Document Coversheet

Study Title: Piloting Pathways, a Hope-enhancing Intervention to Address Activity and Role Function in Metastatic Lung Cancer Patients

Institution/Site:	University of Kentucky
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KEY INFORMATION FOR PILOTING PATHWAYS

We are asking you to choose whether to volunteer for a research study. This study involves completing a couple of brief surveys and participating in a program called Pathways. Pathways is a brief program to help lung cancer patients think about what areas of life matter most to them and to set and pursue goals and activities related to those areas. We are asking you because you are receiving treatment for lung cancer. This gives you key information to help you decide whether to participate. We have included detailed information after this page. Ask the research team questions. If you have questions later, the contact information for the researcher in charge of the study is below.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

We have developed a new program for lung cancer patients called Pathways. We now want to evaluate the program and get feedback on how to improve it prior to offering it others. By doing this study, we hope to learn if the Pathways program is acceptable to patients and can be carried out in clinic. Your participation in this research will last about 4-5 hours total over the course of roughly 6-8 weeks.

Pathways involves:

- 5 “appointments” with a nurse or other healthcare professional: 2 face-to-face appointments when you are at the hospital for cancer treatment (can be done remotely) and 2-3 phone calls to check in
- Face-to-face appointments may take 30 minutes to an hour. Phone calls may take 15-20 minutes.

Surveys and Interview involve:

- Survey: Answering questions about your quality of life, sociodemographics (e.g. income), personality, and experiences with lung cancer and the Pathways program (1 survey before you start Pathways, 1 survey after; ~ 30 minutes each; a brief (~5 minute) phone survey one week into Pathways to ask about your first appointment)
- Interview: Talking with study team member about what you liked and did not like about Pathways and ways we could improve it (can be done in person or over the phone; ~ 15 minutes)

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

You might volunteer to contribute to knowledge that could help other people going through lung cancer in the future.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

You might choose not to volunteer for this study if you think answering survey questions or talking with a nurse about what areas of daily life matter most to you and/or setting goals for those areas of life would be upsetting. For a complete description of risks, refer to the Detailed Consent. If you choose not to participate, you can could access other supportive services. For a complete description of alternate treatment/procedures, refer to the Detailed Consent.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study contact Laurie McLouth, PhD of the University of Kentucky, Department of Behavioral Science at 859-562-2526 or laurie.mclouth@uky.edu. If you have any concerns or questions about your rights as a volunteer in this research, contact staff in the University of Kentucky (UK) Office of Research Integrity (ORI) between the business hours of 8am and 5pm EST, Monday-Friday at 859-257-9428 or toll free at 1-866-400-9428.

DETAILED CONSENT (PILOTING PATHWAYS):

ARE THERE REASONS WHY YOU WOULD NOT QUALIFY FOR THIS STUDY?

You will not quality for this study if you are under 18 years of age.

WHERE WILL THE STUDY TAKE PLACE AND WHAT IS THE TOTAL AMOUNT OF TIME INVOLVED?

The research procedures will be conducted at the Markey Cancer Center/UK Chandler Hospital. You will need to come 2-3 times during the study and complete 2-3 phone sessions as part of the program. In-person visits will take about 30 minutes to an hour. Phone sessions will take about 15-20 minutes. The total amount of time you will be asked to volunteer for this study is 4-5 hours over the next 6-8 weeks.

WHAT WILL YOU BE ASKED TO DO?

Participating in this study involves filling out 2 surveys, participating in a program we have developed for lung cancer patients (described below), and completing a brief interview to give feedback on the program.

This study involves a pilot test of a program we have developed for lung cancer patients. The program is called Pathways.

Pathways involves:

- 5 appointments with a nurse or other healthcare professional: 2 face-to-face appointments when you are at the hospital for cancer treatment (can be done remotely, if needed. For example: phone or video technology) and 2-3 phone calls to check in
- Face-to-face appointments may take 30 minutes to an hour. Phone calls may take 15-20 minutes.
- During face-to-face appointments, we will work with you to identify what matters most to you, goals that fit with your priorities, and ways to work on those goals.
- During phone calls, we will check in with you on the progress you are making on your goals and problem-solve with you about any obstacles to them.

To help us test Pathways, you will be asked to complete an initial survey before you enroll in Pathways. This survey will ask you about your quality of life, personality, and experiences with lung cancer. It should take about 30 minutes to complete. You will be paid for completing it. You will complete a brief (~5 minute) set of questions about a week after your first Pathways appointment to ask how that appointment went. You will complete a survey after you complete Pathways. It will ask many of the same questions as the initial survey and will also ask a few questions about your experience with Pathways. You will be paid for completing it. Finally, you will be asked to complete a brief interview with a study team member to talk more about what you liked and did not like about the Pathways program. This interview should take no longer than 15 minutes. You will be paid for completing it.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

The risk of harm or discomfort that may happen as a result of taking part in this research study is not expected to be more than in daily life or from routine physical or psychological examinations or tests. There is some risk that answering some of the survey questions may be upsetting or that you may become bored answering questions. This happens occasionally. For example, some of the survey questions will ask you about your physical limitations and how others have treated you since being diagnosed with lung cancer. Sometimes questions are asked in different ways, which can be boring and/or frustrating. You can choose not to answer any question that you do not wish to. There is also some risk that you may become upset while talking with the study nurse about your goals, particularly if you are having trouble with a goal. This rarely happens, but if it does, the study nurse will talk with you about it and work with you to develop a plan to manage it. Finally, there is some risk for loss of privacy and confidentiality. Because the nurse may be meeting with you in clinic, it may be difficult to maintain a high level of privacy. You should let the study team know if you are ever uncomfortable discussing anything about the study in your current environment. We will make every effort to keep all of your information confidential. The situations where we are unable to maintain confidentiality are described in detail below. If we have any safety concerns about your or someone else, we will prioritize safety, which may involve sharing your information.

In addition to risks described in this consent, you may experience a previously unknown risk or side effect.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

We do not know if you will get any benefit from taking part in this study. However, some people may find the program helpful or feel positive about participating. Information learned from this study may help others with your condition.

IF YOU DON'T WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?

If you do not want to take part in the study, there are other choices such as seeking existing supportive oncology services at the Markey Cancer Center.

WHAT WILL IT COST YOU TO PARTICIPATE?

You and/or your insurance company, Medicare, or Medicaid will be responsible for the costs of all care and treatment that you would normally receive for any conditions you may have. These are costs that are considered medically necessary and will be part of the care you receive even if you do not take part in this study.

The University of Kentucky may not be allowed to bill your insurance company, Medicare, or Medicaid for the medical procedures done strictly for research.

Therefore, these costs:

- will be your responsibility;
- may be paid by your insurer if you are insured by a health insurance company (you should ask your insurer if you have any questions regarding your insurer's willingness to pay these costs);

- may be paid by Medicare or Medicaid if you are covered by Medicare or Medicaid. (If you have any questions regarding Medicare/Medicaid coverage you should contact Medicare by calling 1-800-Medicare (1-800-633-4227) or Medicaid at 1-800-635-2570.)

Your insurer, Medicare, or Medicaid, may agree to pay for the costs. However, a co-payment or deductible may be needed from you. The amount of this co-payment or deductible may be costly.

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

When we write about or share the results from the study, we will write about the combined information. We will keep your name and other identifying information private.

We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information, or what that information is. We will not include your name or medical record number on surveys you complete or audio recordings from the program sessions or interviews. We will assign you a unique number to link your survey and audio recordings to you. Only a few study staff will be able to access that link. Your unique number will appear on your surveys. All hard copies of files will be stored in locked files in secure buildings. All electronic copies of files will be protected by the UK firewall. Only a few study staff will be able to access files.

You should know that in some cases we may have to show your information to other people. For example, the law may require us to share your information with a court or agencies, if you have a reportable disease/condition; or authorities, if you report information about a child or elder being abused; or if you pose a danger to yourself or someone else. To ensure the study is conducted properly, officials of the University of Kentucky and National Cancer Institute the University of Kentucky, and may look at or copy pertinent portions of records that identify you.

We will make every effort to safeguard your data, but as with anything online, we cannot guarantee the security of data obtained by way of the Internet. Third-party applications used in this study may have Terms of Service and Privacy policies outside of the control of the University of Kentucky.

REDCap is a secure, web-based program to capture and store data at the University of Kentucky. We will make every effort to safeguard your data in REDCap. However, given the nature of online surveys, we cannot guarantee the security of data obtained by way of the Internet.

CAN YOU CHOOSE TO WITHDRAW FROM THE STUDY EARLY?

You can choose to leave the study at any time. You will not be treated differently if you decide to stop taking part in the study.

If you choose to leave the study early, data collected until that point will remain in the study database and may not be removed.

The investigators conducting the study may need to remove you from the study. You may be removed from the study if:

- you are not able to follow the directions,
- we find that your participation in the study is more risk than benefit to you, or
- the agency paying for the study chooses to stop the study early for a number of scientific reasons.

The study intervention will no longer be provided to you and may not be available for purchase. This may occur for a number of reasons.

ARE YOU PARTICIPATING, OR CAN YOU PARTICIPATE, IN ANOTHER RESEARCH STUDY AT THE SAME TIME AS PARTICIPATING IN THIS ONE?

You may take part in this study if you are currently involved in another research study as long as it does not overlap with this study. For example, you can be on a cancer treatment trial and on this study at the same time. It is important to let us know if you are in another research study. You should discuss this with us and your doctor before you agree to participate in another research study while you are in this study.

WHAT HAPPENS IF YOU GET HURT OR SICK DURING THE STUDY?

If you believe you are hurt or if you get sick because of something that is due to the study, you should first seek appropriate medical care and then call Laurie McLouth, PhD, at 859-562-2526 immediately.

It is important for you to understand that the University of Kentucky does not have funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. Also, the University of Kentucky will not pay for any wages you may lose if you are harmed by this study.

Medical costs related to your care and treatment because of study-related harm

- will be your responsibility;
- may be paid by your insurer if you are insured by a health insurance company (you should ask your insurer if you have any questions regarding your insurer's willingness to pay under these circumstances);
- may be paid by Medicare or Medicaid if you are covered by Medicare or Medicaid (If you have any questions regarding Medicare/Medicaid coverage you should contact Medicare by calling 1-800-Medicare (1-800-633-4227) or Medicaid 1-800-635-2570.).

A co-payment/deductible may be needed by your insurer or Medicare/Medicaid even if your insurer or Medicare/Medicaid has agreed to pay the costs. The amount of this co-payment/deductible may be costly.

You do not give up your legal rights by signing this form.

WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THIS STUDY?

You will receive up to $60 ($20 for the initial survey, $30 for the post-survey, and $10 for the interview at the end of the program) for taking part in this study. You will be receiving this compensation as a gift card. You will be paid for each assessment after you complete it.

With a few exceptions, study payments are considered taxable income reportable to the Internal Revenue Service (IRS). A form 1099 will be sent to you if your total payments for research participation are $600 or more in a calendar year.

WHAT IF NEW INFORMATION IS LEARNED DURING THE STUDY THAT MIGHT AFFECT YOUR DECISION TO PARTICIPATE?

We will tell you if we learn new information that could change your mind about staying in the study. We may ask you to sign a new consent form if the information is provided to you after you have joined the study.

