CITY OF HOPE NATIONAL MEDICAL CENTER
1500 E. DUARTE ROAD
DUARTE, CA 91010

DEPARTMENT OF Population Sciences, Division of Nursing Research and Education

TITLE: A Multimedia Self-Management Intervention to Prepare Family Caregivers and Patients for Lung Cancer Surgery

CITY OF HOPE PROTOCOL VERSION: IRB # 17238 Protocol Date: 02/02/2023

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COH Amendment 04	Protocol Dated 10/22/2018	Version 04
COH Amendment 05	Protocol Dated 12/03/2018	Version 05
COH Amendment 06	Protocol Dated 01/27/2019	Version 06
COH Amendment 07	Protocol Dated 03/7/2019	Version 07
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PHASE/TYPE: Phase III Interventional

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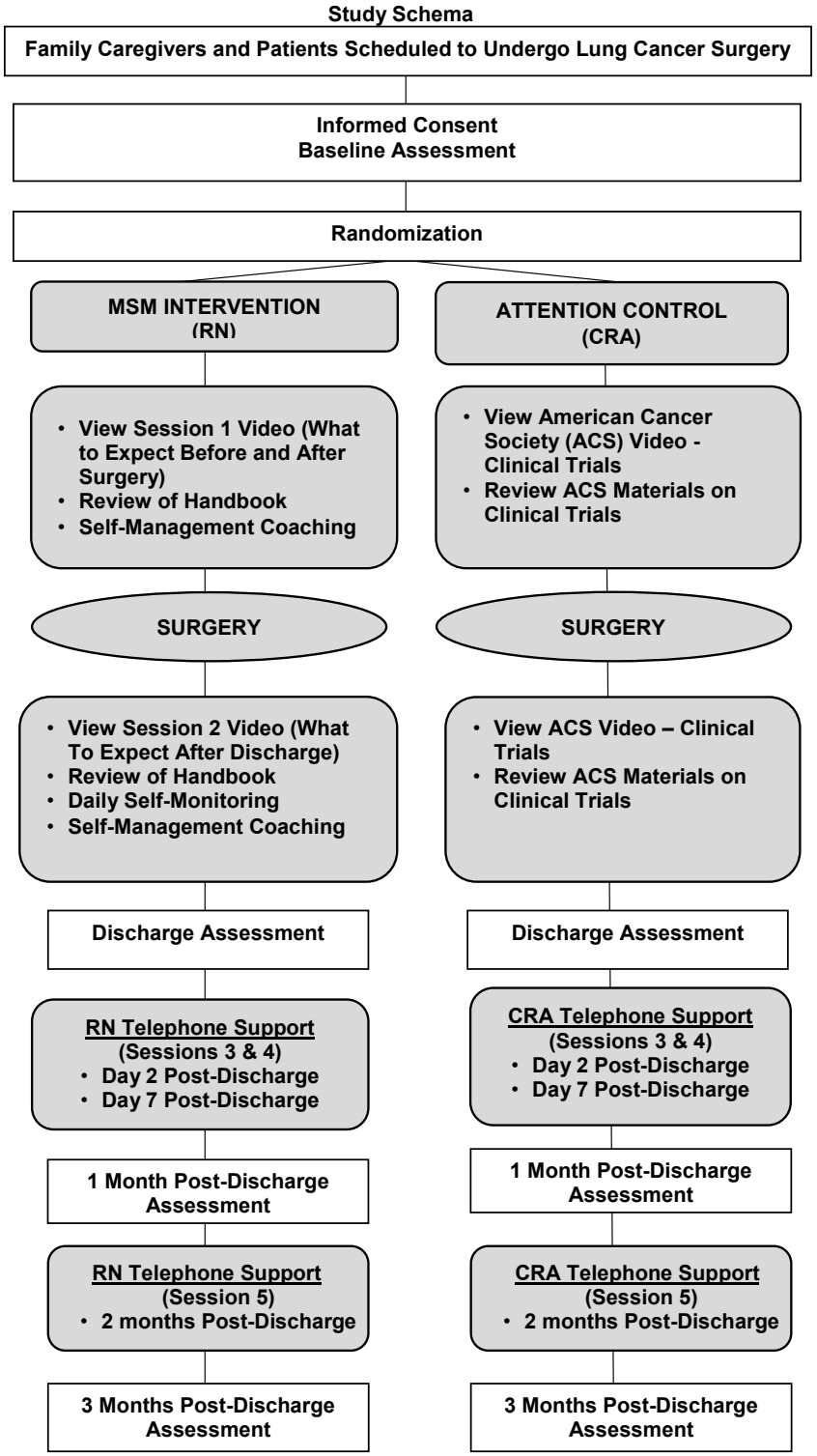
Experimental Design Schema



Protocol Synopsis

Protocol Title:
A Multimedia Self-Management Intervention to Prepare Family Caregivers and Patients for Lung Cancer Surgery
Brief Protocol Title for the Lay Public (if applicable):
Preparing Family Caregivers and Patients for Lung Cancer Surgery using a Multimedia Intervention
Study Phase:
Phase III Interventional
Participating Sites:
None
Rationale for this Study:
Lung cancer surgery patients are a unique population with significant acute and chronic caregiving needs. Patients are older, have greater co-morbidities (pulmonary, cardiovascular), higher psychological distress, and decreased physical functioning. Caregiving demands are high due to acute effects (pain, fatigue) and chronic pulmonary function deficits. As cancer care continues to move further into the home setting, family caregivers (FCGs) and patients may be ill-prepared for recovery at home. This can potentially result in significant morbidity, undesirable healthcare resource use, and immense social and economic costs for both FCGs and patients. Despite the tremendous caregiving burden, family caregiver interventions have been understudied in cancer surgery, and there is a significant, unmet need for family-centered models of care in this area.
Objectives:
The primary purpose of this trial is to test the efficacy of a Multimedia Self-Management (MSM) Intervention in 200 lung cancer surgery caregiver-patient dyads, comparing intervention and attention control groups.
Study Design:
This is a Phase III, prospective, longitudinal, mixed-methods RCT designed to test the efficacy of the MSM Intervention in lung cancer surgery. The use of an attention control condition as the comparison group will minimize the potential for Hawthorne's effect. Building from our previous work and based on the Chronic Care Self-Management Model (CCM), the MSM Intervention is a nurse-led, caregiver-based, telehealth, multimedia care model for lung cancer surgery. Its primary focus is to provide support for FCGs on their post-operative caregiving role and managing their QOL needs through goal setting, proactive planning, and building self-management and problem-solving skills. The MSM Intervention also supports caregiver-patient dyads in preparing for surgery and self-management during post-operative recovery at home. The MSM Intervention includes video, handbook, and post-discharge telephone support. It is administered at five time points: before surgery, during hospitalization, and at Day 2, Day 7, and 2 months post-discharge. It utilizes both in-person encounters as well as telephone for intervention administration.
Endpoints:
Primary: Family Caregivers: Burden, Caregiving Preparedness, Psychological Distress, QOL, Cancer support services use

Patients: Psychological distress, QOL, Healthcare Resource Use (home health nursing care, urgent care/ER visits, readmissions) Outcome Mediators: Activation, Self-Efficacy, Surgery-Related Knowledge Secondary: Moderators of FCG/patient outcomes and reciprocal relationships Additional Studies: Geriatric Assessment for FCGs and patients Social determinants of health Spiritual Well-Being
Sample Size:
200 family caregiver-patient dyads (400 participants total)
Estimated Duration of the Study
60 months
Summary of Subject Eligibility Criteria:
Inclusion Criteria: Family caregiver: 1) A family member or friend identified by the patient as being the primary care provider before and after surgery; 2) A patient/care recipient enrolled in the study; 3) Age 21 years or older; 4) Able to read or understand English or Chinese. Patient: 1) Diagnosis of lung cancer or presumed lung cancer (as determined by surgeons); 2) Scheduled to undergo surgery for treatment; 3) A family caregiver enrolled in the study; 4) Age 21 years or older; and 5) Able to read or understand English or Chinese.
Investigational Product Dosage and Administration:
Not Applicable
Clinical Observations and Tests to be Performed:
Disease and surgical characteristics: date of diagnosis, pre-operative risk factors, pre-operative treatments, pre-operative pulmonary function tests, date of surgery, type of surgical procedures, admission date and status, clinical staging, postoperative events/complications, discharge date and status, discharge disposition, pathological staging, and smoking cessation plans, postoperative urgent care/ER visits, and 30 and 90-day hospital readmissions. Geriatric assessment for FCGs (baseline, 3 months) and patients (baseline, first postoperative clinic visit, and 3 months).
Statistical Considerations:
In Aims 1, 2, and 3, outcomes and mediators will be examined across 3 time points (discharge, 1 and 3 months post-discharge) by treatment group using baseline as covariates. We will also test intervention effects on FCG cancer support services use and patient healthcare resource use. The primary outcome is the change in scores from baseline to discharge (immediate effect) and 3 months post-discharge (sustained effect). In EA 1, we will explore moderators and reciprocal relationships. In EA 2, we will qualitatively explore participants' experience with the MSM Intervention.
Sponsor/Licensee:
National Cancer Institute
Case Report Forms
Not Applicable

Table of Contents

Abbreviations

Abbreviation	Meaning
ACoS	American College of Surgeons
COH	City of Hope
CRA	Clinical Research Associate
DSMC	Data Safety Monitoring Committee
FCG	Family Caregiver
NSCLC	Non-Small Cell Lung Cancer
NCI	National Cancer Institute
PI	Principal Investigator
PMT	Protocol Monitoring Team
PRO	Patient-Reported Outcomes
QOL	Quality of Life
RCT	Randomized Control Trial

1.0 Goals and Objectives (Scientific Aims)

More than 520,000 Americans, most over age 65, carry a diagnosis of lung cancer.[1] The number of individuals diagnosed with early stage lung cancer is projected to increase due to advances in screening and early detection.[2] Surgery is the primary treatment for early stage lung cancer.[1] Due to changes in the healthcare environment as well as advances in surgical care, lung cancer patients are discharged from the hospital earlier after surgery. As such, a greater proportion of the caregiving burden has fallen on family caregivers (FCGs).[3]

Our previous research suggests that lung cancer FCGs experience significant psychological distress and decreased quality of life (QOL) related to their caregiving role.[4-6] Lung cancer surgery patients are a unique population with significant acute and chronic caregiving needs. Patients are older, have greater co-morbidities (pulmonary, cardiovascular), higher psychological distress, and decreased physical functioning. Caregiving demands are high due to acute effects (pain, fatigue) and chronic pulmonary function deficits. As cancer care continues to move further into the home setting, FCGs and patients may be ill-prepared for recovery at home. This can potentially result in significant morbidity, undesirable healthcare resource use, and immense social and economic costs for both FCGs and patients. Despite the tremendous caregiving burden, FCG interventions have been understudied in cancer surgery, and there is a significant, unmet need for family-centered models of care in this area. The **primary purpose** of this trial is to test the efficacy of a Multimedia Self-Management (MSM) Intervention in 200 lung cancer surgery caregiver-patient dyads.

Building from our previous work and based on the Chronic Care Self-Management Model (CCM), the MSM Intervention is a nurse-led, caregiver-based, telehealth, multimedia care model for lung cancer surgery. Its primary focus is to provide support for FCGs on their post-operative caregiving role and managing their QOL needs through goal setting, proactive planning, and building self-management and problem-solving skills. The MSM Intervention also supports caregiver-patient dyads in preparing for surgery and self-management during post-operative recovery at home. The MSM Intervention includes video, handbook, and post-discharge videoconference support. It is administered at five time points: before surgery, during hospitalization, and at Day 2, Day 7, and 2 months post-discharge. It utilizes both in-person encounters as well as videoconferencing for intervention administration. We have preliminary data (N=60) that the MSM Intervention is feasible and acceptable. Our **central hypothesis** is that the MSM Intervention will improve dyadic outcomes and healthcare resource/cancer support services use by enhancing activation, self-efficacy, and knowledge as compared to an attention control group. Accordingly, we propose the following specific aims:

Specific Aim 1: Test the effects of the MSM Intervention on FCG outcomes and cancer support services use at discharge and 3-months post-discharge, comparing intervention and attention control groups.

