PROTOCOL TITLE:
Tailored Self-Management Interventions for Highly Distressed Family Caregivers
Supplement Title: Caregiving Burden and Heart Rate Variability: differences by race and gender

Identifiers: NCT03023332 Unique Protocol ID: 1R01NR016817-01

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INSTRUCTIONS:
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UH FACULTY ADVISOR:
If the principal investigator's primary role at UH is resident, fellow or student, identify a faculty advisor.
N/A
OTHER DEPARTMENTS INVOLVED IN THIS STUDY (IF APPLICABLE):
VERSION NUMBER:
6.2
DATE:
6/30/2020
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3/11/2021

Indicate the origin of this protocol (who conceived of and leads the development of the protocol regardless of funding):

☒ Investigator initiated *(Investigator(s) developed protocol, regardless of funding)*

☐ Industry *(Pharmaceutical, Device, etc.) (Industry developed protocol)*

☐ Federal *(NIH, DOD, etc.)*

☐ Cooperative Group *(SWOG, GOG, etc.)*

☐ Other - *Please specify:*

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Objectives

The study has two aims: the primary aim (A1) is to examine differences across the four groups (control, usual care, SM-need, and SM-preference) on caregiver health (health risks and mental and physical health) over time. We hypothesize that the caregivers who receive a self-management intervention based on need (SM-need) or preference (SM-preference) will have better outcomes than those in the usual care or control groups. Secondary aims are to: A2) explore whether caregiver baseline need or preference for intervention (i.e. choice) is associated with: a) care recipient's symptoms; b) caregiver reactions; and c) caregiver involvement and A3) build caregiver profiles from demographic/contextual factors that are associated with their needs and preferences for the self-management interventions (A3).

We will also conduct a supplemental analysis to examine relationships among psychological stress responses (caregiver reactions and caregiving involvement), physiological stress responses (heart rate variability domains), and caregiver characteristics (race and gender) in caregivers of people with bipolar disorder. The major aims of the supplemental analysis (SA) are to: SA1) determine whether there are differences by caregiver characteristics (race and gender) on measures of psychological stress responses (caregiving involvement and caregiver reactions), SA2) determine whether there are differences by caregiver characteristics (race and gender) on measures of physiological stress responses (heart rate variability domains), SA3) examine associations among indicators of psychological stress responses (caregiver reactions and caregiving involvement) and physiological stress responses (heart rate variability domains), and SA4) explore relationships among time and frequency domains of heart rate variability.

Background

Directions: Describe the relevant prior experience and gaps in current knowledge describing how it will add to existing knowledge. Include any relevant preliminary data.

Family caregivers provide care and support for over 10 million Americans who have bipolar disorder, which is characterized by intensity and fluctuations in mood ranging from depression to mania.[1] With an early onset and chronicity across the lifespan, bipolar disorder

accounts for more disability-adjusted life years than all forms of cancer and major neurologic conditions.[2] It is the most expensive behavioral health care diagnosis,[3] costing more than twice as much as depression per affected person.[4,5] Yet, this does not reflect the adverse effects on the health of the caregivers of persons with bipolar disorder who are highly distressed[6] and experience greater stress due to the unpredictability and severity of bipolar episodes.[7] They have more mental and physical health problems than the general population[8-10] and are less likely to practice adequate self-care to minimize health risks that compromise their health.[7] Chronic stress endured by these caregivers leads to greater use of mental health and primary care services.[11] And, greater stress and declining caregiver health can lead to symptom exacerbation, affective episodes, and re-hospitalization of the diagnosed family member.[12]

Existing psychoeducation[7,13-17] and family therapy interventions[16,18-20] for caregivers of persons with bipolar disorder have shown little effect on caregiver health. Self-management interventions focused on promoting caregiver health, including those specifically tailored to address the family caregivers' needs and preferences for bipolar education, stress-reduction, or self-help and help-seeking strategies (i.e. resourcefulness skills) for maintaining caregiver health, have not been examined. This randomized controlled trial will evaluate how varying levels of participation by family caregivers in selecting self-management interventions (ranging from no input into the selection to selection based on need or preference) affect their health risks and physical and mental health over time.

The findings from this study will generate new scientific knowledge about the effectiveness of novel, easy to use, independently performed interventions that can be individualized and self-tailored to promote family caregiver health through education, biofeedback, or resourcefulness. The study will reveal demographic, contextual, and illness-related factors that are associated with caregiver need and preference for self-management intervention(s) to elucidate for whom and under which circumstances an intervention may be most beneficial. This study is clinically significant in testing self-management interventions in a vulnerable, understudied, highly distressed population of caregivers, for whom interventions to promote their own health are critical for their continued service in the caregiving role Once established, these health self-management interventions can be tailored to match the needs and preferences of other equally distressed family caregivers of persons with other chronic mental or physical conditions.

Bipolar disorder affects men and women equally and rates are not significantly different by race[21]. However, the caregiving experience can differ by gender and race. Female caregivers contribute more time to caregiving and experience greater amounts of role conflict and role strain than male caregivers[22]. Due to caregiving responsibilities, female caregivers are more likely to lose income, lose job benefits, and reduce work hours compared to males[23].

In studies comparing White and African American caregivers, African Americans generally provide more caregiving hours and perform more caregiver tasks than White caregivers[24-26]. However, African American caregivers report lower levels of burden and depression than White caregivers[25-29]. Furthermore, African American caregivers tend to appraise caregiving as less stressful, but are more cognitively impaired and in worse physical health than White caregivers[25, 30]. The supplemental analysis will examine relationships among psychological stress responses, physiological stress responses, and caregiver characteristics in caregivers of people with bipolar disorder. The findings will generate new scientific knowledge about the stress experienced by White and African-American, male and female caregivers of adults with bipolar disorder, using previously untapped measures of heart rate variability to

capture physiological stress. Most importantly, the supplemental analysis holds the potential to significantly advance the sciences of caregiving, self-management, and biobehavioral health by uncovering unknown associations between race and gender and indicators of heart rate variability from which health disparities related to stress and health may be identified and may inform the future tailoring of health self-management interventions.

