A Randomized Trial Addressing Cancer-Related Financial Hardship through Delivery of a Proactive Financial Navigation Intervention (CREDIT): SWOG S1912

Veena Shankaran (vshank@uw.edu)
Fred Hutchinson Cancer Research Center https://orcid.org/0000-0001-8136-6140

Ruth Carlos
University of Michigan Comprehensive Cancer Center: University of Michigan Rogel Cancer Center

Dawn Hershman
Columbia Presbyterian Medical Center: Columbia University Irving Medical Center

Shelby Langer
Arizona State University

Scott Ramsey
Fred Hutchinson Cancer Research Center

Joseph Unger
Fred Hutchinson Cancer Research Center

Amy Darke
Fred Hutchinson Cancer Research Center

Riha Vaidya
Fred Hutchinson Cancer Research Center

Research Article

Keywords: Financial hardship Cancer caregivers, Cancer survivorship

Posted Date: April 21st, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1439367/v1

Abstract

Background

Financial hardship is a growing problem among patients with advanced cancer and their spouse caregivers. Previous studies have shown that the cancer treatment related costs may adversely impact not only patient and caregiver financial status but also quality of life, caregiver burden, treatment adherence, and health care utilization. Financial navigation is a potential solution to help patients and families navigate the cost of cancer care. The goal of this study is to investigate whether a comprehensive oncology financial navigation program will decrease the risk of household financial hardship and lead to improvements in patient and spouse caregiver psychosocial outcomes.

Methods

We will conduct a randomized controlled trial comparing a financial literacy and navigation program (intervention) to financial literacy training alone (control) in patient and spouse caregiver dyads treated at NCI Community Oncology Research Program (NCORP) sites throughout the United States. The intervention will be administered remotely by our community partners, Consumer Education and Training Services (CENTS) and Patient Advocate Foundation (PAF). Eligible patients will be 18 years or older, English- or Spanish-speaking, and be within 120 days of a metastatic solid tumor or advanced hematologic malignancy diagnosis. Spouse caregivers should also be 18 years or older, be residing within the same household as the patient, and be either legally married or filing taxes as “married filing jointly” with the eligible patient. The intervention will be delivered monthly for 6 months. The primary study outcome is risk of financial hardship, as evidenced in patient and spouse credit reports which are collected at baseline and periodically through 12 months. Additional patient and caregiver outcomes will be assessed using questionnaires administered through 12 months.

Discussion

This is one of the first randomized studies to assess the impact of a remotely administered financial navigation program on dyadic financial and psychosocial outcomes. If the financial navigation intervention is shown to decrease financial hardship, then financial navigation should be considered a key component of high-quality cancer care. In addition, study findings would underscore the need for policy level changes to mitigate the financial impact of cancer diagnosis.

Trial registration

: ClinicalTrials.gov Identifier: NCT04960787

Administrative Information

Note

the numbers in curly brackets in this protocol refer to SPIRIT checklist item numbers. The order of the items has been modified to group similar items (see http://www.equator-network.org/reporting-guidelines/spirit-2013-statement-defining-standard-protocol-items-for-clinical-trials/).

Title {1}	**A Randomized Trial addressing cancer-related financial hardship through delivery of a proactive financial Navigation intervention (CREDIT)**
Trial registration {2a and 2b}.	ClinicalTrials.gov Identifier: NCT04960787 NCI-2021-00579 SWOG identifier: SWOG S1912CD
Protocol version {3}	Version date 12/12/2021
Funding {4}	R01CA248656 (U.S. NIH Grant/Contract) UG1CA189974 (U.S. NIH Grant/Contract)
Author details {5a}	Veena Shankaran, M.D., M.S. (Medical Oncology) University of Washington School of Medicine, Division of Medical Oncology Fred Hutchinson Cancer Research Center 1100 Fairview Ave N, M3-B232 Seattle, WA 98109 Ruth Carlos, M.D., M.S., FACR (Radiology) University of Michigan 24 Frank Lloyd Wright Drive Ann Arbor, MI 48106 Dawn L. Hershman, M.D., M.S. (Medical Oncology) Columbia University Medical Center 161 Fort Washington 10th Floor, Room 1068 New York, NY 10032 Shelby Langer, Ph.D. (Psychology) Arizona State University 500 n. Third Street Phoenix, AZ 85004 – 2135 Scott D. Ramsey, M.D., Ph.D. (Internal Medicine) Fred Hutchinson Cancer Research Center 1100 Fairview Avenue N, M3-B232

Title {1}	A Randomized Trial addressing cancer-related financial hardship through delivery of a proactive financial Navigation intervention (CREDIT)
	Seattle, WA 98109 Joseph M. Unger, Ph.D. SWOG Statistics and Data Management Center Fred Hutchinson Cancer Research Center 1100 Fairview Ave N, M3-C102 Seattle, WA 98109 Amy Darke, M.S. SWOG Statistics and Data Management Center Fred Hutchinson Cancer Research Center 1100 Fairview Ave N, M3-C102 Seattle, WA 98109 Riha Vaidya, Ph.D. SWOG Statistics and Data Management Center Fred Hutchinson Cancer Research Center 1100 Fairview Ave N, M3-C102 Seattle, WA 98109
Name and contact information for the trial sponsor {5b}	NCI Funded Research
Role of sponsor {5c}	None

Introduction

Background and rationale {6a}

As the cost of cancer care in the United States increases at an alarming rate, cancer patients are facing higher out-of-pocket healthcare spending, medical debt, and bankruptcy rates compared to individuals without cancer.[1-9] "Financial toxicity" is a term that has gained traction in recent years to capture the spectrum of financial hardships that cancer patients face, including the material, psychological, and behavioral aspects. A growing body of literature suggests that at least 30-50% of all cancer patients experience major financial hardship, which negatively impacts quality of life and survival.[5,7,9] Higher

financial burden early in the disease course may also result in intense hospital-based care, particularly at the end of life.[10]

Family caregivers share the experience of financial hardship. Most spend money on food, medications, and other patient needs; approximately 25% of cancer caregivers report taking two or more months of work leave to perform caregiving duties.[11-16] Spouse caregivers are particularly vulnerable to financial hardship given that they typically share household income, assets, and expenses with patients. Spouses also often assume the responsibility of managing household finances and navigating health insurance and medical bills when patients are ill. As a result of these household financial impacts, spouses of cancer patients can experience poorer quality of life, depression, and higher caregiver burden.[17-22] Moreover, financial concerns may impede spouses' ability to perform the demanding roles of outpatient symptom and medication management, potentially increasing patients' risk of admission to the Emergency Department (ED) or hospital. In a recent study of home-dwelling patient-spouse caregiver dyads, poor caregiver well-being was associated with higher Medicare expenditures and ED use.[22]

Based on evidence supporting the high prevalence and severity of cancer-related financial hardship and its consequences, there is an urgent need to develop and test interventions aimed at reducing financial hardship. Given the interrelatedness of patient and spouse caregiver financial status, we hypothesize that successful interventions implemented at the household level may result in improvements in financial, psychosocial, and clinical outcomes for patients and spouses. Addressing financial hardship at the household level by including spouse caregivers has broad relevance given that over 70% of older American adults (the population at highest risk for cancer) are married or partnered.[23] Moreover, recent research demonstrates the importance of addressing patient and caregiver needs at the individual and dyad level.[24,25]

Tucker-Seeley and Yabroff developed a conceptual model that categorizes financial hardship as material conditions (e.g. debt), psychological responses (e.g. financial worry), and coping behaviors (e.g. cost-related non-adherence).[26,27] We adapted this model to include 1) potential predictors or risk factors for financial hardship, 2) the material, psychological, and coping/behavioral aspects of financial hardship at the patient, spouse, and household levels, and 3) downstream effects on quality of life and outcomes (**Figure 1**).

This model informs the design of interventions aimed at lessening financial hardship by reinforcing its distinct but related aspects. For example, an intervention that focuses solely on providing access to high-cost drugs but ignores impacts on employment and other types of out-of-pocket medical costs is unlikely to be as impactful as one that comprehensively addresses all facets of financial hardship through counseling, education, budget management, and improved medication and treatment access.

Few oncology clinics have specialists that are poised to provide assistance with medical costs and counsel families about management of assets, debts, and household expenses *before* financial status deteriorates.[28-29] A recent landscape survey (PI: Ruth Carlos) of financial navigation practices at NCORP

clinics found that while 69% of participating sites screened for financial toxicity at intake, only 44% provided financial counseling, typically by social workers who lack prerequisite financial training (personal communication, Carlos). A 2016 survey of over 2000 community cancer centers showed a similar trend; only 39% reported that financial navigators met with patients to discuss insurance, cost of care, and copay programs.[28] In a recent study, financial navigators hired and trained by hospital systems led to patient cost savings by way of insurance enrollment, assistance with paying insurance premiums, and copayment assistance for high cost drugs.[30] However, these programs largely focus on recouping and mitigating hospital system financial losses resulting from unpaid patient bills and do not comprehensively address families' various financial concerns.

Recognizing the lack of impartial, highly trained financial navigators in the outpatient oncology setting who can address financial concerns starting at diagnosis, our group has leveraged the expertise of community-based organizations to develop and pilot test a comprehensive financial navigation program that provides education on important financial concepts and *proactively and longitudinally addresses patients' and caregivers' financial needs*.[31-33] Partnering with community organizations to deliver this intervention avoids the real or perceived conflicts of interest that treating clinics might have in offering financial advice to the patients under their care. Moreover, some patients may be reluctant to discuss costs with their medical care teams due to fears that they might receive less optimal treatments if they are transparent about their financial difficulties.[31] We propose a randomized trial to test if providing financial literacy training, and proactive counseling, direct medical cost and healthcare coverage assistance, and indirect and non-medical cost assistance to couples decreases material household financial hardship, improves patient and caregiver psychosocial outcomes, and potentially decreases patient ED and hospital utilization. In a recent study, lay patient navigation that addressed the financial concerns of geriatric cancer patients was associated with a decrease in mean health costs of $781 per patient per quarter and a decline in ED, hospital, and intensive care unit (ICU) visits by up to 10.6%.[34] ***The proposed study will be, to our knowledge, the first randomized trial investigating the impact of financial navigation on financial, clinical, and psychosocial outcomes at the household and individual (patient and spouse) levels. If positive, our study will provide the evidence to support prioritizing proactive financial navigation in the delivery of high-quality cancer care, and potentially inform policies that protect cancer patients from high cost-sharing, employment loss, and adverse credit events.***

Objectives {7}

Obective 1: Determine the impact of a proactive financial navigation program on development of material household financial hardship: We hypothesize that couples in the intervention arm will experience lower risk of major household financial hardship (declines in credit score, exhausting lines of credit, new payment delinquencies, liens/judgments/collections, or bankruptcy filings) compared with those in the control arm.