WILL YOU BE GIVEN INDIVIDUAL RESULTS FROM THE RESEARCH TESTS?

Generally, tests done for research purposes are not meant to provide clinical information. We will not provide you with individual research results.

WILL WE CONTACT YOU WITH INFORMATION ABOUT PARTICIPATING IN FUTURE STUDIES?

The research staff would like to contact you in the future with information about participating in additional studies. If so, it will be limited to 2 times per year.

Do you give your permission to be contacted in the future by Dr. Laurie McLouth regarding your willingness to participate in future research studies?

Yes **No** **Initials_____**

WHAT ELSE DO YOU NEED TO KNOW?

If you volunteer to take part in this study, you will be one of about 55 people to do so.

The National Cancer Institute and UK Markey Cancer Center is providing financial support for this study.

A description of this clinical trial will be available on ClinicalTrials.gov as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

WILL YOUR INFORMATION) BE USED FOR FUTURE RESEARCH?

All identifiable information (e.g., your name, medical record number, or date of birth) will be removed from the information or samples collected in this study. After we remove all identifiers, the information may be used for future research or shared with other researchers without your additional informed consent.

STORING AND SHARING YOUR INFORMATION FOR FUTURE USE:

We would like to store, use, and share your survey data, data obtained from the electronic health record as part of this study, and recordings from your exit interview and Pathways sessions for future research. Having information from many people helps researchers identify trends and discover better ways to diagnose, prevent, and treat many conditions. Researchers can use the stored information to learn more about cancer or research additional scientific questions.

We also would like to have permission to look at your medical records from the time you were diagnosed with lung cancer until at most 12-months after you complete this study. We would collect general information related to your health such as test results, treatments, and doctor's notes. The confidentiality section below provides details about how we will keep your information private.

WHERE WILL INFORMATION BE STORED AND FOR HOW LONG?

The information will be stored at the University of Kentucky Healthy Research Building for no longer than 6 years after study completion.

ARE THERE RISKS FROM ALLOWING YOUR INFORMATION TO BE STORED FOR FUTURE RESEARCH?

There is a risk that someone could get access to the stored information or samples. In spite of the security measures and safeguards we will use, we cannot guarantee that your identity will never become known.

There may be risks that at this time are unknown. As technology advances, there may be new ways of linking information back to you that we cannot foresee now.

HOW WILL YOUR PRIVACY AND CONFIDENTIALITY BE PROTECTED?

We will take careful steps to keep your information confidential.

We will remove your name or other direct identifiers from your information. We will label your information with a code and will store the key separately from the master code list. Only select staff will have access to the list that links the code to you.

We will store hard copies of study materials in a locked filing cabinet in a secure building. These files will only be accessible by designated study staff. We will store your identifiable information, in a password protected database and/or encrypted files. Your audio files from the exit interview and Pathways session recordings will be stored on a computer network with a firewall. These audio files will be labeled with your study code, not your name or other identifying information. Only designated study staff will have access to these files.

The staff follow procedures to protect your identity to the extent allowed by law. In very unusual cases, staff may be required to release your identifiable medical and research information in response to an order from a court of law. Officials of the National Cancer Institute and the University of Kentucky may look at or copy pertinent portions of records that identify you.

HOW WILL WE SHARE YOUR INFORMATION WITH OTHER RESEARCHERS?

The researchers requesting access to information must complete an application process and sign an agreement to obtain any information. The researchers who receive your information will sign an agreement to use the data responsibly.

Before sharing your information, we will remove identifiers such as (e.g., your name, medical record number, or date of birth). Your de-identified information may be shared with other University of Kentucky (UK) researchers and researchers outside of UK, without your additional informed consent. We will use software to track information shared without releasing your identity.

WHAT IF YOU CHANGE YOUR MIND AND WANT TO WITHDRAW YOUR INFORMATION?

You may withdraw your permission to allow your information or samples to be used for future research. To do so, you must send a written withdraw request to:

Laurie McLouth, PhD
Center for Health Equity Transformation
Suite 371, Health Kentucky Research Building
University of Kentucky
760 Press Avenue
Lexington, KY 40508-0679

We will destroy any remaining information that has been stored. In addition, it may be possible to destroy the code that links you with your information. However, we cannot withdraw the information that has already been used.

WILL YOU RECEIVE ANY COMMERCIAL PROFIT FROM FUTURE RESEARCH DISCOVERIES?

The information and samples that you provide will no longer belong to you. The research may lead to new medical knowledge, tests, treatments, or products. These products could have some financial value. There are no plans to provide financial payment to you or your relatives should this occur.

WILL YOU BE GIVEN INDIVIDUAL RESULTS FROM THE FUTURE RESEARCH TESTS?

Tests done for research purposes are not meant to provide clinical information or help care for you. The results are only important for research. Therefore, the results of tests done with your information will not be provided to you. In the rare event that a finding might affect the health of you or your family, we will contact you and you can choose whether to receive or refuse the information.

OPTIONAL FUTURE USE: Do you give permission for Laurie McLouth, PhD to store your survey data, data obtained from the electronic health record as part of this study, and recordings from your exit interview and Pathways sessions for future research? Yes No Initials _____

Remember, you can still be in the main study even if you even if you do not wish to allow your information and/or specimens stored for this investigator's future research.

AUTHORIZATION TO USE OR DISCLOSE YOUR INDENTIFIABLE HEALTH INFORMATION

The privacy law, HIPAA (Health Insurance Portability and Accountability Act), requires researchers to protect your health information. The following sections of the form describe how researchers may use your health information.

Your health information that may be accessed, used and/or released includes:

- Name, address, and medical record number
- age
- gender
- racial and ethnic data
- zip code
- lung cancer diagnosis
- date started lung cancer treatment
- comorbidities (other health conditions)
- type of cancer treatments received and dates received
- types of other services received for cancer care and dates received
- response to cancer treatment
- dates of hospitalizations and reasons hospitalized
- referrals to services for cancer care
- documentation of advance care planning
- date of death, place of death (hospital, home)

The Researchers may use and share your health information with:

- The University of Kentucky's Institutional Review Board/Office of Research Integrity;
- Law enforcement agencies when required by law;
- University of Kentucky representatives;
- UK Hospital
- Center for Clinical and Translational Science (CCTS)
- National Cancer Institute (NCI) who is sponsoring this study
- Your oncologist, if in the course of the project we learn of a medical matter that needs immediate attention

The researchers agree to only share your health information with the people listed in this document.

Should your health information be released to anyone that is not regulated by the privacy law, your health information may be shared with others without your permission; however, the use of your health information would still be regulated by applicable federal and state laws.

You may not be allowed to participate in the research study if you do not sign this form. If you decide not to sign this form, it will not affect your:

- Current or future healthcare at the University of Kentucky;
- Current or future payments to the University of Kentucky;
- Ability to enroll in any health plans (if applicable); or
- Eligibility for benefits (if applicable).

After signing the form, you can change your mind and NOT let the researcher(s) collect or release your health information (revoke the Authorization). If you revoke the authorization:

- Send a written letter to Dr. McLouth at the address below to inform her of your decision.

  Laurie McLouth, PhD
  Center for Health Equity Transformation
  Suite 371, Health Kentucky Research Building
  University of Kentucky
  760 Press Avenue
  Lexington, KY 40508-0679

- Researchers may use and release your health information **already** collected for this research study.
- Your protected health information may still be used and released should you have a bad reaction (adverse event).

The use and sharing of your information has no time limit.

If you have not already received a copy of the Privacy Notice, you may request one. If you have any questions about your privacy rights, you should contact the University of Kentucky's Privacy Officer between the business hours of 8am and 5pm EST, Monday-Friday at (859) 323-1184.

AUDIORECORDING

As part of this research study, your individual sessions with the study nurse and the interview at the end of the study will be audio recorded. The purpose of audio recording the individual sessions with the study nurse is to monitor the sessions for quality. Only the PI and other supervisory team members will review those audio files. If you have a family member or friend present with you during the sessions, their voices will be on the audio file. You will not have access to the individual session recordings.

The interview at the end of the study where you give feedback on the program may be transcribed (typed out word for word). This is being done to make sure that the conversation you have with the interviewer is captured accurately. You may request the recording be stopped at any time during the interview. If you have a friend or family member present with you during the interview and they participate, their feedback will be included. Once the interviews are transcribed, the study team will clean them to remove any instances where your name or other identifying information is used. You

should understand that you will not be able to inspect, review, or approve the audiotapes before they are used in this study.

You can also withdraw your consent to use and disclose the audiotape before it is used. If you choose to withdraw your consent for the audiotapes:

- Send a written letter to Dr. McLouth at the address below to inform her of your decision.

  Laurie McLouth, PhD
  Center for Health Equity Transformation
  Suite 371, Health Kentucky Research Building
  University of Kentucky
  760 Press Avenue
  Lexington, KY 40508-0679

INFORMED CONSENT SIGNATURES

This consent includes the following:

- Key Information Page
- Detailed Consent

You will receive a copy of this consent form after it has been signed.

_____ **Signature of research subject**	_____ **Date**
_____ **Printed name of research subject**	
_____ **Signature of person obtaining informed consent**	_____ **Date**
_____ Printed name of [authorized] person obtaining informed consent and HIPAA authorization	_____ Date

Piloting Pathways, a Hope-enhancing Intervention to Address Activity and Role Function in Metastatic Lung Cancer Patients

Grant Title: Piloting Pathways, a Hope-enhancing Intervention to Address Activity and Role Function in Metastatic Lung Cancer Patients

Grant Number: 1R03CA235171-01A1

Funded by: National Cancer Institute

Protocol Number: 52168

National Clinical Trial (NCT) Identified Number: NCT04161157

Principal Investigator: Laurie McLouth, Ph.D.
Assistant Professor
Behavioral Science
University of Kentucky College of Medicine
laurie.mclouth@uky.edu
Phone: 859-562-2526

