# Incidence and mortality trends of metastatic prostate cancer: Surveillance, Epidemiology, and End Results database analysis

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## Abstract

**Introduction:** In the past decade, prostate cancer screening decreased, raising the concern of delays in diagnosis and leading to an increase in new cases of metastatic prostate cancer. This study evaluated whether these changes may have impacted trends in metastatic prostate cancer incidence and survival.

**Methods:** Metastatic prostate cancer diagnoses from 2008–2016 were identified from the Surveillance, Epidemiology, and End Results (SEER) 18 registries. Age-adjusted incidence rates per 100 000 were calculated by time periods and demographic variables. Two-year all-cause and prostate cancer-specific mortality were calculated for patients diagnosed from 2008–2014, and multivariable Cox proportional hazards models were used to evaluate the impact of demographic and clinical variables.

**Results:** Incidence rates of metastatic prostate cancer increased by 18% from 2008–2009 to 2014–2016 (incidence rate ratio [IRR]=1.18, 95% confidence interval [CI] 1.14–1.21). This trend was observed across multiple subgroups but was greatest in non-Hispanic Whites and patients living in counties 0–10% below poverty level. There was an overall decreased risk of all-cause and prostate cancer-specific mortality, but unmarried men and men living in counties >20% below poverty level showed statistically significant increased risk of prostate cancer-specific mortality.

**Conclusions:** Non-Hispanic Whites and the wealthiest subgroups had the largest increase in incidence of metastatic prostate cancer since 2008. Despite trends of decreased risk of prostate cancer-specific mortality, we found certain populations experienced increases in mortality risk. Studies exploring the role of socioeconomic factors on screening and access to newer treatments are needed.

## Introduction

Prostate cancer is the most common cancer in men in the U.S., with an estimated 191 000 new cases diagnosed in 2020.[1] Despite a five-year relative survival rate of greater than 99% for localized disease, metastatic prostate cancer (mPCa) remains the second leading cause of cancer-related death in men, with a five-year relative survival rate of 30.2%.[2] Prior studies have demonstrated that there has been an increase in the diagnosis of de novo mPCa in the last several years, perhaps related to the U.S. Preventative Services Task Force (USPSTF) recommendation against routine prostate cancer screening for men of all ages in 2012.[3-5] Considering that race/ethnicity and socioeconomic status have been shown to influence incidence and mortality of cancer, we examined demographic differences in incidence of de novo mPCa and survival from 2008–2016.[6,7]

## Methods

### Data sources and study sample

Data were queried from the Surveillance, Epidemiology, and End Results (SEER) Program's 18 Registries Research Data and Hurricane Katrina Impacted Louisiana cases based on the November 2018 submission using SEER*Stat 8.3.6 software.[8] SEER is sponsored by the National Cancer Institute to maintain and distribute cancer incidence and survival data from population-based cancer registries representing approximately 28% of the U.S. population based on the 2010 census.[8] The SEER registries collect information on the site and extent of disease, first course of cancer-directed therapy, and socio-demographic characteristics, with active followup for date and cause of death.[9] mPCA counts and population estimates generated from the incidence rate session, stratified by year of diagnosis, age group, race/ethnicity, region, poverty level, and stage, were extracted; health insurance status could not be considered for incidence rate analysis because it is not defined in the U.S. population

data. Individual data from mPCa cases among males 45 years or older from 2008–2016 were also extracted from the case session. For 2016 cases, SEER classified metastatic stages based on the American Joint Committee on Cancer (AJCC)'s seven staging criteria, with clinical or pathological indication.[10] Cases with any clinical or pathological indication of metastatic cancer were included. However, mPCa was defined using AJCC 6 staging criteria (M1a, M1b, M1c) for 2008–2015, which did not differentiate between clinical and pathological staging.[10] Cases with unknown stage or poverty level, or where survival time was zero months after diagnosis, were excluded.

## Study variables

Demographic variables included age group (45–54, 55–64, 65–74, 75–84, 85+ years), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Non-Hispanic Asian or Pacific Islander, Hispanic [all races]), region (East, Pacific Coast/Alaska, Northern Plains, Southwest), county measure of percent of persons below the federal poverty level (0–10%, >10–15%, >15–20%, >20%), and health insurance (insured, uninsured, unknown). The impact of 2012 screening recommendations was examined using time periods of 2008–2009, 2010–2011, 2012–2013, and 2014–2016.