Objective 2: Investigate whether proactive financial navigation improves patient and caregiver psychosocial and healthcare utilization outcomes: We hypothesize that the intervention will lead to

improved patient and spouse quality of life, lower financial worry, and decreased caregiver burden. We will explore whether the intervention leads to decreased cost-related medication nonadherence and fewer patient emergency department (ED) visits and unplanned hospital admissions compared with control.

Objective 3: Describe the utilization of financial navigation services by younger, financially fragile, and lower income patients and caregivers and evaluate the intervention's effect in these subgroups: We hypothesize that younger patients and households with lower income and higher financial fragility will have higher financial navigation needs and thus derive greater benefit from the intervention.

Trial design {8}

The study is designed as a two-arm randomized controlled study investigating the impact of financial literacy training plus a 6-month remotely-administered proactive financial navigation program (intervention) *versus* financial literacy training alone (control) on patient-spouse caregiver dyadic outcomes (**See Figure 1**). Outcomes will be assessed using medical record, survey, and credit data obtained at baseline, 6 months, and 12 months post-enrollment.

Patient and spouse caregiver dyads will be randomly assigned to Group 1 - Control or Group 2 - Intervention with stratification by:

- Household fragility index: certainly or probably could vs. probably not or certainly not able (to come up with $2,000 in 30 days), from baseline questionnaire
- Patient age (< or ≥ 65)
- Patient sex (male vs. female)
- Hematologic malignancy vs. de novo metastatic solid tumor vs. recurrent solid tumor.

Methods: Participants, Interventions And Outcomes

Study setting {9}

The setting for the proposed study is the National Cancer Institute's (NCI) Community Oncology Research Program (NCORP) network that brings cancer care delivery research (CCDR) studies to over 900 community oncology practices throughout the country. The NCORP is the ideal environment in which to conduct this study because the diverse population and range of clinical settings makes our findings highly generalizable. SWOG Cancer Research Network, an NCI-sponsored national clinical trials network that designs and conducts multidisciplinary cancer clinical trials, will oversee recruitment and data collection. NCORP and SWOG leadership are supportive of this study, as it responds to requests by NCORP investigators and SWOG patient advocates for research studying interventions to lessen financial toxicity and addressing financial hardship at the household, or patient-spouse dyad level.

Eligibility criteria {10}

Each of the criteria in the following section must be met for a patient to be considered eligible for registration.

In calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, as an example, if a test is done on a Monday, the Monday 4 weeks later would be considered Day 28. This allows for efficient patient scheduling without exceeding the guidelines. If Day 28 falls on a weekend or holiday, the limit may be extended to the next working day.

Disease Related Criteria - Patient

a. Patients must have a diagnosis of a metastatic solid tumor or a hematologic malignancy and must receive anti-cancer treatment (i.e. chemotherapy, hormonal therapy, targeted therapy, biologic therapy, immune therapy, bone marrow transplant) per the timing described below (*See Prior/Current Therapy Criteria – Patient*). Registration must occur within 120 days after diagnosis. Patients with indolent hematologic diseases undergoing observation alone are not eligible.
b. Patients with recurrent solid tumors will be allowed if 1) this is the first presentation of metastatic disease and 2) the diagnosis of the metastasis is at least 180 days (6 months) after the diagnosis date of the previous earlier stage cancer.
c. Patients with a history of secondary malignancy are allowed if they were not diagnosed within the previous 24 months, are not on active therapy, and are disease-free. Patients with adequately treated basal cell or squamous cell skin cancer, and *in situ* cervical cancer at any point prior to enrollment are eligible.

Prior/Concurrent Therapy Criteria – Patient

a. Patients who have started anti-cancer treatment for the current diagnosis must have started within 60 days prior to registration.
b. Patients who are planning to start anti-cancer treatment for the current diagnosis must start within (≤) 30 days after registration.
c. Patients are allowed to be co-enrolled on other clinical trials (including non-treatment studies and studies that may or may not include investigational drugs).
d. Patients may not be enrolled in hospice care at the time of registration.

Clinical/Laboratory Criteria - Patient

a. Patients must be at least 18 years of age.
b. Patients must have a Zubrod performance status of 0-2.
c. Patients must complete the baseline patient-reported outcome (PRO) questionnaires prior to registration and must be able to complete questionnaires in English or Spanish.

d. Patients must provide their full name, primary address in the U.S., birth date and social security number at registration for the purposes of accessing credit report data. (This may be obtained directly from the patient, study questionnaires, or the medical record.)
e. Patients must provide email and/or telephone number for the purposes of being contacted by financial navigators.

Spouse Caregiver Criteria

a. Spouse caregivers must be willing to participate in the trial.
b. Spouse caregivers must be legally married, or file their tax returns as married filing jointly.*
c. Spouse caregivers must be living in the same household with the eligible patient enrolling in this trial.
d. Spouse caregivers must be at least 18 years of age.
e. Spouse caregivers must provide their full name, primary address in the U.S., birth date and social security number at registration for the purposes of accessing credit report data.
f. Spouse caregivers must provide email and/or telephone number for the purposes of being contacted by the financial navigators.
g. Spouse caregivers must be able to complete questionnaires in English or Spanish and must complete the baseline questionnaires prior to patient registration.

*The study team acknowledges that other types of caregivers may also face financial hardship following a patient's cancer diagnosis and may similarly benefit from financial education and navigation. The decision to focus solely on *spouse* caregivers was scientific, to facilitate analysis of primary endpoint (household financial hardship).

Regulatory Criteria

a. Participants (patients and spouse caregivers) must sign and give written informed consent in accordance with institutional and federal guidelines. Use of legally-authorized representative is not permissible for this study. Documentation of informed consent via remote consent is permissible.

Who will take informed consent? {26a}

Site staff at participating NCORPs will screen, approach, and consent patient and spouse caregivers. Where possible, patients and spouses will ideally be consented in-person on the same day, while the patient is in the clinic. If a patient is seen in the clinic without his or her spouse or if a patient is identified as a potential study participant subsequent to the clinic visit, staff may also convey the informed consent information via mail, fax, or email and subsequently consent the patient and/or spouse via telephone (remote consent). Both the patient and spouse must be recruited and consented to participate in the

study, however they may be consented at different times if the spouse is not present with the patient at the time of consent.

Additional consent provisions for collection and use of participant data and biological specimens {26b}

Not applicable

Interventions

Explanation for the choice of comparators {6b}

Control group: All participants in the control arm will receive a one-time financial literacy video to standardize their experience and to minimize concerns that a positive study result would be due solely to attention given to the intervention group. Following the video, their experience will follow usual care. Control arm participants may utilize financial resources available in their communities or at their clinic, though the study team will not proactively facilitate access to these resources. NCORP research coordinators may choose to provide subjects with the contact information for the financial counselor or social worker at their practice site if such services are available. To account for institution-level variability in financial assistance infrastructure and dyad-level utilization of clinic or community financial resources, patients and spouses in both arms will be asked to report whether they received any financial resources from the clinic, community, or navigators during the six-month study period.

Within 14 days after registration, all participants in the control arm will view the online financial literacy videos either in clinic or via a link provided by clinical site staff to be accessed at home. Clinics are encouraged to have their own tablet or laptop available to use in clinic should participants choose this option. There are ten videos available in English and Spanish covering a variety of topics relating to cancer care costs and financial concerns during cancer treatment. Each video is 2 to 8 minutes in length and there is not a requirement on the number of videos that should be watched. Participants are asked to watch videos of interest to them. Both patients and spouse caregivers will be asked what videos they watched when they complete the Follow-Up Financial Questionnaire at the 3-month timepoint. Following the videos, their experience will follow usual care.

Intervention description {11a}

There are two community partners that will be delivering the study intervention; 1) Consumer Education and Training Services (CENTS), a Seattle, Washington-based financial literacy and counseling organization; and 2) Patient Advocate Foundation (PAF), a national financial assistance and navigation organization. The financial literacy videos, developed by CENTS, will be delivered to **both** the control and intervention groups. The 6-month remotely administered proactive financial navigation program will be delivered by CENTS and PAF. The financial navigation program consists of financial counseling, direct medical cost and healthcare coverage assistance, and indirect and non-medical cost assistance (**Table 1**). Any or all the issues shown as covered by the counseling partners may be discussed in each session, depending on the needs and interest of the patient and spouse caregiver. There will be 6 scheduled

monthly sessions provided by both CENTS and PAF for a total of 12 scheduled sessions. Within the Medidata RAVE electronic data capture (EDC) system, CENTS counselors will be able to see documentation by PAF case managers (and vice versa) for individual study subjects. CENTS and PAF counselors will be able to view some baseline information about disease type and financial status to assist them in counseling the patient and spouse participants.

PAF and CENTS will provide a bilingual case manager and Spanish-Speaking counselors to work with Spanish speaking study participants.

