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Substantial Family History of Prostate Cancer in Black Men Recruited for Prostate Cancer Screening:

Results from the Prostate Cancer Risk Assessment Program

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Abstract

Background—Black men are at increased risk for prostate cancer (PCA), particularly with a family history (FH) of the disease. Previous reports have raised concern for suboptimal screening of Black men with a FH of PCA. We report on the extent of FH of PCA from a prospective, longitudinal PCA screening program for high-risk men.

Methods—Black men ages 35-69 are eligible for PCA screening through the Prostate Cancer Risk Assessment Program (PRAP) regardless of FH. Rates of self-reported FH of PCA, breast, and colon cancer at baseline were compared with an age-matched sample of Black men from the 2005 National Health Interview Survey (NHIS) using standard statistical methods.

Results—As of January 2007, 332 Black men with pedigree information were enrolled in PRAP and FH of PCA was compared to 838 Black men from the 2005 NHIS. Black men in PRAP reported significantly more first-degree relatives with PCA compared to Black men in the 2005 NHIS (34.3%, 95% CI 29.2-39.7 vs. 5.7%, 95% CI 3.9-7.4). Black men in PRAP also had more FH of breast cancer compared to the 2005 NHIS (11.5%, 95% CI 8.2-15.4 vs 6.3%, 95% CI 4.6-8.0).

Conclusions—FH of PCA appears to be a motivating factor for Black men seeking PCA screening. Targeted recruitment and education among Black families should improve PCA screening rates. Efforts to recruit Black men without a FH of PCA are also needed.

Condensed Abstract—Black men seeking prostate cancer screening have a substantial burden of family history of prostate cancer. Targeted education and enhancing discussion in Black families should increase prostate cancer screening and adherence.

Keywords

prostatic neoplasms; family; mass screening; African Americans; risk factors

Background

Prostate cancer (PCA) remains the most common noncutaneous cancer and the second leading cause of cancer-related death in Black males in the United States (1). The American Cancer Society estimates that over 186,320 men in the United States will be diagnosed with PCA in 2008 and 30,870 (17%) of these cases will be in Black men (1). Race alone places Black men at two times higher risk than Euro-American men for PCA, and having a family history (FH)

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of PCA increases their risk 6.4-fold (2). In addition, PCA in Black men has been reported to be more aggressive (3). Most reports in the literature have focused on quantifying the risk for PCA in Black men based on FH, genetic factors, or epidemiologic factors in case-control studies or from hereditary cohorts (2,4-8). While quantification of PCA risk in Black men is essential, the impact of PCA in these families in the community can be more fully understood if the familial prevalence of PCA is characterized. Estimates of PCA prevalence in Black families have been described in the control arms of previous reports (2,4-8), but not from a prospective cohort of Black men enrolled in a PCA screening program.

PCA screening rates for Black men are suboptimal, even in those men with a FH of the disease (9-14). Weinrich reported that Black men from hereditary PCA families had lower PCA screening rates than age-matched Black men drawn from participants in the 2000 National Health Interview Survey (NHIS), stating a need to replicate screening rates in other cohorts with Black participants (8).

The Prostate Cancer Risk Assessment Program (PRAP) at Fox Chase Cancer Center (FCCC) was established in 1996 to provide screening for men at increased risk for PCA and to gain insight into familial patterns of PCA risk (15). The PRAP cohort is unique because 60% of participants are Black and are followed prospectively. We recently reported a ten-year update of cancer detection from the PRAP cohort, where we found an approximate 10% PCA incidence among the Black participants (16). Furthermore, 79.4% of the Black men were diagnosed with PCA at low prostate-specific antigen (PSA) values (4.0ng/ml or less) and 91.2% had Gleason scores of 6.0 or higher (16). Characterization of pedigrees in this cohort will lend insight into the familial patterns of PCA as well as other cancers in Black families accrued for PCA screening from the community to educate them about the disease and adherence to PCA screening.

Here, we report the detailed pedigrees of Black men enrolled from the community for aggressive PCA screening through the PRAP study at FCCC. Specifically, we examine the extent to which families of Black male PRAP participants harbor PCA. We also compared the rate of familial PCA among these individuals with the rate among a sample of Black men drawn from the nationally representative 2005 NHIS. We also explore the prevalence of other screen-detectable cancers (i.e., breast and colon cancers) reported in the families of Black male PRAP participants and in families of Black male participants in the 2005 NHIS. Finally, we assessed whether the rate of adherence to follow-up PCA screening after an initial screening differed between Black male PRAP participants who had a FH of PCA and those that did not. This information can be used to enhance communication regarding PCA, discuss the importance of adherence to screening schedules, and to discuss PCA early detection with the Black community in order to make strides to prevent mortality from this disease.

