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Factors Influencing Treatment among Veterans with Advanced Prostate Cancer

Running Head: Advanced Prostate Cancer Treatment

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Precis: Clinical factors such as increasing age, comorbidities, and lower prostate specific antigen levels were associated with less toxic oral therapies as first-line treatment. African American

men were more likely to receive ketoconazole first-line than other evidence-based treatments, an effect somewhat attenuated when adjusting for facility characteristics.

Key words: prostate cancer, Veterans, novel agents, variation, care delivery

Text pages: 18

Tables: 3

Figures: 1

Supporting files: 2

Abstract

Background: Treatments for metastatic castration-resistant prostate cancer (CRPC) differ in toxicity, administration, and evidence. We evaluated clinical and non-clinical factors associated with first-line treatment for CRPC in a national delivery system.

Methods: We used national electronic laboratory and clinical data from the Veterans Health Administration to identify patients with CRPC (i.e., rising prostate specific antigen (PSA) on androgen deprivation), who received abiraterone, enzalutamide, docetaxel, or ketoconazole from 2010 through 2017. We determined whether clinical (e.g., PSA) and non-clinical factors (e.g., race, facility) were associated with first-line treatment selection using multilevel, multinomial logistic regression. We calculated the average marginal effects (AME) of patient, disease, and facility characteristics on ketoconazole versus more appropriate CRPC therapy.

Results: We identified 4,998 patients with CRPC who received first-line ketoconazole, docetaxel, abiraterone, or enzalutamide. After adjustment, increasing age was associated with receipt of abiraterone (adjusted odds ratio (aOR) 1.07, 95% credible interval (CrI) 1.06-1.09) or enzalutamide (aOR 1.10, 95% CrI 1.08-1.11) versus docetaxel. Greater pre-existing comorbidity

was associated with enzalutamide versus abiraterone (aOR 1.53, 95% CrI 1.23-1.91). Patients with higher PSA values at start of treatment were more likely to receive docetaxel than oral agents and less likely to receive ketoconazole than others. African American men were more likely to receive ketoconazole than abiraterone, enzalutamide, or docetaxel (AME 2.8%, 95% confidence interval (CI) 0.7-4.9%). This effect was attenuated when adjusting for facility characteristics (AME 1.9%, 95% CI -0.4-4.1%).

Conclusion: Clinical factors had an expected effect on first-line treatment selection. Race may be associated with receipt of guideline discordant first-line treatment.

Background

Prostate cancer is a leading cause of cancer death in men in the United States (US) and the most common non-skin malignancy among US Veterans.[1] Several treatment options exist for men with metastatic castration-resistant prostate cancer (CRPC), including chemotherapy (mitoxantrone, docetaxel, and cabazitaxel), oral androgen inhibitors (ketoconazole, abiraterone, and enzalutamide), immunotherapy (sipuleucel-T), and a radiopharmaceutical (radium-223). Each varies in side effect profile, mechanism of action, and resource use. While most improve survival and palliate symptoms for patients with metastatic CRPC, mitoxantrone and ketoconazole are considered palliative only, and thus are not generally used as a first-line treatment.[2-10]

The extent to which clinical and non-clinical factors impact variation in these treatments has implications for quality and consistency of care. There are some studies that demonstrate age, income, and region of the country may impact treatment patterns for these expensive drugs among commercially-insured patients.[11-13] However, claims-based studies have limited disease-specific information since they lack laboratory or imaging results and thus cannot adjust for disease status or delineate castration-resistant from castration-sensitive disease. We also have limited understanding of racial differences in treatment of advanced prostate cancer as African American men are under-represented in population-based studies and account for only 6% of clinical trial enrollment.[12] Better understanding the contributions of clinical and non-clinical factors in CRPC may guide priorities for clinical quality improvement.

In this context, we used the Veterans Health Administration (VA) national electronic laboratory and clinical data infrastructure to examine CRPC treatment patterns among a diverse

group of men with differing clinical and non-clinical factors. Importantly, the proportion of Veterans who are African American is higher than the general population, allowing us to better illuminate the implications of race on CRPC treatment patterns within a national system.

