

Emergent trends in the reported incidence of prostate cancer in Nigeria

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Background: To date there has not been any nationwide age-standardized incidence data reported for prostate cancer in Nigeria. We examined and integrated diverse trends in the age-specific incidence of prostate cancer into a comprehensive trend for Nigeria, and examined how best the existing data could generate a countrywide age-standardized incidence rate for the disease.

Methods: Data were obtained from studies undertaken between 1970 and 2007 in referral hospital-based cancer registries. Records from at least one tertiary hospital in each of the six geopolitical zones of Nigeria were examined retrospectively. Data were also reported for the rural population in cross-sectional prospective studies. Age-standardized incidence rates and the annual incidence of disease were calculated.

Results: Higher incidence rates for prostate cancer during this period were recorded for patients aged 60–69 years and 70–79 years, with a lower incidence rate for patients aged younger than 50 years. An exponential annual incidence rate of disease was observed in the 50–79 year age group and peaked at 70–79 years before dropping again at age 80 years. The results showed metastasis in more than half of these hospital-based prostate tumors.

Conclusion: Our results suggest that prostate cancer occurs at a relatively young age in Nigerians and that hospital-based registry reports may not appropriately reflect the incidence of the disease in Nigeria. A countrywide screening program is urgently needed. Finally, the difference in reported stages of disease found in Nigerians and African-Americans versus Caucasians suggests biological differences in the prognosis. Nigeria may thus typify one of the ancestral populations that harbor inherited genes predisposing African-Americans to high-risk prostate cancer.

Keywords: prostate cancer, annual age-standardized incidence rate, Nigeria cancer registry

Introduction

Black men of African descent have variously been reported to be at especially high-risk for developing prostate cancer.¹ While the incidence and mortality rates are ostensibly higher in African-Americans than Americans of other racial groups,^{2,3} African-Caribbean men are reported to have the highest rate of prostate cancer in the world.¹ Even worse is the discovery that these African descendants are most likely to present at a younger age with more advanced disease, and historically have a poorer disease prognosis.⁴ This supports autopsy reports showing that African-American men 20 years or older who died of other causes had a higher incidence and higher grade of intraepithelial prostate neoplasia as compared with age-adjusted cohorts of Caucasian men.⁵ In addition, numerous studies of the pathologic characteristics of prostate tumors show that African-American patients have higher tumor volumes

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than Caucasian patients with a similar stage of disease.⁶ All these observations suggest that biological differences in tumorigenesis may be a factor in the course of disease among races.⁶ Indeed, numerous studies have characterized several genes, the expression patterns and variants^{7,8} of which determine the tumoral heterogeneity⁹ which characterizes the disparity in incidence and aggressiveness of disease found among African-American and Caucasian patients.^{10,11} Currently, there is a good deal of literature claiming that lifestyle factors impact the risk of prostate cancer in African-Americans. Accordingly, the wide variations in cancer incidence among populations living in different regions of the world echo the suggestion that the majority of malignant tumors are triggered by environmental factors.¹²

Epidemiological and population studies indicate that lifestyle variables seldom account for the disparities in prostate cancer risk among different groups,¹³ but rather suggest that interaction of specific genetic and lifestyle factors critically predisposes populations to most cancers.^{14–16} Regrettably, there has been no consensus as to whether the higher incidence of prostate cancer or the disturbing two-fold higher mortality rate from this disease among African-Americans¹⁷ is driven by “behavior”, “biology”, or both. Historically, all individuals in this diaspora are people of African descent,

and it is logical that men of African ancestry share common genetic or familial factors that may increase their vulnerability to prostate cancer.¹⁸ Although the contribution of hereditary factors in cancer has been considered minor, the estimated effects of genetic factors for five tumors vary considerably, with the highest effect observed in prostate cancer.¹⁶ This has been corroborated by recent studies showing that African-American patients with gender-specific malignancies like prostate cancer have worse survival than white patients, despite controlling for prognostic, treatment, and socioeconomic factors.¹⁹ This has led to the conclusion that unrecognized interactions of host biological, hormonal, and/or inherited factors may contribute to differential survival outcomes by race in gender-specific malignancies like prostate cancer. The mechanism of inherited genetic predisposition, which is responsible for the varied interethnic response to environmental factors, could be obscured in the genetic framework of ancestral populations in the African diaspora. Mining of such data could reveal trends in the incidence of prostate cancer in these populations. Consistency in incidence trends in such ancestral populations as the African diaspora could encourage the search for an inherited genetic predisposition that responds to behavioral triggers for the disease. In this paper, we present emergent

