LCCC 1941: Addressing Cancer-Related Financial Toxicity in Rural Oncology Care Settings

Principal Investigator
Donald L. Rosenstein, MD
Director, Comprehensive Cancer Support Program
Professor, Medicine and Psychiatry
Vice Chair, Division of Hospital Psychiatry
Physician's Office Building, Room 3134
101 Manning Drive First Floor, Chapel Hill, NC 27514
Business 919 843-8895, 957-6603
Mobile phone 301-594-0859, 302-9295
Email: donald_rosenstein@med.unc.edu

Principal Co-Investigator
Stephanie Brooke Wheeler, MPH, PhD
Professor
Health Policy and Management
Gillings School of Global Public Health
1104E McGavran-Greenberg
CB#7411
Chapel Hill, NC 27599
(919) 966-7374
Stephanie_Wheeler@unc.edu

Co-Investigator(s) at UNC
Katherine Reeder-Hayes, MD
Lisa Spees, PhD

Co-Investigator(s) at other sites
Sarah Birken, PhD
Associate Professor
Department of Implementation Science
Wake Forest School of Medicine
Medical Center Boulevard
Winston-Salem, NC 27157
(919) 357-2662
sbirken@wakehealth.edu

Biostatistician
Allison M. Deal, MS
Senior Biostatistician
919-966-1387
Allison_Deal@med.unc.edu

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Stephanie_Wheeler@unc.edu

Signature Page

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable U.S. federal regulations and ICH guidelines.

Principal Investigator (PI) Names: Donald L. Rosenstein, MD and Stephanie B. Wheeler, MPH, PhD

PI Signature:





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1.0 BACKGROUND AND RATIONALE

1.1 Study Synopsis

Financial toxicity (FT), a term used to describe the high cost and cost-related psychosocial burden that cancer care places on patients and their families, is a major and underappreciated problem affecting at least 20% of all cancer patients, with potentially devastating effects on outcomes. FT disproportionately affects patients in rural settings due to multiple socioeconomic, access, and clinical factors. Importantly, FT is also associated with increased mortality. FN (financial navigation) is one type of evidence-based intervention implemented at the practice or system level that can identify patients at high risk for FT, assess eligibility for existing federal, nonprofit, manufacturer, and local financial support resources, clarify treatment cost expectations, and develop strategies to cope with high costs of care. *Our long-term goal* is to improve cancer care delivery, reduce FT, and improve outcomes in underserved, rural and non-rural populations through sustainable, scalable interventions. The *objectives of this study* are to: (1) assess FN intervention implementation in rural and non-rural oncology practices; and (2) evaluate the effects of FN implementation on patient outcomes, including FT and health-related quality of life, in rural oncology practices.

1.2 Background

It is estimated that at least 20% of all cancer patients experience significant FT as a result of their cancer, including being unable to pay for care, going into debt, filing for bankruptcy, or making other large changes in household spending.[1] A recent review of financial hardship in cancer by Altice and colleagues characterizes the burden associated with cancer care costs as belonging to one of three domains:[2] (1) *material* hardship, including high out-of-pocket expenses and lost wages; (2) *psychological* burden from distress and anxiety caused by high cancer costs; and (3) *behavioral* changes resulting from high cancer care costs, including modifications in both medical spending (such as delaying or declining care) and non-medical spending (such as taking money from savings or skipping nonmedical bills). Across cancer sites and stages, the considerable *material* hardship caused by cancer has been consistently linked to negative *psychological* and *behavioral* outcomes, including lower health-related quality of life (HRQoL),[1; 3; 4; 5] higher emotional distress [6], treatment delay/discontinuation [7], and bankruptcy declaration.[8] Harmful care-altering *behavioral* responses, including delaying or foregoing treatment,[9] may be more common in rural patients who also face greater geographic barriers to care,[10] likely contributing to widely observed rural/urban disparities in cancer mortality.[11; 12]

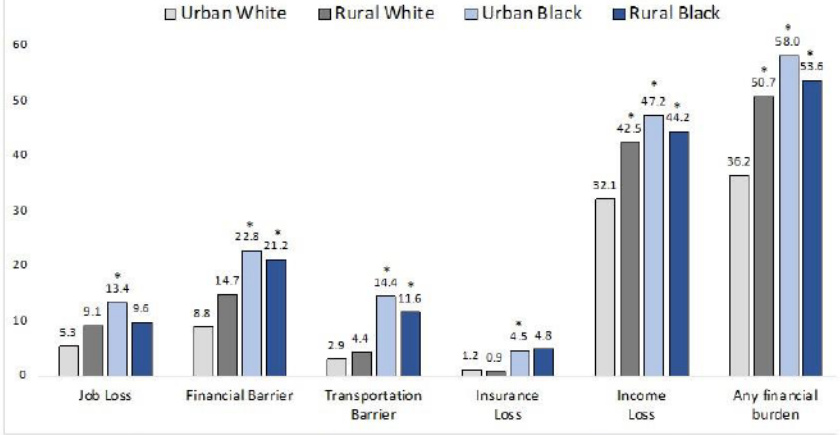
Rural cancer patients experience greater FT than non-rural patients. Several studies have demonstrated higher FT among rural cancer patients, compared to non-rural patients.[13; 14; 15] Although the total cost of cancer *to payers* may be lower among rural, versus non-rural, cancer patients,[16-18] the out of pocket cost burden *to patients* may be greater in rural areas. A review of the literature in 2010 revealed that on average during the first year post-diagnosis, breast cancer patients spend up to $1,180 per month on direct medical expenses and $174 per month on non-medical cancer-related expenses; beyond

one year post-diagnosis, patients spend up to $500 per month on direct medical expenses and $500 per month on non-medical cancer-related expenses.[13] Because rural Americans tend to be lower income, with lower assets, higher unemployment, and higher rates of uninsurance than non-rural populations,[19; 20] such out-of-pocket expenses constitute a greater share of monthly expenditures and thus create more burdensome *material* and *psychological* hardship. This hardship is pronounced among rural communities with large minority populations.[21; 19] Our analysis of a prospective cohort study of 3,000 women with breast cancer surveyed 2 years post-diagnosis, revealed that over 50% of rural black and rural white breast cancer patients report any type of financial hardship from cancer, compared to 36% of urban whites, with rural blacks more often reporting more than one source of financial hardship, compared to urban whites (Figure 1). Rural cancer survivors are also significantly more likely to forego medical care because of cost and transportation barriers, including recommended surveillance after cancer.[22; 23] Rural cancer patients have less access to cancer clinical trials, and when they do enroll in clinical trials, they report high travel costs and other financial burdens associated with participation, including lost wages.[24] In addition, many rural cancer patients travel from their communities to more urban environments to receive treatment, which constitutes a significant economic burden, in terms of transportation, accommodation, lost wages, and opportunity costs of seeking care. In particular, caregivers of children with cancer in rural areas face extraordinary financial hardship, on average missing 24 days of work in a year, compared to 16 days in non-rural households, with one-third losing or leaving a job due to their child's cancer.[25] Despite limited data addressing the full range of negative *material*, *psychological*, and *behavioral* outcomes in the rural setting, *evidence suggests that FT is disproportionately and increasingly harmful to rural cancer patients.*

Rural populations have worse cancer outcomes and greater financial vulnerability, making cancer patients in rural areas an important subpopulation in which to study FT.