Inclusion and Exclusion Criteria

	Inclusion
1.	*English Speaking*
2.	*At least 18 years old*
3.	*Have a family member with bipolar disorder who is at least 18 years old*
4.	*Have cared/supported them for at least 6 months in the last year*
5.	*Be capable of performing informed consent and participating in study procedures*
6.	*Identify as White or African American* ***(supplemental analysis only)***

	Exclusion
1.	*Does not have family member with bipolar disorder*
2.	*Has not cared for a family member for at least 6 months in the last year*
3.	*Has knowledge of another family member in the same household enrolled in the study*
4.	*Currently pregnant*
5.	*Has a pacemaker*
6.	*Lives outside of the study area*
7.	*Currently has acute respiratory condition* ***(supplemental analysis only)***

Number of Research Participants

Directions: Indicate the target number of research participants to be accrued locally, and, if this is a multi-site study, indicate the total number of research participants to be accrued across all sites.
Based on previous research by the PI and Co-Is, we conservatively estimate that 1 in 5 caregivers may not meet eligibility criteria. Thus, we will screen 750 participants to obtain the desired sample of size of 360.

Special/Vulnerable Populations

1. *Indicate specifically if you will include each of the following special populations by checking the appropriate box:*

☐ **Adults unable to consent**
☐ **Minors (infants, children, teenagers)**
☐ Wards of the state

☐ Foster Children
☐ **Pregnant Women**
☐ **Neonates**
☐ **Neonates of Uncertain Viability**
☒ **Employees of CWRU or UHHS**
☐ **Prisoners**

☒ **Illiterate Individuals**
☒ **Non-English Speaking**
☒ **University Students**
☐ **None**

2. If the research involves individuals that are included in a special/vulnerable population, describe the additional safeguards included to protect the rights and welfare of the individuals for each population indicated. *If family caregivers who do not speak/understand the English language come forward with interest in participating and if they meet all other study criteria, we will make accommodations for translating the study measures and intervention materials or for having and interpreter provide appropriate explanations. If an illiterate individual comes forward with interest in participating and if they meet all other study criteria, we will make accommodations to dictate the consent form and all study questions. If a caregiver is an employee or student of CWRU, the consent form identifies participation in this research study is voluntary and if they choose not to participate, it will not affect their current or future relations with the university.*

3. If excluding pregnant women, illiterate or non-English speaking individuals, provide a scientific rationale for the exclusion. Inconvenience or cost is not an acceptable rationale.
Pregnant women are excluded due to the measure of heart rate variability (HRV). The inclusion of pregnant women has the potential to alter the analyses that involve HRV measurement.

Recruitment Methods

Note: Attach all applicable recruitment materials to the last section of the Smart form under "Recruitment Materials."
1. Which of the following methods will be used to recruit research participants. – *Select all that apply*

☐ Email
☐ Phone call
☐ Letter
☒ Advertisement (e.g., poster, flyer, etc.)
☒ Social media
☐ Other. *Please specify:*

2. Describe when, where, and how potential research participants will be recruited .

Study participants (who meet the study criteria) will be recruited through both public and private mental health agencies, counseling centers, support groups, community health centers, health fairs and other community events, print and e-newsletters (e.g. CASE Daily), local magazines and newspapers, the registry of bipolar persons used by CI Sajatovic and other research registries of people with mental illness and/or their family caregivers approved for use from the investigators in the Department of Psychiatry, and private physician offices in Cuyahoga and 6 adjacent counties in Northeastern Ohio. We will post/distribute flyers describing the study and contact information in public venues; caregivers will contact the study office for further information and enrollment. In addition, agency personnel/health care professionals may nominate a caregiver for the study. If additional caregivers are needed, we will use snowball recruitment by asking study participants to refer others like them to the study. We will also recruit via the internet using social media sites (e.g. Twitter, Facebook, Instagram, and other online sources).
3. Describe the source (e.g., from what department, EMR, etc.) of the research participants.

Study participants will be recruited through both public and private mental health agencies, counseling centers, support groups, community health centers, health fairs and other community events, print and e-

newsletters (e.g. CASE Daily), local magazines and newspapers, the registry of bipolar persons used by CI Sajatovic and other research registries of people with mental illness and/or their family caregivers approved for use from the investigators in the Department of Psychiatry, and private physician offices in Cuyahoga and 6 adjacent counties in Northeastern Ohio.

4. Describe the methods that will be used to **identify** potential research participants.

When a person contacts the study to be screened, they will receive a screening ID in the screening log. Contact information will then be collected including name, telephone number(s) and/or email address(es) on all individuals screened will collected for our screening log; this information will be stored in a password-protected computer file.

The project manager or other trained research staff will screen by phone to ensure that caregivers are at least 18 years old, have a family member with bipolar disorder who is at least 18 years old, and have cared/supported them for at least 6 months, but not necessarily in the same household, live in the study area, and have the physical capability to perform the interventions (i.e. does not have a pacemaker, is not currently pregnant). We will also be collecting demographic information (gender, race, ethnicity). All screening documentation will be kept in a screening for on REDCap.

We will also ask study participants if they would like to be contacted for future research; we let them know there is no penalty to them if they do not wish to be contacted. Furthermore, we inform them that agreeing to be contacted does not obligate them to participate in future research, this only permits us to contact them. We will maintain a password-protected list on Box.com of individuals that have consented to be contacted for future research, along with their contact information and contact preferences. This list will be maintained by the Project Manager and may be shared with research team case-by-case basis.

After eligibility is verified during phone screening by team member, the consent form will be reviewed verbally, questions about the study will be answered, and the study enrollment/first data collection appointment will be made.

5. Describe the feasibility of recruiting the required number of suitable research participants within the agreed recruitment period. For example, how many potential research participants do you have access to?

Based on previous research by the PI and Co-Is, we conservatively estimate that 1 in 5 caregivers may not meet eligibility criteria. Thus, we will screen 450 potential participants to obtain the desired sample size of 360.

Setting

Directions: Make sure to describe: 1) sites and locations where your research team will conduct the research; 2) where your research team will identify and recruit potential research participants; and 3) include the physical location where research procedures will be performed.

Study participants will be recruited through both public and private mental health agencies, counseling centers, support groups, community health centers, health fairs and other community events, print and e-newsletters (e.g. CASE Daily), local magazines and newspapers, the registry of bipolar persons used by CI Sajatovic and other research registries of people with mental illness and/or their family caregivers approved for use from the investigators in the Department of Psychiatry, and private physician offices in Cuyahoga and 6 adjacent counties in Northeastern Ohio.

The project manager or other research team member will screen by phone to determine eligibility and schedule first data collection meeting. All data will be collected either in the community (e.g. participants home or other private venue of their choice, including mental health center/physician's office, private/ closed

room in local library, etc.), on the campus of Case Western Reserve University (e.g. the School of Nursing), or Department of Psychiatry Walker Building.

Consent Process

Indicate whether you will be obtaining consent:

☒ Yes ☐ No

If yes, answer the following questions:

1. Describe where the consent process will take place:

After eligibility is verified during phone screening by a team member, the consent form will be reviewed verbally and questions about the study will be answered. During the first appointment with the data collector, the consent form will be reviewed again and signed by both the study participant and data collector before beginning the data collection interview.

