**Enhanced Assistance during Radiotherapy for unmet essential Needs (EARN): a single center hybrid type 1 efficacy-implementation study**

*Short title: EARN*

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# PROTOCOL SUMMARY

## Synopsis

|  |  |
| --- | --- |
| **Title:** | Enhanced Assistance during Radiotherapy for unmet essential Needs (EARN): a single center hybrid type 1 efficacy-implementation study |
| **Study Description:** | This is a non-randomized prospective sequential two-arm study comparing delay-free completion of radiotherapy before and after implementation of an enhanced assistance intervention for patients with unmet essential needs undergoing >10 fractions of radiotherapy. |
| **Objectives:** | The primary objective is to compare proportions of delay-free completion of radiotherapy before and after implementation of an enhanced assistance intervention for patients undergoing radiotherapy with unmet essential needs. Key secondary objectives include comparing changes in patient-reported quality of life and comparing differences in reimbursement for completed radiotherapy fractions and costs of the enhanced assistance intervention before and after implementation of enhanced assistance. We also will be evaluating implementation process measures. |
| **Outcomes :** | Primary Outcome: Delay-free completion of radiotherapy, a composite binary endpoint defined as completing all prescribed fractions of radiotherapy and delaying <5 fractions.  Secondary Outcome: Patient-reported quality of life measures include global quality of life (PROMIS-10), financial well-being (FACIT-COST, additional questions from ECOG-ACRIN EAQ222CD), and physical, social, emotional, and functional well-being (FACT-G).  Differences in reimbursement (total technical and professional reimbursement) and intervention costs (combined monetary assistance provided and social worker costs). |
| **Study group:** | Eligible patients are adults >18 years with cancer who have a prescription for radiotherapy > 10 fractions, a referral to social work for an unmet essential need, and at least one ‘high-risk’ factor for radiotherapy noncompletion. 120 total patients will be enrolled. |
| **Phase:** | 2 |
| **Description of Sites/Facilities Enrolling Participants:** | This is a single-center study enrolling patients from the Department of Radiation Oncology at Barnes-Jewish Hospital / Siteman Cancer Center (main campus). |
| **Description of Study Intervention:** | Patients in the post-implementation arm will receive standard assistance in addition to enhanced assistance targeted to unmet food, transportation, and housing/utility needs. Enhanced assistance includes broader eligibility criteria as well as a higher limit of assistance compared to standard assistance. |
| **Study Duration:** | 26 months. |
| **Participant Duration:** | 4 months. |

## Schema

Pre-enrollment: Patients with cancer with a new prescription for a definitive course of radiotherapy > 10 fractions, an unmet essential need, a high-risk of radiotherapy noncompletion, and referral to a social worker.

Obtain informed consent and baseline PROs.

N = 120

Implementation training (months 0-1 after patient #40 enrolled):

Social worker training for enhanced assistance for unmet essential needs

**Final Assessments**

Primary outcome: DFC; 2ary: PROs, spending and revenue.

**See also Section 1.3, Schedule of Activities**

## Schedule of Activities (SoA)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Procedures** | **Screening** | **Baseline / Pre-radiotherapy (on or before day 1 of radiotherapy)12** | **Radiotherapy** | **Completion of radiotherapy (+/- 7 days)** |
| Meet with clinical team to discuss radiotherapy | X |  |  |  |
| Performance status | X |  |  |  |
| Essential needs screening1 | X |  |  |  |
| Social work evaluation2 | X |  |  |  |
| Assess for eligibility2 | X |  |  |  |
| Informed consent3 | X |  |  |  |
| Questionnaires4 |  | X3 |  | X5 |
| Targeted enhanced financial assistance |  | X7 | X7 |  |
| Collection of radiotherapy treatment information8 |  | X |  |  |
| Collection of essential needs and assistance provided9 |  |  |  | X |
| Collection of medical-record based primary10 and secondary endpoints11 |  |  |  | X |

1In general, the essential needs screening includes a tool in the electronic medical record (or paper equivalent) administered during a visit with the clinical team by the nurse coordinator or designated alternative. If not performed at that time, the screening form can be completed at the time of social work evaluation or on the day of informed consent.

2In general, eligibility for social work evaluation referral is determined by a member of the clinic team using a predefined set of criteria based on patient responses to screening (i.e., positive screen for food, housing, or transportation insecurity) and any request for assistance made by the patient. After social work evaluation, social workers will contact study team about patients who may require additional financial support beyond standard assistance for unmet essential need. Determination about study eligibility will be made using information from essential needs screening, medical record, and social worker evaluation.

3Informed consent and baseline questionnaires can be completed on the same day, ideally prior to the start of radiotherapy. Baseline questionnaires

4PROMIS-10, FACT-G (Version 4), FACIT-COST, and additional questions from ECOG-ACRIN EAQ222CD. Responses will be recorded in REDCap.

5+/-1 week. While in-person completion is recommended, questionnaires can be administered over the phone if needed.

7Assistance can be provided as early as 2 weeks before radiotherapy as long as baseline questionnaires have been administered. Study assistance (enhanced) can be administered through the final day of radiotherapy +/- 1 week.

8Treatment site, number of fractions planned, modality.

9Provided by social work team and transcribed into RedCap.

10Number of missed fractions, duration of radiotherapy, radiotherapy completion status.

11Acute toxicities, weight loss, emergency department visits and hospitalizations, pain scores, and missed on-treatment visits (OTVs) during radiotherapy.

12A patient who has already initiated radiotherapy may with a newly identified unmet need is eligible if: (1) baseline survey can be completed before the patient has ≤10 fractions remaining and (2) patient will start receiving assistance for unmet needs before the patient has ≤10 fractions remaining. Only fractions planned after the patient signs informed consent will be considered for the primary outcome.

# INTRODUCTION

## Study Rationale

Patients with cancer often require multiple weeks of daily radiotherapy sessions as part of a curative-intent treatment course. Unmet essential needs, such as food insecurity, housing insecurity, and transportation insecurity are associated with access to care. Providing financial assistance for unmet needs can decrease delays in radiotherapy, which are associated with worse cancer control and survival. However, prospective studies evaluating interventions addressing multiple domains of unmet essential needs are lacking. Our objective was to compare the proportion of delay-free completion of radiotherapy before and after implementation of an enhanced essential needs intervention among patients undergoing definitive courses of radiotherapy who have unmet essential needs and are at high risk of treatment noncompletion in a hybrid type 1 efficacy-implementation prospective clinical study.

## Background

Over 50% of patients with cancer require radiotherapy,(1) which often involves daily treatment for 5-9 weeks. Social risks include non-medical factors that influence health; essential needs such as food, housing, and transportation insecurity social risk factors that can interfere with timely treatment.(2–5) Food insecurity, or inconsistent access to enough food for a healthy life, is associated with reduced adherence to therapy.(3,6,7) Transportation insecurity, the lack of safe and timely transportation, can lead to patients delaying/missing oncologic care.(2,8,9) Finally, housing insecurity—lack of safe and affordable housing—is also associated with decreased likelihood of timely treatment and increased cancer mortality.(4,5,10) Since lack of timely completion of radiotherapy—for example, missing/rescheduling ≥5 treatments—worsens disease control and survival,(11–15) these factors may also contribute to worse oncologic outcomes through impaired treatment access.(9,10,16) Importantly, given that racial and ethnic minority and other disadvantaged populations experience documented disparities in access to treatment and cancer outcomes due to social risks,(17,18) interventions addressing unmet essential needs may reduce disparities in access to care and survival.

At our institution, clinical and demographic factors associated with decreased odds of timely radiotherapy completion (missing ≥5 treatments or not completing prescribed course) include high neighborhood disadvantage (social deprivation index > 80, OR 0.64, 95% CI = 0.52-0.80, *P*<.001), Medicaid (OR 0.58, 0.45-0.75, *P*<.001), increasing number of treatments, and female pelvis cancer [particularly cervical cancer, associated with lower socioeconomic status] (OR 0.63, 0.43-0.92, *P*=.016) (2023 ASCO Quality Care Symposium). For these at-risk patients, timely radiotherapy completion was achieved in 83.3% vs. 93.8% for all patients. Since these factors are related to social determinants of health, unmet essential needs may contribute substantially to the observed differences in timely treatment completion.

