PROTOCOL
STEPPED TELEMENTAL HEALTHCARE INTERVENTION FOR DEPRESSION

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Principal Investigator:
David C. Mohr, Ph.D.
Northwestern University
Department of Preventive Medicine, Feinberg School of Medicine

1. BACKGROUND

Depression is prevalent and imposes a very high societal burden in terms of cost, morbidity, quality of life, and mortality. While psychological treatments are both effective and acceptable to patients, a variety of barriers exist both to initiating and completing psychotherapy. Approximately 75% of depressed, urban primary care patients experience substantial barriers that limit or prevent access to psychotherapy, and this figure is likely larger among people who do not regularly see a physician or who live outside of urban centers. The most common barrier is cost, however other structural barriers are common, including time constraints, transportation difficulties, caregiving responsibilities, and lack of available services. In addition, cognitive symptoms of depression increase the perception of barriers. Thus, depression itself is both an indicator for treatment and a barrier to receiving it.

Telemental health has been proposed as a method of overcoming barriers to treatment. Research has focused primarily on two treatment delivery media: the telephone and the Internet. The telephone produces outcomes equivalent to face-to-face (F2F) psychological treatments for depression, while also significantly reducing attrition. Internet interventions have the potential to produce moderate gains (*d*=.61-.91) when supported by therapist or TeleCoach via telephone or e-mail; gains are smaller without that guidance (*d*=.25-.29). These two treatment delivery media have complementary strengths and weaknesses. Telephone delivery can extend care and reduce
attrition with no significant loss of efficacy. However, its success at extending care also increases overall costs, which is likely slowing its integration into the American healthcare system. Internet interventions, on the other hand, can be very cost-effective. Australia and many countries in Europe have begun harnessing the economic benefits of Internet treatments for depression by integrating them into their healthcare systems. However, Internet treatments, even when enhanced by human support, are often plagued by attrition, which diminishes efficacy.

Developing healthcare models that integrate treatment delivery media holds the promise of harnessing the advantages of each medium, while minimizing the disadvantages. Stepped care models are a potentially useful framework for achieving a workable integration. We propose to integrate two validated telemental health treatments. Telephone-cognitive behavior therapy (T-CBT) has been validated by our group in two randomized controlled trials and has been found to be equivalent to F2F-CBT in a current trial. ThinkFeelDo is our Internet CBT (iCBT) program, which also has demonstrated efficacy.

The stepped telemental healthcare model we have developed is informed by existing treatment guidelines for depression and data from previous trials. Patients initiating stepped care would receive guided iCBT, a less intensive and less costly modality. Patients who do not benefit from guided iCBT would be “stepped up” to T-CBT.

We propose a comparative efficacy trial in which patients with Major Depressive Disorder (MDD) would be randomized to receive stepped care or T-CBT alone. Patients would receive up to 16 sessions of treatment over the course of 20 weeks, or until they reach criteria for sustained symptom remission (PHQ-9 < 5 over 2 weeks).

Primary Aims and Hypotheses

We will test the following primary hypotheses:

Hypothesis 1: Stepped care will not be inferior to T-CBT alone in reducing depressive symptoms.

Hypothesis 2: Stepped care will be more cost-effective than T-CBT alone.

2. OBJECTIVES AND PURPOSE

To reduce barriers to mental health care, numerous researchers 1-3, as well as the 2003

President's New Freedom Commission on Mental Health 4, have called for evidence-based treatments for depression that can be delivered using telecommunications. The purpose of this study is to pilot a novel intervention that can overcome numerous barriers to treatment for depression, and reduce costs.