Version Number: 7

20 Dec 2021

Table of Contents

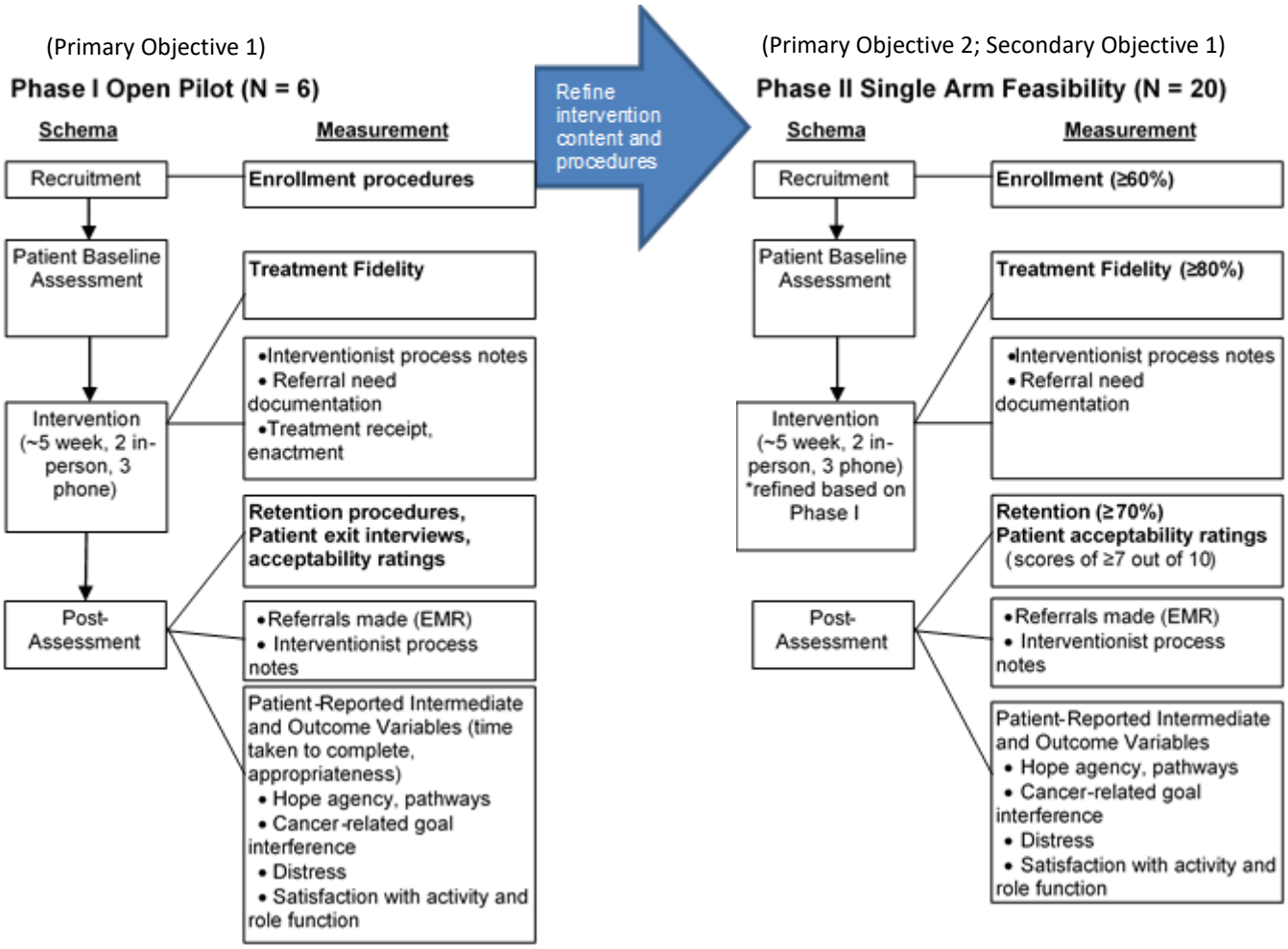
1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title:	Piloting Pathways, a Hope-enhancing Intervention to Address Activity and Role Function in Metastatic Lung Cancer Patients
Grant Number:	1R03CA235171-01A1
Principal Investigator:	Laurie McLouth, PhD Assistant Professor, Behavioral Science
Study Description and Objectives:	This is a Stage I, single-site trial to refine and then test the feasibility and acceptability of a novel intervention, Pathways. Primary Objectives 1. To refine the Pathways intervention and study protocol based on acceptability feedback from an open pilot study (i.e., fully implement the intervention) with patient exit interviews (n = 6). We will use feedback on the acceptability of session content, length, and delivery, and review intervention session recordings to refine the intervention. If necessary, we will refine the procedures for enrollment and retention. 2. To determine Pathways intervention feasibility in a single-arm pilot study (n = 55 Pathways). Feasibility will be defined by enrollment (≥60%; primary feasibility outcome), retention (≥70%), adherence (≥70% of patients completing 3 of 5 sessions), and mean acceptability ratings (scores of ≥7 out of 10 on intervention relevance, helpfulness, and convenience). Secondary Objective 1. To assess preliminary data on intermediate and outcome variables and clinical utility in the single-arm pilot of Pathways. We will assess pre (baseline) to post (~8 weeks after baseline) changes in intermediate (e.g., hope) and outcome (primary: activity and role function) variables related to a future efficacy trial.
Endpoint:	Feasibility, primary endpoint defined as ≥60% eligible and approached patients enrolled
Study Population:	61 (n = 6, Phase I; n = 55, Phase II) patients receiving infusion-based systemic therapy for stage III, IV non-small cell lung cancer, extensive stage small cell lung cancer, 3-12 weeks into tx, ECOG 0-2
Stage:	Stage I (Pilot – Refining and Feasibility testing)
Facilities Enrolling:	UK Markey Cancer Center

Description of Study Intervention:	5-session, supportive care intervention designed to coincide roughly with infusion schedules (2 in-person sessions, 3 phone sessions), delivered 1:1, supporting materials (handouts)
Study Duration:	18 months
Participant Duration:	4.5 hours over ~6-8 weeks

1.2 SCHEMA


(Primary Objective 1)
Phase I Open Pilot (N = 6)
Schema
Measurement
Recruitment
Enrollment procedures
Patient Baseline Assessment
Treatment Fidelity
Intervention (~5 week, 2 in-person, 3 phone)
•Interventionist process notes
• Referral need documentation
•Treatment receipt, enactment
Retention procedures, Patient exit interviews, acceptability ratings
Post-Assessment
•Referrals made (EMR)
• Interventionist process notes
Patient-Reported Intermediate and Outcome Variables (time taken to complete, appropriateness)
• Hope agency, pathways
• Cancer-related goal interference
• Distress
• Satisfaction with activity and role function
Refine intervention content and procedures
(Primary Objective 2; Secondary Objective 1)
Phase II Single Arm Feasibility (N = 20)
Schema
Measurement
Recruitment
Enrollment (≥60%)
Patient Baseline Assessment
Treatment Fidelity (≥80%)
Intervention (~5 week, 2 in-person, 3 phone) *refined based on Phase I
•Interventionist process notes
• Referral need documentation
Retention (≥70%)
Patient acceptability ratings (scores of ≥7 out of 10)
Post-Assessment
•Referrals made (EMR)
• Interventionist process notes
Patient-Reported Intermediate and Outcome Variables
• Hope agency, pathways
• Cancer-related goal interference
• Distress
• Satisfaction with activity and role function

Schedule of Activities

	Pre-screening (Pre-consent)	Visit 1 day 1 (must be within 21 days of screening)	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Day 360
EHR Review Eligibility	X								
Activities involving patient contact									
Patient refusal form		X							
Informed Consent		X							
Baseline (T0) Patient-reported outcome assessment		X							
Post (T2) Patient-reported outcome assessment								X	
Treatment receipt assessment (T1)				X				X	
Treatment expectancy assessment (T1)				X					
Intervention			X	X	X	X	X		
As needed, patient withdrawal, discontinuation form		X	X	X	X	X	X		
Activities involving research staff (No patient contact)									
Fidelity rating			X	X	X	X	X		
Intervention process notes			X	X	X	X	X		
Treatment enactment assessment			X	X	X	X	X		
EHR review for services used, events								X	X

2 INTRODUCTION

2.1 STUDY RATIONALE

Each year, roughly 130,000 people are diagnosed with advanced stage lung cancer. Despite its high incidence and considerable disease burden, patients with lung cancer are psychosocially underserved, with very few interventions developed to meet their needs and address their concerns. Chief among these concerns for 40-65% of patients is concern about difficulty pursuing activities and roles related to family, social, work, and leisure (i.e., activity and role function). These concerns are associated with significant distress, yet are not a focus of existing lung cancer interventions. Our preliminary work has demonstrated that patients with higher hope, defined as perceiving that one is working towards personal goals, is associated with better function. Hope may be an appropriate intervention target to support function.

Based on patient feedback and preliminary data, we have developed a brief intervention, *Pathways*, to improve activity and role function in patients with metastatic non-small cell lung cancer. We propose to implement *Pathways* and conduct patient interviews to refine materials and procedures (Phase I, n = 6) and test intervention feasibility and acceptability in a single arm trial (Phase II, n = 55). It is critical to establish acceptable materials and feasible procedures before testing efficacy.[1]

Premise: Based on theory and preliminary data, increasing patient hope (i.e., patient perception that they are pursuing their goals and have multiple routes to those goals) through an intervention in primary oncology may be a feasible approach to improve activity and role function.
Impact: This intervention is inherently patient-centered and designed to overcome utilization barriers. It may be generalized to other advanced cancers and sustained beyond research to improve care

2.2 BACKGROUND

Lung cancer patients represent a large and underserved population in high need of supportive care interventions that overcome utilization barriers. Lung cancer has the second highest incidence and highest cancer mortality among men and women in the U.S.[2] Each year, 90,000 people are diagnosed with metastatic non-small cell lung cancer (NSCLC).[2] Lung cancer is associated with high physical and psychosocial morbidities,[3] including poorer physical and role function,[4] higher depression,[5,6] and more unmet supportive care needs compared to other cancers.[7] Lung cancer patients face major barriers (e.g., time constraints, stigma about psychosocial care) to utilizing supportive services,[3,8-10] including stigma related to the disease's poor prognosis and association with smoking.[11-14] Stigma reflects perceived negative appraisal from others, constrained disclosure of diagnosis and concerns, and internalized self-blame, shame, or guilt[11,15] and is associated with depression[15-17] and poorer

social, role, and physical function.[18,19] Despite a clear need, few supportive care interventions have been developed for lung cancer patients.[20-22]

Activity and role function concerns are prevalent, distressing, and not addressed by interventions. Between 40-65% of lung cancer patients report impaired activity and role function (i.e., activities and roles related to family, social, work, and leisure) as an unmet supportive care need.[23-25] The consequences of these concerns are decreased survival and quality of life,[26-28] including depression, loss of life purpose, and perceived burden on others.[29-32] Functional concerns are prominent and distressing to lung cancer patients throughout cancer treatment,[33] yet are under addressed in primary oncology[20,34] and supportive care interventions for lung cancer,[21] which emphasize symptom or distress management.[21,22,35,36] This is a critical time to develop interventions to address functional concerns; metastatic NSCLC patients are living longer with potentially more tolerable side effects due to immunotherapy.[37-42] Our work with patients on immunotherapy suggests activity and role function concerns are still common, as are barriers to utilizing supportive care.[43]

Increasing patient hope is a promising approach to improve activity and role function. Patients with metastatic cancer strive to maintain function in valued activities and roles by setting and pursuing personal goals.[23,44-46] Patient hope, a motivational state that reflects goal-directed determination (i.e., agency) and planning to meet goals (i.e., pathways),[47] directly supports goal setting and pursuit. People with higher hope set more goals and ways to reach them and better attain goals.[48,49] Our work suggests increasing hope may improve activity and role function in lung cancer patients, even in the presence of likely goal obstacles such as symptom burden and stigma.[18] Our work also shows higher hope is related to better function, less depression, and less stigma in metastatic NSCLC (Preliminary Data). A person's level of hope varies,[18,50] does not depend on symptom burden,[18] and can be increased through intervention,[51-53] including brief intervention.[54] Hope interventions have reduced distress in other cancer and non-cancer samples.[51-53]

An intervention in primary oncology that incorporates stigma resources could overcome barriers and increase impact. Hope interventions have not been tested with lung cancer patients. Prior hope-enhancing interventions have used mental health providers, but providers are scarce in areas with high lung cancer incidence (ruralhealthinfo.gov) and not acceptable to many patients.[8] Hope interventions help patients overcome obstacles to goals, which, in lung cancer may include symptom or physical concerns and lung cancer stigma. Therefore, an intervention with symptom and stigma resources delivered in primary oncology is a strong approach. Nurses and other healthcare providers know the symptom and psychosocial concerns patients face,[55] are acceptable to patients (Preliminary Data),[55] and are effective in leading supportive care interventions.[55-63] Embedding the intervention in oncology reduces utilization barriers and may help the oncology team address symptom or physical obstacles to goals that often are not detected.[34,64-66] Finally, addressing stigma as a goal obstacle fills a major intervention gap.[11]

Preliminary Data

Study 1: Daily Diary Study of Lung Cancer Patient Quality of Life during Active Treatment (PI: McLouth). Dr. McLouth (PI) designed and conducted a 21-day daily diary study of hope, stigma,

symptoms, and function in 50 lung cancer patients on chemotherapy or chemoradiotherapy.[18] Nearly all patients consented (90%) and completed daily diaries (90%; M daily diaries = 20, SD =1.3). Patients with higher hope had better function and within-person increases in hope related to function, adjusting for stigma, symptoms, and baseline depression.

