Official Title: LiveWell: An Adapted Dialectical Behavioral Therapy Skills Training Protocol for Patients Living With Metastatic Lung Cancer

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Research Abstract

Please type your Research Abstract here:

The Research Abstract should summarize the main points of your study in one paragraph. The following guidelines may help you:

1. Purpose and objective (1-2 sentences)
2. Study activities and population group (2-4 sentences)
3. Data analysis and risk/safety issues (1-2 sentences)

LiveWell is an 8-session Dialectical Behavioral Therapy (DBT) Skills Training-based protocol for patients living with metastatic lung cancer. The first phase of this K99/R00 study (K99, Aim 1) aims to refine the LiveWell intervention protocol (e.g., content) and procedures (e.g., delivery, training, fidelity monitoring). Refinement will be guided by preliminary work (i.e., qualitative feedback from participants in the PI's F32 study), consultation with an advisory board of interested parties, and the Dynamic Sustainability Framework from implementation science. We will conduct user testing (n=10) of the refined protocol. Data collected from user testers will be analyzed using rapid analysis and used to iteratively refine the LiveWell protocol and procedures until unanimously approved by the advisory board. The standardized LiveWell protocol and procedures produced by this K99 study will be used for the future R00 trial. The risks to user testers are minimal.

Research Summary

State your primary study objectives

Aim 1 (K99): To refine and user test the LiveWell protocol and procedures.

State your secondary study objectives

N/A

Please select your research summary form:

Standard Research Summary Template

This is the regular (generic) research summary template which is required for all regular applications (unless your protocol fits under the other research summary templates in this category). Use of these instructions is helpful for ensuring that the research summary contains all necessary elements.

Standard Research Summary

Purpose of the Study

- Objectives & hypotheses to be tested

Survival rates are improving for patients with metastatic lung cancer (i.e., metavivors) due to therapeutic advances. However, living longer with metastatic cancer presents significant challenges. Most metavivors will ultimately die of cancer and must navigate the duality of *living while dying*. As stated by one metavivor, "I feel like a ticking time bomb...I'm scared to be hopeful...I don't know how to live with cancer." Within this challenging emotional context of balancing hope with uncertainty, metavivors must also learn to manage persistent, burdensome symptoms (i.e., fatigue, dyspnea, pain). Metavivors have difficulty navigating these challenges and experience high psychological distress (i.e., depressive symptoms, anxiety, illness non-acceptance), high symptom burden (i.e., fatigue, dyspnea, pain) and poor overall quality of life.

Psychosocial interventions have the potential to improve psychological distress, symptom burden, and quality of life in metavivors. However, existing intervention paradigms are not designed to address metavivors' diverse, fluctuating emotional needs. Metavivors require strategies that can help them to navigate the emotional turbulence of living with and managing metastatic disease. Emotion regulation (i. e., the ability to monitor and manage emotional experiences and responses) is a promising transdiagnostic intervention target to improve metavivors' ability to cope with the challenges of *living while dying*.

Dialectical behavioral therapy (DBT) is an evidence-based psychotherapy that targets emotion regulation. DBT Skills Training teaches core skills (e.g., mindfulness, distress tolerance, emotion regulation, interpersonal effectiveness) to facilitate both acceptance of reality as it is *and* behavior change. Balancing acceptance and change is exceptionally salient for metavivors, as there are emotionally demanding circumstances to accept (e.g., uncertainty about the future, physical changes, life not looking as planned), *and* change (e.g., illness-related thoughts, symptom management behaviors) to reduce psychological distress and symptom burden, and improve quality of life. DBT Skills Training can help metavivors to live well, with lung cancer.

Dr. Hyland (PI) conducted a Phase IB/IIA study (1F32CA265058) to adapt (e.g., dose, delivery, content) and pilot test a DBT Skills Training intervention for lung cancer metavivors. This is the first NCI-funded study to examine DBT Skills Training in cancer patients. Qualitative interviews with metavivors and their providers confirmed that DBT skills are highly relevant and needed. One metavivior noted, "these skills are as important and valuable as treatment". Interviews directly informed and produced LiveWell, an 8-session adapted DBT Skills Training protocol delivered one-on-one via telehealth. Qualitative data and a single-arm pilot (N=30) support proof-of-concept. Building on preliminary data and aligned with the ORBIT behavioral intervention development model, the current study aims to iteratively refine and user test the LiveWell protocol and procedures.

Aim 1 (K99): To refine the LiveWell protocol and procedures. Refine the LiveWell protocol (e.g., content) and procedures (e.g., delivery, training, fidelity monitoring). Refinement will be guided by: 1) preliminary work (i.e., qualitative feedback from F32 participants), 2) The Dynamic Sustainability Framework from implementation science, and 3) consultation with an advisory board composed of interested parties (2 lung cancer metavivors, 1 thoracic oncologist, 1 behavioral clinical trial expert, 1 implementation scientist, 1 DBT expert, 1 member of cancer center leadership). We will conduct user testing (N=10) of the refined protocol and integrate feedback.

