Cover Page for Study Protocol
Social Connections and Late-Life Suicide

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AGING WELL & SOCIAL CONNECTIONS:
Study Protocol for K23MH096936
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I. RATIONALE FOR THE STUDY AND SPECIFIC AIMS

Purpose: With the long-term goal of improving interventions for late-life suicide, the purpose of this study is to examine whether a mechanism by which behavioral interventions reduce risk for suicide is by increasing social connectedness.

Background: Suicide in late-life is a significant public health problem. Older adults have higher rates of suicide than younger individuals in most countries worldwide[1 2] and the size of the older adult population will soon rise dramatically in the U.S.[3 4] We can, therefore, anticipate a very large rise in the number of older adults who die by suicide in coming decades.[5] However, current approaches to late-life suicide prevention are severely limited. It is not known how to prevent suicide among older adults. It *is* known, however, that primary care is a key site for prevention: two-thirds or more of older adults who die by suicide are seen by primary care physicians within a month of their deaths, and up to half within a week.[6 7] Further, depression is a strong risk factor, but the vast majority of depressed older adults do not die by suicide.[8] Social disconnectedness—the degree to which older adults feel connected to, and as if they contribute to, valued relationships—is associated with depression,[9] suicide ideation[10 11] suicide attempts,[12] and suicide deaths[13 14] in later life. There are three intervention studies that have yielded promising outcomes regarding suicide deaths in later life[15-17] and the common element across the studies is the promotion of social connectedness through connections to providers or peers.[18] Thus, among depressed older adult primary care patients, social disconnectedness is both a risk factor for late-life suicide and a potential intervention target.[18] However, despite strong evidence that social disconnectedness increases risk for suicide (and other negative health outcomes) in later life,[13 19-26] scant data are available indicating that *any intervention* is effective in *increasing* social connectedness among older adults.[24 27] Despite the likelihood of this association, the question has simply not been comprehensively addressed. Therefore, this study examines whether a manualized (thus replicable) behavioral intervention does, in fact, increase connectedness. To do so requires establishing that 'connectedness effects' are not fully accounted for by changes in depression (a strong risk factor for late-life suicide)[18] or cognitive functioning (a correlate of late-life depression that impacts capability to engage in interventions).[18]

Overview of the Design: We propose to examine whether a manualized intervention that targets connectedness—ENGAGE—increases connectedness in older adults who report clinically significant social disconnectedness—operationalized as feeling lonely and/or like a burden on others. We propose a randomized controlled trial comparing ENGAGE with care-as-usual (CAU), using n=100 primary care patients aged ≥ 60 years who report social disconnectedness (i.e., loneliness or burdensomeness). At baseline, 3-week, 6-week and 10-week assessments, subjects will report on social connectedness, depression, and suicide risk.

Specific Aims & Hypotheses:

Aim 1: *To examine whether a manualized intervention can increase connectedness among older adults:*

H1a: ENGAGE will produce greater increases in connectedness—measured as greater belongingness and lower burdensomeness—compared to CAU, while adjusting for depression and cognitive functioning.

H1b: ENGAGE will produce comparable increases in connectedness for men and women. Examining this hypothesis will provide effect size estimates, which can be used to guide power analysis for a subsequent R01. This finding will have important implications for prevention, given high suicide rates among elderly men.

Aim 2: *To examine whether an intervention targeting social functioning also reduces late-life suicide risk:*

H2a: ENGAGE will produce greater decreases in depression symptom severity compared to CAU.

H2b: ENGAGE subjects will report lower levels of desire for death (i.e., death ideation) post-treatment than CAU.

Aim 3: *To examine increases in connectedness as a mechanism whereby ENGAGE decreases depression:*

H3a/b: Growth in connectedness over 3 and 6 weeks will be associated with decrements in depressive symptoms over 10 weeks (a), while accounting for baseline influences of cognition (b).

H3c: Connectedness during treatment (i.e., 3 and 6 weeks), will predict depression level post-treatment (i.e., 10 weeks).

H3d: The association in H3c, between connectedness and subsequent depression, will be strongest for those in the intervention condition.

II. CHARACTERISTICS OF THE RESEARCH POPULATION

a) **Number of Subjects:** The study will recruit and enroll 300 subjects into the study using the procedures described below. The target number of randomized subjects is n=50 in each group; in our experience recruiting thus far, 30% of those enrolled are eligible and willing to be randomized, thus we must enroll up to 300 subjects to reach our target number of randomized subjects. After providing informed consent and completing a baseline assessment, subjects will be randomized to receive either the intervention, ENGAGE (n=approximately 50), or care as usual (CAU; n= approximately 50.) Because we are interested in whether men and women respond to the intervention differently, we will stratify the randomization by gender.. We will also stratify on antidepressant medication usage at baseline (i.e., those being prescribed antidepressant medications) in order to ensure that outcomes are due to ENGAGE not medications. Subjects will be primary care patients from practices enrolled in the Greater Rochester Practice-Based Research Network (GR-PBRN).

b) **Gender, Age, Racial, and Ethnic Origin of Subjects:** The GR-PBRN serves approximately 30% of adults in Monroe County and is generally representative of the population of Monroe County. Although we propose to recruit subjects from within the Greater Rochester Practice-Based Research Network (as well as outside sources if needed), we anticipate that our study will include subjects representative of the current Greater Rochester Practice-Based Research Network (GR-PBRN) client mix. That distribution is provided in the Targeted/Planned Enrollment Table below. We intend to purposefully select practices, rather than approach them in a random order, so that we can assure the sample is generally representative of the race/ethnicity of the entire network (i.e., 78% White, 14% African American, 3% Hispanic). We plan to enroll an equal number of men and women. All subjects will be 60 years or older.

TARGETED/PLANNED ENROLLMENT: Number of Subjects			
Ethnic Category	**Sex/Gender**		
	Females	**Males**	**Total**
Hispanic or Latino	6	3	9
Not Hispanic or Latino	144	147	291
Ethnic Category: Total of All Subjects *	150	150	300
Racial Categories			
American Indian/Alaska Native	0	0	0
Asian	2	2	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	21	21	42
White	127	127	254
Racial Categories: Total of All Subjects *	150	150	300

c) **Inclusion Criteria:** age ≥ 60 yrs; English speaking; endorse social disconnectedness, as measured by feeling lonely and/or like a burden on others (in an initial screen in primary care practices); a score of 2 errors or fewer on the 6-item screener (a brief cognitive functioning scale) in the initial phone screen. Social disconnectedness is determined by responses to two questions extracted from the Interpersonal Needs Questionnaire (INQ). Response options for both are "not at all true for me", "somewhat true for me", and "very true for me". Item one reads: "These days I feel like a burden on the people in my life." (Positive = "somewhat" or "very true for me"). Item two reads: "These days, I feel lonely" (Positive = "somewhat" or "very true for me"). My objective in using these criteria is to identify a group of subjects who report feelings consistent with burdensomeness and/or loneliness and who therefore are members of an at risk group appropriate for preventive intervention. Subjects will have sufficient cognitive functioning to provide informed consent and to understand the study requirements and procedures (additional details below).

d) **Exclusion Criteria** are presentation at the baseline interview with any of the following: imminent risk for suicide (thoughts of death or suicide are not cause for exclusion as long as the subject is not at imminent risk); active psychosis; significantly impaired cognitive functioning (i.e., MOCA <20 and/or 3 or more errors on the 6-item cognitive functioning screener); active substance abuse in the last year (AUDIT score of 5 or more for men and 5 or more for women); hearing loss that precludes comfortable communication with an interviewer (and therapist); residence in a long-term care facility. Literacy is not an inclusion or exclusion criterion. I will restrict subjects to those who can speak English because the population of non-English speaking seniors in my region is far too small to enable meaningful analysis, and because several key measures have not been translated and validated in other languages. There is no exclusion for medical conditions or functional impairment other than severe hearing loss, and no exclusion for current or lifetime mental disorders (other than mentioned above regarding psychosis and alcohol abuse). Neither will I restrict participation if a subject is receiving psychopharmacological treatment or psychotherapy.

e) **Vulnerable Subjects:** Individuals who are 60 years of age and older with social risk factors for poor mental and physical health outcomes will be included. The results of this study will inform future research and clinical interventions aimed and improving mental health treatment for older adults.