Study 2: Cross-Sectional Study of Metastatic NSCLC Patients on Immunotherapy (PI: McLouth; NC Lung Cancer Initiative Grant) supports the significance of the intervention in a contemporary treatment era and the intervention design. Dr. McLouth (PI) designed and conducted a cross-sectional survey purposively sampling 60 stage IV NSCLC patients on immunotherapy in 8 months. This study showed (a) activity and role function concerns remain a top unmet supportive care need (reported by 42% of patients); (b) higher patient hope relates to better role function (r = .43), patient goal progress (r = .43), and less depression (r = -.61) and stigma (r = -.40) (p's <.005); (c) low patient supportive care utilization (<12% had used any service, <2% had seen a mental health provider) and multiple barriers (e.g., time concerns, perceptions about services) to using services.[43]

3 OBJECTIVES

PRIMARY OBJECTIVES OF PHASE I

1. To refine the Pathways intervention and study protocol based on acceptability feedback from an open pilot study (i.e., fully implement the intervention; Phase I) with patient exit interviews (n = 6). We will use feedback on the acceptability of session content, length, and delivery, and review intervention session recordings to refine the intervention. If necessary, we will refine the procedures for enrollment and retention.

PRIMARY OBJECTIVES OF PHASE II

1. To determine Pathways intervention feasibility (Phase II; n = 55 Pathways). Feasibility will be defined by enrollment (≥60%; primary feasibility outcome), retention (≥70%), adherence (≥70% of patients completing 3 of 5 sessions), and mean acceptability ratings (scores of ≥7 out of 10 on intervention relevance, helpfulness, and convenience).

2. To assess preliminary data on intermediate and outcome variables and clinical utility in the single-arm pilot of Pathways (Phase II). We will assess pre (baseline) to post (~8 weeks after baseline) changes in intermediate (e.g., hope) and outcome (primary: activity and role function) variables related to a future efficacy trial. We will also describe the number of referrals to supportive services made based on the Pathways intervention.

4 STUDY DESIGN

4.1 OVERALL DESIGN

This is a Stage I, single-site trial to refine and then test the feasibility and acceptability of a novel intervention, Pathways, through a single arm design. Pathways is a 5 session (2 in-person; 3 phone) intervention designed to help patients identify and pursue personal goals and valued activities. To accomplish study objectives, we will 1) fully implement proposed study procedures with 6 patients and conducting patient exit interviews to refine intervention and study procedures (phase I); and 2) conduct a single arm trial of the refined Pathways protocol with 55 patients (phase II). The primary feasibility outcome that will be tested in phase II is enrollment (≥60%). Our secondary objective is to gather preliminary patient-reported outcome and clinical utility data (e.g., referrals to supportive services to support a patient goal) on hypothesized intervention mechanisms (hope) and outcomes (e.g., satisfaction with roles and activities) related to a future efficacy trial. Patient-reported data will be collected at baseline and post-intervention (within 14 days of completing the intervention).

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

We considered a control arm to test the feasibility of randomization, but in accordance with the behavioral clinical trial stage model,[1] decided to maintain focus on identifying appropriate intervention materials, eligibility criteria, enrollment/retention strategies, and fidelity monitoring.

4.3 JUSTIFICATION FOR INTERVENTION

The Pathways intervention was developed based on theory, prior hope-enhancing intervention protocols, consultation with content experts, and patient and provider input. Patient feedback informed the number of sessions, frequency, and interventionist.

4.4 END-OF-STUDY DEFINITION

A patient is considered to have completed the study if he or she has completed the baseline assessment, at least 3 intervention sessions, and the post-assessment. The end of the study is defined as completion of the post-assessment.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. New or recurrent AJCC stage III, IV NSCLC or extensive stage small cell lung cancer
2. 18 years of age or older
3. ECOG performance status 0-2/Karnofsky 60-100;

4. 3-12 weeks into active oncologic treatment (chemotherapy, immunotherapy, chemo-immunotherapy – infusion based systemic treatments).

Rationale: We chose 3-12 weeks into active treatment based on patient input to allow time to begin treatment.

5.2 EXCLUSION CRITERIA

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Unstable brain metastases (i.e., progressive neurological deficits, inadequately controlled seizures, or requiring escalating steroid doses);
2. Cognitive (i.e., dementia) or psychiatric condition (e.g., psychotic disorder) for which participating would be inappropriate
3. Receiving palliative care or actively receiving psychological services at the cancer center (see Rationale for allowances)
4. Unable to speak and read English.

Rationale: Based on preliminary data,[43] most patients will not be using palliative or psychological services. We will consider allowing patients to enroll who are using these services, depending on their focus (e.g., we will allow palliative care for symptom management, counseling for couples' therapy). These cases will be reviewed by the study team. We are unable to include non-English speaking participants in this study because several of the assessment instruments have not been translated or validated in other languages.

5.3 SCREEN FAILURES

Screen failures will be defined as patients who consent to participate in this study but are not subsequently assigned to the study intervention due to ineligibility or are assigned to intervention, but do not meet eligibility criteria and are withdrawn by investigators. Patients who do not meet the criteria for participation in this trial because of meeting one or more exclusion criteria that are likely to change over time may be rescreened. Examples include improvement in functional status and a progression of disease or disease recurrence for which a patient will begin treatment for metastatic disease. Rescreened participants will be assigned the same participant number as for the initial screening.

5.4 STRATEGIES FOR RECRUITMENT AND RETENTION, PARTICIPANT COMPENSATION

Recruitment and Enrollment.
Feasibility of Recruitment. The Markey Cancer Center sees 294 newly diagnosed advanced stage lung cancer patients a year. We estimate 80% will meet performance status and brain

metastases criteria, 85% will receive required active oncologic treatments, and 10% will be excluded for already accessing palliative care or actively receiving psychological services. We estimate 179 patients per year will meet eligibility criteria. With a 50% recruitment rate (based on current estimates during COVID-19), we project recruiting 6 patients in 2 months (Phase I) and 55 patients (Phase II) in 8-9 months.

Recruitment Strategies. As in prior work, we will use two primary recruitment strategies: direct patient referral from oncologists and providers at the Markey Cancer Center and review of patient (per report of patients coming to clinic with diagnostic codes for metastatic lung cancer) and provider appointment schedules at the MCC. To facilitate pre-screening for eligibility, we will use the UK CCTS to have an honest broker build a report in Tableau of patients with upcoming Markey Cancer Center appointments and diagnostic codes for metastatic lung cancer. Tableau will link the CCTS Enterprise Data Warehouse data for this information and generate a report that the study team can access via a dashboard in Tableau. Tableau is a secure system that requires SSL and linkblue authentication. Additional eligibility checks may need to occur from within the UKHC medical record. Study personnel will identify upcoming oncology appointments of patients pre-screened for eligibility. Study personnel will then recruit patients in person at clinic appointments or by telephone.

We are requesting a waiver of HIPAA authorization for recruitment purposes. This waiver will allow us to review appointment schedules at the MCC to pre-screen potential patients for eligibility through the electronic health record. Patients will be pre-screened for documentation in their EHR for inclusion and exclusion criteria.

Inclusion of Women and Minorities. Men and women of all races and ethnicities who meet the above-described eligibility criteria are eligible to participate in this study. We expect approximately 42% of participants to be women. Translating this to our sample size estimate of 61 (6 pilot; 55 single arm), we plan to enroll at least 25 women. We expect to enroll racially and ethnically diverse patients in proportions that reflect our catchment area: Hispanic/Latino (n = 1), Black or African American (n = 3), American Indian/Alaska Native (n = 1), and Asian (n = 1).

Retention. Patients will have up to 12 weeks (from the point of their first session) to complete Pathways. We will use previous retention strategies, including reminding patients of study visits, and offering sessions and assessments when they are in clinic for care. If they are hospitalized and want to participate, the study interventionist will meet them or resume upon discharge.

Participant Compensation. Patients in both Phase I and Phase II will receive a $20 gift card for completing the baseline assessment and a $30 gift card for completing the post-assessment. Patients in Phase I and II will receive an extra $10 for completing the exit interview. Patients will receive gift cards upon completion of an assessment. Patients will receive the full gift card amount even if they elect to skip measures within an assessment, or, in the case of the exit interview, discontinue the interview.

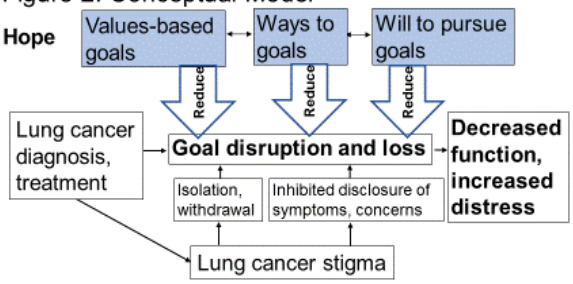
6 STUDY INTERVENTION

6.1 STUDY INTERVENTION ADMINISTRATION

6.1.1 STUDY INTERVENTION DESCRIPTION

Theoretical Basis for Pathways. Hope Theory[49,67] and Hamann's model of lung cancer stigma[15] guide the conceptual foundation of Pathways (**Figure 2**). Hope theory is recommended as a theory-based approach to goal setting interventions in palliative care.[68] It suggests the disruption cancer causes to goal pursuit[67,69-71] can be addressed by setting values-based goals and increasing agency (will to work on goals) and pathways (planning ways to reach goals).[67] In Hamann's model of lung cancer stigma, stigma comprises negative perceptions from others, constrained disclosure, and internalized self-blame, guilt, or shame, with proximal effects of isolation and inhibited disclosure.[15,72] Hope combats these effects by helping patients build ways and will to work toward values-based goals, ultimately supporting function.

Figure 2. Conceptual Model



Adapted from Gum & Snyder, 2002; Hamann et al., 2014, 2018.

Pathways Development was informed by: (a) Dr. McLouth's prior work with 60 stage IV NSCLC patients to establish patient interest in the intervention and modality; (b) Dr. Cheavens' prior hope interventions and Dr. Peterman's cancer goal interference study to develop content (c) review of resources (e.g., Lung Cancer Alliance) and approaches[73,74] for lung cancer stigma and consultation with Dr. Studts to develop stigma content; (d) provider input on the intervention concept; and (e) patient feedback on intervention materials and concept. (see **Figure 3**).

