


Epidemiological Determinants of Advanced Prostate Cancer in Elderly Men in the United States

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ABSTRACT: In this study, we examined the effects of individual-level and area-level characteristics on advanced prostate cancer diagnosis among Medicare eligible older men (ages 70+ years). We analyzed patients from the linked Surveillance, Epidemiology, and End Results (SEER)-Medicare database (2000-2007) linked to US Census and County Business Patterns data. Cluster-adjusted logistic regression models were used to quantify the effects of individual preventive health behavior, clinical and demographic characteristics, area-level health services supply, and socioeconomic characteristics on stage at diagnosis. The fully adjusted model was used to estimate county-specific effects and predicted probabilities of advanced prostate cancer. In the adjusted analyses, low intensity of annual prostate-specific antigen (PSA) testing and other preventive health behavior, high comorbidity, African American race, and lower county socioeconomic and health services supply characteristics were statistically significantly associated with a higher likelihood of distant prostate cancer diagnosis. The fully adjusted predicted proportions of advanced prostate cancer diagnosis across 158 counties ranged from 3% to 15% (mean: 6%, SD: 7%). County-level socioeconomic and health services supply characteristics, individual-level preventive health behavior, demographic and clinical characteristics are determinants of advanced stage prostate cancer diagnosis among older Medicare beneficiaries; other health care-related factors such as family history, lifestyle choices, and health-seeking behavior should also be considered as explanatory factors.

KEYWORDS: prostate cancer screening, stage at diagnosis, socioeconomic status index, health services supply index, geographic disparities

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Introduction

Metastatic prostate cancer is associated with poor prognosis, and distant metastasis is the primary cause of prostate cancer death.¹ The clinical burden of metastatic prostate cancer is disproportionately higher among older men in the United States. Accordingly, 58% of those diagnosed with distant disease, and 89.5% who die of prostate cancer are men aged 65 years or older.^{2,3} In May 2018, the United States Preventive Services Task Force (USPSTF) recommended against annual prostate-specific antigen (PSA)-based prostate cancer screening among men 70 years and older noting that the risk of overdiagnosis and overtreatment may outweigh the benefits of PSA screening in this population.⁴ However, the evidence evaluated for this recommendation also highlights that relatively few men older than 70 years were enrolled in the clinical trials, and that there is limited evidence on the benefits of screening among these older men.⁴ In light of these recommendations, we assessed

individual and area-level factors associated with the incidence of advanced stage prostate cancer among older men (70+ years) in the United States.

The primary goal of prostate cancer screening is to reduce the development of symptomatic metastatic disease, thereby reducing morbidity and mortality associated with advanced prostate cancer.^{5–8} Accordingly, inadequate screening and access barriers to screening may lead to higher incidence of advanced stage prostate cancer diagnosis. Health care environments in the United States are heterogeneous, with substantial geographic variation in locally defined socioeconomic and health services supply (HSS) characteristics across states and counties.^{9–20} The importance of evaluating the impact of geographic characteristics on the uptake of prostate cancer screening and prostate cancer outcomes among relatively younger, uninsured men is well established.^{19–24} However, to our knowledge, no prior study has directly assessed whether differences in contextual characteristics such as area-level socioeconomic status (SES) and HSS in combination with individual preventive

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behavior could explain advanced stage prostate cancer incidence among older (70+ years) Medicare insured men in the United States.

Given the ongoing controversy surrounding USPSTF recommendations for PSA-based screening in elderly men, and the uncertainty of the differential impact of geographic characteristics on prostate cancer outcomes among Medicare eligible older men in the United States, we performed a large retrospective cohort analysis to assess individual and contextual factors associated with the incidence of advanced prostate cancer among elderly Medicare beneficiaries. In contrast to previous studies, we quantified the availability of a wide range of area-level resources to provide a relatively comprehensive assessment of geographic determinants of late-stage prostate cancer diagnosis among older Medicare beneficiaries. The results of this study are intended to inform discussions about the need to develop patient and location-centered strategies to improve health outcomes among older men in the United States.

In this study, we used a unique enriched Surveillance, Epidemiology and End Results (SEER)-Medicare dataset linked with the US Census, County Business Patterns (CBP) and the US Census Equal Employment Opportunity (EEO) Tabulation to assess the combined impact of SES, HSS characteristics and preventive behavior on stage at prostate cancer diagnosis among elderly (70+ years) Medicare eligible men. We hypothesized that older Medicare beneficiaries who received frequent annual PSA testing, and other preventive services, and lived in counties with high HSS and SES are less likely to receive an advanced prostate cancer diagnosis.

