NRG ONCOLOGY

NRG-CC007CD

(ClinicalTrials.gov NCT #NCT03860961)

INCREASING THE DOSE OF SURVIVORSHIP CARE PLANNING IN PROSTATE CANCER SURVIVORS WHO RECEIVE ANDROGEN DEPRIVATION THERAPY

Amendment 4 March 24, 2021

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This trial is sponsored by the National Cancer Institute (NCI), will be led by NRG Oncology and is open to **all affiliated NCORP components and subcomponents** (Alliance for Clinical Trials in Oncology, ECOG-ACRIN Cancer Research Group, NRG Oncology, and SWOG).

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Participating Sites

☒ U.S. (NCORP practices only)

☐ Canada

☐ Approved International Member Sites

Document History

	Version Date
Amendment 4	March 24, 2021
Amendment 3	October 20, 2020
Amendment 2	November 6, 2019
Amendment 1	October 4, 2019
Initial	January 24, 2019

CANCER TRIALS SUPPORT UNIT (CTSU) ADDRESS AND CONTACT INFORMATION (24-Mar-2021)

For regulatory requirements:	**For participant enrollments:**	**For study data submission:**
Regulatory documentation must be submitted to the CTSU via the Regulatory Submission Portal: Regulatory Submission Portal (Sign in at www.ctsu.org, and select the Regulatory > Regulatory Submission.) Institutions with participants waiting that are unable to use the Portal should alert the CTSU Regulatory Office immediately at 1-866-651-2878 to receive further instruction and support. Contact the CTSU Regulatory Help Desk at 1-866-651-2878 for regulatory assistance.	Refer to the participant enrollment section of the protocol for instructions on using the Oncology Patient Enrollment Network (OPEN), which can be accessed at https://www.ctsu.org/OPEN_SYSTEM/ or https://OPEN.ctsu.org. Contact the CTSU Help Desk with any OPEN-related questions at ctsucontact@westat.com.	Data collection for this study will be done exclusively through Medidata Rave. Please see the data submission section of the protocol for further instructions. Do not submit study data or forms to CTSU Data Operations. Do not copy the CTSU on data submissions.
The most current version of the **study protocol and all supporting documents** must be downloaded from the protocol-specific Web page of the CTSU Members' website (https://www.ctsu.org). Access to the CTSU Members' website is managed through the Cancer Therapy and Evaluation Program - Identity and Access Management (CTEP-IAM) registration system and requires user log on with CTEP-IAM username and password.		
For clinical questions (i.e., participant eligibility or study procedure related questions), contact the Clinical Data Coordinator for NRG-CC007CD by phone (215-574-4164) or email (smallt@nrgoncology.org)		
For non-clinical questions (i.e., unrelated to participant eligibility, treatment, or clinical data submission), contact the CTSU Help Desk by phone or email: CTSU General Information Line – 1-888-823-5923 or ctsucontact@westat.com. All calls and correspondence will be triaged to the appropriate CTSU representative.		

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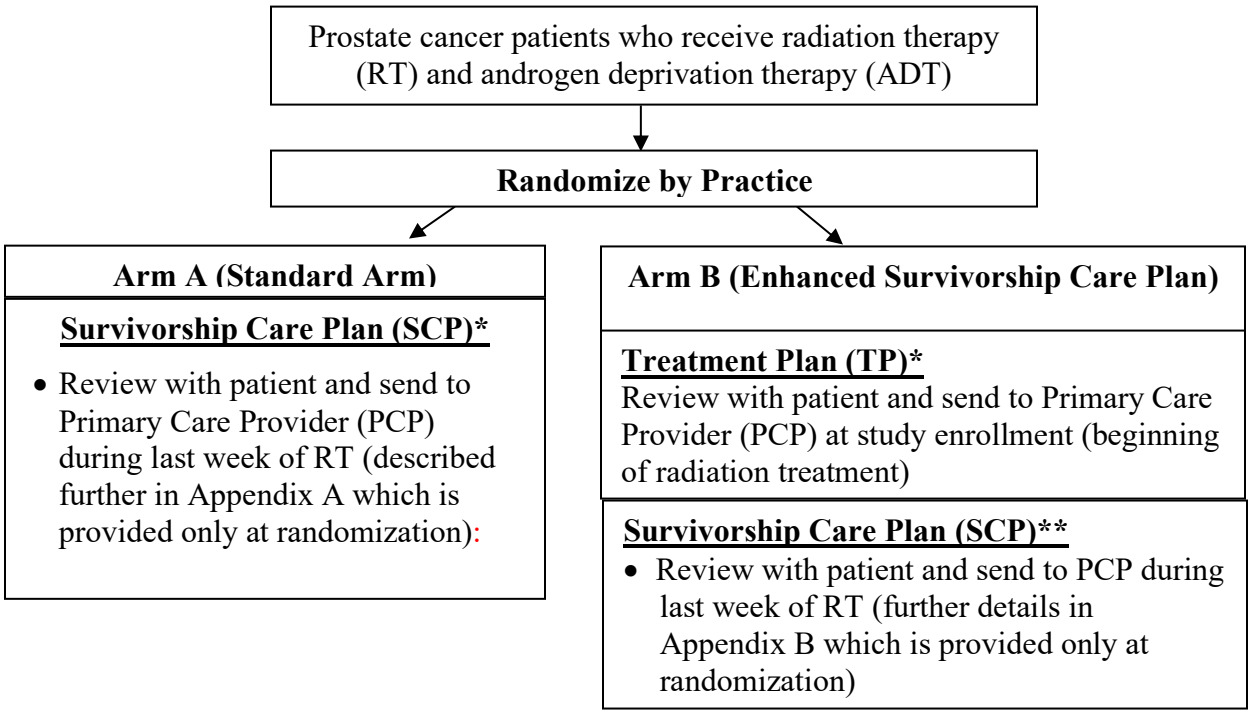
NRG-CC007CD SCHEMA



Patient Screening and Enrollment Process (04-Oct-2019)

Step 0: Screen prostate cancer patients who are to receive radiation therapy and androgen deprivation therapy

Data entered on Step 0: Screening

1. Does the patient meet all eligibility criteria except the PCP requirement? Y/N
2. Does the patient have a PCP or cardiologist? Y/N
3. Is the patient going on study? Y/N

Step 0: Screening

- YES – patient is eligible except PCP requirement
- YES – patient has a PCP or cardiologist
- YES – patient is going on study

Proceed to Step 1: Registration

Step 0: Screening

- YES – patient is eligible except PCP requirement
- YES – patient has a PCP or cardiologist
- NO – patient is not planning on going on study

Complete reason for not going on study and do not proceed to Step 1: Registration

Step 0: Screening

- YES – patient is eligible except PCP requirement
- NO – patient doesn't have PCP or cardiologist
- NO – patient is not planning on going on study

Complete reason for not going on study and do not proceed to Step 1: Registration

Please refer to Section 3.1 for more information concerning how a practice is defined and Section 8 for the enrollment process. Each practice will be provided with arm-specific instructions and assessments after randomization.

***Treatment Plan (TP):** Will be provided at beginning of radiation treatment. The TP will be provided to each practice randomized to Arm B. The TP will be provided to sites randomized to Arm B only.

****Survivorship care plan (SCP)**: Provided during the last week of radiation therapy. Includes all information in Treatment Plan (TP), and summarizes treatment received/is receiving.

1. OBJECTIVES

1.1 Primary Objective

1.1.1 To determine if the experimental arm (increased doses of SCP) has more patients who saw a primary care provider and had blood glucose and cholesterol checked in Year 2 (13-24 months) after finishing RT as compared to the control arm.

1.2 Secondary Objectives

1.2.1 To determine if patients who receive increased doses of SCP have lower cardiovascular disease (CVD) risk score at 2 years as compared to patients who receive a one-time SCP.

1.2.2 To determine if patients who receive increased doses of SCP have improved patient reported coordination and satisfaction with care with respect to their PCP or cardiologist as compared to patients who receive a one-time SCP and whether health literacy modifies the effect of SCP use on patient-reported coordination of care and satisfaction with care with respect to their PCP or cardiologist.

1.2.3 To determine the number of patients eligible, but without a PCP/cardiologist.

1.2.4 To describe the current practice related to SCP delivery and prostate cancer survivor monitoring in participating NCORP practices.

1.3 Exploratory Objectives

1.3.1 To determine if patients who receive increased doses of SCP have improved patient reported coordination and satisfaction with care with respect to their cancer specialist as compared to patients who receive a one-time SCP and whether health literacy modifies the effect of SCP use on patient-reported coordination of care and satisfaction with care with respect to their cancer specialist.