Small studies have evaluated rideshare interventions to address transportation insecurity among radiotherapy recipients, suggesting that these interventions may increase radiotherapy completion percentages by 10-20% (absolute changes; ≥50% relative change) and be financially advantageous.(19–21) One prospective randomized study evaluated food insecurity interventions among patients with cancer, which demonstrated improvements in treatment completion (>10% absolute improvement) and patient-reported quality of life.(7) Leveraging patient navigators, who can assist with unmet essential needs and coordinate logistics of a complicated cancer care process, has also shown some promise. A limited number of studies have examined whether cancer treatment timeliness and adherence can be improved with patient navigators, with mixed results.(22–29) Of these, the only prospective randomized study failed to demonstrate improved treatment adherence, though patient navigators primarily provided education/motivation and assisted with logistical considerations such as transportation. However, since unmet essential needs commonly co-occur, interventions targeting just one unmet need may have limited efficacy.(30–32) Retrospective data suggest that providing financial assistance for possibly multiple unmet essential needs can decrease the proportion of missed radiotherapy appointments, particularly for higher amounts of financial assistance.(33) Prospective studies that test the impact of interventions simultaneously addressing multiple unmet essential needs on cancer treatment adherence are needed.(30–32) As such, we will conduct a prospective study comparing delay-free radiotherapy before and after implementation of an enhanced essential needs for unmet food, housing, and/or transportation needs among patients undergoing definitive radiotherapy who are at high risk of treatment noncompletion.

This study may have implications for institutional practice standards and national policies. Particularly if our intervention targeting unmet essential needs can increase rates of delay-free radiotherapy completion in a multi-center randomized study, institutions nationwide would have a compelling reason to allocate additional funds for unmet essential needs and employ adequate numbers of social workers. Payors may also be motivated to further develop incentives for such services. Finally, given that treatment adherence improves cancer outcomes, these interventions that improve delay-free radiotherapy completion among socioeconomically vulnerable populations may improve cancer outcomes and decrease well-documented disparities in outcomes by race, ethnicity, and place of residence.(17)

## Risk/Benefit Assessment

The risks of the study include feeling uncomfortable about questions asked in the quality of life questionnaires and the risk of breach of confidentiality. Study participants are free to skip any questions, and the research team will seek to maintain data confidentiality. Possible benefits of the study, in addition to gaining knowledge about the efficacy of the enhanced assistance intervention and insights into its implementability, include increased financial assistance for unmet essential needs and possibly higher probability of higher delay-free completion of radiotherapy for some patients.

# STUDY DESIGN

## Overall Design

This is a single-center hybrid type 1 efficacy-implementation study with a pre and post intervention implementation prospective clinical study. Eligible patients include those who are given a new prescription of radiotherapy of >10 fractions, who indicate an unmet essential need on social risks screening and agree to a referral to social work, and who are defined to be at a higher risk of treatment noncompletion. The study intervention consists of increased assistance for identified unmet essential needs. Patients who are enrolled in the study will be assigned to the enhanced assistance arm based on the date of enrollment relative to the pre- or post-implementation period. Forty patients will be enrolled in the pre-implementation period. The post-implementation period will begin a minimum of 1 month after last patient is enrolled in the pre-implementation period to enable training staff prior to enhanced assistance implementation. The primary outcome is delay-free completion of radiotherapy, a composite endpoint defined as completing all prescribed fractions of radiotherapy and delaying fewer than 5 fractions, which delay is associated with cancer outcomes. The study is powered to detect superior delay-free radiotherapy completion in the enhanced assistance arm relative to the standard assistance arm.

# OBJECTIVES

## Primary Objective

To compare proportions of delay-free completion of radiotherapy before and after implementation of an enhanced assistance intervention for patients undergoing radiotherapy with unmet essential needs.

### Primary OBJECTIVE

Delay-free completion of radiotherapy is a composite endpoint defined as (1) completing all fractions of radiotherapy AND (2) delaying fewer than 5 fractions. Patients who do not initiate a recommended course of radiotherapy will be considered as not completing radiotherapy; however, in the rare case where the patient’s radiotherapy treatment recommendation changes by their physician(s) to no longer include radiotherapy, such patients will be dropped from the study and excluded from analyses.

### Justification for the Primary OBJECTIVE

Incomplete courses of radiotherapy involve subtherapeutic radiation doses and are associated with increased risk of cancer recurrence. Similarly, excessively prolonged treatment courses are associated with increased risk of cancer recurrence and death; delays of 5 or days are considered clinically significant as they are associated with worse cancer outcomes, particularly for cervical and head and neck cancers. Hence, we utilize a composite endpoint consisting of treatment completion and clinically significant delays.

## Secondary ObjectiveS

1. To compare changes in patient-reported financial (FACIT-COST, additional questions from ECOG-ACRIN EAQ222CD), functional, emotional, social, and physical (PROMIS-10, FACT-G) well-being before and after implementation of an enhanced assistance intervention for patients undergoing radiotherapy with unmet essential needs.
2. Compare the difference in total reimbursements for completed radiotherapy treatments and costs of delivery of social assistance services before and after implementation of the enhanced assistance intervention.
3. Compare types of reported unmet needs and types and amounts of assistance provided before and after implementation of the enhanced assistance intervention.
4. To evaluate implementation process measures (adherence to study intervention of enhanced assistance, consistency of assistance provided by social worker, timing of assistance provided, characteristics of study participants compared to other patients referred to social work and patients who report unmet needs but are not referred to social work, qualitative assessments of social workers, total numbers of patients per week by social work, time spent by social worker per patient) before and after implementation of the enhanced assistance intervention.

### Secondary OBJECTIVEs

1. General health status QoL will be determined using the PROMIS-10 survey.(34) Further physical, social, emotional, and functional well-being will be assessed using the Functional Assessment of Cancer Therapy general form (FACT-G, Version 4).(35) Financial toxicity will be assessed using FACIT-COST (psychosocial domain) and survey questions from ECOG-ACRIN EAQ222CD (material hardship and care disruption domains).(36) These instruments will be administered at baseline (prior to or on the day of the start of radiotherapy) and at the completion of radiotherapy (+/- 7 days). Surveys should be completed within approximately 20 minutes (per survey).
2. Another secondary endpoint includes the difference between the cost of the unmet essential needs intervention and the potentially increased revenue from potentially increased rates of completed courses of radiotherapy. As such, we will document the amounts of the assistance provided (in dollars), including the category of assistance, costs of the social worker’s time, revenue information (in dollars) from the delivered radiotherapy treatments, and the number of noncompleted treatments.
3. Types of unmet essential needs will be based on screening as well as any additional needs identified by the social worker during their formal evaluation and will be grouped as food insecurity, transportation insecurity, housing insecurity, utility need, or other financial insecurity. Type of assistance provided will be similarly grouped. Monetary amounts of assistance per category will be recorded.
4. During months 1 and 6 (or final month of each period, if accrual to an arm is reached in <6 months) during both the pre- and post-implementation study periods, several process measures will be evaluated. One week of data from the social workers’ workload will be obtained including the number of patients seen, number of encounters, time spent per patient, and time spent per encounter. We will also conduct qualitative interviews periods with social workers and randomly selected participants to understand the acceptability and feasibility of the enhanced assistance intervention. Adherence to study intervention will be assessed by evaluating whether the amount and types of assistance provided extends beyond the guidelines for standard assistance (up to $2000 cap in additional assistance), and will be reported as % of cases. Types and amounts of assistance will be collected as above along with timing of assistance provided (relative to day 1 of radiotherapy) and will be compared across social workers. Characteristics of study participants (sex, age, race, insurance status, ZIP code social deprivation index, cancer site, radiotherapy regimen, and types unmet essential needs) will be compared to other patients with unmet essential needs who received social work referral but did not participate in the study and those who did not receive a social work referral.