Table 1: Financial Navigation Program Components

Component	Description	CENTS Counselor	PAF Case Manager
Financial Literacy Training – Provided at enrollment – (Control and Intervention)			
Financial literacy videos	• Short web-based videos (approximately 2-8 minutes in length) instructive in basic healthcare costs and financial concerns during cancer treatments (developed by CENTS, web links to the videos will be provided by study site staff)		
Proactive Financial Navigation – Provided by CENTS and PAF monthly for 6 months – (Intervention Only)			
Financial Counseling	**(total of 12 sessions)****		
Budget planning	• Review household budget and create monthly expense worksheet • Discuss strategies to increase income or reduce expenses (e.g., mobilizing retirement funds, downsizing home, loans, charity care, crowdfunding)	X	
Medical expenses management	• Instruct couples to save all receipts, medical bills, explanations of benefits (EOBs) for tax purposes • Review guidelines for medical tax deductions and refer patient to tax professional where appropriate	X	
Financial and Legal Planning	• Advise couples about the following: Will, Beneficiary designations, Power of attorney, Estate planning (Discuss state-specific forms or laws or refer couples to resources or legal counsel for state-specific assistance)	X	
Direct Medical Cost and Healthcare Coverage Assistance			
Medical out-of-pocket cost assistance	• Identify eligibility for copay assistance based on disease and income • Identify other patient assistance resources for medical costs		X
Insurance assistance	• Act as a liaison between patient and insurance company (coordinate prior authorizations, insurance denial appeals) • Work with clinic to resolve billing and coding issues • Insurance enrollment and optimization (explaining benefits, help with plan choice and enrollment, Medicare/Medicaid enrollment)		X
Indirect and Non-medical Cost Assistance			
Employment guidance	• Discuss couples' employment status and continued ability for both to work • Negotiate terms of medical leave directly with employers • Explore other types of employment and income sources.		X

	• Review federal workplace protections (Americans with Disabilities Act, Family and Medical Leave Act) and assist with relevant paperwork.		
Disability applications	• Determine eligibility and assist with applications for: Supplemental security income (SSI) and Social security disability (SSDI), Medicaid, VA benefits		X
Debt management and relief	• Determine if couple is in default or behind on medical or other debt • Determine if payment arrangements or waivers can be made	X	
Non-medical OOP cost assistance	• Identify support needs for transportation, housing, utilities, and meals		X

** Both CENTS and PAF will adapt their sessions to address the unique financial needs of the patient and spouse. If they require more frequent meetings based on their circumstances, the counselors and case managers have the option to meet as frequently as needed during the 6-month intervention period.

CENTS counselors and PAF case managers will each set up an initial session (by phone or videoconference) with participants in the intervention arm. The initial sessions are estimated to take 75 minutes for each organization. CENTS and PAF will collect the patient and spouse's preference for how future meetings will be conducted during the initial sessions. After the initial session, enrolled participants will be contacted by CENTS and PAF by phone, videoconference, or email, monthly for 6 months. There will be 6 sessions with each organization for a total of 12 sessions. It is estimated that the follow-up sessions will be less than 1 hour each session, depending on how much financial assistance is needed. Both CENTS and PAF will adapt their sessions to address the unique financial needs of the patient and spouse. If a patient and spouse require more frequent meetings based on their circumstances, the counselors and case managers have the option to meet as frequently as needed during the 6-month intervention. Patients and their spouse will be encouraged to attend all sessions. Both are required to be present for at least the first counseling sessions with CENTS and PAF. For intermediate sessions (sessions 2-5), either the patient or the spouse may be present, as available. If a spouse is unable to be present, they may ask CENTS or PAF about the content of any discussion they have missed. Both patient and spouse should be strongly encouraged (but not required) to both be present for the final monthly counseling sessions with both CENTS and PAF.

Site staff may choose to provide patients with contact information for the financial counselor or social worker at their practice site if such services are available. This does not preclude the patient from participating in the intervention. Patients are allowed to additionally access financial resources available in their communities or at their clinic.

Criteria for discontinuing or modifying allocated interventions {11b}

Criteria for Removal of Patient from Protocol Participation

a. Patient completes 12 months of protocol participation.
b. The patients may withdraw from the protocol participation at any time for any reason. (Research staff should submit the off-protocol forms if the patient refuses both direct and indirect follow-up on the study. If the patient allows for indirect follow-up or is refusing to complete any further patient forms but will allow the site to follow them directly, an off-protocol form should not be completed)
c. Patient death.

NOTE: Patients who divorce or separate may continue to participate in the study.

All reasons for discontinuation of protocol participation must be documented in the off-protocol form

Criteria for Removal for Consented Spouse Caregiver from Protocol Participation

a. Spouse caregiver completes 12 months of protocol participation.
b. Spouse caregiver death.
c. Patient death and the spouse caregiver wishes to discontinue. Patient death is not an automatic criterion for caregiver discontinuation.
d. Patient removed from protocol participation and the spouse caregiver wishes to discontinue.
e. The spouse caregiver may withdraw from the protocol at any time for any reason. *The patient will continue participation even if the consented spouse caregiver discontinues protocol participation.*

NOTE: If the patient is alive and cannot or refuses to complete questionnaires at a study time point, but remains on protocol, the spouse caregiver will continue to complete the spouse caregiver questionnaires at the study time points.

Strategies to improve adherence to interventions {11c}

The financial navigation intervention has been designed to promote flexibility for the patient and spouse-caregiver depending on their needs. While the first financial navigation session must be conducted by phone or videoconference and is required to have both patient and spouse-caregiver attend, subsequent sessions can be by phone, videoconference, or e-mail with the option for just the patient or spouse-caregiver to attend. CENTS and PAF work with study participants to find both times and communication mechanisms that are most convenient for them for the 6 monthly sessions. Additionally, financial

navigation sessions are designed to be tailored to the participant's needs and CENTS and PAF will not utilize time during these sessions to discuss any topics not applicable to the specific participant.

Adherence is tracked via monthly forms that CENTS counsellors and PAF case managers fill out. Forms detail whether they were able to contact the participant for that month's financial navigation session and what topics are discussed with participants.

Relevant concomitant care permitted or prohibited during the trial {11d}

Participants in both study arms may utilize financial resources available in their communities or at their clinic. Site research staff may choose to provide patients with the contact information for the financial counselor or social worker at their practice site if such services are available.

Participants are permitted to concurrently participate in a clinical trial, either treatment-focused on supportive care, at any point during the study duration and 12-month follow up.

Provisions for post-trial care {30}

Not applicable

Outcomes {12}

Primary Endpoint

a. Household Financial Hardship: Defined as one or more of the following: from the patient's and/or spouse's credit report within 12 months: any new loans (bank or home equity); exhausting lines of credit by reaching limits on credit cards and home equity loans; credit or other payment delinquencies; becoming subject to a lien, judgment, or other collection process; personal bankruptcy filings.

Other Endpoints

a. Qualitative Assessment of the Intervention: Intervention arm dyads will be surveyed about availability and use of financial assistance and navigation services with CENTS and/or PAF. CENTS and PAF will document all interactions with the intervention dyads and specific details about all counseling, assistance, and interventions provided for the dyad over the 6-month intervention period.
b. Community/Clinic Assistance: Control arm dyads will be surveyed about availability (or lack), access to, and use of financial assistance via their treating clinic or community-based resources. This information is collected on the Follow-Up Questionnaire – Control Arm (**See Table 2**)
c. Financial Worry: As measured by the Comprehensive Score for Financial Toxicity-Patient Reported Outcome Measure (COST-FACIT Version 2), a 12-item measure developed for patients with advanced

malignancies (scored 0-44).[35,36]

d. Patient Quality of Life: A composite score from the EuroQOL EQ-5D-5L Index (score 0-100). A 6-point score change is considered clinically meaningful in US cancer populations.[37-38]
e. Treatment Adherence: Patient self-reports that they did or did not skip medication doses or refuse/decline recommended therapy due to cost concerns.
f. Emergency Department/Hospital Use: All instances of ED and hospital stays (including reason for visit) will be abstracted from patients' medical records by site staff. Investigators will categorize visits as anticipated (for chemotherapy or planned procedures) versus unanticipated (complication or treatment side-effect).
g. Spouse Caregiver Quality of Life: As measured by the City of Hope Quality of Life Family Version, a 37-item ordinal instrument that measures the QOL of a family member caring for a patient with cancer.[39] The ordinal scale ranges from 0 to 10, with lower scores meaning worse QOL. Four QOL subscales, calculated as mean scores of the items in each, include physical (5 items, scored 0-50), psychological (16 items, scored 0-160), social (9 items, scored 0-90), and spiritual (7 items, scored 0-70) well-being. The revised instrument was tested from 1994 to 1998, with the test-retest reliability of r=.68 and internal consistency of alpha r=.89. Factor analysis confirmed the four QOL domains as subscales for the instrument. A change in score of 2 points per item is considered clinically meaningful. To assess spouse caregiver quality of life, we will use the physical and psychological subscales. Given that 5 items (14, 15, 18, 19, and 20) in the psychological subscale do not relate to the metastatic cancer population, we will administer 11 of the 16 items (score 0-110).
h. Spouse Caregiver Burden: As measured by the social well-being subscale of the City of Hope Quality of Life Family questionnaire.[39]

Participant timeline {13}

Timeline for study enrollment, intervention and assessments are illustrated in **Figure 2** and **Table 2**.

Table 2: Timeline and assessments

REQUIRED FORMS / TASKS	Prestudy/ Baseline	≤ 14 days after reg	Month 3 (+/- 21 days)	Month 6 (+/- 21 days)	Month 12 (+/-21 days)	Off Protocol
PATIENT & SPOUSE		X				
View Financial Literacy Videos						
PATIENT QUESTIONNAIRES						
Baseline Questionnaire - Patient	X					
EQ-5D-5L Health Questionnaire	X		X	X	X	
COST-FACIT(Version 2)	X		X	X	X	
Follow-up Financial Questionnaire - Patient			X	X	X	
SPOUSE CAREGIVER QUESTIONNAIRES						
Baseline Questionnaire - Spouse	X					
COST (Version 2) – Spouse	X		X	X	X	
Quality of Life - Family	X		X	X	X	
Follow-up Financial Questionnaire - Spouse			X	X	X	
PATIENT AND SPOUSE CAREGIVER QUESTIONNAIRES						
Baseline Questionnaire - Patient and Spouse	X					
Follow-up Financial Questionnaire – Patient and Spouse			X	X	X	
Follow-up Questionnaire (Control Arm only)			X	X	X	
Follow-up Questionnaire (Financial Navigation Arm only)			X	X	X	

Primary Objective and Sample size {14}

The primary objective is to determine the impact of a proactive financial navigation program on development of material household financial hardship among eligible patients and their spouse caregivers treated at NCORP sites.

Credit reports provide objective and reproducible measures of financial hardship and will be obtained at four time points (baseline, and Months 3, 6 and 12). Given the death rate by one year in this population, it is possible that only a single assessment will occur in many dyads. As such, we will use a binary outcome measure for the primary outcome- development of financial hardship within one year of enrollment (yes/no).