III. METHODS AND PROCEDURES

a) **Design:** The design is a randomized controlled trial. Subjects will all be randomly assigned to either the intervention condition (ENGAGE) or care-as-usual with their primary care physician (CAU). Those subjects assigned to ENGAGE will receive a 10-session course of psychotherapy delivered in-home over 10 weeks, with the option of phone sessions if necessary. All subjects will receive baseline, mid-treatment (3 and 6 weeks) and post-treatment (10 weeks) assessments. The mid-treatment assessments will be done over the phone.

b) **Setting**: Those randomly assigned to the ENGAGE condition will receive the intervention in their homes (or in an office at URMC if they prefer). Subjects will be recruited from the Greater Rochester Practice Based Research Network. The GR-PBRN is a network of primary care practices coordinated by the University of Rochester's Clinical Translational Science Institute to provide access to subjects and community-based practices for research. The 31 family medicine and internal medicine practices that constitute the network care for approximately 217,000 patients, of which approximately 50,000 are over age 60 and therefore eligible for initial screening for the study.

Having received prior approval for the study from the GR-PBRN executive committee (see attached Letter of Support), we will approach individual practices for their permission to contact patients on their rolls who are ages 60 years and over. **These recruitment procedures are already in place for another of our studies—Social Connections and Healthy Aging (The Senior Connection)—and procedures for this study will be coordinated.** As part of these coordinated procedures, we intend to purposefully select practices, rather than approach them in a random order, so that we can assure the sample is generally representative of the race/ethnicity of the entire network (i.e., 78% White, 14% African American, 3% Hispanic.) Practices will be added sequentially until sufficient subjects have been

recruited into the study. The practices are part of the Strong Health care system, which will allow for access to the electronic medical record for review of antidepressant use (see measures); no paper chart review will be needed.

At the start of the study, one practice had been added—Geriatrics and Medicine Associates (see attached Letter of Support). During the course of the study, we added Highland Family Medicine and UR Medicine Geriatrics (see Letters of Support).

When additional practices have agreed to participation, ***we will submit letters of agreement from individual practices to the RSRB as protocol amendments for review and RSRB approval prior to subject recruitment from any site.***

c) Recruitment Procedures: Recruitment will consist of three stages. First, screening; second, informational phone call; third, home visit for assessment of exclusion criteria and written informed consent. Several strategies will be used for the first stage (screening). Each stage and strategy is described below.

STAGE ONE: SCREENING

- Strategy 1: Primary care office recruitment:
    - A study staff member, identified by their UR name tag, will introduce him or herself to older adults in the waiting rooms of participating primary care practices, show them the study letter and questionnaire, and ask if they have an appointment that day. For individuals who respond that they do indeed have an appointment, the study staff member will explain that we are approaching everyone who is 60 or older (and who has an appointment) with an opportunity to hear more about a study. The staff member will say that "the office is cooperating with the study and your doctor has asked us to hand this information out about it directly to their patients who may qualify." The letter, printed on the letterhead of the practice, will briefly explain that the increasing social engagement. With assurances that participation is voluntary, it will include a card on which the four screening questions are written (one regarding burdensomeness, one regarding belonging, one regarding sadness and a fourth regarding lack of interest in activities), with instructions that if the subject is interested in completing the survey, he/she should approach the study personnel seating in the waiting room with a sign denoting, “Social Connections and Healthy Aging.” The letter will also indicate that a study coordinator may approach them to assess their interest in participating.
    - Individuals interested in participating will then be taken to a private part of the waiting room and provided with a brief description of the study, encouraged to ask questions, reminded that participation is voluntary, and asked to complete the form and to provide information about their age, gender, and race. We will ask them to only complete the survey once. The questionnaire will be completed with research staff in a quiet, private area of the waiting room. Those who screen positive to the screening questions (meet inclusion criteria), and who give verbal consent to have research staff call them with additional information about the study will then be invited to provide their name and contact information so that study personnel may contact them to provide additional information about the study (i.e., Stage 2 of the study, the interview component). Participants will provide verbal consent for the telephone contact (see “in office script” for exact wording) and also verbally acknowledge that by providing their contact information they agree to be contacted by phone by study personnel. No name or other contact information is gathered until the patient is determined to meet inclusion criteria and to be willing to be called with additional information and an invitation to participate. These patients will then be provided with a brief brochure that explains the name of the study and relevant names of key study personnel who will be contacting them.
    - Participants who do not screen as positive on the inclusion criteria questions on the screening form will be thanked for their interest and be provided with community resources related to increasing or maintaining social connections.
- Strategy 2: Letter recruitment:

- We will approach practices that are part of the Greater Rochester Practice-Based Research Network to request their partnership in this recruitment effort. We have approval from the GR-PBRN. After obtaining approval from a given practice, the study coordinator will perform a (secure) data request for patients over age 60 in that practice. The data request will occur via eRecord and will only involve patients within the covered entity. This data pull may be done by the eRecord and Analytics team (EARS) or the study staff (via a tool called i2b2). The research coordinator will review and clean the data on a secure device with enforced password protection. He or she will then give a designee from the practice the opportunity to review the list and exclude patients as needed. These letters, prepared by University Mail Services, will describe the study and invite those who may be interested to call research staff. These letters will state that participation in the study is entirely voluntary, and that participation or non-participation will not influence one's medical care. The letter will also notify the patient that they will be contacted by phone by a research assistant within 2 weeks of the date when the letter was sent out. This strategy was developed in coordinator with Co-Investigator, Dallas Nelson, MD, who is Medical Director of UR Medicine Geriatrics Group. We have found that only a small percentage of potentially eligible subjects call the research coordinator (approximately 2-3%) and of those only 30% are eligible (i.e., most are not socially isolated or depressed). Thus, to reach socially isolated and depressed older subjects, a follow-up phone call is a necessary step to improve recruitment.
- Between 1 and 2 weeks after a letter is sent out, the research assistant will initiate a phone call with potentially eligible patients. The research assistant will follow the phone script, which will reference the letter that was sent. The research assistant will then explain the main points of the study and ask the patient if he or she might be interested in the study. If the patient is interested in the study, the research assistant will conduct the brief phone screen (see Telephone Call below), answer any questions he or she has about the study, and set up a time to meet the patient in his/her home (or URMC office) for the baseline interview. If the patient is not interested, the research assistant will ask the patient whether he or she may be interested in the future. If the patient does not think so, the research assistant will thank the patient and tell the patient he or she will not be contacted again. In order to make sure no more letters are sent out to the same patient in the future (i.e. if the patient is once again identified as potentially eligible using the methods described above), the patient's name will be retained in a secure file until the end of study recruitment. The research assistant will check the list of potentially eligible patients against the names of patients who previously refused to ensure that the patient does not receive another letter. At the close of the study, this list will be securely discarded.

- Strategy 3**:** Behavioral Health Clinic recruitment
  - Identical recruitment strategies to those described above under the section Primary care office recruitment will be used at the geriatric mental health clinic of Strong Behavioral Health (**Older Adults Service [OAS**]), which serves adults aged 60 or older with behavioral health problems such as depression and anxiety. Further, OAS clinicians who screen potential clients for services will provide information about the study to those patients, including verbal information and brochures; no client information will be given to researchers, rather, clients will be given the contact information for the study coordinator and can call if interested in learning more.
- Strategy 4: Direct referral
  - Care managers and physicians at participating practices will have the option of telling subjects about the project by handing out the approved informational letter (see above for letter recruitment) and suggesting patients call the study coordinator to learn more about the project.
  - In coordination with Dallas Nelson, MD, the Medical Director of UR Medicine Geriatrics Group, we have also refined this recruitment method based on her experience with similar studies. Recruitment will involve identification of potential patients (of physicians who have agreed to participate) through coordination with the practice scheduler or the program i2b2; potential patients will be patients with diagnoses of depression or anxiety, without diagnoses of dementia, and scheduled within the next week to see his/her PCP. The scheduler will share dates, times, and locations (the senior living

facility) for appointments that meet eligibility criteria (as these are in-home physician visits); researchers will not have access to names of potentially eligible patients. Research staff will share with the physician the appointment times for which potentially eligible patients are being seen; the physician will thus be prompted to share information about the study with potentially eligible patients. The physician will emphasize to the patient that research staff are not aware of the patient's name and if they decline to learn more about the study, their information will not be released to researchers. If the patient is interested in learning more about the study and gives permission, study staff will join the physician at the end of the visit to share information about the study, conduct the initial screening (if the patient is willing) and schedule a baseline assessment. Research staff will only join the visit if the physician indicates the patient has agreed to this.

