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Diabetes and prostate cancer screening in black and white men

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Abstract

Purpose—Prior studies conducted primarily among white men, find a reduced risk of prostate cancer associated with time since developing diabetes. While biologic explanations are plausible, the association may in part arise from more frequent prostate cancer screening among those with a diabetes diagnosis. The purpose of the present study was to investigate the association between diabetes and prostate cancer screening.

Methods—We examined differences in prostate cancer screening (prostate-specific antigen and/or digital rectal examination) testing practices after a diabetes diagnosis among lower-income persons living in the southeastern United States and enrolled in the Southern Community Cohort Study between 2002 and 2009. Baseline in-person interviews collected information on history of diabetes and prostate cancer screening from 18,809 black and 6,404 white men aged 40-79 years.

Results—After adjustment for confounding, diabetic black (odds ratio (OR) 1.12, 95% confidence interval (CI) 1.01-1.25) and white (OR 1.25, 95% CI 1.03-1.51) men were more likely to undergo recent prostate cancer screening compared to non-diabetic men of the same race. The increased risk for prostate cancer screening, however, occurred primarily within the first 12 months after diabetes diagnosis.

Conclusions—Our results suggest that a diabetes diagnosis modestly increases the likelihood of having a prostate cancer screening test for both black and white men. The prevalence of screening was higher nearer to the time of diabetes diagnosis, which may contribute to an early increase in prostate cancer detection followed by lower prostate cancer detection after an extended time.

Keywords

Race; prostate cancer screening; diabetes; cohort study

Introduction

Increasing evidence suggests that diabetes is associated with reduced prostate cancer risk [1-3], with a summary relative risk (RR) of 0.84 (95% confidence interval (CI) 0.76-0.93) in

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a published meta-analysis [3]. However, two large prospective studies, the Cancer Prevention Study II [1] and Health Professionals Follow-up Study [2], found that prostate cancer risk initially increased for 3 years (RR=1.2) and 1 year (RR=1.3), respectively, following a diabetes diagnosis, before decreasing with longer time since diabetes diagnosis (RR=0.63 and RR=0.75-0.82). Possible explanations for an inverse association between diabetes and prostate cancer include a direct effect of diabetes on reduced prostate cancer growth by lowering insulin [3] or bioavailable testosterone [4] levels, a secondary effect of diabetes drugs such as metformin on prostate carcinogenesis [5], or alternatively an indirect effect due to changes in prostate cancer screening after diabetes diagnosis [6].

Few studies have included black men [3], despite greater diabetes and prostate cancer burdens compared to white men. In the Multiethnic Cohort Study (MEC), a weaker reduction in prostate cancer risk was observed among black (RR=0.89) than white (RR=0.65) men followed for eight years after diabetes diagnosis, despite similar PSA screening frequency by diabetes status in both groups [7]. A cohort study of United States (US) veterans, conducted before the introduction of prostate-specific antigen (PSA) screening, observed similar reductions in prostate cancer risk associated with diabetes among black (RR=0.91) and white (RR=0.88) men, with median follow-up time of 10.5 years for diabetics and 11.9 years for non-diabetics [8].

We investigated the relationship between diabetes and prostate cancer screening, in an attempt to determine its mediating effect on the diabetes and prostate cancer association. Several studies have shown reduced breast cancer screening among diabetic women, but no study has evaluated the association between diabetes and timing of prostate cancer screening. We wished to assess the possibility that decreased prostate cancer screening among diabetics, as seen with the association between diabetes and breast cancer screening, may partially explain the observed reduced risk of prostate cancer associated with diabetes. We hypothesized that prostate cancer screening would be most prevalent near the time of diabetes diagnosis, and, to explain the stronger reduction in prostate cancer risk associated with diabetes among white than black men seen in the MEC [7], that white diabetic men would undergo prostate cancer screening more frequently than white non-diabetic men. In contrast, there would be no association between diabetes and prostate cancer screening among black men.

Methods

Detailed methods of the Southern Community Cohort Study (SCCS), which enrolled black and white men and women in the southeastern US aged 40-79 years, appear elsewhere [9]. Approximately 85 percent of participants completed in-person interviews at the time of enrollment at Community Health Centers (CHC), with the remainder recruited through general population sampling and completion of mailed questionnaires. After exclusion of men of other racial/ethnic groups, men with a history of any cancer or a severe comorbidity (e.g., HIV/AIDS, chronic obstructive pulmonary disease, and history of myocardial infarction) that would preclude screening, and men whose PSA/digital rectal exam (DRE) screening history was not available, the study population for the current analysis comprised 18,809 black and 6,404 white men.

