CME CREDIT *EDUCATIONAL OBJECTIVE:* Readers will educate their African American male patients about prostate cancer and screen them for it.

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Disparities in prostate cancer in African American men: What primary care physicians can do

ABSTRACT

African American men have a higher incidence of prostate cancer than white men, and also a higher rate of death due to prostate cancer. Although both biologic and socioeconomic factors may be to blame, better screening in this population may help to close the gap.

KEY POINTS

African American men have the dual disadvantages of being less likely to receive adequate care and also, possibly, of having biological differences that make them more prone to prostate cancer and more-aggressive cancer.

Prostate-specific antigen (PSA) cutoff levels have not been officially modified according to race, but we believe primary care physicians should have a lower threshold for referring African American men who have a suspiciously high PSA level for further urologic evaluation.

A healthy lifestyle, with a low-fat diet, healthy body mass index, and daily exercise, may decrease the risk of prostate cancer, among other benefits.

Primary care physicians, who are often the gatekeepers to care, play a key role in educating and screening their patients.

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Prostate cancer is the most common cancer affecting American men. In 2010, an estimated 217,730 men were diagnosed with it and 32,050 died of it.[1] African American men are disproportionately affected, with a prostate cancer incidence two-thirds higher than whites and a mortality rate twice as high.[1] Owing to such disparities, the life expectancy of African Americans is several years shorter than that of non-Hispanic whites.[2]

For the primary care provider, who is often the first access point for health care in the United States, it is important to understand what mechanisms may underlie these differences and what can be done to narrow the gap.[3]

WHAT IS THE CAUSE OF THESE DIFFERENCES?

Many studies have looked into the causes of the higher incidence of prostate cancer in African American men and their higher mortality rate from it. The disparity may be due to a variety of factors, some socioeconomic and some biologic.

Poorer access to care, or lower-quality care?

A study of US servicemen who had equal access to care showed that African American men had a higher rate of prostate cancer regardless of access to care and socioeconomic status.[4]

However, the 2002 Institute of Medicine report, *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care*, found evidence that racial and ethnic minorities tend to

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receive lower-quality health care than whites, "even when access-related factors, such as patients' insurance status and income, are controlled."[5]

Genetic predisposition?

Some have proposed that the disparity may be a function of genetic predisposition.

Evidence of a genetic component to the high incidence and mortality rate in African American men comes from epidemiologic studies of men with similar genetic backgrounds. For example, men in Nigeria and Ghana also have a high incidence of prostate cancer, as do men of African descent in the Caribbean islands and in the United Kingdom.[6]

Chromosome 8q24 variants have been shown in several studies to be associated with prostate cancer risk and are more common in African American men.[7–10] Some studies have also shown a higher rate of variations in cell apoptosis genes such as *BCL2*[11] and tumor-suppression genes such as *EphB2* in African American men.[12]

These findings suggest that genetic differences may contribute to the higher prostate cancer incidence and mortality rate seen in African American men.

Studies seem to indicate that prostate cancer really is inherently more aggressive in African American men

More-aggressive cancer, or later detection?

Not only do African American men tend to have a higher incidence of prostate cancer, they also tend to have more-aggressive disease (ie, a higher pathologic grade) at the time of diagnosis, which may contribute to the disparity in mortality rates.[13–19]

Initially, there was some controversy as to whether this observation is a result of genetic and biologic factors that may predispose African American men to more-aggressive disease, or if it is due to inadequate screening and delayed presentation. However, a body of evidence supports the contention that prostate cancer is more aggressive in African American men.

For example, a study of autopsy data from men who died of prostate cancer at ages 20 to 49 showed that the age of onset of prostate cancer was similar between African American and white men.[20] The Surveillance Epidemiology and End Results (SEER) database showed that African American men had a higher incidence of metastatic disease across all age groups.[20] A similar study conducted 10 years later confirmed that rates of subclinical prostate cancer in African American and white men do not differ by race at the early ages, but that advanced or metastatic disease occurred nearly four times as frequently in African American men.[21]

Another study examined prostate biopsies from African American men and found that their tumors expressed higher levels of biomarkers, suggesting they had more-aggressive disease.[22]

SCREENING FOR PROSTATE CANCER

Serum prostate-specific antigen (PSA) testing has become the method of choice for prostate cancer screening. However, PSA screening in asymptomatic men is under debate, because it can lead to overdetection and subsequent overtreatment of indolent disease.[23]

Several recent studies showed differing results from prostate cancer screening.

