The Relationship Between Education and Prostate-Specific Antigen Testing Among Urban African American Medicare Beneficiaries

Mohammad Khalid Hararah • Craig Evan Pollack • Mary A. Garza • Hsin-Chieh Yeh • Diane Markakis • Darcy F. Phelan-Emrick • Jennifer Wenzel • Gary R. Shapiro • Lee Bone • Lawrence Johnson • Jean G. Ford

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Abstract

Purpose We examined the association between socioeconomic status (SES) and prostate-specific antigen (PSA) cancer screening among older African American men.

Methods We analyzed baseline data from a sample of 485 community-dwelling African American men who participated in the Cancer Prevention and Treatment Demonstration Trial. The outcome was receipt of PSA screening within the past year. SES was measured using income and educational

attainment. Sequential multivariate logistic regression models were performed to study whether health care access, patient—provider relationship, and cancer fatalism mediated the relationship between SES and PSA screening.

Results Higher educational attainment was significantly associated with higher odds of PSA screening in the past year (odds ratio (OR) 2.08 for college graduate compared to less than high school graduate, 95 % confidence interval (CI) 1.03–4.24); income was not. Health care access and patient–provider

M. K. Hararah (⊠)

University of Wisconsin Madison School of Medicine and Public Health, Madison, WI, USA e-mail: hararah@wisc.edu

C. E. Pollack · H.-C. Yeh

Department of General Internal Medicine, Johns Hopkins School of Medicine, Baltimore, MD, USA

C. E. Pollack

e-mail: cpollac2@jhmi.edu

H.-C. Yeh

e-mail: hyeh1@jhmi.edu

M. A. Garza

Department of Behavioral and Community Health, School of Public Health, University of Maryland, College Park, MD, USA email: magarza@umd.edu

D. Markakis · D. F. Phelan-Emrick

Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

D. Markakis

e-mail: dmarkak1@jhmi.edu

J. Wenzel

Department of Acute and Chronic Care, Johns Hopkins School of Nursing, Baltimore, MD, USA e-mail: jwenzel@jhu.edu

G. R. Shapiro

Health Partners Cancer Program and Institute for Education and Research, Minneapolis, MN, USA e-mail: grshapiro@gmail.com

G. R. Shapiro

Institute for Advanced Studies in Aging (IASIA), Falls Church, VA, USA

I. Bone

Department of Health Behavior and Society, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA e-mail: lbone@jhsph.edu

I Johnson

Park West Health Systems, Baltimore, MD, USA

J. G. Ford (⊠)

Department of Medicine, The Brooklyn Hospital Center, Brooklyn, NY, USA

e-mail: jgf9001@nyp.org

communication did not alter the relationship between education and screening; however, beliefs regarding cancer fatalism partially mediated the observed relationship.

Conclusion Rates of prostate cancer screening among African American men vary by level of educational attainment; beliefs concerning cancer fatalism help explain this gradient. Understanding the determinants of cancer fatalism is a critical next step in building interventions that seek to ensure equitable access to prostate cancer screening.

Keywords Prostate-specific antigen · Prostate cancer · Cancer screening: African American · Education · Socioeconomic status

Purpose

Socioeconomic status (SES), especially one's level of education and income, is an important determinant of the health care that one receives. Men with lower socioeconomic status, typically as indicated by lower levels of education and income, are less likely to receive prostate-specific antigen (PSA) screening and active treatment for their prostate cancer than those with higher socioeconomic status [1–7]. Less well studied, however, is examining how socioeconomic status affects health *within* racial/ethnic groups [8].

Examining the contribution of socioeconomic status to rates of PSA screening among African American men is especially important given the high burden of prostate cancer morbidity and mortality in this group [9]. While guidelines no longer recommending routine PSA screening for average-risk white men [10], few African American men were included in the large screening trials [11, 12]. With continuing uncertainty regarding the optimal approach for PSA screening among African American men, informed decision-making is frequently recommended [13, 14].