Men were classified as diabetic at baseline if they reported being told by their doctor they had diabetes or high blood sugar, and were further characterized by time since diabetes diagnosis (<1-year, then 5-year categories), year of diagnosis (pre- and post-1994), and use of diabetes medications (oral, insulin). PSA and/or DRE screening was categorized as having occurred within the past 12 months. We stratified by race rather than assess it as an effect modifier because the MEC study reported a stronger association between diabetes and prostate cancer among white than among black men [7]. Covariates of interest included: age, annual household income, educational level, marital status, health insurance coverage, recruitment source, body mass index (BMI, kg/m^2) at age 21 years and maximum, hypertension, cholesterol medication use (previously associated with PSA testing) [10], smoking, and leisure-time moderate and vigorous physical activity during their 30s in hours per week, all self-reported on the baseline questionnaire and categorized as in Table 1. Based on previous studies of diabetes and prostate cancer, age [2, 8] and maximum BMI [2, 8] were assessed as effect modifiers of the diabetes and prostate cancer screening association prior to being assessed as confounders, as were marital status and health insurance, both of which are strong predictors of prostate cancer screening in these data [11].

Statistical analyses were performed in SAS version 9.2. We assessed statistically significant (two-sided, $p<0.05$) differences between diabetics and non-diabetics for potential confounders using chi-square tests. We used unconditional logistic regression to estimate the odds ratios (OR) and 95% CIs for prostate cancer screening associated with diabetes. Interaction terms, the product of diabetes and the putative effect modifiers (age, maximum BMI, marital status and health insurance), were added to logistic regression models and likelihood ratio tests were performed to test for effect modification.

Results

Table 1 presents characteristics of black men who were (n=4,283, 23.8%) and were not (n=13,695) screened for prostate cancer in the past 12 months. Compared to men who were not screened, black men who were screened were significantly older, had a higher household income and educational level, and were more likely to be married or living with a partner, have private insurance, have a higher maximum BMI, have hypertension, be taking cholesterol medications, and be never or former smokers. Similar patterns were seen when comparing screened (n=1,913, 31.3%) and unscreened (n=4,201) white men.

Table 2 presents the association between diabetes measures and prostate cancer screening within the past 12 months by race, adjusted for all variables except smoking whose addition to the model did not materially change OR estimates. Overall, 22.1% of non-diabetic black men and 33.1% of diabetic black men had been screened for prostate cancer. Prostate cancer screening was modestly but significantly more prevalent among men with versus without diabetes (OR 1.12, 95% CI 1.01-1.25). Utilizing <1 year between diabetes diagnosis and prostate cancer screening as the reference, prostate cancer screening among diabetics was greatest in the first year after diabetes diagnosis, after which no excess was observed and screening remained fairly stable with time. There was no significant effect of year of diabetes diagnosis or use of diabetes medications on prostate cancer screening.

Among white men, 29.8% of non-diabetics and 39.8% of diabetics had been screened for prostate cancer. Diabetes was significantly associated with increased odds of prostate cancer screening (OR 1.25, 95% CI 1.03-1.51). Among those with diabetes, we did not observe statistically significant differences according to time since diabetes diagnosis, but similar to the pattern in blacks, there appeared to be an excess of screening in the first year after diabetes diagnosis, after which the prostate cancer screening rate remained stable. Again, similar to black men, there was no effect of year of diabetes diagnosis or use of diabetes medications on prostate cancer screening. Age, maximum BMI, marital status and health insurance did not significantly modify the association between diabetes and prostate cancer screening among blacks or whites (not shown).

We performed a sensitivity analysis among diabetic men only who had been screened for prostate cancer (not shown). Time between diabetes diagnosis and recent prostate cancer screening was categorized as <1 year, 1-2 years, 3-5 years, 6-9 years and 10 or more years. Among diabetic men who were screened for prostate cancer, white men were significantly more likely than black men to have been screened within one year of diagnosis (14.7% vs. 11.6%, p=0.04). In contrast, black men were significantly more likely than white men to have been screened 10 or more years after their diagnosis (34.0% vs. 26.4%, p=0.001).

Discussion

Research on the role of prostate cancer screening in the association between diabetes and prostate cancer risk raised the possibility of a variable effect depending upon timing of the screening. A meta-analysis [3] found a more pronounced inverse association between diabetes and prostate cancer risk for studies conducted after 1994 (RR 0.73, 95% CI 0.64-0.83), when PSA screening became widespread, than those conducted before 1994 (RR 0.94, 95% CI 0.85-1.03). However, a case-control study of black and white men conducted after initiation of widespread PSA testing found no difference in the reduction of prostate cancer risk associated with diabetes among those men who reported they received annual prostate cancer screening (OR 0.68, 95% CI 0.41-1.12) compared to those screened less frequently (OR 0.61, 95% CI 0.36-1.01) [12].

