PROTOCOL Social/Behavioral Research - Expedited/Full Board

Protocol # 14-05-323
Date Printed: 03/23/2015

Protocol Title:	Research Aimed at Improving Both Mood and Weight (RAINBOW)
Protocol Type:	Social/Behavioral Research - Expedited/Full Board
Date Submitted:	01/14/2015
Approval Period:	01/21/2015-08/13/2015
Important Note:	This Print View may not reflect all comments and contingencies for approval. Please check the comments section of the online protocol. Questions that appear to not have been answered may not have been required for this submission. Please see the system application for more details.

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* * * Amendment * * *

Amendment

1. ~~Summarize the proposed changes to the protocol in lay terms.~~

A new recruitment strategy endorsed by our PAMF MD Advisory Committee and RAINBOW Investigator Team is added to address recruitment challenges. This eligibility pre-screening is intended to reduce the burden, and provide incentive from the large pool of patients with no indication of depression in the EHR. Recruitment section 5e is updated with this new step. These participants will be invited to answer 2 preliminary screening questions for an entry to a 1-in-500 to 1,500 chance (based on quarterly cohort estimates) to win an iPad mini 3. If after pre-screening, the patient is eligible and interested, they have the option to continue completing the full initial eligibility ~~screening and a 2nd raffle entry.~~

Proceed to the appropriate section(s) and make your changes.
Make necessary changes in Consent Form(s), when applicable.

2. Indicate Level of Risk involved with the changes proposed. (If level of risk has changed, please update the section 'Risks' in the protocol information.)

No Change

3. Describe any Other Changes

List of Sections (and questions) that have been changed/modified

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* * * Personnel Information * * *

Principal Investigator
This role has editing privileges

Note: All Student/PostDoc Investigators must have a Faculty Sponsor. The Faculty Sponsor is considered by PAMF to be the"Principal Investigator" and is listed as the PI for the IRB submission.

Name of Principal Investigator	Degree (MS/MD/PhD)	Title
Ma, Jun	MD, PhD	Assoc. Scientist/MD/Ph.D
Email	**Phone**	**Fax**
maj@pamfri.org	650-853-4809	
Department Name	**Mailing Address**	
Health Services Research	Palo Alto	

PAMF status (select all that apply):

X	Faculty		PAMFRI Professional Researcher		PAFMG/PMC		Consulting Investigator		Post Doc		Other		

Ethics training completed? Y

Study Coordinator

Name	Degree	Title
Jameiro, Elizabeth	MD	Senior Research Associate
Wittels, Nancy	MS	Senior Research Associate
Luna, Veronica	BA	Project Coordinator III

Project Lead
This role has read-only privileges

Note: Project Lead (Other than PI, the person with day-to-day responsibility for the project, or the student/post doc leading the work)

Name of Project Lead	Degree	Title
Lv, Nan	PhD	Postdoc Fellow
Email	**Phone**	**Fax**
lvn@pamfri.org	650-853-4823	
Department Name		
Health Services Research		

PAMF status (select all that apply):

	Faculty		PAMFRI Professional Researcher		PAFMG/PMC		Consulting Investigator	X	Post Doc		Other	

Ethics training completed? Y

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* * * Subject Population * * *

Subject Population(s) Checklist

Select All That Apply :

- Healthy Subjects
- Children/Minors
- Pregnant Women
- Fetuses
- Neonates
- Subjects for whom fully informed and free consent may be an issue
- Educationally Disadvantaged
- Economically Disadvantaged
- Cognitively Impaired
- Mentally Disabled
- Prisoners
- Employees of PAMF, PAFMG, or Sutter Health
- Students of members of the Research Team
- No particular targeting of vulnerable subjects
- X Other (i.e., any vulnerable subject population(s)not specified above)

Inclusion criteria -

• Body mass index ≥30.0 kg/m2 (non-Asians) or ≥27.0 kg/m2 (Asians)

• Clinically significant depression PHQ9 ≥10

• PAMF patient for ≥1 year and seen in primary care at least once in the preceding 24 months

• Able and willing to enroll and provide written, informed consent, i.e., to: meet the time and data collection requirements of the study; be randomized to one of two intervention arms; participate in follow-up for 24 months; and allow extraction of relevant information from their medical records.

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* * * Study Location * * *

Study Location(s) Checklist

Select All That Apply :

X PAMF: Palo Alto Division
X PAMF: Mountain View Division
PAMF: Santa Cruz Division
X PAMF: Alameda Division
PAMF: Mills Peninsula Division
Menlo Park Surgical Hospital
Mills Peninsula Hospital
Sutter Maternity and Surgical Hospital
El Camino Hospital (discuss their IRB review, if applicable)
Stanford University (discuss their IRB review, if applicable)
Other (Specify other Study Sites)

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* * * General Checklist * * *

General Checklist

X Any federal funding (e.g., NIH, NSF, DOD etc.)?

PAMF Memorandum of Understanding (MOU)?

Inter-institutional IRB Authorization Agreement to rely on PAMF?

X Will subjects be paid for participation?

Other

None of the above

Cover Sheet:

X Check here if you plan to upload a cover sheet to the IRB. Summarize in the box below any special aspects of the submission the IRB and its staff should consider. See What to Include in a Cover Sheet

If you feel that certain methodological or content expertise will help the IRB assess your protocol, please indicate that here. The IRB may solicit advice from non-members and you can offer suggestions about who might be contacted.

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* * * Funding * * *

Funding Checklist

Add funding source(s) below or select "None" if there is no funding for the study or it is funded "out of your own pocket"

NONE

Funding - Grants/Contracts/Fellowships(awarded through PAMFRI)

PAMFRI Proposal 'ShortName'	Sponsor Award#	Sponsor (if multiple sponsors, put the primary one first and add a record for each one)
RAINBOW	1RO1HL119453-01A1	NHLBI

Funding - Other

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* * * Expedited Paragraphs * * *

This section will help in determining the appropriateness of this protocol for this review track.To be expedited, a protocol must be no more than minimal risk (i.e., "not greater than those ordinarily encountered in daily life") AND must only involve human subjects in one or more of the following paragraphs.A subset of those that may be expedited may be eligible for use of the Exempt review track and you will encouraged to use that form.

Select all paragraph(s) describing this protocol:

	1.	Clinical studies of drugs and medical devices.
~~X~~	2.	Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture.
	3.	Prospective collection of biological specimens for research purposes by non-invasive means.
X	4.	Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)
	5.	Research involving materials (data, documents, records, recordings, or specimen) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (NOTE: Some research in this paragraph may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)
X	6.	Collection of data from voice, video, digital, or image recordings made for research purposes.
X	7.	Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects - 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

If none of these boxes apply to this project, consult your Department head.

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* * * Purpose,Study Procedures,Background * * *

If this project was previously reviewed with a paper submitted form, please enter the Legacy Protocol Number: NA

Study Title

Research Aimed at Improving Both Mood and Weight (RAINBOW)

Complete each section. Specify N/A as appropriate. Do not leave any required sections blank.

1. Purpose of the study

a) Provide (in lay language) a brief summary of the purpose and what you expect to learn from the study. (No more than 200 words)

The purpose of the study is to evaluate the clinical and cost effectiveness and implementation potential of an integrated intervention program to improve weight and mood for obese adults with comorbid depression.

The proposed intervention uniquely adapts and integrates the technology-mediated Group Lifestyle Balance (GLB) program, which was derived from the Diabetes Prevention Program lifestyle intervention, with the Program to Encourage Active and Rewarding Lives (PEARLS) for collaborative stepped depression care, which uses problem-solving therapy as first-line, intensified with stepwise increases in doses and number of medications as needed. Each program has proven effective in other populations, and both are nationally recognized in providing standard coach training and support for their original target populations. This study will be the first to test the effectiveness of combining the 2 programs to treat obese and depressed adults in primary care.

2. Study Procedures

a) Describe the study procedures briefly here. More detail will be elicited later.

We will recruit potentially eligible patients identified through Electronic Health Record (EHR) prescreening from selected PAMF primary care clinics located within 25 miles of the PAMF Research Institute. Patients who meet the entry criteria will be enrolled and randomized into a 12-month integrated weight loss and depression treatment intervention program or to the usual care group. All participants will complete baseline, 6-month, 12-month, 18-month, and 24-month assessment visits.

b) State if deception will be used. If so, provide a rationale and describe debriefing procedures. Upload a debriefing script in the Attachments Section.

NA

c) Is this a research project designed to assess the effects of changes in patient care or work processes instituted by PAMF as part of its operations or Quality Improvement efforts? If so, describe the changes, the reasons why they were undertaken, and why such changes are part of routine care as determined PAMF rather than part of a research study. Explain any role members of the research team had in

designing the changes. Upload a letter from the appropriate PAMF "champion" supporting these descriptions.

No

3. Minimal Risk Criteria

Research involving no more than "minimal risk" to subjects and meeting certain additional criteria may be eligible for exempt status. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

a) If you believe the study procedures involve no more than minimal risk, in the box below describe how the proposed research procedures meet the test.