The iterative refinement process will produce a standardized LiveWell protocol and procedures for the independent R00 phase, a Phase IIB randomized pilot trial to examine feasibility, acceptability, and

outcome patterns of LiveWell and Enhanced Usual Care (separate, future IRB application). If successful, Livewell will improve metavivor quality of life and provide a promising psychosocial intervention paradigm for other groups of metavivors and patients living with chronic illness.

Background & Significance

- Should support the scientific aims of the research

Lung Cancer Metavivors Face Unique Challenges. There are over 620,000 people living with metastatic lung, breast, colorectal, or bladder cancer or melanoma in the United States today.[35] With the advent of new therapies, metastatic cancer is often treatable, but not curable, and patients may live for years even after the disease has spread.[36] However, most patients with metastatic cancer will ultimately die of cancer and must navigate the difficult duality of "living while dying". While cancer survivorship encompasses all patients from the time of diagnosis, the needs of survivors living with metastatic disease (i.e., metavivors) likely differ from those of patients treated with curative intent or at the end of life. A meta-analysis of unmet needs in patients living with advanced cancer found that patients endorsed unmet emotional and psychological needs (e.g., anxiety, depression, uncertainty about the future, fear of death), physical needs (symptoms (i.e., fatigue, pain, dyspnea), "not being able to do the things I used to do") and informational needs (i.e., "being informed about things you can do to help yourself").[37] Patients with lung cancer, in particular, endorse higher psychological distress and physical symptom burden compared to other disease types.[38-41] Given the high number of unmet needs, high rates of distress, and high symptom burden, it is unsurprising that patients living with metastatic lung cancer endorse poor quality of life and are at elevated risk for worse overall health outcomes.[42-44] As medical advances continue to extend life expectancy, there is a need for supportive interventions designed to meet the needs of lung cancer metavivors to ensure that these patients are not only living longer, but living well.

Psychosocial Interventions Have Not Been Designed for Metavivors. Literature supports the efficacy of psychosocial interventions to reduce psychological distress and symptom burden and improve quality of life and health outcomes in cancer survivors.[45-48] However, metavivors are under-researched in the psychosocial oncology literature.[49] Most psychosocial interventions are designed for survivors treated with curative intent, or conversely, for patients facing end of life. While symptoms of distress typically decrease with time since diagnosis in cancer survivors, research suggests that trajectories of distress in metavivors are different, such that anxiety, post-traumatic stress, and fear of disease progression persist years after diagnosis.[50-53] These emotional challenges are understandable, as metavivors must balance hope for a positive treatment response and disease control with significant uncertainty about the future, and providers' ability to prognosticate who will respond well to newer therapies and for how long is limited. Early palliative care can help to establish goals of care and provide symptom management and general support to patients with advanced disease, which can improve quality of life.[52] However, these services are not designed to address the emotional challenges of living extended periods of time with metastatic cancer. It is critical to identify interventions that can specifically address the unmet psychosocial needs of metavivors because, as one lung cancer metavivor noted, "the emotional effects of treatment are much worse than the physical".

Dialectical Behavioral Therapy Skills Training: A Promising Psychosocial Intervention for Metavivors. Dialectical behavioral therapy (DBT) is an evidence-based treatment that focuses on the acquisition of skills to optimize emotion regulation and promote a "life worth living."[54,55] DBT is a third-wave cognitive behavioral therapy (CBT) that integrates change-oriented strategies found in traditional CBT (e.g., change dysfunctional cognitions, unhelpful behaviors), with acceptance-focused strategies (e.g., mindfulness of the present moment, accept reality as it is), and dialectical thinking. Dialectical thinking is the ability to hold onto two seemingly opposite things as true at the same time, like living and dying or acceptance and change. Whereas traditional CBT protocols emphasize change (e.g., how we think, feel, act) as a strategy to improve outcomes, third-wave therapies, including DBT, acceptance and commitment therapy (ACT), and mindfulness-based treatments, integrate acceptance-focused strategies (e.g., accepting things as they are).[56] Both DBT and ACT teach patients to accept things that they cannot change. This is extremely validating and important for patients with problems that cannot be changed (e. g., a metastatic cancer diagnosis). However, whereas ACT encourages patients to choose to act according to their values regardless of emotional or physical symptom burden, DBT includes several unique ingredients that may be particularly valuable to lung cancer metavivors: 1) DBT teaches strategies to change emotions and physical symptoms (when appropriate), and 2) DBT addresses interpersonal effectiveness and communication skills, which metavivors identify as important (e.g., communicating wants and needs with loved ones, asking the medical team questions). While ACT has been widely adopted

for patients with chronic illness,[57,58] research on DBT in chronic physical illness has been limited, likely due to 1) inaccurate perceptions of DBT as a lengthy treatment for psychopathology, 2) siloes in treatment, and relatedly, 3) a lack of providers with adequate training to translate DBT into health settings. DBT Skills Training is a component of DBT treatment that may offer particular benefit as it teaches a compendium of easy-to-use strategies from across psychology (mindfulness, distress tolerance, emotion regulation, interpersonal effectiveness). The modular nature of DBT Skills Training and focus on a transdiagnostic process (i.e., emotion regulation) make it broadly applicable to various stressors and symptoms and suitable for adaptation.[59] DBT Skills Training has been adapted for a variety of populations (e.g., people with anxiety, depression, PTSD, substance abuse disorders, eating disorders, chronic pain) and demonstrated efficacy in improving emotion regulation, distress, symptom coping and acceptance, quality of life, and other important health outcomes.[60-63] However, applications of DBT Skills Training in cancer patients have been limited.

