


Changes in Prostate-Specific Antigen at the Time of Prostate Cancer Diagnosis After Medicaid Expansion in Young Men

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BACKGROUND: The objective of this study was to determine the effect of Medicaid expansion under the Patient Protection and Affordable Care Act (January 1, 2014) on the epidemiology of high-risk prostate-specific antigen (PSA) levels (≥ 20 ng/mL) at the time of prostate cancer (PCa) diagnosis. The authors hypothesized that better access to care would result in a reduction of high-risk features at diagnosis. **METHODS:** A retrospective cohort study was performed of 122,324 men aged <65 years who were diagnosed with PCa within the National Cancer Database. Difference-in-difference (DID) analyses adjusting for sociodemographic variables using linear regression compared PSA levels at diagnosis before expansion (2012-2013) and after expansion (2015-2016) between men residing in states that did or did not expand Medicaid. **RESULTS:** From 2012 to 2016, the proportion of men with PSA levels ≥ 20 ng/mL increased (from 18.9% to 19.8%) in nonexpansion states and decreased (from 19.9% to 18.2%) in expansion states. Compared with men in nonexpansion states, men in expansion states experienced a decline in PSA ≥ 20 ng/mL (DID, -2.33% ; 95% CI, -3.21% to -1.44% ; $P < .001$). Accordingly, the proportion of men presenting with high-risk disease decreased in expansion states relative to nonexpansion states (DID, -1.25% ; 95% CI, -2.26% to 0.25% ; $P = .015$). A similar statistically significant decrease in PSA levels ≥ 20 ng/mL was noted among black men (DID, -3.11% ; 95% CI, -5.25% to 0.96% ; $P = .005$). **CONCLUSIONS:** In Medicaid expansion states, there was an associated decrease in the proportion of young men presenting with PSA ≥ 20 ng/mL at the time of PCa diagnosis. These results suggest that Medicaid expansion improved access to PCa screening. Longer term data should assess oncologic outcomes. *Cancer* 2020;126:3229-3236. © 2020 American Cancer Society.

KEYWORDS: epidemiology, Medicaid, Patient Protection and Affordable Care Act, prostatic neoplasms, United States, young adult.

INTRODUCTION

Men without health insurance harbor a greater risk of metastases at the time of diagnosis of prostate cancer (PCa) compared with the general population in the United States¹ and present with higher levels of prostate-specific antigen (PSA) (a marker of disease severity).² It has been demonstrated that uninsured patients have greater odds of presenting with advanced disease and experience worse cancer-specific survival compared with those with Medicaid.^{2,3} Therefore, increasing health insurance coverage through Medicaid expansion could result in improved cancer-specific outcomes.

Implementation of the Patient Protection and Affordable Care Act allowed states to expand Medicaid eligibility to cover a larger group of low-income Americans; 24 states and the District of Columbia had opted to expand by January 1, 2014. After expansion, states that had *opted in* saw an increase in rates of Medicaid coverage and a subsequent reduction in uninsured rates relative to states that did not expand.⁴ Previous studies have associated Medicaid expansion with an increase in cancer screening and a decrease in late-stage diagnoses for some.⁵⁻⁷ Because of the prolonged natural history of prostate cancer, it is not surprising that there were no decreases in late-stage PCa in the first year of expansion (2014).⁶ One way to detect improvements in PCa care is to assess PCa screening by measuring PSA levels before diagnosis. As noted in screening trials, PSA values ≥ 20 ng/mL are associated with a poor prognosis, and PSA-based PCa screening can reduce the number of men who present with high-risk PSA values before diagnosis.^{8,9}

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Primary Exposures

Our main exposures of interest were year of diagnosis—pre-Medicaid expansion (2012-2013) versus post-Medicaid expansion (2015-2016)—and residence in states that expanded Medicaid on January 1, 2014 versus states that expanded Medicaid after the study period or never expanded Medicaid during the study period (Fig. 1). Other exposures considered in multivariable analyses are discussed in the Supporting Methods.