The time that will be devoted to the consent discussion:

There are no time constraints to the consent discussion. The consent discussion will take place during the screening phone call and again at the enrollment meeting, prior to data collection.

3. Any waiting period available between informing the prospective subject and obtaining the consent:

Yes. After verifying eligibility and reviewing the consent form during the screening phone call, there is a period of time between the phone call and the enrollment meeting. The length of time between the two varies depending on the meeting time selected by the research participant and team member.

4. Steps that will be taken to ensure the research participants' understanding:

Study participants will have time to ask questions about the study and review the consent form before signing it.

5. Any process to ensure ongoing consent:

Within approximately one month of the first data collection session, the participants will be made aware of which of the four groups (control, usual care, SM-need, or SM-preference) that they have been randomly assigned to. Those who are randomly assigned to usual care, SM-need, or SM-preference will need a second-level consent, obtained at the beginning of the training session for that particular intervention. The second-level consent process is needed in order to keep the control group and usual care groups blinded to the content of the interventions being tested. Knowledge of the other interventions could motivate them to seek out similar strategies on their own and confound the study.

6. Steps that will be taken to minimize the possibility of coercion or undue influence to the subjects:

The study participants will be informed that his or her participation in the research study is completely voluntary. If he or she chooses not to participate, it will not affect their current or future relations with the University or with physicians, mental health centers, or community venues from whom they may have obtained information about the study. Study participants will also be informed that there is no penalty of loss of benefits for not participating of for discontinuing participation in the study.

For Adult Participants

Indicate if you will be asking for a waiver or alteration of consent process or documentation (consent will not be obtained, written consent will not be documented)

☐ Yes ☒ No

If yes, indicate which part of the consent process you are requesting be waived or altered and the rationale for requesting the waiver or alteration:

☐ I will obtain consent, but not participant's signature

☐ I will obtain consent, but request a waiver for pre-screening purposes

☐ I will obtain consent, but request a waiver of some of the elements of consent (e.g. use of deception)

☐ I will not obtain consent, and I am requesting a full waiver of consent

1. Give the rationale for the request of a waiver or alteration of the consent process or documentation.

N/A

2. Explain how the research involves no more than minimal risk.

N/A

3. Explain why the waiver or alteration of consent will not adversely affect the rights and welfare of the participants.

N/A

4. Explain why the research could not practicably be carried out without the waiver or alteration of consent.

N/A

5. Indicate if the subjects will be provided with additional information about the study after participation.

N/A

6. If you will obtain consent, but not document consent in writing (e.g. over the phone, verbally, electronic survey, etc.), please describe and provide a rationale.

☒ N/A

7. Describe how you will be documenting that a research participant has consented.

N/A

Additional Considerations for Consent Process with Adults

Non English Speakers *(Please select one)*

☐ I am **not** enrolling non-English speaking individuals in this research study. The following is justification for why non-English speaking individuals cannot be enrolled:

☐ I will be targeting non-English speaking adults

1. Describe the process to ensure that the oral and written information provided to those research participants will be in that language during initial consent as well as throughout the study.

2. List the language(s) other than English that will be targeted:

☒ I am **not** targeting non-English speaking individuals. If a non-English speaking individual is eligible for the study, we will use the following procedures to enroll:
1. Describe the process to ensure that the oral and written information provided to those research participants will be in that language during initial consent as well as throughout the study.

If family caregivers who do not speak/understand the English language come forward with interest in participating and if they meet all other study criteria, we will make

accommodations for translating the study measures and intervention materials or for having an interpreter provide appropriate explanations.
2. List the language(s) other than English that will be targeted:

Adults Unable to Consent
☒ I am **not** enrolling adults unable to consent in this research study – *please leave the rest of this section blank.*
☐ There is an anticipated direct benefit to the subject. Explain:
☐ There is NOT an anticipated direct benefit to the subject. Explain:
1. Describe the process to determine whether an individual is capable of consent.

2. List the individuals from whom permission will be obtained in order of priority (e.g. durable power of attorney for health care, court appointed guardian for health care decisions, spouse, and adult child).

3. For research conducted outside of the state, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the procedure(s) involved in the research.

☒ N/A
4. Describe the process for assent of the research participants. Indicate:
1. Which subjects that are unable to consent will be required to give assent? If not all, explain why.

2. Describe whether assent of the research participants will be documented and the process to document assent.

☐ The subject will be informed about the research to the extent compatible with the subject's understanding.
☐ Subjects will be closely monitored.
☐ The subject will be withdrawn if they appear unduly distressed.
Research Participants Who Are Not Yet Adults (infants, children, teenagers)
☒ I am not enrolling participants who are not yet adults in this research study. – *please leave the rest of this section blank*
1. Will parental permission be obtained from:

One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child

☐ Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child

☐ Requesting a waiver of parental permission

If you are getting parental/guardian permission:

1. Indicate how you will be documenting the permission:

☐ Signed consent form

☐ Requesting a waiver of documentation of parental permission

2. Describe whether permission will be obtained from individuals other than parents, and if so, who will be allowed to provide permission. Describe the process used to determine these individuals' authority to consent to each child's participation in research.

If a waiver of parental permission is being requested:

1. Describe how the study is designed for a subject population for which parental/guardian permission is not a reasonable requirement to protect the subjects, if applicable.

2. Describe how the research could not practicably be carried out without the waiver of parental permission.

a. Indicate if the subjects will be provided with additional information about the study after participation.

3. Will assent be obtained from:

☐ all of the children

☐ some of the children

☐ none of the children

If assent will be obtained from some children, indicate which children will be required to assent.

When assent of children is obtained, describe how it will be documented.

4. For children who are pregnant, describe how assent and permission are obtained.

☐ N/A

Sharing of Results with Research Participants

Results will be shared with research participants:

☒ Yes ☐ No

If yes, describe how the results will be shared.

Study participants will receive a one-page summary of the results by mail or email based on contact preference.

Results will be shared with others:

☒ Yes ☐ No
If yes, describe with whom and how the results will be shared.
Results of the study will be shared with others through manuscripts and presentations.

Study Design/Procedures

Directions: 1) Describe the overall study design. 2) Provide a description of all study-related research procedures being performed, including the length of time involved. 3) Include procedures being performed to monitor research participants for safety or minimize risks. 4) Describe the source records including medical or educational records, which will be used to collect data about subjects.

