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TITLE: Racial differences in financial impact of prostate cancer treatment and outcome

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14. ABSTRACT The North Carolina-Louisiana Prostate Cancer Project (PCaP) used rapid case ascertainment in North Carolina (NC) and Louisiana (LA) to recruit 2258 research subjects with newly diagnosed prostate cancer (CaP); African Americans (AAs). Treatments received and oncological outcomes were gathered about 4 years later from 79% of research subjects enrolled in NC and 4.4 years later from 65% of research subjects enrolled in LA. Estimations based on that initial follow-up experience and actuarial assumptions suggest that information should be collectable from 1233 living PCaP research subjects and from the surviving family members about the impact of death from CaP in 110 (about 65 AAs and 45 CAs) versus another cause in 300 (about 150 of each race) family units, respectively. The central hypothesis is that the financial impact of CaP treatment and oncologic outcome differs between AAs and CAs newly diagnosed with CaP. LA State University School of Public Health Epidemiology Data Center (EDC) will contact all PCaP research subjects who provided consent for future contact (97% allowed future contact). Treatments received and oncologic outcome will be collected using PCaP's CaP Follow-up Form and QoL will be reassessed using the same validated instruments administered by PCaP at baseline and first re-contact. Current household income, treatment costs, QoL, financial distress and caregiver QoL and stress will be ascertained using validated questionnaires. EDC will obtain the pertinent medical records and abstract them using the PCaP Follow-up Medical Records Abstraction Database. Oncologic outcome will be displayed graphically for all LA research subjects and updated for all NC research subjects using the same methodology as used to produce oncologic outcome for NC research subjects. Mortality and cause of death information is obtained via the NC State Center for Health Statistics and the LA State Tumor Registry. When PCaP research subjects have died, next-of-kin will be consented and asked to provide treatments received and physician caregivers and to complete financial, caregiver QoL and healthcare system satisfaction questionnaires modified for use by next-of-kin. Greater cost and intensity of treatment translates to greater financial burden and stress that may impact those more with less insurance, financial reserves and medical system sophistication. More non-treatment resources may be required to support men, in general, and African-American men, specifically, who suffer from CaP, but survivorship deficits require better and data-driven definition for precise intervention.					
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TABLE OF CONTENTS

	Page
1. Introduction	4
2. Keywords	4
3. Accomplishments	4
4. Impact	37
5. Changes/Problems	37
6. Products	39
7. Participants & Other Collaborating Organizations	40
8. Special Reporting Requirements	64
9. Appendices	64

1. INTRODUCTION:

The North Carolina-Louisiana Prostate Cancer Project (PCaP) used rapid case ascertainment in North Carolina (NC) and Louisiana (LA) to recruit 2258 research subjects with newly diagnosed prostate cancer (CaP); African Americans (AAs). Treatments received and oncological outcomes were gathered about 4 years later from 79% of research subjects enrolled in NC and 4.4 years later from 65% of research subjects enrolled in LA. Estimations based on that initial follow-up experience and actuarial assumptions suggest that information should be collectable from 1233 living PCaP research subjects and from the surviving family members about the impact of death from CaP in 110 (about 65 AAs and 45 CAs) versus another cause in 300 (about 150 of each race) family units, respectively. The central hypothesis is that the financial impact of CaP treatment and oncologic outcome differs between AAs and CAs newly diagnosed with CaP. LA State University School of Public Health Epidemiology Data Center (EDC) will contact all PCaP research subjects who provided consent for future contact (97% allowed future contact). Treatments received and oncologic outcome will be collected using PCaP's CaP Follow-up Form and QoL will be reassessed using the same validated instruments administered by PCaP at baseline and first re-contact. Current household income, treatment costs, QoL, financial distress and caregiver QoL and stress will be ascertained using validated questionnaires. EDC will obtain the pertinent medical records and abstract them using the PCaP Follow-up Medical Records Abstraction Database. Oncologic outcome will be displayed graphically for all LA research subjects and updated for all NC research subjects using the same methodology as used to produce oncologic outcome for NC research subjects. Mortality and cause of death information is obtained via the NC State Center for Health Statistics and the LA State Tumor Registry. When PCaP research subjects have died, next-of-kin will be consented and asked to provide treatments received and physician caregivers and to complete financial, caregiver QoL and healthcare system satisfaction questionnaires modified for use by next-of-kin. Greater cost and intensity of treatment translates to greater financial burden and stress that may impact those more with less insurance, financial reserves and medical system sophistication. More non-treatment resources may be required to support men, in general, and African-American men, specifically, who suffer from CaP, but survivorship deficits require better and data-driven definition for precise intervention.

Table 2. Estimated PCaP Research Subject Participation about 10 Years after Enrollment

	NC	LA
Enrolled (n)	1031	1021
4 yr F/U		
- Deceased	5%	12%
- Not found	5%	7%
- Declined	1%	13%
- Participation Rate	89%	65%
10 yr F/U (estimated)		
- Deceased	10%	14%
- Not found	5%	5%
- Participation Rate	74%	46%
Research Subjects (n)	763	470

2. **KEYWORDS:** Prostate cancer; Financial distress; Financial toxicity; Caregiver; Racial disparity; Survivorship; Quality of life

3. ACCOMPLISHMENTS:

Y1 Progress

There are no significant changes in the project or its direction.

What were the major goals of the project?

There are no significant changes in the major goals of the approved research:

Aim 1) Locate and contact PCaP research subjects to update CaP status, CaP treatments received and comorbidities, repeat the QoL assessments performed at baseline and follow-up, and administer new surveys on financial burdens and stress and caregiver QoL and support;

Aim 2) Locate and contact PCaP research subjects' treating physicians to update treatments received and oncologic outcome data;

Aim 3) Obtain and link vital status data and cause of death in PCaP research subjects; and

Aim 4) Examine the role financial burden and stress have on CaP survival and QoL and whether this relationship was modified by race.

Y2 Progress

We are considering a significant change in a major goal of the approved research. The updating of oncologic outcome graphs on NC Research Subjects and the construction of oncologic outcome graphs on LA research subjects will require identification of treating primary care physicians for research subjects discharged from specialty oncologic follow-up and identification of specialty physicians providing oncologic care (urologist, radiation oncologist or medical oncologist) for 1616 research subjects. Two factors suggest a need for a change in strategy. Sharing of personal health information (PHI) has become more challenging due to medico-legal concerns and more expensive because of office charges for the time necessary to access and provide PHI. The continuing evolution in clinical data availability may allow more efficient collection of these data. We have initiated a pilot project of 20 NC Research Subjects and 20 LA research subjects to determine how much oncologic outcome data can be acquired electronically. In LA, PCaP research subjects are flagged already in SEER. Dr. Peters is meeting with SEER officials to determine if we can conduct a pattern-of-care study to identify treatments received, oncologic status, and interval PSA results. In NC, Dr. Bensen will explore the use of the UNC Tumor Registry and an ongoing UNC project to access claims data for research use, which should include data from NC research subjects who have BC/BS, Medicare or Medicaid (an estimated 80-90% of NC research subjects). We will know soon if Aim 2 can be performed more efficiently and completely, which would prompt the following change:

Aim 2) Collect data electronically, when possible, and locate and contact PCaP research subjects' treating physicians, when necessary, to update treatments received and oncologic outcome data

Y3 Progress

NC The health insurance claims data to be used for the PCaP Financial Toxicity project on NC participants will be reused from UNC's Cancer Information and Population Health Resource (CIPHR). CIPHR-linked data include cancer case data from the North Carolina Central Cancer Registry (NCCCR). Original NC PCaP cases were defined from the NCCCR using rapid case ascertainment. NCCCR data are linked to administrative and claims data for a 100% sample of North Carolinians from Medicare, Medicaid, and Blue Cross Blue Shield of North Carolina (BCBS). These data are subject to data use agreements (DUAs) between CIPHR and the data owner (BCBS or Centers for Medicaid & Medicare Services (CMS)). Per the terms of these DUAs, each reuse of this data for individual research studies must be approved by the individual data owners. This study requested and received data use approval from the NCCCR (required 2 weeks) and BCBS (required 4 months). The remaining review and approval process for CMS has taken approximately 1 year and should require approximately 2 more months. CMS data use approval processes usually take 6 months, but CMS has received an unusually high demand for data use requests as a result of the COVID-19 pandemic. Documents for CMS approval are at the DoD pending signature. Once signed, these documents will be reviewed by the CMS Research Data Assistance Center (ResDAC) for final approval. Once approved at ResDAC, CMS will issue a study-specific data use agreement granting access to its data as housed at CIPHR for the purposes of this research study.

LA The LA SEER Registry will be queried for date of last contact, vital status and recurrence information for all LA PCaP participants as has been done annually. In addition, the PCORI supported Louisiana REACHnet will be used to obtain clinical electronic health record (EHR) data for LA PCaP participants. REACHnet contains electronic health record data for more than 8 million patients standardized to a common data model to support pragmatic clinical research conducted under real-life practice conditions. REACHnet is one of nine Clinical Research Networks (CRNs) nationwide that constitute PCORnet®—The National Patient-Centered Clinical Research Network. Louisiana Public Health Institute (LPHI) is the REACHnet Coordinating Center. REACHNET contains data from several LA health care systems, which include Tulane Medical Center, Ochsner Health System, and University Medical Center. REACHnet has archived claims data from BCBS of LA, LA Medicaid, and Humana. Examples of data elements available through REACHnet include procedures for medical interventions and diagnostic testing, such as surgical procedures and laboratory orders, and records of medications administered to patients by healthcare providers. These may take place in any setting, including inpatient,

outpatient or home health encounters. REACHnet data conforms to the PCORnet common data elements model and permits efficient data linkages to collect the clinically relevant data necessary to achieve the study aims. REACHnet's academic partners include the Louisiana State University Health Sciences Center (LSUHSC). A Data Sharing and Use Agreement (DSUA) is required for data linkage that outlines the specifications of the dataset to be provided and the terms for data use. The DSUA is between the REACHnet Coordinating Center and the PCaP investigative team. LA PCaP participants will have medical claims data abstracted using the same search terms as used in NC).

Therefore, **Aim 2)** Locate and contact PCaP research subjects' treating physicians to update treatments received and oncologic outcome data **was changed** 07/31/2018 to **Aim 2)** Collect data electronically, when possible, and locate and contact PCaP research subjects' treating physicians, when necessary, to update treatments received and oncologic outcome data.

Y4 Progress

NC The remaining review and approval process for Centers for Medicaid & Medicare Services (CMS) was completed in this reporting period. Once signed, documents were reviewed by the CMS Research Data Assistance Center (ResDAC) for final approval. Once approved at ResDAC, CMS issued a study-specific data use agreement granting access to its data as housed at CIPHR for the purposes of this research study. This data use agreement was executed fully. Appropriate PCaP staff received CIPHR training, which was required to access linked PCaP-health insurance claims data files. PCaP Biostatistician provided LA team with physician contact list for PCaP participants completing the financial toxicity follow-up study survey to support physician recontact for clinical follow-up data.

LA The treating physicians of the PCaP participants who completed the financial toxicity survey were contacted to collect participant's current disease and treatment status. At the time of the financial toxicity survey, participants were asked to update their treating physicians. Of 562 participants, approximately 450 provided information about their physicians. We then searched the NC and LA state board of medical examiners databases and Google to validate and obtain the most recent address for each physician. An introductory letter and medical record data collection form, and a pre-paid envelope, were sent to the physician's clinic address on file. Forms asked about disease status, progression, PSA values, and treatments received since the file's last contact date. Completed data collection forms can be returned by US mail, scanned, and securely uploaded to REDCap or fax. Letters to physicians were sent during May 2021, and reports are being returned to the study office.

What was accomplished under these goals?

Specific Aim 1: Locate and contact PCaP research subjects to update CaP status, CaP treatments received and comorbidities, repeat the QoL assessments performed at baseline and follow-up, and administer new surveys on financial burdens and stress and caregiver QoL and support

Major Task 1 Obtain follow-up from PCaP research subjects

Subtask 1 Development: IRB approval at all sites, develop electronic and paper questionnaire forms, install and update patient and clinical medical records data tracking and collection system

Y1 Progress

IRB approval at all sites

A notice of probable award was received 02/07/2017. The PCaP Executive Committee discussed the potential award and what steps may be necessary to assist at its quarterly meeting 02/03/2017. Dr. Mohler traveled to LSUHSC 03/17/2017 to meet with Dr. Peters and the LSUHSC research team to begin the process of assembling

and modifying the survey instruments and set a timeline for IRB approvals at UNC, LSUHSC, RPCCC and DoD. The PCaP Executive Committee reviewed progress at its quarterly meeting 07/21/2017. Dr. Mohler traveled to UNC 01/29/2018 to meet with Dr. Benson and the UNC research team to review progress toward PCaP central data base modification and data transfer agreement, and IRB approval at UNC and DoD. Dr. Mohler returned to LSUHSC 02/02/2018 to meet with Dr. Peters and the LSUHSC research team to review the final survey instruments, update the Medical Record Abstraction (MRA) form, and review the status of IRB approvals at UNC, LSUHSC, RPCCC and DoD. After collaboration with the PCaP Executive Committee and Dr. Fontham, Drs. Peters, Benson and Mohler decided to prioritize the collection of data from living PCaP research subjects and their caregivers over the caregivers for deceased PCaP research subjects.

IRB approval proved challenging for several reasons. First, LSUHSC had closed the original PCaP study, which required re-opening. Second, the DoD approval mechanism required extra time because of the complexity of the proposed research. Three institutions were involved. Two states provided research subjects who enrolled on the PCaP study 11 years ago and were re-consented to follow-up studies, one in NC and one in LA conducted at different times by different investigators. The proposed research will be conducted at LSUHSC but all data, once de-identified, will be housed at UNC. Finally, the survey instruments required that IRB applications be amended as the survey instruments were customized for the proposed research, then approved, and then submitted to DoD for final approval BEFORE we could contact the first PCaP research subject.

- **UNC** IRB protocol #17-0530, approved 01/17/2018.
- **RP** IRB protocol #212/BDR 083017, approved 03/10/2017; amended protocol approved 06/11/2018.
- **LSUHSC** IRB protocol #9813, approved 08/01/2017- 07/31/2018; amended 03/15/2018 (re-ordering and re-wording of study instruments); amended 05/09/2018 (revision of primary care giver recruitment call script); renewed 07/03/2018- 07/02/2019.
- **DoD** USAMRMC, ORP, HRPO approved 07/02/2018.

Y2 Progress

- **UNC** IRB protocol #17-0530, approved 01/17/2019.
- **RP** IRB protocol #212/BDR 083017, approved 06/11/2018.
- **LSUHSC** IRB protocol #9813, approved 08/01/2017- 07/31/2018; amended 03/15/2018 (re-ordering and re-wording of study instruments); amended 05/09/2018 (revision of primary care giver recruitment call script); renewed 07/03/2019- 07/02/2020.
- **DoD** USAMRMC, ORP, HRPO approved 07/02/2018.

Y3 Progress

- **UNC** IRB protocol #17-0530, approved 01/17/2019.
- **RP** IRB protocol #212/BDR 083017, approved 06/11/2018.
- **LSUHSC** IRB protocol #9813, approved 08/01/2017- 07/31/2018; amended 03/15/2018 (re-ordering and re-wording of study instruments); amended 05/09/2018 (revision of primary care giver recruitment call script); renewed 07/03/19- 07/02/20; renewed 06/15/2020- 06/14/2021.
- **DoD** USAMRMC, ORP, HRPO approved 07/02/2018.

Y4 Progress

- **UNC** IRB protocol #17-0530 underwent an annual review and was approved for one year 11/12/2020; there were no amendments in Y4 other than the addition of new personnel.
- **RP** IRB protocol #212/BDR 083017, approved 06/11/2018, and remains active through 03/09/2025.

- **LSU IRB Protocol IRB: #1157** underwent an annual continuing review and was approved for one year 06/15/2020. An amendment to collect limited clinical information from PCaP participants' physicians needed to achieve the study's aims was submitted to the LSUHSC IRB 03/29/2021 and approved 03/30/2021.

Develop electronic and paper questionnaire forms

Y1 Progress

Research subject, caregiver and medical abstraction instruments were built in REDCap, validated and tested (see Appendix items 1, 2 and 3). Pilot testing of survey instruments and REDCap database functionality has been completed. Conversion of the electronic survey instruments from REDCap to TeleForm for ease of data transfer is ongoing. Paper-based versions of all questionnaires are being prepared.

Data collection instruments: Research subjects (Appendix 1)

- Contact info
- EPIC-26
- SF 12 Version2 Health Survey
- Charlson Comorbidity Index (CCI)
- Medical Expenditure Panel Survey (MEPS)
- Comprehensive Score for Financial Toxicity (COST)
- NCCN Distress Thermometer and Problems List for Patients
- PHQ-9
- Service Satisfaction Scale of Cancer Care for PT(SSS-PT)
- Patient Satisfaction Questionnaire Short Form (PSQ-18)
- Follow-up (Health Insurance/Disease History/PA)

Data collection instruments: Caregivers (Appendix 2)

- Contact Info
- Charlson Comorbidity Index (CCI)
- EPIC Short Form for Partners or Spouses
- Service Satisfaction Scale of Cancer Care of Partners (SSS-PA)
- NCCN Distress Thermometer and Problems List for Caregivers
- PHQ-9
- Caregiver Quality of Life-Cancer
- Montgomery-Borgatta Caregiver Burden Scale

Medical Record Abstraction (MRA) form (Appendix 3)

- A REDCap instrument with more than 300 data collection fields was created to store the data extracted from PCaP research subject's electronic and paper health records.

Y2 Progress

Expansion of questionnaire methodology

The telephone-based questionnaire set was reviewed 05-13-19 and reduced in length by about 20% by eliminating redundancy brought to the investigators' attention by interviewers and their research subjects' comments (Appendix 6). Skip patterns were developed to minimize un-necessary questions. Telephone interviews using the streamlined questionnaires require < 1 hour if research subjects are not "chatty." Even so, many research subjects requested a different format than telephone interviews.

A web-based questionnaire set was developed (Appendix 7). An email with a link to the questionnaires was sent to a test group of 85 research subjects, all of whom had requested a web-based instrument. A total of 64 research subjects have completed the online questionnaires, 21 online questionnaires are yet to be completed, and reminder emails are being sent and follow-up phone calls made.

A paper-based questionnaire set was developed (Appendix 8) and mailed to a test group of 125 research subjects. A total of 16 questionnaires have been completed and returned to the PCaP office in LA. Since most of the paper questionnaires were sent April-May 2019, more completed questionnaires are expected. Going forward, paper-based questionnaires will be sent out to those who don't answer the phone. This should increase the rate of questionnaire completion.

The impression of the enrollment and interview team is that research subjects prefer paper over web-site over telephone interviews for questionnaire completion.

Y3 Progress

PCaP participants were offered three vehicles for survey completion. The vehicle preferred was paper for 70%, online for 22%, and telephone for 8%. PCaP participants were reluctant to spend the time necessary for a telephone interview and preferred paper 3:1 over web-based questionnaires, a preference that probably reflects their age.

Y4 Progress

Survey collection was completed in early Y4 with a total of 562 surveys completed from participants in LA (N=287) and NC (N=275).

Install and update patient and clinical medical records data tracking and collection system

Dr. Farnan, the PCaP Biostatistician, began work 03/01/2017 on the creation of the recruitment re-contact dataset. This required her to merge the NC-LA PCaP baseline dataset with the most current contact information for each study research subject in NC and LA from multiple datasets; the re-contact information from the 2014 re-contact effort for PCaP, the existing contact data from the 5-year HCaP-NC follow-up study, and the 2015 re-contact effort for the LA follow-up study, Q-PCaP. Vital status for all research subjects was updated from the LA SEER database (updated annually) in January 2018 and from the NC Vital Statistic database updated monthly in June 2018. This dataset was distributed to LA after DoD IRB approval was secured in July 2018.

Subtask 2 Locate, contact and re-consent

Subtask 3 Collect treatment, oncologic outcome information and identify treating MDs

Subtask 4 Administer questionnaires

Y1 Progress

We must locate, recruit, and consent PCaP research subjects. Letters of study introduction and request to update contact information are being printed and envelopes ordered. The packets will be mailed to PCaP research subjects by 08/20/2018. Additional staff are being hired. We are anticipating to start the enrollment process 09/10/2018 (2 weeks after initial letters are sent). We will send letters in batches of 100, over time increasing to batches of 200.

PCaP research subjects will be asked to provide information on treating MD(s) if different from those recorded and identify and provide contact information for their caregiver(s).

Y2 Progress

Enrollment timeline

07/09/2018 First batch of 100 invitation letters and a form to update their contact information sent to PCaP research subjects.

10/12/2018 First telephone interview conducted

10/26/2018 Online survey made available for research subjects who wanted to complete the survey online

03/15/2019 First batch of paper-based surveys (TeleForm) mailed

04/02/2019 First completed paper-based survey received

Enrollment progress

Research subjects' contact information/vital status databases were updated when research subject/family member reports a change of phone number/email address or vital status. Research subjects who returned the contact form to LSUHSC PCaP office with their updated contact information are the priority of the interviewers. As an alternative method, the online survey or paper-version of survey are offered to research subjects who are reluctant to complete the survey over the phone.

In a batches of 200, the PCaP follow-up letters-were mailed starting 07/09/2018 and ended on 04/30/2019. An invitation for participation and a request to update contact information were sent to all verified alive PCaP research subjects. If the mailing to a research subject returned undeliverable, contact information/vital status was searched on LexisNexis Accurint (<https://www.accurint.com/>). Acumint has found about 40 LA research subjects, 50 NC research subjects and more research subjects should be found, especially in LA where research subjects have relocated more frequently as a result of Hurricane Katrina. PCaP databases were updated when new information was found. Invitation letters were sent again to those who didn't receive it before because of a wrong or old address. PCaP research subjects received 6 phone call contact attempts for recruitment before being classified as lost to follow-up.

The enrollment and interview team of 5 are performing well.

PCaP had a total of 1,616 living research subjects when the data collection began, based on the data received from UNC 06/12/2018. Prior to that an update on vital status of PCaP LA research subjects was received 03/13/2018 from Louisiana Tumor Registry (LTR). Another update on vital status from LTR was received 05/14/2019.

A total of 566 research subjects have been contacted via telephone and 1000 contacts remain in progress. A total of 206 questionnaires have been completed: 41 over the phone; 95 online; and 70 paper-based.

Y3 Progress

Enrollment status

A total of 562 PCaP participants have been enrolled, survey completed, data transferred to Dr. Farnan, data cleaned, and data reported. Participation rate was 42% of 1331 original PCaP participants who were neither deceased nor who declined future contacts at initial enrollment on the original PCaP study. Follow-up calls continued in Y3 to obtain missing information from those enrolled and to try to enroll new participants, but very few new enrollees are anticipated.

Y4 Progress

Enrollment was completed with a total of 562 PCaP participants.

Major Task 2 Obtain follow-up from caregiver/wife/partner/child(ren) of deceased PCaP research subjects

Subtask 1 Locate, contact and consent

Y1 Progress

Based on the progress of PCaP research subject agreement and interviews (subtasks 2 and 3), we plan to contact caregivers within 4 weeks of PCaP research subject data completion.

Subtask 2 Collect treatment, oncologic outcome information and identify treating MDs

Based on the progress of PCaP research subject agreement and interviews (subtasks 2 and 3), we plan to contact treating MD(s) within 4 weeks of PCaP research subject data completion.

Subtask 3 Administer questionnaires

Additional staff are being hired.

Y3 Progress

Executive decision was made to abandon major task 2 for several reasons. First, both UNC and LSUHSC IRBs balked at initial inquiries about a strategy to obtain consent from those who were identified as contacts by PCaP participants at the time of initial enrollment on the PCaP study. The original PCaP study identified a “contact person,” which was to address lost to follow-up issues, not to identify caregivers. Second, in this study, only 30% of PCaP participants identified a caregiver and almost all caregivers were the spouse. Therefore, we would only have caregivers to contact for about 36 men who died of other causes and about 9 men who died from CaP in years 3 and 4. Instead, Dr. Peters will submit an MPI R01 to study a large number of men who present with bone metastatic CaP.

Specific Aim 2: Collect data electronically, when possible, and locate and contact PCaP research subjects’ treating physicians, when necessary, to update treatments received and oncologic outcome data

Major Task 1 Obtain follow-up electronically

Subtask 1 Conduct feasibility test on 20 NC research subjects and 20 LA research subjects

Subtask 2 Collect electronic treatment and oncologic outcome data on NC research subjects

Subtask 3 Collect electronic treatment and oncologic outcome data on LA research subjects

Major Task 2 Obtain follow-up from treating MDs

Subtask 1 Obtain follow-up from UNC in NC PCaP research subjects followed at UNC

Subtask 2 Obtain follow-up from NC MDs in NC PCaP research subjects not followed at UNC

Subtask3 Obtain follow-up from SEER for LA PCaP research subjects

Subtask 4 Obtain follow-up from LA MDs on LA PCaP research subjects without follow-up in SEER

Subtask 5 Abstract data using the PCaP Follow-up Form

Y2 Progress

The updating of oncologic outcome graphs on NC research subjects and the construction of oncologic outcome graphs on LA research subjects will require identification of treating primary care physicians for research subjects discharged from specialty oncologic follow-up and identification of specialty physicians providing oncologic care (urologist, radiation oncologist or medical oncologist) for 1616 research subjects. The continuing evolution in clinical data availability may allow more efficient collection of these data. We have initiated a pilot project of 20 NC research subjects and 20 LA research subjects to determine how much oncologic outcome data can be acquired electronically. In LA, PCaP research subjects are flagged already in SEER. Dr. Peters is meeting with SEER officials to determine if we can conduct a pattern-of-care study to identify treatments received, oncologic status, and interval PSA results. In NC, Dr. Bensen will explore the use of the UNC Tumor Registry and an ongoing UNC project to access claims data for research use, which should include data from NC research subjects who have BC/BS, Medicare or Medicaid.