The prevalence of major material financial hardship among cancer patients has been estimated between 30-50% based on several large retrospective studies.[5,7,9] Our prior work suggests that, for metastatic colorectal cancer (mCRC) patents, the cumulative incidence for major financial hardships by 12 months post-diagnosis may be as high as 75%, significantly higher than previous estimates.[40] Given that this study will enroll patients with a variety of cancers (some perhaps less financially burdensome than mCRC) and that we will be focusing on more severe financial hardships, we estimate that 30% of dyads in the usual care arm will experience major financial hardship in the year after diagnosis.

A two-arm binomial design without continuity correction will be used with a one-sided alpha=.05 test. With these specifications, 312 patient and spouse caregiver dyads (156 in each arm) will provide 80% power to detect a relative 40% decrease in the proportion of households experiencing financial hardship within the first year (from 30% down to 18%, a 12% absolute percentage reduction). A risk reduction of this magnitude could potentially impact practice, guidelines, and policy, as suggested by similar observed differences observed in recent high profile practice changing trials.[41,42] Given that financial hardship accumulates over the course of disease as evidenced by our preliminary data,[40] we believe that intervening proactively at diagnosis by providing debt relief, assistance with out-of-pocket expenses, and other services described earlier has the potential to mitigate escalating debt which leads to household credit strain. If the incidence of material household financial hardship in the control arm is higher than we estimate, then power will increase; for instance, if the control arm rate is 40%, we can detect a 40% reduction (from 40% down to 24%) with 90% power.

To account for 40% expected dropout at 1 year, we would need to enroll 520 eligible dyads; in addition, given the historical 3% ineligible registration rate in NCORP trails, we will enroll 536 total dyads to achieve the necessary sample size for our analysis. One-year survival is 70-80% in the most common cancers (breast and colorectal cancer) expected to comprise most of our study population.[43-44] Thus, we project a 30% dropout due to death. Through endpoint data may be captured for some of these dyads, we will conservatively assume no information from these dyads for design purposes. A further 10% of dyads will contribute no endpoint data for reasons other than death (e.g., transferring care to another institution, withdrawal of consent, “credit invisibles” for whom we are unable to obtain credit data).[45] Based on accrual rates to our prior SWOG study, we estimate 16-17 dyads accrued per month, with a total time of 33 months to complete accrual. To enroll 536 dyads, we anticipate screening 1,276 patients based on our preliminary work that suggests 70% of eligible patients will be married to a living spouse and that, among these 60% will agree to participate as a dyad.[40]

Recruitment {15}

To maintain balance by cancer type and address the potential concern that patients with hematologic malignancies may accrue more rapidly than patients with solid tumors, we will cap the total enrollment of hematologic malignancy patient + caregiver dyads at 268 (50% of the total accrual goal) (**Table 3**).

Table 3: Recruitment and Retention Estimates

Enrollment goal (# dyads)	Ineligible registrations	1-year survival	1-year retention*	Retention goal (# dyads)
536	3%	70%	90%	312
* retention refers to lack of dropout for reasons other than death (e.g. transfer of care, withdrawal of consent) (536*(1-.4)*(1-.03))				

Assignment of interventions: allocation

Sequence generation {16a}

Randomization will occur at the dyad level. A practice- or provider-level clustered randomization approach is not advantageous because the intervention is delivered by outside entities (i.e. no change in usual care with implementation of this study) and because the delivery of proactive financial navigation is generally lacking across NCORP sites (thus we hypothesize that location of care will not significantly influence outcomes).

Household financial fragility will be determined prior to randomization using a widely accepted metric assessing one's ability to come up with $2,000 in 30 days to cope with an unexpected expenditure.[46] This $2,000/30 day metric is a more precise measure of financial resiliency than income in the setting of an unanticipated health shock. In the 2015 National Financial Capability Study, approximately 34% of American adults across a range of income levels could not manage an unexpected expense of this magnitude; 30% of individuals with income $50K - $75K and 20% of individuals with incomes $75K to $100K were considered 'financially fragile.'[46] Couples will be asked to come to a consensus response to this question based on current household resources.

To achieve balance between arms with respect to household financial fragility and other factors that have been shown to influence financial status, randomization will be stratified by 1) household financial fragility (certainly/probably able vs. probably/certainly *not* able to come up with $2,000 in 30 days), 2) patient age (< or ≥ 65) and 3) patient gender (male vs. female) given potential gender differences in employment and thus financial security. Randomization within these three strata will be assigned via a computerized system at the SWOG statistical center, using a dynamic balancing approach. Participants will remain on study until voluntary withdrawal, death, or completion of all planned follow-up.

Concealment mechanism {16b}

Concealment mechanisms will not be required.

Implementation {16c}

The Oncology Patient Enrollment Network (OPEN) is a web-based registration system available on a 24/7 basis. OPEN is integrated with CTSU regulatory and roster data and with the Lead Protocol Organizations (LPOs) registration/randomization systems or the Theradex Interactive Web Response System (IWRS) for retrieval of patient registration/randomization assignment. OPEN will populate the patient enrollment data in NCI's clinical data management system, Medidata Rave.

Communication of Randomization to Study Participants

Sites will receive randomization assignment from the OPEN Registration system. It is the responsibility of the site to communicate the randomization assignment to study participants. Sites may use local procedures (as long as they are IRB approved).

Exceptions to SWOG registration policies will not be permitted.

a. Patients and Spouse-Caregivers must meet all eligibility requirements.
b. Institutions must be identified as approved for registration.
c. Registrations may not be cancelled.
d. Late registrations (after initiation of intervention) will not be accepted.

Assignment of interventions: Blinding

Who will be blinded {17a}

Study is not blinded

Procedure for unblinding if needed {17b}

Not applicable

Data collection and management

Plans for assessment and collection of outcomes {18a}

The questionnaires used for this study are derived from validated instruments as described above under Outcomes. The schedule of administration of these questionnaires is outlined in **Table 3**. Credit reports will be collected at baseline, 6, and 12 months following registration.

Plans to promote participant retention and complete follow-up {18b}

The financial navigation intervention has been designed to promote flexibility for the patient and spouse-caregiver depending on their needs. While the first financial navigation session must be conducted by

phone or videoconference and is required to have both patient and spouse-caregiver attend, subsequent sessions can be by phone, videoconference, or e-mail with the option for just the patient or spouse-caregiver to attend. Adherence is tracked via monthly forms that CENTS counsellors and PAF case managers fill out. Forms detail whether they were able to contact the participant for that month's financial navigation session and what topics are discussed with participants. Participants will receive questionnaires and credit reports will be pulled regardless of engagement with the intervention. If patients request to drop out of the study (but allow the study team to continue inactive follow up), medical records will still be reviewed for evidence of ED or hospital use.

Data management {19}

Data Submission Procedures

a. Medidata Rave is a clinical data management system being used for data collection for this trial/study. Access to the trial in Rave is controlled through the CTEP-IAM system and role assignments.

Upon initial site registration approval for the study in Regulatory Support System (RSS), all persons with Rave roles assigned on the appropriate roster will be sent a study invitation e-mail from iMedidata. To accept the invitation, site staff must log into the Select Login (https://login.imedidata.com/selectlogin) using their CTEP-IAM user name and password and click on the "accept" link in the upper right-corner of the iMedidata page. Site staff will not be able to access the study in Rave until all required Medidata and study specific trainings are completed. Trainings will be in the form of electronic learnings (eLearnings) and can be accessed by clicking on the link in the upper right pane of the iMedidata screen. If an eLearning is required and has not yet been taken, the link to the eLearning will appear under the study name in iMedidata instead of the Rave EDC link; once the successful completion of the eLearning has been recorded, access to the study in Rave will be granted, and a Rave EDC link will display under the study name.

Site staff that have not previously activated their iMedidata/Rave account at the time of initial registration approval for the study in RSS will receive a separate invitation from iMedidata to activate their account. Account activation instructions are located on the CTSU website in the Data Management section under the Rave resource materials (Medidata Account Activation and Study Invitation Acceptance). Additional information on iMedidata/Rave is available on the CTSU members' website in the Data Management > Rave section at www.ctsu.org/RAVE/_or by contacting the CTSU Help Desk at 1-888-823-5923 or by e-mail at ctsucontact@westat.com.

Research staff may also access Rave® via the SWOG CRA Workbench via the SWOG website (www.swog.org) and contact the CRA Workbench technicalquestion@crab.org with any questions.

b. Data Quality Portal

The Data Quality Portal (DQP) provides a central location for site staff to manage unanswered queries and form delinquencies, monitor data quality and timeliness, generate reports, and review metrics.

The DQP is located on the CTSU members' website under Data Management. The Rave Home section displays a table providing summary counts of Total Delinquencies and Total Queries. DQP Queries, DQP Delinquent Forms and the DQP Reports modules are available to access details and reports of unanswered queries, delinquent forms, and timeliness reports. Review the DQP modules on a regular basis to manage specified queries and delinquent forms.

The DQP is accessible by site staff that are rostered to a site and have access to the CTSU website. Staff that have Rave study access can access the Rave study data using a direct link on the DQP.

To learn more about DQP use and access, click on the Help icon displayed on the Rave Home, DQP Queries, and DQP Delinquent Forms modules.

Note: Some Rave protocols may not have delinquent form details or reports specified on the DQP. A protocol must have the Calendar functionality implemented in Rave by the Lead Protocol Organization for delinquent form details and reports to be available on the DQP. Site staff should contact the LPO Data Manager for their protocol regarding questions about Rave Calendar functionality.

Data Submission Overview and Timepoints

Research staff will be required to submit baseline forms within 15 days of registration (along with onstudy form and cover sheet) and within a +/- 21 day window of the 3, 6, and 12 month follow-up questionnaire time points. The following questionnaires will be administered: the following: Vital Status Form, Onstudy form, Cover Sheet for Patient- and Spouse-completed questionnaires, Patient / Spouse / Patient & Spouse baseline questionnaires.

a. Participants will complete the following questionnaires at baseline (after consent and prior to registration):

- Baseline Questionnaire – Patient
- EQ-5D-5L Health Questionnaire
- COST-FACIT (Version 2)
- Baseline Questionnaire – Spouse
- COST (Version 2) - Spouse
- Quality of Life – Family
- Baseline Questionnaire Patient and Spouse

b. Participants will complete the following questionnaires at 3, 6 and 12 months following registration:

- Follow-up Financial Questionnaire - Patient
- EQ-5D-5L Health Questionnaire
- COST-FACIT (Version 2)
- Follow-up Questionnaire (Control Arm or Financial Navigation Arm as appropriate)
- Follow-up Financial Questionnaire – Spouse
- COST (Version 2) - Spouse
- Quality of Life - Family
- Follow-up Financial Questionnaire – Patient and Spouse

Within 15 days of participant discontinuation from the study, research staff will be required to submit the vital status form and an Off Protocol Notice.