In this context, we sought to first examine the association between socioeconomic status and PSA screening among older African American men living in Baltimore and, second, explore potential mechanisms that may mediate any observed association. We specifically examined whether lower access to health care, difficulties with doctor–patient communication, and higher beliefs around cancer fatalism may help explain socioeconomic differences in PSA screening [2, 4–6, 15, 16]. Each of these factors have been previously associated with rates of PSA screening among men and are more likely to be found among men with lower socioeconomic status [2, 4, 3].

Methods

This analysis is based on data from the baseline interview of 485 Baltimore City, community-dwelling African

American men, age 65–75 years participating in the Cancer Prevention and Treatment Demonstration Project (CPTD). CPTD was funded by the Centers for Medicare & Medicaid Services (CMS) between April 2006 and December 2010. The Johns Hopkins University Institutional Review Board approved the study.

Study Participants

Study participants were recruited using two strategies. First, between October 2006 and June 2008, individuals were recruited using the Medicare membership database as well as from clinical (Johns Hopkins affiliated clinics and federally qualified health centers) and community-based settings, such as senior centers, apartment buildings, and community events. During this period, 744 individuals (27 % male, 73 % female) were recruited into the study. Second, in July 2008, enhanced population-based recruitment was initiated wherein participants were recruited through Medicare enrollment rosters provided by CMS. During this second phase of recruitment, which continued through March 2010, 1,849 individuals were enrolled in the study (26.5 % male, 73.5 % female).

African American residents of Baltimore City were eligible to participate in the CPTD study if they were aged 65 years or older, enrolled in Medicare Parts A and B, and had either no known history of cancer or cancer in remission for five years or longer. Study exclusion criteria included inability to provide informed consent and residence in an institutionalized setting, including a chronic care facility. Patients who were not enrolled in fee-for-service Medicare were excluded as the larger trial planned to obtain insurance claims data on patients. A total of 685 men completed the in-person, baseline interview. We excluded 7 men who did answer the main outcome questions on PSA screening and 193 men who were over 75 years and older as PSA screening was not routine recommended for this age group at the time when the study was conducted [17].

Variables

PSA Screening In a baseline interview, participants were asked "Have you ever had a PSA test?" and for those who responded affirmatively, "How long ago was it since you have your last PSA?" Screening in the past year was our primary outcome.

Socioeconomic Status Socioeconomic status was measured using educational attainment (categorized as less than high school, high school, some college, and college graduate) and household income measured by increments of \$10,000 (categorized as less than \$10,000, \$10,000 to \$30,000, and greater than \$30,000 based on the sample distribution).



Demographic Characteristics Marital status (married/living with partner vs single/separated/divorced), family history of prostate cancer in a first-degree relative, and self-reported health status (excellent/very good/good vs fair/poor) were included.

Health Care Access We examined three measures of access to health care: (1) whether they have a usual place for health care, (2) whether there is a particular doctor, nurse practitioner, or physician's assistant they usually see, and (3) whether respondents have Medicaid and/or Medigap enrollment.

Patient–Provider Relationship Participants were asked how often the following statements reflected their experiences with the health care system: "Health care professional listens to you carefully," "Health care professional explains things in way you can understand," "Health care professional shows you respect," and "Health care professional spends enough time with you." Responses were dichotomized into always/usually versus sometimes/never.

Cancer Fatalism Cancer susceptibility and beliefs were assessed by how much a participant agreed or disagreed with the following statements: "There is nothing you can do to lower your chance of getting cancer" and "It seems everything causes cancer." [18] Responses were categorized as "strongly agree/agree," "no opinion", and "disagree/strongly disagree."