Y3 Progress

NC The health insurance claims data to be used for the PCaP Financial Toxicity project on NC participants will be reused from UNC's Cancer Information and Population Health Resource (CIPHR). CIPHR-linked data include cancer case data from the North Carolina Central Cancer Registry (NCCCR). Original NC PCaP cases were defined from the NCCCR using rapid case ascertainment. NCCCR data are linked to administrative and claims data for a 100% sample of North Carolinians from Medicare, Medicaid, and Blue Cross Blue Shield of North Carolina (BCBS). These data are subject to data use agreements (DUAs) between CIPHR and the data owner (BCBS or Centers for Medicaid & Medicare Services (CMS)). Per the terms of these DUAs, each reuse of this data for individual research studies must be approved by the individual data owners. This study requested and received data use approval from the NCCCR (required 2 weeks) and BCBS (required 4 months). The remaining review and approval process for CMS has taken approximately 1 year and should require approximately 2 more months. CMS data use approval processes usually take 6 months, but CMS has received an unusually high demand for data use requests as a result of the COVID-19 pandemic. Documents for CMS approval are at the DoD pending signature. Once signed, these documents will be reviewed by the CMS Research Data Assistance Center (ResDAC) for final approval. Once approved at ResDAC, CMS will issue a study-specific data use agreement granting access to its data as housed at CIPHR for the purposes of this research study.

LA The LA SEER Registry will be queried for date of last contact, vital status and recurrence information for all LA PCaP participants as has been done annually. In addition, the PCORI supported Louisiana REACHnet will be used to obtain clinical electronic health record (EHR) data for LA PCaP participants. REACHnet contains electronic health record data for more than 8 million patients standardized to a common data model to support pragmatic clinical research conducted under real-life practice conditions. REACHnet is one of nine Clinical Research Networks (CRNs) nationwide that constitute PCORnet®—The National Patient-Centered Clinical Research Network. Louisiana Public Health Institute (LPHI) is the REACHnet Coordinating Center. REACHNET contains data from several LA health care systems, which include Tulane Medical Center, Ochsner Health System, and University Medical Center. REACHnet has archived claims data from BCBS of LA, LA Medicaid, and Humana. Examples of data elements available through REACHnet include procedures for medical interventions and diagnostic testing, such as surgical procedures and laboratory orders, and records of medications administered to patients by healthcare providers. These may take place in any setting, including inpatient, outpatient or home health encounters. REACHnet data conforms to the PCORnet common data elements model and permits efficient data linkages to collect the clinically relevant data necessary to achieve the study aims. REACHnet's academic partners include the Louisiana State University Health Sciences Center (LSUHSC). A Data Sharing and Use Agreement (DSUA) is required for data linkage that outlines the specifications of the dataset to be provided and the terms for data use. The DSUA is between the REACHnet Coordinating Center and

the PCaP investigative team. LA PCaP participants will have medical claims data abstracted using the same search terms as used in NC for procedures (Appendix 10) and medications (Appendix 11).

Y4 Progress

NC The remaining review and approval process for Centers for Medicaid & Medicare Services (CMS) was completed in this reporting period. Once signed, documents were reviewed by the CMS Research Data Assistance Center (ResDAC) for final approval. Once approved at ResDAC, CMS issued a study-specific data use agreement granting access to its data as housed at CIPHR for the purposes of this research study. This data use agreement has been fully executed. Appropriate PCaP staff received CIPHR training (required to access linked PCaP-health insurance claims data files). PCaP Biostatistician provided LA team with physician contact list for PCaP participants completing the financial toxicity follow-up study survey to support physician recontact for clinical follow-up data. We began analysis of CIPHR health insurance claims data, by creating 2011-2018 oncographs to describe patterns of prostate cancer care during this follow-up period. Together with baseline information, HCaP 4-year follow-up data, vital status, and PCaP financial toxicity questionnaires, we have extended our clinical follow-up to 10 or more years after diagnosis. Furthermore, 156 NC men were found to have received prostate cancer follow-up care at UNC Health during the 2011-2018 follow-up period. Medical records abstraction is underway to provide detailed clinical data to complement the health insurance claims data as well as assess the accuracy of progression assignment using electronic data. In addition, mailings to health care providers identified by PCaP participants on the recent financial toxicity 10-year follow-up survey have requested information about progression status including interval PSA values and new treatments.

LA 562 LA and NC PCaP participants completed the financial toxicity survey. Of these, physician addresses have been confirmed for 417, and physician contact information was either not provided or not found for 145 participants. The form for the clinical follow-up date was developed to collect the most relevant information necessary to achieve study aims. The document was sent to those 417 physicians with confirmed and validated addresses by the LA study team in May 2021. The completed forms can be returned by physicians' office staff to the LA PCaP study office through US mail, fax, or securely scanned and uploaded as a PDF to REDCap. Forms are being received daily in May and June, with an expected completion date of 06/30/2021.

Major Task 3 Construct progression graphs

Subtask 1 Update progression graphs on NC PCaP research subjects

Subtask 2 Construct progression graphs on LA PCaP research subjects

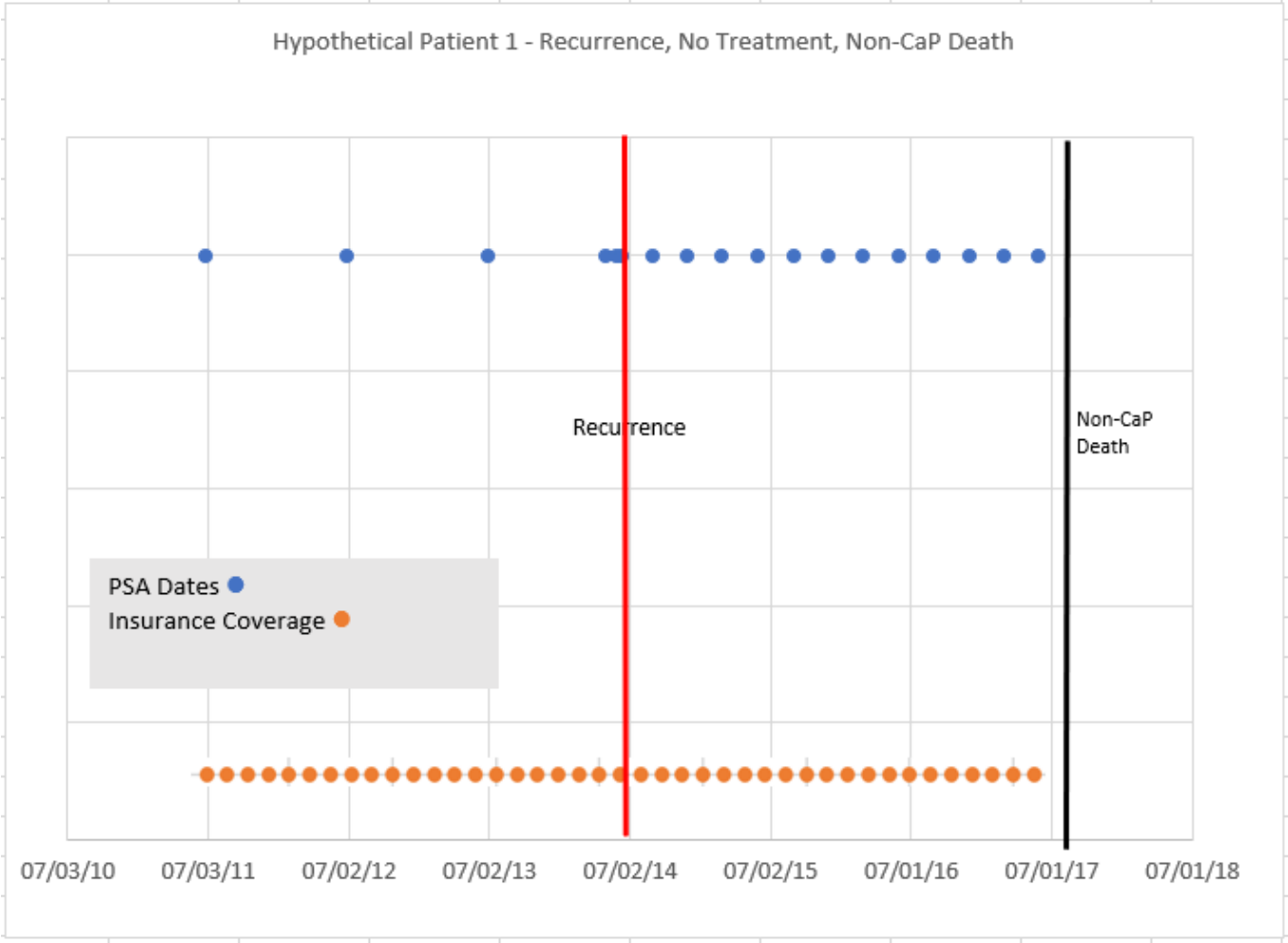
Y3 Progress

The oncologic outcomes will be inferred from procedures undergone and medications prescribed as ascertained using CIPHR in NC and REACHnet in LA. Uncertainties will be addressed by contacting physicians' offices; most PCaP participants see only their urologist for CaP follow-up. A manuscript has been added that will outline our methods. In preparation for the EHR-based construction of OncoGraphs that was performed previously in NC using medical record review, 5 hypothetical patients were constructed (see below). A test set of 30 PCaP participants (15 from NC and 15 from LA and 15 African Americans and 15 European Americans) are having OncoGraphs constructed using the EHR method and the OncoGraphs reviewed in the context of medical record information from all sources (EHR, paper medical records, participant interview, and personal physician(s) contact(s), where necessary). Again, and fortunately, most PCaP participants see only their urologist for CaP follow-up so contact to obtain additional information about oncologic outcome should be practical.

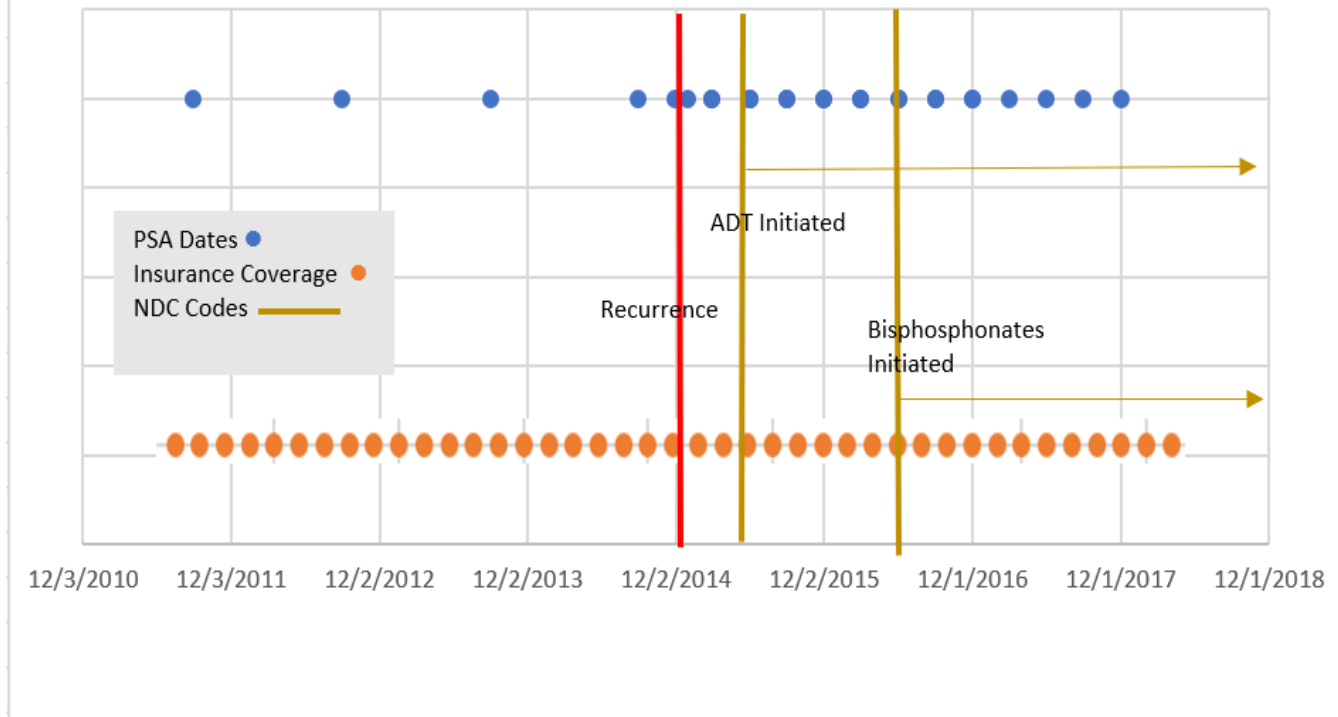
Y4 Progress

NC. We have made progress on determination of oncologic outcomes among PCaP men greater than 10 years after diagnosis utilizing CIPHR data in NC. There are 652 PCaP participants in NC (of the original 1031) linked to health insurance data in CIPHR (Medicaid, Medicare and BCBS) between 2011-2018. Oncographs specific to the 2011-2018 time period were created using the available CIPHR data related to prostate cancer care (PSA tests, treatments including surgery, radiation, and medications, such as ADT). Many men with CIPHR oncographs also had oncographs utilizing electronic medical record (EMR) data the 4 years after diagnosis (HCaP-NC). For these men (N= 563), we have extensive details about patterns of care and prostate cancer outcomes. Of men who participated in the PCaP financial toxicity survey, 190 linked with CIPHR claims data during the follow-up period.

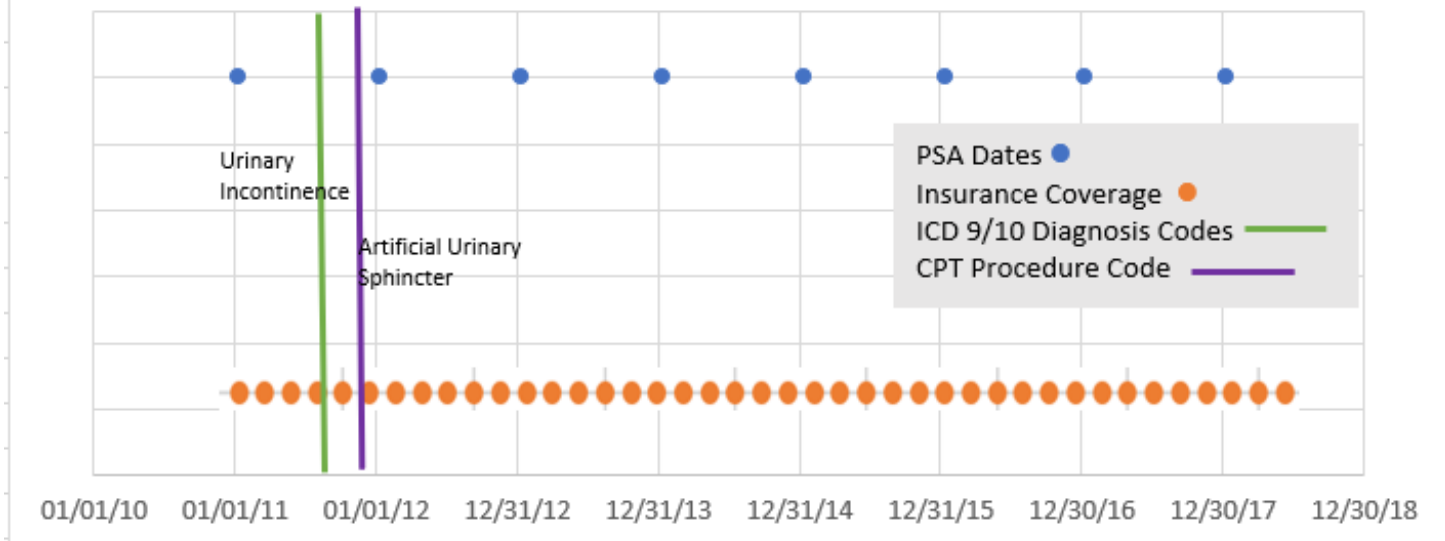
LA Awaiting receipt of clinical progression data (PSA levels and new treatments) from physicians’ offices.

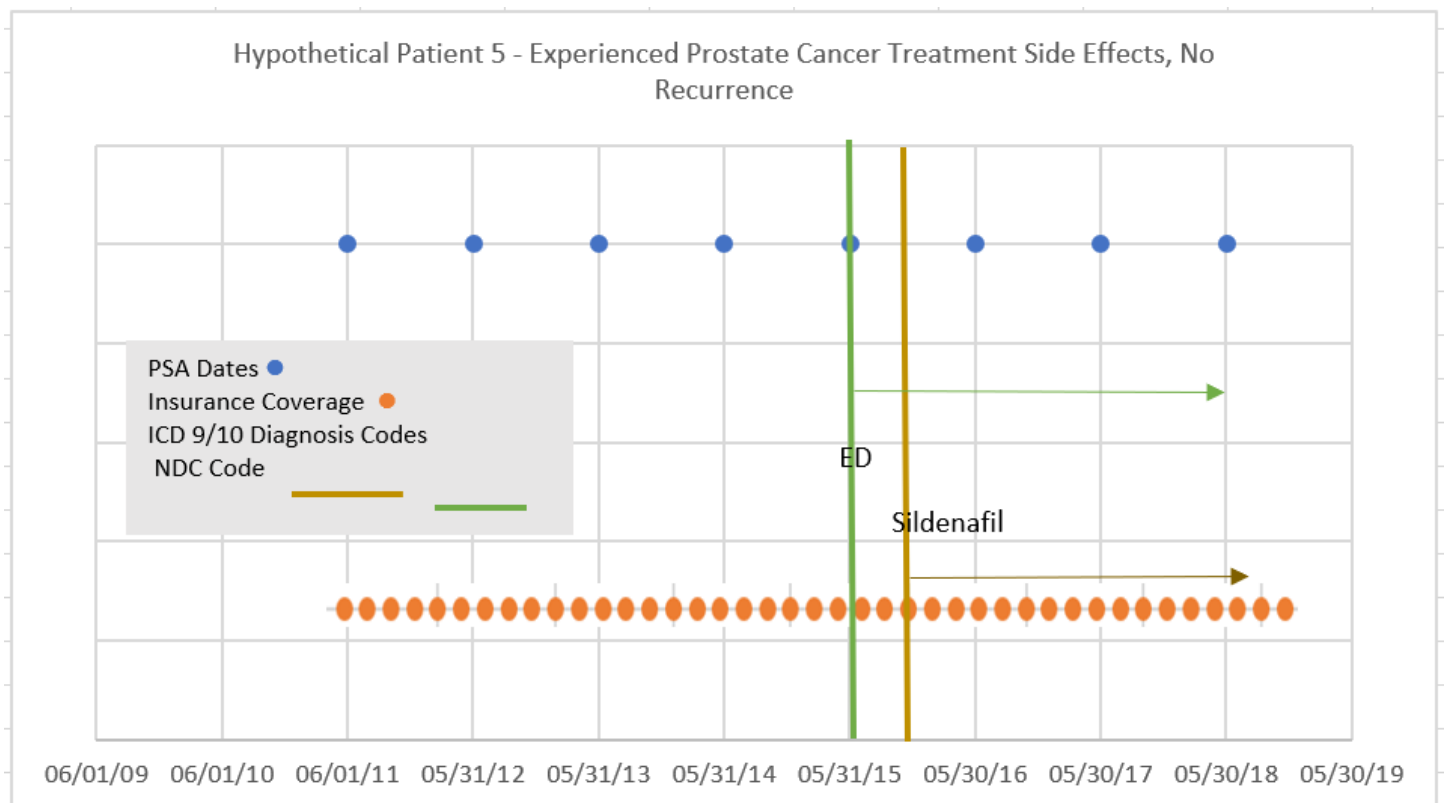
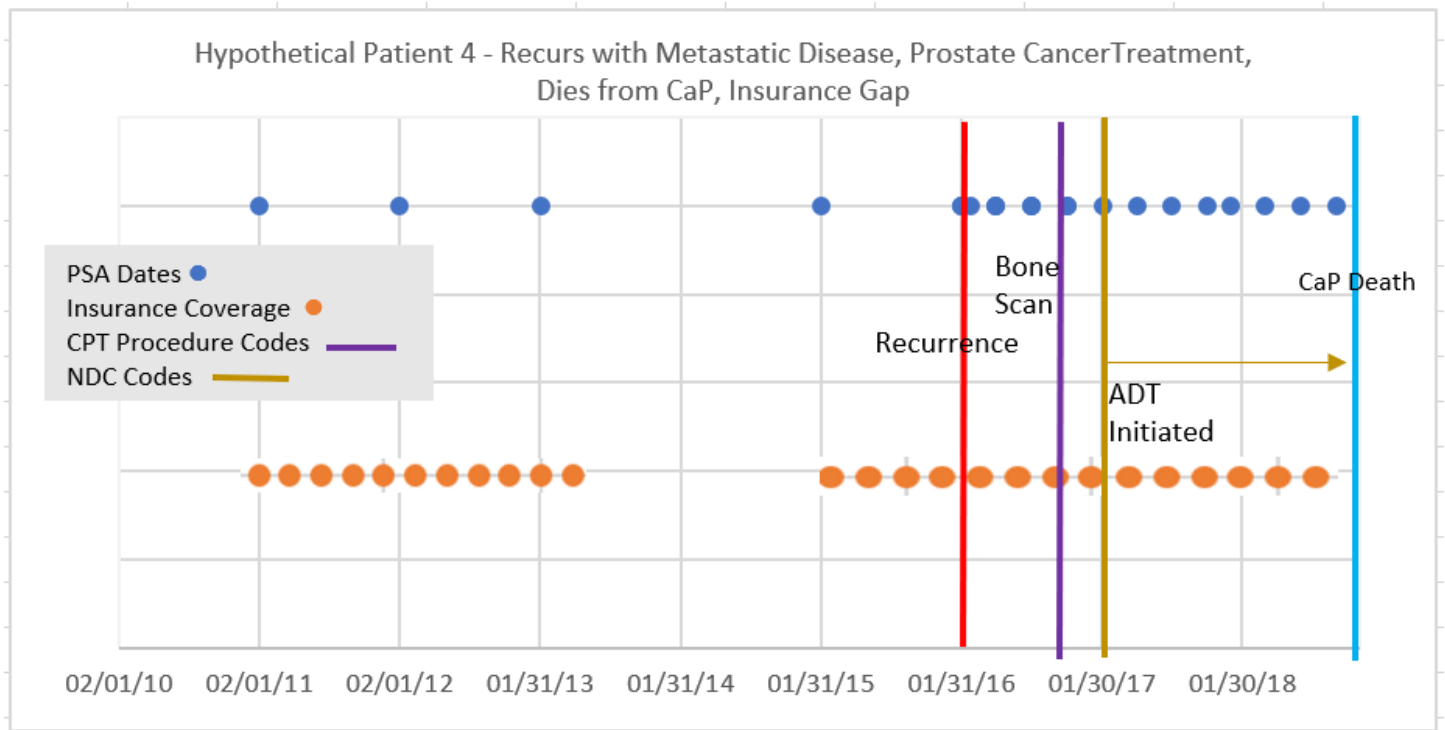


Hypothetical Patient 2 -Recurrence with Prostate Cancer Treatment



Hypothetical Patient 3- Experienced Prostate Cancer Treatment Side Effects, No Recurrence





Specific Aim 3: Obtain and link vital status data and cause of death in PCaP research subjects

Major Task 1 Obtain vital statistics of NC PCaP research subjects

Subtask 1 Obtain vital statistics from NC Vital Records

The most current data on NC PCaP research subjects is obtained monthly and is reported below through end of June 2018 (see below).

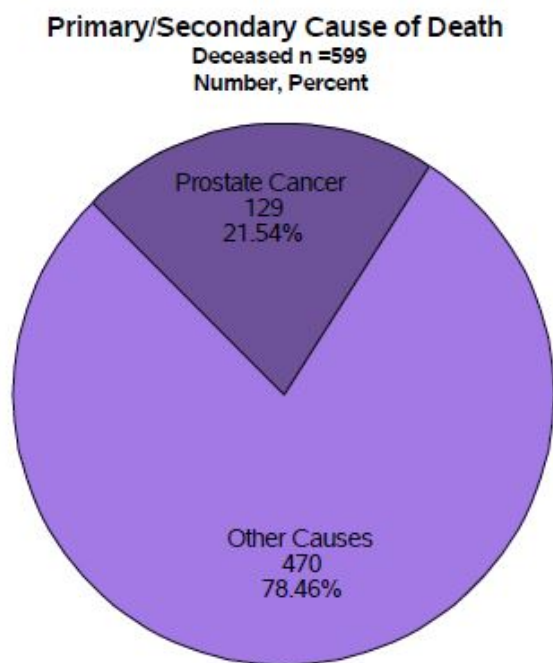
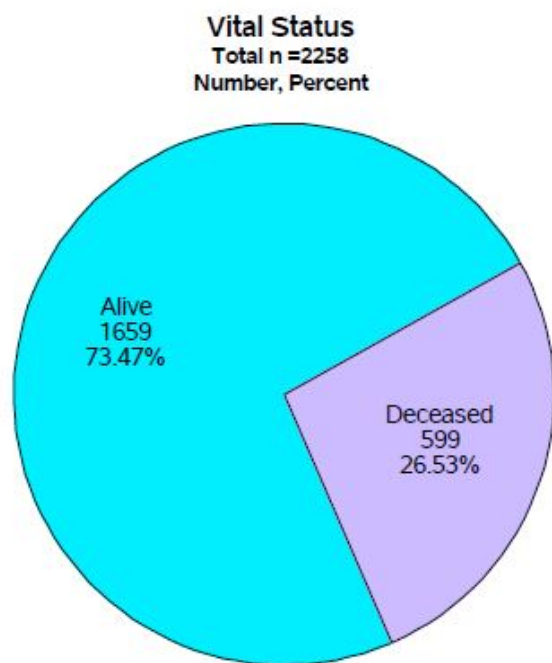
Major Task 2 Obtain vital statistics of LA PCaP research subjects

Subtask 1 Obtain vital statistics from LA State Tumor Registry in Year 1

Y1 Progress

A copy of vital status of LA PCaP research subjects were sent to UNC (Laura Farnan) March 2018 (see below) that provided LA research subjects' status as of 01/01/2018 (see below). The most current data on LA PCaP research subjects will be delivered from the Louisiana Tumor Registry (LTR) in the next few days. Data received from LTR will be shared monthly going forward.