Outcomes

Our outcomes were based on changes in the annual proportion of measurements relative to measurements from 2012 and 2013 in states that expanded Medicaid. Our primary outcome was changes in the proportion of men presenting with PSA level ≥ 20 ng/mL at the time of diagnosis. A cutoff of 20 ng/mL was chosen for 3 reasons.

First, PSA levels ≥ 20 ng/mL are considered by National Comprehensive Cancer Network (NCCN) criteria and clinical series to be high-risk and associated with high-grade disease and a high likelihood of disease recurrence after optimal local treatment.¹²⁻¹⁴ In addition, in a large PCa screening trial, in the earlier years of screening, there were higher proportions of men being diagnosed with PSA ≥ 20 ng/mL, which was associated with worse survival.⁸ Second, in that same screening trial, declines in the percentage of men being diagnosed with PSA ≥ 20 ng/mL were noted only within 2 screening rounds, suggesting that it can serve as a marker of screening access in the few years after Medicaid expansion.⁸ Finally, the NCDB codes PSA values >99 ng/mL only as such; therefore, assessment of PSA as a continuous variable would not be possible.¹²

Secondary outcomes included changes in the proportion of men diagnosed with intermediate-risk or low-risk disease (biopsy Gleason grade groups 1-3, PSA <20 ng/mL, and clinical tumor classification 1-2 [cT1-cT2]) and high-risk disease (biopsy Gleason grade groups 4-5, PSA ≥ 20 ng/mL, or cT3-cT4), as defined by the NCCN.¹² In addition, metastatic disease at diagnosis (clinical metastatic classification 1 [cM1] or clinical lymph node status 1 [cN1] according to the American Joint Committee on Cancer *AJCC Cancer Staging Manual*, 7th edition¹⁵) and insurance coverage (yes vs no) for men with PCa was assessed.

Statistical Analyses

We compared the median age of patients from expansion and nonexpansion states using the Mann-Whitney *U* test

and compared categorical variables using chi-square tests. Analyses simply comparing outcomes preintervention and postintervention would not account for temporal trends before the intervention or other external factors. Therefore, our primary and secondary outcomes were assessed using a difference-in-difference (DID) analysis,¹⁶ with patients residing in Medicaid expansion states serving as the intervention group and those residing in nonexpansion states serving as controls. DID values were calculated as percentages by performing linear regression analyses with an interaction term between Medicaid expansion and time and multiplying by 100. Two separate dummy variables were created to represent time preintervention and postintervention: 1) 2012 to 2013 versus 2015 to 2016, and 2) 2012 to 2013 versus 2015 or 2016. To test our hypothesis and to avoid multiple testing, we would reject the null hypothesis if there was statistical significance ($P < .05$) only when comparing 2012 to 2013 with 2015 to 2016 (for additional information on the use of the DID analysis, see Supporting Methods). Unadjusted annual rates for each outcome were displayed as percentages.

We performed an exploratory analysis by limiting our analyses to black men, a racial group with previously documented higher risks of PCa death and presentation with later stage disease.¹⁷ Additional univariable comparisons were made between patients who did and did not meet exclusion criteria, and we also performed a sensitivity analysis of our primary outcome, including excluded patients who had *unknown* dummy variables for all missing data. All analyses were conducted using Stata 13.0 (Stata Corp).

RESULTS

Cohort Characteristics

The cohort consisted of 65,954 men from nonexpansion states and 56,370 men from expansion states (see Supporting Table 1). Over the entire study period, patients from expansion states were more likely to be white (74% vs 67%; $P < .001$) and more likely to have no comorbidities (84.4% vs 82.6%; $P < .001$). More patients in expansion states lived in regions of high median household income (\$64,000 annually; 47% vs 29%; $P < .001$). Approximately 19% of the cohort presented with PSA levels ≥ 20 ng/mL at the time of diagnosis, and a high PSA level was associated with high-grade disease at biopsy (see Supporting Table 2).

