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**TITLE:** Active Surveillance for African-American Men with Prostate Cancer

**PRINCIPAL INVESTIGATOR:** Dr. Brent Rose

**CONTRACTING ORGANIZATION:** University of California, San Diego, La Jolla, CA

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# REPORT DOCUMENTATION PAGE

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<b>13. SUPPLEMENTARY NOTES</b>						
<b>14. ABSTRACT</b> Active surveillance (AS) is an appropriate method to avoid overtreatment for many men with early prostate cancer (PC). However, whether African-American (AA) men can safely undergo AS is controversial due to the higher risk of death from PC and the lack of data on AS in this population. We identified 5,774 men (1,456 AA, 4,318 non-Hispanic White (NHW)) that were initially managed with AS. Progression to definitive treatment was more common in AA men than NHW men (10-year cumulative incidence: 60.7% AA vs. 49.1% NHW, subdistribution hazard ratio (SHR) 1.18, p< 0.01). However, there were no significant differences in the cumulative incidence of metastases (10-year cumulative incidence: 1.96% AA vs. 2.80% NHW, SHR: 0.92, p=0.81), death from prostate cancer, (10-year cumulative incidence: 1.00% AA vs. 0.86% NHW, SHR: 1.16, p=0.69), or all-cause mortality (10-year cumulative incidence: 15.9% AA vs. 17.4% NHW, SHR: 0.91, p=0.14). We found that PSA velocity was strong predictor of progression to Gleason Grade Group 2 and 3. Furthermore, AA men were likely to experience progression at lower PSA velocities. These results show that surveillance can be a successful way to manage low-risk PC in AA men and to identify the safest way to follow AA men on surveillance.						
<b>15. SUBJECT TERMS</b> Prostate cancer, active surveillance, African-American, Race, Disparity						
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## TABLE OF CONTENTS

	<u>Page</u>
<b>1. Introduction</b>	<b>4</b>
<b>2. Keywords</b>	<b>4</b>
<b>3. Accomplishments</b>	<b>4</b>
<b>4. Impact</b>	<b>8</b>
<b>5. Changes/Problems</b>	<b>10</b>
<b>6. Products</b>	<b>11</b>
<b>7. Participants &amp; Other Collaborating Organizations</b>	<b>12</b>
<b>8. Special Reporting Requirements</b>	<b>14</b>
<b>9. Appendices</b>	<b>15</b>

## 1. INTRODUCTION:

Active surveillance (AS) is an appropriate method to avoid overtreatment for many men with early prostate cancer (PC). However, whether African-American men can safely undergo AS is controversial. Black men are 70% more likely to be diagnosed and 240% more likely to die from PC than White men suggesting their disease may behave more aggressively. Furthermore, very few Black men have been included in AS studies. We hypothesize that African-American men managed in a high quality, equal access health care system can safely undergo with AS with rates of disease progression and oncologic outcomes that are comparable to non-AfricanAmerican patients. Our study will employ the novel dataset of Veterans Affairs Health System patients from within the VINCI research platform. To test our hypothesis, we will identify Black and White men with low-risk PC who underwent active surveillance. We will then determine the rates of PSA progression, pathologic upgrading, and subsequent definitive therapy. We will report cancer outcomes for Black and White men managed with AS. We will seek to identify specific triggers for definitive therapy by investigating risk factors for metastases and PCSM in those undergoing AS. We also hypothesize that NLP tools can extract information from unstructured or semi-structured health records. This will unlock an enormous amount of information to enhance outcomes research for this and many other projects. These data will serve to differentiate indolent from aggressive disease and improve the physical health and quality of life of African-American men with PC by limiting overtreatment and unnecessary side effects.

