CITY OF HOPE NATIONAL MEDICAL CENTER
1500 E. DUARTE ROAD
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DEPARTMENT OF Nursing Research & Education

TITLE: Conquer Fear SUPPORT: A Psychosocial Intervention in Patients with Advanced Cancer

CITY OF HOPE PROTOCOL NUMBER: IRB # 18305 Protocol Date 10/12/20

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STAGE (If applicable): III and IV
MODALITY: Psychoeducation/intervention
TYPE: Pilot

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CITY OF HOPE PROTOCOL NUMBER: 18305 **VERSION: 05**

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SPONSOR/IND NUMBER: to be assigned
DISEASE SITE: Gynecologic and Lung Cancer
STAGE (if applicable): III and IV
MODALITY: Psychoeducation/intervention
PHASE/TYPE: Pilot

PRINCIPAL INVESTIGATOR:
Designs protocol, responsible for study conduct and data analysis

Anne Reb PhD, NP
City of Hope

COLLABORATING INVESTIGATOR(S):
Key individual(s); Assist in study design and development; May be involved in analysis of data

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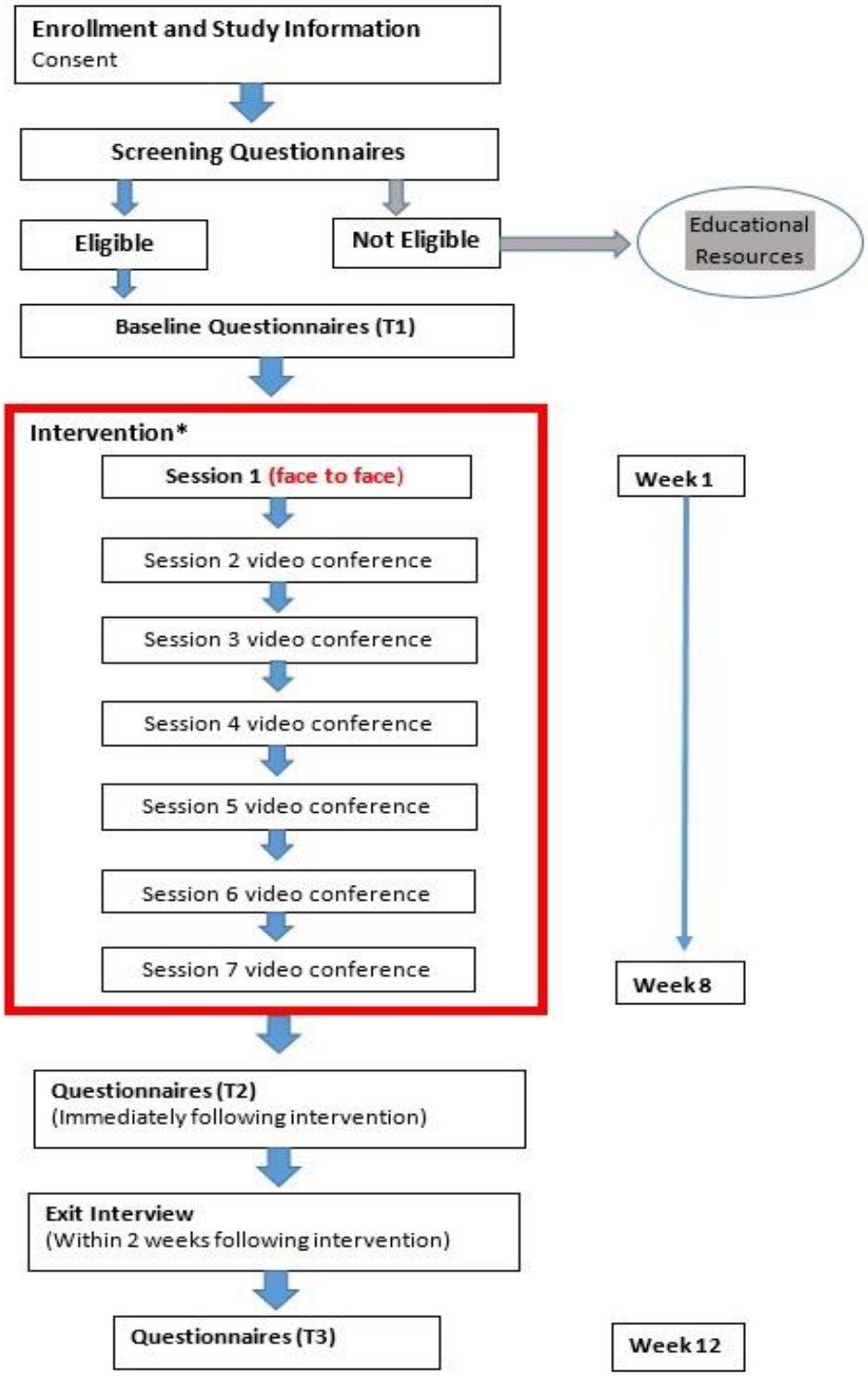


Figure 1. Conquer Fear SUPPORT Flowchart

* The intervention will be delivered by APN; the first session will be approximately 60 minutes, sessions 2-7 will be 45-60 minutes

**Sessions 2-7 will utilize a video conferencing platform

ABSTRACT

Approximately 49% of cancer survivors overall and up to 70% of vulnerable groups experience moderate to high levels of fear of cancer recurrence (FCR) or progression (FOP) (P. Butow et al., 2018; Lebel et al., 2017). Research supports that patients with more advanced disease are at higher risk for persistently elevated FCR due to the progressive nature of their illness (Savard & Ivers, 2013). This study will pilot a nurse-led psychosocial SUPPORT intervention in patients with advanced gynecologic (GYN) or lung cancer. The intervention is adapted from a novel intervention called "Conquer Fear," which has been tested in breast, colorectal, and melanoma cancer survivors treated with curative intent (P. N. Butow et al., 2017). Conquer Fear SUPPORT (CFS) is a manualized intervention that teaches patients more effective strategies for controlling worries and responding to their fears about cancer progression. **The primary aim** is to assess the feasibility and acceptability of the CFS in patients with advanced lung and GYN cancer who have moderate to high levels of FOP or cancer-related distress. **The secondary aim** is to assess preliminary effects of CFS on FOP, cancer-specific distress, anxiety, depression, metacognitions, and mindfulness. If feasibility is shown in this pilot study, the data will be used to refine the intervention to support a future RO1 submission. A single group mixed methods pilot study will be conducted to assess the feasibility of CFS in patients with stage III or IV gynecologic (GYN) or lung cancer who are at least 3 months from initial diagnosis. The intervention will consist of 7 sessions, approximately45 minutes each, delivered over an 8 week period and home practice assignments. The initial session will be in-person followed by 6 video conferencing sessions and will be delivered by an advance practice nurse (APN) trained in Conquer Fear and mindfulness based practices. Bimonthly team meetings will be conducted to review cases with oversight from a clinical psychologist. We will consent patients and screen them for eligibility until we enroll 33 eligible patients in the study. Measures of feasibility and acceptability include enrollment rate, attrition, attendance, and compliance with home practice assignments. The participants will complete questionnaires assessing FOP, anxiety, depression, cancer-specific distress, overall symptom distress, metacognitions, and mindfulness at baseline, 8 weeks, and 12 weeks. Chart audits will be conducted to assess referrals to palliative care and psychosocial services and unscheduled encounters or visits for symptoms or other concerns; and patient requests for additional surveillance testing. Exit interviews will be conducted to assess acceptability; benefits; barriers; self-initiated or community referrals for palliative care and psychosocial services; and experience with the intervention. Content analysis will be used to analyze the interview data.