Hypothesis 1.1: The intervention group will experience lower psychological distress and caregiver burden.

Hypothesis 1.2: The intervention group will experience higher caregiving preparedness and QOL.

Hypothesis 1.3: The intervention group will have lower social work referrals and higher family resource center use.

Specific Aim 2: Test the effects of the MSM Intervention on patient outcomes and healthcare resource use at discharge and 3-months post-discharge, comparing intervention and attention control groups.

Hypothesis 2.1: The intervention group will experience lower psychological distress and higher QOL.
Hypothesis 2.2: The intervention group will have lower in-home nursing care, lower urgent care/ER visits, and lower hospital readmissions.

Specific Aim 3: Test the effects of the MSM Intervention on outcome mediators at discharge and 3-months post-discharge, comparing intervention and attention control groups.
Hypothesis 3.1: FCGs and patients in the intervention group will experience higher activation, self-efficacy, and knowledge.

Exploratory Aims:
EA 1: Explore moderators (age, sex, marital status, caregiver relationship to patient, caregiver employment status, co-morbidities) of FCG and patient outcomes and reciprocal relationships.
EA 2: Determine, through exit interviews, participant's experience with the MSM intervention.

This application addresses key research priorities specified in NCI PAR-16-317, "Intervening with Cancer Caregivers to Improve Patient Health Outcomes and Optimize Health Care Utilization."[7] It addresses two key priorities of the American College of Surgeons (ACoS): 1) the critical role of patients and families as integral members of the surgical team, and 2) that the active involvement of patients and families as partners in surgical care can decrease complications through timely identification of risks.[8] With regards to **impact**, this trial seeks to fill critical knowledge gaps in cancer surgical care where FCG needs are not addressed. Our **long-term goal** is to prove that the CCM can be applied to patients with lung cancer and their FCGs to better prepare them for surgery, improve postoperative outcomes, and optimize healthcare resource/cancer support services use.

2.0 Background

2.1 Introduction/Rationale for Development

Lung cancer is one of the most common cancers and the leading cause of cancer death for both men and women in the United States.[1] Lung cancer patients report higher levels of distress, anxiety, fatigue, and dyspnea than other cancer patients at baseline.[9, 10] The majority of lung cancer patients are older; median age at diagnosis is 70.[11] Tobacco-related comorbid conditions, such as chronic obstructive pulmonary disease (COPD) and cardiovascular diseases, are common.[12] Lung cancer treatments often exacerbate these problems. Surgery is a key component in the treatment for most patients with non-metastatic lung cancer, but by its very nature, lung resection can significantly worsen QOL.[13] Patients experience pain, fatigue, loss of respiratory capacity, and decreased physical function after lung cancer surgery.[14] The most common resection performed for lung cancer is a lobectomy, which typically removes about 20-25% of a patient's lung. After lobectomy, pulmonary function declines to less than half of baseline in the immediate post-operative period.[15] More extensive resections result in even greater decline in lung function. Some aspects of QOL remain compromised long-term, for 6 months or longer after lung cancer surgery.[16]

Due to the impact of lung cancer surgery on patients who have existing severe co-morbidities, this population has an ongoing need for care and major resource use after discharge from the hospital. Whereas only 6% of patients die during the initial hospitalization after lung cancer surgery, twice that number will die in the six months after discharge.[14] Almost a third of patients are discharged with some type of formal, paid home health care, 9% of patients are

transferred to another facility, and 20% of patients are readmitted within 90 days.[17] This is occurring while patients are being discharged earlier after surgery, ultimately resulting in FCGs taking on greater responsibility for recovery at home.

Post-operative caregiving is an intense experience for lung cancer FCGs. During care transitions such as hospital discharge, only 54% of FCGs report having ever been asked about their caregiving needs.[18] Alarmingly, only 29% of cancer caregivers report addressing their own self-management needs.[19] The caregiving role is a major source of stress and burden for FCGs of lung cancer patients and has a negative impact on their QOL.[4, 5, 20] FCGs report significant negative physical health and emotional effects of caregiving.[21, 22] Common adverse economic and social effects of lung cancer caregiving include less engagement with social activities and reduced work hours.[23, 24] Key caregiving challenges for lung cancer FCGs include a profound sense of uncertainty in the patient's potential for functional decline, distress related to managing the patient's emotional reactions to lung cancer, and managing the practical challenges of caregiving.[25] Despite the significant QOL issues, few FCGs report using mental health and support services.[26] Beyond utilizing existing mental health and support services, lung cancer FCGs also desire skills for self-management of QOL concerns.[27]

FCGs and patients often experience heightened feelings of powerlessness before and after lung cancer surgery.[28, 29] The transition from postsurgical hospitalization to self-management post-discharge is frequently threatened by unmet discharge needs[30], decreased patient functional health status, and increased caregiving burden.[31, 32] In this setting, FCGs and patients are often expected to take responsibility for self-managing recovery at home while still experiencing the physical and psychological effects of surgery.[33, 34] Being adequately prepared for surgery and self-management has the potential to empower patients and families, lower distress, and improve QOL.[35] This model of care enables and empowers FCGs and patients to achieve their own goals of care.[34, 36] The IOM defines self-management support as the "systematic provision of interventions to increase skills and self-efficacy in managing health problems, including regular assessment of problems, goal setting and problem-solving support."[37]

Previous research indicates the need for interventions that jointly examine dyadic outcomes. In general, significant effects were observed for emotional distress[38], improvements in problem-solving ability[39], decreased negative appraisal of caregiving[40], and psychosocial well-being.[41] Despite the tremendous caregiving burden associated with cancer surgery, there is an unmet need for evidence-based interventions for FCGs in this population. Caregiving for cancer surgery patients is fundamentally different than the non-surgical population, characterized by multiple transitions in caregiving burden, but FCG interventions in lung cancer have focused primarily on advanced/metastatic stage populations. Out of 27 published RCTs of FCG interventions in adults with cancer, none were specific to surgical populations.[42] A recent systematic review of preparatory interventions for cancer patients undergoing surgery found there were no trials involving FCGs and concluded that "further work should be directed at multi-modal interventions, and those that include FCGs, given their role in assisting patients to prepare and recover from surgery."[43] There is an even greater need for interventions specific for lung cancer surgery given the high level of caregiving demands in this population.

Our scientific premise is based on three key areas. First, there is high quality evidence to support the use of the CCM in the cancer population. Multiple RCTs have demonstrated the efficacy of self-management approaches in the setting of chronic illness.[44] The positive benefits of the CCM are found in COPD[45], diabetes[46], and cancer survivorship.[47] They suggest that self-management coaching-based interventions are effective in improving physical and psychosocial health status, health behaviors, and healthcare resource use (ER visits, at home nursing care,

readmissions).[45-49] Over 40 RCTs have examined self-management interventions for cancer patients, with many demonstrating improved QOL.[50] A significant weakness of the evidence is the heterogeneity of interventions and a relative lack of mechanistic data to clearly indicate which core elements are most essential. Observational evidence in lung cancer suggest that 1) patients with low self-efficacy who also had an FCG with low self-efficacy reported worse physical and psychological well-being; 2) dyads with high self-efficacy reported better QOL; and 3) low FCG self-efficacy is associated with higher FCG distress and caregiver burden.[51] This suggests that interventions targeted at increasing self-efficacy and self-management may be beneficial for this population. There is much more limited data for the use of self-management strategies specific to cancer surgery.[52, 53] Second, multiple studies have demonstrated that in a variety of settings, multimedia approaches to intervention delivery are superior in knowledge-transfer and skills building compared to print materials only. Recent meta-analyses found that video interventions in cancer were as effective, and in some RCTs, superior in knowledge transfer to print materials alone.[54] Videos may be especially suitable for participants with low health literacy, and are more scalable for future dissemination purposes.[54] A weakness in the evidence is the lack of studies demonstrating the effectiveness of multimedia interventions for self-management in FCGs of surgical patients. Third, our previous work with a nurse-led palliative care intervention found that dyadic interventions for symptom management can improve QOL outcomes in lung cancer surgery. However, the intervention was a) not conceptually-based, b) not scalable, and c) focused on traditional educational approaches rather than self-management skills-building.

This randomized trial is innovative in several aspects. 1) The timing of the intervention is novel, with delivery beginning in the preoperative setting. Very few FCG interventions have been examined in cancer surgery and there are virtually no FCG interventions that begin prior to surgery. Beginning the intervention before surgery offers potential advantages to FCGs and patients. Early patient discharge has meant less time to intervene with FCGs after surgery before caregiving begins at home. Beginning support in the lead up to surgery allows dyads to become familiar with elements of the intervention before they undergo the physical and psychological stress of surgery. Data from pulmonary rehabilitation studies indicate that the addition of preoperative education may be more effective than post-operative teaching intervention alone.[55] We have found that the preoperative period is a time of great psychological distress for both FCGs and patients, and is an area of significant unmet need.[56] 2) The application of the self-management (CCM) model to the surgical setting is novel. Previous CCM interventions for FCGs have focused on chronic illnesses. Application of the CCM to cancer surgery represents an important step in the use of self-management for FCG well-being and a significant change in surgical practice paradigm. Previous CCM-based content do not address caregiving needs after cancer surgery. The caregiving experience after lung cancer surgery is characterized by an acute increase in caregiving burden followed by a gradual decrease and a more chronic phase.[56] Our study uniquely allows us to assess the efficacy of self-management through these transitions in peri-operative caregiving. In contrast with most chronic illnesses, the surgical setting also allows for the self-management intervention to be delivered in a more anticipatory fashion. 3) Scalability of the intervention. Our trial builds on our previous work with a palliative care intervention for lung cancer dyads of all stages. The intervention was relatively resource intensive, requiring multiple hour-long, face-to-face education sessions with an advanced practice nurse. It also required weekly, face-to-face interdisciplinary care meetings, which was challenging to implement given clinicians' busy schedules. The intervention also resulted in less QOL benefits for FCGs of surgical patients compared to advanced stage patients. Guided by this

previous experience, we developed the proposed intervention with multimedia resources that specifically addresses the post-operative recovery needs of FCGs and patients. The multimedia resources are readily adaptable for any hospital that performs lung cancer surgery and can easily be accessed over the internet, making the intervention easily scalable. In addition, successful application of the CCM to this cancer population could lead to similar interventions for other surgical patients and their FCGs. There is data that self-management interventions may be particularly useful in resource poor populations.[57]

In summary, overwhelming evidence illustrates: 1) Significant QOL issues and healthcare resource utilization for lung cancer patients after surgery; 2) Significant QOL issues and caregiving burden for FCGs after cancer surgery; and 3) Large unmet need for evidence-based FCG interventions in cancer surgery. Our trial has great potential for success based on the evidence supporting our scientific premise.

2.2 Overview of Proposed Study

This prospective, longitudinal, mixed-methods RCT is designed to test the efficacy of the MSM Intervention in lung cancer surgery. In Aims 1, 2, and 3, outcomes and mediators will be examined across 3 time points (discharge, 1 and 3 months post-discharge) by treatment group using baseline as covariates We will also test intervention effects on FCG cancer support services use and patient healthcare resource use. The primary outcome is the change in scores from baseline to discharge (immediate effect) and 3 months post-discharge (sustained effect). In EA 1, we will explore moderators and reciprocal relationships. In EA 2, we will qualitatively explore participants' experience with the MSM Intervention.

This study will be conducted in compliance with the protocol, Good Clinical Practice (GCP) and the applicable regulatory requirements.

