PROTOCOL TITLE: Evaluation of a Proactive Identification and Digital Mental Health Intervention Approach to Address Unmet Psychosocial Needs of Individuals Living with Cancer

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1.0 Objectives

Primary: To evaluate the feasibility of conducting a randomized clinical trial (RCT) comparing a proactive identification + digital mental health intervention (DMHI) approach vs treatment as usual (TAU) among individuals living with likely incurable cancer (ILLIC) with depression.

Secondary: To determine the acceptability, appropriateness, and adoption of a proactive identification + DMHI approach and TAU among ILLIC with depression.

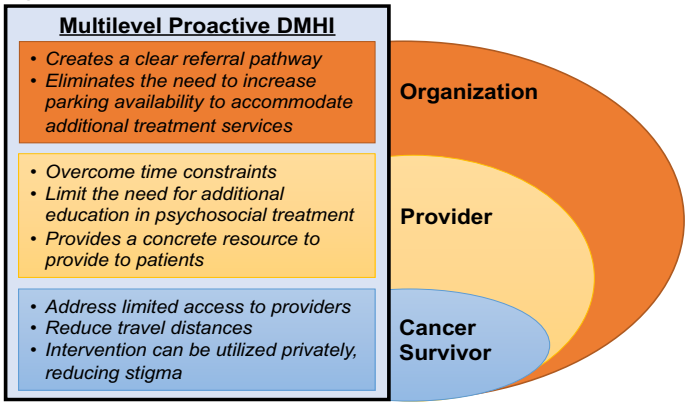
Secondary: To examine the fidelity of Moodivate approach among ILLIC with depression.

Exploratory: To explore the effect of a proactive + DMHI approach on depression, anxiety, and quality of life among ILLIC with depression relative to TAU.

2.0 Background

ILLIC are a heterogeneous, growing subpopulation of cancer survivors who have unique survivorship care needs[1,2]. Principal among these is the need for psychosocial treatment[3]. Treatment of depression is particularly critical as up to half of ILLIC report depressive symptoms[4-7]. Negative sequalae of depression include lower quality of life[8], reduced adherence to anti-cancer therapies[9], suicidal ideation[10], and desire for hastened death[10-12]. Numerous trials[13-16] and meta-analyses[6,17] have documented that evidence-based psychosocial treatment improves depression outcomes for ILLIC. However, multilevel barriers, including transportation issues, stigma, and a scarcity of oncology mental health providers[18-20] limit treatment access (**Figure 1**). Thus, ILLIC need feasible, accessible evidence-based depression treatment options.