Protocol Synopsis

Protocol Title:
Conquer Fear SUPPORT: A Psychosocial Intervention in Patients with Advanced Cancer
Brief Protocol Title for the Lay Public (if applicable):
Conquer Fear SUPPORT in Advanced Cancer
Study Phase:
Pilot
Participating Sites:
City of Hope, Duarte campus
Rationale for this Study:
This study will pilot a nurse-led psychosocial support intervention in patients with advanced GYN or lung cancer. This population was selected as they are at high risk of progression; experience similar fears; and there are few resources or interventions to help patients deal with their concerns. Most interventions for FOP have been delivered by psychologists and are time and resource intensive. A nurse-led model to address FOP may be translatable to community and underserved settings where mental health providers may not be readily available.
Objectives:
Aim 1. We will assess the feasibility and acceptability of CFS in patients with advanced lung and GYN cancer (stages III or IV) who have clinically significant levels of fear of cancer progression (FOP) OR cancer-related distress. Aim 2 (Exploratory). We will assess preliminary effects of the intervention on FOP, cancer-specific distress, anxiety, depression, overall symptom distress, metacognitions, and mindfulness.
Study Design:
A single group mixed methods pilot study will be conducted to assess the feasibility of the CFS in patients with stage III or IV GYN or lung cancer who score ≥34 on the FoP-Q-SF or ≥24 on the IES-R. The CFS consists of 7 sessions (45 minutes each) delivered over an 8 week period with home practice assignments (Figure 1). The initial session will be in person when possible and followed by 6 video conferencing sessions. The CFS will be delivered by an APN (advance practice nurse) trained in CFS methods and mindfulness based practices. Bimonthly team meetings will be conducted to review cases with the clinical psychologist. We will consent patients and screen for eligibility until we enroll 33 eligible patients in the study. We plan to enroll approximately 40% of patients in surveillance mode and 60% in active treatment mode as the concerns and symptoms may be different for these groups. The participants will complete questionnaires assessing fear of progression, anxiety, depression, overall symptom distress, cancer-specific distress, overall symptom distress, metacognitions, and mindfulness at baseline, 8 weeks, and 12 weeks. An exit interview will be conducted immediately post-intervention or at time of drop-out to assess acceptability, benefits, barriers, referrals to psychosocial services, and experience with CFS. Chart audits will be conducted to assess referrals to palliative care and psychosocial services; unscheduled encounters for symptoms or other concerns; and patient requests for additional surveillance testing. Participants will also be asked about self-initiated referrals for such services to outside facilities during the exit interview.

Endpoints:
Primary: Feasibility & acceptability (enrollment rate, attrition, attendance, compliance with home practice exercises). Secondary (Exploratory): FOP, cancer-specific distress, anxiety, depression, overall symptom distress, metacognitions, mindfulness
Sample Size:
We will enroll 33eligible patients in the study.
Estimated Duration of the Study:
12 months, (approximately 9 months will be needed for accrual of 33 eligible patients at ~4 pts/mo., and 3 additional months to follow the last patient)
Summary of Subject Eligibility Criteria:
Inclusion Criteria: 1) Lung and GYN cancer, stage III or IV disease; 2) at least 3 months from initial diagnosis; 3) receiving disease-focused treatment or in surveillance mode; and 4) a score of ≥34 on the Fear of Progression Questionnaire-SF or a score of ≥24 on the Impact of Event Scale-Revised. Exclusion Criteria: 1. Current severe depression or psychosis; significant cognitive impairment. 2. Patients enrolled in hospice care or who opt to receive no further disease-focused treatment. 3. Currently receiving ongoing psychiatric therapy 4. Non-English speaking
Investigational Product Dosage and Administration:
n/a
Clinical Observations and Tests to be Performed:
Self-Report questionnaires, exit interview
Statistical Considerations:
Descriptive statistics will be used for primary outcomes, and analysis of variance will be used to study secondary aims over time. Distributions of the demographics, medical history, and results obtained from assessment tools will be generated. Means, standard deviations, and ranges will be calculated for continuous variables, and frequencies and percentages for categorical variables. All questionnaires will be scored according to instrument scoring guidelines.
Sponsor/Licensee:
n/a
Case Report Forms
n/a

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Abbreviations

Abbreviation	Meaning
ACT	Components of Acceptance and Commitment therapy
AE	Adverse Event
ATT	Attention Training technique
APN	Advance Practice Nurse
CFR	Code of Federal Regulations
CFS	Conquer Fear SUPPORT
COH	City of Hope
CTCAE	Common Terminology Criteria for Adverse Events
DLT	Dose Limiting Toxicity
DSMC	Data Safety Monitoring Committee
FCR	Fear of Cancer Recurrence
FDA	Food and Drug Administration
FOP	Fear of Progression
HIPAA	Health Information Portability and Accountability Act
ICF	Informed Consent Form
IDS	Investigational Drug Services
IND	Investigational New Drug
IRB	Institutional Review Board
NCI	National Cancer Institute
NINR	National Institute of Nursing Research
PCRC	Palliative Care Research Consortium
PD	Progressive Disease
PI	Principal Investigator
PMT	Protocol Monitoring Team
PR	Partial Response
RC	Research Coordinator

REDCap	Research Electronic Data Capture
S-REF	Self-Regulation of Executive Function Model
SAE	Serious Adverse Event
SD	Stable Disease

1.0 Goals and Objectives (Scientific Aims)

Fear of cancer recurrence is very common among cancer survivors and associated with a range of negative outcomes. Approximately 49% of cancer survivors overall and up to 70% of vulnerable groups experience moderate to high levels of fear of cancer recurrence (FCR) (P. Butow et al., 2018; Lebel et al., 2017). FCR is closely linked with survival and existential issues and represents one of the most common unmet needs among cancer survivors (Simard et al., 2013; Simonelli, Siegel, & Duffy, 2017). Fear of recurrence has been defined as the "fear, worry, or concern related to the possibility that cancer will come back or progress" (Lebel et al., 2016). The terms "FCR" and "fear of progression" (FOP) are used interchangeably; we will use the term "FOP" as it may be more relevant for advanced patients who may experience remitting- recurring illness (Dinkel & Herschbach, 2018). FOP is associated with a preoccupation with the cancer returning; hypervigilance about symptoms; intrusive thoughts and worries about the future; unhelpful coping behaviors; and fears preceding follow-up tests and appointments (Simonelli et al., 2017). High levels of FOP can negatively impact follow-up screening behaviors and health care costs (P. N. Butow et al., 2017). Most of the research has been conducted in cancer survivors with good prognosis and in particular women with early stage breast cancer, and relatively good prognosis. However, recent data shows that FOP is an even more pressing issue for patients with advanced disease. In particular, patients with advanced lung and gynecologic cancer report significant FOP. This population was selected as they are in need of psychological support and palliative care and cancer progression is common. There are now a range of evidence-based treatments to treat FOP but all have been done in patients with early stage disease. The proposed intervention, "Conquer Fear SUPPORT" (CFS) is adapted from a novel program called "Conquer Fear," which was developed by researchers in Australia and has shown efficacy in reducing FCR in patients with stages I-III breast, colorectal, and melanoma cancers (P. N. Butow et al., 2017; Lebel et al., 2017). The overall goal of this study is to pilot test CFS in patients with advanced GYN and lung cancer. The primary aim is to assess the feasibility and acceptability of CFS in patients with advanced lung and GYN cancer who have clinically significant levels of fear of cancer progression (FOP) or cancer-related distress. The secondary aim is to assess preliminary effects of CFS on FOP, cancer-specific distress, anxiety, depression, metacognitions, and mindfulness.

Aim 1: We will assess the feasibility and acceptability of the CFS intervention in patients with advanced lung and GYN cancer (stages III or IV) who have clinically significant levels of fear of cancer progression (FOP) or cancer-related distress.

Feasibility and acceptance will be assessed by enrollment rate, attrition, attendance, compliance with home practice exercises, and observance of unanticipated problems, as defined below:

a) Enrollment rate will be deemed sufficient if at least 33 eligible patients (out of 50 possible patients) are accrued within 9 months.
b) Attrition will be deemed manageable if the percentage of accrued subjects who drop out of the study does not exceed 25% by T2 and 50% by T3.
c) Attendance is defined as percentage of the 7 sessions attended. An average of 5 sessions attended will indicate high acceptance.
d) Compliance with home practice exercises will be assessed by: 1) the percentage of assignments completed, 2) the percentage of attention training and mindfulness practice sessions performed, as recorded on daily tracking logs; and 3) Responses to a question on the exit interview asking participants about the frequency of their adherence to home practice exercises. Average 50% compliance on at least one of these measures will be deemed adequate.
e) Observance of anticipated problems will be defined as detection of any problems or barriers to the implementation of the protocol or the intervention sessions.