### Justification for Secondary OBJECTIVEs

1. Screening for essential needs can improve quality of life.(37) Better addressing unmet essential needs, which may decrease stress driven by financial concerns and enable better nutrition or transportation or living situation in some individuals, may further improve quality of life. For this study, we utilize patient-reported quality of life endpoints include questionnaires tested in similar studies.(36,38)
2. Assessment of cost of intervention delivery versus potential increased reimbursement from radiotherapy completion provides evidence for institutional resource allocation for sustainability of the enhanced assistance intervention.
3. As part of evaluating the implementation process, it is important to understand the extent of additional assistance that is being provided. The types of assistance and correlations to previously reported needs will also be helpful in determining how forthcoming patients are during screening for essential needs and in assessing whether the enhanced assistance intervention needs to be modified.
4. Routine evaluation of the implementation of the enhanced assistance intervention is crucial to ensure that adoption is appropriate, which could have impacts on our primary outcome. Additionally, issues causing poor study intervention compliance or adverse workflow consequences affecting patient care (e.g., overburdened social worker due to increased workload) need to be addressed in a timely manner.

## Tertiary/Exploratory Objective

Compare acute toxicity, weight loss, emergency department visits and hospitalizations, pain scores, and missed weekly check-in visits during radiotherapy before and after implementation of the enhanced assistance intervention.

Explore associations between delay-free completion of radiotherapy and baseline sociodemographic factors, responses to essential needs screening, and responses to quality of life surveys.

### Tertiary/Exploratory OBJECTIVE(s)

Acute toxicity will be assessed by the treating physician during standard of care weekly visits during radiotherapy and will be extracted from the medical record retrospectively. Pain scores will be reported by patients and recorded by nurses during standard of care weekly visits during radiotherapy and will be extracted from the medical record retrospectively. Similarly, weight loss will be assessed relative to the patient’s pre-treatment weight (at time of consultation) compared to weight recorded by the nurse at each weekly visit during radiotherapy; the maximum % weight loss relative to baseline during radiotherapy will be extracted retrospectively. The number of emergency department visits and hospitalizations will also be retrospectively extracted from the medical record.

Definitions of the baseline sociodemographic factors, baseline essential needs screening responses, and responses to the patient-reported quality of life questionnaires are based on previously collected/defined information.

### Justification for Tertiary OBJECTIVE(s)

Acute toxicities, such as pain-related symptoms, nausea/vomiting, etc., can be affected by access to medications, which may be related to the assistance provided. Acute toxicities may also influence some patients’ decisions to discontinue radiotherapy. Collection of weight loss, which may be impacted by acute toxicities, and pain scores will be done for similar reasons. Downstream utilization measures such as emergency department visits and hospitalizations, which may be avoided with consistent outpatient management, may also be improved with assistance-mediated access to care.

The patients at highest risk of noncompletion or delayed courses of radiotherapy have not been clearly defined by essential needs screening responses or quality of life. We suspect that some of these factors may contribute to impaired access to care, in addition to known associations with socioeconomic status. Better understanding of the factors associated with impaired access will be helpful in tailoring additional interventions to specific populations with the greatest needs of assistance.

# STUDY GROUP

## Inclusion Criteria

In order to be eligible to participate in this study, an individual must meet all the following criteria:

1. Male or female, age > 18 years.
2. Have a new prescription for a course of curative-intent (neoadjuvant, definitive, or postoperative) radiotherapy consisting of greater than 10 fractions.
3. Indicate at least 1 unmet essential need, including food insecurity, transportation insecurity, housing instability, utility needs, childcare needs, or other financial insecurity.
4. Accept referral to social work
5. Have unmet essential needs that will not be able to be fully addressed by standard assistance, as determined by the assigned social worker.

Note that a patient who has already initiated radiotherapy may with a newly identified unmet need is eligible if: (1) baseline survey can be completed before the patient has ≤10 fractions remaining and (2) patient will start receiving assistance for unmet needs before the patient has ≤10 fractions remaining. In such a case, only fractions planned after the patient signs informed consent will be considered for the primary outcome.

## Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study:

1. A patient who is receiving financial assistance through a social worker at the time of study entry or within the prior 3 months.
2. The patient is not planned to undergo radiotherapy simulation for more than 1 month (though the patient may become eligible once the date of simulation is within 1 month).
3. The patient is admitted to the hospital and is not expected to undergo >10 fractions of radiotherapy as an outpatient. Patients admitted to a rehabilitation center or skilled nursing facility who require transportation assistance to continue radiotherapy are considered transportation-insecure and are eligible.
4. A patient who requires lodging in/near St. Louis to avoid excessive daily transportation will not be eligible unless they have other (non-transportation- or lodging-related) essential needs. However, patients who utilize local lodging for treatments are still eligible for the study if they require financial assistance for rent/mortgage/utilities.
5. The patient is being treated for anaplastic thyroid cancer.

## Strategies for Recruitment

Patients will be screened for unmet essential needs during intake as part of an outpatient consultation visit, which is part of a standard clinical workflow and overseen by a nurse coordinator. Patients with unmet needs are offered referral to a social worker. Potentially eligible patients will be identified by a social worker, who will inform them about the option of the study. Approximately 70 patients per year are expected to be eligible for the study based on estimated numbers of patients who establish care with a social worker (110 patients per year who undergo >10 fractions of radiotherapy), with 75% meeting eligibility criteria and 90% consenting to the study. As such, accounting for 1 months washout between the pre- and post-implementation aspects of the study, we anticipate recruitment will occur over 22 months.

# STUDY INTERVENTION

## Study Intervention(s)

During standard of care radiotherapy and up to two weeks prior to a scheduled simulation, study participants will either receive standard or enhanced financial assistance for unmet essential needs (see Table below)

**TABLE: Description and Examples of Enhanced Assistance Intervention**

|  |  |  |
| --- | --- | --- |
|  | **Standard assistance** | **Enhanced assistance** |
| **Eligibility restrictions** | Income ≤ 200% federal poverty level. | No household income restrictions. |
| **Food insecurity resources provided** | Food items in clinic, voucher, referral for community resources *(voucher & referral limited to select patients based on where they live and cancer type).* | Grocery store gift cards, vouchers for groceries, food delivery services, paid transportation to community food banks beyond standard assistance. |
| **Transportation insecurity resources provided** | Gas card, taxi/van arrangement, arranging rides through insurance company *(note ambulance from nursing or rehabilitation facility not covered by insurance and not routinely permitted per institutional guidelines).* | Rideshare vouchers, taxi/van vouchers, other transportation arrangements for transportation needs not covered by insurance or current institution guidelines. |
| **Housing insecurity resources provided** | Rent/utilities/etc. payment (institutional limit of one-time payment). Partial lodging assistance for patient traveling from out of town (limited to patients traveling >75 miles). | Additional month(s) of rent/utilities/etc. payment(s) during radiotherapy beyond standard assistance. |

## Measures to Minimize Bias

This is a nonrandomized study. We include a pre-intervention implementation period to minimize the risks of confounding due to patients being enrolled in a clinical trial, which involves increased monitoring from clinical study coordinators, which may also affect delay-free completion of radiotherapy. The pre- and post-implementation design will reduce the effects of patient self- selection bias to accept referral, though there is the potential for temporal factors to affect delay-free completion proportions. In a separate study, we also will retrospectively collect data for patients who indicate social risk factors / unmet basic needs who do not desire a social work referral, we will conduct a planned sensitivity analysis modeling the temporal trends in this population relative to the difference between the pre- and post-implementation arms using a difference-in-differences design.

## Concomitant Therapy

Patients will undergo standard of care radiotherapy per the treating radiation oncologist. Patients may also receive concurrent systemic therapy at the discretion of the treating medical/gynecologic oncologist (if applicable). Data regarding the intended treatment site, radiotherapy modality, radiotherapy dose and fractionation, and concurrent chemotherapy will be collected at study entry.

