Racial disparities in late-stage prostate cancer: a SEER analysis 2005-2015

Stephanie Rodriguez, BS, Andrew D. Sparks, MS, Hanbing Zhou, MS, Richard L. Amdur, PhD, Jianqing Lin, MD

Department of Medicine and Surgery, George Washington University, Washington DC, USA

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Introduction: *To evaluate the impact of prostate cancer screening guidelines on different racial and ethnic populations.*

Materials and methods: *Data was collected from the 2005-2015 Surveillance, Epidemiology, and End Results (SEER) program. Incidence of prostate cancer diagnosis was categorized and analyzed by stage, race/ethnicity, and age group. Appropriate univariate and multivariable statistical analysis was performed.*

Results: *The odds of being diagnosed with regional-stage prostate cancer in 2013-2015 were 1.3 times higher for black men, 1.3 times higher for Asian American/Pacific Islander (AAPI) men, and 1.2 times higher for white men when compared to 2005-2008. The odds of being diagnosed with distant-stage prostate cancer in 2013-2015 were 1.6 times higher for black men, 1.8 times higher for AAPI men, and 2.1 times higher for white men when compared to 2005-2008. In 2005-2008, 2009-2012, and 2013-2015 respectively, the odds of being diagnosed with distant-stage prostate cancer were 1.8 times higher, 1.7 times higher, and 1.4 times higher for black men compared to white men, and 1.5 times higher, 1.5 times higher, and 1.4 times higher for AAPI men compared to white men (all respective $p < .001$).*

Conclusions: *The proportion of late-stage prostate cancer has increased significantly in all US males regardless of race and/or ethnicity. From 2013-2015, all men had a higher chance of being diagnosed with regional or distant stage disease compared to years prior. Newly-diagnosed regional-stage disease increased the most over time in AAPI and black men, while distant prostate cancer increased the most over time in white men.*

Key Words: racial disparity, prostate cancer, SEER database

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Address correspondence to Dr. Jianqing Lin, George Washington University, 2150 Pennsylvania Ave, NW, Suite 1-208, Washington DC, 20037 USA

Introduction

Prostate cancer is the second most common cancer in U.S. males. Screening for prostate cancer began in 1992 when the American Urological Association (AUA) and the American Cancer Society (ACS) recommended annual prostate-specific antigen (PSA)-based screening for men 50 years and older.[1] During that time, PSA screening was widely adopted and

associated with increases in prostate cancer incidence. Since the adoption of these screening methods, recommendations by various entities have influenced prostate cancer incidence trends.

The US Preventive Services Task Force (USPSTF) recommended against screening for men 75 years of age and older in 2008 and for all men in 2012, citing "moderate certainty that the benefits of PSA-based screening for prostate cancer do not outweigh the harms".[2,3] The controversial recommendation was largely based on the conflicting results of the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO) and the European Randomized Study of Screening for Prostate Cancer.[4,5] The U.S.-based PLCO trial showed no mortality benefit from screening while the European trial showed a small reduction in prostate-cancer–related mortality.[5,6] Since the 2012 USPSTF recommendation to omit PSA screening, both the incidence of early-stage prostate cancer and rates of PSA screening have declined.[7,8] However, a 2016 National Cancer Data Base (NCDB) study found an increase in incidence of metastatic prostate cancer from 2007 to 2013.[9]

Few studies have demonstrated the effects of the USPSTF recommendation on minority groups specifically.[10,11] Racial and ethnic differences in prostate cancer incidence and mortality are well documented.[12,13] Disparities range the full spectrum of patient care including PSA-based screening and response to treatment.[11,14] Further examination of differences in initial rates of prostate cancer diagnosis by race/ethnicity is needed to distinguish factors precipitating disparity.

We hypothesize that the publication of the 2012 USPSTF recommendation posed a disproportionately negative impact on minority groups, thus leading to higher incidence of late stage disease in these populations. By examining the trends in stage-specific prostate cancer incidence for men aged 45 to 75 prior and subsequent to the 2008 and 2012 USPSTF recommendations, we hope to elucidate the impact of reduced screening on different patient populations by focusing on temporal trends in prostate cancer incidence by specifically investigating the year and race effect on the proportion of regional and distant-stage cancer diagnoses.

Materials and methods

Study population

Prostate cancer incidence data from 2005 through 2015 were obtained from 18 population-based cancer registries participating in the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute, which records all new cancer cases in 34% of the US population (SEER), and includes records obtained from hospital registries, pathology laboratories, and physician offices. The study was based on de-identified publicly available data, which is considered non-human participants research under the US Department of Health and Human Services' Office for Human Research Protection and does not require institutional review board review or informed consent. In this report, the study population of interest is all men with diagnosed prostate cancer.