2. BACKGROUND (20-OCT-2020)

Practitioners are increasingly aware of coordinated health care's importance in cancer survivorship. The 2013 Institute of Medicine report "Delivering High-Quality Cancer Care: Charting a New Course for a System in Crisis," (IOM 2013) specifically highlights a need for coordinated care between the cancer care team with the primary care team. This is especially relevant for prostate cancer survivors who receive androgen deprivation therapy (ADT) in conjunction with radiation therapy (RT). These prostate cancer survivors need routine oncologic follow-up with their radiation oncologist and also coordinated routine follow-up with their primary care provider (PCP). The latter is particularly important because ADT heightens a patient's risk for developing diabetes, hypercholesterolemia, and cardiovascular events.

A joint publication from the American Heart Association, American Cancer Society and American Urological Association made specific recommendations regarding cardiovascular follow-up for prostate cancer patients who receive ADT (Levine, 2010):

- ADT's metabolic effects warrant PCP referral for periodic follow-up evaluation. This evaluation should include assessments of blood pressure, lipid profile, and blood glucose level. Since some of the effects of ADT occur within 3 months of treatment, initial evaluation should occur within 3-6 months after starting ADT;
- Blood glucose and lipids should be checked at least yearly;

- The referring physician (i.e. cancer specialist) should provide PCPs information on ADT's potential side effects, including glucose intolerance and dyslipidemia.

Currently, practitioners lack evidence regarding the best way to improve coordination of follow-up care for prostate cancer survivors so that they receive the necessary cardiovascular follow-up care. Survivorship Care Plan (SCP), initially described by the Institute of Medicine (Hewitt, Greenfield and Tovall, 2006), is a tool developed to facilitate care coordination for cancer survivors. The SCP documents a summary of the patient's cancer diagnosis, treatment(s) received, and follow-up care recommendations. For this trial, radiation oncologists will create SCPs and specifically include information about ADT and recommended cardiovascular follow-up care; both the patient and his primary care provide will receive the SCP.

While SCPs have face validity there is little evidence clarifying whether or how SCPs improve patient care and patient outcomes. There are 5 published randomized trials comparing routine care without SCP vs. the provision of a one-time SCP document (see Figure 1).

Figure 1: Comparison of randomized trials with and without SCP

	Patient Population	**Study Findings**
Grunfeld 2011; Boekhout 2015	Breast	No difference in patient-reported outcomes or adherence to breast cancer surveillance
Hershman 2013	Breast	No difference in patient-reported outcomes
Brothers 2013	Gynecologic	No difference in patient-perceived quality of care
Nicolaije 2015	Endometrial	No difference in patient-reported satisfaction with information or care
Maly 2017	Breast	SCP improved physician breast cancer follow-up care in Latina breast cancer patients

Four of these first-generation SCP trials showed no improvement in any measured outcome suggesting a single "dose" of SCP to patients fails to exert a demonstrable effect on survivor outcomes. A more recent trial demonstrated a benefit in care received by Latina breast cancer patients (Maly et al. 2017). Recently observed impact notwithstanding, the predominant null findings indicate a strong need for further studies specifically addressing the optimization of SCPs use in order to improve patient outcomes. This study addresses this need by examining whether increasing the dose of survivorship care planning improves patient care and outcomes.

Specifically we hypothesize that patients whose primary care providers receive an initial treatment plan, and subsequently receive the increased doses of SCP post-treatment (all of which describe the potential risks of ADT and need for primary care follow-up and monitoring) will demonstrate improved care as measured by completion of the recommended cardiovascular follow-up. The secondary objectives address lower CVD risk scores and patient-reported outcomes including coordination of and satisfaction with care. We

hypothesize that increased dose of SCP will improve patients' perception of coordination of and satisfaction with care compared to the standard arm. Additionally one factor that may modify the patient outcomes is health literacy. Health literacy is the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions (Ratzan & Parker 2000). Inadequate health literacy has been associated with lower patient satisfaction and lower preventive service compliance (MacLead et al, 2017). In this trial, we will assess each patient's health literacy to see if literacy is a modifier of the primary and secondary trial outcomes.

Description of study

The present study will specifically evaluate whether increasing the "dose" of survivorship care planning (SCP) improves care and outcomes in prostate cancer patients receiving RT plus ADT. The impact of increasing the dose of survivorship care on patient care and outcomes, including adherence to AHA guidelines, control of cardiovascular disease (CVD) risk factors, and coordination of and patient satisfaction with care will be compared with that of standard care (i.e., a one-time provision of the SCP to patients).

This is a cluster-randomized trial in which 35 practices (defined in Section 3.1) will be randomized to receive standard of care (single post-treatment SCP) or experimental care (increased dose of SCP). All patients will be screened for potential eligibility in the study from all participating practices regardless of treatment arm. Completion of study specific training will be required prior to trial participation with additional details provided in Section 8.3. More information regarding the screening portion of the trial can be found in Section 3.2 and information regarding practices and registration procedures can be found in Section 8.

3. PARTICIPANT ELIGIBILITY AND INELIGIBILITY CRITERIA

Per NCI guidelines, exceptions to inclusion and exclusion criteria are not permitted. For questions concerning eligibility, please contact the Biostatistical/Data Management Center (see protocol cover page).

3.1 Practice Eligibility Criteria (20-Oct-2020)

Practices (defined as a single NCORP component or subcomponent; or NCORP component and/or subcomponents that share the same physicians and/or staff, but are in different locations) will be randomized to receive standard of care (control arm) or increased SCP dose (experimental arm) once all of the eligibility criteria specified below have been met.

3.1.1 All institutions participating in a practice are NCORP components or sub-components.

3.1.2 Have a mechanism for delivering SCPs to prostate cancer patients. Practices that currently provide SCPs are eligible but for this trial will need to use the study-provided SCP template (Appendix C).

3.1.3 See at least 10 patients meeting eligibility criteria per year

3.1.4 Completion and submission of the NRG-CC007CD Letter of Intent (LOI) (posted on the CTSU website) by each practice to nrg-cc007CD@nrgoncology.org).

3.1.5 IRB approval

3.1.6 Each PI and RA at a NCORP practice must complete NRG-CC007CD SCP training. A training certificate will need to be completed and uploaded to the CTSU Regulatory Submission Portal. (See NRG-CC007CD Training Memo and Slides; located on the CTSU website). Note: staff and physicians cannot be part of multiple practices.

3.1.7 For a practice that is participating on Wake Forest study, WF-1804CD is not able to participate in this trial in order to not impact the fidelity of either trial. As long as the clinicians (physicians, APPs) are different for the patient populations of the two trials, a practice is eligible to participate in both trials.

3.2 Guidelines for Screening (04-Oct-2019)

3.2.1 Investigators should consider the factors below when selecting patients for this trial. Investigators also should consider all other relevant factors (medical and non-medical), as well as the risks and benefits of the study therapy, when deciding if a patient is an appropriate candidate for this trial. NRG Oncology is requesting a waiver of documentation of informed consent to screen eligible participants for the study. This process presents no more than minimal risk of harm to the subjects.

3.2.2 Patients must have the psychological ability and general health that permits completion of the study requirements and required follow up.

3.2.3 Screening (Step 0)

This step is for screening purposes only. Sites must use a screening log to record all patients screened. Screening logs should be maintained with no identifying information. The NRG-CC007CD screening log template can be found on the CTSU website. All screened patients will be entered on step 0 of the study.

When patients are screened for this study they should be asked whether or not they have a PCP or cardiologist, then record the information on the screening log. If an eligible patient who chooses not to participate on the trial (either due to not wanting to obtain a PCP or another reason), the reason should also be recorded. PCP can be a physician, physician assistant or nurse practitioner, in family practice or internal medicine. A cardiologist also meets this requirement.

The following script should be used to discuss with potential participants for this trial: ""You could be eligible for a clinical trial focused on prostate cancer survivorship care. Please tell me if you have a primary care provider or a cardiologist. If you do not have a primary care provider or cardiologist, I need to know if you are willing to have a primary care provider."

Below are scenarios:

- Patients with or without a PCP or cardiologist meeting eligibility criteria 3.3.1 and 3.3.2 stated below will be entered on the screening step.

- Patients with a PCP or cardiologist meeting all eligibility criteria stated below will be consented and step 1: registration can take place immediately after step 1: screening. If a patient with a PCP or cardiologist is eligible but chooses not to consent for another reason, this reason will be collected on step 0 and no registration on step 1 is needed.
- Patients without a PCP or cardiologist, but meeting all eligibility criteria stated below and are planning on establishing a PCP or cardiologist no more than 14 days after starting RT, can be consented. Step 0: Screening and Step 1: Registration can occur once the PCP or cardiologist is established. Establishing a PCP or cardiologist means that an appointment to see this provider has been made.
- Patients without a PCP or cardiologist, but meeting all other eligibility criteria below who do not plan on establishing a PCP or cardiologist will be entered on step 0: screening; however, they will not be consented or entered onto step 1: registration.