Within 4 weeks of knowledge of patient or spouse death, research staff will be required to submit a vital status form and off protocol notice.

Questionnaire Administration

Options for distribution of questionnaires by sites:

a. Sites may provide paper copies of questionnaires to consented participants at clinic visit, or they may be sent by mail or email. If emailed, participant must print and complete questionnaires by hand since questionnaires are not formatted for electronic completion. Participants are to return the completed questionnaires at the next clinic visit, by mail, or via secure email. (Participating sites must adhere to local institutional policies for secure exchange of electronic protected health information if receiving participant completed scanned questionnaires.)
b. Questionnaires will be self-administered and are anticipated to require no more than 30 - 60 minutes to complete at each study time point.
c. Target follow-up assessment dates should be based on the date of registration. A window of ± 21 days is allowed for each assessment to provide more flexibility in scheduling.
d. In order to minimize patient and spouse caregiver burden and streamline clinic visits, it is preferable for questionnaires to be given to the patient and spouse at the clinical visit immediately prior to the study time point, or completed at home and returned at the routine clinical visit coinciding with the study time point. It is allowable for baseline forms to be done at home (after consent). Sites should be mindful of timelines as baseline forms must be completed prior to registration. Study staff should accommodate the participant's preferences for filling out the questionnaires as described below. Some questionnaires will require detailed financial information, so it is recommended that the site staff contact the patient a week before their scheduled visit to remind him/her to bring the appropriate information to the visit to complete the questions on the forms. At the time of consent, the patient and spouse caregiver should be provided with a copy of the forms for reference.

e. The research site should encourage the patient and spouse caregiver to review the questionnaires after completing them. The patient and spouse's review may help them decide if they need more time to find the information. The patient and spouse may also be more comfortable completing the questionnaire(s) at home. It is not required that forms be completed together (by the patient and spouse). The options for the patient and spouse caregiver are as follows:

- Complete questionnaires at home. Provide the patient and spouse caregiver with the questionnaires in advance and instructions to return them to the site at the clinical visit corresponding to the study time point (e.g., give patient and spouse caregiver questionnaires 2 weeks in advance at a routine clinical visit). Review the returned questionnaires for completeness at the clinical visit and clarify answers while the patient and spouse are at the clinic. If the patient and spouse caregiver do not return the completed questionnaires as scheduled, the patient and spouse caregiver should complete the questionnaires at the clinical visit or schedule a phone contact. Completed questionnaires may be scanned and sent back to the site if the site has provided a secure email to ensure protection of PHI.
- Complete the questionnaires in the clinic or practice. Due to the sensitive information being asked, when possible, offer the patient and spouse caregiver a private location to sit and complete the questionnaires. After completion of the questionnaires, the site staff should immediately review the questionnaires for completeness and confirm the patient and spouse caregiver answered the questions per the directions on the form and clarify questions with the patient while they are still at the clinic or practice.
- Partially complete the questionnaires in the clinic or practice. If due to illness, not enough time or any reason the patient and spouse caregiver begin completing the questionnaires in the clinic or practice but then decide they cannot finish one or more questionnaires, make a photocopy of the incomplete questionnaire(s), give the patient and spouse caregiver a copy and keep the original in the patient's research chart. Give the patient a pre-addressed stamped envelope to return the questionnaire(s) by mail to the clinic or practice but also schedule a phone call with the patient 1 week later. If the questionnaire(s) are returned (by email, mail or in person) within 1 week, use the scheduled phone call to clarify any missing or unclear responses (if applicable). If questionnaire(s) are not returned, use the scheduled phone call to complete the questionnaire(s) by phone interview.
- Complete questionnaires by phone or video conference interview. If the patient and spouse caregiver are unable to come in for the patient's clinic visits or questionnaires are not completed before or at the clinic visit, questionnaires may be completed by phone or video conference interview. Phone or video conference interviews should be scheduled within 1 week of the clinic visit corresponding to the study time point. The patient and spouse caregiver should be given a copy of blank forms (or partially-completed, if applicable) so that the patient and spouse caregiver may look at a copy of the questionnaires while the site staff conducts the interview. The date of the interview is to be noted on the Cover Sheet for Patient- and Spouse- Completed Questionnaires. If the interview is to complete data on a partially-completed form, review all the

questions with the patient and spouse caregiver, even those previously completed, in case the patient and spouse caregiver needs to change a previously answered question. If the phone interview is not completed as scheduled, reschedule to remain within the ± 21 day window for the study time point.

f. Completed questionnaires will be reviewed to ensure that all of the questions have been answered and, when the patient and spouse caregiver are directed to mark only one response, that only one answer is marked. If the patient and spouse caregiver have marked more than one answer per question, ask which answer reflects how the patient and/or spouse is feeling. If the patient and spouse caregiver have skipped a question, research staff will indicate that a question was not answered and ask them if they would like to answer the question. If they are unable to answer the question at the time of the visit, site staff are encouraged to retain the questionnaire and contact the patient and spouse caregiver by phone to obtain outstanding information. If patient and spouse caregiver do not want to answer a particular question, the site staff will enter "Not answered by the participant" in Medidata RAVE®.

g. Spouse caregivers may assist patients with their questionnaires by administering the questionnaire orally to the patient, helping the patient find information and/or recording the patient's answers. Spouse caregivers cannot answer for the patient. For patients who are too sick to complete the questionnaires (even with assistance from the Spouse caregiver) or who are not able to come to a clinical visit, the site staff will record, on the **S1912CD** Cover Sheet for Patient- and Spouse-Completed Questionnaires, that the patient was too sick to complete the questionnaire.

Cover Sheet for Patient and Spouse-Completed Questionnaires

For each time point, site staff completes the Cover Sheet for Patient and Spouse-Completed Questionnaires. The Cover Sheet is submitted with the set of patient and spouse-completed forms at each scheduled assessment. The Cover Sheet is very important for tracking how and when the patient and spouse caregiver forms were completed. When a patient-completed form is not administered at a scheduled time point, it is important to know why the assessment did not occur; the form includes potential reasons for a patient not completing a form. All issues of noncompliance are noted on the Cover Sheet for Patient- and Spouse- Completed Questionnaires.

Confidentiality {27}

All data collection, including approach and consent of potential participants, is handled by trained Clinical Research Associates (CRAs) at NCORP sites. Data is entered into secure Electronic Data Capture (EDC) system forms and transmitted securely to CRAB. All data collected is reported to the assigned

SWOG Data Safety and Monitoring Committee (DSMC). Signed consent forms and any completed paper surveys are stored in locked files at the respective site.

Data identifying individual subjects is restricted to those directly involved in the study. The data are stored in Oracle data tables. Study investigators from CRAB and Fred Hutch have direct access to these data tables through a common network maintained by CRAB. All participant data is stored in secure databases. At CRAB, the computing infrastructure and the associated network are maintained continuously to safeguard criticaland sensitive information, e.g., the patient database. Data are stored across a variety of systems including a NetApp® network attached storage system (NAS) and an Equalogic® storage area network (SAN). Researchdata and servers are backed up to tape nightly, utilizing high-speed tape libraries and fault-tolerant RAID arrays. Tapes are removed from the Statistical Center daily and stored in a fire-proof safe until transported to a secureoff-site facility on a regular basis for disaster recovery purposes.

Names and other identifying information from subjects are obtained for requesting credit reports and record keeping purposes only, and no individual will be identified in any study report. Written reports and manuscripts will only include de-identified data in aggregate form.

Credit reports will be obtained by CRAB using a password-protected web-based portal. Credit report attributes will be posted by TransUnion and will be available for download by CRAB for 7 days before automatically expiring. Credit report data will then be entered into the study database at CRAB and will not be accessible by investigators on the research team, investigators and research associates at NCORP sites, patients, or spouses. Once the credit data have been input into the master CRAB database, these reports will not be retained either electronically or in hard copy form. Access to credit reports for this study will be considered a ‘soft pull’ and will not affect the participant’s credit score.

Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

Not applicable

Statistical methods

Statistical methods for primary and secondary outcomes {20a}

To address the primary objective, we will conduct a multivariable logistic regression (outcome = household financial hardship; independent variable = intervention vs. control), adjusting for the demographic, clinical, financial and practice characteristics in Table 4.

Table 4: Covariates

Covariates	
Variable	**Data source**
Joint or combined household factors	
Financial fragility: Couples' ability to come up with $2000 in 30 days for an unexpected expense (Scale: certainly, probably, probably not, certainly not) – dyad measure	Collected by site staff at registration
Baseline financial status: Combined household income category (< $50,000 versus ≥ $50,000); Combined household income (continuous); Baseline averaged credit score; Combined credit utilization > 70%	Household budget worksheet; baseline credit report
Patient and Spouse-Caregiver demographic factors	
Demographics: Age group (< vs. ≥ 65); Age (continuous); Race; Gender; Education level; Insurance type (patient) – (Commercial, Medicare, Medicaid, other)	Medical record (patient) and Survey (patient and spouse)
Patient clinical factors	
Zubrod PS (0,1,2); Cancer type (solid vs. hematologic); de novo vs recurrent	Medical record
NCORP Site-Level variables	
Existing financial resources (NCORP): Financial screening process; Dedicated financial navigator or counselor	Collected from individual NCORP affiliates and sub-affiliates as a protocol specific requirement for activation

Secondary Objectives

Investigate whether proactive financial navigation improves patient and Spouse-Caregiver psychosocial and healthcare utilization outcomes.

