# Study Protocol and Statistical Analysis Plan

**LCCC2030:** A Pilot Study Evaluating the Feasibility, Acceptability, and Preliminary Evidence of Efficacy of the Families Addressing Cancer Together (FACT) Tool

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**Study Synopsis**

This is a single-arm pilot study using a pretest-posttest design to evaluate the feasibility and acceptability of a novel psychosocial intervention, *Families Addressing Cancer Together (FACT)*. In this single-center study, we will recruit up to 60 patients with a new or recurrent diagnosis of cancer who also have minor children to participate in a newly developed psychosocial intervention for parents with cancer. The purpose of the intervention is to decrease parental distress by facilitating parental communication about cancer with their children. The primary hypothesis being tested is that an intervention that assists parents with their communication needs with their children can be feasible, acceptable, and reduce parental psychological distress. Findings from this study will inform a future grant application to further test this intervention in a randomized controlled trial.

**Background**

Parents with cancer are encouraged to be "honest and open" with their minor children about their illness. Parental communication about illness is linked to better emotional adjustment for both themselves and their children,[1-3] yet most cancer centers lack the resources to address these patients' needs. Lay publications to support parental illness communication exist, but patients prefer tailored resources specific to their concerns and disease.[4,5] The few evidence-based interventions to facilitate parental cancer communication demonstrate high acceptability, yet are limited by the need for extensive infrastructure or highly specialized providers, thus limiting dissemination. What remains unknown is how to deliver timely, customized parental communication guidance across cancer treatment settings. Without this support, parents with cancer and their children experience avoidable psychosocial distress. In order to better support parental communication needs in cancer, psychosocial interventions that can be implemented across clinical practice settings are needed.

To address this gap, we have developed a novel psychosocial intervention, *Families Addressing Cancer Together (FACT)*. FACT is a theory-guided, tailored psycho-educational communication resource for parents with cancer. FACT was developed through an extensive review of the scientific literature and publicly-available resources, consultation with mental health, social work, oncology, and palliative care clinicians, patient and caregiver stakeholder interviews, and data from the PI's prior observational studies with parents living with advanced cancer.

**Purpose and Rationale**

This pilot study will provide the necessary data to inform the development and testing of a communication intervention to support parents in their communication with children about cancer. The research questions to be answered by this study are whether the intervention being tested can be feasible and acceptable, and provide preliminary estimates of improvement in parental psychological distress.

**Primary Objective**

The primary objective of this study is to evaluate the acceptability of a pilot psychosocial intervention for parents with cancer. Acceptability will be defined through satisfaction ratings.

**Secondary Objective**

A secondary objective of this study is to evaluate the feasibility of the study and study

procedures in preparation for a future RCT of the intervention. We will report on participant screening, recruitment, and retention.

**Exploratory Objectives**

An exploratory objective of this study is to explore the impact of the intervention on target outcomes of anxiety symptom severity (Hospital Anxiety and Depression Scale, HADS) depression symptom severity (HADS), social/family well-being (Social/Family Well-Being subscale of the Functional Assessment of Cancer Therapy-General, FACT-G), quality of life (FACT-G), family functioning (McMaster Family Assessment Device General Functioning Scale) and communication self-efficacy in parents with cancer. Data from this study will be used for preliminary estimates to power a future R01 testing the intervention.

An exploratory objective of this study is to explore the impact of the intervention to promote parents' communication about cancer with their children as measured by an investigator-designed survey of parental cancer communication concerns and behaviors.

**Study Population**

**Inclusion Criteria**

Confirmation of eligibility criteria is required for all potential study subjects prior to study enrollment. Subjects will be eligible for study participation as defined by the inclusion and exclusion criteria as follows:

1. Informed consent reviewed and signed;
2. Age equal to or above 18 years;
3. Ability to understand and comply with study procedures;
4. Able to complete all study measures and visits in English;
5. Be a parent, primary caregiver, or guardian of at least one child between the ages of 3-18 years old with whom the subject has regular contact. The child must have cognitive ability to understand verbal communication;
6. Have a new or recurrent/progression diagnosis of invasive solid tumor within the past six months, or have a solid tumor cancer diagnosis with disease that is either stage IV or equivalent. Staging determined to be "equivalent" to cancer with distant metastases reflects disease in which long-term survival is poor, and will be defined as:
    a. Stage III lung (extensive stage or NSCLC) cancer;
    b. Ovarian cancer with platinum resistant/persistent/refractory disease;
    c. Stage III cervical cancer with recurrence;
    d. Head/neck cancer considered stage IV in the absence of distant metastases;
    e. Stage III endometrial cancer with recurrence after chemotherapy;
    f. Stage III pancreatic cancer;
    g. Glioblastoma multiforme (GBM);
    h. Anaplastic oligodendroglioma with grade 3 or above.
7. Have a cancer diagnosis that is likely to require systemic anti-neoplastic therapy, non-office based surgical intervention, radiation therapy, or palliative care/hospice within the next three months.