3.3 Patient Eligibility Criteria (24-Mar-2021)

Prior to Registration (Step 1)
A participant cannot be considered eligible for this study unless ALL of the following conditions are met.

3.3.1 The participant must be able to complete required questionnaires in English.

3.3.2 The participant must have a diagnosis of prostate adenocarcinoma that will be treated with RT plus ADT with curative intent. Both definitive RT (intact prostate) and post-prostatectomy RT patients are eligible.

- The ADT must be planned for at least 4 months and must include LHRH agonist or LHRH antagonist.
- ADT may have started for no more than 120 days before registration.

3.3.3 The participant must have a primary care provider and/or cardiologist or plan to obtain one per Section 3.2.

3.3.4 Comorbidities assessed at study entry using the ACE-27 instrument (located on the CTSU website).

3.3.5 The patient or a legally authorized representative must provide study-specific informed consent prior to study entry.

3.4 Ineligibility Criteria

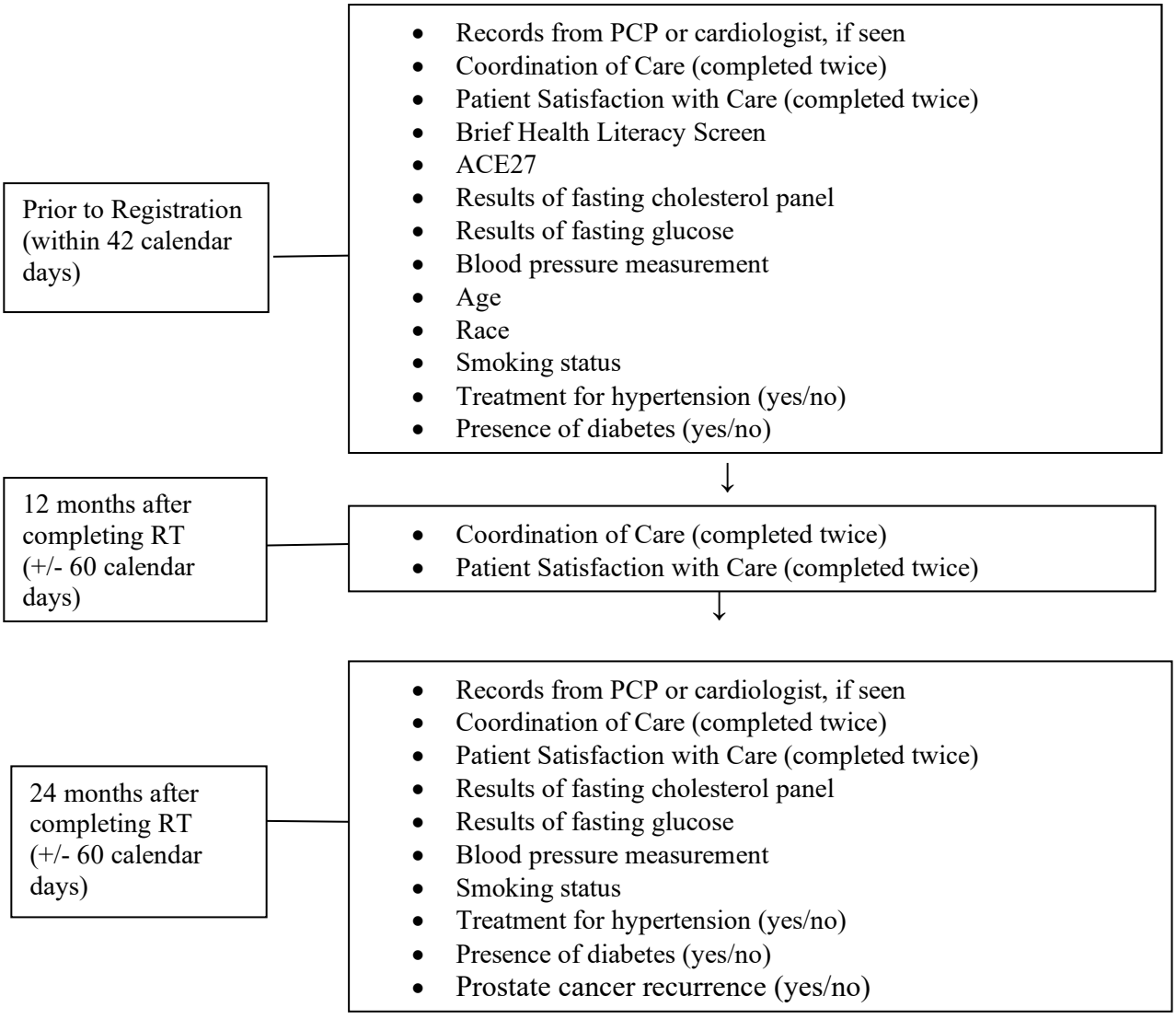
Not applicable

4. STUDY REQUIREMENTS (04-OCT-2019)

Below is a list of required assessments on this study for both arms. Time points of data collection are baseline, end of RT, 12 months post-RT, and 24 months post-RT. There will be no

data collection after 2 years. All baseline data will be entered at the time of registration in OPEN except for the Coordination of Care and Patient Satisfaction with Care surveys regarding the PCP. This is because patients who are planning to establish a PCP or cardiologist will not have seen their PCP or cardiologist at the time of registration (see Section 3.2.3).

Below is an overview of the data collection that doesn't relate to implementation of the TP and/or SCP. The TP and SCP schedule are provided separately. Please note that detailed information for these assessments, times of collection and an arm specific informed consent form template will be provided to each practice based on the arm to which the practice has been randomized. The arm specific document will not be posted to the CTSU website and will be provided within 5 business days of practice notification of the randomization assignment.



Assessment	Notes
Coordination of Care (twice)	Both the Coordination of Care and Patient Satisfaction with Cancer Care questionnaires need to be completed twice, once regarding the cancer specialist and once regarding the PCP. If the patient did not see a PCP or cardiologist within 365 calendar days prior to each time point, the Coordination of Care and Patient Satisfaction with Care questionnaires will only be completed regarding the cancer specialist.
Patient Satisfaction with Care (twice)	
Brief Health Literacy Screen	Baseline only; To be completed within 42 calendar days of registration
ACE27	
Records from PCP or cardiologist, if seen	Must record whether patient saw PCP or cardiologist within 365 calendar days of baseline and 24 months and if fasting glucose and fasting cholesterol were checked.
Results of fasting cholesterol panel	At baseline, only required if the patient has seen a PCP within 365 days prior to registration and had these blood tests checked. At 24 months, these are assessed at NCORP practice unless medical records provide results within previous 365 calendar days.
Results of fasting glucose	
Blood pressure	
Age	Baseline only
Race	
Smoking status	
Treatment for hypertension	Only required to record if this occurred or not (yes/no) at the specified time points.
Presence of diabetes	
Prostate cancer recurrence	

This study uses Medidata Patient Cloud ePRO. Remember to register the patient to the Patient Cloud ePRO. For instructions on registering the patients, please refer to Section 8.5 and the Medidata Patient Cloud ePRO operational instructions on the CTSU website for additional instructions.

5. STUDY PROCEDURES (20-OCT-2020)

The plans below depict the study arms. Randomization will be by practices (defined in Section 3.1).

Participating practices must have a mechanism for delivering SCPs and must see at least 10 prostate cancer patients meeting study eligibility per year (see Section 3.1 for

practice eligibility criteria); however, no NCORP practice will be allowed to enroll more than 25 patients.

5.1 Eligible participants will be identified by the treating radiation oncologist, together with study staff. Institutions must record on a screening log the number of patients who are eligible; regardless of whether they have a PCP or cardiologist. **Patients who do not have a PCP or cardiologist will not be registered to the trial. No further information about these patients will be collected (i.e. date of birth or other identifiable information). See Section 3.2.**

5.1.1 ***Standard arm (Arm A):***

Appendix A will be provided by NRG Oncology to the lead institution of each practice, post randomization, which will include details about the intervention and assessments for Arm A. Note: the arm specific assessments will be sent to practices on Arm A only and not posted on CTSU.

- Provided SCP template (see Appendix C) must be used
- Personnel utilized to create and review the SCP with the patient is per institutional protocol
- Methods for sending the SCP to PCP can include: fax, mailed letter, and/or sent through electronic medical record system.
- For patients who receive external beam RT and brachytherapy, "last week of RT" is defined by the last modality of planned radiation.