- Strategy 5: Advertisement
    - Subjects can also learn of the study through ads in local newspapers. For potential subjects who call study staff, additional information will be provided to the potential subject, the screening conducted (see Stage 2 below), and if interested, an in-person interview will be scheduled.

STAGE 2: Telephone call:

- Participants who provide their contact information will be called by a member of the study team who will explain the study in more detail, including the randomized, controlled aspect of the study.
- Participants who hear about the study from a letter will call research staff. A member of the study team will then screen the potential subject for eligibility, and explain the study in more detail, including the randomized, controlled aspect of the study.
- If the participant agrees to an interview with the CRC, an appointment will be made for that interview, in the person's home.

STAGE 3: In-home interview:

- A Clinical Research Coordinator (CRC interviewer) will conduct two home visits for the baseline interview. First, the CRC interviewer will explain the study and obtain written, informed consent for the subject to participate. The process of obtaining informed consent also involves completing procedures to ensure the potential subject has the capacity to provide informed consent (see document "Determination of Capacity for Informed Consent). These procedures involve asking the potential subject a series of questions to ensure they understand the purpose of the study as well as risks and benefits, as well as the fact that participation is voluntary. These procedures are described in detail below in the section on "Informed Consent Procedures" (p. 15). It is at this point in the process that the person is considered to be an identified subject in the study. An additional Behavioral and/or Medical release will be signed and initialed at this time so that the PI will be able to contact the subject's mental health provider in the event that a subject's presentation indicates the presence of a research diagnosis of depression, or if the subject reports suicidal thoughts. If such a release form is not signed, the PI will not contact subjects' mental health providers (this includes those subjects who were consented prior to beginning this process) but will contact the primary care provider. Our exclusionary screens will be completed. Next, the CRC will explain the need to interview the subject *alone* (to assure unbiased responses). She will then administer an additional set of baseline research measures that document standard demographic information; social and financial resources; physical health (providers, pain assessment, assistive devices), functioning (ADL/IADL ratings), well-being, depression, anxiety, suicide risk, and social connectedness. If during the interview, research staff suspects elder abuse or severe neglect, or identifies unsafe living conditions (lack of heat in the winter months), the CRC will provide the subject with information about care management services and the option of the CRC making a referral for case management (if consent to release the subject's name and contact information to case management services is provided). Breaking the interview into two parts is done for two reasons: first, to minimize participant fatigue; second, to allow the CRC to discuss eligibility with the PI before randomization. In the second interview, the remainder of the measures will be administered followed by assignment of the subject by random selection to ENGAGE or CAU. Finally, the CRC will again explain the follow-up interview schedule, answer any remaining questions, and end the home visit.

- Audio-taping of assessments: The in-person assessments will be audio-recorded because of the need to examine inter-rater reliability for the depression assessments and ensure that the assessors are providing unbiased assessments. This information is included in the consent form. The PI will review the audiotapes.
- **Assessment information provided to physicians**: As a service to the physicians who will be assisting with recruiting, we will provide a brief letter describing clinical information gathered from the assessments to PCP's and mental health providers (if subjects provide this additional permission). Specifically, depression symptoms, anxiety symptoms, scores on neuropsychological measures, alcohol use, functional impairment, and suicide risk. Subjects will be informed of this in the consent form. Based on provider preference, information will be provided via eRecord (for URMC practices), secure email, or hard copy letter.
- **Follow-up assessments:** Subjects will be maintained in the study, either in the ENGAGE or CAU arm, for 10 weeks. For subjects assigned to ENGAGE, the intervention will begin within two weeks of the baseline assessment and study enrollment. Follow-up research assessments will be conducted for both ENGAGE and CAU groups *by phone at 3 weeks and 6 weeks and in-person at 10 weeks*. For subjects with significant sensory impairment that precludes scheduling via phone, a separate email consent form will be used to allow the coordinator and subject to communicate via email. All emails will be encrypted using University of Rochester encryption procedures.

d) Assessment Measures & Administration Schedule:

The following tables specify the measures we propose to use in the study:

Screening measures

Measure Name and Citation	*Construct Measured*	*Description & Psychometric Data*	*Estimated Administration Time*
Demographic characteristics	Not applicable	Age, gender.	1 minute
INQ Screener	Social disconnectedness	These two items ask about feelings of loneliness and being a burden on others.	1 minute
PHQ-2[28]	Depression	These two items ask about feelings of sadness and anhedonia.	1 minute
6-Item Screener	Cognitive functioning	These 6 items ask questions measuring orientation and short-term memory.	1-2 minutes

Descriptive measures, and psychiatric/medical covariates

Measure Name and Citation	*Construct Measured*	*Description & Psychometric Data*	*Estimated Administration Time*
Demographic characteristics	Not applicable	Age, race/ethnicity, gender, education, living situation, marital status, PCP name, emergency contact.	3 – 5 minutes
WHOQOL-BREF[29]	Health-related quality of life	This brief 36 item measure assesses several domains of health related functioning and quality of life. It has excellent psychometric properties and can be used cross culturally.	5 – 10 minutes baseline and final interview
Medical conditions and medications[30]	Physical health	This measure is checklist of self-reported medical conditions derived from the Minimum Data Set Version 2.0. Data on medications will be	10 – 15 minutes baseline only

		used to create the Composite Antidepressant Scale (CAD), a measure of antidepressant dosage. Questions about adherence to medicines will also be asked to determine if the prescribed dosage is being taken.	
WHO Disability Assessment Schedule 2.0 WHODAS 2.0	Functional impairment	Functional impairment will be measured by client self-reporting of six domains: cognition, mobility, self-care, social, life activities, and participation. In order to adequately characterize our sample, we will obtain the degree to which subjects experience functional impairment.	5 – 20 minutes baseline and final interview
Pittsburgh Sleep Quality Index (PSQI)[31]	Sleep problems	The PSQI is a self-report index of sleep difficulties. Research has demonstrated good internal consistency of the items and high sensitivity in the detection of clinically significant sleep problems.	5 – 10 minutes baseline and final interview
Audit-C[32,33]	Alcohol abuse	The Audit-C is validated for use as a screener for substance use disorders.[32,33] This measure will be used as an exclusion screen.	3 – 7 minutes baseline only
Modified Cornell Services Index (CSI) [34]	Formal & informal health/ social services usage.	Adequate test-retest (r=.54-1.00) and inter-rater (modal intraclass coefficient for all items was 1.00) reliabilities are reported [34].	3 – 7 minutes baseline and final interview
Structured Clinical Interview for DSM-IV (SCID-IV), Mood disorders & psychosis module[35]	Mental disorders	The SCID-IV is the current gold standard for diagnosis of mental disorders as defined by the DSM-IV. The mood disorders module will be used as an inclusion criteria measure and the psychosis module will be used as an exclusion criteria screen. The SCID is only administered at the baseline interview	10 – 35 minutes baseline only
Quick Inventory of Depressive Symptomatology (QIDS)[36]	Depression severity	This assessor-rated scale involves 16 items rated on a 0 to 3 point scale. The scale was designed to be sensitive to change for use in clinical trials.	5-7 minutes at all interviews
GAD-7[37]	Anxiety	This self-report scale is brief and has been found to be sensitive to clinically significant symptoms of generalized anxiety disorder.	3-5 minutes baseline and final interview
SHARE ALLIANCE Mood Improvement Protocol (MIP)	Self-perceived distress (before and after interview) and coping strategy (i.e., mood improvement activity)	The research interview may elicit negative reactions in individuals who are having difficulties in areas of their life related to questions in the assessment. Thus, this measure, adapted from procedures designed by Linehan and colleagues, is designed to enhance retention and	5 – 10 minutes only in-person, unless needed during phone interviews

		improve subjects' experience in the research assessments.[30]	
Ten Item Personality Inventory [38]	Personality traits	This very brief self-report measure (10 items) assesses the "Big Five" personality traits. This measure is included because personality may moderate (or effect) treatment outcome.	3-5 minutes baseline only
PHQ-9[39]	Depression symptom severity	This brief depression screening measure has been found to be sensitive in detecting clinically significant depression.	3-5 minutes intervention sessions only
Total estimated time for this portion of interview			70 – 141 minutes