Disease groups

Yearly cancer diagnosis frequency was categorized by stage (in situ/localized, regional, and distant), race/ethnicity (white, Asian/Pacific Islander, black, American Indian/Alaska Native), and age (45-54, 55-69, 70-75 years).

The stage category is based on SEER summary stage, which has been used for cases consistently since 2001. The SEER summary stage is a combination of the most precise clinical and pathological documentation of the extent of disease available in the medical record. In this study, regional-stage is defined as direct extension of the prostate tissue, regional lymph node involvement, or both (so any T3, any N1 or T3N1); distant-stage is defined as distant site with or without lymph node involvement (M1). Regional- and distant–stage disease were grouped together as late-stage disease for the focus of this study because the prostate cancer specific mortality is higher than in earlier disease states, though potentially reversible if appropriate screening is adopted. Cases categorized as "unknown/ unstaged/ unspecified" were excluded from our study.

Data analysis

The variables of this study includes year of diagnosis, age of diagnosis, race/ethnicity. The temporal analysis was conducted by comparing the proportion of incidence of same category from 2005 to 2015. Chi-square tests were used to examine the association between year of diagnosis and stage, race/ethnicity, and age. In order to make the pattern over time more clear, and to see the potential impact of 2008 and 2012 USPSTF recommendations, years of diagnosis were categorized into three groups (2005 to 2008, 2009 to 2012, and 2013 to 2015). To examine the independent effect of diagnosis year within each race, we used race-stratified, age-adjusted multivariable logistic regression models predicting diagnostic group (regional vs. in situ/ local and distant versus in situ/local). To examine the

independent effect of race within each year group, we used year group-stratified, age-adjusted multivariable logistic regression models predicting diagnostic group. We examined the race by year interaction to determine whether the temporal pattern differed by race, after adjusting for age group. SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) was used for data analysis with $p < 0.05$ considered significant.

Results

Demographic characteristics of study population from SEER

The study included all men diagnosed with prostate cancer in the SEER registry aged 45 to 75 from 2005 to 2015. The number of prostate cancer diagnoses initially increased from 2005 to 2007, then remained fairly stable from 2007 to 2011, and then declined in 2012, Figure 1a. White men (n = 137,754) made up the largest proportion of the study sample, followed by black men (n = 26,638) and AAPI (n = 9,150), Figure 1b. Men aged 60 to 69 had the highest proportion of diagnoses during the 10-year period, Figure 1c. During the 10-year period, distant-stage prostate cancer had the lowest incidence (3.9%) and in situ/localized prostate cancer had the highest incidence (81.6%), Figure 1d.

Racial/ethnic differences in regional- and distant-stage prostate cancer diagnoses

The proportion of regional- and distant-stage prostate cancer diagnoses over time

Of the 174,398 men included in our study, 6 785 men or 3.9% had distant-stage prostate cancer at diagnosis.

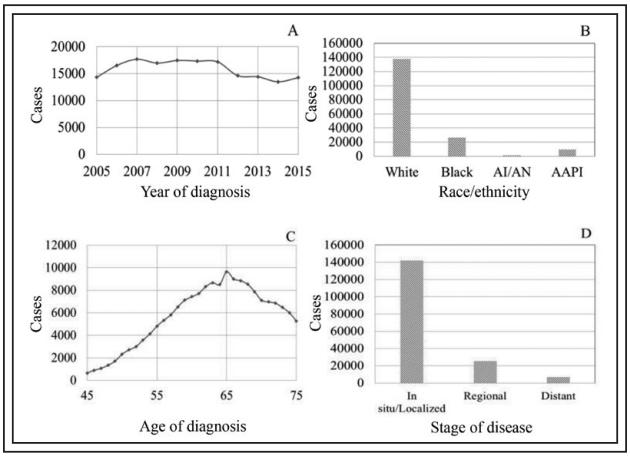

Figure 1. Frequency of prostate cancer diagnosis by year **(A)**, race/ethnicity **(B)**, age **(C)** and stage **(D)**, SEER 18, 2005-2015.