5.1.2 ***Experimental arm (Arm B)***:

The study intervention is enhanced survivorship care planning exposure which, in addition to SCP (identical to the standard arm), consists of several additional components. Appendix B will be provided by NRG Oncology to the lead institution of each practice, post randomization, which will include details about the additional components for Arm B. Note: the additional components for Arm B will be sent to practices on Arm B only and not posted on the CTSU.

6. TREATMENT MODIFICATIONS/MANAGEMENT

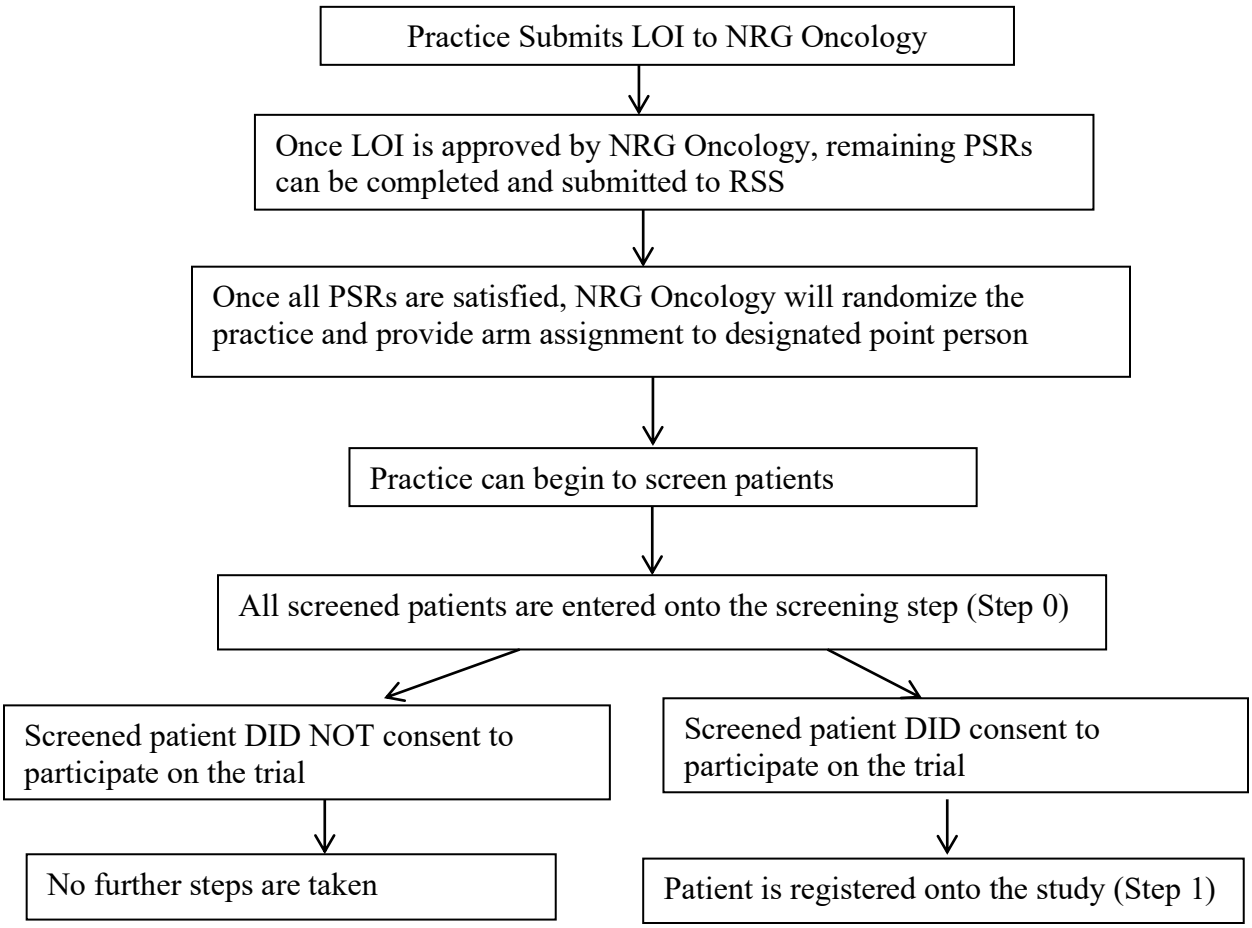
Not applicable.

7. ADVERSE EVENTS REPORTING REQUIREMENTS

Not applicable.

8. REGISTRATION AND STUDY ENTRY PROCEDURES (04-OCT-2019)

Practice Randomization and Patient Registration



8.1 CTEP Registration Procedures and Access requirements for OPEN, Medidata Rave (20-Oct-2020)

Food and Drug Administration (FDA) regulations and National Cancer Institute (NCI) policy require all individuals contributing to NCI-sponsored trials to register and to renew their registration annually. To register, all individuals must obtain a Cancer Therapy Evaluation Program (CTEP) Identity and Access Management (IAM) account at https://ctepcore.nci.nih.gov/iam. In addition, persons with a registration type of Investigator (IVR), Non-Physician Investigator (NPIVR), or Associate Plus (AP) must complete their annual registration using CTEP's web-based Registration and Credential Repository (RCR) at (https://ctepcore.nci.nih.gov/rcr.

RCR utilizes five person registration types.

- IVR — MD, DO, or international equivalent;
- NPIVR — advanced practice providers (e.g., NP or PA) or graduate level researchers (e.g., PhD);

- AP — clinical site staff (e.g., RN or CRA) with data entry access to CTSU applications such as the Roster Update Management System (RUMS), OPEN, Rave,, acting as a primary site contact or with consenting privileges;
- Associate (A) — other clinical site staff involved in the conduct of NCI-sponsored trials; and
- Associate Basic (AB) — individuals (e.g., pharmaceutical company employees) with limited access to NCI-supported systems.

RCR requires the following registration documents:

Documentation Required	IVR	NPIVR	AP	A	AB
FDA Form 1572	✓	✓			
Financial Disclosure Form	✓	✓	✓		
NCI Biosketch (education, training, employment, license, and certification)	✓	✓	✓		
GCP training	✓	✓	✓		
Agent Shipment Form (if applicable)	✓				
CV (optional)	✓	✓	✓		

An active CTEP-IAM user account and appropriate RCR registration is required to access all CTEP and Cancer Trials Support Unit (CTSU) websites and applications. In addition, IVRs and NPIVRs must list all clinical practice sites and Institutional Review Boards (IRBs) covering their practice sites on the FDA Form 1572 in RCR to allow the following:

- Addition to a site roster
- Assign the treating, credit, consenting, or drug shipment (IVR only) tasks in OPEN
- Act as the site-protocol Principal Investigator (PI) on the IRB approval

In addition, all investigators acting as the Site-Protocol PI (investigator listed on the IRB approval), or consenting/treating/drug shipment investigator in OPEN, must be rostered at the enrolling site with a participating organization.

Additional information can be found on the CTEP website at <http://ctep.cancer.gov/branches/pmb/associate_registration.htm>. For questions, please contact the ***RCR Help Desk*** by email at <RCRHelpDesk@nih.gov>.

8.2 Practice Randomization Assignment (24-Mar-2021)

Each practice will be notified of their randomization assignment via an email to the lead institution within the practice (designated on the Letter of Intent [LOI]). Once 35 practices have met all study entry requirements, no other institutions, not part of the 535 practices, will be able to enroll patients. Once a practice enrolls 25 patients; no institution within that practice will be able to enroll additional patients. If a practice does not enroll at least 1 patient within one year of randomization, the practice will be considered for possible removal and replacement. The practice will be notified and provided with sufficient time, and assistance from the study team, to enroll at least 1 patient.

8.3 Site Registration Requirements (24-Mar-2021)

This study is supported by the NCI Cancer Trials Support Unit (CTSU).

IRB Approval

For CTEP and Division of Cancer Prevention (DCP) studies open to the National Clinical Trials Network (NCTN) and NCI Community Oncology Research Program (NCORP) Research Bases after March 1, 2019, all U.S.-based sites must be members of the NCI Central Institutional Review Board (NCI CIRB). In addition, U.S.-based sites must accept the NCI CIRB review to activate new studies at the site after March 1, 2019. Local IRB review will continue to be accepted for studies that are not reviewed by the CIRB, or if the study was previously open at the site under the local IRB. International sites should continue to submit Research Ethics Board (REB) approval to the CTSU Regulatory Office following country-specific regulations.

Sites participating with the NCI CIRB must submit the Study Specific Worksheet for Local Context (SSW) to the CIRB using IRBManager to indicate their intent to open the study locally. The NCI CIRB's approval of the SSW is automatically communicated to the CTSU Regulatory Office, but sites are required to contact the CTSU Regulatory Office at CTSURegPref@ctsu.coccg.org to establish site preferences for applying NCI CIRB approvals across their Signatory Network. Site preferences can be set at the network or protocol level. Questions about establishing site preferences can be addressed to the CTSU Regulatory Office by emailing the email address above or calling 1-888-651-CTSU (2878).