**Exclusion Criteria**

Eligible subjects must not have any of the following to be enrolled in the study:

1. Unable to complete self-report instruments due to illiteracy, neurologic illness, inability to speak or read English, or other causes.
2. Unwilling to be audio recorded during the feedback interview portion.

**Study Details**

**Screening**

Potential study subjects will be identified through conversations with clinicians and review of oncology service rosters. The principal investigator (PI), study coordinator, or the research assistant (RA) will confirm study eligibility with patients' oncology provider prior to approaching potential subjects.

**Recruitment and informed consent**

All subjects will provide informed consent for the study and HIPAA authorization. When approaching an eligible patient, the study team member will describe the nature of the study questions and their purposes and written informed consent will be sought. When the treating oncology team believes it may be more acceptable to an individual patient, a member of the oncology team may first introduce the study. The provider will briefly describe the study, provide an approved brochure or "quick-sheet" to the patient, and assess willingness to be contacted by the study team.

In addition to in-person recruitment, recruitment will occur by email and telephone. These methods of recruitment will be used to recruit potential subjects when in-person recruitment is not feasible (and during COVID-19 restrictions for in-person research contacts). This method will also be used to recruit potential subjects who express interest in the study but who do not provide written informed consent at the time of initial in-person recruitment. As with in-person recruitment, telephone and email recruitment will only occur after receiving healthcare provider permission to approach the patient and verbal statements from the patient that the study team can call them to further discuss the study.

In addition to the above methods, patients may self-identify for potential enrollment in the study. The study will be listed in Research for Me @UNC. Flyers and brochures will be available in waiting rooms or other common areas in NCCH. Self-identifying patients may complete a pre-screen link via Qualtrics to ascertain whether the patient meets eligibility criteria. Ineligible patients will be provided with information about existing resources and services.

We will make all attempts to obtain written informed consent from all individuals. Under circumstances in which individuals cannot provide written consent due to convenience, burden, or UNC COVID-19 guidelines, verbal telephone consent will be sought. In these circumstances, the study team will email a copy of the consent form to the individual and provide a hard copy if possible. When collecting verbal consent, study staff will employ similar procedures for written informed consent

Participation in this study is voluntary. Patients who choose not to participate in this study will not be subject to prejudice in the delivery of health care by their physicians and clinical staff nor by the research institution.

**Baseline study assessment (T0)**
After receiving consent, the study team member will obtain baseline assessment information from the subject. Subjects will complete the study forms online via a secure REDCap link or via pen and paper if they wish to complete them immediately after providing informed consent. The baseline study assessment consists of a demographic form and several patient-reported outcome measures. Baseline assessments must be completed before the intervention study visit.

**Study visit (T1)**
For the study visit, the subject will first complete a web-based questionnaire that guides the selection of tailored materials and resources. Subjects will only be able to access the questionnaire after they have received a unique de-identified study ID which they will use when completing the questionnaire. If the subject does not have internet access or does not wish to complete the study visit electronically then they will be scheduled for an in-person study visit in a private room of the NCCH. They will complete the web-based questionnaire via a password-protected iPad provided by the study team.

Items on the study visit assessment measure will be forced-response, as missing items would result in being unable to generate participants' customized content. Subjects will be told during the informed consent process that those specific items will be forced-response, will have the opportunity to preview the items before consenting if desired, will be informed that all other study questions may still be skipped if preferred, and will be informed as to the rationale for making these items forced-response.

**Post-intervention assessments (T2)**
After reviewing their customized communication materials, subjects will be contacted 2-weeks (with an additional 2-week window) to complete the first post-intervention assessments. Subjects will be asked to complete study measures as well as a semi-structured interview. Subjects will complete the study measures via a secure REDCap link or via pen and paper if they do not have internet access.

The post-intervention semi-structured interview consists of a face-to-face or telephone interview addressing barriers and facilitators to intervention use, communication content areas not addressed in the current communication tool, feedback on their experiences communicating with their children, suggestions for improvement, review of the future prototype of the intervention, and any psychosocial follow-up needs. The interview is expected to last approximately 30 minutes and will be conducted by a trained member of the study team. Subjects are not required to answer questions they find emotionally distressing. All interviews will be audiotaped and then transcribed to facilitate analysis. To allow flexibility for participants, we will allow the semi-structured interview to occur between 2-12 weeks post-intervention.

