Cover Page

Study Title: Treatment Preference and Patient Centered Prostate Cancer Care

NTC number: NCT02032550

Date: July 30, 2014

Modification

Basic Info

Confirmation Number:	**bdgacceg**
Protocol Number:	**818201**
Created By:	**JAYADEVAPPA, RAVISHANKAR**
Principal Investigator:	**JAYADEVAPPA, RAVISHANKAR**
Protocol Title:	**Treatment Preference and Patient Centered Prostate Cancer Care**
Short Title:	**Patient Centered PCa Care**
Protocol Description:	**To test the comparative effectiveness of a conjoint analysis intervention and identify preferred attributes of alternative prostate cancer treatments that will aid in designing ways to help patients weigh treatment attributes. We employ values markers, to represent clusters of values for particular aspects of treatments that are valued most by individual patients. We will test if concordance between values markers and treatment received is predictive of objective and subjective outcomes.**
Submission Type:	**Biomedical Research**

PennERA Protocol Status

Approved

Resubmission*
No

Are you submitting a Modification to this protocol?*

Yes

Current Status of Study

Study Status

Currently in Progress

If study is currently in progress, please enter the following

Number of subjects enrolled at Penn since the study was initiated

0

Actual enrollment at participating centers

0

If study is closed to further enrollment, please enter the following

Number of subjects in therapy or intervention

0

Number of subjects in long-term follow-up only

0

IRB Determination
If the change represents more than minimal risk to subjects, it must be reviewed and approved by the IRB at a convened meeting. For a modification to be considered more than minimal risk, the proposed change would increase the risk of discomfort or decrease benefit. The IRB must review and approve the proposed change at a convened meeting before the change can be implemented unless the change is necessary to eliminate an immediate hazard to the research participants. In the case of a change implemented to eliminate an immediate hazard to participants, the IRB will review the change to determine that it is consistent with ensuring the participant′s continued welfare. Examples: Convened Board Increase in target enrollment for investigator initiated research or potential Phase I research Expanding inclusion or removing exclusion criteria where the new population may be at increased risk Revised risk information with active participants Minor risk revisions that may affect a subject′s willingness to continue to participate Expedited Review Increase in target enrollment at Penn where overall enrollment target is not exceeded or potentially sponsored research Expanding inclusion or removing exclusion where the new population has the same expected risk as the previous, based on similarities of condition Revised risk information with subjects in long-term follow-up Minor risk revisions with no subjects enrolled to date
Expedited Review

Modification Summary
Please describe any required modification to the protocol. If you are using this form to submit an exception or report a deviation, enter 'N/A' in the box below.
We are here by submitting modifications to our approved protocol entitled "Treatment Preference and Patient Centered Prostate Cancer Care (protocol 818201)" for your review and approval. Following are the modifications: (1) Additional Research Assistants added to the list (2) Introductory letter for focus group or interview (3) Modified consent for focus group or interview (4) Flyer for focus group or interview

Risk / Benefit
Does this amendment alter the Risk/Benefit profile of the study?
No

Change in Consent
Has there been a change in the consent documents?
Yes

If YES, please choose from the options below regarding re-consenting

Our site does not plan to obtain re-consent

Deviations

Are you reporting a deviation to this protocol?*

No

Exceptions

Are you reporting an exception to this protocol?*

No

Protocol Details

Resubmission*
Yes

Study Personnel

Principal Investigator

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Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**

Study Contacts

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Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**

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Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**

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4243 - DM-Geriatrics

Key Study Personnel

Name:	**LUCAS, STEVEN A**
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Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**

Name:	**BAVARIA, THOMAS**
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Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**

Name:	**JACOBS, LISA M**
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HS Training Completed:	**Yes**
Training Expiration Date:	**01/29/2015**
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**

Name:	**BABBAR, SHAILI**
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HS Training Completed:	**Yes**
Training Expiration Date:	**09/15/2016**
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**

Name:	**ADEJARE, ADERINOLA A**
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HS Training Completed:	**Yes**
Training Expiration Date:	**05/26/2014**
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**

Name:	**KELLOM, KATHERINE**
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Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**

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HS Training Completed:	**Yes**
Training Expiration Date:	**01/31/2016**
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**

Name:	**VACCARO, KAREN**
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HS Training Completed:	**Yes**
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Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**

Name:	**PACIOTTI, BREAH L**
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HS Training Completed:	**Yes**
Training Expiration Date:	**10/03/2015**
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**

Name:	**EASLEY, EBONY**
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HS Training Completed:	**Yes**
Training Expiration Date:	**05/14/2015**
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**

Disclosure of Significant Financial Interests*
Does any person who is responsible for the design, conduct, or reporting of this research protocol have a **FINANCIAL INTEREST**?
No

Certification
I have reviewed the *Financial Disclosure and Presumptively Prohibited Conflicts for Faculty Participating in Clinical Trials* and the *Financial Disclosure Policy for Research and Sponsored Projects* with all persons who are responsible for the design, conduct, or reporting of this research; and all required Disclosures have been attached to this application.
Yes

Biomedical Research

Investigator Initiated Trial
Is this an investigator-initiated trial?
No

Drugs or Devices*
Does this research study involve Drugs or Devices?
No

IND Exemption

For studies that fall under an IND exemption, please provide the number below

For studies including IND or IDE's, please provide the number(s) below

IDE Review*
NOTE: For research involving investigational devices, you are required to review the guidance on Managing Research Device Inventory. Consult the Penn Manual for Clinical Research: https://somapps.med.upenn.edu/pennmanual/secure/pm/storage-drugsdevices Please check the box Yes if you have reviewed the guidance.
Yes

Research Device Management*
Please indicate how research device(s) will be managed.
Not Applicable (no investigational devices)

Drug, Herbal Product or Other Chemical Element Management *
Please indicate how drugs, herbal products or other chemical entities will be managed.
Not Applicable (no drugs, herbal products or other chemical entities)

Radiation Exposure*
Are research subjects receiving any radiation exposure (e.g. X-rays, CT, Fluoroscopy, DEXA, pQCT, FDG, Tc-99m, etc.) that they would not receive if they were not enrolled in this protocol?
No

Gene Transfer*
Does this research involve gene transfer (including all vectors) to human subjects?
No

Human Source Material*
Does this research include collection or use of human source material (i.e., human blood, blood products, tissues or body fluids)?
No

CACTIS and CT Studies*
Does the research involve Center for Advanced Computed Tomography Imaging Services (CACTIS) and CT studies that research subjects would not receive if they were not part of this protocol?
No

CAMRIS and MRI Studies*
Does the research involve Center for Advanced Magnetic Resonance Imaging and Spectroscopy (CAMRIS) and MRI studies that research subjects would not receive if they were not part of this protocol?
No

Investigational Agent or Device within the Operating Room*
Does the research project involve the use of an investigational agent or device within the Operating Room?
No

Cancer Related research not being conducted by an NCI cooperative group*
Does this protocol involve cancer-related studies in any of the following categories?
Yes

Processing of Materials*
Will the research involve processing (such as over encapsulating, or compounding)?
No

In-House Manufacturing of Materials*
Will the research involve processing (such as over encapsulating, or compounding)?
No

Medical Information Disclosure*
Does the research proposal involve the use and disclosure of research subject's medical information for research purposes?
Yes

If the answer is YES, indicate which items is is provided with this submission:

Modified research informed consent document that incorporates HIPAA requirements

CTRC Resources*
Does the research involve CTRC resources?
No

Pathology and Laboratory Medicine Resources*
Will samples be collected by hospital phlebotomy and/or processed or analyzed by any of the clinical laboratories of the University of Pennsylvania Health System?
No

Research Involves Apheresis, Cell Collection, and/or Blood Product Collection*
Does this research involve collection of blood products and/or the use of apheresis for treatment or for collection of cells or other blood components?
No

Research involving blood transfusion or drug infusions*
Will your research involve blood transfusion or infusion of study drug in 3 Ravdin Apheresis Unit for research purposes?
No

Trial in Radiation Oncology
Is this research a prospective trial being done in Radiation Oncology, and if so, has this protocol been approved by the Radiation Oncology Protocol committee?
No

Study in Radiation Oncology
Is this research a retrospective study being done in Radiation Oncology, and if so, has this project been reviewed by the Radiation Oncology Clinical Research Group?
No

Use of UPHS services*
Does your study require the use of University of Pennsylvania Health System (UPHS) services, tests or procedures* whether considered routine care or strictly for research purposes?
No

Primary Focus*
Sociobehavioral (i.e. observational or interventional)

Protocol Interventions

	Sociobehavioral (i.e. cognitive or behavioral therapy)
	Drug
	Device - therapeutic
	Device - diagnostic (assessing a device for sensitivity or specificity in disease diagnosis)
	Surgical
	Diagnostic test/procedure (research-related diagnostic test or procedure)
	Obtaining human tissue for basic research or biospecimen bank
x	**Survey instrument**
	None of the above

The following documents are currently attached to this item:

There are no documents attached for this item.

Sponsors

Business Administrator

Name:	**CAULFIELD, LUCILLE D**
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Funding Sponsors

Name:	**PATIENT CENTERED OUTCOMES RESEARCH INSTITUTE**
Type:	**UPENN Other Non-Profit Organizations**

Regulatory Sponsor

Name:	**PATIENT CENTERED OUTCOMES RESEARCH INSTITUTE**
Type:	**UPENN Other Non-Profit Organizations**

IND Sponsor

none

Industry Sponsor

None

Project Funding*
Is this project funded by or associated with a grant or contract?
Yes

Selected Proposals

Proposal No	**Title**
10040362	**Treatment Preference and Patient Centered Prostate Cancer Care2804**

Sponsor Funding
Is this study funded by an industry sponsor?
No

Status of contract

The following documents are currently attached to this item:

Grant Application (pgreportoutputreader-rj-fullapplication.pdf)

Multi-Site Research

Other Sites

Site:	**Philadelphia Veterans Adminstration Medical Center (PVAMC)**
Contact:	**Ravishankar Jayadevappa, PhD**
Pi:	**Ravishankar Jayadevappa, PhD**
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Site:	**Fox Chase Cancer Center**
Contact:	**Yu-Ning Wong MD MSCE**
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Management of Information for Multi-Center Research
Reporting unanticipated problems involving risks to participants or others: An Adverse Event is any untoward medical occurrence in participants or clinical investigation subject who was administered a medicinal product and which does not necessarily have a causal relationship with this treatment. An AE can therefore any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with intervention. As per our knowledge, there are no known AEs due to intervention. The AEs will be closed monitored and recorded under the direction of Drs. Malkowicz, Guzzo, and Wong (co-Investigators). All unanticipated problems at the Fox Chase Cancer Center will be monitored by Dr. Wong who will then communicate with the study principal investigator, Dr. Jayadevappa. Additionally, Drs. Jayadevappa and Malkowicz will monitor the unanticipated problems involving risks to participants or others at the PVAMC. The following AE information will be collected: 1.Severity. 2.Relationship to the intervention. 3. Whether or not it is considered serious. Note the distinction between severity and seriousness. A severe AE is not necessarily serious. For Example, a headache may be severe in intensity, but would not be classified as serious unless it met one of the criteria listed below. Criteria for serious adverse event: a. Results in death, b. Is life-threatening; c. Requires inpatient hospitalization or prolongation of existing hospitalization; d. results in persistent or significant disability or incapacity. All continuing adverse events will be reported at each subsequent study visit until resolution. The date and time when the adverse even began and ended will be recorded so that the adverse even duration can be estimated. Scoring of adverse is performed by a physician who is guaranteed blinded to the treatment modality.

Adverse events labeled as serious require expeditious handling and reporting within 24 hours, and non-serious adverse events require reporting within seven days. Upon occurrence of serious adverse, the research team must complete any serious adverse event form. The data Safety Monitoring Board will determine if the serious adverse event requires updating the consent form. The principal investigator will be responsible for reporting the adverse event to the University of Pennsylvanias Institutional Review Board, the Universities Office of Human Research, as well as the PCORI. Reporting of Interim Results Interim results of unanticipated problems will be reported to by the Fox Chase Cancer Center and PVAMC by Dr. Wong and Dr. Jayadevappa respectively during annual review process and to the DSMB meetings. Coordination of protocol modifications All modifications to the protocol will be coordinated through the primary site principal investigator, Dr. Jayayadevappa in close coordinator with the DSMB and Penn IRB.