Rural cancer patients across the US are diagnosed more often at later stages [26] and experience increasingly higher cancer mortality than nonrural populations,[11; 12] due in part, to differences in geographic access to timely and high-quality cancer screening, diagnosis, and treatment.[10; 23; 27; 28] At the end of life, rural cancer patients less often receive recommended home health, hospice and palliative care services.[16; 18] Rural populations also may be more likely to experience FT because they have fewer protections, including health

Figure 1: Financial Burden by Race and Rurality



* Statistically significant difference versus urban whites (p<.05)

insurance, against financial setbacks.[29] Even though the Affordable Care Act narrowed health insurance disparities by rurality, rural Americans remain more likely to be uninsured.[30; 31] Moreover, states that failed to expand Medicaid to low income adults disproportionately denied insurance coverage to rural and minority residents.[29,30,31] Uninsured or "self-pay" individuals are generally responsible for paying the full cost of their care unless they are able to navigate the complex and uneven safety net of resources, including hospital charity care, entitlement programs, manufacturer assistance, and non-profit organizations' aid.[32; 33] Privately insured patients in rural areas may have insurance plans that require more out of pocket contributions, in the form of higher premiums, deductibles and cost-sharing, due to the disproportionate share of smaller employers with less generous health plans and self-employed, self-insured patients in rural areas relative to non-rural areas.[29; 34] Yet insurance coverage—regardless of plan type or degree of coverage—does not sufficiently protect against financial burden of cancer;[1; 4; 35] 42% of insured cancer patients report significant or catastrophic financial hardship.[4]

The complex *material*, *structural*, and *psychological* needs in rural settings, fragmentation of existing financial support resources, and complicated aid eligibility requirements suggest that financial navigation (FN) is needed to reduce FT and harmful care-altering behaviors. Although FT is a major burden that affects patients' health-related quality of life (HRQOL) and treatment outcomes, cancer centers generally fail to identify FT and assist their patients with this common consequence of cancer, a situation that warrants intervention. The science on FT, to date, has focused primarily on the identification of the problem, leaning on convenience sample cohorts and descriptive studies. The stage is set for the next phase of research, which should include intervention development, testing, implementation and dissemination to relieve cancer-related financial burden, particularly in rural populations. A variety of financial assistance programs exist and provide much-needed financial assistance to cancer patients; however, these programs are fragmented, uncoordinated, and difficult to access, with cumbersome eligibility and paperwork requirements.[33] In addition, providers and support staff report that they lack both the time and knowledge to help patients navigate the increasingly complex and patchwork web of resources that do exist.[33; 36] *Financial navigation (FN)* is the only evidence-based intervention that coordinates access to these existing financial assistance programs. FN works by identifying patients at risk for high FT, assessing eligibility for existing federal, nonprofit, manufacturer, and local financial support resources, clarifying treatment cost expectations, and helping patients develop a plan to cope with high costs of care.[37; 38; 36; 39] A financial navigator is at the helm of FN and is trained to work with patients and their families to reduce the stress of the cost of cancer treatment by helping them access healthcare services, find cost-saving treatments, and understand and pay their bills.[40] *FN has been shown to be feasible to implement and effective in reducing cancer patients' out-of-pocket costs by tens of thousands of dollars, reducing cost-related anxiety, and generating millions in hospital savings.*[38; 39]

FN has substantial potential to reduce FT in rural settings, yet its implementation and effectiveness in these settings has yet to be demonstrated. Rural settings are expected to be different from the non-rural settings in which FN has previously been tested because of the aforementioned financial vulnerability of rural cancer patients. In addition,

rural healthcare providers may have greater competing financial demands, lack access to ongoing, professional training, be less well-resourced to manage FN, have fewer financial support resources available locally, and lack sufficient knowledge and self-efficacy to deliver FN.[41-43] These contextual realities may make FN more difficult to implement in rural oncology practices. As such, rural oncology practices are likely to benefit from strategies that have demonstrated effectiveness in promoting the implementation of evidence-based interventions, such as enhanced technical support through a peer-learning network and tailored coaching to aid implementation.[44-46] *In summary, our prior work with patients, cancer care professionals, and a regional network of oncology practices argues strongly for enlisting trained financial navigators to prevent and mitigate FT in rural oncology settings and suggests that patient outcomes will be improved through this multilevel intervention;*[33] *however, FN's scalability depends upon clear evidence that FN can be implemented and is effective in rural and non-rural settings.*

1.3 Purpose and Rationale

The financial burden of cancer is a serious and growing problem, particularly for rural patients, who face disproportionate hardship due to multiple socioeconomic, access, and clinical factors. For patients with cancer who are already coping with the physical and emotional demands of their disease, FT only adds greater distress and increased complexity. It is important to improve our understanding of how FN can reduce the *material*, *psychological*, and *behavioral* burden of high direct and indirect costs associated with the cancer experience, particularly for rural and minority patients--already vulnerable populations.

This prospective, multi-site, interventional study is designed to evaluate the implementation and effectiveness of FN within 5 rural oncology settings and 4 non-rural oncology settings (see Study Schema). We will first engage practice-based financial navigators in training, technical support and coaching to facilitate FN implementation for n=700 cancer patients, and assess, through navigator and key informant interviews, FN implementation outcomes (e.g., fidelity to FN, uptake, acceptability, costs, and perceived sustainability) and its determinants (Aim 1). In Aim 2, we will use patient surveys to evaluate the effect of FN on FT, HRQoL, harmful care-altering behavior, FN acceptability and FN responsiveness.

We are conducting this interventional study of 700 rural and non-rural NC cancer patients, with any type of cancer diagnosis, to answer the following research question: **What is the feasibility, acceptability and preliminary effect on patient outcomes of financial navigation among rural and non-rural NC cancer patients?**

2.0 STUDY OBJECTIVES AND ENDPOINTS

2.1 Primary Objective

2.1.1 To evaluate the change from baseline to follow-up in scores from the Comprehensive Score for Financial Toxicity (COST) measure after participation in the financial navigation program among 700 rural and non-rural NC cancer patients with high baseline financial distress.

2.2 Secondary Objectives

2.2.1. To evaluate the change from baseline to follow-up in scores from HRQoL, care-altering behaviors and patient perspectives on the intervention itself.

3.0 PATIENT ELIGIBILITY

3.1 Inclusion Criteria

Eligibility for Patients:

3.1.1 Patients over the age of 18 with any type and stage of cancer and a confirmed cancer diagnosis within 5 years or currently living with advanced disease
3.1.2 Patients who score 22 or lower on the COST measure indicating high financial distress
3.1.3 Patients must be able to read and speak English

Eligibility for Financial Navigators and Key Stakeholders:

3.1.4 Employee of the organization
3.1.5 Over the age of 18
3.1.6 Ability to read and speak English

3.2 Exclusion Criteria

Individuals meeting any of the following exclusion criteria at baseline will be excluded from study participation.