Emotion Regulation in Cancer: Emerging Evidence. Emotion regulation, the process by which individuals monitor and manage their emotional experiences and responses, may be a mechanism by which DBT Skills Training impacts health outcomes.[64] Research suggests that high negative emotionality and greater use of maladaptive emotion regulation strategies (e.g., suppression, avoidance) is linked to greater psychological distress and worse overall health outcomes (e.g., disease, death).[65,66] Conversely, greater use of adaptive emotion regulation strategies (e.g., cognitive reappraisal, acceptance) has been associated with greater emotional vitality, greater symptom tolerance, greater physical vigor and better immune functioning.[65,67] Taken together, changes in emotion regulation may be a mechanism by which DBT Skills Training reduces metavivor psychological distress and symptom burden and improves quality of life.[65,68-70] However, research on interventions to improve emotion regulation in cancer patients has been limited.

The Current Project: LiveWell. We recognized the exceptional fit of DBT Skills Training for lung cancer metavivors and conducted the first NCI-funded study to examine DBT Skills Training in cancer (1F32CA265058). We adapted DBT Skills Training for lung cancer metavivors (e.g., dose, delivery format, materials) creating LiveWell, an eight-session adapted DBT Skills Training protocol delivered one-on-one via telehealth. The current study will allow for timely progression of intervention development and testing aligned with the ORBIT model for behavioral treatment development.[71] In the current study (K99 phase), we will use an iterative, collaborative approach to refine the LiveWell study protocol and procedures (Aim 1).

Design & Procedures

- Describe the study, providing details regarding the study intervention (drug, device, physical procedures, manipulation of the subject or the subject's environment, etc.). Discuss justifications for placebo control, discontinuation or delay of standard therapies, and washout periods if applicable. Identify procedures, tests and interventions performed exclusively for research purposes or more frequently than standard of care. Include alternative therapies, concurrent therapies discontinued per protocol, risk benefit ratio, and use of tissue/specimens. Discuss monitoring during washout periods if applicable. Include brief description of follow-up, if any.

Intervention. LiveWell is an 8-session protocol of Dialectical Behavioral Therapy Skills Training, adapted specifically for patients with metastatic lung cancer. Sessions are 45-60 minutes in length and are delivered approximately weekly, one-on-one, via telehealth. Participants learn concrete, easy-to-use skills to: 1) tune into the present moment, and how they are thinking and feeling (*mindfulness*), understand emotions, how to change them, and how to experience more positive feelings (*emotion regulation*), tolerate distressing emotions and symptoms (e.g., fatigue, pain, dyspnea) and to accept reality as it is (*dist ress tolerance)*, and tools to communicate wants and needs effectively with others (*interpersonal effectiveness*).). An overview the protocol is provided in the table below. The goal is to teach patients skills to live well, *with* metastatic cancer. All sessions follow a standardized structure that is customary in skills training and grounded in social cognitive theory: 1) engage in a brief mindfulness experiential exercise; 2) review homework to reinforce application of skills taught the previous week; 3) facilitate learning of new skills through a) skill acquisition (modeling, teaching), b) strengthening (practice, role play), and c) generalization (assign home practice to promote flexible use in the real world); 4) closing ritual (dialectic of the week).[91]

Wk	Domain	Function	Skills	Practice/HW
1	Mindfulness	Non-judgmental awareness present moment, noticing internal and external experience	Mindfulness "What" Skills (Observe, Describe, Participate)	Mindful eating exercise Applying mindfulness to everyday activities
2	Emotion Regulation	Understand what emotions are, what they are not, and how to manage them	Model of emotions "Name it to tame it": how to identify and label emotions	Busting myths about emotions Applying name it to tame it
3	Emotion Regulation	Impact of Thoughts & Behaviors on Emotions, and how to change them!	How unhelpful thoughts impact emotion: Check the Facts to change thinking How actions/habits influence emotions (vulnerability factors, PLEASE to take care of body and mind	Review common cognitive distortions Identify and attend to vulnerability factors Taking care of the mind and body in context cancer
4	Emotion Regulation	Tools to create more positive emotions	Accumulate positives (doing pleasant things) Living aligned with values (what is important)	Pleasant activity planning Values identification
5	Distress Tolerance	Dealing with difficult circumstances (physical and emotional)	MAPPP Skills to change body chemistry (Movement, Airflow, Paced Breathing, Posture, Progressive Muscle Relaxation (PMR))	How to use fan + posture for dyspnea, practice paced breathing, Practice PMR
6	Distress Tolerance	Making things just a little bit better in the moment	IMPROVE the Moment (Imagery, Meaning, Prayer, Relaxing Actions, One Thing, Vacation, Encouragement	Practice pleasant imagery Encouraging words/mantra
7	Distress Tolerance	Accepting things as they are	Radical Acceptance of things as they are, using body language to practice acceptance	Discuss acceptance, practice half smiling and willing hands
8	Interpersonal Effectiveness	Plan ahead for emotional situations, communicating wants and needs	Cope Ahead for emotionally challenging situations (rehearsal) Identifying Goals in Interpersonal Situations Communicating effectively	Practice coping ahead Role play effective communication