3. SELECTION OF PATIENTS – ELIGIBILITY CRITERIA

RCT Inclusion Criteria: 1) Has a DSM-IV diagnosis of non-psychotic MDD as assessed using the Mini International Neuropsychiatric Interview (MINI), plus a score of 12 or greater on the Quick Inventory of Depressive Symptomatology – Clinician Rated (QIDS-C). 2) Has a phone, access to the Internet, and basic internet skills (assessed using "Web-Use Skills" form – see Appendix A); 3) is at least 18 years of age (age 19 in Nebraska). 4) Is able to speak and read English. 5) Is a United States Citizen/Resident; 6) If currently taking an antidepressant medication, patient must have been on a stable dose for at least 14 days, and have no plans to change the dose.

Exclusion Criteria: 1) Has visual, hearing, voice, or motor impairment that would prevent completion of study procedures; 2) Is diagnosed with a psychotic disorder, bipolar disorder, dissociative disorder, or other diagnosis for which participation in this trial is either inappropriate or dangerous. 3) Is severely suicidal (has ideation, plan, and intent). 4) Is currently receiving or planning to begin psychotherapy during the study treatment period; 5) Is planning to be out of town or unavailable for 4 weeks or more during the scheduled treatment time; 6) Participated in phase 1a or 1b.

4. PATIENT REGISTRATION

Subject Recruitment

Individuals with major depressive disorder will be recruited from clinics, in the community via fliers, patient registries, mass email, websites, listserves, CTA and newspaper ads.

Clinic-based recruitment: The primary care clinics of Northwestern Medicine (including but not limited to NMFF, NMPG, REACH), the Rehabilitation Institute of Chicago, NorthShore University Health System, Alexian Brothers Medical Group, and the Southern Illinois Research Practice Organization (SIPRO), and the University of Illinois at Chicago clinics, will serve a primary recruitment sites. Fliers will be available in all exam rooms. Physicians will be alerted to recommend the study when depression is noted. The physician will also be able to indicate patient interest in the chart, which will trigger an automated message to study staff, who will then contact the patient.

Additionally, PCPs in the Northwestern system will be provided a list of patient names from EPIC and they will be instructed to identify the names of patients whom we should not contact. Potential participants will be contacted via mail and invited to participate, after study staff have received approval to contact the patient from their PCP.

Printed materials describing study aims, eligibility criteria and treatment will be distributed to physicians to educate them about study procedures.

Online Recruitment: Recruitment may use print and online classified ads (placed on websites such as Craigslist, Research Match, Reddit), ads placed with online search services such as Google Ads, and through emails sent via services such as Constant Contact. Study information will also be posted on Northwestern websites including the Department of Preventive Medicine and the GIM websites and in department newsletters, as well as Facebook, Twitter and other

social media pages. Participants may call, email or be directly linked to a brief screening measure if interested.

Group Health Cooperative:
Group Health (GH) will identify potentially-eligible patients from automated data systems. Group Health will mail potentially-eligible patients a letter introducing the Northwestern University Telehealth study and will follow up by telephone to assess interest. For those patients that are interested, GH will obtain oral consent to pass their contact information along to NU study staff. Contact information of those that consent will be transferred securely via an SFT site to NU. The NU study staff will then contact GH patients for screening, etc.

Northwestern University Enterprise Data Warehouse (EDW): In addition to identifying potential participants through GIM Epic, participants will be identified via the Northwestern Clinical Enterprise Data Warehouse (EDW). As with the mailing via GIM, physicians will be provided a list of patient names and will be instructed to identify the names of patients whom we should not contact. Once physician approval has been received, potential participants will be sent a letter describing the study and inviting them to participate. Potential participants will not receive more than one letter per year about the trial. In order to avoid an individual receiving multiple letters, the list will be reviewed for duplicate names first by a computer analyst and re-examined by study staff. Individuals may also request not to receive future recruitment letters.

Northwestern University NUCATS Registry:
The NUCATS General Research Registry will be used as a recruitment method. The NUCATS General Research Registry consists of individuals who have indicated that they are interested in being contacted to participate in research studies occurring at Northwestern University. People can join the NUCATS Registry in one of three ways.

1) If the person is a patient at Northwestern Memorial Hospital or an NU affiliate, they can opt- in by logging into MyChart and signing up for MyResearch.
2) The person can call the NU Study telephone line and be added to the registry.
3) The person can be added to the registry when they screen fail for a study but want to be contacted for future studies.

