


Sociodemographic and Geographic Disparities of Prostate Cancer Treatment Delay in Tennessee: A Population-Based Study

American Journal of Men's Health
November–December 1–10
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DOI: 10.1177/15579883211057990
journals.sagepub.com/home/jmh


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Abstract

The relationship of social determinants of health, Appalachian residence, and prostate cancer treatment delay among Tennessee adults is relatively unknown. We used multivariate logistic regression on 2005–2015 Tennessee Cancer Registry data of adults aged ≥ 18 diagnosed with prostate cancer. The outcome of treatment delay was more than 90 days without surgical or nonsurgical intervention from date of diagnosis. Social determinants in the population-based registry were race (White, Black, Other) and marital status (single, married, divorced/separated, widow/widower). Tennessee residence was classified as Appalachian versus non-Appalachian (urban/rural). Covariates include age at diagnosis (18–54, 54–69, ≥ 70), health insurance type (none, public, private), derived staging of cancer (localized, regional, distant), and treatment type (non-surgical/surgical). We found that Black and divorced/separated patients had 32% (95% confidence interval [CI]: 1.22–1.42) and 15% (95% CI: 1.01–1.31) increased odds to delay prostate cancer treatment. Patients were at decreased odds of treatment delay when living in an Appalachian county, both urban (odds ratio [OR] = 0.89, 95% CI: 0.82–0.95) and rural (OR = 0.83, 95% CI: 0.78–0.89), diagnosed at ≥ 70 (OR = 0.59, 95% CI: 0.53–0.66), and received surgical intervention (OR = 0.72, 95% CI: 0.68–0.76). Our study was among the first to comprehensively examine prostate cancer treatment delay in Tennessee, and while we do not make clinical recommendations, there is a critical need to further explore the unique factors that may propagate disparities. Prostate cancer treatment delay in Black patients may be indicative of ongoing health and access disparities in Tennessee, which may further affect quality of life and survivorship among this racial group. Divorced/separated patients may need tailored interventions to improve social support.

Keywords

Tennessee, Appalachia and non-Appalachia, health inequality/disparity, epidemiology of men's health, population-based, prostate cancer

Received August 4, 2021; revised October 14, 2021; accepted October 19, 2021

Introduction

Prostate cancer (PCa) is the second most common cancer among men in the United States, as well as the second leading cause of cancer death (American Cancer Society, 2020). Approximately 192,000 new PCa cases have been estimated in 2020 where 33,330 are projected to be fatalities in the United States (American Cancer Society, 2020; Siegel et al., 2020). Over the years, the 5-year relative survival rate for PCa has increased significantly to 98%

for all Surveillance, Epidemiology, and End Results (SEER) stages and nearly 100% when detected at the localized stage (Howlader et al., 2019; Siegel et al., 2020). This has been attributed to an earlier stage of diagnosis through prostate-specific antigen (PSA) testing and advances in treatments (Etzioni et al., 2008; Tsodikov et al., 2017).

Despite this improvement, disparities still exist in PCa treatment (Borno et al., 2019; Rawla, 2019; Wu & Modlin, 2012). African Americans or Black men have



both higher incidence and mortality rates compared to White men (Barsouk et al., 2020; Rawla, 2019). A study that examined temporal and spatial trends of highly aggressive PCa over a 10-year period reported that Black men in comparison to White men were more likely to have aggressive PCa (Wang et al., 2020). In addition to limited access to quality healthcare, Black men have significantly higher PSA levels and are less likely to undergo PSA screening (Hosain et al., 2011). Thus, the risk of developing and dying from advanced PCa disease and related complications compared to other racial/ethnic groups is increased (Ellis et al., 2018). While racial and ethnic groups are differentially affected by PCa outcomes in morbidity and mortality, geographic disparities have been reported to contribute to differential outcomes even among the same racial and ethnic groups (Ellis et al., 2018; Taitt, 2018). In the United States, the Appalachian region presents a unique geographical context concerning PCa due to the unique disparities that occur within this region in contrast to the non-Appalachian US (Yao et al., 2017). While cancer mortality has been reported to be in decline in the United States in general, disparities have been identified in Appalachian regions where rural Appalachia had the highest cancer incidence compared to urban non-Appalachian areas (Yao et al., 2017).