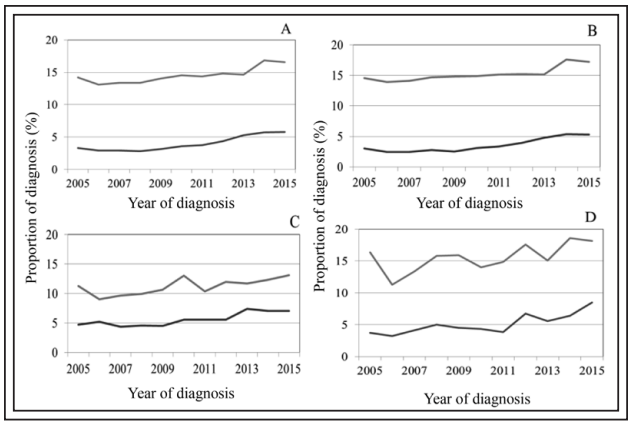

Figure 2. Proportion of regional- and distant-stage prostate cancer by year 2005-2015 (black = distant, grey = regional). **(A)** all men, **(B)** white men, **(C)** black men, **(D)** Asian or Pacific Islander men.

The proportion of regional- and distant-stage prostate cancer diagnoses for men aged 45-75 increased from 2005 to 2015 in all races, Figure 2. Distant-stage cancer diagnoses rose steadily beginning in 2009, with regional cancers following a similar trend beginning in 2010, Figure 2a. Regional-stage cancer increased from 14.2% of diagnoses in 2005 to 16.6% in 2015 ($p < .0001$). Distant-stage cancer increased from 3.3% of diagnoses in 2005 to 5.8% of diagnoses in 2015 ($p < .0001$). Overall, the largest year-to-year increase for distant-stage prostate cancer occurred from 2012-2013 with a 21.1% increase. The largest year-to-year increase for regional-stage prostate cancer occurred from 2013-2014 with a 15.0% increase, Figure 2a.

Late stage prostate cancer diagnosis among different racial/ethnic groups

The largest year-to-year increase in regional-stage diagnoses for white and AAPI men occurred from 2013-2014, following the overall group trend, Figure 2b and 2d. White men experienced a 16.1% increase and AAPI men experienced a 23.7% increase. Unlike white and AAPI men, black men display a lower proportion (11.2%) of regional-stage diagnoses relative to the overall population. However, an upward trend in regional-stage diagnoses has emerged since 2006, Figure 2c.

AAPI and black men experience higher proportions of distant-stage prostate cancer diagnoses, 5.1% and 5.6%, respectively, when compared to white men. The largest increase in the proportion of AAPI men diagnosed with distant-stage prostate cancer was seen from 2011-2012 with a 75.1% increase, Figure 2d. The largest increase in the proportion of black men

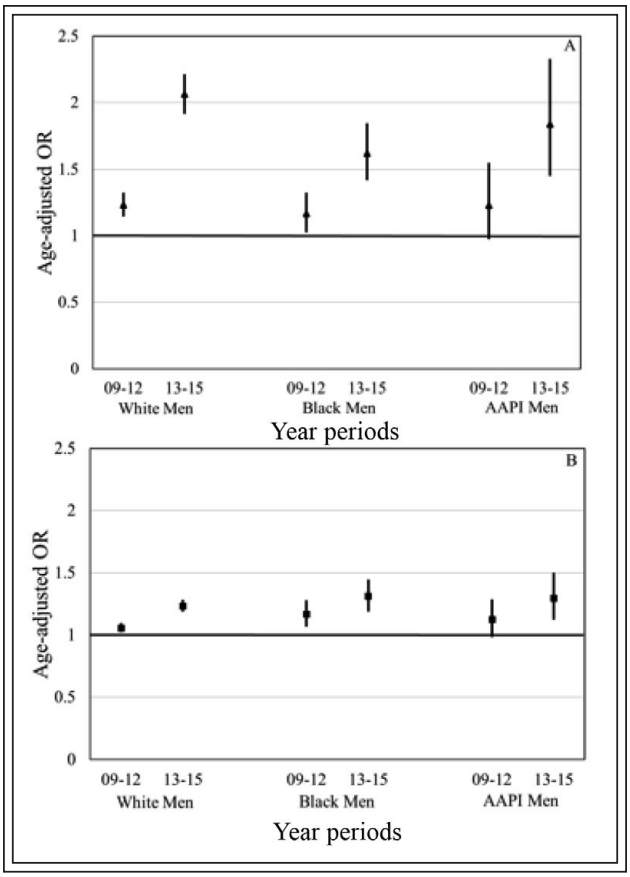

Figure 3. Adjusted odds ratio (OR, with 95% confidence interval) for prostate cancer in 2009-12 and 2013-15 versus 2005-08, stratified by race. Adjusted for age. **(A)** distant vs. in situ/localized. **(B)** regional vs. in situ/localized. Black line shows the odds for the reference group.

diagnosed with distant-stage prostate cancer was seen from 2012-2013 with a 32.3% increase, Figure 2c. The second largest increase for black men was seen from 2009 to 2010 with a 23.4% increase in the proportion of distant-stage diagnoses, Figure 2c. For white men, the proportion of distant-stage diagnoses closely mirrors the overall population trend with a steady rise beginning in 2009, Figure 2b.