The following documents are currently attached to this item:

Site Information (reportingunanticipatedproblemsinvolvingriskstoparticipantsorothers.docx)

Protocol

Abstract
Objectives: To test the comparative effectiveness of a conjoint analysis intervention compared to usual care and identify preferred attributes of alternative prostate cancer treatments (including active surveillance) that will aid in designing ways to help patients weigh treatment attributes. We employ values markers, to represent clusters of values for particular aspects of treatments that are valued most by individual patients. Study hypothesis is that conjoint task may have an effect on treatment choice and prostate cancer patients whose treatment is more concordant with their values markers will have improved outcomes. Study Design: We propose a two phase study design. In Phase1, to identify the attributes, we will conduct six focus groups of prostate cancer patients and two focus groups with physicians who treat prostate cancer. Next, we will develop a conjoint task instrument using the attributes identified in focus groups and pilot test it. This task requires the patients to trade-off various treatments by assessing relative importance of particular treatment attributes. Results of Phase1 will yield a conjoint analysis instrument to identify profiles of treatment values markers, and will be used in Phase 2 to determine common values markers, or profiles of treatment attributes prostate cancer patients value most. Phase 2 consists of a stratified (UPHS, Fox Chase, and PVAMC) randomized controlled trial study of men with localized prostate cancer, aged 45 and randomized to either the conjoint task intervention group or usual care control group, and followed for up to 24 months for objective and subjective outcomes.

Objectives

Overall objectives
Objectives: To test the comparative effectiveness of a conjoint analysis intervention compared to usual care and identify preferred attributes of alternative prostate cancer treatments (including active surveillance) that will aid in designing ways to help patients weigh treatment attributes.

Primary outcome variable(s)
objective outcomes: cancer recurrence and complications; and subjective outcomes: health related quality of life, psychological well-being, satisfaction with decision and satisfaction with care. Outcomes Assessment: As part of Specific Aim 2, following instruments will be used to measure preferences for participation in treatment decision, decision conflict and physician trust for both intervention group and the usual care control group at baseline, immediately after treatment decision, but prior to initiation of treatment. Control Preferences Scale (CPS): The CPS assesses the role that patients want to play and perceive playing in treatment decisions [259]. It consists of five sort-cards to assess different roles in decision making, ranging from a fully active to a fully passive role. This survey will be administered at baseline only. Decision Conflict Scale (DCS): The DCS is based on a conceptual framework of decision conflict, which is a state of uncertainty about which course of action to take. This scale is well studied in cancer area and has good psychometric properties [260]. We will administer this survey at baseline (before treatment). Patient Trust-Wake Forest Physician Trust Scale: This 10-item instrument is

based on a multi-dimensional conceptual model of trust and measures trust in physicians and other health care providers [128-130]. Compared with previous scales, it showed improved internal consistency and variability [129, 131-132, 261]. Trust is measured by the sum of the 10 item scores, ranging from 10 to 50, with a higher score indicating higher trust [129, 131-132, 261]. As part of Specific Aim 3, the following outcomes will be measured for both intervention group and the usual care control group after initiation of treatment. Treatment choice: We will obtain data on primary and secondary treatments received, such as active surveillance, RP, RALP, EBRT, BT or PT via self report and verified from medical chart review. Satisfaction with Decision (SWD): The SWD scale measures satisfaction with healthcare decisions. It was developed in the context of postmenopausal hormone-replacement therapy decisions. The six-item scale has excellent reliability (Cronbachs alpha = 0.88) [262]. Regret scale: Regret represents the unsettling feeling of having made a poor choice of treatment, persistent doubt, and a wish to change one's mind. The Regret scale is defined by three items that assess (1) the mans wish that he could change his mind about the kind of treatment he has received, (2) his feeling that he would be better if he had chosen the other treatment, and (3) whether he is bothered by the fact that other men received very different treatments for their PCa [33]. This scale exhibited good psychometric properties and has been extensively studied [33, 174, 263-265]. Following objective and subjective outcome measures will be assessed at baseline and at each post-treatment follow-up period (3,6,12 and 24 months) for intervention group and usual care control group. Biochemical recurrence: We will define progression of PCa as a change in PCa stage to an advanced stage or PSADT, post treatment [11, 44-45, 55, 160, 203]. We will obtain PSA data at baseline, prior to treatment, and post treatment at three months interval for 18 months. A PSA value of greater than 0.2 ng/ml indicates disease recurrence for surgery patients. For radiation therapy patients, we will adopt the Houston / Phoenix definition of the current PSA nadir + 2 ng/mL, with date of failure determined at call as the biochemical recurrence after radiation therapy [11, 44-45, 55, 160, 203]. Any treatment within six-month of diagnosis will be considered as adjuvant (review by investigators Drs. Malkowicz, Guzzo, and Wong). D.2.4.3.2 Medical complications: We will identify complications that occur during either index or subsequent hospital admissions within 30 days of treatment [266]. Alibhai, et al. (2005), has grouped complications after RP into seven mutually exclusive categories: cardiac; respiratory; genitourinary; wound or bleeding; vascular; miscellaneous medical; and miscellaneous surgical [266]. Similarly, a list of complications for each treatment type will be developed by literature review and the physician investigators and consultants. Generic HRQoL- Medical Outcome Study Short Form: HRQoL data will be obtained using the Medical Outcome Study Short Form (SF-36) a multi-item scale that assesses eight health domains. This instrument can be self-administered or administered by a trained interviewer, either in person or by telephone. It has been tested extensively for reliability (r=0.80 - 0.93) and validity (Cronbachs =0.92). Scores on each sub-scale range from 0 to 100, with higher scores indicating better HRQoL [267-271]. Prostate Cancer HRQoL- Expanded Prostate Cancer Index (EPIC): The EPIC was developed for comprehensive assessment of HRQoL in men with PCa. It is a 50-item expanded edition of the 20-item UCLA Prostate Cancer Index (PCI) and complements other instruments by measuring a broad spectrum of urinary, bowel, sexual and hormonal symptoms. It has good psychometric properties: test-rest reliability and internal consistency are high for EPIC and for most of the subscales [189, 272-273]; construct validity was established using SF-36 as a generic core measure and a cancer-related HRQoL instrument, the Cancer Rehabilitation System-Short Form [189, 272-273]; and is easy to understand and complete [192]. American Urological Association Symptom Index (AUA-SI): The AUA-SI, a clinically sensible, reliable, valid and responsive index widely used for clinical and research purposes [274], has good internal consistency (Cronbachs =0.86), excellent test-retest reliability (r=0.92) and sensitivity to change with preoperative scores decreasing from a mean of 17.6 to 7.1 by four weeks after prostatectomy (p0.001). D.2.4.3.6 Patient Satisfaction Questionnaire (PSQ-18): This 18-item survey [a shorter version of the original Patients Satisfaction Questionnaire [275], assesses global satisfaction with medical care and satisfaction with six aspects of care: technical quality; interpersonal manner; communication; financial aspects of care; time spent with doctor; and accessibility of care. It has demonstrated good internal consistency (Cronbachs =0.86) and excellent test-retest reliability (r=0.92). Memorial Anxiety Scale for Prostate Cancer (MAX-PC): The 18-item MAX-PC identifies three aspects of PCa-related anxiety. It has high internal consistency and concurrent and discriminant validity[276]. The Center for Epidemiologic Studies Depression (CES-D) scale: This 20-item, self-report scale to identify depression in the general population covers major components of depression, with an emphasis on affective components: depressed mood; feelings of guilt and worthlessness; feelings of helplessness and hopelessness; psychomotor retardation; loss of appetite; and sleep disorder [277]. Potential confounding variables: Disease severity: We will adjust for disease severity using information on PCa stage or TNM stage, grade and histology from electronic medical records. Gleason score: The Gleason score is a sum of the predominant pattern and the second most

common pattern of the Gleason grade. Gleason score ranges from 2 -10 classified as low (2-4), intermediate (5-7) or high-grade (8-10). Elixhauser comorbidity index: The Elixhauser comorbidity index is a medical record-based metric designed to predict death in longitudinal studies, with an integer score representing increasing burden of illness [278]. We will use diagnostic information from inpatient encounters in 180 days prior to the month of PCa diagnosis to adjust for comorbidity, following the method of Elixhauser et al. [167,168,] and will obtain comorbidity scores using PICARD and VA inpatient and outpatient databases. Demographic variables: We will gather baseline data on patient age, income, education, health insurance, occupation, marital status, smoking status, height, weight and family history of PCa as possible covariates in our analyses.

Secondary outcome variable(s)
None

Background
This section reviews the significance and innovation of patient centered prostate cancer care in the context of patient-centered care and comparative effectiveness of prostate cancer care to improve quality of care and concludes with our approach to accomplish the specific aims. Impact of the Condition on the Health of Individuals and Populations (Criterion 1) A.1 Prostate cancer as a public health problem: Prostate cancer (PCa) accounts for 33% of all newly diagnosed malignancies in men, with an estimated 241,740 new PCa cases and 28,170 PCa related deaths in 2012 [1]. Ethnicity, age and family history of PCa are the only well established risk factors for PCa [2-13]. Overall mortality trends vary by age and ethnicity for all stages of PCa [2, 7, 14-15]. In population-based cancer registry data, African American PCa patients had poorer stage-specific survival and higher rate of presentation with late-stage disease than whites [2, 7, 10, 12, 14, 16-22]. Prostate cancer incidence rates increase more sharply with age than for any other cancer: 60% of all newly diagnosed PCa cases and almost 80% of all deaths occur in men aged 70 years. Age also has a strong influence on treatment: younger men are more likely to receive radical prostatectomy, middle-aged men radiation and older men either hormone therapy or no treatment [2-3]. After adjusting for clinical covariates, age disparities persisted in progression-free survival of localized PCa patients treated with radical prostatectomy [2-3, 7, 12-13, 16, 23-24]. A.2 Prostate cancer treatment choice and decision uncertainty: For PCa patients, treatment decisions are complicated. Especially, men with early stage PCa face difficult treatment decisions since optimal treatment for PCa remains unclear [2-13, 25-59]. For localized PCa patients, treatment choices include active surveillance, watchful waiting, or aggressive, potentially curative therapies, such as radical prostatectomy (RP), robotic-assisted laparoscopic prostatectomy (RALP), external-beam radiation therapy (EBRT), brachytherapy (BT) and proton therapy (PT), all with clinically significant side effects. Patient-centered care, a key component of high quality of care, involves application of scientific knowledge to patient care, tailored to each individuals unique characteristics, circumstances, needs and preferences [11, 36-45, 51, 55, 60-65]. In patient-centered PCa care, concordance between patient preferences and treatment attributes may optimize outcomes [66-74]. Uncertainties confronted by physicians and patients in the course of PCa care call for improved measures to understand patient preferences [11, 36-45, 51, 55, 60-64]. This is particularly important because we still know little about the optimal management strategies for PCa, (especially so, since most treatments have troublesome adverse effects) and how best to advise patients regarding treatment choice [11, 36-45, 51, 55, 60-64]. Few studies have assessed patient treatment preferences, the role desired by patients in decision making, and the association of patient treatment preferences with outcomes, as we propose here. Our study addresses the need for studying values markers and their potential relationship to outcomes in order to determine if matching values markers to attributes of treatment will improve quality of care and outcomes. A.3 Preference assessment-conjoint analysis: Patients newly diagnosed with localized PCa face difficult decisions regarding treatment choice and management of disease. One way to explore treatment related risk-benefit tradeoff entails assessment of patient preferences for key outcomes associated with PCa treatment. Conjoint analysis is a method with strong theoretical roots in mathematical psychology [75], and asks respondents to make a series of holistic decisions from which tradeoffs among conflicting attributes (such as treatment outcomes) can be disentangled and deduced. Conjoint analysis methods thus seek to uncover the underlying preference function of a treatment in terms of its attributes [75-79]. Conjoint analysis is a method that uncovers respondent tradeoffs among various attributes of competing products or services, such as treatment options for PCa and allows the assessment of treatment attribute weights as opposed to the preferences themselves. Profiles of treatment attributes (value markers) are identified that are associated with particular choices since the preference profile is more or less aligned with the characteristics of the treatment provided. Conjoint analysis generates a preference (utility) score that has a numeric value that refers to the part-worth

