of the studies planned. Given the nature of the protocol, the risks are likely limited to breach of confidentiality. The Principal Investigator will be responsible for monitoring the data and assuring protocol compliance. The PI will meet with the clinical research coordinator and Data Manager bi-weekly to review enrollment, eligibility, participant follow-up and outcome assessment. The PI and study coordinator will monitor for breaches of confidentiality on an ongoing basis. Study-related adverse events will be reported per IRB guidelines. All serious adverse events (SAE) will be recorded and adjudicated by a CPMH Principal Investigator and reported per IRB guidelines. Any endorsement of suicidal ideation will be managed acutely as detailed in the section 2.5.4. If study staff becomes aware of a reportable adverse event, it will be reported to necessary stakeholders according to Washington University Human Protection Office guidelines. This type 1 hybrid randomized study does not require a Data and Safety Monitoring Board.

3. HUMAN SUBJECTS RESEARCH

3.1 Protection of Human Subjects

The study will be conducted under appropriate Washington University Institutional Review Board protocols and consent forms approvals. The study will be conducted under the supervision of the PI, who has extensive of experience in the conduct of human research studies.

3.2 Sources of Materials

Preoperative assessments along with preoperative and postoperative questionnaires regarding quality of life, depression, and anxiety will be obtained from all study participants. The results of follow-up questionnaires will be obtained via e-mail, mail, or telephone survey. Data will be collected at baseline, one, two, and 3 months following surgical procedure.

3.2.1 List of Protected Health Information Collected for Study

The HIPAA protected identifiers that will be collected for this study include:

- Name
- Dates
    - Date of birth
    - Date of services (surgical procedure)
- Contact information
    - Mailing address
    - Phone number
    - Electronic mail address
- Medical record number

3.2.2 Data Management

All paper data will be stored under lock and key (office, file cabinet) and all electronic data will be stored in REDCap, only accessible to the research team members. Surveys that are completed electronically will be administered via the REDCap server. All REDCap email correspondence will be sent using secure survey links. All survey information will be coded with the patient's unique study ID number and no personal health information that may directly identify patients will be included.

3.3 Recruitment and Informed Consent

Participants will be recruited either from the cardiac surgery and cardiology clinics or procedure schedules at Washington University or the Center for Preoperative Assessment and Planning (CPAP) at Barnes-Jewish Hospital/Washington University. Patients under the care of WashU Anesthesiology providers undergoing eligible cardiac procedures requiring anesthesia at either BJH or MBMC will be included. Flyers will also be available in clinical areas for interested patients to contact the study team to screen. Participants with pre-screening scores of PHQ-4 $\geq$3 will be recruited, and eligibility confirmed if PHQ-ADS $\geq$10. Retention strategies will include flexibility in scheduling follow-up visits and coordination of research visits with any in-person clinical visits. Subjects will be given verbal and then written descriptions of the study aims, procedures, risks, and benefits, and will be required to give informed consent. A member of the research team will be available to present study descriptions, informed consent, and answer any questions. Subjects are informed verbally and in writing that participation is voluntary and they may refuse to participate and may withdraw from the study at any time without penalty. Remuneration for each data collection study visit will be provided to encourage retention as well.

3.4 Potential Benefits of the Proposed Research to the Subjects and Others

Although the study is designed to improve symptoms of depression and anxiety and other outcomes of care, there is no guarantee that the study participants will receive any clinical benefits by participating in the study. This may lead to a clinical intervention that is lifesaving and may not have occurred had the participant not been participating in the study. Given the undertreatment of depression and anxiety in older adults, the minimal risks are acceptable in comparison to the potential benefits in improving the mental health of older adults undergoing surgery.

3.5 Remuneration

Patients will receive remuneration by a reloadable debit card of $25 for completion of the following data collection study visits: Standard Care (control arm) participants will be compensated for their time at Baseline, 1, and 3 month post-op, up to $75 for completion of all data collection time points. Wellness Program (intervention arm) participants will also be compensated for their time at Baseline, 1, and 3 month post-op, plus a post-EOS semi-structured interview, so up to $100 for completion of all eligible data collection time points.

3.6 Inclusion of Women

Eligible individuals will be offered the opportunity to participate in the study regardless of gender or minority status. Thus, the sample composition will reflect the composition of community-living older adults in the St. Louis area.

3.7 Inclusion of Minorities

All of our studies actively encourage the participation of minorities in the research. Our minority recruiting typically matches the demographic composition of the Washington University community from which subjects will be recruited (78% white, 21% Black, <1 % Hispanic).

3.8 Inclusion of Children

We will not be including children in this study.

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