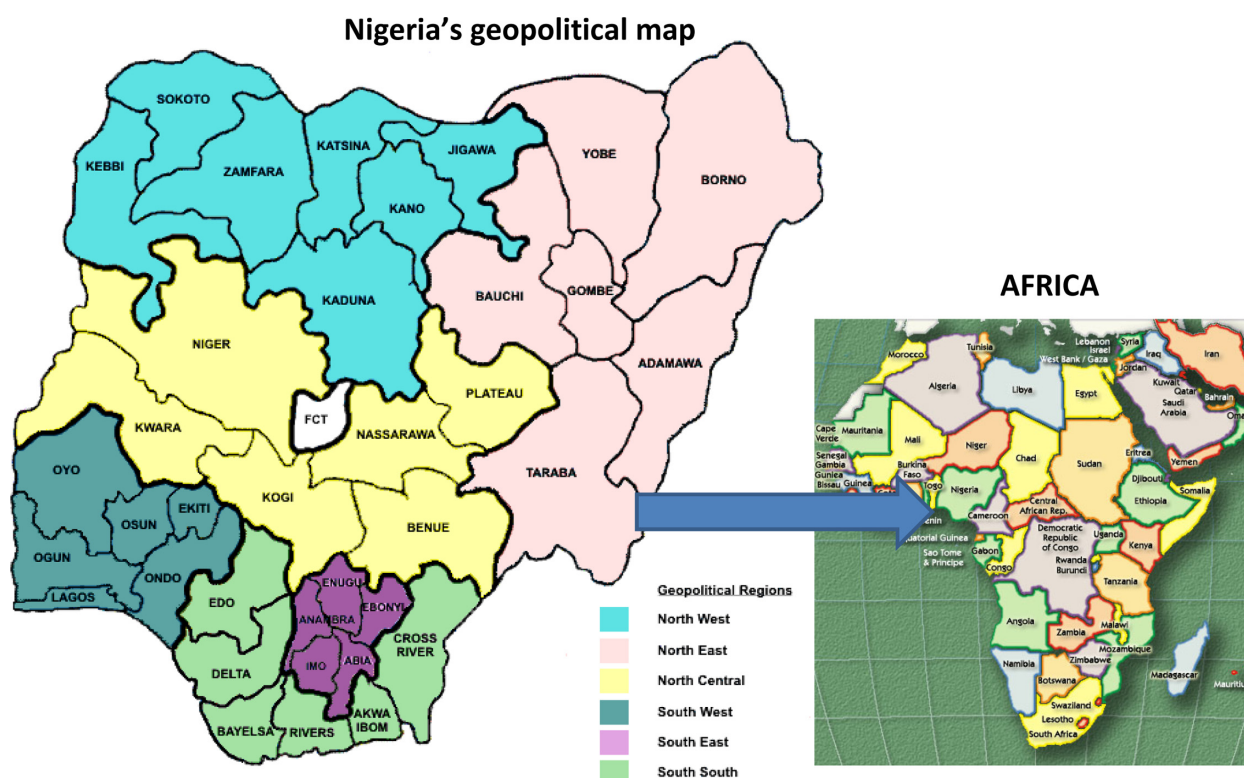


Figure 1 Geopolitical map of Nigeria.

Abbreviation: FCT, Federal Capital Territory.

trends in the reported incidence of prostate cancer in modern day Nigeria, a country that accounts for a highly significant proportion of the African diaspora.²⁰ Correlation in features of the disease in these two populations could guide the search for the biology of the disease in these populations.

Methods

Design and study population

We grouped together prospective and retrospective data previously obtained from histologic and clinical records at the tertiary referral or university teaching hospitals serving the six Nigerian geopolitical zones (Figure 1), each of which covers a core state and several peripheral states. The data provided by the teaching hospitals in each of the geopolitical zones and their peripheral states are shown in Table 1. Our study population was broadened because we examined data from two or more such tertiary health institutions in a zone. Because our data embraced all of the geopolitical zones in Nigeria, the information it provides may constitute the most extensive hospital-based prostate cancer incidence report for Nigeria so far. Nonetheless, the present data compensate for the lack of satisfactory prostate cancer incidence data that ought to be coordinated and collated by the Ibadan University