The US Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial found that the mortality rate was no lower with combined PSA screening and digital rectal examination during a median follow-up of 11 years than in a control group that had a lower rate of screening.[24] However, further analysis of these data, with stratifying by comorbidities, showed that PSA screening in young and healthy men reduces the risk of death from prostate cancer, with minimal overtreatment.[25]

The European Randomized Study of Screening for Prostate Cancer found a statistically significant 20% reduction in deaths from prostate cancer with PSA screening, but that it was necessary to treat 48 men in order to save one life.[26]

Another study, published in 2010, showed that regular PSA screening reduced the rate of prostate cancer mortality by half over 14 years.[27]

African American men generally present with disease that is more advanced than in white men.[28] This historically has been attributed to the fact that African Americans have been less likely to be screened for prostate cancer, though recent data indicate the gap is lessening.[29–31] A cross-sectional study from

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the Texas Medical Center showed that 54.4% of African American men had received PSA screening, compared with 63.2% of white men.[32]

Another study showed that African Americans were more likely to have had a longer interval between PSA screenings before diagnosis, and that a longer PSA screening interval was associated with greater odds of having advanced disease at diagnosis.[33] However, when the researchers controlled for the PSA screening interval, they found that African Americans had the same odds of being diagnosed with advanced prostate cancer as white patients did. They concluded that more frequent or systematic PSA screening may reduce the racial differences in cancer stage at diagnosis and in deaths.

Reasons for the disparities in screening

Many reasons have been proposed to explain why African Americans receive less screening, including poor communication between physicians and minority patients due to lack of cultural competency among physicians, lack of health insurance (and poor access to quality care as a result), and deficiency of knowledge about screening. Though awareness is rising, many African Americans are unaware of early detection methods for prostate cancer (eg, PSA testing), and other barriers such as cost and transportation exist that may prevent African American men from being screened.[34,35]

As gatekeepers, primary care physicians are in a position to address these shortcomings in patient education and to enhance the physician-patient relationship.[36]

Black men have higher PSA levels, with or without cancer

Physicians must also be aware of racial differences in PSA levels and realize that the predictive value of PSA in the diagnosis of prostate cancer may differ between African Americans and whites.

Black men, with or without prostate cancer, have been found to have higher PSA levels. Kyle and colleagues[37] found that African American men without prostate cancer had significantly higher mean PSA levels than white men across all age groups. Furthermore, Vijayakumar et al[38] found that African Americans with newly diagnosed localized prostate cancer had higher serum PSA levels than whites at diagnosis.

Although PSA cutoff levels have not been officially modified according to race, primary care physicians should have a lower threshold for referring African American men who have a suspiciously high PSA level for further urologic evaluation. Close partnership between the internist, family practitioner, and urologist will aid in the optimal use of PSA testing for the early detection of prostate cancer.

When to start PSA screening? How often to screen?

The age at which African American men should begin to have their PSA levels checked (with or without a digital rectal examination) continues to debated. However, the American Cancer Society[39] recommends that African American men who have a father or brother who had prostate cancer before age 65 should begin having discussions with their physician on this topic and, with their informed consent, screening at age 45.

The frequency of PSA screening depends on the individual's PSA level. The National Comprehensive Cancer Network[40] recommends that men at high risk be offered a baseline PSA measurement and digital rectal examination at age 40 and, if the PSA level is higher than 1 ng/mL, that they be offered annual follow-ups. If the PSA level is less than 1 ng/mL, they recommend screening again at age 45. Risk factors for prostate cancer include family history as well as African American race.[41]

Elevated PSA does not necessarily signify prostate cancer

How should PSA levels be interpreted?

Interpreting PSA results is important in detecting prostate cancer at early stages.

At first, we believed the normal range of PSA for all men was 4.0 ng/mL or less. However, the American Urological Association now recognizes that the normal PSA range, in addition to varying along racial lines, also is age-dependent.[42] The Cleveland Clinic Minority Men's Health Center's suggested normal ranges of PSA in African American men are:

- Age 40–49: ≤ 2.5 ng/mL
- Age 50–59: ≤ 3.0 ng/mL

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- Age 60–69: ≤ 3.5 ng/mL
- Age 70–79: ≤ 4.5 ng/mL
- Age > 80: ≤ 5.0 ng/mL.