Methods

Cohort Identification

Using the VA Corporate Data Warehouse, consisting of aggregated medical record data from 130 facilities, we identified men with a diagnosis of prostate cancer using International Classification of Diseases, Ninth Revision (ICD-9) code 185 for 2010 through 2015, and ICD-10 code C61 for 2016 and 2017. Using pharmacy claims, we identified men with prostate cancer who received at least one of 8 medications used for CRPC treatment during this time period: mitoxantrone, ketoconazole, docetaxel, cabazitaxel, sipuleucel-T, abiraterone, enzalutamide, or radium-223. Since some patients enroll in the VA system while already receiving CRPC treatment, we further restricted the cohort to men confirmed to be receiving their prostate cancer care (i.e., androgen deprivation therapy (ADT)) within the VA system.

To ensure patients were castration-resistant, we required patients to be receiving ADT for at least six months prior to first therapy and to have a rising PSA while receiving ADT. Identifying castration-resistance has been challenging in claims data since ICD codes do not specify castration-sensitivity or resistance; thus, our utilization of PSA values allowed us to be confident in identification of men with CRPC. ADT was defined as at least two injections of a gonadotropin-releasing hormone analogue within the 8 months prior to receipt of first CRPC treatment or an orchiectomy in the prior 12 months. Medications were identified using inpatient and outpatient pharmacy data, Healthcare Common Procedure Coding System and Current Procedural Terminology codes. Finally, since only 29 patients (0.6%) received cabazitaxel, mitoxantrone, sipuleucel-T, or radium-223 as first-line CRPC treatment, we excluded these patients in the final analysis. Figure 1 illustrates development of the final cohort.

Exposure

Using the rigorous approach detailed above to ensure patients had castration-resistant disease, our primary exposure was first-line therapy for CRPC. First-line CRPC treatment is generally most effective given the relative naivety of the CRPC and thus an important choice.

Clinical and non-clinical factors

To determine *non-clinical* factors associated with first-line treatments, we collected information on race, year of treatment, and the facility where a patient was treated. Race was self-reported. Prior work among commercially-insured patients demonstrated African American men may be less likely to receive docetaxel than abiraterone or enzalutamide.[12] Year of treatment was assigned based on first administration of a treatment of inquiry. We expected patients would receive more docetaxel and ketoconazole in the earlier years of study with increasing use of abiraterone and enzalutamide in later years as they were approved midway through data collection.[11] Patients were assigned to a facility based on where the patient's first treatment was dispensed. The VA is divided into 130 health systems over 18 regional networks. We identified workforce capacity at the facility as the ratio of clinical full-time equivalent (FTE) units of physicians in a specialty clinic divided by the total number of patients in that specialty clinic. We expected patients treated in facilities with a lower workforce capacity would use more ketoconazole or docetaxel and have less access to novel oral therapies abiraterone and enzalutamide.

Clinical factors we expected to affect CRPC treatment selection included age, Charlson Comorbidity Index, and PSA indicators of cancer severity. We used the patient's age at time of first-line treatment initiation. Comorbidities were determined from those reported within the year prior to start of first treatment. We expected patients who were older and had more comorbid conditions would be less likely to receive docetaxel than the oral therapies since docetaxel has more associated toxic side effects. Finally, we used the PSA level at time of treatment and PSA doubling time as biomarkers of disease severity.[14,15] PSA at start of first-line treatment was determined by the PSA most proximal to time of first treatment. PSA doubling time was calculated using the PSA most proximal to first-line treatment and the lowest PSA value within the six months prior to first treatment. We expected patients with more aggressive disease based on higher PSA values and faster PSA doubling time would be more likely to receive docetaxel than oral therapies.

Statistical Analysis

We evaluated the association of different patient, facility, and time variables on receipt of first-line CRPC treatment. We first fit a Bayesian multilevel multinomial regression model to calculate odds ratios (OR) and 95% credible intervals (CrI) for each variable in the model. We included treating facility in the model as a random intercept. Weakly-informative normal (0,8) priors were chosen for each regression coefficient. Trace plots were checked to ensure parameter convergence.