Acceptability will also be assessed qualitatively based on responses to an exit interview asking about participants' experience with the intervention, including benefits and barriers.

Aim 2. We will assess preliminary effects of the intervention on FOP, cancer-specific distress, anxiety, depression, overall symptom distress, metacognitions, and mindfulness, using the following instruments.

a) The Fear of Progression Questionnaire-SF will be used to assess fear of cancer progression at T1, T2, and T3 and scores will be compared over time.
b) The Impact of Events Scale-Revised will be used to assess cancer-specific distress at T1, T2, and T3 and scores will be compared over time.
c) The PROMIS-Anxiety 8a will be used to assess anxiety at T1, T2, and T3 and scores will be compared over time.
d) PHQ-9 will be used to assess depression and scores will be compared over time.
e) The Memorial Symptom Assessment Scale will be used to assess overall symptom distress at T1, T2, and T3 and scores will be compared over time.
f) The Metacognitions questionnaire (MCQ-30) will be used to assess beliefs about worry at T1, T2, and T3 and scores will be compared over time.
g) The Five Facet Mindfulness Questionnaire (FFMQ-15) will be used to evaluate mindfulness at T1, T2, and T3 and scores will be compared over time.

2.0 Background

2.1 Introduction/Rationale for Development

Palliative care provides support for patients with serious illness across the trajectory of disease, including psychosocial support which is one of the key domains of palliative care. Research supports that patients with more advanced disease are at higher risk for FOP due to the progressive nature of their illness (Savard & Ivers, 2013). Psychological distress and FOP are frequent concerns among women with GYN cancers and there are few resources or interventions to help women deal with this concern (Dawson, Madsen, & Dains, 2016; Maheu et al., 2016). FOP is a significant concern among women with advanced ovarian cancer as it is associated with high recurrence rates (Ozga et al., 2015). Similarly, the majority of patients with advanced lung cancer experience progressive disease and have unmet needs that exceed those of other cancer patients (Mosher et al., 2014). A recent survey study of 89 lung cancer survivors found that concerns about recurrence and death were among the most frequent unmet psychological needs (Giuliani et al., 2016). Despite the prevalence of psychological distress, there is an underutilization of supportive care services including mental health services (Giuliani et al., 2016; Mosher et al., 2013) and a need for well-designed psychosocial intervention studies to support patients with advanced lung (Lehto, 2017) and GYN cancer. This pilot study aligns with the mission of the Palliative Care Research Consortium (PCRC) to contribute to evidence-based approaches to improve palliative care for advanced cancer patients and fits within the Psychological and Psychiatric Aspects of Care domain of the National Consensus Project for Quality Palliative Care. CFS will employ an interdisciplinary approach to address FOP and will likely lead to identification of patients in need of palliative care consultation and mental health services. If feasibility is shown in the pilot, the data will be used to refine CFS to support a future RO1 clinical intervention trial in October, 2019.

Significance: Research supports that having a cancer recurrence or a diagnosis of advanced disease is significantly associated with FCR (Savard & Ivers, 2013; Simard et al., 2013). Most of the FCR interventions have been tested in patients with early-stage disease who were treated with curative intent (P. Butow et al., 2018). Only one nurse-led intervention was identified that targeted FCR in patients with head and neck cancer disease that included patients with both early and advanced disease (Humphris & Rogers, 2012). The introduction of new targeted therapies and immunotherapies has led to significant increases in survival for a subset of advanced cancer patients. These patients are being treated for extended durations and are monitored frequently for signs of progression, which may contribute to

uncertainty and increased vulnerability to FOP (P. N. Butow et al., 2017; Thewes et al., 2017). For example, the initial treatment strategy for advanced lung cancer patients with an identified mutation is oral immune and targeted therapies. Similarly, those with newly diagnosed advanced ovarian and cervical cancers are treated with regimens including targeted therapies. Despite the high prevalence of FOP in these groups, cancer providers only refer about 21% of patients for psychosocial services and are unsure about the best treatment approach (Lebel et al., 2017). Research is needed on psychosocial interventions to address FOP and distress in patients with advanced cancers as many are living longer due to treatment advances and struggling with existential fears without a roadmap to guide them. If the proposed aims are achieved, this study could provide preliminary data to support a nurse-led model to address FOP which significantly impacts quality of life. This model may be translatable to community and underserved areas where psychologists or mental health providers may not be readily available.

Innovation: Most of the evidence for interventions targeting FCR is based on patients with early stage breast cancer and it is unclear if the benefits extend to patients with advanced cancer or cancers with different trajectories. Further, most interventions have been delivered in one-on-one formats or group settings administered by trained psychologists and have been time and resource intensive (P. N. Butow et al., 2017). Research is needed on alternative delivery models that are cost-effective and accessible to patients who may be struggling with physical symptoms and existential concerns related to advanced disease or its treatment. A nurse-led intervention that is flexible in terms of the timing and delivery and allows the patient to stay at home for the sessions may be acceptable and feasible for patients with advanced disease. Conquer Fear SUPPORT is a novel, evidence-based intervention that teaches patients more effective ways to respond to their fears. The proposed intervention would be the first study to investigate a nurse-led model of CFS and one of the first studies to specifically target patients with advanced cancer.

Theoretical Framework:
The goals of CFS are to teach strategies for controlling worry; modify unhelpful beliefs about worry; encourage acceptance of uncertainty; and encourage values-based goal setting (P. N. Butow et al., 2013). The intervention is guided by a new cognitive processing model of FCR that was developed by international experts on FCR (Fardell et al., 2016) (Figure 2). According to this model, distress and intrusive thoughts are a normal following a cancer diagnosis. However, for some patients, their thoughts trigger an unhelpful style of cognitive processing that exacerbates worry and distress (Sharpe, Thewes, & Butow, 2017). CFS is based on Meta-cognitive therapy and the Self-Regulation of Executive Function Model (S-REF). The S-REF model posits that a cognitive appraisal system consisting of beliefs about the benefits of worry, together with the appraisal of the perceived level of threat are associated with FCR. For example, a person may become more attentive to physical symptoms which may trigger intrusive thoughts and rumination (Simonelli et al., 2017). This model suggests that cognitive factors may be targets for treatment including self-focused attention; worry; and maladaptive coping behaviors. The S-REF model underpins the behavioral components of CFS related to frequent checking in related to symptoms or requests for testing and developing a contract for appropriate behaviors. Further, certain vulnerability factors may exacerbate FCR such as previous losses; traumatic events; and other life stressors (P. Butow et al., 2018). Components of Acceptance and Commitment therapy (ACT) are incorporated to address the existential concerns related to FCR and to promote living consistent with one's values (P. N. Butow et al., 2013). Both ACT and the S-REF models emphasize informal mindfulness practices and learning new skills to help accept distressing thoughts while simultaneously giving these experiences less attention (Fashler, Weinrib, Azam, & Katz, 2018).