In contrast with studies of diabetes and breast cancer screening which reported negative associations [13-16], we found that diabetes is modestly but significantly associated with increased likelihood of having a recent prostate cancer screening test among black and white men. However, the influence of diabetes on screening practices appeared largely restricted to the first year after a diabetes diagnosis, with similarly elevated OR estimates for screening during the first year among black and white men, albeit statistically significant only among black men. The associations between diabetes and breast and prostate cancer also differ, with greater likelihood of postmenopausal breast cancer associated with diabetes [17-20] and less likelihood of prostate cancer associated with diabetes [21].

Healthcare access, insurance coverage, and other socio-economic characteristics, as well as race, are all associated with PSA testing practices and cancer stage at detection. In our study population of black and white men with similarly low socioeconomic status (SES) and similar access to care, a positive association between diabetes and prostate cancer screening may be expected. Additionally, past prostate cancer screening recommendations [22-24], are consistent in suggesting increased prostate cancer screening for black men, who are at higher risk of prostate cancer compared with white men. Thus, primary care physicians face the challenge of not only considering the patient's age and race, but also overall health and co-morbidity status, in guiding the patient to an informed judgment as to the benefits of screening. Additionally, diabetes has been linked to increased risk of benign prostatic hyperplasia [25], suggesting the possibility that diabetes patients experiencing lower urinary tract symptoms should be preferentially screened at diagnosis to remove prostate cancer as a differential diagnosis. Furthermore, obesity is more prevalent among diabetes patients and thus may contribute to lower blood PSA levels [26-28], increasing the need for more frequent screening; however, we controlled for BMI in our analyses.

Preferential screening of men with diabetes may impact the interpretation of epidemiologic findings [1, 2] that prostate cancer risk initially increased following a diabetes diagnosis, before decreasing with extended follow-up. Thus, the long-term decreased risk of prostate cancer may result in part from enhanced detection near the time of diabetes diagnosis, as the lead time induced by active screening and removal of latent prostate cancers early during the follow-up period may remove prostate cancers that would have been diagnosed during extended follow-up. Future cohort investigations of diabetes and prostate cancer should consider collecting detailed data on PSA screening history to control for time varying effects

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of prostate cancer detection. Indeed, interpretation of past prostate cancer analyses have been altered with adjustment for prostate cancer screening [29].

Our study relied on self-reports of diabetes and prostate cancer screening which may have been affected by faulty memory or low literacy, or misclassification due to undiagnosed diabetes or inaccurate reports of timing of prostate cancer screening. However, the majority of SCCS participants were patients at CHCs, which provide primary healthcare to the underserved, and a validation sub-study found over 95% of self-reported diabetes in the SCCS could be confirmed through medical chart review [9]. It is possible that initiation of prostate cancer screening preceded or occurred simultaneously with a diabetes diagnosis in a subset of the baseline cohort, however we analyzed prostate cancer screening in the 12 months prior to cohort entry so that diabetes preceded prostate cancer screening for the vast number of study participants reporting a diabetes diagnosis. While we adjusted for health care coverage as a dimension of health care access, we were unable to adjust for usual source of care.

Study strengths include the large size of the population allowing for investigation of associations in black and white men separately. Confounding by socioeconomic factors is likely to be minimal, because blacks and whites were of similar SES upon recruitment and residual differences in education and income were accounted for in the statistical analyses. We adjusted for a wide range of confounders including obesity, hypertension, and cholesterol medication use, as well as health insurance coverage to isolate the effect of diabetes on prostate cancer screening apart from its effect on access to care.

In conclusion, diabetes was positively associated with prostate cancer screening especially during the short term following a diabetes diagnosis. Although racial differences in healthcare recommendations have been described by the Institute of Medicine [30], we found similar results for prostate cancer screening by diabetes status among black and white men. The early increase in prostate cancer detection, followed by lower prostate cancer detection over time, may partially explain the overall reduction in prostate cancer risk associated with diabetes.