The study is a four-year randomized controlled trial in Northeastern Ohio and includes a convenience sample of family caregivers of adults with bipolar disorder. After eligibility is verified during phone screening by team member, the consent forms will be reviewed verbally, questions about the study will be answered, and the study enrollment/first data collection appointment will be made.
There are three structured data collection time points (T1/enrollment, T2/ 6months after initiation of intervention, T3/ 12 months after initiation of intervention); these will be face-to-face with a research assistant, using a desktop, laptop, or iPad with secure REDCap software. During the enrollment and first data collection meeting, we will obtain informed consent from the caregiver. Caregivers will have time to ask questions about the study and review the consent form before signing it.
***COVID-19 Modifications:** Some T2 and T3 data collection will take place remotely, as a response to the COVID-19 pandemic (beginning in April 2020). We will use phone (Google voice) or Zoom (computer video) to complete the data collection. An email will be sent, if possible, to participants with the answer response choices for each survey. If we are using phone for data collection, the Research Assistant (RA) will ask the participant each question and record the responses in our REDCap Surveys project. If collecting data using Zoom video, the RA will share the screen of the REDCap Surveys project, and record the answers for the participant as they review each survey question. If neither of those two options are available for the participant (e.g., limited phone minutes, inability to use Zoom), the study may email the REDCap surveys to study participants for them to complete on their own at an agreed upon date / time (similar to in-person appointment); in this instance, the RA can be available to answer questions or clarify information as needed, by phone or email. It may be that none of these options will work for a study participant, in which case we will consider that data "missed" if we cannot wait to collect the data in person at a later date (when we resume normal study activities). The precise method(s) will depend on the ability and resources of the study participant. For these data collection sessions, HRV data (collected by placing electrodes on the wrists) may not be collected and will be considered missing data (see following page for more detail regarding remote HRV data collection). We will contact active participants with Zoom/ phone instructions, by phone/text and/or email, as needed, and we will record the methods used*

for each data collection done remotely. A COVID-19 questionnaire will be asked at remaining T2 and T3 data collections; script to obtain consent for these questions is included in the questionnaire.
Individuals will be assigned a study ID using our enrollment log. In addition, at enrollment we will collect demographic information including age, gender, race, ethnicity, marital status, education, income, occupation, hours of work/week, if the participant is an employee or student at CWRU, health conditions, current medications, relation to person with bipolar, age of family member with bipolar, how many years ago was family member diagnosed with bipolar disorder, specific diagnosis of family member, predominant behavior style of family member with bipolar, whether or not caregiver lives with this family member, whether or not caregiver provides care/assists with basic needs (and how many hrs/day), how many years caregiver has been providing care, if other adults help provide care for family member with bipolar disorder. Some, but not all of the demographic and other questions asked at baseline will also be asked at T2 and T3. We will then proceed with data collection, consisting of surveys to measure bipolar symptoms, caregiver reactions, caregiving involvement, bipolar knowledge, resourcefulness, health risks, and health outcomes. They will also have their heart rate variability (HRV) measured using a non-invasive device on the wrists; it

will take approximately 10 minutes to collect the data. The entire first meeting will take approximately 60-90 minutes. The second and third data collection meeting will be approximately 60 minutes. In the event there is an equipment malfunction or a poor reading is obtained by a research team member, we may need to re-collect the HRV and/or survey data again after a data collection meeting. ***COVID-19 modification:*** *HRV data will may not be collected when data collection is done remotely (T2 or T3 only) and will be considered missing data. When we are able to collect HRV data, we will do so by bringing an HRV device to the study participant at a set date and time, providing instructions on how to use the HRV device, safety information on the HRV device, and also providing support via phone or video. HRV data collected this way will be collected for 15-20 minutes instead of 10 minutes, to ensure reliable data is collected. A study team member will collect the HRV device the same day or within 28 hours, at a mutually convenient time. Each HRV device will be sanitized before and after each study participants' use.*

Following the T1 data collection, the project manager will randomize each caregiver into one of four groups using Qminim, a secure online minimization program. Research assistants will be blinded as to which intervention arm caregivers are assigned to. The four groups are: 1) control group- no intervention; 2) usual care group- will receive bipolar education; 3) Self-management (SM)- need based, determined by baseline cut scores from T1- either bipolar education (ED), biofeedback (BF), resourcefulness training (RT), or no need; 4) SM-preference-based, caregiver selects intervention (ED, BF, RT, or no intervention). For SM-need, for example, caregivers scoring <70% on bipolar knowledge would be assigned to ED, < 97 on the resourcefulness scale to RT, and low HRV as determined by SDNN parameter for age and gender to BF. Those in the SM-need and SM-preference groups will perform one SM intervention (as listed above). Those in the usual care group will receive the same bipolar educational intervention as others in the SM-need or SM-preference groups. All interventions will take 4 weeks and these 4 weeks will occur between the T1 and T2 data collections; the T2 data collection is planned to occur 6 months after the initiation of the intervention. The T3 data

we are excluding pregnant women from joining the study (due to the variance in HRV data which would affect scoring for minimization), if someone becomes pregnant while they are enrolled in the study, we will not exclude them from the remainder of the study.

Caregivers in the control group will receive a phone call (or email/text depending on their preferred method of contact) letting them know of their assignment; they will also have access to three interventions at the end of the study. Caregivers in the usual care, SM-need and SM-preference groups will receive training by a trained interventionist, which consists of a single face-to-face session in the caregiver's home/private venue. The session includes training/education via a voice-over PowerPoint presentation on iPad or laptop, and print materials to keep/review regarding the intervention. Other commonalities during the single session for ED, RT and BF are: 1) all caregivers will keep a structured journal, though the content will differ by intervention; journals will be collected after 4 weeks/ 28 days; 2) all will be taught to indicate day and time of the journal entry with the suggestion to do it at the same time each day; and 3) all will have the opportunity to complete a journal entry during the training session. During the 28-days after the initial session, all caregivers will: 1)perform the assigned intervention independently; 2) have print access to intervention content for review as they wish; 3) receive weekly follow-up from interventionists (3-5 minute phone call or email).

The ED and RT interventions involve providing educational information about bipolar disorder or teaching self-help (stress management, problem-solving) and help-seeking skills, respectively. BF training consists of the use of a hand-held device that shows the participant their changes in heart rate based on changes in their breathing patterns (as they relax); caregivers who need or prefer the biofeedback will be given a device to use for the study (for 28 days). Caregivers may use their intervention whenever and as often as they wish (i.e. self-tailoring). Dosing (number of times intervention is performed) and fidelity (using checklists) will be monitored. After 28 days, we will collect the BF hand-held devices and journals from all three interventions.