assigned to particular attributes and its levels. Process of conjoint analysis involves four steps: 1) Identifying treatment attributes; 2) assigning levels to attributes; 3) developing choice scenarios; and 4) establishing choice preferences and analysis. It has been used in many health-related applications [75-105]. For example, conjoint analysis was employed to study the factors important to patients in choosing a hospital [92], to elicit patient priorities in womens health [77, 79, 94], to establish consumer preferences for dental services [82, 89], and to elicit patient perspectives in medical conditions [80, 87-88, 90, 93, 95, 98, 100, 106]. In clinical research, conjoint analysis has begun to be recognized as a valuable means of assessing patient preferences for healthcare [107-109]. It has been successfully used in elderly to understand their preferences for cataract surgery options [102], hearing aids [97], and osteoarthritis treatment options [101]. In mental health, conjoint analysis has been used to assess features of treatment that low-income Latinos thought would improve acceptability of treatment [85] and to inform the design of a alcohol and smoking cessation program [86]. Relative weights (utilities) derived from conjoint task can be used to form profiles (sets or patterns of utilities) representing values markers that may be associated with treatment outcomes. In our proposed study, we will classify patients based on latent profiles of utilities to study the relationship among profiles (values markers), treatment received and outcomes such as Health related Quality of Life (HRQoL), satisfaction with care, complications and psychological well-being. Concordance between value markers and outcomes: Prostate cancer patients face a series of choices during all phases of their PCa care (pre-treatment, treatment, follow-up and terminal phase). While a wealth of information regarding these choices is available, it can often be confusing to a patient to sort it out and can affect the patient centeredness of care. This can also lead to difficulties in decision making, treatment regrets etc. from a patients' perspective, and can be exasperating to both patients and providers. An important goal of patient centered PCa care is to help PCa patients reach satisfying resolutions of difficult problems by reaching treatment decisions with which they can live. To facilitate informed patient centered PCa decision making, strategies are being proposed that include innovative ways of presenting complex information to the patients, and developments of devices that will aid patients in articulating their preferences and facilitate decisions that are concurrent with their values [63, 110]. Currently, one understudied area is the magnitude and direction of concordance with value markers and treatment choice, degree and quality of satisfaction that men subsequently experience, as they do indeed live with their decisions. A.4 Informed clinical decision making and physician's role: Informed decision making is at the core of patient centered care and is a process that implies that a physicians unbiased knowledge is transferred to the patient, who then has the knowledge and preferences necessary to make a decision. Studies have discussed non-systematic process of decision making in PCa care. Many patients with localized PCa choose surgery instead of other treatments thinking that surgery is the best way to cure PCa [111-114]. Prostate cancer treatments frequently are complex and unfamiliar to many patients. A majority of PCa patients report that their physicians recommendation was the most important factor in their treatment choice [11-12, 37-46, 51, 55-56, 60-64]. This is appropriate if the physician is an efficient agent for the patient, i.e., making the decision the patient would if the patient had physicians medical knowledge. The physician agency model presupposes that the physician knows and understands the patients attitudes, beliefs, preferences and values. However, patient and physician beliefs differ in many respects, such as prioritizing outcomes, conceptualization of the illness, and ranking available options [11-12, 25, 37-46, 51, 55-56, 60-64, 68, 115-117]. Thus, physicians opinion as a credible source may inappropriately bias a patients systematic decision process. Preferences cannot be based on misinformation or missing information, so physicians need to ascertain that they and their patients have sufficient knowledge to construct informed preferences in concordance with the patients values. Respecting and responding to patient preferences - the hallmark of patient centered care requires accurately eliciting preferences and aiding patients in constructing them. A.5 Decision making, decision conflict and trust: Enabling PCa patients to assume a more active role in decision making is associated with reduction of decision conflict [36-43, 60, 62-63, 67-68, 118-127]. Decision conflict means perceiving a poor quality of the decision, feeling unsupported, unclear about the values and uncertain about a treatment decision. Acknowledging that PCa patients desire a role in decision making provides a foundation to foster active involvement and negotiate a treatment plan to which both patient and physician agree. Patients trust in their health care providers may affect their satisfaction and outcomes. Trust is a fundamental aspect of healthcare and of the patient-physician relationship. Due to uncertainty in all stages of PCa care, trust can play a crucial role in treatment decisions. In addition to giving medical relationships intrinsic value, trust is critical to a patients willingness to seek care, reveal sensitive information and submit to and obtain treatment. Trust is central to the ongoing debate about structure and regulation of healthcare delivery [128-133]. Differences in levels of trust among patients may help explain variations in care seeking and use of preventive and treatment services [128-132]. In addition to biological and other risk factors, mistrust of physicians is associated with lower use of

preventive and curative services, and disparities in outcomes [128-132, 134]. In uncertain and ambiguous situations, such as choosing a PCa treatment, patients often find it difficult to choose and defer their decisions. In this regard, decision conflict, preference to participate in treatment choice and physician trust may play pivotal roles. A.6 Treatment and outcomes: Currently there is no consensus about optimum management of localized PCa that often with no treatment might never become life threatening. Due to the slow growth of some malignant PCa cells, many cancers remain latent and a great proportion of patients may not need aggressive treatment [135-155]. Active surveillance is an alternative strategy that allows individualized management of low-risk PCa with PSA tests, digital rectal exam (DRE) and repeat biopsies without compromising the potential for curative treatment. Low risk patients on active surveillance potentially avoid complications related to treatment while meeting goals of metastasis-free survival, thereby enhancing HRQoL. While several treatment options are available for localized PCa, they often have significant short and/or long term effects [56]. Treatment for PCa can affect a patients sense of identity, particularly his masculine identity, HRQoL, psychological wellbeing and cost. Table1 presents a comparison synopsis of outcomes associated with treatments. Detailed discussion of each outcome [45, 47, 56, 156-158] follows. A.6.1 Disease progression: Prostate cancer disease severity affect treatment outcomes and must be considered in outcome evaluation. Introduction of the PSA serum marker in1988 dramatically altered PCa diagnosis. Biochemical recurrence also has important implications for HRQoL and is a key issue in the PCa clinical decision making process [159]. Two-thirds of PCa patients are treated with either radiation or surgery; up to 40% may eventually relapse, with early progression in terms of PSA only, and receive follow-up treatment. The PSA level at which to define failure after RP varies between 0.2 ng/ml and 0.5ng/ml. Phoenix definition of PSA nadir +2 has been accepted definition of PSA recurrence[160]. PSA doubling time is an important predictor of systemic progression and local or systemic clinical progression [36, 95,117]. A.6.2 Patient centered outcomes-Health-Related Quality of Life: Patient reported outcomes such as HRQoL and satisfaction with care provide real time information for general and disease-specific domains [46, 161-162]. The conceptual model of HRQoL described by Wilson and Cleary includes five levels of outcomes: biological and physiological factors, symptoms, functioning, general health perceptions and overall quality of life [161, 163]. Age at diagnosis, and type of and time to treatment are associated with impaired HRQoL[164-167]. Men with early stage PCa often live long after diagnosis and desire to maximize the quality of their life [2-10, 13, 25-37, 39-43, 54, 58, 60, 62, 168-170]. Past studies on HRQoL in PCa patients have found inconclusive results [16, 23-24, 49-50, 61, 168-169, 171-192]. Men treated with RP for localized PCa continued to experience impaired urinary and sexual function, whereas, men treated with EBRT had worse sexual and bowel function [16, 23-24, 26-30, 49-50, 56, 58, 61, 168-169, 171-191, 193]. Many studies of HRQoL comparing patients treated with RP or EBRT reported that men receiving RP had frequent problems with urinary incontinence [16, 23-24, 49-50, 61, 168-169, 171-191, 194-195]. Long-term (five year) study of localized PCa patients receiving RP showed that most of the prostate-specific HRQoL functions needed time to recover to pre-operative baseline values [196-198]. These results demonstrate that variations occur in generic and prostate-specific HRQoL across treatment and time (short and long-term) and thus HRQoL is critical elements of treatment choice. A.6.3 Satisfaction with care: Satisfaction with care is an important patient reported outcome and consists of three dimensions-patient level attributes, satisfaction with treatment choice/decision and process, and satisfaction with outcomes. Some personality traits are associated with satisfaction with care [199] and satisfaction with care is associated with outcomes and treatment type [29, 193, 198]. In a study of 2,365 men with clinically localized PCa, believing oneself to be free of cancer, avoiding complications and having good health and social support were positively related to satisfaction [200]. Improved patient-reported clinical outcomes was associated with higher satisfaction with care. Also, confidence in medical system, regular source of care and being satisfied with life are important predictors of satisfaction. Thus, a satisfaction with care measure may be sensitive to patient level attributes, and outcomes and process of care [44, 130]. A.6.4 Psychological wellbeing: Stress, anxiety and depression are implicated in the pathogenesis and progression of PCa and impaired HRQoL [24, 32-33, 111, 177, 201-204]. Depression is common in PCa patients and leads to poorer outcomes and higher costs [84, 201, 205-212]. Prostate cancer specific worry was significantly associated with abnormal PSA level [208, 210-211, 213-215]. Innovation and Potential for Improvement Through Research: patient centered care as providing care that is respectful of and responsive to individual patient preferences, needs, and values, and ensuring that patient values guide all decisions [118, 216-217]. Patient centered care that encompasses informed decision making is a process of decision making by patient and physician whe Conceptual Framework: The Institute of Medicine defined re the patient: 1) understands the risk or seriousness Outcomes of the disease or condition to be prevented; 2) understands the preventive service, including the risks, benefits, alternatives and uncertainties; 3) has evaluated his values regarding the potential benefits and harms

associated with treatment; and 4) has engaged in decision making at a level at which he desires and feels comfortable [41, 63, 69, 118, 216, 218-221]. As seen from Figure 1, a conceptual model of individual decision making in the context of patient centered care consists of multiple domains (patient and clinical characteristics, attributes and values; patient preferences; physician recommendation; treatment choice; concordance and outcomes) that influence treatment choice and outcomes [66, 72, 222-226]. Patients differ in the extent to which they wish to be involved in decision making for their medical care [218, 227]. While some prefer active participation, others opt for a more passive role and defer decisions to their physician. Physicians are thus encouraged to tailor care according to patient preferences [33, 37, 41, 48, 63, 80, 87, 118, 218-219, 228]. Patient-centered care requires knowledge of how patients preferences and reasoning affects choice of alternative therapeutic options. Per preference assessment theory, PCa patients will be aided in deciding what treatment strategy they should receive on the basis of information about the choices. The healthcare provider, as the patients agent, will support the patient in this process, rather than deciding the treatment for them. As physicians are more likely to recommend treatments related to their specialty [229], patient centered care with the addition of uniform preference assessment can help minimize physician decision bias and help better inform patients. Concordance between patient preference and treatment choice is at the core of patient centered care.

Study Design

Phase*
Not applicable

Design
We will study the comparative effectiveness of conjoint analysis intervention compared to usual care, and identify preferred attributes of alternative PCa treatments (including active surveillance) that will aid us design ways to help patients weigh the attributes of treatment. We employ values markers, to represent clusters of values for particular aspects of treatments that are valued most by individual patients. We propose a two phase study (Figure 2). In Phase 1, we will identify the PCa treatment attributes most salient to patients and providers in order to develop the conjoint analysis tasks to be used in Phase 2. In Phase 2, we will analyze the comparative effectiveness of patient centered conjoint analysis intervention and assess the relationships among attributes of treatment received, profiles of valued treatment attributes (values markers), and patient outcomes using a stratified randomized controlled trial. We propose to test if the concordance between values markers and treatment received is predictive of subjective and objective outcomes among PCa patients. In Phase1 of the study, we will develop an instrument to assess patient treatment preferences using conjoint analysis. Phase 1 will also ensure significant involvement of stakeholders (patients and physicians). First we will identify the salient attributes related to PCa treatment and outcomes using: (1) results from our prior studies and literature review; (2) six patient focus group meetings, each with 6-10 participants; and (3) two physician focus group meetings, each with 6-10 physicians (urologists, oncologists, radiation oncologist, primary care and geriatricians) who provide PCa care. Next, using the salient attributes, we will develop a conjoint task instrument to assess patient preferences and pilot test the instrument. Conjoint analysis is a technique for estimating the relative importance of different attributes for the valuation of treatment and outcome. The process of eliciting preferences via conjoint analysis involves following steps: (1) Identifying and defining attributes. After identifying attributes from literature review, our prior research and the prior physician focus group, we will conduct six focus groups with PCa patients, each consisting of 6-10 men with localized PCa and two physician focus groups, each with 6-10 physicians who treat PCa. Focus group participants will identify and further define attributes and their levels. Attributes will be identified using health and non-health categories, such as generic and PCa specific HRQoL, psychological well-being (depression, stress and anxiety); time away from work, travel time; out-of-pocket costs; caregiver burden; and other. (2) Focus groups. After obtaining informed consent from physicians, we will recruit ~60 eligible PCa patients from urology clinics for the six focus groups (n 6 to 10 each). Both practical and substantive considerations form the basis for the rule of thumb that specifies the range of 6 to 10 participants [254]. Each focus group will have equal representation of age groups. Participants first will undergo a standardized educational session with the study team regarding PCa treatment and outcomes. Initially, we will identify salient attributes of PCa treatments and outcomes as perceived by patients. The research team will use the focus group themes and responses to guide design and conduct of subsequent focus groups and development of the conjoint task. We will conduct audio/video recording of all focus groups. Conjoint analysis is a method that combines qualitative and quantitative methods to capture consumer preferences. The initial qualitative