Individuals in the registry are contacted once a year to update their information. Individuals that indicate that they are no longer interested in being in the registry are removed and are no longer contacted.

Initial Contact Method
Participants recruited through online advertisements as well as flyers and print methods will complete a brief pre-consent screening to determine eligibility. (For those who are recruited online, some portions of this may be completed online, but all participants will finish the pre-consent screening via telephone with a research assistant). If eligible, they will then be provided with a link to access the consent form before proceeding with the full screening assessment. Those who are not eligible will be informed of this, thanked, and sent a list of mental health related referrals.

Consent Process and Documentation
The consent process will utilize the process employed in our TABI study (IRB #2288-007). Following the initial pre-consent screening phone call but prior to the screening assessment, the participant will be emailed a link to the detailed digital version of the consent form. The consent form may be administered via one of two electronic platforms: (1) a secure e-consenting system

built by our team of software developers (consent data is stored on FSM servers) which enables subjects agree to participate by checking a yes box and typing in their name, or (2) via REDcap in which case subjects will use their mouse to sign their name and agree to participate by submitting the REDcap form (REDcap consent data is also stored on FSM servers). On the consent form, participants will have additional opportunities to provide separate consent for: 1.) contact regarding future research opportunities and 2.) permission to use anonymous quotes from opinions they express about the ThinkFeelDo website during the course of the study for use in the design of future digital interventions, promotional recruitment materials, the Center for Behavioral Intervention Technologies website, research papers, presentations, and media stories. They are instructed to print out the consent form for their records. After the electronic study consent form is signed, detailed information regarding the consent will be reviewed with the participant over the phone and study staff will ask the participant to affirm their signature verbally. Witnessing of the consent form will take place at this time by study staff. A date and time for the screening assessment will then be scheduled. The day before their appointment, the participant will be sent an email with a link to the self-report measures, asking them to fill these out as close to the interview as possible.

Communication from the research study may occur across a participant's involvement in the trial to increase participant retention. Such contact would be limited (e.g. sending greeting cards via mail or email (thank you, birthday, etc.) or sending small tokens of appreciation (keychains, pens, stress balls).

RCT Treatments:

310 participants will be randomized to either received Stepped Care or T-CBT. A description of the stepped care model follows (I-CBT +T-CBT). The T-CBT only arm will look the same as the T-CBT provided in the Stepped Care arm. All coach and therapist sessions will be audiotaped for treatment fidelity ratings.

Stepped care. The stepped care intervention will be initiated with guided iCBT, which can be stepped up to T-CBT if the patient does not respond. While the treatment will change, the therapist will remain the same. There are two conditions under which the participant will be offered T-CBT:

1) Stepping Due to Poor Engagement

1. Weeks 4-16: If a participant is not engaged in iCBT for 3 treatment weeks and is not responding to coaching, and if last known PHQ-9>10, coach offers to step the participant up to T-CBT on the 4th week of no engagement. If agreeable to stepping up, starts T-CBT the following treatment week. Participants will not be offered to step to T-CBT if they have had > 12 sessions/weeks of coaching or if they are past Week 16 of treatment. If participant does not respond to attempts to step to T-CBT within a week, participant's treatment will be discontinued.

2) Stepping Based on PHQ score

The algorithm below was developed to determine when patients should be stepped-up from iCBT to T-CBT due to poor response to treatment.

Week 4-8
If PHQ-9 ≥ 17 at two consecutive weeks, then "step" t-CBT
If PHQ-9 < 17 at Week 5-8, then "stay" i-CBT
If PHQ-9 < 5 at two consecutive weeks, schedule final coach call

Week 9 - later
If PHQ-9 ≥ 13 at two consecutive weeks, then "step" t-CBT

If PHQ-9 < 13 and ≥ 5 at Week 10-13, then "stay" i-CBT
If PHQ-9 < 5 at two consecutive weeks, schedule final coach call

Missing PHQ-9 Data: If we do not have 2 consecutive weeks of PHQ-9 data, stepping decisions will be made based on data collected by RA and missing data filled in (estimated PHQ score) by the system.