Methods

Data source

Data for the study were obtained from the National Cancer Institute's SEER database and the linked Medicare enrollment and claims files.²⁵ SEER is a national cancer surveillance network of 18 regional cancer registries covering about 28% of the US population. The SEER program collects data on patient's demographic characteristics, primary tumor site, tumor morphology, stage at diagnosis, and first course of treatment on all diagnosed cancers within its region. Medicare enrollment and claims files are linked to SEER data at the patient-level to record health care utilization by Medicare beneficiaries before their cancer diagnoses. The study was developed using claims data from 2000 through 2007 for men diagnosed with prostate cancer between 2004 and 2007.

Counties are considered legislative areas with 100 000 persons on average. In the United States, counties provide a socioeconomic, political, and community context within which many social and public health policies are formulated and implemented.²⁶⁻²⁸ County-level indicators of socioeconomic characteristics were extracted from the year 2000 US

census. The 2000 CBP data were used to obtain data on health care facilities and services available in counties.²⁹ Information regarding the availability of physician and non-physician health care providers available within the counties were obtained from the year 2000 US Census EEO Tabulation.³⁰

Study population

The study sample included men diagnosed with incident prostate cancer between 2004 and 2007, with continuous fee-for-service Medicare coverage (i.e., with both Parts A and B coverage) in the 60 months prior to cancer diagnosis. Men enrolled in Medicare Advantage plans or health maintenance organization coverage during this 60-month period were excluded due to incomplete Medicare claims data on these patients. Men with missing data for clinical stage at diagnosis and those with an unknown stage at diagnosis were excluded (4%). The men included were aged 70+ years at the time of diagnosis.

Study design

We employed a retrospective cohort study design to explore the variation in the effects of individual and county-level characteristics on stage at prostate cancer diagnosis among elderly Medicare beneficiaries.

Individual-level characteristics. The outcome of interest was stage at prostate cancer diagnosis identified using the SEER historic staging categories. SEER historic stage uses all information available in the medical record to provide a combination of the most precise clinical and pathological documentation of the extent of disease.³¹ Accordingly, localized prostate cancer is identified based on the number of clusters (foci) seen on microscopic examination, or the presence of clinically palpable (or visibly seen) nodule(s) in the prostate; regional prostate cancer includes capsular invasion microscopically; and distant prostate cancer includes metastatic disease identified either clinically or microscopically.^{32,33} Prostate cancer tumors were grouped as localized/regional and distant per SEER coding protocol.³³ SEER data were also used to obtain baseline individual-level information on age, year of diagnosis, marital status, SEER region, urban/rural location, and race/ethnicity. PSA tests administered before prostate cancer diagnosis were identified using Health Care Common Procedure Coding System (HCPCS) codes 84153, 84154, and G0103 in Medicare claims. Receipt of annual PSA testing was combined as those who received 4-5, 2-3, or 0-1 PSA tests annually over a period of 5 years before prostate cancer diagnosis. "No PSA testing" and "PSA testing once a year" were grouped together because PSA screening cannot be distinguished from diagnostic PSA testing in Medicare claims, where men may have received a PSA test because of symptoms.³⁴ We counted multiple PSA

tests men received during a single year as a single test.^{34,35} Use of other covered preventive and cancer screening services could correlate with healthy behavior and opportunities to discuss signs and symptoms of illness with health care providers, subsequently lowering probability of advanced cancer at the time a beneficiary is first diagnosed with cancer.³⁵ Therefore, use of colon cancer screening (82270, 82272, 82274, 82270, G0328, and G0107) at least once during the observation period and receipt of annual influenza vaccination (90732, 90724, 90658, 90659, 90669, and G0008), 5 years prior to prostate cancer diagnosis were also identified using Medicare claims data.³⁶ The ICD-9 diagnostic codes associated with health services utilization during the 12-month period prior to prostate cancer diagnosis (baseline) were used to calculate a baseline Charlson comorbidity index (CCI) score for each patient. We also identified baseline performance status proxies from Medicare claims that are distinct from comorbidity measures: use of walking aid, wheelchair, oxygen and related supplies, hospitalizations, and admissions to skilled nursing facilities. We captured state buy-in coverage of Medicare beneficiaries for whom states pay the Part B premium. Beneficiaries with state buy-in coverage are likely to have higher resource use and worse utilization-based outcomes because they tend to be in poorer health.³⁷