2.3 Preclinical Studies

Not Applicable

2.4 Human Studies

This trial builds directly from an NCI-funded Program Project (P01CA136396, 2009-2014 - PI: Ferrell) that tested a palliative care intervention in lung cancer.[58, 59] We conducted several subset analyses using data from the Program Project that informed this trial:

FCG's Distress Levels, QOL, Burden, and Preparedness – Using usual care group data of 163 FCGs, we found that high caregiver burden and low QOL were common. Subjective stress (emotional impact of caregiving) was high. Caregiving demands increased progressively through including surgery and as the patient's conditions worsened.[5] FCG psychological distress was correlated with QOL, subjective stress burden, and perceived preparedness for caregiving. We identified 3 constructs were that were associated with FCG well-being: 1) ability to manage their own healthcare and QOL needs; 2) perceived preparedness for caregiving and its impact on burden; and 3) perceived emotional distress caused by the caregiving role.[4]

QOL and Psychological Distress Trajectories in Lung Cancer Patients and FCGs After Surgery – To further investigate the effects of lung cancer surgery on QOL, we performed a subset analysis of 41 dyads of lung cancer patients and FCGs (N=82). We observed significant incongruence between patient and FCG outcomes. Psychological distress levels were high for

both patients and FCGs before surgery (3.8/10 patients, 5.1/10 caregivers). Distress levels in patients significantly decreased at 6 and 12 weeks after surgery (2.9/10 and 2.2/10, p=.001). However, distress levels did not improve for FCGs from 6 to 12 weeks (4.2/10 and 4.4/10, p=.157). FCGs did not experience significant improvements in emotional QOL.[6]

FCG and Patient Informational Needs in Lung Cancer Surgery - Using implementation process data, we described the most important QOL topics for early stage lung cancer FCGs and patients. For FCGs (N=65), fatigue, pain, breathing problems/cough, and sleep problems were the most frequently selected physical well-being topics. For psychological well-being, worry/fear and depression were most common. For social well-being, changes in relationships and social support were the most frequently selected topics.[60] Patient's preference for educational topics (N=123) was similar compared to FCGs. Based on these findings, we developed a preliminary version of the MSM Intervention. This version was presented to seven FCGs and patients for review. They confirmed the importance of including community resources, practical caregiving tips, and addressing anxiety. Areas for improvements included emphasizing breathing exercises and minimizing sleep disturbance, and cough.[61]

Pilot Study of the MSM Intervention - A quasi-experimental pilot study was conducted to evaluate the feasibility and acceptability of the MSM Intervention (published in Clinical Lung Cancer).[62] The study enrolled FCGs and patients with cancer who were treated with lung resection. Participants were enrolled before surgery (baseline) and followed for 2-4 weeks after discharge. The first 20 dyads received usual care, and the second group of 20 received the MSM Intervention. The MSM Intervention was delivered at 4 time points: 1) before surgery, 2) before discharge, and 3) twice after discharge via telephone calls. A total of 60 participants (22 FCGs, 38 patients) completed the pilot study. Enrollment rate over 12 months was 70% for all eligible participants. A total of 13 participants (6 patients, 7 FCGs) dropped out of the study (17.8% attrition). Thirty-eight percent of participants were ethnic minorities. Mean age for FCGs was 61.6, and 70.2 for patients. FCGs assigned to the MSM Intervention (N=11) were highly satisfied with the overall intervention (3.6/4.0), the amount of information provided (70% "just right"), and the intervention timing (100% "just right"). FCG surgery-related knowledge scores were significantly improved post-intervention (8.1 to 9.6, 1.5 point difference, p=0.02). A trend for improvement was observed for the subjective demand subscale (p=0.09) for caregiver burden (defined as the extent to which FCGs feel care responsibilities are overly demanding). Emotional QOL was significantly improved post-intervention for MSM Intervention group patients (15.8 to 19.8, p=0.001). Trends for significant improvements in self-efficacy (p=0.09) and patient surgery-related knowledge (p=0.06) were seen. Activation scores improved an average of 4.6 points post-intervention; this difference is clinically meaningful.[63] Unscheduled visits were similar (8 patients for intervention group versus 7 in usual care).

3.0 Patient Eligibility

3.1 Inclusion Criteria

The study sample will consist of 200 caregiver-patient dyads (100 per randomization group) who are scheduled to undergo lung cancer surgery. Participants will be enrolled as dyads only. FCG eligibility criteria include: 1) A family member or friend identified by the patient as being the primary care provider before and after surgery; 2) A patient/care recipient enrolled in the study; 3) Age 21 years or older; and 4) Able to read or understand English or Chinese - the intervention and outcome measures are not validated in other languages. Our intent is to adapt

and test the intervention in a future study with linguistically and culturally diverse populations. Patient eligibility criteria include: 1) Diagnosis of lung cancer or presumed lung cancer (as determined by surgeons); 2) Scheduled to undergo surgery for treatment; 3) A FCG enrolled in the study; 4) Age 21 years or older; and 5) Able to read or understand English or Chinese.

3.1.1 Disease Status

This trial will be conducted in FCGs and patients who are scheduled to undergo lung cancer surgery for treatment. We are targeting patients with stage I-III disease with resectable disease only.

3.1.2 Age Criteria, Performance Status and Life Expectancy

Age criterion for this trial is based on the NIH's age criteria, which defines an adult as individuals aged 21 years and over. There are no restrictions related to performance status or life expectancy.

3.1.3 Child Bearing Potential

Not Applicable

3.1.4 Protocol-Specific Criteria

Not Applicable

3.1.5 Informed Consent/Assent

This protocol is eligible for waiver of informed consent documentation because the risk level is low. All subjects must have the ability to understand and the willingness to provide verbal informed consent.

3.1.6 Prior Therapy

Not Applicable

3.2 Exclusion Criteria

Not Applicable

3.2.1 Study-Specific Exclusions

Not Applicable

3.2.2 Non-Compliance

Subjects, who in the opinion of the investigator, may not be able to comply with the safety monitoring requirements of the study.

3.3 Inclusion of Women and Minorities

The study is open to anyone regardless of gender or ethnicity. Efforts will be made to extend the accrual to a representative population.

4.0 Screening and Registration Procedures

4.1 Screening Procedures

All eligible FCGs and patients who meet study inclusion criteria will be identified through the Division of Thoracic Surgery (Dr. Kim, Dr. Raz, and Dr. Erhunmwunsee). This trial will employ 1 Research Nurse and 2 CRAs to implement the study. The Research Nurse and CRAs, working closely with the Division of Thoracic Surgery, will attend key clinics and meetings (ambulatory clinics, tumor boards) on a weekly basis to identify eligible participants. They will contact eligible participants and explain the study purpose, answer questions, and ascertain interest in participation. If the participant agrees to enroll, informed consent will be obtained. The Research Nurse and one CRA will be responsible for obtaining informed consent, intervention implementation, and data collection. Chinese-speaking participants will be consented using IRB translated and approved Chinese version of the forms. The study employs bilingual research staff that will complete informed consent and all study activities in the appropriate language; no translators will be used.

4.2 Informed Consent

Study objectives and procedures, and their attendant risks and discomforts, will be carefully explained to the potential participants. Informed consents will be obtained in person or via mail, electronic mail, or other electronic applications (i.e. DocuSign™) to obtain electronic signatures from each patient per standard practice. If necessary (i.e. if potentials have left the clinic), a telephone/verbal informed consent will be obtained first in order to begin study in a timely manner. Signed informed consent will then be obtained for this study either in person when participants are at COH or via mail, electronic mail, or other electronic applications (i.e. DocuSign™). For FCGs who may not accompany participants to clinic visits, the consent for signature will be emailed or mailed to them and returned to COH when signed, or completed by other electronic application (i.e. DocuSign™) to obtain electronic signature per standard practice.

4.3 Registration Requirements/Process

The Research Nurse and CRA will establish eligibility and consent before contacting the registrar at the time of enrollment. The registrar will enter the patient on a pre-established randomization log, and report the assignment to the Research Nurse and CRA, who will then communicate the assignments to the participants in both study arms. Participants will complete baseline assessment following informed consent.

4.4 Randomization and/or Dose Level Assignment

Each FCG-patient dyad will be randomly assigned to either the MSM Intervention or attention control group, using a stratified and blocked randomization. Strata are defined by surgical approach (open or minimally-invasive). Variable block sizes will be used to maintain approximate balance and pre-assignment masking.

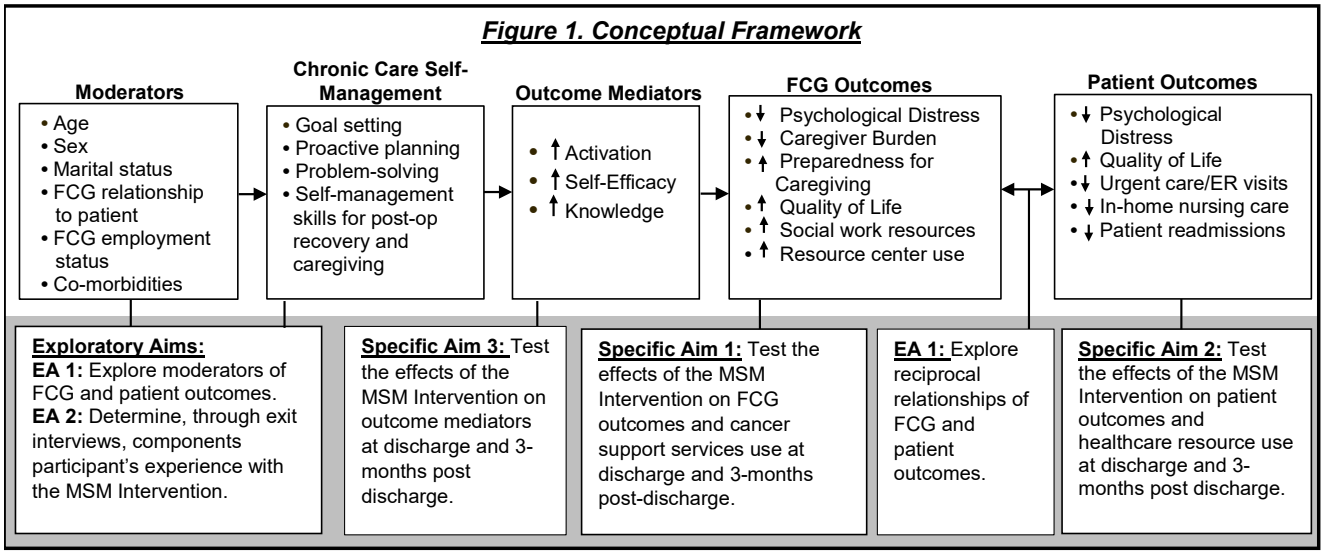
5.0 Treatment Program

5.1 Intervention Overview – Conceptual Framework

The MSM Intervention is based on the Chronic Care Self-Management Model (CCM).[64-66] The CCM transforms a reactive health system into one that improves FCG and patient outcomes through proactive planning and self-management skills building.[67] The CCM is based on social cognitive theory and focuses on skills building to empower and engage individuals in their own care. Self-management includes goal setting, problem solving, and post-operative recovery/caregiving skills building. Self-management coaching complements traditional education in supporting patients and FCGs to live the best possible QOL before and after surgery. The MSM Intervention combines both traditional (information and technical skills) and self-management education (enhance activation, self-efficacy, and confidence in using the information and technical skills).