Individuals will be encouraged to continue with the interventions if they found them helpful (for BF, caregivers will have been given information on deep-breathing techniques without using a device). Caregivers who cannot be reached by phone or email for follow-up (either intervention or data collection) will have a letter sent to them if they have consented to having a letter sent to their home. Occasionally, calls will need to be made to study participants outside of the office (e.g., evenings/ weekends; when a research team member is working remotely/ in the field) or participants will request to be contacted by text. In these instances, the research team will use Google Voice, which allows users (research team) to set up a phone number through their CWRU email and is connected to their personal mobile phones. Calls and texts can be made to/ from the mobile phones while masking the actual phone number. When the research team is not working, calls will be directed to voicemail.
From Modification #8 (approved 03/06/2019)-- At the end of the T3 data collection, study participants will receive a brochure from each of the three interventions being researched, as well as an answer sheet for Caregiver Knowledge of Bipolar Disorder Questionnaire. Study participants who received an intervention will be asked a series of questions (up to 16) about their experience with, and opinion of, the intervention they received. Study participants who have already completed all three data collection sessions and have already agreed to be contacted for any questionnaire follow-up will be called and asked questions over the phone.

The supplemental analysis will use baseline data (T1) to explore relationships among caregiver characteristics (race and gender), psychological stress (caregiver reactions and caregiving involvement), and physiological stress (heart rate variability time and frequency domains). De-identified baseline data from the demographic measures, psychosocial measures (caregiver reactions, caregiver involvement) and the HRV measurements will be used for this analysis.

Study Timeline (optional)

ClinicalTrials.gov Information

Directions: If this study has been registered on ClinicalTrials.gov, provide the ClinicalTrials.gov identifier and the investigator/sponsor responsible for registering. If this study has not been registered on ClinicalTrials.gov, provide the rationale as to why and if/when it will be. If it does not meet the requirement for being registered on ClinicalTrials.gov, please state that.
NCT03023332

List of Data to be Collected

• *Indicate what identifiers you will collect*

☒ Name
☒ Address *(e.g., Zip code, other geographical designation, etc.)*
☐ Dates related to an individual *(e.g., Date of admission, birth, surgery, etc.)*
☒ Telephone number
☐ Fax number
☒ Email address
☐ Social security number
☐ Medical record number
☐ Health plan beneficiary number
☐ Account number
☐ Certificate/license number
☐ Any vehicle or other device serial

☐ Device identifiers or serial numbers
☐ Web URL
☐ Internet protocol (IP) address
☐ Finger or voice prints *(includes audio recordings)*
☐ Photographic images *(includes video recordings)*
☒ Other: Any characteristic that would uniquely identify the individual
If other, please explain:
Heart rate variability requires non-invasive electrocardiography
1. List all other data to be collected for the research study. Attach all data collection tools on the Local Site Documents page of the SpartaIRB smart form (Other Attachments).
• *Questionnaires to measure bipolar symptoms, caregiver reactions, caregiving involvement, bipolar knowledge, resourcefulness, health risks, and health outcomes. (Listed under site related documents as 'questionnaires.pdf')*
• *Intervention evaluation questionnaire*

(Listed under site related documents as 'script intervention eval questionnaire.pdf')
• *Intervention journals*

(Listed under site related documents as 'resourcefulness sample journal page.pdf', 'biofeedback sample journal page.pdf', 'bipolar education sample journal page.pdf')
• *COVID-19 questions at remaining data collection sessions (consent included with questionnaire)*

Data Analysis Plan

Directions: Describe the data analysis plan, including any statistical procedures. If applicable, provide a power analysis, and study/safety endpoints.

*The primary aim **(A1)** is to examine differences across four groups of family caregivers on caregiver health over time. The underlying analyses for **A1** are built around the repeated measures analysis of variance (RMANOVA). The primary analysis will be a set of 4 group X 3 time waves RMANOVA. These analyses will compare the four groups: 1) a control group (no intervention); 2) education (usual care); 3) SM-need; or 4) SM-preference across three time waves of health risks and physical and mental health outcomes. When using RMANOVA, one not only assesses mean differences across time, but also assesses group differences and the interaction of time X group, which allow us to test the trend of the means over time across the four groups. The RMANOVA, not only can be used to determine if there are mean differences across the three time periods, it can utilize orthogonal polynomial contrasts to determine if there are mean and quadratic trends of the means across time. Orthogonal polynomials are weights assigned to each time period that model a linear or quadratic non-linear trend. RMANOVA can determine if these trends in the mean are significant. A linear trend is indicated if there is a change in direction based on scores across the tome waves. The major assumption to be tested with RMANOVA is sphericity. Sphericity is a form of compound symmetry and refers to the equality of variances of the differences between time waves. If the assumption of sphericity is violated based on the Mauchly's test, SPSS provides and adjusted F, df, and P-value in RMANOVA to account for the violation.*
*Secondary aims are to: **A2)** explore whether caregiver need or their preference for interventions associated with: a) care recipient's symptoms; b) caregiver reactions; and c)*

*caregiving involvement; and **A3)** build caregiver profiles from demographic/contextual factors that are associated with their needs and preferences for the self-management interventions. Accordingly, **A2** will be tested with a series of bivariate analyses including correlations, one way analyses of variance (ANOVA) and independent samples t-tests. We will run correlations when both variables are continuous. If the independent predictor variable is categorical and the dependent outcome is continuous, we will run an ANOVA. When the independent variable is dichotomous and the outcome is continuous, an independent samples t-test will be run. **A3** will build profiles 8 groups from two of the study arms: 1) SM-need and 2) SM-preference. To identify the unique characteristics of each group. Univariate descriptive statistics will be run on the contextual variables within the caregiver, care recipient, and caregiving situation. We will also examine cut points from measures of the self-management processes (knowledge, resourcefulness, and heart rate variability). These analyses will build profiles to show which caregivers may benefit most from a specific self-management intervention. We will prescreen for potential violations of assumptions for correlations. Scatter plots between two variables will identify influential cases, patterns of nonlinearity and constant-error variance that may reduce Parson's r. To address potential violation of the assumptions, influential cases can be removed. Data transformations can be used to remedy issues such as non-linearity, non-constant error variance, and non-normal error variance. For ANOVAs and t-tests, assumptions of normality and homogeneity of variance will be tested. Non-parametric equivalence tests will be used if assumptions are violated.*

For the supplemental analysis, VivoSense software will be used to perform automatic cleaning and computation of heart rate variability measures (SDNN, RMSSD, TP, VLF, LF, HF, LF/HF). Data analysis will consist of descriptive and inferential statistics using SPSS. Description of the sample will include age, gender, race/ethnicity, marital status, education level, annual income, and caregiver relationship. Additionally, descriptive statistics will be calculated for the study measures.