County-level characteristics. We extracted 30 county-level SES characteristics belonging to the domains of employment, education, poverty, income, housing, ownership, and living crowdedness from the 2000 US census data.^{11,26,38–42} All health care personnel, facilities, and services available within counties that could potentially influence the uptake of screening services and early detection of cancer were extracted from the CBP and EEO databases. To capture health care resource availability considering county size, the number of facilities or providers available within the county was divided by the total land area of the county and then multiplied by 1000 to express each health care characteristic as the number available per 1000 square miles.^{12,43}

Area-level characteristics (eg, income, poverty, and occupation) tend to be highly correlated, which can lead to multicollinearity in a multivariable analysis.^{44,45} Therefore, we created two separate composite indices to capture area-level SES and HSS characteristics. Composite measures have greater validity, robustness, statistical efficiency, and explanatory power than single area measures in documenting the impact of area-level characteristics on disease outcomes.^{26,45} Factor analysis using the SAS PROC Factor procedure with a maximum likelihood (ML) parameter estimator was used to arrive at the number and nature of latent constructs needed to account for correlations, and to capture the commonality among the measured variables.⁴⁶ All measures were normalized using rank transformations prior to being entered into factor analysis; tied values were assigned an average rank.⁴⁴ Factor coefficients were used

to construct weighted SES and HSS scores for each county. SES and HSS county scores were merged with patient-level SEER data based on where individuals lived at the time of prostate cancer diagnosis using Federal Information and Processing Standards (FIPS) code information. Factor scores were sorted and divided as closely as possible into quintiles based on the distribution of SEER county populations.

Statistical analysis

Descriptive statistics were constructed to examine the distribution of characteristics among elderly Medicare beneficiaries diagnosed with incident prostate cancer. Chi-square tests were used for bivariate comparisons of patient and county characteristics by stage at diagnosis. We assessed geographic variation in the incidence of distant prostate cancer using (1) random intercept/slope models, (2) variance partition coefficients, (3) a caterpillar plot of predicted proportions of distant prostate cancer diagnoses across counties, and (4) caterpillar plots of the predicted proportion of distant prostate cancer diagnoses by county-level HSS and SES characteristics.

Cluster-specific logistic regression models were used to examine the effects of annual PSA testing intensity on prostate cancer outcomes considering county-level random effects. To account for possible county-level heterogeneity, we allowed the intercept of each county to vary, using a random intercepts model. Random slopes for the intensity of annual PSA testing (4 or more and 2–3 times) were introduced to the models to examine the variation of the effect of annual PSA testing across the 158 counties. Variance partition coefficients were calculated using a null model to measure the variance in stage at prostate cancer diagnosis that was attributable to county-level effects. The partially adjusted model consisted of patient-level characteristics including annual PSA testing, demographic, clinical characteristics, and other preventive health behavior. A second model was fitted with urban/rural location, SES and HSS measures to examine the role of county-level characteristics in explaining the variation in stage at prostate cancer diagnosis across counties. Using this model, we calculated the proportional change in variance attributable to the added county-level predictors and quantified the amount of variance “explained” by county-level predictors. This second fully adjusted model was used to estimate predicted proportions of distant prostate cancer diagnoses in the SEER covered counties. We created a caterpillar plot with rank ordered predicted proportions of distant prostate cancer diagnoses and 95% confidence intervals (CIs).

Analyses were performed using SAS software, version 9.2 (SAS Institute, Inc., Cary, NC) and STATA software, version 10.0 (StataCorp LP, College Station, TX). This research study was approved by the University of Maryland Baltimore Institutional Review Board (approval no. HCR-HP-0004 9426-4).

Results

Factor analysis

The final composite measure of county-level SES consisted of county employment rate, percentage of families below poverty level, median family income and the level of education measured by an education index (measures, factor loadings and fit statistics are provided in Supplemental Appendix 1).⁴⁶ The county-level HSS measure captured the availability of physician offices, diagnostic laboratories, general medical and surgical hospitals and health care professionals including physicians, nurses, pharmacists, laboratory technicians and social workers (Supplemental Appendix 1).⁴⁶ Spearman's rank correlation coefficient between SES and HSS categorical measures was 0.36, indicating a low positive correlation between the SES and HSS.

Descriptive and bivariable analysis

Application of the inclusion criteria resulted in 43 890 older Medicare beneficiaries diagnosed with prostate cancer from 2004 to 2007. Due to privacy concerns, the EEO tabulation provides information only on those counties with more than 50 000 residents. Thus, after combining the county-level composite HSS and SES measures with the SEER-Medicare dataset, the final study sample consisted of 37 760 Medicare beneficiaries diagnosed in 158 counties in SEER covered regions.