Methods

PRAP Procedures and Eligibility

The objectives and design of PRAP have been described previously (15). Briefly, PRAP was established in 1996 with the objectives of providing screening and education for men at high risk for PCA and to perform research regarding the increased risk. Black men, ages 35-69 years, with no personal history of PCA are eligible to enter the program regardless of a FH of PCA. Screening measures and biopsy criteria have been reported previously (16). Recruitment of Black men has been shown to be most successful when targeted to communities where these men live and/or work (13). Therefore, PRAP primarily focuses efforts for recruiting Black men from the community through radio advertisements broadcast in the Philadelphia metropolitan area. In addition to FCCC, participants are also recruited at three community Partner hospitals. At an initial visit, PRAP participants undergo PCA screening consisting of PSA testing and a

digital rectal examination (DRE). Individuals with no abnormal screening test results are scheduled to return for subsequent PCA screening in 12 months' time. Criteria for prostate biopsy in PRAP have changed over time. Prior to November 2005, criteria for prostate biopsy were (1) PSA > 4 ng/mL, (2) PSA 2.0-4.0 with fPSA less than 27%, (3) any abnormality on DRE, or (4) PSAv of 0.75 ng/mL/year. Since PCA detection rates have been high with these criteria (16), the criteria for prostate biopsy were lowered after November 2005 to detect earlier changes in screening parameters. The criteria for biopsy after November 2005 were changed to (1) PSA > 2.0 ng/mL, (2) PSA 1.5-2.0 ng/mL with fPSA <25%, (3) any abnormality on DRE, or (4) PSAv of 0.75 ng/mL/year.

PRAP Measures and Data Management

Participants in the PRAP complete a 400+ item questionnaire assessing demographic factors and a broad range of health-related issues. For the purposes of the current report, we used self-reported responses to a comprehensive Family History of Cancer form from the Health History Questionnaire (HHQ) that is completed at the initial screening visit. Data entry is performed via a custom Oracle Forms (version 10.1.2.0.2) application used by the Risk Assessment Programs at FCCC. The data are maintained by an Oracle RDBMS, version 9i.

Since FH information is self-reported, standard criteria are utilized for imputation of dummy parents whenever an offspring is listed in order to create complete pedigrees. Imputed individuals were added by the Data Management staff in order to complete a mother/father link for any child reported by the PRAP participant. FH information is updated during follow-up visits by self-report.

Informed consent is obtained from all PRAP participants and the PRAP study is approved by the Institutional Review Board at FCCC.

PRAP Participants

As of January 2007, 403 Black men were enrolled in PRAP for PCA screening. FH information was provided by 83.2% (337/405) of participants. Five Black participants had other relatives who are in PRAP. For these families, only the initial PRAP participant (proband) with FH information provided was detailed in this report in order to prevent duplication of results. These pedigrees are described as "unique" pedigrees. Among the 332 individuals with unique pedigrees, the mean age was 49.3 years (SD=8.3 years) and 33.3% reported having at least a college education.

2005 NHIS Methodology and Sample

The NHIS is an annual, cross-sectional, national probability health survey of non-institutionalized U.S. adults. NHIS interviews are completed in person in participants' homes. The NHIS uses a complex sample survey design and oversamples Hispanic and Black populations. The 2005 NHIS included a Cancer Control Supplement that contained questions about cancer history among FDRs (i.e., biological mother and father, full biological sisters and brothers, and biological daughters and sons). We used data from the 2005 NHIS to estimate reported rates of prostate, breast, and colon cancer among FDRs of Black males aged between 35 and 69 years who reported no personal history of PCA. The number of individuals who met these criteria and had complete data regarding the history of prostate, breast, and colon cancer in their FDRs were 838, 869, and 813, respectively. Additional details regarding the 2005 NHIS are available elsewhere (17).

Overview of Statistical Analyses

Frequency and univariate methods (using SAS version 9.1) were used for the analyses of PRAP data. The 2005 NHIS data were analyzed using SUDAAN (version 9.0.1). We consider percentages with non-overlapping 95% confidence intervals to be significantly different with at least a $p<0.05$. We used Fisher's Exact test (with a statistical significance cutoff of $p < 0.05$) to examine whether the rate of adherence to follow-up PCA screening within 15 months of an initial screening differed according to whether Black male PRAP participants had or did not have a FH of PCA.

Results

A summary of the pedigrees of the Black PRAP participants is shown in Table 1. Of the 332 Black probands with unique pedigrees, 28 (8.4%) have been diagnosed with PCA after enrollment into PRAP. Of the 2,411 males aged at least 18 years in Black PRAP families, 228 (9.5%) have been diagnosed with PCA. Table 2 provides a detailed breakdown of the FH of PCA reported by Black PRAP participants and Black 2005 NHIS participants. As shown in Table 2, substantially more Black PRAP participants report having a FDR with PCA compared to a representative sample of Black males from the 2005 NHIS (34.3% vs. 5.7%, respectively). A more in-depth analysis of these families shows that 30.1% of Black males in PRAP report a father having had PCA and 6.6% report having a brother with PCA, which is substantially higher than the comparison group from the 2005 NHIS. In addition, within the PRAP cohort, marital status of Black men with at least one FDR with PCA (66.7% married) did not differ significantly ($p = 0.42$) from that for Black men with no history of PCA among FDRs (59.4% married).