## 2. KEYWORDS:

Prostate cancer, active surveillance, African-American, Race, Disparity

## 3. ACCOMPLISHMENTS:

**What were the major goals of the project?**

Major Task 1: Development of active surveillance cohort and assessment of follow-up

- Subtask 1: Obtain UCSD IRB
- Subtask 2: DoD-Level human research protection approval
- Subtask 3: Acquire and clean VINCI data in preparation for data analysis
- Subtask 4: Characterize the frequency of repeat PSA testing and prostate biopsy
- Subtask 5: Identify AS cohort defined by PSA frequency and repeat biopsy
- Subtask 6: Obtain important baseline covariates not included in standard structured databases through manual chart-review

Major Task 2: Investigate rates of disease progression and need for definitive treatment in men undergoing active surveillance

- Subtask 1: To determine the rates of PSA progression and PSA doubling time
- Subtask 2: To determine the rates of Gleason and volume upgrading on repeat biopsy
- Subtask 3: To determine the rate of subsequent definitive therapy

Major Task 3: Investigate oncologic outcomes and triggers for intervention in men undergoing active surveillance

- Subtask 1: To determine the rate of metastasis, prostate cancer-specific mortality and overall survival for African American and White men managed with active surveillance
- Subtask 2: To identify specific triggers for definitive therapy in men undergoing active surveillance

Major Task 4: Development and validation of Natural Language Processing (NLP) algorithms

- Subtask 1: To develop NLP algorithm to extract and classify biopsy data from pathology reports
- Subtask 2: To validate the NLP biopsy algorithm in an independent group of patients
- Subtask 3: To develop NLP algorithm to identify the first diagnosis of metastases from radiology reports and clinical notes
- Subtask 4: To validate the NLP metastasis algorithm in an independent group of patients

### **What was accomplished under these goals?**

Major Task 1

Major Task 1 and all associated sub tasks were completed in the prior reporting period.

Major Task 2

Major Task 2 and all associated sub tasks were completed in the prior reporting period.

Major Task 3

Major Task 3 and all associated sub tasks were completed in the prior reporting period.

Major Task 4

During the final reporting period, Major Task 4 and its subtasks were completed and published. In order to develop and validate an NLP tool to identify patients with metastatic prostate cancer, we identified 1,144,610 patients with prostate cancer within the Veterans Health Administration (VHA) identified through either diagnostic codes, biopsy results, or cancer registry inclusion. NLP logic required text describing a diagnosis or history, metastases, cancer and anatomy describing prostate cancer (Figure 1).