To better understand differences in treatments observed by race and disease status after multivariable analysis, we conducted a series of sensitivity analyses. We first assessed whether disease status at start of first-line treatment differed by race. Furthermore, due to effects observed by race with regards to receipt of ketoconazole (considered a suboptimal comparator to the other first-line therapies due to lack of evidence for a survival benefit), we conducted a univariate logistic regression identifying patient, disease, and facility variables associated with ketoconazole versus other first-line CRPC therapies. To determine whether additional variables affected the association of race with receipt of ketoconazole, we then used an innovative analytic method of calculating the average marginal effects (AME) by sequentially adding covariates back into the model.[16] Finally, since ketoconazole and docetaxel were used most commonly in the earlier years, we conducted a similar analysis limited to the years 2013-2017 when all therapies were available for use.

We used R version 3.6.0 for our analyses; the Bayesian multilevel modeling was done using the brms R package.[17] This study followed the Strengthening the Reporting of Observational Studies in Epidemiology guideline for cohort studies.[18] This study was approved by the Veterans Affairs Ann Arbor Healthcare System Internal Review Board.

Results

Among 569,432 Veterans identified with prostate cancer between 2010-2017, 3.16% (n=17,991) received at least one of the CRPC treatments. After cohort restriction to patients with a rising PSA receiving ADT within the VA system, (i.e., considered castration-resistant), and excluding the <1% of patients who received the less commonly used first-line therapies, our final

cohort included 4,998 men with CRPC at 127 facilities who received abiraterone, enzalutamide, docetaxel, or ketoconazole as first-line treatment. (Figure 1)

Mean age was 73 (range 42-100 years), with 3,197 (64.0%) patients identified as white, 1,424 (28.5%) African American, and 377 (7.6%) other or unidentified race. (Table 1) The Supplemental Figure illustrates the marked shift in treatments used throughout the years, with ketoconazole and docetaxel used most commonly in earlier years (2010-2011) and a gradual substitution of abiraterone and enzalutamide for docetaxel and ketoconazole in later years.

Clinical and non-clinical factors associated with first-line CRPC treatment

After adjustment for other covariates, patients who were older had greater odds of receiving first-line abiraterone (adjusted odds ratio (aOR) 1.07, 95% CrI 1.06-1.09 for every year of age), or enzalutamide (aOR 1.10, 95% CrI 1.08-1.11) compared to docetaxel. There was also a preference for enzalutamide versus abiraterone in patients who were older (aOR 1.02, 95% CrI 1.01-1.03).

As shown in Table 2, patients with a Charlson Comorbidity Index of 2 or greater were more likely to receive enzalutamide compared to any of the other therapies (aOR 1.79, 95% CrI 1.31-2.45 versus docetaxel; aOR 1.53, 95% CI 1.23-1.91 versus abiraterone; and aOR 1.50, 95% CrI 1.08-2.08 versus ketoconazole).

We also found treatment year had an expected effect on first-line treatment with docetaxel and ketoconazole more likely to be used than abiraterone or enzalutamide in earlier years, and abiraterone more likely to be used than enzalutamide in years prior to enzalutamide approval, as demonstrated in Table 2.

Prostate cancer characteristics were associated with first-line therapy selection. Patients with a higher starting PSA (i.e., more severe disease) were more likely to receive docetaxel (aOR 1.44, 95% CrI 1.33-1.55), abiraterone (aOR 1.27, 95% CrI 1.18-1.37), or enzalutamide (aOR 1.17, 95% CrI 1.06-1.28) compared to ketoconazole. Those with higher starting PSA values were less likely to receive oral therapies abiraterone (aOR 0.89, 95% CrI 0.83-0.95) or enzalutamide (aOR 0.82, 95% CrI 0.75-0.89) compared to docetaxel. Similarly, Table 2 demonstrates patients with a slower PSA doubling time (i.e. > 3 months), suggesting less aggressive disease, had greater odds of receiving oral therapies abiraterone or enzalutamide versus docetaxel.

After adjusting for clinical and facility-level variables, race was not associated with first-line abiraterone, enzalutamide, or docetaxel over the others. There was a trend toward African American men having lower odds of receiving docetaxel or abiraterone over ketoconazole first-line (aOR 0.78, 95% CrI 0.60-1.02 for docetaxel; aOR 0.83, 95% CrI 0.64-1.08 for abiraterone), but the credible intervals crossed 1.