The family history of breast and colon cancers (screen-detectable cancers) in FDRs reported by PRAP and 2005 NHIS participants is shown in Table 3. Black PRAP participants reported significantly more FDRs with breast cancer than Black men from the 2005 NHIS (11.5% vs. 6.3%, respectively). FH of colon cancer or combination of breast and colon cancers was not significantly different between the two groups.

The rate of adherence to a follow-up PCA screening appointment after the first visit to PRAP did not differ between Black men with and without a FH of PCA (29.6% vs. 35.1%, respectively, $p = 0.34$).

Conclusions

Black men have among the highest reported incidence rates for PCA and a considerably higher mortality than men of other racial backgrounds (1). In addition, Black men are frequently diagnosed with more aggressive PCA and at a younger age (18,19). Screening younger, high-risk men (such as Black men especially with a FH) could detect potentially dangerous cancers, with a higher likelihood of organ confinement at the time of treatment (16,18). Since Black men with a FH of PCA are at particularly increased risk, efforts need to be targeted to the Black community (and to families in particular) to raise awareness of enrolling in PCA early detection programs. Though previous literature has described the risk for PCA in Black men from case-control cohorts (2,4-8), this report gives a detailed description of the familial patterns of PCA as reported by Black men recruited from the community and enrolled in PCA screening to begin to understand the burden of PCA in these families in order to target education efforts for PCA early detection.

The familial characteristics of PRAP probands described in this report were quite revealing. While Black men are not required to have a FH of PCA for entry into PRAP, we found that 34.3% of our Black families have strong familial susceptibility to PCA with a FDR with the

disease, which is substantially higher than the rate reported by a comparative sample of Black men from the 2005 NHIS. Men with affected brothers are at significantly higher risk for the development of PCA (20), and our report found that 6.6% of the Black probands report having at least one affected brother. Screening these men is particularly important since Black men with a FH of PCA have been reported to have more aggressive disease (3). Our results indicate that FH of PCA may be a leading factor in motivating Black men to seek screening for PCA. Encouraging discussions between family members (such as between brothers) may lead to enhanced uptake of PCA early detection programs.

Numerous studies have described low PCA screening rates in Black men (9-14). Weinrich examined PCA screening in Black men with a FH of the disease from the African American Hereditary Prostate Cancer (AAHPC) Study Network and found that these men had lower screening rates compared to men from the 2000 NHIS (8). They reported that 46% of men in the AAHPC study had PSA screening at some time point compared to 65% of Black men surveyed in the 2000 NHIS, raising cause for concern and the need for replication in other cohorts. Our data report on FH of PCA in Black men from a prospective, longitudinal screening cohort. Our targeted recruitment efforts are effective in enrolling Black men with a strong FH of PCA from the community for aggressive PCA screening. Additional efforts may be needed to further enhance recruitment of Black men without a FH of PCA since they are also at elevated risk. One challenge that still exists is compliance with adherence to PCA screening follow-up. Around one in three men had received follow-up PCA screening within 15 months of their first screening, and this rate did not differ between those with and without a FH of PCA. These data highlight the need to encourage and facilitate regular follow-up PCA screening among high-risk Black men who have received an initial screening.

Our report also details other cancers in families of Black men participating in PCA screening. We chose to focus on cancers for which screening is available in order to expand the scope of education efforts to include all family members (male and female) for early cancer detection. Breast cancer was reported in FDRs of 11.5% of Black PRAP participants, much higher than from the 2005 NHIS representative sample. This could represent another point to target education and behavioral interventions to motivate Black women from PRAP families to pursue breast cancer screening. These data support the critical need to educate the Black community regarding the importance of families discussing cancer risk assessment for not just PCA but other cancers for which screening is available for early detection and cure.