Social connectedness measures

Measure Name and Citation	*Construct Measured*	*Description & Psychometric Data*	*Estimated Administration TIme*
Berkman Social Network Index (SNI)[40]	Social network size and frequency of contact.	This set of self-report questions has been shown to predict premature mortality.	3 – 5 minutes; baseline and final interview
Interpersonal Needs Questionnaire (INQ) [41] [42]	Thwarted belongingness (TB), perceived burdensomeness (PB).	Van Orden et al. [41] report high internal consistency coefficients for the thwarted belongingness (α=.85) and perceived burdensomeness subscales (α=.89). In support of construct validity, both subscales were found to positively correlate with suicidal ideation.	5 – 7 minutes at all interviews
Perceived Burdensomeness Questionnaire[43]	The type and nature of relationships characterized by perceptions of burdensomeness.	Jahn and Cukrowicz report acceptable reliability and convergent validity (i.e., with suicidal ideation) for scores derived from this measure.	1 – 2 minutes at all interviews
Interpersonal Support Evaluation List[44]	Social support	This brief self-report scale measures three components of social support: tangible, belonging, and self-esteem.	3-5 minutes baseline and final interview
National Social Life, Health, and Aging Project Social Network Module (NSL-SN)[45]	Social network density and quality (closeness).	Cornwell et al.[45] report that these measures of the social network were designed for use with older adults. In support of their construct validity, density and quality were significantly related, but the magnitude was small (r=.27), as would be expected.	10-15 minutes baseline and final interview
Behavioral Activation Scale for Depression (BADS)[46]	Social and behavioral activation.	Kanter and colleagues[46] present evidence of the scale's psychometric properties, including solid factor structure, internal consistency, and test-retest reliability.	5-10 minutes. baseline and final interview

UCLA Loneliness Scale, short form[47]	Loneliness	Hughes and colleagues present acceptable psychometric properties for this shortened form of the UCLA Loneliness Scale; this short form was designed for telephone administration,	1-3 minutes at all interviews
The Anticipatory and Consummatory Interpersonal Pleasure Scale (ACIPS)[48]	Social anhedonia	Gooding and colleagues[48 49] report acceptable internal consistency and evidence for convergent validity of the ACIPS.	5-10 minutes. baseline and final interview
Jacelon Attributed Dignity Scale[50]	Dignity	Jacelon[50] reports convergent and divergent validity as well as high internal consistency.	3-5 minutes. baseline and final interview
Total time for this portion of the interview			36-64 minutes

Suicide Risk Measures

Geriatric Suicidal Ideation Scale (GSIS)[20]	Death ideation (DI), suicidal ideation (SI), personal/ social worth (PSW), meaning in life (ML)	Heisel and Flett [21] report high internal consistency for both the death ideation (α=.82) and suicide ideation subscales (α=.82), as well as significant criterion validity (i.e., positive correlations with another measure of suicide ideation, depression, & hopelessness).	5 – 10 minutes baseline and final interview (shorter 5 item version only for phone interviews)
Columbia Suicide Severity Rating Scale (CSSRS)[51]	History of suicidal ideation and behaviors.	The CSSRS is an interview that assesses for worst-point lifetime and past month suicidal ideation and behavior. It has been shown to predict future suicidal behavior[51] and is the current gold standard for assessing suicide risk in clinical trials.	5 –15 minutes at all interviews (time frame is "since last visit" for follow-up interviews)
Acquired Capability for Suicide—Fearlessness about Death Scale[52]	Perceived fear of death and perceived pain tolerance.	The ACSS is a 7-item self-report scale designed to measure fearless about death and perceived level of pain tolerance and is posited to be a distal risk factor for suicidal behavior.	1 – 3 minutes baseline only
Communication about Suicidal Thoughts	Willingness and evidence of communication about suicide risk with others.	This is a measure that is under-development and is being pilot tested in the current study	1-3 minutes baseline only
Firearm Safety Management Form	Presence of firearms in the home	This measure assesses for the presence of firearms and ammunition in the home for the purposes of suicide risk assessment and management.	1-3 minutes baseline only
Total estimated time for this portion of interview			11 – 28 minutes

Cognitive functioning measures

Measure Name and Citation	*Construct Measured*	*Description & Psychometric Data*	*Estimated Administration TIme*

Montreal Cognitive Assessment (MOCA)[53]	Global cognitive functioning	The Montreal Cognitive Assessment (MoCA) was designed as a rapid screening instrument for mild cognitive dysfunction. It assesses different cognitive domains: attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation. Time to administer the MoCA is approximately 10 minutes. The total possible score is 30 points; a score of 26 or above is considered normal. Nasreddine and colleagues report high sensitivity and specificity for MOCA scores in detecting MCI.[53] The MOCA has three alternate forms in English to prevent practice effects with repeat administration, as well as a form for blind individuals.	10 – 15 minutes baseline and final interview (alternate form used at final interview)
Delis-Kaplan Executive Function System[54]	Executive Dysfunction	This brief neuropsychological battery assesses executive functioning. Only select tests will be used to minimize subject burden.	30-45 minutes baseline only
Total estimated time for this portion of interview			40 –60 minutes

Total estimated time for entire baseline interview (completed over 2 sessions)		225 – 257 minutes

e) Study Conditions:

a) ENGAGE is a form of cognitive behavioral therapy (CBT) that specifically targets increased social activity. ENGAGE is relatively simple for patients and therapists to master[55] and results in significant changes in depression in as few as 6-8 sessions.[56] The study will use the ENGAGE manual developed by Drs. Alexopoulos, Arean and their colleagues,[57] focusing the behavioral activation on activities that allow subjects to be social (targeting thwarted belongingness) or contribute to the well-being of others (targeting perceived burdensomeness). Sessions will be audio recorded for supervision of therapists and completion of ratings of fidelity to the ENGAGE protocol. Sessions will be rated for adherence by a certified ENGAGE therapist at the University of California San Francisco (UCSF) given that there are no trained ENGAGE therapists on site at the University of Rochester. A secure ftp server will be used to provide access to the tapes, described in detail below. This collaboration will only involve rating of audiotapes for fidelity and providing feedback to study therapists; the rater will not have access to other study data.

Session	Session Objectives (per Treatment Manual)
1	Obtain psychosocial history and build rapport. Meet with family. Socialize the patient to the ENGAGE intervention, including relating current feelings of loneliness and/or burdensomeness to social inactivity. Assess suicide risk and review the safety plan created by the assessor. Work with the patient to clarify values involved in a "valued life" and Make a list of rewarding social engagement goals that address chosen values. Develop an "action plan" with the patient consisting of activities that the patient should pursue between sessions. This session may last 1.5 hours.
2	Continue making social engagement action plans. Highlight the relationship between social re-engagement and improvement in mood.
3	Decision-making session: Continue with action planning if patient is engaging well in the therapeutic task. If not, move to Step Two to address barriers to social re-engagement.