Exclusion criteria for Patients:

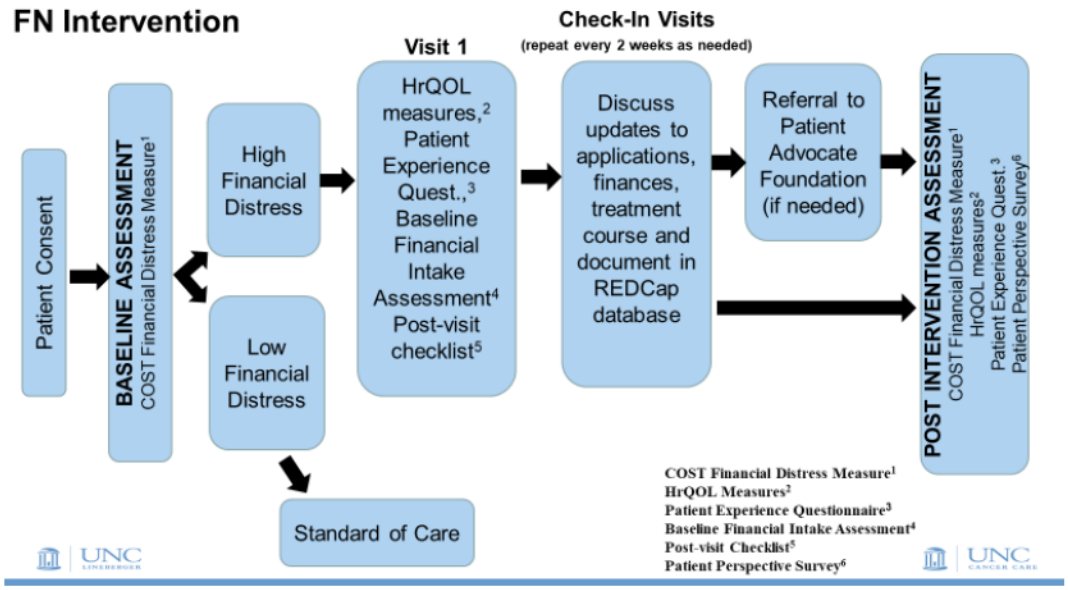
3.2.1 Participants without a cancer diagnosis
3.2.2 Patients or caregivers under the age of 18
3.2.3 Patients who do not sign the consent form
3.2.4 Patients who do not complete the baseline COST survey
3.2.5 Patients who cannot read and speak English

Exclusion criteria for Stakeholders (Year 1 only):

3.2.6 Not employed by the participating organization
3.2.7 Less than 18 years of age
3.2.8 Inability to read and speak English

4.0 STUDY PLAN

4.1 Schema



This is a multi-site, single arm, intervention study of cancer patients in rural NC (n=500) and cancer patients in non-rural NC (n=200). The total number of patients in this study is 700. The primary purpose of this study is to evaluate the change from baseline in COST financial distress scores after the financial navigation intervention. We anticipate that patient active participation will last approximately 4 months but possibly longer depending on the complexity of the patient's financial need.

4.2 Duration of Study

This study will last 4 years. Patient participation begins in Year 2 and includes completion of consent, baseline assessments, and from 1 up to 6 individual appointments with a financial navigator over a period of approximately 4 months. Patient participation length will vary depending on the complexity of their financial assistance needs with more complex patients needing more appointments. It is estimated that patients will need 15 minutes to complete all baseline and post-intervention surveys. The initial financial navigation appointment including completion of the intake form with the financial navigator may take 45-90 minutes depending on the complexity of patient needs.

4.3 Study Details

This prospective study is designed to evaluate the implementation and effectiveness of FN within rural and non-rural oncology settings (See Study Schema). We will engage practice-based financial navigators in training, technical support and coaching to facilitate FN implementation, and assess, through navigator and key informant interviews, FN implementation outcomes (e.g., fidelity to FN, uptake, acceptability, costs, and perceived sustainability) and its determinants. In addition, we will use patient surveys to evaluate the effect of FN on FT, HRQoL, care-altering behaviors and patient perspectives on the intervention itself.

Setting and Population

Five rural oncology practice sites were chosen for participation in this study based on their rural location (according to 2010 Rural-Urban Commuting Area (RUCA) codes) and their prior active participation in the NC-CSPAN statewide network: Carteret Health Care Cancer Center, Harris Regional Hospital, Outer Banks Hospital, UNC Lenoir Cancer Center, and Nash UNC Health Care. Four non-rural oncology practices were chosen based on their more urban setting and their participation in NC-CSPAN: CarolinaEast Cancer Center, Novant Health, Vidant Health and Wake Forest University Health Services. These clinical setting sites are diverse in terms of ownership structure, geographic location, and racial composition, with two out of five rural practices based in counties with high percentages of black residents (Nash, 40.7%; Lenoir 41.2%).

Aim 1. Identify FN implementation determinants and implementation outcomes in rural and non-rural practices.

Aim 1 Rationale. In order for FN to be adopted and sustained in rural and non-rural settings, it must be demonstrated that FN can be successfully implemented in both settings. Determinants of implementation, according to CFIR,[47] exist within 5 key domains: intervention characteristics, outer setting, inner setting, individual characteristics and implementation processes. It is critical to understand the role of these determinants in impeding or promoting effective implementation, as measured by fidelity, uptake, acceptability, efficiency, and perceived sustainability. Training, group-based technical support and tailored coaching are strategies that can enhance implementation of evidence-based interventions;[48-50] these were provided to NC-CSPAN implementers and increased satisfaction, self-efficacy, and confidence. Thus, we plan to leverage similar strategies here.[51; 52]

Aim 1 Intervention. The FN intervention is designed to: (1) build capacity and improve quality of care, while reducing duplication of effort and integrating workflows; (2) educate patients about programs and services that may mitigate their financial distress; and (3) assist patients in applying for, and receiving the benefits from, existing programs and services (e.g., disability, subsidized insurance coverage, SNAP benefits, etc.). The FN intervention will be delivered

by full- or part-time financial navigators currently employed by or hired at each rural and non-rural oncology practice, with modest financial support provided by the grant for hiring, training, supervising, and offsetting practice-level costs associated with employing staff financial navigators. The FN intervention consists of 3 components: (1) systematic identification of cancer patients at high risk for FT; (2) connecting patients experiencing FT or at high risk for FT to dedicated and trained oncology financial navigators, who use a comprehensive assessment tool to determine financial needs and one-on-one appointments to direct patients to specific financial support resources and assist with applications; and (3) routine electronic tracking and monitoring of FN patients' financial and health outcomes. Patients referred to a financial navigator will have at least 2 visits with the navigator with some patients receiving more intensive, needs-dependent support. Repeated visits with the navigator are often important for navigators to review patients' applications for financial support services, correct simple errors, and assist with submission; our experience with UNC's FN program has taught us, for example, that 60% of financial assistance applications were incomplete prior to FN. The anticipated duration of intervention for patients is between 2 weeks and 6 months, with an average intervention time of 4 months, depending on needs.