Approximately 6% of the beneficiaries were diagnosed with incident distant prostate cancer. As shown in Table 1, 45% of the beneficiaries received annual PSA testing four or more times and 24% received once or no PSA tests over a period of 5 years before prostate cancer diagnosis. The mean age of the sample was 76.5 years (SD \pm 5.3) years and a majority (77%) reported their race/ethnicity as White non-Hispanic. Bivariable analysis shows that a higher proportion of men received four or more annual PSA tests (47%) prior to localized/regional prostate cancer diagnosis, while a higher proportion of men received one or no PSA tests (54%) prior to metastatic prostate cancer diagnosis ($P < .01$). African American race, older age (80 years or older), higher CCI, poor performance status proxies, and no colon cancer screening and receipt of 0-1 influenza shots 5 years prior to prostate cancer diagnosis were statistically significantly associated with a higher likelihood of late-stage prostate cancer diagnosis. Rural location and low HSS characteristics were also associated with a higher likelihood of advanced prostate cancer diagnosis.

Multivariate analysis

According to the null model, between-county variance was 0.1 (95% CI: 0.06-0.16) indicating that 3% of the variation in distant prostate cancer diagnosis across counties was attributable to county-effects. Multivariate analyses showed that greater intensity of annual PSA testing was associated with a

statistically significant lower likelihood of distant prostate cancer diagnosis compared with receiving 0 or 1 PSA test 5 years prior to prostate cancer diagnosis (Table 2). Other preventive health behavior measured by receipt of colon cancer screening was also negatively associated with advanced prostate cancer diagnosis. Older age, higher comorbidity, and African American race were consistently associated with an increased likelihood of distant prostate cancer diagnosis. Men living in rural counties were more likely to be diagnosed with distant prostate cancer compared with men living in urban or big metro counties. Increasing HSS and SES scores were associated with a lower likelihood of distant prostate cancer diagnosis. After adjusting for patient and county-level characteristics, the variation in distant prostate cancer diagnosis that was attributable to county-effects reduced to 2%; rural location (8%) and SES and HSS characteristics (13%) of the counties explained 21% of the variation in distant prostate cancer diagnosis. Random slopes for annual PSA testing were not statistically significant, indicating that the effects of annual PSA testing did not statistically significantly vary across the counties. Figure 1 illustrates the variation in the predicted proportions of distant prostate cancer diagnoses after adjusting for individual and county-level characteristics; the predicted proportions of distant prostate cancer diagnosis ranged from 3.5% to 15.1% (mean: 6.1%, SD: 6.7%) across the 158 SEER covered counties. Figure 2A and B illustrates the variation in adjusted predicted proportions of prostate cancer diagnoses across county-level HSS and SES characteristics; counties with higher SES and HSS characteristics showed lower proportions of advanced stage diagnoses, while counties with lower SES and HSS characteristics showed relatively higher proportions of advanced stage prostate cancer diagnoses.

Discussion

This study provides an assessment of individual- and area-level epidemiological determinants of advanced stage prostate cancer among older Medicare beneficiaries, using a unique enriched dataset linking SEER-Medicare data with several other data sources that helped characterize the contexts within which older men live and make health care decisions in the United States. While previous studies have evaluated area-level socioeconomic variations in prostate cancer incidence overall and specifically among younger, uninsured men,²⁰⁻²⁵ there has been limited focus on evaluating these differences among older Medicare beneficiaries. In contrast to previous studies, our findings highlight that even with insurance coverage, county-level characteristics could still contribute to significant variation in late-stage prostate cancer incidence in older men. This study demonstrates how health care environments characterized by SES and HSS indicators interact with individual characteristics and preventive health behavior to determine subsequent health outcomes among Medicare insured older men.

Table 1. Sample characteristics of Medicare eligible older men diagnosed with incident prostate cancer in 158 SEER covered counties, stratified by stage at diagnosis, 2004-2007.