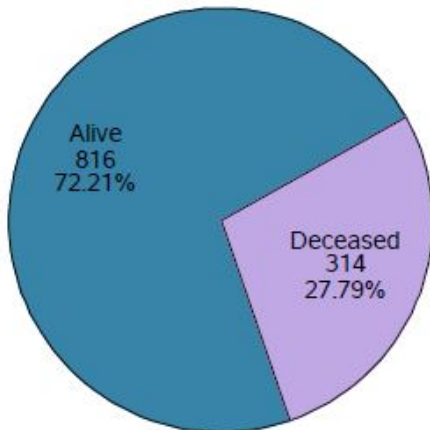
Vital Statistics for NC and LA PCaP subjects



Vital Statistics for PCaP subjects by race

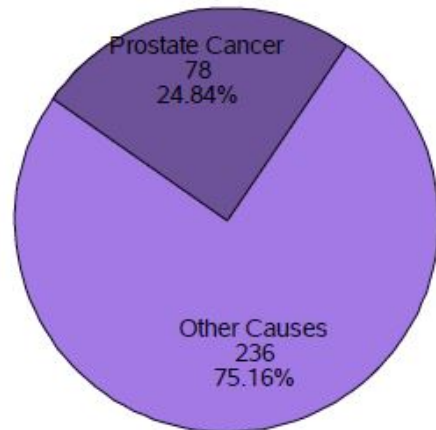
Vital Status of AA subjects

Total n =1130
Number, Percent



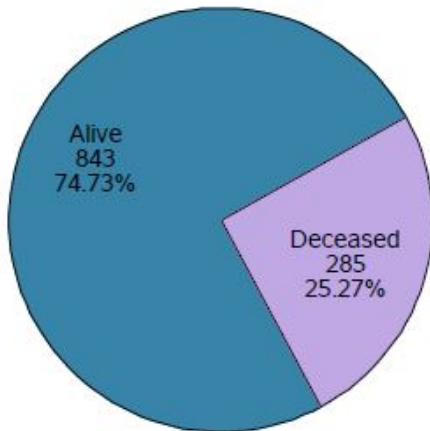
Primary/Secondary Cause of Death of AA subjects

Deceased n =314
Number, Percent



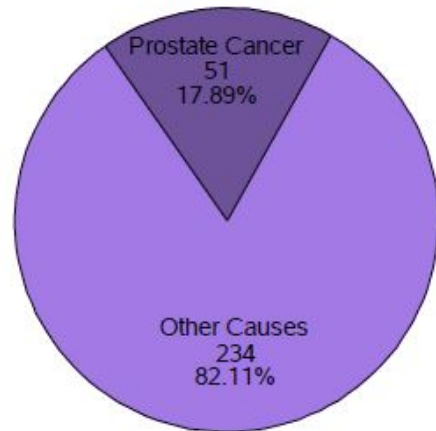
Vital Status of CA subjects

Total n =1128
Number, Percent



Primary/Secondary Cause of Death of CA subjects

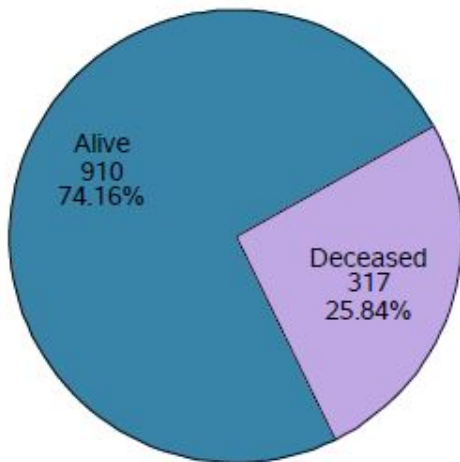
Deceased n =285
Number, Percent



Vital Statistics for NC and LA PCaP subjects

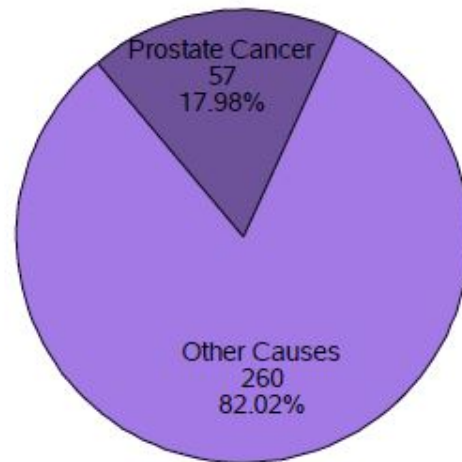
Vital Status of LA subjects

Total n =1227
Number, Percent



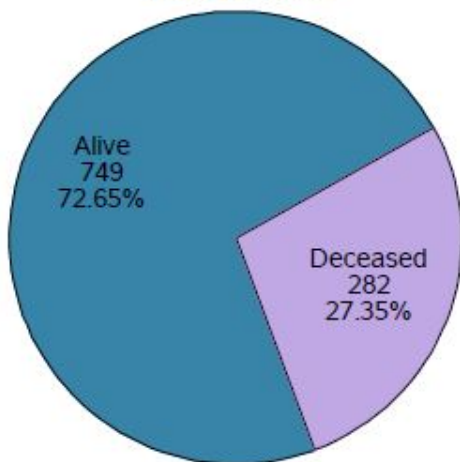
Primary/Secondary Cause of Death of LA subjects

Deceased n =317
Number, Percent



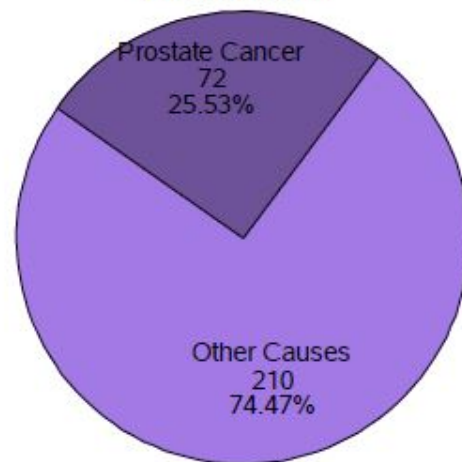
Vital Status of NC subjects

Total n =1031
Number, Percent



Primary/Secondary Cause of Death of NC subjects

Deceased n =282
Number, Percent

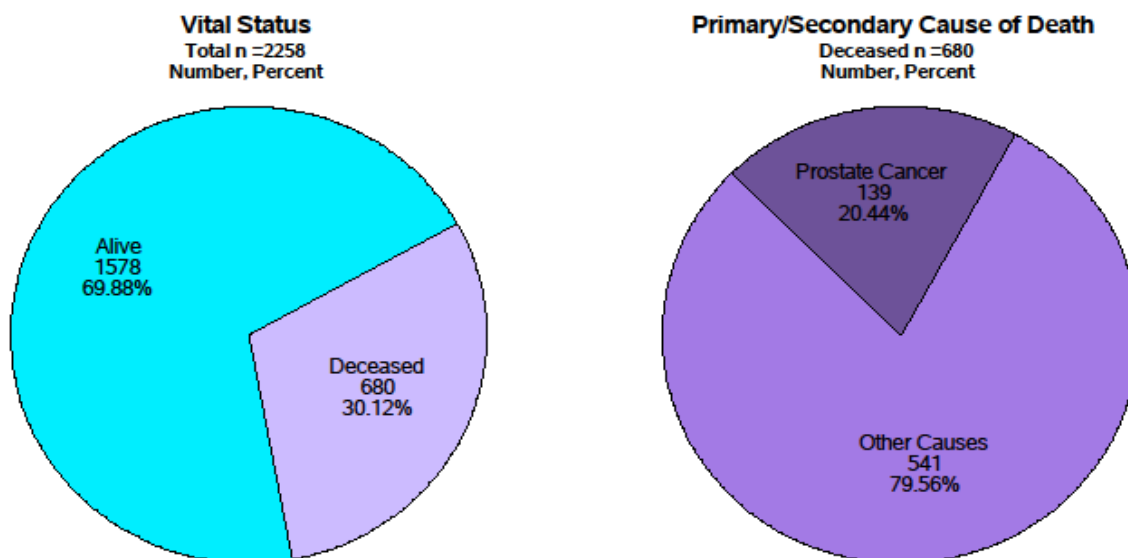


Y2 Progress

The vital statistics data reveal that we continue to have research subjects die: 81 research subjects died in the last year and 71% of all origin PCaP research subjects remain alive. The rate at which these deaths occur from CaP remains relatively stable at about 21%.

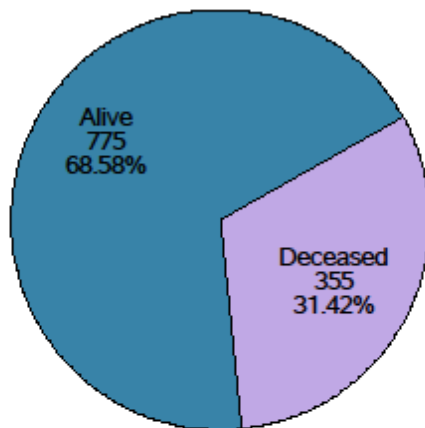
Vital Statistics for NC and LA PCaP subjects

1



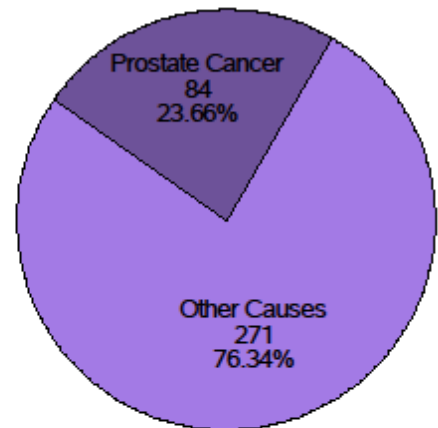
Vital Status of AA subjects

Total n =1130
Number, Percent



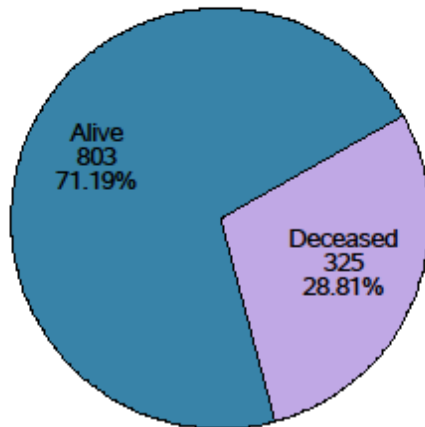
Primary/Secondary Cause of Death of AA subjects

Deceased n =355
Number, Percent



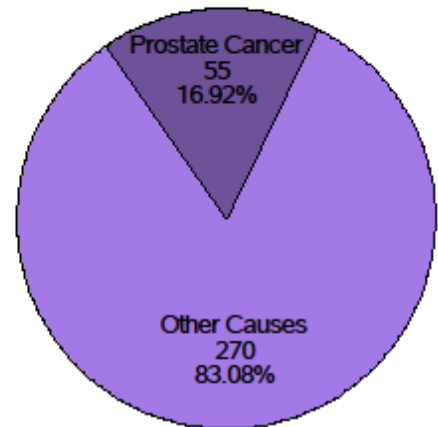
Vital Status of CA subjects

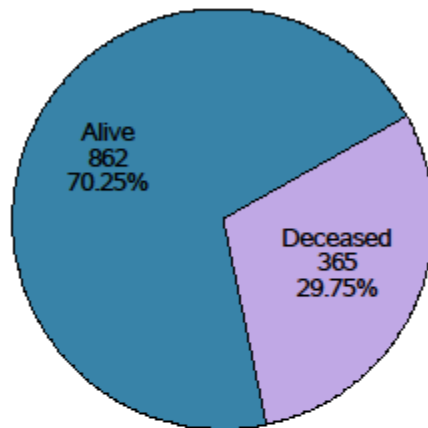
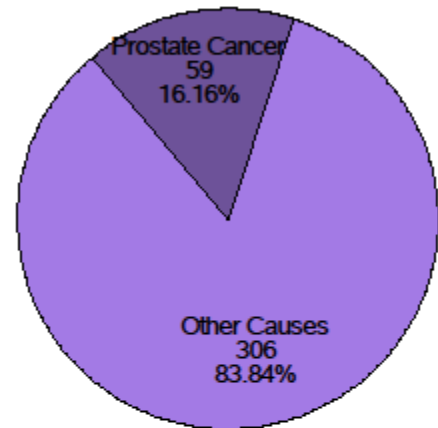
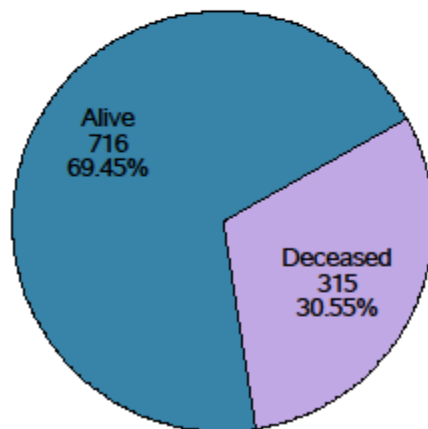
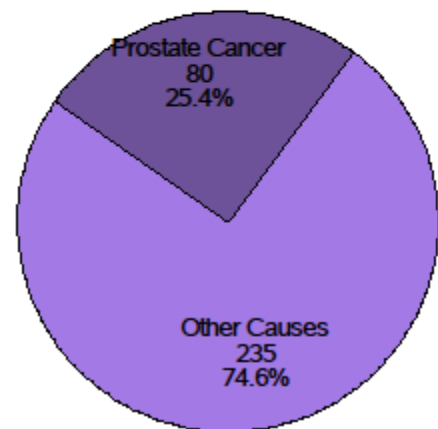
Total n =1128
Number, Percent



Primary/Secondary Cause of Death of CA subjects

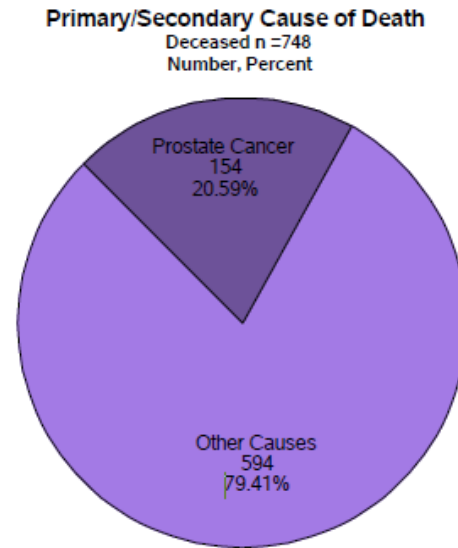
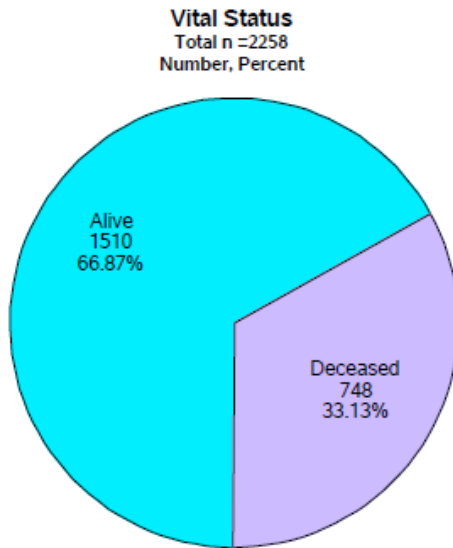
Deceased n =325
Number, Percent



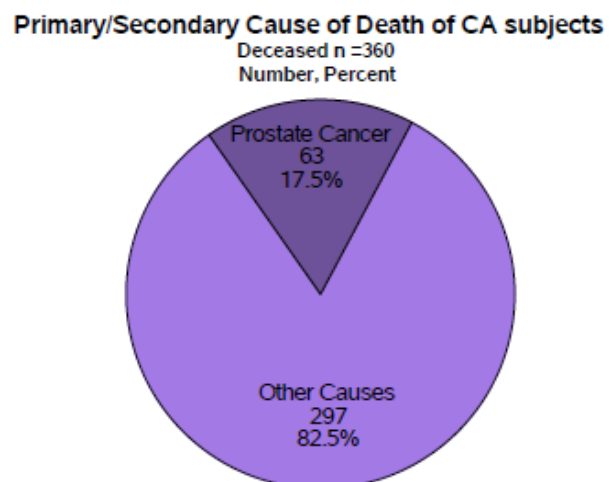
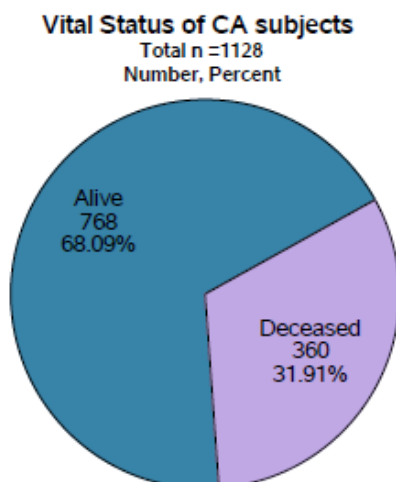
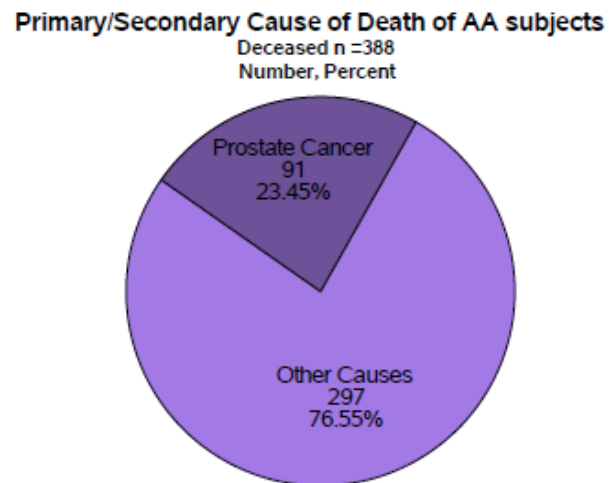
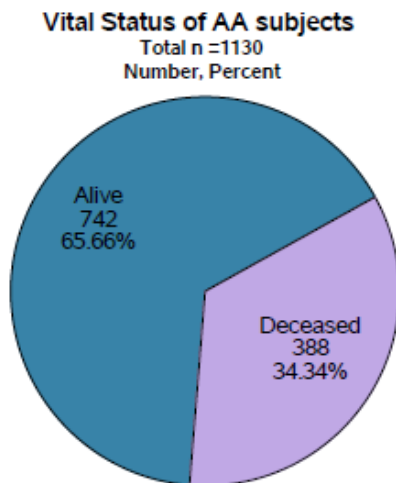
Vital Status of LA subjectsTotal n =1227
Number, Percent**Primary/Secondary Cause of Death of LA subjects**Deceased n =365
Number, Percent**Vital Status of NC subjects**Total n =1031
Number, Percent**Primary/Secondary Cause of Death of NC subjects**Deceased n =315
Number, Percent**Y3 Progress**

The vital statistics data reveal that we continue to have research subjects die: 68 research subjects died in the last year and 67% of all original PCaP research subjects remain alive. The rate at which these deaths occur from CaP remains relatively stable at about 21%.

Vital Statistics for NC and LA PCaP subjects



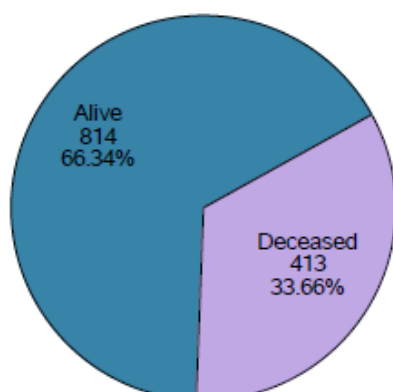
Vital Statistics for PCaP subjects by race



Vital Statistics for NC and LA PCaP subjects

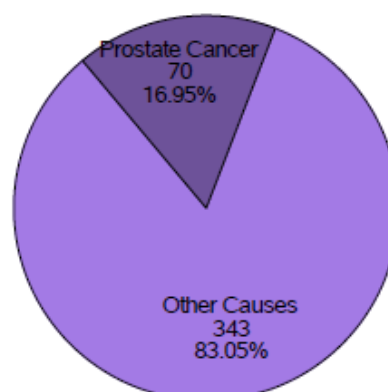
Vital Status of LA subjects

Total n =1227
Number, Percent



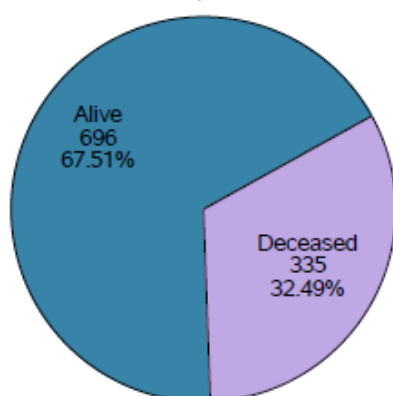
Primary/Secondary Cause of Death of LA subjects

Deceased n =413
Number, Percent



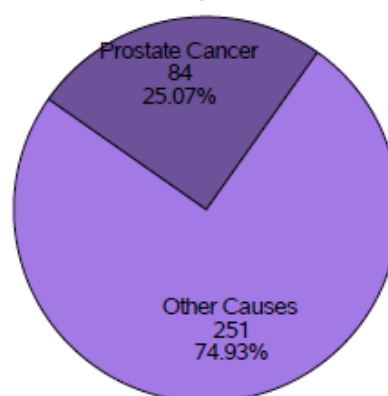
Vital Status of NC subjects

Total n =1031
Number, Percent



Primary/Secondary Cause of Death of NC subjects

Deceased n =335
Number, Percent

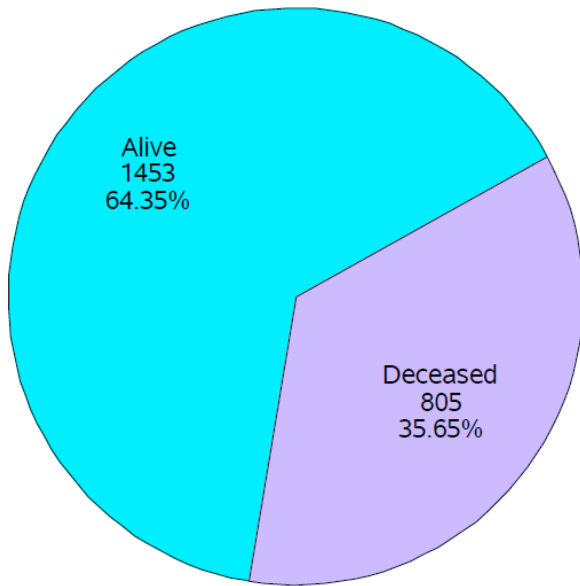


Y4 Progress

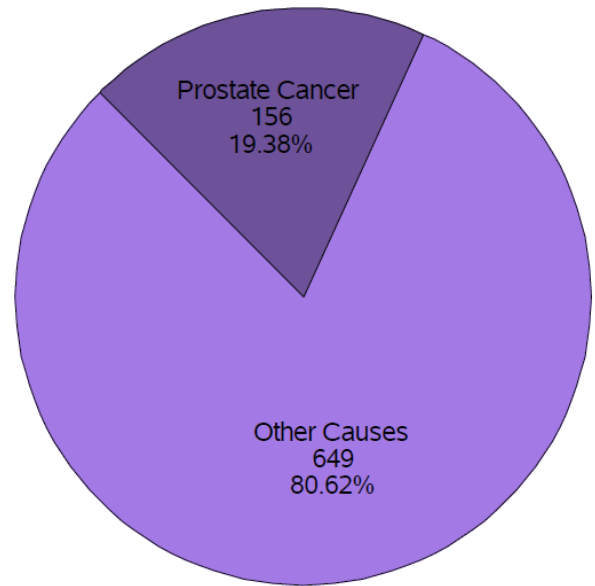
The vital statistics data reveal that we continue to have research subjects die: 57 research subjects died in the last year and 64% of all original PCaP research subjects remain alive. 19% of all deaths are attributed to CaP.