4-5	Continue making social engagement action plans. Highlight the relationship between social re-engagement and improvement in mood. If patient has moved to Step Two, continue addressing barriers as well as creating action plans.
6	Decision-making session: Continue with action planning if patient is engaging well in the therapeutic task. If not, move to Steps Two/Three to address barriers to social re-engagement.
7	Continue making social engagement action plans. Highlight the relationship between social re-engagement and improvement in mood. If patient has moved to Steps Two/Three, continue addressing barriers as well as creating action plans.
8	Begin discussing termination. Begin reviewing progress and creating a relapse prevention plan; meet with family. Continue with action planning and addressing barriers.
9	Continue making social engagement action plans. Highlight the relationship between social re-engagement and improvement in mood. If patient has moved to Steps Two/Three, continue addressing barriers as well as creating action plans.
10	Review relapse prevention plan with family and patient. Give additional copies of Action Planner, PHQ-9, and INQ-2. Congratulate patient on completing the Engage course.

b) Care-as-Usual (CAU): CAU will involve care-as-usual in *primary care with research assessments at baseline, 3-weeks, 6-weeks and 10 weeks*. In other words, no psychotherapy will be provided. However, this condition will involve suicide risk management and depression symptom monitoring with the research assessor.

c) Analytic Procedures:

i) Overview. Linear mixed effect models (LMM) and weighted generalized estimating equations (WGEE) will be used to examine the longitudinal hypotheses concerning treatment differences across the 2 conditions, ENGAGE (n=50), and CAU (n=50).[58 59] All subjects are assessed at 4 points: baseline, 3 weeks, 6 weeks, and 10 weeks (i.e., end of ENGAGE treatment).. All measures are assessed at each point. For the hypotheses in Aim 3 concerning the interplay between the treatment conditions, social connectedness, and depression we will employ structural equation models (SEM).[60] All statistical tests are two-sided with the significance level alpha = 0.05.

LMM and WGEE are the two most popular approaches for investigating differences at the population level.[58-60] Although both provide inference for fixed-effects—parameters describing the characteristics of interest such as treatment differences—WGEE provides valid inference under missing completely at random (MCAR) and missing at random (MAR), two conditions general enough to accommodate most missing data mechanisms arising in practice,[59 61] while LMM does so only if the parametric distribution assumptions are met.[62] Biased estimates may arise if missingness follows neither MCAR nor MAR. Although such non-ignorable non-response (NINR) is rare in practice and unanticipated in this study, we will examine this issue using the joint modeling approach.[63 64] As this approach is not applicable under WGEE, we will perform sensitivity analyses by assuming some plausible NINR models.[64 65]

Descriptive statistics such as mean and standard deviation for continuous variables and frequency and proportion for categorical variables will be used to depict the social-demographical and mental health characteristics for the study sample. The intervention groups will be compared to determine if imbalances occur in demographics and other pre-treatment measures, by conducting T-test/Wilcoxon rank sum test or chi-square tests, depending on the nature of the scale. Any potential confounders will be included in all subsequent analytic models. All analyses will be conducted for the intent-to-treat sample on the primary outcomes and other secondary outcomes of interest. Analyses will be conducted with SAS 9.2 for LMM and GEE/WGEE. The false discovery rate (FDR) will be used to control for study-wide type 1 error.

ii) Power analysis: Since Aims 1 and 2 form the primary hypotheses, power was estimated for testing the hypotheses in these Aims. With n = 50 for BA and n = 50 for CAU, power set at 0.8, a two-sided alpha = 0.05 and 10% attrition rate, the minimum detectable effect size for comparing the two means is 0.51 (Cohen's *d*) for comparing BA vs. CAU.

iii) Analyses for Aim 1, to compare depressed older adults who receive either ENGAGE or CAU on levels of connectedness: this analysis proposes a longitudinal analysis on the effect of condition (i.e., ENGAGE, CAU) on social connectedness (i.e., loneliness, burden).

H1a: There will be a condition effect on both loneliness and burdensomeness (higher scores indicate disconnectedness), at 3 months and 6 months, indicating differing levels of disconnectedness in the direction: CAU > ENGAGE. Longitudinal models described above will be employed to examine the hypothesis, with loneliness (or burden) as the response, and treatment group, time and their interaction as the predictors, controlling for the covariates (depression and cognitive decline). If a significant difference exists (as indicated by a significant time by group interaction), appropriate linear contrasts will be followed to confirm the hypothesized directional effects.

H1b: This hypothesis proposes to examine the role of gender as a potential moderator of the intervention's effectiveness. The moderation analysis will be examined by including gender and the interaction of condition and gender in the GLMM/GEE or WGEE analyses for each of the primary outcomes (i.e., loneliness and burden) described in H2a. A significant interaction indicates that gender moderates the effect of treatment condition on the primary outcomes.

iv) Analyses for Aim 2, to compare ENGAGE and CAU on indicators of suicide risk.

H2a/b: As with H1a, longitudinal models will be employed to examine the condition effect, but with depression severity (H2a) and death ideation severity (H2b) as the dependent variables.

v) Analyses for Aim 3, to examine connectedness as a mechanism whereby BA reduces depression.

H3a/b: A latent growth model with concurrent growth processes[66] and cross lagged components[67] will examine the hypotheses for Aim 3. First, that growth in connectedness (slope loneliness; $S_{lon)}$ will be associated with decrements in depressive symptoms (slope depression, S_{dep}; H3a), while accounting for baseline influences of cognition (H3b). The directional hypothesis (H3c) will be examined with the cross-lag component of the model; specifically, whether level of connectedness at 3 months (after the acute phase of BA) predicts depressive symptoms at 6 months. Finally, to model the effect of experimental condition (H3d), a multiple group model[68] will be specified to test whether the parameters of interest differ significantly as a function of condition. Separate models will be run for loneliness and burdensomeness. Cognitive functioning at baseline will be added as a time-invariant covariate to the model.

d) Data and Safety Monitoring Plan: The purpose of the Data and Safety Monitoring Plan (DSMP) is to specify the procedures and rationales of the current study to ensure the safety of participants and the validity and integrity of the data. This specifies who will look at the data and review any adverse events, how often, and what they are authorized to do. The use of Data and Safety Monitoring Boards (DSMBs) may be indicated if the studies have multiple clinical sites, are blinded (masked), and/or employ particularly high-risk interventions or vulnerable populations. This study on the other hand will be conducted at one site utilizing a low risk intervention. Therefore, we have chosen to include a modified DSMB that, while constituted by individuals connected to the study, will systematize monitoring safety issues throughout its duration.

***DSMB Membership*:** Nancy Talbot, Ph.D. will chair the DSMB. Other members will include Kimberly Van Orden, Ph.D., Yeates Conwell, M.D and Jeffrey Lyness, MD. Dr. Talbot is Associate Professor of Psychiatry, in the Department of Psychiatry at the University of Rochester. Dr. Talbot has directed two NIMH-funded clinical trials among depressed women with trauma histories -- a population at high risk for self-harming and suicidal behaviors. Dr. Van Orden is the principal investigator of the project and Dr. Conwell is the primary mentor. Dr. Lyness is the outside member of the DSMB and is Associate Professor of Psychiatry at URMC and an expert in research and clinical care of older adults.

***DSMB Responsibilities and Actions*:** The DSMB will maintain an overview of the quality of the accumulating data and provide guidance to the PI on interim analyses and stopping rules. The DSMB will also serve as liaison among study investigators and the University of Rochester Medical Center Research Subjects Review Board (RSRB) and the NIH. It will review and approve, disapprove, or suggest modifications to the study protocol and/or consent documents to assure both scientific integrity and that studies adhere to human subject protection policies. It will monitor, provide feedback, and report on scientific and ethical issues related to study implementation for the protection of human subjects and advise on ethical issues related to adverse events. The DSMB will monitor adverse event reports for purposes of determining whether their nature, frequency and severity are consistent with

expectations. It will report to the RSRB and NIH any unanticipated problems involving risks to subjects (per 45CFR46). If considered related to the study, unanticipated adverse events involving risks to subjects or to others must be reported by the P.I. and/or DSMB to the RSRB. The RSRB will promptly inform NIH. Along with the RSRB and NIH staff, the DSMB can recommend remedies or other appropriate actions such as introducing new monitoring protocols, altering inclusion or exclusion criteria, or recommending changes in the informed consent documents. As well, the DSMB will be charged with ensuring that the study protocol maintains subjects' confidentiality in a manner that is appropriately balanced with issues of clinical care and safety, where relevant, and will monitor data management activities. The DSMB will review requests for interim analyses and approve, disapprove, require additional information, or defer decisions. The DSMB will be kept apprised of all severe adverse events on an ongoing basis and will serve as the final arbiters of whether individual subjects should be removed from the protocol. The DSMB will be called upon whenever possible to render judgments in the advent of a severe adverse event. We acknowledge that there may be rare instances where some emergent situation occurs that was unanticipated regarding the welfare of the subject. In these situations, the University of Rochester Medical Center's RSRB or the DSMB may be contacted to help resolve the situation.