phase is critical for determining the salient characteristics of a product or service. Typically, researchers use focus groups that consist of end-users or "experts", to learn from people who have the most experience with the service, but researchers also convene focus groups of people who have little or no experience with a service to learn what may be important for a new user. Focus groups typically are comprised of 6 to 10 participants who do not know one another and who have similar associations to the topic being investigated (i.e., newly diagnosed localized PCa patients). We will make an effort to recruit equal number of surgical and radiation treatment patients and men younger than age 65 and age 65. It is recommended that one conduct at least two focus groups to capture experiences from similar groups of individuals [254-256]. Drs. Chhatre, Johnson, and Schwartz each have extensive experience in racial and ethnic disparity research and will carefully construct each focus group. Thus, we will conduct focus groups with good representation from minority and non-minority patients. Of the six patient focus groups, three will be with newly diagnosed patients yet to make treatment decision; and three will be with those who underwent treatment one year ago, providing additional insight into what they wish they had known about the less immediate outcomes and aspects of treatment. In contrast to individual interview, focus group participants relate their experiences and reactions among peers with whom they likely share some common frame of reference. The discussions stimulated in a group setting and listening to others' experiences has the potential to stimulate memories, ideas and experiences relevant to the topic at hand [254-256]. Overarching goal of focus groups is to obtain perspectives of two of the key stakeholders (patients and physicians) about those components or features of PCa care are important to consider in choosing a treatment. The most commonly mentioned and strongly weighted features of treatment across the focus groups will be used to create the conjoint task (to be used in Phase2). If saturation of emerging themes is not reached after six focus groups, we will conduct additional focus groups until saturation occurs. (See Appendix for interview guide that was developed using results of our prior focus group of physicians, discussed in preliminary work). (3) Assigning levels to the attributes. Levels of an attribute may be cardinal (e.g. waiting time, missed work), ordinal (e.g. level of pain) or categorical (e.g. surgery or radiation treatment). Attribute levels will be identified and aligned with the active surveillance (AS) and five active treatment options being studied (RP, RALP, BT, EBRT, PT), reviewed for appropriateness and wording by the study investigators and advisory board members. (4) Developing choice scenarios. Scenarios will describe services, treatment options and outcome configurations for the attributes and level chosen. We will use a fractional factorial design to reduce the number of paired comparisons to the smallest number necessary for efficient estimation of utility weights [49,183,188]. (5) Conjoint task instrument testing. We will pilot test the conjoint task instrument for appropriateness of attributes, levels, language and ease of administration in 20 PCa patients. PHASE 2 Study Population: We will use stratified randomized control trial to study association between value markers and objective (complications and cancer recurrence) and subjective (HRQoL, psychological wellbeing) outcomes across intervention groups, over 24 month period. We will recruit newly diagnosed localized PCa patients from UPHS (Hospital of University of Pennsylvania, Presbyterian Medical Center, and Pennsylvania Hospital), Fox Chase Cancer Center and Philadelphia Veterans Administration Medical Center (PVAMC) and randomize them to conjoint analysis intervention (n=360) or control group (n=360). D.2.1.1 Participants: The sample will consist of 720 newly-diagnosed PCa patients. Inclusion criteria are: (1) treated for PCa at UPHS, Fox Chase Cancer Center or PVAMC; (2) aged 45 yearsr; (3) newly diagnosed with localized PCa and TNM stage T3a; (4) community dwelling; (5) Gleason score 8; (6) low (PSA 10 ng/ml, Gleason 6, clinical stage T1-2a), intermediate (PSA 10 -20 ng/ml, Gleason 7, clinical stage T2b), and high risk (PSA 20, Gleason 8, clinical stage T2c-3a) group [45] and (7) provide informed consent. Exclusion criteria are: (1) Distant, metastatic or un-staged PCa at diagnosis; (2) visited the clinics to obtain second opinion only; (3) moved to another location; (4) unable to communicate in English and (5) cognitive impairment (Mini Mental State Exam or MMSE score 21). MMSE is a standardized mental status examination widely used for clinical and research purposes [197,198]. D.2.1.2 Recruitment and participant availability: Participants will be recruited from UPHS, PVAMC and Fox Chase Cancer Center's urology and radiation oncology clinics using recruitment protocols that we have successfully used in our prior and ongoing PCa studies. Recruitment will occur in seven steps: 1) determining potential eligibility; 2) obtaining consent from patients urologist/physician; 3) confirming eligibility; 4) screening via phone and interview to assess willingness to participate; 5) obtaining informed consent and HIPAA permissions; 6) baseline assessments; and 7) follow-up assessments. The study and consent form comply with HIPAA Standards for Privacy of Individually Identifiable Health Information. The draft study design and protocol have been approved by the University of Pennsylvania IRB. Future changes will be reviewed and approved prior to implementation. Participant availability: UPHS is a large hospital and physician network in greater Philadelphia area. Approximately 1,600 patients with newly diagnosed PCa are evaluated annually: 40-50% undergo surgery (RP or RALP); 30-40% undergo EBRT

or BT; 10-20% undergo PT. The urology clinic at PRINCIPAL INVESTIGATOR (LAST, FIRST, MIDDLE): Jayadevappa, Ravishankar PCORI Research Plan: Research Strategy 9 the Hospital of the University of Pennsylvania (HUP) treats more than 60% of this group; the rest are treated at Presbyterian Medical Center and Pennsylvania Hospital. Additionally, UPHS has a proton therapy center, providing a unique opportunity to study this new technology. The Philadelphia Veterans Administration Medical Center (PVAMC) cares for 33,000 veterans in Philadelphia area and evaluates ~400 patients with newly diagnosed PCa each year. Fox Chase Cancer Center evaluates ~500 patients with newly diagnosed PCa each year. Together, UPHS, PVAMC, and Fox Chase Cancer Center provide care to socio-demographically diverse population of ~2,500 men newly diagnosed with PCa each year. Thus, our study sample requirement of 720 patients (33% of the available pool) can be fulfilled comfortably, as demonstrated by the successful recruitment for our earlier studies. Recruitment: Prior to study initiation, investigators will explain the study objectives to physicians who actively treat PCa at the UPHS, PVAMC, Fox Chase urology clinics. During a patients initial visit, Drs. Malkowicz, Guzzo, or Wong will briefly introduce the study to the patient. Each week, the research assistant will contact the participating physician offices to obtain contact information for those patients who have expressed an interest in the study. Potential participants will be contacted during their office visits, at which time those eligible may agree to participate and provide informed consent, request additional information and/or time to think or request to be contacted later. Patients who request to be contacted later will be sent study information, a consent form and a prepaid return envelope. Participants will discuss the consent form with research assistant prior to signing, at which time all questions will be answered. During enrollment, compensation of $20 will be provided. Using a similar recruitment strategy in our prior PCa studies, we had achieved enrollment and retention rates of 85% or higher. The expected number of 60 participants in each treatment group (AS, RP, RALP, EBRT, BT or PT) will be achieved as follows: (1) each recruited participant randomly assigned to the conjoint analysis intervention group will meet with research assistant to complete the computer-based conjoint analysis tasks and other surveys before initiation of treatment or making a treatment decision; (2) after treatment decision is made, patients (both cases and controls) will be assigned to the appropriate group based on treatment; (3) this process will continue until we reach the required number of participants in each group. To achieve this, we may evaluate and obtain baseline data including conjoint tasks from patients in excess of the required 360 participant each in the intervention and control groups. Based on our prior prospective cohort studies, to fulfill sample requirement of 60 participant in each treatment group (60x2x6 =720), allowing for attrition we expect to obtain baseline assessment including conjoint tasks for 800 participants (10% excess). The cohort that doesnt get assigned for further follow-up due to targeted group enrollment accrual will be analyzed to ensure comparability. D.2.2 Process of stratified randomization: We will recruit 720 participants stratified by three hospitals-UPHS, PVAMC, or Fox Chase Cancer Center (Figure 3). Dr. Morales will create randomization sequences for each hospital using a pseudo-random number generator with random blocking and will place the treatment assignments in sealed, opaque envelopes. All investigators, staff and referring physicians will be masked to the treatment assignment, except the research assistant who will open the envelope and notify participants of group assignment. Participants will be instructed not to reveal their group status to physicians or study personnel, except in case of emergency or if necessary for medical reason, which we believe to be unlikely. D.2.2.1 Conjoint analysis intervention The primary goal of patient-centered PCa care is to engage patients and their families in meaningful and thorough interactions with their healthcare providers to develop accurate and well-conceived treatment choice, using all available medical information appropriately, while also considering the medical, social and cultural needs and desires of the patient and family. It is important for providers to solicit patient preferences and not make assumptions about which treatment and associated side effects patients are more likely to prefer or feel is best for them. Results of conjoint analysis will be shared with the participants of the intervention group, family members, and treating physicians prior to treatment decision. D.2.2.2 Usual care controls: Participants from this group will receive usual care that consists of standard educational material about various treatment options. D.2.3 Data collection and follow-up: After obtaining informed consent, baseline data will be obtained in person prior to the initiation of treatment. Participants will meet with the research assistant to complete the PRINCIPAL INVESTIGATOR (LAST, FIRST, MIDDLE): Jayadevappa, Ravishankar PCORI Research Plan: Research Strategy 10 computer-based conjoint analysis tasks. Patient identifiers will be removed to maintain data confidentiality. Only the PI will have access to the master files. For conjoint analysis, each participant will be asked to express his preference for attributes and attribute levels for active surveillance and five active treatments for clinically localized PCa (RP, RALP, EBRT, PT, BT) based on choice sets presented. The choices will vary based on the differing attributes of various treatments ascertained in prior work and focus groups. After pilot testing and refining the conjoint task in Phase 1, final attributes and levels will be used. Trade-offs

among treatment features will be calculated in patient-specific utilities or part-worths associated with the attribute levels in the study. For other outcomes, participants will receive the following surveys via mail within 1-2 weeks after enrollment and prior to treatment initiation: SF-36, EPIC, AUA-SI, regret scale, CES-D, MAX-PC, SWD, PSQ-18, CPS, DCS and trust scale. Demographics, health and family history, clinical covariates and cancer progression data will be collected at 3, 6, 12 and 24 month follow-up. Histological tumor grade Gleason score and PSA and annual Elixhauser comorbidity score [257-258] will be obtained from the Pennsylvania Integrated Clinical and Research Database (PICARD), a UPHS, Fox-Chase Cancer Center electronic database, and PVAMC administrative and patient HER database. Retention and survey administration: During enrollment, importance of active participation will be emphasized. All participants will complete self-administered surveys at baseline within 1-2 weeks after enrollment (prior to treatment initiation) and again 3,6,12 and 24 months post-enrollment (see Appendix for copies of instruments, consent and medical chart review form). Non-respondents will be contacted via telephone after 10 days. In case of non-response due to death, cause of death will be noted and the physician investigators will determine cause of death (PCa or non-PCa related). The PCa conjoint analysis task, DCS, CPS and trust scale will be administered at baseline only, immediately after diagnosis of PCa and before treatment decision. D.2.4 Outcomes Assessment: D.2.4.1 As part of Specific Aim 2, following instruments will be used to measure preferences for participation in treatment decision, decision conflict and physician trust for both intervention group and the usual care control group at baseline, immediately after treatment decision, but prior to initiation of treatment. D.2.4.1.1 Control Preferences Scale (CPS): The CPS assesses the role that patients want to play and perceive playing in treatment decisions [259]. It consists of five sort-cards to assess different roles in decision making, ranging from a fully active to a fully passive role. This survey will be administered at baseline only. D.2.4.1.2 Decision Conflict Scale (DCS): The DCS is based on a conceptual framework of decision conflict, which is a state of uncertainty about which course of action to take. This scale is well studied in cancer area and has good psychometric properties [260]. We will administer this survey at baseline (before treatment). D.2.4.1.3 Patient Trust-Wake Forest Physician Trust Scale: This 10-item instrument is based on a multi-dimensional conceptual model of trust and measures trust in physicians and other health care providers [128-130]. Compared with previous scales, it showed improved internal consistency and variability [129, 131-132, 261]. Trust is measured by the sum of the 10 item scores, ranging from 10 to 50, with a higher score indicating higher trust [129, 131-132, 261]. D.2.4.2 As part of Specific Aim 3, the following outcomes will be measured for both intervention group and the usual care control group after initiation of treatment. D.2.4.2.1 Treatment choice: We will obtain data on primary and secondary treatments received, such as active surveillance, RP, RALP, EBRT, BT or PT via self report and verified from medical chart review. . D.2.4.2.2 Satisfaction with Decision (SWD): The SWD scale measures satisfaction with healthcare decisions. It was developed in the context of postmenopausal hormone-replacement therapy decisions. The six-item scale has excellent reliability (Cronbachs alpha = 0.88) [262]. D.2.4.2.3 Regret scale: Regret represents the unsettling feeling of having made a poor choice of treatment, persistent doubt, and a wish to change one's mind. The Regret scale is defined by three items that assess (1) the mans wish that he could change his mind about the kind of treatment he has received, (2) his feeling that he would be better if he had chosen the other treatment, and (3) whether he is bothered by the fact that other men received very different treatments for their PCa [33]. This scale exhibited good psychometric properties and has been extensively studied [33, 174, 263-265]. D.2.4.3 Following objective and subjective outcome measures will be assessed at baseline and at each post-treatment follow-up period (3,6,12 and 24 months) for intervention group and usual care control group. D.2.4.3.1 Biochemical recurrence: We will define progression of PCa as a change in PCa stage to an advanced stage or PSADT, post treatment [11, 44-45, 55, 160, 203]. We will obtain PSA data at baseline, prior to treatment, and post treatment at three months interval for 18 months. A PSA value of greater than 0.2 ng/ml indicates disease recurrence for surgery patients. For radiation therapy patients, we will adopt the Houston /Phoenix definition of the current PSA nadir + 2 ng/mL, with date of failure determined at call as the biochemical recurrence after radiation therapy [11, 44-45, 55, 160, 203]. Any treatment within six-month of diagnosis will be considered as adjuvant (review by investigators Drs. Malkowicz, Guzzo, and Wong). D.2.4.3.2 Medical complications: We will identify complications that occur during either index or subsequent PRINCIPAL INVESTIGATOR (LAST, FIRST, MIDDLE): Jayadevappa, Ravishankar PCORI Research Plan: Research Strategy 11 hospital admissions within 30 days of treatment [266]. Alibhai, et al. (2005), has grouped complications after RP into seven mutually exclusive categories: cardiac; respiratory; genitourinary; wound or bleeding; vascular; miscellaneous medical; and miscellaneous surgical [266]. Similarly, a list of complications for each treatment type will be developed by literature review and the physician investigators and consultants. D.2.4.3.3 Generic HRQoL- Medical Outcome Study Short Form: HRQoL data will be obtained using the Medical Outcome Study Short Form (SF-36) a multi-