UNC will provide centralized optimization of the intervention that is responsive to Aim 1 contextual needs, to include, but not limited to: comprehensive FN *training*, monthly group-based navigator *technical support* calls to build a peer learning network and facilitate shared problem-solving, and site-specific *tailored coaching* (delivered remotely and in-person). The Patient Advocate Foundation (PAF) will provide external complex case management to those patients for whom local navigation has reached its limits—i.e., we will refer to PAF those patients with severe and complex financial needs that extend beyond what local financial resources can support. In this way, we triage patients according to the severity and complexity of their financial needs. PAF is a national 501 (c)(3) non-profit charity that, for 20 years, has provided direct financial support to patients with chronic, life threatening and debilitating diseases to help access recommended treatment.[53] PAF case managers "advocate and mediate on behalf of patients to provide avenues of access for therapies, therapeutic agents and devices deemed medically efficacious by the medical and scientific communities while working to find sources of reimbursement for care."

Aim 1 Implementation Strategies. For our purposes, FN *training* is the modularized, interactive FN curriculum that we will provide to financial navigators, including a 12-hour Financial Bootcamp offered online by the Association of Community Cancer Centers (ACCC).[54] FN group-based *technical support* includes monthly teleconferences and annual in-person meetings for financial navigators from the oncology practices and the UNC study team to discuss caseloads, offer best practices and lessons learned, problem-solve difficult situations, and share information across sites in a peer-to-peer format. FN *tailored coaching* includes direct, site-specific interactions between financial navigators at an individual site and UNC study team members, whereby specific implementation challenges can be discussed and resolved in a more targeted

manner. Tailored coaching will involve at least one visit to each rural site in each year of implementation.

The part-time financial navigator(s) at each of the 5 sites will attend a comprehensive and intensive virtual training via Zoom webconferencing software, led by the study team, which will include modules on cancer-related FT, financial distress screening, intake processes, description of local financial support resources and eligibility, program evaluation metrics, and team-building/peer support activities. At the beginning of this training, we will assess through a questionnaire navigators' baseline knowledge, self-efficacy and confidence related to implementation of a FN intervention. In addition to our virtual training, each financial navigator will complete the 12-hour ACCC Financial Advocacy Bootcamp.[54] This national, online resource provides basic information on federal financial aid programs and eligibility requirements, patient communication strategies and problem-solving. After completion of the online training, financial navigators will be asked to complete a post-training knowledge, self-efficacy and confidence questionnaire.

Financial navigators will participate in monthly group technical support sessions that will be delivered and audio-recorded via Zoom. Attendance will be monitored and CFIR-derived templates for meeting notes will record participation of navigators, content introduced and discussed at each meeting, and thematic observations around implementation barriers, unanticipated challenges (and solutions), changes in organizational climate and leadership, reported fidelity to the intervention, and protocol deviations. In addition to monthly peer support opportunities, UNC will work with each of the 9 sites individually to help them navigate any patient-, practice- or provider-level barriers that arise by meeting on a monthly basis with them to offer tailored coaching. These tailored coaching sessions also will be delivered and audio-recorded via Zoom, with CFIR-derived templates for meeting notes summarizing discussions. During these site-specific sessions, the UNC team will assist local financial navigators with problem-solving, including determining when to refer to PAF.

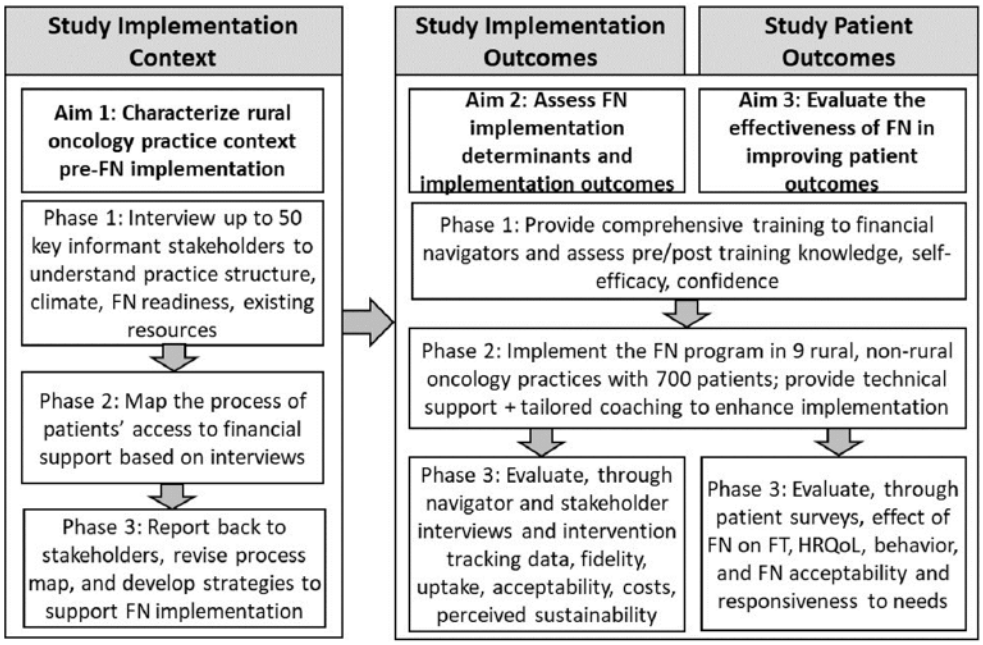
Aim 1 Procedures and Recruitment. Following training, financial navigators will implement the FN program at their respective sites. We will enroll 700 oncology patients with moderate or severe financial distress through our 9 NC-CSPAN oncology practices. Each participating site provides care to uninsured and insured patients. The trial will enroll men and women, ages 18+, with a confirmed cancer diagnosis in the past 5 years or those living with advanced disease. Given the prevalent and indiscriminate nature of FT among oncology patients, we plan to enroll all cancer types. Participants must speak English, plan to continue receiving care at the current oncology study site and be willing to complete all study activities. With regard to biologic sex, we will include, and analyze data for, both sexes since FT affects both male and female patients. Intervention procedural detail is elaborated more fully in the Clinical Trial/Human Subjects Form.