*The aims for the supplemental analysis are to: **SA1)** determine whether there are differences by caregiver characteristics (race and gender) on measures of psychological stress responses (caregiving involvement and caregiver reactions), **SA2)** determine whether there are differences by caregiver characteristics (race and gender) on measures of physiological stress responses (heart rate variability domains), **SA3)** examine associations among indicators of psychological stress responses (caregiver reactions and caregiving involvement) and physiological stress responses (heart rate variability domains, and **SA4)** explore relationships among time and frequency domains of heart rate variability. **SA1** and **SA2** will be tested with a series of independent samples t-tests. **SA3** and **SA4** will be tested with a series of bivariate correlations. Potential violations of assumptions for correlations and t-test will be assessed. To address violations of the assumptions for correlation, influential cases may be removed. Data transformations may be used to remedy issues such as non-linearity, non-constant error variance, and non-normal error variance. To address violations of the assumptions for t-test, non-parametric equivalence tests will be used if assumptions are violated.*

Confidentiality of Data

1. To maintain the confidentiality of the data: ☒ I will use a unique study identifier to code individuals' identifiable data and will store the master list separate from the study data..

HRP-

☐ Other (please explain)

Provide a plan to destroy identifiers including how and when.

2. How are you storing your electronic data? ☐ UH Redcap ☒ CWRU Redcap ☐ Secure Research Environment (SRE) ☒ CWRU Box ☐ OnCore ☐ UH Secure Network Drive ☒ CWRU Secure Network Drive ☐ Other - List storage method and provide justification:

3. Storage location of the paper research data and documents, if applicable:

☒ Paper research data and documents will be stored in a double-locked secure environment in the following location: *France Payne Bolton School of Nursing study office*

4. Will data be shared?

☐ Yes

1. List the exact data elements that will be shared:
2. Describe how data will be sent:

☒ No

☐ N/A

(Please note: if sharing data, please contact the UH Grants and Contracts Specialist or CWRU Tech Transfer Office to ensure the proper contracts/agreements are in place.)

HIPAA Authorization

Does this study collect, access, use, or distribute any Protected Health Information (PHI)?

☒ Yes ☐ No

If yes, indicate how HIPAA authorization will be obtained (check all that apply):

☒ HIPAA authorization is in the consent form

☐ Requesting a full or partial waiver of HIPAA for prescreening

☐ I will complete the Request for Waiver of HIPAA Authorization form. *See SpartaIRB Library*

☐ Requesting a full or partial waiver of HIPAA

☐ I will complete the Request for Waiver of HIPAA Authorization form. *See SpartaIRB Library*

Devices

☒ This is **not** device study. The protocol is considered non-therapeutic (non-therapeutic is defined as research not intended to diagnose, prevent, cure, mitigate, treat, etc. a disease or condition) by the FDA. – *You may delete the rest of this section.*
OR
☐ This is a device study. The protocol is considered therapeutic (research intended to diagnose, prevent, cure, mitigate, treat a disease or condition) by the FDA.
1. Is there an IDE (Investigational Device Exemption) for the proposed study?

☐ Yes, provide an official letter of support or proof of approval which identifies the IDE holder and IDE number.
☐ No
2. Is the device (and its use) a non-significant risk device for the proposed study design?

☐ Yes
☐ No
☒ N/A
3. If the research involves device(s), describe your plans to use, store, handle, administer and track those device(s) to ensure that they will be used only on research participants and be used only by authorized investigators.

Risks to Research Participants

1. List the reasonably foreseeable risks such as breach of confidentiality, discomforts, hazards, or inconveniences to the research participants related to their participation in the research. Include a description of the probability, magnitude, duration, and reversibility of the risks. Include the physical psychological, social, legal, and economic risks.

No physical, psychological, social, legal, or economic risks other than associated with daily living, are expected for the caregiver who participates in this study. Thus, the risks for emotional/physical distress should be minimal. Several measures will be taken to minimize the potential risk for distress while completing study questionnaires, HRV measurement, or during the interventions that involve journaling about the use of education, resourcefulness skills or breathing techniques, or use of the biofeedback device. If a caregiver becomes upset during a data collection interview or intervention meeting or phone call/email/text, the team member will offer to end it immediately, provide emotional support and/or make a referral to a mental health professional as needed. It is possible that discussion of stresses related to having a family member with bipolar disorder may stimulate emotional responses in the caregiver during the 4 week interventions. All weekly phone call/email/text field notes will be stored in REDCap. In addition, there will be ongoing supervision by the intervention supervisor (Suresky), who is an experienced, doctorally-prepared, advanced practice psychiatric nurse. The data collectors and interventionists will report adverse effects to Dr. Suresky and PI Zauszniewski as soon as discovered.

In regard to the use of the HRV measuring instrument, there have been no reported safety risk with the use of this instrument thought participants may fear it. It has passed electromagnetic interference and compatibility tests. Thus, there is no danger of electric shock from use of the device. We let the individual know that the device is for research purposes only and not meant to be diagnostic, the data obtained from the device will record heart rhythm but will not give information about treatments needed for heart health. If the individual would like more information about heart health or risk, they will be encouraged to talk to their doctor.

2. If applicable, indicate which experimental procedures may have risks to the research participants that are currently unforeseeable.

☒ N/A

3. If applicable, describe the risks to others who are not research participants.

☒ N/A

4. Describe the availability of medical or psychological resources that research participants might need.

☒ N/A

Provisions to Protect the Privacy Interests of Research Participants

Directions: Describe the steps that will be taken to protect research participants' privacy interests. (consider issues such as physical space, proximity to other, and participant preferences)

After eligibility is verified during phone screening by a team member, we will confirm with all study participants whether or not we can leave a voicemail message on their phone(s), and whether or not we can send mail to their home (in the event we cannot reach them by phone, and/or if they are randomized to the control group). We will ask if there are any disclosure concerns and make note if applicable in REDCap contact form. We will also ask study participants if they would like to be contacted for future research; we let them know there is no penalty to them if they do not wish to be contacted. Furthermore, we inform them that agreeing to be contacted does not obligate them to participate in future research, this only permits us to contact them. We will maintain a password-protected list on Box.com of individuals that have consented to be contacted for future research, along with their contact information and contact preferences. This list will be maintained by the Project Manager and may be shared with research team members, Co-Investigators, and/or other CWRU CREC-certified administrators on a case-by-case basis.