We further characterized whether the disease state of patients in our cohort at the time of first treatment differed by race. The median PSA at the time of first treatment was 41.2 ng/mL (interquartile range (IQR) 14.4-126.1) for all patients, and 58.8 ng/mL (IQR 18.2-180.2) for African American men, suggesting that the disease state at time of first CRPC treatment may be more advanced in African American men. In the entire cohort, men with higher PSA at start of first treatment were more likely to be started on docetaxel, abiraterone, or enzalutamide than ketoconazole. We saw a trend for the opposite effect among African American men despite the fact that African American men had higher starting PSA values. To understand why we were observing this opposite effect in African American men, we conducted additional sensitivity analyses with a multivariable logistic regression to determine the marginal effects of an African American man receiving ketoconazole, as a presumably less effective, or guideline discordant comparator, versus any of the other three therapies, with step-wise addition of the different therapies into the model.

The results of these sensitivity analyses demonstrate the change in predicted probability of an African American man receiving ketoconazole versus one of the other evidence-based treatments. (Table 3) Patient characteristics such as age and comorbidities, and year of treatment had little effect on whether African American men were more likely to receive ketoconazole. However, after adjusting for severity of disease, African American men were more likely than white men to receive ketoconazole versus other first-line treatments (AME 2.8%, 95% confidence interval (CI) 0.7%-4.9%). This effect was partially attenuated by accounting for facility characteristics (AME 1.9%, 95% CI -0.4%-4.1%). These effects remained when we limited this analysis to the years 2013-2017, but were not statistically significant. (Supplemental Table)

Discussion

In this cohort of US men with CRPC, we demonstrated clinical and non-clinical factors were associated with first-line treatment. Patients who were older or had more comorbidities were more likely to receive less toxic oral therapies compared to docetaxel, and more likely to receive enzalutamide versus abiraterone. Overall, patients with more aggressive prostate cancer characteristics were more likely to receive first-line docetaxel versus an oral therapy such as abiraterone, enzalutamide, or ketoconazole. However, despite having a higher starting PSA suggesting more advanced disease at the start of first treatment, African American men were more likely to receive ketoconazole (a drug with no known survival benefit) than the other first-line therapies, an effect that may be partly explained by a patient's treating facility. Taken together, these results identify the complexities in understanding CRPC care delivery, even in a national system aiming to mitigate financial and other access to care issues, including those impacted by race.

Older patients and those with more comorbidities receiving abiraterone or enzalutamide over docetaxel supports previous work among commercially-insured patients.[12] Docetaxel chemotherapy has more toxicities and can be more difficult to administer in elderly patients or those with more comorbid conditions. Less expected was that older and sicker patients were more likely to be prescribed enzalutamide over abiraterone. Since abiraterone has more potential cardiovascular complications and is administered with prednisone, providers may view this therapy with trepidation in patients with pre-existing hypertension or diabetes, measureable comorbid conditions commonly included in comorbidity indices. Interestingly, abiraterone was found to be better tolerated than enzalutamide in a recent study,[19] so this propensity for enzalutamide over abiraterone in older and sicker populations may change in the coming years.

Because abiraterone and enzalutamide were not approved for first-line use in CRPC until 2013 and 2014, respectively, our temporal effects were also expected.[3,5] Moreover, it is generally common for patients with higher PSA values or faster PSA doubling time, and thus more aggressive disease, to be prescribed docetaxel first-line rather than an oral agent. None of these treatments have been compared head to head, so it is unknown whether disease factors such as PSA doubling time should impact first-line treatment for CRPC. However, chemotherapy is generally expected to work more quickly in crisis situations with more aggressive disease and oncologists may be less likely to wait for an oral therapy to take effect.