Medicaid Expansion and PSA at Diagnosis

The unadjusted proportion of men with PSA ≥ 20 ng/mL increased from 18.9% to 19.8% during 2012 through

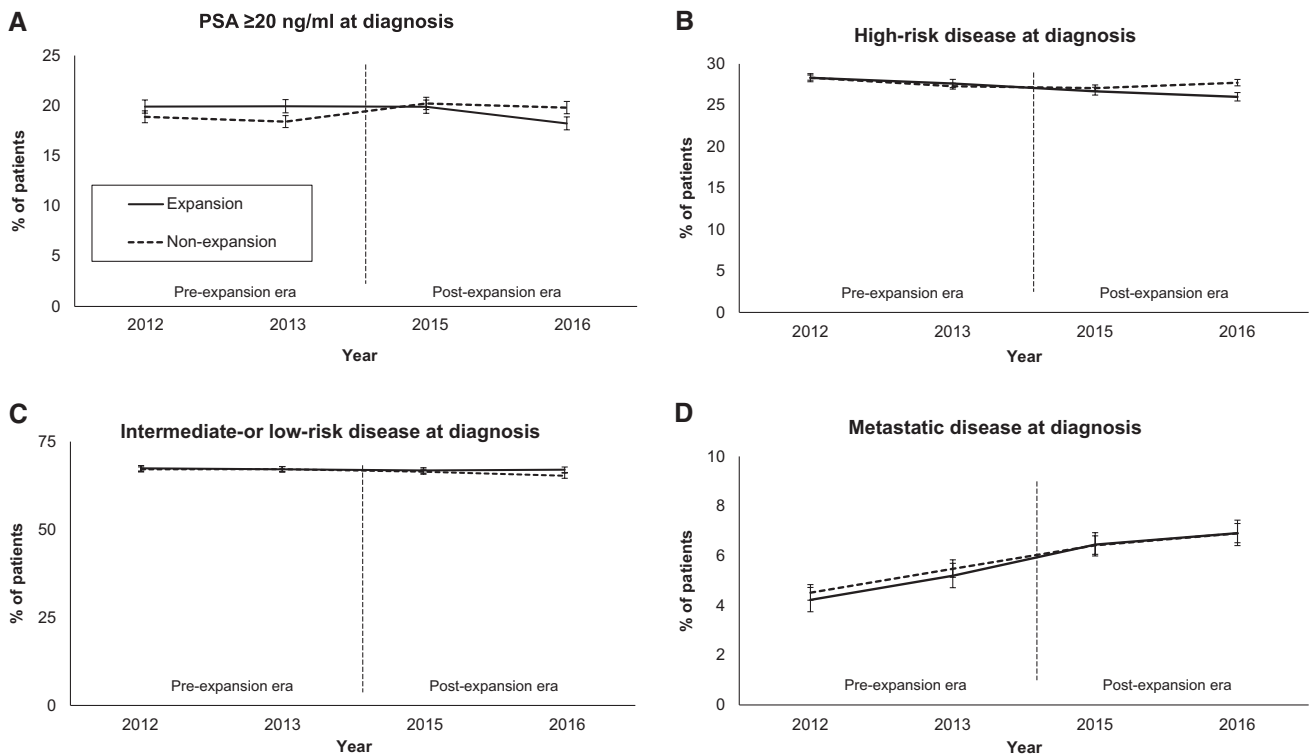


FIGURE 2. (A-D) Unadjusted temporal trends in outcomes at diagnosis are illustrated among states that expanded and did not expand Medicaid. Error bars represent 95% confidence intervals. Vertical dashed lines demarcate the division between pre-Medicaid expansion and post-Medicaid expansion. PSA indicates prostate-specific antigen.