Figure 3. Completed Stepwise Process to Develop Pathways

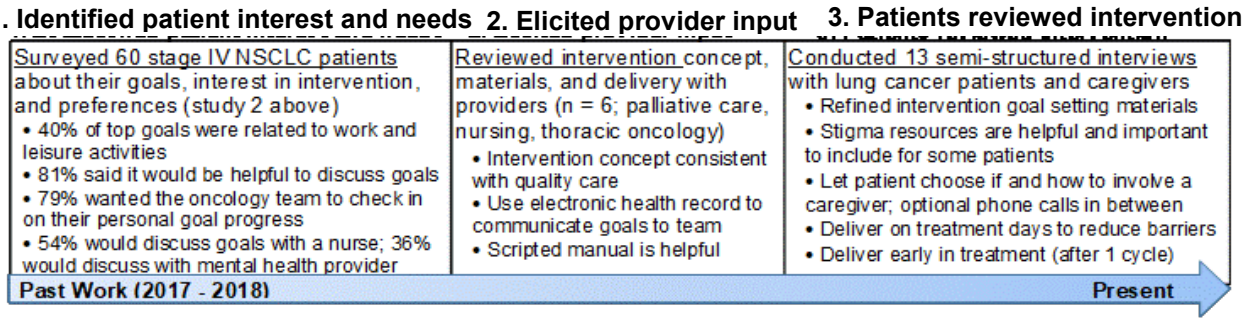


Table 1. Overview of Intervention Components

Component	IP	IP	P	P	P	Main Purpose
Values Clarification Exercise - Review list of potential values and priorities (e.g., family, spirituality)	X	*	*	*	*	**To Increase** - Intrinsic motivation to work on goals
Values-Based Goals - Generate list of potential goals aligned with top values and priorities - Select goals to pursue based on importance and desire for progress	X	*	*	*	*	**To Increase** - Agency, Awareness of important goals still available to pursue
Identify Pathways for Goals - Generate list of all potential ways to pursue top goal, including action that is consistent with the goal and feasible even on high symptom days - Select pathways to use and plan to implement pathways	X	X	X	X	X	**To Increase** - Pathways thinking - Agency thinking - Goal setting skills (specific, realistic)
Plan Ways around Goal Obstacles, Responding to Blocked Goals		X			X	**To Increase** - Pathways thinking

- Identify potential obstacles to goals (e.g., symptoms, stigma, treatment information or resource needs) and plan (e.g., if [obstacle], then [solution]) - Identify new goals to pursue if goal is blocked (i.e., not feasible)						- Agency thinking **To Reduce-** impact of goal blockages
Review Past Success, Personal Strengths -Identify time when persisted in goal when it was difficult -Identify personal strengths from list of potential characteristics		X				**To Increase** - Agency thinking
Stigma Resources (Workbook) - Responses: what to do if someone asks you if you smoked; people are distancing themselves or unsure how to act; feelings about lung cancer creating isolation - Lung cancer advocacy resources; Peer support networks	*	*	*	*	*	**To Reduce** - Stigma's impact on patient-identified goals
Symptom Resources (Workbook) - Cancer center patient guides for coping with fatigue, dyspnea, and pain - Strategies to communicate symptoms to the oncology team	*	*	*	*	*	**To Reduce** - Undermanaged symptom's impact on patient-identified goals
Documentation of Patient Goals and Obstacles in EHR (as needed)	X	X	X	X	X	**To Reduce** patient goal obstacles
Note. IP = in-person session; P = Phone session; X = component is main focus of session; * = as needed; EHR = electronic health record						

Pathways Content and Procedures. See Appendix A for a draft of the intervention manual and Appendix B for a draft of patient materials. The ~6-8 week intervention focuses on increasing patient hope, including reducing obstacles to patient goals, through 5 sessions: 2 in-person and 3 phone-based (Table 1 Overview of Intervention Components). The treatment manual is scripted, with scenario guides (e.g., "goal of living long enough to see…"; self-blame as obstacle to goal related to family). To reduce patient burden, in-person sessions align with typical 3-4 week infusion schedules. To increase adherence, the study coordinator will remind them of sessions.

6.1.2 ADMINISTRATION AND/OR DOSING

As described in Table 1, the intervention will be delivered in 5 sessions over approximately 5-8 weeks. Two sessions will be in-person when patients are in clinic; 3 sessions will be delivered on the phone when patients are not in clinic. In-person sessions are expected to take 30-45 minutes; phone sessions are expected to take 15-20 minutes. In-person sessions can be completed via Zoom or phone, if needed. Phone sessions can be delivered in-person, if needed, when patients are in clinic. The interventionist will be a member of the health profession (e.g., training as nurse, nurse navigator, rehabilitation or occupational therapist). A full dose of the intervention will be defined as completing 2 in-person sessions and at least 1 phone session.

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

Interventionist training and fidelity monitoring will follow guidelines of the Fidelity Workgroup of the Behavior Change Consortium. Multiple interventionists will be trained in case of interventionist attrition. Dr. McLouth (PI) and the study team will conduct an in-person training with review of procedures, treatment manual, and role plays. To minimize drift and evaluate fidelity, the interventionist will audiorecord all sessions and complete fidelity self-checklists each session (topics covered, session duration, and proscribed behaviors; Appendix E). Dr. McLouth and the study team will review recordings to rate fidelity (topics, length, interventionist competence; Appendix F).

For Phase I, which is intended to inform refinements needed to the treatment manual or fidelity forms, the study interventionist will have regular (e.g., every week a patient is seen) supervision with Dr. McLouth, and Dr. McLouth and the study team will review all recorded intervention sessions. For Phase II, the single arm feasibility test of the refined intervention, the study interventionist will have regular (e.g., every week a patient is seen) supervision with Dr. McLouth. To determine if remedial training is needed (fidelity <80%), the study team will review all sessions for the first 10 patients. Two members of study team will randomly select 10% of remaining sessions and rate fidelity.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

This is a single arm intervention design. To help minimize bias, the study coordinator, not the interventionist, will collect patient-reported data and data from the electronic health record related to referrals that could be associated with the intervention.

6.4 STUDY INTERVENTION

Treatment adherence will be defined by patient participation (“yes/no” to whether a patient was present and agreed to participate in the session) in at least 3 of 5 intervention visits. We will also track engagement through study interventionist ratings of patient engagement in each session (Appendix G)
Treatment receipt will be assessed through patient ratings of components received and non-specific factors after in-person session 1 and post-intervention with the coordinator and a pre-posttest goal setting exercise (Appendix H).[75]
Treatment enactment will be assessed from review of recordings for demonstration of skills.[75]

6.5 CONCOMITANT THERAPY

Patients will be able to receive concomitant treatment while on study. This may include counseling, palliative care, complementary and alternative therapies, psychotropic medications, and rehabilitation. Indeed, one of the anticipated effects of the intervention is a facilitated referral to supportive services. We will track concomitant treatment use through review of

electronic health record for services used during the study intervention period as well as by asking patients at follow-up whether they engaged services while completing the intervention.

7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION

If a patient discontinues the intervention, but not the study, remaining study procedures will be completed (e.g., post-assessment). Patients who discontinue the intervention will be asked to indicate the reason why they are discontinuing (e.g., intervention burden, decline in functional status, etc.; Appendix I). If a patient's post-assessment is due to be completed within 2 weeks of discontinuing the intervention, the post will be administered at the time of discontinuation. If the post assessment is scheduled for more than 2 weeks from the date they discontinue the intervention, the post assessment will be administered at the originally scheduled assessment.

Patients may be discontinued from the intervention by the investigative team if the study team or treating physician has concerns about the patient's mental status or psychological wellbeing, at which point procedures for managing patient safety and evaluating adverse events will be followed. The study will document reasons for discontinuing a patient (Appendix I).

7.2 PATIENT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue a participant from the study for the following reasons:

- Significant study intervention non-compliance
- Lost-to-follow up; unable to contact subject (see Section 7.3, Lost to Follow-Up)
- Any event or medical condition or situation occurs such that continued collection of follow-up study data would not be in the best interest of the participant (Note: patients who are hospitalized during the study period will be offered the opportunity to continue the intervention in the hospital or resume upon discharge. Patients who become hospitalized and elect to discontinue the intervention will still have option to continue the study to complete assessments).
- The participant meets an exclusion criterion (either newly developed [e.g., change in mental status] or not previously recognized) that precludes further study participation.

The reason for participant discontinuation or withdrawal from the study will be recorded (Appendix I). Patients who sign the informed consent form but do not receive the study intervention may be replaced. Patients who sign the informed consent form and receive the

study intervention and subsequently withdraw, or are discontinued from the study, will not be replaced.

7.3 LOST TO FOLLOW-UP

A patient will be considered lost to follow-up if he or she fails to appear for 3 intervention visits or return an assessment and study staff are unable to contact the participant after at least 3 attempts.

The following actions will be taken if a patient fails to return to the clinic for a required study visit:

- Staff will attempt to contact the participant, reschedule the missed intervention within 10 days, counsel the participant on the importance of maintaining the assigned visit schedule and determine if the participant wishes to and/or should continue in the study
- Before a participant is deemed lost to follow-up, the investigator or staff will make every effort to regain contact with the participant (where possible, 3 telephone calls and check-in at upcoming cancer care visit, and if necessary, a certified letter to the participant's last known mailing address). These contact attempts will be documented in the participant tracking log (Appendix J).
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

Screening. We will build a separate REDCap project for screening. This screening project will include an eligibility database (i.e., REDCap form) of patients who are screened for eligibility, and a master list database (i.e., separate REDCap form) linking patient names, MRNs, and screening IDs (Appendix K). Because all patients in the study will have an MRN (which includes contact information in it), we will not extract contact information for patients at the screening stage. The eligibility screening database will include patient screener ID, date screened, date must be enrolled by (21 day window), eligibility criteria (e.g., performance status, time on cancer treatment, age, etc.), whether the patient is being rescreened for eligibility, and, if rescreened, the last date of screening (Appendix L). If deemed potentially eligible, additional fields will appear in the eligibility database for tracking dates of upcoming appointments and contact with patients. Patients must be enrolled within 21 days of screening or else they will need to be rescreened.

Administration of Questionnaires. Patient-reported measures related to a future efficacy trial and of treatment processes were chosen based on their validity and sensitivity to change in cancer patients[76] and recommendation for clinical trials. These measures will be completed by

patients in both Phase I and Phase II pre-intervention (TP0), during (T1), and post-intervention (TP2) on paper, online (REDCap), or by phone. Patients will use a participation ID on their questionnaires. See **Table 2** for a list of measures to be administered, psychometric properties, assessment schedule, and role in analysis plan. All patient-reported measures will be entered in REDCap (Appendix M, N, O) in the REDCap project built for those patients who enroll.