Sites using their local IRB or REB, must submit their approval to the CTSU Regulatory Office using the Regulatory Submission Portal located in the Regulatory section of the CTSU website. Acceptable documentation of local IRB/REB approval includes:

- Local IRB documentation;
- IRB-signed CTSU IRB Certification Form; and/or
- Protocol of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption Form.

In addition, the Site-Protocol Principal Investigator (PI) (i.e. the investigator on the IRB/REB approval) must meet the following criteria in order for the processing of the IRB/REB approval record to be completed:

- Holds an Active CTEP status;
- Rostered at the site on the IRB/REB approval and on at least one participating roster;
- If using NCI CIRB, rostered on the NCI CIRB Signatory record;
- Includes the IRB number of the IRB providing approval in the Form FDA 1572 in the RCR profile; and
- Holds the appropriate CTEP registration type for the protocol.

Additional Requirements For NRG-CC007CD Site Registration:

- An active Federal Wide Assurance (FWA) number;

- An active roster affiliation with the Lead Protocol Organization (LPO) or a Participating Organization (PO);
- Compliance with all protocol-specific requirements (PSRs).

Protocol Specific Requirements For NRG-CC007CD:

- Letter of Intent (LOI) completed and submitted by each practice to nrg-cc007cd@NRGOncology.org (The form and instructions are posted on the CTSU website).
- Once the LOI is approved, each PI and RA at a NCORP practice must complete NRG-CC007CD study specific training, which includes details related to the study and cultural competency. A training certificate is provided at the end of the training and will need to be completed and submitted to the CTSU via the Regulatory Submission Portal. See the CTSU website for the training memo and training slides.

Downloading Site Registration Documents:

Download the site registration forms from the protocol-specific page located on the CTSU members' website. Permission to view and download this protocol and its supporting documents is restricted based on person and site roster assignment. To participate, the institution and its associated investigators and staff must be associated with the LPO or a Protocol Organization (PO) on the protocol. One way to search for a protocol is listed below.

- Log on to the CTSU members' website (https://www.ctsu.org) using your CTEP-IAM username and password;
- Click on *Protocols* in the upper left of the screen
    - Enter the protocol number in the search field at the top of the protocol tree, or
    - Click on the By Lead Organization folder to expand, then select *NRG* and protocol number NRG-CC007CD*;*
- Click on *Documents*, select *Site Registration*, and download and complete the forms provided. (Note: For sites under the CIRB initiative, IRB data will load automatically to the CTSU.)

Submitting Regulatory Documents:

Submit required forms and documents to the CTSU Regulatory Office via the Regulatory Submission Portal on the CTSU website.

To access the Regulatory Submission Portal log in to the CTSU members' website, go to the Regulatory section and select Regulatory Submission.

Institutions with patients waiting that are unable to use the Regulatory Submission Portal should alert the CTSU Regulatory Office immediately at 1-866-651-2878 in order to receive further instruction and support.

Checking Your Site's Registration Status:
Site registration status may be verified on the CTSU members' website.

- Click on *Regulatory* at the top of your screen;
- Click on *Site Registration*;
- Enter your 5-character CTEP Institution Code and click on Go
  - Additional filters are available to sort by Protocol, Registration Status, Protocol Status, and/or IRB Type.

Note: The status shown only reflects institutional compliance with site registration requirements outlined within the protocol. It does not reflect compliance with protocol requirements for individuals participating on the protocol or the enrolling investigator's status with the NCI or their affiliated networks.

8.4 Patient Enrollment (20-Oct-2020)

Patient registration can occur only after evaluation for eligibility is complete, eligibility criteria have been met, and the study site is listed as 'approved' in the CTSU RSS. Patients must have signed and dated all applicable consents and authorization forms.

8.4.1 Oncology Patient Enrollment Network (OPEN)

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 LPOs registration/randomization systems or 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.

Requirements for OPEN access:

- A valid CTEP-IAM account;
- To perform enrollments or request slot reservations: Must be on a LPO roster, ETCTN Corresponding roster, or participating organization roster with the role of Registrar. Registrars must hold a minimum of an AP registration type; and
- Have an approved site registration for a protocol prior to patient enrollment.

To assign an Investigator (IVR) or Non-Physician Investigator (NPIVR) as the treating, crediting, consenting, drug shipment (IVR only), or receiving investigator for a patient transfer in OPEN, the IVR or NPIVR must list the IRB number used on the site's IRB approval on their Form FDA 1572 in RCR.

Prior to accessing OPEN, site staff should verify the following:

- Patient has met all eligibility criteria within the protocol stated timeframes; and
- All patients have signed an appropriate consent form and HIPAA authorization form (if applicable).

Note: The OPEN system will provide the site with a printable confirmation of registration and treatment information. Please print this confirmation for your records.

Access OPEN at https://open.ctsu.org or from the OPEN link on the CTSU members' website. Further instructional information is in the OPEN section of the CTSU website at https://www.ctsu.org or https://open.ctsu.org. For any additional questions, contact the CTSU Help Desk at 1-888-823-5923 or ctsucontact@westat.com.

In the event that the OPEN system is not accessible, participating sites can contact NRG web support for assistance with web registration: websupport@acr.org or call the NRG Registration Desk at 215-574-3191, Monday through Friday, 8:30 a.m. to 5:00 p.m. ET. The registrar will ask the site to fax in the eligibility checklist and will need the registering individual's e-mail address and/or return fax number. This information is required to assure that mechanisms usually triggered by the OPEN web registration system (e.g. drug shipment and confirmation of registration) will occur.

8.5 Medidata Patient Cloud ePRO Registration (20-Oct-2020)

This study includes the use of Medidata Patient Cloud ePRO (electronic patient-reported outcomes). After the patient is registered to the trial via OPEN, and if the patient is willing to participate in electronic data collection, the site staff will then complete a registration for the patient to the Patient Cloud ePRO through iMedidata. Note: Site staff must have already completed required eLearning for the Patient Cloud ePRO application to register a patient and information about the training is in the Medidata Patient Cloud ePRO Operational Instructions on the CTSU website. The registration to the Patient Cloud ePRO will create a unique patient registration code that the site staff will provide to the patient. The patient (with assistance from the site staff) should be instructed to download the Patient Cloud ePRO app onto his/her own device (IOS, Android, phone or tablet) and use the unique patient registration code to create an account. Once the patient's account is set up, the patient will be able to complete the submission of patient reported outcomes electronically for the trial. There are multiple versions of the app available. The **Patient Cloud** App (the version with the cloud logo) will be used on this study. Ensure that the patient downloads the correct version of the ePRO app. Note only 1 version of the app is active per protocol.

For sites providing a shared institutional device for use by multiple patients on site:

- The site staff should assist the patient with access and registration to the Patient Cloud ePRO app, and the patient can then complete the electronic data submission independently. Site staff may need to assist patients with logging on to the device at each visit.

8.5.1 CRA Patient Registration Instructions for ePRO

Please visit the CTSU website for reference information on Patient Cloud ePRO for CRAs.

i. The subject registration process starts in iMedidata. Begin by selecting the Patient Cloud ePRO Registration link for your study
ii. The patient management app will display, select your STUDY and SITE from the drop downs and click Launch.
iii. Now you can register your first patient. Create a subject ID and select a Country / Language from the drop down, (these are the only required data fields). The subject initials are optional, but are helpful in identifying which subject ID maps with which activation code. When finished, click Add.
iv. The subject added and will include the date the patient was added, the subject ID, subject initials, (if included) and a unique auto-generated activation code. The activation code is unique for each patient and linked to the subject ID, it is not interchangeable. In addition, there is a status section, which indicates if the patient has registered. When the patient has registered the status will change from "invited" to "registered".

Reminder- site staff must have already completed the Medidata Patient Cloud training in order to register study participants. Please visit the CTSU website for information on Patient Cloud ePRO for CRAs.

9. DRUG INFORMATION

Not applicable

10. PATHOLOGY/BIOSPECIMEN

Not applicable

11. SPECIAL STUDIES (NON-TISSUE)

11.1 Adherence to AHA guideline recommendations (04-Oct-2019)

Adherence to AHA guideline recommendations is assessed using data collected at the24 month time point, as described in Section 4. Guideline adherence requires a "yes" response to all 3 elements:

1) The patient saw his PCP or cardiologist within the previous 365 days;
2) Fasting glucose was checked within the previous 365 days;
3) Fasting cholesterol panel was checked within the previous 365 days.