If a patient discloses financial distress to either a staff member or on a screening instrument (such as the Distress Thermometer), the financial navigator will let them know about the study, obtain consent, and then use the COST measure, a

validated nationally recognized measure of FT, to measure their level of financial distress. Patients who report mild or no financial distress will receive each site's standard of care and an educational packet including a tri-fold brochure providing basic information about financial resources and FN. Patients with moderate or severe financial concerns will receive either: (1) an immediate same day appointment with the financial navigator; or (2) a separate scheduled appointment with the financial navigator. Both appointments will involve one-on-one consultation with the financial navigator, who will assess patients' individual financial situation and financial assistance goals, as well as collect information about employment status, billing information, insurance status and other indicators used to triage patients to the appropriate financial resource(s). Patients will leave this initial appointment with a checklist of resources they are potentially eligible for and a list of the personal paperwork (tax forms, W-2, pay stubs) needed to apply. During the follow-up appointment, the financial navigator will review the initial intake forms, verify that the patient has the necessary paperwork and work with the patient to complete resource applications. Patients will be educated on and referred to financial resources such as local charity care, foundation-provided financial support, medication assistance programs, Medicaid, Medicare, private health insurance plans, Social Security and Disability, and legal aid. Patients will be re-contacted by the financial navigator 2-3 weeks after each financial clinic visit to assess progress toward their financial assistance goals. If patients screen positive on the financial distress screening but do not want to attend the FN appointments and participate in the study, they will be given the educational packet including basic information about financial resources and FN.

Aim 1 Data and Measures. The critical measures of implementation determinants will be obtained through in-depth, structured post-implementation interviews with both the financial navigators and key practice-level stakeholders at each site Interviews will be guided by CFIR constructs[47] and include measures of: intervention complexity; outer setting patient needs and resources; inner setting implementation climate, learning climate, resources and access to information; individual characteristics of knowledge, self-efficacy and confidence; and the process of reflecting and evaluating (Figure 2).

Figure 2: CFIR Constructs By Aim



Implementation outcome measures[55] will include fidelity to the FN intervention, uptake, acceptability, costs, and perceived sustainability. Intervention acceptability and perceived sustainability will be explored during the structured post-implementation interviews of financial navigators and practice-level stakeholders. The research team will measure fidelity by reviewing a 10% random sample of all FN intake forms and appointment notes recorded by financial navigators in a patient tracking database built in REDCap to assess: whether the full comprehensive intake form was completed, whether participants received at least two visits with the financial navigator, whether the financial navigator re-contacted participants within 2-3 weeks after each financial clinic visit, and level of completeness of tracking data (e.g., were financial assistance applications submitted, and was the resolution status recorded?) **Uptake** will be assessed as the ratio of the number of patients served by FN to the number of patients screened positive for financial distress and referred to FN), and the percentage of patients who are successfully navigated to specific financial aid resources. Costs will be measured on a per-practice level as the sum of all wages associated with intervention-related navigator activity for the duration of the study period, specifically: time spent training, time spent with patients delivering financial navigation services, time spent conducting administrative functions (e.g., patient scheduling and tracking, researching financial assistance resources, and submitting and resolving financial assistance applications), and time spent engaged in technical support and tailored coaching. These cost data will be captured through activities recorded in the patient tracking database and random navigator weekly time-audits.

Aim 2 Analysis. We will follow a CFIR-derived template analysis[56] approach using Dedoose qualitative analysis software to develop themes from post-implementation interviews with navigators and stakeholders and produce practice-

specific and general summaries of findings in a matrix format, following prior work. In addition, we will use standardized barrier/facilitator ratings (ranging from -2 to +2) based upon coded interview data to score the extent to which CFIR-derived constructs were viewed as impediments or accelerants to FN implementation. We will describe FN fidelity qualitatively using a checklist and the range in uptake and costs across practices.

Aim 2. Evaluate the effectiveness of FN in improving patient outcomes in rural and non-rural oncology practices.

Aim 2 Rationale. In order for FN to be adopted and maintained in rural and non-rural oncology practices, its effects on patient outcomes must be measurable and compelling. In our single-arm FN intervention among 700 cancer patients with high levels of financial distress, we will evaluate baseline and post-FN intervention change in FT (primary outcome), HRQoL, care-altering behaviors, and patient perspectives on the intervention itself.

Aim 2 Recruitment and Procedures. Following the procedure described in Aim 1, 700 eligible oncology patients will be recruited to participate in the FN intervention (100 each from our 5 rural NC-CSPAN oncology practices and 50 each from our 4 non-rural NC-CSPAN oncology practices listed previously). After obtaining informed consent, each patient will be assigned a unique study identifier, complete the baseline survey, receive an appointment with the FN, and receive $25 for completing the baseline and HrQOL surveys. Two to three months after the second FN visit (to allow time for FN to have an effect on outcomes), patients will complete the follow-up surveys and receive $25 each for completing the post-intervention surveys. Additional financial incentives for study participation include the possibility of receiving benefits from financial aid resources.

Aim 2 Measures and Analysis Plan. The research team will administer patient surveys to collect Aim 2 measures (see below) using a pre- and post-FN single-arm intervention approach. We acknowledge that a randomized, controlled design may be preferred from a statistical perspective; however, none of our oncology practices were willing to be randomized to a control arm (or a delayed-onset intervention control), so in order to be responsive to their needs, a single-arm design was chosen.

Study Instruments (also see time and events table)

Comprehensive Score for Financial Toxicity – The COST measure has been validated among advanced cancer patients. It is an 11 item scale with scores ranging from 0 to 44 that measures financial toxicity, with lower scores indicating higher financial toxicity. Individual items are scored from 0 to 4 with 4 indicating a high score. *Note: items: #2,3,4,5,8,9, 10 must be reverse scored as lower scores mean a higher level of financial distress.* A total score is calculated by performing reversals as indicated, and summing individual items to obtain a score, then multiplying the sum of the item scores by the number of items in the scale, and

then dividing by the number of items answered. This produces the final score and lower scores reflect greater financial toxicity. Possible scores range from 0 to 44, with scores 22 or lower considered to indicate higher than normal levels of financial worry. Because items must be summed to obtain a score, only respondents who answer all 11 of the COST items will be included in our analysis.

PROMIS Emotional Distress-Anxiety Short Form 6a- This is a 6-item measure of anxiety over the past 7 days. Each question has five response options ranging in value from one to five. To find the total raw score for a short form with all questions answered, sum the values of the response to each question. All questions must be answered in order to produce a valid score using the scoring tables. If a participant has skipped a question, we will use the HealthMeasures Scoring Service (https://www.assessmentcenter.net/ac_scoringservice) to generate a final score. Locate the applicable score conversion table in Appendix 1 of the scoring manual and use this table to translate the total raw score into a T-score for each participant. The T-score rescales the raw score into a standardized T-score with a mean of 50 and a standard deviation (SD) of 10. Therefore, a person with a T-score of 40 is one SD below the mean.