More concerning was the observed racial differences in both the disease state at start of treatment, and subsequently, in prescribing patterns. Prior research among commercially-insured men with prostate cancer demonstrated African American men were more likely to be prescribed an oral agent over docetaxel compared to white men, but the reasons for this are not known and could be due to unmeasured factors such as patient preference.[12] In this study, we did not see that African American Veterans were more likely to receive abiraterone or enzalutamide over docetaxel, but we did see a trend by race in the use of ketoconazole over the other three evidence-based treatments. Ketoconazole is an oral antifungal agent that was found to have anti-androgen effects and thus was used traditionally for treatment of CRPC before other more effective agents were available. Unlike docetaxel, abiraterone, and enzalutamide, ketoconazole has not been demonstrated to improve overall survival in patients with CRPC and is not included in the guidelines for the treatment of CRPC. NCCN guidelines in 2010, before abiraterone or enzalutamide were available, list ketoconazole as a potential strategy to lower PSA but indicate that there is no known benefit to survival, unlike docetaxel.[20] When we looked at this association in a step-wise manner and adjusted for PSA, African American men appeared more likely to receive ketoconazole than the other guideline concordant therapies. That the unadjusted model did not demonstrate this difference likely reflects the fact that African American men in our cohort had higher PSA values at the time of first-line treatment. If African American men were being prescribed therapies based on their starting PSA alone, we should have seen in the unadjusted model that African American men were less likely to be prescribed ketoconazole than the other three therapies. Adjusting for treating facility, and less so for workforce capacity, mitigated some of the effect, suggesting that facility characteristics beyond workforce may explain this difference. Prior work has demonstrated that the hospital where a patient is treated, including demographics of the hospital patient population can affect treatment and quality of treatment a patient receives, even within the VA.[21-24] Quality of care associated with racial composition of a facility is an example of structural racism within the healthcare system.[25] Furthermore, while total drug costs and out-of-pocket expenses in the civilian setting may be higher for abiraterone and enzalutamide compared to ketoconazole, differences in out-of-pocket costs do not apply in an integrated single-payer system such as the VA where all medications have minimal copay.

A strength of this analysis was the high proportion of African American patients in our cohort. African American men account for 17% of men in the VA system, and 20% of men with prostate cancer in the VA. Yet, close to 30% of patients in our final cohort were African American. This large cohort of African-American men may reflect the increased rates of advanced disease among African American men since we only included men with CRPC. Furthermore, this analysis included ketoconazole, a therapy that was commonly used off-label to treat prostate cancer, but which is frequently not discussed in the current era of advanced therapeutics and not included in prior trials. A limitation, however, is that unlike abiraterone and enzalutamide, docetaxel and ketoconazole have indications for use other than CRPC. Since all patients included in this cohort started their treatment after being identified to have newly castration-resistant disease, we believe that treatment with these therapies was most likely directed at their CRPC. Another limitation was that we did not include diagnosis codes for metastatic disease so it is possible that patients may have had non-metastatic CRPC. Considering median PSA values at the start of any of the treatments were similar, we did not expect the presence of metastases to differ by first-line treatment. We did, however, consider the potential that coding for metastases may have been affected by pharmacy formulary restrictions for more expensive abiraterone or enzalutamide. For these reasons, we chose not to include a metastatic variable. Finally, all patients included in our final analysis received one of the treatments of inquiry and thus did not include patients with CRPC for which no treatment is given. Whether patient and facility-level factors influence whether a patient is offered treatment at all deserves further study. These limitations notwithstanding, our investigation highlights some of the important CRPC treatment predictors in a diverse cohort of men with advanced prostate cancer.

Conclusion

Comorbidity, age, and starting PSA were factors that accounted for some of the variation in how men were treated for CRPC in the US. Importantly, African American race may be associated with guideline discordant first-line treatment for CRPC. Some of this disparity was partially mediated through site of care; thus, future work should explore how structural racism impacts facility- and individual-level mediators of racial disparities. Furthermore, considering the disproportionately high number of African American patients in our cohort and the imbalance in PSA between African American men and white men at the start of treatment,

further study must be done to understand the extent to which race impacts the development and severity of CRPC. Now that additional therapies are being used in the metastatic castration-sensitive setting for longer periods of time, better understanding disparities in treatment will be critical to ensuring that all Veterans and non-Veterans are receiving optimal care.