This report has some limitations. Due to obtaining FH information by self-report, a small percentage of individuals needed to be imputed in order to complete pedigree structures. However we were able to capture a significant number of the most important familial relationships that are relevant for cancer risk assessment (such as parent:offspring and sibling:sibling). Mother/father imputations had to be performed 7.0% of the time in order to complete the pedigree structures. This is not unexpected since we are relying on individual report of FH information. However, our 93% data completion rate is comparable to segregation analyses which have rigorous FH data collection (21). Another limitation of self-reported FH is recall bias. This is a known limitation regarding the accuracy of FH information obtained by questionnaire. An additional limitation is selection bias. PRAP participants are contacting PRAP based on hearing about the program primarily on the radio. However, when comparing our findings of PCA in Black PRAP families to a sample of Black men from the general population (2005 NHIS), we find that targeted recruitment efforts for PCA screening are effective and should be employed more to reach these high-risk families. Other people can also motivate Black men to seek PCA screening, such as close friends and spouses or partners. We did not find that the marital status of Black men in PRAP with at least one FDR with PCA differed at enrollment compared to Black men without an FDR with PCA. Education efforts can also be directed at spouses or partners of Black men to determine if this enhances PCA

screening uptake. We did not obtain detailed information about individuals (e.g., close friends, a spouse, partner, or other family members) who may motivate Black men to seek PCA screening and adherence to follow-up, although this is an important issue and should be explored further. Finally, future analyses will focus on whether probands have more aggressive disease and younger age of diagnosis according to FH of PCA. Our current sample size was too small to evaluate this issue.

This report indicates that FH of PCA is a large motivator for Black men to seek screening for the disease, and targeted recruitment measures are successful at accruing these men for PCA screening. We also see a sizable familial burden of PCA in Black men, which highlights the need to increase awareness and education in the Black community to discuss cancer screening and to comply with screening schedules for the early detection of PCA. In addition, this report showed many of the Black men reported not only PCA but other cancers within their families for which screening is available. Targeted education efforts are needed to bring this information to the Black community to move toward the ultimate goal of early detection and cure of PCA in Black men.

In summary, a substantial number of Black men taking part in the FCCC PRAP have significant familial burden of PCA as well as other cancers. Knowledge of this burden coupled with understanding PCA risk is the first step to raising awareness in the Black community of the importance of cancer risk assessment for early detection of PCA. Targeted efforts are needed to educate the Black community regarding the importance for performing cancer screening measures and to overcome barriers for cancer prevention efforts. Challenges still exist in improving adherence to PCA screening follow-up.

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Table 1

Summary of Pedigrees for Male Black Participants (Aged 35-69 Years) in the Prostate Cancer Risk Assessment Program

	N
Total participants	403
Participants with pedigrees	337
Probands with unique pedigrees†	332
Probands affected with prostate cancer due to program protocol	28

†*Note*. For the purpose of the current study, the first family member enrolled was considered the proband for the pedigree.

Table 2

Family History of Prostate Cancer Reported by Male Black Participants (Aged 35-69 Years) in the Prostate Cancer Risk Assessment Program and by Male Black Participants (Aged 35-69 Years) in the 2005 National Health Interview Survey

	PRAP Participants		NHIS Participants	
	n	**% (95% CI)**	***n***	**% (95% CI)**
≥ 1 FDR with prostate cancer	114	34.3 (29.2-39.7)	52	5.7 (3.9-7.4)
Father with prostate cancer	100	30.1 (25.2-35.4)	41	4.4 (2.9-6.0)
Brother with prostate cancer	22	6.6 (4.2-9.9)	11	1.2 (0.4-1.9)
PRAP probands with ≥ 1 FDR with prostate cancer and ≥ 2 same-side SDRs with prostate cancer	8	2.4 (1.1-4.7)	-	-
PRAP probands with no FDRs with prostate cancer and ≥ 2 same-side SDRs with prostate cancer	10	3.0 (1.5-5.5)	-	-

Note. FDR = first-degree relative; SDR = second-degree relative; PRAP = Prostate Cancer Risk Assessment Program; NHIS = National Health Interview Survey; CI = confidence interval. For PRAP participants, *N* = 332; for NHIS participants, *N* = 838. Percentages from the NHIS are weighted.

Table 3

Family History of Breast and Colon Cancers in First-Degree Relatives Reported by Male Black Participants (Aged 35-69 Years) in the Prostate Cancer Risk Assessment Program and by Male Black Participants (Aged 35-69 Years) in the 2005 National Health Interview Survey

	PRAP Participants		NHIS Participants	
FDR Family History	***n***	**% (95% CI)**	***n***	**% (95% CI)**
Breast cancer	38	11.5 (8.2-15.4)	56	6.3 (4.6-8.0)
Colon cancer	18	5.4 (3.2-8.4)	40	4.9 (3.2-6.6)
Breast and colon cancer	1	0.3 (0.0-1.7)	3	0.4 (0.0-0.8)

Note. FDR = first-degree relative; PRAP = Prostate Cancer Risk Assessment Program; NHIS = National Health Interview Survey; CI = confidence interval. For PRAP participants, $N = 332$; for NHIS participants, $N = 869$ for breast cancer family history, $N = 813$ for colon cancer family history, and $N = 813$ for breast and colon cancer family history combined. Percentages from the NHIS are weighted.