The Appalachian region of the United States is a 13-state geographic area that extends from New York to Mississippi, which is segmented into five subregions: Central, South Central, Southern, Northern, and North Central (Pollard et al., 2020). These subregions accommodate approximately 25.6 million or 8% of the U.S. population (Myint et al., 2019). According to the Appalachia Regional Commission, Whites are the largest racial group that reside in these Appalachian regions (Pollard et al., 2020). Kentucky's Appalachian communities provide an insight into the diversity that exists among these communities; that is, 94.7% of the Appalachian population is White (Myint et al., 2019). The Appalachian region while primarily White and having low racial/ethnic diversity, is still reported to have differential PCa outcomes within the region (Myint et al., 2018; 2019; Yao et al., 2017). There is a public health need for increased research in Appalachian regions concerning PCa and

disparities therein due to the limited existing studies (Yao et al., 2017), especially in the state Tennessee.

Disparities can be accounted for using the social determinants of health as well as availability and access to diagnostic and treatment services, type of health insurance or healthcare payer, marital status, neighborhood characteristics, and recommendations regarding PCa testing that may contribute to disparities in the form of treatment delay (Ellis et al., 2018; Taitt, 2018). While treatment delay does not generally equate to increased mortality, surgical treatment delay may be associated with PCa disparities through increased morbidity and decreased quality of life (Halpern & Holden, 2012). To further understand PCa treatment delay and disparities in Tennessee, we take into consideration sociodemographic characteristics as social determinants of health and geography of patients living within Appalachian counties.

The present study aimed to understand PCa disparities in Tennessee between Appalachian and non-Appalachian counties using surgical treatment delay as the outcome. In addition, we examined the relationship of social determinants of health and Appalachian residence on PCa surgical treatment, while accounting for multiple treatment and diagnostic confounders. The purpose of this study was not to make a clinical recommendation as we recognize the current debate on overtreatment of PCa (Lazzeri et al., 2020; Sun et al., 2012; van den Bergh et al., 2013; Xiao et al., 2013). This study intended to identify factors associated with the social determinants of health in PCa treatment delay and examine the relationship of racial and geographic differences among men in Tennessee.

Methods

Study Population

We used multivariate logistic regression on Tennessee Cancer Registry (TCR) data managed by Tennessee Department of Health. The TCR is a population-based registry and was established by Tennessee law to collect and monitor cancer among those diagnosed and/or treated for cancer in Tennessee (<https://www.tn.gov/health/>

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health-program-areas/tcr/tennessee-cancer-registry-data.html). The study population included all Tennessee residents with histologically confirmed prostate cancer based on the International Classification of Diseases for Oncology, third edition (ICD-O-3) behavior code diagnosed from January 1, 2005 to December 31, 2015. Analysis was performed on adults 18 years and older ($N = 48,341$). Data used for this analysis are restricted but available by request to the Tennessee Department of Health—Tennessee Cancer Registry (<https://www.tn.gov/education/data/data-downloads/request-data.html>). All statistical analyses were conducted between September and December 2019 and results obtained January 2020. All analytical files are available by reasonable request.

Model of Prostate Cancer Treatment Delay

Outcome of Treatment Delay. Treatment delay was defined as more than 90 days (Freedland et al., 2006; Khan Masood et al., 2004; Korets et al., 2012). Delay was based on when patient was diagnosed with prostate cancer to the date when treatment, whether surgical or non-surgical, was provided and recorded in the TCR. It should be noted that there is no manner to distinguish observational strategies (e.g., active surveillance, watchful waiting) from the TCR. As such, the treatment delay may include individuals being treated with an observational approach.

Social Determinants of Health. From the TCR, we were able to use the following social determinants based on collected sociodemographic factors from the population-based registry. Race categories were non-Hispanic White, non-Hispanic Black, and Other; where other race included American Indian/Alaska Native and Asian or Pacific Islander. Marital status was categorized into single/never married, married/common law, divorced/separated, and widow/widower.