Remember that an elevated PSA does not necessarily signify prostate cancer, and that these are reference ranges only and may vary in individual men.

SURVIVAL AFTER DIAGNOSIS

African American men with prostate cancer have significantly higher mortality rates than white men. The possible causes of worse outcomes are many, and there have been many studies that attempted to address this disparity. The question of a more biologically aggressive cancer was previously discussed, but additional factors such as socioeconomic factors, comorbidities, and treatment received have also been studied, and data are mixed.[43–45]

In a large SEER database review, once confounding variables of socioeconomic status, cancer stage, and treatment received were eliminated, African Americans had similar stage-for-stage survival from prostate cancer.[46] Another study found, in 2,046 men, that differences in socioeconomic status explained the difference in mortality rates between white and black patients.[47]

However, other studies that adjusted for socioeconomic status as well as patient and tumor characteristics found that African American and Hispanic men were more likely to die of prostate cancer than white men.[48]

African American men have historically been less likely to be screened, although the gap is lessening

Do African American men receive less-aggressive care?

Studies have also determined that there may be differences in treatments offered to patients, which in turn negatively affect survival.[28,49–53] Potentially curative local therapies (including radical surgery or radiation) may be recommended less often to black men because of major comorbidities or socioeconomic considerations.[49–52]

Additionally, potential metastatic disease may be identified in a less timely and accurate manner, as African American men are less likely to undergo pelvic lymph node dissection. This was associated with worse survival in men with poorly differentiated prostate cancer.[53]

However, returning to the possibility that prostate cancer is biologically more aggressive in African American men, some studies have shown that even after adjusting for treatment, African Americans continue to have worse survival rates.[54,55] One study in men with stage T1 to T3 prostate cancer who chose brachytherapy for treatment reported that after adjusting for PSA, clinical stage, socioeconomic status, and comorbidities, African American and Hispanic race were associated with higher all-cause mortality rates.[55]

Equal care, equal outcomes?

In total, these results suggest that factors unrelated to tumor biology may be additional reasons for the poorer survival rates in African American men with prostate cancer. More favorable survival outcomes for African Americans with localized disease may be achieved with uniform assignment of treatment.

Fowler and Terrell[56] reviewed the outcomes of 148 black and 209 white men with localized prostate cancer treated with surgery or radiation therapy over an 11-year period at a Veterans Administration hospital. Not surprisingly, the black men presented more often with advanced disease. However, survival outcomes were equivalent between whites and blacks when treatment was assigned in a uniform manner without regard to race. After a median follow-up of 96 months, there were no significant differences in all-cause, cause-specific, metastasis-free, clinical disease-free, or PSA recurrence-free survival rates in 109 black and 167 white men with low-stage cancer treated with surgery or radiation therapy or in 39 black and 42 white men with high-stage disease treated with radiotherapy.[56]

Similarly, Tewari et al[57] studied a cohort of 402 African American and 642 white men, all of whom underwent radical prostatectomy for clinically localized prostate cancer. They were followed for PSA recurrence to determine if race-specific differences in PSA doubling time or histopathologic variables might account for the higher mortality rate in black men. While there were race-specific differences in baseline serum PSA and incidence of high-grade prostatic intraepithelial neoplasia, race was not an independent risk factor for biochemical recurrence. Instead, other variables such as the

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Gleason pathology score, bilateral cancers, and margin positivity were independently associated with biochemical recurrence.

Furthermore, researchers at Louisiana State University[58] retrospectively analyzed data from 205 men of different races with early-stage prostate cancer. The African American men had a higher serum PSA level, suggesting more advanced disease or greater tumor burden at presentation, but no statistically significant differences were found among the pretreatment biopsy variables, including prostate volume (measured by ultrasonography), Gleason score, millimeters of cancer within the biopsy specimen, and percentage of cancer within the biopsy specimen. After treatment, there were no significant differences in survival outcomes along racial lines, leading the authors to conclude that early detection and treatment of prostate cancer in African Americans would be the best approach to lowering mortality rates.

Taken together, these data suggest that if localized prostate cancer is treated adequately and appropriately, African American patients may have improved survival rates.