## Statistical analysis

Multivariable Poisson regression models for rate analyses were used to calculate mPCA incidence rates and evaluate whether they differed by period, while adjusting for demographic variables and tumor stage. They included an offset using the log (population). Interactions between period and demographic variables or stage were included in separate models to assess whether there were differential trends by these factors. Adjusted incidence rates, presented as the number of mPCa cases per 100 000 persons, as well as adjusted incidence rate ratios (IRR) and Bonferroni-corrected 95% confidence intervals (CI), were reported. The Bonferroni correction using p=0.0019 (21 subgroup comparisons and five tests for interaction) was applied due to testing multiple comparisons.

Multivariable Cox proportional hazards models were used to determine whether there was a difference in two-year all-cause mortality and prostate cancer mortality between time periods and whether it was modified by demographic variables or stage. Time to the event (all-cause mortality and prostate cancer mortality) was the interval in months between diagnosis and the date of death, loss of followup, or December 2016, whichever was earliest. This analysis was restricted to patients diagnosed between 2008 and 2014 so that all patients had at least two years of followup after diagnosis. The time periods 2008–2009, 2010–2011, and 2012–2014 were compared. Because hazards of treatment

variables (chemotherapy, radiation, surgery) and stage were not constant over time, they were not included in the main analyses. As a sensitivity to the results, we performed models stratified by these treatment variables and the observed effects of time period and other adjustment variables were similar (Supplementary Table 1).

mPCa counts and population estimates were extracted from SEER*Stat software, version 8.3.6 (Surveillance Research Program, National Cancer Institute). All other statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, U.S.). Statistical significance was defined as p<0.05.

## Results

The study cohort consisted of 24 407 men diagnosed with mPCa from 2008–2016 (Table 1). More than half of patients (55.9%) were aged 65–84 years, non-Hispanic White (64.9%), and married (57.1%). The majority of the patients lived in the Pacific Coast (50.8%) and East regions (35%). Stage M1b disease was most frequent (74.3%), followed by M1c (19.6%) and M1a (6.2%). Poverty level varied among the cohort, with the highest number of patients falling 10–15% below the federal poverty level (33.3%).

Multivariable Poisson regression models of incidence trends are presented in Table 2. The increase in incidence trend was observed across several subgroups, including age, race/ethnicity, regions, and poverty levels (p<0.05 for all interactions). Comparing 2008–2009 to 2014–2016, patients 75–84 years of age showed a 24% increase in the mPCa incidence rate (IRR 1.24, 95% CI 1.15–1.35, p<0.001). Similarly, there was a 31% increase in incidence for patients living in counties 0–10% below federal poverty level (IRR 1.31, 95% CI 1.22–1.40, p<0.001). Patients living in counties >10–15% and >20% below poverty level also showed increases in mPCa incidence of 19% (IRR 1.19, 95% CI 1.18–1.454, p<0.001) and 18% (IRR 1.18, 95% CI 1.06—1.31, p<0.001), respectively.

The impact of interactions between time period and each variable on mortality rates was evaluated in separate survival models. Because none of these interactions were statistically significant (p<0.05), interactions were removed and models were re-run with main effects only, adjusted for all demographic variables (Table 3).

Despite increased incidence rates, men diagnosed with mPCa from 2012–2014 had a lower two-year cancer-specific mortality (hazard ratio [HR] 0.93, 95% CI 0.89–0.97, p=0.002) and overall mortality (HR 0.95, 95% CI 0.90–1.00, p=0.033) compared to those diagnosed in 2008–2009. Slight decreases in overall and cancer-specific mortality from 2008–2009 until 2010–2011 were not significant.