Geographic Residence. Patient residence was categorized as being in either an Appalachian or non-Appalachian county as defined by the Appalachian Regional Commission (Pollard et al., 2020). Appalachian Tennessee was further classified as urban or rural Appalachian based on the distressed and at-risk counties as defined by the Tennessee Department of Economic and Community Development in conjunction with metro and nonmetro categorizations using Rural-Urban Continuum Codes. Urban Appalachian counties included Hamilton, Knox, Sullivan, and Washington.

Covariates and Controls of Prostate Cancer Screening and Treatment. Age was categorized into 18–54, 55–69, and ≥ 70 based on the United States Preventive Services Task

Force prostate cancer screening recommendations. Type of health insurance categorized into non-insured/self-pay, publicly insured, or privately insured. Derived staging of cancer was categorized as localized, regional, or distant. Lastly, if patient with PCa opted for surgical treatment (e.g., radical prostatectomy) as intervention.

Statistical Analysis

Multivariate logistic regression was used to examine the relationship between social determinants, geographic residence, and prostate cancer treatment delay. All findings are reported in odds ratios (ORs) using a 95% confidence interval (CI) for significance criteria. Stata SE 16.1 (Stata Corp LLC., College Station, TX) was used for all analyses.

Ethics Approval

The research protocol and access to the data for this study went to full review by the Tennessee Department of Health Institutional Review Board (IRB) and was approved on 01 February 2018 (TDH-IRB-1057486). The National Institutes of Health—Intramural Research Program IRB—Human Research Protections Program—Office of Human Subjects Research Protections determined that our protocol did not involve human subjects and was excluded from IRB review (18-NIMHD-00722).

Results

Sample Descriptives

The mean age of patients with PCa was 66.6 years of age, with a range of 33 to 104 years of age. The sample was predominantly non-Hispanic White ($n = 39,563$; 82.2%) and married ($n = 28,951$; 78.4%). Patients were found to be living almost equally in non-Appalachian ($n = 25,331$; 52.5%) and Appalachian counties ($n = 22,947$; 47.6%); of the Appalachian sample, 18.3% (8,820) resided in urban Appalachia and 29.3% (14,127) in rural Appalachia. In addition, the sample was between the ages of 55–69 ($n = 26,229$; 54.3%), had public health insurance ($n = 23,768$; 56.4%), had localized staging ($n = 38,767$; 83.9%), opted for surgical intervention ($n = 23,595$; 52.8%), and did not delay treatment ($n = 32,654$; 80.1%). See Table 1 for complete sample descriptives.

Multivariate Logistic Regression

Non-Hispanic Black patients were associated with 32% increased odds (95% CI: 1.22–1.42) to delay prostate cancer treatment by more than 90 days when compared to non-Hispanic Whites. Divorced/separated patients

Table 1. Descriptives of Invasive Prostate Cancer Patients ($N = 48,341$).

	<i>N</i>	%	Mean	<i>SD</i>
Age (R:33,104)	48,341	-	66.6	9.3
Race				
White	39,563	82.1		
Black	8,168	17.0		
Other	429	0.9		
Marital status				
Single	3,383	9.1		
Married (common law)	28,951	78.4		
Divorced/Separated	2,763	7.5		
Widow/Widower	1,853	5.0		
Appalachian				
No	25,331	52.5		
Urban	8,820	18.3		
Rural	14,127	29.3		
Age group				
18–55	4,640	9.6		
55–69	26,229	54.3		
70 and older	17,472	36.1		
Insurance type				
No insurance/self-pay	638	1.5		
Public insurance	23,768	56.4		
Private insurance	17,756	42.1		
Derived staging				
Localized	38,767	83.9		
Regional	5,637	12.2		
Distant	1,793	3.9		
Surgical intervention				
No	21,123	47.2		
Yes	23,595	52.8		
Surgical treatment delay				
≤90 days	32,654	80.1		
>90 days	8,095	19.9		