PROMIS Depression Short Form 8a- This is a 8-item measure of depression over the past 7 days. This form assesses the pure domain of depression in individuals age 18 and older and the measure is completed by the individual prior to a clinical visit. Each item on the measure is rated on a 5-point scale (1=never; 2=rarely; 3=sometimes; 4=often; and 5=always) with a range in score from 8 to 40 with higher scores indicating greater severity of depression. The raw scores on the 8 items should be summed to obtain a total raw score. Next, the T-score table should be used to identify the T-score associated with the individual's total raw score and the information entered in the T-score row on the measure. *Note:* The look-up table in the scoring manual works only if all items on the form are answered. If 75% or more of the questions have been answered; you are asked to prorate the raw score and then look up the conversion to T-Score. The formula to prorate the partial raw score to Total Raw Score is:

$$\frac{\text{(Raw sum x number of items on the short form)}}{\text{Number of items that were actually answered}}$$

If the result is a fraction, round to the nearest whole number. For example, if 6 of 8 items were answered and the sum of those 6 responses was 20, the prorated raw score would be 20 X 8/ 6 = 26.67. The T-score in this example would be the T-score associated with the rounded whole number raw score (in this case 27, for a T-score of 64.4).

The T-scores are interpreted as follows:

Less than 55 = None to slight
55.0—59.9 = Mild

60.0—69.9 = Moderate
70 and over = Severe

PROMIS Global Health Questionnaire- The PROMIS Global Health measures assess an individual's physical, mental, and social health.This is a 10-item measure of symptoms, functioning, and healthcare-related quality of life (HRQoL in which the response options are presented as 5-point (as well as a single 11-point) rating scales. The results of the questions are used to calculate two summary scores: a Global Physical Health Score and a Global Mental Health score. These scores are then standardized to the general population, using the "T-Score". The average "T-Score" for the United States population is 50 points, with a standard deviation of 10 points. Higher scores indicate a healthier patient.

PROMIS Psychosocial Illness Impact Short Form-Pos 4a- This is a 4-item measure of positive emotional and social outcomes of illness. Each question has five response options ranging in value from two to five. The first two response categories are collapsed which results in the response score being the same (2) for response options "Not at all" and "A little bit." To find the total raw score for a short form with all questions answered, sum the values of the response to each question. For the 4-item form, the lowest possible raw score is 8; the highest possible raw score is 20. The 4-item short form can only be scored with complete data.

Patient Experience Questionnaire- This form will be used to collect additional patient-reported data on financial vulnerability, employment disruption, caregiver cost burden, food insecurity, and care altering behaviors. These measures will be captured using ad-hoc instruments, as well as other previously used instruments from other studies. This information is critical to understanding the full scope of experiences and responses following financial hardship caused by cancer and we will describe frequencies and proportions.

Financial Intake Form -This form will be used to collect patient data describing their individual financial situation including employment status, total monthly income, current billing information, insurance status and other indicators used to triage patients to the appropriate financial resource(s). This information is needed for most financial assistance programs and by using a single form to collect these data, they can be applied to multiple applications.

Post First Visit Checklist- This form will be used at the end of the first visit to capture the financial navigation visit information for the patient. The checklist includes the next appointment date, resources the patient is eligible for and documents needed in addition to the financial resource application.

Check In Form- This form will be used to check in with the patient every 2 weeks to check on application progress and additional patient needs.

Patient Perspective Survey- This form will capture patients' perspectives on the intervention's acceptability, responsiveness and alignment with needs, patient-centeredness and timeliness. This is an investigator-developed questionnaire used in prior studies.

Patient Recruitment:

Patients will be referred to the financial navigator if they express concerns about paying for their cancer treatment, medications, transportation, or other aspects of their cancer care during their visit with their oncology clinician, a social worker or other healthcare personnel. Upon referral to the financial navigator, the navigator will discuss the study with the patient and if the patient is eligible and interested in the study, the financial navigator will follow the informed consent process. After consent, patients will complete the COST measure and the financial navigator will score their answers to determine study eligibility.

If patients score low (22 or lower) on the COST measure, they will be eligible to participate in the study. This includes participation in the full financial navigation program which consists of: 1) an initial appointment at the time of the positive screening result (if the patient's schedule permits), and 2) one or more follow-up appointment(s) to return to the financial navigator with the paperwork and applications necessary to apply for the resources identified during their initial appointment. Both appointments will include one-on-one consultation with a trained financial navigator. At the initial appointment, the financial navigator will review patients' individual situations, including employment status, current billing information, insurance status and other indicators used to triage patients to the appropriate financial resource(s) using the Baseline Intake Assessment Form. At the end of this initial appointment, patients with be provided with a checklist of the resources that they are eligible for and the personal paperwork (tax forms, W-2, pay stubs) needed to apply. During the follow-up appointment(s), the financial navigator will review the initial appointment sheet, verify that the patient has the necessary paperwork, and review applications for completeness or work with the patient to complete the resource application(s). Patients will be educated about and referred to the following potential financial resources, including but not limited to: Charity Care, Pharmacy Assistance, Co-Pay Assistance Programs, Medicaid, Social Security and Disability, and Legal Aid. Patients will receive 2 follow up contacts after their financial navigation program visits in order to assess progress toward their financial assistance goals.

Post-Intervention After participation in the intervention ends (approximately 3 months after consent), patients will complete a post-intervention COST survey, HrQOL surveys, patient experience survey and a patient perspectives survey to measure their financial distress post-intervention and to evaluate the financial navigation program. These outcomes will also inform scalability and sustainability efforts for future grants.

Program Evaluation. The research team will gather process data on all patients participating in this study from screening to final financial assistance application funding decisions through Research Electronic Data Capture, or REDCap. REDCap is a secure web application is used to build and manage case report forms, surveys and other data capture mechanisms for clinical research. We will track the number of patients screened, the number of patients who screen positive for financial distress, the number of patients who attend financial navigation appointments, and the number of financial navigation appointments/patient. In addition, the project coordinator and financial navigator will record the type of financial resources the patient is eligible for including internal programs e.g. Medication Assistance and Pharmacy Assistance and external programs e.g. Medicare, Medicaid, SNAP, and Veterans Affairs. Researchers will also track the number of programs the patient is referred to, how many applications are submitted and application outcomes (success or denial).

4.4 Expected Risks

Risks to participants are minimal due to the largely educational nature of the financial navigation intervention. Risks may include emotional distress while talking about the patients' cancer and financial experiences. Patients will have completed a financial distress screening (as part of the study) prior to their financial navigation appointments which should minimize this risk. However, if patients experience emotional distress during the intervention, each site will follow their individual protocol for referring patients for psychosocial support.

There is also a very minimal risk of breach of confidentiality. Since personal health information will be collected during this study, there is a minimal risk of loss of privacy. Investigators will make every effort to ensure that HIPAA regulations are properly enforced, and study data will be carefully protected. In addition, all subjects will be assigned subject IDs. A master list with the patient's name and study ID assignment will be maintained and accessed only by the principal investigator, study coordinator, and site-specific financial navigator on a secure network. All other electronic data will be maintained within the REDCap database. All hardcopy data (if patients prefer to complete paper vs. online surveys) will be maintained in a locked office suite within a locked cabinet. As stated above, we will use a study ID number rather than participant names on study records and the code sheet will be kept electronically and separately from the survey data.

4.5 Removal of Patients from Protocol

Every effort will be made to encourage participants to attend all of their financial navigation appointments. Patients will receive reminder calls prior to their appointment dates and appointment options will be flexible so we do not

anticipate problems with study completion. There are no study criteria for removal of patients from the study by the principal investigator; however, study participation will be completely voluntary and participants can end their participation at any time.