Figure 1: Conceptual Model



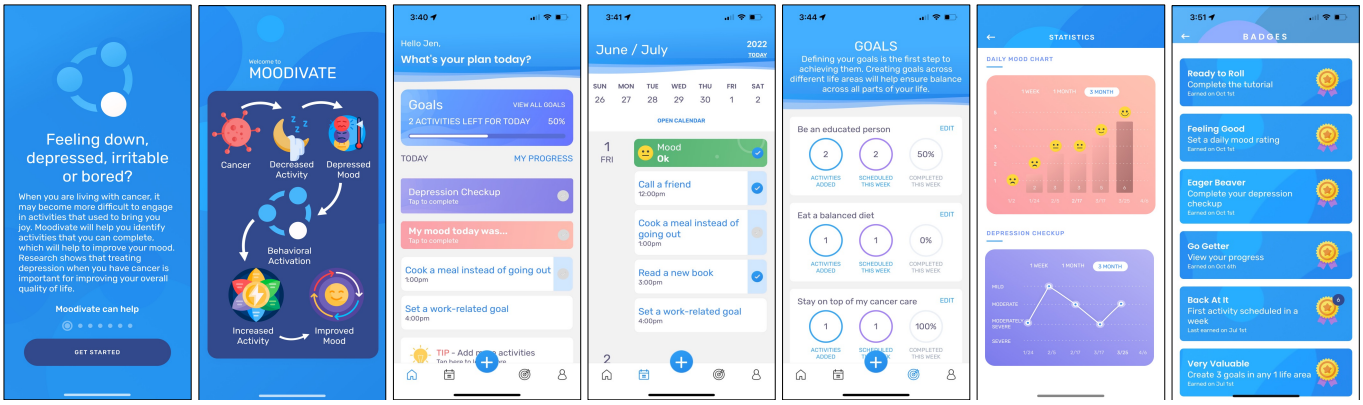
Best practice guidelines for comprehensive survivorship care suggest that screening and assessment of psychosocial concerns should be part of every clinical encounter[11,12,21]. Short depression screeners (e.g., the PHQ-2[22]) are now routinely administered in oncology settings[21,23] and these data can be used to ***proactively*** (i.e., outside of a clinical encounter) identify survivors in need of psychosocial treatment and link them to scalable options. While psychosocial screening data are recorded in structured Electronic Health Record (EHR) fields and can be readily used for proactive identification of patients with depression, efficient identification of ILLIC is more challenging. Data necessary to determine likelihood of curability, such as advanced stage at diagnosis or progression to metastatic cancer, are typically recorded in unstructured EHR fields[24], necessitating labor-intensive, manual chart review to identify ILLIC. To realize the goal of proactive identification and delivery of scalable evidence-based depression care for ILLIC, accurate, efficient, automated identification approaches are needed.

Self-guided digital mental health interventions (DMHIs) can be paired with proactive identification to deliver scalable evidence-based depression treatment[25]. Our team previously adapted one evidence-based depression treatment[26-29], Behavioral Activation (BA), for delivery via a DMHI called "Moodivate." Of available psychosocial depression treatments, BA is an ideal fit for ILLIC because of its: 1) strong clinical evidence base among cancer survivors[26-29] and 2) appropriateness for an underlying mechanism of depression faced by ILLIC. Our pilot work among primary care patients with depression demonstrated that Moodivate is a feasible, acceptable, and efficacious DMHI[30,31]. While a proactive treatment delivery model using a DMHI such as Moodivate may be a promising approach to deliver evidence-based depression treatment to ILLIC, additional work is needed to determine feasibility and efficacy of the approach.

3.0 Intervention to be studied

Moodivate: When users first download Moodivate, they complete a psychoeducational interactive tutorial, practice generating goals and activities, and receive instruction on app use. Users are then taken to their Home screen where they can see an overview of their activities for the day, plan additional activities, and track mood. Users are prompted to continuously generate new goals across life areas (Relationships, Daily Responsibilities, Recreation, Career and Education, Health) and multiple activities within each goal. By being connected to what the user values, this goal-driven framework ensures that activities will be positively reinforced[32]. Once a user has identified activities across goals, activities are scheduled and monitored via the Calendar (for future planning) and Home (for today) screens. After completing an activity, the user receives reinforcement (e.g., "Great job!"). Moodivate users can track daily mood to monitor progress and are prompted to complete a clinical assessment of depressive symptoms[33] once every two weeks. Users can view a graph of fluctuations in mood and depressive symptoms overlaid upon a graph of the number of completed activities, illustrating the connection between activity and mood. Users are reinforced for treatment engagement via badges[31]. Users are encouraged to use the app regularly, at least once per day, for the treatment of depressed mood[34]. If randomized to receive Moodivate, study staff will provide the participant with a Moodivate app download code and will ensure successful download. Study staff will then give the participant a brief, scripted overview (as utilized in our R41 and R42) regarding app utilization and will provide the participant with 10 minutes to use the app and ask questions.

Figure 2: Moodivate



TAU: TAU mimics existing depression treatment for ILLIC. Participants in both conditions will be provided educational mood management material available via the EHR with the suggestion to discuss questions with their oncology provider. Across conditions, participants will not be precluded from obtaining additional treatment (e.g., pharmacotherapy, palliative care), which will be tracked throughout the study via self-report.