had 15% increased odds (95% CI: 1.01–1.31) to delay prostate cancer treatment by more than 90 days when compared to single/never married patients. Patients living in urban Appalachian and rural Appalachian counties were at 11% lower odds (95% CI: 0.82–0.95) and 17% lower odds (95% CI: 0.78–0.89), respectively, to delay prostate cancer treatment by more than 90 days when compared to those living in non-Appalachian counties. Patients diagnosed at 70 and older were at 41% decreased odds (95% CI: 0.53–0.66) to delay prostate cancer treatment by more than 90 days when compared to 18–54-year-olds. Patients with regional and distant derived staging had lower odds of prostate cancer treatment delay (i.e., odds ratio [OR] = 0.81, 95% CI: 0.75–0.88; OR = 0.17, 95% CI: 0.14–0.22, respectively) compared to patients with localized staging. Patients that received surgical intervention were at 28% decreased odds (95% CI: 0.67–0.76) to delay prostate cancer

treatment compared to those that did not receive any surgical intervention. See Table 2 for more detail.

Discussion

This study examined social determinants of health and geographic residence of PCa treatment delay in Tennessee. Racial/ethnic disparities between Black and White men were found in our study. Previous studies have indicated that Black men had 32% increased odds of experiencing treatment delay for more than 90 days compared to Whites, ultimately indicating that racial/ethnic disparities remain crucial in addressing PCa treatment delay (Ellis et al., 2018). Similar findings have been previously reported (Kinlock et al., 2016; Mahal et al., 2014; Moses et al., 2016; Sacramento et al., 2019; Stokes et al., 2013). Stokes et al. (2013) used SEER database and observed longer time from diagnosis to treatment in Blacks than in

Table 2. Multivariate Regression of Surgical Treatment Delay in Prostate Cancer ($N = 33,413$).

	OR	95% CI		<i>p</i> -value
		Lower	Upper	
Race				
White	ref.	-	-	-
Black	1.32	1.22	1.42	0.000
Other	0.90	0.65	1.25	0.544
Marital status				
Single	ref.	-	-	-
Married (common law)	0.96	0.87	1.06	0.410
Divorced/Separated	1.15	1.01	1.31	0.032
Widow/Widower	0.86	0.73	1.01	0.064
Appalachian				
No	ref.	-	-	-
Urban	0.89	0.82	0.95	0.001
Rural	0.83	0.78	0.89	0.000
Age group				
18–54	ref.	-	-	-
55–69	0.96	0.88	1.05	0.344
70 and older	0.59	0.53	0.66	0.000
Insurance type				
No insurance/self-pay	ref.	-	-	-
Public insurance	0.93	0.74	1.17	0.527
Private insurance	0.92	0.73	1.16	0.484
Derived staging				
Localized	ref.	-	-	-
Regional	0.81	0.75	0.88	0.000
Distant	0.17	0.14	0.22	0.000
Surgical intervention				
No	ref.	-	-	-
Yes	0.72	0.67	0.76	0.000
Constant	0.46	0.36	0.59	0.000

White men, which becomes even more pronounced in high-risk groups. The resulting higher rates of recurrence and mortality in Black men were attributed to this racial/ethnic disparity (Stokes et al., 2013). Similarly, Sacramento et al. (2019) reported that non-Whites had 30% increased odds of experiencing treatment delay compared to Whites. Black men were significantly less likely to receive radical prostatectomy, brachytherapy, cryotherapy, and combination therapy compared to White men due to lack of medical insurance (Mahal et al., 2014; Moses et al., 2016). Mahal et al. (2014) has suggested that having medical insurance may reduce the health disparity between White and Black men with regards to PCa treatment (Mahal et al., 2014). Black men also tend to develop PCa at an earlier age, however, are more likely to be diagnosed with advanced-stage disease (Pietro et al., 2016; Powell et al., 2014; Trantham et al., 2013). Black men have a higher risk for early biochemical recurrence and metastasis, have shorter cancer-specific survival, and

are more likely to undergo PSA testing less frequently (Pietro et al., 2016; Powell et al., 2014; Trantham et al., 2013). Several studies have suggested Black patients with metastatic castration-resistant prostate cancer respond better than White men, (Borno et al., 2019; Halabi et al., 2019; Zhao et al., 2020) although the participation rate of Black men in treatment trials remain significantly low (Spratt & Osborne, 2015).