The interaction between year of diagnosis and race/ethnicity

Both distant-stage and regional-stage models show significant year, race and age effects. The interaction terms of year of diagnosis x race are significant ($p < .001$) in both models, indicating that the effect of race on diagnosis significantly varied by year group and the effect of year group on diagnosis significantly varied by race. Figure 3 shows the age-adjusted odds ratio estimates of distant-stage and regional-stage prostate cancer, versus in situ/local cancer, stratified by race. The odds of being diagnosed with distant-stage prostate cancer increased through time for all men, with white men showing the highest odds ratio, Figure 3a. The odds of being diagnosed with distant-stage prostate cancer for white men was 2.1 times higher during 2013-2015 than during 2005-2008 (95% CI: 1.9-2.2), 1.8 times higher for AAPI (95% CI: 1.5-2.3) and 1.6 times higher for black men (95% CI: 1.4-1.9). Black men showed the largest increase over time in the odds of being diagnosed with regional-stage prostate cancer, Figure 3b. Their odds were 1.3 times higher during 2013-2015 than during 2005-2008 (95% CI: 1.2-1.5), while the odds were 1.3 times higher for AAPI (95% CI: 1.1-1.5) and 1.2 times higher for white men (95% CI: 1.2-1.3).

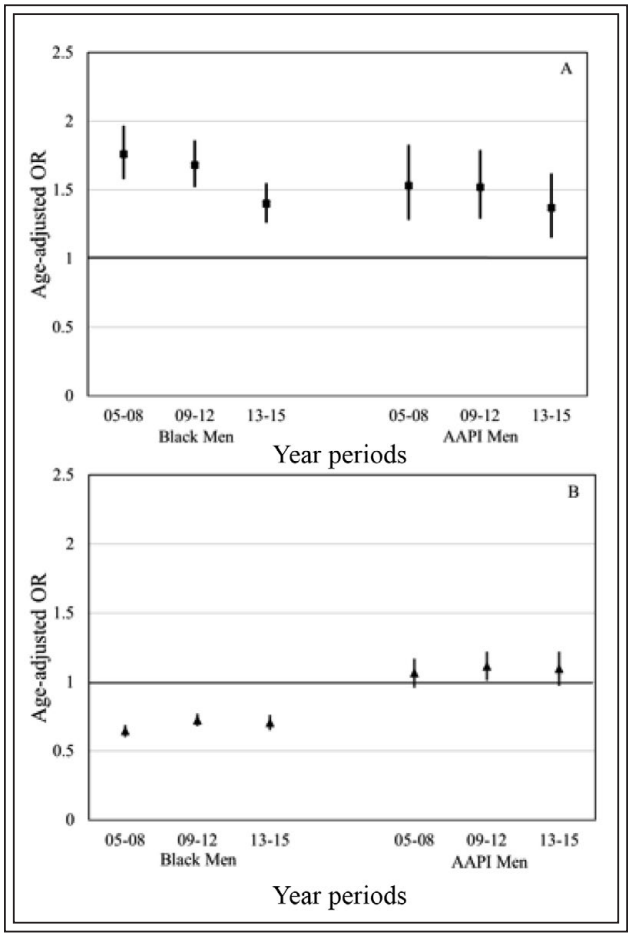

Figure 4. Adjusted OR (with 95% confidence interval) for prostate cancer in black and AAPI men when compared to white men, stratified by year. Adjusted for age. **(A)** distant vs. in situ/localized. **(B)** regional vs. in situ/localized. Black line shows the odds for the reference group.