2016 in nonexpansion state, whereas this proportion decreased in expansion states from 19.9% to 18.2% (Fig. 2A; see Supporting Table 3). On the basis of the multivariable DID analysis, Medicaid expansion was associated with a 2.33% decrease (95% CI, 3.21%-1.44%; $P < .001$) in the proportion of men presenting with PSA ≥ 20 ng/mL in expansion states relative to nonexpansion states from the pre-Medicaid expansion era (2012-2013) to the post-Medicaid expansion era (2015-2016) (Table 1). The adjusted DID comparing year 3 of expansion (2016) versus the pre-Medicaid expansion era showed a decrease of 2.95% (95% CI, 4.03%-1.86%; $P < .001$) in expansion states relative to nonexpansion states.

Similarly, adjusted DID analyses limited to black men revealed that expansion was associated with a decrease of 3.11% (95% CI, 5.25%-0.96%; $P = .005$) in expansion states relative to nonexpansion states from the pre-Medicaid expansion era to the post-Medicaid expansion era (Table 2). The adjusted DID comparing year 3 of expansion alone with the pre-Medicaid expansion era showed a decrease of 4.51% (95% CI, 7.13%-1.88%;

$P = .001$) in expansion states relative to nonexpansion states.

Medicaid Expansion and Risk Group at Diagnosis

Next, we sought to determine whether decreases in the proportion of men presenting with PSA levels ≥ 20 ng/mL resulted in decreases among men categorized as having a high risk of disease progression based on NCCN high-risk localized disease criteria at diagnosis.¹² In adjusted DID analysis, expansion was associated with a significant decrease in the proportion of high-risk disease at diagnosis in expansion states relative to nonexpansion states from the pre-Medicaid expansion era to the post-Medicaid expansion era (-1.25%; 95% CI, -2.26% to 0.25%; $P = .015$) (Fig. 2B and Table 1; see Supporting Table 3). Among black men, the overall DID was not statistically significant ($P = .083$) (Table 2). However, the adjusted DID comparing year 3 of expansion alone with the pre-Medicaid expansion era did demonstrate a significant decrease of 3.42% (95% CI, -6.25% to -0.59%; $P = .018$) in expansion states relative to nonexpansion states among black men.

TABLE 1. Adjusted Difference-in-Difference Analysis for All Men With Prostate Cancer^a

| Outcome at Diagnosis | Post-Medicaid Expansion Years Combined: 2015-2016 | | Post-Medicaid Expansion Year 2: 2015 | | Post-Medicaid Expansion Year 3: 2016 | |
|--------------------------|---|--------------------|--------------------------------------|-------------------|--------------------------------------|--------------------|
| | DID (95% CI), % | <i>P</i> | DID (95% CI), % | <i>P</i> | DID(95% CI), % | <i>P</i> |
| PSA >20 ng/mL | -2.33 (-3.21, -1.44) | <.001 ^b | -1.73 (-2.81, 0.65) | .002 ^b | -2.95 (-4.03, -1.86) | <.001 ^b |
| Intermediate or low risk | 0.99 (-0.07, 2.05) | .067 | 0.38 (-0.91, 1.67) | .6 | 1.60 (0.30-2.91) | .016 ^b |
| High risk | -1.25 (-2.26, -0.25) | .015 ^b | -0.63 (-1.86, 0.59) | .3 | -1.88 (-3.12, -0.64) | .003 ^b |
| Metastatic | 0.26 (-0.26, 0.78) | .3 | 0.26 (-0.38, 0.90) | .4 | 0.26 (-0.38, 0.90) | .4 |

Abbreviations: DID, difference-in-difference; PSA, prostate-specific antigen.

^aDID values were calculated using multivariable linear regression with an interaction term between a time variable for pre-Medicaid expansion and post-Medicaid expansion and patient residence in a state that did or did not expand Medicaid. All covariates in Supporting Table 1, from age to regional high-school attainment, were included in each regression.