Vital Statistics for NC and LA PCaP subjects

Vital Status
Total n =2258
Number, Percent



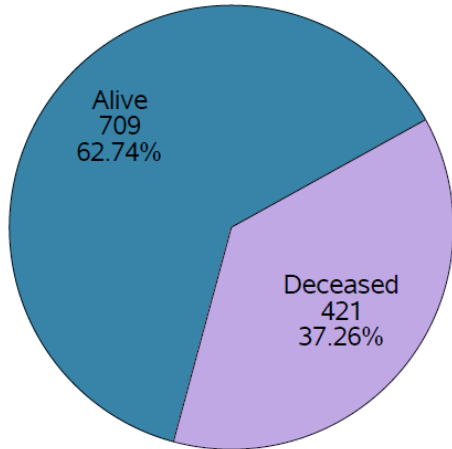
Primary/Secondary Cause of Death
Deceased n =805
Number, Percent



Vital Statistics for PCaP subjects by race

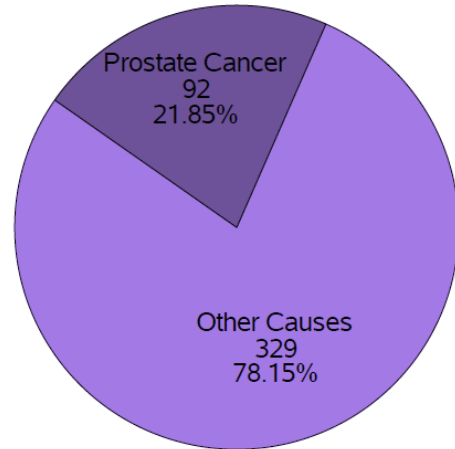
Vital Status of AA subjects

Total n =1130
Number, Percent



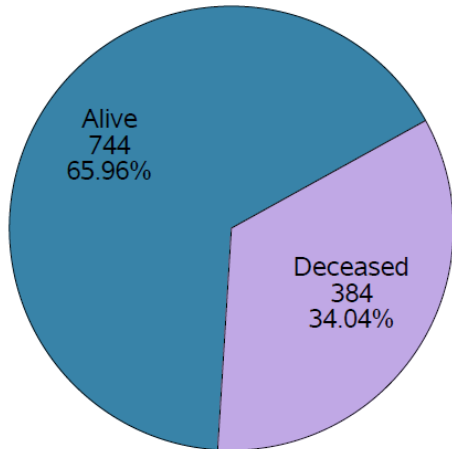
Primary/Secondary Cause of Death of AA subjects

Deceased n =421
Number, Percent



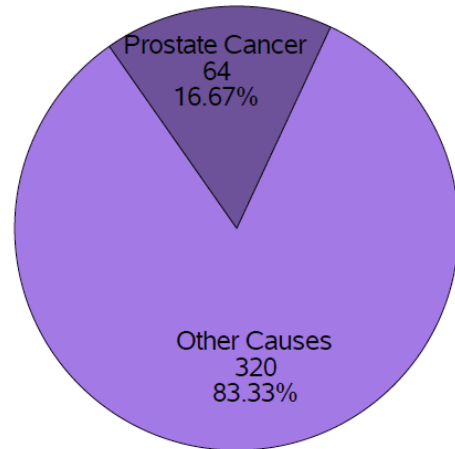
Vital Status of CA subjects

Total n =1128
Number, Percent



Primary/Secondary Cause of Death of CA subjects

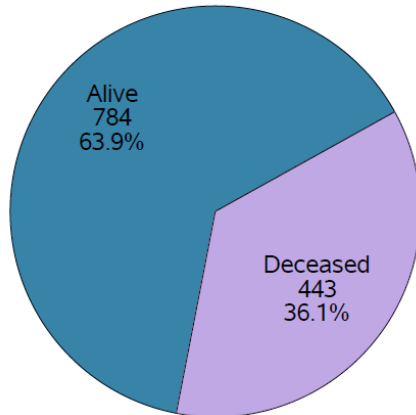
Deceased n =384
Number, Percent



Vital Statistics for NC and LA PCaP subjects

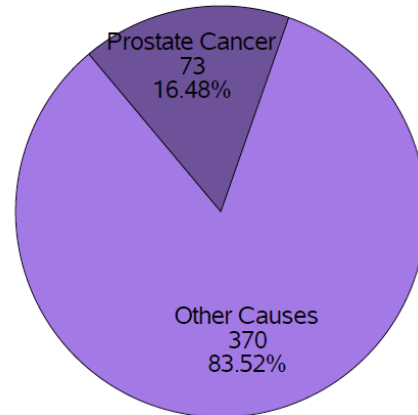
Vital Status of LA subjects

Total n =1227
Number, Percent



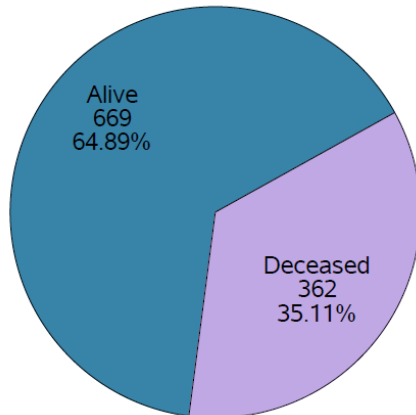
Primary/Secondary Cause of Death of LA subjects

Deceased n =443
Number, Percent



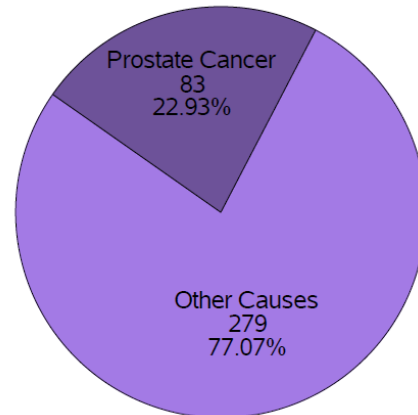
Vital Status of NC subjects

Total n =1031
Number, Percent



Primary/Secondary Cause of Death of NC subjects

Deceased n =362
Number, Percent



Major Task 3 Obtain vital statistics of NC and LA research subjects living outside NC and LA

Subtask 1 Obtain vital statistics form NDI of NCHS in year 1

Subtask 2 Obtain vital status of any remaining PCaP research subjects by contacting their treating physicians and family members

Y3 Progress

Drs. Bensen and Farnan tried to get all PCaP participants linked to NDI for vital status determination in Year 1. Application forms were completed and reviewed with the NDI senior manager. They were not willing to move past 2 issues. The first was a deal breaker. NDI would not agree to comply with our IRB in that we cannot share PHI with them. We were asking for access to the NDI to link our patients ourselves, not to send them a file with PHI. The second was impossible. NDI wanted PCaP to agree that PCaP would destroy all NDI data/information after 5 years. After several meetings with NDI, they would not budge from PCaP removing all vital status data from our PCaP dataset after 5 years. UNC Lineberger Comprehensive Cancer Center remains without a contract with NDI of NCHS due to expense.

LSUHSC SPH LTR performs an annual download of NDI vital statistics that is reflected in the data LA share with NC. However, NDI linkage has not been made yet for 2018 and 2019 (NDI usually is a few years behind). LA queried the state vital records for 140 LA PCaP participants who could not be located of whom 30 had died

but LA has no additional information. LA is following a total of 15 PCaP participants who have been found living outside of LA and are alive in FL, GA, OH, DE and TX.

Specific Aim 4: Examine the role financial burden and stress have on CaP survival and QoL and whether this relationship was modified by race

Y1 Progress

Major Task 1 Data management

Subtask 1 Maintain PCaP Data Sharing and Tracking System

PCaP diligently maintains a state-of-the-art Data Sharing Tracking System developed and maintained by the UNC Cancer Information and Population Resource (CIPHR) program. CIPHR incorporates a world class computing system with systems for data management and project tracking (ancillary studies, manuscripts), and expert staff to support and maintain these data and systems. The CIPHR secure server environment is maintained by UNC Information Technology Services and Research Computing. The CIPHR project management and tracking system is a web-based application that allows groups to manage and track studies/projects in accordance with their data governance policies. CIPHR system developers tailor each implementation of the tracking system to the particular organization. They employ the latest stable version of PHP and perform quarterly updates with emergency patching as needed. The system is housed in a Tier II Data Center with 24/7 surveillance, electronic key-card entry or sign-in with escort, redundant power sources, and climate control. The servers are behind UNC campus perimeter firewalls and have host-based firewalls exposing only ports necessary for the services in use. Servers are scanned twice weekly for vulnerabilities using QualysGuard SaaS and patched/upgraded accordingly. Over 140 PCaP investigators, nearly 20 completed ancillary studies/grants, 16 ancillary studies in progress, 40 published manuscripts and 10 manuscripts in development are archived in our Data Sharing Tracking System along with many other manuscript and grant statuses.

Subtask 2 Create project-specific data repository

PCaP maintains a robust Central Analytic Dataset on a secure server supported and managed by the UNC Lineberger Comprehensive Cancer Center's Bioinformatics/Biostatistics Core Facility, complete with fully annotated data dictionary describing source (baseline, follow-up, or other project-specific sources), a Data and Specimen Guide, and detailed description of questionnaires available for use. User friendly, supporting documents described above can be found on the PCaP website (<https://pcap.bioinf.unc.edu/resources-protocols.php>). Details of data available are shared by Drs. Bensen (UNC PCaP/HCaP-NC PI) and Farnan (Biostatistician) with interested investigators via phone or in-person. Numerous de-identified project-specific data repositories have been deposited via project-specific folders on the secure PCaP website and this data merged with the Central PCaP Analytic Dataset by Dr. Farnan. Recently, to comply with current HIPAA and PHI standards, we established a secure Office 365 folder for transfer of datasets that contain PHI shared with PCaP established sites that have fully executed Data Use Agreements (LSUHSC, UNC and RPCCC). Office 365 is rated for storage and sharing internally and externally for most classifications of UNC-Chapel Hill owned and managed information, including the type of information stored and shared by PCaP. This compliant secure folder was used for the transfer of the recruitment and re-contact dataset created specifically for the DoD-funded PCaP Financial Toxicity grant. This same mechanism will be utilized for re-deposit of updated data returned to the PCaP Central Database from LSUHSC following PCaP Financial Toxicity grant recruitment and data collection.

Data collected from PCaP research subject and their caregiver surveys including abstraction of PCaP medical records will be entered into Research Electronic Data Capture (REDCap). REDCap is a secure, HIPAA-complaint web application for building and managing online surveys and databases.

A PCaP research subject tracking database specific for the proposed research was developed at LSUHSC in REDCap that was based on and incorporated data received from UNC. Two Excel documents were received from UNC containing contact and demographic data for LSU and UNC PCaP research subjects, which were merged and imported into the REDCap tracking database. The tracking database will serve as monitoring dashboard for interviewers, since it allows us to keep track of call and data collection activities for all PCaP research subjects.

Subtask 3 Perform continuous data quality control

Data use agreements were negotiated and executed between UNC and LSUHSC. Transfer from UNC of data for PCaP research subject tracking was completed and data were validated (see below).

Y2 Progress

Telephone and Online REDCap has inbuilt validation features, so most of the data that were collected over the phone or online have been clean. Some of the inbuilt validation features include date structure, text only fields, and only one option from given choices can be selected. Questionnaires done online are reviewed for completeness and, if instruments are left blank, research subjects are contacted to complete the survey. Research subjects who open the link and submit the questionnaires in multiple parts created more than one record, which required that all parts of all questionnaires surveys to be combined to create a single record. PCaP ID is assigned and entered once online questionnaires are complete.

Teleform A quality control of the scanned questionnaires is done before exporting the data into .csv format. The number of scanned copies and number of data points are matched to ensure accurate data export. Most fields are double-checked manually during the process of form evaluation.

Once the questionnaire data gets to PCaP, they are checked for completeness, accuracy and uniformity, and scrubbed for duplicate records. Quality control reports are generated and returned to each site (NC, LA) for resolution. All questionnaire data are merged with PCaP baseline data for analysis once the data analyst confirms all quality control report issues have been resolved. Of the 206 questionnaires completed, 181 questionnaires have been completed QC and have had data entered.

Subtask 4 Perform statistical analysis of quality-controlled data

Y3 Progress

All questionnaire data were merged with PCaP baseline data for analysis once the data analyst confirmed all quality control report issues were resolved. Of the 561 questionnaires completed, all have been completed QC and have had data entered. Most participants have had insurance of some type all the time so that their oncologic outcomes should be accessible electronically. Only 9% are under treatment for their cancer and only 2% are in poor health. Our PCaP participants are equally distributed by state but more European than African Americans are represented, a difference that will require further analysis to assess for bias.

Table 1

	AA				CA				TOTAL	
	LA		NC		LA		NC			
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
aggressive:tumor aggressiveness(derived)										
Missing	4	3.8	0	0	11	6.0	1	0.5	16	2.9
Low	53	50.5	47	52.8	100	54.9	115	62.2	315	56.1

	AA				CA				TOTAL	
	LA		NC		LA		NC			
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Intermediate	34	32.4	33	37.1	49	26.9	54	29.2	170	30.3
High	14	13.3	9	10.1	22	12.1	15	8.1	60	10.7
What is your current marital status?										
Missing	2	1.9	1	1.1	3	1.6	2	1.1	8	1.4
Married or Living as Married	69	65.7	64	71.9	141	77.5	153	82.7	427	76.1
Widowed	14	13.3	9	10.1	18	9.9	19	10.3	60	10.7
Separated	2	1.9	2	2.2	0	0	2	1.1	6	1.1
Divorced	13	12.4	10	11.2	13	7.1	7	3.8	43	7.7
Never married	5	4.8	3	3.4	7	3.8	2	1.1	17	3.0
At any time from when you were first diagnosed with cancer until now, were you working for pay at a job or business?										
Missing	8	7.6	6	6.7	8	4.4	1	0.5	23	4.1
No	42	40.0	29	32.6	62	34.1	60	32.4	193	34.4
Yes	55	52.4	54	60.7	112	61.5	124	67.0	345	61.5
Since our last interview, have you had any kind of health insurance or health benefits? This includes: Medicare, Medicaid or other public assistance programs, military insurance or VA health benefits, private insurance (through a job or union, or that you										
Missing	18	17.1	21	23.6	26	14.3	8	4.3	73	13.0
ALL of the time	79	75.2	57	64.0	141	77.5	168	90.8	445	79.3
PART of the time	3	2.9	5	5.6	7	3.8	2	1.1	17	3.0
NONE of the time	3	2.9	3	3.4	3	1.6	4	2.2	13	2.3
I don't know	2	1.9	3	3.4	5	2.7	3	1.6	13	2.3
Are you currently being treated for cancer* - that is are you planning or recovering from cancer surgery, or receiving chemotherapy, radiation therapy, or hormonal therapy for your cancer?										
Missing	3	2.9	5	5.6	5	2.7	4	2.2	17	3.0
No	96	91.4	79	88.8	155	85.2	163	88.1	493	87.9
Yes	6	5.7	5	5.6	22	12.1	18	9.7	51	9.1
In general, would you say your health is:										
Missing	1	1.0	4	4.5	0	0	1	0.5	6	1.1
Excellent	8	7.6	7	7.9	23	12.6	24	13.0	62	11.1
Very Good	29	27.6	25	28.1	76	41.8	81	43.8	211	37.6
Good	44	41.9	38	42.7	62	34.1	58	31.4	202	36.0
Fair	23	21.9	14	15.7	13	7.1	20	10.8	70	12.5
Poor	0	0	1	1.1	8	4.4	1	0.5	10	1.8
TOTAL	105	100.0	89	100.0	182	100.0	185	100.0	561	100.0

* Any cancer, not necessarily CaP.

Demographics information for 561 FT participants

site				
site	Frequency	Percent	Cumulative Frequency	Cumulative Percent
LA	287	51.16	287	51.16
NC	274	48.84	561	100.00

bc6: race				
BC6	Frequency	Percent	Cumulative Frequency	Cumulative Percent
AA	194	34.58	194	34.58
CA	367	65.42	561	100.00

Survey method				
method	Frequency	Percent	Cumulative Frequency	Cumulative Percent
Telephone	47	8.38	47	8.38
Online	123	21.93	170	30.30
Paper	391	69.70	561	100.00

Y4 Progress

All questionnaire data were merged with PCaP baseline data for analysis once the data analyst confirmed all quality control report issues were resolved. Of the 562 questionnaires completed, all have completed QC and have had data entered. Most participants have had insurance of some type all the time so that their oncologic outcomes should be accessible electronically. Only 9% are under treatment for their cancer and only 2% are in poor health. Our PCaP participants are distributed equally by state but more European Americans than African Americans are represented, a difference that will require further analysis to assess for bias.

Table 1

	AA				CA				TOTAL	
	N	LA (%)	N	NC (%)	N	LA (%)	N	NC (%)		
aggressive:tumor aggressiveness(derived)										
Missing	4	3.8	0	0	11	6.0	1	0.5	16	2.8
Low	53	50.5	47	52.2	100	54.9	115	62.2	315	56.0
Intermediate	34	32.4	33	36.7	49	26.9	54	29.2	170	30.2
High	14	13.3	10	11.1	22	12.1	15	8.1	61	10.9
What is your current marital status?										
Missing	2	1.9	1	1.1	3	1.6	2	1.1	8	1.4
Married or Living as Married	69	65.7	65	72.2	141	77.5	153	82.7	428	76.2
Widowed	14	13.3	9	10.0	18	9.9	19	10.3	60	10.7
Separated	2	1.9	2	2.2	0	0	2	1.1	6	1.1
Divorced	13	12.4	10	11.1	13	7.1	7	3.8	43	7.7
Never married	5	4.8	3	3.3	7	3.8	2	1.1	17	3.0
At any time from when you were first diagnosed with cancer until now, were you working for pay at a job or business?										
Missing	8	7.6	6	6.7	8	4.4	1	0.5	23	4.1

	AA				CA				TOTAL	
	LA		NC		LA		NC			
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
No	42	40.0	29	32.2	62	34.1	60	32.4	193	34.3
Yes	55	52.4	55	61.1	112	61.5	124	67.0	346	61.6
Since our last interview, have you had any kind of health insurance or health benefits? This includes: Medicare, Medicaid or other public assistance programs, military insurance or VA health benefits, private insurance (through a job or union, or that you										
Missing	18	17.1	21	23.3	26	14.3	8	4.3	73	13.0
ALL of the time	79	75.2	58	64.4	141	77.5	168	90.8	446	79.4
PART of the time	3	2.9	5	5.6	7	3.8	2	1.1	17	3.0
NONE of the time	3	2.9	3	3.3	3	1.6	4	2.2	13	2.3
I don't know	2	1.9	3	3.3	5	2.7	3	1.6	13	2.3
Are you currently being treated for cancer - that is are you planning or recovering from cancer surgery, or receiving chemotherapy, radiation therapy, or hormonal therapy for your cancer?										
Missing	3	2.9	5	5.6	5	2.7	4	2.2	17	3.0
No	96	91.4	79	87.8	155	85.2	163	88.1	493	87.7
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In general, would you say your health is:										
.	1	1.0	4	4.4	0	0	1	0.5	6	1.1
Excellent	8	7.6	7	7.8	23	12.6	24	13.0	62	11.0
Very Good	29	27.6	25	27.8	76	41.8	81	43.8	211	37.5
Good	44	41.9	38	42.2	62	34.1	58	31.4	202	35.9
Fair	23	21.9	15	16.7	13	7.1	20	10.8	71	12.6
Poor	0	0	1	1.1	8	4.4	1	0.5	10	1.8
TOTAL	105	100.0	90	100.0	182	100.0	185	100.0	562	100.0

* Any cancer, not necessarily CaP.

Demographics information for 562 FT participants

site				
site	Frequency	Percent	Cumulative Frequency	Cumulative Percent
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NC	275	48.93	562	100.00

bc6: race				
BC6	Frequency	Percent	Cumulative Frequency	Cumulative Percent
AA	195	34.70	195	34.70
CA	367	65.30	562	100.00

Survey method				
method	Frequency	Percent	Cumulative Frequency	Cumulative Percent
Telephone	47	8.36	47	8.36
Online	124	22.06	171	30.43
Paper	391	69.57	562	100.00

Major Task 2 Data Reporting

Subtask 1 Produce annual progress reports for PCaP

Y1 Progress

Year 1 progress report completed.

Y2 Progress

Year 2 progress report completed.

Y3 Progress

Year 3 progress report completed.

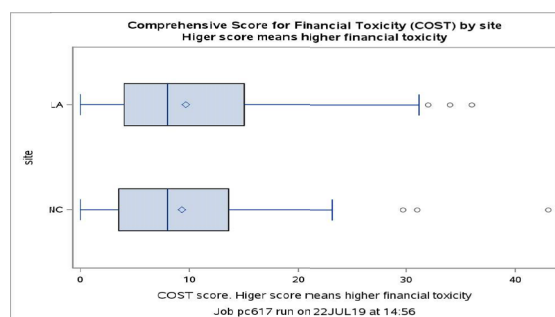
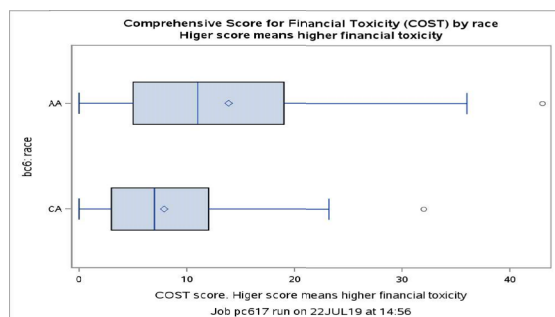
Y4 Progress

Year 4 progress report completed.

Subtask 2 Produce manuscripts

Y2 Progress

A very preliminary analysis compared financial distress (COST only) in research subjects (n= 194) by site (NC; n= 76 versus LA; n= 118) and by race (AA; n= 53 versus CA; n= 141).



Y3 Progress

Manuscripts Our planned manuscript list continues to evolve and was increased from 4 to 5 manuscripts:

- 1) report on racial differences in financial burden/stress the financial burden/stress posed by CaP
- 2) methods report on the use of the global medical record based on our experience and its challenges with audience of future researchers, state legislatures

- 3) report on reasons for imperfect follow-up in a longitudinal, long-term, population-based study
- 4) validation of Comprehensive Score for Financial Toxicity (COST) that has never been used in CaP before
- 5) report on racial differences in caregiver stress in families of men with CaP

Grant proposal Year 3 was to produce a grant proposal to fund prospective study of financial distress in men with newly diagnosed CaP. However our preliminary results suggest that we should focus on men who present with, or develop, bone metastatic CaP, since we see little financial distress in PCaP participants 10-12 years after diagnosis most of whom die of other causes, not CaP, and appear to have little financial distress from their disease, most of which is clinically localized and effectively cured. About 10% and possibly as many as 15% of men present with metastatic disease and these men will have mean survival 5 years. A larger sample of men are needed that necessitates a multi-institutional study. Other participants may include JoEllen Schilkroft/Emory, Kevin Ward/Georgia Cancer Registry, Melissa Bondy/Stanford, Michelle Cote/Karmanos, and Allison Mondul/UMichigan. Dr. Peters has requested a SEER analysis to determine what proportion of men fit this category so that he can extrapolate to the other 3 SEER sites to determine the power of the above described analysis. Dr. Peters will be the PI and Drs. Mohler and Bensen will be co-investigators on a prospective examination of financial distress in men newly diagnosed with bone metastatic CaP (Race- black or white; any age; bone metastases on imaging; tissue/prostate biopsy confirming CaP; English speaking; capable of providing informed consent). COVID-19 has delayed these activities.

What opportunities for training and professional development has the project provided?

Saira Khan PhD, Assistant Professor, College of Health Sciences, University of Delaware, has joined the UNC PCaP team as a new data analyst. She produced the OncoGraphs for the NC PCaP Follow-up Study (HCaP-NC) when she was a UNC School of Public Health doctoral student in Epidemiology. She obtained her PhD at UNC and pursued a post-doctoral position at the Washington University, St. Louis, MO where she secured grant funding (DoD Prostate Cancer Research Program Early Investigator Grant) and continued her research focus on CaP. Dr. Khan has reliance agreements in place and is approved as study personnel for both IRB #17-0530 Financial Toxicity DoD grant and IRB #15-3017 PCaP-CIPHR claims project. Drs. Mohler and Bensen are members of her mentoring committee. Dr. Khan is working to develop a grant application to interrogate the Veterans Health Administration (VHA) national medical care datasets (VA cohort) and the PCaP dataset to examine the incidence of new chronic disease development by CaP treatment type and to elucidate the extent to which chronic disease management, as measured by consistent prescription medication use, can reduce these adverse CaP treatment side effects.

Madhav KC continues as a graduate research assistant/project manager for this project. As a result of this experience, he has chosen Dr. Peter as his thesis advisor and a thesis has been proposed that will geocode all LA PCaP participants to enable a comprehensive analysis of the role of societal/neighborhood and individual factors to discover which factors alone or jointly predict CaP aggressiveness, quality of life, and mortality and whether these relationships are modified by race (Appendix 12).

How were the results disseminated to communities of interest?

Nothing to report

Y4 Progress

Manuscripts Our planned manuscript list continues to evolve and was increased from 5 to 7 manuscripts (M#s are assigned within the PCaP Data Sharing Tracking system for manuscripts with submitted and approved Letters of Intent: The 7 manuscripts are:

- 1) Prostate cancer aggressiveness and financial toxicity (PCaP #M0171)
- 2) Using health insurance claims data to assess long-term disease progression in a prostate cancer cohort (PCaP #M0172)
- 3) The influence of physician trust and shared decision making on long-term patterns of care in a racially diverse population of prostate cancer survivors (#M0173)
- 4) Progression and financial toxicity among PCaP participants (PCaP #M0176)

- 5) Patterns of insurance coverage using insurance claims linked to PCaP (PCaP #M0177)
- 6) Association between neighborhood deprivation and prostate cancer aggressiveness in a population-based study (PCaP #M0178; submitted to *Cancer Epidemiology, Biomarkers & Prevention*)
- 7) The effect of neighborhood deprivation on prostate cancer survival PCaP (PCaP #M0179)

Grant proposal

What opportunities for training and professional development has the project provided?

Shekinah Elmore, MD, MPH, Department of Radiation Oncology, University of North Carolina at Chapel Hill, graduated from the Harvard Radiation Oncology Residency Program in Boston, and has joined the UNC PCaP team as a new investigator. She is clinically trained in genitourinary cancers and will focus her research on prostate cancer, global health, and healthcare equity research. Dr. Elmore will supervise her GRA who will be responsible for the medical records abstraction of clinical follow-up data on the 156 PCaP participants who have had follow-up care at UNC Health between 2011-2018. Drs. Elmore, Mohler and Bensen had a training session in March to standardize EMR clinical data abstraction. This EMR abstraction will support and assist in confirming the evaluation of long-term prostate cancer progression from health insurance claims data (in progress manuscript M#0172).

Saira Khan PhD, Assistant Professor, College of Health Sciences, University of Delaware, has joined the UNC PCaP team as a new epidemiologist. She produced the OncoGraphs for the NC PCaP Follow-up Study (HCaP-NC) as a GRA during her training as a UNC School of Public Health doctoral student in Epidemiology. She obtained her PhD at UNC and pursued a post-doctoral position at the Washington University, St. Louis, MO where she secured grant funding (DoD Prostate Cancer Research Program Early Investigator Grant) and continued her research focus on prostate cancer. During Y4, she has overseen the analysis and development of the 2011-2018 health insurance claims based oncographs by new UNC GRA, Sanah Vohra. Dr. Khan has reliance agreements in place and is approved as study personnel for both IRB #17-0530 Financial Toxicity DoD grant and IRB #15-3017 PCaP-CIPHR claims project. Drs. Mohler and Bensen are members of her mentoring committee. Last year, Dr. Khan submitted a DOD IDEA Award, which scored 2.3 but was not funded. This year, Dr. Khan is refining the grant and plans to submit the revised proposal to the DOD Prostate Cancer Research Project Health Disparities Award opportunity (July 2021), which will allow her to leverage the racially diversity of the PCaP cohort. The grant will interrogate the Veterans Health Administration (VHA) national medical care datasets (VA cohort) and the PCaP dataset to identify unique clusters of comorbidities, using data science methods, that can be used to predict adverse outcomes, with a particular focus on the interaction of comorbidities with newer agents for ADT.

Madhav KC continues as a graduate research assistant/project manager for this project. As a result of this experience, he chose Dr. Peter as his thesis advisor. In Y4, all PCaP participants have had Area Deprivation Index (ADI) scores calculated. He conducted a comprehensive analysis of the role of societal/neighborhood and individual factors to discover which factors alone or jointly are risk factors for aggressive CaP. This work and the associated findings have been reported in a manuscript (#M0178) submitted to *CEBP* (see manuscript list above). Mr. Madhav is working on several additional follow-up papers on the impact of ADI on mortality and quality of life and whether these relationships are modified by race (Appendix 12).

Sanah Vohra, is a fourth-year Epidemiology doctoral student at UNC Gilling School of Global Public Health. She is skilled in SAS and has received training in health insurance claims data. She joined the PCaP team in Y4 and serves an essential role in evaluating the CIPHR health insurance claims data, creating claims-based oncographs of prostate cancer care in the 2011-2018 follow-up period, and continuing to mine the claims data for other key variables for future research (e.g., side effects). She also participates in manuscript development and writing. She may continue this work in the no cost extension period, which was approved 06/07/2021.

In June 2020, Laura Farnan, the PCaP Biostatistician, attended two virtual workshops organized by Research Data Assistance Center (ResDAC): “Introduction to Medicare Data for Research” and “Introduction to Medicare Part D”. The workshops provided an introduction to the Medicare program and the underlying Medicare population, taught how to use the claims data to measure health services utilization and outcomes, and familiarized the audience with the Medicare Part D program.

How were the results disseminated to communities of interest?