11.2 Cardiovascular disease (CVD) risk score

CVD score will be calculated by NRG Oncology according to the 2013 ACC/AHA Guidelines on the Assessment of Cardiovascular Risk (Levine 2010). This is assessed using data collected at baseline and the 24 month time point, as described in Section 4. **The following data elements are required for this score calculation**: Age, race, smoking status, hypertension treatment (yes/no), fasting total cholesterol and HDL, systolic blood pressure, and diabetes (yes/no). Systolic blood pressure should be measured by enrolling NCORP practice at each time point. Fasting glucose and total cholesterol and HDL should also be measured by the NCORP practice, unless documented values can be obtained by medical records within 365 calendar days prior to the 24 month time point. If a patient has multiple fasting glucose/total cholesterol/HDL

results within 365 days, the results most recent to the time point should be used. Patients will only have the CVD risk score calculated at baseline if they saw a PCP or cardiologist within 365 days prior to registration and had the required blood tests checked.

11.3 Patient-reported outcomes

Brief Health Literacy Screen (BHLS) (3 items, no subscales) – completed at baseline only. BHLS is a validated instrument that consists of three items on a 5-point response scale. After reverse-scoring the item addressing confidence with forms, responses to the three items are summed; scores range between 3 and 15, with higher scores indicating higher subjective health literacy (Wallston et al, 2014). The BHLS can be found in on the CTSU website.

Items and Response Options for the Brief Health Literacy Screen include:

- How confident are you filling out medical forms by yourself? (Extremely, Quite a bit, Somewhat, A little bit, Not at all)
- How often do you have someone help you read hospital materials? (All of the time, Most of the time, Some of the time, A little of the time, None of the time)
- How often do you have problems learning about your medical condition because of difficulty understanding written information? (All of the time, Most of the time, Some of the time, A little of the time, None of the time)

Coordination of care (6 items): The Components of the Primary Care Index is a validated instrument specifically designed to measure aspects of primary care delivery from the patient's perspective (Flocke 1997). The coordination of care subscale measures "the patients' perception of their physician's knowledge of other visits and visits to specialists, as well as follow-up of problems."

Patients respond to each item on a 6-point Likert scale: strongly disagree (1), to strongly agree (6). Scoring is based on a mean of the 6 items, with negatively-worded questions scored in reverse. A higher score indicates better coordination of care. **Participants will complete the questionnaire twice per time point** (baseline, 12 months and 24 months): one set of questionnaires is regarding coordination/satisfaction toward the radiation oncologist, one set toward PCP (or cardiologist if patient does not have a PCP).

Patient Satisfaction with Care (18 items, no subscales): The NCI-funded Patient Navigation Research Programs developed and validated this instrument, specifically to evaluate patient-reported outcomes related to satisfaction with cancer-related care. This instrument has been used in patients from diverse backgrounds (Jeanne-Pierre 2011) and was developed to assess potential benefits (i.e. satisfaction) of patient navigation.

This tool was developed and validated to be administered by a member of the research staff. Patients respond to each item on a 5-point Likert scale from strongly disagree (1) to strongly agree (5). A total scale score is calculated by adding scores on all 18 items, with a higher score indicating higher satisfaction (Jeanne-Pierre 2011; Fiscella 2012).

12. DATA MANAGEMENT/COLLECTION (20-OCT-2020)

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.

Requirements to access Rave via iMedidata:

- A valid CTEP-IAM account;
- Assigned a Rave role on the LPO or PO roster at the enrolling site of: Rave CRA, Rave Read Only, Rave CRA (LabAdmin), Rave SLA, or Rave Investigator.

  Rave role requirements:
  - Rave CRA or Rave CRA (Lab Admin) role must have a minimum of an Associate Plus (AP) registration type;
  - Rave Investigator role must be registered as a Non-Physician Investigator (NPIVR) or Investigator (IVR); and
  - Rave Read Only role must have at a minimum an Associates (A) registration type.

Refer to https://ctep.cancer.gov/investigatorResources/default.htm for registration types and documentation required.

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 users 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 site registration approval for the study in RSS will also 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.

12.1 Summary of Data Submission

Blank Rave forms and Summary of Data Submission are available on the CTSU website.

12.2 Quality Portal (04-Oct-2019)

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 (LPO) 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 Calendaring functionality.

12.3 Global Reporting/Monitoring

This study will be monitored by the Clinical Data Update System (CDUS) version 3.0. Cumulative CDUS data will be submitted quarterly to CTEP by electronic means. Reports are due January 31, April 30, July 31, and October 31.

13. STATISTICAL CONSIDERATIONS

13.1 Study Design (20-Oct-2020)

This is a prospective, cluster-randomized trial of survivorship care plans (SCPs). Practices (defined in Section 3.1) will be randomized using block randomization to the standard arm (one-time SCP given during the last week of radiation) or experimental arm. The TP and SCP will be standardized for this trial, and based upon the published ASTRO SCP template (Chen 2015). The SCP will indicate that the patient received androgen deprivation therapy and outline the American Heart Association guideline (Levine 2010) recommendation for primary care follow-up. The SCP is reviewed with the patient and sent to the PCP and/or cardiologist.

The target maximum accrual is 544 patients from approximately 35 practices. Patients will be analyzed according to the intent-to-treat principle using all randomized at-risk patients.

13.2 Study Endpoints

13.2.1 Primary Endpoint

Patients who saw a primary care provider (PCP) or cardiologist and had fasting blood glucose and fasting cholesterol checked by their PCP (or cardiologist) in Year 2 (13-24 months) after completing RT. This will be assessed using medical record abstraction.

13.2.2 Secondary Endpoints

- Calculated CVD risk score
- Coordination of care with respect to the PCP or cardiologist
- Satisfaction with care with respect to the PCP or cardiologist
- Eligible patients with a PCP or cardiologist screened
- Current practice related to SCP delivery and prostate cancer survivor monitoring

13.2.3 Exploratory Endpoints

- Coordination of care with respect to the cancer specialist
- Satisfaction of care with respect to the cancer specialist

13.3 Primary objectives and study design (20-Oct-2020)

13.3.1 Primary Endpoint and Hypothesis

The primary endpoint is the proportion of patients who saw a PCP (or cardiologist) and had fasting blood glucose and fasting cholesterol checked in Year 2 (13-24 months) after completing RT. The primary *hypothesis* is that increased doses of SCP will improve adherence to the American Heart Association recommendations for monitoring of CVD risk factors in prostate cancer survivors as compared to a one-time SCP.

13.3.2 Definition of Primary Endpoint and How It Will Be Analyzed

The primary endpoint will be assessed at the 24 month time point after completing RT. Medical records from the PCP and cardiologist will be reviewed to determine if each patient received care that met all 3 AHA guideline recommendations within 365 calendar days prior to this time point. Patients who received care that met all 3 criteria have "yes" for the primary endpoint; otherwise, "no" for the primary endpoint.

The primary endpoint will be evaluated on the individual level using an adjusted chi-square test that computes clustering correction factors computed separately in each treatment (Donner 1989) and tested with a 2-sided type I error of 0.05. A generalized estimating equation (GEE) (Liang 1986), adjusting for practice as a random covariate as part of a 2 level hierarchy (patients nested within clusters) will be used to determine the effect of intervention, ADT duration, person delivering the SCP, whether the patient saw a PCP or cardiologist, and possible confounders such as age, race, and number of baseline cardiovascular disease risk factors (none, hypertension, diabetes, hypercholesterolemia, and/or known coronary heart disease).

Since patients with missing data (either in part or whole) will be excluded from the primary endpoint analysis, a sensitivity analysis will be conducted assuming patients who have missing data at 24 months did not have their glucose and cholesterol checked or see their PCP or cardiologist.

Subgroup analyses based on race and ethnicity as well as in men without prostate cancer recurrence will be conducted where feasible. It is projected that 37 patients will be Hispanic or Latino and 117 will be of a minority race. In order to increase sample size within this subgroup, race and ethnicity will be combined to assess treatment effect (noting that 10 patients are projected to be both Hispanic and of a minority race). Additional subgroup analyses for Black or African American men and Hispanic or Latino men will be conducted on an exploratory basis. The rate of prostate cancer recurrence by 2 years is expected to be too low to allow for a subgroup analysis of progressed patients but a subgroup analysis of recurrence-free patients at 2 years will be conducted.