^bThese *P* values indicate statistical significance.

TABLE 2. Adjusted Difference-in-Difference Analysis for Black Men With Prostate Cancer^a

| Outcome at Diagnosis | Post-Medicaid Expansion Years Combined: 2015-2016 | | Post-Medicaid Expansion Year 2: 2015 | | Post-Medicaid Expansion Year 3: 2016 | |
|--------------------------|---|-------------------|--------------------------------------|----------|--------------------------------------|-------------------|
| | DID (95% CI), % | <i>P</i> | DID (95% CI), % | <i>P</i> | DID (95% CI), % | <i>P</i> |
| PSA >20 ng/mL | -3.11 (-5.25, -0.96) | .005 ^b | -1.76 (-4.36, 0.85) | .186 | -4.51 (-7.13, -1.88) | .001 ^b |
| Intermediate or low risk | 2.40 (-0.05, 4.84) | .055 | 1.52 (-1.44, 4.48) | .3 | 3.31 (0.32-6.30) | .030 ^b |
| High risk | -2.05 (-4.36, 0.27) | .083 | -0.73 (-3.53, 2.07) | .6 | -3.42 (-6.25, -0.59) | .018 ^b |
| Metastatic | -0.36 (-1.69, 0.98) | .6 | -0.79 (-2.41, 0.82) | .3 | 0.10 (-1.54, 1.73) | 0.9 |

Abbreviations: DID, difference-in-difference; PSA, prostate-specific antigen.

^aDID values were calculated using multivariable linear regression with an interaction term between a time variable for pre-Medicaid expansion and post-Medicaid expansion and patient residence in a state that did or did not expand Medicaid. All covariates listed in Supporting Table 1, from age to regional high-school attainment, were included in each regression.

^bThese *P* values indicate statistical significance.

On the basis of the above results, we surmised that decreases in high-risk localized disease would accompany increases in the proportion of men presenting with NCCN intermediate-risk or low-risk PCa, which is associated with a greater likelihood of cure with local treatment.¹² In adjusted DID analysis, expansion was associated with a nonsignificant increase in the proportion of intermediate-risk or low-risk disease in expansion states relative to nonexpansion states from the pre-Medicaid expansion era to the post-Medicaid expansion era (0.99%; 95% CI, -0.07% to 2.05%; *P* = .067) (Fig. 2B and Table 1). However, the adjusted DID comparing year 3 of expansion alone with the pre-Medicaid expansion era showed a significant increase of 1.60% (95% CI, 0.30%-2.91%; *P* = .016) in expansion states relative to nonexpansion states. Similarly, among black men, the DID analysis showed an increase in intermediate-risk or low-risk disease when comparing all pre-Medicaid expansion and post-Medicaid expansion years for changes that approached significance (2.44%; 95% CI, -0.05% to 4.48%; *P* = .055) (Table 2). The adjusted DID comparing year 3 of expansion alone with the pre-Medicaid expansion era showed a significant

increase of 3.31% (95% CI, 0.32%-6.30%; *P* = .016) in expansion states relative to nonexpansion states.

Finally, we assessed trends in the presentation of metastatic disease at diagnosis. From the pre-Medicaid expansion era to the post-Medicaid expansion era, the unadjusted proportion of men presenting with metastatic disease at diagnosis increased in both expansion states (from 4.2% to 6.9%) and nonexpansion states (from 4.5% to 6.9%) during 2012 through 2016 (Fig. 2D). There was no significant DID when comparing pre-Medicaid expansion years versus all post-Medicaid expansion years (*P* = .4) or comparing pre-Medicaid expansion years versus year 3 of expansion (*P* = .4) (Table 1). These results were similar among black men (*P* = .3 and *P* = .9, respectively) (Table 2).