College Hospital (UCH) National Headquarters for Cancer Registries in Nigeria. Such data ought to be generated by population-based screening for prostate and other cancers in the presently existing university teaching hospital-based registries at Maiduguri, Zaria, Jos, Kano, Ilorin, Calabar, Enugu, Lagos, and Ife-Ijesha. The data presented in this report were retrieved by researchers from these teaching hospital-based registries, except for the Usman Danfodiyo UCH records, which were obtained from a cancer patient register in the department of histopathology. The histology and cytology specimens^{21,22} used for some of these studies were obtained from tertiary, secondary, and private hospitals located close to the core tertiary hospital and the surrounding peripheral states, towns, and villages²³ within that particular geopolitical zone. In a few surveys of prostate cancer risk from a seldom-screened cohort of the rural population, participants were invited for a health survey after alerting them to the procedures involved, including a blood test and digital rectal examination (DRE) by a local nurse.²⁴ In many of the retrospective studies, information on the age of patients at presentation,^{21,25–27} histopathological grading, mode of presentation, clinical and biochemical response to chemotherapy, their relative frequencies,²⁸ and the level of

Table 1 Teaching hospitals and cancer registries with published data and information on prostate cancer incidence in the geopolitical zones of Nigeria

Geopolitical zones/population# (% of national population)	Teaching/tertiary hospital*/** (other hospitals in the zone)	Core and peripheral states
South-South 21,014,655 (15.01%)	University of Calabar Teaching Hospital, Calabar; University of Benin Teaching Hospital, Benin; University of Uyo Teaching Hospital, Uyo; Niger Delta University Teaching Hospital, Yenogoa; University of Port Harcourt Teaching Hospital, Port Harcourt; Delta State University Teaching Hospital, Oghara; other hospitals (n = 111)	Akwa-Ibom, Bayelsa, Cross River Delta, Edo and Rivers
South-East 16,381,729 (11.7%)	University of Nigeria Teaching Hospital, Enugu; Abia State University Teaching Hospital, Aba; Ebonyi State University Teaching Hospital, Abakaliki; Imo State University Teaching Hospital, Owerri; Enugu State University Teaching Hospital, Enugu; Nnamdi Azikiwe University Teaching Hospital, Nnewi; other hospitals (n = 120)	Abia, Anambra, Ebonyi, Enugu, Imo
South-West 27,581,992 (19.65%)	University College Hospital, Ibadan; Lagos University Teaching Hospital, Lagos; University Teaching Hospital, Ado Ekiti; Olabisi Onabanjo University Teaching Hospital, Sagamu; Lagos State University, Teaching Hospital, Ikeja; Obafemi Awolowo University Teaching Hospital, Ile-Ife; Ladoke Akintola University Teaching Hospital, Osogbo; other hospitals (n = 412)	Ekiti, Lagos, Ogun, Ondo, Osun, Oyo
North-East 18,971,965 (13.55%)	University of Maiduguri Teaching Hospital, Maiduguri; Abubakar Tafawa Balewa University Teaching Hospital, Bauchi; other hospitals (n = 84)	Adamawa, Bauchi, Borno, Gombe, Taraba, Yobe
North-Central 20,266,257 (13.46%)	University of Ilorin Teaching Hospital, University of Abuja Teaching Hospital, Abuja; Benue State University Teaching Hospital, Makurdi, Jos University Teaching Hospital; other hospitals (n = 175)	Benue, Abuja (Federal Capital Territory), Kogi, Kwara, Nasarawa, Niger, Plateau
North-West 35,786,998 (25.56%)	Ahmadu Bello University Teaching Hospital, Zaria; Aminu Kano Teaching Hospital, Kano; Usmanu Danfodiyo University Teaching Hospital, Sokoto; other hospitals (n = 80)	Kaduna, Katsina, Kano, Kebbi, Sokoto, Jigawa, Zamfara

Notes: *Other tertiary, secondary hospitals, or health facilities (public, mission, and private) not enumerated here exist in all zones, but had no published data or information for this study. Core states where listed hospitals are located are italicized; **Other hospitals include federal medical centers, specialist hospitals, mission hospitals, private hospitals, and general hospitals; #Population figures based on the provisional National Population of Nigeria March 2006 census results.