Stepping is not offered unless the participant has enough sessions/time to have at least 4 weeks of T-CBT. Thus, participants are not offered T-CBT if they have had >12 sessions of coaching or are on Week 16 of the study.

Guided iCBT. Guided iCBT will consist of access to the *ThinkFeelDo* treatment site, supported by our manualized *TeleCoaching* program.

ThinkFeelDo is a highly interactive CBT web-based treatment. It consists of didactic material presented in "lessons" that include text, animation, and short video clips. Each lesson focuses on a specific component of a CBT principle or skill. For example, behavioral activation is introduced over two sequential lessons focused, first, on monitoring behaviors, and then on scheduling positive behaviors. Each lesson requires 10-15 minutes to complete. Each lesson is coupled with a tool that supports the CBT skill (e.g. a calendaring tool for scheduling and monitoring pleasant events or a thought record tool to support cognitive restructuring). Patients are asked to complete a tool every 1-2 days. Tools require 2-3 min to complete. New lessons can be completed by the patient at a rate of approximately one every 4-7 days.

ThinkFeelDo also contains an interface for a coach or therapist that displays the patient's activity and work on the site, and provides alerts for safety issues such as suicidality. Participants will communicate with their therapists via telephone and/or secure messaging through the site each week. The initial session will be conducted via telephone and will last about 30 - 45 minutes long in order to facilitate engagement with the coach and the program, with subsequent sessions of approximately 5-15 minutes per week. Coaching sessions will follow a motivational interviewing based format focused on increasing participants' motivation to continue logging in to the website. Communication between patients and coaches will also occur via the site's secure messaging. Coaches will be Licensed clinical social workers, Ph.D. level psychologists or PhD students who are trained and supervised by licensed psychologists. Data regarding participants' use of the *ThinkFeelDo* website for logins that occur during active coaching phase of treatment and after completion of treatment will be collected.

T-CBT will be administered by Licensed clinical social workers, Ph.D. level psychologists or PhD students who are trained and supervised by licensed psychologists. The goal of T-CBT is to reduce depression by teaching methods of managing negative emotions and depressive thought patterns, improving social functioning, and improving coping with stressful life events. Techniques to meet these goals include cognitive-behavioral strategies focused on reframing unhelpful automatic thoughts, pacing activities, time management skills, planning and organization, increasing pleasant events, anxiety management, anger management, and social skills training. To facilitate T-CBT, patients receive a workbook which contains the explanatory materials as well as worksheets used in standard CBT. The patient workbook serves to facilitate communication over the telephone.

Research staff may communicate with participants electronically (via SMS, email, video conference etc.) regarding study related treatments and to facilitate scheduling of assessments.

Length of Treatment

Patients in both treatment arms will receive treatment until sustained symptom remission

(See stepping algorithm above) within the 16 session treatment protocol (that is to be completed within 20 calendar weeks to allow for vacation and time off). When a patient reaches the PHQ- 9 < 5 the first time, the therapist or TeleCoach will discuss the patient's progress, and begin to end therapy in a manner consistent with standard treatment. The therapist (whether in T-CBT or TeleCoaching) will indicate to the patient that if s/he continues to remain free of symptoms for 2 weeks, there will be no need to continue treatment and that the focus for the coming week will be maintenance of gains. Thus, if the PHQ-9 score remains below 5 during the second week, the following week will be the final termination session. No treatment will last beyond 20 weeks.

Reimbursement of Subjects
Subjects earning more than $100 per calendar year will be compensated via check for each completed assessment. Monetary incentives will be distributed in amounts that increase as participants complete study milestones. Since the Telehealth Study has several milestones, spaced several weeks apart (e.g. completion of screening assessment, completion of mid-point assessment, etc.) incentives will increase slightly over time to encourage the participant to reach the next milestone.