Sensitivity Analyses

Men who were excluded from the primary analysis differed only marginally in terms of sociodemographic variables from those who were included (see Supporting Table 4). A sensitivity analyses including these excluded men demonstrated similar DID for PSA ≥20 ng/mL for the entire cohort (DID, -1.76%; 95% CI, -2.65% to

−0.89%; $P < .001$) and black men (DID, −2.30%; 95% CI, −4.37% to −0.823%; $P = .030$) (see Supporting Table 5).

Trends in Insurance Coverage

From Census data we found a similar magnitude change in insurance coverage for men age 18 to 64 years in expansion states relative to nonexpansion states over our study period (Crude DID: −1.1%) (see Supporting Fig. 1). A similar trend was noted among men with PCa in the NCDB (adjusted DID, −0.38%; 95% CI, −0.78 to 0.01; $P = .061$) (see Supporting Fig. 2).

DISCUSSION

We sought to measure the correlation between Medicaid expansion and access to PCa screening by assessing the proportion of men presenting with a high-risk PSA level (≥ 20 ng/mL) at the time of PCa diagnosis, which is associated with a greater risk of disease recurrence after PCa treatment and worse survival after a PCa diagnosis.^{8,13} By using a multivariable DID approach comparing PSA values between men in expansion and nonexpansion states, we observed that Medicaid expansion was associated with decreases in the proportion of men presenting with PSA ≥ 20 ng/mL, a surrogate for disease with a high-risk of recurrence after treatment.¹²⁻¹⁴ Similarly, we also noted a decrease in the proportion of men presenting with high-risk disease in expansion states relative to nonexpansion states.

These results are encouraging given the multitude of studies demonstrating sociodemographic disparities in PCa outcomes.¹⁸⁻²¹ Previous work from population-based data in the United States noted that men with any insurance were much less likely than men without any insurance to present with metastatic disease at the time of PCa diagnosis.²¹ Additional prior work from the NCDB demonstrated that men aged < 65 years who had Medicaid insurance were more likely to present with metastatic disease compared those who had private insurance.²⁰ In the NCDB, Medicaid expansion was not associated with changes in the proportion of men with newly diagnosed PCa presenting with metastatic disease. However, this was not surprising based on large screening trials, which showed that reductions in metastatic disease at diagnosis took 4 to 6 years after randomization.^{22,23} Meanwhile, reductions in the number of men presenting with high-risk PSA ≥ 20 ng/mL were seen after only 2 rounds of screening,⁸ and significant increases in intermediate-risk or low-risk disease were seen within 3 years of randomization.²³

In the United States, decreases in the proportion of men with PCa presenting with PSA ≥ 20 ng/mL and high-risk PCa in Medicaid expansion states may reflect improvements in access to health care and PCa screening. Thus lower PSA levels and less high-risk disease at diagnosis in the first few years after expansion may precede decreases in incident de novo metastatic disease in expansion states and decreases in death from PCa. Importantly, however, the greatest impact of Medicaid expansion would likely take place in states with the highest incidence of PCa-related deaths. As demonstrated by Mokdad et al, the states with the highest incidence of PCa-related deaths are concentrated in the southeast United States and include Mississippi, Alabama, Georgia, and South Carolina.²⁴ Notably, these states still have not expanded Medicaid (Fig. 1), suggesting that our findings actually may underestimate the potential positive impact of Medicaid expansion on PCa outcomes because states with the worst outcomes did not expand.

In addition, during the study period, PCa screening practice patterns were likely influenced by the US Preventive Services Task Force 2012 guidelines, which recommended against any routine PCa screening.^{25,26} Since then, the US Preventive Services Task Force has assigned a *grade C* recommendation to PCa screening for men aged 55 to 69 years after a shared decision-making conversation between patients and clinicians.²⁷ With potentially increased acceptance of PCa screening related to these new guidelines and increases in young men with health insurance in expansion states, as demonstrated by our analysis of Census data, Medicaid expansion states may continue to see improvements in PSA levels, and potentially disease stage, at PCa diagnosis.