VARIABLE	FULL SAMPLE (N ^a =37 760)		LOCALIZED/ REGIONAL (N ^a =35 451)	DISTANT (N ^a =2309)	P-VALUE ^b
	N	%	COL. ^c %	COL. ^c %	
Individual-level characteristics					
Annual PSA-testing 5 years before diagnosis					<.01
4 or more times	16 926	44.8	46.5	18.8	
2 or 3 times	11 672	30.9	31.1	27.4	
0 or 1 times	9162	24.3	22.3	53.8	
Demographics					
Race					<.01
White non-Hispanic	29 202	77.3	77.4	76.6	
African American	3295	8.7	8.5	11.6	
Other ^d	5263	13.9	14.1	11.8	
Age at diagnosis					<.01
70 to 74	17 051	45.2	46.5	24.4	
75 to 79	11 272	29.8	30.1	25.9	
80 to 84	6568	17.4	16.8	27.1	
85+	2869	7.6	6.6	22.7	
Married	24 335	64.4	64.9	57.2	<.01
State buy-in (at least 1 month)	3325	8.8	8.5	13.4	<.01
Clinical characteristics (baseline)					
Charlson comorbidity index ^e					<.01
Zero	23 154	61.3	61.8	53.6	
One	8308	22.0	22.1	20.4	
Two or higher	5263	13.9	13.7	18.2	
Missing	1035	2.7	2.4	7.9	
Performance status proxies ^e					
Walking aids	761	2.0	1.9	4.1	<.01
Wheelchair	710	1.9	1.7	4.5	<.01
Oxygen and related supplies	1602	5.0	4.8	8.1	<.01
Skilled nursing facility use	802	2.1	1.9	5.2	<.01
Hospital use	6000	15.9	15.3	24.4	<.01
Preventive health behavior ^f					
Colon cancer screening					<.01

(Continued)

Table 1. (Continued)

VARIABLE	FULL SAMPLE (N ^a =37 760)		LOCALIZED/ REGIONAL (N ^a =35 451)	DISTANT (N ^a =2309)	P-VALUE ^b
	N	%	COL. ^c %	COL. ^c %	
No screening over 5 years	31 677	83.9	83.4	91.7	
1 or more times over 5 years	6083	16.1	16.6	8.3	
Annual influenza shots					<.01
0 to 1 time	9338	24.7	24.4	29.6	
2 to 3 times	9701	25.7	25.9	22.4	
4 or more times	18 721	49.6	49.7	48.0	
Year ^g					<.01
2004	9479	25.1	25.1	25.9	
2005	8946	23.7	23.6	25.8	
2006	9561	25.3	25.3	25.6	
2007	9774	25.9	26.1	22.8	
All-cause death	7861	20.8	17.3	75.0	<.01
Prostate cancer death	1944	30.8	17.3	70.6	<.01
County-level characteristics					
Big metro/urban/rural location					<.01
Big metro	35 521	94.1	94.2	92.3	
Urban	2152	5.7	5.6	7.1	
Rural	87	0.2	0.2	0.6	
Socioeconomic status					.42
Low	6968	18.4	18.4	19.1	
2	7365	19.5	19.5	19.4	
3	7155	18.9	18.9	19.7	
4	7024	18.6	18.5	19.9	
High	9248	24.5	24.7	22.0	
Health services supply					<.01
Low	5637	14.9	14.9	16.2	
2	6917	18.3	18.2	20.2	
3	6285	16.6	16.6	16.7	
4	9665	25.6	25.8	22.4	
High	9256	24.5	24.5	24.5	

Abbreviation: PSA, prostate-specific antigen; SEER, Surveillance, Epidemiology, and End Results.

^aN represents the number of patients.

^bThe P-values were calculated using chi-square tests.

^cCol. %: Column percentage is calculated as the ratio of the frequency count for a single cell to the total frequency count for the column that contains the cell. The ratio is represented as a percentage. For example, Col. % for White non-Hispanics with distant prostate cancer = $(1768/2309) \times 100 = 76.57\%$.

^dOther includes Asian, Hispanic, American Indian/Alaska Native, and Unknown.

^eDuring the 12-month period prior to prostate cancer diagnosis.

^fOther preventive health behavior assessed over a period of 5 years prior to prostate cancer diagnosis.

^gYear of prostate cancer diagnosis.