Study Overview. The aim of the current study is to refine the LiveWell intervention protocol (e.g., content) and procedures (e.g., delivery, training, fidelity monitoring). Refinement will be guided by preliminary work (i.e., qualitative feedback from PI's fellowship study pilot participants), consultation with an advisory board of interested parties, and the Dynamic Sustainability Framework from implementation science. We will conduct user testing (n=10) of the refined protocol and integrate feedback. The iterative refinement process and elements are described below. This will produce a standardized LiveWell protocol and procedures that will be tested in the R00 trial (separate, future IRB application).

Advisory board: The advisory board will include members of interested parties with expertise relevant to the project, including a thoracic oncologist (Dr. Thomas Stinchcombe), a behavioral clinical trial expert (Dr. Frank Keefe), an implementation scientist (Dr. Leah Zullig), a DBT expert (Dr. Andrada Neacsiu), a member of cancer center leadership (Dr. Kevin Oeffinger) and two lung cancer metavivors. The two patient advisors will be lung cancer metavivors who previously participated in the PI's F32 fellowship study (Pro00108640). The advisory board will convene for bi-monthly, one-hour meetings. These meets may be held virtually or in-person, depending on board preference. The purpose of these meetings is to discuss refinement of the LiveWell intervention protocol and procedures and to review and provide feedback on iterations of the protocol and procedures. Minutes will be circulated following each meeting. Refinements will be made by the PI in between meetings. A detailed log of changes made will be maintained. This process will continue until the protocol and procedures are unanimously approved by the board.

Preliminary work: All participants in the PI's F32 fellowship study (Pro00108640), which tested LiveWell using a single-arm pilot trial design, were invited to participate in a qualitative exit interview to provide feedback on the LiveWell intervention, study procedures, and their overall experience in the program. Exit interviews were audio recorded and will be transcribed and analyzed using rapid analysis. Summaries of this data will be circulated to advisory board members and discussed at the initial board meeting to inform the first round of intervention refinement.

Implementation Science: The proposed project will leverage several pillars of the Dynamic Sustainability Framework, including 1) ongoing adaptation with a focus on fit, 2) ongoing stakeholder involvement, 3) standardization and streamlining, and 4) use of practical, relevant measures. As described above, exit interview data from the F32 fellowship study will help us to identify content that participants identify as 1) critical, 2) missing, and 3) unnecessary, and provide information about the feasibility of LiveWell in its current form. We will emphasize standardization of LiveWell content delivery and study procedures. We will ensure standardization by 1) automating some content (e.g., developing videos to explain key study concepts, recorded mindfulness e-library), 2) developing a protocol for interventionist training, 3) establishing clear procedures for intervention delivery (e.g., refined interventionist manual) and study operations (e.g., SOPs), and 4) developing a strategy to thoroughly assess fidelity. The advisory board will also review the assessment battery to ensure measures are as concise as possible and that they clearly reflect outcomes of interest. The baseline (A1) and post-treatment (A2) assessments will be uploaded with a future amendment.

User testers: Once a revised LiveWell protocol and procedures have been approved by the advisory board, we will conduct user testing. User testers (n=10) will meet eligibility criteria and be identified using the same procedures for the future R00 trial *(see Participants section).* User testers will complete the baseline assessment (A1), then receive the refined LiveWell intervention protocol. Following each session, participants will complete Likert scale ratings of perceived usefulness of the material, applicability to the patients' needs, and overall session quality. Following intervention completion, user testers will complete a post-treatment assessment (A2) consisting of self-reported outcome measures and additional Likert scale ratings of the acceptability of LiveWell procedures (i.e., recruitment and enrollment, assessment

procedures). User testers will complete an in-depth qualitative interview to discuss their experience with the program and to provide feedback. This will include additional questions about the acceptability, feasibility, and enjoyableness of the refined intervention, particularly the refined content (e.g., relevance, usefulness) and its delivery (e.g., recorded videos). Exit interviews will be transcribed and evaluated using a rapid analysis approach to rapidly inform further intervention refinement. User tester feedback will be presented during advisory board meetings and integrated.

Selection of Subjects

- List inclusion/exclusion criteria and how subjects will be identified.