4.0 Study Endpoints

Table 1. Study Objectives and Endpoints

OBJECTIVES	ENDPOINTS
Primary: To evaluate the feasibility of conducting a RCT comparing a proactive identification + DMHI approach vs TAU among ILLIC with depression	ILLIC case identification
	Accrual
	Retention
Secondary: To determine the acceptability, appropriateness, and adoption of a proactive identification + DMHI approach among ILLIC with depression.	System Usability Scale (SUS)[35] score
	Number of Moodivate app sessions
	Average time per Moodivate session
	Total time using the Moodivate app
	Number of goals created within Moodivate

Table 1. Study Objectives and Endpoints	
OBJECTIVES	ENDPOINTS
	Number of activities created within Moodivate
	Number of activities scheduled within Moodivate
	Number of activities completed
Exploratory: To explore the effect of a proactive + DMHI approach on depression, anxiety, and quality of life among ILLIC with depression relative to TAU.	Change in the PHQ-9[36] score from baseline to 1-month follow-up.
	Change in the Hospital Anxiety and Depression Scale, Anxiety subscale (HADS-A) score from baseline to 1-month follow-up.
	Change in the Functional Assessment of Cancer Therapy-General (FACT-G7) score from baseline to 1-month follow-up.

5.0 Inclusion and Exclusion Criteria/ Study Population

Inclusion criteria:
1) elevated depressive symptoms, defined as a score of ≥ 10 on the PHQ-9[36]
2) ILLIC (as determined during manual chart review)
3) age 18+
4) currently own an iOS- or Android-compatible smartphone
5) report willingness to utilize a mobile app for the treatment of depressed mood (response of "yes" on yes/no item)
6) have a valid e-mail address that is checked regularly *or* have regular access to text messages (to access follow-up assessments)
7) English fluency

Exclusion criteria:
1) Severe cognitive impairment that precludes completion of informed consent
2) current suicidal ideation on the PHQ-9 at screening or final study eligibility, defined as a response ≥1 (several days) on item nine

6.0 Number of Subjects

We will recruit 15 participants to examine the feasibility, acceptability, and preliminary efficacy of proactive identification + DMHI vs TAU among ILLIC with depression.

7.0 Setting

This study will be conducted within the NCI-Designated Hollings Cancer Center (HCC) and recruitment will leverage the HCC Survivorship and Cancer Outcomes Research (SCOR) infrastructure (Director: mPI Graboyes). As the only NCI-Designated Cancer Center in SC, HCC serves a diverse racial, socioeconomic, and geographic population. More than 3,500 new patients are diagnosed or treated at HCC annually.

8.0 Recruitment Methods

Study participants will be recruited proactively and remotely via the EHR using the same procedures utilized in our team's prior proactive behavioral health intervention trials. We will utilize available EHR data via a research data request to obtain a recruitment report of HCC patients with depressive symptoms with likely incurable cancer. Free-text and other fields (e.g., radiology reports, lab values) will be manually reviewed to identify survivors with likely incurable cancer. Discrete fields (e.g., PHQ-2 screening, depression-related diagnostic or billing codes) will be used to identify those with likely depressive

symptoms. Herein, we define ILLIC as persons who are diagnosed with advanced cancer that is likely incurable or diagnosed with or progressing to metastatic cancer. This definition, which varies by cancer type and available treatments and includes a range of survival trajectories, will be defined for each patient based on the assessment and plan of the treating oncologist and/or consensus discussion at the multi-disciplinary tumor board documenting an advanced cancer stage that is deemed likely incurable and/or cancer that is metastatic upon diagnosis and/or progresses to metastatic following prior treatments. Depression will be defined as 1) a score of $\geq$ 3 on the last PHQ-2 (the optimal cut-point to identify depression[37]), 2) depression listed on the problem list, or 3) a depression-related billing code associated with the last visit. To facilitate chart review, EHR data and clinical notes will be imported into a secure REDCap database[38]. Labels (ILLIC/non-ILLIC) will be provided as fields in REDCap and team members will assign an outcome. Clear guidelines will be created based on the ILLIC definition and linked in the REDCap project for easy reference.