Risks associated with participation in this study may include the potential for the following: worsening depression and self-harm; new onset or worsening anxiety; side effects or adverse reactions to a newly initiated medication for depression; risks associated with behavioral strategies to reduce weight and obesity-related risk factors through moderately reduced caloric intake and gradually increased physical activity; breach of research participant privacy and confidentiality; discomfort associated with the procedures for clinical ~~and laboratory~~ measurements; discomfort or distress with completing survey instruments; and inconvenience caused by study contacts. These risks are largely associated with the characteristics of the patient population to be studied and the guideline-consistent treatments (e.g., FDA-approved antidepressant medications and evidence-based behavior change strategies). The risks are reasonable in relation to the anticipated benefits and will be minimized by using procedures that are consistent with sound research design, that do not unnecessarily expose participants to risk, and that are based on established research and clinical protocols.

b) In the box below, discuss any potential organizational risks that might arise from the publication of study findings and how you will address such risks. If the research involves such risks, complete a separate[Organizational Risk Assesment Form] (ORA).Enter below any specific mitigations or risk management approaches requested by the Advisory Committee Concerning Organizational Risk and Dissemination. Also indicate if any ACCORD members scored the project as a 5. Upload the ORA as reviewed and scored by the ACCORD.

NA

4.Criteria for exempt status:

Human subjects research that falls within one of 6 categories described in CFR 46.101(b) may be categorized as exempt by the IRB. For the two categories commonly applicable to research at PAMFRI, the following questions (a) and (b) are particularly relevant. If this project meets, the criteria any of the other 4 categories, please explain here:

NA

Note: The key distinction between the questions under (a) and those under (b) is that the former relate to data, observations, etc., that are to be collected for this research. The questions under (b) relate to the use of data, specimens, etc., that were collected previously for some other reason and are now to be accessed for this project.

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a1. Does this research involve "the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior"? (Include focus groups in this category.) Enter No or Yes. If yes, explain:

Yes. This research will use surveys and individual interviews to screen participants and to examine the effects of the integrated intervention program. Participants are free to choose not to answer any questions and the following language will be added to all self-completed surveys in order to clarify the voluntary nature of study questions:

NOTE ABOUT DECLINE TO STATE OPTION:
Participation in research is voluntary. As a research participant, you have the right to decline to answer any question. Please be advised that your decision to do so may prevent us from being able to determine your eligibility for enrollment. Note: We have indicated with an asterisk (for example, Decline to state*) the questions for which choosing not to answer will result in your ineligibility. Also, if you are enrolled into the study, providing complete data is important to the scientific validity of our findings, and we thank you for keeping these considerations in mind.

a2. Is the information obtained through such means or "recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects"? Enter No or Yes. If yes, explain:

Yes. We will collect the following individually identifiable private information from research participants: names, street addresses/post office box numbers, telephone/handheld device, and email addresses, which will be used only by trained study personnel who have a need to know to carry out recruitment, intervention, and assessment activities proposed in this study. We will destroy the personal identifiers of individuals who refuse to participate, are ineligible, or who are otherwise not enrolled in the study at the earliest opportunity. Our standard practice is to use anonymous, unique study IDs to label all participant data, which will be stored separately from personal identifiers needed for study contact. Only de-identified study sets will be stored on the PAMFRI network. Recordings of individual interviews may contain patient identifiers because, for example, participants may be addressed by name during the sessions. The main informed consent contains the IRB required language for protocols that include audio recordings.

a3. Could "any disclosure of the human subjects' responses outside the research … reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation"? Enter No or Yes. If yes, explain:

No

In general, with respect to all aspects of the project, if the answer to a1 is yes AND the answers to a2 OR a3 are no, a protocol may be determined by the IRB to be exempt.

b1. Does the research rely on "the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens"? In the context of this question, "existing" can also be considered not in a temporal sense, but in the sense that the data etc. have been, or will be collected for purposes other than this research project, such as in ongoing patient care or administration. An example would be data extracted from electronic health records or claims files, even if some of that data is to be generated in the future. Enter No or Yes. If yes, describe the nature of the data:

Yes. We will obtain participants' written HIPAA authorization (in combination with the informed consent for randomization, intervention, and follow-up) at baseline assessment visits for the research team to use and disclose data from the PAMF EHR on health insurance types, encounters, diagnoses, prescriptions, procedures, and other health services (e.g., health education programs, telephone or secure email consultations) for psychiatric and general medical conditions.

b2. Are the sources of these data "publicly available?" Enter No or Yes. If yes, explain the source and any restrictions on its use.

No

b3. Are the data "recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects"? A commonly used process at PAMFRI involves access to identifiable data by the Information Management Group (IMG) which prepares a data file that only includes a study ID for each case. If the IMG maintains this "key" and does not share it with the research team, the above test (b3) can be met. Enter No or Yes. If yes, please describe how the procedures in this study meet this criterion.

No

b4. If the data to be accessed (b1) are patient data, they may be protected health information (PHI). Even if the research team only has access to a fully de-identified data set, there may be HIPAA concerns that must be addressed. (See question 9 below). In the space below, indicate whether the study involves PHI or explain why the data being used in this study are not PHI. Note: if the IMG is responsible for preparing a research file from identifiable files, the study is considered to be using PHI. The study is not using PHI if all the study data sets are derived from other data sets that have been previously de-identified. Upload in the attachments section the Data Access Plan as completed by the IMG.

The study requires access to PHI in 2 stages of its conduct, initially for recruitment purposes and also for outcome analyses.

PHI for Recruitment Purposes:
The EHR will be used to pre-screen and identify an enriched pool of potentially eligible patients. Minimally necessary patient identifiers will be used to recruit potentially eligible patients (e.g., names, telephone numbers, and mailing addresses)

PHI for Outcome Analyses:
Only after HIPPA Authorization has been obtained from participants will health care utilization data be abstracted for analysis. Data will be de-identified by the IMG per PAMFRI standard practice (e.g., using the anonymous study ID and wobbled dates). Only de-identified data will be used for baseline characterization and outcome evaluation (e.g., cost-effectiveness analyses), and if indicated, to conduct exploratory analyses of the potential confounding of treatments outside the study protocol (e.g., psychiatric or weight-loss medications, mental health or nutrition counseling referrals) on the primary intention-to-treat findings.

If data are transferred to PAMFRI from other sources under a HIPAA data use agreement, the study is considered to be using PHI. Agreements simply restricting the recipient from passing on the data to others are not necessarily in this category. If in doubt, consult with the PAMFRI Director. Upload any data use agreements for the use of data derived from sources outside PAMF.

In the space below, indicate whether the study involves PHI or explain why the data being used in this study are not PHI.

See section 4b4 above.

If this project only relies on the use of publicly available data, even if there are non-HIPAA restrictions on how the Investigator can use or redistribute the data, it will qualify as Exempt and the Exempt form may be used.

This study may qualify for exempt status under 4(b1) and 4(b3) by using only data not collected for this research.

If there are no subjects to consent, skip to question 9.

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* * * Subject Population * * *

5. Subject Population from Whom Consent/Assent will be Requested

a) Describe the proposed subject population, stating any exclusion or inclusion criteria with respect to age, gender, race, ethnicity, language and literacy. If any inclusion/exclusion criteria are based on gender, race, or ethnicity, please provide the rationale. Note that consent forms should take account of the subjects' language and literacy capabilities.

Inclusion criteria-

•Age (as of date of enrollment)
Lower limit: 18 years;
Upper age limit: none; (Only exclude for cause, e.g. disease and functional limitations, as detailed below.)
•Gender: both women and men;
•Ethnicity: all ethnic groups;
•Obesity: Body mass index ≥30 kg/m2 (non-Asians) or ≥27 kg/m2 (Asians);
•Clinically significant depression: PHQ-9≥10;
• Having established care at PAMF: PAMF patient for ≥1 year and seen in primary care at least once in the preceding 24 months;
• Able and willing to enroll and provide informed consent, i.e., to meet the time and data collection requirements of the study, be randomized to one of two study arms, participate in follow-up for 24 months, and authorize extraction of relevant information from the EHR.

Exclusion Criteria-

Psychiatric exclusions:
• Active suicidal ideation per PHQ-9 interview that includes active plan and/or intent (item #9 ≥2) ;
• Any Axis I disorder other than Minor or Major Depressive Disorder and/or Dysthymia, with the exception of any comorbid Anxiety Disorder;
• Active Bulimia Nervosa within the past 3 months (however Binge Eating Disorder without purging is not an exclusionary condition);
• Ongoing psychiatric care with a provider outside of PAMF
• Active alcohol or substance use disorder (including prescription drugs)

Medical exclusions related to weight loss:
• Had bariatric surgery within the past 12 months or plan to undergo bariatric surgery during the study period;

Other medical exclusions:
• Pre-existing diabetes (other than during pregnancy);
• Pre-existing cardiovascular disease: e.g., coronary heart disease (myocardial infarction, angina pectoris, percutaneous coronary intervention, coronary artery bypass graft surgery), cerebrovascular disease (stroke, transient ischemic attack), peripheral vascular disease, heart failure, or aortic aneurysm.
• Diagnosis of cancer (other than non-melanoma skin cancer) that is/was active or treated with radiation or chemotherapy within the past 12 months;
• Severe medical comorbidities that require aggressive treatment, e.g., stage 4 or greater renal disease, liver failure;
• Diagnosis of a terminal illness and/or residence in long-term care facility;
• Cognitive impairment based on the Callahan 6-item Screener

Other exclusions:
• Inability to speak, read or understand English;
• Having no reliable telephone service, or no regular Internet access via a computer and/or mobile device

(e.g., smartphone);
• Plan to move out of the area or transfer care outside PAMF during the study period;
• Currently pregnant or lactating, or planning to become pregnant;
• Already enrolled, or planning to enroll, in a research study that would limit full participation in the study or confound the observation and interpretation of the study's findings;
• Family/household member of another study participant or of a study staff member;
• Investigator discretion for clinical safety or protocol adherence reasons.

b) Estimate the total number of subjects planned for the study and approximately how many must be approached to obtain this sample size. The number of subjects should be adequate to answer the research question(s) posed in this study. Please indicate the rationale for the target number of subjects.