5.0 TIME AND EVENTS TABLE

5.1 Time and Events Table

Data Source	Measurement Description	Pre-FN Intervention	During Intervention	Post-FN Intervention
Financial Navigators				
Financial navigator questionnaire	Financial navigator questionnaire regarding knowledge, self-efficacy and confidence related to FT and FN	X		X
Financial navigator and practice **stakeholder structured interviews**	**Outer setting** patient needs and resources **Inner setting** implementation climate, learning climate, resources and access to information **Process** of reflecting and evaluating **Acceptability** of financial navigation to practices Perceived **sustainability** of financial navigation			X
Patient				
COmprehensive Score for financial Toxicity (COST)	Cancer-related financial toxicity	X		X
PROMIS Emotional Distress-Anxiety Short Form 6a	Emotional distress and anxiety 6-item measure of anxiety over the past 7 days	X		X
PROMIS Depression Short Form 8a:	Depression 8-item measure of depression over the past 7 days	X		X
PROMIS Global Health Questionnaire:	Health Related Quality of Life 10-item measure of symptoms, functioning, and healthcare-related quality of life (HRQoL)	X		X
Psychosocial Illness Impact Short Form-Pos 4a:	Illness impact 4-item measure of positive emotional and social outcomes of illness	X		X
Patient Experience Questionnaire	COST Plus questions Employment disruption questions Caregiver cost burden Hunger Vital Sign Care-altering behaviors (foregoing, delaying care)	X		X
Intake Form: Socio-	Patient survey of age, race, ethnicity,		X	

demographic variables	marital status, education, income, employment status, health insurance, household size and dependents			
Intake Form:	Form collects patient data describing their individual financial situation including employment status, total monthly income, current medical billing information, insurance status and other indicators used to triage patients to the appropriate financial resource(s).		X	
Post 1st Visit Summary	Form will be used at the end of the first visit to capture the financial navigation visit information for the patient. The checklist includes the next appointment date, resources the patient is eligible for and documents needed in addition to the financial resource application.		X	
Check-In Form	Form will be used during the follow-up appointment with patients. The financial navigator will review the initial appointment sheet, verify that the patient has the necessary paperwork, and review applications for completeness or work with the patient to complete the resource application(s).		X	
Patient Perspective Survey	Patient perspectives on FN acceptability, responsiveness and alignment with needs, patient-centeredness, and timeliness			X

1. COST Financial Distress Measure
2. PROMIS Emotional Distress-Anxiety
3. PROMIS Depression
4. PROMIS Global Health Questionnaire
5. Psychosocial Illness Impact
6. Patient Experience Questionnaire
7. Baseline Financial Intake Assessment
8. Post-Visit Checklist
9. Check In Form
10. Patient Perspective Survey

6.0 UNANTICIPATED PROBLEMS

6.1 Definition

As defined by UNC's IRB, unanticipated problems involving risks to study subjects or others (UPIRSO) refers to any incident, experience, or outcome that:

- Is unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- Is related or possibly related to a subject's participation in the research; and
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized.

6.2 Reporting

Any UPIRSO that occurs during the conduct of this study and that meets all three criteria listed in 6.1 must be reported to the UNC IRB using the IRB's web-based reporting system.

7.0 STATISTICAL CONSIDERATIONS

7.1 Study Design

This is a non-randomized, multi-center, single-arm, interventional study. The primary objective of this study is to evaluate the change from baseline in COST scores following the financial navigation intervention among 700 patients with any type of cancer diagnosis. Secondary objectives include (1) evaluating the change from baseline in scores for HRQoL measures after participation in the financial navigation program as well as feasibility and acceptability of the financial navigation program.

7.2 Sample Size and Accrual

We anticipate enrolling a total of 700 patients into the study with approximately 100 patients enrolled per site at our five rural cancer center sites and 50 patients per site at our 4 non-rural cancer centers. We considered a very conservative pre/post-FN intervention effect (difference in COST scores) as small as 0.5 as well as a more considerable intervention effect as large as 3.0. A one-sample paired t-test (pre/post analysis of the change in COST FT score) with alpha=.05, will have 80% power to detect an effect size of 0.126. This may be seen with an average difference of 1 point, and a standard deviation of 7.966, or a mean difference of 3 points, and a standard deviation of 23.898.

In order to account for attrition, we will recruit up to 80 patients/site (8-10 additional patients/site), if needed. Given our 2% (1/50) attrition rate for the UNC pilot project this study is based on, we do not expect much attrition. If patients are lost to follow-up between consent and their first financial navigation visit, we will replace them since they did not receive the intervention.

7.3 Data Analysis Plans

Our primary outcome measure is FT as reflected by changes in pre-/post-FN intervention scores on the COST tool. For the primary outcome of change in FT pre/post-FN intervention, we will assess change in pre-/post-FN intervention COST scores, which range from 0-44 with a population mean of 22, and use a paired sample t-test to test the null hypothesis that FN does not result in statistically significant changes in FT, at an alpha level = 0.05. Where feasible (depending on enrollment sample sizes), we will assess racial/ethnic, gender, and age-specific effect modification using sub group analyses. Additionally, linear regression modeling may be performed to evaluate the combined effect of these patient characteristics on COST scores. For the secondary outcome of change in HRQoL pre/post-FN intervention, we will again use a paired sample t-test to test the null hypothesis that FN does not result in statistically significant changes in HRQoL, at an alpha level = 0.05, with attention to potential effect modification by race/ethnicity, gender, and age (where feasible). For the secondary outcome of change in care-altering behavior (e.g., a dichotomous outcome of foregoing or delaying care in a paired pre/post intervention sample), we will use a McNemar test to test the null hypothesis that the probability of foregoing or delaying care is reduced post-FN is the same as the probability that foregoing or delaying care is increased post-FN. In addition, we will describe frequencies, proportions, means and standard deviations, as appropriate, of patient-reported post-FN intervention convenience, accessibility, satisfaction, responsiveness (alignment with needs), patient-centeredness and timeliness.

7.4 Data Management/Audit

All electronic data will be collected via REDCap. All hardcopy data, consisting of consent and intake forms, and paper versions of the COST survey and patient satisfaction survey for those patients who choose to complete paper surveys vs. online surveys via iPad will be kept in a locked filing cabinet. For patients who choose to complete paper surveys, we will use a study number rather than participant names on the instrument and the project coordinator or financial navigator will input all hardcopy data into REDCap. Patient name will be kept separately from the survey data. Only consent forms will contain identifying information and they will be kept separate from the questionnaire data in a locked filing cabinet at each participating site. The REDCap data is on a protected server

accessible only by research staff. All REDCap data will be stored on UNC's REDCap's secure servers.

All hard copies of study data will be destroyed within 2 years of study completion. After the study is completed, all electronic copies of the data will be stored on the Lineberger Biostatistics Core servers which are maintained by the University.