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Table 1

Demographic characteristics of men who were and were not screened for prostate cancer within the past 12 months, Southern Community Cohort Study, 2002-2009

	Screened[a]		Not screened		
Characteristic	**n**	**%**	**n**	**%**	**p-value**
Black Men					
Age (years)					<0.0001
40-44	711	16.6	4341	31.7	
45-49	931	21.7	3751	27.4	
50-54	980	22.9	2833	20.7	
55-59	713	16.7	1521	11.1	
60-64	504	11.8	708	5.2	
65-69	256	6.0	326	2.4	
70-74	134	3.1	151	1.1	
75-79	54	1.3	64	0.5	
Annual household income					<0.0001
<$15,000	2065	48.9	8321	61.3	
$15,000-$24,999	885	21.0	3045	22.4	
$25,000-$49,999	726	17.2	1581	11.7	
$50,000-$99,999	420	9.9	507	3.7	
≥$100,000	128	3.0	115	0.9	
Educational level					<0.0001
<9 years	355	8.3	1009	7.4	
9-11 years	812	19.0	3572	26.1	
Completed high school or GED	1372	32.1	5263	38.5	
Vocational/Some college	1085	25.3	2936	21.5	
Graduated from college	390	9.1	657	4.8	
Graduate school	267	6.2	250	1.8	
Marital status					<0.0001
Single	956	22.5	4790	35.1	
Married/living with a partner	1729	40.7	3856	28.2	

	Screened[a]		Not screened		
Characteristic	n	%	n	%	p-value
Black Men					
Divorced/widowed/separated	1560	36.8	5015	36.7	
Health insurance coverage					<0.0001
None	1436	33.7	7482	54.8	
Medicare/Medicaid only	1123	26.3	2827	20.7	
Any private/CHAMPUS/other	1709	40.0	3337	24.5	
Recruitment source					<0.0001
Community Health Centers	3613	84.4	12941	94.5	
General population	670	15.6	754	5.5	
Body mass index (kg/m^2) at age 21					0.03
<18.5	284	7.0	953	7.3	
18.5-24.9	2428	59.7	8088	61.8	
25-29.9	1058	26.0	3081	23.6	
30-34.99	224	5.5	681	5.2	
35-39.99	51	1.3	178	1.4	
40	24	0.6	101	0.8	
Body mass index (kg/m^2) maximum					<0.0001
<20	25	0.6	137	1.0	
20-24.99	578	13.8	2684	19.9	
25-29.99	1468	35.0	4848	35.9	
30-39.9	1771	42.3	4872	36.1	
40	350	8.4	959	7.1	
Hypertension					<0.0001
No	1652	38.6	7736	56.5	
Yes	2630	61.4	5954	43.5	
Cholesterol medications					<0.0001
No	3464	81.3	12564	91.8	
Yes	797	18.7	1117	8.2	
Smoking					<0.0001

Characteristic	Screened[a] n	Screened[a] %	Not screened n	Not screened %	p-value
Black Men					
Never	1144	26.9	2997	22.0	
Former	1160	27.3	2214	16.2	
Current	1944	45.8	8427	61.8	
Moderate physical activity during their 30s (hours per week)					0.12
0	244	5.9	916	6.8	
0.01-2.00	56	1.3	171	1.3	
2.01-4.99	69	1.7	255	1.9	
≥5	3802	91.2	12160	90.1	
Vigorous physical activity during their 30s (hours per week)					0.20
0	397	9.5	1340	9.9	
0.01-2.00	182	4.4	494	3.7	
2.01-4.99	134	3.2	434	3.2	
≥5	3463	82.9	11247	83.2	
White Men					
Age (years)					<0.0001
40-44	152	8.0	1169	27.8	
45-49	261	13.6	1090	26.0	
50-54	348	18.2	758	18.0	
55-59	428	22.4	577	13.7	
60-64	360	18.8	334	8.0	
65-69	222	11.6	161	3.8	
70-74	99	5.2	85	2.0	
75-79	43	2.3	27	0.6	
Annual household income					<0.0001
<$15,000	441	23.6	1922	46.2	
$15,000-$24,999	222	11.9	787	18.9	
$25,000-$49,999	382	20.5	683	16.4	

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Characteristic	Screened[a] n	Screened[a] %	Not screened n	Not screened %	p-value
Black Men					
$50,000-$99,999	525	28.1	515	12.4	
≥$100,000	298	16.0	253	6.1	
Educational level					<0.0001
<9 years	102	5.3	316	7.5	
9-11 years	144	7.5	656	15.6	
Completed high school or GED	433	22.7	1400	33.4	
Vocational/Some college	467	24.5	1034	24.6	
Graduated from college	372	19.5	427	10.2	
Graduate school	392	20.5	364	8.7	
Marital status					<0.0001
Single	153	8.4	764	18.4	
Married/living with a partner	1271	69.3	1889	45.6	
Divorced/widowed/separated	409	22.3	1493	36.0	
Health insurance coverage					<0.0001
None	350	18.4	2043	48.8	
Medicare/Medicaid only	281	14.8	739	17.7	
Any private/CHAMPUS/other	1272	66.8	1405	33.6	
Recruitment source					<0.0001
Community Health Centers	887	46.4	3217	76.6	
General population	1026	53.6	984	23.4	
Body mass index (kg/m^2) at age 21					0.04
<18.5	103	5.5	254	6.2	
18.5-24.9	1165	62.6	2480	60.3	
25-29.9	478	25.7	1067	25.9	
30-34.99	92	4.9	223	5.4	
35-39.99	11	0.6	63	1.5	
40	13	0.7	29	0.7	
Body mass index (kg/m^2) maximum					<0.0001