Privacy language is included in the informed consent form. Participants have the option of withdrawing from the study at any time and can request that no further information be shared about them from that point on. Participant names will not be shared in any report of the finding or with other study participants. Data collection interviews and intervention sessions will be conducted in a private setting (i.e. participant's home or other venue where others, including the persons with bipolar disorder, will not be present).

Confidentiality will be assured during all phases of the project by the following procedures. Screening and Study ID numbers will be used for all caregivers. A list of screening and study ID numbers with identifying names, phone numbers, and addresses will be kept locked in password-protected files in Box.com and REDCap. The survey data will be kept in a separate

file from the data collected during the study and will only be accessible to the PI and research staff that need access to assure accurate follow-up in this longitudinal study. This identifiable information will be destroyed after all data have been collected.
Confidentiality issues will be addressed during training of research staff that will do the data collection and the interventionists. All data collected throughout the study, including signed consent forms, quantitative data using the REDCap system, HRV parameters, journals, emails, and field notes maintained by research assistants and interventionists will be stored in locked files and password protected computer databases only accessible to the PI, Co-I's, project manager, and research staff. These data will not include any identifiable information that may have been obtained during recruitment and screening. These measures have been used successfully to protect the rights of human subjects in our previous studies. In addition, we will implement the following specific strategies to protect data obtained from the journals or emails used by the caregivers.
1) Structured journal – caregivers receiving an intervention will be provided with a structured journal for their use during the four weeks between the first (T1) and second (T2) data collection interviews. They will be instructed to store the journal in a private place (known only to them) in their home during the four weeks. They will be directed to not use real names of friends, relatives, etc. within the journal entries; they may use alternative names if they wish. Interventionists will review the journals immediately upon retrieval (after the 28 day period) and if names are found, they will be blackened out and not appear within the transcribed text data files. The journals will be stored in a locked cabinet in the research office and the text files will be stored in a password protected computer database. Both the journal and text files will be kept for a period not to exceed 3 years. 2) Email - Individuals may use email to get more information about the study, and/or to contact staff once enrolled in the study. Email contacts and outcomes will be recorded generally on our contact forms, which use Study ID number and not names. If an email needs to be printed or otherwise saved, it will be securely downloaded to a PDF file, with names and other contact information redacted, and delete the original email message. The PDF file will be stored in the password protected computer file for a period not to exceed 3 years.

Potential Benefit to Research Participants

☐ There is potential benefit to research participants.
Describe the potential benefits that individual research participants may experience from taking part in the research. Include the probability, magnitude, and duration of the potential benefits.
☒ There is **no** direct benefit to research participants.
If no direct benefit, state the potential benefit to society or others. *Do not list compensation.*

Withdrawal of Research Participants

Directions: Describe the anticipated circumstances under which research participants will be withdrawn from the research without their consent. Also include the procedures that will be followed when a research participant withdraws or are withdrawn from the research, including partial withdrawal from procedures with continued data collection.

☐ N/A

Participants have the option of withdrawing from the study at any time and can request that no further information be shared about them from that point on. If a study participant withdraws consent to participate in the study, a research team member will notify the project manager to complete end of study documentation.

The project manager will review cases regularly with research staff to determine which study participants should be withdrawn from the study. Research participants will be withdrawn from the research without their consent if they are non-responsive to phone calls, emails, texts, or letters and considered lost to follow up.

Data that were collected prior to a study participant's withdrawal will be de-identified and still be used in the data analysis for the study. After withdrawal, no further data will be collected for that participant.

Alternatives to Participation

Directions: List other options to participation. If subjects will be compensated with extra course credit, the course instructor offering extra course credit must provide alternatives to earn extra course credit. The alternative assignment must require equal or less time and effort for the same amount of earned extra credit that you can earn through participation in research. If there are other available clinical treatments, what would be included if a subject continued on standard of care therapy. If there is a viable alternative you must list it in the consent.

☒ The alternative is for research subjects not to participate.

Costs to Research Participants

☒ There are **no** costs to research participants or their insurance companies (there are no clinical visits or billable procedures.) – *You may delete the rest of the section.*

1. Describe what costs research participants will be responsible for as a result of their participation in the research, including but not limited to: clinical services required by the protocol deemed billable to insurance, transportation to study visits, parking, costs of drugs, cost of therapy, lost broken or stolen devices, etc.
2. Explain who will be responsible for payment of provided services in the event of insurance denials.
3. List what procedures, drugs, devices, supplies will be paid by the study sponsor or covered by other funding. List the other funding source.

Research Participant Compensation

☐ There is no compensation for research participants – *please leave rest of this section blank*

☒ There is compensation for research participants.

Describe the schedule, payment method, and payment total of any incentives or compensation that research participants will receive for participation in the research (e.g., gift cards or cash with amount, t-shirts, devices, bags, swag, etc.)
Incentive will be provided as follows: completion of entire data collection at T1 (enrollment): $20; T2 (6 months post intervention or from the date of enrollment if randomized to the control group): $25; and T3 (6 months after second data collection): $30 for a maximum total of $75.
COVID-19 modification: *For T2 and T3 data collected remotely, study participants will receive a gift card mailed to them. The study will have 1-3 gift card vendor options to choose from/ the amount of the gift card will be $25 for T2 and $30 for T3.*
☒ There will be reimbursement for research participants.
Describe the schedule, payment method, and payment total of any reimbursement that research participants will receive for participation in the research (e.g., gift cards or cash with amount, etc.)
If someone takes a bus or drives to CWRU or other community location to meet a research team member for T1, T2, T3, or an intervention meeting, we will reimburse that individual a 2-trip bus pass or parking voucher as appropriate.

Compensation for Research Related Injury

Describe who will pay for the costs of medical treatment and/or compensation in the event of a research related injury:
☐ Funding agency is providing some/all payment for injury
☐ Funding agency is providing no payment for injury
☒ N/A

Provisions to Monitor the Data to Ensure the Safety of Research Participants

1. Describe how often the data will be monitored for completeness, accuracy and adherence to the protocol.

2. Indicate if there will be a Data and Safety Monitoring Board or Committee:

☐ There will **not** be a formal Data and Safety Monitoring Board/Committee.
☒ There will be a formal Data and Safety Monitoring Board/Committee.
Provide information about the DSMB/C including the contact information of the committee member(s) (as applicable); whether it is independent from the study sponsor; how often it meets; the type of data that will be used; written reports, etc.
A Safety Monitoring Committee (SMC) has been formed as the monitoring entity for this grant. The SMC is independent from the study sponsor and consists of:
• Dr. Ronald Hickman , SMC chair, who serves as the Associate Dean for Research and is Associate Professor, Frances Payne Bolton School of Nursing, CWRU