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

Data and Safety Monitoring Plan

The Principal Investigators will provide continuous monitoring of patient safety in this trial with periodic reporting to the Data and Safety Monitoring Committee (DSMC) as required.

Meetings/teleconferences will be held at a frequency dependent on study accrual, and in consultation with the study Biostatistician. At these meetings, the research team will discuss all issues relevant to study progress, including enrollment, safety, regulatory, data collection, etc. and the team will produce summaries or minutes of these meetings. These summaries will be available for inspection when requested by any of the regulatory bodies charged with the safety of human subjects and the integrity of data including, but not limited to, the oversight (Office of Human Research Ethics (OHRE) Biomedical IRB, the Oncology Protocol Review Committee (PRC) or the North Carolina TraCS Institute Data and Safety Monitoring Board (DSMB).

8.0 STUDY MANAGEMENT

8.1 Institutional Review Board (IRB) Approval and Consent

It is expected that the IRB will have the proper representation and function in accordance with federally mandated regulations. The IRB should approve the consent form and protocol.

In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirement(s), and should adhere to Good Clinical Practice (GCP) and to ethical principles that have their origin in the Declaration of Helsinki.

Before recruitment and enrollment onto this study, the patient will be given a full explanation of the study and will be given the opportunity to review the consent form. Each consent form must include all the relevant elements currently required by the FDA Regulations and local or state regulations. Once this essential information has been provided to the patient and the investigator is assured that

the patient understands the implications of participating in the study, the patient will be asked to give consent to participate in the study by signing an IRB-approved consent form.

Prior to a patient's participation in the trial, the written informed consent form should be signed and personally dated by the patient and by the person who conducted the informed consent discussion.

8.2 Required Documentation

Before the study can be initiated at any site, the following documentation must be provided to the Clinical Protocol Office (CPO) at the University of North Carolina.

- A copy of the official IRB approval letter for the protocol and informed consent
- CVs and medical licensure for the principal investigator and any associate investigators who will be involved in the study
- A copy of the IRB-approved consent form

8.3 Registration Procedures

Participant enrollment will be tracked in REDCap. Adherence to the Protocol Except for an emergency situation in which proper care for the protection, safety, and well-being of the study patient requires alternative treatment, the study shall be conducted exactly as described in the approved protocol.

8.4 Adherence to the Protocol

Except for an emergency situation in which proper care for the protection, safety, and well-being of the study patient requires alternative treatment, the study shall be conducted exactly as described in the approved protocol.

8.4.1 Emergency Modifications

UNC investigators may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard(s) to trial subjects without prior UNC IRB approval.

For any such emergency modification implemented, a UNC IRB modification form must be completed by UNC Research Personnel within five (5) business days of making the change.

8.4.2 Single Patient/Subject Exceptions

Eligibility single subject exceptions are not permitted for Lineberger Comprehensive Cancer Center Investigator Initiated Trials under any circumstances. Other types of single subject exceptions may be allowed if proper regulatory review has been completed in accordance with Lineberger Comprehensive Cancer Center's Single Subject Exceptions Policy.

8.4.3 Other Protocol Deviations/Violations

According to UNC's IRB, a protocol deviation is any unplanned variance from an IRB approved protocol that:

- Is generally noted or recognized after it occurs
- Has no substantive effect on the risks to research participants
- Has no substantive effect on the scientific integrity of the research plan or the value of the data collected
- Did not result from willful or knowing misconduct on the part of the investigator(s).

An unplanned protocol variance is considered a violation if the variance meets any of the following criteria:

- Has harmed or increased the risk of harm to one or more research participants.
- Has damaged the scientific integrity of the data collected for the study.
- Results from willful or knowing misconduct on the part of the investigator(s).
- Demonstrates serious or continuing noncompliance with federal regulations, State laws, or University policies.

If a deviation or violation occurs please follow the guidelines below:

Protocol Deviations: UNC personnel will record the deviation in OnCore® (or other appropriate database set up for the study), and report to any sponsor or data and safety monitoring committee in accordance with their policies. Deviations should be summarized and reported to the IRB at the time of continuing review.

Protocol Violations: Violations should be reported by UNC personnel within one (1) week of the investigator becoming aware of the event using the same IRB online mechanism used to report UPIRSO.

Unanticipated Problems Involving Risks to Subjects or Others (UPIRSO: Any events that meet the criteria for "Unanticipated Problems" as defined by UNC's IRB (see section 6.1) must be reported by the Study Coordinator using the IRB's web-based reporting system.

8.5 Amendments to the Protocol

Should amendments to the protocol be required, the amendments will be originated and documented by the Principal Investigator at UNC. It should also be noted that when an amendment to the protocol substantially alters the study design or the potential risk to the patient, a revised consent form might be required.

The written amendment, and if required the amended consent form, must be sent to UNC's IRB for approval prior to implementation.

8.6 Record Retention

Study documentation includes all Case Report Forms, data correction forms or queries, source documents, Sponsor-Investigator correspondence, monitoring logs/letters, and regulatory documents (e.g., protocol and amendments, IRB correspondence and approval, signed patient consent forms).

Source documents include all recordings of observations or notations of clinical activities and all reports and records necessary for the evaluation and reconstruction of the clinical research study.

Government agency regulations and directives require that all study documentation pertaining to the conduct of a *clinical* trial must be retained by the study investigator. In the case of a study with a drug seeking regulatory approval and marketing, these documents shall be retained for at least two years after the last approval of marketing application in an International Conference on Harmonization (ICH) region. In all other cases, study documents should be kept on file until three years after the completion and final study report of this investigational study.

8.7 Obligations of Investigators

The Principal Investigator is responsible for the conduct of the clinical trial at the site in accordance with Title 21 of the Code of Federal Regulations and/or the Declaration of Helsinki. The Principal Investigator is responsible for personally overseeing the treatment of all study patients. The Principal Investigator must assure that all study site personnel, including sub-investigators and other study staff members, adhere to the study protocol and all FDA/GCP/NCI regulations and guidelines regarding clinical trials both during and after study completion.

The Principal Investigator at each institution or site will be responsible for assuring that all the required data will be collected and entered onto the Case Report Forms. Periodically, monitoring visits will be conducted and the Principal Investigator will provide access to his/her original records to permit verification of proper entry of data. At the completion of the study, all case report forms will be reviewed by the Principal Investigator and will require his/her final signature to verify the accuracy of the data.

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10.0 APPENDICES

Appendix A: Comprehensive Score for Financial Toxicity (Screening Instrument)
Appendix B: PROMIS Emotional Distress-Anxiety
Appendix C: PROMIS Depression
Appendix D: PROMIS Global Health Questionnaire
Appendix E: PROMIS Psychosocial Illness Impact
Appendix F: Patient Experience Questionnaire
Appendix G: Financial Intake Form
Appendix H: Post First Visit Checklist
Appendix I: Check In Form
Appendix J: Patient Perspective Survey

All appendices are located in the password-protected section of our website: cancercosts.org