13.3.3 Sample Size and Power Calculations

The primary endpoint is the proportion of patients who saw a primary care provider in Year 2 after completing RT and had their glucose and cholesterol checked. This is a cluster randomized study in which practices will be randomized to the standard or experimental arm. Ideally, each practice would enroll the same number of patients; however, that is unlikely in the NCORP. Therefore, sample size for a patient-level randomization will be determined and then inflated by a design effect that also adjusts for unequal cluster size (Rutterford 2015). It is assumed that there will be approximately 9 patients enrolled per practice ($\bar{n}$). A coefficient of variation (CV) of cluster size of 0.5 will be assumed (van Breukelen 2012) along with an intra-cluster correlation (ρ) of 0.05. van Breukelen recommends $0.0 < \rho < 0.10$ (van Breukelen 2012). Based on national data from 2011-2015 [investigator's analysis of National Health Interview Survey/NHIS data, unpublished], 59.83% of prostate cancer survivors met the primary endpoint of this study. Clinically, an absolute improvement by 15% for the intervention arm is deemed a clinically-meaningful difference (thus, 74.8%). This improvement is reasonable based on a recently reported randomized trial which demonstrated that providing PCP with cardiovascular disease guidelines vs routine care improved physician adherence to anti-hypertensive medication use by 30%, and patient-reported adherence by 19% (Wei 2017).

Using a 2-sample test of proportions with a 2-sided α=0.05, 300 patients would provide 80% statistical power. Using equation 17 from Rutterford et al (Rutterford 2015), the design effect is:

$$DE = 1 + \big((CV^2 + 1)\bar{n} - 1\big)\rho = 1.51.$$

This results in 454 evaluable patients. After inflating by 5% for loss to follow-up and 5% due to consent withdraw as patients with missing data will not be included in the analysis, 504 patients from approximately 50 practices will be required for this study.

13.3.4 Revised Sample Size Calculation

The study design and sample size calculation are being modified in order to allow practices to enroll more patients and reduce the number of practices required. Initially ρ=0.05 and CV=0.5 but will now be ρ=0.4 and CV=0.45. This is because the primary endpoint is dependent on the patient's PCP/cardiologist who is not participating in the trial and is likely to be different from patient to patient within the same practice, thus decreasing the variance between clusters. After simulating likely accrual scenarios based on the current accrual by each practice, a slightly lower CV (calculated as the standard deviation/mean) is reasonable. Increasing the average number of patients from $\bar{n}$=9 to $\bar{n}$=14 will increase

the number of evaluable patients to 490 from approximately 35 practices. Inflating by 10% for consent withdraw and loss to follow-up results in a maximum target accrual of 544 patients. The current consent withdraw rate is 1.6%. The target accrual is 527 after inflating by 7% (2% for consent withdraw and 5% for loss to follow-up). The consent withdraw rate will be monitored semi-annually and if it remains below 2%, then the trial will close to accrual once 527 patients are enrolled. **Otherwise, the trial will continue until 544 patients are enrolled. The maximum accrual is increased to 25 patients per practice.**

13.4 Study Monitoring of the Primary Objective

The NRG Oncology Data Monitoring Committee (DMC) will review the study twice a year with respect to patient accrual and data submission. The DMC also will review the study on an "as needed" basis. No interim analysis is planned.

Once 10 practices have been enrolled, a hold will be put on randomizing additional practices. This hold will serve to ensure that all questions and issues regarding the practice randomization and study enrollment processes have been resolved. We anticipate this hold to take 1-2 months. The 10 randomized practices are able to continue screening and registering patients during this randomization hold.

13.5 Accrual Considerations

Many prostate cancer studies utilizing ADT conducted by NRG Oncology have high accrual rates. For example, RTOG 0534, a phase III trial of short-term ADT with pelvic lymph node or prostate bed only RT in prostate cancer patients with a rising PSA after radical prostatectomy, accrued patients at a rate of 23.5 per month. RTOG 0924, a phase III trial of ADT with high dose RT with or without whole pelvic RT in unfavorable intermediate or favorable high risk prostate cancer, is currently enrolling patients at a rate of 36.7 per month. Given the broad eligibility, the ability to be on a treatment trial as well as this trial, but accounting for the limited number of sites, the projected accrual is 20 patients per month. Thus, this study is projected to accrue 544 patients in 25 months, after a ramp up period of 6 months with negligible accrual. The primary endpoint will be reported approximately 4 years from study activation, once all patients have had at least 2 years on study. Accrual will be monitored by NRG Oncology's DMC according to DCP guidelines.

Given that African American men are disproportionately affected by prostate cancer, this study will aim to recruit African American men to consist of at least 15% of the study sample. Enrollment by ethnicity and race will be monitored on a semi-annual basis. If the proportion of African American men falls below 17%, the study chairs will reach out to practices to provide individualized recommendations to recruit more minorities, specifically African American men.

13.6 Secondary Endpoints (04-Oct-2019)

13.6.1 Secondary Endpoints and Hypotheses

- Calculated CVD risk score using the American Heart Association Risk Calculator

Hypothesis: Increased doses of SCP will reduce calculated CVD risk score as compared to a one-time SCP.

- Coordination of care of the PCP or cardiologist as measured by the Components of the Primary Care Index
  Hypothesis: Increased doses of SCP will improve patient-reported coordination of PCP or cardiologist care as compared to a one-time SCP.
- Satisfaction with care of the PCP or cardiologist as measured by the Patient Satisfaction with Care questionnaire
  Hypothesis: Increased doses of SCP will improve patient-reported satisfaction with PCP or cardiologist care as compared to a one-time SCP.
- To explore whether high health literacy levels are associated with improved patient-reported coordination of care and satisfaction with care.
- Collect number of eligible screened patients who do not have a PCP or cardiologist
- Describe current practice related to SCP delivery and prostate cancer survivor monitoring

13.6.2 Definitions of Secondary Endpoints and How These Will be Analyzed

Calculated CVD Risk Score
The American Heart Association Risk Calculator (Goff et al, 2013) will be used to calculate CVD risk score at baseline and at 24 months. For patients who have not seen a PCP within 365 days prior to registration, and therefore do not have results for fasting glucose and cholesterol levels at baseline, baseline CVD risk score will not be calculated.

Factors included in the Risk Calculator are: male/female, (all participants are male in this trial), age, race (White, African American, Other), HDL, total cholesterol, systolic blood pressure, diabetes (yes/no), treatment for hypertension (yes/no), smoker (yes/no). It is expected that all patients will be able to be assessed for the 24 month endpoint. Specifically, for participants with missing data at 24 months due to lack of primary care follow-up (i.e. the patient did not see a PCP or cardiologist within 365 days prior to this time point), necessary tests for CVD score calculation will be assessed by study personnel at 24 months after completing RT so that all participants contribute data toward this secondary endpoint. If patients are missing the appropriate variables to calculate CVD risk score regardless of whether the patient saw his PCP, they will be excluded from the analysis however this rate is expected to be low. If this rate is $\geq$ 15% appropriate missing data techniques, as described below for the PRO analysis, will be utilized. A linear mixed model (Laird 1982) with practice as a random covariate as part of a 2 level hierarchy (patients nested within clusters) will be used to compare the treatment arms using a significance level of 0.05.

Patient-Reported Outcomes
An expected benefit of the intervention is to improve coordination of care and patient satisfaction with care: both are ideally assessed by patient report using validated instruments. Both PROs will be collected twice at each time point: one in regards to the cancer specialist and one for the PCP or cardiologist.

It is expected that the Coordination of Care and Satisfaction with Cancer Care for the PCP or cardiologist may have a higher missing data rate on the control arm as these patients may not see their PCP. Therefore, the distribution of the Coordination of Care and Satisfaction with Cancer Care for the PCP or cardiologist will be provided for the entire study cohort only and not by arm; statistical testing using a t-test (Wilcoxon test if the data is not normal) will only be performed if there is sufficient data on the control arm to allow for between treatment arm differences.

A linear mixed effects model with practice as a random covariate as part of a 3 level hierarchy (surveys nested within patients nested within clusters) will be used to assess the effect of the intervention on the Coordination of Care and Satisfaction with Cancer Care for the PCP or cardiologist, with baseline score as a covariate, at 12 months and 24 months after completing RT (Liang 1986). Similar models will be used to determine the effect of various baseline covariates, including ADT duration, number of cardiovascular risk factors, person delivering the SCP, BHLS score, and race/ethnicity on the Coordination of Care and Satisfaction with Cancer Care scores. Treatment arm, time, and their interaction will be included in the models.

Missing data will be assessed. If ≥15% of the data is missing at any time point for any of the PROs, patient characteristics will be compared between patients with completed assessments and those with missing assessments. If the missingness is determined to be ignorable, no additional analyses need to occur since mixed effects modeling is valid under data that is missing at random (MAR). If the missingness is determined to be non-ignorable, other methods, such as imputation and pattern mixture models, may be performed (Fairclough 2010). Ceiling effects will be evaluated for both tools to aid in the interpretation of the results.