As depicted in **Figure 1**, FCGs and patients bring personal and health status factors that will influence their capacity to integrate self-management strategies into their daily activities. These factors (e.g. age, sex, marital status, FCG relationship to patient, FCG employment status, co-morbidities) are potential moderators based on the current literature that influence intervention uptake.[20, 68-71] We hypothesize that the MSM Intervention, as guided by the Chronic Care Self-Management Model, will enhance outcome mediators, such as activation (confidence in their ability to manage their health) and self-efficacy (confidence to carry out behaviors necessary to achieve a desired goal), and knowledge.[34, 72] The mediator effects, based on CCM evidence[72], are hypothesized to serve as the mechanisms whereby the MSM Intervention improves FCG and patient outcomes (psychological distress, caregiver burden, preparedness for

Figure 1. Conceptual Framework



caregiving, QOL, healthcare resource/cancer support services use). Reciprocal interactions (EA 1) between FCG and patient outcomes are hypothesized to be interrelated.[4-6] Evidence from our work suggest that lung cancer FCGs' and patients' psychological distress are correlated; FCG distress is associated with perceived burden, caregiving preparedness, as well as patient physical and psychological well-being.[4, 5, 20]

Intervention Design and Content - The MSM Intervention, Preparing for your Lung Cancer Surgery, is a nurse-led, caregiver-based, multimedia intervention. The intervention coaches lung cancer FCGs on pre- and post-operative caregiving skills building and managing their own QOL needs.[61] The current literature provides evidence that FCGs suffer from symptoms such as sleep disturbance and fatigue, forget to manage their own healthcare, and have decreasing ability to cope with the stresses of caregiving.[73-76] In addition, the MSM Intervention also targets FCG-patient dyadic knowledge and self-management skills in preparing for surgery and post-operative recovery activities. The intervention uses a multimedia approach (15 minute video + handbook – available in English or Chinese) to facilitate intervention delivery. Content in the video and handbook are identical. The video specifically re-enforces content that involves skills building for postoperative recovery activities and caregiving (e.g. step-by-step instructions on using an incentive spirometer (IS) for deep breathing exercises).

The MSM Intervention is divided into five sessions, provided before surgery, before discharge, and at day 2, 7, and 2-months post-discharge (**Table 1**). Intervention doses are based on current evidence for pre-operative educational support in breast, cardiothoracic, and orthopedic surgery[77-81], and established post-operative recovery activities that are associated with

Table 1. "Preparing for Your Lung Cancer Surgery" – MSM Intervention Content

Component	Family Caregiver Content	Caregiver-Patient Content
Session 1 (before surgery) • What to expect before surgery • What to expect day of surgery • What to expect after surgery	• Goal Setting • Importance of FCG self-care • Managing FCG psychosocial well-being • Problem solving coping skills	• Understanding your surgery • Tobacco cessation • Breathing exercise (incentive spirometer) • Physical activity before surgery • Coping with anxiety • Day of surgery admissions information • Pain assessment and management • Chest tube • Breathing exercise (incentive spirometer) • Early ambulation • Daily self-monitoring plan
Session 2 (before discharge) • What to expect after discharge (Healing at home)	• Goal Setting • Managing FCG physical well-being • Managing FCG healthcare needs • National and local cancer support services	• Recognizing and managing symptoms and medications at home • Pain assessment and management • Cough and breathing • Nutrition • Physical activities, intimacy, return to work • Sleep disturbance • When to call your doctor
Sessions 3, 4, 5 (days 2, 7, 2-months post-discharge • RN Videoconference Support	• Re-enforce problem-solving and self-management skills • Assess FCG QOL needs • Review goals	• Re-enforce self-management skills • Assess patient symptoms and QOL needs

outcomes (pulmonary exercise, early ambulation).[82, 83] Session 1 focuses on what to expect before surgery and during hospitalization after surgery. The information is first presented in an 8 minute video viewed by both FCGs and patients through provided ipads, followed by goal setting and self-management skills coaching using the handbook. Coaching and self-management skills assessment will be focused on caregiving skills to support patient post-operative recovery as well as skills to manage caregivers own QOL needs. FCGs will learn about the importance of managing their own physical and psychosocial well-being (anxiety, roles and relationships, social support). FCGs will also be coached on using problem-solving skills to enhance preparedness in caregiving. Problem solving skills coaching involves identification of perceived barriers to caregiving, prior plans or strategies to overcome these barriers, and identification of new strategies to facilitate caregiving responsibilities. Together as a dyad, FCGs and patients will learn about what to expect before and after surgery (understanding lung cancer surgery, importance of tobacco cessation, breathing exercises using an IS, physical activity, coping with

anxiety, day of surgery information). Dyadic content for what to expect after surgery focuses on promoting postoperative recovery activities (pain assessment and management, use of IS and breathing exercises, early ambulation). Patients, along with FCG participation, will complete daily self-monitoring on pain severity, frequency of deep breathing exercises, and frequency of ambulation during hospitalization.

Session 2 focuses on what to expect after discharge and will be delivered within 24 hours of discharge. If patients are discharged from hospital over the weekend, participants will only view the video before discharge. A separate telephone call will be scheduled for Monday morning with the Research Nurse to deliver the rest of the content for Session 2. Session 2 video lasts 7 minutes, and will be followed by goal setting and self-management skills coaching using the handbook. FCGs will learn about tending to their own physical well-being and healthcare needs. Physical symptoms of caregiving, such as sleep disturbance and fatigue, will also be addressed. FCGs will receive content on managing their own healthcare needs (medications, co-morbid conditions, doctor's appointments). National and local cancer support services for FCGs will be provided. Dyadic content will re-enforce postoperative recovery activities to be continued at home (recognizing and managing symptoms, medications at home, pain assessment and management, breathing exercises, physical activity). Common postoperative symptoms, such as cough, dyspnea, fatigue, and sleep disturbance will be reviewed. Content also addresses nutrition, intimacy, return to work, and when to contact the surgical team.

Participants will be able to view the videos at home after initial viewings during Sessions 1 and 2. Videos will be accessible through a trial-specific secure website made available only to participants randomized to the MSM Intervention group. The website will be accessible via computers, smartphones, or tablets.

Sessions 3, 4, and 5 involves three RN support sessions after discharge through telephone calls (separate sessions for FCGs and patients). During these sessions, the Research Nurse will re-enforce problem-solving approaches with the FCGs and self-management with both FCGs and patients. They will also review goals, assess the participants' QOL needs and facilitate any care coordination and communication with the surgical team as needed. Based on our pilot study experience, the estimated time to complete sessions 1 and 2 is about 40-60 minutes (video viewing and RN coaching). Each videoconference (sessions 3, 4, 5) will last 20-30 minutes.

Study Procedures - The Experimental Design Schema on page 2 of the protocol provides the study schema for this trial.

For the MSM Intervention group, Session 1 video will be viewed by FCGs and patients approximately 3-7 days before surgery. The video will be delivered during a routine clinic visit in the pre-anesthesia clinic. If needed, the video can be administered remotely. Participants will receive the handbook (English or Chinese) either in person or by mail following viewing, and the Research Nurse will coach participants on session 1 content, and answer any questions related to the MSM Intervention. After surgery, FCGs/patients will view the Session 2 video within 24 hours of planned discharge. Session 2 video can be administered in person or remotely by internet and telephone. In addition, nurses in 4 West will also be able to show session 2 video to participants. Handbook content will be reviewed, and the Research Nurse will coach participants on completing daily self-monitoring during hospitalization. For participants discharged over the weekend, they will view Session 2 video before discharge, and receive a scheduled call Monday morning with the Research Nurse to review rest of the content for Session 2. Outcomes will be re-assessed at discharge. Research Nurse will complete Sessions 3, 4, and 5 of the MSM

Intervention (RN telephone support) at day 2, day 7, and 2 months post-discharge. Outcomes will be re-assessed at 1-month and 3-months post-discharge.

For the attention control group, FCGs and patients will view Session 1 video (American Cancer Society video on "Clinical Trials") approximately 3-7 days before surgery. This will be delivered during a routine clinic visit in the pre-anesthesia clinic. If needed, the video can be administered remotely. Participants will receive American Cancer Society print materials either in person or by mail on the topic following viewing, and the CRA will answer any questions related to the materials. After surgery, participants will view Session 2 video (American Cancer Society video on "Clinical Trials") within 24 hours of planned discharge. Session 2 video can be administered in person or remotely by internet and telephone. In addition, nurses in 4 West will also be able to show session 2 video to participants. American Cancer Society print materials on the topic will be reviewed, and the CRA will answer any questions related to the materials. All videos and written materials are available in English and Chinese. Three telephone calls at day 2, day 7, and 2 months post-discharge will be initiated by the CRA. During these calls, the CRA will ask participants if they have any questions with the American Cancer Society materials. Outcome assessments will be the same as the MSM Intervention group.

For lung cancer surgery, a 3-month follow-up is the most appropriate time period to address the main outcomes in this study. From a patient QOL perspective, pulmonary function declines immediately after surgery, but continues to improve for about 3 months afterwards.[15] Beyond that point, respiratory capacity plateaus, such that the lung function 3 months after lung cancer surgery closely approximates the permanent status of the patient. In terms of healthcare resource use, about half of readmissions occur within 30 days, but almost an equal number of readmissions occur between 30 and 90 days.[17] In addition, the 90 day period after major surgery is included in the "global surgical package" by the Centers for Medicare and Medicaid Services (CMS), which reflects the period of time that should be considered the peri-operative period.[84]

Several approaches are included to ensure intervention rigor and prevent experimental drift. Design for establishing intervention fidelity is guided by the Technology Model of Intervention Fidelity.[85-87] First, interventionist manual will be developed to layout intervention goals, and strategies to achieve these goals. Second, training and supervision of the Research Nurse and CRAs will be undertaken. Third, intervention fidelity will be monitored during study implementation using an intervention fidelity measure. The PI will monitor intervention fidelity. Rigor will be established by double-coding of monitoring results. When study accrual begins, sessions for the first 5 participants will be tape-recorded and every 10th session thereafter will be recorded and reviewed by the PI. Fidelity issues and review results will be discussed with the research staff during team meetings.

5.2 Planned Duration of Therapy

Study participation is planned for approximately 3-4 months. The timeframe covers before surgery, postop acute care, and 3 months post-discharge.

5.3 Criteria for Removal from Treatment

The only criterion for disenrollment is if participants desire to discontinue with study participation.

5.4 Subject Follow-Up

Subjects will be followed for approximately 3 months.

5.5 Supportive Care, Other Concomitant Therapy, Prohibited Medications

The Research Nurse and CRAs will review participant's responses to all self-reported outcome measures and alert the attending thoracic surgeon if participants show risk of self-harm or other serious conditions. These participants will be referred to supportive care and social work as necessary after evaluation by the attending surgeon. Otherwise, there are no restrictions to the use of supportive care medications, other concomitant therapy and no prohibited medications.

5.6 Additional Studies

Patients enrolled in the study will be consented to provide permission to access their routine CT scans for future research purposes. The future use involves improving the knowledge on accurate methods of measuring muscle mass. The study will access routine CT scans before surgery and scans at 6-months after surgery. Patients will not incur additional costs or harms because only routine CT scans completed for treatment preparation and for follow-up will be used.

All outcome measures, as described below, are available and validated in both English and Chinese.

FCGs and patients will also complete Geriatric Assessments (GA), available in both English and Chinese. All participants, regardless of age, will complete GA throughout the study. In our previous Program Project grant in lung cancer, we had completed GA for all patients, regardless of age. Many key components of the GA (such as comorbidities, social support, social activity, weight loss, body mass index) are relevant outcomes to consider for all surgical patients, regardless of age. In addition, we anticipate that many FCGs will be older. Our administration of the GA in FCGs is exploratory, and will provide an innovative approach to expand the utility of GA in oncology.