PCaP’s website continues to provide an updated list of manuscripts and links to abstracts and full text articles and will update this as journal submitted publications such as PCaP #M0178, entitled ‘Association between neighborhood deprivation and prostate cancer aggressiveness in a population-based study,’ which was submitted to *CEBP* 04/24/2021.

What do you plan to do during the next reporting period to accomplish the goals?

Y1 Progress

Year 2 will focus on data collection. We are poised to contact living PCaP research subjects in both states. We are hiring the staff necessary to manage contact and conduct surveys of research subjects and their caregiver(s) and contact their treating physicians to obtain medical records for abstraction. Once underway and proceeding smoothly, we will adapt our process for living PCaP research subjects to approach the family, caregiver(s), and treating physician(s) of deceased PCaP research subjects to collect research data. Once medical record abstraction is underway and proceeding smoothly, we will hire the graduate research assistant at UNC and begin the updating of progression graphs on NC research subjects and construction of progression graphs on LA research subjects.

Y2 Progress

Year 3 will collect all questionnaire data on PCaP research subjects and their caregiver (if any), Q/C all data and begin its analysis, acquire oncologic outcome information (update treatments received and obtain most recent PSA values, and conduct the pilot “study-within-the-study” of the PCaP research subjects who die in the next year. Effort will be maintained at the current levels for Year 3 and funds will be sequestered for the anticipated effort needed in the no-cost extension period beginning July 2020 as outlined in the timeline in the revised Statement of Work to complete data analysis, produce manuscripts and prepare a new proposal to seek new funding for an intervention to address financial distress where financial distress is most problematic.

Y3 Progress

A planned no-cost extension (see above) was granted 06/15/2020. Year 4 will focus on two major areas. First, we will collect missing data from enrolled PCaP participants, secure oncologic outcome data electronically, construct OncoGraphs of PCaP participants’ oncologic outcome, and collect any missing data from non-electronic sources necessary to complete the OncoGraphs. Second, we will produce 5 manuscripts and submit one MPI R01 focused on financial distress in men with bone metastatic CaP.

Y4 Progress

A second planned no-cost extension was requested 05/27/2021 and approved 06/07/2021. This extension was requested as the result of delays in work due to COVID-19 since our participating institutions shut down for a period of time and reorganized and reassessed operations. Specifically, institutional resources were diverted at LSUHSC that slowed data collection (in particular, clinical follow-up data). Our PCaP biostatistician had to take significant time away to meet the needs of her school age children. Finally, hiring and then the work situation of a graduate research assistant (GRA) at UNC was delayed by institutional decisions about student safety. UNC will carry over funds to support our GRA and Biostatistician beyond June 30, 2021 to allow the

completion of data cleaning, documentation, analysis, and manuscript development. Roswell Park plans to move some funds (about \$8000) to UNC to assist with support of the GRA from carry over funds we will retain to allow for review of our work product and manuscript strategy, and recommendations for dissemination of our findings by our External Advisory Committee, Dr. Mohler's travel, and salary support for a small portion of his effort .

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report

What was the impact on other disciplines?

Nothing to report

What was the impact on technology transfer?

Nothing to report

What was the impact on society beyond science and technology?

Nothing to report

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Y2 Progress

The updating of oncologic outcome graphs on NC research subjects and the construction of oncologic outcome graphs on LA research subjects will require identification of treating primary care physicians for Research Subjects discharged from specialty oncologic follow-up and identification of specialty physicians providing oncologic care (urologist, radiation oncologist or medical oncologist) for 1616 research subjects. The continuing evolution in clinical data availability may allow more efficient collection of these data. We have initiated a pilot project of 20 NC research subjects and 20 LA research subjects to determine how much oncologic outcome data can be acquired electronically. In LA, PCaP research subjects are flagged already in SEER. Dr. Peters is meeting with SEER officials to determine if we can conduct a pattern-of-care study to identify treatments received, oncologic status, and interval PSA results. In NC, Dr. Bensen will explore the use of the UNC Tumor Registry and an ongoing UNC project to access claims data for research use, which should include data from NC research subjects who have BC/BS, Medicare or Medicaid.

Actual or anticipated problems or delays and actions or plans to resolve them

Y1 Progress

DoD IRB approval was not secured until 07/02/2018 for the reasons described above. Time between the probable notice of award 02/07/2017 and IRB approval 07/02/2018 was utilized to adapt the survey tools, create a project space within the PCaP Central Database, update PCaP research subject vital status, and prepare for data exchange between LSUHSC and UNC. PCaP research subjects could not be contacted, and the staff could not be hired who

are necessary to manage contact and conduct surveys of research subjects and their caregiver(s) and contact their treating physicians to obtain medical records for abstraction. The approved Statement of Work (Appendix 4) has been revised (Appendix 5) to reflect a reordering of work that is still accomplished within the 3 year funding period. However, the compression of data acquisition and analysis and reporting into 2 years is unrealistic. A further revision will most likely be necessary to extend “Major Task 2 Data Reporting Subtask 2 Produce manuscripts” from year 3 to year 4 in a no-cost extension.

Y2 Progress

The LSUHSC IRB raised an issue about the “study-within-a-study.” The families of deceased PCaP Research Subjects would fall into 1 of 2 categories: dead of CaP (dead of disease [DOD]) or dead of other causes (DOC). The IRB asked how we could enroll the primary caregiver in a study when the PCaP research subject is deceased: how would that caregiver be identified; how could they be contacted; and how both would pose a HIPAA risk that cannot be resolved. We have decided to obtain the primary caregiver from the research subject and enroll them as part of the current study. We will conduct the “study-within-a-study” of those family units where the PCaP research subject dies going forward. Hence, this portion of the proposed research will be converted to “pilot status” to accrue data as our PCaP research subjects succumb DOD or DOC. The current data suggest that PCaP Research Subjects are dying in a ratio of about 4 to 1 (DOC vs DOD) and at a rate of about 80 per year. Hence, during the last 2 years of the proposed study (Year 3 and a no-cost extension Year 4), we should enroll a pilot group of approximately 160 families who suffered the loss of about 128 men from DOC versus 32 men from DOD.

Y3 Progress

We decided to abandon the above strategy to conduct a “study-within-a-study” of the families of deceased PCaP participants by studying those men who died in Y 3 and Y4 for two reasons. First, both UNC and LSUHSC IRBs balked at initial inquiries about a strategy to obtain consent from those who were identified as contacts by PCaP participants at the time of initial enrollment on the PCaP study. The original PCaP study identified a “contact person,” which was to address lost to follow-up issues, not to identify caregivers. Second, in this study, only 30% of PCaP participants identified a caregiver and almost all caregivers were the spouse. Therefore, we would only have caregivers to contact for about 36 men who died of other causes and about 9 men who died from CaP in years 3 and 4. Instead, Dr. Peters will submit an MPI R01 to study a large number of men who present with bone metastatic CaP.

Y4 Progress

COVID-19 significantly affected our study progress in this reporting period. Participating institutions shut down for a period during Y4 and also reorganized and reassessed operations. Institutional resources were diverted at LSUHSC that slowed data collection (in particular, clinical follow-up data collection from physician offices – many of which also experienced shutdowns, staffing challenges and delays). Our PCaP biostatistician had to take significant time away to meet the needs of her school age children. Finally, hiring, and continued work of a graduate research assistant (GRA) at UNC was delayed by institutional decisions about student safety. We will carry over funds at UNC to support our GRA and Biostatistician beyond June 30, 2021 that will allow the completion of data cleaning, documentation, analysis, and manuscript development.

Changes that had a significant impact on expenditures

Y1 Progress

The delay in securing DoD IRB approval until 07/02/2018 produced a delay in hiring study personnel that has moved Year 1 funds to Year 2. Further adjustments may be necessary since the revised timeline (see revised statement of work) is ambitious.

Y2 Progress

We propose an additional revision of our timeline (Statement of Work) due to the delay in securing DoD IRB approval until 07/02/2018 that produced a delay in hiring study personnel that in turn moved Year 1 funds in to Year 2. We have now moved year 2 funds to Year 3 and will have funds left over to fund a Year 4 no cost extension, if approved. We are in the midst of very successful data collection that make it highly likely that we will meet all the goals of the study.

Y3 Progress

Year 4 NCE granted June 15, 2020.

Y4 Progress

COVID-19 significantly affected our study progress in this reporting period. Participating institutions shut down for a period during Y4 and also reorganized and reassessed operations. Institutional resources were diverted at LSUHSC that slowed data collection (in particular, clinical follow-up data collection from physician offices – many of which also experienced shutdowns, staffing challenges and delays). Our PCaP biostatistician had to take significant time away to meet the needs of her school age children. Finally, hiring, and continued work of a graduate research assistant (GRA) at UNC was delayed by institutional decisions about student safety. We will carry over funds at UNC to support our GRA and Biostatistician beyond June 30, 2021, that will allow the completion of data cleaning, documentation, analysis, and manuscript development.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

None

6. PRODUCTS:

Publications, conference papers, and presentations

Manuscript (PCaP #M0178) submitted 04/24/2021 to *CEBP* entitled “Association between neighborhood deprivation and prostate cancer aggressiveness in a population-based study.”

Manuscript (PCaP #M0179) to be submitted June 2021 to *Cancer* entitled “The effect of neighborhood deprivation on prostate cancer survival PCaP.”

Journal publications

Nothing to report

Books or other non-periodical, one-time publications

Nothing to report

Other publications, conference papers, and presentations

Nothing to report

Technologies or techniques

Nothing to report

Inventions, patent applications, and/or licenses

Nothing to report

Other Products

Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Y1 Progress

Name: James L. Mohler

Project Role: Principal Investigator

Research Identifier: ORCID ID: 0000-0002-7726-3795

Nearest person month worked: 1

Contribution to project: No change- Dr. Mohler will serve as the Principal Investigator. He will be responsible for project initiation (7% Y1), project oversight and annual progress report generation (3% Y1-3), clinical graph quality (10% Y2), data analysis oversight (2% Y1-3) generation of 4 manuscripts (15% Y3). Dr. Mohler will be responsible for the overall scientific integrity, management and reporting of results. He will interact with Drs. Bensen and Peters at UNC and LSUHSC, respectively. He will serve as a resource to Dr. Peters for clinical issues and to Dr. Bensen for PSA measurement and treatment graphing. He will continue to oversee all immunohistochemistry, visual scoring and image analysis.

Funding Support: National Cancer Institute, National Institute of Diabetes and Digestive and Kidney Diseases, Department of Defense

Name: Jeannette T. Bensen

Project Role: Co-Investigator

Research Identifier: ORCID ID: 0000-0003-4972-0087

Nearest person month worked: 1

Contribution to project: No change- Dr. Bensen will oversee and facilitate data collection and distribution and assist in interpretation of the follow-up data for PCaP research subjects in North Carolina. Dr. Bensen will assist in preparation of the 4 planned study-related manuscripts. She, Dr. Mohler and Dr. Bensen's graduate research assistant, assisted by Mr. Gerstel, will construct the CaP disease status/treatment graphs (update those made already for NC research subjects and construct graphs for LA research subjects). Dr. Bensen will coordinate all UNC-based aspects of the study. She will join Drs. Mohler and Peters in quarterly teleconferences that will occur during Dr. Mohler's quarterly visits mostly to LSUHSC but occasionally, especially in Year 3, to UNC.

Funding Support: NIH/National Human Genome Research Institute, University Cancer Research Fund (North Carolina), NIH/National Institute of Environmental Health Sciences, National Cancer Institute

Name: Edward Peters

Project Role: Co-Investigator

Research Identifier: ORCID ID: 0000-0003-4928-6532

Nearest person month worked: 1

Contribution to project: No change- Dr. Peters will supervise all EDC research staff and closely coordinate with Drs. Mohler and Bensen to ensure the successful execution, validity and integrity of the study aims. Dr. Peters will be responsible for assuring that subject recontact, data collection, data processing and data linkage are conducted properly through the EDC. He also is an Epidemiologist with the Louisiana State Tumor Registry and will liaison with Louisiana State Tumor Registry staff to ensure appropriate follow-up, outcome and clinical linkages are made for LA research subjects. He will be available for weekly staff project meetings and assure that quality control procedures for data collection are followed, and sufficient EDC resources are available at all times for the project.

Dr. Peters will provide monthly status reports of case contact and data collection as well as address any study-related issues with Drs. Mohler and Bensen. Dr. Peters will be available to Dr. Mohler to coordinate all LSUHSC-based aspects of the study. He will join Drs. Mohler and Bensen in quarterly teleconferences that will occur during Dr. Mohler's quarterly visits mostly to LSUHSC but occasionally, especially in Year 3, to UNC.

Funding Support:

Name: Laura Farnan

Project Role: Other, Biostatistician

Research Identifier: ORCID ID: 0000-0001-9240-4974

Nearest person month worked: 1

Contribution to project: No change- Dr. Farnan will organize data and quality control in Years 1 and 2. She will analyze data and participate in preparation of the 4 manuscripts in Year 3.

Funding Support: University Cancer Research Fund (North Carolina)

Other Personnel

Madhav KC 2 calendar months

Y2 Progress

Name: James L. Mohler

Project Role: Principal Investigator

Research Identifier: ORCID ID: 0000-0002-7726-3795

Nearest person month worked: 1

Contribution to project: No change- Dr. Mohler will serve as the Principal Investigator. He will be responsible for project initiation (7% Y1), project oversight and annual progress report generation (3% Y1-3), clinical graph quality (perhaps now 5% Y3 and 5% Y4), data analysis oversight (perhaps now 2% Y1-4) generation of 4 manuscripts (perhaps now 5% Y3 and 10% Y4). Dr. Mohler will be responsible for the overall scientific integrity, management and reporting of results. He will interact with Drs. Bensen and Peters at UNC and LSUHSC, respectively. He will serve as a resource to Dr. Peters for clinical issues and to Dr. Bensen for PSA measurement and treatment graphing.

Funding Support: National Cancer Institute, National Institute of Diabetes and Digestive and Kidney Diseases, Department of Defense

Name: Jeannette T. Bensen

Project Role: Co-Investigator

Research Identifier: ORCID ID: 0000-0003-4972-0087

Nearest person month worked: 1

Contribution to project: No change- Dr. Bensen will oversee and facilitate data collection and distribution and assist in interpretation of the follow-up data for PCaP research subjects in North Carolina. Dr. Bensen will assist in preparation of the 4 planned study-related manuscripts. She, Dr. Mohler and Dr. Bensen's graduate research assistant, assisted by Mr. Gerstel, will construct the CaP disease status/treatment graphs (update those made already for NC research subjects and construct graphs for LA research subjects). Dr. Bensen will coordinate all

UNC-based aspects of the study. She will join Drs. Mohler and Peters in quarterly teleconferences that will occur during Dr. Mohler's quarterly visits mostly to LSUHSC but occasionally, especially in Year 3 or 4, to UNC. Funding Support: NIH/National Human Genome Research Institute, University Cancer Research Fund (North Carolina), NIH/National Institute of Environmental Health Sciences, National Cancer Institute, Department of Defense

Name: Edward Peters

Project Role: Co-Investigator

Research Identifier: ORCID ID: 0000-0003-4928-6532

Nearest person month worked: 1

Contribution to project: No change- Dr. Peters will supervise all EDC research staff and closely coordinate with Drs. Mohler and Bensen to ensure the successful execution, validity and integrity of the study aims. Dr. Peters will be responsible for assuring that subject recontact, data collection, data processing and data linkage are conducted properly through the EDC. He also is an Epidemiologist with the Louisiana State Tumor Registry and will liaison with Louisiana State Tumor Registry staff to ensure appropriate follow-up, outcome and clinical linkages are made for LA research subjects. He will be available for weekly staff project meetings and assure that quality control procedures for data collection are followed, and sufficient EDC resources are available at all times for the project.

Dr. Peters will provide monthly status reports of case contact and data collection as well as address any study-related issues with Drs. Mohler and Bensen. Dr. Peters will be available to Dr. Mohler to coordinate all LSUHSC-based aspects of the study. He will join Drs. Mohler and Bensen in quarterly teleconferences that will occur during Dr. Mohler's quarterly visits mostly to LSUHSC but occasionally, especially in Year 3 or 4, to UNC.

Funding Support: Department of Defense, National Cancer Institute

Name: Laura Farnan

Project Role: Other, Biostatistician

Research Identifier: ORCID ID: 0000-0001-9240-4974

Nearest person month worked: 1

Contribution to project: No change- Dr. Farnan will organize data and quality control in Years 1, 2 and 3. She will analyze data and participate in preparation of the 4 manuscripts in Years 3 and 4.

Funding Support: University Cancer Research Fund (North Carolina), NIH/National Human Genome Research Institute, Department of Defense

Y3 Progress

Name: James L. Mohler

Project Role: Principal Investigator

Research Identifier: ORCID ID: 0000-0002-7726-3795

Nearest person month worked: 2

Contribution to project: No change- Dr. Mohler will serve as the Principal Investigator. He will be responsible for project initiation (7% Y1), project oversight and annual progress report generation (3% Y1-3), clinical graph quality (5% Y3 and 5% Y4), data analysis oversight (2% Y1-4) generation of 4 manuscripts (5% Y3 and 10% Y4). Dr. Mohler will be responsible for the overall scientific integrity, management and reporting of results. He will interact with Drs. Bensen and Peters at UNC and LSUHSC, respectively. He will serve as a resource to Dr. Peters for clinical issues and to Dr. Bensen for PSA measurement and treatment graphing. He has been and will continue to work closely with Dr. Saira Kahn for construction of the OncoGraphs.

Funding Support: National Cancer Institute, National Institute of Diabetes and Digestive and Kidney Diseases, Department of Defense

Name: Jeannette T. Bensen

Project Role: Co-Investigator

Research Identifier: ORCID ID: 0000-0003-4972-0087

Nearest person month worked: 1

Contribution to project: No change- Dr. Bensen will oversee and facilitate data collection and distribution and assist in interpretation of the follow-up data for PCaP research subjects in North Carolina. Dr. Bensen will assist in preparation of the 5 planned study-related manuscripts. She, Dr. Mohler, Dr. Saira Khan, and Dr. Bensen's graduate research assistant, assisted by Mr. Gerstel, will construct the CaP disease status/treatment graphs (update those made already for NC research subjects and construct graphs for LA research subjects). Dr. Bensen will coordinate all UNC-based aspects of the study. She will join Drs. Mohler and Peters in quarterly teleconferences that will occur during Dr. Mohler's quarterly visits mostly to LSUHSC but occasionally, especially in Year 4, to UNC.

Funding Support: NIH/National Human Genome Research Institute, University Cancer Research Fund (North Carolina), NIH/National Institute of Environmental Health Sciences, National Cancer Institute, Department of Defense

Name: Edward Peters

Project Role: Co-Investigator

Research Identifier: ORCID ID: 0000-0003-4928-6532

Nearest person month worked: 1

Contribution to project: No change- Dr. Peters will supervise all EDC research staff and closely coordinate with Drs. Mohler and Bensen to ensure the successful execution, validity and integrity of the study aims. Dr. Peters will be responsible for assuring that subject recontact, data collection, data processing and data linkage are conducted properly through the EDC. He also is an Epidemiologist with the Louisiana State Tumor Registry and will liaison with Louisiana State Tumor Registry staff to ensure appropriate follow-up, outcome and clinical linkages are made for LA research subjects. He will be available for weekly staff project meetings and assure that quality control procedures for data collection are followed, and sufficient EDC resources are available at all times for the project.

Dr. Peters will provide monthly status reports of case contact and data collection as well as address any study-related issues with Drs. Mohler and Bensen. Dr. Peters will be available to Dr. Mohler to coordinate all LSUHSC-based aspects of the study. He will join Drs. Mohler and Bensen in quarterly teleconferences that will occur during Dr. Mohler's quarterly visits mostly to LSUHSC but occasionally, especially in 4, to UNC.

Funding Support: Department of Defense, National Cancer Institute, National Institutes of Health

Name: Laura Farnan

Project Role: Other, Biostatistician

Research Identifier: ORCID ID: 0000-0001-9240-4974

Nearest person month worked: 1

Contribution to project: No change- Dr. Farnan will organize data and quality control in Years 1, 2 and 3. She will analyze data and participate in preparation of the 4 manuscripts in Year 4.

Funding Support: University Cancer Research Fund (North Carolina), NCI, NIH/National Human Genome Research Institute, Department of Defense

Y4 Progress

Name: James L. Mohler

Project Role: Principal Investigator

Research Identifier: ORCID ID: 0000-0002-7726-3795

Nearest person month worked: 2

Contribution to project: No change- Dr. Mohler will serve as the Principal Investigator. He will be responsible for project initiation (7% Y1), project oversight and annual progress report generation (3% Y1-3), clinical graph quality (5% Y3 and 5% Y4), data analysis oversight (2% Y1-4), generation of 7 manuscripts (5% Y3 and 10%

Y4). Dr. Mohler will be responsible for the overall scientific integrity, management and reporting of results. He will interact with Drs. Bensen and Peters at UNC and LSUHSC, respectively. He will serve as a resource to Dr. Peters for clinical issues and to Dr. Bensen for PSA measurement and treatment graphing. He has been and will continue to work closely with Dr. Saira Kahn for construction of the updated OncoGraphs. He served and will continue to serve as a resource to Dr. Elmore for questions about the medical record abstraction of PCaP participants who remain in the UNC Healthcare System.

Funding Support: National Cancer Institute, National Institute of Diabetes and Digestive and Kidney Diseases, Department of Defense

Name: Jeannette T. Bensen

Project Role: Co-Investigator

Research Identifier: ORCID ID: 0000-0003-4972-0087

Nearest person month worked: 1

Contribution to project: No change- Dr. Bensen will oversee and facilitate data collection and distribution and assist in interpretation of the follow-up data for PCaP research subjects in North Carolina. Dr. Bensen will assist in preparation of the 7 planned study-related manuscripts. She, Dr. Mohler, Dr. Saira Khan, and Dr. Bensen's graduate research assistant, assisted by Mr. Gerstel, will construct the CaP disease status/treatment graphs (update those made already for NC research subjects and construct graphs for LA research subjects). Dr. Bensen will coordinate all UNC-based aspects of the study. She will join Drs. Mohler and Peters in monthly teleconferences.

Funding Support: NIH/National Human Genome Research Institute, University Cancer Research Fund (North Carolina), NIH/National Institute of Environmental Health Sciences, National Cancer Institute, Department of Defense

Name: Edward Peters

Project Role: Co-Investigator

Research Identifier: ORCID ID: 0000-0003-4928-6532

Nearest person month worked: 1

Contribution to project: No change- Dr. Peters will supervise all EDC research staff and closely coordinate with Drs. Mohler and Bensen to ensure the successful execution, validity and integrity of the study aims. Dr. Peters will be responsible for assuring that subject recontact, data collection, data processing and data linkage are conducted properly through the EDC. He also is an Epidemiologist with the Louisiana State Tumor Registry and will liaison with Louisiana State Tumor Registry staff to ensure appropriate follow-up, outcome and clinical linkages are made for LA research subjects. He will be available for weekly staff project meetings and assure that quality control procedures for data collection are followed, and sufficient EDC resources are available at all times for the project.

Dr. Peters will provide monthly status reports of case contact and data collection as well as address any study-related issues with Drs. Mohler and Bensen. Dr. Peters will be available to Dr. Mohler to coordinate all LSUHSC-based aspects of the study. He will join Drs. Mohler and Bensen in quarterly teleconferences.

Funding Support: Department of Defense, National Cancer Institute, National Institutes of Health

Name: Laura Farnan

Project Role: Other, Biostatistician

Research Identifier: ORCID ID: 0000-0001-9240-4974

Nearest person month worked: 1

Contribution to project: No change- Dr. Farnan will organize data and quality control in Years 1, 2 and 3. She will analyze data and participate in preparation of the 4 manuscripts in Year 4.

Funding Support: University Cancer Research Fund (North Carolina), NCI, NIH/National Human Genome Research Institute, Department of Defense

Name: Sanah Vohra

Project Role: Other, GRA (graduate research assistant)

Research Identifier: ORCID ID: 0000-0003-4461-5157

Nearest person month worked: 1

Contribution to project: Ms. Vohra will organize data, clean data, create/update OncoGraphs, analyze data with a focus on claims data, create tables/figures for publications and participate in manuscript development.

Funding Support: Department of Defense

Name: Shekinah Elmore

Project Role: Other, Radiation Oncologist

Research Identifier: ORCID ID: 0000-0002-7136-1597

Nearest person month worked: 0

Contribution to project: Dr. Elmore provides updates and reviews of current prostate cancer NCCN guidelines, contributing especially to the radiation therapy guidelines in interpreting PCaP oncographs, oversees research assistant performing medical records abstraction to verify PCaP participant progression status (for men with prostate cancer visits at UNC at Chapel Hill and participates in manuscript development)

Funding Support: UNC start-up

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Y1 Progress

Yes, active other supports for Dr. James L. Mohler, Dr. Jeannette Bensen, and Dr. Edward Peters were updated below. Nothing to report for Dr. Laura Farnan.

Changes in active support

MOHLER, JAMES L.

Pending to active

Title: Genetic and Epigenetic Prostate Cancer Related alterations in early onset disease in African American Men (Woloszynska-Read)

Time Commitments: 1.20 calendar months

Supporting Agency: DoD

Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Department of Defense, USA MED RESEARCH ACQ ACTIVITY 820 CHANDLER ST FORT DETRICK MD 21702-5014/ LYMOR BARNHARD

Performance Period: 04/01/2017-03/31/2020

Level of funding:

Brief description of project's goals: Proposed research aims to identify molecular alterations that distinguish aggressive forms of early onset prostate cancer commonly found in African-American men will contribute to the development of African American tumor (epi)genetic signature(s) and ultimately will lead to personalized medicine strategies for this group of patients.

List of specific aims:

1. Determine the relative frequency of genetic lesions found in PCa in AAs and EAs.
2. Determine novel, clinically relevant methylomic and transcriptomic differences in PCa from AAs and EAs
3. Obtain and link vital status data and cause of death in PCaP research subjects

Overlap: None

Active to completed

Title: Prostate Cancer: Transition to Androgen Independence, Project 1: Interference with the Androgen Receptor and Its Ligands in Recurrent Prostate Cancer (French - PI)

Time Commitments: 0.60 calendar months

Supporting Agency: National Cancer Institute P01-CA77739

Name and address of the Funding Agency's Procuring Contracting/Grants Officer:

Mark Kramer, Administrative Director, UNC Lineberger Comprehensive Cancer Center Campus Box 7295
102 Mason Farm Road, Chapel Hill, NC 27599-7295, Phone: (919) 966-0233, Fax: (919) 966-3015,
mkramer@med.unc.edu

Performance Period: 04/01/2005-03/31/2017 (NCE)

Level of Funding:

Brief description of project's goals: Renewal of a project that tests the hypothesis that recurrence of prostate cancer during androgen deprivation therapy can be prevented or delayed by preventing the accumulation of tissue androgens and/or inhibiting the androgen receptor.