Statistical Analyses

Exploratory data analysis was used to determine the variability and distribution of the data, followed by bivariate analyses. Bivariate analyses with chi-square tests or twosided Fisher's exact test were performed with each independent variable and PSA within the past year. We then examined the independent association between income and education and the main outcome (PSA testing within the past year) in logistic regression analyses that adjusted for marital status, family history, and self-reported health status. To test whether health care access, patient-provider relationship, and beliefs regarding cancer fatalism individually mediated the observed relationship between socioeconomic status and PSA testing, we followed the approach of Baron and Kenny in which we (1) tested whether each potential mediator was associated with PSA screening in unadjusted analyses, (2) tested whether each potential mediator was associated with socioeconomic status, and (3) examined whether the association between socioeconomic status and PSA screening was attenuated after adjustment for the potential mediator [19]. Because we did not observe a significant association between income and PSA screening, we focused on the relationship between potential mediators and education only in the tests of the association between mediators and socioeconomic status. Analyses were conducted using STATA version 11.2 for Windows (StataCorp LP, College Station 148 TX).

Results

Demographic information, patient–provider relationship, beliefs around cancer fatalism, and health access characteristics are presented in Table 1. Among the 485 African American men between 65 and 75 years old, 56 % of the sample reported having a PSA screening within the past year, and 81 % reported having a PSA screening during their lifetime. With regard to education, 36 % of the sample had less than a high school education and 13 % had earned a bachelor's degree or greater.

In bivariate analyses, participants who had higher levels of education and those with higher incomes were significantly more likely to report PSA screening in the past year. With regard to potential mediators, men who reported screening in the past year were more likely to have a usual place of health care and a particular health care professional they usually see, report that their health care professional explained things understandably and showed respect for what they had to say, and disagree with the statement that there is nothing that you can do to lower your chance of prostate cancer and that everything causes cancer.

In Table 2, the association between education and the potential mediators is reported. We focus on education because, as discussed later, income was not independently associated with PSA screening in adjusted analyses. Higher educational attainment is significantly associated with Medigap supplemental enrollment, while no other health access variables had an association with education. Higher education was not significantly associated with measures of the patient–provider relationship. Higher beliefs in cancer fatalism were found among men with lower levels of education (p value <0.01 for each statement).

Results of the unadjusted and adjusted logistic models are presented in Table 3. In unadjusted models, we find similar results as the bivariate analyses in Table 1, where men who reported screening in the past year were at higher odds of having a bachelor's degree or higher, having an income of greater than or equal to \$30,000, being married or living with a partner, and having better reported health. Again, we find that men who reported screening in the past year were at higher odds of having a usual place of care and a particular health care professional they usually see, and reporting that their health care professional explained things understandably and showed respect for what they had to say. Notably, we also see that men who agreed with the statements that there is nothing that you can do to lower your chance of prostate cancer and that



Table 1 Baseline characteristics by PSA screened status within the past year (n=485)