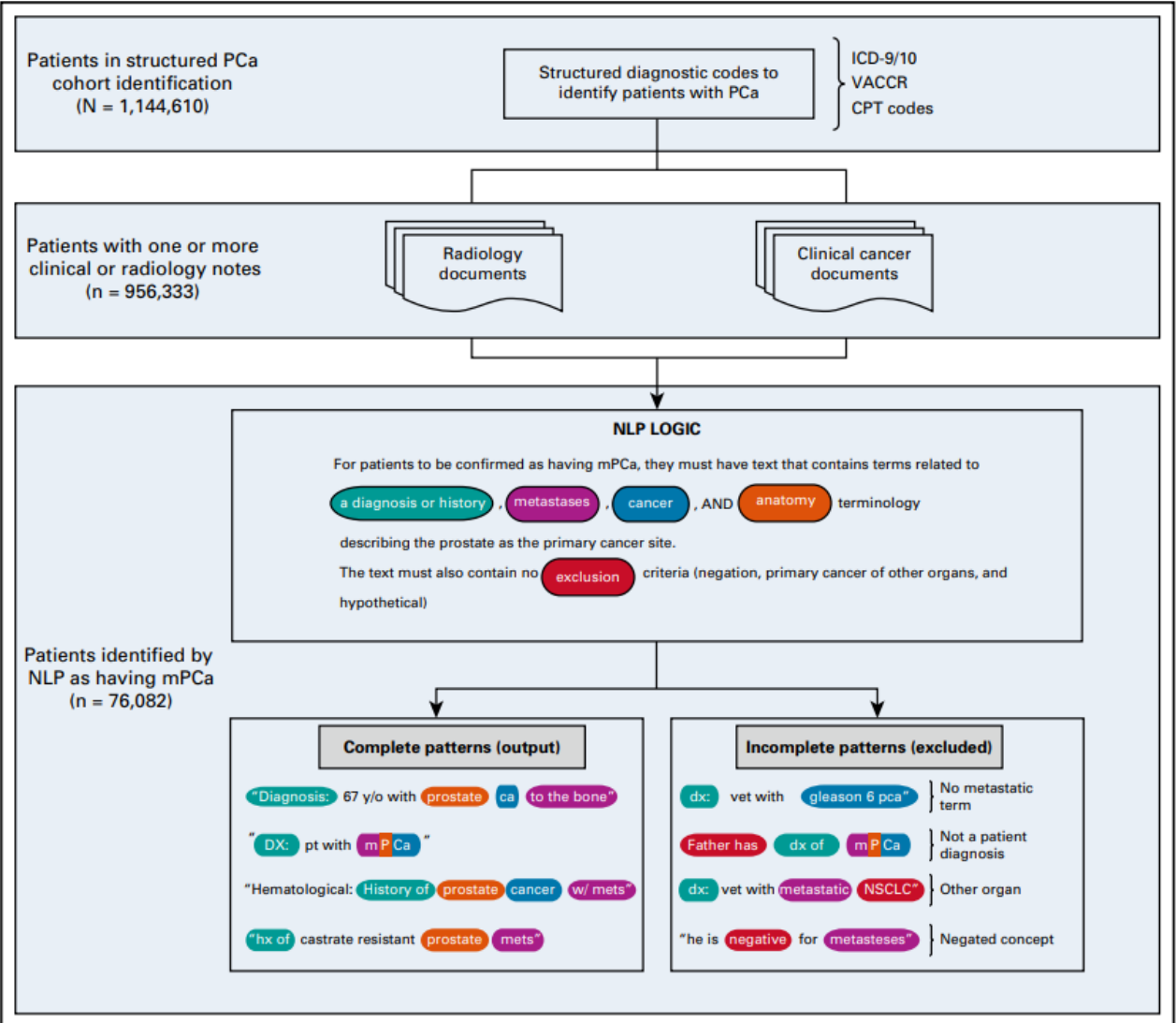


Figure 1. Simplified visualization of the complete system to identify patients with metastatic prostate cancer.

We identified 76,082 patients with metastatic prostate cancer and 1,068,528 patients with non-metastatic cancer. Patients with metastatic cancer tended to be younger, unmarried, and more likely to be African-American. We went on to validate the results of the NLP tool through manual review of 327 records. We found that the NLP tool had a specificity and sensitivity of 97.9% and 91.9%, respectively. The NLP tool also had a positive predictive value and negative predictive value of 96.9% and 94.4%, respectively (Table 1). Together, these results indicate excellent performance for identifying patients with metastatic prostate cancer. These findings were published in Alba et al, JCO Clin Cancer Inform, 2021.

Table 1. Performance comparison of alternative structured metastatic definitions.

mPCa Classification Method	Specificity	Sensitivity	PPV	NPV
NLP	0.979	<b>0.919</b>	0.969	<b>0.944</b>
Prescription alone <sup>a</sup>	<b>0.995</b>	0.596	<b>0.988</b>	0.776
Secondary ICD alone	0.953	0.809	0.924	0.875
Prescription or ICD	0.921	0.897	0.891	0.926

Abbreviations: ICD, International Classification of Diseases; mPCa, metastatic prostate cancer; NLP, natural language processing; NPV, negative predictive value; PPV, positive predictive value.

<sup>a</sup>Any patient prescribed abiraterone or enzalutamide before October 2019.

Bold text shows the highest performing definition for each performance metric in this validation.

We also developed a rule-based natural language processing (NLP) system to extract Gleason scores from clinical documents, including pathological reports from prostate specimens and reporting of pathological results in other cancer-related clinical notes, including clinical notes from Oncology, Radiation Oncology, Urology, and chemotherapy infusion providers. The NLP system extracted the highest reported Gleason score from each document. The system was evaluated with two validation studies. First, performance was assessed on 200 randomly selected pathology documents involving a prostate specimen. The system showed excellent performance, with an accuracy of 0.995, recall of 1.0, and precision of 0.988. We next validated the performance of the NLP algorithm on cancer-related non-Pathology documents by manually reviewing 100 extracted Gleason scores derived from these documents. This system showed a precision of 97%. This analysis was published as an appendix in Bryant et al. JAMA Oncology 2022.