Subjects earning less than $100 per calendar year may be compensated via an amazon.com giftcard. The decision to pay participants with an Amazon.com gift card or check will be made depending on preference and availability at the time of participation. The Amazon.com gift card can be used for making online purchases through the Amazon.com website and there are no fees associated with this payment type.

RCT incentive plan (total compensation up to $200):

- Completion of screening assessment: $30
- Completion of assessment 1 (approximately half way through treatment): $20
- Completion of assessment 2 (when treatment ends): $45
- Completion of assessment 3 (three months after treatment ends): $50
- Completion of assessment 4 (six months after treatment ends): $55

5. Response Assessment

Assessments: Assessments will consist of both web based self-report and telephone interviews. Internet administered surveys will use REDCap, a secure, web-based application for building and managing online surveys and databases. Interview measures will be administered by telephone. All interviews will be audiotaped to monitor the reliability of the assessment administration. *Mini-International Neuropsychiatric Interview (MINI)* [5] will be used to evaluate MDD diagnosis. Telephone administration of diagnostic interview has been well validated [6-8] *Quick Inventory of Depressive Symptomatology* will be used to evaluate more objective, evaluator-rated symptom severity. *Patient Health Questionnaire – 9 (PHQ9)* to evaluate self-reported depression.

Assessments will occur at baseline (screening assessment), approximately half way through treatment, at the end of treatment and at 3 and 6 month post-treatment follow-ups. All interview assessments will be conducted over the telephone. Self-report questionnaires will be completed by Internet administration. Participants in iCBT will also be asked about their impressions of the website and the individual modules. Participants who feel strongly, either positively or negatively, about the site may be invited to come in to the Behavioral Medicine Research Laboratory in the Department of Preventive Medicine in order to provide in person feedback

about the current website and propose changes to its design and content. If a participant is not interested in participating in the in-person interview, it will not affect his or her ability to participate in the rest of the study. Participants will also have the option to provide separate consent for the study team to use anonymous portions of a participant's expressed opinions and impressions of the ThinkFeelDo website for use in the design of future digital interventions, promotional recruitment materials, the Center for Behavioral Intervention Technologies website, research papers, presentations, and media stories.

The primary danger to the patient with depression is self harm. No study procedures are known to aggravate that risk, but we have nevertheless developed procedures to ensure safety of participants. Suicidality is assessed both by interview using the MINI and the QIDS, and by self-report using the PHQ-9. If participants score >=2 on the PHQ-9 item 9 regarding suicidality, the REDcap questionnaire will branch to suicide item (item 9) from Beck Depression Inventory. If the Beck Depression Inventory item is 2 or 3, a message will be displayed in the Redcap questionnaire making participant aware we are not an emergency service and should they need immediate help or be in danger, call 911 or go directly to nearest emergency room. Staff will review this item within one business day and the CBITS Suicidality protocol document will be enacted via phone. As our clinicians do not provide after-hours emergency support, the safety assessment would be performed the next business day if the alert is received after hours. However, the website will immediately refer patients scoring a 2 or 3 on the Beck Depression Inventory item 9 to call 911 or 1-800-SUICIDE for emergency services. If the patient reports suicidal ideation and intent upon interview, the study coordinator and PI will be notified immediately. In either case, the patient will be contacted and evaluated, and all necessary steps will be taken to ensure the patient's safety, up to and including calling emergency services to go out to the patient's location, perform a safety check and hospitalize the patient if necessary.

Initial Interview: The initial interview will take place after the participant has completed the digital consent. The initial interview will last approximately 30-45 minutes and will be audiotaped to ensure reliability in assessment. The participant will complete the self-report questionnaires on-line as close to the interview as possible. The questionnaires will take approximately 45-60 minutes to complete. Based upon these results a determination will be made as to the patient's eligibility. The patient will be informed of his/her eligibility within approximately 72 hours of his/her assessment. If the patient is eligible, the patient will be randomized.