Exit Interviews. Patients participating in Phase I (n = 6) and Phase II (n = 55) of the study will complete an exit interview (Appendix P). The interview will last approximately 15-20 minutes and will query overall satisfaction with the intervention, reactions to the session content, length, and delivery, and assessment relevance. The interviews will take place over the phone or in-person, according to patient preference. Interviews will be conducted by the study team (not the interventionist) and audiorecorded. After each interview, the interviewer will write up observations in the form of field notes (Appendix Q), which will include information about the setting (e.g., details about room if in-person vs. on the phone), personal environment (e.g., respondent's attitude and openness), social environment (e.g., presence of caregiver or others in room), and summary of patient's responses. Recordings will be transcribed verbatim, the transcripts checked for accuracy and deidentified.

Table 2. Patient-Reported Measures Related to a Future Efficacy Trial

Construct	Role	Time	Measure	Description
Activity and Role Function	Primary outcome in future trial	T0, T2	PROMIS Satisfaction with Social Roles and Activities 8a Short Form	8 items; Alpha reliability of T-score of 50 = .98; high correlation with well-validated functioning measures.[77] Recommended for longitudinal research on function in cancer.[78,79]
Distress	Secondary outcome	T0, T2	PROMIS Depression Short Form 8a	8 items; Alpha reliability of T-score of 50 = .98. The PROMIS depression measure has been validated for use in cancer patients. [80]
Purpose	Secondary outcome	T0, T2	PROMIS Meaning and Purpose 4a[81]	4 items; Assesses one's sense of purpose and that there are reasons for living. Alpha reliability of T-score of 50 = .98.
Hope	Intermediate outcome	T0, T2	State Hope Scale[47]	6 items; e.g., "I can think of many ways to reach my current goals"; 2 subscales: agency, hope pathways. Good internal consistency in lung cancer patients (α = .88).[18]
Goal Interference	Intermediate outcome	T0, T2	Cancer-Related Goal Interference Scale[82]	8 items; e.g., "To what extent did the effects of disease/treatment interfere with progress on this project?" Has shown internal (α = .90) and concurrent validity.[82]
Stigma	Intermediate outcome	T0, T2	Lung Cancer Stigma Inventory[72]	25 items; Assesses internalized, perceived, and constrained disclosure. Correlates with previous measures of stigma used in our studies with lung cancer patients.
Physical Function	Covariate	T0, T2	PROMIS Physical Function Short Form 6	6 items; This measure has been validated in lung cancer patients, with high internal consistency (α = .92) and strong correlations with the FACT-G Physical Wellbeing.[83]
Symptom Severity	Covariate	T0, T2	FACT- Lung Symptom Index[84,85]	7 items; Items are an independent subscale of the Functional Assessment of Cancer Therapy – Lung/NCCN Lung Symptom Index. Immunotherapy-specific items used in C1.2 or FACIT system (if available) will be incorporated.

Tobacco use Comorbidity	Covariate	T0	Cancer Patient Tobacco Use Questionnaire[86,87];	4 items; Assesses lifetime and current tobacco use.
Social Support	Covariate	T0	PROMIS Emotional Support, Instrumental Support V2. 4a;	4 items; Assesses perceived emotional support and instrumental support (e.g., help with tasks).
Demoralization	Secondary outcome	T0, T2	Demoralization Scale –II	16 items; 2 factors: meaning and purpose; distress and coping ability. Patients with low and or/moderate levels are less likely to have major depressive disorder; those with high levels are more likely to have major depressive disorder.
Care Quality	Secondary outcome	T0, T2	Patient-centered communication in cancer care	8 items; (e.g., To what extent do you and your doctor discus how cancer is affecting your everyday life?...what is important to you when planning your care?")
Treatment Expectancy	Covariate	T1	HEAL Treatment Expectancy	6 items; Assesses expectations for treatment (e.g., "I am confident in this treatment")
Treatment Receipt	Covariate	T1, T2		7-9 items; (Assesses whether patients perceived that they set goals, discussed values, etc. with the interventionist)
Survey Length			***30 minutes based on prior use with this population***	

Review of Existing Data in EHR. As part of the consent, all patients will be asked to consent to a HIPAA release for permission to collect the following protected health information for up to 12 months post-enrollment:

- age
- gender
- racial and ethnic data
- zip code
- lung cancer diagnosis
- date started lung cancer treatment
- comorbidities (other health conditions)
- type of cancer treatments received and dates received
- types of other services received for cancer care and dates received
- response to cancer treatment
- dates of hospitalizations and reasons hospitalized
- referrals to services for cancer care
- documentation of advance care planning
- date of death, place of death (hospital, home)

This information will be collected by study staff and entered in REDCap or obtained through clinical informatics service.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

Primary Endpoint: We hypothesize that at least 60% of eligible patients approached will enroll in the Pathways intervention in the Phase II feasibility study.

9.2 SAMPLE SIZE DETERMINATION

The target sample of 6 patients for Phase I is based on the aim of refining procedures and content.[88-90] We anticipate that 6 will be sufficient given that we have already had patients review proposed intervention materials to provide feedback and initial refinement.

The target sample size of 40 evaluable cases for Phase II is based on the goal of estimating the probabilities and means for 3 feasibility outcome measures (enrollment ≥ 60% [primary], retention ≥ 70%, adherence [defined as completing at least 3/5 sessions] >=70%). We will use feasibility outcomes to inform an efficacy trial. Here we present some basic power calculations for the above 3 outcomes. Assuming a negative binomial distribution and true probability of enrollment of 60%, the probability that we would have to approach 55 or more people to recruit 40 is <0.05. If we approach ≥55 patients to enroll 40, it is unlikely the true probability of enrollment is 60% or greater, concluding a future efficacy study with our criteria may not be feasible. Out of 40 patients, if the true probability of retention is 60% we expect at least 19 patients will be retained (i.e., probability of n≤19 retained given true retention probability of 60% is <0.05), so if more than 21 patients are not retained, an efficacy study may not be feasible. We have 80% power (using a 2-tailed alpha of 0.05) to detect an adherence proportion of 0.72 if we assume a null hypothesis adherence proportion of 0.50.

9.3 POPULATIONS FOR ANALYSES

The sample from phase I (n = 6) will be used to refine procedures and the intervention protocol. The sample from phase II (n = 55) will be used to analyze feasibility and acceptability data and describe pre-post changes in patient-reported outcomes.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

For Phase I we will use qualitative methods to analyze patient feedback from the exit interviews and descriptive statistics to summarize participants' acceptability ratings of the intervention. The interviews will be transcribed verbatim and managed in ATLAS.ti or other qualitative software for analysis. The PI and study coordinator will code interviews by domains (e.g., session relevance, delivery mode, ease of participation). Data will be analyzed using thematic content analysis[91] to describe patient perceptions and identify patterns in the patient experience. Quantitative and qualitative findings from Phase I will be synthesized along with interventionist process notes and

included in a report. This report will be used to determine potential refinement in the recruitment procedures, intervention content, intervention delivery, fidelity forms, and retention strategies. The study team will review this report to reach consensus on refinements needed for Phase II testing.

For Phase II, we will use descriptive statistics (means, standard deviations, median, range) to examine the distribution of continuous variables. We will calculate 95% CIs for each of the feasibility measures to determine the range of estimates that are consistent with our data.

We will use one-sample negative binomial probabilities and tests of binomial proportions to compare rates of feasibility to hypothesized values. We will also summarize reasons for patient ineligibility and refusal to participate. In exploratory analyses, we will monitor and compare the patients who drop out or do not complete 3 or more sessions by demographic and clinical characteristics, and baseline scores of the measures (e.g., distress, lung cancer stigma). We will also investigate any differences in patient enrollment, retention, or adherence by treatment type (chemotherapy vs. immunotherapy) to identify an optimal patient population for a future study.

We will calculate inter-rater reliability for fidelity scores between raters of intervention fidelity.

Statistical significance will be indicated by $p < .05$.

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

The primary outcome of the feasibility is enrollment (≥60%). A one-sample binomial test will be used to compare the observed enrollment percentage to 60%.

Enrollment (primary): Number of patients enrolled divided by the number of eligible patients approached

Retention: The percentage of patients who complete baseline and post-treatment questionnaires

Adherence: The percentage of patients who complete at least 3 of 5 sessions in 10 weeks.

Acceptability: Mean post-treatment patient ratings ≥ 7/10 on intervention satisfaction (primary), convenience, helpfulness, relevance, recommendation to others, worth doing (0 = not at all to 10 = extremely); and a brief semi-structured interview to explore factors associated with acceptability

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

We will describe pre-post changes in intermediate (e.g., hope) and outcome (primary: activity and role function; secondary: distress, purpose) variables using descriptive statistics. The primary goal of these analyses will be to estimate the standard deviations (SD) for use in future studies. Exploratory analyses will include intermediate variables as covariates to model the relation between outcome variables and hypothesized mediators.

We will calculate means, sd, and range of minutes per session (including preparation and documentation), interventionist post-session ratings (e.g., ease of delivering content), and mean caseload (i.e., number of patients) a week.

10 RISK/BENEFIT ASSESSMENT

10.1.1 KNOWN POTENTIAL RISKS

The proposed study poses minimal risks. Potential risks that might exist fall into three categories: (a) risks associated with the intervention; (b) risks associated with research assessments, and (c) risks associated with potential loss of confidentiality. We describe each below.

Risks of the intervention. The intervention asks patients to think about their personal goals, to identify actions to take towards those goals, and to identify potential barriers. For some patients, thinking about goals may cause frustration or prompt thoughts related to the ways that cancer has disrupted their lives. However, our pilot work with 60 stage IV non-small cell lung cancer patients indicates that patients can complete assessments related to their personal goals and the interference cancer has caused, identify goals that are meaningful, and view assessments of their goals and goal progress as important. As patients are asked to set goals for themselves during the week, there is a possibility that patients will not be able to meet their planned goals that week and will become distressed or discouraged as a result. We have considered this in developing our intervention protocol and identified ways to minimize risk. An additional potential risk of the intervention could be that patients may identify physical goals (i.e., activities that are physically demanding). Our pilot work suggests 10% of patients may identify a physical goal (e.g., “to start walking more”).

Risks associated with research assessments. Research assessments include questions about depression, demoralization, lung cancer stigma, interference from cancer with personal goals, physical function, and disease-related symptoms. The instruments and methodologies are well tested and are not known to cause problems or distress on the part of the participants; however, there is the possibility that some individuals may find answering the questions distressing.

Risks associated with potential loss of confidentiality and privacy. There is a risk of loss of confidentiality and privacy as patients will be met in person at the Interdisciplinary Lung Clinic at Markey Cancer Center and will receive phone calls from the study coordinator.

10.1.2 KNOWN POTENTIAL BENEFITS

Participants may experience some benefit from feeling that they have contributed to a study that can help inform ways to help future lung cancer patients. Participants may benefit from being asked about their personal goals and monitoring their own behavior to identify areas of their lives that they want to pay more attention to for their own benefit. Participants may experience an increase in goal-directed thought and decrease in lung cancer stigma as a result of treatment. These benefits may or may not occur for any and all participants. For society as a whole, the findings will inform future intervention development and testing with lung cancer patients. Future patients may benefit from an intervention that is low burden in terms of time and cost, potentially widely available due to delivery mode, and aligned with personal values and unmet supportive care needs.