The study projects to randomize 404 participants. We estimate that about 7,500 patients will be contacted in order to reach the proposed number of subjects. This study will recruit women and men meeting the inclusion and exclusion criteria.

c) If any proposed subjects are children/minors, prisoners, pregnant women, those with physical or cognitive impairments, mental illness, or others who are considered vulnerable to coercion or undue influence, state the rationale for their involvement. Please explain any special precautions and procedures you have incorporated to address the special circumstances of including such subjects.

NA

d) State whether any of subjects are PAMF/PAMFRI employees and/or students. Describe the precautions to be taken to ensure they do not feel any pressure to participate.

At no point will we reach out to staff through means (e.g. supervisors) that may exert or be perceived to exert coercion or undue influence.

e) Describe how potential subjects will be identified for recruitment (e.g., chart review, referral from individual's treating physician, those individuals answering an ad). Describe how subjects will be recruited and how they will initially learn about the research, e.g., clinics, advertising (attach recruitment material). Potential subjects may not be contacted before IRB approval.

The following steps will be used to identify potential subjects for recruitment:

• Identification of potentially eligible participants: Potential participants will be identified through electronic health record (EHR) data extraction using pre-specified exclusion criteria.

• Patient PCP authorization of study contact: Research staff will obtain PCP authorizations of study contact of identified patients in their panels.

• Pre-screening strategy for patients WITH NO INDICATION of depression in the EHR: These patients will be sent a brief email from the PI inviting them to answer 2 preliminary screening questions (PHQ2 for depressive symptoms), for a chance to win an iPad mini 3. If eligible in the pre-screening, the patient has the option to continue with the full Initial Eligibility Screening and a 2nd entry to the drawing. For patients with no email on file, a letter will be sent. All interested patients may self-screen online or by phone with a research staff.

• Recruitment letter/email sent to patients WITH INDICATION of depression in the EHR: These patients will be sent a letter on behalf of their PCPs with a description of the study and invitation to screen. The letter will also include instructions for interested participants to complete the Initial Eligibility Screening themselves online or with a research staff over the phone. The patient is also given the option to decline

and refuse further contact. When there is an email on file, patient will be sent an email as alternative to a letter with a link to the online survey to complete or decline screening.

• Online or telephone Initial Eligibility Screening: The screening begins with an online or phone consent procedure which covers the initial screening, baseline questionnaire and dietary recalls. Potentially eligible patients who consent will be screened online or by telephone using questions pertaining mainly to the exclusion criteria listed above (section 5a), and they will provide their contact information.

• Online baseline questionnaire: Patients who pass the initial screening will be invited by email to complete the online baseline questionnaire prior to the study visit. Patients may receive up to two reminder emails and/or phone calls.

• Dietary Recall: In addition, patients who pass the initial screening will be asked to complete a 24-hour dietary recall over the phone with a trained research associate.

• Baseline visit: The visit will begin with the written informed consent process. They will be asked to confirm their willingness and motivation to enroll in the study. Those who consent will complete the full Baseline Clinical Measurement Visit. ~~Patients who are eligible at baseline and gave consent will complete their blood draw at a PAMF clinical laboratory for future research.~~

• Study physician chart review and approval: A study physician will review all participants who completed the baseline visit for study enrollment. Patients needing further evaluation as determined by the study physician will need medical clearance from their primary care providers to be enrolled in the study.

• Randomization: Fully eligible and consenting patients will be randomized into the study.

f) Payment. Explain the amount and schedule of payment, if any that will be paid for participation in the study. Include provisions for prorating payment, if applicable.

At the conclusion of the baseline assessment (visit 1), all eligible patients will receive and keep a Fitbit ZIP™ WIRELESS ACTIVITY TRACKER, which measures daily total steps, aerobic steps, time spent walking, calories and distance traveled. In addition, participants will receive:

$20 6-month assessment (Visit 2)
$20 12-month assessment (Visit 3)
$20 Bonus for completion of both first year visits
$20 18-month assessment (Visit 4)
$20 24-month assessment (Visit 5)
$20 Bonus for completion of both second year visits

g) Estimate the probable duration of the entire study. This estimate should include the total time each subject is to be involved and the period about which the data about the subject is to be collected (e.g., During this 3-year study, data will be collected from subjects using four surveys taking about 3 hours in total over a 12 month period). Subjects will also be asked to authorize access to their medical record information at PAMF for the past 5 years as well as during the study period).

The entire study will last for 5 years. Each eligible, consenting participant will be randomized to receive the integrated treatment or usual care for 12 months. The health coach facilitated intervention will involve eight (9) one-on-one in-person sessions over 5-6 months, six (6) 15-20 minute phone calls over 5-6 months and concurrent coach support via MyHealth Online over the 12 months. Coach contact will cease after 12 months, although participants will be followed for another 12 months in order to assess intervention durability and cost-effectiveness. Regardless of group assignment, all participants will be asked to complete 4 follow-up assessments at 6, 12, 18, and 24 months post randomization). An estimate of the total time each subject is to be involved is below.

All Participants	Estimated Time*
Initial Screen	10 minutes
Baseline Assessment:	
Baseline questionnaire	30 minutes
Baseline dietary recall by phone	20 minutes
~~Baseline fasting blood draw~~	~~Varies~~
Baseline visit	90 minutes
6-month, 12-month, 18-month, and 24-month assessments, each:	
Follow-up questionnaires	30 minutes
Follow-up dietary recalls by phone	20 minutes
~~Follow-up fasting blood draws~~	~~Varies~~
Follow-up visits	60-75 minutes
Group B I-CARE Participants	Estimated Time,* each:
Orientation session	60 minutes
In-clinic sessions (8)	60 minutes each
Telephone sessions (6 or more)	15-20 minutes each
DVD sessions at home (12)	30 minutes each
Self-monitoring and physical activities	Varies

*Please note that these time estimates do not include commute time to and from the clinic.

h) If the study may affect the workflow at PAMF sites or clinicians, please explain how the impact will be minimized and upload a letter from the relevant department head or administrator.

NA

i) Please review the PAMFRI database of ongoing studies that are not “data-only.” Describe any targeting the same patient population that will be targeted in this protocol. Discuss issues of overlap, respondent burden, and potential confounding effects and how they will be handled.

None

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* * * Risks * * *

6. Risks

HHS Regulations define a subject at risk as follows: "...any individual who may be exposed to the possibility of injury, including physical, psychological, or social injury, as a consequence of participation as a subject in any research, development, or related activity which departs from the application of those accepted methods necessary to meet his needs, or which increases the ordinary risks of daily life, including the recognized risks inherent in a chosen occupation or field of service."

If audio/video taping will be used, state if it could increase potential risk to subject's confidentiality.

All study audio records will be protected according to the same standards and procedures used for all study data. These records will be generated and accessed by authorized study personnel only and securely stored in locked cabinets or on password-protected, encrypted network drive (if electronic).

a) For the following categories, describe the potential risks and how you plan to minimize them.

Physical well-being.

• Risks associated with weight-loss strategies and increased physical activity

The proposed weight-loss intervention promote a balanced, calorie-controlled diet approach and recommend against very low calorie diets (<1200 kcal/day) or losing weight too rapidly (>2lbs/week). Participants will be advised to avoid crash or fad diets that promise marked, rapid weight loss. Instead we will recommend a moderate caloric reduction by 500-1000 kcal/day through healthy substitutions and portion control, rather than omission or elimination of specific foods.

To minimize risks associated with increased physical activity, potential participants will be screened prior to enrollment for angina and peripheral vascular disease using the Rose Questionnaire. Those screening positive may only participate with approval by a study physician and a written clearance from their PCP. Screening for angina and peripheral vascular disease will also be conducted at each follow-up assessment, irrespective of group assignment. If positive, the Co-PI, study physician and the patient's PCP will be notified and the patient will be advised to schedule an appointment with his/her PCP for further evaluation. Consistent with the latest physical activity recommendations for Americans, the proposed intervention promotes achieving 150 minutes or more per week of moderate-intensity physical activity in a gradual manner. Participants will be informed during the consent process and will be reminded during regular follow-up visits if they experience new or increasing physical symptoms (e.g., chest pain, palpitations, etc.) with physical activity, they should consult their PCP for evaluation and possible treatment.