Quality of Life and Spouse-Caregiver Burden

We will use available scoring systems to determine composite EQ-5D-5L (patient) and City of Hope Quality of Life Family (spouse caregiver) scores at baseline, 3, 6, and 12 months. We will determine mean composite score for each of the 3 City of Hope Quality of Life Family subscales. We will focus on the change in score between baseline, 3 and 6 months, which represents the end of the intervention. 2-sided p values <0.05 will indicate statistical significance for all tests described below. The proportion of patients in each arm who experience improved, unchanged, or worsened EQ-5D scores from baseline to 3, 6 (and 12) months will be compared using Fisher's exact test. This analysis will be conducted for a level of

change from baseline and for a 6-point change, which is considered clinically meaningful. Mean score changes from baseline will be compared using two group t tests. A multivariate linear regression model, with worsening score as the dependent variable and study arm (intervention vs usual care) as the independent variable will be performed, adjusting for covariates in Table 4. As above, we will determine the proportion of spouse caregivers in each arm who experience improved, unchanged, or worsened Quality of Life Family scores (composite scores for physical, emotional, and social well-being subscales) from baseline to 3, 6 (and 12) months and compare using Fisher's exact test. Mean score changes will be compared using two group t tests. A multivariate linear regression model, with worsening score as the dependent variable and study arm as the independent variable will be performed, adjusting for covariates in **Table 4**.

Financial Worry

Financial worry measured by the COST-FACIT (Version 2) tool will be scored from 0-44, with lower scores representing higher levels of financial toxicity. Mean scores (and SD) at 3, 6 and 12 months will be compared between intervention and usual care patients and spouses using two sample t tests. Unlike household financial hardship which represents a composite household endpoint, financial worry may diverge between patients and spouses and thus should be measured separately. Additionally, we will explore the extent to which financial worry correlates with financial hardship by comparing mean scores in those who experience financial hardship in each study arm versus those who do not.

Healthcare Utilization

We will explore the impact of the intervention on the health utilization outcomes of treatment adherence and emergency department (ED)/hospital use. This analysis is exploratory given that these outcomes are more distal to the intervention and may not differ between arms due to the high rates of ED/hospital use and low anticipated rates of cost-related non-adherence in this population. Based on previous work, we anticipate that approximately 7% of patients will report non-adherence due to cost.[9] We will determine the proportion of patients in each arm reporting cost-related non-adherence and compare using chi-squared test. The sample size of 520 total eligible patients will enable us to detect an absolute reduction in the proportion of treatment non-adherent patients of 5.0% (from 7% to 2%) with 81% power. The cumulative incidence of ED and unanticipated hospital use will be calculated by arm to account for death as a competing risk and compared using Cox regression, adjusting for covariates in Table 4. If we do see a trend towards lower ED/hospital use and higher treatment adherence in the intervention arm, then we will consider this finding hypothesis-generating and warranting further study including a detailed investigation into the mediators and moderators of these effects.

Other Objectives

Describe the utilization of financial navigation services by younger, financially fragile, and lower income patients and households and evaluate the intervention's effect in these subgroups.

Qualitative Evaluation

We will evaluate CENTS' and PAF's documentation and characterize the interventions made on behalf of dyads within each of these subgroups. We will look for differences in proportions of dyads within each subgroup requiring assistance with each of the key navigator functions (financial counseling, direct medical cost and healthcare coverage assistance, and non-medical and indirect cost assistance). We will review all unresolved issues reported by CENTS and PAF and describe the frequency and type by subgroup. We will also describe usual care group dyads' self-reported pursuit and use of clinic and community-based financial assistance resources, noting barriers to access if present.

Moderator Analysis

We will examine the extent to which the relationship between the intervention assignment and the development of financial hardship potential differs by demographic and socioeconomic factors including patient age, household income, and household financial fragility. Interaction tests will be used representing, in the regression model, the product of the intervention assignment and the factor in the presence of the main effects for both. The absence of any interactions will suggest no statistical evidence that the relationship between intervention assignment and financial hardship differs substantially based on these factors. However, if a statistically significant interaction is evident ($p<.05$), examinations of the intervention effect within each factor level will be conducted to enable interpretation of the observed differences for hypothesis generation. In the absence of a significant main effect of the intervention, it is likely that significant effects in a subset could be spurious and should only be regarded as suggestive. A significant overall main effect but an effect size that is close to the null in certain subgroups might suggest heterogeneity.

Different Aspects of Household Financial Hardship

The primary endpoint reflects a composite measure of different aspects of household financial hardship assessed over time. Thus households are at risk of experiencing more than one component of financial hardship, and may experience multiple components over time. We will further explore potential differences by arm in different aspects of household financial hardship by comparing the number of different events patients experience as well as the individual components of the composite event by arm .

Sensitivity Analysis

SWOG's prior study evaluating major financial hardship (S1417CD) showed that new loans are a major component of the financial hardship measure. To evaluate the potential sensitivity of the primary endpoint assessment to the accumulation of new loans, we will explore whether the comparison by arm in household financial hardship is robust to different levels of the magnitude of new loans (e.g., >$1,000, >$5,000).[40]

Although all secondary and exploratory objectives will be evaluated at the two-sided alpha=.05 level, statistically significant findings will be considered hypothesis-generating, requiring confirmation in independent study.

Interim analyses {21b}

No interim analyses will be performed. The study team will hold quarterly meetings throughout the recruitment period and will evaluate the need for protocol modifications to improve enrolment and meet the anticipated enrolment timeline.

Methods for additional analyses (e.g. subgroup analyses) {20b}

See above section Statistical methods

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

Sample size calculation takes into account death or drop out for various reasons. An “intention to treat” analysis will be performed such that patients assigned to the treatment arm will be considered in this group for the purposes of analysis, regardless of their compliance or adherence to all aspects of the intervention.

Plans to give access to the full protocol, participant level-data and statistical code {31c}

There are no plans to grant public access to the full protocol, participant-level dataset, or statistical code.

Oversight and monitoring

Composition of the coordinating centre and trial steering committee {5d}

Composition of the data monitoring committee, its role and reporting structure {21a}

A Data and Safety Monitoring Committee (DSMC) will oversee the conduct of the study. The Committee consists of four members from outside of the SWOG Cancer Research Network, three SWOG members, three non-voting representatives from the National Cancer Institute (NCI), and the Group Statistician (non-voting). The members of this Committee will receive confidential reports every six months from the SWOG Statistics and Data Management Center and will meet at the Group's bi-annual meetings, as necessary. The Committee will be responsible for decisions regarding possible termination and/or early reporting of the study. The emphasis of DSMC oversight of this study will be on accrual feasibility.

Adverse event reporting and harms {22}

No dose modifications or adverse event information will be collected.

Frequency and plans for auditing trial conduct {23}

The standing SWOG DSMC oversees the conduct of the study. The Committee consists of four members from outside of SWOG, three SWOG members (who do not participate in the trial), two non-voting representatives from NCI, and a statistician from the SWOG Statistical Center (non-voting). The members of this Committee will receive confidential reports from the SWOG Statistical Center and will meet in person or by conference call every 6 months. The primary responsibility of the DSMC is to review interim analyses of outcome and to recommend whether the study needs to be changed or terminated based on these analyses.

Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, ethical committees) {25}

Protocol modifications will be submitted to the central IRB for review and will be communicated with research teams at all enrolling sites. The modified protocol and relevant forms will be uploaded to the Cancer Trials Support Unit (CTSU) and SWOG portals.

Dissemination plans {31a}

Trial results will be disseminated via academic publications in health and medical journals, presentation at oncology and other relevant society meetings (e.g. American Society of Clinical Oncology), and at twice yearly SWOG group meetings and NCORP meetings, when appropriate. There are no restrictions on publication imposed by either the funder or by the community partners (CENTS and PAF) or credit agency (TransUnion)

Discussion

Enrollment began in October 2021 and, as of February 28th 2022 the study has enrolled 15 subjects. This enrollment is slower than anticipated given COVID-related delays and ramp up period for sites to activate the study. This is typical of enrollment for other cancer care delivery studies conducted through SWOG and NCORP. The study team is planning a series of webinars and roundtables with NCORP sites and research staff to discuss enrollment challenges and barriers with an eye towards potential protocol modifications in the future, if appropriate.

Trial status

Protocol version date: 12/21/2021

Recruitment start: 10/12/2021

Approximate anticipated recruitment completion: 10/01/2023

Abbreviations

NCORP

NCI Community Oncology Research Program
CENTS
Consumer Education and Training Services
PAF
Patient Advocate Foundation
SWOG
SWOG Cancer Research Group
NCI
National Cancer Institute
CCDR
Cancer Care Delivery Research
ED
Emergency Department; ICU = Intensive Care Unit
DSMC
Data Safety and Monitoring Committee
EDC
Electronic Data Capture
CRA
Clinical Research Associate
PRO
patient reported outcome
OOP
out-of-pocket
OPEN
Oncology Patient Enrollment Network
CTSU
Clinical Trials Support Unit
IWRS
Theradex Interactive Web Response System
DQP
Data Quality Portal
RSS
Regulatory Support System
LPO
Lead Protocol Organization

Declarations

Acknowledgements

Thank you to Christa M. Braun-Inglis, MS, APRN-Rx, FNP-BC, AOCNP Oncology/Hematology Clinic Kaiser Permanente Hawaii Region, Honolulu HI (Hawaii Minority Underserved NCORP) who contributed significantly to the content for the S1912CD Staff Talking Points document.

Authors' contributions {31b}

VS is the Principal Investigator; she conceived the study, secured the funding, and led the proposal and protocol development. RC, DH, SL, and SR contributed to study design and to development of the proposal. JU (lead), RV, and AD serve as biostatisticians on this trial. All authors read and approved the final manuscript.

Funding {4}

This trial is funded by National Institutes of Health/National Cancer Institute grant awards R01CA248656 and UG1CA189974. The funder did not play a role in the design of the study nor will it play a role in the study conduct, interpretation of data, analysis, and manuscripts or publication.

Availability of data and materials {29}

In accordance with SWOG policies, the final trial dataset will be accessible only by the SWOG statistical team and housed at the SWOG statistical center at CRAB. All reports and analytic data sets (de-identified) will be supplied to the investigative team by the SWOG statistical team.

Ethics approval and consent to participate {24}

Approval for the original protocol has been obtained from the Single Central Institutional Review Board (CIRB) for cooperative group research. All protocol modifications will be submitted to CIRB for approval. Written, informed consent to participate will be obtained from all participants.

Consent for publication {32}

Study team is willing to provide a model consent form on request

Competing interests {28}

The authors declare that they have no competing interests

References

1. Bach PB. Limits on Medicare's Ability to Control Rising Spending on Cancer Drugs. N Eng J Med. 2009;360(6):626–33.
2. Bernard DS, Farr SL, Fang Z. National Estimates of Out-of-Pocket Health Care Expenditure Burden Among Nonelderly Adults With Cancer: 2001 to 2008. J Clin Oncol. 2011;29(20):2821–6.