**Table 1. Patient characteristics**

| Variable | Total (n=24 407) |
|---|---|
|  | n (%) |
| Age group |  |
| 45–54 years | 1513 (6.2) |
| 55–64 years | 5615 (23.0) |
| 65–74 years | 7236 (29.6) |
| 75–84 years | 6426 (26.3) |
| 85+ years | 3617 (14.8) |
| Marital status |  |
| Married | 13 930 (57.1) |
| Unmarried | 8832 (36.2) |
| Unknown | 1645 (6.7) |
| Insurance status |  |
| Uninsured | 840 (3.4) |
| Insured | 22 709 (93.0) |
| Insurance status unknown | 858 (3.5) |
| Geographic region |  |
| Alaska, Pacific Coast | 12 396 (50.8) |
| East | 8535 (35.0) |
| Northern Plains | 2385 (9.8) |
| Southwest | 1091 (4.5) |
| Race/ethnicity |  |
| Non-Hispanic White | 15 845 (64.9) |
| Non-Hispanic Black | 4271 (17.5) |
| Non-Hispanic American Indian/Alaska | 165 (0.7) |
| Non-Hispanic Asian or Pacific Islander | 1404 (5.8) |
| Hispanic (all races) | 2722 (11.2) |
| Poverty level |  |
| 0–10% | 5060 (20.7) |
| >10–15% | 8136 (33.3) |
| >15–20% | 7583 (31.1) |
| >20% | 3628 (14.9) |
| Stage |  |
| M1a | 1502 (6.2) |
| M1b | 18124 (74.3) |
| M1c | 4781 (19.6) |

## Discussion

Previous reports have shown that the incidence of mPCa increased after 2007, which may be partially attributed to the 2008 USPSTF recommendation against screening in those 75 and older.[5] Advances in imaging and screening techniques in the past decade is another plausible explanation for this trend. However, newer guideline changes in 2012 recommending against routine screening for men of all ages further supports the argument that this trend is most likely related to reduced screening and/or access to care. This study explores whether this trend is similar among different demographic subgroups and the interaction with disease and overall survival.

We found that there was a significant increase in incidence among certain groups, most notably those who were non-Hispanic White, those who were 0–10% below federal poverty level, and those 75–84 years old. We hypothesize that non-Hispanic Whites, men who lived in counties 0–10% below poverty level, i.e., the least impoverished group, and men over 65, the age that Medicare begins, likely had better access to screening in the past and therefore were impacted the most during this time period.

Previous studies have demonstrated that lower socioeconomic status is associated with diagnoses of more aggressive cancers, such as prostate and breast, both of which have established screening methods.[11,12] After the changes in USPSTF guidelines on prostate cancer screening, patients in the lowest income brackets were likely impacted the least.[13]

Previous studies also described discrepancies in prostate cancer screening use in patients of different races. Caucasian men had shorter prostate cancer screening intervals as compared to African American men.[14] Likewise, there were more diagnoses of prostate cancer without prior history of screening in African American men as compared to in Caucasian men.[15] Interestingly, after controlling for socioeconomic factors, the disparity in prostate cancer mortality from 1992–1999 between African Americans and Caucasians was reduced significantly.[7] The recent trends in incidence of mPCa illustrated in our study further reinforces many of the conclusions drawn from the literature by highlighting certain demographic subgroups that benefited most from screening prior to the USPSTF guideline change.

Our results show that despite increases in mPCa incidence over time, the risk of prostate cancer-specific mortality decreased in later time intervals. Specifically, patients diagnosed from 2012–2014 showed a 7% reduction in prostate cancer-specific mortality, while patients diagnosed from 2010–2011 only showed a 4% reduction in prostate cancer-specific mortality when compared to those diagnosed from 2008–2009. These findings may reflect the recent advances in treatment for prostate cancer and/or improved access to care through the Patient Protection and Affordable Care Act, enacted in 2010. Studies using more granular data, including treatment information and insurance status, should be considered to examine these trends.

Certain subgroups demonstrated a lower risk of cancer-specific mortality, including those who were insured compared to uninsured and non-Hispanic Asian or Pacific Islander compared to non-Hispanic White. Not only is there an increased likelihood of advanced prostate cancer in uninsured patients compared to insured patients, but also insurance status acts as an important predictor for favorable treatment outcomes in patients with low-grade disease.[13] The decreased risk of cancer-specific mortality in patients of non-Hispanic Asian or Pacific Islander background for multiple types of cancer (lung, colorectal, prostate, breast) is less well-described in the literature and warrants further investigation.[16]

