Prostate cancer in the African–Caribbean community

Niyukta Thakare and Frank Chinegwundoh

African–Caribbean men have the highest risk of prostate cancer, which is the second most common male cancer worldwide. The authors present an overview of the epidemiology, genetic factors and disparities in management of prostate cancer in the African–Caribbean community.

Figure 1. Age-standardised prostate cancer incidence and mortality rates worldwide

In the UK, prostate cancer is the most common male cancer and the second most common cause of cancer death in men after lung cancer. In their current strategy, the UK Department of Health has addressed the impact of inequalities on cancer outcomes. African–Caribbean ethnicity is a known risk factor for prostate cancer. Ethnic disparity in prostate cancer has become an important issue worldwide because of the higher incidence and mortality in the African–Caribbean population.

The National Cancer Institute defines ‘cancer health disparities’ as ‘adverse differences in cancer incidence (new cases), cancer prevalence (all existing cases), cancer death (mortality), cancer survivorship, and burden of cancer or related health conditions that exist among specific population groups in the United States.’ The focus on identifying areas of research in ethnic disparity in prostate cancer is increasing.

We have examined the current knowledge of epidemiological features and genetic and

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molecular characteristics of prostate cancer in African-Caribbean men. We also aim to provide an insight into the existing evidence for differences in prostate cancer diagnosis and management between ethnic groups of men.

**Epidemiology**

The International Agency for Research on Cancer has assimilated incidence and mortality data for cancer throughout the world as part of the GLOBOCAN project. In 2012, an estimated 1.1 million men were diagnosed with prostate cancer worldwide.

A 25-fold variation in incidence rates is seen globally, with the rates being higher in the developed world (Figure 1). Australia/New Zealand has the highest age-standardised rate of 111.6 per 100,000, followed by North America and western Europe. The lowest rates are seen in Asian countries. The higher incidence rate in developed countries is mainly attributed to widespread PSA testing and readily available diagnostic modalities. In the Caribbean and South Africa, a relatively high incidence rate of 79.8 and 61.8 per 100,000 respectively is observed. This is in spite of the fact that PSA testing is not very prevalent in these regions.

In contrast, there is only a 10-fold global variation in mortality rates, which are predominantly high in less developed regions. The Caribbean has the highest age-standardised mortality of 29 per 100,000, followed by sub-Saharan Africa (19–24 per 100,000). Moreover, these are the only countries where prostate cancer is the leading cause of death. These disproportionate geographical trends suggest that ethnicity plays a vital role as a risk factor in prostate cancer.

According to the US Surveillance, Epidemiology, and End Results (SEER) program, the 2000–11 age-standardised incidence rates for African-American men are 202.5 per 100,000, the highest in the world. A reduction in incidence has been seen after the end of an 'enthusiastic PSA testing' era in white as well as African-American men. Mortality rates are invariably higher at 44.0 per 100,000 among African-American men in comparison to 19.2 per 100,000 among white-American men.

In the UK in 2008–10, the National Cancer Intelligence Network (NCIN) reported that incidence and mortality rates for prostate cancer were 89.0–116.0 and 22.7–23.9 per 100,000, respectively. Within the UK, ethnicity-related epidemiological data are currently available only for England. The NCIN has published incidence rates for ethnic groups of men diagnosed with prostate cancer in England (2000–06). Age-standardised incidence rates were significantly higher in the 'black' ethnic group (120.8–247.9 per 100,000) compared to the 'white' ethnic group (96.0–99.9 per 100,000). Mortality statistics related to ethnicity for 2007–09 show that in England, African-Caribbean men have a 30% higher mortality rate compared to white men.

In terms of prostate cancer survival, the global CONCORD study showed a wide variation in rates from 40% to 95% throughout the world. SEER data (1998–2010) show that African-American men have lower 5-year relative survival rates than their white counterparts (95.7% versus 99%). However, in the UK, no significant differences in survival have been seen. The reported relative survival rates in England are in fact higher for men of 'black' ethnicity (Table 1).

It is challenging to interpret and compare data from various sources, mainly because of variations and limitations in methodology of epidemiological studies. Cancer cases are also likely to be under-reported in the less developed countries. Moreover, ethnicity recording itself is not robust or accurate and under-representation of African-Caribbean groups is common. These shortcomings should be considered before drawing inferences regarding ethnic disparities in epidemiological research.

**Biological Factors**
The presumed factors contributing to ethnicity-related differences are socio-economic status, cultural beliefs and genomic differences. Ongoing research in the field of genetic and molecular basis for prostate cancer disparity in African-American men has identified the following areas:

- Inherited risk alleles
- Tumour genes
- Androgen receptors
- Epigenetics.