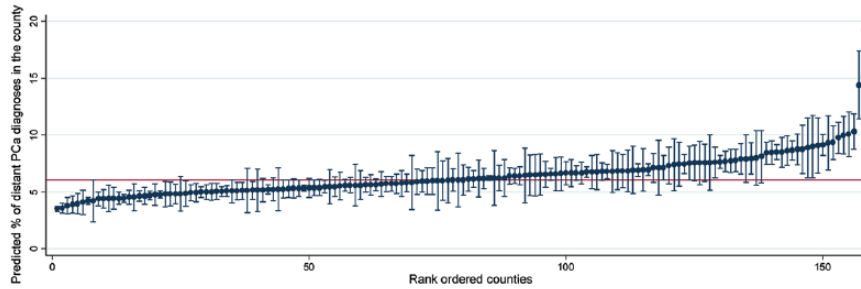


Figure 1. Caterpillar plot illustrating county-level variation in the predicted proportion of distant (advanced) prostate cancer (PCa) diagnoses among Medicare eligible older men shown in rank order together with 95% confidence intervals (N = 158). Figure displays the predicted proportions of distant prostate cancer diagnosis across 158 counties with at least 14 prostate cancer patients. The model was adjusted for individual demographic, clinical characteristics and other preventive health behavior, rural location, and county-level socioeconomic and health services supply characteristics. The x-axis shows the 158 counties ordered from smallest proportion to largest proportion of distant prostate cancer cases. Average percentage across all counties was 6.1% (shown by the horizontal line).

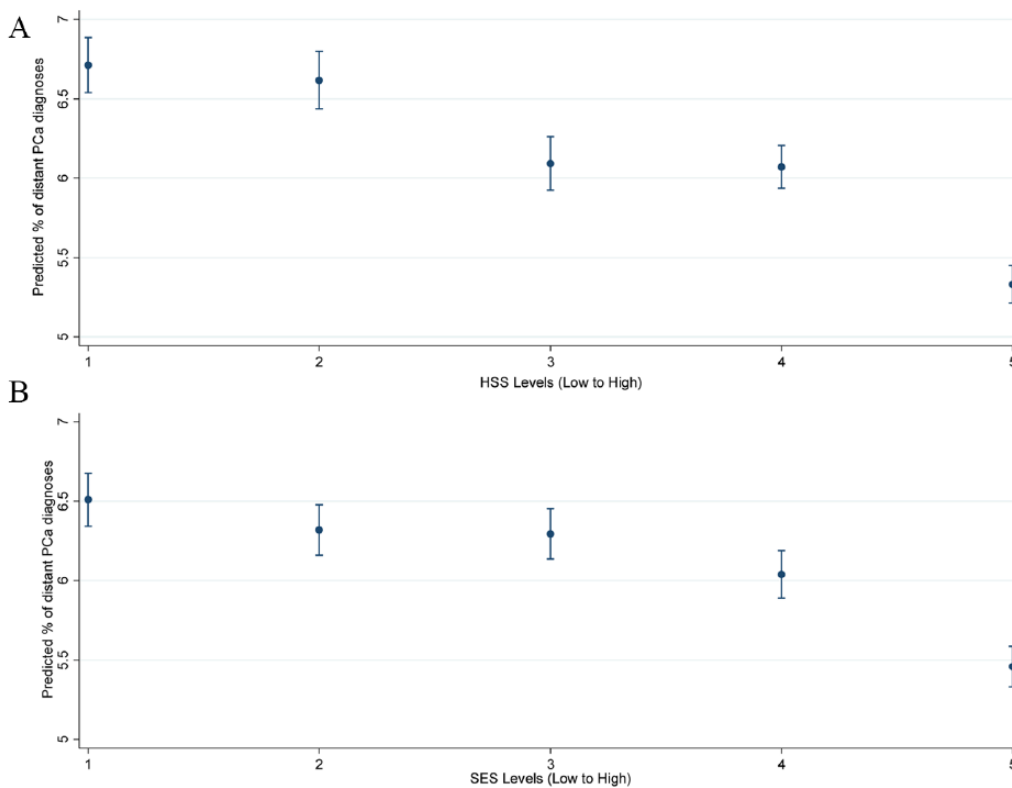


Figure 2. Caterpillar plots illustrating variation in the predicted proportion of distant (advanced) prostate cancer (PCa) diagnoses among Medicare eligible older men shown by (A) county-level health services supply (HSS) and (B) county-level socioeconomic status (SES) characteristics. The models were adjusted for individual demographic, clinical characteristics and other preventive health behavior, rural location, and county-level SES and HSS characteristics. The x-axis shows county-level HSS and SES characteristics ordered from lowest to the highest.

While our results confirm that county-level characteristics are significant contributors to the prostate cancer burden in older men, the possible explanatory pathways for these effects are complex. The protective effect of SES may be related to individual resources that support a healthy lifestyle including consuming a healthy diet, engaging in exercise, health-seeking behavior, greater health knowledge, and motivation to seek care. HSS may contribute to greater access to health care, the quality of care received, and the timeliness or thoroughness of workup and diagnosis. In this study, the observed additional benefit from county-level resources suggests that regardless of

an individual’s health motivation (measured by preventive health behavior, e.g., the intensity of annual PSA testing), the availability of health care services within counties can influence stage at prostate cancer diagnosis among older Medicare beneficiaries.