Rlh4@case.edu

Dr. Sara Douglas, Assistant Dean for Research, and Professor, Frances Payne Bolton School of Nursing, CWRU
Sld4@case.edu
• Dr. Joseph Calabrese, Professor of Psychiatry from the CWRU School of Medicine, who has studied persons with bipolar disorder for more than three decades

Joseph.calabrese@UHhospitals.org
• Study team members will include Dr. Jaclene A. Zauszniewski, PI, and Dr. Christopher J. Burant, statistician cxb43@case.edu

1. Monitoring Study Safety
a) Monitoring schedule - Twice per year throughout the project, the SMC will review data on the study regarding study safety. For example, the SMC will review any occurrences of caregiver emotional distress that required intervention by data collector or interventionist as well as those requiring referral and follow-up and instances where caregivers withdrew from the study.
b) Audits for compliance with IRB requirements – Random internal audits of 10% of the files will be done twice annually to insure the approved IRB protocol is being followed. The SMC will review recruitment procedures, compliance with meeting the inclusion/exclusion criteria, consistency with random assignment process to the treatment conditions, provision of interventions within timeframe defined within the protocol, and scheduling of data collection sessions as outlined within the protocol.
c) Conformance with informed consent requirements – Random internal audits will be conducted twice per year to verify that informed consent requirements are being met. For example, the SMC will review 10% of the consent forms for signatures and dates, make sure all consent forms are accounted for and stored in locked files and that the correct form is being used. Data collectors will be asked to describe the consent process quarterly to re-assess their knowledge of this process quarterly and review / retraining will be done as needed.
d) Verification of source documents – This study does not involve printed or written documents; data will be collected through electronic data capture using REDcap software and then downloaded directly into SPSSPC files. Heart rate variability data will be downloaded from the assessment device and transcribed into the SPSSPC files. These sources will not include any data that would be personally identifiable.
The SMC will review 1) all causes of mortality (e.g., caregiver death); 2) issues with participation (e.g., numbers and reasons for withdrawing from the study or refusing interventions, etc.) as well as recruitment refusal (percent and reasons) and subject attrition (percent and reasons); 3) missing data (including whether there are systematic patterns or whether data are missing at random); and 4) errors in data entry (which are expected to be minimal given the use of software for data collection with direct download into SPSS). In addition, differential attrition from the intervention groups (including the control and usual care groups, and the groups assigned to intervention based on need or personal preferences) will be monitored.

If concerns or problems are identified by the SMC, they will be reported to the IRB and NINR/NIH via email by Dr. Zauszniewski and Dr. Hickman, respectively, within 3 business days after they are identified. If there are recommendations made by the SMC, the action plan for response or notice of any actions taken by the IRB regarding the research and any responses to those actions will be provided to NINR Officials within 2 weeks.
e) Investigator compliance – Compliance of the investigators and all research team members who will have access to the data will be monitored annually. All research team members will be CREC certified; the CWRU intranet hosts a website where verification of compliance with continuing education for all investigators and team members can be evaluated.
2.) Reviewing and Reporting Adverse Events/unanticipated problems
a) Event identification- At the onset and for the duration of the study, all research staff and investigators will have instructional review of the nature and types of unanticipated and adverse events as described by the CWRU IRB. Potential risks for this study may include caregiver distress and breach of confidentiality (as described above). Caregiver distress may be identified by the data collector (during data collection) or the interventionist (during the interventions or phone follow-up). Breach of confidentiality may be identified by any research team member.
b) Reviewing and reporting- As they occur, all unanticipated events and adverse events will immediately be reported to Dr. Zauszniewski (PI) who will report them to the IRB according the CWRU IRB protocol reporting procedures for both serious and non-serious adverse events and unanticipated problem reporting. These will be summarized in the semi-annual reports to the SMC. Annual progress reports to the CWRU IRB and NINR/NIH will include a summary of the SMC's activities and findings as well as any adverse events regarding human subjects. Program Officials at NINR will be informed in a timely manner (3 business days) of unanticipated problems (e.g., a data breach) or unexpected serious adverse events that may be related to the study protocol or IRB-approved revisions to the study protocol that indicate a change in risk for participants. All adverse events and protocol deviations will be reviewed with the staff involved within 3 business days. Factors leading up to the event or deviation will be discussed and strategies for preventing recurrence will be developed and implemented immediately.

Community-Based Participatory Research

☒ This is **not** a community-based participatory research project – please leave the rest of this section blank

☐ This is a community-based participatory research project

Describe the involvement of the community in the design and conduct of the research.

Note: Community based research is research that is conducted as an equal partnership between academic investigators and members of a community. In Community Based Participatory Research (CBPR) projects, the community participates fully in all aspects of the research process.

MULTI-SITE RESEARCH (when UH or CWRU is the IRB of Record)

Does this project have multiple sites?

☐ **Yes**

☒ **No** – please leave the rest of this section blank

Non-Local Site Information for Multi-Site Studies

*If this is a multi-site study where you are the **lead investigator,** list the following information for each relying site:*

1. Name of site:
2. PI of relying site:
3. Name of IRB contact:
4. Phone number of IRB contact:
5. Email address of IRB contact:

Non-Local Recruitment Methods for Multi-Site Studies

*If this is a multi-site study and research participants will be recruited by methods **not under the control of the local site** (e.g. call centers, national advertisements) describe those methods. Local recruitment methods are described above.*

1. Describe when, where, and how potential research participants will be recruited.

2. Describe the methods that will be used to identify potential research participants.

3. Describe the materials that will be used to recruit research participants.

Multi-Site Research Communication Plan (when you are the lead investigator)

*If this is a multi-site study where you are the **lead investigator**, describe the processes to ensure communication among sites including:*

☐ *All sites will have the most current version of the protocol, consent document, and HIPAA authorization*

☐ *All required approvals (initial, continuing review and modifications) have been obtained at each site (including approval by the site's IRB of record)*

☐ *All modifications have been communicated to sites, and approved (including approval of the site's IRB of record) before the modification is implemented*

☐ *All engaged participating sites will safeguard data, including secure transmission of data, as required by local information security policies*

☐ *All engaged participating sites will safeguard data, including secure transmission of data, as required by local information security policies*

☐ *All local site investigators conduct the study in accordance with applicable federal regulations and local laws*

☐ *All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy*
If this is a multi-site study where you are the ***lead investigator,*** *describe the method for communicating to engaged participant sites the following:*
1. Problems:
2. Interim results:
3. The closure of the study:

Additional Information

If you have any additional information regarding your study not covered in the template, please include it here.

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