prevailing tumor biomarkers were obtained from patient files.^{29–31} In prospective studies, data were obtained from patients presenting with histologically diagnosed carcinoma of the prostate during the study period.³² Again, in the prospective studies, various patient information was documented including, but not limited to, prevailing biomarker levels such as serum acid phosphatase, DRE, blood electrolyte profile, prostate biopsy, transabdominal ultrasonography, and a survey of the skeleton.^{32,33} In some of the more recent cases, detection of prostate cancer by prostate-specific antigen (PSA) was preceded by DRE. In most cases, the diagnosis was made on the basis of DRE, an ultrasound scan (which when combined with artificial neural network classification tools enabled encouraging differentiation between cancerous and noncancerous tissue),³⁴ and confirmed by Tru-Cut (UK Medical Limited, Sheffield, UK) prostatic biopsy.²¹ In certain cases too, the clinical staging of the disease was determined using the tumor, node, metastasis (TNM) system at the time of DRE.²⁹ In others, the prostate was carefully assessed for size, hardness, nodularity fixation, and discomfort.³³ Staff at the registries was centrally trained through programs run by the National Headquarters for Cancer Registries in Nigeria and delivered as instructed data items abstracted from pathology reports, medical charts, and questionnaires to treating physicians in order to obtain complete data on therapies. To avoid duplication, all retrieved records were reported to have been double-checked by name and matched with hospital numbers. Cases presented by the reports ranged from 125 to 4686, where large number of cases represented retrospective studies of all malignant diseases studied over a longer period. Age-standardized rates were calculated using Nigerian census figures for the appropriate study periods. The mean sample size for assessment of prostate tumors and

benign prostatic hyperplasia was 327 ± 280.12 . Studies were variously approved by the research and ethics committees of the tertiary health institutions involved.²⁴

Statistical analysis

Many statistical measures have been developed to compare the incidence rates of particular cancers for different age groups in two or more populations. A long list of references and sources of information indicate extensive discussion on the subject.^{35–37} We used some of the accepted standards to calculate different statistics for estimating and comparing the incidence rate of prostate cancer for different age groups in different zones of Nigeria. In order to delineate the different age structures of the populations in each geopolitical region, the direct method of standardization was applied to the data shown in Tables 2 and 3. The primary statistics in the direct method are age-specific rates, a_i ,³⁸ calculated as the incidence rate per 100,000 by the formula:

$$a_i = \frac{d_i}{y_i} * 100,000$$

where d_i is the number of cases in the i th age group and y_i is the person-years of observation in the i th age group. Person-years are the population at risk and the time it contributes. The above formula indicates the age incidence rate of prostate cancer per 100,000 of each age group for the population covered by a particular hospital calculated by dividing the number of new prostate cancer cases by the number of person-years at risk for every age group and multiplying that by 100,000.³⁸ Person-years at risk were found by multiplying the number of males in different age groups in the Nigerian population (obtained from population pyramids of Nigeria)³⁹ during the observation period. Then, in order to compare the age-specific

Table 2 Hospital-based age structure of patients with prostate cancer within the various zones of Nigeria (Pre-PSA era 1970–1999)

Age, years	Geopolitical zones					
	SS ²⁹⁺ n (%)	SE ⁵⁰ n (%)	SW ²⁶⁺ n (%)	NE n (%)	NC ⁵⁶ n (%)	NW ³¹ n (%)
<50	3 (2)	19 (16)	18 (6)	Data N/A	4 (2.7)	4 (4)
50–59	30 (21)	40 (33)	57 (18)		14 (9.5)	19 (20)
60–69	44 (30)	49 (40)	99 (32)		51 (34.7)	41 (43)
70–79	58 (40)	13 (11)	97 (31)		43 (29.3)	29 (31)
≥80	10 (7)		39 (13)		23 (15.6)	2 (2)
Unspecified					12 (8.2)	
Period	(1984–1994)	(1970–1980)	(1990–1996)		(1979–1996)	(1993–1999)
Biomarkers	Pre-PSA	Pre-PSA	Pre-PSA		Pre-PSA	Pre-PSA
Total	145 (100)	121 (100)	310 (100)		147* (100)	95 (100)

Notes: Figures in superscript denote citation references. *Figures derived from histograms; *Denote mistaken data count in original manuscript; Data N/A denote Journal article was not easily accessed online or in most libraries.

Abbreviations: PSA, prostate-specific antigen; SS, South-South; SE, South-East; SW, South-West; NE, North-East; NC, North-Central; NW, North-West.

Table 3 Age structure of patients with prostate cancer within various zones in Nigeria (PSA era 1991–2007)

Age, years	Geopolitical zones						
	SS ²⁴ n (%)	SS ⁶¹ n (%)	SE	SW ^{43,#} n (%)	NE n (%)	NC n (%)	NW ²⁵ n (%)
<50	na	na	Data N/A	8 (4.2)	Data N/A	Data N/A	5 (14)
50–59	3 (21)*	8 (17.8)		44 (23.3)			4 (11)
60–69	3 (21)	12 (26.7)		68 (36)			10 (27)
70–79	4 (29)	25 (55.6)**		57 (30.2)			14 (38)
≥80	4 (29)			12 (6.3)			4 (11)
Period	(2003)	(2001–2004)		(1991–2007)			(2000–2002)
Biomarkers	PSA era	PSA era		PSA era			PSA era
Total	14 (100)	45 (100)		189 (100)			37 (100)

Notes: Figures in superscripts denote citation references. *Figures derived from men with PSA level ≥ 4.0 in rural prospective cross-section studies of prostate cancer incidence. #Figures derived from histograms. Na indicates cases were not available for that particular age-group; *Indicates data that include patients in the age group <60 years. **Indicates that data include all patients in the age group ≥ 70 years. Data N/A denote journal article was not easily accessed online or in most libraries.