Participants

Patient advisory board members will be N=2 lung cancer metavivors who previously participated in the PI's F32 fellowship study. Patient advisors hold unique knowledge and expertise as persons with lived experience with the disease, and personal experience participating in the LiveWell program. Lung cancer metavivors will be recruited from Duke Cancer Institute (DCI) using procedures listed under *Subject Recruitment.*

Eligible patients will:
1) be diagnosed with metastatic (AJCC stage IV) non-small cell lung cancer
2) have completed the LiveWell program as a study participant on Pro00108640, the PI's F32 fellowship study, and expressed a willingness to be contacted for future research
5) be able to understand, speak, and read English
6) be able to provide informed consent.

Exclusion criteria include:
1) under the direct care of the advisory board thoracic oncologist, Dr. Thomas Stinchcombe. This will ensure there is no compromising the patient/provider relationship.

Recruitment procedures are described in detail in the "Subject Recruitment" section.

User Testers will be N=10 lung cancer metavivors who meet eligibility criteria for the proposed R00 trial**.** Lu ng cancer metavivors will be recruited from Duke Cancer Institute (DCI) and Duke Cancer Center (Raleigh, NC), using procedures listed under *Subject Recruitment.*

Eligible patients will:
1) be diagnosed with metastatic (AJCC stage IV) non-small cell lung cancer
2) be undergoing lung cancer treatment with non-curative intent
3) endorse $\geq$3 out of 10 on the NCCN distress thermometer over the past week
4) be $\geq$ 18 years of age
5) be able to understand, speak, and read English
6) be able to provide informed consent.

Exclusion criteria include:
1) reported or suspected cognitive impairment
2) presence of untreated serious mental illness (e.g., schizophrenia) indicated by the medical chart or treating oncologist
3) expected survival <6 months.

At least four user testers will be recruited from each of the study sites (e.g., Duke Cancer Center Clinics in Durham, Raleigh). Recruitment procedures are described in detail in the "Subject Recruitment" section.

Subject Recruitment and Compensation

- Describe recruitment procedures, including what method(s) will be used, when the study will be introduced to potential participants and by whom. If any follow-up contact is planned, describe the proposed method and timing. Describe how you will ensure that subject selection is equitable and all relevant demographic groups have access to study participation (per 45 CFR 46.111(a) (3)). Include information about how many DUHS participants will be recruited. If participants are to be compensated and/or reimbursed, provide specific prorated amounts to be provided for expenses such as travel and /or lost wages, and/or for inducement to participate.

Patient Advisory Board Members

Subject Recruitment: The research team will recruit 2 patient advisory board members from the pool of study participants from the PI's F32 study, Pro00108640. During this trial, participants were asked if they would be open to being contacted for future research. We will contact patients who agreed to being contacted for future research, who are not patients of the thoracic oncologist on the advisory board, Dr. Thomas Stinchcombe. Patients will be contacted by highly trained study staff via telephone, no more than three times, to assess interest in advisory board membership. We will contact participants until two have been identified as eligible and interested. If a patient is interested when contact is made with a study team member, they will be provided with information about the advisory board and the K99 study, including the purpose, requirements, and time commitment. Eligible patients who wish to participate as advisory board members and enroll in the study will complete an electronic consent form via REDCap or, if preferred, be mailed a hard copy consent form to be reviewed by telephone, executed, and returned by mail. Consent procedures may also be completed in-person at the cancer center. In-person visits will be scheduled at a time that is convenient for the patient. In all cases, a member of the study team will review consent in a private space and answer any questions that the potential participant may have. Informed consent will be documented by signature on an IRB-approved consent form. Remote, direct-to-patient recruitment approaches have allowed the PI and research team to efficiently reach more patients while reducing numerous obstacles encountered with methods that require physician time and clinic resources (e.g., space).

Compensation: Patient advisors will be compensated $200 quarterly for one year for their participation. Compensation will be in service of patient board members' attendance at in approximately bi-monthly, 1-hour advisory board meetings, preparation time to review materials prior to and following each meeting, and travel to and from meetings, if held in-person (potential total compensation=$800).