DIETARY AND LIFESTYLE FACTORS

The incidence of prostate cancer is increasing in other countries where Western diets and lifestyles have been adopted,[59,60] suggesting that nutritional factors may also contribute partly to prostate carcinogenesis. Culture- and race-specific differences in diet may play an important role in prostate cancer risk in certain racial minorities. Many aspects of diet and nutrition have been studied for their impact on prostate cancer.

Dietary risk factors

Too much red meat and processed meat? Although some have suggested that diets high in red and processed meats may lead to a higher risk of prostate cancer, a meta-analysis showed no association.[61,62]

Too much calcium? The European Prospective Investigation Into Cancer and Nutrition study found that high dietary intake of dairy protein and calcium from dairy products was associated with a higher risk of prostate cancer.[63] A cohort study in the United States had similar findings with regard to calcium.[64] However, the higher risk of prostate cancer was associated with consumption of 2,000 mg or more of calcium per day, which was consumed by only 2% of the study's cohort and, as the study's authors reported, fewer than 1% of US men. As such, only a small population of American men seem to be exposing themselves to a higher risk of prostate cancer by high calcium consumption.

High fat intake? Certain fatty acids have been implicated in general tumor genesis, and that risk has been extrapolated to prostate cancer.[65] For example, high fat intake and obesity are associated with increased levels of insulin-like growth factor 1, which in turn has been shown to correlate with a significantly elevated risk of prostate cancer.[63,65]

Obesity has been shown to increase the risk of more-aggressive prostate cancer, but not of less-aggressive tumors.[66] Moreover, men who lost weight had a lower risk of prostate cancer than those who maintained their weight over 10 years.[66] Obesity may be particularly risky for African American men, in whom it was found to be associated with shorter biochemical relapse-free survival, whereas it was not an independent risk factor in white men.[67]

Preventive dietary agents have been elusive

Unfortunately, despite attempts to identify preventive dietary agents, none has yet been confirmed.

No benefit from selenium or vitamin E. The Selenium and Vitamin E Cancer Prevention Trial was discontinued, as there was no evidence that either agent prevented prostate cancer in relatively healthy men.[68]

Vitamin D? It has been suggested that lower levels of vitamin D could contribute to the higher rates of prostate cancer in African Americans, as vitamin D deficiency is more common in African Americans.[69] However, several meta-analyses have shown no association between vitamin D and prostate cancer.[70–72]

Soy? Attempts at correlating the relatively low incidence of prostate cancer in Asians have revealed that high soy intake may be protective. Asians consume more soy than Americans do (100 vs 3 mg/day), and soy isoflavones such as genistein, glycitein, and daid-

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zein lower the incidence of prostate cancer in laboratory mice.[73]

Other lifestyle factors

Other lifestyle factors have also been analyzed to see if they contribute to prostate cancer.

Pollution. Some studies have suggested that the etiology of prostate cancer may lie in environmental exposures to pesticides,[74] metal industrial facilities,[75] and urban living.[76]

Smoking. Watters et al[77] found that current and former cigarette smokers were actually at a lower risk of being diagnosed with nonadvanced prostate cancer, but current smokers were at higher risk of dying from prostate cancer.

Physical activity. A prospective study of lifetime physical activity of more than 45,000 men found that men who were not sedentary during work and who walked or bicycled more than 30 minutes per day during adult life had an approximately 20% lower incidence of prostate cancer.[78]

In sum, primary care providers who are generally promoting healthy lifestyles can point to a reduction in risk for prostate cancer as yet another benefit to a low-fat diet, a healthy body mass index, and daily exercise.

HOW PRIMARY CARE PHYSICIANS CAN HELP CLOSE THE GAP

Primary care physicians serve as the first point of health access for many in the United States today.

The diagnosis of prostate cancer is made more frequently in African American men than in other American men, often at a higher pathological grade, and with a worse mortality rate. Primary care physicians can help improve these statistics. Interventions targeting overall health, such as promotion of a healthy diet, could be established at primary care visits and could also reduce the incidence of prostate cancer in African American men. Patient education regarding prostate cancer screening, the impact of family history, and the rate of PSA screening could be improved.

Primary care physicians serve a vital role in health education and prostate cancer screening, and therefore they begin the process in potentially reducing the impact of prostate cancer in African American men. The racial disparity seen in prostate cancer may begin to be minimized with primary care physicians and specialists working together to ensure that all men receive appropriate treatment.

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