item scale that assesses eight health domains. This instrument can be self-administered or administered by a trained interviewer, either in person or by telephone. It has been tested extensively for reliability (r=0.80 - 0.93) and validity (Cronbachs =0.92). Scores on each sub-scale range from 0 to 100, with higher scores indicating better HRQoL [267-271]. D.2.4.3.4 Prostate Cancer HRQoL- Expanded Prostate Cancer Index (EPIC): The EPIC was developed for comprehensive assessment of HRQoL in men with PCa. It is a 50-item expanded edition of the 20-item UCLA Prostate Cancer Index (PCI) and complements other instruments by measuring a broad spectrum of urinary, bowel, sexual and hormonal symptoms. It has good psychometric properties: test-rest reliability and internal consistency are high for EPIC and for most of the subscales [189, 272-273]; construct validity was established using SF-36 as a generic core measure and a cancer-related HRQoL instrument, the Cancer Rehabilitation System-Short Form [189, 272-273]; and is easy to understand and complete [192]. D.2.4.3.5 American Urological Association Symptom Index (AUA-SI): The AUA-SI, a clinically sensible, reliable, valid and responsive index widely used for clinical and research purposes [274], has good internal consistency (Cronbachs =0.86), excellent test-retest reliability (r=0.92) and sensitivity to change with preoperative scores decreasing from a mean of 17.6 to 7.1 by four weeks after prostatectomy (p0.001). D.2.4.3.6 Patient Satisfaction Questionnaire (PSQ-18): This 18-item survey [a shorter version of the original Patients Satisfaction Questionnaire [275], assesses global satisfaction with medical care and satisfaction with six aspects of care: technical quality; interpersonal manner; communication; financial aspects of care; time spent with doctor; and accessibility of care. It has demonstrated good internal consistency (Cronbachs =0.86) and excellent test-retest reliability (r=0.92). D.2.4.3.7. Memorial Anxiety Scale for Prostate Cancer (MAX-PC): The 18-item MAX-PC identifies three aspects of PCa-related anxiety. It has high internal consistency and concurrent and discriminant validity[276]. D.2.4.3.8. The Center for Epidemiologic Studies Depression (CES-D) scale: This 20-item, self-report scale to identify depression in the general population covers major components of depression, with an emphasis on affective components: depressed mood; feelings of guilt and worthlessness; feelings of helplessness and hopelessness; psychomotor retardation; loss of appetite; and sleep disorder [277]. D.2.4.4. Potential confounding variables: Disease severity: We will adjust for disease severity using information on PCa stage or TNM stage, grade and histology from electronic medical records. Gleason score: The Gleason score is a sum of the predominant pattern and the second most common pattern of the Gleason grade. Gleason score ranges from 2 -10 classified as low (2-4), intermediate (5-7) or high-grade (8-10). Elixhauser comorbidity index: The Elixhauser comorbidity index is a medical record-based metric designed to predict death in longitudinal studies, with an integer score representing increasing burden of illness [278]. We will use diagnostic information from inpatient encounters in 180 days prior to the month of PCa diagnosis to adjust for comorbidity, following the method of Elixhauser et al. [167,168,] and will obtain comorbidity scores using PICARD and VA inpatient and outpatient databases. Demographic variables: We will gather baseline data on patient age, income, education, health insurance, occupation, marital status, smoking status, height, weight and family history of PCa as possible covariates in our analyses.

Study duration

We will use stratified randomized control trial to study association between value markers and objective (complications and cancer recurrence) and subjective (HRQoL, psychological wellbeing) outcomes across intervention groups, over 24 month period. We will recruit newly diagnosed localized PCa patients from UPHS (Hospital of University of Pennsylvania, Presbyterian Medical Center, and Pennsylvania Hospital), Fox Chase Cancer Center and Philadelphia Veterans Administration Medical Center (PVAMC) and randomize them to conjoint analysis intervention (n=360) or control group (n=360). Length of a Subject's participation time In study: 24 months All participants will complete self-administered surveys at baseline within 1-2 weeks after enrollment (prior to treatment initiation) and again 3,6,12 and 24 months post-enrollment. Projected Date of the Proposed Study: July 2013 to June 2016.

Resources necessary for human research protection

Describe research staff and justify that the staff are adequate in number and qualifications to conduct the research. Describe how you will ensure that all staff assisting with the research are adequately informed about the protocol and their research related duties. Describe access to a population that would allow recruitment of the targeted number of subjects. If medical or psychological services as a consequence of the research, describe how the subject will be referred to those services. Describe your facilities and justify that the facilities are adequate. Verify that there is sufficient time to conduct and complete the research.

The study Principal Investigator and all co-investigators are well qualified to conduct this research. The

PI, Dr. Jayadevappa is a health services researcher with expertise in cancer outcomes research. Similarly, all co-investigators of the study are well qualified to support the proposed research and bring multiple expertise to this project. The investigators have completed the necessary human research protection training. We will also ensure that the research coordinator and research assistant will complete all necessary training certifications prior to engaging in study activities. Participants will be recruited from UPHS, PVAMC and Fox Chase Cancer Center's urology and radiation oncology clinics using recruitment protocols that we have successfully used in our prior and ongoing PCa studies. Recruitment will occur in seven steps: 1) determining potential eligibility; 2) obtaining consent from patients urologist/physician; 3) confirming eligibility; 4) screening via phone and interview to assess willingness to participate; 5) obtaining informed consent and HIPAA permissions; 6) baseline assessments; and 7) follow-up assessments. The study and consent form comply with HIPAA Standards for Privacy of Individually Identifiable Health Information. The draft study design and protocol have been approved by the University of Pennsylvania IRB. Future changes will be reviewed and approved prior to implementation. Participant availability: UPHS is a large hospital and physician network in greater Philadelphia area. Approximately 1,600 patients with newly diagnosed PCa are evaluated annually: 40-50% undergo surgery (RP or RALP); 30-40% undergo EBRT or BT; 10-20% undergo PT. The urology clinic atthe Hospital of the University of Pennsylvania (HUP) treats more than 60% of this group; the rest are treated at Presbyterian Medical Center and Pennsylvania Hospital. Additionally, UPHS has a proton therapy center, providing a unique opportunity to study this new technology. The Philadelphia Veterans Administration Medical Center (PVAMC) cares for 33,000 veterans in Philadelphia area and evaluates ~400 patients with newly diagnosed PCa each year. Fox Chase Cancer Center evaluates ~500 patients with newly diagnosed PCa each year. Together, UPHS, PVAMC, and Fox Chase Cancer Center provide care to socio-demographically diverse population of ~2,500 men newly diagnosed with PCa each year. Thus, our study sample requirement of 720 patients (33% of the available pool) can be fulfilled comfortably, as demonstrated by the successful recruitment for our earlier studies.

Characteristics of the Study Population

Target population
Study Population: We will use stratified randomized control trial to study association between value markers and objective (complications and cancer recurrence) and subjective (HRQoL, psychological wellbeing) outcomes across intervention groups, over 24 month period. We will recruit newly diagnosed localized PCa patients from UPHS (Hospital of University of Pennsylvania, Presbyterian Medical Center, and Pennsylvania Hospital), Fox Chase Cancer Center and Philadelphia Veterans Administration Medical Center (PVAMC) and randomize them to conjoint analysis intervention (n=360) or control group (n=360). Participants: The sample will consist of 720 newly-diagnosed PCa patients.

Subjects enrolled by Penn Researchers
580

Subjects enrolled by Collaborating Researchers
220

Accrual
Participant availability: UPHS is a large hospital and physician network in greater Philadelphia area. Approximately 1,600 patients with newly diagnosed PCa are evaluated annually: 40-50% undergo surgery (RP or RALP); 30-40% undergo EBRT or BT; 10-20% undergo PT. The urology clinic atthe Hospital of the University of Pennsylvania (HUP) treats more than 60% of this group; the rest are treated at Presbyterian Medical Center and Pennsylvania Hospital. Additionally, UPHS has a proton therapy center, providing a unique opportunity to study this new technology. The Philadelphia Veterans Administration Medical Center (PVAMC) cares for 33,000 veterans in Philadelphia area and evaluates ~400 patients with newly diagnosed PCa each year. Fox Chase Cancer Center evaluates ~500 patients with newly diagnosed PCa each year. Together, UPHS, PVAMC, and Fox Chase Cancer Center provide care to socio-demographically diverse population of ~2,500 men newly diagnosed with PCa each year. Thus, our study sample requirement of 720 patients (33% of the available pool) can be fulfilled comfortably, as demonstrated by the successful recruitment for our earlier studies. We estimated sample

size based on the observed differences in outcomes such as HRQoL (SF-36 and prostate cancer index, PCI) and cost of PCa care across groups. The primary outcome is HRQoL as measured by the SF-36 and PCI sub-scales. A change of 5 to 9 points on PCI is clinically meaningful [272]. Similarly, a difference of 7 points or more on the SF subscales is considered clinically meaningful [272, 275, 301]. Based on our prior research and that of Litwin et al [253, 272], the standard deviations for the PCI and SF-36 scales in samples of men with PCa mostly range from 8 to 14; hence standardized differences (SDs) of 7/14=0.5 to 7/8=0.87 will be clinically relevant. The power calculations for Aims 2-4 assume availability of 720 participants who are eligible for randomization into one of the two intervention groups. We assume a conservative intra-class correlation of 0.3 and 4 follow-up measures per subject. The sample size is adjusted to accommodate a 10% missing or dropout rate by 24 months based on rates over a similar period of time in previous studies [272, 275, 301]. We assume 80% power and two-sided level of significance of = 0.05. We have 80% power to detect a 1.2 point difference in PCI or SF-36 sub-scale. Within treatment type, the sample size is reduced to 60 per intervention arm. We have 80% power to detect a 3.0 point difference in sub-scale with 60 patients in each arm. Thus, we will have adequate power to detect differences between treatment groups [302]. Power for identifying utility based profiles and outcomes: We analyzed the levels of power for differences in outcomes between profiles defined by latent classes of attributes-specific utilities with a conservative allocation of subjects to each profile (25 in one vs. 10 in other profile) and less conservative allocation (35 in one profile vs. 35 in other profile) using a logistic model based comparison for a binary outcome (e.g. recovery of baseline HRQoL) with a 2-sided alpha of .0125 (Holms adjustment profiles). In the first allocation, the group difference of 0.56 yields 80% power; for the second allocation an effect size of 0.42 corresponds to power of 90. Thus, with our anticipated effect size of 0.51, we will have adequate power with n=60 in each group. (Adjusting for patient characteristics may reduce the effect sizes of the differences between profiles.)

Key inclusion criteria
The sample will consist of 720 newly-diagnosed PCa patients. Inclusion criteria are: (1) treated for PCa at UPHS, Fox Chase Cancer Center or PVAMC; (2) aged 45 yearsr; (3) newly diagnosed with localized PCa and TNM stage T3a; (4) community dwelling; (5) Gleason score 8; (6) low (PSA 10 ng/ml, Gleason 6, clinical stage T1-2a), intermediate (PSA 10 -20 ng/ml, Gleason 7, clinical stage T2b), and high risk (PSA 20, Gleason 8, clinical stage T2c-3a) group [45] and (7) provide informed consent.

Key exclusion criteria
Exclusion criteria are: (1) Distant, metastatic or un-staged PCa at diagnosis; (2) visited the clinics to obtain second opinion only; (3) moved to another location; (4) unable to communicate in English and (5) cognitive impairment (Mini Mental State Exam or MMSE score 21). MMSE is a standardized mental status examination widely used for clinical and research purposes [197,198].