**Post-intervention assessments (T3)**
12-weeks (with an additional 2-week window before/after), subjects will be asked to complete the same survey measures that they completed at T0 and T2. Subjects will complete the study measures via a secure REDCap link or via pen and paper if they do not have internet access.

**Chart abstraction**

The PI and RA will also abstract basic data from the medical record such as cancer type and treatment at the time of study enrollment.

**Subject self-report study measures**
Subjects will complete several outcome measures. Subjects may complete some or all of the surveys and they can skip any questions they find distressing.

**Demographic form**
The investigator-designed demographic form is a brief self-administered questionnaire.

**Eastern Cooperative Oncology Group Performance Status Scale (ECOG)**
The ECOG evaluates the severity of symptoms and amount of assistance the participant requires to complete "normal activities" using a 5-point scale. The ECOG is used to assess how the disease affects the daily living abilities of the patient and determine appropriate treatment and prognosis.[6] It has been modified for patient self-report. Subjects are also asked two questions assessing their appraisals of illness severity.

**Parental Cancer Communication Questionnaire**
Subjects will be asked several investigator-designed questions assessing their parental communication concerns, their beliefs about anticipated consequences of discussions with their children about cancer, and their communication behaviors with their children about cancer. Parents who have engaged in any communication with their children about cancer will also be asked questions about their child(ren)'s response to these discussions.

**Hospital Anxiety and Depression Scale (HADS)**
The HADS is a 14-item self-administered rating scale to assess depression and anxiety symptoms in patients with physical illness. The HADS has two 7-item sub-scales addressing depression and anxiety. It is graded on a 4-point scale with scores ranging from 0 to 42 (or 0-21 for each subscale) with higher scores representing greater degrees of mood symptoms. The HADS is a well-validated instrument frequently used in oncology populations.[7,8]

**Functional Assessment of Cancer Therapy – General (FACT-G)**
The FACT-G is a 27-item self-administered assessment of general quality-of-life measures in cancer patients. It has been extensively validated in the literature and permits measurement of a number of symptoms including nausea, pain, and insomnia. It is graded on a five-point scale and has four sub-scales addressing emotional, social/family, physical and functional well-being. The general adult population norm is a mean total score of 80.1 (standard deviation = 18.1) with a total score range from 0-108.[9]

**Communication Self-Efficacy scale**
The nine-item Communication self-efficacy scale is adapted from Murphy et. al.'s maternal HIV disclosure self-efficacy scale.[10] Subjects rate nine statements assessing their level of confidence in their ability to tell their child about their diagnosis using a visual analogue scale. This scale has been extensively used in the parental HIV communication literature. In prior studies the Cronbach's alpha for the scale was 0.90.

**FACT Satisfaction scale**
The intervention satisfaction assessment includes four investigator-designed core question items assessing the relevance and acceptability of the study intervention with an additional 6 items assessing specific intervention components. Subjects rate each item on a 4-point ordinal scale. The questions have been adapted from other assessments of psychosocial intervention satisfaction/acceptability in the literature.

**McMaster Family Assessment Device – General Functioning Scale (GFS)**
The GFS is a 12-item self-administered scale that measures the overall health of the family unit. It is measured on a 4-point scale and the sum of values is divided by 12 to give a total score ranging from 1-4. Higher scores indicate unhealthier levels of family functioning. The GFS is widely used in research and clinical practice to identify families experiencing problems.

**Post-intervention study interview**
Subjects will participate in a semi-structured interview with a member of the study team to obtain feedback on the intervention.

**Medical record abstraction**
The PI or RA will abstract demographic and medical history data from the subject's chart including illness history and treatment and medical co-morbidities.

**Expected Risks**
Approaching patients about enrollment in the clinic poses a risk to privacy. We expect this risk to be low. In the UNC ambulatory oncology clinics, RAs routinely approach patients for enrollment in clinical studies, and members of our team have completed prior studies with careful attention to patient privacy and high acceptability on the part of subjects. Approaching patients via telephone also poses a risk to privacy although we expect this risk to be low.

Loss of confidentiality could occur if the study database was breached. This risk will be minimized as a result of numerous steps to protect confidentiality. The alternative of not keeping identifiable information is not possible, because we will need to access the medical record.

Eligible subjects may be at higher risk for brief additional emotional discomfort or distress due to this study. Questions about communication concerns may be temporarily uncomfortable or distressing for some subjects. We expect the risks of discomfort or distress to be low relative to the overall distress that the patients experience due to their serious illness.