**Table 2. Adjusted metastatic prostate cancer incidence rates and incidence rate ratios by demographic subgroups, stage at diagnosis, and period with Bonferroni corrected CI, SEER 2008–2016**

| | Estimated incidence rates (CI) per 100 000 | | | | Estimated incidence rate ratios (CI) per 100 000 (ref=2008–2009) | | |
|---|---|---|---|---|---|---|---|
| | 2008–2009 | 2010–2011 | 2012–2013 | 2014–2016 | 2010–2011 | 2012–2013 | 2014–2016 |
| Overall | 4.22 (3.98–4.46) | 4.29 (4.05–4.53) | 4.63 (4.37–4.88) | 4.97 (4.72–5.22) | 1.02 (0.97–1.06) | 1.10 (1.05–1.14) | 1.18 (1.14–1.22) |
| Age group | | | | | | | |
| 45–54 years | 0.54 (0.47–0.62) | 0.57 (0.50–0.65) | 0.56 (0.49–0.64) | 0.63 (0.56–0.70) | 1.05 (0.88–1.27) | 1.03 (0.86–1.24) | 1.16 (0.98–1.37) |
| 55–64 years | 2.54 (2.33–2.75) | 2.49 (2.28–2.69) | 2.69 (2.48–2.90) | 2.87 (2.68–3.06) | 0.98 (0.89–1.08) | 1.06 (0.96–1.17) | 1.13 (1.04–1.23) |
| 65–74 years | 5.44 (5.01–5.88) | 5.86 (5.41–6.30) | 6.06 (5.62–6.49) | 6.55 (6.15–6.96) | 1.08 (0.98–1.18) | 1.11 (1.02–1.21) | 1.20 (1.11–1.3) |
| 75–84 years | 10.14 (9.34–10.95) | 10.43 (9.61–11.24) | 11.27 (10.42–12.11) | 12.61 (11.81–13.41) | 1.03 (0.94–1.13) | 1.11 (1.02–1.21) | 1.24 (1.15–1.35) |
| 85+ years | 18.10 (16.35–19.85) | 16.83 (15.21–18.45) | 20.22 (18.45–21.98) | 19.87 (18.40–21.35) | 0.93 (0.82–1.05) | 1.12 (1.00–1.25) | 1.10 (0.99–1.22) |
| Poverty level | | | | | | | |
| 0–10% | 4.26 (3.94–4.58) | 4.44 (4.12–4.76) | 4.72 (4.39–5.05) | 5.08 (4.77–5.39) | 1.04 (0.96–1.13) | 1.11 (1.02–1.20) | 1.19 (1.11–1.28) |
| >10–15% | 4.2 (3.89–4.51) | 4.07 (3.77–4.37) | 4.4 (4.08–4.71) | 4.63 (4.34–4.92) | 0.97 (0.89–1.05) | 1.05 (0.97–1.13) | 1.10 (1.03–1.18) |
| >15–20% | 4.31 (3.89–4.74) | 4.36 (3.94–4.78) | 4.83 (4.41–5.25) | 5.10 (4.73–5.47) | 1.01 (0.89–1.14) | 1.12 (1–1.26) | 1.18 (1.06–1.31) |
| >20% | 3.97 (3.59–4.35) | 4.24 (3.85–4.63) | 4.58 (4.18–4.98) | 5.19 (4.82–5.56) | 1.07 (0.95–1.20) | 1.15 (1.03–1.29) | 1.31 (1.18–1.45) |