# EFFICACY AND SAFETY ASSESSMENTS

## Outcome (survival, quality of life, etc.) Assessments

Patient eligibility will be based on (1) age, (2) radiotherapy prescription, (3) responses to screening for essential needs, and a (4) social worker assessment. In the screening process, items 1-3 may be determined from existing data in the medical record by study team members. Item 4 are disclosed to social workers and not recorded in the medical record.

**The primary and secondary endpoints in the study include:**

1. **Delay-free completion of radiotherapy.** Radiotherapy completion information, consisting of number of fractions completed, duration of radiotherapy (days from first to final day of radiotherapy), number of delayed fractions, completion status (yes/no; lack of initiation of a recommended course of radiotherapy will be considered noncomplete) will be collected from the medical record after radiotherapy completion.
2. **Patient-reported quality of life.** Patient-reported outcomes for financial (FACIT-COST, additional questions from ECOG-ACRIN EAQ222CD), functional, emotional, social, and physical (PROMIS-10, FACT-G) well-being will be collected prior to (or on the first day of) radiotherapy initiation and at the completion of radiotherapy (+/- 7 days from the final day of radiotherapy).
3. **Difference in reimbursement and costs of the essential needs intervention.** Costs of the enhanced assistance intervention, consisting of study financial assistance provided and estimated social worker time will be collected from the social workers. Reimbursement information about completed radiotherapy fractions will be collected from department and institutional billing offices at the time of study completion.
4. **Implementation process measures.** See section 4.2 (items 3 and 4).

**Timeline of assessments:**

1. **Baseline.** Patient-reported quality of life will be obtained via surveys administered between the time of informed consent and the first day of radiotherapy.
2. **Completion of radiotherapy.** Within 1 week of completion of radiotherapy, patient-reported quality of life will again be obtained.
3. **After completion of radiotherapy:** delay-free radiotherapy completion, reimbursement, cost, and other outcomes will be extracted from the medical record.
4. **During months 1 and 6 of the post-implementation period.** Implementation process measures will be obtained.

**Standard of care procedures** (not related to study intervention but will occur while patient is enrolled in the study):

Standard of care procedures that will occur during the study period include radiotherapy simulation (may involve making of patient immobilization device such as an alpha cradle or plastic face mask, CT and/or MRI with and/or without contrast) and delivery of radiotherapy (will also typically include daily onboard imaging with kV x-rays and/or cone-beam CT), which will be delivered at the discretion of the treating radiation oncologist. Concurrent systemic therapy may also be administered at the discretion of the patient’s treating medical oncologist (or gynecologic oncologist if the patient has a gynecologic malignancy). Labs during concurrent chemoradiotherapy will be obtained at the discretion of the treating medical (or gynecologic) oncologist.

Any results of standard of care tests to be provided to patients will be at the discretion of the treating oncologists; no results from study interventions or procedures from this study will be provided to patients.

## Safety and Other Assessments

At baseline, patients will have their performance status (Karnofsky and/or ECOG) assessed by their treating radiation oncologist. Karnofsky (or Karnofsky-equivalent score based on recorded ECOG score as assessed by the investigators) will be collected.

Details of the patients’ radiotherapy treatment recommendation will be recorded as follows:

* Modality: IMRT/VMAT without brachytherapy, IMRT/VMAT with brachytherapy, 3D conformal, proton.
* Dose: (total dose in Gy)
* Fractions: (total number of planned fractions; if brachytherapy included, list numbers of both external beam and brachytherapy fractions)
* Treatment site: CNS, head and neck, thoracic (including esophagus), abdominal, pelvis, bone/extremity

A number of process measures will be collected as follows:

* Essential needs identified during essential needs screening: food insecurity, transportation insecurity, housing insecurity / utility needs, other financial insecurity
* Other essential needs identified by social worker: food insecurity, transportation insecurity, housing insecurity / utility needs, other financial insecurity, no additional needs
* Type of assistance provided: food, transportation, housing/utility, other
* Amount of assistance provided: (dollar amount for each category of assistance)

To evaluate the implementation process, several measures will be obtained during months 1 and 6 (or final month of the period, if accrual to the arm is reached in <6 months) during the post-implementation study period. One week of data from the social workers’ workload will be obtained including the number of patients seen, number of encounters, time spent per patient, and time spent per encounter (this information will also be obtained at two points during the pre-implementation period to establish a baseline). We will also conduct qualitative interviews periods with social workers and randomly selected participants to understand the acceptability and feasibility of the enhanced assistance intervention. Adherence to study intervention will be assessed by evaluating whether the amount and types of assistance provided extends beyond the guidelines for standard assistance, and will be reported as % of cases. Types and amounts of assistance will be collected as above and will be compared across social workers. Characteristics of study participants (sex, age, race, insurance status, ZIP code social deprivation index, cancer site, radiotherapy regimen, and types unmet essential needs) will be compared to other patients with unmet essential needs who received social work referral but did not participate in the study and those who did not receive a social work referral.

Acute toxicity, weight loss, emergency department visits and hospitalizations, pain scores, and missed weekly check-in visits during radiotherapy will be obtained by review of the medical record.

# STUDY INTERVENTION NOT OR INCOMPLETELY PERFORMED AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

## Study Intervention Not or Incompletely Performed

If a patient’s physician recommends discontinuing (or not initiation radiotherapy, in the case that it has not yet been started), the patient will be removed from the study, no further data will be collected, and the patient will be excluded from final analyses (see **Section 8.2**). Patients who do not complete all questionnaires will still be included in the study, though efforts will be made by study team to ensure participants are given ample opportunities to complete the questionnaires in the designated time windows.

## Participant Discontinuation/Withdrawal from the Study

An investigator may discontinue or withdraw a participant from the study for the following reason:

* The treating radiation oncologist recommends NOT proceeding with radiotherapy (e.g., progression of disease identified at radiation treatment planning, warranting surgery or systemic therapy instead of radiotherapy).

Participants are free to withdraw from participation in the study at any time upon request.

The reason for participant discontinuation or withdrawal from the study will be recorded on the Case Report Form (CRF).

Data collected from participants who voluntarily withdraw will be included in the final analysis, though no further patient-reported outcomes will be obtained. Missing questionnaires or specific responses to the questionnaires will be imputed. Endpoints available from the medical record will be extracted.

Patients withdrawn from the study due to change in treatment recommendation will not be included in the final analysis.

## LosS to Follow-Up

Follow-up will continue until the last day of radiotherapy (+/- 7 days days for questionnaire completion). For purposes of the study, patients will be considered lost to follow-up if they do not complete the post-radiotherapy questionnaires and cannot be contacted for questionnaire completion within 1 week of radiotherapy completion. To minimize loss to follow-up, study coordinators will seek to obtain final questionnaires while the patient is in the radiation oncology department during the final week of their radiotherapy. Patients who are lost to follow-up due to early discontinuation of radiotherapy will be considered as having noncompletion of radiotherapy and their primary outcome data will be reported, though final questionnaires will be unavailable.

Patients who do not initiate radiotherapy within 3 months of study entry or who do not complete radiotherapy within 3 months of initiation of radiotherapy will be considered as having noncompletion of radiotherapy; final questionnaires in these patients are to be completed prior to the end of the 3 month period.

# STATISTICAL CONSIDERATIONS

## Executive Summary

This is a single-center hybrid type 1 efficacy-implementation study with a (nonrandomized) pre and post intervention implementation prospective clinical study. The study is powered to detect superior delay-free completion of radiotherapy in the post-intervention implementation arm. The study population includes cancer patients undergoing curative-intent radiotherapy with >10 fractions who are at high risk of treatment noncompletion and have unmet essential needs that are being addressed by a social worker. Patients will be followed until the completion of radiotherapy. The primary objective is to compare proportions of delay-free completion of radiotherapy before and after implementation of an enhanced assistance intervention for patients undergoing radiotherapy with unmet essential needs. Secondary objectives include estimating patient-reported quality-of-life measures, estimating the differences in reimbursement and intervention costs, and evaluating process measures.