List of specific aims:

1. Prevent the changes in androgen metabolism that provide AR ligand(s) in the immediate post-castration period
2. Degrade AR ligand(s) formed in the immediate post-castration period
3. Diminish or eliminate AR in the immediate post-castration period

Overlap: None

Title: Diet changes among prostate cancer patients under expectant management (Marshall - PI)

Time Commitments: 0.60 calendar months

Supporting Agency: National Cancer Institute

Name and address of the Funding Agency's Procuring Contracting/Grants Officer: Program Official:

Howard L. Parnes, Email: hp24c@nih.gov Phone: 301-594-0920 Fax: 301-435-1564

Performance Period: 09/28/2009-01/31/2017 (NCE)

Level of Funding:

Brief description of project's goals: The focus of this study is to assess whether a diet emphasizing plant consumption decreases the probability that low grade, low-volume prostate cancer (LGLV) in expectant management (EM) patients progresses to a more aggressive form of cancer that merits active treatment. The intervention will be conducted through one of the leading cooperative oncology research groups: Cancer and Leukemia Group B (CALGB).

List of specific aims:

1. Assess the effect of a telephone-based dietary intervention on PSA, PSA doubling time, Gleason score and tumor extension in LGLV prostate cancer patients treated with EM.
2. Assess the effect of a telephone-based dietary intervention on treatment seeking, anxiety and coronary heart disease in prostate cancer patients treated with EM.

Overlap: None

Title: Deplete prostate cancer of DHEAS to prevent castration-recurrent prostate cancer (Wu – PI)

Time Commitments: 0.12 calendar months

Supporting Agency: NIH/NCI 1R21CA191895-01 **Name and address of the Funding Agency's Procuring**

Contracting/Grants Officer: Viviana Knowles, 9609 Medical Center Drive, West Tower, Bethesda, MD 20892, phone: 240-276-5157, viviana.knowles@nih.gov

Performance Period: 09/17/2014-02/28/2018 (NCE)

Level of Funding:

Brief description of project's goals: This research seeks to address the racial differences in prostate cancer aggressiveness from a biological perspective.

List of specific aims:

1. Characterize the expression of STS and potential STS regulators in CRPC

2. Evaluate the value of targeting DHEAS usage by prostate cancer cells to prevent post-castration tumor growth

3. Identify DHEAS uptake mechanisms

Overlap: None

BENSEN, JEANNETTE T.

Pending to active

Title: North Carolina Clinical Genomic Evaluation by Next-Gen Exome Sequencing 2

Time commitment: 7.20 calendar months

Supporting Agency: NIH, National Human Genome Research Institute (NHGRI)

Name and Address of the Funding Agency Procuring Contracting/Grants Officer: Unavailable

Performance Period: 08/01/17-05/31/21

Level of Funding:

Brief description of projects goals:

NCGENES 2 will generate the necessary evidence to support the use of Whole Exome Sequencing (WES) as a standard tool in the management of patients with genetic disorders and enable its implementation in populations that experience health disparities.

Overlap: None

FARNAN, LAURA

Nothing to report

PETERS, EDWARD S.

Pending to active

Title: Mid-South Transdisciplinary Collaborative Center for Health Disparities Research

Time Commitments: 1.2 calendar

Supporting Agency (and grant #): NIH 4U54MD008176

Address:

Name and address of the Funding Agency's Procuring Contracting/Grants Officer:

Performance Period: 8/1/2016-7/31/2018

Level of Funding:

Project Goals: Test the feasibility of recruitment and participation of our population into a trial of a mindfulness training using a novel smartphone application (HeadSpace), which integrates mindfulness training cues and assessment, and determine whether it improves trait mindfulness.

List of specific aims:

1. To estimate changes in mindfulness practice from baseline to follow-up

Overlap: None

Active to completed

Title: Women and their Children's Health Study, Trapido (PI), Peters (Co-PI)

Time Commitments: 1.08 calendar

Supporting Agency (and grant #): NIH/NIEHS 1UO1ES021497-01

Address:

National Institute of Environmental Health Sciences

P.O. Box 12874

Research Triangle Park, North Carolina USA 27709

Contracting/Grants Officer: Donald Ellis

Performance Period: 6/27/11-4/30/2017

Level of Funding:

Project Goals: A network of researchers will evaluate potential harmful effects of the Deepwater Horizon disaster on reproduction and birth outcomes, the cardiorespiratory system, cancer, and other chronic diseases as well as behavior and mental health. The network will conduct research to evaluate the level of potentially harmful contaminants in air, water, and seafood, and assess their relationship to health outcomes.

List of specific aims:

1. To establish a prospective cohort study population representing the women and children living in seven parishes heavily affected by the Deepwater Horizon oil spill. This cohort will be an extremely valuable and unique resource for future investigations and collaborations to examine the health effects associated with a massive oil spill.
2. To examine among the adult women the association between seafood consumption and heavy metal accumulation (i.e. arsenic, cadmium, chromium, nickel, manganese and lead) measured in participants' urine. Further to examine whether heavy metal accumulation is associated with a greater presence of neurological, respiratory or immunologic disorders at baseline and prospectively.
3. To estimate among adult women the association between oil spill exposure and physical and emotional health outcomes such as respiratory disease, rashes, headaches, depression and emotional distress, controlling for potential confounders. In addition, to assess whether this relationship is modified by estimates of community and individual resilience and social capital.
4. To identify and enroll the study population for the Assessment of Community Stressors on Children sub-study (Columbia University-David Abramson). The overall goals of this project are to: (1) understand the impacts of the Deepwater Horizon oil spill on children's development and well-being, and (2) examine how parental and social forces, and alternative treatment models, can mediate or modify the spill's effects on children.

Overlap: None

Title: Reassessment of Monitoring the Impact of a Prophylactic HPV Vaccine on HPV Types in Cancers Using Tissues from Central Cancer, Peters (PI)

Time Commitments: 0.9 calendar

Supporting Agency: Centers of Disease Control and Prevention (via Battelle)

Address:

1100 Dexter Ave N, Suite 400
Seattle, WA 98109

Contracting/Grants Officer: April Greek

Performance Period: 01/1/17-12/31/17

Level of Funding:

Project Goals: To measure the HPV prevalence and type distribution among a sample of HPV associated cancers 10 years after the baseline initial effort

List of specific aims:

1. To re-establish the infrastructure for the systematic monitoring of HPV types in cervical and other HPV-associated cancers;
2. Using infrastructure to type HPV distribution of cervical cancer and other HPV-associated cancer cases from participating population-based central cancer registries for 2014-2015.

Overlap: None

Title: Patient Generated Health Data (PGHD) to Enhance SEER Data Collection, Peters (PI)

Time Commitments: 1.0 calendar

Supporting Agency (and grant #): NIH/SEER H HHSN261201300016I/HHSN26100015I

Address:

National Cancer Institute/ OA
9609 Medical Center Drive
Bethesda, MD 20892

Contracting/Grants Officer: William Neal

Performance Period: 9/19/16-9/18/17

Level of Funding:

Project Goals: To develop the requisite infrastructure using smartphone based technology to capture patient generated health data to assess treatment adherence, social support, stress and other psychosocial characteristics in cancer survivors.

List of specific aims:

1. To assess the feasibility of PGHD methods to serve as a complement to traditionally collected registry data, focusing on patients' personal experiences in adhering to cancer treatment as a starting point for this evaluation.
2. To investigate the feasibility of collecting PGHD at a minimum of two points in time, for a longitudinal view of patients' personal experiences in adhering to cancer treatment regimens.
3. To provide value back to patients by offering reports or journaling capabilities as a record of personal experiences during treatment
4. To generate knowledge on best practices, costs, and benefits for utilizing PGHD methodologies in the context of cancer treatment surveillance.

Overlap: None

Title: SEER Linked Virtual Tissue Repository, Wu (PI)

Time Commitments: 0.24 calendar months

Supporting Agency: NIH/NCI/SEER NHHSN2612013000161

Address:

National Cancer Institute / OA
9609 Medical Center Dr.
RM#1E160, MSC 9705

Contracting/Grants Officer:

Marla Jacobsen

Performance Period: 9/17/2015-9/16/2017

Level of Funding:

Project goals: To develop and test the capacity of a SEER Registry to establish a virtual biospecimen locator service to provide high quality annotated cancer specimens for molecular epidemiologic investigations.

List of specific aims:

1. To assess the ability of Louisiana Tumor Registry to serve as a resource for biospecimen research as a SEER Contractor Registry.
2. To locate cases with biospecimens in pathology laboratories in Louisiana and for the LTR to retrieve those biospecimens as a resource for future biospecimen research.
3. To provide custom annotation of specimens.
4. To assess availability of tissue blocks from subjects with pathology reports meeting inclusion criteria.
5. To secure tissue blocks slated for destruction that meet study eligibility criteria.

Overlap: None

Title: National Comprehensive Cancer Control Program, Wu (PI)

Time Commitments: 0.5 calendar months

Supporting Agency (and grant #): CDC/NPRC

Name and address of the Funding Agency's Procuring Contracting/Grants Officer:

Olivia Maar

Performance Period: 6/30/20012-6/29/2017

Level of Funding:

Brief description of project's goals: The major goal of this project was to conduct population based cancer surveillance in Louisiana.

Overlap: None

Y2 Progress

Yes, other supports for Dr. Jeannette Bensen, Dr. Edward Peters and Dr. Laura Farnan were updated below. Dr. James Mohler had no changes.

BENSEN, JEANNETTE

Active to Completed

Title: UNC Cancer Survivorship Cohort (Bensen- PI)

Time commitment: 9 Calendar months

Supporting Agency: University Cancer Research Fund - NC State Funding

Name and Address of the Funding Agency Procuring Contracting/Grants Officer:

Unavailable

Performance Period: 4/1/17 - 3/31/18

Level of Funding:

Brief description of projects goals:

The main goals of this application are to expand and enhance this large novel and ethnically diverse adult cancer cohort to 10,000 cancer survivors with comprehensive data collection and follow-up, maintain extensive infrastructure that links clinical, biospecimen and patient -reported outcomes, and to create novel data linkages to facilitate research on critical cancer survivorship issues.

Specific Aims:

1. Create a large, well-characterized cohort of adult cancer survivors that includes biospecimens, medical history and patient interview data
2. Understand long-term effects of cancer, evaluate interventions to reduce adverse symptoms, assess the burden of comorbid conditions, examine treatment side effects, and improve the cost-effectiveness of survivorship care and services.
3. Determine the impact of racial and economic disparities, investigate genetic predisposition that may influence treatment efficacy, toxicity, and survival, and improve the quality of life (QoL) of cancer survivors

Overlap: None

PETERS, EDWARD S.

New to Current

Title: Louisiana Rural Oral Health Network Peters (Co-PI)

Time Commitments: 0.5 calendar months

Supporting Agency (and grant #): HRSA (P10RH32093)

Name and address of the Funding Agency's Procuring Contracting/Grants Officer:

Sara Afayee

Federal Office of Rural Health Policy

Health Resources and Services Administration (HRSA)

U.S. Department of Health and Human Services

5600 Fishers Lane - 17W49C Rockville, MD 20857

Performance Period: 8/1/2018-7/31/2020

Level of Funding:

Brief description of project's goals: The goals of this project is to establish the infrastructure to support and sustain a rural oral health network (LaROHN), complete a Community Oral Health Needs Assessment, and assess service delivery models that will be used to address identified needs

List of specific aims:

1. Undertake a Community Rural Oral Health Needs Assessment;
2. Evaluate potential service delivery models and study policy that would be necessary for successful implementation of selected models.

Overlap: None

Title: Surveillance, Epidemiology and End Results (SEER) Program Wu (PI)

Time Commitments: 0.6 calendar

Supporting Agency (and grant #): NIH/NCI/SEER HHSN261201800007I/HHSN26100002 (P00001)

Address:

National Institutes of Health

National Cancer Institute

Bethesda, MD 20892-7511

Name and address of the Funding Agency's Procuring Contracting/Grants Officer:

John O. Turner

Performance Period: 5/1/2019-4/30/2028

Level of Funding:

Project Goals: The major goal of this project is to conduct population based cancer surveillance in Louisiana

Specific Aims:

1. Assemble and report, on a periodic basis, estimates of cancer incidence.
2. Monitor annual cancer incidence trends to identify unusual changes in specific forms of cancer occurring in population subgroups defined by geographic, demographic, and social characteristics.
3. Provide continuing information on changes over time in extent of disease at diagnosis, trends in therapy, and changes in cancer patient survival.
4. Identify the occurrence of possible iatrogenic cancers, i.e., cancers that are caused by cancer therapy.
5. Serve as a research resource to the National Cancer Institute, and conduct studies dealing with current cancer control issues as well as issues related to the operation of the SEER Program which may lead to improved and/or more cost-effective operating procedures.

Overlap: None

New to Completed

Title: Mid-South Transdisciplinary Collaborative Center for Health Disparities Research

Time Commitments: 1.2 calendar

Supporting Agency (and grant #): NIH 4U54MD008176

Address:

Name and address of the Funding Agency's Procuring Contracting/Grants Officer:

Performance Period: 8/1/2016-7/31/2018

Level of Funding:

Project Goals: Test the feasibility of recruitment and participation of our population into a trial of a mindfulness training using a novel smartphone application (HeadSpace), which integrates mindfulness training cues and assessment, and determine whether it improves trait mindfulness.

Specific Aims: To estimate changes in mindfulness practice from baseline to follow-up.

FARNAN, L.

Active to Completed

Title: UNC Cancer Survivorship Cohort (Bensen- PI)

Time commitment: 12 Calendar months (100.00%)

Supporting Agency: University Cancer Research Fund - NC State Funding

Name and Address of the Funding Agency Procuring Contracting/Grants Officer:

Unavailable

Performance Period: 4/1/17 - 3/31/18

Level of Funding:

Brief description of projects goals:

The main goals of this application are to expand and enhance this large novel and ethnically diverse adult cancer cohort to 10,000 cancer survivors with comprehensive data collection and follow-up, maintain extensive

infrastructure that links clinical, biospecimen and patient -reported outcomes, and to create novel data linkages to facilitate research on critical cancer survivorship issues.

Specific Aims:

1. Create a large, well-characterized cohort of adult cancer survivors that includes biospecimens, medical history and patient interview data
2. Understand long-term effects of cancer, evaluate interventions to reduce adverse symptoms, assess the burden of comorbid conditions, examine treatment side effects, and improve the cost-effectiveness of survivorship care and services.
3. Determine the impact of racial and economic disparities, investigate genetic predisposition that may influence treatment efficacy, toxicity, and survival, and improve the quality of life (QoL) of cancer survivors

Overlap: None

What other organizations were involved as partners?

Nothing to report

Y3 Progress

Yes, active other supports for Dr. James L, Mohler, Dr. Jeannette Bensen, Dr. Laura Farnan and Dr. Edward Peters were updated below.

Changes in active support

MOHLER, JAMES L.

Active support - Change to end date

Title: Genetic and Epigenetic Prostate Cancer Related alterations in early onset disease in African American Men (Woloszynska-Read)

Time Commitments: 1.20 calendar months

Supporting Agency: DoD

Grants Officer: USA MED RESEARCH ACQ ACTIVITY 820 CHANDLER ST FORT DETRICK MD 21702-5014/ LYMOR BARNHARD

Performance Period: 04/01/2017-03/31/2021

Level of funding:

Brief description of goals: Proposed research aims to identify molecular alterations that distinguish aggressive forms of early onset prostate cancer commonly found in African American men will contribute to the development of African American tumor (epi)genetic signature(s) and ultimately will lead to personalized medicine strategies for this group of patients.

List of specific aims:

1. Determine the relative frequency of genetic lesions found in PCa in AAs and EAs.
 2. Determine novel, clinically relevant methylomic and transcriptomic differences in PCa from AAs and EAs
- Obtain and link vital status data and cause of death in PCaP research subjects

Overlap: None

Active support - Change to effort

Title: The NF-kappaB-androgen Receptor Axis Drives Failure of Medical Therapy in Human Benign Prostatic Hyperplasia

Time Commitments: 0.24 calendar months (Matusik, PI)

Supporting Agency: NIH/NIDDK R01DK111554

Grants Officer: Melissa Haney, Manager, Dept of Urologic Surgery, Vanderbilt University. 615-322-3172, Melissa.haney@vanderbilt.edu

Performance Period: 09/16/2016 – 07/31/2021

Level of funding: (sub)

Brief description of goals: NF κ B and AR signaling controls the failed response to 5ARIs in BPH.

List of specific aims:

1. Determine cross-talk between NF κ B and AR signaling to regulate failure of medical therapy
2. Determine the SRD5A isoforms contribution during resistance to medical therapy
3. Determine if failure of medical therapy is driven by NF κ B and/or AR-V7 in BPH patients. New insight into how BPH patients fail 5 α -reductase inhibitors holds the promise to identify pathways to apply novel approaches to medical therapy in the treatment of BPH.

Overlap: None

Active support - Change to end date, total costs, and effort

Title: Cancer Center Support Grant (Johnson, PI)

Time Commitments: 3.6 calendar months as Director of Bioanalytics, Metabolomics and Pharmacokinetics Shared Resource (BMPK)

Supporting Agency: National Cancer Institute P30CA016056

Funding Agency's Procuring Contracting/Grants Officer: Hasnaa Shafik; shafikh@mail.nih.gov

Performance Period: 5/1/19 – 04/30/24

Level of Funding: (annual direct)

Project Goals: Roswell Park is an independent, free-standing research, education and clinical cancer care Institute. Roswell has been continuously recognized as a Cancer Center since NCI first designated centers in 1974 and has been designated as a comprehensive center since that term was first employed. Roswell occupies a 27 acre campus near downtown Buffalo. The Roswell campus consists of 1.6 million square feet (sf) of laboratory, office, clinical and education. An additional 142,000 sf clinical care, clinical research and office building began construction on April 18, 2013. An additional 16,000 sf of clinical space have been opened at three affiliate sites. While the population of the Roswell catchment area (the 8 county region of WNY from which ~86% of Roswell patients are drawn) has been generally stable at ~1.5M, the number of analytic cases in the RPCI tumor registry has increased 25% since 2008.

Specific Aims: Roswell Park's Cancer Center Support Grant (CCSG) includes five programs and 15 core resources. Support is provided for leadership, development funds, planning, and evaluation, and administration.

Overlap: None

Active support - Change to end date, total costs, and grant number

Title: Network Lead Academic Participating Site Grant from the Roswell Park Cancer Inst. (UG1CA233191)

Time Commitments: 0.60 calendar months (Levine, PI)

Supporting Agency: NIH/NCI

Name and address of the Funding Agency's Grants Officer: Margaret M. Mooney, mooneym@mail.nih.gov

Performance Period: 3/06/2019-2/28/2025

Level of funding:

Brief description of goals/Aims: Roswell Park has had a long tradition of contributing to the national cooperative groups over many decades. Roswell Park is committed to the many strengths inherent to cooperative group research: therapeutic advances; a better understanding of the biology of cancer; cancer prevention; means to improve the quality of life of cancer patients; piloting of new drugs and radiology and radiation and surgical techniques; establishing the relevance of new cellular and molecular advances to the predictive, prognostic, and therapeutic approaches to patients; and the advancement of patient advocacy.

Overlap: None

Active support - Change to end date

Title: Qualifying Multi-Transcript Signatures for Active Surveillance of Prostate Cancer (R01CA182438)

Time Commitments: 0.6 calendar months (Kim, PI)

Supporting Agency: NIH/NCI

Grants Officer: Peter Ogunbiyi, ogunbiyi@mail.nih.gov

Performance Period: 09/02/14 - 08/31/20

Level of Funding: (subcontract)

Brief description of goals: The consortium is well-positioned to rapidly translate and promote validated signatures since all assays will be performed in a CLIA-approved laboratories, and study investigators have leadership positions in cooperative groups, national professional societies, and national guidelines committees.

List of specific aims:

1. to validate biomarkers in prostate needle biopsies predictive of adverse pathology and progression in men considering active surveillance
2. to test the effects of African-American ethnicity on the biomarker signatures.

Overlap: None

Active support - Change to end date

Title: Cholesterol Lowering Intervention for Prostate Cancer Active Surveillance/Jr. Faculty Award to Alliance NCORP Research Base – Pilot Project (Kim/Mohler - PIs)

Time Commitments: 0.60 calendar months (UG1CA189823)

Supporting Agency: Cedars/NCI

Grants Officer: Subcontract with Cedars Sinai. Cedars-Sinai Medical Center, Margaret Jenkins, Administrative Program Coordinator, Department of Surgery, Research Division, 8635 W. 3rd Street, Suite 973W, Los Angeles, CA 90048, margaret.jenkins@cshs.org

Performance Period: 04/01/2015 – 07/31/2020

Level of funding: (subcontract)

Brief description of goals: The proposed research tests the hypothesis that intensive cholesterol lowering will decrease the growth rate of benign and malignant prostate epithelium. The proposed research could provide the data necessary to justify a phase III clinical trial to address one of the major problems in urologic oncology how to prevent the progression of low risk prostate cancer to provide men higher levels of confidence for selection of active surveillance.

Overlap: None

Active support - Change to end date

Title: Understanding the Relative Contributions of and Critical Enzymes for the 3 Pathways for Intracrine Metabolism of Testicular Androgens in Advanced Prostate Cancer (Mohler/Watt/Bies)

Time Commitments: 1.65 calendar months

Supporting Agency: DOD

Grants Officer: Thomas S. Winter, USAMRAA, Thomas.s.winter2.civ@mail.mil, 240.357.1590

Performance Period: 09/30/16 - 09/29/20

Level of Funding:

Brief description of goals: This research seeks a better understanding of intracrine androgen metabolism acutely in response to initiation of issuing in vivo models and sophisticated PK/PD modeling.

List of specific aims:

1. Determine the relative use of the 3 pathways for intracrine androgen metabolism in vitro, in vivo and in clinical specimens
2. Identify the principal androgen metabolism enzymes (ie. 3a-oxidoreductases) responsible for primary backdoor DHT synthesis from androstenediol

3. Determine the requirements for SRD5A1-3 in the frontdoor pathway of DHT synthesis from T and its precursors and of SRD5A1 and HSD17B3 in the secondary backdoor pathway of DHT synthesis from androstenedione.

Overlap: None

New Pending

Title: Characterization of a novel critical interplay between VHL inactivation and iron metabolism in clear cell renal cell carcinoma tumorigenesis (Kauffman)

Time Commitments: 0.3 calendar months

Supporting Agency: DOD KCRP

Grants Officer: To be determined

Performance Period: 7/1/2020-6/30/2022 (Final dates to be determined)

Level of funding:

Brief description of goals: This study uses an innovative combined carcinogenic/gene-knockout animal model generated by introducing *vhl* loss into the FeNTA mouse model, and performs complementary experiments in human tissues, to test the novel *central hypothesis that* VHL inactivation and renal iron accumulation cooperate to promote ccRCC tumorigenesis.

Overlap: None

Active to Completed

Title: The Thoc1 Ribonucleoprotein as a Novel Biomarker for Prostate Cancer Treatment Assignment (Goodrich - PI)

Time Commitments: 0.30 calendar months

Supporting Agency: USAMRAA PC130746P1

Grants Officer: Lance Nowell, lance.l.nowell.civ@mail.mil, Phone: 301-619-1357

Performance Period: 09/15/2014-09/14/2018

Level of funding: (partnering PI)

Brief description of goals: The central objective of this application is to test the utility of a novel molecular biomarker, *THOC1*, which may improve assignment of patients to appropriate therapy.

List of specific aims:

1. Characterize pThoc1 levels in independent cohorts of human prostate cancer radical prostatectomy specimens.
2. Characterize pThoc1 levels in a cohort of human prostate cancer patients on active surveillance.
3. Test whether pThoc1 or autoantibodies against pThoc1 can be detected in the blood of prostate cancer patients.

Overlap: None

Active to Completed

Title: Genetic variations in SLCO transporter and racial disparity in aggressiveness of PCa Time Commitments: 0.12 calendar (PI-Wu)

Supporting Agency: DOD (W81XWH-14-0453)

Grants Officer: Mirlene Desir, mirlene.desir.civ@mail.mil

Performance Period: 04/01/14-3/14/19

Level of Funding: annual direct

Brief Description of Goals: The objective seeks to address how transporter-regulated androgen availability to cancer cells may contribute to the difference in prostate cancer aggressiveness between African-American (AA) and European-American (EA) men. The hypothesis is: Genetic variations in solute carrier family of organic anion transporting peptides (SLCO) androgen transporter genes and expression profiles of SLCO androgen

transporters in prostate tissue are associated with aggressiveness of prostate cancer, and contribute to racial differences in prostate.

List of Specific Aims:

1. Aim 1 is to examine genetic variations in SLCO transporters genes and to investigate the associations of the variations with prostate cancer aggressiveness in AA and EA.
2. Aim 2 is to examine in situ expression profiles of SLCO transporters in prostate tissue and to investigate the associations of the expression profiles with prostate cancer aggressiveness in AA and EA.
3. Aim 3 is to characterize the functions of candidate SLCO transporters in androgen uptake and to evaluate the biological effects on androgen receptor signaling in human prostate cancer cell lines.

Overlap: NONE

Active to Completed

Title: A Small-Molecule Inhibitor of the Terminal Steps for Intracrine Androgen Synthesis in Advanced Prostate Cancer (Mohler)

Time Commitments: .97 calendar months

Supporting Agency: NCI-R21CA205108

Grants Officer: Nicole Franklin, Grants Management Specialist, 9609 Medical Center Drive, West Tower, Room 2W556, Bethesda, MD 20892 (regular mail), Phone: 240-276-5210, nicole.franklin@nih.gov

Performance Period: 04/10/2016-03/31/2020 (NCE)

Level of Funding:

Brief description of goals: This research seeks to explore if a small-molecule inhibitor of the catalytic site shared by the five 3α -oxidoreductases will decrease T and DHT metabolism through the frontdoor and backdoor pathways.