	Not screened		Screened		Total		p value
	\overline{N}	%	\overline{N}	%	\overline{N}	%	
Socioeconomic Status							
Income							< 0.01
<\$10,000	42	(19.7 %)	29	(10.7 %)	71	(14.6 %)	
\$10,000–\$30,000	77	(36.2 %)	89	(32.7 %)	166	(34.2 %)	
≥\$30,000	55	(25.8 %)	121	(44.5 %)	176	(36.3 %)	
Unknown	39	(18.3 %)	33	(12.1 %)	72	(14.9 %)	
Education	0.7	(41.6.07)	0.2	(20.0.0/)	1.70	(25.6.04)	< 0.01
<high school<="" td=""><td>87</td><td>(41.6 %)</td><td>83</td><td>(30.9 %)</td><td>170</td><td>(35.6 %)</td><td></td></high>	87	(41.6 %)	83	(30.9 %)	170	(35.6 %)	
High school	57	(27.3 %)	73	(27.1 %)	130	(27.2 %)	
Some college	49	(23.4 %)	65	(24.2 %)	114	(23.9 %)	
≥Bachelors degree	16	(7.7 %)	48	(17.8 %)	64	(13.4 %)	
Demographic characteristics							
Marriad dives with portner	97	(41.6.0/)	166	(62.4.9/)	252	(52.2.0/)	< 0.01
Married/lives with partner Widowed/divorced/lives alone	87	(41.6 %)	166	(62.4 %)	253	(53.3 %)	
	122	(58.4 %)	100	(37.6 %)	222	(46.7 %)	0.20
Family Hx of PCa No	185	(86.9 %)	230	(85.5 %)	415	(86.1 %)	0.29
Yes	15	(7.0 %)	28	(10.4 %)	43	(8.9 %)	
Self-reported health	13	(7.0 70)	20	(10.4 70)	-13	(0.5 70)	< 0.01
Excellent/very good/good	156	(73.2 %)	226	(83.4 %)	382	(78.9 %)	\0.01
Fair/poor	57	(26.8 %)	45	(16.6 %)	102	(21.1 %)	
Health care access		,		, ,		,	
Usual place for health care?							< 0.01
No	21	(10.0 %)	1	(0.4 %)	22	(4.6 %)	
Yes	189	(90.0 %)	268	(99.6 %)	457	(95.4 %)	
Particular doctor/NP/PA usually see?							< 0.01
No	47	(22.1 %)	22	(8.1 %)	69	(14.2 %)	
Yes	166	(77.9 %)	250	(91.9 %)	416	(85.8 %)	
Enrolled in Medigap/Supplement?							0.17
No	111	(53.9 %)	128	(47.6 %)	239	(50.3 %)	
Yes	95	(46.1 %)	141	(52.4 %)	236	(49.7 %)	
Enrolled in Medicaid, i.e., dual?	170	(96.4.0/)	224	(99.2.0/)	412	(94 5 0/)	0.54
No	178	(86.4 %)	234	(88.3 %)	412	(84.5 %)	
Yes	28	(13.6 %)	31	(11.7 %)	59	(12.5 %)	
Provider–patient relationship							0.02
Doctor listens to you carefully?	22	(10.6.07)	10	(4.0.0/)	2.5	(7.2.0/)	0.02
Sometimes/never	22	(10.6 %)	13	(4.8 %)	35	(7.3 %)	
Usually/always	186	(89.4 %)	257	(95.2 %)	443	(92.7 %)	0.04
Doctor explains things in way you un Sometimes/never	derstand?	(12.0 %)	15	(5.6 %)	40	(8.4 %)	0.01
Usually/always	183	(88.0 %)	255	(94.4 %)	438	(91.6 %)	
Doctor show respect for what you had		(88.0 /0)	233	(94.4 /0)	436	(91.0 /0)	< 0.01
Sometimes/never	20	(9.7 %)	7	(2.6 %)	27	(5.7 %)	\0.01
Usually/always	187	(90.3 %)	263	(97.4 %)	450	(94.3 %)	
Doctor spends enough time with you		(/*/		(· · · / • /		, . ,	< 0.01
Sometimes/never	28	(13.5 %)	16	(6.0 %)	44	(9.2 %)	
Usually/always	180	(86.5 %)	253	(94.1 %)	433	(90.8 %)	
Cancer fatalism							
There is nothing you can do lower ch	ance of gettin						0.02
Disagree	140	(65.7 %)	208	(76.5 %)	348	(71.8 %)	



Table 1 (continued)

	Not screened		Screened	Screened		Total	
	\overline{N}	%	\overline{N}	%	\overline{N}	%	
Agree	60	(28.2 %)	50	(18.4 %)	110	(22.7 %)	
It seems everything causes cancer Disagree	93	(43.7 %)	156	(57.4 %)	249	(51.3 %)	0.01
Agree	111	(52.1 %)	108	(39.7 %)	219	(45.2 %)	

everything causes cancer were at lower odds of having been screened in the prior year (odds ratio (OR) 0.56, 95 % confidence interval (CI) 0.36–0.86, and OR 0.58, 95 % CI 0.40–0.84), respectively.

Adjusted model I includes both income and education along with demographic factors. Only men with a bachelor's degree or higher were significantly associated with having a PSA screening within the past year (odds ratio (OR) 2.08, 95 % confidence interval (CI) 1.03–4.24) compared to less than high school diploma. Income level was not significantly associated with screening. Marital status remains significantly associated with PSA screening (OR 1.91, 95 % CI 1.27–2.88).