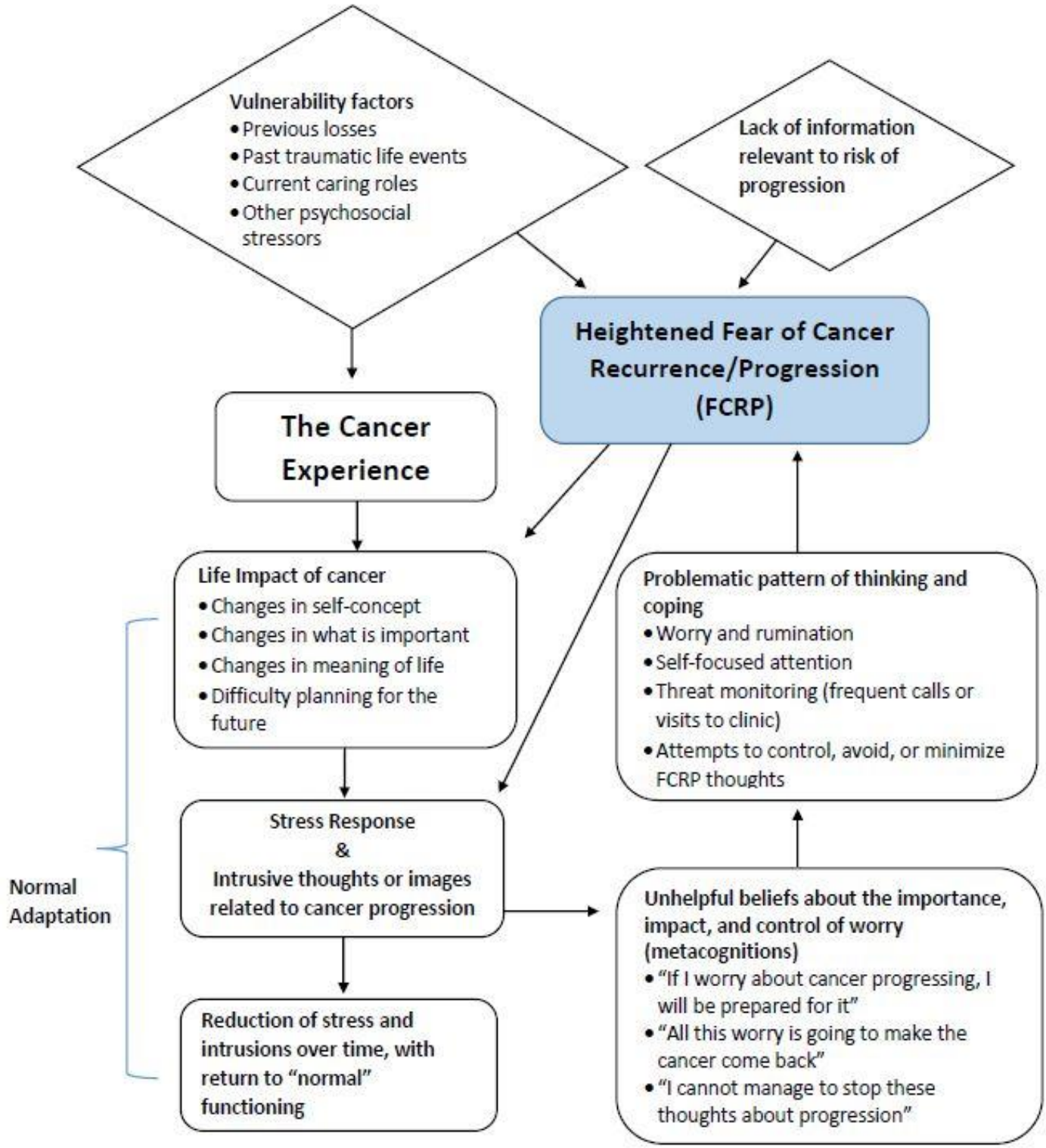


Figure 2. Cognitive Processing Model of Fear of Cancer Recurrence/Progression. Adapted from Fardell et al. J Cancer Surviv. 2016.

Overview of Proposed Study

Research Design/Methods:

A single group mixed methods pilot study will be conducted to assess the feasibility of CFS in patients with stage III or IV GYN or lung cancer who score ≥34 on the Fear of Progression Questionnaire-SF or ≥24 on the Impact of Event Scale-Revised. We will try to attain some balance by planning to enroll approximately 40% of patients in surveillance mode and 60% in active treatment mode. The CFS consists of 7 sessions (45 minutes each) delivered over an 8 week period with home practice assignments (Figure 1). The initial session will be in –person when possible and followed by 6 video conferencing sessions. The CFS will be delivered by an APN (advance practice nurse) trained in CFS methods and mindfulness based practices. Bimonthly team meetings will be conducted to review cases with the clinical psychologist. We will consent patients and screen them for eligibility until we have enrolled 33 eligible patients in the study. Measures of feasibility and acceptance include enrollment rate, attrition, attendance, and compliance with home practice assignments. The participants will complete questionnaires assessing FOP, anxiety, cancer-specific distress, depression, overall symptom distress, metacognitions, and mindfulness at baseline, 8 weeks; and 12 weeks. Chart audits will be conducted to assess referrals to palliative care and psychosocial services; unscheduled encounters for symptom management or other concerns; and patient requests for additional surveillance testing. An exit interview will be conducted immediately post-intervention or at time of drop-out to assess acceptability; benefits; barriers; self-initiated or community referrals to psychosocial services; and experience with CFS. Content analysis will be used to analyze the interview data.

Preclinical Studies

N/A

2.2 Human Studies

N/A

3.0 Patient Eligibility

The GYN Oncology department treats an average of 76 patients with advanced GYN cancer per year, and the Department of Medical Oncology treats approximately 158 patients with advanced lung cancer/year (includes patients with newly diagnosed and recurrent disease). Based on these numbers, we anticipate enrolling 3-4 patients/month. Up to 50 patients may be consented and further screened for eligibility until 33 eligible participants have enrolled. Due to an expected attrition of 25%, we anticipate a final sample size of 25. Patients receiving active disease-focused treatment at the COH Duarte campus are eligible. The majority of patients with advanced lung cancer will be on active therapy, including targeted therapy, immunotherapy or chemotherapy. A smaller number of patients treated at City of Hope have stage IIIa lung cancer and will be in "surveillance" mode. The GYN population treated at City of Hope includes patients with advanced uterine and cervical cancer who are treated for cure and will be in "surveillance mode" as well as patients with recurrent disease on active therapy. Based on discussions with the lung and GYN oncologist co-investigators and assessment of the types of patients seen at City of Hope, we plan to enroll approximately 40% of patients who are in "surveillance" mode and 60% undergoing "active therapy."

The investigators gave considerable thought to the eligibility criteria including reviewing the literature; speaking with clinicians caring for lung and GYN patients as well as international researchers who have studied fear of cancer recurrence. We opted for broad eligibility criteria since FOP tends to have a more variable course in patients with advanced disease and is higher in patients who have experienced a recurrence or progression.

Inclusion Criteria

Patients with GYN and lung cancer will be recruited who meet the following inclusion criteria: 1) stage III or IV disease; 2) at least 3 months from initial diagnosis; 3) receiving disease-focused treatment or active surveillance mode; and 4) a score of ≥34 on the Fear of Progression Questionnaire-SF or ≥24 on the Impact of Event Scale-Revised.

3.1 Age Criteria, Performance Status and Life Expectancy

N/A

3.1.1 Child Bearing Potential:

N/A

3.1.2 Protocol-Specific Criteria

N/A

3.1.3 Informed Consent/Assent

All subjects must have the ability to understand and the willingness to sign a written informed consent.

3.1.4 Prior Therapy

N/A

3.2 Exclusion Criteria

1. Current severe depression or psychosis; significant cognitive impairment.
2. Patients enrolled in hospice care or who opt to receive no further disease-focused treatment.
3. Patients who are currently receiving ongoing psychiatric treatment.
4. Non-English speaking

Inclusion of Women and Minorities

The study is open anyone regardless of gender or ethnicity. Efforts will be made to extend the accrual to a representative population, but in a trial which will accrue approximately 33 eligible subjects, a balance must be struck between subject safety considerations and limitations on the number of individuals exposed to potentially toxic or ineffective treatments on the one hand and the need to explore gender, racial, and ethnic aspects of clinical research on the other. If differences in outcome that correlate to gender, racial, or ethnic identity are noted, accrual may be expanded or additional studies may be performed to investigate those differences more fully.

4.0 Screening and Registration Procedures

4.1 Screening Procedures

The research coordinator and APN will review clinic schedules and consult with the attending oncologist to identify eligible participants.

4.2 Informed Consent

The investigational nature and objectives of the trial, the procedures and treatments involved and their attendant risks and discomforts, and potential alternative therapies will be carefully explained to the subject and a signed informed consent will be obtained. Documentation of informed consent for screening will be maintained in the subject's research chart and medical record.