Patients on the study recruitment report identified as having likely incurable cancer and depressive symptoms will be sent a study invitation by the research team. Invitations will be sent via MyChart, text message, e-mail, and/or phone call and we will follow all requirements of the POR process. The study team will not cold-contact any patients who have opt-ed out of receiving contact about research or who have met the maximum number of contact attempts at the time of recruitment. If interested, participants will complete an online screening within REDCap to determine preliminary study eligibility.

9.0 Consent Process

After completing determination of preliminary eligibility, a member of the research team will schedule a phone call with the participant to determine final study eligibility (no suicidal ideation reported on the PHQ-9 and a score >=10 on the PHQ-9). After determination of final study eligibility, a study team member will complete remote electronic informed consent (e-consent) with the participant via REDCap. Participants will receive a link to an electronic consent form, available via REDCap, that they can review and sign. Review of the consent form will be paired with a phone call with a member of the research team to ensure that all questions are answered prior to enrollment. This remote consent procedure is currently utilized across all of Dr. Dahne's current NIH-funded awards. As smartphone ownership is an inclusion criterion (to use Moodivate), all participants will have internet access and thus access to the electronic consent form. All participants will electronically sign informed consent forms that have been IRB-approved once the study is explained to them in full and they have stated that they understand what is being asked of them. Participants will be given the opportunity to ask questions about their participation throughout the course of the study. A copy of the informed consent will be kept centrally at our study office within locked filing cabinets and a copy will also be given to each study participant. Participants will be given a study phone number and e-mail address to contact for questions.

10.0 Study Design / Methods

ILLIC with depressive symptoms identified chart review will be randomized 2:1 to proactive identification + DMHI vs TAU via a two-arm remote pilot feasibility RCT (N=15). The purpose of this pilot trial is to refine trial methods in preparation for a larger future grant (e.g., R01) and examine the feasibility, acceptability, and preliminary efficacy of proactive identification + self-guided DMHI approach vs TAU.

In addition to baseline assessments completed following e-consent, all participants will be text messaged and/or emailed a REDCap link, accessible via smartphone, to complete follow-ups weekly for 4 weeks. Assessments are estimated at 10 minutes each and participants will be compensated $40 in electronic gift codes for completion of baseline assessments, $40 for completion of each follow-up assessment, and $100 as a bonus if all study assessments are completed. Additionally, participants will be invited to attend a post-study interview (~30-45 minutes) to help further refine trial procedures. Individual interviews may occur either remotely using an MUSC-approved HIPAA compliant video conferencing platform (e.g., Microsoft Teams, MUSC Pro Zoom) Those who participate in these interviews will earn an additional $40 (total

potential compensation = $340). Procedures for remote remuneration are well-established through our prior trials[39].

We will collect the following study measures from the EHR or patient self-report as indicated below.

Baseline Demographics (Assessed via self-report at baseline)
Participants will self-report age, race, sex, ethnicity, marital status, insurance, and home address (which will be used to determine rurality).

Clinical characteristics (Assessed via EHR data and self-report at baseline)
Clinical and mental health characteristics are assessed using clinical documentation within the EHR unless otherwise indicated.

We will collect data via the EHR and participant self-report regarding include type of cancer (breast, lung, colon, etc), type of ILLIC [locally advanced, metastatic], current cancer treatment (chemotherapy, immunotherapy, etc), and ECOG performance status[40]. We will also collect self-report data regarding use of psychotherapy, pharmacotherapy, DMHIs, and supportive care services (e.g., palliative care, support groups).

Technological Experience (Assessed via self-report at baseline)
Pew Research Center's technology adoption survey: This validated survey will be used to assess experience using technology and internet access (home broadband, access via mobile device)[41].

Mobile Device Proficiency Questionnaire (MDPQ-16)[42]: The MDPQ-16 is a validated 16-item measure of mobile device proficiency.