In model II, we added measures of health care access to model I. Individuals who reported having a usual place of care had approximately 28 times higher odds of having a PSA test within the past year though with wide confidence intervals

indicating instability of the estimate (OR 27.89, 95 % CI 3.59-216.64). Reporting supplemental insurance was not significantly correlated with having PSA testing. The addition of health access variables did not appear to alter the relationship between education and PSA screening. Model III adds patient-provider communication variables to model I. None of the communication variables were associated with PSA screening status within the past year, and the inclusion of these variables also did not alter the point estimate between education and PSA screening status. In model IV, we added variables measuring fatalism about cancer to model I. The inclusion of these items attenuated the point estimate between educational attainment and PSA testing in the negative direction, making it no longer statistically significant. Individuals who reported having a bachelor's degree or higher had approximately 1.83 times higher odds of being screened in the

Table 2 Baseline characteristics by educational level (n=478)

	Education Level								
	<high school<="" th=""><th colspan="2">High school</th><th colspan="2">Some college</th><th colspan="2">≥Bachelor's</th><th>p value</th></high>		High school		Some college		≥Bachelor's		p value
	\overline{N}	%	\overline{N}	%	\overline{N}	%	\overline{N}	%	
Total (n=478)	250	(100 %)	181	(100 %)	141	(100 %)	95	(100 %)	
PSA screened within past year	83	(30.9 %)	73	(27.1 %)	65	(24.2 %)	48	(17.8 %)	< 0.01
Health care access									
Usual place for health care	162	(35.5 %)	124	(27.2 %)	107	(23.5 %)	63	(13.8 %)	0.58
Usual Doctor/NP/PA	146	(35.2 %)	114	(27.5 %)	100	(24.1 %)	55	(13.3 %)	0.95
Enrolled in Medigap/Supplement	66	(28.1 %)	64	(27.2 %)	60	(25.5 %)	45	(19.2 %)	< 0.01
Provider–patient relationship									
Doctor listens to you carefully usually/always	157	(35.8 %)	117	(26.7 %)	103	(23.5 %)	62	(14.1 %)	0.48
Doctor explains things in way you understand <i>usually/always</i>	149	(34.3 %)	120	(27.7 %)	105	(24.2 %)	60	(13.8 %)	0.27
Doctor shows respect for what you had to say <i>usually/always</i>	158	(35.4 %)	120	(26.9 %)	105	(23.5 %)	63	(14.1 %)	0.45
Doctor spends enough time with you usually/always	148	(34.5 %)	118	(27.5 %)	103	(24.0 %)	60	(14.0 %)	0.05
Cancer fatalism									
Agrees there is nothing you can do lower chance of getting cancer	53	(50.0 %)	23	(21.7 %)	21	(19.8 %)	9	(8.5 %)	< 0.01
Agrees, it seems everything causes cancer	94	(43.3 %)	64	(29.5 %)	40	(18.4 %)	19	(8.8 %)	< 0.01