The Geriatric Assessment (GA) Tool developed by Hurria and colleagues is composed of a group of instruments, some of which are completed by the research staff and some by the patient. Each of these is described below. Time for patients to complete the group of questionnaires is 27 minutes.[88, 89]

1) Instrumental Activities of Daily Living (IADL): [subscale of the Older American Resources and Services (OARS)]The OARS Multidimensional Functional Assessment Questionnaire (MFAQ) was developed to provide a profile of the level of functioning and need for services of older persons who live at home but may have some degree of impairment. The MFAQ has been tested on over 6,000 older community residents.[90] The Instrumental Activities of Daily Living (IADL) subscale consists of 7 questions rated on a three-point Likert scale of degree to which the activity can be performed independently. Norms are available for the MFAQ based on 2,146 elderly community residents.[90]

2) Activities of Daily Living: [subscale of Medical Outcomes Study (MOS) Physical Health] The MOS Physical Health Scale contains measures of higher levels of physical functioning than

those described in other activities of daily living scales. The variation in functioning among healthier patients in the study will be examined through asking about higher order functioning. The scale includes items on vigorous activities (running, lifting heavy items) as well as basic activities (bathing and dressing). The 10 items are rated on a three-point Likert scale of independent performance of the activity. At least six items must be answered to obtain a total score. A total score is created by summing the item scores and transforming them to range from 0 to 100. Internal consistency of the physical function score is high at 0.92.[91]

3) Karnofsky Physician-Rated Performance Rating Scale (KPS): The Karnofsky Performance Status, has been widely used in the evaluation of cancer patients.[92] It is a general measure of patient independence in carrying out normal activities. Patients are given a score on a numerical scale of 0-100 as a global indicator of functional status. Studies on inter-rater reliability between nurse and social worker KPS ratings indicate good correlation ($r = 0.69$, $p<.001$). KPS was most strongly correlated with variables related to physical functioning (difficulty with stairs: $r = 0.63$; difficulty with balance: $r = 0.61$).[93]

4) Timed Up & Go: The timed "up and go" is a test of physical mobility. The test, measured in seconds, is the time it takes for an individual to stand up from a standard arm-chair (approximate seat height of 46 cm), walk a distance of 3 meters (10 feet), turn, walk back to the chair, and sit down again. Intra-rater and inter-rater reliability was extremely high (intra-class correlation 0.99). Performance on the timed "up and go" test significantly correlated with scores of other performance measures including Berg Balance Scale ($r = -0.81$), gait speed ($r = -0.61$), and Barthel Index of ADL ($r = -0.78$).

5) Number of Falls in Last 6 Months: Older patients are at risk for falls and injury secondary to falls because of gait and balance impairments. In patients with cancer the risk is even greater for a number of reasons. First, bony metastases may place them at risk of a pathologic fracture with falls. Secondly, patients receiving chemotherapy may have a low platelet count which puts them at greater risk of hemorrhage. Lastly, commonly used chemotherapy drugs may have neurologic complications resulting in falls. For example, paclitaxel and cisplatin may cause neuropathy, fluorouracil and cytarabine may cause cerebellar toxicity. For these reasons, knowing a patient's risk of falling before treatment could help providers make treatment decisions.

6) Physical Health Section [subscale of The Older American Resources and Services Questionnaire (OARS)]: The OARS Physical Health Section is a comorbidity scale which contains a list of concurrent illnesses and the degree to which they impair daily activities, rated on a three-point scale of "not at all" to "a great deal." Medication use is recorded. Test-retest reliability was good ($r=.66$) over a five-week period. In terms of validity, the Physical Health subscale correlated significantly with health professional ratings (Kendall's tau co-efficient $=.75$). We will also capture the patient's medication list, so as to confirm that the comorbidity list reported by the patient is complete.

7) Blessed Orientation-Memory-Concentration Test: The BOMC consists of 6 questions designed to screen for gross cognitive impairment. A score >11 signifies cognitive impairment. The test-retest reliability is high (Spearman Rank Correlation 0.96; $p < 0.001$). The BOMC has excellent validity as a screening instrument, correlates highly with clinicians' ratings of dementia severity ($r=0.89$), predicts results from a longer (26 item) mental status questionnaire, and discriminates between patients with mild, moderate, and severe cognitive deficits.

8) Hospital Anxiety and Depression Scale (HADS):The Hospital Anxiety and Depression Scale (HADS) is a 14-item self-administered measure that has been well tested in cancer populations. It has two 7-item subscales that assess depression and anxiety. The scale is considered

particularly appropriate for use with medically ill patients because of the absence of somatic items that often confound the determination of psychiatric problems in a medically ill population. Reported anxiety and depression cutoff scores on the HADS have varied from 8 to 11. The total cutoff score for psychological distress has ranged from 13, reflecting adjustment disorder, to 19, reflecting major depressive disorders. Ibbotson and colleagues found that an overall cutoff score of 15 or greater resulted in 80% sensitivity, 76% specificity, and a positive predictive value of 41% for psychological distress.[94]

9) Medical Outcomes Study (MOS) Social Activity Limitations Measure: The impact of cancer on patients' social functioning will be assessed by the Social Activity Limitations scale from the Medical Outcome Study (MOS).[91] As with all MOS measures, the Social Activity Limitations scale was developed from a national sample of medically ill patients being treated in outpatient facilities. The four-item scale assesses the extent to which physical or emotional problems have interfered with social activities. All items are rated on a 5-point Likert scale, with response categories varying with each item. The mean of the total score is transformed to a scale of 0-100, with a higher number indicating greater support. Internal consistency was good (alpha coefficient = .77). The scale correlates significantly with a range of measures: role limitations due to physical (r= .52) and emotional (r = .49) health, psychological distress (r= .64) and pain (r = .55).

10) Medical Outcomes Study (MOS) Social Support Survey: Emotional/Information and Tangible Subscales: This is a 20-item measure of social support, with four subscales: emotional/informational, tangible, affectionate, and positive social interactions. The scale was developed as part of the Medical Outcome Study, tested on 2987 patients, and designed to assess quality of life across medical conditions. In this study, we use the Tangible (access to material aid or behavioral assistance) and Emotional/Information (the expression of positive affect and empathetic understanding; the offering of advice, information, guidance, or feedback) subscales. All but one item is rated on a five-point Likert scale from "None of the Time" to "All of the Time." Internal consistency of the subscales and total score are excellent (alpha coefficient > 0.91). Convergent validity was demonstrated by significant correlations of social support total score with measures of mental health (r =.45).[91]

11) Percent Unintentional Weight Loss: Patients will be asked to quantify the amount of unintentional weight loss in the past 6 months and to record their baseline body weight 6 months ago. The following is the calculation for % unintentional weight loss: unintentional weight lost in last six months = (unintentional weight loss in last 6 months/baseline body weight) x100.

12) Body Mass Index: Weight and height will be measured in order to calculate body mass index, by the following formula:

$$\text{BMI} = \frac{\text{Weight in kg}}{\text{Height in m}^2}$$

The assessments will be completed in-person on an iPad during a routine clinic visit, or by telephone. Patients will complete GA at baseline, first postoperative clinic visit, and 3 months. FCGs will complete GA at baseline and 3 months).

13) Mini-Cog: The mini-cog is a validated tool recommended for use to assess Chinese speaking participants in place of the blessed-orientation-memory-concentration test. A score of <3 is a validated cut off for dementia screening, although a score of <4 may be used for more sensitive screening of cognitive impairment.

COVID-19 Questions- These questions will be asked 1 month post-discharge to obtain qualitative data from patients and FCGs on the impact of the COVID-19 pandemic. FCGs and patients will provide answers separately. We will only collect this data going forth with newly enrolled patients/FCGs. We will not ask patients/FCGs already enrolled in the study to complete the questions.

COVID-19 Interview Questions for Healthcare Professionals – These interview questions will be used to obtain qualitative data from thoracic surgeons and thoracic surgery nurse practitioners on the impact of COVID-19 on cancer care. Interviews will be conducted individually with each surgeon/NP (total = 5). Interviews will be conducted once only.

Social Determinants of Health (SDH) – Key Informant Interviews: Six participants (3 FCGs, 3 patients) will be invited to participate in individual (Key Informant) interviews. The purpose of the 6 interviews is to inform the development of the interview guide to determine social determinants of health-related needs of FCGs/patients in relation to lung cancer surgery. A total of 30 participants (15 FCGs, 15 patients) will then be invited to participate in individual (Key Informant) interviews. A total of 36 FCGs/patients (3 FCG/patient dyads) will be randomly invited to participate in six focus groups. Open-ended questions will be used to garner discussions around SDH and QOL outcomes for FCGs and patients.

Invitation letters will be sent to potential participants via email and postal mail; the letters will instruct interested participants to contact the investigators (Dr. Teteh). Each key informant interview will last approximately 30 minutes and each focus group session will last approximately 60 minutes. Both will be conducted via Zoom or MS Teams videoconferencing to minimize travel burden for participants. Set-up for the Zoom/MS Teams system and instructions for use will be provided prior to each interview. Only newly enrolled dyads after IRB approval will be invited to participate in the interviews. Dyads that are already enrolled will not be invited.

Social Determinants of Health (SDH) – Quantitative Survey: FCGs and patients will complete the following questionnaire about the impact of social determinants of health. For English-speaking participants who enrolled in the study but did not complete the SDH quantitative survey, they will be retrospectively invited to complete the survey at one time only. Participants will be consented using IRB approved addendum consents before survey completion.

Protocol for Responding to and Assessing Patients' Assets, Risks, and Experiences (PRAPARE)[95]: This 21-item instrument measures SDH domains for patients related to environment, economic stability and social and emotional health factors. PRAPARE is a standardized patient and social risk assessment tool informed by research on SDH and aligns with national initiatives (e.g. Department of Health and Human Services' Healthy People 2020), federal reporting requirements, and International Classification of Diseases-10 clinical coding system.

Spiritual Well-Being – Quantitative Survey: Patients will complete the following questionnaire about spiritual well-being. For English-speaking participants who enrolled in the study but did not complete the Spiritual Well-Being quantitative survey, they will be retrospectively invited to complete the survey at one time only. Participants will be consented using IRB approved addendum consents before survey completion.

Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being Scale (FACIT-Sp-12): This 12-item tool assesses a patient's spiritual well-being using a 5-point Likert scale. FACIT-Sp-12 measures sense of meaning and peace (8-item subscale), and the role of faith in illness (4-item subscale). The internal consistency ranges from 0.81 to 0.88 for the total scale and subscales. Items score ranges from 0 to 48 and a higher score indicates better spiritual well-being. The tool was previously tested in a sample of lung cancer patients.[96] FCGs will not complete the survey.

5.6.1 Laboratory Studies

Not Applicable

5.7 Definition of Dose-Limiting Toxicity (DLT)

Not Applicable

6.0 Dose Delays/Modifications for Adverse Events

Not Applicable.

7.0 Data and Safety Monitoring, Unanticipated Problems and Adverse Event Reporting

7.1 Data and Safety Monitoring

Definition of Risk Level

This is a Risk Level 1 study, as defined in the City of Hope Institutional Data and Safety Monitoring Plan [policy effective date: 07/09/14], because it involves an educational/behavioral intervention and surveys.

7.2 Monitoring and Personnel Responsible for Monitoring

The Principal Investigator (PI) is responsible for monitoring protocol conduct and reporting to the City of Hope (COH) Data and Safety Monitoring Committee (DSMC) and Institutional Review Board (IRB) as indicated in the sections below.

7.3 Unanticipated Problems (UP) Involving Risks to Subjects or Others

An unanticipated problem is any incident, experience or outcome that **meets all three** of the following criteria:

1. Unexpected (in terms of nature, severity, or frequency) given the following: a) the research procedures that are described in the protocol-related documents such as the IRB approved research protocol, informed consent document or Investigator Brochure (IB); and b) the characteristics of the subject population being studied; **AND**
2. Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcomes may have been caused by the procedures involved in the research); **AND**

3. Suggests that the research places participants or others at greater risk of harm (including physical, psychological, economic, or social harm) than previously known or recognized.

Any UP that occurs during the study conduct will be reported to the DSMC and IRB in accordance with the City of Hope's Institutional policy [policy effective date: 05/14/14] using the electronic submission system, iRIS.

7.4 Deviations

A deviation is a divergence from a specific element of a protocol and that occurred without prior IRB approval. Deviations from the approved protocol should be avoided, except when necessary to eliminate an immediate hazard to a research participant. A Corrective and Preventative Action (CAPA) plan should be developed by the study staff and implemented promptly to avoid similar issues in the future. All deviations from the protocol must be documented in study source documents and promptly reported to the DSMC and IRB.

Reporting Deviations

Investigators may deviate from the protocol to eliminate immediate hazards for the protection, safety, and well-being of the study subjects without prior IRB approval. For any such deviation, the PI will notify the DSMC and IRB, within 5 calendar days of its occurrence by electronic submission of a Deviation Notice via iRIS.