Computer Proficiency Questionnaire (CPQ-12)[43]: The CPQ-12 is a validated 12-item measure of computer proficiency.

Implementation (Assessed via self-report Week 4 [SUS] and via app analytics across study duration)
System Usability Scale (SUS[35]): The SUS is a 10-item self report measure of acceptability.

Adoption: Adoption will be characterized as 1) number of app sessions, 2) average time per session, and 3) total time using the app.

Retention: Retention will be defined as any app use within each week following enrollment.

Fidelity: Fidelity will be measured as 1) number of goals created, 2) number of activities created, 3) number of activities scheduled, and 4) number of activities completed.

Clinical Efficacy (Assessed at baseline and at all study timepoints via self-report)
PHQ-9[36]: The PHQ-9 is a validated 9-item measure of depression. The PHQ-9 has high sensitivity and specificity for identifying individuals with depressive symptoms, particularly among cancer survivors[44-46].

Functional Assessment of Cancer Therapy-General (FACT-G7)[47]: The FACT-G7 is a patient-reported outcome measure of health-related quality of life with good validity and reliability in patients with cancer[47].

Hospital Anxiety and Depression Scale, Anxiety subscale (HADS-A). The HADS-A is a validated 7-item patient-report measure of anxiety symptoms in the past week which has been used extensively among patients with advanced cancer[48].

11.0 Data Analysis and Data Management

Data Analysis

Data analysis for Aims 1 and 2 will primarily focus on descriptive analysis of feasibility and acceptability metrics. Descriptive statistics will be summarized overall and within each intervention group for baseline demographic and clinical variables and for primary study outcomes. Descriptive analyses will be used to help determine feasibility of a future larger scale clinical trial with this patient population using these approaches.

Data Management

Participants will enter data in REDCap, a secure, web-based application designed exclusively to support data capture for research studies. REDCap provides: 1) an intuitive interface for data entry (with data validation); 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages (SPSS, SAS, Stata, R); 4) procedures for importing data from external sources; and 5) advanced features, such as branching logic and calculated fields. These procedures are effective in minimizing data entry errors (e.g., missing or errant data). All data from Moodivate will be stored on a HIPAA-compliant server and data will be transmitted securely to the research team via industry standard protocols as in our prior trials. Recruitment projects are housed in REDCap and only IRB approved study team members will have access to the recruitment project database. The research team will only have access to the REDCap recruitment project while actively enrolling for the study.

12.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

Quality Assurance

Accuracy and completeness of the data collected will be ensured by weekly review. The REDCap system does not accept outliers, illogical response patterns, etc. The PIs and research staff will have weekly meetings to discuss any qualitative comments received during data collection and any problems in data collection. The PIs will examine the database for potential irregularities monthly. Initial data analyses will examine distributions of variable scores and comparability of baseline characteristics across conditions in case analyses need to be adjusted for these. Confidentiality procedures are outlined above.

Regulatory Issues

All serious AEs will be reported to the MUSC Committee on Human Research within 48-hours. Follow-up of all unexpected and serious AEs will also be reported. All AEs will be reviewed weekly by the PI and yearly by the IRB. Any significant actions taken by the local IRB and protocol changes will be relayed to the funding agency. We estimate the significant AE rate to be very low (< 5%). Potential conflicts of interest (COI) will be reported using the rules of MUSC's COI committee.

Trial Safety

The contact PI (Dr. Dahne) will serve as the lead Program Manager for AEs. All unexpected AEs will be monitored while they are active to determine if treatment is needed. We anticipate that AEs will be rare given that the Moodivate app is non-invasive and that all participants will be engaged with current healthcare. For each weekly study meeting, the research assistant will prepare a summary of all AEs, including their severity, whether they caused a dropout, required treatment, and presumed relation to app utilization. The PIs will review this at the weekly study meeting (or before if more urgent). At the weekly meeting (or before if urgent), the research staff will report any premonitory symptoms to suggest emergence of a serious psychiatric condition (e.g., suicidality). The mPI, Dr. Graboyes, a board-certified head and neck

microvascular reconstructive surgeon-scientist, will be available on an ad-hoc basis for on-site medical supervision for any issues that cannot be resolved by Dr. Dahne.