4.3 Registration Requirements/Process

n/a

4.4 Randomization and/or Dose Level Assignment

n/a

5.0 Treatment Program

5.1 Treatment Overview

Intervention.
CFS is a manualized intervention that focuses on patients' beliefs about their thoughts and worries with the goal of teaching them more effective ways to respond to their fears about a potential recurrence. CFS focuses on the needs and concerns of patients with advanced GYN and lung cancer. CFS consists of 7 sessions including the following topics: psychosocial assessment focusing on FOP; values-based goal setting; vulnerability factors; Attention Training technique (ATT), worry management; and detached mindfulness exercises (Table 1). Sessions will include experiential exercises to facilitate engagement. Participants will be given the option to email or call the APN if they have questions about the sessions or home practice assignments. Participants will complete weekly practice logs to record the frequency of ATT and mindfulness practices and completion of practice assignments. Dr. Louise Sharpe will train the APNs, the principal investigator (PI), and clinical psychologist; and answer questions that arise regarding CFS. Dr. Cangin and the PI will oversee intervention fidelity and consult with Dr. Sharpe if any questions arise about CFS. The APN will complete a Session checklist following each session and review cases with the clinical psychologist and PI during bimonthly team meetings. Dr. Cangin will review 30% of randomly selected session audiotapes for quality; provide guidance to the APN; and recommend referrals for patients needing additional mental health services.

Data Collection: Study Website

Participants will complete web-based surveys through the Research Electronic Data Capture (REDCap) internet based platform. Following the informed consent meeting, the participant will be given education regarding how to complete the web based study questionnaires. The patient will be emailed a secure link to the REDCap website to complete the study questionnaires on-line at home. Participants who do not have access to a computer or internet will be able to complete paper questionnaires to be returned with a stamped envelope.

Study Procedures

Following informed consent, patients will complete two brief screening questionnaires, the FoP-Q-SF and the IES-R to confirm eligibility. If patients score below the cut-off for eligibility on both questionnaires, they will be provided with a list of resources on managing fear of cancer progression and distress. These patients will also be given the option to meet with a social worker to discuss their concerns, and the RC or APN will facilitate a referral to Supportive Care Services. Patients who are accrued will be emailed a link to complete web-based surveys through the Research Electronic Data Capture (REDCap) internet based platform. Participants will complete a web-based Personal Data Form (T-1 only), and questionnaires assessing FOP, anxiety, depression, cancer-specific distress, overall symptom distress, metacognitions, and mindfulness at baseline (T1), 8 weeks (T2); and 12 weeks (T3 (Figure 1). Chart audits will be conducted to assess referrals to palliative care and psychosocial services; and unscheduled encounters or patient requests for additional surveillance testing. An exit interview will be conducted within two weeks of T2 or time of drop-out. Exit interviews will be conducted by a qualified research team member who will be trained in open-ended interviewing techniques. The interviews will be digitally recorded and recorders will be stored in a locked file cabinet. The transcripts will be stored on a password protected computer. The digital recordings will be erased once the study is completed.

The CFS will be delivered by the APN and consists of 7- sessions delivered over 8 weeks. The first session will be 60 minutes and face-to-face when possible; followed by 6 video-conferencing sessions lasting approximately 45-60 minutes. Sessions will be delivered weekly with flexibility built in based on the patient's circumstances. Patients who do not have access to a computer will be provided with a tablet with built-in Wi-Fi if available he research coordinator will review with the participant how to sign on to the sessions and will assist with any technical difficulties or issues affecting the delivery of the sessions. Following each session, patients will complete home practice assignments including ATT and mindfulness exercises and document their practice on a daily log. The APN will audio-record sessions for intervention fidelity, and the recordings will be stored on password protected computers. The APN will complete a session checklist following each session to document content covered; self-monitoring behaviors (frequent self-exam; calls to clinicians about symptoms or concerns; requests for additional surveillance tests); and any significant concerns or questions. Interdisciplinary team meetings will be conducted bimonthly in which the APN will present the psychosocial assessment and summary of the sessions to the clinical psychologist and other team members. Patients who experience significant ongoing distress based on questionnaire responses or during the sessions will be referred to a social worker, psychologist, or palliative care specialist. Participants who respond 1 or greater ("several days) on the PHQ-9 question "Thoughts that you would be better off dead, or of hurting yourself") will be assessed by a member of the study team and referred to the social worker or psychologist or urgent care clinic if appropriate. Their attending physician will also be notified. The APN will provide resources for patients and their caregivers as needed.

Post-Study Activities

For patients who agreed to be contacted about potential future studies, we will ask if they are willing to participate in a video and/or audio recording (testimonial) about their experience with the intervention. The recordings/testimonials will be used in upcoming studies to test the revised version of the program. We may also add excerpts from the testimonial (s) as written statements in the patient

workbook. The RA, PI or APN will explain the purpose and procedures related to the recordings. The RA/research team will explain that participation is optional and that declining to participate will not affect their future care. If interested, participants will sign an addendum consent form that explains the purpose and potential use of the recordings. If the participant agrees to provide an audio testimonial, it will be conducted in a manner to ensure confidentiality of their identity. However, they may opt to include their picture alongside the audio testimonial (this is optional).

To help participants prepare for the recordings, they will be given a list of potential questions. The RA, PI or APN will be available to assist with preparing their script for the recording and to answer any questions. The recordings will take place in the Biller Center or other private location in the medical center.

In the future, the testimonials may be used or disclosed by City of Hope to third parties as part of business operations and City of Hope or its affiliates may derive revenue from these activities. Examples may include training or coaching programs for health care providers, patients, or caregivers.