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Figure 1 Title: Final Cohort of Veterans with Castration-Resistant Prostate Cancer

Figure 1 Legend: VA, Veterans Health Administration; ADT, Androgen Deprivation Therapy; PSA, Prostate Specific Antigen

[a]Treatment of inquiry: Abiraterone, Cabazitaxel, Docetaxel, Enzalutamide, Ketoconazole, Mitoxantrone, Radium-223, Sipuleucel-T

[b]Mitoxantrone: No patients received mitoxantrone as first-line treatment of inquiry

Supplemental Figure Title: First-Line Treatment Received Among Final Cohort by Year

Supplemental Figure Legend: Frequency of first-line treatments by year. Due to our required 6 months of pre-treatment follow-up, 2010 numbers only account for half of 2010 and thus may appear lower on this figure.

Table 2. Bayesian multilevel[a] multinomial regression of first line treatment among patients treated 2010 to 2017

	Abiraterone vs Docetaxel		Enzalutamide vs Docetaxel		Enzalutamide vs Abiraterone		Abiraterone vs Ketoconazole		Enzalutamide vs Ketoconazole		Docetaxel vs Ketoconazole	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Age at First Treatment, years	**1.07**	**(1.06, 1.09)**	**1.10**	**(1.08, 1.11)**	**1.02**	**(1.01, 1.03)**	0.99	(0.98, 1.00)	**1.02**	**(1.00, 1.03)**	**0.92**	**(0.91, 0.93)**
Race												
White	1.00		1.00		1.00		1.00		1.00		1.00	
African American	1.07	(0.85, 1.36)	1.12	(0.84, 1.50)	1.05	(0.84, 1.31)	0.83	(0.64, 1.08)	0.86	(0.62, 1.19)	0.78	(0.60, 1.02)
Other	0.92	(0.41, 2.15)	1.29	(0.48, 3.51)	1.38	(0.66, 2.89)	0.68	(0.30, 1.53)	0.95	(0.36, 2.60)	0.78	(0.34, 1.71)
Charlson Comorbidity Index												
0	1.00		1.00		1.00		1.00		1.00		1.00	
1	1.11	(0.86, 1.43)	1.18	(0.87, 1.62)	1.06	(0.84, 1.34)	1.22	(0.92, 1.61)	1.30	(0.93, 1.82)	1.06	(0.80, 1.40)
2+	1.16	(0.90, 1.51)	**1.79**	**(1.31, 2.45)**	**1.53**	**(1.23, 1.91)**	0.98	(0.74, 1.28)	**1.50**	**(1.08, 2.08)**	0.82	(0.61, 1.10)
Starting PSA, ng/mL	**0.89**	**(0.83, 0.95)**	**0.82**	**(0.75, 0.89)**	**0.92**	**(0.86, 0.99)**	**1.27**	**(1.18, 1.37)**	**1.17**	**(1.06, 1.28)**	**1.44**	**(1.33, 1.55)**
PSA Doubling Time												
< 3 months	1.00		1.00		1.00		1.00		1.00		1.00	
3 - <6 months	**1.51**	**(1.01, 2.27)**	**1.85**	**(1.09, 3.15)**	1.22	(0.80, 1.88)	0.91	(0.55, 1.52)	1.11	(0.60, 2.02)	**0.61**	**(0.37, 0.98)**
6 - <10 months	**1.85**	**(1.23, 2.80)**	**2.31**	**(1.35, 3.97)**	1.25	(0.82, 1.93)	0.86	(0.51, 1.42)	1.07	(0.58, 1.98)	**0.46**	**(0.28, 0.75)**
≥ 10 months	**1.74**	**(1.09, 2.76)**	1.64	(0.91, 3.00)	0.95	(0.59, 1.51)	1.02	(0.60, 1.75)	0.96	(0.48, 1.86)	0.58	(0.34, 1.00)
Year at Time of First Treatment												
2017	1.00		1.00		1.00		1.00		1.00		1.00	
2016	0.94	(0.64, 1.39)	0.81	(0.55, 1.22)	0.87	(0.68, 1.12)	1.17	(0.49, 2.83)	1.02	(0.41, 2.53)	1.26	(0.50, 3.33)
2015	0.96	(0.65, 1.43)	0.81	(0.54, 1.22)	0.83	(0.65, 1.08)	**0.32**	**(0.16, 0.66)**	**0.27**	**(0.13, 0.55)**	**0.34**	**(0.15, 0.74)**
2014	0.91	(0.63, 1.30)	**0.19**	**(0.12, 0.29)**	**0.21**	**(0.16, 0.29)**	**0.18**	**(0.09, 0.35)**	**0.04**	**(0.02, 0.08)**	**0.20**	**(0.10, 0.42)**
2013	1.00	(0.67, 1.50)	**0.06**	**(0.03, 0.10)**	**0.06**	**(0.03, 0.09)**	**0.07**	**(0.04, 0.13)**	**0.00**	**(0.00, 0.01)**	**0.07**	**(0.03, 0.15)**
2012	**0.19**	**(0.13, 0.28)**	**0.00**	**(0.00, 0.01)**	**0.00**	**(0.00, 0.03)**	**0.01**	**(0.01, 0.02)**	**0.00**	**(0.00, 0.00)**	**0.07**	**(0.03, 0.14)**
2011	**0.05**	**(0.03, 0.08)**	**0.00**	**(0.00, 0.00)**	**0.00**	**(0.00, 0.02)**	**0.00**	**(0.00, 0.01)**	**0.00**	**(0.00, 0.00)**	**0.06**	**(0.03, 0.12)**
2010	**0.00**	**(0.00, 0.00)**	**0.00**	**(0.00, 0.00)**	0.01	(0.00, 55.6)	**0.00**	**(0.00, 0.00)**	**0.00**	**(0.00, 0.00)**	**0.07**	**(0.04, 0.15)**
Site-level Urologist FTE Ratio[b]	0.99	(0.92, 1.06)	1.06	(0.96, 1.16)	1.05	(0.96, 1.14)	0.94	(0.88, 1.01)	1.01	(0.92, 1.12)	0.97	(0.89, 1.06)