User Testers

Subject Recruitment: The research team will recruit 10 user testers using the same direct-to-patient recruitment method that has been successful in PI's F32 project with the same patient population. This includes using DEDUCE and PACE (Protected Analytics Computing Environment) software to identify patients who meet initial eligibility criteria. Under a HIPAA waiver, study staff will query for patients that meet study eligibility criteria, then screen the Duke electronic medical record (EMR) to identify potentially eligible patients on a weekly basis. After a careful chart review to verify initial eligibility (e.g., age $\geq$18 years, diagnosis is metastatic non-small cell lung cancer, receiving treatment with non-curative intent), study staff will mail or email a recruitment letter to potential participants. The letter will state that the patient may be eligible to participate in a research study evaluating a skills training intervention (i.e., LiveWell) for patients with advanced lung cancer. The letter includes a number to call if the patient is interested in learning more about the study (or would like to opt out) and explains that a study staff member will contact them about the study. Patients may also be referred to the study by their medical providers. The medical team will introduce the study, and, if interested, the PI or a study staff member will contact the patient to further describe the study and discuss questions and/or concerns.
Patients will be contacted by highly trained study staff to assess interest. All patients who meet initial eligibility criteria will be contacted unless they opt out. Consistent with Duke's direct-to-patient recruitment guidelines, patients will be contacted a maximum of three times. These contact attempts include telephone calls (using an IRB-approved telephone script), recruitment emails (using an IRB-approved email template), and/or in-person visits to the outpatient thoracic oncology clinic(s). If a patient is interested when contact is made with a study team member, they will be provided with information about the study, including the purpose, requirements, and time commitment. Interested patients will complete a brief screening interview (e.g., NCCN distress rating), either via phone, Zoom, or in person (based on patient preference) to confirm full eligibility. Those who do not pass the screening interview will be provided with a list of free resources available through the institution (e.g., individual and couple counseling through the Duke Cancer Patient Support Program, financial support). Eligible patients who wish to enroll in the study will complete an electronic consent form via REDCap or, if preferred, be mailed a hard copy consent form to be reviewed by telephone, executed, and returned by mail. Consent procedures may also be completed in-person at the cancer center. In-person visits will be scheduled at a time that is convenient for the patient. In all cases, a member of the study team will review consent in a private space and answer any questions that the potential participant may have. Informed consent will be documented by signature on an IRB-approved consent form. Remote, direct-to-patient recruitment approaches have allowed the PI and research team to efficiently reach more patients while reducing numerous obstacles encountered with methods that require physician time and clinic resources (e.g., space).

Compensation: User testers participants will be compensated $40 for each self-report assessment and $30 for the exit interview (potential total compensation=$40 baseline assessment, $40 post-intervention assessment, $30 exit interview=$110).

Consent Process

- Complete the consent section in the iRIS Submission Form.

Subject's Capacity to Give Legally Effective Consent

- If subjects who do not have the capacity to give legally effective consent are included, describe how diminished capacity will be assessed. Will a periodic reassessment occur? If so, when? Will the subject be consented if the decisional capacity improves?

Cognitive impairment will be assessed via medical record review, or by a baseline Folstein Mini-Mental Status Examination of <25. If patient is cognitively impaired, they will be excluded from the study per study protocol.

Study Interventions

- If not already presented in the Design & Procedures section, describe study-related treatment or use of an investigational drug or biologic (with dosages), or device, or use of another form of intervention (i. e., either physical procedures or manipulation of the subject or the subject's environment) for research purposes.

The LiveWell Intervention and procedures that will be used to refine the intervention are described above.

Risk/Benefit Assessment

- Include a thorough description of how risks and discomforts will be minimized (per 45 CFR 46.111(a) (1 and 2)). Consider physical, psychological, legal, economic and social risks as applicable. If vulnerable populations are to be included (such as children, pregnant individuals, imprisoned persons or cognitively impaired adults), what special precautions will be used to minimize risks to these subjects? Also identify what available alternatives the person has if he/she chooses not to participate in the study. Describe the possible benefits to the subject. What is the importance of the knowledge expected to result from the research?

No adverse events are anticipated. Study participation is voluntary and participants can withdraw at any time. The risks associated with this study are minimal and rare. The potential risks are associated with (1) confidentiality related to videoconferencing, and self-report data; and (2) emotional upset due to questioning about thoughts, feelings, and personal history of cancer when completing intervention sessions and assessments.

First, breach of confidentiality is a possible risk. This will be clearly stated in the consent form. All efforts will be made for confidentiality to be maintained by using study ID numbers to identify participants' research records participant names to study ID numbers will be stored separately from data and research records in a password- protected database. All paper research records (e.g., paper consent and assessment documents) will be kept in a locked file cabinet in the PI's locked office in the PPTRP laboratory housed within the Department of Psychiatry and Behavioral Sciences' Clinical Research Facility at the Duke North Pavilion (2400 Pratt Street, 7th Floor, Durham, NC, 27705). There is some risk of loss of confidentiality inherent to the use of videoconferencing to conduct the study intervention sessions. To protect patient privacy, we will use Zoom videoconferencing, which has standard internationally-recognized and accepted encryption algorithms. Only approved research team members will have access to the research records. All research team members will be required to complete the DUMC IRB online training course (i.e., Protecting Research Subjects) as well as human research subjects' protection training and certification through the Collaborative Institutional Training Initiative (CITI) program, both of which address confidentiality.