• Risks associated with clinical/~~laboratory~~ testing

There are no greater risks associated with completing the required clinical ~~and laboratory~~ measurements in this study than those ordinarily associated with such measurements in routine health care. All measurements will be performed by trained personnel according to standardized protocols and procedures. Patients with a mean systolic BP ≥180mmHg or mean diastolic BP ≥120mmHg will be further assessed for hypertensive urgency by asking about associated symptoms: headache, vision changes, chest pain, shortness of breath, severe new back pain, nausea/vomiting. If no urgency detected, the patient will be advised to see their PCP the same/next day. If urgency detected, the research associate will

immediately take the patient to urgent care for further evaluation. Patients with mean BP above the threshold will be rescheduled and asked to complete a Participant Advisory Acknowledgment. Patient PCP will be notified immediately via staff message in EPIC.

Psychological well-being.

• Risks of worsening depression and self-harm.

Some of the questions about depression, thoughts of death and other psychiatric symptoms and conditions as a part of the screening may be distressing to some patients. However, in general the questions will not be particularly intrusive or distressing, and stress will likely be transient. In addition, participants are free to choose not to answer any questions. It is widely accepted that asking questions about thoughts of death or suicide does not lead to increased risk of suicide. Nevertheless, in the event that a patient is identified as being suicidal in the screening or follow-up phase of the study (not because of being asked questions), we have a self-harm protection protocol (see 6e) in place that will alert the study supervising psychiatrist to assess the patient's suicidal thoughts by telephone, followed by notification of the patient's primary care provider and appropriate clinical action if necessary.

• Risk of worsening anxiety.

The Generalized Anxiety Disorder 7-Item (GAD-7) Scale is a screening tool that has been developed to screen for 4 anxiety disorders: Post Traumatic Stress Disorder, Panic Disorder, Generalized Anxiety Disorder, and Social Phobia. A score of ≥10 indicates a high probability of 1 or more of these disorders. Patients with coexisting anxiety who meet all inclusion and exclusion criteria will be eligible to participate. They can usually be effectively treated by starting on citalopram or sertraline. Patients carrying a diagnosis of bipolar or psychotic disorder will not be eligible to participate. However, patients with undiagnosed anxiety disorders or panic attacks can have an exacerbation of anxiety symptoms if an antidepressant is started at therapeutic dose or if an antidepressant like buproprion is used. Patients screening positive on the GAD-7 will be asked follow-up questions to screen for panic disorder. Patients with suspected panic disorder should be discussed with a psychiatrist before starting or increasing the dosage of a patient's planned antidepressant. SSRIs are effective treatments for both panic disorder and depression, but patients with comorbid panic should be started on lower dosages initially.

• Protection against adverse reactions to antidepressant medications (ADMs).

Consistent with the stepped depression care strategies, the study supervising psychiatrist will contact PCPs of intervention participants with unremitting symptoms (e.g., PHQ-9 score remains >50% of baseline by weeks 10 of PST) to recommend initiating or adjusting ADMs. Health coaches will support and educate intervention participants regarding ADM management in preparation for potential recommendations by the study psychiatrist and action by their PCP.

Economic well-being.

NA

Social well-being.

In-person visits will be required of all study participants for the purposes of data collection at baseline and follow-up. In addition, intervention participants will attend nine (9) one-on-one sessions and receive ongoing counseling by phone and EHR-integrated secure email. Although some degree of inconvenience will be associated with these contacts, it likely will not be excessive and will largely be related to additional services that participants receive. Further, our use of phone and email contacts as means of long-term follow-up in the intervention eliminates inconvenience associated with face-to-face visits.

b) Explain how the training and expertise of Principal Investigator and other key personnel listed in the application will help minimize any risks to subjects and maximize the potential value of the study.

Dr. Ma is a nationally recognized, dually trained, MD and PhD scientist with expertise in the delivery of behaviorally-based, prevention-oriented interventions. Dr. Ma has led and collaborated on numerous intervention trials with all-age adults with multiple chronic conditions such as obesity, diabetes, cardiovascular disease, and asthma.

The research associates conducting recruitment and assessments will undergo protocol-specific training and standardization of administration of survey instruments and clinical measurements. They will learn recruitment and retention strategies that we have successfully used before to foster rapport building, motivation, and study identity among participants.

Health coaches will be trained and medically supervised. The training will include self-study, training video and audiotapes, in-person lectures, and extensive role-playing. Role plays with pilot patients will be recorded (with patient consent) and evaluated for adherence and skillfulness. Coach consultations with patients will be audiotaped, and secure email communications will be extracted from the EHR. Only coaches who achieve satisfactory performance will intervene with trial participants. One psychiatrist and 1 primary care physician will be identified from among local PAMF providers and trained to provide study psychiatric and medical supervision.

c) Review the vulnerable populations you may be including as subjects and any particularly sensitive issues you may be touching upon or settings in which the research will be done, including communities and cultures. Describe the expertise you have, or have access to, which prepares you to conduct research in this location and/or with this subject population, including specific qualifications (e.g., relevant coursework, background, experience, training).

NA

d) Considering the nature of the study and the likely risks it may entail, how will serious negative outcomes/experiences or adverse events be identified and managed? (NOTE: This may apply in social-behavioral as well as biomedical research, e.g., unanticipated stress or anxiety of subject in an interview, loss of laptop computer with study data.) See PAMF IRB website for policies regarding the reporting of adverse and serious adverse events.

We will follow the study data and safety monitoring plan (DSMP), and the self-harm protection plan (see 6e below).

DATA AND SAFETY MONITORING PLAN-

The following procedures will be followed to ensure the safety of study participants and the validity and integrity of data in compliance with NIH requirements.

Functions of the Data and Safety Monitoring Board (DSMB). We will empanel a DSMB prior to enrollment of the first study participant. A DSMB in the context of this investigator-initiated randomized controlled trial exists for the purpose of providing the investigators, the cognizant IRB(s) and the sponsor with objective, scientific monitoring of the conduct of the study from the standpoint of ensuring (1) the protection and safety of human subjects and (2) the validity and integrity of the trial. The DSMB will be an independent, advisory body to the investigators and funding agency. To fulfill its functions, the DSMB will review the original protocol and any subsequent amendments, perform expedited monitoring of serious adverse events (SAEs) that are unexpected and at least possibly related to the study, perform ongoing monitoring of drop-outs and non-SAEs, determine whether study procedures should be changed or the study should be halted because of serious safety concerns and/or major problems with the study conduct, and perform periodic review of the completeness and validity of data to be used for analysis of effectiveness and safety. The DSMB will also monitor implementation of procedures to ensure research participant privacy and data

confidentiality.
As in any clinical trial, it is not possible to anticipate all possible adverse events (AEs). We will conduct extensive training with our staff in ascertaining, monitoring, and documenting AEs—serious or not. The study investigators have extensive experience in clinical trial organization and management, including data and safety monitoring for single site and multi-site trials. We have established procedures for rendering first aid and life threatening emergencies. Study physicians will oversee these procedures.

Membership of the DSMB. The DSMB will consist of 3-5 outside members (not part of the investigative team) with expertise in a variety of disciplines including mental health, biobehavioral medicine, preventive medicine, nutrition, physical activity, biostatistics, clinical trial designs, and bioethics of research conduct. In the event of an award, we will work with NIH-designated Project Official to appoint an appropriate DSMB. The expertise of the members will include the disciplines and skills needed to initially review the protocol and then to monitor trial progress, data quality, and participant safety. The voting members must have no personal stake in the scientific outcomes of the study. They will not be included as authors of publications from the study, but will be acknowledged for their contribution. The PI and Reporting Investigator (Ma) will be responsible for overseeing the preparation of AEs and SAEs and all statistical reports to the DSMB.
Functional Organization of the DSMB. One individual will serve as Chairperson of the DSMB and will communicate by e-mail and telephone conference with the other members on an as-needed basis. Communication pertaining to expedited review of unexpected and possibly study-related SAEs will occur within a week of receiving the report of such events from Dr. Ma. Reporting and communication about routine trial monitoring will occur during DSMB meetings throughout the study.

DSMB Meetings and Recommendations. The DSMB will convene every 4-6 months, in person or by conference call, with the investigators to review summaries of patient accrual, data collection, the timeliness of data transfer to analysis files, group balance and data concerning the execution of the randomization process, analysis plans and results, and the numbers and characteristics of any SAEs, and the numbers and rates of non-SAEs. At the end of each meeting, DSMB members will make a recommendation regarding the continuation of the trial and the time interval and format of the next meeting. In addition, there will be an evaluative statement regarding SAEs, protocol exceptions, and other matters of data quality, integrity of the trial, and timeliness. The DSMB's findings and recommendations will be documented in the meeting minutes and transmitted to the investigators and sponsor for their information and action. A draft of the meeting minutes will be made available to the DSMB Chair for approval prior to distribution of a final version to other DSMB members, the funding agency, and the investigators.