3. Davidoff AJ, Erten M, Shaffer T, et al. Out-of-Pocket Health Care Expenditure Burden for Medicare Beneficiaries with Cancer. Cancer. 2013;119(6):1257–65.
4. Guy GP Jr, Yabroff KR, Ekwueme DU, et al. Healthcare Expenditure Burden Among Non-elderly Cancer Survivors, 2008–2012. Am J Prev Med. 2015;49(5 Suppl 5):489–97.
5. Banegas MP, Guy GP Jr, de Moor JS, et al. For Working-Age Cancer Survivors, Medical Debt and Bankruptcy Create Financial Hardships. Health Aff (Millwood). 2016;35(1):54–61.
6. Ramsey S, Blough D, Kirchhoff A, et al. Washington State Cancer Patients Found to be at Greater Risk for Bankruptcy than People Without a Cancer Diagnosis. Health Aff (Millwood). 2013;32(6):1143–52.
7. Yabroff KR, Dowling EC, Guy GP Jr, et al. Financial Hardship Associated With Cancer in the United States: Findings From a Population-Based Sample of Adult Cancer Survivors. J Clin Oncol. 2016;34(3):259–67.
8. Kaiser Family Foundation. 2016 Employer Health Benefits Survey. 2016; http://www.kff.org/report-section/ehbs-2016-section-one-cost-of-health-insurance/. Accessed Aug 7, 2017.
9. Shankaran V, Jolly S, Blough D, Ramsey SD. Risk Factors for Financial Hardship in Patients Receiving Adjuvant Chemotherapy for Colon Cancer: a Population-Based Exploratory Analysis. J Clin Oncol. 2012;30(14):1608–14.
10. Tucker-Seeley RD, Abel GA, Uno H, Prigerson H. Financial Hardship and the Intensity of Medical Care Received Near Death. Psychooncology. 2015;24(5):572–8.
11. Kamal KM, Covvey JR, Dashputre A, et al. A Systematic Review of the Effect of Cancer Treatment on Work Productivity of Patients and Spouse-Caregivers. J Manag Care Spec Pharm. 2017;23(2):136–62.
12. de Moor JS, Dowling EC, Ekwueme DU, et al. Employment Implications of Informal Cancer Caregiving. J Cancer Surviv. 2017;11(1):48–57.
13. Balfe M, Butow P, O'Sullivan E, Gooberman-Hill R, Timmons A, Sharp L. The Financial Impact of Head and Neck Cancer Caregiving: a Qualitative Study. Psychooncology. 2016;25(12):1441–7.
14. Gott M, Allen R, Moeke-Maxwell T, Gardiner C, Robinson J. 'No Matter What the Cost': A Qualitative Study of the Financial Costs Faced by Family and Whanau Spouse-Caregivers Within a Palliative Care Context. Palliat Med. 2015;29(6):518–28.
15. Hanly P, Ceilleachair AO, Skally M, et al. How Much Does it Cost to Care for Survivors of Colorectal Cancer? Spouse-Caregiver's Time, Travel, and Out-of-Pocket Costs. Support Care Cancer. 2013;21(9):2583–92.
16. Van Houtven CH, Ramsey SD, Hornbrook MC, Atienza AA, van Ryn M. Economic Burden for Informal Spouse-Caregivers of Lung and Colorectal Cancer Patients. Oncologist. 2010;15(8):883–93.
17. Kent EE, Rowland JH, Northouse L, et al. Caring for Spouse-Caregivers and Patients: Research and Clinical Priorities for Informal Cancer Caregiving. Cancer. 2016;122(13):1987–95.
18. Romito F, Goldzweig G, Cormico C, Hagedoorn M, Andersen BL. Informal Caregiving for Cancer Patients. Cancer. 2013;119(Suppl 11):2160–9.

19. Hanratty B, Holland P, Jacoby A, Whitehead M. Financial Stress and Strain Associated with Terminal Cancer- a Review of the Evidence. Palliat Med. 2007;21(7):595–607.
20. Bradley SE, Sherwood PR, Kuo J, et al. perceptions of Economic Hardship and Emotional Health in a Pilot Sample of Family Spouse-Caregivers. J Neurooncol. 2009;93(3):333–42.
21. Yun YH, Rhee YS, Kang IO, et al. Economic Burdens and Quality of Life of Family Spouse-Caregivers of Cancer Patients. Oncology. 2005;68(2–3):107–14.
22. Ankuda CK, Masut DT, Kabeto MU, McCammon RJ, Langa KM, Levine DA. Association Between Spousal Spouse-Caregiver Well-Being and Care Recipient Healthcare Expenditures. J Am Geriatr Soc. 2017.
23. The United States Census Bureau. The Population 65 Years and Older in the United States: 2016. 2016; https://www.census.gov/content/dam/Census/library/publications/2018/acs/ACS-38.pdf. Accessed May 23, 2019.
24. Langer S, Lehane C, Yi J. Patient and Spouse-Caregiver Adjustment to Hematopoietic Stem Cell Transplantation: a Systematic Review of Dyad-Based Studies. Curr Hematol Malig Rep; 2017.
25. Badr H, Acitelli LK. Re-thinking Dyadic Coping in the Context of Chronic Illness. Curr Opin Psychol. 2017;13:44–8.
26. Tucker-Seeley RD, Yabroff KR. Minimizing the “Financial Toxicity” Associated with Cancer Care: Advancing the Research Agenda. J Natl Cancer Inst. 2016;208(5).
27. Tucker-Seeley RD, Thorpe RJ. Material-Psychosocial-Behavioral Aspects of Financial Hardship: A Conceptual Model for Cancer Prevention. Gerontologist. 2019;59(Supplement_1):88–93.
28. Association of Community Cancer Centers. Trends in Cancer Programs. 2016; https://www.accc-cancer.org/surveys/pdf/Trends-in-Cancer-Programs-2016.pdf. Accessed Sept 28, 2017.
29. Sherman DE. Transforming Practices Through the Oncology Care Model: Financial toxicity and Counseling. J Oncol Pract. 2017;13(8):519–22.
30. Yezefski T, Steelquist J, Watabayashi K, Sherman D, Shankaran V. Impact of Trained Oncology Financial Navigators on Patient Out-of-Pocket Spending. Am J Manag Care. 2018;24(5 Suppl):74–9.
31. Shankaran V, Linden H, Steelquist J, et al. Development of a Financial Literacy Course for Patients with Newly Diagnosed Cancer. Am J Managed Care. 2017;23(3 Suppl):58–64.
32. Shankaran V, Leahy T, Steelquist J, et al. Pilot Feasibility Study of an Oncology Financial Navigation Program. J Oncol Pract. 2018;14(2):e122–9.
33. Watabayashi K, Steelquist J, Overstreet KA, Leahy A, Bradshaw E, Gallagher KD, Balch AJ, Lobb R, Lavell L, Linden H, Ramsey SD, Shankaran V. A Pilot Study of a Comprehensive Financial Navigation Program in Patients With Cancer and Caregivers. J Natl Compr Canc Netw. 2020 Oct 1;18(10):1366–1373.
34. Rocque GB, Pisu M, Jackson BE, et al. Resource Use and Medicare Costs During Lay Navigation for Geriatric Patients With Cancer. JAMA Oncol. 2017;3(6):817–25.

35. de Souza JA, Yap BJ, Hlubocky FJ, et al. The development of a financial toxicity patient-reported outcome in cancer: The COST measure. Cancer. 2014;120(20):3245–53.
36. de Souza JA, Yap BJ, Wroblewski K, et al. Measuring financial toxicity as a clinically relevant patient reported outcome: The validation of the COmprehensive Score for financial Toxicity (COST). Cancer. 2017;123(3):476–84.
37. Sullivan PW, Ghushchyan V. Preference-Based. EQ-5D index scores for chronic conditions in the United States. Med Decis Making. 2006;26(4):410–20.
38. Sullivan PW, Ghushchyan V. Mapping the EQ-5D index from the SF-12: US general population preferences in a nationally representative sample. Med Decis Making. 2006;26(4):401–9.
39. The City of Hope Quality of Life Family Version. Accessed February 15. 2022 at https://prc.coh.org/QOL-Family.pdf.
40. Shankaran V, Unger JM, Darke AK, et al. S1417CD: A Prospective Multicenter Cooperative Group-Led Study of Financial Hardship in Metastatic Colorectal Cancer Patients. J Natl Cancer Inst. 2022. https://doi.org/10.1093/jnci/djab210. epub ahead of print.
41. Basch E, Deal AM, Dueck AC. et. Overall Survival Results of a Trial Assessing Patient-Reported Outcomes for Symptom Monitoring During Routine Cancer Treatment. JAMA. 2017.
42. Basch E, Wood WA, Schrag D, et al. Feasibility and clinical impact of sharing patient-reported symptom toxicities and performance status with clinical investigators during a phase 2 cancer treatment trial. Clin Trials. 2016;13(3):331–7.
43. Mariotto AB, Etzioni R, Hurlbert M, Penberthy L, Mayer M. Estimation of the Number of Women Living With Metastatic Breast Cancer in the United States. Cancer Epidemiol Biomarkers Prev. 2017;26(6):809–15.
44. Venook AP, Niedzwiecki D, Lenz HJ, et al. Effect of First-Line Chemotherapy Combined With Cetuximab or Bevacizumab on Overall Survival in Patients With KRAS Wild-Type Advanced or Metastatic Colorectal Cancer: A Randomized Clinical Trial. JAMA. 2017;317(23):2392–401.
45. Brevoort K, Grimm P, Kambara M. Data Point: Credit Invisibles. 2015; http://files.consumerfinance.gov/f/201505_cfpb_data-point-credit-invisibles.pdf.Accessed September 15, 2017.
46. Hasler A, Lusardi A, Oggero N. Financial Fragility in the US: Evidence and Implications. *Global Financial Literacy Excellence Center (GFLEC) Working Paper Series.* 2018;WP 2018(1):1–49.