Abbreviations: PSA, prostate-specific antigen; SS, South-South; SE, South-East; SW, South-West; NE, North-East; NC, North-Central; NW, North-West.

rates between different age groups within a geopolitical region and between geopolitical regions, the observed age-specific rates were standardized against the reference population, ie, the standard world population for each age group. This became the hypothetical value for age-specific rates, which would have occurred in the i th age class of the reference population. Standardization in the i th age class was found by the product $a_i w_i$, where w_i was the reference population for the age group i . The total of all the incidence rates ($\sum a_i w_i$) gave the age-standardized incidence rate per 100,000 world population for prostate cancer among Nigerians. Finally, the most important statistic is the mean annual age-standardized incidence rate (ASR) of prostate cancer per 100,000 of males in Nigeria, and is calculated as:

$$ASR = \frac{\sum a_i w_i}{\sum w_i}$$

Variance is given by the formula:

$$Var(ASR) = \frac{\sum \frac{a_i w_i^2 (100000 - a_i)}{y_i}}{(\sum w_i)^2}$$

And the 95% confidence interval by:

$$(ASR - 1.96 * \sqrt{Var(ASR)}, ASR + 1.96 * \sqrt{Var(ASR)})$$

For data in Tables 4 and 5, the ASR, the standard error (SE = $\sqrt{Var(ASR)}$), and 95% confidence interval were calculated for each region and provided summary comparison statistics. Two more statistics were also included in the data, ie, firstly, the crude (all-ages) rates per 100,000 person-years for all regions, which were used to amplify the effect of age and the geopolitical zone on the average incidence

rate of prostate cancer and, secondly, the cumulative rate and the corresponding measure for cumulative risk. The cumulative rate was the total $\sum a_i t_i$ where t_i was the observation period of i 'th age class of each geopolitical zone, and cumulative risk was the percentage risk a Nigerian residing in one of the geopolitical regions could have of developing prostate cancer (if no other causes of death were present). Cumulative risk was calculated from cumulative rate using the relationship:

$$100 \left(1 - \text{Exp} \left(-\text{cumulative rate} \frac{\text{rate}}{100} \right) \right)^{40}$$

Results

Demographic information from the registries was divided into the pre-PSA and PSA eras. The “pre-PSA era” comprised data recorded between 1970 and 1999, and only included reports in the 1990s that did not detect prostate cancer by any of the PSA assays. The “PSA era” encompassed cases that were detected between 1991 and 2007, and considered mostly prostate cancer cases that were detected by any of the PSA assays. This classification considered the late 1980s as the period when PSA became the diagnostic tool for prostate cancer in the Western world, while its countrywide application in Nigeria was only very recent. Data from the pre-PSA era comprised various prospective and retrospective hospital-based records of prostate cancer across the geopolitical zones, except for the inaccessible figures from the North-East (NE), arranged according to age and incidence (Table 2). Representative data obtained from countrywide registries revealed that approximately 98% of the prostate cancer cases were adenocarcinoma.^{23,29,30,50} Nonetheless, two patients (1.4% and 1.1%) presented with squamous cell

Table 4 Statistical analysis of crude and average annual age-standardized incidence rate of prostate cancer for pre-PSA era per 100,000 of Nigerian males

Region	Period of study	Crude rate per 100,000	ASR per 100,000	SE (ASR) per 100,000	95% CI for ASR per 100,000		Cumulative rate (%)	SE (cumulative rate) (%)	95% CI for cumulative rate		Cumulative risk (%)	Rank
					Lower	Upper			Lower	Upper		
SS	1984/94	7.53	6.54	0.55	5.47	7.62	0.62	0.061	0.5	0.74	0.62	3
SE	1970/80	3.47	3.5	0.33	2.86	4.14	0.18	0.018	0.14	0.21	0.18	5
SW	1990/96	21.06	19.41	1.14	17.19	21.64	1.1	0.075	0.96	1.25	1.1	2
NC	1979/96	12.28	13.85	1.25	11.14	16.29	2.23	0.21	1.82	2.63	2.2	1
NW	1993/99	5.41	5.28	0.35	4.19	6.36	0.23	0.03	0.18	0.28	0.23	4

Abbreviations: ASR, age-standardized incidence rate; SE, standard error; SS, South-South; SE, South-East; SW, South-West; NE, North-East; NC, North-Central; NW, North-West; CI, confidence interval.