Single Subject Exception (SSE) Amendment Request

Deviations from the written protocol that are not done to eliminate an immediate hazard(s) for the protection, safety and well-being of study subjects but may increase risk and/or alter the protocol integrity require prior IRB approval. The deviation is submitted as a Single Subject Exception (SSE) amendment request. An IRB approved SSE does not need to be submitted as a protocol deviation to the DSMC. The SSE should be submitted according to the IRB guidelines and Clinical Research Protocol Deviation policy [policy effective date: 11/07/11] and submitted via iRIS.

A deviation that is not an SSE (i.e., discovered after the occurrence) must be reported to the COH DSMC and IRB according to the Clinical Research Protocol Deviation policy [policy effective date: 11/07/11] and submitted via iRIS.

8.0 Agent Information and Risks

Not Applicable.

9.0 Correlative/Special Studies

No correlative studies will be performed during this trial.

10.0 Study Calendar

	Baseline	Before Surgery	Treatment	Before Discharge	Day 2 Post-Discharge	Day 7 Post-Discharge	First Postop Clinic Visit	1 Month Post-Discharge	2 Month Post-Discharge	3 Month Post-Discharge
Informed Consent	R									
Baseline Assessment	R									
*Intervention – Session 1		R								
SURGERY			X							
*Intervention – Session 2 (note: for participants discharged over the weekend, video will be viewed before discharge, and rest of the session will be delivered via phone on Monday morning				R						
Before Discharge Assessment				R						
*Intervention – Session 3					R					
*Intervention – Session 4						R				
1 Month Post-Discharge Assessment								R		
*Intervention – Session 5									R	
3 Month Post-Discharge Assessment										R
Geriatric Assessment (FCGs)	R									R
Geriatric Assessment (Patients)	R						R			R
Social Determinant of Health Questionnaire (Patients)	R									

Social Determinants of Health Questionnaire (FCGs)	R									
Spiritual Well-Being (Patients only)	R									R

* Will only be administered to subjects in MSM intervention group

11.0 Endpoint Evaluation Criteria/Measurement of Effect

11.1Response Criteria

Not Applicable.

12.0 Data Reporting/Protocol Deviations

12.1Data Reporting

12.1.1 Confidentiality and Storage of Records

A REDCap database will be developed by COH's Research Informatics for this study. All completed outcome surveys will stored electronically in the REDCap database. The database is passcode-protected, and only the PIs and research staff will have access to the REDCap database. Recordings of key informant and focus group interviews will be stored in the City of Hope firewall protected network. Only the PIs and research staff will have access to the recordings. These recordings will be transcribed for data analysis purposes and then deleted after completion of the study. When results of this study are reported in medical journals or at meetings, identification of those taking part will not be disclosed. Medical records of subjects will be securely maintained in the strictest confidence, according to current legal requirements. They will be made available for review, as required by the FDA, HHS, or other authorized users such as the NCI, under the guidelines established by the Federal Privacy Act and rules for the protection of human subjects.

12.1.2 Subject Consent Form

Initial verbal consenting will only be used when potential participants are not in the clinic. In these situations, the Research Nurse and CRA will use the approved information sheet (available in both English and Chinese) for verbal consent process. An informed consent (available in both English and Chinese) will then be obtained either in writing in person, by mail, or electronic mail, or electronically via other electronic applications (i.e. DocuSign™). Otherwise, all participants will complete either a written or electronic informed consent (i.e. DocuSign™) prior to study participation. The study will use one written or electronic informed consent (with signature line) and one information sheet (without signature line) for FCGs, and one written or electronic informed consent (with signature line) and one information sheet (without signature line) for patients. Documentation of initial verbal consent for study participation will be charted through progress notes and maintained in the patients' electronic medical records as required by the Institutional Review Board.

12.1.3 Data Collection Forms and Submission Schedule

Table 2 provides outcome measures and the corresponding evaluation time points. All outcome measures completed by patients/FCGs are available and validated in both English and Chinese. We will collect sociodemographic and health status data (e.g. age, sex, race/ethnicity, education, employment, relationship to patient, religious preference, marital status, living

situation, income, co-morbidities, and tobacco history) for both FCGs and patients at baseline. Outcomes are assessed at baseline (before surgery), discharge, 1 month, and 3-months post-discharge. They will take about 30 to 45 minutes to complete. Outcomes were selected based on our conceptual model, previous research in lung cancer, and recommendations on common data elements for self-management research.[97]

Table 2. Outcome Measures by Aims and Assessment Time Points

	Measures	Baseline	Discharge	1 month	3 months
Family Caregivers	Distress Thermometer	x	x	x	x
	Montgomery Borgatta Caregiver Burden Scale	x	x	x	x
	Preparedness for Caregiving Scale	x	x	x	x
	COH-QOL-Family	x	x	x	x
	Family Caregiver Healthcare Use Survey		x	x	x
Patients	Distress Thermometer	x	x	x	x
	FACT-L	x	x	x	x
	Patient Healthcare Use Survey (non-COH)			x	x
	Medical Chart Audit Form				x
Outcome Mediators	Family Caregiver Activation in Transitions (FCAT) Tool	x	x	x	x
	Patient Activation Measure (PAM)	x	x	x	x
	Self-Efficacy Scale	x	x	x	x
	Surgery-Related Knowledge Tool	x	x	x	x
Exploratory	Sociodemographic and Health Status	x			
	STS General Thoracic Surgery Data Collection Form				x
	Exit Interview Discussion Guide				x
Process	RN Debriefing Form	After each intervention session			
	Intervention Fidelity Checklist	1st five participants and every 10th session thereafter			

Family Caregivers:

Distress Thermometer (DT) – The DT is an efficient, low subject burden measure to evaluate psychological distress over the past week, based on a scale of 0 (no distress) to 10 (extremely distressed). According to the National Comprehensive Cancer Network (NCCN), psychological distress is defined as mixed anxiety and depression symptoms.[98] A cut-off of 3/10 indicates a need for intervention, with acceptable sensitivity (94.1%) and specificity (71.2%) compared to

the Hospital Anxiety and Depression Scale (HADS).[71] The DT has been validated in FCGs, with receiver operating characteristics (ROC) of 0.88 relative to the HADS.[71, 99] It is also validated in lung cancer patients.[70]

Montgomery Borgatta Caregiver Burden Scale (MBCBS) – This 14-item tool was designed to measure the impact of caregiving on three dimensions of burden: objective, subjective demand, and subjective stress. Internal consistency for the three dimensions ranges from .81 to .90.[100] The ordinal scale ranges from 1-5 (a lot less to a lot more). The following cutoff scores are interpreted as high burden: 1) a score of 23 or > for objective burden, 2) a score of 15 or > for subjective demand, and 3) a score of 13.5 or > for subjective stress.

Preparedness for Caregiving Scale – This is an 8-item scale of the Family Care Inventory by Archbold and colleagues.[101] Items are scored from 0 to 4, with higher scores indicating better preparedness. A mean score is tabulated for all items. Internal consistency ranges from 0.88 to 0.93.[102, 103]

City of Hope-Quality of Life–Family (COH-QOL-Family) – This is a 37-item instrument that measures the FCG QOL in the physical, psychological, social, and spiritual well-being domains. Ordinal scale ranges from 0-10, with higher scores indicating better QOL. The instrument was revised and tested from 1994-1998 in a study of 219 FCGs of cancer patients. The test-retest reliability was r=.89 and internal consistency was alpha r=.69.[104, 105]

Family Caregiver Healthcare Use Inventory – This is a self-report measure of 4 yes/no items on cancer support services use (social work referrals, family resource center use). This inventory was adapted from Given and colleagues[106] and Meneses and colleagues.[107]

Patients:

Distress Thermometer (DT) – this is the same measure used to assess FCG psychological distress.

Functional Assessment of Cancer Therapy-Lung (FACT-L) - The FACT-L is a cancer specific version of the FACIT System developed specifically for lung cancer. It contains the FACT-G scales with 27-items divided into physical, social/family, emotional, and functional well-being domains. A 10-item disease-specific symptom index (LCS) is included. For each item, the respondent indicates on a 5-point Likert scale (0=not at all; 4=very much) how true each statement is during the past 7 days. Reliability was tested in 116 lung cancer patients. Cronbach's alpha for the FACT-L is 0.89.[108] A 2 to 3 point change in scores for the FACT-L subscales is considered to be the minimal clinically important difference (MCID).[109]

Medical Chart Audit Form – This form will be used to record healthcare resource use provided at the cancer center as documented in electronic medical records (EHR). These include in-home nursing care, urgent care/ER visits, and 30 and 90-day hospital readmissions.

Patient Healthcare Use Inventory – This is a self-report measure of 23 yes/no items on non-COH healthcare resource use (hospital admissions, urgent care/ER visits, support services visits). It was adapted from Given and colleagues[106] and Meneses and colleagues.[107] McCorkle and colleagues used a similar method for an intervention study, and reported a 95% agreement between patient self-report data and medical chart audits.[110]

Outcome Mediators:

FCG Activation in Transitions Tool (FCAT) – This 10-item survey was designed to assess FCG's level of engagement and preparedness to care for patients during care transitions. Psychometric assessment was conducted in two randomly equivalent waves of participants

(N=434), including FCGs of patients with cancer and/or chronic lung disease. The estimated person-separation reliability was 0.84.[111]
Patient Activation Measure (PAM) – This measure assesses patient "activation", which uses a Guttman-like scale that reflects a patient's level of engagement and empowerment in their healthcare.[112] Cronbach's alpha from our pilot study was 0.92.
Self-Efficacy Scale - This tool is a modified version of the Self-Efficacy Scale developed by Lorig and colleagues.[113] It contains 8 items that assesses FCG's and patient's perceived confidence in self-management. Items are rated on a 4-point Likert scale, and higher scores represent higher confidence. Cronbach's alpha from our pilot study was 0.89.
Surgery-Related Knowledge Tool - This tool was developed by the investigators to assess FCG and patient post-operative recovery knowledge. Each item addresses specific content within the MSM intervention to assess changes in knowledge. Scoring is based on the number of questions answered correctly.

Exploratory:
Society of Thoracic Surgeons General Thoracic Surgery Database Data Collection Form – This form will be used to record clinical and surgical characteristics. These include date of diagnosis, pre-operative risk factors, pre-operative treatments, pre-operative pulmonary function tests, date of surgery, type of surgical procedures, admission date and status, clinical staging, postoperative events/complications, discharge date and status, discharge disposition, pathological staging, and smoking cessation plans.
Exit Interview Discussion Guide – Qualitative data will be obtained through semi-structured interviews using a discussion guide. The guide contains a series of overarching questions, presented in an open-ended fashion. The questions are designed to solicit FCGs' and patients' experiences with participating in the intervention. FCGs and patients will be interviewed separately.
Key Informant Discussion Guide – This discussion guide will be used to obtain qualitative data for the key informant interviews. The questions in this guide will solicit information about patient's and FCG's living environment, social and community context, economic stability, healthcare access and quality, and education. FCGs and patients will be interviewed separately.

Process: We will also include the following process measures to assess intervention implementation and fidelity:
RN Debriefing Form - This form will be used to assess intervention implementation by the Research Nurse. It includes 7 scored items and 2 open-ended questions. The form documents session length, and assesses, on a scale of 0-10 (0=poorly, 10=very well), the participant's level of intervention participation during each session.
Intervention Fidelity Checklist – This checklist will be used to monitor intervention fidelity by the MPIs and self-management consultant (Dr. McCorkle). Using a present/absent response format, each intervention key element will be assessed by determining whether the interventionist behaviors were completed.

12.1.3.1 Eligibility Checklist

No eligibility checklist will be used in this study as the eligibility criteria is short.

12.1.3.2 Prior Therapy Forms and On-Study Forms

No prior therapy forms and on-study forms will be used in this study.

12.2 Protocol Deviations

12.2.1 Deviation Policy

This protocol will be conducted in accordance with COH's "Clinical Research Protocol Deviation Policy" located at http://www.coh.org/dsmc/Documents/Institutional%20Deviation%20Policy.pdf.