## Statistical Hypotheses

* Primary Objective(s):

To compare proportions of delay-free completion of radiotherapy (completing all planned fractions and delaying <5 fractions) before and after implementation of an enhanced assistance intervention for patients undergoing radiotherapy with unmet essential needs. Compared to the null hypothesis of no difference, we hypothesize that delay-free completion of radiotherapy will increase from 83% to 92% following implementation of enhanced assistance.

* Secondary Objective(s):

To compare changes in patient-reported financial (FACIT-COST), functional, emotional, social, and physical (QLC-C30 global health status, FACT-G) well-being before and after implementation of an enhanced assistance intervention for patients undergoing radiotherapy with unmet essential needs. We hypothesize that financial and emotional well-being will improve from pre- to post-radiotherapy and that the improvement will be greater in the post- relative to the pre-implementation period.

To compare the difference in total reimbursements for completed radiotherapy treatments and costs of delivery of enhanced social assistance services before and after implementation of the enhanced assistance intervention. We hypothesize that total reimbursements will be greater than the costs of delivery of assistance and that the difference in reimbursements and costs will be greater after implementation of the enhanced assistance intervention.

Other secondary objectives including evaluating implementation process measures. No formal hypothesis testing will be performed for these endpoints.

## Sample Size Projections

Our primary outcome is delay-free completion (DFC) of radiotherapy, which is a binary composite endpoint. Higher values are better.

H0: DFCpost-implementation = DFCpre-implementation = 0.83

Ha: DFCpost-implementation > DFCpre-implementation

Based on institutional data from 2018-2022, the percentage of delay-free radiotherapy among patients likely eligible for the study who established with a social worker was 83%. This number is consistent with data for patients not receiving financial assistance reported in a retrospective UNC experience.(33) In recent retrospective series, the proportion of missed radiotherapy visits or percentage of noncompleted visits decreased on the order of 50% relative change or 5-20 percentage point absolute change with increased institutional financial and/or food and/or transportation assistance.(7,21,33) As such, we anticipate a similar degree of change and assume the percentage of delay-free radiotherapy will increase from 83% to 92%.

Under the aforementioned assumptions about proportion of DFC, we need to enroll 40 patients in the pre-implementation and 80 patients in the post-implementation arms to detect a 9% increase in the primary outcome with 80% power and α=15%. Note that we utilize a Bayesian analysis (see Appendix III), so α is not directly applicable. However, we tested the characteristics of our testing procedure in simulation studies to estimate the Type I error under the aforementioned null hypothesis and under other scenarios (Appendix III).

Due to minimal expected dropout rate due to the definition of the primary outcome, we will plan to enroll 40 patients in the pre-implementation arm and 80 patients in the post-implementation arm. In recent years, approximately 90 patients undergoing >10 fractions of radiotherapy see our social workers. Assuming a 25% increase due to improved essential needs screening (being implemented separately), 75% of whom will meet eligibility criteria, and 90% will sign consent for the study, approximately 70 patients per year will be enrolled. Hence, including the ≥1 month between pre- and post-implementation periods, we anticipate that accrual will be completed over 22 months. Allowing for delayed completion of radiotherapy of the final patients, the study will be completed in 26 months.

## STudy GROUP for Analyses

The primary analysis will include all enrolled subjects.

A per-protocol analysis will be conducted excluding patients from the post-implementation arm whose ‘enhanced assistance’ did not adhere to the protocol.

Analyses of patient-reported quality-of-life measures will include a complete-case analysis and an analysis including all patients utilizing multiple imputation to account for missing data.

A sensitivity analysis of the primary outcome will involve a difference-in-differences analysis comparing the change in delay-free radiotherapy from pre- to post-implementation in the study population relative to changes in delay-free radiotherapy over the same time periods among individuals who reported unmet essential needs but did not receive social work referral (and, as an alternative, who received social work referral enroll in the study). Data for the non-study comparison group will be obtained retrospectively from the medical record.

## Statistical Analyses

### General Approach

Baseline characteristics and treatment details will be described by study arm using descriptive statistics such as minimum, maximum, median, mean and standard deviation for continuous variables. Categorical variables will be described in tabular form as counts and percentages.

The primary outcome will be analyzed using Bayesian methods, which enabled prior knowledge to increase the precision of the pre-implementation period and decrease the required sample size for the pre-implementation arm (see Appendix III for details). For other inferential statistics, we will use 2-tailed tests and consider P < .1 statistically significant. Covariates for regression models will be pre-specified.

### Analysis of the Primary OBJECTIVE(s)

The primary outcome (delay-free radiotherapy; defined as completing all fractions of radiotherapy and delaying fewer than 5 fractions) will be reported as a proportion. The comparison between arms will be presented as a difference in proportions. Formal testing will be done in using hierarchical Bayesian linear probability model (see **Appendix III**). We will reject the null hypothesis if the posterior probability that the (1-sided) probability that the post-implementation effect was greater than 0 was greater than 80% (i.e., Pr(βpost-implementation > 0) > 80%). This probability must be greater than 90% in the interim analysis. We will present a visual depiction of the posterior distribution along with reporting the posterior mean and lower bound of the 1-sided 80% (or 90%, for the interim analysis) credible interval.

The primary analysis will not include any adjustment for covariates beyond a post-implementation dummy variable [effect of primary interest] due to relatively limited sample size.

However, a multivariable regression model will be utilized in a sensitivity analysis due to the nonrandomized design. The covariates included are those associated with delay-free completion of radiotherapy based on institutional data and basic demographics: age, sex, performance status, cancer site, treatment modality, unmet needs, Medicaid status, and neighborhood disadvantage.

Another sensitivity analysis of the primary outcome will utilize a similar approach but will be expanded to a difference-in-differences framework by also including non-study participants who reported unmet essential needs. The linear probability model will be expanded with additional covariates including a dummy variable indicating the study participants and an interaction between the study participant and post-implementation variables; the effect of interest will be the coefficient for the interaction term).

Due to the nature of the outcome, there will be no missing data (all patients will have defined completion status and/or number of fractions delivered).

The individual components of the primary outcome, the proportion completing all fractions of radiotherapy and the proportion delaying fewer than 5 fractions will also be reported.

### Analysis of the Secondary OBJECTIVEs

Secondary endpoints will be reported regardless of the results of the primary outcome. No adjustments to account for multiple comparisons will be made.

Patient reported physical, emotional, social, and financial outcomes at baseline and at completion of radiotherapy. We will use the PROMIS-10, FACT-G, FACIT-COST, and additional questions from ECOG-ACRIN EAQ222CD surveys, utilized in similar studies, which provide outcome scores that are scaled means of multiple Likert-type scale responses or binary responses. Since each participant will complete the surveys twice, data will be treated as repeated measures. Changes from baseline in each patient-reported outcome will be assessed in a linear (or generalized linear, for binary responses) mixed model with sandwich estimators, with random effects for each subject. Covariates include a post-implementation effect and an interaction between change from baseline and study arm. Estimates of the changes from baseline will be reported as mean differences (or odds ratios, for binary outcomes). We will account for missing data utilizing multiple imputation procedures utilizing baseline covariate information utilized in our other analyses (age, sex, performance status, cancer site, treatment modality, unmet needs, Medicaid status, and neighborhood disadvantage).

The difference between the cost of the unmet essential needs intervention and the potentially increased revenue from potentially increased rates of completed courses of radiotherapy will be based on amounts of the assistance provided (in dollars), including the category of assistance, costs of the social worker’s time, revenue information (in dollars) from the delivered radiotherapy treatments, and the number of noncompleted treatments. The differences in costs will be reported for each arm.

There will be no formal testing of evaluations of intervention implementation process measures.