Table 5 Statistical analysis of crude and average annual age-standardized incidence rate of prostate cancer for PSA era per 100,000 of Nigerian males

Region	Period of study	Crude rate per 100,000	ASR per 100,000	SE (ASR) per 100,000	95% CI for ASR per 100,000		Cumulative rate (%)	SE (cumulative rate) (%)	95% CI for cumulative rate		Cumulative risk (%)	Rank
					Lower	Upper			Lower	Upper		
SS	1984/94	15.4	16.42	1.4	13.67	19.17	0.86	0.09	0.67	1.04	0.85	1
SS	2001/04	15.09	16.31	2.47	11.47	21.13	0.3	0.04	0.2	0.39	0.3	2
SW	2002/04	4.68	4.38	0.33	3.74	5.03	0.07	0.006	0.06	0.08	0.07	3
NC	2000/02	0.92	0.88	0.15	0.59	1.17	0.016	0.003	0.01	0.02	0.016	4

Abbreviations: PSA, prostate-specific antigen; ASR, age-standardized incidence rate; SE, standard error; SS, South-South; SE, South-East; SW, South-West; NE, North-East; NC, North-Central; NW, North-West; CI, confidence interval.

carcinoma or adenosquamous carcinoma in the South-South (SS) and South-West (SW), respectively.^{29,43} However, the report from the NE indicated that most of these patients presented with symptoms similar to those of benign prostatic hyperplasia.²¹ Apart from specifying the differentiated types of adenocarcinomas, identification of specific histologic subtypes as, eg, small cell, ductal, and mucinous, was not reported. Data from these zonal registries showed that the highest incidence rate for prostate cancer was among patients in the 60–69 year and 70–79 year age brackets. In contrast, the age cohorts below 59 years presented with the lowest incidence of prostate cancer in all the zones during the study period. Despite the sparse tertiary hospital-based incidence data obtained for each geographic population, we computed a crude and age-standardized incidence rate of prostate cancer for the different age groups (Tables 4 and 5). Furthermore, even in the PSA era, we observed a trend similar to the age-specific incidence of disease found in the pre-PSA data (Table 3). However, in most data from the PSA era, age-specific incidence rates of disease in cohorts below 59 years were surprisingly high, especially in the SS₁, SW₂, and North-West (NW) zones. The detection of some concealed cases of prostate cancer in the SS and a section of the SE by PSA tests is presented in Tables 6 and 7. Distribution of PSA values according to patient age (Table 6) shows that the mean values for prospective, cross-sectional, and prospective hospital-based studies ranged between 1.17 ng/mL and 18.0 ng/mL. Each of these studies also confirmed that PSA values are age-dependent. Furthermore, the complementarity of PSA and DRE in predicting prostate cancer was also established in these populations (Table 7). Here, between 41.4% and 46.15% of prostatic cases detected by a PSA cutoff ≥ 4.0 were confirmed as symptomatic and palpable by DRE tests. In contrast, between 23.08% and 96% of prostatic cases detected by a PSA cutoff ≥ 4.0 were shown to

be enlarged but asymptomatic by DRE. Irreconcilable data from the zones for the detection of prostate cancer by PSA measurements were omitted.

Figures 2 and 3, respectively, show our calculated crude pre-PSA and PSA era annual incidence rates for prostate cancer per 100,000 of defined age groups for the estimated census populations serving the specific zonal tertiary health institutions. These curves show an exponential annual incidence rate of disease in the age group 50–79 years, with a peak annual incidence at 70–79 years in most cases except in the cross-sectional studies from SS₁ (Figure 2) where the incidence rate reached a peak at ≥ 80 years. In both eras, the calculated annual incidence rate for all zonal populations dropped beyond the age of 79 years, except for the reported rise in incidence in SS₁. Overall, the annual incidence rate recorded for the SW geopolitical zone in both eras was dramatically different from that in the other zones. The crude rate and the average annual age-standardized rate for prostate cancer by region in the period before and during the PSA era are shown in Tables 4 and 5, respectively. Based on these data, further cumulative risk (%) ranking conferred the SW and North-Central (NC) zones with the highest crude and age-standardized rates in the pre-PSA era (Table 4). This cumulative risk ranking was surpassed by values obtained from the SS zone during the PSA era (Table 5).