We found in our study that PCa patients that were divorced or separated had higher odds of experiencing treatment delay, which may be due to low social support. The impact of social support on treatment delay and overall quality of life among men with PCa and other malignancies has been well documented (Aizer et al., 2013; Du et al., 2012; Huang et al., 2018; Imm et al., 2017; Kamen et al., 2015; Matthews et al., 2012; Tyson et al., 2013; Zhou et al., 2010). For instance, Zhou et al. (2010) examined the longitudinal effect of social support on general health-related quality of life in men treated for localized

PCa and reported that high levels of social support may protect survivors against the stressful burden of treatment. Huang et al. (2018) reported that PCa patients who were divorced or separated at the time of their study reported worst survival outcomes independent of age, ethnicity, grade, stage, and sequence number. Aizer et al. (2013) also reported significantly higher risk of presenting with metastatic cancer, undertreatment, and lower survival in unmarried patients. Moreover, non-White men were reported to have lower survival when compared to White men due to low levels of social support (Du et al., 2012; Imm et al., 2017). Conversely, non-health profession social support networks that include male friends and family members may predispose Black men to avoid seeking medical care and treatment (Imm et al., 2017). Thus, identifying and connecting with the right social groups can serve as a coping mechanism and buffer for Black men dealing with PCa (Imm et al., 2017). For instance, Black women can play an instrumental role in the informed decision-making process for PCa screening among Black men (Allen et al., 2018; Owens et al., 2015). PCa screening becomes a shared decision-making process with romantic partners (e.g., spouse, partner, girlfriend) where Black women can provide health information and social support to their Black counterparts (Allen et al., 2018; Owens et al., 2015). While Black women may be eager to provide the necessary information and support in some cases (Allen et al., 2018), Black men will also often rely and seek guidance from their partners on issues concerning PCa screening and treatment (Owens et al., 2015). Future prostate cancer screening, prevention and intervention efforts among Black men should then include their romantic partners throughout the process.

We must also then consider geographic context, and the relationship place has with PCa and treatment delay. In our study, we found that patients in Appalachian counties with PCa were less likely to delay compared to non-Appalachian counties. We found, specifically, that rural Appalachians were less likely to delay than urban Appalachians when compared to non-Appalachians. While there are no current epidemiological studies on PCa of Appalachian and non-Appalachian Tennessee, the limited studies in other Appalachian states help put our findings in context. In the state of Kentucky, Myint et al. (2019) reported that the Appalachian regions had lower incidence of PCa but higher mortality rate in comparison to non-Appalachian regions and the US. Moreover, Appalachian Kentucky PCa patients had an increased probability of presenting advanced clinical cases, higher Gleason scores, higher PSA values, stage IV disease, and poorly differentiated tumor histology (Myint et al., 2019). Furthermore, McDonald et al. (2020) reported that urban non-Appalachia Pennsylvania had the highest incidence rate of PCa and aggressive PCa compared to rural and

urban Appalachian Pennsylvania. (2017) reported that US Appalachian areas may be experiencing increased PCa burden due to treatment delay, sometimes due to the rural or remote nature within the region. PCa disparities, however, may not only be attributable to only geography but possible interrelated factors ranging from access to screening and health services (Yao et al., 2017). Nonetheless, PCa patients from our study residing in Appalachian counties while having decreased odds of treatment, may be at increased risk of mortality.