Site-level HemeOnc FTE Ratio[b]	1.00	(0.98, 1.01)	1.00	(0.98, 1.02)	1.00	(0.98, 1.02)	1.02	(1.00, 1.05)	1.02	(0.99, 1.05)	**1.03**	**(1.00, 1.06)**

Abbreviations: OR, Odds Ratio; CI, Credible Interval; PSA, Prostate-Specific Antigen; FTE, Full-Time Equivalent

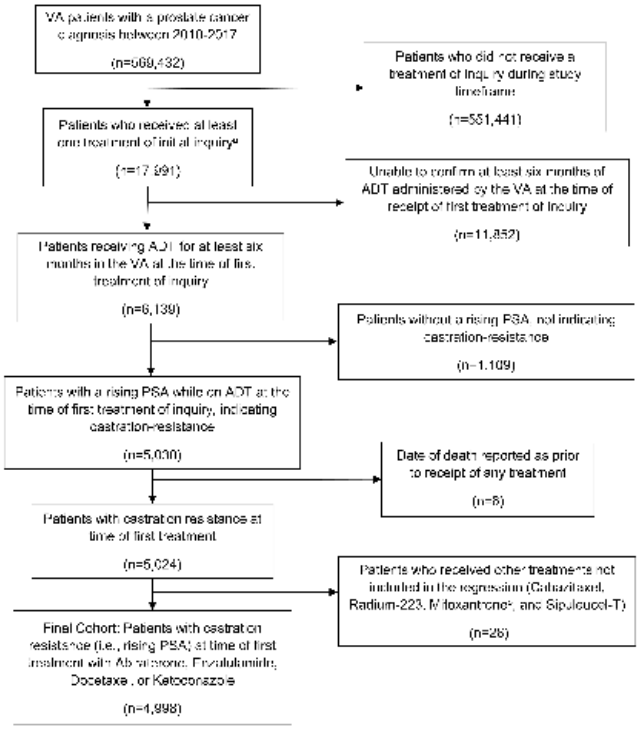
[a]Facility was included in the model as a random intercept.

[b]Site-level FTE Ratio defined as FTE per 10k patients in specialty.

The bolded numbers are statistically significant.

Bayesian multilevel multinomial regression of first-line treatment among patients with castration-resistant prostate cancer. This model includes 4,685 patients from the 118 facilities for which complete information on race and FTE ratio could be used. Patients from 9 sites (n=313) were not included in this regression analysis due to incomplete information on race or FTE ratio.

Figure 1. Final Cohort of Veterans with Castration-Resistant Prostate Cancer



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