### Safety Analyses

There are no adverse or other safety events that could possibly or probably be associated with the study intervention of increasing the amount of financial assistance for unmet needs.

### Baseline Descriptive Statistics

Baseline characteristics of the pre- and post-implementation of the enhanced assistance intervention arms will be compared. Numbers and percentages will be presented for the following factors: age group, sex, performance status, cancer site, treatment modality, unmet needs, Medicaid status, and neighborhood disadvantage.

### Planned Interim Analyses

A planned interim analysis for efficacy will be conducted a minimum of 3 months after 30 patients have enrolled in the post-implementation period (to allow for completion of radiotherapy). If the posterior probability is >90% that the effect of the intervention is greater than 0, then the trial will be closed early for efficacy.

### Sub-Group Analyses

Subgroup analyses of the primary outcome will include the following subgroups: 1 vs >1 unmet need, Medicaid status or eligibility vs. others, <25 fractions vs. ≥25 fractions, cancer site groups, and amounts of assistance provided (stratified by median).

There are no prespecified subgroup analyses for the secondary or exploratory endpoints.

### Tabulation of Individual participant Data

With the exception of the quality of life survey data, which will be collected twice per patient, individual participant data will only be listed by measure.

### Exploratory Analyses (Tertiary objectives)

Acute toxicities (grade 2+, grade 3+), weight loss (% body weight, treated as continuous measure), emergency department visits (binary) and hospitalizations (binary), pain scores (integer), and missed weekly check-in visits during radiotherapy (% of scheduled visits, treated as continuous measure) will be collected from the medical record. These outcomes before and after implementation of the enhanced assistance intervention will be compared utilizing logistic regression (binary outcomes) or linear regression (continuous outcomes) with and without adjustment for baseline covariates (age, sex, performance status, cancer site, treatment modality, unmet needs, Medicaid status, and neighborhood disadvantage). Missing data will be accounted for with multiple imputation utilizing the aforementioned covariates.

Associations between delay-free completion of radiotherapy and baseline sociodemographic factors, responses to essential needs screening, and responses to quality of life surveys will be performed utilizing logistic regression.

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# APPENDIX I: SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

## Regulatory, Ethical, and Study Oversight Considerations

### Informed Consent Process

#### Consent/assent and Other Informational Documents Provided to participants

Consent forms describing in detail the study intervention, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention/administering study intervention. The consent materials are submitted with this protocol in Appendix V.

#### Consent Procedures and Documentation

Informed consent is a process that is initiated prior to the individual’s agreeing to participate in the study and continues throughout the individual’s study participation. Consent forms will be Institutional Review Board (IRB)-approved and the participant will be asked to read and review the document. A study team member will explain the research study to the participant and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant’s comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. Participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the participants for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

### Study Discontinuation and Closure

Not applicable

### Confidentiality and Privacy

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their interventions. This confidentiality is extended to cover the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor, representatives of the Institutional Review Board (IRB), regulatory agencies or pharmaceutical company supplying study product may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

The study participant’s contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be deidentified prior to statistical analyses and will not include the participant’s contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by research staff will be secured and password protected. Identifiable patient information will only be available to the investigators listed in the protocol, institutional research coordinators, and the IRB. Study team members including the PI and co-PIs and study coordinators will have the key for the study identification numbers. Deidentified patient information may be shared with researchers from other institutions upon a reasonable request after appropriate IRB approvals have been obtained from both applicable institutions.

### Future Use of Stored Specimens and Data

Not applicable

### Key Roles and Study Governance

*Provide the name and contact information of the Principal Investigator and the Medical Monitor.*

|  |  |
| --- | --- |
| **Principal Investigator** | **Medical Monitor** |
| *Name, degree, title* | *Name, degree, title* |
| *Institution Name* | *Institution Name* |
| *Address* | *Address* |
| *Phone Number* | *Phone Number* |
| *Email* | *Email* |

### Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

These practices are consistent with ICH GCP:

* 4.5 Compliance with Protocol, sections 4.5.1, 4.5.2, and 4.5.3
* 5.1 Quality Assurance and Quality Control, section 5.1.1
* 5.20 Noncompliance, sections 5.20.1, and 5.20.2.

It is the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 10 working days of identification of the protocol deviation, or within 10 working days of the scheduled protocol-required activity. All deviations must be addressed in study source documents, reported to reviewing Institutional Review Board (IRB) per their policies. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements.

## Abbreviations

|  |  |
| --- | --- |
| AE | Adverse Event |
| CFR | Code of Federal Regulations |
| CMP | Clinical Monitoring Plan |
| CRF | Case Report Form |
| DFC | Delay-free completion (of radiotherapy) |
| HIPAA | Health Insurance Portability and Accountability Act |
| NIH | National Institutes of Health |
| PI | Principal Investigator |
| QA | Quality Assurance |
| SAE | Serious Adverse Event |
| SAP | Statistical Analysis Plan |
| SDoH | Social determinants of health |
| SMC | Safety Monitoring Committee |
| SOA | Schedule of Activities |
| US | United States |

## Protocol Amendment History

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| --- | --- | --- | --- |
| **Version** | **Date** | **Description of Change** | **Brief Rationale** |
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# APPENDIX II: ADVERSE EVENTS AND UNANTICIPATED PROBLEMS

*.*

## AdversE Events

This study does not incorporate any deviation from standard of care treatment.There are no adverse events that can potentially, probably, of definitely be related to the study intervention of providing additional financial assistance for unmet essential needs.

### Definition of Adverse Events (AE)

Not applicable

### Definition of Serious Adverse Events (SAE)

Not applicable

### Classification of an Adverse Event

#### Severity of Event

All AEs that occur during radiotherapy will be assessed by the treating clinician. Note that there are no adverse events that can potentially, probably, of definitely be related to the study intervention of providing additional financial assistance for unmet essential needs. No AEs that occur during the study will be reported.

#### Relationship to Study INTERVENTION

There are no adverse events that can potentially, probably, of definitely be related to the study intervention of providing additional financial assistance for unmet essential needs. No AEs that occur during the study will be reported.

#### Expectedness

Not applicable

### Time Period and Frequency for Event Assessment and Follow-Up

Not applicable

### Adverse Event Reporting

There are no adverse events that can potentially, probably, of definitely be related to the study intervention of providing additional financial assistance for unmet essential needs.

Patients may experience expected events due to their underlying disease or course of standard-of-care radiotherapy while enrolled in the study. Such events often depend on the location of cancer but can include fatigue, nausea, vomiting, headache, hair loss, skin redness, skin peeling, pain, dry mouth, dysphagia, odynophagia, diarrhea, proctitis, urinary frequency, and urinary urgency. These events will not be reported. However, these events will be recorded in the medical record by the treating physician and will be obtained from the medical record as exploratory endpoints.