Deviations from the written protocol that could increase patient risk or alter protocol integrity require prior IRB approval of a single subject exception (SSE) request. In addition, if contractually obligated, the sponsor must also approve the deviation. IRB pre-approved SSE protocol modifications are considered an amendment to the protocol and not a deviation. The submission of a deviation report is not required.

Brief interruptions and delays may occasionally be required due to travel delays, airport closure, inclement weather, family responsibilities, security alerts, government holidays, etc. This can also extend to complications of disease or unrelated medical illnesses not related to disease progression. The PI has the discretion to deviate from the protocol when necessary so long as such deviation does not threaten patient safety or protocol scientific integrity. Examples include, but are not limited to: a) dose adjustments based on excessive patient weight; b) alteration in treatment schedule due to non-availability of the research participant for treatment; c) laboratory test results which are slightly outside the protocol requirements but at levels that do not affect participant safety. These instances are considered to be deviations from the protocol. A deviation report will be submitted to the DSMC/IRB within five days.

12.2.2 Reporting of Deviations

All deviations will be reported to the COH DSMC within five days. The DSMC will forward to report to the IRB following review.

12.2.3 Resolving Disputes

The COH Investigational Drug Service (IDS) cannot release a research agent that would cause a protocol deviation without approval by the PI. Whenever the protocol is ambiguous on a key point, the IDS should rely on the PI to clarify the issue.

In situations where there is misperception or dispute regarding a protocol deviation among the persons involved in implementing the protocol, it is the responsibility of the PI to resolve the dispute and the PI may consult with the DSMC chair (or designee) to arrive at resolution.

13.0 Statistical Considerations

13.1Study Design

Our target sample size for this study will be 200 caregiver-patient dyads (after 20% attrition). The planned sample size is 100 caregiver-patient dyads per treatment group. The power of statistical tests (two-sided 0.05 level of significance) is shown below for the primary outcomes of each specific aim. The effect sizes are shown as pairs of numbers representing the expected control group mean, based on published data, and the hypothetical population mean for the intervention care group. The SD column is based on published data, and power is conservatively estimated for a simple t-test on a single post-intervention measurement. The planned analysis, described in section E.5, will adjust for baseline values, and will combine longitudinal assessments, both of which will improve power.

A total of 80 new cases of stage I-III surgically treated NSCLC were available at City of Hope in fiscal year 2015. Our institutional race distribution is 56.2% Caucasian, 20.5% Hispanic, 4.7% Black, 13.5% Asian, and 5.1% other (38.7% ethnic minorities overall). These statistics should reflect the anticipated race distribution for participants. All efforts will be made to accrue minorities. Our pilot study demonstrates that we are able to accrue minorities (38%) to match the population at City of Hope.

A sample size of 100 per arm was calculated, based primarily on outcome means and variation observed in our previous studies (see Section E.1 for sample size calculations and power analysis). We have projected attrition based on previous studies. We will enroll 100 participants per arm to allow for 20% drop-out/attrition during the course of the study. We will enroll a total of 200 dyads in order to retain 160 dyads at 3-months. With a 52 month accrual plan, we estimate that 4 caregiver-patient dyads will need to be accrued per month. With a total pool of 80 potential dyads per year, this yields approximately 7 dyads per month that are eligible for the study. Hence, we will have a sufficient pool of eligible participants for study accrual. In our lung cancer Program Project (N=366), we were able to enroll 4 FCGs and patients per month.[59, 114]

We will study FCGs and patients age 21 and over to obtain participants across a spectrum of chronological ages. A range of ages is expected although we anticipate at least 68% of NSCLC patients will be ≥ 65 years. We anticipate that the majority of FCGs will be spouses and ≥ 60 years old given the patient age distribution. Based on our experiences, 90% of patients have an identified FCG. We acknowledge that the aging spectrum is heterogeneous and that older patients have a higher risk of surgical morbidity.[115] We anticipate that the majority of FCGs will be female (75%), but expect an equal representation by sex for patients. We recognize that age and sex are important influencing factors. We will examine the moderating effect of these biological variables on outcomes in Exploratory Aim 1.

Specific Aim 1 addresses the effects of the MSM Intervention on FCG outcomes, and **Table 3** provides FCG outcome effect size and power based on 80 participants per group. **Hypothesis 1.1** will address FCGs' psychological distress and burden. The study by Zwahlen et al[71] provides distress thermometer (DT) scores for 306 family members, including 32 relatives of lung cancer patients. The mean score was 3.7, and the standard deviation was 2.6. With this SD, a reduction of the mean by 1.2 points could be detected with 83% power. Caregiver burden is described by the research team's previous work[114] with mean objective burden subscale scores of near 22.0, with a pooled standard deviation of 4.0. With 80 subjects per group, a reduction by 1.8 points could be detected with 81% power. **Hypotheses 1.2** address preparedness for caregiving and QOL. In our previous work, preparedness has been reported on a 1 to 5 scale with a mean of approximately 3.7 and SD of 0.72.[114] An increase in mean score from 3.7 to 4.1 could be detected with 93% power. Total QOL scores for 157 FCGs are reported by our previous work[114], with a mean total score of 5.93 and a standard deviation of 1.42. An increase in mean total QOL score of 0.7 could be detected with 87% power. **Hypothesis 1.3** address changes in FCG cancer support services use. Here, we will classify each FCG as to whether they had an encounter with social work services and family resource center. A difference of 20 percentage points for social work referrals and 30 percentage points for family resource center would be detectable with 80 subjects per group.

Table 3. FCG Outcomes Effect Size and Power

Outcome	Measure	Effect	SD	Power
H1.1 Psychological distress	Distress thermometer	3.7 v 2.5	2.6	83%
H1.1 Caregiver burden	Objective burden score	22.0 v 20.2	4.0	81%
H1.2 Caregiver preparedness	Preparedness score	3.7 v 4.1	0.72	93%
H1.2 Caregiver QOL	Total QOL score	5.9 v 6.6	1.42	87%
H1.3 Social work referrals	FCG healthcare use	20% v 40%	NA	80%
H1.3 FCG center resource use	FCG healthcare use	30% v 60%	NA	97%

Specific Aim 2 addresses the effects of the MSM Intervention on patient outcomes, and **Table 4** provides patient outcome effect size and power. **Hypothesis 2.1** addresses patients' psychological distress and QOL, and **Hypothesis 2.2** addresses healthcare resource use. For each of these outcomes, the mean control group value, the root mean square (RMS) standard deviation, and the detectable improvements (Delta) in mean score was calculated for a two-sided 0.05 significance level test using 80 subjects per group. For resource use, we will classify each patient as to whether they had in-home nursing care, urgent care/ER visits, or a readmission. In preliminary data, 20 of 38 subjects had such an event, indicating that a difference of 22 percentage point would be detectable with 80 subjects per group.

Table 4. Patient Outcomes Effect Size and Power

Outcome	Measure	Detectable effect	SD	Power
H2.1 Psychological distress	Distress thermometer	3.5 v 2.4	2.4	82%
H2.1 QOL	FACT-L	93.7 v 101.3	17.0	80%
H2.2 Resource use	Any use (y/n)	53% v 31%	NA	80%

Specific Aim 3 addresses the effect of outcome mediators on FCG and patient outcomes (**Table 5**). Standard deviations (SD) were estimated from previous data. For activation, an improvement of the mean by 8.0 points could be detected with 80% power. For self-efficacy, an improvement of 2.0 points could be detected

Table 5. Outcome Mediator Effect Size and Power

Outcome	Measure	Detectable effect	SD	Power
H3.1 Activation	PAM and FCAT	72.0 v 80.0	18.0	80%
H3.1 Self-Efficacy	Self-Efficacy Tool	20.0 v 22.0	22.0	80%
H3.1 Knowledge	Knowledge Tool	8.5 v 9.0	1.0	88%

with 80% power. For knowledge, a difference of 5.0 points can be detected with 88% for 80 dyads per group.

Sample Size and Power Calculation for Social Determinants of Health and Spiritual Well Being – Sample size calculation is based on linear multiple regression method using G*power (Version 3.1.9.4). This method tests the null hypothesis that the proportion of variance of the outcome explained by a set of predictors is zero (i.e., $R^2=0$), while the alternative hypothesis is $R^2>0$. Significance level is 0.05 and power is 0.8. 20% of attrition was considered in calculation.

Table 2. Sample size considering 20% attrition

Number of predictors	Effect size		
	0.15	0.25	0.35
9	137	87	65
14	162	104	80
19	184	119	92
24	203	132	102

Two parameters need to be specified for sample size calculation[74]: effect size and number of predictors. The effect size is the ratio of proportion of variance explained by a set of predictors and error variance[74]. Since there is no published data for correlation between our outcomes and predictors in the target population (lung cancer), and due to the exploratory nature of the analyses, the effect sizes are estimates only. To cover potential effect sizes that our data may reveal, we employed different levels of effect size defined by Cohen[75]: small 0.15, medium 0.25, and large 0.35. The total number of predictors is 24 for FCG arm and 23 for patient arm. However, some predictors come from the same SDH domain, thus they would be highly correlated. To avoid multicollinearity in multiple regression model, some predictors may be removed from the final model. Therefore, we also used different number of predictors to calculate sample size (**Table 2**). Assuming the effect size 0.35 and 20% attrition, our target sample size will be 51 dyads (102 total participants) to detect deviation of R^2 from zero with 0.05 significance level and 80% power.

Data management is of key importance in this study. Our institutional research informatics core will develop an electronic data entry, capture, and storage system that will perform tracking functions (accrual, enrollment, consenting, data collection, and intervention delivery). We will develop a query system to address data validity and integrity by making early identification of cases of recruitment irregularity, data collection inconsistency, data inaccuracy or incompleteness. Data will be audited for accuracy prior to scoring and analysis.

Our primary data analysis will be according to intention-to-treat, i.e. all participants will be included in the analysis whether or not they received all prescribed intervention components. Participants who are lost to follow-up due to mortality will not be included. Reasons for study dropout will be recorded. Participants with missing items will be compared with those having non-missing items to determine whether missing data are random or can be accounted for by other variables. Broadly, our data may be missing at random (MAR) or missing not at random (MNAR). Generalized linear model with robust (sandwich) variance estimator model will be fitted to the data, with time, baseline, treatment arms, and interaction of time and treatment as explanatory variables. This approach provides valid standard errors with repeated measurement of individuals. It also accommodates missing time points by using the model of time effects to reduce bias. For MNAR, a pattern mixture model[55] will be fitted to the data to correct for informative drop-out. In particular, three patterns will be defined: a pattern consisting of participants who died during the study period, a pattern of participants with relapse, and a pattern of participants who remained disease free. Within each pattern, data will be modeled by the random effects model. To compare treatment arms, the effects of both arms will be respectively estimated using a weighted average across all patterns weighted by their sample proportions.

E.4. Preliminary Analysis - Initially, standard data descriptions, along with q-q plots and similar diagnostics will be used to check each outcome measure prior to analyses addressing hypotheses. Transformations will be considered, if necessary, to improve symmetry, variance homogeneity, and distribution, and to accommodate floor and ceiling effects. For several outcomes with high coefficient of variation, we anticipate using analysis on a logarithmic scale, potentially permitting presentation of geometric means and multiplicative effects.

E.5. Statistical Methods by Study Aims - Our general approach is to produce a confidence interval and corresponding hypothesis test for the effect of treatment (as intended) on each outcome, with the stratum used in randomization, and the baseline value of the outcome of interest included as covariables (i.e. analysis of covariance). This approach reduces residual variance and improves power, and randomization removes potential bias due to baseline differences. For the sake of robustness, secondary analyses will include a simple comparison without covariables, as well as a three-covariable model that includes a propensity score to address any residual imbalance in medical or socio-demographic variables. This approach generally minimizes the missing data problem for the primary analysis. **Multiplicity:** Planning is based on significance levels of 0.05, as each primary outcome is well-motivated a priori, and the merits of the intervention are expected to be seen in multiple outcomes. Statistically significant change in a single outcome, as would be controlled by family-wise adjustment procedures, would not be enough to motivate continued pursuit of the intervention. Two-sided significance levels are quoted. All of the hypotheses are also dividing hypotheses in the sense of Cox[116] so both the a priori direction, and the decision argument of Lehman[117] justify two-sided tests.