The USPSTF recommends against PSA-based prostate cancer screening in older men regardless of place of diagnosis.⁴⁸ However, our findings indicate that the benefits of PSA-based screening may vary across US counties. Each county in the United States represents a unique health care environment governed by local and regional politics, social systems, and

Table 2. Multilevel logistic regression models for incident distant prostate cancer diagnosis controlling for individual and county-level characteristics (N=37 760).

VARIABLES	PARTIALLY ADJUSTED: DEMOGRAPHIC AND CLINICAL CHARACTERISTICS ONLY	FULLY ADJUSTED
	OR (95% CI)	OR (95% CI)
Individual level		
Annual PSA-testing 5 years before diagnosis		
4 or more times	0.20 (0.18, 0.22)**	0.20 (0.17, 0.22)**
2 or 3 times	0.41 (0.37, 0.46)**	0.41 (0.37, 0.46)**
0 or 1 times	Reference	Reference
Race		
White non-Hispanic	Reference	Reference
African American	1.20 (1.03, 1.40)*	1.23 (1.06, 1.44)**
Other ^a	0.65 (0.56, 0.76)**	0.65 (0.56, 0.75)**
Age at diagnosis		
70 to 74	Reference	Reference
75 to 79	1.77 (1.57, 2.00)**	1.77 (1.57, 2.00)**
80 to 84	3.26 (2.89, 3.69)**	3.26 (2.88, 3.68)**
85+	6.09 (5.33, 6.95)**	6.10 (5.34, 6.97)**
State buy-in (at least 1 month)	1.51 (1.31, 1.75)**	1.50 (1.30, 1.74)**
Charlson comorbidity index ^b		
Zero	Reference	Reference
One	1.05 (0.94, 1.18)	1.05 (0.94, 1.18)
Two or higher	1.25 (1.11, 1.41)**	1.25 (1.11, 1.42)**
Missing	1.76 (1.46, 2.12)**	1.75 (1.45, 2.11)**
Colon cancer screening ^c		
No screening over 5 years	Reference	Reference
1 or more times over 5 years	0.72 (0.61, 0.84)**	0.72 (0.61, 0.84)**
Annual influenza shots ^c		
0 to 1 time	Reference	Reference
2 to 3 times	0.96 (0.86, 1.07)	0.96 (0.86, 1.07)
4 or more times	0.92 (0.81, 1.04)	0.92 (0.81, 1.04)
County-level		
Urban/rural location		
Big metro/urban		Reference
Rural		3.26 (1.54, 6.91)**
Socioeconomic status		
Low		Reference
2		1.05 (0.85, 1.30)
3		0.99 (0.81, 1.22)
4		0.94 (0.75, 1.78)

Table 2. (Continued)

VARIABLES	PARTIALLY ADJUSTED: DEMOGRAPHIC AND CLINICAL CHARACTERISTICS ONLY	FULLY ADJUSTED
	OR (95% CI)	OR (95% CI)
High		0.76 (0.69, 0.98)*
Health services supply		
Low		Reference
2		0.80 (0.61, 1.06)
3		0.75 (0.56, 1.02)
4		0.66 (0.49, 0.89)**
High		0.70 (0.52, 0.93)*
Number of counties	158	158
Variance partition coefficients	2.5%	2.0%
Variance of random intercept	0.08 (0.05, 0.14)	0.07 (0.04, 0.12)
Likelihood ratio	-7607.59	-7602.06

Abbreviations: CI, confidence interval; OR, odd ratio; PSA, prostate-specific antigen.

^aOther includes Asian, Hispanic, American Indian/Alaska Native, and Unknown.

^bDuring the 12-month period prior to prostate cancer diagnosis.

^cOther preventive health behavior assessed over a period of 5 years prior to prostate cancer diagnosis.