7.0 STASTICAL CONSIDERATIONS

Rationale for Sample Size

The sample size was determined by Hypothesis 1, as non-inferiority requires a larger sample size than the cost-effectiveness analysis in Hypothesis 2. Using a one-sided two sample t-test on the difference between groups of the primary outcome of change in QIDS-C, and a margin of equivalence of 0.33, an analytic sample of 115/group would provide 80% power for equivalence. We will conservatively allow for an 8-9% attrition rate between assessments across 3 assessment points (total attrition of 26%), resulting in enrollment of 155 per group. Additionally, we will analyze the data using repeated measurements on an intent–to-treat basis, which would have adequate power to assess equivalence. To the best of our knowledge, power calculations for non- inferiority of two groups for longitudinal designs with attrition have yet to be derived (see communication from Don Hedeker, Appendix E). For outcomes that are not focused on non-inferiority, but rather more traditional inequality tests, the initial sample size of 155/group would have 80% power to detect effect sizes between 0.48 and 0.51 for a linear trend effect between groups and between 0.35 and 0.40 for constant group effects across time, assuming a correlation structure of compound symmetry, autoregressive(1), or Toeplitz(2).

Statistical Analyses

Noninferiority is established by showing that the true difference between two treatment arms is likely to be smaller than a prespecified noninferiority margin that separates clinically important from clinically negligible (acceptable) differences (D'Agostino, Massaro, & Sullivan, 2003; Nutt, Allgulander, Lecrubier, Peters, & Wittchen, 2008). Noninferiority trials of pharmaceuticals have used 30%–50% of the difference between treatment and control conditions to define noninferiority margins (Jones, Jarvis, Lewis, & Ebbutt, 1996; Nutt et al., 2008). A meta-analysis of CBT found an overall effect size of d = 0.82 (Cuijpers, Smit, Bohlmeijer, Hollon, & Andersson, 2010). We use face-to-face CBT rather than tCBT as the effect-size as this literature is far larger and therefore more reliable, and because there is no reason to believe that the effects of t-CBT are different from face-to-face CBT (Mohr et al., 2012). Using the midpoint of 40% for the acceptable criterion, we set d = 0.33 as the noninferiority criterion. A 1-sided test at a type I error rate of 5%, testing whether the difference in treatment groups is less than the noninferiority margin, is equivalent to testing whether a 2-sided 90% CI for the difference does not contain the noninferiority margin (Walker & Nowacki, 2011).

A sample of 115 per group provided 80% power to detect noninferiority using a one-sided, confidence interval for the difference in two independent means with type I error rate of 5% and a standardized margin of equivalence of 0.33. Assuming a 25% dropout rate, the study was designed to enroll 155 per treatment group.

Current literature suggests not directly imputing missing data for noninferiority analyses, but instead using mixed-effects models with repeated measures (Wiens & Rosenkranz, 2013). This method can estimate the difference between treatments at each time while accounting for observations that may be missing and adjusting for covariates. Hence, we used these models to estimate differences in primary outcomes (QIDS) between treatment allocation, assuming a random intercept and unstructured covariance structure. Additionally, we parameterized time as a nominal variable to not impose any structure to the trajectory of outcome over time. We provide the difference and 90% CI for treatment differences on the QIDS scale for interpretability. MDE, a secondary outcome, is binary and therefore used the effect size, *h*. All clinical outcome models were fit in SAS v.9.04. To verify that each arm produced reductions in symptoms, we evaluated the mean QIDS over time using mixed models with random intercepts and categorical indexing of time. Analyses for the primary clinical outcome was conducted using modified intention-to-treat, where all participants with at least one QIDS assessment after baseline were used in analyses. Additionally, as ITT analyses may increase the likelihood of falsely concluding non-inferiority, we performed a secondary analysis using a hybrid ITT/per-protocol (PP) approach, where participants who did not complete treatment were excluded. Non-trivial missing data was addressed using MLE-based ITT analysis via mixed models, as in our primary analysis (Matilde Sanchez & Chen, 2006).