In subgroup analyses, PSA and high-risk disease at diagnosis also decreased among black men residing in expansion states relative to those in nonexpansion states. This indicates that Medicaid expansion may help reduce PCa outcome disparities among vulnerable racial groups, consistent with previous work.^{17,28,29} Previous work has noted that men with PCa and insurance more often receive definitive treatment and have improved cancer-specific survival.^{21,30} However, even among men with health insurance, those with Medicaid are less likely than those with private insurance to receive definitive treatment for PCa.²⁰ Thus future work should assess the association between Medicaid expansion and access to PCa treatment for men in vulnerable populations. Notably, however, Medicaid expansion only applies to men aged < 65 years, suggesting that further work and interventions

will be needed to reduce racial outcome disparities after a PCa diagnosis that largely may be caused by differences in health care access.³¹

Our study is not without limitations. The NCDB is not a population-based data set; therefore, its trends are reflective of the hospital patient population within the database, and most hospitals within this data set are academic or comprehensive treatment centers (see Supporting Table 1). Comparisons to non-NCDB cohorts have shown that hospitals included in the NCDB comprise different proportions of hospitals by state, are less likely to represent critical access hospitals or rural hospitals, and may offer more cancer-related services.³² The NCDB is also limited by the variables it captures, thus we cannot account for any unmeasured relevant factors. Follow-up for this study was relatively short after Medicaid expansion, and ongoing study is warranted to discern the downstream effects on PCa outcomes, including survival and incidence rates. In data from a large screening trial in Europe, up to 6 years were required to see reductions in incident metastatic disease, and up to 8 years were required before there were reductions in death from PCa.^{23,33} Although our data suggest that Medicaid expansion improved access to optimal PCa care, as measured by disease risk at the time of diagnosis, we did not assess actual screening rates in expansion states. Previous work has suggested that screening did not change in expansion states by 2015, but these data require longer follow-up.³⁴ Finally, although our analysis of insurance coverage does suggest that Medicaid expansion resulted in more men with health insurance, our analysis of Census data included all men aged 18 to 64 years regardless of cancer diagnosis, and our analysis within the NCDB included men who already had been diagnosed with PCa. A more thorough insurance analysis on the subject of PCa screening would assess men in the screening age range without a prior diagnosis of PCa.

In the context of these limitations, to our knowledge, our study is the first to assess changes in PSA values at the time of PCa diagnosis after statewide Medicaid expansion on January 1, 2014. In the years after Medicaid expansion, there was a decrease in men presenting with high-risk PSA values at diagnosis, suggesting an increase in access to PCa screening in expansion states. However, we suspect that, with longer follow-up, Medicaid expansion may result in decreases in the diagnosis of metastatic disease and PCa death, as observed in PCa screening trials with improved access to screening.²³ In addition, future work should be directed at assessing the effects of

Medicaid expansion on vulnerable populations, such men of African heritage.

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CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

AUTHOR CONTRIBUTIONS

Adam B. Weiner: Conception and design, acquisition of data, analysis and interpretation of data, writing—initial draft, critical revision of the article for important intellectual content, statistical analysis, and obtaining funding. **Amanda X. Vo:** Conception and design, acquisition of data, analysis and interpretation of data, and writing—initial draft. **Anuj S. Desai:** Analysis and interpretation of data, writing—initial draft, and critical revision of the article for important intellectual content. **Jim C. Hu:** Analysis and interpretation of data, writing—initial draft, and critical revision of the article for important intellectual content. **Daniel E. Spratt:** Analysis and interpretation of data, writing—initial draft, and critical revision of the article for important intellectual content. **Edward M. Schaeffer:** Conception and design; analysis and interpretation of data; writing—initial draft; critical revision of the article for important intellectual content; obtaining funding; administrative, technical, or material support; and supervision.

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