| Race/ethnicity | | | | | | | |
| Hispanic (all races) | 4.21 (3.76–4.66) | 4.14 (3.71–4.56) | 4.45 (4.03–4.87) | 4.21 (3.89–4.53) | 0.98 (0.85–1.13) | 1.06 (0.92–1.21) | 1.00 (0.88–1.13) |
| Non-Hispanic American Indian/Alaska | 4.42 (2.56–6.29) | 4.11 (2.38–5.84) | 5.09 (3.24–6.94) | 5.02 (3.60–6.45) | 0.93 (0.51–1.69) | 1.15 (0.66–2.01) | 1.14 (0.68–1.89) |
| Non-Hispanic Asian or Pacific Islander | 2.78 (2.38–3.17) | 2.20 (1.86–2.53) | 2.6 (2.25–2.95) | 2.79 (2.51–3.07) | 0.79 (0.65–0.97) | 0.94 (0.77–1.13) | 1.00 (0.85–1.19) |
| Non-Hispanic Black | 9.45 (8.64–10.26) | 9.54 (8.75–10.32) | 9.52 (8.76–10.28) | 9.88 (9.24–10.51) | 1.01 (0.90–1.13) | 1.01 (0.90–1.12) | 1.05 (0.95–1.15) |
| Non-Hispanic White | 3.58 (3.41–3.76) | 3.74 (3.56–3.93) | 4.09 (3.90–4.28) | 4.54 (4.36–4.72) | 1.04 (0.98–1.11) | 1.14 (1.08–1.21) | 1.27 (1.20–1.33) |
| Region | | | | | | | |
| East | 3.78 (3.50–4.05) | 4.01 (3.73–4.29) | 4.15 (3.87–4.44) | 4.59 (4.32–4.87) | 1.06 (0.98–1.15) | 1.1 (1.02–1.19) | 1.22 (1.13–1.31) |
| Northern Plains | 4.15 (3.66–4.65) | 4.61 (4.10–5.13) | 4.84 (4.32–5.36) | 5.35 (4.88–5.82) | 1.11 (0.95–1.29) | 1.17 (1.00–1.35) | 1.29 (1.13–1.47) |
| Alaska, Pacific Coast | 4.91 (4.60–5.22) | 4.73 (4.44–5.03) | 5.23 (4.91–5.54) | 5.48 (5.19–5.77) | 0.96 (0.90–1.03) | 1.06 (1.00–1.13) | 1.12 (1.05–1.18) |
| Southwest | 3.46 (2.85–4.08) | 3.75 (3.13–4.37) | 4.57 (3.90–5.24) | 4.8 (4.25–5.35) | 1.08 (0.86–1.37) | 1.32 (1.06–1.65) | 1.39 (1.13–1.70) |
| Stage | | | | | | | |
| M1a | 1.04 (0.88–1.20) | 1.13 (0.96–1.29) | 1.24 (1.08–1.41) | 1.68 (1.52–1.84) | 1.09 (0.89–1.34) | 1.2 (0.98–1.46) | 1.62 (1.36–1.93) |
| M1b | 14.24 (13.41–15.06) | 15.38 (14.52–16.25) | 16.65 (15.74–17.55) | 17.79 (16.91–18.67) | 1.08 (1.02–1.14) | 1.17 (1.11–1.23) | 1.25 (1.19–1.31) |
| M1c | 5.02 (4.62–5.42) | 4.10 (3.75–4.44) | 4.35 (4.00–4.7) | 4.42 (4.12–4.72) | 0.82 (0.74–0.90) | 0.87 (0.79–0.95) | 0.88 (0.81–0.96) |