Overall, PCa patients are more likely to delay treatment when compared to patients diagnosed with other cancer types. This delay may be in part due to the minimal to no significant impact on oncological outcomes when PCa treatment is delayed for a few months, especially for patients with low or intermediate risks (Helsper et al., 2017; Morini et al., 2018; O'Callaghan et al., 2017; Sun et al., 2012). Treatment delay in high-risk PCa patients has been associated with worse clinical outcomes (Fossati et al., 2017; Hsu et al., 2015; Qu et al., 2019; van den Bergh et al., 2013; Zanaty et al., 2018). A systematic review of 17 studies that assessed the timing of curative treatment on PCa outcomes reported that treatment delay with high risk PCa patients may increase the likelihood of incurable and lethal PCa (van den Bergh et al., 2013). In context of our findings, Black men and divorced or separated patients had significantly higher odds of treatment delay; that is, 32% and 15% respectively. As such, both Black and divorced/separated men could be considered to be high risk given that both have worse survival outcomes.

Public health researchers and medical practitioners must take into consideration the dynamic factors that may exacerbate health and access disparities among PCa patients in Tennessee. The state of Tennessee presents a unique public health dynamic circumstance when it comes to Appalachian versus non-Appalachian regions and urban versus rural distinctions to understand the geographic effects of PCa disparities. Distinctions must be made as Appalachian regions do not always equate as rural areas, as evidenced by our study. This is essential to take into consideration for future studies to not only account for geographical but ecological features within Appalachian and non-Appalachian counties. By focusing on these nuanced features from Appalachian and non-Appalachian counties we could better understand risk factors and attend the community effectively to then tailor prevention and intervention programs and mitigate ongoing disparities.

Limitations

Our current study contributed to the limited literature on PCa treatment delay in Tennessee, as well as assessed the

sociodemographic and geographic factors associated. While Tennessee is currently not covered in the Surveillance, Epidemiology, and End Results program (Seiber et al., 2015), we were able to leverage the TCR population-based database to examine treatment delay among racial/ethnic minorities in a unique geographical region. While our study was among the first and presents with many strengths, there are some limitations we must acknowledge. First, we were limited by the retrospective administrative variables available to us. For instance, the TCR did not collect socioeconomic status data (e.g., income, education), quality of treatment received by patients, nor treatment using observational approaches. Due to the progression and nature of prostate cancer, observational approaches are an important treatment option that need to be considered and collected by cancer registries. This is especially critical considering the risk-specific context of certain men, prostate cancer screening and treatment options, and other comorbidities. Also, some demographic variables collected may not be up-to-date since these variables are only collected at the time of diagnosis. Secondly, the results may not be generalizable to other regions or the entire US population. Tennessee is a unique geographic location due to its blend of large cities and remote communities. Nevertheless, the findings are important because they provide a better understanding of PCa health disparities and what affects at risk underserved or underrepresented groups as it relates to treatment delay in Tennessee.

Conclusion

We found that sociodemographic factors and geography were associated with PCa treatment delay. While PCa treatment delay was more pronounced in Black patients, we found that Appalachian compared to non-Appalachian differences emerged. Appalachian states have unique geographic factors to disentangle between urban and rural counties. Underlying factors such as quality and access to medical care, low participation in clinical trials, and levels of social support must be included in future studies to understand the contributors to the ongoing racial/ethnic and geographic/ecological cancer health disparities in Tennessee. Thus, all these factors need to be considered when developing tailored prevention programs to understand and address the disparities occurring among Black and divorced/separated patients residing in Appalachian and non-Appalachian counties with PCa. Future studies must assess the nuanced profiles within Appalachian region between urban and rural areas.

Acknowledgments

The content is solely the responsibility of the authors and does not necessarily reflect the views of the National Institutes of

Health. Tennessee Department of Health restricted data used in this study were obtained from the Office of Cancer Surveillance, Tennessee Department of Health. The use of these data does not imply the National Institutes of Health or Tennessee Department of Health agree or disagree with any presentations, analyses, interpretations, or conclusions herein, nor had any involvement with analyses, interpretations, conclusions, or manuscript development.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Drs. F. A. Montiel Ishino and F. Williams, and Mr. Kevin Villalobos were supported by the Division of Intramural Research, National Institute on Minority Health and Health Disparities, National Institutes of Health. No other funding to report.

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