N=478, because 7 persons did not answer the educational attainment question



Table 3 Factors associated with PSA screening within the past year

	Unadjusted OR (95 % CI)	Model I	Model II	Model III	Model IV
Socioeconomic status					
Income					
<\$10,000	1.00	1.00	1.00	1.00	1.00
\$10,000–30,000	1.67 (0.95, 2.93)	1.30 (0.71, 2.35)	1.45 (0.78, 2.70)	1.25 (0.68, 2.30)	1.33 (0.73, 2.42)
≥\$30,000	3.18 (1.80, 5.64) ^a	1.68 (0.86, 3.28)	1.88 (0.93, 3.79)	1.61 (0.81, 3.17)	1.66 (0.84, 3.26)
Unknown	1.22 (0.63, 2.37)	0.81 (0.39, 1.70)	1.04 (0.48, 2.24)	0.89 (0.42, 1.88)	0.85 (0.40, 1.79)
Education					
<high school<="" td=""><td>1.00</td><td>1.00</td><td>1.00</td><td>1.00</td><td>1.00</td></high>	1.00	1.00	1.00	1.00	1.00
High school	1.34 (0.85, 2.12)	1.09 (0.67, 1.77)	1.14 (0.69, 1.88)	1.10 (0.67, 1.82)	1.01 (0.61, 1.65)
Some college	1.39 (0.86, 2.24)	1.23 (0.73, 2.05)	1.35 (0.79, 2.31)	1.29 (0.76, 2.19)	1.09 (0.65, 1.86)
≥Bachelors degree	3.14 (1.66, 5.96) ^a	2.08 (1.03, 4.24) ^b	2.11 (1.03, 4.37) ^b	$2.07 (1.01, 4.21)^{b}$	1.83 (0.89, 3.77) ^c
Demographics					
Married/lives with partner	2.32 (1.61, 3.37) ^a	1.91 (1.27, 2.88) ^a	1.76 (1.14, 2.70) ^a	1.71 (1.12, 2.60) ^b	1.94 (1.28, 2.94) ^a
Family history of PCa	1.50 (0.78, 2.89)	1.37 (0.68, 2.79)	1.54 (0.73, 3.26)	1.48 (0.71, 3.06)	1.43 (0.69, 2.92)
Fair/poor self-reported Health	$0.54 (0.35, 0.85)^{a}$	0.69 (0.43, 1.11)	0.65 (0.40, 1.06) ^c	0.69 (0.43, 1.11)	0.73 (0.45, 1.18)
Health care access					
Usual source of care	29.78 (3.97, 223.29) ^a		27.89 (3.59, 216.64) ^a		
Usual Doctor/NP/PA	3.22 (1.87, 5.54) ^a	-	-		
Medigap/Supplement insurance	1.29 (0.89, 1.85)		0.73 (0.50, 1.11)		
Enrolled in Medicaid	0.84 (0.49, 1.46)	-			
Provider-patient relationship					
Doctor listens to you carefully usually/always	2.34 (1.15, 4.76) ^b		-	1.09 (0.36, 3.34)	
Doctor explains things in way you understand usually/always	2.32 (1.19, 4.53) ^b		-	1.04 (0.35, 3.06)	
Doctor show respect for what you have to say <i>usually/always</i> .	4.01 (1.67, 9.70) ^a		-	1.65 (0.32, 8.45)	
Doctor spends enough time with you usually/always Cancer fatalism	2.46 (1.30, 4.70) ^a		-	1.58 (0.61, 4.13)	
Agrees there is nothing you can do lower chance of getting cancer	0.56 (0.36, 0.86) ^a		-	-	0.64 (0.40, 1.04) ^c
Agrees that everything causes cancer	$0.58 (0.40, 0.84)^{a}$		_	_	0.68 (0.45, 1.02) ^c

OR odds ratio, CI confidence interval

previous year than those without a high school diploma (OR 1.83, 95 % CI 0.89–3.77).

Discussion

Among older African American men living in Baltimore, we found that education was positively significantly associated with reported prostate cancer screening by PSA testing. Beliefs concerning cancer fatalism (i.e., that "there is nothing you can do to lower cancer risk" and "everything causes cancer") were more common among men with lower

socioeconomic status and, after the inclusion of these beliefs in a multivariable model, education was no longer significantly associated with PSA screening. The results present important evidence on socioeconomic differences in cancer screening within racial/ethnic group as well as potential factors that may be targeted in addressing these differences.