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

This project has provided immense opportunities for professional development. Dr. Rose has closely collaborated with the mentors of the grant who are international leaders in the fields of prostate cancer and health disparities. They have been collaborating in both informal work and mentoring sessions as well as formal departmental and Health System-wide research presentations.

**How were the results disseminated to communities of interest?**

Nothing to report

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

Nothing to report

#### **4. IMPACT:**

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

Our publication in JAMA showed that active surveillance is safe and effective in African American men. This finding is critically important for the African American community for several reasons. First, low risk prostate cancer is extremely common in Black men. Prior to our work, the prevailing opinion was that active surveillance was not safe for Black men. This led to aggressive treatment and the associated side effects including erectile dysfunction, urinary incontinence and bowel problems. Due to our work many men will be able to safely undergo active surveillance and avoid these side effects. Additionally, the availability of active surveillance makes PSA screening more palatable since it reduces the main harm of screening which is overdiagnosis and overtreatment of indolent disease.

**What was the impact on other disciplines?**

These findings have clear and important implications for urologists, medical oncologists, and radiation oncologists. However, these results are also very important for primary care providers as they can substantially reduce the risk of PSA screening by reducing overtreatment of indolent disease. Finally, these results are very important for those who care about the role of access to medical care as a determinant of health care outcomes. We believe that one of the strengths of the study and the reason outcomes were similar is that the Veterans Health Administration reduces barrier to receipt of medical care which helps to reduce racial disparities.

**What was the impact on technology transfer?**

Nothing to report

**What was the impact on society beyond science and technology?**

The impact on society from this project is substantial. We believe that one of the strengths of the study and the reason outcomes were similar is that the Veterans Health Administration reduces barrier to receipt of medical care which helps to reduce racial disparities. This project is part of a line of research in our lab that is actively attempting to clarify whether poorer outcomes for African Americans is due to differences in biology or rather the result of barriers to receiving optimal medical care. On balance, we have found that when receiving care in an equal access 11 medical system like the Veterans Health Administration outcomes for African American men are equal to similar Non-Hispanic White men. These results have critical implications for health policy and social justice.

**5. CHANGES/PROBLEMS:**

Nothing to report.

**Changes in approach and reasons for change**

Nothing to report.

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

Nothing to report

**Changes that had a significant impact on expenditures**

Nothing to report

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

**Significant changes in use or care of human subjects**

Nothing to report

**Significant changes in use or care of vertebrate animals**

Nothing to report

**Significant changes in use of biohazards and/or select agents**

Nothing to report

**6. PRODUCTS:**

- **Publications, conference papers, and presentations**

**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

- **Website(s) or other Internet site(s)**

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?**

<i>Name:</i>	<i>Brent S. Rose</i>
<i>Project Role:</i>	<i>PI</i>
<i>Nearest person month worked:</i>	<i>6</i>
<i>Contribution to Project:</i>	<i>Dr. Rose performed and oversaw the entire project</i>
<i>Funding Support:</i>	<i>DOD grant PC171106 (present award), DOD grant PC 200113</i>
<i>Name:</i>	<i>Rishi Deka</i>
<i>Project Role:</i>	<i>Post-doctoral scholar</i>
<i>Nearest person month worked:</i>	<i>6</i>
<i>Contribution to Project:</i>	<i>Data processing and analysis</i>
<i>Funding Support:</i>	<i>DOD grant PC171106 (present award)</i>

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

During the study period, the PI received another DOD award (PC200113) for an unrelated project. There is no overlap with the present study.

**What other organizations were involved as partners?**

Organization Name: UC San Diego

Location of Organization: (if foreign location list country) 9500 Gilman Dr, La Jolla, CA 92093

Partner's contribution to the project (identify one or more) Facilities

Organization Name: VA San Diego health care

Location of Organization: (if foreign location list country) 3350 La Jolla Village Drive

San Diego, CA 92161-0002

Partner's contribution to the project (identify one or more) Facilities including the VINCI platform

**8. SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:**

**QUAD CHARTS:**

**9. APPENDICES:**