Figures

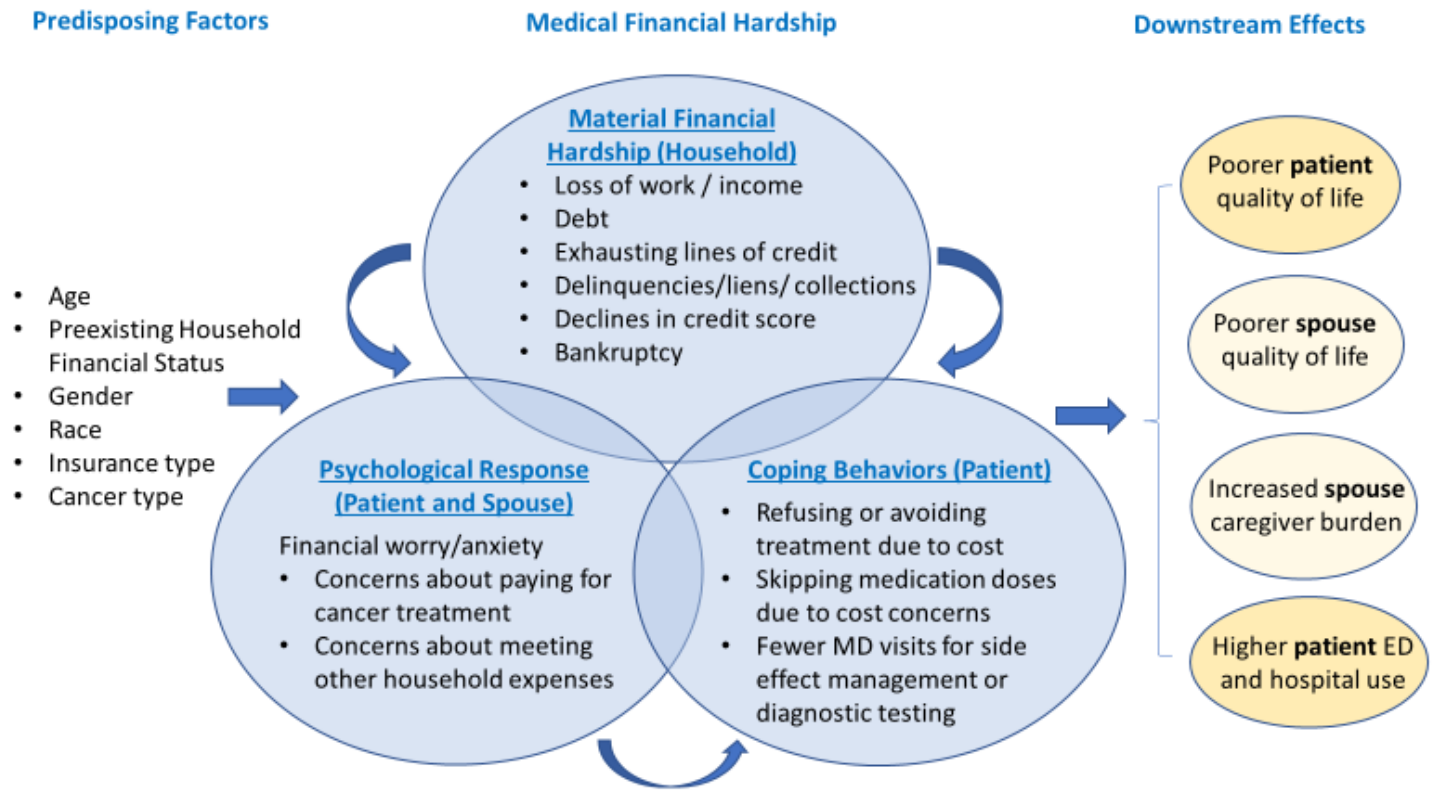

Figure 1

Conceptual Framework for Medical Financial Hardship and Potential Downstream Effects

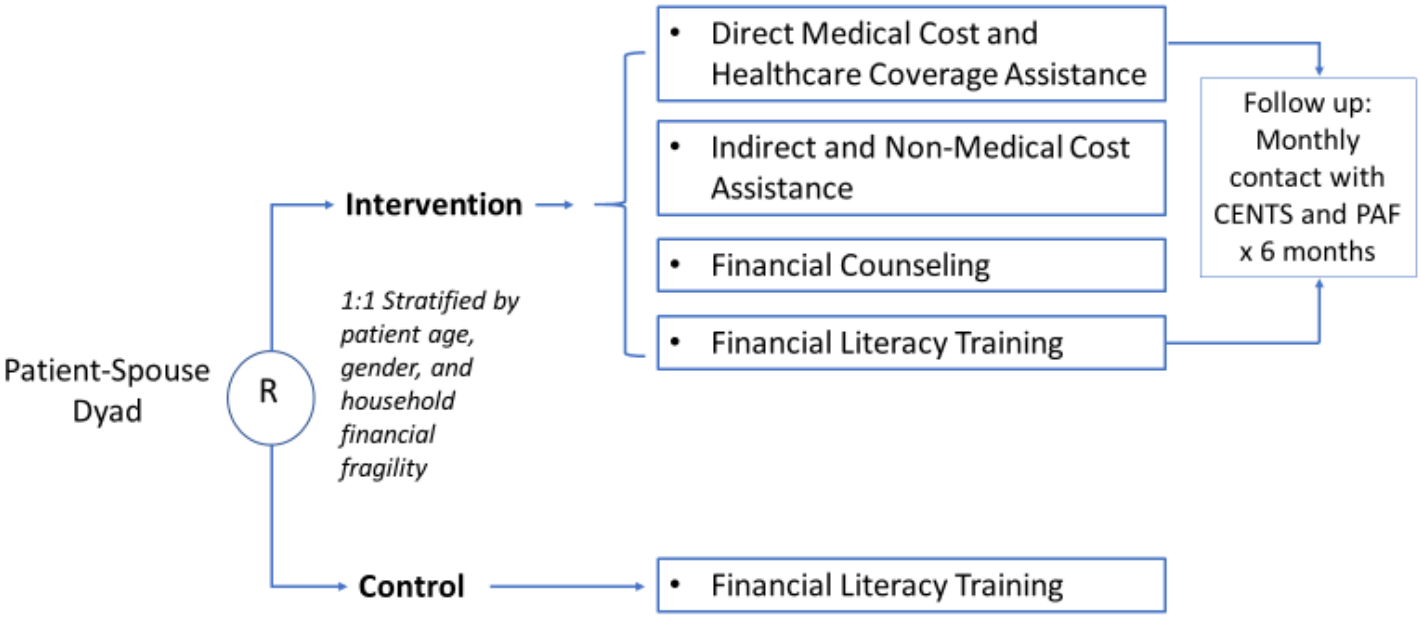

Figure 2

Figure 1: Trial schema

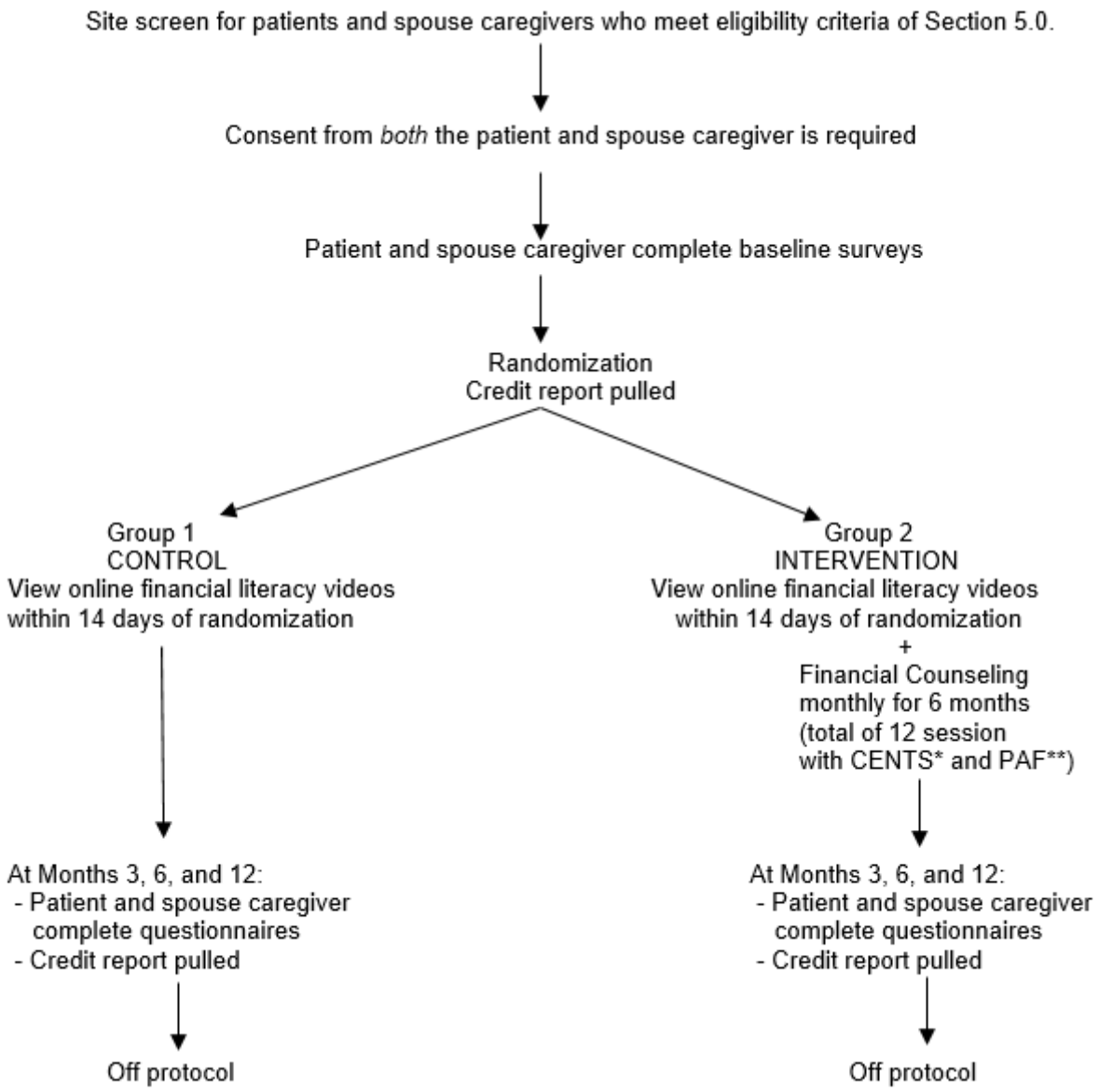

Figure 3

Figure 2: Study Flow