Two password-protected databases will be used for this study to ensure confidentiality. First, a tracking database will be used for recruitment and follow-up. This database will house information related to tracking the participants in the study, such as phone numbers and addresses. Identifying information will be kept separate from research records. No medically sensitive or outcome data will be stored in this database. This database will also track non-participants (i.e., those who have declined participation) only

to the bare minimum to ensure that they are not contacted again about participation. At the end of the study, all identifiable data of non-participants will be deleted. Tracking data on participants will be retained for the usual required period. Second, all study data (i.e., self-report assessment data) will be stored in a separate password-protected REDCap database without any personal identifiers. Data in this database will be derived from patients' direct input into the electronic patient reported outcomes system which is an online survey system; data entered into this system is stored on a secure server housed behind the DUMC firewall. Only a unique study ID number will link the electronic data to the study data file. The tracking data and study data will be stored in a file on a secure DUMC Psychiatry server which can only be accessed by research team members. Access to the Duke network requires a password-protected, 128-bit encrypted virtual private network connection provided by Cisco systems.

Second, participants will be asked about their thoughts and feelings regarding cancer diagnosis, treatment, and symptoms; thus, it is possible they may experience psychological distress. The psychological risk associated with answering questions is expected to be minimal. Although some participants may find certain questions or topics to be upsetting, heightened awareness of psychosocial needs may be the first step in resolving these concerns. If a participant reports significant distress during study participation, the research team will consult with the PI, who is a licensed clinical psychologist. If the participant requires additional treatment outside the context of the study, the PI will work with the mentoring team to initiate an appropriate referral. Patients with cancer often report benefits from participating in psychosocial research. Thus, the risk of psychological distress is minimal and these safeguards should be adequate. The benefits to society could include increased knowledge of skill-based strategies that can help to meet the needs of lung cancer metavivors.

Costs to the Subject

- Describe and justify any costs that the subject will incur as a result of participation; ordinarily, subjects should not be expected to pay for research without receiving direct benefit.

Patient advisory board members may incur costs from traveling to and from any meetings that are held in-person. It is estimated that the majority of meetings will be held virtually, with a potential for 1-2 meetings in-person. Patient advisors will receive quarterly compensation that would cover such costs plus their time.
There is no cost to the user testers.

Data Management, Analysis and Statistical Considerations

- Describe endpoints and power calculations. Provide a detailed description of how study data will be analyzed, including statistical methods used, and how ineligible subjects will be handled and which subjects will be included for analysis. Include planned sample size justification. Provide estimated time to target accrual and accrual rate. Describe interim analysis including plans to stop accrual during monitoring. Phase I studies, include dose escalation schema and criteria for dose escalation with definition of MTD and DLT.
- **For external collaborators/personnel** who are NOT ENGAGED in the research but are handling de-identified or a limited data set of **Duke** data, include their name, role and a description of the data.

Data Collection.
Quantitative Data: User testers with complete assessments at baseline and post-treatment and provide feedback on questionnaire length and acceptability. User tester survey data is being collected to evaluate the assessment process and no formal statistical analysis will be done with this outcome data. User testers will also provide Likert scale ratings (1-5) to assess intervention content relevance and enjoyableness, following each session and at intervention completion. This data will be summarized using descriptive statistics (means, frequencies) and presented to the advisory board to guide refinement.
Qualitative Data: User testers will participate in in-depth interviews to obtain feedback on the LiveWell protocol and procedures (e.g., intervention content, presentation). Interviews will be audio recorded and transcribed verbatim. Rapid analysis will be used to analyze qualitative interview data from user testers. Findings from rapid analysis will be summarized and used by the PI and advisory board to guide iterative intervention refinement.

Data Management. Participant identifying information will be stored in a secure study database. It will not be stored with questionnaire or interview data to protect patient confidentiality. External collaborator (and prior study PI) Kelly Hyland will have access to non-identifiable research data in order to collaborate

as a contributing author on papers and presentations. This non-identifiable data will be shared with Kelly Hyland through Duke Box. No data will be shared outside of Duke until any and all necessary agreements are fully executed.

Statistical Considerations. Literature suggests that 85% of usability problems can be reliably identified in 5 user testers. However, iterative user testing may require more testers, and if conducting research at multiple sites, it can be beneficial to conduct testing with 3-5 people per site. Given this, we will use 10 user testers. Given this, we will recruit 10 user testers over 4 months.

Analytic Approach. We will use several metrics to signal completion of Aim 1, and readiness to progress to the next phase (R00 study). Recurrent themes identified in user tester exit interviews will inform adjustments to LiveWell content and procedures. Quantitative data will include Likert scale ratings of feasibility, acceptability, and enjoyableness of the LiveWell intervention and procedures. This information will be reviewed in consultation with the advisory board and adjustments will be made accordingly. Potential adjustments include: updates to recruitment or other operating procedures, changes in the self-report battery based on user tester feedback (e.g., relevance, length), and changes in intervention delivery (e.g., session length, content). We will iteratively refine the LiveWell protocol and procedures until unanimously approved by the advisory board. The data collected in Aim 1 does not meet the NIH definition of "scientific data" and is considered preliminary.

Data & Safety Monitoring

- Summarize safety concerns, and describe the methods to monitor research subjects and their data to ensure their safety, including who will monitor the data, and the frequency of such monitoring. If a data monitoring committee will be used, describe its operation, including stopping rules and frequency of review, and if it is independent of the sponsor (per 45 CFR 46.111(a) (6)).