Characteristic	Screened[a] n	Screened[a] %	Not screened n	Not screened %	p-value
Black Men					
<20	7	0.4	27	0.7	
20-24.99	182	9.7	599	14.4	
25-29.99	697	37.0	1458	35.1	
30-39.9	819	43.5	1673	40.3	
40	179	9.5	394	9.5	
Hypertension					<0.0001
No	942	49.2	2586	61.6	
Yes	971	50.8	1614	38.4	
Cholesterol medications					<0.0001
No	1309	68.8	3622	86.5	
Yes	593	31.2	567	13.5	
Smoking					<0.0001
Never	685	36.5	1031	24.8	
Former	789	42.1	1033	24.8	
Current	402	21.4	2102	50.5	
Moderate physical activity during their 30s (hours per week)					<0.0001
0	92	5.0	281	6.8	
0.01-2.00	26	1.4	62	1.5	
2.01-4.99	80	4.4	100	2.4	
≥5	1635	89.2	3672	89.2	
Vigorous physical activity during their 30s (hours per week)					<0.0001
0	180	9.8	447	10.9	
0.01-2.00	116	6.3	155	3.8	
2.01-4.99	111	6.1	124	3.0	
≥5	1427	77.8	3392	82.4	

[a]Prostate-specific antigen or digital rectal exam.

Table 2

Odds ratios of prostate cancer screening within the past 12 months associated with diabetes measures by race, Southern Community Cohort Study, 2002-2009

	Screened[a]		Not screened			
Characteristic	**n**	**%**	**n**	**%**	**OR[c]**	**95% CI[d]**
Black Men						
Self-reported diabetes						
No	3327	77.7	11761	85.9	1.0	Referent
Yes	956	22.3	1934	14.1	1.12	1.01-1.25
Time since diabetes diagnosis (years)[b]						
<1	86	9.2	158	8.3	1.0	Referent
1-4	291	31.1	599	31.5	0.74	0.53-1.02
5-9	227	24.3	475	25.0	0.69	0.49-0.96
10-14	150	16.0	302	15.9	0.64	0.45-0.92
15-19	82	8.8	145	7.6	0.71	0.47-1.08
≥20	100	10.7	223	11.7	0.51	0.35-0.76
Year of diabetes diagnosis[b]						
Pre-1994	290	31.0	571	30.0	1.0	Referent
Post-1994	646	69.0	1331	70.0	1.11	0.92-1.35
Diabetes medications[b]						
No	134	14.1	310	16.1	1.0	Referent
Yes	819	85.9	1621	83.9	1.06	0.83-1.36
White Men						
Self-reported diabetes						
No	1559	81.5	3666	87.3	1.0	Referent
Yes	354	18.5	535	12.7	1.25	1.03-1.51
Time since diabetes diagnosis (years)[b]						
<1	41	11.8	54	10.2	1.0	Referent
1-4	112	32.2	186	35.2	0.65	0.36-1.16

Characteristic	Screened[a] n	Screened[a] %	Not screened n	Not screened %	OR[c]	95% CI[d]
Black Men						
5-9	91	26.2	137	25.9	0.71	0.39-1.29
10-14	44	12.6	77	14.6	0.59	0.30-1.16
15-19	24	6.9	27	5.1	0.74	0.32-1.69
≥20	36	10.3	48	9.1	0.76	0.37-1.57
Year of diabetes diagnosis[b]						
Pre-1994	85	24.4	116	21.9	1.0	Referent
Post-1994	263	75.6	413	78.1	0.86	0.59-1.26
Diabetes medications[b]						
No	71	20.1	116	21.7	1.0	Referent
Yes	282	79.9	419	78.3	1.18	0.79-1.78

[a]Prostate-specific antigen or digital rectal exam.

[b]Among diabetics.

[c]Odds ratio adjusted for age, annual household income, educational level, marital status, health insurance coverage, recruitment source, BMI at age 21 years and maximum, hypertension, cholesterol medications, and leisure-time moderate and vigorous physical activity during their 30s as categorized in Table 1.

[d]95% Confidence interval.