Racial disparities in late-stage prostate cancer considering all the major variables

Figure 4 shows the age-adjusted odds ratio estimates of distant-stage and regional-stage prostate cancer versus in situ/local between races, stratified by year-group. In 2005-2008, 2009-2012, and 2013-2015 respectively, the odds of being diagnosed with distant-stage prostate cancer were 1.8 times higher, 1.7 times higher, and 1.4 times higher for black men compared to white men (all respective $p < .0001$), and 1.5 times higher, 1.5 times higher, and 1.4 times higher for AAPI men compared to white men (all respective $p < .001$), Figure 4a. In 2005-2008, 2009-2012, and 2013-2015 respectively, the odds of being diagnosed with regional-stage prostate cancer were 36% lower, 28% lower, and 30% lower for black men compared to white men (all respective $p < .0001$), Figure 4b. In 2005-2008 there was no significant difference for regional-stage prostate cancer diagnosis between AAPI and white men ($p = 0.2547$), nor was there a significant difference in 2013-2015 ($p = 0.1351$). In 2009-2012 the odds of being diagnosed with regional-stage prostate cancer were 1.1 times higher for AAPI compared to white men ($p = 0.0342$).

Discussion

Using the most recent population-based incidence data, we found a significant increase in the proportion of men diagnosed with prostate cancer presenting with late-stage disease from 2005 to 2015. The frequency of distant- and regional-stage prostate cancer rises steadily over this time period with significant increases after 2012 and 2013 in all U.S. male populations. We report some disproportionate trends of late-stage cancer among the racial/ethnic groups in the population studied. Men from minority groups experienced a larger increase over time in rates of newly diagnosed regional-stage prostate cancer from 2005 to 2015 in SEER registry areas, while white men experienced the largest increase in newly diagnosed distant cancers. Our data is consistent with data published by Dalela et al who found a significant increase in the incidence of metastatic prostate cancer among white men from 2009-2013.[10]

It is well documented that minority men experience higher rates of prostate cancer and aggressive disease when compared to their white counterparts.[11,12,14] Our study focused on the trend of late stage disease over the most recent 10 year period during which recommendation against PSA screening was published. These findings are important as the cure rate decreases when prostate cancer is diagnosed at later stages. We surmise the influence of PSA screening guidelines is the most likely reason all men experienced an increase in incidence of late-stage diagnoses. Other attributing factors may include the changes of biological aggressiveness of the disease, diagnostic imaging, etc.

Further studies should examine the effects of decreased screening recommendations on prostate cancer mortality rate by race/ethnicity to advise future PSA-based screening practices. Additional research is recommended to explore the relationship between insurance and minority status on the incidence of late-stage prostate cancer. Perhaps insurance status, as a health care and socioeconomic indicator, contributes to the incidence and diagnosis of late-stage prostate cancer. So underlying disparities faced by racial/ethnic minorities may enhance the adverse effects of the 2012 USPSTF grade D recommendation against PSA screening. As the minority community continues to exceed the average rate of late-stage prostate cancer, examination of factors to prevent metastases may be beneficial for patients from all backgrounds.

Most recently in May 2018, the USPSTF recommended shared decision making between patient and provider when discussing potential harms and benefits of PSA screening.[15] This is encouraging but it is possible that the recommendations did not adequately take into account the racial/ethnic differences among U.S. males. There is significant variability in PSA baseline, density, and velocity when comparing black and white men and patients with different ethnic backgrounds.[16-18] An individualized approach is needed since there might be differences in optimal PSA cutoff values among patients with different genetic backgrounds.[19] Physicians should always consider the factor that the diagnosis, management, and treatment of prostate cancer is adversely complicated by racial/ethnic and healthcare disparities.[14]

Despite the use of nationally representative data, our study is limited by a number of factors. First, we examined changes in the proportion of early-, regional-, and distant-stage prostate cancer but not incidence or incidence rates. However, given the large number of patients and healthcare facilities analyzed, it is likely the trends in proportion reflect national incidence patterns. Second, white men make up a large proportion (79%) of our study sample, thus highly influencing the overall trends. Third, we examined changes in prostate cancer frequency trends but not mortality rates, which require a longer monitoring period because of the long natural history of the disease. Fourth, we analyzed the year effects on prostate cancer diagnosis but not directly the PSA screening rates.

In summary, men from minority groups experienced a larger increase over time in the incidence of newly

diagnosed regional-stage prostate cancer after 2012 and 2013, the period after which the USPSTF recommending against PSA screening, while white men experienced a larger increase in newly diagnosed distant-stage cancers over the same time period. Changes in guidelines for screening may be responsible for this increase, although this was not directly investigated. In an effort to reduce racial/ethnic disparities in prostate cancer care, we propose careful consideration of patient's ethnic background when developing PSA-based screening guidelines.[1] □

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