List of specific aims:

1. Identify a candidate inhibitor against the catalytic site shared by the five 3α -oxidoreductases
2. Synthesize and test re-designed candidate inhibitors and conduct PK/PD and toxicity studies to produce a lead compound inhibitor of the five 3α -oxidoreductases
3. Determine whether the inhibitor of the 3α -oxidoreductases decreases tissue T and DHT levels and impairs CRPC growth

Overlap: None

FARNAN, LAURA

Active support – Not previously reported

Title: North Carolina Clinical Genomic Evaluation by Next-gen Exome Sequencing 2

Effort: 5.40 Calendar

Supporting Agency: NIH/NHGRI

Grants Officer: Anneliese B. Galczynski, National Institutes of Health, Building 31, Room 4B09, 31 Center Drive, MSC 2152, 9000 Rockville Pike, Bethesda, MD 20892-2152

Performance Period: 06/01/2018 – 05-31/2021

Funding Amount:

Project Goals: NCGENES 2 will generate the necessary evidence to support the use of Whole Exome Sequencing (WES) as a standard tool in the management of patients with genetic disorders and enable its implementation in populations that experience health disparities.

Specific Aims:

Specific Aim 1: Assess the analytic performance of ES/GS and genomic variant interpretation by: 1A) Improving analytic efficiency and diagnostic yield by including deep phenotypic information during molecular analysis, improving copy number variant detection, and conducting whole genome sequencing in a subset of “negative” cases; and 1B) Determining impact of genetic ancestry on genomic variant interpretation. This Aim will also explore the distribution of genomic data by: 1C) Fostering data sharing, and piloting integration of

genomic data in a healthcare system through a real-world implementation of ClinGen data standards; and 1D) Implementing tools for collaborative interpretation involving clinicians and laboratorians at geographically distributed sites.

Specific Aim 2: Test the hypothesis that patients will benefit from a theory-based, multi-component pre-visit preparation intervention designed to maximize active engagement.

Specific Aim 3: Test the hypothesis that ES/GS provides a more efficient diagnostic evaluation, curtailing the costly and difficult “diagnostic odyssey” experienced by many patients. We will collect comprehensive longitudinal clinical data and utilize a randomized controlled trial study design that compares usual care plus exome sequencing versus usual care to examine: 3A) Impact of ES/GS on condition-specific and general clinical outcomes; and 3B) Provider expectations at baseline and diagnostic thinking after return of results; and 3C) Effect of ES/GS on management planning, follow-up tests, and referral patterns.

Specific Aim 4: Establish healthcare utilization models to examine: 4A) Net Monetary Benefit to payers; 4B) Cost effectiveness of ES/GS as a firstline test for suspected genetic disorders; and 4C) Identification of health disparities that limit the benefits of genomic medicine.

Overlap: None

Active support – Not previously reported

Title: Cancer Center Core Support Grant (Core 12)

Effort: 1.80 Calendar

Supporting Agency: NCI

Grants Officer: Cornice Young, National Institutes of Health, BG 9609 MSC 9760, 9609 Medical Center Drive, Bethesda, MD 20892-9760

Performance Period: 06/01/1997 – 11/30/2020

Funding Amount:

Project Goals: The mission of the Tissue Procurement and Biospecimens Processing Shared Resource is to support and enhance cancer-related translational, clinical, population and basic science research. This is achieved by providing UNC LCCC members with a centralized, coordinated, quality-controlled, quality-assured facility for the procurement, processing, storage, distribution and clinical annotation of biologic specimens.

Specific Aims:

The Specific Aims for the Tissue Procurement Facility and Biospecimens Processing SR include the following:

1. Procure clinical specimens from all consented cancer patients at UNC for inclusion in the cancer biobank and for the support of cancer related clinical trials. Specimens collected include: fresh tissue, frozen tissues, formal-fixed paraffin-embedded tissues, blood, urine, buccal swabs and other tissue types as, needed.

2. Provide clinical annotations for all specimens procured and banked by the Core and maintain a database to securely and effectively link clinical annotations with specimens.

3. Provide extraction of nucleic acids from various blood and tissue products, comprising both large and small sample volumes. Sample normalization and preparation for genotyping and expression studies is also provided.

4. Provide processing services for procured blood and tissue specimens. For blood specimens, this includes separating whole blood into different components (plasma, serum and buffy coat) or isolating viable peripheral blood mononuclear cells. For tissue specimens, this includes histologic processing and sectioning of tissue samples (both FFPE and frozen) and disassociation of specimens to obtain viable Cells.

Overlap: None

PETERS, EDWARD S.

New pending

Title: Epidemiology of Ovarian Cancer in African-American Women (Schildkraut)

Time Commitments: 1.2 calendar

Supporting Agency: NCI/NIH

Grants Officer: To be determined

Performance Period: 7/1/20-6/30/25 (Final dates to be determined)

Level of funding: (annual direct)

Brief description of goals: This study proposes to undertake a novel integrative and comprehensive approach to understand the complex causes of poor survival in AA women after EOC diagnosis. Our study approach uses established methods in a new paradigm with the potential to provide more detailed information that can be used to inform prevention strategies and targeted interventions and therapies to improve survival in AA women.

Specific Aims:

1. To investigate the role of the neighborhood social and physical environment on overall survival of EOC among AA women.
2. To evaluate the association between patient characteristics and EOC survival in AA women.
3. To examine the association between inflammatory pathway biomarkers and invasive EOC survival among AA women.
4. To use multi-level modeling to integrate the impact of the Aim 1-3 variables from the macro environment and individual factors on survival in AA women with ovarian cancer.

Overlap: None

BENSEN, JEANNETTE T.

Active - Change to effort

Title: North Carolina Clinical Genomic Evaluation by Next-Gen Exome Sequencing 2

Time commitment: 8.40 calendar months

Supporting Agency: NIH, National Human Genome Research Institute (NHGRI)

Performance Period: 08/01/17-05/31/21

Level of Funding:

Brief description of projects goals/Aims: NCGENES 2 will generate the necessary evidence to support the use of Whole Exome Sequencing (WES) as a standard tool in the management of patients with genetic disorders and enable its implementation in populations that experience health disparities.

Overlap: None

Year 4

Yes, active other supports for Dr. James L. Mohler, Dr. Jeannette Bensen, and Dr. Laura Farnan were updated below.

MOHLER, JAMES L.

Active to Completed

Title: Genetic and Epigenetic Prostate Cancer Related alterations in early onset disease in African American Men (Woloszynska-Read)

Time Commitments: 1.20 calendar months

Supporting Agency: DoD

Grants Officer: USA MED RESEARCH ACQ ACTIVITY 820 CHANDLER ST FORT DETRICK MD 21702-5014/ LYMOR BARNHARD

Performance Period: 04/01/2017-03/31/2021

Level of funding:

Brief description of goals: Proposed research aims to identify molecular alterations that distinguish aggressive forms of early onset prostate cancer commonly found in African American men will contribute to the development of African American tumor (epi)genetic signature(s) and ultimately will lead to personalized medicine strategies for this group of patients.

List of specific aims:

1. Determine the relative frequency of genetic lesions found in PCa in AAs and EAs
2. Determine novel, clinically relevant methylomic and transcriptomic differences in PCa from AAs and EAs
3. Obtain and link vital status data and cause of death in PCaP research subjects

Overlap: None

Active support - Change to effort

Title: The NF-kappaB-androgen Receptor Axis Drives Failure of Medical Therapy in Human Benign Prostatic Hyperplasia

Time Commitments: 0.24 calendar months (Matusik, PI)

Supporting Agency: NIH/NIDDK R01DK111554

Grants Officer: Melissa Haney, Manager, Dept of Urologic Surgery, Vanderbilt University. 615-322-3172, Melissa.haney@vanderbilt.edu

Performance Period: 09/16/2016 – 07/31/2021

Level of funding: (sub)

Brief description of goals: NkB and AR signaling controls the failed response to 5ARIs in BPH.

List of specific aims:

1. Determine cross-talk between NFkB and AR signaling to regulate failure of medical therapy
2. Determine the SRD5A isoforms contribution during resistance to medical therapy
3. Determine if failure of medical therapy is driven by NFkB and/or AR-V7 in BPH patients. New insight into how BPH patients fail 5 α -reductase inhibitors holds the promise to identify pathways to apply novel approaches to medical therapy in the treatment of BPH.

Overlap: None

Active support -

Title: Cancer Center Support Grant (Johnson, PI)

Time Commitments: 3.6 calendar months as Director of Bioanalytics, Metabolomics and Pharmacokinetics Shared Resource (BMPK)

Supporting Agency: National Cancer Institute P30CA016056

Funding Agency's Procuring Contracting/Grants Officer: Min He; min.he@nih.gov

Performance Period: 5/1/19 – 04/30/24

Level of Funding: (annual direct)

Project Goals: Roswell Park is an independent, free-standing research, education and clinical cancer care center. Roswell has been continuously recognized as a Cancer Center since NCI first designated centers in 1974 and has been designated as a comprehensive center since that term was first employed. Roswell occupies a 27 acre campus near downtown Buffalo. The Roswell campus consists of 1.6 million square feet (sf) of laboratory, office, clinical and education. An additional 142,000 sf clinical care, clinical research and office building began construction on April 18, 2013. An additional 16,000 sf of clinical space have been opened at three affiliate sites. While the population of the Roswell catchment area (the 8 county region of WNY from which ~86% of Roswell patients are drawn) has been generally stable at ~1.5M, the number of analytic cases in the RPCI tumor registry has increased 25% since 2008.

Specific Aims: Roswell Park's Cancer Center Support Grant (CCSG) includes five programs and 15 core resources. Support is provided for leadership, development funds, planning, and evaluation, and administration.

Overlap: None

Active support -

Title: Network Lead Academic Participating Site Grant from the Roswell Park Cancer Inst. (UG1CA233191)

Time Commitments: 0.60 calendar months (Levine, PI)

Supporting Agency: NIH/NCI

Name and address of the Funding Agency's Grants Officer: Margaret M. Mooney, mooneym@mail.nih.gov

Performance Period: 3/06/2019-2/28/2025

Level of funding:

Brief description of goals/Aims: Roswell Park has had a long tradition of contributing to the national cooperative groups over many decades. Roswell Park is committed to the many strengths inherent to cooperative group research: therapeutic advances; a better understanding of the biology of cancer; cancer prevention; means to improve the quality of life of cancer patients; piloting of new drugs and radiology and radiation and surgical techniques; establishing the relevance of new cellular and molecular advances to the predictive, prognostic, and therapeutic approaches to patients; and the advancement of patient advocacy.

Overlap: None

Active support -

Title: Mechanisms of Metabolic Stress Induced Transcriptional Regulation in Prostate Cancer (Dasgupta)

Time Commitments: 0.6 calendar

Supporting Agency: NCI/NIH (R01CA252092)

Grants Officer: Neeraja Sathyamoorthy, ns61r@nih.gov

Performance Period: 4/1/2021-3/31/2026

Level of funding:

Brief description of goals: To uncover molecular links between mitochondrial metabolism and transcriptional regulation that enables hormone refractory PCa adaptation, survival and ultimately metastatic competency.

Specific Aims: (1) to investigate the mechanisms regulating sustained activation of mitochondrial ACO2 to promote lipogenesis, (2) define the role of nuclear receptor coregulator SRC-2 regulating SIRT3 expression, and (3) evaluate the impact of this nuclear-mitochondrial regulatory axis on prostate tumor survival and adaptation leading to bone colonization and growth.

Overlap: None

PENDING SUPPORT

Title: Novel Approaches for Assessing Chronic Comorbidities and Predicting Adverse Outcomes Among Ethnically-Diverse Populations of Prostate Cancer Survivors (Khan)

Time Commitments: 0.30 calendar months (W81XWH-20-PCRP-IDA)

Supporting Agency: DOD

Grants Officer: TBD

Performance Period: 9/1/2021-8/31/2024

Level of funding: (subcontract)

Brief description of goals/Aims: This proposal represents a continuation of, and takes advantage of, the DOD Prostate Cancer Research Program funded "North Carolina-Louisiana Prostate Cancer Project (PCaP)," the largest population-based CaP study ever conducted (2258 men with newly diagnosed CaP; involved 11 institutions).

Overlap: None

Active to Completed

Title: Qualifying Multi-Transcript Signatures for Active Surveillance of Prostate Cancer (R01CA182438)

Time Commitments: 0.6 calendar months (Kim, PI)

Supporting Agency: NIH/NCI

Grants Officer: Peter Ogunbiyi, ogunbiyi@mail.nih.gov

Performance Period: 09/02/14 - 08/31/20

Level of Funding: (subcontract)

Brief description of goals: The consortium is well-positioned to rapidly translate and promote validated signatures since all assays will be performed in a CLIA-approved laboratories, and study investigators have leadership positions in cooperative groups, national professional societies, and national guidelines committees.

List of specific aims:

1. to validate biomarkers in prostate needle biopsies predictive of adverse pathology and progression in men considering active surveillance
2. to test the effects of African-American ethnicity on the biomarker signatures.

Overlap: None

Active to Completed (change in end date)

Title: Cholesterol Lowering Intervention for Prostate Cancer Active Surveillance/Jr. Faculty Award to Alliance NCORP Research Base – Pilot Project (Kim/Mohler - PIs)

Time Commitments: 0.60 calendar months (UG1CA189823)

Supporting Agency: Cedars/NCI

Grants Officer: Subcontract with Cedars Sinai. Cedars-Sinai Medical Center, Margaret Jenkins, Administrative Program Coordinator, Department of Surgery, Research Division, 8635 W. 3rd Street, Suite 973W, Los Angeles, CA 90048, margaret.jenkins@cshs.org

Performance Period: 04/01/2015 – 03/31/2021

Level of funding: (subcontract)

Brief description of goals: The proposed research tests the hypothesis that intensive cholesterol lowering will decrease the growth rate of benign and malignant prostate epithelium. The proposed research could provide the data necessary to justify a phase III clinical trial to address one of the major problems in urologic oncology how to prevent the progression of low risk prostate cancer to provide men higher levels of confidence for selection of active surveillance.

Overlap: None

Active to Completed

Title: Understanding the Relative Contributions of and Critical Enzymes for the 3 Pathways for Intracrine Metabolism of Testicular Androgens in Advanced Prostate Cancer (Mohler/Watt/Bies)

Time Commitments: 1.65 calendar months

Supporting Agency: DOD

Grants Officer: Thomas S. Winter, USAMRAA, Thomas.s.winter2.civ@mail.mil, 240.357.1590

Performance Period: 09/30/16 - 09/29/20

Level of Funding:

Brief description of goals: This research seeks a better understanding of intracrine androgen metabolism acutely in response to initiation of issuing in vivo models and sophisticated PK/PD modeling.

List of specific aims:

1. Determine the relative use of the 3 pathways for intracrine androgen metabolism in vitro, in vivo and in clinical specimens
2. Identify the principal androgen metabolism enzymes (ie. 3 α -oxidoreductases) responsible for primary backdoor DHT synthesis from androstenediol
3. Determine the requirements for SRD5A1-3 in the frontdoor pathway of DHT synthesis from T and its precursors and of SRD5A1 and HSD17B3 in the secondary backdoor pathway of DHT synthesis from androstenedione.

Overlap: None

Pending to Active – change in dates

Title: Characterization of a novel critical interplay between VHL inactivation and iron metabolism in clear cell renal cell carcinoma tumorigenesis (Kauffman)

Time Commitments: 0.3 calendar months

Time Commitments: 0.3 calendar months

Supporting Agency: DOD KCRP (W81XWH-20-1-0721)

Grants Officer: Elena G. Howell, elena.g.howell.civ@mail.mil, 301-619-6871, 1077 Patchel St., Fort Detrick, MD 21702

Performance Period: 8/15/2020-8/14/2022

Level of funding:

Brief description of goals: This study uses an innovative combined carcinogenic/gene-knockout animal model generated by introducing *vhl* loss into the FeNTA mouse model, and performs complementary experiments

inhuman tissues, to test the novel *central hypothesis that* VHL inactivation and renal iron accumulation cooperate to promote ccRCC tumorigenesis.

Overlap: None

Active to Completed

Title: The Thoc1 Ribonucleoprotein as a Novel Biomarker for Prostate Cancer Treatment Assignment (Goodrich - PI)

Time Commitments: 0.30 calendar months

Supporting Agency: USAMRAA PC130746P1

Grants Officer: Lance Nowell, lance.l.nowell.civ@mail.mil, Phone: 301-619-1357

Performance Period: 09/15/2014-09/14/2018

Level of funding: (partnering PI)

Brief description of goals: The central objective of this application is to test the utility of a novel molecular biomarker, *THOC1*, which may improve assignment of patients to appropriate therapy.

List of specific aims:

1. Characterize pThoc1 levels in independent cohorts of human prostate cancer radical prostatectomy specimens.
2. Characterize pThoc1 levels in a cohort of human prostate cancer patients on active surveillance.
3. Test whether pThoc1 or autoantibodies against pThoc1 can be detected in the blood of prostate cancer patients.

Overlap: None

Active to Completed

Title: Genetic variations in SLCO transporter and racial disparity in aggressiveness of PCa Time Commitments: 0.12 calendar (PI-Wu)

Supporting Agency: DOD (W81XWH-14-0453)

Grants Officer: Mirlene Desir, mirlene.desir.civ@mail.mil

Performance Period: 04/01/14-3/14/19

Level of Funding: annual direct

Brief Description of Goals: The objective seeks to address how transporter-regulated androgen availability to cancer cells may contribute to the difference in prostate cancer aggressiveness between African-American (AA) and European-American (EA) men. The hypothesis is: Genetic variations in solute carrier family of organic anion transporting peptides (SLCO) androgen transporter genes and expression profiles of SLCO androgen transporters in prostate tissue are associated with aggressiveness of prostate cancer, and contribute to racial differences in prostate.

List of Specific Aims:

1. Aim 1 is to examine genetic variations in SLCO transporters genes and to investigate the associations of the variations with prostate cancer aggressiveness in AA and EA.
2. Aim 2 is to examine in situ expression profiles of SLCO transporters in prostate tissue and to investigate the associations of the expression profiles with prostate cancer aggressiveness in AA and EA.
3. Aim 3 is to characterize the functions of candidate SLCO transporters in androgen uptake and to evaluate the biological effects on androgen receptor signaling in human prostate cancer cell lines.

Overlap: NONE

Active to Completed

Title: A Small-Molecule Inhibitor of the Terminal Steps for Intracrine Androgen Synthesis in Advanced Prostate Cancer (Mohler)

Time Commitments: .97 calendar months

Supporting Agency: NCI-R21CA205108

Grants Officer: Nicole Franklin, Grants Management Specialist, 9609 Medical Center Drive, West Tower, Room 2W556, Bethesda, MD 20892 (regular mail), Phone: 240-276-5210, nicole.franklin@nih.gov

Performance Period: 04/10/2016-03/31/2020 (NCE)

Level of Funding:

Brief description of goals: This research seeks to explore if a small-molecule inhibitor of the catalytic site shared by the five 3 α -oxidoreductases will decrease T and DHT metabolism through the frontdoor and backdoor pathways.

List of specific aims:

1. Identify a candidate inhibitor against the catalytic site shared by the five 3 α -oxidoreductases
2. Synthesize and test re-designed candidate inhibitors and conduct PK/PD and toxicity studies to produce a lead compound inhibitor of the five 3 α -oxidoreductases
3. Determine whether the inhibitor of the 3 α -oxidoreductases decreases tissue T and DHT levels and impairs CRPC growth

Overlap: None

BENSEN, JEANNETTE T.

Active Support – Change to end date

Title: North Carolina Clinical Genomic Evaluation by Next-Gen Exome Sequencing 2

Time Commitment: 4.80 calendar months

Supporting Agency: NIH, National Human Genome Research Institute (NHGRI)

Grant No: 5U01HG006487-08

Grants Officer: Devon R. Bumbray-Quarles, Grants Management Specialist (GMS), devon.bumbray-quarles@nih.gov, 301-451-7928

Performance Period: 08/01/17-05/31/22

Level of Funding:

Brief description of goals:

Overlap: None

Title: North Carolina Clinical Genomic Evaluation by Next-Gen Exome Sequencing 2

Time Commitment: 3.60 calendar months

Supporting Agency: NIH, National Human Genome Research Institute (NHGRI)

Grant No: 5U01HG006487-08S1

Grants Officer: Deanna L. Ingersoll, Grants Management Specialist (GMS), Deanna.Ingersoll@nih.gov, 301-435-7858

Performance Period: 08/01/17-05/31/22

Level of Funding:

Brief description of goals: This large multidisciplinary project will examine the utility of whole exome sequencing as a diagnostic test in diverse patient populations, the discovery and impact of clinically relevant incidental findings, and ultimately provide insight into the best practices for genomic medicine.

Overlap: None

FARNAN, LAURA

Active Support – Change to end date

Title: North Carolina Clinical Genomic Evaluation by Next-Gen Exome Sequencing 2

Time Commitment: 4.80 calendar months

Supporting Agency: NIH, National Human Genome Research Institute (NHGRI)

Grant No: 5U01HG006487-08S1

Grants Officer: Deanna L. Ingersoll, Grants Management Specialist (GMS), Deanna.Ingersoll@nih.gov, 301-435-7858

Performance Period: 08/01/17-05/31/22

Level of Funding:

Brief description of goals: This large multidisciplinary project will examine the utility of whole exome sequencing as a diagnostic test in diverse patient populations, the discovery and impact of clinically relevant incidental findings, and ultimately provide insight into the best practices for genomic medicine.

Overlap: None

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

Nothing to report

9. APPENDICES:

Y1 Progress

1. Survey Instrument: Research Subject
2. Survey Instrument: Caregiver(s)
3. Medical Record Abstraction (MRA)
4. Statement of Work: Approved
5. Statement of Work: Revised (2018)

Y2 Progress

6. Survey Instrument: Research Subject, Telephone-based
7. Survey Instrument: Research Subject, Web-based
8. Survey Instrument: Research Subject, Paper-based
9. Statement of Work: Revised (2019)

Y3 Progress

10. PCaP Procedure Codes
11. PCaP NDC Medication Codes
12. Proposed Thesis, Madhav KC

Y4 Progress

13. Manuscript submitted to *Cancer Epidemiology, Biomarkers & Prevention*

Association between Neighborhood Deprivation and Prostate Cancer Aggressiveness in a Population-Based Study

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Running title: Neighborhood deprivation and prostate cancer aggressiveness

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Abstract: 242 words; Text: 3333 words; Tables: 4; Figure: 0; References: 57

Abstract

Background: Prostate cancer (PCa) is a multifactorial disease that involves genetics and socio-environmental factors. Aggressive PCa likely results from complex multilevel interaction of biological, individual, and neighborhood factors. This study examines the role of neighborhood deprivation on PCa aggressiveness while adjusting for individual-level factors.

Methods: A total of 2,034 individuals diagnosed with PCa enrolled in the North Carolina-Louisiana Prostate Cancer Project (PCaP) were included in this study. A composite variable, the Area Deprivation Index (ADI), was used to assess the level of neighborhood deprivation. ADI was calculated using US Census Bureau data. Multilevel logistic regression models were performed to assess the effect of neighborhood deprivation on PCa aggressiveness.

Results: Association between neighborhood deprivation and high aggressive PCa was observed. Participants residing in the most deprived neighborhood had a greater odds of high aggressive PCa (aOR=1.50, 95% CI=1.10-1.96). Upon adjustment for race, this association was no longer observed. However, interaction between ADI and race indicated a presence of a super-additive interaction; the relative excess rate due to interaction (RERI) was 0.61 (95% CI=0.10-1.14).

Conclusions: This study found that neighborhood deprivation was a risk factor for aggressive PCa, and this association was modified by race. African Americans (AAs) residing in more deprived neighborhoods experienced a higher degree of aggressive PCa compared to European Americans (EAs).

Impact: Neighborhoods with greater deprivation should be targeted for PCa screening programs, and public health cancer intervention efforts should take into consideration social determinants of health associated with cancer disparities.

86

87 **Introduction**

88 Prostate cancer (PCa) is one of the most common cancers in the world with an
89 estimated 1.3 million new cases and 360,000 deaths in 2018 (1, 2). In the United
90 States, PCa is the second leading cause of death in men, accounting for 33,330 deaths
91 in 2020. The number of new cases is estimated to be 191,930, which represents more
92 than 10% of all new cancer cases in 2020 (3). PCa aggressiveness is the result of a
93 complex multilevel interaction of biological, individual, and societal factors. Previous
94 studies that have assessed risk factors for PCa aggressiveness were limited to the
95 individual or biological level (4-7). Age, family history of PCa, genetic factors, diet,
96 obesity, physical activity, and smoking behavior are the most common individual or
97 biological level risk factors that have been studied previously (5, 8-12). However,
98 identifying risk factors at one level is not sufficient to inform public health policies and
99 programs to prevent PCa cancer and associated adverse health outcomes. Since PCa
100 is a multifactorial disease, the holistic evaluation of individual and neighborhood-level
101 risk factors is needed.

102 Neighborhood factors include the socioeconomic, physical, and social
103 characteristics of residential neighborhoods that may influence an individual's health
104 outcomes. Such characteristics include lack of access to health care facilities,
105 employment opportunities, or social support (13-16). Compared to neighborhoods with
106 little deprivation, deprived neighborhoods are characterized by higher levels of
107 socioeconomic disadvantage, income inequality, overcrowding, less social cohesion,
108 less access to health care, lack of access to healthy food, and poor physical

environments that adversely affect human behavior and health outcomes (15). Deprived neighborhoods are also often correlated with higher levels of environmental pollutants, less walkability, and less greenery, all of which increase the likelihood of chronic diseases (17, 18). Neighborhood deprivation has therefore been identified as a critical social determinant of health and is considered as one of the fundamental causes of health inequalities (19-22).

Features of deprived neighborhoods, such as lack of access to health care, low quality education, and poor patient-provider relationships, may lead to less screening for PCa among men and ultimately more aggressive PCa (23-28). A study that assessed neighborhood-level risk factors demonstrated an association between neighborhood deprivation and a high PCa Gleason score (29).

While the number of studies that assess neighborhood effects on human health has increased significantly over the past 20 years, most of these studies are conducted at the census tract level. The census block group, the smallest geographical unit for which the census bureau publishes data, is however the unit of geography considered best suited to examine small-area level influences of socioeconomic resources on cancer outcomes (30-32). In addition, little research has examined the potential sociobiological mechanisms of health disparities in PCa aggressiveness. The goal of this study is to investigate the relationship between neighborhood deprivation and PCa aggressiveness in the North Carolina-Louisiana Prostate Cancer Project (PCaP) cohort using data from the census block group level. Neighborhood deprivation was measured by the Area Deprivation Index (ADI). ADI is a robust and validated composite index of neighborhood socioeconomic measurement that takes into consideration of 17 census

132 indicators that are highly relevant social determinants of health (33-35). The use of ADI
133 may help explain the sociobiological mechanism of the disparities in PCa
134 aggressiveness.