Screening study
Each NCORP practice will screen (step 0) and keep a log of all patients who are eligible, regardless of whether the patient has an existing PCP and/or cardiologist. The only information that will be collected is whether the patient signed consent (Y/N), is eligible excluding the PCP and/or cardiologist requirement (Y/N), if the patient has a PCP and/or cardiologist (including one that was recently established) (Y/N), and the reason for not registering to the trial (such as no PCP/cardiologist nor will obtain one, doesn't speak English, patient not interested in participating on a clinical trial, other). Patients who have a PCP and/or cardiologist or establish one as outlined in Section 3.2.3, will provide additional eligibility information when registered (step 1). This will provide the study team an idea of the amount of potential bias caused in this study due to the exclusion of these patients. Since no patient level information will be collected, no additional analyses will be performed or adjustments will be made to the specified analyses. The percentage of the enrolled patients out of all eligible patients (excluding the PCP requirement) will be provided along with the percentages broken down by practice.

Current SCP practice
Information regarding participating sites current practices for treatment plans, SCP, and fasting blood glucose and cholesterol testing will be collected prior to randomization.

Descriptive statistics, such as frequencies for the number of sites that currently use a treatment plan and/or SCP, and routinely perform testing and means for the percent of patients and/or their PCPs who receive a treatment plan and/or SCP, will be performed. Comparisons by arm will be made using a chi square test or t-test. If significant differences exist, at a two-sided significance level of 0.05, the respective covariates may be added to the models for the primary and secondary endpoints.

13.7 Exploratory Endpoints

Patient-Reported Outcomes
The distribution of the Coordination of Care and Satisfaction with Cancer Care for the cancer specialist by treatment arm and the entire study cohort will be provided with between treatment arm differences tested using a t-test (Wilcoxon test if the data is non-normal).

A linear mixed effects model with practice as a random covariate as part of a 3 level hierarchy (surveys nested within patients nested within clusters) will be used to assess the effect of the intervention on the Coordination of Care and Satisfaction with Cancer Care for the cancer specialist, with baseline score as a covariate, at 12 months and 24 months after completing RT (Liang 1986). Similar models will be used to determine the effect of various baseline covariates, including ADT duration, number of cardiovascular risk factors, person delivering the SCP, BHLS score, and race/ethnicity on the Coordination of Care and Satisfaction with Cancer Care scores. Treatment arm, time, and their interaction will be included in the models. Missing data will be assessed as specified in Section 13.6.2.

13.8 Gender/Ethnicity/Race Distribution (20-Oct-2020)

NRG Oncology remains committed to improving the awareness and involvement of racial and ethnic minority participants and underserved populations and will devote financial and personnel resources to accomplishing those goals. Since this trial is only open NCORP practices, there will be no international accrual. The prognostic effect of race/ethnicity will be evaluated using statistical models. Effects for the different cultural or racial groups will be compared between treatment arms, depending on the distributions. No differences across the patient subsets below are anticipated.

Expected racial and ethnic composition of NRG-CC007CD

DOMESTIC PLANNED ENROLLMENT REPORT					
Racial Categories	**Ethnic Categories**				**Total**
	Not Hispanic or Latino		**Hispanic or Latino**		
	Female	**Male**	**Female**	**Male**	
American Indian/Alaska Native	0	7	0	1	8
Asian	0	12	0	0	12
Native Hawaiian or	0	6	0	1	7

DOMESTIC PLANNED ENROLLMENT REPORT					
Other Pacific Islander					
Black or African American	0	92	0	1	93
White	0	388	0	31	419
More than One Race	0	2	0	3	5
Total	0	507	0	37	544

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APPENDIX A: ARM A STUDY REQUIREMENTS

This document will include further details about requirements for Arm A. It will be provided to each lead institution of a practice at time of site randomization only.

APPENDIX B: ARM B STUDY REQUIREMENTS

This document will include further details about requirements for Arm B. It will be provided to each lead institution of a practice at time of site randomization only.

APPENDIX C: SURVIVORSHIP CARE PLAN (SCP) (04-OCT-2019)

Dear _____, your patient was diagnosed with prostate cancer and received the following treatment. The treatment received and potential side effects are described below.

Patient History

Patient name: _____ Date of birth: __/__/____ MRN: _____
Treating radiation oncologist: _____ Phone: _____
Primary care provider: _____ Phone: _____
Surgeon: _____ Phone: _____
Medical oncologist: _____ Phone: _____
Other providers: _____ Phone: _____

Diagnosis

Primary site: _____ Histology: _____

PSA at diagnosis (ng/mL):
Biopsy Gleason score:
Clinical stage:

Surgery: ☐ Prior to RT ☐ Planned to follow RT ☐ Not planned

Optional free text box for details

Systemic treatment (e.g. hormone therapy): ☒ Yes ☐ No

☐ Before radiation	*Optional free text box for details*
☐ During radiation	*Optional free text box for details*
☐ After radiation	*Optional free text box for details*

Radiation Treatment: Start Date: __/__/____ End Date: __/__/____

Body Area Treated	

Total Dose: _____ (Gy) Total Number of Treatments: _____

On therapeutic clinical trial: ☐ Yes ☐ No

Optional free text box for details

Treatment Course and Side Effects

Did the patient complete treatment as planned?

☐ Yes ☐ No, due to toxicity ☐ No, due to cancer progression ☐ Other

Optional free text box for details

Treatment interruptions: ☐Yes ☐No

Optional free text box for details

Side effects during and at the end of treatment:

Free text box for details on side effects and management (interventions, medications)

Possible side effects which may occur later:

Free text box for details on side effects and when to seek medical care

Survivorship

The following two sections include health concerns and lifestyle/behavior changes that the Primary Care Provider should discuss with the patient based on your recommendation. Check all that apply.

Please discuss the following concerns with your patient:

☐ Emotional and Mental Health ☐ Fatigue ☐ Weight changes
☐ Physical functioning ☐ Insurance ☐ Work/School ☐ Parenting
☐ Financial Assistance ☐ Fertility ☐ Sexual functioning ☐ Memory loss
☐ Other _____

Please discuss these lifestyle/behavior changes with your patient to improve his overall health:

☐ Smoking/tobacco cessation ☐ Healthy diet ☐ Physical activity
☐ Weight management (gain/loss) ☐ Alcohol use ☐ Sunscreen use
☐ Other _____

Next appointment:

☐ With Radiation Oncologist, in____weeks/months

☐ None or only as needed with Radiation Oncologist

☐ With other provider(s) | *Free text*

☐ Follow-up testing | *Free text*

Instructions given to patient (optional):

Optional free text box for details

Additional Details for a Radiation Completion Note

Prior radiation therapy (any site): ☐ Yes ☐ No

Optional free text box for details

On clinical trial: ☐ Yes ☐ No

External beam and stereotactic radiotherapy treatments:

Treatment site	Treatment technique / Modality	Dose per fraction	Total number of fractions	Total dose	Start Date	End Date	Fractions per day	Fractions per week
e.g. Site 1					_/_/__	_/_/__		
e.g. Site 2								
Total								

Special technical considerations: details to be included here can include (as relevant) 4D techniques, image guidance/gating, simulation technique, image fusion during planning, prescription point, etc.

Brachytherapy treatments:

Treatment site	Treatment technique (LDR/ HDR/other)	Isotope	Dose per fraction	Total number of fractions	Total dose	Start Date	End Date	Fractions per week

Applicator used (for HDR only)**:** _____

Special technical considerations: details to be included here can include (as relevant) simulation technique, image fusion during planning, prescription point, etc.

Person completing this form:

Role: ☐ Physician ☐ Physician assistant ☐ Nurse ☐ Nurse Practitioner

Name:_____

Androgen Deprivation Therapy (ADT)

How it works**:** ADT works by lowering the amount of testosterone (the hormone that makes prostate cancer cells grow).

How ADT is given: Usually as an injection into the buttock muscle or under the skin of your abdomen.

Possible Side Effects of ADT

Hot flashes
- Feeling waves of heat in the face, head, upper body; night sweats may interfere with sleep.

Diabetes
- ADT increases the risk of type 2 (adult) diabetes
- Men who have diabetes before starting ADT may find that medication alone isn't enough to control diabetes.

Heart health
- Men on ADT can experience higher blood pressure, blood sugar, and other factors that raise the chance of having heart problems.
- **Make an appointment with your primary care doctor within 12 months** to check your numbers: blood sugar, cholesterol levels, blood pressure.
- Based on American Heart Association recommendations, **you also need to have your primary care doctor check these (blood sugar, cholesterol levels, blood pressure) every year.**

Possible Side Effects of Radiation Therapy

Bladder problems
- Needing to go urgently or frequently
- Burning sensation
- Slower urine flow

Bowel problems
- Loose stools
- Blood in stool

Erectile dysfunction

Cancer Monitoring

You need to have a checkup with your radiation oncologist every 6 months.