Although PSA screening remains controversial, most guidelines recommend informed decision-making for African American men [10, 13]. Patients with lower socioeconomic status are often less likely to engage in shared decision-making [20]. In previous studies, patients with fatalistic beliefs about cancer are at decreased likelihood of



 $^{^{}a}p$ value ≤0.01

 $^{^{\}rm b}p$ value ≤0.05

 $^{^{\}rm c}p$ value ≤ 0.10

engaging in preventative behaviors [21]. In our current study, we found that those with higher beliefs in cancer fatalism were less likely to undergo screening, although the results did not remain significant in our fully adjusted model. It is possible that addressing cancer fatalism may be an important way to reduce socioeconomic disparities within racial/ethnic groups.

Studies using short education programs or brief media interventions targeting cancer fatalism have been successful in reducing fatalistic beliefs about cancer survivorship; this suggests that cancer fatalism is modifiable [22, 23]. Future research should be aimed at sources of cancer fatalism and assess the impact of interventions to reduce cancer fatalism. If fatalistic beliefs about cancer prevention are largely attributable to information overload or are culturally related, health educators might target these areas. Health care workers and educators could develop simpler cancer prevention messages that can be widely disseminated and understood by less educated individuals.

Annual income was not the major determinant of screening status after adjusting for education and other known confounders. The finding that varying income levels are insufficient to explain socioeconomic differentials of cancer screening is consistent with previous research on PSA screening and other health service use, particularly in relation to countries with universal health care (in comparison to the Medicare) [24, 8]. Moreover, focusing on urban African American Medicare beneficiaries in Baltimore City may lead to less heterogeneity in income distribution and have limited our ability to see significant associations, especially for those at the higher end of the income distribution [25]. There also may be other markers of socioeconomic status such as wealth, which may be particularly meaningful among older adults when yearly income may not be stable [26, 27].

Although access to care did not mediate the role of education, it was a strong predictor for PSA screening in its own right. Men who have a usual place of care were 28 times more likely to have had a PSA within the past year, albeit with wide confidence intervals. Increasing access to care may be an important step in increasing rates of screening among urban, African American Medicare beneficiaries, regardless of level of education.

Limitations

Our findings contain several limitations that should be considered in the interpretation of the results. First, we focus on African American Medicare beneficiaries in Baltimore City. We do not have comparison data for the rates of PSA screening among African Americans in Baltimore based solely on a population-based sample. Moreover, annual screening rates were slightly higher in this study than other previous national estimates that

described frequency in screening [28, 5, 3]. Thus, our results may not be broadly generalizable. Second, questions on cancer fatalism were not specific to prostate cancer. Similarly, patient-provider communication was measured using general self-reported communication items, which may not capture the full extent of the patient-provider relationship and were not specific to prostate cancer screening. Third, the outcome measure of having undergone prostate cancer screening within the past year was self-reported and subject to recall bias [29, 30]. Fourth, consistent with previous studies, our measure of income included a high degree of missing values. Incomes were reported to be low, which is consistent with Baltimore City's relative deprivation compared to the remainder of the state [25]. The lower range of incomes likely limited our ability to detect significant associations between income and PSA, especially among men with higher incomes. In addition, with a small sample size, our ability to detect significant associations is diminished. Finally, this study occurs in the context of uncertainty over the optimal use of PSA screening among African American men [13, 10]. Related to this, while it is possible that educational differences in the observed rates of PSA screening reflect differences in informed choices, such explanations based on patient preferences are often misleading [31]. Patients with lower socioeconomic status have been found to have lower levels of informed decision-making [15].

Conclusion

The results demonstrate that urban, African American men with lower levels of education status tend to have lower rates of PSA screening. These differences may, at least in part, be explained by cancer fatalism. Understanding the determinants of cancer fatalism and why it is more prominent among low-income men is a critical next step in building interventions that seek to ensure equitable access to prostate cancer screening.

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Conflict of interest Mohammad Khalid Hararah, Craig Evan Pollack, Mary A. Garza, Hsin-Chieh Yeh, Diane Markakis, Darcy F. Phelan-Emrick, Jennifer Wenzel, Gary R. Shapiro, Lee Bone, Lawrence Johnson, and Jean G. Ford all declare that they have no conflict of interest.

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Informed consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was obtained from all patients for being included in the study.

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