***Meeting Schedule*:** At a minimum, the DSMB will convene on an annual basis. DSMB conferences will be assembled in-person, and conducted in accordance with federal and state health privacy legislation and relevant standards. The Chair and the P.I. will determine meeting logistics based upon urgency and the availability of DSMB members.

e) Data Storage & Confidentiality:

Study data will be collected on hard-copy forms of the measures during the in-home interviews. These hard copies will remain in the possession of the CRC for immediate transport back to the University site and placed in a locked file drawer in a locked office.

Data will be entered into a password protected, secure web-based application called REDCap (Research Electronic Data Capture). The electronic data capture system provides a secure, HIPAA-compliant web-based application that is flexible enough to be used for a variety of types of research, provides an intuitive interface for users to enter data and has real time validation rules (with automated data type and range checks) at the time of entry.

REDCap servers are housed in a local data center at the University of Rochester and all web-based information transmission is encrypted. REDCap was developed in a manner consistent with HIPAA security requirements and is recommended to University of Rochester researchers by the URMC Research Privacy Officer and Office for Human Subject Protection.

No protected health information will be stored on portable media, including laptop computers or removable hard drives. The data (including names and all identifiable information) will be encrypted using SSL. Only authorized study personnel and regulatory personnel (e.g. auditors) will be allowed access to data. All access to the database will be controlled by passwords with varying levels of security and access. The data on the audio recorder will be identified only by an ID number, with no PHI. In the case that a study subject states information during the sessions that would be considered PHI, the audio recorder will be password protected and the audio recording deleted immediately upon transfer to the hard drive of the PI's desktop computer. Audio recordings for the ENGAGE sessions will be uploaded onto a secure, HIPAA compliant FTP server behind the UCSF (University of California San Francisco) firewall. The UCSF Psychiatry Cerberus FTP Server is HIPAA compliant; it provides the necessary access controls to ensure that data is not accessed by unauthorized users. Cerberus FTP Server provides full logging of all FTP activity.

Users will be assigned access to the application by personnel in the Department of Biostatistics and/or study personnel. REDCap also tracks who enters the data.

In addition, all applications, projects, and user accounts are stored on mirrored disks. If one disk should fail, the remaining disk of the mirror is used, and no data loss or downtime is experienced. Weekly, a backup is removed from the site and stored in a secure location. Only specific users are allowed access to projects; the system administrator specifies these users. Watcher programs are used to keep a close eye on disk utilization, rogue, user and daemon processes, as well as rogue system alterations.

These programs help to tune the system for maximum performance and help maintain the reliability of the system. Security monitoring programs are used to alert us to possible security holes, which may be exploited by would-be crackers. The University of Rochester Medical Center also maintains a firewall in front of their Enterprise network, providing an additional level of security.

In order to protect the confidentiality of subject information, we will take a number of precautions. These include training of research interviewers in confidentiality procedures; entry and storage of data using coded identification labels; maintenance of project computers (both PRN and clinical research hardware) in secure locations with restricted access by enforced password protection.

IV. RISK BENEFIT ASSESSMENT

1. Risk Category

Greater than minimal risk.

2. Potential Risks

For the questionnaires and interviews, the primary risk is invasion of privacy, breach of confidentiality (if high risk for suicide, elder abuse, or other safety issues are detected), or mild reactions of distress or fatigue. Given that assessments and treatment are conducted/provided in the subjects' homes, others could be present, which risks revealing the subject's participation in the study; subjects will have full discretion in having others present. All assessment measures and procedures have been safely used in previous research with older adults; no sustained negative effects from assessments are expected, but negative outcomes cannot be ruled out. Subjects were selected due to the presence of social disconnectedness and depression, which are risk factors for suicide. Therefore, all subjects are at higher than average risk for suicide. However, that risk is moderated by the fact that we will exclude all potential subjects at imminent risk for suicide and initiate indicated interventions to assure their safety, which might include referral to a comprehensive geriatric psychiatry clinic that provides both psychopharmacology and psychotherapy and/or emergency psychiatric services, including the psychiatric emergency department at Strong Memorial Hospital (the Comprehensive Psychiatric Emergency Room, CPEP).

The treatment, ENGAGE, carries the risk of worsening subjects' moods or causing emotional distress. ENGAGE has been used in numerous studies with suicidal and/or depressed older adults with overall good effects. No sustained negative effects are expected, but negative outcomes from psychotherapies cannot be ruled out. The study therapists are experienced in working with depressed and socially disconnected older adults. Progress notes for each session must include a suicide risk assessment. Subjects who exhibit or describe heightened distress during treatment or assessments will be immediately assessed for safety and suicide risk by therapists or assessors. All subjects will have access to hospital crisis intervention services, evaluation in the psychiatric emergency department (CPEP). Subjects who describe active suicidal ideation with intent to act will be evaluated for inpatient or partial hospital admission. Decisions about suicidal intent will be based on the risk assessment protocol (described below).

Regarding alternative interventions, subjects will not be prohibited from seeking out supportive social services, or volunteering their services to others (for ethical reasons). If a subject in the ENGAGE group does engage these services, he/she will be followed for the duration of the study, with documentation of the nature and extent of that engagement, and evaluation of its impact on the outcomes of interest.

No restriction on medications or concurrent psychotherapy is made for subjects in either arm, but subjects will be asked to refrain from initiating new psychotherapeutic treatment during the 10-week trial.

3. Protection Against Risks

- We propose to manage potential distress elicited by the research assessment with implementation of a "Mood Improvement Protocol" (MIP) adapted from procedures designed by suicide prevention researchers at the University of Washington. The MIP is designed to enhance retention and improve subjects' experience in the research assessments. The researchers at UW found that some subjects become distressed when answering questions about suicide risk, and in similar studies, we have received feedback from subjects that

they find the suicide questions distressing. While these subjects are in the minority, we propose to include procedures to help such subjects manage distress that arises during the research assessments. Specifically, the MIP involves the research assessor (study staff) collaboratively creating a coping plan for managing distress with the subject prior to completing the interview. Such coping strategies include: engaging in chit chat with study staff, sharing a cup of tea, etc. (please see attached MIP for other activities). The protocol also involves having the subject rate his/her level of distress at the start of the interview and after the interview,. This will allow study staff to better manage the risk of distress by providing a gauge of subjects' change in level of distress at the conclusion of the interview.. If a subject remains highly distressed after the interview (highly unlikely), study staff will engage in a coping activity with the subject and/or call the Project Director, a clinical psychologist, for guidance.

- The CRC's will be trained in the study's suicide risk screening protocol, which involves the Columbia Suicide Screening form, Geriatric Suicide Ideation Scale, Firearm Safety Management Form, and clinical interview. Any subject who endorses death or suicidal ideation will be asked additional questions to assess his/her safety. Any endorsements of active suicidal ideation will involve notifying Dr. Van Orden (or Dr. Conwell) for review of risk and protective factors and consideration of emergency psychiatric services.
- Subjects in the ENGAGE arm will be monitored for increases in depressed mood each week and discussed at a meeting with the study therapist and PI each week. These meetings will be held to promote subject safety and well-being. Further, after the research assessments a standardized review process will be conducted for each subject, including a review of depression symptom change (or lack thereof), treatments received (both pharmacological and behavioral), and suicide risk.