Monitoring of Safety Data by the DSMB.
Blinded Reporting – Safety information for this study will be reported to the DSMB by group but with the true identity of the treatment groups masked. This will maintain proper blinding of the investigators, outcome assessors, and the DSMB. However, if there are extraordinary concerns regarding patient safety, the DSMB may request unblinded data, e.g., on unexpected SAEs or unanticipated problems, in order to determine the nature and extent of toxicity of the intervention under study or the integrity of the trial conduct. When this occurs, the unblinded results will not be released to the investigators unless warranted for safety protection of the research participants.
No formal interim analyses are proposed of study outcomes by study group before primary data analyses. Follow-up data will be reported for all participants, irrespective of random assignment, during the course of the study. For purposes of study monitoring, including review of planned primary outcome analyses, the DSMB may wish to review results with permuted group assignments to test the analysis programs.

SAEs – For ongoing monitoring of this study, all SAEs will be reported to the DSMB during its regularly scheduled meetings, regardless of any judgment of their expectedness or relatedness to the study. Expedited reviews will occur for all unexpected and possibly study-related events meeting the NIH definition of SAEs, i.e., any fatal event, immediately life-threatening event, permanently or substantially disabling event, event requiring or prolonging inpatient hospitalization, or any congenital anomaly. Dr. Ma will concurrently notify the DSMB and the IRB by email within 72 business hours of the detection of an SAE requiring expedited review and will submit all relevant information about the event and a proposed

corrective and preventive action plan (CAPA). The relevant information may include, but is not limited to, that about the event and its outcome, dosing history of a suspect medication/treatment, concomitant medications, the subject's medical history and current conditions, and all relevant laboratory data. Within one week of receiving the notification, the DSMB will render their determination of the event and recommendations about the CAPA in a letter signed by the chair and transmitted by email to Dr. Ma and the IRB.

Non-SAEs – At periodic intervals, the DSMB will be provided with summaries of the numbers and rates of all AEs by blinded treatment group. "Blinded treatment group" means an arbitrary labeling (e.g., 1 and 2) that does not reveal the true identity of the groups. These reports will include types of events, affected body system(s), severity, expectedness, study relatedness, and treatment phase. Data on individual non-SAEs is not expected to be needed for this review. At the discretion of the DSMB, however, the Chair may request unblinded and/or individual-level results to determine the nature and extent of adverse consequences.

Other Safety-Related Reports – It is considered necessary for the purpose of monitoring the safety of the study that the DSMB review not only AEs and SAEs, but other data that may reflect differences in safety between treatment groups. For example, these may include treatment retention rates and reasons for drop-outs. In addition, mean (SD) changes in SCL-20 score, weight, BMI, and cardiovascular risk factors from baseline to follow-up will be reported for all participants, irrespective of random assignment, because as noted above, interim outcome analyses by group are not planned in this trial.

Study Stopping Rules – Formal stopping rules for safety, efficacy, and futility are not proposed as part of this application but may be established per recommendations of the DSMB following the funding of the grant. If at any time during the course of the study, the DSMB judges that risk to participants may significantly outweighs the potential benefit, the DSMB shall have the discretion and responsibility to request all necessary information for detailed analyses, and if warranted, recommend that the study be terminated. Stopping rules for the trial could include stopping because of a significant number of injuries or illnesses that can reasonably be attributed to participation in the study, inability to recruit and measure the required number of participants to conduct the primary outcome analyses, poor intervention quality and delivery, serious deviation from study protocols, or other circumstances that would render the study unlikely to produce scientifically valid findings. The DSMB will carefully weigh the risk of completing the trial as planned against the risk of prematurely stopping the trial for safety or futility.

Monitoring of Data Quality by the DSMB. For each DSMB meeting, Dr. Ma will submit a detailed report on data quality and completeness. At a minimum, this will include the following: (1) patient accrual and follow-up completion/retention in relation to goals and timeline; (2) the randomization process and group comparability on the balancing variables; (3) key baseline characteristics of the sample, by blinded group, related to the primary and secondary outcome variables and proposed effect modifiers and mediators; (4) indices of intervention adherence; and (5) protocol violations.

Annual Report to the sponsor. As part of each annual progress report to the NIH, Dr. Ma will include a summary of findings regarding safety and quality based on data received to that point in the study and any new DSMB recommendations about patient safety, protocol adherence, and data quality.

e) Describe plans regarding appropriate medical or professional intervention in the event of a subject who appears distressed by the research or discloses information regarding suicide or other high-risk behavior.

The study staff will receive training regarding how to handle situations in which a participant, or a potential participant, responds negatively to study data collection instruments. If a participant seems to enter a highly distressed state or discloses information regarding suicide or other high-risk behavior, the Self-Harm Protection Protocol will be followed.

Self-Harm Protection Protocol

Rationale:
1. The Patient Health Questionnaire-9 (PHQ-9) has a question regarding self-harm risk. If a participant reports frequently contemplating suicidal ideation (“more than half the days” or “nearly every day” over the last 2 weeks), a clinical response is indicated. The Symptom Checklist (SCL-20) questionnaire also has a question regarding self-harm risk. If a participant reports frequently contemplating suicidal ideation (“quite a bit” or “extremely” over the past 2 weeks), a clinical response is indicated.

2. This protocol includes two self-harm protection procedures: one for participants self-screening online and the other for research staff conducting the telephone (e.g., during phone screening or intervention phone consult) or in-person (e.g., during a baseline or follow-up assessment or intervention visit) interviews.

3. The research staff conducting the telephone or in-person interviews are non-clinicians.

4. Current suicidal ideation is the only interview finding that clearly requires further clinical assessment and possible intervention.

5. This protocol refers to self-harm risk responded to an online self-screening (PHQ-9 only), telephone or in-person interview (PHQ-9 or SCL-20) as follows:

- Responding “2” (“more than half the days”) or “3” (“nearly every day”) to the PHQ-9 question - “Over the last 2 weeks, how often have you been bothered by thoughts that you would be better off dead or thoughts of hurting yourself in some way?”

- Responding “3” (‘quite a bit”) or “4” (“extremely”) to the (SCL-20) question - “Overall in the past 2 weeks how much were you distressed by thoughts of ending your life?”

6. Either question can be endorsed at several different time points. The PHQ-9 is administered during online self-screening or phone screening by a research associate, and during every in-person or phone intervention sessions. The SCL-20 is completed at the clinic during baseline and follow-up assessments (6, 12, 18, and 24 months).

Procedures:

A. For participants self-screening online

1. During the online self-screening, if a participant responds “2” (“more than half the days”) or “3” (“nearly every day”) to the PHQ-9 question “Over the last 2 weeks, how often have you been bothered by thoughts that you would be better off dead or thoughts of hurting yourself in some way?” the participant will be shown the following instructions:

"Please note: we do not monitor this screener in real time; if this is an emergency call 911.

For more immediate attention, because you have been bothered by thoughts that you would be better off dead or of hurting yourself in some way in the last 2 weeks, you should call your physician or other healthcare professional right away, or go to the emergency room.

You may also call the National Suicide Hotline at 800-SUICIDE / 800-784-2433 or the National Suicide Prevention Lifeline at 800-273-TALK / 800-273-8255. The helplines are available 24 hours every day.

We will have a study clinician contact you within 1-2 days. In the meantime, do not delay seeking medical attention."

2. The research staff will generate daily reports (except for weekends and holidays) on any positive suicidality responses from the newly completed PHQ-9s since the last report. The research staff will follow the following procedural steps based on the participant’s answers to screening questions and should not

attempt to perform any independent assessment of self-harm risk.

3. If positive suicidality responses are identified, the research staff will contact the study psychiatrist via a high priority staff message in EPIC. The study psychiatrist is licensed and has clinical privileges at PAMF. The study psychiatrist will notify the research staff of receipt of message within 24 hours; otherwise staff will call to confirm receipt. The assessment request and study psychiatrist's follow-up attempts and actions will be documented in the study Safety Monitoring Database.

4. If the study psychiatrist is not available, the research staff will send a high priority staff message in EPIC to the participant's PCP or covering physician (using the dot phrase in the appendix below) requesting that he/she contact the patient and enter an urgent mental health referral into EPIC as deemed appropriate. The PCP or covering physician may in addition schedule a follow up appointment with the patient as deemed appropriate.

5. The study psychiatrist will attempt to contact the participant as soon as possible (within 1-2 days) to conduct a PHONE assessment of current suicidal ideation for level of lethality and need for further referral. This assessment will be based on characteristics of suicidal patients (low-, moderate-, or high-risk) and clinical strategies for managing suicidal patients at these different thresholds. These strategies could include prompt emergency intervention by a licensed mental health professional when the immediate suicide risk is high and the participant has refused other interventions.

6. If there is an IMMINENT/HIGH risk of harm, including but not limited to: an active plan to harm oneself or another person, grave disability impacting the participant's ability to care for him/herself or severely impairing participant's judgment and/or without reasonable supportive resources, then the study psychiatrist will ask for participant's location and advise the participant that she is obligated to take immediate action to get help for the participant. The study psychiatrist will call 911, giving participant's name, date of birth, location, medical conditions and current risk factors and notify any immediate family member or emergency contact if relevant.

The study psychiatrist will check study database to see whether patient is an I-CARE participant.