Study procedures will follow as much as possible the FDA's Good Clinical Practice Guidelines and our research team has found Spilker's comprehensive text on conducting clinical trials to be useful[49]. We will encourage participants to notify their physicians that a) they are in a randomized controlled research study examining a treatment for depressed mood, and b) the physician should contact the PI directly if the physician has any questions.

The research staff will be instructed not to reveal whether a person is a participant in the study and will report to the PI any outside requests for information about a participant or any breaches in confidentiality. All requests by participant's physicians and other medical providers will be referred directly to the PI.

Data and Safety Monitoring Plan Administration

The PIs will be responsible for monitoring the trial, with additional oversight provided by study co-Investigators. The PIs will examine monthly the outcomes database for missing data, unexpected distributions or responses, and outliers. The PIs will check weekly the AE database prepared by the research staff immediately prior to the weekly lab meeting.

13.0 Risks to Subjects

This is considered a minimal risk study. Minimal risk means the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. The potential risks in this study include those related to: a) depressive symptoms, b) clinical deterioration, c) confidentiality, d) potential data breach from the app database, and e) frustration. All risk mitigation strategies outlined have previously been approved by the MUSC IRB and implemented with success during our team's prior Moodivate evaluation trials.

a) Depressive symptoms: Depressive symptoms will be monitored via the PHQ-9. All participants will complete the PHQ-9 weekly online via a REDCap survey that is accessible via mobile phone web browsers. All participants will own smartphones. Thus, all participants should have access to the online PHQ-9 assessments.

b) Clinical deterioration: Drs. Dahne, Graboyes, and their research team will monitor participant PHQ-9 scores for possible clinical deterioration (i.e., increasing depressive symptoms and/or the development of suicidal ideation) throughout the course of the study as participants complete the PHQ-9 weekly. Clinical deterioration will be defined as an increase of 5 or more points on the PHQ-9 from the baseline PHQ-9 assessment or a response of "More than half the days" or "Nearly every day" on item 9 ("Thoughts that you would be better off dead, or thoughts of hurting yourself in some way") of the PHQ-9. Our team has developed real-time alerts in REDCap which alert the investigative team if a participant completes a PHQ-9 assessment and evidences clinical deterioration. This system was developed during our prior Moodivate evaluation studies and has now been implemented with success across multiple studies. In the event that a participant evidences clinical deterioration, Dr. Dahne, a licensed clinical psychologist, or other IRB-approved clinical personnel will contact the participant via phone and will provide referrals for local mental health resources for depression treatment. Dr. Dahne (or other IRB-approved clinical personnel) will suggest that the participant seek treatment and then will follow-up with the participant via phone one week later. In the event that a participant reports suicidal ideation either during study screening or during subsequent assessments, Dr. Dahne will complete a risk assessment with the participant via phone. Dr. Dahne will query the participant for details regarding the suicidal ideation, including a likelihood of harming oneself imminently and a plan for committing

suicide. If the participant reports an imminent likelihood of harming themself or a plan for committing suicide, Dr. Dahne will call emergency services and will remain on the phone with the participant until emergency services arrive. Contact information including home address will be collected during study screening and will be provided if necessary to emergency services personnel. If the participant does not respond to Dr. Dahne's phone call within 24 hours, Dr. Dahne will contact the participant's designated emergency contact (contact information for emergency contact will be collected at baseline). If neither the participant nor the emergency contact responds to Dr. Dahne within 48, Dr. Dahne will call local emergency services and will provide them with the participant's name and home address for the purposes of completing a well check. These risk mitigation procedures will be reviewed with all participants during the informed consent process and are currently approved across all of our team's IRB protocols. Dr. Dahne has more than 10 years of experience conducting suicide risk assessments. In the event that a participant evidences clinical deterioration, the participant will be allowed to continue in the trial, but we will recruit an additional participant for data collection purposes.