SEER: Surveillance, Epidemiology, and End Results.

Conversely, we also found that certain subgroups demonstrated an increased risk of cancer-specific mortality, notably patients who were unmarried compared to married and who lived in counties >20% below federal poverty level compared to 0–10% below poverty level. Unmarried men may lack the social support systems that are critical for cancer treatment and survival as compared to married men. Prior studies demonstrate marital status as a predictor of cancer mortality and prostate cancer-specific mortality.[17] Using the SEER registry data, unmarried men had higher risk of pros-tate cancer-specific mortality compared to that of unmarried men between 1988 and 2003.[18] Men living in areas below poverty level (>20%) likely suffer from lack of access to cancer-related treatments and care, which may contribute to the significantly higher risk of both prostate cancer-specific and all-cause mortality.[19] Although the results of our study show a direct association between percent below poverty level and increased risk of prostate cancer-specific mortality, only the >20% below poverty level group is found to be statistically significant.

**Table 3. Multivariable Cox proportional hazards models for all-cause and prostate cancer-specific mortality in men with metastatic prostate cancer, SEER 2008–2014**

| | All-cause mortality | | Prostate cancer mortality | |
|---|---|---|---|---|
| | HR[†] | p | HR[†] | p |
| Period (ref=2008–2009) | | | | |
| 2010–2011 | 0.97 (0.92–1.02) | 0.2 | 0.96 (0.92–1.01) | 0.09 |
| 2012–2014 | 0.95 (0.90–1.00) | 0.03 | 0.93 (0.89–0.97) | 0.002 |
| Age group (ref=20–54 years) | | | | |
| 55–64 years | 0.93 (0.85–1.01) | 0.08 | 0.99 (0.91–1.07) | 0.7 |
| 65–74 years | 0.96 (0.89–1.05) | 0.4 | 1.10 (1.01–1.19) | 0.02 |
| 75–84 years | 1.27 (1.16–1.38) | <0.0001 | 1.52 (1.41–1.65) | <0.0001 |
| 85+ years | 1.80 (1.64–1.97) | <0.0001 | 2.31 (2.13–2.51) | <0.0001 |
| Insurance status (ref=uninsured) | | | | |
| Insured | 0.85 (0.77–0.95) | 0.003 | 0.88 (0.80–0.97) | 0.01 |
| Insurance status unknown | 0.88 (0.76–1.02) | 0.1 | 0.91 (0.80–1.04) | 0.2 |
| Marital status (ref=married) | | | | |
| Unmarried | 1.20 (1.15–1.26) | <0.0001 | 1.23 (1.19–1.28) | <0.0001 |
| Unknown | 0.98 (0.90–1.06) | 0.6 | 0.99 (0.92–1.06) | 0.7 |
| Geographic region (ref=East) | | | | |
| Alaska, Pacific Coast | 1.04 (0.99–1.09) | 0.1 | 1.01 (0.97–1.05) | 0.8 |
| Northern Plains | 0.99 (0.92–1.06) | 0.7 | 1.00 (0.94–1.06) | 0.9 |
| Southwest | 0.97 (0.87–1.07) | 0.5 | 0.94 (0.86–1.03) | 0.2 |
| Race/ethnicity (ref=White) | | | | |
| Non–Hispanic Black | 1.02 (0.96–1.08) | 0.5 | 1.04 (0.99–1.09) | 0.1 |
| Non–Hispanic American Indian/Alaska Native | 1.04 (0.81–1.32) | 0.8 | 1.04 (0.84–1.28) | 0.7 |
| Non–Hispanic Asian or Pacific Islander | 0.73 (0.67–0.81) | <0.0001 | 0.77 (0.71–0.84) | <0.0001 |
| Hispanic (all races) | 0.94 (0.88–1.01) | 0.07 | 0.95 (0.89–1.00) | 0.06 |
| Poverty level (ref=0–10%) | | | | |
| >10–15% | 1.01 (0.96–1.07) | 0.7 | 1.00 (0.95–1.05) | 1.0 |
| >15–20% | 1.04 (0.98–1.11) | 0.2 | 1.04 (0.99–1.09) | 0.17 |
| >20% | 1.09 (1.02–1.17) | 0.01 | 1.10 (1.04–1.17) | 0.002 |

[†]Numbers represented as hazard ratio with 95% confidence intervals adjusted for age, race (White, Black, other), year of prostate cancer diagnosis, poverty level, marital status, insurance status, and geographic region of SEER registry. HR: hazard ratio; SEER: Surveillance, Epidemiology, and End Results.

Several limitations should be noted that are inherent in the SEER research data and were described previously.[9] First, this study is not able to assess whether screening guidelines were implemented for individual cases and can only make inferences based on time periods. Second, factors such as access to health insurance may influence these trends and were not accounted for in the incidence rate analysis because this is not collected for the general population in the U.S. census data. Likewise, SEER data does not include important risk factors and clinical factors, such as smoking, alcohol intake, diet, family history, and comorbidities, which may impact incidence and survival analyses by acting as confounding variables. Finally, this study did not incorporate a time-series design because there were too few years (nine years) for this type of analysis.

It is possible that the increased rates by periods are consistent from 2008–2016 and do not represent a change in the existing trend. It is also possible that there may be lagged effects. For example, in some subgroups, rates for 2012–2013 were not markedly higher than 2010–2011 rates.

This could reflect the early adoption in the clinical community for restrictive screening guidelines before they were officially recommended in 2012. Nonetheless, the fact that only certain groups seem to be driving the increasing trend in mPCa incidence rates is worth noting. Furthermore, in order to ensure that all patients had at least two years of followup from diagnosis of mPCa, the survival analysis was restricted to patients diagnosed between 2008 and 2014. This poses a limitation because the patients had unequal followup time and two-year followup time, rather than the more standard five-year follow up period, may not be adequate for assessing cancer-specific or overall mortality.