A. For enrolled I-CARE participants, the study psychiatrist will contact the study health coach via phone or confidential email, who will contact the participant weekly thereafter (unless currently hospitalized) to complete the PHQ-9 (until patient's PHQ-9 score <5, or score decreases by 50%), assess progress, and coordinate patient's follow up care with the study psychiatrist. The study psychiatrist will also send a staff message to inform patient's PCP of this action (using the dot phrase in the appendix below).

B. For patients excluded from enrollment, or enrolled control participants, the study psychiatrist will send a high priority staff message in Epic (using the dot phrase in the appendix below) to inform participant's PCP or covering physician of the action of calling 911 and give potential resources for follow up following hospitalization. The PCP may in addition choose to call or schedule a follow up appointment with the patient as deemed appropriate.

7. If there is MODERATE RISK of harm, with the participant having significant symptoms, but able to tend to basic needs, expressing willingness to get help, possibly having suicidal thoughts but denying an active suicidal plan:

A. For enrolled I-CARE participants, the study psychiatrist will contact the study health coach, via phone or confidential email, who will contact the participant weekly thereafter by phone to complete the PHQ-9 (until patient's PHQ-9 score <5, or score decreases by 50%), assess progress, and assist participant with follow-up. The study psychiatrist will send a staff message to inform patient's PCP of this action. The study psychiatrist will be available as needed to consult with the health coach and the participant's PCP.

B. For patients excluded from enrollment, or enrolled control participants, the study psychiatrist will send a high priority staff message in Epic (using the dot phrase in the appendix below) to inform participant's PCP or covering physician of follow up plan.

8. If there is LOW RISK of harm, with participant denying suicidal or homicidal thoughts, able to carry out basic activities of daily living, with reasonable social supports and agreeable to getting help:

A. For enrolled I-CARE participants, the study psychiatrist will staff message the study health coach who will contact the participant weekly thereafter to complete the PHQ-9 (until patient's PHQ-9 score <5, or score decreases by 50%), assess progress, and coordinate the patient's follow up care with the study psychiatrist. The study psychiatrist will send a staff message to inform patient's PCP of this action.

B. For patients excluded from enrollment, or enrolled control participants, the study psychiatrist will send a staff message in Epic (using the dot phrase in the appendix below) to inform participant's PCP of follow up plan.

9. The study psychiatrist in scenarios 6-8 above will complete a study Self-Harm Risk Clinician Assessment Form that is part of the study Safety Monitoring Database.

B. PROCEDURES for telephone or in-person interviews with research staff

During telephone or in-person interviews with research staff, if a participant's response suggests suicidal ideation on PHQ-9 or SCL-20 per definition in Rationale #5, the interviewer will ask "Do you have a plan for how you would commit suicide?"

1. If yes, the interviewer stop the interview, get the participant's location (if phone interview), let the participant know that you are concerned for his/her safety and therefore need to call for help, and call 911 immediately. You do NOT need participant's consent to call 911 if you feel there is a possibility of immediate risk of harm to self or others.

2. If no, the interviewer will tell the participant that the study psychiatrist will contact him/her within 24-48 hours and give the participant the Resource Contact Information Form or verbally give the participant the resource contact phone numbers if interviewing participant by phone. The interviewer will then offer to continue with the interview. Before moving on, it may be helpful to acknowledge to the patient that we will continue to monitor suicidal thoughts throughout the study, as they are a fairly common symptom of depression, and part of the depressive illness itself. Also helpful to instill hope: "We will work together to get you feeling better."

APPENDIX: Dot Phrases for use in EPIC

RESEARCH STAFF high priority dot phrases to alert PCP or covering physician via Epic if the study psychiatrist is unavailable:

*This message is to inform you that your patient recently endorsed suicidal thoughts on the PHQ-9 and/or SCL-20 while participating in the RAINBOW study.

As the study psychiatrist is not immediately available, we urge you to contact your patient and initiate an Urgent Mental Health referral in Epic if deemed appropriate.

In addition, you may choose to schedule a follow up appointment with the patient at your discretion.

-For enrolled I-CARE participants: Our health coach will contact your patient within one week and weekly thereafter to complete PHQ-9 and assess progress, consulting with the study psychiatrist as needed.

Study psychiatrist dot phrases to alert PCPs via Epic:

For HIGH RISK PATIENTS:
**This message is to inform you that your patient was recently assessed by the RAINBOW study

psychiatrist to be at high risk for self harm based on responses to PHQ-9 and/or SCL-20. As a result, 911 has already been contacted and patient is en route to being evaluated in an emergency room setting for possible psychiatric and/or medical admission to the hospital. Appropriate family member/emergency contact has already been contacted.

-For enrolled I-CARE participants, our health coach will contact your patient within one week and weekly thereafter to complete PHQ-9 and assess progress, consulting with the study psychiatrist as needed.

For MODERATE RISK PATIENTS:
***This message is to inform you that your patient recently endorsed having suicidal thoughts over the past two weeks on the PHQ-9 and/or SCL-20 and has been contacted and assessed by the RAINBOW study psychiatrist by phone.

We urge you to contact your patient and initiate an Urgent or Routine Mental Health referral in Epic as deemed appropriate.

In addition, you may choose to schedule a follow up appointment with the patient at your discretion.

-For enrolled I-CARE participants: Our health coach will contact your patient within one week and weekly thereafter to complete PHQ-9 and assess progress, consulting with the study psychiatrist as needed.

For LOW RISK PATIENTS:
****This message is to inform you that your patient recently endorsed having significant depressive and/or anxiety symptoms over the past two weeks on the PHQ-9 and/or SCL-20.

A. For enrolled I-CARE participants, our study health coach will contact the participant within one week and weekly thereafter to complete the PHQ-9 and assess progress, consulting with the study psychiatrist as needed.

B. For patients excluded from enrollment, or enrolled control participants, we recommend you advise your participant who is in network to contact PA (650-853-4726) or Fremont (510-498-2942) Behavioral Health intake referral line to schedule a routine appointment with a mental health provider. If participant is out of network, we recommend that you advise he/she to contact their insurance provider for an in-network mental health provider. If neither of the above options are available, the patient should be advised to schedule an appointment with their PCP or covering physician within the next 1-2 weeks to discuss treatment options.

RESOURCE CONTACT INFORMATION

I am not a clinician; however, our study has clinicians who speak with any participant who tells us they've been feeling this way recently. I will have a study doctor call you within the next day or so. I would also like to give you three local emergency contact numbers that you may find helpful. All numbers are available 24 hours/7 days per week.

ALAMEDA COUNTY:1-(800)-309-2131

SAN MATEO COUNTY: 1-(650)-579-0350

SANTA CLARA COUNTY:1-(855)-278-4204

Further numbers that may be useful:

National Hopeline Network: 1-(800)-SUICIDE or 1-(800)-784-2433

National Suicide Prevention Lifeline: 1-(800)-273-TALK or 1-(800)-273-8255

f) Describe foreseeable risks to the members of the research team, e.g., if doing interviews in high-crime areas, your plans for minimizing/coping with such risks.

NA

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* * * Benefits,Procedures to Maintain Confidentiality * * *

7. Benefits

a) Describe the potential benefit(s) to be gained by the subjects or by the acquisition of important knowledge which may benefit future subjects, etc.

There are several benefits that are reasonable to expect from participating in this study. Participants may benefit through increased knowledge of obesity and depression and the associated risks for high-risk, high-cost chronic diseases such as Type 2 DM and CVD. Study eligibility screenings may identify underlying medical disorders so that appropriate treatment and referral can be made. Participants enrolled in the study have an equal chance of being assigned to the intervention. The intervention is expected to reduce depression, body weight, and cardiometabolic risk. It may also reduce the need for intensive health care use (hospitalizations and ER visits). The coaching and self-management support for participants also may provide other, less tangible, benefits in terms of general well-being. Finally, subjects often express great satisfaction from knowing that they have been able to make a personal contribution to the advancement of scientific knowledge and to the search for solutions to health problems–either their own or others'. From the perspectives of health systems and society, the increased understanding gained through this study may advance the treatment of comorbid depression and obesity in primary care and reduce the associated morbidity and mortality. All the benefits are likely to be long-term and outweigh any possible short-term risks.

Despite the possibility for personal benefit from study participation described above, it must be clearly stated that we cannot and do not guarantee or promise that they will receive any benefits from this study.

NOTE: Do not include compensation/payment of subjects in this section, as remuneration is not considered a "benefit" of participation in research.

b) Describe any potential benefits to people with whom the subject may identify, e.g., others with the same disease.

While efficacious treatments exist for obesity and depression separately, the evidence is lacking on effective treatment for patients with both conditions, who often have other cardiometabolic risk factors (e.g., metabolic syndrome). The latter is a pressing clinical need, especially in primary care, that is expected to only grow with the rising prevalence. The proposed intervention capitalizes on the theoretical and practical similarities between the 2 evidence-based, efficient behavioral treatments. Further, it harnesses the advantages of blending traditional (e.g., office visits and phone consults) and emerging care delivery channels (e.g., secure email and mobile texting) to optimize scalability and sustainability in usual practice for substantial public health impact. Hence, this study has high potential to advance the science and practice of managing patients with comorbid obesity, depression, and increased cardiometabolic risk in primary care. If shown to be effective, this research could influence how obese and depressed adults receive care to improve mood and weight in primary care.

c) Describe potential benefits to Society as whole.