Vulnerable Populations

	Children Form
	Pregnant women (if the study procedures may affect the condition of the pregnant woman or fetus) Form
	Fetuses and/or Neonates Form
	Prisoners Form
	Other
x	**None of the above populations are included in the research study**

The following documents are currently attached to this item:

There are no documents attached for this item.

Populations vulnerable to undue influence or coercion
NA

Subject recruitment
Participants will be recruited from UPHS, PVAMC and Fox Chase Cancer Center's urology and radiation oncology clinics using recruitment protocols that we have successfully used in our prior and ongoing PCa studies. Recruitment will occur in seven steps: 1) determining potential eligibility; 2)

obtaining consent from patients urologist/physician; 3) confirming eligibility; 4) screening via phone and interview to assess willingness to participate; 5) obtaining informed consent and HIPAA permissions; 6) baseline assessments; and 7) follow-up assessments. The study and consent form comply with HIPAA Standards for Privacy of Individually Identifiable Health Information. The draft study design and protocol have been approved by the University of Pennsylvania IRB. Future changes will be reviewed and approved prior to implementation. Participant availability: UPHS is a large hospital and physician network in greater Philadelphia area. Approximately 1,600 patients with newly diagnosed PCa are evaluated annually: 40-50% undergo surgery (RP or RALP); 30-40% undergo EBRT or BT; 10-20% undergo PT. The urology clinic atthe Hospital of the University of Pennsylvania (HUP) treats more than 60% of this group; the rest are treated at Presbyterian Medical Center and Pennsylvania Hospital. Additionally, UPHS has a proton therapy center, providing a unique opportunity to study this new technology. The Philadelphia Veterans Administration Medical Center (PVAMC) cares for 33,000 veterans in Philadelphia area and evaluates ~400 patients with newly diagnosed PCa each year. Fox Chase Cancer Center evaluates ~500 patients with newly diagnosed PCa each year. Together, UPHS, PVAMC, and Fox Chase Cancer Center provide care to socio-demographically diverse population of ~2,500 men newly diagnosed with PCa each year. Thus, our study sample requirement of 720 patients (33% of the available pool) can be fulfilled comfortably, as demonstrated by the successful recruitment for our earlier studies. Recruitment: Prior to study initiation, investigators will explain the study objectives to physicians who actively treat PCa at the UPHS, PVAMC, Fox Chase urology clinics. During a patients initial visit, Drs. Malkowicz, Guzzo, or Wong will briefly introduce the study to the patient. Each week, the research assistant will contact the participating physician offices to obtain contact information for those patients who have expressed an interest in the study. Potential participants will be contacted during their office visits, at which time those eligible may agree to participate and provide informed consent, request additional information and/or time to think or request to be contacted later. Patients who request to be contacted later will be sent study information, a consent form and a prepaid return envelope. Participants will discuss the consent form with research assistant prior to signing, at which time all questions will be answered. During enrollment, compensation of $20 will be provided. Using a similar recruitment strategy in our prior PCa studies, we had achieved enrollment and retention rates of 85% or higher. The expected number of 60 participants in each treatment group (AS, RP, RALP, EBRT, BT or PT) will be achieved as follows: (1) each recruited participant randomly assigned to the conjoint analysis intervention group will meet with research assistant to complete the computer-based conjoint analysis tasks and other surveys before initiation of treatment or making a treatment decision; (2) after treatment decision is made, patients (both cases and controls) will be assigned to the appropriate group based on treatment; (3) this process will continue until we reach the required number of participants in each group. To achieve this, we may evaluate and obtain baseline data including conjoint tasks from patients in excess of the required 360 participant each in the intervention and control groups. Based on our prior prospective cohort studies, to fulfill sample requirement of 60 participant in each treatment group (60x2x6 =720), allowing for attrition we expect to obtain baseline assessment including conjoint tasks for 800 participants (10% excess). The cohort that doesnt get assigned for further follow-up due to targeted group enrollment accrual will be analyzed to ensure comparability. D.2.2 Process of stratified randomization: We will recruit 720 participants stratified by three hospitals-UPHS, PVAMC, or Fox Chase Cancer Center (Figure 3). Dr. Morales will create randomization sequences for each hospital using a pseudo-random number generator with random blocking and will place the treatment assignments in sealed, opaque envelopes. All investigators, staff and referring physicians will be masked to the treatment assignment, except the research assistant who will open the envelope and notify participants of group assignment. Participants will be instructed not to reveal their group status to physicians or study personnel, except in case of emergency or if necessary for medical reason, which we believe to be unlikely.

Will the recruitment plan propose to use any Penn media services (communications, marketing, etc.) for outreach via social media avenues (examples include: Facebook, Twitter, blogging, texting, etc.) or does the study team plan to directly use social media to recruit for the research?
No

The following documents are currently attached to this item:

There are no documents attached for this item.

Subject compensation*
Will subjects be financially compensated for their participation?
Yes

The following documents are currently attached to this item:

There are no documents attached for this item.

If there is subject compensation, provide the schedule for compensation per study visit or session and total amount for entire participation, either as text or separate document

Compensation: Participants who complete the study will be compensated $20 during the consent. Next, at each follow-up period (3, 6, 12 and 24 months), the participant will receive $20 after completion of the measurements.

Study Procedures

Procedures
After obtaining informed consent, baseline data will be obtained in person prior to the initiation of treatment. Participants will meet with the research assistant to complete the computer-based conjoint analysis tasks. Patient identifiers will be removed to maintain data confidentiality. Only the PI will have access to the master files. For conjoint analysis, each participant will be asked to express his preference for attributes and attribute levels for active surveillance and five active treatments for clinically localized PCa (RP, RALP, EBRT, PT, BT) based on choice sets presented. The choices will vary based on the differing attributes of various treatments ascertained in prior work and focus groups. After pilot testing and refining the conjoint task in Phase 1, final attributes and levels will be used. Trade-offs among treatment features will be calculated in patient-specific utilities or part-worths associated with the attribute levels in the study. For other outcomes, participants will receive the following surveys via mail within 1-2 weeks after enrollment and prior to treatment initiation: SF-36, EPIC, AUA-SI, regret scale, CES-D, MAX-PC, SWD, PSQ-18, CPS, DCS and trust scale. Demographics, health and family history, clinical covariates and cancer progression data will be collected at 3, 6, 12 and 24 month follow-up. Histological tumor grade Gleason score and PSA and annual Elixhauser comorbidity score [257-258] will be obtained from the Pennsylvania Integrated Clinical and Research Database (PICARD), a UPHS, Fox-Chase Cancer Center electronic database, and PVAMC administrative and patient HER database. Retention and survey administration: During enrollment, importance of active participation will be emphasized. All participants will complete self-administered surveys at baseline within 1-2 weeks after enrollment (prior to treatment initiation) and again 3,6,12 and 24 months post-enrollment (see Appendix for copies of instruments, consent and medical chart review form). Non-respondents will be contacted via telephone after 10 days. In case of non-response due to death, cause of death will be noted and the physician investigators will determine cause of death (PCa or non-PCa related). The PCa conjoint analysis task, DCS, CPS and trust scale will be administered at baseline only, immediately after diagnosis of PCa and before treatment decision. Procedure for Data Sharing and Modification coordination: In Phase-1 on the study, data will be generated from focus group meetings that will take place on Pennn campus. Focus group data will not be shared with other sites. This data will be used to generate a conjoint analysis instrument. This conjoint analysis instrument will be administered to participants in the intervention arm at all three sites during the Phase-2 of the study. The paper copies of various instruments that all participants complete will be stored at Penn campus in a secure office. In addition, clinical data obtained through chart abstraction will also be stored at Penn campus in a secure office. All electronic data bases will be pass word protected and only the study personal will have access to this data. Raw data will not be shared with other sites, only results in aggregate format with de-identified information will be made available to other sites. Each site PI will be responsible for addressing modifications. Additionally, the Penn site PI Dr. Jayadevappa will have overall responsibility of tracking all modifications. In case of a reportable event at a site, the site PI will inform Penn IRB and Penn site PI regarding the reportable events. Additionally, during Phase-1 of the study, we will conduct audio/video recording of focus group meetings.

The following documents are currently attached to this item:

There are no documents attached for this item.

Analysis Plan

Analytic Methods General: The statistical analysis will proceed in three stages: First, we will check the data quality and carry out descriptive analyses of demographics and key outcome variables. Next, we will assess preferences using conjoint analysis and inferential analysis. For continuous outcome variables, we will check for homogeneity of errors using spread-vs.-level plots and will consider transforming variables that either are highly skewed or have variance that depends strongly on the mean. We will use methods based on general linear model (univariate and repeated-measures ANOVA, mixed models) to analyze uncensored continuous outcomes, such as generic and prostate-specific HRQoL, psychological wellbeing and satisfaction with care. For potentially censored outcome variables such as time to PSA recurrence, we will use Kaplan-Meier curves and Cox proportional hazard models. Poisson regression (zero-inflated) will be used for count data. We will use Bonferroni correction for multiple testing. We will use propensity-score and instrumental variable approach to minimize observed and unobserved bias within groups (i.,e intervention group and usual care control group). Missing Data: We will attempt to prevent missing data by ensuring that data collection is as complete as possible. Should there be substantial missing data, however, we will employ analysis and imputation methods to reduce bias and increase efficiency [279-282]. Based on the proportion of missing data, we will use complete-case analysis, or explore available techniques, such as standardized score imputation, simple means imputation, maximum likelihood model-based imputation, data augmentation, etc. [281]. When data are evidently non-missing at random, we will conduct explicit non-ignorable modeling and sensitivity analysis [278]. Propensity score matching: In observational studies, comparisons between treatment groups that do not adjust for factors associated with treatment choice may be biased. Propensity score technique offers a highly practical approach to address such bias [283]. Here, the probability of each participant being in the treatment arm (i.e., the propensity score), is estimated. Participants are sorted by their propensity scores; the sample is divided into strata based on estimated scores, the treatment effect within each stratum estimated and overall estimate computed by aggregating across strata in a weighted analysis. When the model for predicting treatment status includes all relevant covariates, within strata treatment groups will be balanced on all predictors and the overall comparison of treatment arms will have substantially lower bias. We will use a model relating PCa treatment (RP, RALP, EBRT, PT, BT or AS) to baseline factors [283-284]. To study the extent to which treatment groups are now matched, we will compare t-statistics for these covariates before and after adjusting for propensity score. This will be done separately for intervention group and usual care controls. Instrumental variable analysis: Another limitation of observational research is the strong potential for confounding bias, due to differences in comparison groups that are not reflected in the data (i.e., unobserved bias). The instrumental variable (IV) approach is useful in reducing this bias. This technique uses one or more observable factors that influence outcome only indirectly (the IV). This allows one to mimic randomization with different likelihoods of receiving a particular treatment [227, 285-291]. Physicians play an important role in patients treatment choice- a majority of the PCa patients report that their physicians recommendation was the most important factor in their treatment choice [11-12, 37-46, 51, 55-56, 60-64]. We will use specialty of the first physician (urologist, urologic oncologist, oncologist, radiation oncologist) who the patient saw during PCa diagnosis as an IV. We will explore other potential IVs, such as absolute distance between patients residence to the hospital where they will receive care (Hospital of University of Pennsylvania, Presbyterian Medical Center, PVAMC, Pennsylvania Hospital, or Fox-Chase Cancer Center). Validity of the IV(s) is assessed as following. First, we will use Pearsons correlation coefficient to examine the correlation between IV, primary exposure (treatment) and outcomes. We will then perform a partial F-test using a linear regression where treatment group is regressed on physician specialty along with patient attributes. For a valid IV, test statistic should be very high (e.g., physician specialty will strongly predict treatment after adjusting for covariates). Next, we will perform a partial F-test using a linear probability model in which HRQoL outcomes are regressed on specialty and patient demographic and clinical variables. For an IV to be valid, this test statistic should be very low. Finally, we will compare observable attributes across patient groups cared for by different physician specialty (initial). For the IV be valid, these groups should have comparable observable attributes. Phase 1 Focus group analysis-development of conjoint task instrument: The goal of focus groups is to identify attributes of PCa treatment that are most salient to localized PCa patients. This process includes following steps: (1) identifying and defining attributes; (2) assigning attribute levels; and (3) creating scenarios and choice sets. Attributes will be defined based on input from patient focus groups, literature, our prior research, and prior physician focus group. Once an attribute and its extreme values are defined, we will assign them appropriate levels. A large number of possible combinations of attributes and levels will preclude