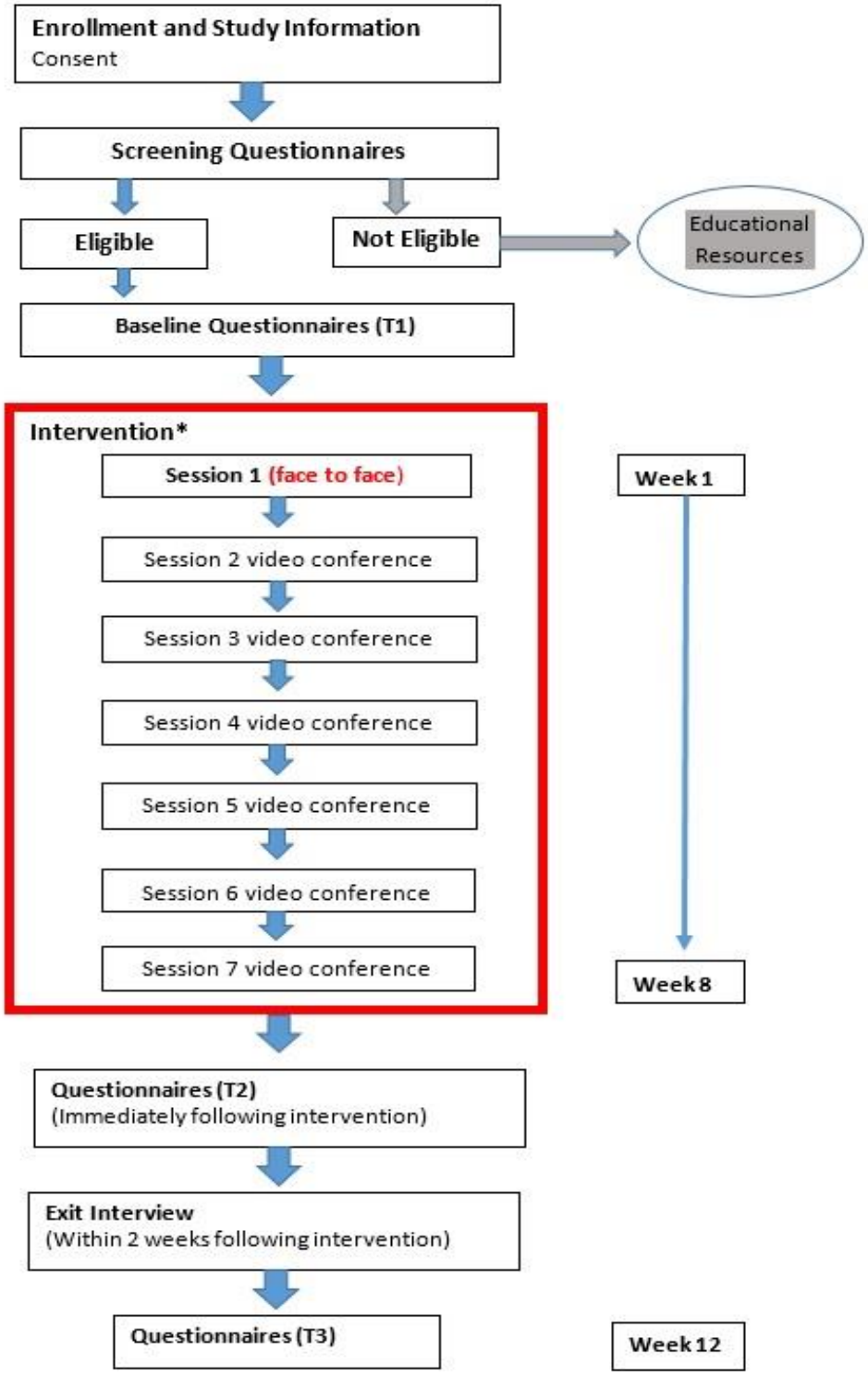


Figure 1. Conquer Fear SUPPORT Flowchart

* The intervention will be delivered by APN; the first session will be approximately 60 minutes, sessions 2-7 will be 45-60 minutes

**Sessions 2-7 will utilize a video conferencing platform

5.1.1 Schedule

For a tabular view of the treatment, monitoring, and follow-up schedule, see study calendar in Section 10.

5.2 Planned Duration of Therapy

Study participation will be for 12 weeks.

5.3 Criteria for Removal from Treatment

Participants who become too ill to participate will be discontinued from the study.

5.4 Subject Follow-Up

Participants will be followed for approximately 12 weeks.

5.5 Supportive Care, Other Concomitant Therapy, Prohibited Medications

The RC or APN will review participant's responses to web-based surveys. If participants report significant symptoms or distress on the surveys or during the intervention sessions, the APN will notify the attending physician and refer the patient to supportive care or social worker for further evaluation. The APN will discuss any clinical concerns with the clinical psychologist on the study team.

5.6 Additional Studies

N/A

5.6.1 Laboratory Studies

N/A

5.7 Definition of Dose-Limiting Toxicity (DLT)

N/A

6.0 Dose Delays/Modifications for Adverse Events

N/A

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

7.1 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 a psychosocial support intervention in patients with advanced GYN or lung cancer and questionnaires assessing fear of progression, cancer-specific distress, anxiety, depression, metacognitions, and mindfulness.

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.

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

N/A

9.0 Correlative/Special Studies

No correlative studies will be performed during this trial.

10.0 Study Calendar

Week	0	0	1	2	3	4	5	6	7	8	9	10	11	12
Time point	**Pre-Study**	**Baseline T1**								**T2**				**T3**
Informed consent	RC/RN													
Screening Questionnaires*	RC/RN													
Personal Data Form (PDF)		RC												
Fear of Cancer Progression Questionnaire-Short Form (F0P-SF)		*RC								RC				RC
Impact of Events Scale Revised (IES-R)		*RC								RC				RC
Patient-Reported Outcomes Measurement Information System (PROMIS –Anxiety 8a)		RC								RC				RC
Patient Health Questionnaire (PHQ-9)		RC								RC				RC
Memorial Symptom Assessment Questionnaire (MSAS)		RC								RC				RC
Metacognitions Questionnaire (MCQ-30)		RC								RC				RC
The Five Facet Mindfulness Questionnaire (FFMQ-15)		RC								RC				RC
Intervention			RN	RN	RN	RN	RN	RN	RN					
Exit Interview										RC/RN				
Chart Audit		RN/RC								RN/RC				RN/RC

*Screening questionnaires (FoP-Q-SF and IES-R) will also serve as baseline questionnaires

11.0 Endpoint Evaluation Criteria/Measurement of Effect

11.1 Response Criteria

N/A

12.0 Data Reporting/Protocol Deviations

12.1 Data Reporting

12.1.1 Confidentiality and Storage of Records

Data collection and management will be captured through the Research Electronic Data Capture (REDCap) internet based platform (Harris et al., 2009). This platform allows researchers to create a unique study-specific website to securely capture patient data. REDCap includes domain specific questionnaires from their library (e.g., PROMIS measures). Researchers can also add other measures/instruments to be used in the study(Bevans, Ross, & Cella, 2014)

REDCap provides 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2700030/.(Harris et al., 2009)

REDCap is a secure, HIPPA and, FISMA compliant web application for building and managing online forms / surveys and databases. This application is hosted at City of Hope. Server security and application compliance is jointly managed by the administrators in the departments of Information Technology Services (ITS) and Research Informatics (RI). Where feasible, validation rules (e.g., logic checks, format restrictions, min/max range, etc.) will be added to ensure that the data entered is valid and accurate. Users are able to complete forms/surveys on any computer with internet access or a compatible mobile application. Data will be stored in password protected, secure computers that meet all HIPAA requirements. Digital audio recorders will be used for this study. Transcripts will be stored on a password protected computer and labeled with only the study ID to protect confidentiality. The digital recorder will be stored in a locked file cabinet. Data will be made available for review, as required by the FDA, HHS, or other authorized users such as the NCI, National Institute of Nursing Research (NINR), and Palliative Care Research Consortium (PCRC) under the guidelines established by the Federal Privacy Act and rules for the protection of human subjects.

12.1.2 Information Sharing

A grant from PCRC is funding this study. The PCRC is the only US research cooperative focused specifically on the science of palliative and end-of-life research, and houses the PCRC De-identified Data Repository. As part of the NIH data sharing directive, deidentified data from this study will be transferred to the PCRC De-identified Data Repository located at the University of Colorado. Any deidentified data that are collected and entered will remain in the PCRC Data Repository indefinitely. All future data analysis will be performed on de-identified data in the PCRC Data Repository. While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, patient identity will not be revealed. Data will be presented in aggregate reports without patient-level identifiers.

Consistent with the PCRC Data Sharing Policy, the data from this study will be deidentified and will be transferred and stored on a server maintained by the PCRC at the University of Colorado (U of CO). U of CO's Office of Information Technology (OIT) Department provides University employees with centralized file sharing services. Centralized file servers are Windows-based virtual systems hosted in OIT's VMware server environment. These servers are proactively monitored by the automated monitoring system, patched on a monthly basis with latest security patches and updates, and backed up nightly by OIT's Enterprise backup solution, consistent with good data storage practices.

12.1.3 Subject Consent Form

At the time of registration, the original signed and dated Informed Consent form, HIPAA research authorization form, and the California Experimental Subject's Bill of Rights (for the medical record) and three copies (for the subject, the research record, and the Coordinating Center) must be available. All Institutional, NCI, Federal, and State of California requirements will be fulfilled.12.1.4 Data Collection Forms and Submission Schedule

Figure 1 lists the outcome measures and corresponding evaluation time points. Categories of outcomes in this study include: 1) Patient-reported outcomes; 2) Medical record documentation; and 3) Interview data. Data will be sent to the location identified in Section 12.1.1 and stored in a secure location.

Data Collection Tools

Personal Data Form: This self-report survey was developed by the investigators and documents demographics, medical history, use of supportive care services, and medications.

FOP-Q-SF consists of 12 items pertaining to 4 of the subscales of the original 43-item FOP questionnaire (excluding coping) (Mehnert, Herschbach, Berg, Henrich, & Koch, 2006). The longer questionnaire consists of 5 subscales: affective reactions; partnership/family; occupation; loss of autonomy; and coping with anxiety. The 12 items are scored on a 5-point Likert scale (1=never to 5=very often). Scores range from 12-60 with higher levels indicating greater FOP. Researchers have used a cut-off of 34 and above to indicate dysfunctional FOP. The FOP-SF has been validated in a large sample of breast cancer patients and shows adequate reliability (α =.87); the correlation between the long and short form of the questionnaires is r=0.92.The scale showed good internal consistency in a large sample of patients with various cancer diagnoses who completed a cancer rehabilitation program (α =.90) (Hinz, Mehnert, Ernst, Herschbach, & Schulte, 2015). Convergent validity was demonstrated by correlation with other psychosocial measures.