## Conclusions

The overall incidence of mPCa increased from 2008 to 2016. We were able to show an increase in incidence of mPCa over time in patients living in the least impoverished areas and in non-Hispanic Whites, reflecting that the increase in diagnoses may be driven by demographic subgroups that benefited most

from routine screening prior to the USPSTF recommendation against screening in 2012. We also demonstrated that despite decreased prostate cancer-specific mortality in recent years, perhaps due to the advances in treatment and access to care, certain demographic subgroups saw an increase in risk of prostate cancer-specific mortality. The differences in mortality risk were largely explained by these groups lacking access to resources and social support systems that are critical for favorable treatment outcomes. Future studies should examine the impact of more recent USPTSF guidelines for re-instituting screening and implementation of newer prostate cancer therapies in different subgroups.

This paper has been peer-reviewed.

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**Supplementary Table 1. Sensitivity analysis of multivariable Cox proportional hazards models stratified by treatment variables for all-cause and prostate cancer-specific mortality in men with metastatic prostate cancer, SEER 2008–2014**

| | All-cause mortality | | Prostate cancer mortality | |
|---|---|---|---|---|
| | HR[†] | p | HR[†] | p |
| Period (ref=2008–2009) | | | | |
| 2010–2011 | 0.96 (0.92–1.01) | 0.1 | 0.97 (0.92–1.02) | 0.2 |
| 2012–2014 | 0.94 (0.90–0.98) | 0.006 | 0.95 (0.91–1.00) | 0.06 |
| Age group (ref=20–54 years) | | | | |
| 55–64 years | 0.99 (0.92–1.08) | 0.9 | 0.94 (0.86–1.02) | 0.1 |
| 65–74 years | 1.09 (1.01–1.19) | 0.03 | 0.97 (0.89–1.06) | 0.5 |
| 75–84 years | 1.51 (1.39–1.64) | <0.0001 | 1.27 (1.16–1.39) | <0.0001 |
| 85+ years | 2.29 (2.11–2.49) | <0.0001 | 1.81 (1.65–1.99) | <0.0001 |
| Insurance status (ref=uninsured) | | | | |
| Insured | 0.91 (0.83–1.00) | 0.06 | 0.88 (0.79–0.98) | 0.02 |
| Insurance status unknown | 0.93 (0.81–1.06) | 0.3 | 0.90 (0.79–1.05) | 0.2 |
| Marital status (ref=married) | | | | |
| Unmarried | 1.22 (1.18–1.27) | <0.0001 | 1.20 (1.15–1.25) | <0.0001 |
| Unknown | 0.98 (0.91–1.05) | 0.5 | 0.97 (0.89–1.06) | 0.5 |
| Geographic region (ref=East) | | | | |
| Alaska, Pacific Coast | 1.00 (0.96–1.04) | 0.9 | 1.03 (0.98–1.08) | 0.2 |
| Northern Plains | 0.99 (0.93–1.05) | 0.8 | 0.98 (0.91–1.05) | 0.6 |
| Southwest | 0.93 (0.85–1.02) | 0.1 | 0.96 (0.86–1.06) | 0.4 |
| Race/ethnicity (ref=White) | | | | |
| Non–Hispanic Black | 1.03 (0.98–1.08) | 0.3 | 1.01 (0.96–1.07) | 0.7 |
| Non–Hispanic American Indian/Alaska Native | 1.03 (0.83–1.27) | 0.8 | 1.04 (0.81–1.32) | 0.8 |
| Non–Hispanic Asian or Pacific Islander | 0.77 (0.71–0.83) | <0.0001 | 0.73 (0.66–0.80) | <0.0001 |
| Hispanic (all races) | 0.94 (0.89–1.00) | 0.05 | 0.94 (0.88–1.00) | 0.07 |
| Poverty level (ref=0–10%) | | | | |
| >10–15% | 1.01 (0.96–1.06) | 0.8 | 1.02 (0.96–1.08) | 0.5 |
| >15–20% | 1.03 (0.98–1.09) | 0.2 | 1.04 (0.98–1.10) | 0.2 |
| >20% | 1.11 (1.04–1.18) | 0.001 | 1.10 (1.02–1.18) | 0.01 |

[†]Numbers represented as hazard ratio with 95% confidence intervals adjusted for age, race (White, Black, other), year of prostate cancer diagnosis, poverty level, marital status, insurance status, and geographic region of SEER registry. HR: hazard ratio; SEER: Surveillance, Epidemiology, and End Results.