10.1.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS AND PROCEDURES TO MINIMIZE RISKS

The risk of harm or discomfort that may happen as a result of taking part in this research study is not expected to be more than in daily life or from routine physical or psychological examinations or tests. This study will determine whether a hope-enhancing intervention is feasible for advanced stage lung cancer patients in primary oncology. Results of this study will inform whether an efficacy study is warranted.

Procedures to Minimize Risks.

Protection for risks associated with the intervention. The biggest risk we perceive with the intervention is distress resulting from the potential of patients in the intervention to not meet their personal goals. We aim to reduce the risk of patients not meeting their goals by helping them evaluate the feasibility of goals they are setting for themselves and emphasizing small actions to help set themselves up for success. Dr. Cheavens (consultant) has been able to implement a hope-enhancing protocol that this intervention is based in with patients with depression where self-efficacy is low and sensitivity to perceived failure may be high. Patients will have the option of calling the study interventionist during the week if they are encountering problems with their goal. During these calls, the study interventionist will query their mood, reinforce effort and consistency in working towards meaningful activities and goals, and help problem-solve. The interventionist will help the patient set more feasible goals for the next week if needed.

As mentioned above, 10% of our sample may identify a physical health goal (e.g., to start walking more). To help minimize risk if patients identify physical goals (e.g., exercise-related or physically demanding goals), the study interventionist will communicate patient-identified goals with the oncology team, will discuss physical limitation and safety concerns related to the goal with the patient, and, if necessary, will ask the patient to wait to pursue the goal until the oncology team has cleared the activity.

Protection for risks associated with assessment. Patients will give voluntary responses to questions; they are told that they can decline to answer any questions that they choose. If patients express distress or frustration with the questions, study staff will remind them that these questions are voluntary and that they are meant to apply to a broad range of patients

and may not necessarily reflect each person's experience. If patients remain distressed, the study PI, Dr. McLouth or other qualified member of the study team will contact them. If concerns remain, participants will be directed either to the chair of the IRB to discuss their concerns about the assessments and will be referred for psychological services at the Markey Cancer Center.

Protection for risks associated with potential loss of confidentiality. Prior to any contact with study participants or data, the Principal Investigator will ensure study team members have completed required institutional training in maintaining confidentiality of study data. Further, all study staff will complete training in Good Clinical Practice, which is required for clinical trial research.

Assessments completed on paper will have the participant's assigned unique ID and not the participant's name on it. Assessments completed online will be done through a secure survey site, REDCap. REDCap requires HTTPS login access. Hypertext Transfer Protocol Secure (HTTPS) is a combination of the Hypertext Transfer Protocol with the SSL/TLS protocol to provide encryption and secure identification of the server. HTTPS connections are used for payment transactions on the Internet and for sensitive transactions in corporate information systems. Assessments completed on the phone with the study coordinator will be conducted an agreed upon time by the participant when they believe they will not be interrupted. The study coordinator will complete the phone assessments from a private office. At the start of the call, the study coordinator will query whether it is a good time and whether the participant is comfortable answering questions in their current location.

Data for all participants will be kept strictly confidential, except as mandated by law. All research files will be kept on secure, password protected departmental and medical school servers. All electronic data will be stored on secure servers behind firewalls. Any paper documentation will be kept in locked file cabinets or a locked file room. Participants will be assigned a numerical code for identification in the files. Names and other identifiers will be kept in separate password protected files. Audio data will be stored on secure servers with password protected files. Study team members who are not at UK will access audio data of intervention session recordings through an FTP server. FTP divides files into segments and assigns a reference number to each segment, which are transmitted in a sequence for the receiving computer to reassemble. FTP performs automatic error detection and correction in file transfers. FTP files are considered encrypted.
All data presentation will be of aggregate-level data; patients will not be individually named.

Psychiatric emergencies. In the case of psychiatric emergencies, patient care will take precedence over treatment protocol. If the study coordinator or interventionist identifies concerns about a patient's mental state, the study PI or other qualified member of the study team will contact the participant and determine whether a referral to psychological counseling is needed or whether emergency services are needed. If the patient is able to continue the study, the PI or other qualified member of the study team will develop a follow-up plan using clinical judgment based upon the data and any additional information acquired through interview. This may include assessing distress prior to interventionist check-in calls or periodic telephone check-ins by the PI or other qualified member of the study team Referrals and assistance will be given in obtaining appropriate treatment for any participant terminated from the study for safety

issues. Reports will be filed with all necessary governing bodies, including the University of Kentucky IRB and the NCI program officer.

10.2 SAFETY MONITORING AND ADVERSE EVENTS

10.2.1 DEFINITION OF ADVERSE EVENTS

This study is considered to carry a low risk to patients. All AEs will be recorded regardless of whether they are study related. AEs will be reported if they are study related. For example, patient hospitalization or death due to disease is expected in this population and unlikely to be an AE related to the study. However, if the AE could be related the study (i.e., there is a temporal relationship between the study procedures and the event or reasonable possibility means that there is evidence to suggest a causal relationship between the study procedures and the AE), it will be reported as an AE. An example of an AE for this study would be severe distress during the intervention session that requires additional clinical management for safety. Any psychiatric condition that is present at the time the patient is screened and enrolled will be considered as baseline and not reported as an AE. However, if the patient's condition deteriorates during the study, it will be reported as an AE.

The PI and/or other qualified Co-I will be responsible for reviewing the AE to grade its severity (mild, moderate, severe) and relatedness (definitely, probably, potentially) to the study intervention.

10.2.2 MONITORING FOR AE'S AND FOLLOW-UP

Several mechanisms for monitoring the occurrence of adverse events will be employed. The study coordinator will oversee day-to-day monitoring of the study activities and will have daily contact with the PI.

There will be ongoing communication among the research team. This will be facilitated by: 1) regular (weekly or bi-weekly) meetings with project staff and investigators to discuss study progress, reactions to the intervention, and any adverse events; 2) supervision of the study interventionist, study coordinator, and data manager; 3) the principal investigator and other member of the study team will monitor the audiotaped intervention sessions; and 4) a study phone number patients may call in the event of a non-medical adverse event. For medical adverse events, patients will contact their oncology care team or emergency medical services as they would in routine care.

The study interventionist will receive training on how to effectively communicate via telephone and assess for actual or potential adverse psychological reactions. For patients who exhibit excessive or worrisome emotional reactions, the study interventionist or PI will follow-up with the patient by telephone within 24 hours and again within 1 week of the session to ensure that these patients receive adequate mental health care.

10.2.3 ADVERSE EVENT REPORTING

The PI or designated personnel will be responsible for reporting the results of an AE evaluation to the NIH and the IRB as soon as possible, but no later than 14 working days after the study team first learns of the event.

10.3 UNANTICIPATED PROBLEMS

10.3.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). OHRP considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

An example of an unanticipated problem would include loss of data or sensitive information due to a study laptop being stolen or a complaint from a participant or participant family member. If a participant complaint identifies a newly recognized risk, the informed consent document will be updated and previously enrolled participants will be informed of the additional potential risk.

10.3.2 UNANTICIPATED PROBLEMS REPORTING

The PI or designated personnel will report unanticipated problems to the IRB. This information will include a detailed description of the event, an explanation of the basis for determining that the event constitutes an unanticipated problem, and a description of any changes to the protocol or other corrective actions that have been take or are proposed in response to the unanticipated problem.

11 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

11.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

11.1.1 INFORMED CONSENT PROCESS

11.1.1.1 CONSENT

Written documentation of informed consent will be required prior to starting the intervention (Phase I, Phase II).

For Phase I, the consent form will describe the intervention, study procedures, including audiorecording of the semi-structured interview and intervention sessions, risks, and potential benefits (Appendix R).

For Phase II, the consent form will describe the intervention, study procedures, including audiorecording of intervention sessions and semi-structured interview, risks, and potential benefits.

11.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Once patients are deemed eligible and express interest in the study, they will be consented in person at either an upcoming clinic appointment or as a unique clinic visit. Consent will take place in a private space within the clinic (e.g., consultation room, infusion suite with curtain drawn). Consent will review information that will be collected from the electronic medical record and how it will be used. Consent will include information for the process and purpose of the study interventionist documenting their activity and role-related goals and potential sources of disease or treatment interference in the electronic medical record. These notes will briefly describe the type of activity the patient wants to engage in and potential obstacles they need help overcoming (e.g., “The patient wants to be able to go on a fishing trip in a month, but is worried about fatigue.”).. The consent will also describe information about the rationale for audiorecording intervention sessions and procedures to protect confidentiality of session data. Patients will be informed that they can request that the recording be paused if they are discussing sensitive information they do not want on the recording.

Patients will review the consent form with study personnel and have the opportunity to ask questions. To check understanding, patients will be asked to describe their understanding of key aspects of the study (rationale, intervention topic, what is involved to participate, decision not to participate not affecting their medical care) and study staff will review any aspects that do not appear understood.

As part of the consent, all patients will be asked to consent to a HIPAA release for permission to use the following protected health information:

- age

- gender
- racial and ethnic data
- zip code
- lung cancer diagnosis
- date started lung cancer treatment
- comorbidities (other health conditions)
- type of cancer treatments received and dates received
- types of other services received for cancer care and dates received
- response to cancer treatment
- dates of hospitalizations and reasons hospitalized
- referrals to services for cancer care
- documentation of advance care planning
- date of death, place of death (hospital, home)

A copy of the consent form will be sent with the patient on paper or electronically and retained via paper or electronically for study records.

11.1.2 CONFIDENTIALITY AND PRIVACY

Confidentiality will be protected by collecting only information needed to assess study outcomes, minimizing to the fullest extent possible the collection of any information that could directly identify subjects, and maintaining all study information in a secure manner. To help ensure subject privacy and confidentiality, only a unique study identifier will appear on the data collection forms. All interactions with patients will be conducted in as private atmosphere as possible. Any collected patient identifying information corresponding to the unique study identifier will be maintained on a linkage file, store separately from patient data. The linkage file will be kept secure, with access limited to designated study personnel. Following data collection subject identifying information will be destroyed 6 years after the closure of the study, producing an anonymous analytical dataset. Data access will be limited to study staff. Data and records will be kept locked and secured, with any computer data password protected. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study. Specific procedures for protecting confidentiality and privacy by study stage are detailed below.

Screening. We will build a separate REDCap project for screening. This screening project will include a database (i.e., RedCap form) of patients who are screened for eligibility and a master list database (i.e., separate RedCap form or Excel file) linking patient names, MRNs, and screening IDs. Because all patients in the study will have an MRN (which includes contact information in it), we will not extract contact information for patients at the screening stage. Only the minimum necessary information will be collected prior to ascertaining desire to participate. The eligibility screening database will include patient screener ID, eligibility criteria (e.g.,

performance status, time on cancer treatment, age, etc.), and, if deemed potentially eligible, dates of upcoming appointments.

Patient Interactions. Study staff will ask patients for permission to discuss anything related to the research study with them and whether patients are comfortable to proceed. Consent will take place in a private space within the clinic (e.g., consultation room, infusion room). Based on our preliminary work, patients prefer to receive the intervention during infusion. Patients will be offered the option of completing the intervention in a private consultation room in clinic or in infusion clinic space, based on patient preference. Patients who choose to complete their in-person sessions via Zoom will have their session conducted using a UK-HIPAA compliant Zoom account. Prior to interacting with patients in any clinic space, the study interventionist and/or study staff will confirm with the patient whether they are comfortable to proceed and take precautions to help protect privacy (e.g., closing infusion suite curtains if in shared space, pausing recordings and the intervention or interaction if medical staff approach the patient, reminding the patient they can ask to pause the recording if they wish to discuss something they do not want recorded, etc.). Phase I testing will help inform whether the intervention can be delivered to most patients during infusion or whether it will require a separate appointment to assure an enclosed, private room.