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Materials and methods

Study Design & Population

Data from the North Carolina-Louisiana Prostate Cancer Project (PCaP) baseline survey was used in this study. PCaP is a multidisciplinary study of social, individual, and tumor-level causes of racial differences in PCa that includes residents of the North Carolina and Louisiana study area who were diagnosed with histologically confirmed adenocarcinoma of PCa after July 1, 2004. Participant recruitment for the baseline survey was started in 2004 and completed in 2009.

A total of 2,258 men were successfully enrolled in the PCaP baseline survey: 1,227 in Louisiana, and 1,031 in North Carolina. The eligibility criteria included age between 40-79 years at the time of diagnosis, ability to complete the study interview in English, not living in an institution, not cognitively impaired or in a severely debilitated physical state, and not under the influence of alcohol, severely medicated, or psychotic at the time of the interview. Eligible men also must have self-identified as either African American or European American to the open-ended question, "What is your race?" Detailed information on the methods and design of the PCaP study can be found in a prior publication (36).

Outcome assessment: PCa aggressiveness

A combination of prognostic factors such as clinical tumor stage, biopsy Gleason grade, and Prostate Specific Antigen (PSA) score were used to define PCa aggressiveness as they accurately estimate the pathologic stage and assist in treatment planning (37). PCa was classified as 1) high aggressive (Gleason sum ≥ 8 , or PSA >20

ng/ml, or Gleason sum ≥ 7 , and clinical tumor stage cT3–cT4); 2) low aggressive (Gleason sum < 7 and clinical stage cT1–cT2 and PSA < 10 ng/ml), or 3) intermediate (all other cases) (36, 38, 39).

Exposure assessment: neighborhood deprivation

Calculation of the Area Deprivation Index (ADI)

Data were extracted from the US census bureau for North Carolina and Louisiana for the year 2000 using the IPUMS National Historical Geographic Information System (NHGIS) (40). The year 2000 was chosen because PCaP study participant enrollment began in 2004. Factor analysis and principal-components analysis of US census indicators were conducted to select 17 indicators that had larger loadings; the larger the loadings the higher the correlation between the factors (33). The census-derived indicators include percent of the population with less than 9 years of education, percent of the population with 12 or more years of education, median family income, median home value, median gross rent, median monthly mortgage, income disparity, unemployment rate, percent of employed persons in white-collar occupations, percent of families below poverty, percent of the population below 150% poverty threshold, single-parent household rate, homeownership rate, percent of the household without a telephone, percent of the household without a motor vehicle, percent of occupied housing units without complete plumbing, and percent of occupied housing units with more than one person per room (crowding) (40).

Singh coefficients, also known as factor weights, were used in the calculation of the ADI scores (33). Each of the 17 US census indicators were multiplied by their corresponding factor weight for all Louisiana and North Carolina block groups, and their

scores were summed to obtain the base score for a census block group. The base score of each block group was standardized by dividing the difference between the individual block group score and the mean of entire Louisiana and North Carolina block groups by the standard deviation. Finally, the standardized score was adjusted to the base mean of 100 and standard deviation of 20. Higher ADI scores indicate more deprived neighborhoods. Neighborhoods were ranked and categorized into quintiles based on their ADI scores. The most deprived neighborhoods were grouped as quintile 5, and the least deprived neighborhoods were grouped as quintile 1. Detailed information on the calculation of ADI can be found elsewhere (35, 41). The dataset with ADI scores was then merged with the participant's individual-level data using the Federal Information Processing Standard (FIPS) code. Participants' postal addresses were geocoded at the US census block group level using Texas A&M web-based geocoding services (42).

Covariates

A Directed Acyclic Graph (DAG) was developed based on existing evidence to identify potential confounding variables (43-46). Patient's age at diagnosis, race, ethnicity, income, education, health insurance status before diagnosis, family history of PCa, PCa screening history, Body Mass Index (BMI), marital status, smoking history, and comorbidity status were included in the analysis.

Age at diagnosis was classified as: 1) ≤ 50 years; 2) 51 to 60 years; 3) 61 to 70 years; 4) more than 70 years. Education level was dichotomized as more than high school degree or high school degree or less. Income was classified into 5 categories: 1) less than \$10,000; 2) \$10,001 - \$40,000; 3) \$40,001 - \$60,000; 4) \$60,001 - \$80,000; 5)

more than \$80,000 per year. The Charlson Comorbidity Index (CCI) was used to assess comorbidity level among the participants. The CCI was categorized into none (CCI=0), mild (CCI<2), moderate (CCI=2-4), and severe (CCI>4) morbidity.

The final analytical dataset included 2,034 participants after excluding participants; 85 participants had missing values for PCa aggressiveness and 139 participants did not have a complete home address at diagnosis. Participants who were excluded from this study (n=139) were more likely to have high aggressive PCa (low=2.90% vs intermediate=1.33% vs high=3.79%, p=0.0311). The final analytical dataset that included 2,034 participants had missing values for ethnicity (n=5), BMI (n=20), marital status (n=1), insurance status (n=14), income (n=186), CCI (n=8), smoking status (n=3), Pca screening history (n=186), and family history (n=76).

Statistical Analysis

Descriptive statistics were computed to examine the distribution of participant characteristics and neighborhood deprivation (ADI quintiles). Differences by study site and PCa aggressiveness were compared using chi-square tests for categorical variables and t-tests or ANOVA for continuous variables. The effect of ADI on PCa aggressiveness was first assessed with a simple multilevel logistic regression model that accounted for the geographical clustering of PCa cases. Then, multivariable multi-level models were used to estimate the effect of neighborhood deprivation on PCa aggressiveness that adjusted for various confounding factors. The interaction between ADI and race was tested. The interaction between ADI and race was tested on both multiplicative and additive scale. The multiplicative interaction was used to measure the extent to which the effect of both ADI and race together exceeded the product of the

effects of ADI and race considered separately. Whereas, interaction on the additive scale was used to measure the difference by which the joint effect of ADI and race exceeded the individual effects of ADI and race. The additive interaction was assessed with Relative Excess Risk due to Interaction (RERI). Odds ratios from logistic regression models were used to calculate the RERI. All analyses were performed using SAS 9.4 software (SAS Institute Inc., 2013).

Results

Characteristics of participants by study site

A total of 1,064 participants from Louisiana and 970 participants from North Carolina were included in this study. Table 1 shows the overall and state-stratified distribution of participants' characteristics. Louisiana participants were slightly older than North Carolina participants (64 vs. 63 years, $p < 0.0012$). PCa aggressiveness was distributed evenly by state. The neighborhoods represented by PCaP participants in Louisiana were more deprived than the neighborhoods in North Carolina; mean ADI score of 99.44 (SD 19.08) vs 90.49 (SD 24.47). The distribution of other individual level covariates including ethnicity, education, income also differed by state ($p < 0.05$). There were more Hispanic/Latino participants in Louisiana compared to North Carolina. Similarly, North Carolina participants were more educated and had higher income compared to Louisiana participants.

Characteristics of participants by PCa aggressiveness

Of 362 participants with high aggressive PCa, 26.52% were residents of the most deprived neighborhoods and 17.40% were residents of the least deprived neighborhoods (Table 2). High aggressive PCa was more prevalent among older participants (69% of all high aggressive PCa occurred among participants older than 60 years, $p < 0.0001$). Among those who had high aggressive PCa, 57% were African American (AA) and 43% were European American (EA). Among participants who were

diagnosed with high aggressive PCa, 64% were never screened, compared to 82% in the low aggressive PCa group who were never screened.

Characteristics, such as marital status, education, income, insurance, comorbidity, and smoking status, also differed by PCa aggressiveness ($p < 0.05$) (Table 2).

Association between neighborhood deprivation and high aggressive PCa: crude model

A greater odds of high aggressive PCa (Table 3, crude model) was observed among participants residing in the most deprived neighborhood (quintile 5) compared to those in the least deprived neighborhoods (quintile 1) (OR=1.57, 95% CI=1.20-2.05).

Associations between neighborhood deprivation and high aggressive PCa: multivariable multi-level model

In the model adjusted only for age (Table 3, Model 1), 57% increased odds of high aggressive PCa was observed among participants who were residing in the most deprived neighborhoods compared to participants residing in the least deprived neighborhoods (aOR=1.57, 95% CI=1.20-2.05). Participants grouped as quintile 4 also had 44% increased odds of high aggressive PCa compared to quintile 1 (aOR=1.44, 95% CI=1.10-1.88).

Model 2 adds race to Model 1 and Model 3 adds income to model 2. The association between neighborhood deprivation and PCa aggressiveness was attenuated when race was added to Model 1 (Model 2: aOR=1.27, 95% CI=0.94-1.70). No association between neighborhood deprivation and PCa aggressiveness was observed in Model 3 after adjustment for age, race, and income (aOR=1.07, 95% CI=0.77-1.48).

The final model (Model 4) adjusted for age, education, insurance status, and family history of PCa showed an association between neighborhood deprivation and PCa aggressiveness. Participants residing in the most deprived neighborhood had 50% increased odds of high aggressive PCa compared to participants in the least deprived neighborhoods (aOR=1.50, 95% CI=1.10-1.96) (Table 3).

Interaction between ADI and race

Since both ADI and race have an individual effect on PCa aggressiveness, interaction is likely present between ADI and race. Therefore, the modification of neighborhood effect on PCa aggressiveness by race was tested by calculating interaction on both additive and multiplicative scales.

Additive interaction between ADI and race was observed that indicated modification of the effect of neighborhood deprivation on high aggressive PCa by race (Table 4). A substantial increase in the odds of high aggressive PCa was observed among the AA men residing in the most deprived neighborhoods (OR=1.55, 95% CI=1.30-2.25) compared to EA residing in the least deprived neighborhoods.

The RERI of 0.61 (95% CI=0.10-1.14) suggests the presence of a super-additive interaction, where the combined effect of ADI and race is larger than the sum of the individual effects of ADI and race. Since the 95% CI does not include 0, the interaction test on an additive scale is statistically significant. The presence of additive interaction between ADI and race suggests that the risk of high aggressive PCa among AA men is increased if they live in a deprived neighborhood. The test for multiplicative interaction indicates no presence of interaction between ADI and race.

Discussion

The objective of this study was to assess the effect of neighborhood deprivation on PCa aggressiveness. Increased odds of high aggressive PCa among participants residing in deprived neighborhoods was observed. The results of this study are consistent with the findings from previous studies (29, 47-50). A study by Zeigler-Johnson et al. using Pennsylvania State Cancer Registry data found that the highest quartile of neighborhood deprivation, measured by six US census indicators, was associated with a high Gleason score at diagnosis (29). Another study that evaluated 14,663 census variables also reported positive associations between neighborhood level indicators and PCa aggressiveness (47). There is a wide range of literature about the effect of neighborhood-level factors on PCa, however, only few studies take into consideration the role of multiple neighborhood-level indicators.

The association between ADI and high aggressive PCa was no longer present after adjusting for race in the model (Models 2 and 3). This is likely because of the interacting effect between race and ADI. Race represents a complex social construct rather than a biological categorization. In many epidemiologic studies, self-reported race is used to simply classify participants into two or more large groups that ignore the underlying social construct and health care disparities that may lead to adverse health outcomes. The present study adds the role of underlying social construct and health care disparities as assessed by ADI to the body of literature. A study conducted by

357 Dess et al. reported that when there was equal access to health care, the PCa
358 outcomes do not differ by race (51). The same study concluded that factors that
359 characterize the social determinants of health, such as education, insurance status, and
360 family history of PCa were important risk factors for PCa aggressiveness. Findings from
361 the final model and sequential models (Models 2 and 3) along with interaction tests
362 provide comprehensive findings of the relationships between neighborhood deprivation
363 and race with PCa aggressiveness.

364 The existence of additive interaction suggests modification of the effect of neighborhood
365 deprivation on high aggressive PCa by race. Findings from this study indicate that AA
366 men residing in the most deprived neighborhood had greater odds of high aggressive
367 PCa than the sum of the individual effects of race and neighborhood deprivation. The
368 synergistic effect between race and neighborhood deprivation augmented the effect of
369 neighborhood deprivation on high aggressive PCa among AA men. This result supports
370 the research findings that AAs residing in deprived neighborhoods experience greater
371 health consequences compared to other racial groups (52-55). The additive interaction
372 between ADI and race reflects greater public health importance since it can inform
373 decision-makers to target AA residing in deprived neighborhoods, for which the public
374 health intervention is most effective (36-39). The increased odds of high aggressive
375 PCa among AAs residing in deprived neighborhoods might be the consequence of
376 many things including long-term discrimination, racial segregation, and inequalities in
377 access to health care. A study by Major et al. also found an interacting effect between
378 race and neighborhood deprivation among PCa patients (48). Another study using
379 Veterans Affairs health care system data found that access to care was the most

important determinant of aggressive PCa (26). The study concluded that given equal access to healthcare, cancer outcomes are likely to be similar among AAs and EAs.

To our knowledge, this is the first study to examine the effect of neighborhood deprivation, measured using ADI, on high aggressive PCa. Unlike other independent measures of neighborhood deprivation, such as neighborhood socioeconomic status, median household income, median high school education, % population with public assistance, ADI takes into account a total of 17 relevant neighborhood indicators of social determinants of health (33). While many neighborhood-level studies were analyzed at the census tract level using only a few indicators, this study used the data from smaller geographical units (census block groups) to identify the neighborhood deprivation by calculating a composite socioeconomic disadvantage score.

This study noted substantial disparities between the neighborhoods; the mean ADI score ranged from -111.89 to 136.08 for the block groups (data not shown). The distribution of participants by ADI quintile was different by race, and other individual-level risk factors, such as income, marital status, insurance status, smoking status, CCI, and PCa screening status (Supplementary Table S1). As documented in many previous studies, this study also found that AAs are more likely to reside in deprived neighborhoods and have many individual-level risk factors compared to EAs, which substantially increase the odds of high aggressive PCa (29, 56). Maybe because of the lack of access to health care in the deprived neighborhoods, there is a synergistic effect of individual-neighborhood level risk factors that contributed to high aggressive PCa. By contrast, a study by Haas et al. showed that an area that was racially segregated did not have an association with high aggressive PCa (57). The contrasting result may be

due to the differences in study population size, age group, and size of the geographical unit.

This study has several limitations. Although relatively few, neighborhoods for participants missing complete address information could not be examined, and these participants on average had more aggressive PCa than the remainder of the cohort. Additionally, while this study is population-based and thus generalizable, it is limited to men with PCa residing in North Carolina and Louisiana who self-reported race as AA or EA. Furthermore, while a comprehensive ADI score with 17 factors was used, there were neighborhood level factors that were not captured in this score, including health care access and food environment that should be taken into consideration.

Despite the limitations, this study presents a comprehensive evaluation of individual and neighborhood-level risk factors in a large population-based PCa study while considering PCa aggressiveness. The study is one of the few that examines neighborhood socioeconomic disadvantage using the ADI, a measure that encompasses a broad range of 17 US census indicators that are highly relevant social determinants of health that may help explain the socio biologic mechanism of disease. As a composite measure, the ADI permits greater explanatory power than a single neighborhood socioeconomic status measure. Similarly, the use of census block group level data more accurately represents the socio-economic characteristics of a neighborhood.

Neighborhood deprivation is a significant risk factor for aggressive PCa, and AA are more likely to reside in deprived neighborhoods and thus have the greatest odds for

425 high aggressive PCa. AA men residing in deprived neighborhood should be targeted for
426 PCa early detection.

427

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Table 1. Characteristics of participants by state (N=2,034)

Characteristics	State			p-value
	Overall (N=2034)	Louisiana (n=1067)	North Carolina (n=970)	
Individual level				
Mean $\pm$ S.D Age	63 $\pm$ 8	64 $\pm$ 8	63 $\pm$ 8	0.0012*
Age group				
≤50 years	114 (5.60)	41 (3.85)	73 (7.53)	0.0017*
51 to 60 years	667 (32.79)	340 (31.95)	327 (33.71)	
61 to 70 years	852 (41.89)	464 (43.61)	388 (40.00)	
More than 70 years	401 (19.71)	219 (20.58)	182 (18.76)	
Ethnicity				
Not Hispanic/Latino	2007 (98.12)	1042 (98.30)	965 (99.59)	0.0031*
Hispanic/Latino	22 (1.08)	18 (1.70)	4 (0.41)	
Race				
African American	999 (49.12)	525 (49.34)	474 (48.78)	0.8301
European American	1035 (50.88)	539 (50.66)	496 (51.13)	
BMI				
Underweight	22 (1.09)	13 (1.23)	9 (0.94)	0.6696
Normal weight	368 (18.27)	201 (19.05)	167 (17.41)	
Overweight	860 (42.70)	441 (41.80)	419 (43.69)	
Obese	764 (37.93)	400 (37.91)	364 (37.96)	
Marital Status				
Married	1533 (75.41)	794 (74.70)	739 (76.26)	0.3703
Separated	76 (3.74)	36 (3.38)	40 (4.13)	
Divorced	215 (10.58)	121 (11.37)	94 (9.70)	
Single/never married	92 (4.53)	45 (4.23)	47 (4.85)	
Widowed	117 (5.76)	68 (6.39)	49 (5.06)	
Education				
High school or less	908 (44.64)	500 (47.00)	408 (42.06)	0.025*
More than high school	1126 (55.36)	564 (53.00)	562 (57.94)	
Insurance before diagnosis				
No	196 (9.70)	97 (9.18)	99 (10.28)	0.4027
Yes	1824 (90.30)	960 (90.60)	864 (89.72)	
Income				
Less than \$10,000	171 (9.25)	100 (10.70)	71 (7.78)	0.0038*
\$10,001 - \$40,000	698 (37.77)	378 (40.43)	320 (35.05)	
\$40,001 - \$60,000	324 (17.53)	156 (16.68)	168 (18.40)	
\$60,001 - \$80,000	216 (11.69)	106 (11.34)	110 (12.05)	
\$80,000+	439 (23.76)	195 (20.86)	244 (26.73)	
Charlson Comorbidity Index				

Table 1. Characteristics of participants by state (N=2,034)

Characteristics	State			p-value
	Overall (N=2034)	Louisiana (n=1067)	North Carolina (n=970)	
Mean (S.D)	1.01 (1.45)	1.02 (1.43)	1.00 (1.50)	0.6472
None	1016 (50.15)	515 (48.54)	501 (51.92)	0.8118
Mild	500 (24.68)	272 (25.64)	228 (23.63)	
Moderate	445 (21.96)	242 (22.81)	203 (21.04)	
Severe	65 (3.21)	32 (3.02)	33 (3.42)	
Smoking				
Never	677 (33.33)	354 (33.30)	323 (33.37)	0.9687
Past	1039 (51.16)	546 (51.36)	493 (50.93)	
Current	315 (15.51)	163 (15.33)	152 (15.70)	
Family History of PCa				
No	1461 (74.62)	752 (73.94)	709 (75.35)	0.4762
Yes	497 (25.38)	265 (26.06)	232 (24.65)	
Screening History				
Yes	1426 (77.16)	212 (21.63)	210 (24.19)	0.1906
No	422 (22.84)	768 (78.37)	658 (75.81)	
PCa Aggressiveness				
Low	1029 (50.59)	532 (50.00)	497 (51.24)	0.5348
Intermediate	643 (31.61)	333 (31.30)	310 (31.96)	
High	362 (17.80)	199 (18.70)	163 (16.80)	
Neighborhood level				
ADI				
Mean (S.D)	95.17 (22.26)	99.44 (19.08)	90.49 (24.47)	<0.0001*
ADI Quintiles				
Quintile 1 (least Deprived)	406 (20.00)	162 (15.23)	244 (15.15)	<0.0001*
Quintile 2	406 (20.00)	191 (17.95)	215 (22.16)	
Quintile 3	409 (20.00)	201 (18.89)	208 (21.44)	
Quintile 4	407 (20.00)	226 (21.24)	181 (18.66)	
Quintile 5 (most Deprived)	406 (20.00)	284 (26.69)	122 (12.58)	

*Significant p-values indicate differences by state at type I error=0.05. P-values were calculated from t-tests for continuous variables and Pearson chi-square or Fisher's exact tests for categorical variables.

Table 2. Characteristics of participants by PCa aggressiveness (N=2,034)

Characteristics	PCa Aggressiveness			p-value
	Low (N=1,029)	Intermediate (N=643)	High (N=362)	
Mean $\pm$ S.D Age	62 $\pm$ 8	63 $\pm$ 8	65 $\pm$ 8	<0.0001*
Age group				
≤50 years	69 (6.71)	34 (5.29)	11 (3.04)	<0.0001*
51 to 60 years	363 (35.28)	203 (31.57)	101 (27.90)	
61 to 70 years	423 (41.11)	281 (43.70)	148 (40.88)	
More than 70 years	174 (16.91)	125 (19.44)	102 (28.18)	
Site				
Louisiana	532 (51.70)	333 (51.79)	199 (54.97)	0.5348
North Carolina	497 (48.30)	310 (48.21)	163 (45.03)	
Ethnicity				
Not Hispanic/Latino	1016 (98.93)	634 (98.75)	357 (99.17)	0.8312
Hispanic/Latino	11 (1.07)	8 (1.25)	3 (0.83)	
Race				
African American	459 (44.61)	334 (51.94)	206 (56.91)	<0.0001*
European American	570 (55.39)	309 (48.06)	156 (43.09)	
BMI				
Underweight	11 (1.08)	7 (1.10)	4 (1.14)	0.1587
Normal weight	196 (19.16)	110 (17.21)	62 (17.61)	
Overweight	457 (44.67)	270 (42.25)	133 (37.78)	
Obesity	359 (35.09)	252 (39.44)	153 (43.74)	
Marital Status				
Married	805 (78.23)	487 (75.74)	241 (66.76)	0.0084*
Separated	34 (3.30)	25 (3.89)	17 (4.71)	
Divorced	101 (9.82)	62 (9.64)	52 (14.40)	
Single/never married	38 (3.69)	30 (4.67)	24 (6.65)	
Widowed	51 (4.96)	39 (6.07)	27 (7.48)	
Education				
High school or less	431 (41.89)	288 (44.79)	189 (52.21)	0.0031*
More than high school	598 (58.11)	355 (55.21)	173 (47.79)	
Insurance before diagnosis				
No	83 (8.11)	59 (9.25)	54 (15.04)	0.0006*
Yes	940 (91.89)	579 (90.75)	305 (84.96)	
Income				
Less than \$10,000	65 (6.92)	51 (8.69)	55 (17.08)	<0.0001*
\$10,001 - \$40,000	339 (36.10)	222 (37.82)	137 (42.55)	
\$40,001 - \$60,000	167 (17.78)	114 (19.42)	43 (13.35)	
\$60,001 - \$80,000	118 (12.57)	67 (11.41)	31 (9.63)	
\$80,000+	250 (26.62)	133 (22.66)	56 (17.39)	
Charlson Comorbidity Index				

Table 2. Characteristics of participants by PCa aggressiveness (N=2,034)

Characteristics	PCa Aggressiveness			p-value
	Low (N=1,029)	Intermediate (N=643)	High (N=362)	
Mean (S.D)	0.94 (1.39)	1.03 (1.50)	1.17 (1.51)	0.0285*
None	530 (51.61)	321 (50.16)	165 (45.96)	0.0196*
Mild	265 (25.80)	157 (24.53)	78 (21.73)	
Moderate	205 (19.96)	137 (21.41)	103 (28.69)	
Severe	27 (2.63)	25 (3.91)	13 (3.62)	
Smoking Status				
Never	375 (36.51)	206 (32.04)	96 (26.59)	0.0001*
Past	517 (50.34)	337 (52.41)	185 (51.25)	
Current	135 (13.15)	100 (15.55)	80 (22.16)	
Family History of PCa				
No	742 (74.87)	446 (72.40)	273 (77.78)	0.1754
Yes	249 (25.13)	170 (27.60)	78 (22.22)	
Screening History				
Yes	167 (17.63)	141 (24.31)	114 (35.51)	<0.001*
No	780 (82.37)	439 (75.69)	207 (64.49)	
ADI				
Mean (S.D)	93.70 (22.94)	96.10 (21.41)	97.70 (21.53)	0.0060*
ADI Quintiles				
Quintile 1 (least Deprived)	222 (21.57)	121 (18.82)	63 (17.40)	0.0009*
Quintile 2	223 (21.67)	117 (18.20)	66 (18.23)	
Quintile 3	219 (21.28)	134 (20.84)	56 (15.47)	
Quintile 4	183 (17.78)	143 (22.24)	81 (22.38)	
Quintile 5 (most Deprived)	182 (17.69)	128 (19.91)	96 (26.52)	

*Significant p-values indicate differences by PCa aggressiveness at type I error=0.05.

P-values were calculated from ANOVA for continuous variables and Pearson chi-square or Fisher's exact test for categorical variables.

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Table 3. Associations between neighborhood deprivation and high aggressive prostate cancer: multivariable multi-level model

	Crude Model	Model 1	Model 2	Model 3	Model 4
Characteristics	OR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)
ADI					
Quintile 1 (least deprived)	Reference	Reference	Reference	Reference	Reference
Quintile 2	1.00 (0.77-1.32)	1.03 (0.78-1.35)	0.95 (0.72-1.26)	0.86 (0.64-1.16)	1.01 (0.75-1.38)
Quintile 3	1.00 (0.68-1.21)	1.04 (0.79-1.36)	0.92 (0.70-1.21)	0.80 (0.60-1.08)	0.99 (0.74-1.32)
Quintile 4	1.45 (1.10-1.90)*	1.44 (1.10-1.88)*	1.25 (0.95-1.65)	1.08 (0.80-1.46)	1.34 (1.01-1.80)*
Quintile 5 (most deprived)	1.57 (1.20-2.05)*	1.57 (1.20-2.05)*	1.27 (0.94-1.70)	1.07 (0.77-1.48)	1.50 (1.10-1.96)*

Model 1: Adjusted for age

Model 2: Adjusted for age and race

Model 3: Adjusted for age, race, and income

Model 4: Adjusted for age, education, insurance status, and family history of PCa

*Significant association with high aggressive PCa: OR=Odds Ratio; aOR=adjusted Odds Ratio

Table 4: Measure of interaction on an additive scale

Exposures	OR	95% CI
African American and least deprived neighborhood	1.10	0.75-1.53
European American and most deprived neighborhood	1.03	0.72-1.47
African American and most deprived neighborhood	1.55	1.30-2.25
<u>Interaction test</u>		
Relative Excess Risk due to Interaction (RERI)	0.61	0.10-1.14

OR= Odds Ratio; CI= Confidence Interval

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