The few reports that described the extent of prostate cancer spread were based on TNM classification (Table 8) and Whitmore-Jewett stages (Table 9). From the TNM classification, 81.5% of the tumors in hospital-based cases from the SE zone had spread through the prostatic capsule, as opposed to 19.3% of such cases reported in the SS zone. Worse still, within the SS zone, most patients reporting to hospitals had tumors that had invaded nearby structures, as observed by T4 clinical staging (62.1%). Approximately one-third or more of the patients whose tumors were scored by Whitmore-Jewett

Table 6 Age distribution of prostate-specific antigen values from some zones in Nigeria

Age, years	PSA (ng/mL)		
	SS ^{24,48} n (%) Mean (median)	SS ⁶⁸ n% Mean \pm SD	SS ⁴⁹ /SE ⁴⁸ n% Mean \pm SD
<50	56 (37.1) 1.17 (0.60)	522 (39.4) 2.15 \pm 1.62	N/A
50–59	34 (22.5) 1.57 (0.55)	416 (31.4) 3.03 \pm 1.81	6 (12.8) 7.3 \pm 2.7
60–69	32 (21.2) 2.05 (0.90)	245 (18.5) 4.85 \pm 2.74	18 (38.3) 9.3 \pm 3.0
70–79	16 (10.6) 5.69 (1.25)	105 (7.9) 6.32 \pm 3.06	21 (44.7) 11.9 \pm 4.0
≥ 80	8 (5.3) 13.75 (4.45)	37 (2.8) 9.74 \pm 4.51	2 (4.2) 18.0 \pm 8.0
Period	(2003)	2007–2010	2002–2003
Total	146	1325	47*

Notes: *Mean PSA values reported here are from 47 prostate cancer patients. PSA for 71 age-matched control subjects are, respectively, 2.5 \pm 0.9, 2.3 \pm 0.5, 1.9 \pm 0.7, and 2.1 \pm 0.7 ng/mL; **Study subjects overlapped two geopolitical zones, ie, SS and SE; #Data reported as mean and median.

Abbreviations: SS, South-South; SE, South-East; PSA, prostate-specific antigen; SD, standard deviation; SE, standard error of the mean.

Table 7 Distribution of percentage of men with elevated PSA and their prostate cancer status

Region	PSA (ng/mL)	Prostate status by DRE			
		Normal Enlarged		Enlarged nodular	
		No symptoms n (%)	With symptoms n (%)	Cancer suspected n (%)	Confirmed n (%)
SS ²⁴	≥4.0	3 (23.08)	3 (23.08)	6 (46.15)	1 (7.69)
SS ⁶⁸	≥4.0	58 [#] (59)	N/A	41 (41.41)*	41 (41.41)
SS ⁷⁰	≥4.0	162 (57.7)	96 (34.2)	N/A	N/A [@]

Notes: [#]Men in this category had raised PSA with prostate enlargement, prostatitis, or benign prostatic hyperplasia; *All men having enlarged prostate with symptoms were confirmed with prostate cancer; [@]Data did not explain status of enlarged prostates.

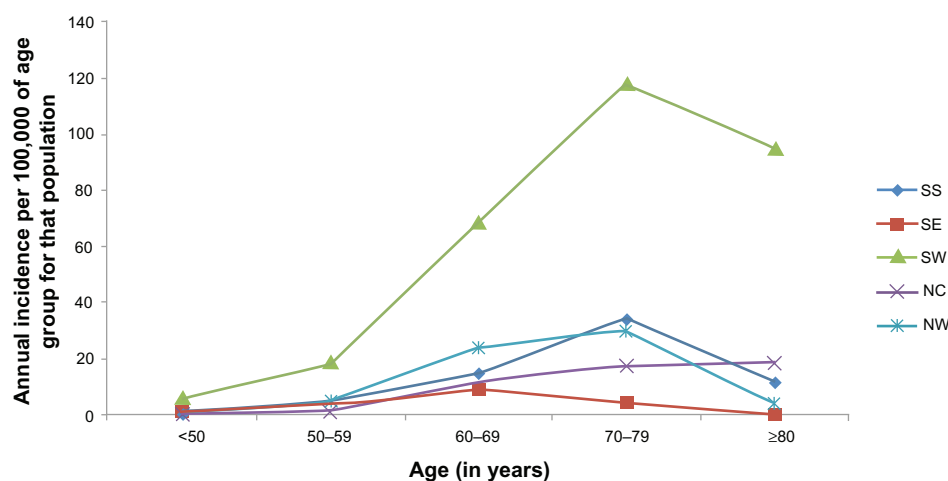
Abbreviations: SS, South-South; N/A, cases not available; PSA, prostate-specific antigen; DRE, digital rectal examination.