Specific Aim 1: Test the effects of the MSM Intervention on FCG outcomes and cancer support services use at discharge and 3-months post-discharge, comparing intervention and attention control groups. **Hypothesis 1.1:** The intervention group will experience lower psychological distress and caregiver burden. **Hypothesis 1.2:** The intervention group will experience higher caregiving preparedness and QOL.

These two hypotheses will be tested in the same way. We will address the effect of the intervention on FCG psychological distress, burden, preparedness for caregiving, and QOL at months 1 and 3, adjusted for baseline response. Scores for all outcome measures will initially be summarized graphically and numerically at baseline, month 1, and month 3, for each stratum, along with simple diagnostic plots. The need for transformation will be accessed. A generalized linear mixed model will be fit to estimate the distribution of 1 month and 3 month score as a function of treatment, stratum, occasion (month 1 or 3) and baseline value. The robust (sandwich) variance estimator will be used to accommodate the correlation of the two occasions, and the estimated treatment effect for the adjusted average of the 1 and 3 month outcomes will be estimated and tested, in order to limit multiplicity with respect to occasions, and to improve upon the designed power by combining information, effectively reducing standard deviations relative to those used for planning. This is similar to the analysis of average outcome for the two post-treatment occasions, except that it accommodates missing outcome evaluations by attributing observations to the appropriate occasion (comparing like with like), and avoids overstating information. Analysis of average outcome does provide a convenient robustness check. Each analysis will be a repeated measures ANCOVA statistical design, removing variances prior to examining mean squares for the group by occasion interactions, and covarying the baseline scores. The independent variable will be group (intervention vs. attention control). **Hypothesis 1.3:** The intervention group will have higher social work referrals and family resource center use.

FCG cancer support services will be evaluated by recording social work referrals and family resource center use. Each subject will be classified as having an event or not. There is no baseline value, but the data will be tabulated by surgery stratum, and tested for homogeneity (interaction) before estimating and testing the overall treatment effect.

Specific Aim 2: Test the effects of the MSM Intervention on patient outcomes and healthcare resource use at discharge and 3-months post-discharge, comparing intervention and attention control groups.
Hypothesis 2.1: The intervention group will experience lower psychological distress and higher QOL.

For this hypothesis, we will address patient psychological distress and QOL. Distress and QOL are each quantitative scales measured at both 1 month and 3 months. These will be analyzed by the same plan described for Specific Aim 1, hypothesis 1.1 and 1.2. Each analysis will be a repeated measures ANCOVA statistical design, removing variances prior to examining mean squares for the group by occasion interactions, and covarying the baseline scores. The independent variable will be group (intervention vs. attention control).
Hypothesis 2.2: The intervention group will have lower in-home nursing care, lower urgent care/ER visits, and lower hospital readmissions.

Similar to Specific Aim 1, hypothesis 1.3, patient healthcare resource use will be evaluated by recording in-home nursing care, urgent caregcp/ER visits, and readmissions (COH and non-COH encounters). Each subject will be classified as having an event or not. There is no baseline value, but the data will be tabulated by surgery stratum, and tested for homogeneity (interaction) before estimating and testing overall treatment effect.

Specific Aim 3: Test the effects of the MSM Intervention on outcome mediators at discharge and 3-months post-discharge, comparing intervention and attention control groups. **Hypothesis 3.1:** FCGs and patients in the intervention group will experience higher activation, self-efficacy, and knowledge.

For this hypothesis, we will address outcome mediators, including FCG and patient activation, self-efficacy, and knowledge. These outcomes are each quantitative scales measured at both 1 month and 3 months. These will be analyzed by the same plan described for Specific Aim 1 & 2. Each analysis will be a repeated measures ANCOVA statistical design, removing variances prior to examining mean squares for the group by occasion interactions, and covarying the baseline scores. The independent variable will be group (intervention vs. attention control). In addition, we will use structured equation modeling (SEM) to evaluate whether a mediator accounts for all or part of the effect between treatment and outcome. We will focus on the following: 1) estimating how treatment affects mediators, 2) how mediators are associated with outcomes, and 3) estimating, at least roughly, the relative strengths of mediation by activation, self-efficacy, and knowledge, as well as direct effects on outcomes. Each FCG model will involve variables describing: intervention (treatment assignment), 3 mediational variables (1-month activation, self-efficacy, knowledge), baseline values of 3 mediational variables, and primary outcomes (baseline values and 1-month). Intervention effect on patient outcomes is also proposed to be mediated by activation, self-efficacy, and knowledge. Each patient model will involve 11 observed variables: intervention (treatment assignment), 3 mediational variables (1-month activation, self-efficacy, knowledge), baseline values of 3 mediational variables, and primary outcomes (baseline values and 1-month).

Exploratory Aim 1: Explore moderators (age, sex, marital status, caregiver relationship to patient, caregiver employment status, co-morbidities) of FCG and patient outcomes and reciprocal relationships.

In EA 1 we will examine moderators and reciprocal relationships of FCG and patient outcomes. Potential moderating variables to be examined include, for FCGs: age, sex, relationship to patient (spouse vs. others), employment, and co-morbidities. For patients, potential moderators include: age, sex, marital status, and co-morbidities. These will be explored for interactions with treatment in affecting outcomes (psychological distress, caregiver burden, preparedness, QOL at discharge and 3 months), and for interactions with treatment in affecting potential moderators. Reciprocal relationships between FCG and patient outcomes are proposed. FCG (psychological distress, caregiver burden, caregiving preparedness, QOL) and patient (psychological distress, QOL) data will be pooled and structured so that the family (FCG +

patient) is the unit of analysis. We will test the effects of FCG characteristics on patient outcomes through structural equation modeling (SEM). These models will allow for the simultaneous calculation of effects of FCG experiences on patient outcomes. The models will also account for the intercorrelation among caregiver-patient dyads for both predictors and outcomes. Model will be estimated using maximum likelihood estimation; this will allow patients to be included when FCG information is missing, and vice versa. This will be explored both by graphical display, and considering patient outcomes as time-varying predictors of caregiver outcomes.

Exploratory Aim 2: Determine, through exit interviews, participant's experience with the MSM intervention.

We will use semi-structured interviews to examine dyadic experiences with the MSM Intervention. Qualitative data will be analyzed by the PIs using the conventional content analysis approach.[118] This approach is used to describe a phenomenon where existing theory or research literature is limited. Data from the tape-recorded interviews will be transcribed and analyzed using HyperRESEARCH™ qualitative software. Transcripts will be imported allowing for the development of analytic categories, data coding, and review of coded data. All data will be read repeatedly to achieve immersion and obtain a sense of the whole. Then, data will be read word by word to derive codes. Codes will then be sorted into themes based on links and relationships. Separate investigators with experience in qualitative data analysis (Dr. Sun and Dr. Ferrell) will conduct a final validation review of the codes and themes to ensure consistency and clarity across all qualitative data. Data discordantly coded will be discussed for refinement and consensus purposes.

Geriatric Assessment (GA) data for both FCGs and patients will be analyzed descriptively. We will use descriptive statistics (mean [SD], median [range], percentage [95% confidence interval]) to summarize GA scores and domains. We will also describe the patterns of changes in GA over time for both FCGs and patients. Changes will be calculated as post-surgery scores minus pre-surgery scores. Exploratory logistic regression models (univariate and multivariate) will be fitted to study the correlation between GA and FCG/patient outcomes.

COVID-19 qualitative data will be analyzed using content analysis approaches as described under exploratory aim 2.

Social determinants of health (SDH) data will be scored according to guidelines descriptively summarized. We will use multiple linear regression to test associations between baseline outcomes and SDH predictors. Baseline scores of outcomes activation, burden preparedness, self-efficacy, QOL and distress will be summarized with descriptive statistics. Distributions of SDH predictors will be summarized. For each outcome, we will use bivariate regression to assess the effect of one predictor at a time. Stepwise multivariate analysis will be performed to select all significant predictors ($p<0.05$). In addition, multicollinearity issues will be examined by calculating correlation matrix for all predictors and by checking variance inflation factors.

Spiritual well-being data will be scored according to guidelines and descriptively summarized. Two subscale scores of spiritual well-being outcomes will be measured before (baseline) and after surgery (3-months post-discharge). Pre and post-surgery data will be compared to assess potential changes in each subscale scores for patient and FCG arms separately. We will use Generalized Estimation Equations (GEE) for comparison, adjusting for sociodemographic covariates. Similar to multiple regression analyses for research questions 1.1 and 1.2, both bivariate and multivariate GEE models will be performed. Multicollinearity will also be examined.

Key Informant/Focus Group Data Analysis

A codebook will be co-developed by the principal investigators of the parent R01 and the diversity supplement, along with study participants. Grounded Theory methods of emerging coding will be used and facilitated by QDA Miner. To ensure data validity, constant comparison method—each theme and interpretation will be compared with emerging findings from data analysis— will be used to confirm emerging themes. Member checking techniques—results will be returned to participants for accuracy and resonance of experiences— will be utilized to validate focus group results.

14.0 Human Subject Issues

14.1Institutional Review Board

In accordance with City of Hope policies, an Institutional Review Board (IRB) that complies with the federal regulations at 45 CFR 46 and 21 CFR 50, 56 and State of California Health and Safety code, Title 17, must review and approve this protocol and the informed consent form prior to initiation of the study. All institutional, NCI, Federal, and State of California regulations must be fulfilled.

14.2Recruitment of Subjects

Subjects will be recruited on the COH Duarte campus and South Pasadena community site and through the Division of Thoracic Surgery.

14.3Advertisements

No advertisements will be used for study accrual.

14.4Study location and Performance Sites

This study will be performed at COH.

14.5Confidentiality

This research will be conducted in compliance with federal and state of California requirements relating to protected health information (PHI). The PHI that will be recorded includes name and medical record number. This information will be contained in a password protected database created by COH Research Informatics and monitored by the Study Personnel. Surveys administered to the subjects will not contain PHI information.

14.6Financial Obligations and Compensation

Subjects will not incur any financial obligations; they will be remunerated $50 each at completion of baseline and 3-month surveys ($100 per participant).

14.7Informed Consent Processes

The Research Nurse and CRAs will contact eligible participants and explain the study purpose, answer questions, and ascertain interest in participation. The primary approach for informed consent will be during an in-person encounter. Obtaining a signature of the consent form by the patient/caregiver may also be completed by sending the consent form by mail or electronic mail, and returned to City of Hope, or electronically via other electronic applications (i.e. DocuSign™). We will only use telephone verbal consents in situations where patients are not returning to COH prior to surgery date. If, during, the first phone call, participants are willing to consent for enrollment, the Research Nurse and CRAs will proceed with verbal consent. The Research Nurse and CRAs will document the provision of verbal consent via progress note as required by IRB policies.

The Principal Investigator or IRB approved named designate will explain the nature, duration, purpose of the study, potential risks, alternatives and potential benefits, and all other information contained in the IRB approved Consent Forms and Information Sheets. In addition, they will review the experimental subject's bill of rights and the HIPAA research authorization form. Research subjects will be informed that they may withdraw from the study at any time and for any reason without prejudice, including as applicable, their current or future care or employment at COH or any relationship they have with COH. Research subjects will be afforded sufficient time to consider whether or not to participate in the research.

Should sufficient doubt be raised regarding the adequacy of comprehension, further clarifications will be made and the study information repeated until a satisfactory result is obtained. Prospective research subjects who cannot adequately comprehend the fundamental aspects of the research study with a reasonable amount of discussion, education and proctoring will be ineligible for enrollment. For those subjects who do comprehend the fundamental aspects of the study, verbal consent will be obtained and documented via progress note charted through electronic medical record system.

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