Genome-wide association studies have identified single nucleotide polymorphisms (SNPs) on several gene loci and chromosomes in prostate cancer. This genetic inheritance has been studied to explain the differences in tumour biology in African-American and white men. Multiple SNPs within the 8q24 region are known to confer increased risk

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<td></td>
<td>1-Year relative survival (%)</td>
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<td>3-Year relative survival (%)</td>
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<td>standardised</td>
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Table 1. Relative survival of African-Caribbean and white men in the UK.
of prostate cancer in African-American men. SNPs within the CYP3A4 gene cause a genetic variant CYP3A4*1B, which is associated with aggressive characteristics in African-American men diagnosed with prostate cancer.\(^{14}\)

TMPRSS2 is an androgen-responsive protease specific to prostate cells and ERG is an ETS (E-twenty six) related gene. TMPRSS2-ERG fusions have also been studied to explain the differences in prostate cancer in African-American and white men.\(^{15}\) EphB2 tyrosine kinase, a prostate cancer tumour-suppressor gene, is thought to be associated with increased risk of prostate cancer in African-American men.\(^{16}\) Genomic gains and losses relevant to oncogene function have been studied by detection of copy number variations and show higher amplification in prostate tumours of African-American men.\(^{17}\)

The role of androgen receptor (AR) gene structure and function has been investigated in several studies. It has been reported that fewer CAG repeats in the AR gene contribute to higher AR activity in African-American men,\(^{18}\) although evidence to the contrary also exists.\(^{19}\) Higher genomic AR function leading to higher levels of AR proteins in African-American men is also reported.\(^{20}\)

Epigenetic changes, including glutathione S-transferase-pi gene (GSTP1) hypermethylation, are observed in prostate cancer tissue, although similar levels have been observed between African-American and white men.\(^{21}\) On the other hand, regulatory genes including TIMP3 and NKX2–5 are more likely to be methylated in African-American men.\(^{22}\) Reduced signalling of vitamin D pathway-related genes including vitamin D receptors is considered to be associated with higher risk in African-American men.\(^{23}\)

Unfortunately, the exact role of these molecular factors is not yet established and the majority of these studies include African-American men. However, these early attempts have provided a direction for future research and advances.

**MANAGEMENT AND OUTCOMES**

The management pathway of prostate cancer starts at the detection stage. Screening is a controversial issue and, although selective screening of high-risk groups seems reasonable, screening studies focused on ethnic minorities are lacking. In the large screening trials, including the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial, which constitute the existing evidence, ethnic groups including African-Caribbean men were under-represented.\(^{24}\) There is an ongoing argument for selective screening of African-Caribbean groups\(^{25}\) and it remains to be seen whether it will become common practice.

In the UK, the Prostate Cancer in Ethnic Subgroups (PROCESS) study investigated differences in prostate cancer between African-Caribbean and white men.\(^{26}\) The study comprised a retrospective cohort of men diagnosed with prostate cancer in the London and Bristol areas over a 5-year period. It concluded that African-Caribbean men were at a substantially higher risk of developing prostate cancer compared to white men, especially in the younger age group. Several studies, particularly in the US, have queried the differences in disease presentation, tumour stage and tumour burden among ethnic groups. A systematic review of these disparities revealed that African-American men present at a younger age and also have higher-risk disease and higher tumour volumes.\(^{27}\)

Similarly, the management of low-risk disease in African-Caribbean men has also been scrutinised. There is increasing concern regarding the role of active surveillance in low-risk prostate cancer in African-Caribbean men. A recent review on active surveillance in African-American men suggests that it is a safe option for low-risk prostate cancer in these men.\(^{28}\) However, the quality of evidence contributing to this is far from adequate. It is also somewhat contradictory given the higher rates of pathological upgrading after radical prostatectomy in African-American men with low-risk disease.\(^{29}\) Moreover, adverse oncologic outcomes and lower biochemical recurrence-free survival are also reported after radical prostatectomy in African-American men.\(^{30}\)

Despite persistent efforts to tackle these issues, there are still significant mortality differences in prostate cancer among ethnic groups. In fact a recent study comprising the SEER data in the US showed that there has been no reduction in disparity in prostate cancer mortality in African-American men over the past 20 years.\(^{31}\) This means that more needs to be done to identify and narrow the gap in current management of prostate cancer in African-Caribbean men in order to achieve discernible results.

**SUMMARY**

There is undoubtedly a disparate burden of prostate cancer in the African-Caribbean community. Mounting evidence indicates that prostate cancer in African-Caribbean men is a biologically distinct entity. Further research into biological determinants is required to determine the exact cause of these disparities. There is a crucial need to conduct larger outcome-related studies and establish new pathways to improve prostate cancer care in African-Caribbean men.

**Declaration of interests:** none declared.

**REFERENCES**