**Adequacy of Protection Against Risks**
The PI, study coordinator, or RA will receive permission from the patient's oncology provider before approaching any eligible patients. As such, patients whom the oncology team believes are at high risk of emotional distress from study participation will not be approached. All subjects will provide informed consent for the study and HIPAA authorization. When approaching an eligible patient, the study member will describe the nature of the study questions and their purposes and written informed consent will be sought. For telephone recruitment, written consent via secure Qualtrics link or verbal consent will be sought. Participants providing Qualtrics or verbal consent will provide HIPAA consent electronically through secure Qualtrics link.

Participation in this study is voluntary. Patients who choose not to participate in this study will not be subject to prejudice in the delivery of health care by their physicians and clinical staff nor by the research institution. All subjects will be specifically reminded that they may withdraw at any time without impacting their treatment or relationship with their clinical team and that they may choose not to answer any study question they would rather not answer.

All members of the study team will undergo and maintain training in the responsible conduct of research. To protect against loss of privacy, all study-related interactions will be conducted in private rooms at UNC hospital or clinics or via telephone after ascertaining with the subjects that the location is private. To protect against the risk of a loss of confidentiality, study files will be password-protected and housed on a secure server within the UNC School of Medicine. Consent and HIPAA forms will be kept in a locked cabinet in the locked office of the PI and will be destroyed upon study completion. For analysis, identifiable information will be removed from the analytic dataset and interviews, and subjects will be assigned a unique study identifier. To protect against the risk of emotional distress to subjects from study questions, the study team will review all study components and materials prior to starting the study. Should study staff observe emotional reactions necessitating clinical intervention, the study subjects will be offered immediate support services in the form of psycho-oncology assessment by a member of the UNC Comprehensive Cancer Support Program psycho-oncology service. The PI will report to the IRB any adverse events that occur during the study and will notify the subject's primary oncologist.

**Removal of Patients from Protocol**

Subjects will be removed from the study when any of the exclusion criteria apply or the subject elects to withdraw from the study. If this occurs, the PI will be notified and the reason for study removal and the date the subject was removed will be documented in the Case Report Form.

**Sample Size and Accrual**

We will recruit up to 60 patients over 12 months for the proposed study. A 95% exact binomial confidence interval will be calculated for the acceptability rate. For qualitative interview data, sample size estimation is based on projections of the number of subjects needed to reach saturation of the concept. The sample size for the proposed study is adequate for qualitative analysis and consistent with psychosocial intervention development.[11,12]

**Data Analysis Plans**

**Evaluate acceptability of the intervention**

To evaluate acceptability of the intervention, we will administer a satisfaction assessment to each participant after each follow-up study visit (T2 and T3) and conduct post-intervention interviews at T2. In the post-intervention interviews, we will use content analysis, a widely accepted qualitative analysis approach in health research, to identify major themes from interviews.[13] The study team will review interview transcripts, coding and categorizing the data by expanding and collapsing categories until thematic saturation is reached.[14] We will use best practices for qualitative research such as member checking, and creation of an audit trail.[15] We will use this feedback to refine the intervention prior to launching the randomized controlled trial. We will use qualitative analysis software to aid with analyses. Descriptive statistics from the quantitative rating scale and qualitative interview data will be collected concurrently, analyzed separately,

and the two sets of findings converged.[16]

**Evaluate feasibility of the intervention**

To evaluate feasibility of intervention, we will report the percentage of patients who are approached about the study who: (1) enroll in the intervention (percent approached), (2) complete the intervention at each time point. We will use descriptive statistics to assess the demographic characteristics of patients who enter, remain in, and drop out of the study. We will evaluate feasibility of study procedures including: (1) Number of patients screened, (2) Number of contacts, (3) Duration of study visits, and (4) Proportion of completed study measures at each visit. Although adverse events are unlikely, we will examine the procedures for adverse event reporting and the study teams' response to such events. We will use qualitative analyses of post-intervention semi-structured interview data to explore barriers and facilitators to participation, including reasons for enrollment, non-participation, ineligibility, or withdrawal and use this information to refine study procedures in preparation for a larger-scale study.

**Explore impact of intervention on target outcomes**

We will report on changes in patient-reported outcomes of interest and will use paired t-tests to evaluate whether mean scores pre- (T0) and post-intervention (T2) are significantly different from 0. This pilot study is not designed nor powered to detect differences as the primary objectives are to evaluate the acceptability and feasibility of the intervention. We will use descriptive statistics to report on the percentage of patients who engage in any communication behaviors about cancer with their children, the depth of their discussion, and their assessments of how their children responded to these conversations.

**Data Management/Audit**

As an investigator-initiated study, this trial will be audited by the Lineberger Cancer Center audit committee every six or twelve months, depending on the participation of affiliate sites.

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