11.1.3 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator:

Laurie McLouth, Ph.D.
Assistant Professor
Behavioral Science
University of Kentucky College of Medicine
Laurie.mclouth@gmail.com
Phone: 620-532-6425

Co-Investigator(s):

Susanne Arnold, MD
Professor
Internal Medicine
University of Kentucky College of Medicine
Associate Director of Clinical Translation, University of Kentucky Markey Cancer Center

Jessica Burris, PhD
Assistant Professor
Psychology
University of Kentucky College of Arts and Sciences
Burris.jessica@gmail.com; jessica.burris@uky.edu

Biostatistician:

Brent Shelton, PhD
Professor
Division Chief of Cancer Biostatistics

University of Kentucky Markey Cancer Center
bshelton@kcp.uky.edu

Andrew Shearer
SAS Programmer I
Markey Cancer Center Core Support
Ajsh225@uky.edu

Study Interventionists:

Lexandra Overby
Lexandra.overby@uky.edu

Constance Murrie, RN
Constance.murrie@uky.edu

Study Coordinators:

Amy Christian
Research Associate
UK Markey Cancer Center Behavioral and Community Oncology Shared Resource Facility
Amy.christian@uky.edu

Vilma Bursac, MPH
Research Program Manager
UK Center for Health Equity Transformation
Vbu222@uky.edu

Shaylla Shelton
Undergraduate study research assistant
Srsh234@uky.edu

Kaitlyn Weyman, BA
Medical student research assistant
Kaitlyn.weyman@uky.edu

Regulatory Contact:

Laura Ashe
Regulatory Manager
Center for Clinical and Translational Science (CCTS)
Llashe2@email.uky.edu

11.1.4 QUALITY ASSURANCE AND QUALITY CONTROL

Quality control procedures will be implemented as follows:

Informed consent. Study staff will review both the documentation of the consenting process as well as a percentage of the completed consent documents. This review will evaluate compliance with Good Clinical Practice, accuracy, and completeness. Feedback will be provided to the study team to ensure proper consenting procedures are followed.

Source documents and the electronic data. Some data will be initially captured on source documents (see **Section 11.1.5, Data Handling and Record Keeping**), but all will ultimately be entered into the study database.

The biostatistician and programmer will download the patient-reported outcome REDCap data and examine it for errors after completing Phase I to identify any refinements that need to be made in the Manual of Procedures regarding data entry procedures. The PI will review all data sources for accuracy with study staff in Phase I.

In the single arm pilot (Phase II), biostatistician and programmer will download the REDCap data after the first 5 patients have enrolled to check for errors. We will perform logic and range checks. Patient-reported data and medical record data entered by the study coordinator in REDCap will be examined for accuracy. Specifically, the study team will compare the patient-reported packet with entries in REDCap for 50% of the data. The study team will review medical record data extracted for accuracy and consult with Dr. Arnold or other member of the thoracic oncology team on the protocol if there are questions about clinical data.

Intervention Fidelity. Consistent delivery of the study intervention will be monitored throughout the intervention phase of the study. Procedures for ensuring fidelity of intervention delivery are described in **Section 6.2.1, Interventionist Training and Tracking**.

Protocol Deviations. Protocol compliance will be monitored and discussed at weekly team meetings. The study team will review protocol deviations and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern.

Should independent monitoring become necessary, the PI will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor/funding agency, and inspection by local and regulatory authorities.

11.1.5 DATA HANDLING AND RECORD KEEPING

11.1.5.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data sources include:

- Information from the electronic medical record (e.g., eligibility screening and upon enrollment demographic, clinical data; electronic only)
- Audiorecorded intervention sessions (electronic only)
- Audiorecorded exit interviews and transcripts (Phase I and II; electronic)
- Patient-reported treatment receipt, enactment (paper source then electronic)
- Patient-reported measures (T0, T1, T2; Phase I and Phase II; paper and/or electronic source; electronic management)
- Interventionist process notes (e.g., session length, ratings of patient engagement; paper source; electronic management)
- Fidelity ratings (paper source; electronic management)
- Participant tracking (e.g., upcoming appointments; withdrawal; discontinuation; electronic)

All data except for audiofiles and transcripts will be stored in REDCap, a secure electronic data capture system, or Excel behind a UK firewall on a study-specific shared drive. REDCap provides a real-time record of any changes made to data.

Patient-reported outcome data will be collected via mail, telephone, or in-person. Based on our prior studies, we anticipate that most patients will complete the assessments in-person with the study coordinator when they are at the Markey Cancer Center for other oncologic appointments.

11.1.5.2 STUDY RECORDS RETENTION

All records pertaining to the study will be retained for 6 years.

11.1.6 PROTOCOL DEVIATIONS

A protocol deviation is defined as any noncompliance with the clinical trial protocol or Manual of Procedures. Deviations will be reported to the IRB and corrective actions will be developed by the study team and implemented.

11.1.7 PUBLICATION AND DATA SHARING POLICY

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals.

11.2 ABBREVIATIONS AND SPECIAL TERMS

AE	Adverse Event
NSCLC	Non-small cell lung cancer
HIPAA	Health Insurance Portability and Accountability Act
MOP	Manual of Procedures
NCT	National Clinical Trial
NIH	National Institutes of Health
NIH IC	NIH Institute or Center
OHRP	Office for Human Research Protections
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SOA	Schedule of Activities
SOP	Standard Operating Procedure
UP	Unanticipated Problem

12 APPENDICES LIST

Appendix A	**Draft Intervention Manual**
Appendix B	**Draft Intervention Patient Materials**
Appendix C	**Electronic health record note template about patient goals**
Appendix D	**Letter template: patient goals for patient to share with oncology team**
Appendix E	**Interventionist fidelity self-checklist**
Appendix F	**Fidelity reviewer rating form**
Appendix G	**Interventionist process notes**
Appendix H	**Patient assessment of treatment receipt**
Appendix I	**Patient discontinuation/withdrawal form**
Appendix J	**Patient tracking log (enrolled)**
Appendix K	**Masterlist template**
Appendix L	**Patient screening form & recruitment tracking log**
Appendix M	**Patient baseline (T0) questionnaire**
Appendix N	**Patient post (T2) questionnaire**
Appendix O	**Patient treatment enactment, expectancy questionnaire (T1)**
Appendix P	**Patient exit interview**
Appendix Q	**Patient exit interview field note template**
Appendix R	**Phase I patient consent form**
Appendix S	**Patient refusal questionnaire**

13 AMENDMENT HISTORY

Version	Date	Description of Change	Brief Rationale
2	8/25/19	Added project members (Dr. Shelton, BCBR staff, CCTS staff); updated questionnaires and treatment information	Previous forms were rough drafts and missing information (e.g., treatment receipt items)
	11/25/2019	Added project members (Mary Valen, study nurse; Vilma Bursac, Program Manager; Hannah Bowlds, CCTS regulatory)	
3	12/09/2019	Updated tracking forms, questionnaires, templates for participant postcard, magnet	Identified formatting changes that were needed to improve questionnaires. Identified formatting and minor changes needed to administrative tracking forms for study.
4	02/11/2020	Updated participant handouts, added S. Shelton, K. Weyman, and B. Estridge to protocol, added CCTS Tableau for recruitment pre-screening	Identified formatting changes needed to improve patient materials. New study personnel (research assistants, study interventionist). Tableau through CCTS added to help

			reduce screening to potentially eligible patients
	10/23/2020	Removed Studts, Edwards, and Westgate from personnel list	Co-Is were not actively involved in study and roles were replaced by other faculty on campus
	12/14/2020	Added Burris to protocol	Dr. Burris is replacing Dr. Studts on the protocol.
6	1/26/2021	Increased aim 2 sample size to 40; expanded eligibility criteria to include advanced stage lung cancer patients; added income question to patient baseline questionnaire	Recruitment opportunities have lessened during COVID (patients coming into clinic less often). Dr. Arnold, Co-I, and NCI program officer, Dr. Lee were supportive of expanding to advanced stage LC patients given similar treatment and disease characteristics. Increasing sample size to strengthen single arm pilot data and potentially allow for subgroup comparisons to identify ideal eligibility criteria for future trial. Discovered income was erroneously omitted from paper version of patient baseline questionnaire.
7	11/10/2021	Increased aim 2 sample size to 55; added Lexandra Overby as additional study interventionist	We need 40 evaluable cases (pre-post data) for aim 2 patient-reported outcome analyses. Based on attrition and patients who had to be discontinued, we expect enrolling 55 will yield 40 evaluable cases. Ms. Overby is replacing Brittany Estridge and Mary Valen as a study interventionist, as both are no longer working for the study.
8	12/15/2021	Updated Word version of protocol and consent forms to reflect increased aim 2 sample size approved in 11/2021.	The protocol and consent forms should have been updated during the last modification request.

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Analysis Plan. Protocol 52168; Pathways R03 (PI McLouth)

For Phase II, we will use descriptive statistics (means, standard deviations, median, range) to examine the distribution of continuous variables. We will calculate 95% CIs for each of the feasibility measures to determine the range of estimates that are consistent with our data.

We will use one-sample negative binomial probabilities and tests of binomial proportions to compare rates of feasibility to hypothesized values. We will also summarize reasons for patient ineligibility and refusal to participate. In exploratory analyses, we will monitor and compare the patients who drop out or do not complete 3 or more sessions by demographic and clinical characteristics, and baseline scores of the measures (e.g., distress, lung cancer stigma). We will also investigate any differences in patient enrollment, retention, or adherence by treatment type (chemotherapy vs. immunotherapy) to identify an optimal patient population for a future study.

We will calculate inter-rater reliability for fidelity scores between raters of intervention fidelity.

Statistical significance will be indicated by $p < .05$.

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

The primary outcome of the feasibility is enrollment (≥60%). A one-sample binomial test will be used to compare the observed enrollment percentage to 60%.

Enrollment (primary): Number of patients enrolled divided by the number of eligible patients approached

Retention: The percentage of patients who complete baseline and post-treatment questionnaires

Adherence: The percentage of patients who complete at least 3 of 5 sessions in 10 weeks.

Acceptability: Mean post-treatment patient ratings ≥ 7/10 on intervention satisfaction (primary), convenience, helpfulness, relevance, recommendation to others, worth doing (0 = not at all to 10 = extremely); and a brief semi-structured interview to explore factors associated with acceptability

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

We will describe pre-post changes in intermediate (e.g., hope) and outcome (primary: activity and role function; secondary: distress, purpose) variables using descriptive statistics. The primary goal of these analyses will be to estimate the standard deviations (SD) for use in future studies. Exploratory analyses will include intermediate variables as covariates to model the relation between outcome variables and hypothesized mediators.

We will calculate means, sd, and range of minutes per session (including preparation and documentation), interventionist post-session ratings (e.g., ease of delivering content), and mean caseload (i.e., number of patients) a week.