c) Confidentiality: Participants will be made aware of limits to confidentiality at the beginning of screening and during informed consent which includes a report of suicidal or homicidal intent or report of abuse or neglect. If the participant reports suicidal or homicidal intent or abuse/neglect during screening or at any point during the trial, Dr. Dahne will take appropriate action as outlined by the MUSC IRB, NIH, and the State of South Carolina, which may include paging the participant's oncologist, contacting the authorities and/or pursuing involuntary commitment at a mental health facility. If participants present no imminent danger but also need more extensive treatment of mental health concerns, they will be given appropriate referrals. All individual interviews will be recorded, transcribed, and destroyed within 12 months of completion of the entire study to protect confidentiality.

d) Data breach: Although health information will be collected within Moodivate (e.g., daily mood ratings, activities, values), personally identifiable information will intentionally not be collected within the app (e.g., name, phone number, email address, etc), and thus we will not collect nor will we retain protected health information (PHI). In the event of a data breach, it is important to note that health information will not be able to be tracked back to specific individual users. By refraining from collecting PHI within the mobile app, we ensure HIPAA compliance while also protecting the identities of our users. In the event of a data breach, all app users will be notified via email.

e) Frustration: Participants may become frustrated while completing questionnaires or while using Moodivate. Participants will be informed that they may refuse to answer any question(s) that they do not wish to answer and that they may discontinue use of Moodivate at any time.

f) Randomization: The treatment participants receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments.

e) Unknown risks: The experimental treatments may have unknown side effects. The researchers will let participants know if they learn anything during the course of the study that might make participants change their mind about participating in the study.

Since patients will all currently be receiving medical care at HCC, there are no additional risks associated with participation in this study.

Adequacy of Protection Against Risks

Recruitment and Informed Consent

Study participants will be recruited proactively and remotely via the EHR using the same procedures utilized in our team's prior proactive behavioral health intervention trials. We will utilize available EHR

data to identify HCC patients with likely incurable cancer and depressive symptoms. Patients on the study recruitment report who have likely incurable cancer as denoted within the medical record will be sent a study invitation by the research team. If interested, participants will complete an online screening within REDCap to determine preliminary study eligibility. After completing determination of preliminary eligibility, a member of the research team will schedule a phone call with the participant to determine final study eligibility (no suicidal ideation reported on the PHQ-9 and a score >=10 on PHQ-9). After determination of final study eligibility, a study team member will complete remote electronic informed consent (e-consent) with the participant via REDCap. Participants will receive a link to an electronic consent form, available via REDCap, that they can review and sign. Review of the consent form will be paired with a phone call with a member of the research team to ensure that all questions are answered prior to enrollment. This remote consent procedure is currently utilized across all of Dr. Dahne's current NIH-funded awards. As smartphone ownership is an inclusion criterion (to use Moodivate), all participants will have internet access and thus access to the electronic consent form. All participants will electronically sign informed consent forms that have been IRB-approved once the study is explained to them in full and they have stated that they understand what is being asked of them. Participants will be given the opportunity to ask questions about their participation throughout the course of the study. A copy of the informed consent will be kept centrally at our study office within locked filing cabinets and a copy will also be given to each study participant. Participants will be given a study phone number and e-mail address to contact for questions.

Protections Against Risk

All screening information will be kept in a password protected REDCap database. Only key study personnel will have access to the database. If an individual is not eligible to participate, his/her screener will include his/her first name and last initial and the reason for disqualification. Eligible participants' full name, telephone number and e-mail address will be recorded in the database. This is the only place where participants' names and subject identification numbers appear together. Eligible participants will be assigned a subject number, will complete informed consent (see procedures above), will be randomized, will complete baseline assessments, and subsequently will receive their randomized intervention.