studying all possible combinations using designed scenarios. Thus, we will use a fractional factorial design to reduce the number of paired comparisons to the smallest number necessary for efficient estimation of attribute utility weights [292-295]. (See Appendix for a draft interview guide for the patient focus group developed from our prior physician focus group). We will elicit information about how decisions regarding alternative treatments for PCa will be made or were made (i.e., reasons for and against initiation of specific treatments). Participants also will be asked what they wish someone would have told them about treatment before they began it. Physicians will be asked what their patients want to know about treatments and what they think patients dont realize about various options. Physician focus group will include urologists (including at least one with robotic surgery sub-specialization), radiation oncologists (including at least one with proton beam experience), geriatricians, family medicine and internists. Focus group sessions will be tape recorded and transcribed. Participant names and identifying information will be removed from the transcripts. Transcribed data will be stored and analyzed using N6 software, which facilitates thematic coding, inter-rater coding (and inter-rater reliability), and correlation of themes with demographic variables. Attributes and their levels will be derived for conjoint analysis based on the main themes that come up in the focus groups. The conjoint analysis tasks will then be pilot tested to ensure comprehension, feasibility and response burden. We have extensive experience employing the qualitative methods proposed here [105, 220, 296-300]. 2.2.7 Phase 2 2.2.7.1 Specific Aim 1: To develop values markers, we first will assess individual level utilities, followed by latent profile analysis based on these individual level utilities as described below. Individual utilities for attributes of treatment (conjoint task): The conjoint task requires PCa patients to make choices between hypothetical treatment options based on the attributes identified in the Phase 1 focus groups. Each participant will be asked to express his preference for attributes of various PCa treatments based on choice sets presented, varying in the attribute levels of the various treatment choices ascertained in Phase 1. Precisely which attributes will be used will be refined based on piloting the conjoint task with a small number of participants (n=20). The balancing or trade-off of treatment features will be captured in the patient-specific utilities or part-worths associated with the attribute levels in the study. The discrete choice conjoint analysis is based on a mixed effects logistic model with a pair of fixed and random effects defined for each attribute, which is treated as a covariate. We assume two attributes, x1 and x2 with binary discrete choice response variable Y. The corresponding mixed effects logistic model for the mean of Y (=E(Y | x1, x2)) is: Estimation of 1, 2 and is based on an empirical Bayes approach using maximum likelihood estimates (MLE) of 1 and2.Under this approach, we assume that 1, 2 and have a multivariate normal distribution with mean zero and variance-covariance . MLE of 1, 2 and is based on marginal likelihood derived from integrating 1, 2 and from the likelihood. With estimates of 1, 2 and we obtain empirical Bayes estimates of 1, 2 and . This estimation will be performed in SAS (Proc NLMIXED), which also will allow us to assess the sensitivity of this modeling approach to assumptions of normality of the random effects utility parameters by trying non-normal random effects distributions. Values markers (latent profiles based on individual utilities): We will carry out additional analyses of individual-level utilities to classify patients according to profiles or patterns of utilities using latent profile analysis. The profiles that are derived from the latent profile analysis will determine the value markers representing patterns of treatment attributes that the patients value. The empirical Bayes estimates of the subject-level utilities then can be used as inputs to a growth curve mixture model (i.e, Latent Profile Analysis) to obtain patterns of treatment preferences as represented by the estimated utilities from the conjoint analysis. Such patterns correspond to latent classes based on a random effects linear model with multivariate set of utilities as the continuous dependent variables [300]. This model will be implemented in Mplus Version 6.12. The number of classes will be determined using the Lo-Mendell-Rubin (LMR) adjusted likelihood ratio test. Mplus reports a bootstrapped p-value to account for departures from model assumptions, such as the multivariate normal distribution of the attribute-specific utilities. We will describe these profiles in terms of descriptive statistics of the multivariate set of attribute-set utilities. Specific Aim 2: Hypothesis 2: Poorer objective (cancer recurrence and complications) and subjective (HRQoL, psychological wellbeing, satisfaction with decision and satisfaction with care) outcomes are directly log[/(1)] = (1 + 1) x1 + (2 + 2) x2 + 1= the log odds ratio for option A vs. option B with respect to attribute 1 (estimate of this parameter will allow us to obtain part-worth for this attribute) 2= the log odds ratio for option A vs. option B with respect to attribute 1 (estimate of this parameter will allow us to obtain part-worth for this attribute) = overall patient-level utility 1 = patient-level utility for attribute 1 2 = overall patient-level utility for attribute 2 and indirectly (moderated by treatment received) associated with decision conflict, physician trust and preference to participate in decision making. Figure 4 presents a conceptualization of the association between decision conflict, physician trust and preference for participation in decision making, treatment choice and outcomes. First, we will test the association denoted by the path a (Figure 4) and model treatment received as a function of role desired by PCa

patients in decision (measured using CPS) using multi-nominal regression model to adjust for observed covariates. Then we will examine if these associations vary across intervention and usual care control groups. We then will repeat the model with other independent variables (decision conflict and trust). Next, we will test the association denoted by path c (direct effect of DCS, CPS, and trust on outcomes). For continuous outcomes (HRQoL, AUA-SI, MAX-PC, CES-D, SWD, and PSQ-18), we will compute area under the curve (AUC) for each measure for each patient. We will analyze AUC summaries with univariate linear models. In our main analysis we will analyze the series of functional status measures using linear mixed models that predict the outcome from time, independent variables and their interaction. We will repeat the analyses described for path c, this time by including treatment received in the models. We will test if the observed effects of DCS, CPS or trust on outcomes will be weaker after controlling for treatment. These analyses will be performed within and between groups (intervention and usual care controls). Specific Aim 3: Hypothesis: Prostate cancer patients in the intervention group undergoing conjoint analysis-value clarification exhibit improved treatment choice, satisfaction with decision, lower regrets, and improved objective and subjective outcomes. Analysis for Specific Aim 3 uses intent-to-treat approach: all randomized participants will be included regardless of whether they drop out of the intervention or study. Analysis will involve comparison of the primary outcomes between intervention and usual care control groups. Improved treatment choice is operationalized as the likelihood of low-risk PCa patients receiving active surveillance than active treatment, and will be compared between intervention and usual care control group. To allow for different trajectories of the outcome measures and to afford flexibility in making contrasts within participants over time and across participants, while simultaneously controlling for potential confounders, we propose the participant-specific or mixed effects linear model, in which the mean outcome depends on fixed covariates and random effects. The primary fixed effects will be indicators for intervention group and hospital. We will also stratify the analysis by type of treatment. The random effects represent the unobserved factors that lead to variation of the individual participants outcome. Random intercepts for each participant permit modeling of natural variation across participants at baseline. In addition, random slopes or random effects for the trajectory of each participant over time, allow for variation of each participant about a mean, overall trajectory across all participants. Although less robust to model misspecification, the mixed effects paradigm offers special flexibility in longitudinal data when exposures vary over time and when dropout and missed visits lead to unbalanced groups. The target of inference is the participant-specific response to treatment over time. At each time point of interest, we will estimate from the fitted model the difference from baseline in outcome for the treatment and control groups and test the difference between these differences. Both univariate and multivariate results will be reported in terms of Wald test, point estimates, and 95% confidence intervals. Specific Aim 4: Hypothesis 4: Prostate cancer patients whose treatment is more concordant with their values markers will experience improved subjective and objective outcomes. This specific aim s for intervention group only. We will analyze the association of the concordance between stated individual preferences and actual treatment received with objective (PCa recurrence and complications), subjective (HRQoL, psychological wellbeing, SWD, and satisfaction with care) outcomes, across treatment groups, adjusting for covariates. Association between the value markers (profiles) and measures of outcomes and personal and clinical characteristics: The value markers will be studied for their relationship with socio-demographic and clinical characteristics. We will also assess the association of value markers with outcomes. We will perform logistic regression with outcomes as the dependent variable and dummy variables for the utility-based profiles obtained earlier as independent variables. We will perform this evaluation with and without adjusting for patient attributes in the logistic model. For each case (adjusting and not adjusting for patient attributes), the evaluation of association between these profiles and outcomes will be based on a likelihood ratio test of the set of odds ratios corresponding to the dummy variables of the profiles. Additionally, we will perform a sequence of pair wise tests of comparisons of the profiles in terms of the proportion of type of treatment received based on the Holms multiple comparisons approach. This procedure is hierarchical in that it will identify the utility-based profile at the start of the process before making other comparisons, thus protecting the Type I error from additional comparisons. Specifically, Holms approach tests each pair-wise comparison in ascending order of p-values. Successively larger p-values have less rigorous alpha. The sequential Holm tests terminate after the first non-significant comparison so no subsequent comparison is significance. Concordance and its assessment: Understanding and respect for the patients preference and values is the main aspect of concordance [69, 73]. Thus a first step in concordance involves the physician extracting and understanding the patients view, followed by an agreement between the physician and patient regarding a management plan that integrates their views. There exist many definitions of concordance. For the purpose of this study, we operationalized concordance as agreement between a patients value markers and the attributes (or characteristics) of the treatment that

the patient receives (choice). Association of concordance between stated preference and attributes of treatment received will be studied separately for each treatment using Kappa statistics. The degree of concordance then will be used as an independent variable to test its association with outcomes. For objective/clinical outcomes (i.e., complications and PCa recurrence), we will test the hypothesis that degree of concordance is associated with PCa recurrence (measured by PSA doubling time). To evaluate the effects of concordance on biochemical recurrence of PCa, we will analyze PSA levels on the log scale over time using a mixed model approach. We also will apply survival analyses (Kaplan-Meier, logrank and Cox model) to model effects concordance of treatment and covariates on time to PSA recurrence. For subjective outcomes of urologic symptoms (AUA-SI), generic and prostate specific HRQoL, psychological well-being (CES-D, MAX-PC), satisfaction with decision and satisfaction with care, we will perform inferential analysis with t, chi-squared and non-parametric tests. Wilcoxon matched-pairs test will be used for comparisons within concordance and non-concordance groups. A concordance group will be defined as at least 75% agreement between values markers and treatment related attributes. We will perform sensitivity analysis to test robustness of results. Primary analyses will compare baseline with six and 24 months assessments, as literature suggests these are the clinically most relevant time points. Secondary analyses will compare baseline with three month and one year outcomes. Proportion returning to baseline over time will be compared using chi-squared tests, using procedures such as Bonferroni, Scheffé, and step-down Holm corrections to adjust for multiple testing. We will use loglinear regression models with psychological well being, HRQoL and satisfaction with care scores (log) as dependent variables, logistic regression with return to baseline as the dependent variable, and degree of concordance as the independent variable. For repeated measures outcomes we will use linear mixed models (Proc Mixed).

The following documents are currently attached to this item:

There are no documents attached for this item.

Deception
Does your project use deception?
No

Data confidentiality

- x **Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study.**
- x **Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords.**
- x **Prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information.**
- x **Wherever feasible, identifiers will be removed from study-related information.**

  A Certificate of Confidentiality will be obtained, because the research could place the subject at risk of criminal or civil liability or cause damage to the subject's financial standing, employability, or liability.

  A waiver of documentation of consent is being requested, because the only link between the subject and the study would be the consent document and the primary risk is a breach of confidentiality. (This is not an option for FDA-regulated research.)
- x **Precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys.**
- x **Audio and/or video recordings will be transcribed and then destroyed to eliminate audible identification of subjects.**

Subject Confidentiality
Protection of Participants and Procedure of Protection of Confidentiality: We will institute strict procedures to maintain confidentiality and will adhere to 2003 HIPAA Standards for Privacy of Individually Identifiable Health Information (the Privacy Rule). Blood draw will be conducted at the Outpatient clinic, which, as a geriatric outpatient clinic, is a very safe setting for any medical tests. All information on participants will be maintained confidentially, and will be shared with collaborating institutions and PCORI only by means of code. The patients physician will have the right to know of the

patients participation in this study, and may be informed of which group the patient is in if the patient chooses or if there is a medical reason to necessitate this. The research coordinator will meet with the participants at the urology and radiation oncology clinics, and the participant will know whom to contact in case of emergency. Release of participant information to other parties not affiliated with the research team will be governed by the HIPAA Privacy Rule Guidelines. Disposition of data: The raw data will be stripped of participant identifiers immediately and each participant will be assigned a unique identifier. Our unique participant identifier is a number that is incremented by one for each new consented participant accrued in the study. This identifier number is not derived or linked to the participants social security number, hospital ID number, medical record number, or some other number that can also be used to directly identify the data source. The participant identifier information will be held highly confidential and only the principal investigator will have access to it. The principal investigator will maintain a master file linking the participants medical record number and the assigned unique participant identifier. This file will be password protected on a secured computer. The data will be stored on a secure and password protected computer. Every attempt will be made by the investigators to maintain all information collected in this study strictly confidential. In any publications or presentations resulting from this research, data will be presented in aggregate format only and the participants will not be identified individually. To ensure accuracy of data while transferring raw data to computerized database, data will be verified in three steps. First, double entry will be done for raw data that are entered into a computer. Next, the principal investigator will perform a random data check. Finally a one-way frequency of all the variables will be run and checked to see if any incorrect or out of range information appears in the database. If so, the necessary corrections will be made. In order to generate the final report and publications, data will be stored for approximately four years beyond the end of the study period. Sharing Study Results: We will seek advice from institutional review and data safety monitoring board regarding sharing the study results with participants over the study duration. The published results will be made available to all the participants, caregivers and physicians. Ethical Considerations: This study will not modify a participants prescribed medical regimen in any way. The major ethical considerations involve issues of notification of physicians when participants are worsening. Since our research coordinator and research assistant are not medical practitioners, their role will be to remind the participant that they must take action if their condition is worsening (e.g. notify the physician). The research coordinator will be given guidelines by the medical co-investigators to identify extreme cases. In these instances, the investigators will contact the participants physician.