The cost-effectiveness and implementation potential evaluations in this study will have important practical and policy implications.

8. Procedures to Maintain Confidentiality and Privacy

NOTE: Click here for a copy of Sutter Data Security Policy

a) Explain how the subject's privacy will be protected and how confidentiality of the subject's information will be maintained. Discuss who will have access to identifiable study records / specimens and how these will be secured.

All information to be obtained during the study will be considered strictly confidential and will be only used and disclosed as permitted under the HIPAA regulations. All eligible subjects must sign a HIPAA authorization form as part of the consent process in order to participate. Only aggregate data will be included in scientific presentations and publications resulting from this study. The identity of individual participants will not be revealed. All study team members involved in this study respect participant privacy.

b) State if audio or video recording will occur. Will these be initially made, or subsequently modified in such a way as to make the subjects non-identifiable? Describe how these will be used and by whom. What will become of the tapes or digital files after the project? Please include the PAMF form regarding permission for recording [link] in the Attachments section.

The audio recording resulting from this study will be used solely for intervention, evaluations, and quality improvement in this study. It is possible that, during the course of conversation among participants or with the interventionist, patient first names will be captured on the recording. We will not modify the recording. Patient names will not be included in any transcripts derived from the recording. The recording will be saved on a firewall protected PAMFRI server and be permanently erased as soon as the research is completed. All participants will consent using the Social Behavioral Research ICF before any recording. The consent contains IRB required language for protocols that include audio recording.

c) If patient names and identifiers are to be removed, describe whether a study ID will be used to maintain a link between the underlying data or specimens and a subject list. If so, how is this ID generated, stored and protected? Who will have access to the key linking study IDs with subject identifiers?

The PHI collected for the purpose of the research study will be assigned a unique anonymous research ID number and any obvious patient identifiers (e.g., name, social security number, medical record number) will be removed from this information. The study IDs will be used on all study forms and for data storage, tracking and reporting. Both the anonymized health information and the information linking the research ID numbers to the patients' identities will be stored in a secure manner (e.g., locked file cabinet, password protected database on a secure network fitted for protection of such information) accessible only to the research personnel who have a need to know. The information linking the research ID numbers to the patients' identities will be stored separately from the anonymized health information. We will follow the latest industry standards for data encryption, server authentication, and client authentication to ensure secure data transmissions at all times. No participant data, even if de-identified, shall be saved onto laptop computers.

d) Describe the stages through which data/specimens pass, e.g., original data collection instruments, video recordings, or slides with patient names, to machine-readable format, to records with study IDs only. Indicate when each type will be destroyed. If destruction is not planned at the close of this research protocol, what are the plans for secure storage thereafter?

Only de-identified data will reside on the PAMFRI network for analyses.

HIPAA allows the IRB to waive authorization by individuals under certain circumstances. See 45 CRF46.117. A frequent use of such waivers is for the initial recruitment of subjects to a study who will then be asked to provide authorization and/or consent. A second frequent use is to access large quantities of

previously collected data that include PHI and for which obtaining individual authorization is impractical.

e) Are you requesting a waiver of authorization under HIPAA for the purposes of recruitment? If so, please describe the recruitment procedures you plan. The IRB site includes a "Recruitment Plan Template" that can be completed and then uploaded. If doing so, indicate here.

Yes. Please see section 5e

f) If information derived from the study will be provided to the subject's personal physician, a government agency, or any other person or group, describe to whom the information will be given, the nature of the information and the rationale.

NA

g) A certificate of confidentiality can protect identifiable research information from forced disclosure. This allows the investigator and others who have access to research records to refuse to disclose identifying information on research participants in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. See GRANTS Do you plan to request such protection and if so, why?

No

h) Are you requesting a waiver of authorization under HIPAA for the purposes of accessing data including PHI? If so, explain why it is impractical to obtain individual authorization and upload the Data Access Plan completed by the Information Management Group.

Yes, EHR data extraction process will be used to identify potential participants for research recruitment; therefore, it is impractical to obtain individual authorization before that.

i) Specify where and under what conditions study data will be kept, how samples will be labeled, who has access to the data, and what will be available and to whom. Alternatively, get the template labeled "Access and Handling of Confidential Data and Protected Health Information," complete and upload it.

The anonymous, unique study IDs will be used on all study forms and for data storage, tracking and reporting. Both the anonymized health information and the information linking the research ID numbers to the patients' identities will be stored in a secure manner (e.g., locked file cabinet, password protected database on a secure network fitted for protection of such information) accessible only to the research personnel who have a need to know.

j) If there are any expectations or plans for the participants in this study to be re-contacted for follow-up studies, please describe this below. Note that participants should be informed of this potential for re-recruitment during the current study's consent process.

All participants will complete evaluation at baseline and follow-up visits (6-months, 12-months, 18-months, and 24-months). All participants will be given a reminder and contacted when it is time for their follow-up visits. All participants will be informed of this during the study's consent process at baseline.

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* * * Potential Conflict of Interest * * *

9. Potential Conflict of Interest

Please answer the following questions a through e:

a)	N	Do any of the involved Investigators or their immediate family (as described below) have consulting arrangements, management responsibilities or equity holdings in the sponsoring company, vendor(s), provider(s) of goods, or subcontractor(s)?
b)	N	Do any Investigators or their immediate family have any financial relationship with the sponsoring company, including the receipt of honoraria, income, or stock/stock options as payment?
c)	N	Is any Investigator(s) a member of an advisory board with the Sponsoring company?
d)	N	Do any investigators receive gift funds from the Sponsoring company?
e)	N	Do any investigators or their immediate family have an ownership or royalty interest in any intellectual property utilized in this protocol?

"Immediate family" means a spouse, dependent children as defined by the IRS, or a domestic partner.

If one or more of the above relationships exist, please include a statement in the consent form to disclose this relationship. i.e., a paid consultant, a paid member of the Scientific Advisory Board, has stock or stock options, or receives payment for lectures given on behalf of the sponsor. The consent form should disclose what institution(s) or companies are involved in the study through funding, cooperative research, or by providing study drugs or equipment.

If you answer Yes to any of the questions above, you must file a Conflict of Interest disclosure statement available by going to http://portal.pamfri.org

Please discuss any potential findings that would be particularly beneficial or problematic to you, other research team members, sponsors, PAMF, or Sutter Health. What are your plans to ensure that findings of this project will be submitted for publication?

NA

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* * * Informed Consent * * *

10. Informed Consent

Add the Consent Forms, Unsigned Consents, Altered Consent Forms, Altered and Unsigned Consents, and/or Consent Waivers needed for this research using the table below. You will be asked to provide relevant background. information for each consent document or waiver. If this is a minimal risk study, see the guidelines developed by the Agency for Healthcare Research and Quality at [link: http://www.ahrq.gov/fund/informedconsent/] (Note: Do not include child/minor assent forms and assent waivers or parental permission forms and permission waivers here, as these are addressed in the next section. Translated/foreign language versions of any consent materials must be attached in the Attachments section.)

In some circumstances it is appropriate for consent to be given, but to not have a signed form collected and retained by the researcher. For example, if the primary risk to the subject is a loss of confidentiality and the only identifying information would be a signed consent form, the IRB may waive the requirement for documentation of consent or alter the items included in the consent. If this is the case for this project, please describe the rationale and the consent process.

NA

Note: * denotes mandatory field.

Consent Form - a document that embodies all of the required information (elements of informed consent) designed to help an individual make an informed decision about whether or not to participate in the research. The form must include a signature line and date line for the individual to sign if he or she agrees to participate. The Consent Form can also be presented as a "short form" document stating that the required elements of informed consent have been presented orally to the participant. When the short form method is used, a "summary" of the information that is presented to the participant must also be provided for IRB approval and there must be an impartial witness to the oral presentation. The witness must sign the summary as well as the short form and the participant must sign the summary. The "short form" method may be used in circumstances where oral presentation of consent is preferable or necessary, e.g., subjects are illiterate in English or their native language.

Unsigned Consent – (sometimes called an “information statement”) a document that embodies all of the required information (elements of informed consent), but does not include a place for a participant to indicate with a signature that he or she agrees to take part in the research. This means that the IRB is asked to waive the requirement for documented (signed) consent. For example, if consent will be obtained verbally or using a button on the web, this option should be selected. Unsigned consent is preferred in situations in which the there is minimal risk to the subject other than a loss of confidentiality and the only identifying information would be the signed consent.

Altered Consent Form - a consent form that has omitted required information. This means that the IRB is asked to waive one or more required elements of informed consent. For example, if the purpose of the study will not be disclosed to participants in order to avoid bias, this option should be selected because the "purpose" is a required element of informed consent. The form must include a signature line and date line for the individual to sign if he or she agrees to participate. Indicate separately what aspects of the usual consent are omitted.

Consent Waiver - no consent will be sought at all. This means that the IRB is asked to waive the requirement for informed consent. This option is often appropriate for research that involves use of existing data or samples.