Impact of Event Scale-Revised (IES-R). A 22- item Likert scale that measures cancer related distress(Sundin & Horowitz, 2002). It consists of 3 subscales- a) Intrusion; b) Avoidance; and c) Hyperarousal. Items are scored on a 0-4 response format. Subscale scores are calculated by taking the mean of the subscale responses. Total scores range from 0-88. A score of 24 or greater indicates clinical levels of distress. It has good internal consistency (α = 79-.92). The IES has been used in several studies with cancer patients and has been found to be sensitive in cancer patients (P. N. Butow et al., 2017).

PROMIS Anxiety 8a: PROMIS-Anxiety measures fear, worry/dread; hyper arousal and related somatic symptoms (Cella et al., 2010). The short-form consists of 8 items that are scored on a 0-5 response format. The raw score is calculated by summing the values of the response to each question (range 8-40). Scores are standardized such that the scale produces continuous T scores with a mean of 50 and a SD of 10; higher scores reflect higher distress. PROMIS T score thresholds for anxiety are: < 55 normal; 55-64 mild; 65-74 moderate; ≥75 severe. Validity was tested in a large sample of participants with chronic

illnesses including cancer. Construct validity was demonstrated using the anxiety scale from the MASQ as the convergent measure (r=.80) and the CES-D as the divergent measure (r=.75).

Patient Health Questionnaire (PHQ-9) is a 9-item depression screening tool based on the diagnostic criteria for major depressive disorder in the Diagnostic and Statistical Manual Fourth Edition (DSM-IV). The PHQ-9 includes the two major symptom domains characteristic of depression: affective and somatic symptoms. It is rated from a 0 (not at all) to 3 (nearly every day) scale. Items are summed and a score of 10 or greater is considered clinically significant symptoms of depression. Scores of 0-4, 5-9, 10-14, and ≥15 represent minimal, mild, moderate, and severe levels of symptom burden. It is well-validated and widely-used in medical settings such as primary care. The scale showed good internal consistency (α = 86- .89) and sensitivity to change (Kroenke, Spitzer, Williams, & Löwe, 2010).

The Memorial Symptom Assessment Scale (MSAS) is a measure of overall symptom distress and assesses 32 common symptoms experienced by cancer patients. A modified version of the MSAS will be used to evaluate the occurrence, severity, and distress of symptoms. Symptom severity is rated on a 4 point Likert scale (1=slight) to 4=very much). Distress is rated on a 0-4 Likert scale ranging from not at all (0) to very much (4). The physical symptom subscale is the average of the severity and distress associated with 12 prevalent physical symptoms. The psychological symptom subscale is the average of the severity and distress associated with 6 prevalent psychological symptoms. The total MSAS score (TMSAS) is the average of the symptom scores of all 32 symptoms; higher scores indicate greater symptom severity and distress. Cronbach alpha coefficients for the subscales were .83 (psychologic), .and .88 (physical) for high prevalence symptoms (Portenoy et al., 1994)

The Metacognitions questionnaire (MCQ-30) is a 30 item Likert scale that assesses different beliefs about worry, also referred to as "metacognitive beliefs and processes." It consists of 5 subscales: Positive beliefs about worry; Negative beliefs about worry, Cognitive confidence; Need to control thoughts; and Cognitive self-consciousness (tendency to focus attention on thought processes). Items in each subscale are scored on a 1-4 Likert scale. Subscale scores range from 6-24 and total scores range from 30 to 120. Higher scores indicate more dysfunctional metacognitions. Internal consistency was α =.93 for the total score and ranged from .72-.93 for the subscale scores (Wells & Cartwright-Hatton, 2004). It has been validated in cancer patients and showed good convergent validity; internal consistency of the subscales ranged from .73-.89 pre-treatment) and .79-.91 (post-treatment) (Cook, Salmon, Dunn, & Fisher, 2014).

The Five Facet Mindfulness Questionnaire (FFMQ-15) assesses five facets of overall mindfulness: observing, describing, acting with awareness, non-reactivity to inner experience, and non-judging of inner experience. Items are rated on a 5-point Likert scale ranging from 1 (never or rarely true) to 5 (very often or always true). Three items comprise each subscale; and the facet subscale scores range from 3-15. Higher scores indicate greater engagement with mindfulness skills. The measure is sensitive to change over the course of mindfulness-based cognitive therapy. However, psychometric testing found that a four-factor structure without the observing scale best fit the data prior to the intervention while a 5-factor structure provided the best fit following the MBCT intervention (Gu et al., 2016). For scoring they recommend excluding the observing facet score from comparisons of subscale and total scores before and after mindfulness interventions. Thus, one would combine only the 4 subscale scores into a total FFMQ score (Gu et al., 2016). Internal consistency is adequate for the FFMQ-15 with Cronbach's alphas for the 4 subscales ranging from .66 to .83. The FFMQ has been used in studies of advanced cancer patients (Chambers et al., 2017).

Interview Guide: A structured interview guide was developed based on qualitative interviewing methods. It includes open-ended questions asking about participants' experience with CFS; perceived benefits, barriers, and whether they received the help they needed. A question addressing referrals or participation in supportive care; mental health services; and integrative therapies. We will also ask

patients to describe self-monitoring behaviors during the exit interview e.g. requests for additional surveillance testing; unscheduled visits related to symptom concerns.

Chart Audit Form: The chart audit form consists of three sections and will document: 1) Clinical data including staging, treatments, comorbidities, and baseline symptoms and medications. 2) Referrals for supportive services and to other medical specialists (type, reason for referral) and 3) Unscheduled encounters including unscheduled clinic visits for symptom concerns (phone calls or in-person); urgent care and emergency room visits (type & reason); or unscheduled surveillance tests (lab tests, scans). We will also document self-initiated and other referrals to supportive care services in the community. This form will be completed by the APN.

Practice Log and Client Handouts: Patient handouts include worksheets and exercises to supplement session content. Practice logs will document compliance with home practice exercises (e.g. attention training).

Session Checklist: This form is to be completed by the APN following each session. It consists of a checklist to document the key topics covered in each session, and assessment of self-monitoring and avoidance behaviors. It includes a free-text section to note any participants concerns, comments about the intervention, and questions that arose during the session. The APN will also note any referrals made or resources given to the participant.

12.1.2.1 Eligibility Checklist

No Eligibility Checklist will be used for this study as the eligibility criteria are short.

12.1.2.2 Prior Therapy Forms and On-Study Forms

N/A

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

13.1 Study Design

This is a single group mixed methods pilot study. GYN and lung cancer patients with advanced stage (3 or 4) will be invited to participate as their eligibility is identified. We plan to enroll approximately 40% of patients in surveillance mode and 60% in active treatment mode. There is no randomization involved, and patients will be accessioned in the order in which they consent for participation. We will employ a 2-stage eligibility screening process. Once patients are identified as satisfying the first three eligibility screening criteria: 1) Lung or GYN cancer: stage III or IV disease; 2) ≥ 3 months from initial diagnosis; 3) receiving disease-focused treatment or in surveillance mode, they will be invited to sign a consent for enrollment. A second stage of the screening process will further identify patients who score 34 or higher on the Fear of Progression Questionnaire-SF *or* 24 or higher on the Impact of Event Scale-Revised. We will consent patients and screen them for eligibility until we have enrolled 33 subjects. Consented but ineligible patients will represent false starts and therefore will not be included in the analysis. An exit interview will be sought with all accrued subjects, regardless of whether they dropout or complete the intervention. We anticipate that the enrollment distribution will be approximately 50 lung and 50 GYN patients. Descriptive statistics will be used for primary outcome metrics, and analysis of variance will be used to study secondary outcome measures over time. All analyses are described in 13.3. Sample Size Accrual Rate

COH sees 110 patients with GYN and 210 patients with lung cancer in advanced stages (III/IV) annually. Therefore, we anticipate that our screening and enrollment of n=33 subjects will be completed within 9 months (approximately 4pts/mo.).