- **Informed Consent Procedures:** A CRC will obtain verbal consent from subjects before beginning the phone screening. At the conclusion of the phone screening, the CRC will explain that written informed consent will be obtained at the next assessment in the home, and that if they have privacy concerns the consent process can be completed in an office at the medical center (with transportation reimbursement provided). The CRC will obtain written consent from subjects before the baseline in-person assessment only after subjects have received both verbal and written explanations of the study and indicated their full understanding. They will be informed that the study is designed to examine the effects of counseling on social supports of older adults in the community. They will be informed of their rights as research subjects, including the right to refuse to participate in the study, and to withdraw their consent at any time, as well as potential risks and benefits of participation, including financial compensation, and rights to privacy and confidentiality. Specifically, individuals will be told that questions asked may cause them to feel uncomfortable or upset. They will be informed that: they may withdraw from an assessment at any time for any reason and still receive full reimbursement for that assessment; and they may withdraw from the research study at any time without negative consequences to their treatment in the Strong Memorial Hospital healthcare system. Moreover, participants will be informed that they will be asked to participate in assessments whether or not they complete treatment, that they will be financially compensated for participation in assessments whether or not they complete treatment, that they have the right to refuse to participate in any study assessment session. Subjects will be compensated for the assessment sessions for their time and effort ($40 for each baseline interview, $10 for phone follow-ups and $20 for follow-up in person interviews). Data storage and safety will also be described to them. Informed consent will also include information about costs of psychotherapy (i.e., no cost). Subjects will be informed that psychotherapy during the trial will be provided free of charge in the subject's home. Subjects will be asked to provide a release of information for relevant medical records and social services records if referred for case management. The process of random assignment will be described to subjects as "the flip of a coin."
    - Subjects will be informed that study staff will perform an immediate evaluation of their dangerousness towards self or others should safety concerns arise during assessments or treatment sessions. Subjects will also be informed that their confidentiality may be breached should concerns arise about their dangerousness to self or others. Finally, they will be informed that suspected child abuse will be reported, as mandated by law.
    - A small minority of participants may experience elder abuse. In the case of suspected elder abuse, subjects will be given an immediate referral to the Elder Abuse Prevention Program (EAPP) of Rochester, which provides crisis intervention services. A phone call will be made to the primary care provider. Any suspected cases of elder abuse will be immediately reviewed with the PI before the

CRC leaves the home. The PI will also be in contact with Dr. Conwell regarding potential imminent dangerousness, which may involve the use of emergency services and law enforcement authorities.

- When obtaining informed consent, a "Determination of Capacity for Informed Consent" protocol developed will be utilized. The consent form will be read aloud to subjects, who will be encouraged to ask questions throughout the process. At the conclusion of the consent process and prior to requesting that they sign the form, all clients are asked the following questions:
  - Could you please tell me what this study is about?
  - What are the potential risks to you of participating in this study?
  - What are the benefits for participating in this study?
  - Do you understand that your participation in this study is voluntary and that you may stop at any time or not answer any questions that you feel uncomfortable answering?
  - Do you have any questions about the interview or the treatment?
  - If in answering these questions the subject is unable to demonstrate an understanding or appreciation of the issues, the investigator and subject further review the consent form and repeat the pertinent questions. Subjects who achieve a demonstrated understanding of the study are determined to have capacity to provide informed consent. For those who do not, they are thanked for their time, informed that they are not eligible for the study, and provided reimbursement for the assessment. Subjects' answers are characterized on a checklist that is kept with the research record as documentation of the consent process.

- In order to protect the confidentiality of subject information, we will take a number of precautions. These include training research interviewers in confidentiality procedures; entry and storage of data using coded identification labels; maintenance of project computers in secure locations with restricted access by enforced password protection. Back-ups of all study files will be made daily to allow for recovery of data due to disk failure. Risks associated with subject burden or distress will be minimized by employment of research personnel with appropriate backgrounds and experience and work with psychological factors and elderly subjects. The baseline research interview will last approximately two hours in total. Given the length of time involved for this assessment, and concerns regarding subject health and well-being, subjects will be reminded that if they become fatigued, they may terminate the interview at any time, and that the interview can be conducted over multiple sessions as needed. Research personnel will further be trained to recognize potential signs of fatigue among elderly subjects, and to actively suggest alternative data collection strategies (including telephone-based and mail-in interviews), in order to reduce the possibility of overwhelming study subjects and to ensure completeness of data collection. These strategies have been employed effectively in Dr. Van Orden's and Conwell's past research involving older adult populations.

  All patient data, including assessment measures and audiotaped sessions, will be obtained with the written consent of the patient. Information pertaining to individual participants will be released with the patient's informed and written consent only, except in unusual cases where withholding the information might pose a serious risk or danger to the participant or others. All patient data will be identified by a uniquely coded study number assigned to each participant. Access to the master list of study numbers will be restricted to Dr. Van Orden and the CRC. Confidentiality will be further maintained by the storage of "hard copy" data in locked files in a locked office. Access to computerized data is restricted and subject to review by Dr. Van Orden and Dr. Tu. Publications or presentations will report only cumulative data or descriptions certain to maintain participants' anonymity.

  All data collection involving human subjects will be HIPAA compliant. All data involving human subjects will be stripped of any identifiers; a unique ID will be generated to link to a file and will not be stored in the central database repository. The data will be encrypted by applying a special scrambling code that makes the data unreadable to anyone who does not have a decryption key. Authorized personnel with access to the this key can unscramble it. This file will be stored on a separate server and will only be accessible to database administrators with the appropriate permissions.

  In order to protect confidentiality during the provision of the intervention, subjects will be given information at the time of randomization that the ENGAGE sessions should be treated like any other medical appointment, including that if they have privacy concerns, they should arrange for others in the home to be

out of the home at the time. As an alternative, subjects may complete ENGAGE sessions in an office at the medical center.

- *Monitoring of Subjects and Crisis Management Procedures*

Risk to study subjects will be minimized by only employing experienced and well-trained and clinically experienced interviewers, supervised by clinicians with expertise in geriatric mental healthcare. Subject well-being will be carefully monitored throughout the study. If the clinical information obtained in the course of research assessments pertains to patient safety, (e.g., intent to harm one's self or others), then confidentiality will not be maintained and appropriate treating professionals will be informed. Previous studies by the investigators have successfully employed a risk management protocol that involves the assessment of elder research subjects for potential suicidality, including presence, frequency, and intensity of suicidal thoughts and impulses, and presence of a plan to harm one's self. See attached measures: Safety Protocol Worksheet and Firearm Safety Management Form. In the event that a subject reports either no suicidal thoughts or only transient or fleeting suicidal thoughts without a suicide plan or specific suicidal intent within the past month, they will be encouraged to discuss these issues with the physician or other healthcare professional(s). In the event that an older adult reports having seriously considered suicide in the past month or a strong desire or impulse to harm one's self, current risk will be assessed in terms of the subject's likely control over his or her suicidal thoughts and impulses. If the subject can convincingly demonstrate control over his or her suicidal thoughts and impulses to study staff, the staff member will contract for safety with the subject and will contact Dr. Van Orden (or Dr. Conwell) and report their concerns to them. Additional resources may then be notified, including the subject's physician or other healthcare professional(s), and/or family member(s). If the subject cannot convince the study personnel that they are capable of controlling their suicidal impulses, the study staff member will remain with the subject and will call Dr. Van Orden and/or other clinical backup for assistance. Additional clinical resources may be notified, including the subject's physician or other healthcare professional(s), a mobile crisis unit of the Department of Psychiatry of the University of Rochester, and/or emergency response services. Family member(s) may additionally be notified.

- *Monitoring Adverse Events (AEs) and Serious Adverse Events (SAEs).*

We will abide by the rules governing reporting of adverse events as defined in NIMH Policy on Data and Safety Monitoring in Clinical Trials (September 2002, revised 2007). Any event will be reported to the RSRB if it is “serious,” “unexpected,” and “related.”

Reportable Events: Definition of terms

- “Serious” means any event that causes a prolonged or permanent harm that is psychological, social, legal or financial. Examples most pertinent to this study include a subject’s death from any cause; a suicide attempt or hospitalization due to depression.
- “Unexpected” means that the event was unforeseen and has not been previously encountered, known, or recognized and was not identified in nature, severity, or degree of incidence in the protocol, supporting documentation, the informed consent document, or the RSRB application.
- “Related to the study” means that there is some aspect of the study (e.g., a research procedure, existence of a laptop database, etc.) that is directly related to the event. An example pertinent to this study is breach of confidentiality by which private information about the subject was made known to other community members. Events for which the relationship to the study cannot be clearly determined based on review of all available data will be classified as “possibly related to the study” and reported according to the same guidelines as for related events.
- “Event” is an incident, experience, or outcome that occurs to a subject participating in an RSRB-approved research study.