Therapist cost differences and satisfaction across treatments were analyzed using *t*-tests. We calculated confidence intervals using bootstrapping and Fieller's theorem (a probabilistic model) (Chaudhary & Stearns, 1996; Willan & O'Brien, 1996). Differences in acceptability were compared using logistic regression (to determine if dropout differed between groups), and linear regression was used to determine if satisfaction was different across groups after adjusting for covariates. Analyses of acceptability (treatment preferences, dropout, and satisfaction) and time to remission were analyzed using t-tests and chi-squared tests. These analyses were done in R v3.4.3.

QUALITY CONTROL

Withdrawal Criteria

There are no specific criteria for removal of a patient from the study. A patient will be removed if continued participation is determined to constitute a danger to the patient's health or well- being by the PI based on input from the therapists and/or evaluators. Clinical evaluators and study clinicians are required to inform the PI and study coordinator if they suspect deterioration or adverse effects in the patient. The PI and study coordinators will perform all necessary evaluations. If the PI determines the patient must be removed from the study immediately, the patient will be removed and all appropriate referrals will be made. The IRB will be informed.

Risks/Discomforts
The risks from completing the self-report measures and interviews are minimal, but it is possible that the participant may experience emotional discomfort or increased anxiety as a result of answering questions about their mental health. The participant will be reminded that s/he has the option of stopping if s/he finds completing the self-report measures to be overly distressing. There are no known risks associated with iCBT or T-CBT. Patients will be permitted to continue antidepressant medications. As such, participation in this study is not expected to pose any significant risk to participants.

Treatment and Compensation for Injury
Participant risks in this study are minimal. The only risk is emotional discomfort. The participant will be reminded that s/he has the option of stopping if s/he finds completing the self- report measures to be overly distressing.

Confidentiality of Records
Study data will be kept in locked filing cabinets and in password protected databases stored on secure servers maintained by Northwestern University FSM IT. Participants' direct personal identifiers will not be released without prior consent except as specifically required by law. Efforts will be made to limit the use and disclosure of research study data to people who have a need to review this information. Study data may be shared for research purposes with collaborators outside of the research team at Northwestern University. Collaborators may include researchers at other academic institutions or foundations and/or government agencies. A data use agreement will be established before study data is released to a researcher or organization that is not part of the study team. The data use agreement will specify whether and how potential PII (e.g. demographic information like Age, Gender, Race, Salary) will be transferred to another organization. Study consent forms will explain the range of information that may be shared with collaborators.

Data Safety Monitoring
Study procedures will include the use of a Data Safety Monitoring Board (DSMB) that is comprised of a broad range of specialists who can oversee the study and offer guidance to the PI. The board will be chaired by Gregory Simon, M.D. Dr. Simon is a psychiatrist and researcher with Group Health who is a noted expert on research involving the treatment of depression in primary care and telemental health. Current study procedures have been developed in accordance with recommendations from the DSMB. The Project Coordinator will review all screening data prior to enrollment to exclude patients who may be at risk (e.g., who show signs of severe psychiatric disturbance such as psychosis, bi-polar disorder, or active suicidality). Follow-up data are also routinely checked immediately after receipt by the CEs for signs of deterioration and/or suicidality by CEs. Therapists and CEs are instructed to inform the DSMB immediately if any participant is experiencing psychiatric or medical deterioration. In addition, CEs are specifically asked by the PI to report any suspected deterioration during weekly lab meetings.
The DSMB will be informed of all instances of deterioration or suicidality. Northwestern

University's Office for the Protection of Research Subjects and IRB will be contacted immediately at all suspected adverse events (AEs), signs of medical or psychiatric deterioration, unexpected diagnostic findings or other incidents. For all events deemed significant by the Northwestern University IRB, reports will then be provided to all DSMB members.

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