The proposed study carries minimal risk. There are not physical or side effects involved in taking part in this study. The protocol does not use an investigational drug, procedure, or device.

Data obtained from participants will include information from medical chart review and self-report measures. The PI (Dr. Somers), mentors (Drs. Neasciu and Zullig, co-mentors), and collaborators (Drs. Stinchcombe, Samsa) consider the secure and ethical management of participant information and data as a key priority. Best practices for data management and confidentiality will be observed.

All participants enrolled in the study will continue to receive their usual medical care during the course of the study and be informed that choosing to participate in the study will in no way impact the medical treatment they receive at the Duke University Medical Center (DUMC). All enrolled participants will continue to be monitored by their physicians at the Duke Cancer Institute (DCI) throughout the duration of the proposed study; thus participants' physicians (e.g., oncologists) will provide usual and ongoing monitoring of their overall medical status. If a health concern is identified during contact with study staff, the participants' treating oncologist will be contacted, and appropriate referrals for medical treatment will be provided to participants. All research personnel who have direct contact with participants will be trained to observe and report any adverse events. The PI will report any adverse event to DUMC Institutional Review Board (IRB) in real time. An adverse event is defined as *any untoward medical event occurring during the clinical evaluation, which is causally related to the study protocol*. A serious adverse event is defined as *any event which results in death, is immediately life threatening, results in persistent or significant disability/incapacity, results in patient hospitalization, or is serious for any other reason representing significant hazard*.

Potential Risks: Risks associated with the proposed study are minimal and rare. Psychological risks include anxiety or distress due to questioning about thoughts, feelings, and personal/family history of cancer. There is the possibility of a breach of confidentiality due to the use of mailing of information and technology. The consent form will address this possibility. All efforts will be made for confidentiality to be maintained by using case numbers to identify participants' research records and by having a limited number of individuals with access to identifying information. Identifying information will be kept separate from research records. All research records will be kept in a locked file cabinet and password protected computer files. Only the PI
and other trained staff will have access to the research records. To ensure that there are no changes in potential risk during the course of the study and that confidentiality is maintained the PI and sponsors will implement a Data and Safety Monitoring Plan.

Data and Safety Monitoring: We will appoint two data safety officers. One data safety officer will be a physician (i.e., MD) who is not associated with the study. The appointed MD data safety officer will have thorough experience with clinical trial research and an advanced understanding of adverse events and their reporting. The other data safety officer will be a senior investigator (i.e. PhD) who has experience

with clinical trial research and expertise in behavioral oncology research. Responsibilities of the data safety offers will include: 1) attend an annual Data and Safety Monitoring Meeting convened by the PI; 2) become familiar with the research protocol and plans for data and safety monitoring; 3) review accrual, attrition, adverse events, and protocol compliance; 4) review major proposed modifications to the study prior to their implementation (e.g., termination, significantly altering a study arm, etc.); and 5) provide relevant recommendations related to continuing, changing, or terminating the study. All adverse events will be reported to IRB and data safety officers in real time. Given the low risk nature of the study, the data and safety monitoring committee will convene at least annually.

Protection Against Risk: All data will be stored on a secure server with multiple backups created regularly. All interactions with study participants will be under the direction of three licensed clinical psychologists including Dr. Hyland (PI), Dr. Somers, and Dr. Neacsiu. Audio recordings of intervention sessions with participants will be obtained and reviewed to ensure fidelity of intervention delivery and that the interventionists are providing effective, ethical treatment. As a licensed and practicing clinical psychologist, the PI has experience with distressed patients with chronic disease. If a participant shows signs of experiencing high levels of physical or emotional distress that need to be addressed outside the context of this trial, the PI will work directly with the participant to move forward in a way that is in the participant's best interest. No participant will be kept in the trial if they are experiencing increased, extreme distress that requires a higher level of clinical management. Study staff will be carefully trained to monitor participants' psychological status and will report to the PI when increased emotional distress is identified. The PI will work directly with the Cancer Patient Support Program at the DCI to place appropriate referrals for participants reporting increased emotional distress. Drs. Hyland and Somers are integrated into the Cancer Patient Support Program at the DCI and have experience referring cancer patients who are distressed to appropriate psychosocial or psychiatric care within this large team of mental health professionals (e.g., medical family therapists, social workers, psychiatrists, psychologists). They will utilize these valuable resources when making referrals for distressed participants in this study.

There is the possibility of a breach of confidentiality. The consent form will address this possibility. All efforts will be made for confidentiality to be maintained by using case numbers to identify participants' research records and by having a limited number of individuals who have access to identifying information. Identifying information will be kept separate from research records. All research records will be kept in a locked file cabinet and password protected computer files. Only the PI and other trained research staff will have access to the research records. The PI has completed Duke University Health System Institutional Review Board's online training course: Protecting Research Subjects, which addresses confidentiality. All other individuals involved in this study will be required to complete this course and ongoing training.

Privacy, Data Storage & Confidentiality

- Complete the Privacy and Confidentiality section of the iRIS submission form.