Informed Consent

Title	Consent Type	Created Date
Screening Consent	Consent	07/30/2014
Informed Consent Coversheet	Consent	12/15/2014
Infomred consent	Consent	12/15/2014
Infomred consent -clean	Consent	12/15/2014

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* * * Assent Background * * *

11. Assent Background

All minors must provide an affirmative consent to participate by signing a simplified assent form, unless the Investigator provides evidence to the IRB that the minor subjects are not capable of assenting because of age, maturity, psychological state, or other factors.

See sample Assent forms at Assent Sample

Provide assent process background information, in the table below, for each Assent Form, Alteration Form, and Waiver.

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* * * Attachments * * *

12. Attachments

Add appropriate attachments (e.g., questionnaires, surveys, advertisements, etc.) in this section

To update or revise any attachments, please delete the existing attachment and add the revised document to replace it.

Document Type	Document Name
Conflict of Interest Information	COI Disclosure form-PI-JMa
Recruitment Material (e.g., flyers, email text, verbal scripts)	RAINBOW_210_E-mail Invitation or Reminder for Online Study Questionnaire_v1
Recruitment Material (e.g., flyers, email text, verbal scripts)	RAINBOW_330_Motivation_and_Commitment_Review_v1
Other supplemental information	RAINBOW_350_Randomization_Assignment_Notification
Data Access Plan(DAP) Prepared by IMG	RAINBOW_Data_Access_Plan_v1.1
HIPAA Waiver Form	RAINBOW Waiver of Patient Authorization_v1.1
Other supplemental information	RAINBOW_500_Authorization_for_non-secure_Communication_v1.1
Recruitment Material (e.g., flyers, email text, verbal scripts)	RAINBOW_110_Telephone_Scripts_v1.1
Recruitment Material (e.g., flyers, email text, verbal scripts)	RAINBOW_220_E-mail or letter reminder of Study Visit with Instructions _v1.1
Recruitment Material (e.g., flyers, email text, verbal scripts)	RAINBOW_310_Welcome_Video_Script_v1.1
Recruitment Material (e.g., flyers, email text, verbal scripts)	RAINBOW_200b_StudyInitialEligibility_v1.2
Other supplemental information	RAINBOW Measures table_v2Tracked
Questionnaires	301_Addendum_SelfAdministered_Quest_v1
Questionnaires	341_Addendum_Clinic_Visit_Forms_v1
Recruitment Material (e.g., flyers, email text, verbal scripts)	RAINBOW_100_Recruitment_Letter_From PCPs_v2tracked
Recruitment Material (e.g., flyers, email text, verbal scripts)	RAINBOW_100_Recruitment_Letter_From PCPs_v2clean
Other supplemental information	370_RAINBOW_Pedometer_Instructions_v1
Other supplemental information	570_RAINBOW_Technology_Tool_Instructions_For_I-CARE_v1
Other supplemental information	400_RAINBOW Adverse Event Patient Query Form_v1
Other supplemental information	401_RAINBOW Adverse Event Physician Report_v1
Other supplemental information	360_RAINBOW MD Clearance Form_v2_clean
Other supplemental information	360_RAINBOW MD Clearance Form_v2_TRACKED

Other supplemental information	361_RAINBOW Participant Advisory Acknowledgement_v2_ TRACKED
Other supplemental information	361_RAINBOW Participant Advisory Acknowledgement_v2_clean
Recruitment Material (e.g., flyers, email text, verbal scripts)	RAINBOW_101_Recruitment_Email_From PCPs
Questionnaires	RAINBOW_300_Self_Administered_Questionnaires_ v2
Questionnaires	RAINBOW_340_Clinic_Visit_Forms_v2
Other supplemental information	800_RAINBOW_REAIM Process Evaluation_v1
Coversheet	IRB amendment cover letter_12Jan2015
Recruitment Material (e.g., flyers, email text, verbal scripts)	RAINBOW_102_Prescreening_Email_from_PI_v1
Recruitment Material (e.g., flyers, email text, verbal scripts)	RAINBOW_201_PHQ2_Prescreen_Form_v1
Recruitment Material (e.g., flyers, email text, verbal scripts)	RAINBOW_103_Prescreening_Letterl_from_PI_v1

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* * * Obligations * * *

Obligations

FOR NON-EXEMPT STUDIES, THE OBLIGATIONS OF THE PRINCIPAL INVESTIGATOR TO THE IRB INCLUDE:

Modifications - Changes in any aspect of the study (for example, project design, procedures, consent forms, advertising materials, additional key personnel or subject population) will be submitted to the IRB for approval before instituting the changes;

Consent/Assent/Authorization Forms - All subjects will be given a copy of the signed forms unless the IRB has approved the use of unsigned forms or waived the need for consent/authorization. Investigators will be required to retain signed documents for six (6) years after close of a funded project or three (3) years if unfunded;

Training - Human subject training certificates, including those for any newly added personnel, will be provided for all key personnel;

If the data used in this project are patient-level observations, maintain the data consistent with PAMFRI data use protocols, even if the data are fully de-identified.

Maintain Linkages - Enter the “shortname’ for this project in the PAMFRI Activity Database and keep those entries updated with new publications and presentations arising from the use of these data.

Adverse Events - All adverse events occurring in the course of the protocol will be reported to the IRB as soon as possible, but not later than ten (10) working days;

Continuing Review - IRB Protocol Report Forms will be submitted annually at least two weeks prior to expiration, six weeks for protocols that require full review;

Completion Report - The IRB will be notified when the study is complete. To do this, complete the IRB Protocol Report Form and select "Final Report."

X The Principal Investigator has read and agrees to abide by the above obligations.

FOR EXEMPT-TRACKED STUDIES, THE OBLIGATIONS OF THE PRINCIPAL INVESTIGATOR TO THE IRB INCLUDE:

If the data used in this project are patient-level observations, maintain the data consistent with PAMFRI data use protocols, even if the data are fully de-identified.

Maintain Linkages - Enter the “shortname’ for this project in the PAMFRI Activity Database and keep those entries updated with new publications and presentations arising from the use of these data.

Adverse Events - All adverse events, including data breaches, occurring in the course of the protocol will be reported to the IRB as soon as possible, but not later than ten (10) working days;

Continuing Review - IRB Protocol Report Forms will be submitted annually at least two weeks prior to expiration, six weeks for protocols that require full review;

Completion Report - The IRB will be notified when the study is complete. To do this, complete the IRB Protocol Report Form and select "Final Report."

X The Principal Investigator has read and agrees to abide by the above obligations.

Protocol Title: Research Aimed at Improving Both Mood and Weight (RAINBOW)

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* * * Event History * * *

Event History

Date	Status	View Attachments	Consent Forms	Letters
05/23/2014	NEW FORM CREATED			
07/16/2014	NEW FORM SUBMITTED	Y		
07/24/2014	NEW FORM RETURNED			
07/30/2014	NEW FORM RESUBMITTED	Y		
07/31/2014	NEW FORM PANEL ASSIGNED			
07/31/2014	NEW FORM REVIEWER(S) ASSIGNED			
08/02/2014	NEW FORM SUBMITTED (CYCLE 1)	Y		
08/19/2014	NEW FORM SUBMITTED (CYCLE 2)	Y		
08/19/2014	NEW FORM APPROVED	Y	Y	Y
09/10/2014	AMENDMENT 1 FORM CREATED			
09/16/2014	AMENDMENT 1 FORM SUBMITTED	Y		
09/18/2014	AMENDMENT 1 FORM RETURNED			
09/22/2014	AMENDMENT 1 FORM RESUBMITTED	Y		
09/24/2014	AMENDMENT 1 FORM REVIEWER(S) ASSIGNED			
10/10/2014	AMENDMENT 1 FORM APPROVED	Y	Y	Y
10/20/2014	AMENDMENT 2 FORM CREATED			
10/20/2014	AMENDMENT 2 FORM SUBMITTED	Y		
11/03/2014	AMENDMENT 2 FORM PANEL MANAGER REVIEW			
11/04/2014	AMENDMENT 2 FORM SUBMITTED (CYCLE 1)	Y		
11/19/2014	AMENDMENT 2 FORM APPROVED	Y	Y	Y
11/19/2014	AMENDMENT 2 FORM UNDO APPROVED		Y	
11/19/2014	AMENDMENT 2 FORM APPROVED	Y	Y	Y
12/05/2014	AMENDMENT 3 FORM CREATED			

12/05/2014	AMENDMENT 3 FORM SUBMITTED	Y		
12/10/2014	AMENDMENT 3 FORM RETURNED			
12/10/2014	AMENDMENT 3 FORM RESUBMITTED	Y		
12/12/2014	AMENDMENT 3 FORM APPROVED	Y	Y	Y
12/12/2014	AMENDMENT 4 FORM CREATED			
12/15/2014	AMENDMENT 4 FORM SUBMITTED	Y		
01/14/2015	AMENDMENT 4 FORM APPROVED	Y	Y	Y
01/14/2015	AMENDMENT 5 FORM CREATED			
01/14/2015	AMENDMENT 5 FORM SUBMITTED	Y		
02/19/2015	AMENDMENT 5 FORM APPROVED	Y	Y	Y