Upon completing eligibility screening, if study eligible, individuals will be provided with a verbal overview of the study, asked to review a consent form, and asked to provide informed consent. Participants will be informed of limitations of confidentiality (i.e., abuse or neglect, intention to harm self or someone else) both verbally and in writing during the informed consent process. The consent form will include the participant's name, but not his/her subject number. Consent forms will be provided in English. As utilization of Moodivate requires that participants are able to read, participants unable to read the consent form on their own will not be included.

Regarding questionnaire data, data will be obtained for research purposes only. All data will be collected, stored, and managed via REDCap, which is a secure, web-based application designed exclusively to support data capture for research studies. REDCap includes real time validation rules with automated data type and range checks at the time of entry. The underlying database is hosted in a secure data center at MUSC and includes redundancy, failover capability, backups and extensive security checks. The system has several layers of protection including user/group account management, "Data Access Groups" which allow data to be entered by multiple groups in one database with segmented user rights for entered data, audit trails for all changes, queries and reports, and Secure Sockets Layer (SSL) encryption. Name and relevant contact information will be obtained to provide compensation and every effort will be made to maintain subject confidentiality, in accordance with HIPAA. All data will be identified only by code numbers (participant IDs). Participant IDs will be linked to participants' names in a password-protected file that is accessible only to the PI and trained research staff.

Regarding user privacy while using Moodivate, users will create a username and password in order to login to their account without storing their true identity. In Moodivate, we will store a one-way hashed version of the patient's email address to support password reset and unique identification, but that identification will not be traceable back to the user's true identity. We will not store any personally identifiable information (e.g., first name, last name, email address, phone number) of users in our app database. We will use a HIPAA-compliant server protected by industry-standard safeguards to prevent unauthorized access. Since we are not associating patient health information with personally identifiable information there would not be a risk of unauthorized release of patient medical data in the event of a security breach. User personal information will be contained behind secured networks and will only be accessible by the investigators, who will have special access rights to such systems. In addition, all sensitive information users supply will be encrypted via Secure Socket Layer (SSL) technology. We will not sell, trade, or otherwise transfer personally identifiable information to outside parties. Our privacy policy will be available within the app for users to view at any time.

Protection against risk resulting from depressive symptoms includes the following: Regarding suicidal ideation and broader mental health concerns, Dr. Dahne, a licensed clinical psychologist, will take appropriate action as outlined by the MUSC IRB, NIH, and the State of South Carolina, which may include contacting the authorities and/or pursuing involuntary commitment at a mental health facility. If participants present no imminent danger but also need more extensive treatment of mental health concerns, they will be given appropriate referrals. As noted above, PHQ-9 data will be monitored over time in order to detect any possible clinical deterioration. PHQ-9 data will be monitored using only the participants' subject numbers. Should a participant evidence clinical deterioration, Dr. Dahne will then use the participant database to obtain contact information for the participant based on their subject number.

Regarding recordings, all interviews will be audio recorded and transcribed with recordings stored on an MUSC secure, password protected server. Recordings will be destroyed within one year of recording. Only IRB approved research staff will have access to recordings. Recordings will be destroyed within 12 months of completion of the entire study. Only IRB approved research staff will have access to recordings.

14.0 Potential Benefits to Subjects or Others

All participants in this trial will receive at minimum treatment as usual. We will not augment treatment as usual as provided by HCC. The majority of participants will also receive a mobile app developed to improve depressive symptoms, therefore there is a possibility of reduced depressive symptoms through the use of Behavioral Activation for those that receive the Moodivate app. The major benefit to society will be whether a proactive identification + DMHI approach improves depression treatment outcomes relative to TAU for ILLIC. Potential issues of clinical deterioration, confidentiality, data security, and frustration are a high priority and will be closely monitored throughout the study. Consequently, the risk to benefit ratio in the proposed study appears to be acceptable.

15.0 Sharing of Results with Subjects

Study outcomes will not be shared with subjects.

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