### Serious Adverse Event Reporting

Not applicable

### Reporting Events to Participants

*Include content in this section if applicable, otherwise note as not-applicable.*

Not applicable

### Events of Special Interest

*Not applicable*

### Reporting of Pregnancy

Not applicable

## Unanticipated Problems

### Definition of Unanticipated Problems (UP)

Not applicable

### Unanticipated Problem Reporting

Not applicable

### Reporting Unanticipated Problems to Participants

Not applicable

# APPENDIX III: Details of Bayesian Analyses of Primary Outcome

Our Bayesian model for binary primary outcome variable *Y* for subjects i=1,…N, **β =** β*post-implementation*, β2,…, β*q* for *q* number of variables and matrix of corresponding covariate information **X** was parameterized as follows:

***Yj*** ~ Bernoulli(*pi)*

*pi ~* μ + **Xj** \* **β**

μ ~ N(mean = 0.16, var = 0.0582)

βpost-implementation ~ N(mean = 0, var = 0.152)

β2,…, β*q ~* N(mean = 0, var = 12)

The mildly informative prior for μ was selected to contain 60% of the density within 0.8 and 0.9, the limits of likely proportions of the primary outcome based on institutional data, previously reported data of similar patients from another institution,(33) and clinical experience. Note such a parameterization has minimal (<10%) density outside of 0.75 and 0.95, which are not feasible based on previously published retrospective data and clinical experience. The prior for βpost-implementation was chosen to be centered at 0 to conform to the null hypothesis; the standard deviation was selected to result in a distribution that was neither too narrow or too broad based on evaluations of posterior distribution and simulation studies of power and alpha with standard deviation values ranging from 0.095 to 1. Note the selected prior contains 50% of the density between -0.1 and 0.1, the likely values of the effect size, with 80% of the density between -0.2 and 0.2, the practical limits of the effect size. We utilized a linear probability model formulation under the central limit theorem to facilitate creation of clinically appropriate priors and to enable direct estimation of both the marginal and conditional effects after adjustment for covariates. Note *pi* was truncated at 1.0, and for purposes of power calculations, no covariates were included (i.e., equal distribution of covariates between arms was assumed). The posterior distribution will be obtained via MCMC using R (R2jags package). Convergence will be assessed visually and using the Geweke, Heidelberger-Welch tests including the halfwidth mean, and Raftery-Lewis diagnostic (superdiag R package).

We will reject the null hypothesis if the posterior probability that the (1-sided) probability that the post-implementation effect was greater than 0 was greater than 80% (i.e., Pr(βpost-implementation > 0) > 80%). For the interim analysis, this probability must be greater than 90%. We will present a visual depiction of the posterior distribution along with reporting the posterior mean and lower bound of the 1-sided 80% credible interval.

We conducted sensitivity analyses of projected power and Type I error accounting for the interim analysis under a variety of scenarios. In a sensitivity analysis assuming DFC increases from 85% to 93%, power was estimated to be 0.81. Power was estimated to be 0.55 to detect a DFC increase from 85% to 90% and 0.86 for a DFC increase from 88% to 94%. In simulation studies estimating α, estimates of α varied with the assumed proportion of DFC, which was held equal between arms. Estimates of α included: 0.08 for DFC=80%, 0.14 for DFC=83%, 0.16 for DFC=84%, 0.17 for DFC=85%, and 0.29 for DFC=88%.

# APPENDIX IV: Quality of Life Survey Instruments

Name:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Date:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

|  |
| --- |
| **Section 1: Material Hardship** |
| This set of questions is about your finances. |

1. In order to pay bills, have you had to do any of the following in the last 1 month (mark all that apply):

* Reduced spending on vacation or leisure activities
* Reduced spending on basics (e.g., food and clothing)
* Refinancing/second mortgage on your home
* Sell your home
* Move to a less expensive residence (e.g., lower rent or smaller mortgage)
* Sell your car
* Sell stocks or other investments
* Withdraw money from retirement accounts
* Withdraw money from savings accounts
* Incur credit card debt
* Take on a loan
* Maxed out your credit card
* Borrowed money from family or friends
* Declared bankruptcy
* None of above

1. Did your income go down in the last 3 months? If so, by how much (choose one)?

* Income did not decrease
* up to 10% decrease
* 11% to 20% decrease
* 21% to 30% decrease
* 31% to 50% decrease
* > 50% decrease

|  |
| --- |
| **Section 2: Impact of financial burden on health care** |
| This set of questions is about the impact of cancer financial burden on your cancer care. |

1. **In the last 1 month,** have you done any of the following due cost? Mark all that apply.

* Did not fill a prescription medication due to cost
* Delay the filling of a prescription medication due to cost
* Filled only part of a prescription medication due to cost
* Skip doses of prescribed medication in order to save money
* Stopped taking a medication due to cost
* Refused or delayed recommended lab tests, e.g. blood draws, due to cost
* Refused or delayed recommended imaging tests due to cost
* Refused or delayed recommended procedures due to cost
* Refused or delayed visits to doctor due to cost

|  |
| --- |
| **Section 3: COST Financial Worry** |

R

|  |
| --- |
| **Section 4: PROMIS-10 Overall Quality of Life** |

1. Please respond to each question or statement by marking one box per row.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Excellent** | **Very Good** | **Good** | **Fair** | **Poor** |
| 1. In general, would you say your health is: | 5 | 4 | 3 | 2 | 1 |
| 1. In general, would you say your quality of life is: | 5 | 4 | 3 | 2 | 1 |
| 1. In general, how would you rate your physical health? | 5 | 4 | 3 | 2 | 1 |
| 1. In general, how would you rate your mental health, including your mood and your ability to think? | 5 | 4 | 3 | 2 | 1 |
| 1. In general, how would you rate your satisfaction with your social activities and relationships? | 5 | 4 | 3 | 2 | 1 |
| 1. In general, please rate how well you carry out your usual social activities and roles. (This includes activities at home, at work and in your community, and responsibilities as a parent, child, spouse, employee, friend, etc.) | 5 | 4 | 3 | 2 | 1 |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Please respond to each question or statement by marking one box per row**. | **Completely** | **Mostly** | **Moderately** | **A little** | **Not at all** |
| 1. To what extent are you able to carry out your everyday physical activities such as walking, climbing stairs, carrying groceries, or moving a chair? | 5 | 4 | 3 | 2 | 1 |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **In the past 7 days…** | **Never** | **Rarely** | **Sometimes** | **Often** | **Always** |
| 1. How often have you been bothered by emotional problems such as feeling anxious, depressed or irritable? | 5 | 4 | 3 | 2 | 1 |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **In the past 7 days…** | **None** | **Mild** | **Moderate** | **Severe** | **Very severe** |
| 1. How would you rate your fatigue on average? | 5 | 4 | 3 | 2 | 1 |

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **In the past 7 days…** | **No pain** |  |  |  |  |  |  |  |  |  | **Worst pain** |
| 1. How would you rate your pain on average? | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

|  |
| --- |
| **Section 5: FACT-G Physical, Social, Emotional, and Functional Quality of Life** |

ADDITIONAL QUESTION TO ADD TO POST-RT SURVEY:

Did you finish all your radiation treatments (or, if you’re not done yet, do you think you will finish all your radiation treatments)?

If you answered “no,” please say why:

# APPENDIX V: Informed consent document

**INFORMED CONSENT DOCUMENT**

**Project Title: Radiotherapy completion with or without enhanced assistance for unmet essential needs: a single center hybrid type 1 efficacy-implementation study**

**Principal Investigator: Justin Barnes, MD, MS**  
**Research Team Contact: \*\*\***

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant.

**WHAT IS THE PURPOSE OF THIS STUDY?**

This is a research study. We invite you to participate in this research study because you will receive radiation to treat your cancer and you have indicated that you are interested in receiving assistance for a non-medical financial need.

The purpose of this research study is to learn more about the well-being of our patients who have unmet needs. We use the term “insecurity” to describe when our patients are not able to afford adequate food, safe housing, and reliable transportation. Many of our patients deal with these insecurities, and we know that food, housing, and transportation insecurity can keep patients from getting care they need. We are trying to improve how we give assistance for food, housing and transportation needs for patients receiving radiation treatments. We hope that by doing so we will be able to help more people finish their radiation treatments and avoid delays in treatment.

**WHAT WILL HAPPEN DURING THIS STUDY?**

As part of this study you will complete two surveys. Before and near the end of your radiation treatments (care that you will receive outside of this research study) you will complete surveys asking you about your quality of life. Questions will ask how your financial situation affects you and how you feel physically and emotionally. The surveys will take about 20 minutes to complete both times.

**Before you begin study treatment:**

You will need to have the following screening exams, tests, or procedures to find out if you can continue to be in the study. Most of these procedures may have already been done, and many of these may be done even if you do not join the study. If you have had some of them recently, they will not need to be repeated.

• Physical exam, including taking of vital signs, measuring your height and weight, reviewing your medical history, and talking about any symptoms or health problems you’re having

• Screening for essential needs, which involves answering a questionnaire about possible food, housing, or transportation needs.