Sensitive Research Information*

Does this research involve collection of sensitive information about the subjects that should be excluded from the electronic medical record?

No

Subject Privacy

Privacy refers to the person's desire to control access of others to themselves. Privacy concerns people, whereas confidentiality concerns data. Describe the strategies to protect privacy giving consideration to the following: The degree to which privacy can be expected in the proposed research and the safeguards that will be put into place to respect those boundaries. The methods used to identify and contact potential participants. The settings in which an individual will be interacting with an investigator. The privacy guidelines developed by relevant professions, professional associations and scholarly disciplines (e.g., psychiatry, genetic counseling, oral history, anthropology, psychology).

Protection of Participants and Procedure of Protection of Confidentiality: We will institute strict procedures to maintain confidentiality and will adhere to 2003 HIPAA Standards for Privacy of Individually Identifiable Health Information (the Privacy Rule). Blood draw will be conducted at the Outpatient clinic, which, as a geriatric outpatient clinic, is a very safe setting for any medical tests. All information on participants will be maintained confidentially, and will be shared with collaborating institutions and PCORI only by means of code. The patients physician will have the right to know of the patients participation in this study, and may be informed of which group the patient is in if the patient chooses or if there is a medical reason to necessitate this. The research coordinator will meet with the participants at the urology and radiation oncology clinics, and the participant will know whom to contact in case of emergency. Release of participant information to other parties not affiliated with the research team will be governed by the HIPAA Privacy Rule Guidelines. 2.6.7 Disposition of data: The raw data will be stripped of participant identifiers immediately and each participant will be assigned a unique identifier. Our unique participant identifier is a number that is incremented by one for each new consented participant accrued in the study. This identifier number is not derived or linked to the participants social security number, hospital ID number, medical record number, or some other number

that can also be used to directly identify the data source. The participant identifier information will be held highly confidential and only the principal investigator will have access to it. The principal investigator will maintain a master file linking the participants medical record number and the assigned unique participant identifier. This file will be password protected on a secured computer. The data will be stored on a secure and password protected computer. Every attempt will be made by the investigators to maintain all information collected in this study strictly confidential. In any publications or presentations resulting from this research, data will be presented in aggregate format only and the participants will not be identified individually. To ensure accuracy of data while transferring raw data to computerized database, data will be verified in three steps. First, double entry will be done for raw data that are entered into a computer. Next, the principal investigator will perform a random data check. Finally a one-way frequency of all the variables will be run and checked to see if any incorrect or out of range information appears in the database. If so, the necessary corrections will be made. In order to generate the final report and publications, data will be stored for approximately four years beyond the end of the study period. Sharing Study Results: We will seek advice from institutional review and data safety monitoring board regarding sharing the study results with participants over the study duration. The published results will be made available to all the participants, caregivers and physicians. Ethical Considerations: This study will not modify a participants prescribed medical regimen in any way. The major ethical considerations involve issues of notification of physicians when participants are worsening. Since our research coordinator and research assistant are not medical practitioners, their role will be to remind the participant that they must take action if their condition is worsening (e.g. notify the physician). The research coordinator will be given guidelines by the medical co-investigators to identify extreme cases. In these instances, the investigators will contact the participants physician.

Data Disclosure
Will the data be disclosed to anyone who is not listed under Personnel?
NA

*Data Protection**

- x **Name**
- x **Street address, city, county, precinct, zip code, and equivalent geocodes**
- x **All elements of dates (except year) for dates directly related to an individual and all ages over 89**
- x **Telephone and fax number**
- x **Electronic mail addresses**
- x **Social security numbers**
- x **Medical record numbers**
- **Health plan ID numbers**
- **Account numbers**
- **Certificate/license numbers**
- **Vehicle identifiers and serial numbers, including license plate numbers**
- **Device identifiers/serial numbers**
- **Web addresses (URLs)**
- **Internet IP addresses**
- **Biometric identifiers, incl. finger and voice prints**
- **Full face photographic images and any comparable images**
- **Any other unique identifying number, characteristic, or code**
- **None**

Tissue Specimens Obtained as Part of Research*
Are Tissue Specimens being obtained for research?
No

Tissue Specimens - Collected during regular care*
Will tissue specimens be collected during regulator clinical care (for treatment or diagnosis)?
No

Tissue Specimens - otherwise discarded*
Would specimens otherwise be discarded?
No

Tissue Specimens - publicly available*
Will tissue specimens be publicly available?
No

Tissue Specimens - Collected as part of research protocol*
Will tissue specimens be collected as part of the research protocol?
No

Tissue Specimens - Banking of blood, tissue etc. for future use*
Does research involve banking of blood, tissue, etc. for future use?
No

Genetic testing
If genetic testing is involved, describe the nature of the tests, including if the testing is predicative or exploratory in nature. If predictive, please describe plan for disclosing results to subjects and provision of genetic counseling. Describe how subject confidentiality will be protected Note: If no genetic testing is to be obtained, write: "Not applicable."
Not applicable

Consent

1. Consent Process

Overview
Consent Procedures: This study involves a one-stage consent process. After confirming eligibility, participants will receive detailed information about the study and expected outcomes. Those interest will complete informed consent at the end of this information session from those willing to participate. Informed consent will be obtained from all persons interested in participating in the study by the research coordinator. This will be done in person after the potential participant is fully informed of all aspects of the research study and after the person has had the opportunity to discuss the project with his physician. The consent will be administered after a detailed study explanation by the principal investigator or the study research coordinator. Participants will then be given 30-90 minutes to read over the consent form, at which time the PI, investigators, or the study research coordinator will ask if they have any further questions. The final component of the consent process will be reviewing of a brief checklist that outlines the major aspects of the study to confirm that the subject fully understands the protocol. Participants will also be asked to review and sign a Research Subject Authorization: Confidentiality and Privacy Rights consent at the time they sign the general study consent form. This document, written to ensure compliance with HIPAA Privacy Rule guidelines, provides detailed information about what information is being collected, the participants privacy rights, and to whom the information may be disclosed. Participants will be given a signed copy of the consent forms for their records. This consent process was tested in our pilot study and has been effective. The research coordinator will obtain informed consent only after the patient demonstrates full understanding of all aspects of the study protocol. We will obtain informed consent from all focus group patient participants. We request a waiver of documentation of consent for the physician group only, since the research presents no more than minimal risk of harm to subjects and involves no procedures or activities for which written consent is normally required outside of the research context. The protocol and consent will be received and approved by the Committee on Studies Involving Human Beings of the University of Pennsylvania Institutional Review Board prior to initiating the study. It will be documented by the participant signing the consent forms in the presence of a witness. A copy of the

consent and HIPAA forms have been included the Appendix. In the event of Adverse Events (AEs), the consent forms may be revised at the discretion of the Data and Safety Monitoring Committee. In these cases, all patients who are currently enrolled in the protocol and patients who have already completed the protocol will be given the revised consent forms for their review and signature.

Children and Adolescents
Not applicable

Adult Subjects Not Competent to Give Consent
Not applicable

2. Waiver of Consent

Waiver or Alteration of Informed Consent*
Waiver of written documentation of informed consent: the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context

Minimal Risk*

Impact on Subject Rights and Welfare*

Waiver Essential to Research*

Additional Information to Subjects

Written Statement of Research*
Yes

If no written statement will be provided, please provide justificiation

We request a waiver of documentation of consent for the physician group only, since the research presents no more than minimal risk of harm to subjects and involves no procedures or activities for which written consent is normally required outside of the research context.

The following documents are currently attached to this item:

Written Statement of Research (jayadevappapcorifocusgroupconsentsept192013.docx)

Written Statement of Research (jayadevappapcoriphyicianfocusgroupinfojune132013.docx)

Written Statement of Research (jayadevappapcoriphyicianfocusgroupinfojune142013.docx)

Risk / Benefit

Potential Study Risks
Potential Risks: This is an observation study and no medical risks are known to be associated specifically with the study. Any discomforts, physical or psychological, that a specific participant may experience may not currently be anticipated, but are anticipated to be minimal. The blood chemistry analysis involves a blood draw, which is a routine procedure at the Outpatient clinic. Blood samples will be stored at the PENN-CTRC. The research coordinator will closely monitor the participant for any adverse reactions. In addition to Independent Data and Safety Monitoring Board, numerous protocol measures will be instituted to protect research participants. Most have been used during our research teams previous work and are thus familiar to the staff and have proven to be highly effective.

Potential Study Benefits
Potential benefits: Prostate cancer is a slow progressing, chronic and debilitating disorder that substantially limits quality and quantity of life for nearly millions of Americans. There exists significant ambiguity regarding the best treatment for prostate cancer for a particular patient since prostate cancer treatments involve inherent tradeoffs between quantity and quality of life. Thus, the treatment for

prostate cancer presents a clinical dilemma even with perfect data. Clinically similar patients can receive different treatments, given that their preferences may differ. The results of this study will add new knowledge regarding the extent to which the newly diagnosed prostate cancer patients prefer to be involved in decision making, the extent to which prostate cancer patients perceive decision conflict, preferences and the role of demographic and clinical characteristics in relation to involvement in decision making and decision conflict. Evidence shows that there are substantial opportunities to improve the care delivered to prostate cancer patients by analyzing preferences and by adopting patient centered care. We propose a two phase study, in the first phase of the study we will use conjoint analysis to derive patient preference and develop an instrument, in the second phase we will implement a stratified randomized controlled trial to analyze the effects of conjoint analysis (value markers) intervention on treatment choice and outcomes and variation in preference and actual treatment received and its impact on outcomes, and will analyze the effectiveness of active surveillance and active treatment [surgery (RP or RALP), or radiation therapy (EBRT, BT or PT)], on outcomes for low-risk prostate cancer patients. This is a novel study in four ways: (1) assessment of preference using conjoint analysis; (2) development of new tool for assessment of preferences; (3) Comprehensive assessment (HRQoL, and psychological well-being) within and between treatment groups; (4) focus on general population; and (5) rigorous analysis of trust, stress, regrets and depression; Thus, the outcome of this study will facilitate effective clinical decision through patient centered care model so as to achieve optimal outcomes across ethnic and age groups of prostate cancer patients. Also, the results will help understand the effectiveness of prostate cancer care. This study can benefit and aid clinical decision, policy and effective management of prostate cancer.

Alternatives to Participation (optional)

Data and Safety Monitoring

Independent Data and Safety Monitoring Board: The data and safety monitor board (DSMB) will be composed of 4-6 individuals from the Abramson Cancer Center and Fox-Chase Cancer Center, each with their own area of expertise and will include a medical ethicist and public ombudsman as per recommendations of PCORI. Its members will be appointed after consultation with the PCORI and Penn IRB. They will be completely independent of the study staff, and will have no scientific, financial or other conflict of interest with the study as attested by written documentation. The DSMB will meet in person at least once a year, with the first meeting occurring face to face prior to study initiation. In addition, the DSMB may meet via telephone conference as often as believed necessary to review the progress of the study. Emergency meetings may also be called at any time by the Chairperson of the DSMB, or by the PCORI funding agency. The DSMB will report directly to the PCORI concerning study continuation. The format of DSMB meetings will be an initial open forum during which the principal investigator (Dr. Jayadevappa) summarizes overall study issues, then the study investigators will be excused while a closed session is conducted. During this session, the members will meet with the study statistician to review the interim reports (which will be provided to the DSMB members at least five days before the meetings). If appropriate, the DSMB will then hold an executive session to discuss the general conduct of the study and outcomes, and offer recommendations after voting. The DSMB will be charged with the following responsibilities: 1) Review the research protocol, informed consent documents and plans for data safety and monitoring prior to study initiation. 2) Assess accrual rate and baseline comparability between the groups to ensure that changes in the blocking scheme are not required. 3) Assess resource availability as the study proceeds. 4) Examine data quality with special emphasis on eligibility data and timeliness of follow-up visits 5) Evaluate safety of research subjects Based on the DSMBs assessment of each of these issues, the DSMB will then make formal report in which it will make recommendations to the PCORI and the P.I. regarding whether the study should continue, the study protocol should be modified, further data needs to be reviewed, and at what frequency the DSMB should continue to meet. If appropriate, these reports will be distributed to the local IRB. So as to allow the DSMB to effectively examine safety data, as such, no investigator directly related to this study will be included on the data monitoring board. However, if particular expertise related to the operation of the study or to other issues related to the study are required, the DSMB can ask for the investigators to participate in the DSMB meetings.

The following documents are currently attached to this item:

There are no documents attached for this item.