* $P < .05$, ** $P < .01$.

baseline conditions.^{47,49} The observed variation in late-stage prostate cancer incidence across counties highlights the differences in US health care environments, and the reciprocal relationships between older men, and these environments leading to geographic disparities in cancer outcomes. However, in this context, it must also be noted that potential gains of screening could be countered by harms of overdiagnosis and overtreatment including reductions of quality of life related to follow-up procedures, increase in immediate risk of suicide or death from cardiovascular causes, burdensome cancer treatment, and long-term treatment-related adverse events.⁵⁰⁻⁵² A substantial proportion of prostate cancers shows late onset and slow progression; therefore, overdiagnosis and overtreatment are common consequences of screening, especially when it is performed frequently or in men with relatively short remaining life expectancy due to life-shortening comorbidity.⁵¹ Therefore, older men living in certain areas may benefit more from the provision of information on the nature and magnitude of the trade-off involved with early cancer detection, while in other areas equitable access to health care workforce, facilities and screening services might be necessary to reduce the burden of advanced diagnoses. Our findings also indicate that future screening policies focused on location-based interventions could potentially play an important role in reducing geographic disparities in prostate cancer outcomes among Medicare eligible older men.⁴⁷ Further research is warranted to inform how resource allocation or tailored interventions and policies may ultimately reduce geographic variation in distant prostate cancer diagnosis among older men.

Our findings are supported by other studies conducted using SEER-Medicare data. Hu and colleagues⁵³ observed that greater frequency of PSA testing was associated with a lower likelihood of advanced prostate cancer diagnosis among older men. According to Shao et al,³³ increasing numbers of PSA tests before cancer diagnosis were associated with lower PSA levels, lower biopsy Gleason scores, lower clinical stages, and lower risk disease at diagnosis ($P < .001$). However, these studies have paid limited attention to assessing the effect of frequent PSA testing on stage at diagnosis while examining the “contexts” within which older men make health care decisions. Several studies have reported separately the protective effects of increasing county-level resources with respect to socioeconomic characteristics, density of hospitals, and urologists on the incidence of advanced prostate cancer.^{19,54,55} However, these studies have paid limited attention to quantifying the impact of individual preventive health behavior such as PSA-based screening patterns on stage at diagnosis among older Medicare beneficiaries.

Although our findings are policy relevant, they must be interpreted in the context of the study design. First, this study included only men aged 70 years or older living in SEER areas and those who were enrolled in fee-for-service Medicare. Thus, study findings may not generalize to younger men or older men enrolled in health maintenance organizations and Medicare Advantage plans or those who received health care in non-SEER areas in the United States. Medicare began covering PSA testing for all male beneficiaries over 50 years old in 2000.²⁵ In addition to individual preventive health behavior and better access to health care services within counties, it is

possible that men who received frequent PSA testing had a family history of prostate cancer and other risk factors such as smoking or symptoms of prostate cancer.⁵⁶ Furthermore, there are a number of lifestyle choices that impact risk of prostate cancer. For example, several studies have shown that lifestyle modifications such as smoking cessation, exercise, maintaining a healthy body weight and dietary factors may reduce the risk for advanced and aggressive prostate cancer in men.^{57–59} However, these measures were not available in claims data; as a result, we were unable to assess the impact of these measures on prostate cancer outcomes in the current analysis. Receipt of PSA screening from diagnostic PSA testing cannot be distinguished in Medicare claim data. Diagnostic PSA testing occurs when men receive PSA testing due to symptoms of the disease. Therefore, we examined PSA testing patterns over a period of 5 years before the incident prostate cancer diagnosis and combined receipt of one PSA test during the 5 years with no testing. In this study, we did not assess the effects of digital rectal examination (DRE) as a screening procedure due to underreporting of DREs in claims data. Medicare covers DREs separately if it is the only service provided during a physician visit or if it is part of a visit that is not covered by Medicare. However, DREs administered during a routine office visit would not be covered separately by Medicare, as a result these procedures are underreported in Medicare claims.⁶⁰ We assumed that patient's county at the time of diagnosis was the county of residence at Medicare enrollment, which is consistent with previous studies that have shown that the vast majority of Americans (approximately 95%) do not change residences after age 55.^{61,62}

In conclusion, differences in stage at prostate cancer diagnosis among older Medicare beneficiaries were associated with demographic and clinical characteristics, preventive health behavior and contextual characteristics of the counties they lived in at the time of diagnosis. Moreover, after adjusting for patient-level and county-level characteristics, we observed significant geographic variation in the risk of advanced prostate cancer incidence among older Medicare beneficiaries in 158 SEER covered US counties. Counties with significantly low or high predicted rates of advanced prostate cancer diagnosis provide interesting geographic areas for further research into resources allocation for knowledge sharing and/or screening.

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Author Contributions

JJ was responsible for conception, design, data analyses, interpretation of results, manuscript preparation, and approval of the final manuscript. EO was responsible for conception, interpretation of results, and approval of the final manuscript. CC, DH, ST, MN were responsible for interpretation of results, and approval of the final manuscript.

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Supplemental Material

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