AEs are reported to the sponsor on an adverse events form as part of annual progress reports, regardless of whether they are considered study related. The date and time of onset and outcome, course, intensity, action taken, and causality to study treatment will be assessed.

The Principal Investigator has the final decision regarding what is to be reported on the adverse event form, and has the option to reclassify an AE as a serious adverse event (SAE).

In case of an SAE: The date and time of onset and outcome, course, intensity, action taken, and relationship to study treatment will be assessed. SAEs will be reviewed by the PI weekly. SAE’s will be reported to the RSRB in the form of a written report per the URMC RSRB “Guidance for Reporting Reportable Events to the RSRB”

document. SAE's will only be reported to the RSRB when they are unexpected and related to participation in the study. In this case, the report will be made within 10 calendar days of the investigator's discovery of the event.

Information about AEs and SAE's will be obtained through ongoing interactions with the primary care providers of subjects in both arms of the study, and from the therapists of those subjects assigned to the intervention arm.

- *Confidentiality: Limits and Precautions*

The present study includes a documented plan for the collection, storage, protection and analysis of research data. The key components of this plan include restriction from unauthorized access to identifiable subject data, storage of data to protect against inadvertent loss, and use of appropriate database software tools to maintain integrity of data for subsequent analyses. All research files will be coded using a study identification number. Subject identifying information and PHI will be stored separately from other data collected for this study and will only be accessible by those investigators, Lifespan or University clinicians, or staff who have a need to know this information for the purpose of conducting the study. All identifying data will be stored in locked cabinets and locked offices or in password-encrypted files. Access to these files is limited to investigators and support personnel with the need to enter or analyze data.

All research and clinical information obtained is kept confidential unless the subject is an immediate danger to him or herself or to others (Note: clinically relevant but not life threatening information may be shared with outside personnel with subject permission). During crisis situations, this clinical information may be provided to other clinicians (or family members) in order to facilitate appropriate treatment and minimize the risks of self-harm or harm to others. This information may include the subject's clinical diagnosis, psychiatric and medical history, current medication and treatment status, response to psychiatric or substance abuse treatment, financial and social resources, and history of suicidal behavior, if known.

If study personnel identify inappropriate treatment practices by an outside professional (e.g., inappropriate/ dangerous medication combinations given to a vulnerable elder) key study personnel will be consulted and a course of action will be planned that balances subject confidentiality with his or her safety. Normally, consent will be obtained from the subject to speak to the other treating professional and express concerns. If the subject refuses to provide consent to speak with the professional, the degree of danger to the subject will be the primary barometer to determine the appropriate steps.

- *Certification of Research Personnel in the Protection of Human Subjects*

In order to ensure appropriate human research knowledge, all study personnel interacting with subjects or with access to subject research will have completed mandatory training in the protection of human research participants per guidelines issued by the U. S. Department of Health and Human Services, Office for Human Research Protections (see http://ohrp.osophs.dhhs.gov/) and per guidelines of the University of Rochester Medical Center. Any additional personnel will complete this training before interacting with study subjects.

Consistent with University of Rochester Research Subjects Review Board (RSRB) policy, all investigators and research staff will complete certification by the RSRB—required completion of a course that contains seven modules dealing with topics such as "Ethics and Federal Regulations," "Roles and Responsibilities of the Investigator and the Study process," and "Roles and Responsibilities of Institutions in Human Subjects Research," among others. The program provides a substantial resource to the investigator for understanding the ethics and regulations governing research with human subjects.

It is also University of Rochester policy that all research and clinical staff who may be in contact with protected health information (PHI) demonstrate a working understanding of the University of Rochester's Notification of Health Policies and Practices form. This information form describes to patients and research subjects the University's policies and procedures regarding PHI, consistent with the federal Health Insurance Portability and Accountability Act (HIPAA) and with other relevant university regulations and local, state, and national legislation. All investigators and research staff will complete an information and training session on HIPAA legislation, the University's Notification of Privacy Practices, and on ethical conduct of research in accordance with this legislation and with University regulations. This training session will be developed, in tandem, by training staff in the Department of Psychiatry and by the HIPAA compliance officer for Lifespan.

4. Potential Benefits to the Subjects

Half of the study subjects will receive a psychotherapy aimed to increase connectedness – an intervention that target significant risk factors for suicide, namely social isolation and depression. Thus, the potential benefit to the individual may be significant. Subjects may additionally benefit from participating in research interviews and completing the questionnaire measures, as these assessments provide them with the opportunity to be carefully listened to and comprehensively evaluated. They may further benefit from feelings of altruism connected with participation in research designed to better understand the mental health needs and experiences of community-residing older adults. Given the level of risks associated with the proposed research and the substantial gains both to the individual and older adults more broadly, benefits appear to outweigh the risks.

5. Alternatives to Participation

Regarding alternative interventions, as mentioned above, subjects assigned to ENGAGE or CAU will not be prohibited from seeking out medication for treatment for depression. We will ask that subjects assigned to the ENGAGE condition refrain from engaging in other psychotherapies while they are engaged in ENGAGE.

VII. SUBJECT IDENTIFICATION, RECRUITMENT AND CONSENT/ASSENT

1. Method of Subject Identification And Recruitment

Recruitment strategies involve:

1) initial contact:
    a. information and invitation letter in primary care practices;
    b. informational letter sent to home inviting interested individuals to call to learn more
    c. advertisement – newspaper ad, blog article, flyers, etc.
    d. Direct referral via providing an informational letter from physicians and care managers.
2) informational phone call;
3) home visit for written informed consent and assessment.

As described in the Procedures section,

2. Process of Consent

The CRC will obtain written consent from subjects before the baseline in-person assessment only after subjects have received both verbal and written explanations of the study and indicated their full understanding. They will be informed that the study is designed to examine the social supports of older adults in the community, and whether people receive benefit from companionship. They will be informed of their rights as research subjects, including the right to refuse to participate in the study, and to withdraw their consent at any time, as well as potential risks and benefits of participation, including financial compensation, and rights to privacy and confidentiality. Data storage and safety will also be described to them. Finally, the process of randomization to one of two conditions will be described; subjects will be told that if they choose to participate they will randomly assigned to one of two conditions: one condition that involves only the baseline and follow-up assessments, or a condition that involves participation in ENGAGE.

3. Subject Comprehension and Capacity to Consent

A Capacity for Informed Consent protocol will be implemented for all potential participants (see attached document: “Determination of Capacity for Informed Consent”). The capacity assessment will consist of a series of open ended questions administered to the subject that follow explanation of the study. It will address the subject’s knowledge and understanding of the study’s objectives, the voluntary nature of participation, ability to withdraw at any time, consequences of withdrawing, possible risks and benefits of participation. For subjects who have difficulty in one or more of these areas, further review of the relevant elements of the study will be provided in order to improve their knowledge and understanding to a level that enables them to make a meaningful choice about participation. A form (i.e., “Determination of Capacity for Informed Consent”) will be completed for each subject documenting the results of the decision-making capacity determination, a copy of which is maintained with the consent form.

4. Debriefing Procedures

Participants are given feedback about their level of depressive symptoms (and other psychiatric symptoms endorsed) in a manner that is understandable and useful (i.e., psychoeducation). At the end of the follow-up

period, those assigned to CAU will be given information about ENGAGE and should they desire psychotherapy, referrals will be made to agencies providing these services.

5. Consent Forms

See attached.

6. Documentation of Consent

All signed consent forms will be stored in a locked file in a locked office, separate from other non-identifying subject data. Only study staff will have access to these files. All subjects will receive a signed copy of the consent form for their records.

7. Costs to the Subject

There are no costs to the subject. All assessments are completed in-home.

8. Payment for Participation

Participants will be paid $40 for the baseline interview and $20 for each in person follow-up interview, and $10 for phone follow-up interviews. Each participant, therefore, may be reimbursed a maximum of $80 for their time and effort.

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