13.2 Statistical Analysis Plan

Statistical Analysis Plan: Statistical analyses will include all accrued subjects, regardless of whether they complete the multi-session intervention. Consented but ineligible patients will represent false starts and therefore will not be included in the analysis. Among the 50 subjects, we anticipate that at least 33 subjects will complete the pre-treatment assessment and enroll in the study; and at least 25 of them will complete at least one intervention session. With those 33 subjects, the study will allow detection (in at least 1 patient in our sample) of any cause that prevents follow-through with any component of the intervention and data gathering that has at least 10% prevalence in the general population, with a probability of 0.97. We will be able to estimate the rate of adherence with attendance and home practice assignments, with a confidence interval with half-width no greater than 0.16, as long as the true proportion exceeds 0.7. Descriptive statistics will be used for the primary outcome metrics, and analysis of variance will be used to study the secondary outcome measures over time. Aims outside of the feasibility scope are exploratory. Distributions of the participant demographics, medical history, and results obtained from assessment tools will be generated. Means, standard deviations, and ranges will be calculated for continuous variables, and frequencies and percentages for categorical variables. All

questionnaires and assessment tools will be scored according to instructions. An exit interview will be sought with all accrued subjects, regardless of whether they dropout or complete the intervention.

Aim 1.
We will assess the feasibility and acceptability of the CFS intervention in patients with advanced lung and GYN cancer (stages III or IV) who have clinically significant levels of fear of cancer progression (FOP) or cancer-related distress.

Feasibility and acceptance will be assessed by enrollment rate, attrition, attendance, compliance with home practice exercises, and observance of unanticipated problems, as defined below:

a) Enrollment rate will be deemed sufficient if at least 33 eligible patients are accrued within 9 months.
b) Attrition will be deemed manageable if the percentage of accrued subjects who drop out of the study does not exceed 25%% by T2 and 50% by T3.
c) Attendance is defined as percentage of the 7 sessions attended. An average of 5 sessions attended will indicate high acceptance.
d) Compliance with home practice exercises will be assessed by: 1) the percentage of assignments completed, 2) the percentage of attention training and mindfulness practice sessions performed, as recorded on daily tracking logs; and 3) Responses to a question on the exit interview asking participants about the frequency of their adherence to home practice exercises. Average 50% compliance on at least one of these measures will be deemed adequate.

Observance of anticipated problems will be defined as detection of any problems or barriers to the implementation of the protocol or the intervention sessions.

Acceptability will also be assessed qualitatively based on responses to an exit interview asking about participants' experience with the intervention, including benefits and barriers.

Aim 2. We will assess preliminary effects of CFS on FOP and other outcomes. Analysis of variance (ANOVA) will be used to study patterns of change over time in self-report questionnaires administered at T1, T2, and T3. For self-reported questionnaires that were not completed at either T2 or T3, we will use the last observation carried forward approach, and carry forward responses reported at T1 (or T2 if only T3 data missing), in order to avoid bias resulting from patients who drop out early due to finding the intervention less effective. This will provide a more conservative approach in measuring the effectiveness of the intervention.

a) The Fear of Progression Questionnaire-SF – to assess fear of cancer progression
b) The Impact of Events Scale-Revised – to assess cancer-specific distress
c) The PROMIS-Anxiety 8a – to assess anxiety
d) The PHQ-9 will be used to assess depression
e) The MSAS will be used to assess overall symptom distress
f) The Metacognitions questionnaire (MCQ-30) – to assess metacognitive beliefs and processes (beliefs about worry)
g) The Five Facet Mindfulness Questionnaire (FFMQ-15) -to evaluate overall mindfulness and engagement with mindfulness skills.

Qualitative Analysis: Acceptability will be assessed based on participants' responses to an exit interview assessing benefits, barriers, and participant's experience with CFS. A convergent-parallel mixed methods approach will be used to gain a better understanding of feasibility and participants' experience. Content analysis will be used to identify, code, and categorize themes in the data (Patton, 1990). We will include data from the exit interview and participant comments as recorded by the APN on the session checklist. Transcripts will be read several times to identify preliminary themes. The content of the data

will be analyzed and categories of responses identified for each interview question (Fonteyn & Bauer-Wu, 2005). Preliminary codes or key phrases will be generated using open-coding. Preliminary subcategories will be created and reviewed for each survivor across all data sources (Sandelowski, 2000). The data will be analyzed independently by two team members. Team members will meet to refine the subcategories and themes. Any discrepancies in coding or subcategories/themes will be discussed and refined based on consensus. The quantitative and qualitative data will be analyzed separately and compared and integrated in the discussion section.

14.0 Human Subject Issues

14.1 Institutional 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.

14.2 Recruitment of Subjects

Potentially eligible patients will be identified by the disease team as well as the research coordinator (RC). The RC and APN will review the GYN and lung clinic appointment schedules and the surgery schedules to identify potentially eligible participants. The RC/APN will also review SUPPORT screen questionnaires that assess distress including FOP as another way to screen for eligibility. In addition, the RC/APN will attend the outpatient lung and GYN clinics on a regular basis to discuss eligibility with the clinical team and identify potential participants. We plan to enroll approximately 40% of patients in surveillance mode and 60% in active treatment mode as the concerns and symptoms may be different for these groups.

The RC or APN will meet with the patient to explain the study procedures and obtain informed consent. In addition, study flyers with contact information for the study team will be posted in the clinic exam and waiting rooms.

14.3 Advertisements

Advertisements to include print, media (radio, television, billboards), telephone scripts, lay summary to be posted on City of Hope's public Clinical Trials On-Line^{SM} website, etc., will be reviewed and approved by the IRB prior to their use to recruit potential study subjects.

14.4 Study location and Performance Sites

This study will be performed at COH, Duarte campus.

14.5 Confidentiality

This research will be conducted in compliance with federal and state of California requirements relating to protected health information. The PHI that will be recorded include name, date of birth, date of diagnosis and surgery, e-mail, and telephone number. If the participant agrees to provide testimonials, optional PHI may include their picture or facial image; e.g. an audio or video recording. This information will be linked to the subject's identify using a coded study number. The PI, co-investigators, RC, and RN will have access to this information. No identifiers will be used in any subsequent publication of the results.

14.6 Financial Obligations and Compensation

Subjects will not incur any financial obligations, and they will not be compensated for participation. Subjects will receive financial compensation for completing sessions and the study surveys at T2 and T3. We will provide a $25 gift card following completion of the T2 surveys and exit interview and another $25 gift card following completion of the T3 surveys. For participants who agree to provide a video and/or or audio testimonial, we will provide a $30 gift card following completion of the recording.

14.7 Informed Consent Processes

The Principal Investigator, APNs, RC 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 informed consent document. 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 City of Hope or any relationship they have with City of Hope. Research subjects will be afforded sufficient time to consider whether or not to participate in the research.

The RC or APN will meet with the patient during a follow-up visit to review study procedures and answer any questions. Consenting will take place in a private area in the GYN or lung outpatient clinics. Alternatively, the RC may call the patient to determine interest and review the study procedures and consent form. If necessary (i.e. if potential participants have left the clinic or would like additional time to consider participation), a telephone/verbal informed consent will be obtained first in order to begin the study in a timely manner. Signed informed consents will be obtained in person or via mail, fax, electronic mail, or other electronic applications (i.e. DocuSign). Mailed consent forms will include a return, stamped envelope. If the patient declines, no coercive tactics or pressure will be used. Following the consent meeting, the RC/APN will administer and review the scores on the screening questionnaires to determine eligibility. If patients score below the cut-off for eligibility on both questionnaires, they will be provided with a list of resources on managing fear of cancer progression and distress. Patients will also be given the option to meet with a social worker to discuss their concerns, and the RC or APN will facilitate a referral to Supportive Care Services if needed. For patients who are eligible (score ≥34 on the FOP-SF or ≥24 on the IES-R), the RC/RN will review the procedures for completing the study questionnaires and provide a copy of the signed Informed Consent document. The RC will follow-up by phone to answer any further questions about the study or data collection procedures.

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