• Questionnaires to assess your symptoms and quality of life; this may take up to 20 minutes to complete.

It is possible that after your medical history, tests, and procedures are reviewed, you will not be able to continue in this study. Your study doctor will go over any reasons why you might not be able to continue in the study with you.

**Procedures throughout the study:**

There will be no procedures related to the study while you are getting your standard of care radiation treatments.

**Follow-up procedures:**

Near the end of radiation or right after you finish your radiation treatments, you will fill out another questionnaire to assess your symptoms and quality of life. This may take up to 20 minutes to complete.

**HOW MANY PEOPLE WILL PARTICIPATE?**

Approximately 120 people will take part in this study conducted by investigators at Washington University.

**HOW LONG WILL I BE IN THIS STUDY?**

If you agree to take part in this study, your involvement will last for approximately 3 months. Your involvement will be completed after you fill out the final questionnaire around the end of your radiation treatments.

**WHAT ARE THE RISKS OF THIS STUDY?**

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Risks of Questionnaires  
There is a risk you will be asked questions that make you uncomfortable. You can skip any questions that you don’t wish to answer.

Risk of Breach of Confidentiality  
One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled *“How will you keep my information confidential?”* for more information.

**WHAT ARE THE BENEFITS OF THIS STUDY?**

You may or may not benefit from being in this study.

However, you may receive improved assistance for food, transportation, or housing needs and these benefits may make it more likely that you will finish radiation treatments on time. And we hope that, in the future, other people might benefit from this study because the results of the study may help researchers learn more about how to best give assistance for food, housing, and transportation needs and how to best help patients with unmet needs to finish radiation treatments on time.

**WHAT OTHER TREATMENT OPTIONS ARE THERE?**

Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. Instead of being in this study, you could

• Receive assistance for food, transportation, and housing needs, without being in a study

**WILL IT COST ME ANYTHING TO BE IN THIS STUDY?**

You will not receive any bills for any of the procedures related to this study. Participation in this study will not affect how your health plan/insurance company will pay for radiation treatments or bill you for radiation treatments.

**WILL I BE PAID FOR PARTICIPATING?**

You will not be paid for being in this research study. The surveys you will complete as part of this study will help us to better understand your quality of life, but the food, housing, and transportation assistance you may receive will be provided to you outside of this study. However, as we improve how we give financial assistance over time, some research participants may receive higher amounts of financial assistance for their unmet needs than they would have received outside of the study. No research participants will receive less financial assistance than they would be able to receive outside of the study.

**WHO IS FUNDING THIS STUDY?**

\*\*\*

**WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?**

It is very unlikely that participation in this study, whichinvolves only questionnaires asking about your quality of life, will lead to injury. Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator at \*\*\* and/or the Human Research Protection Office at 1-(800)-438-0445.

**HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?**

Other people such as those listed below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you. We will keep your participation in this research study confidential to the extent permitted by law.

* Government representatives (including the Office for Human Research Protections) to complete federal or state responsibilities
* The U.S. Food and Drug Administration
* Hospital or University representatives to complete Hospital or University responsibilities
* Information about your participation in this study may be documented in your health care records

and will be available to anyone with access to your health care record, including your health insurance company. This information may also be released as part of a release of information request.

* The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures.
* Washington University’s Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The Institutional Review Board has reviewed and approved this study.
* Siteman Cancer Center
* The Quality Assurance and Safety Monitoring Committee, to monitor the conduct of this study

Any report or article that we write will not include information that can directly identify you. The journals that publish these reports or articles require that we share your information that was collected for this study with others to make sure the results of this study are correct and help develop new ideas for research. Your information will be shared in a way that cannot directly identify you.

To help protect your confidentiality, we will make sure that your study information is kept secure. We will keep study information in a secure database that requires a username and password. To help protect your confidentiality, no identifying information such as your name, date of birth, or social security number will be made available to researchers who receive your health information. Furthermore, the study team will keep the master code list that links your unique study number with your name and other identifying information in locked storage in a locked office (for paper copies), or on a secured network on a password-protected computer (for electronic copies). Access to either paper or electronic copies will be limited to the Principal Investigator and members of the study team. Any research specimens collected for this study will be labeled with a code and will be stored in a secured lab in a locked building.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

**Are there additional protections for my health information?**

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, “How will you keep my information confidential?”

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University’s Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

**If you decide not to sign this form, it will not affect**

• your treatment or the care given by your health provider.  
• your insurance payment or enrollment in any health plans.  
• any benefits to which you are entitled.  
However, it will not be possible for you to take part in the study.

**If you sign this form:**

• You authorize the use of your PHI for this research  
• This authorization does not expire.  
• You may later change your mind and not let the research team use or share your information

• To revoke your authorization, complete the withdrawal letter found in the Participant section of the Human Research Protection Office website at hrpo.wustl.edu or you may request that the investigator send you a copy of the letter.

o **If you revoke your authorization:**♣ The research team may only use and share information already collected for the study.

♣  Your information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant’s withdrawal from the research study or for safety reasons.

♣  You will not be allowed to continue to participate in the study.

**Can we contact you by email and/or text?**

We would like to contact you by email and/or text for the purposes listed below. Some of these messages may contain health information that identifies you.

• We may contact you be email or text to set up appointments, remind you of upcoming visits, or check on the status of your health

Only the research team will have access to your email and/or text communications. We will only communicate in this method to send you the information listed above. If you have any questions, wish us to stop sending these messages or need to contact us for an urgent or emergent situation, please contact the research team member identified at the top of this document.

You should be aware that there are risks associated with sending your health information via email and/or text.

• Text messaging is not a secure communication method.  
• There is always a risk that the message could be intercepted or sent to the wrong email address and/or phone number. To avoid this, we will send a test message to ensure we have the correct email address and/or telephone number.  
• When using any computer you should be careful to protect your username and password. Make sure you log-out before getting up from the computer.  
• If you share a home computer or cell phone with other family members, and do not want them to know you are participating in this study make sure you provide an email address that only you can access.  
• Your employer will have access to any messages sent or received on any electronic devices used for work or through a work server.  
• If you lose your phone, others may be able to access the messages that we send.

Do you agree to allow us to send your health information via email?

**\_\_\_\_\_ Yes \_\_\_\_\_ No Initials Initials**

Do you agree to allow us to send your health information via text?

**\_\_\_\_\_ Yes \_\_\_\_\_ No Initials Initials**

If you have a MyChart account we may use this as a way to communicate with you about the treatment and/or medical care you are receiving as part of this study.

**IS BEING IN THIS STUDY VOLUNTARY?**

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you won’t be penalized or lose any benefits for which you otherwise qualify.

**What if I decide to withdraw from the study?**

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found in the Participant section of the Human Research Protection Office website at hrpo.wustl.edu.

**Will I receive new information about the study while participating?**

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we’ll promptly provide you with that information.

**Can someone else end my participation in this study?**

Under certain circumstances, the investigator might decide to end your participation in this research study earlier than planned. This might happen because your doctor no longer thinks radiation treatments that you are or will be receiving outside of the study are no longer a good option for you or the study is stopped for another reason.

**WHAT IF I HAVE QUESTIONS?**

We encourage you to ask questions. If you have any questions about the research study itself, please contact \*\*\*. Please be sure to tell this person you are a research participant.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office at 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, hrpo.wustl.edu. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

• To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.

* To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
* To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
* To give the research team accurate and complete information.
* To tell the research team promptly about any problems you have related to your participation, or

if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

**Do not sign this form if today’s date is after EXPIRATION DATE: \*\*\*\*\*\*\*** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

(Signature of Participant) (Date)

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (Participant's name – printed)

**Statement of Person Who Obtained Consent**

The information in this document has been discussed with the participant or, where appropriate, with the participant’s legally authorized representative. The participant has indicated that they understand the risks, benefits, and procedures involved with participation in this research study.

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\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (Signature of Person who Obtained Consent)

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (Name of Person who Obtained Consent - printed)

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (Date)