staging presented with prostate tumors extending through the capsule at the time of reporting to hospital (28.6%, 42.9%, and 27.2% reported in the SE, SW₁, and SW₂, respectively). Expectedly, Whitmore-Jewett staging also showed that not less than half of the patients seen in tertiary hospitals in all the reported zones presented with tumors that had spread to other organs (59.7%, 51.3%, and 59.2% in the SE, SW₁ and SW₂, respectively, Table 9). This trend is thus similar to the picture presented by previous grading of patients on the TNM classification. Finally, from the histologic subtypes (Table 10), 20%–49.5% of tumors recorded in the northern zones were considered to be high grade or poorly differentiated. Again, using this scoring system, 51%–80% of tumors were classified as generally low grade tumors. Generally, in this case, a little less than a third or more of the tumors seen were defined as high grade, which is close to the proportion seen for TNM and Whitmore-Jewett staging reported earlier.

Discussion

No study to date has evaluated the nationwide annual incidence rate and clinical characteristics of prostate cancer

in Nigeria. In the present study, data from all university teaching hospital-based registries in the geopolitical zones of Nigeria except for the NE zone showed that patients aged 60–69 years and 70–79 years had the highest rate of prostate cancer. The only available information on prostate cancer demographics²¹ from the NE zone is a PubMed abstract indicating that the majority (56%) of affected patients were 65 years of age or younger. The report also showed that most patients in this group presented with symptoms similar to benign prostatic hyperplasia. However, details such as histologic tumor grade and age distribution of patients were inaccessible for our study. In addition, the high incidence of the disease observed in men aged 60 years and older in all geopolitical zones of Nigeria is consistent with the observation that age-specific incidence rates of prostate cancer rise steadily with advancing age worldwide.⁴¹ These results corroborate those of previous studies identifying the 65–70 year age group in males from Ibadan and Washington, DC, as presenting with the peak incidence of carcinoma of the prostate.⁴² The average peak incidence according to age in most of the reports predated the seventh decade of life. This

**Figure 2** Pre-PSA annual incidence rate of prostate cancer per 100,000 of age cohorts in different zones of Nigeria.

Abbreviations: SS, South-South; SE, South-East; SW, South-West; NC, North-Central; NW, North-West.

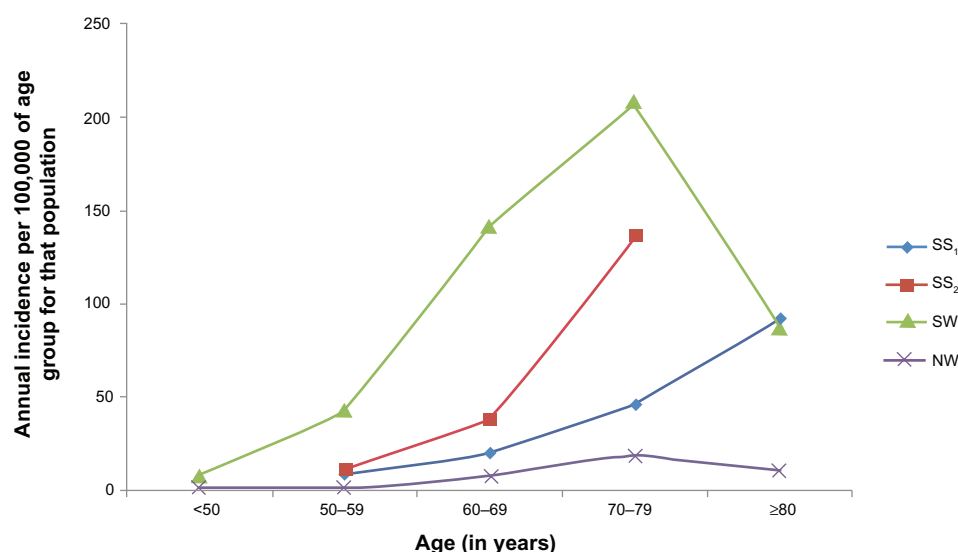


Figure 3 PSA-era annual incidence rate of prostate cancer per 100,000 of age cohorts in different zones of Nigeria.

Abbreviations: SS₁, South-South (first data set); SS₂, South-South (second data set); SW, South-West; NW, North-West.

is slightly lower than the mid years of the seventh decade reported for Caucasians in Europe and the US,⁴³⁻⁴⁵ leading us to suspect that prostate cancer occurs at a relatively younger age among Nigerians.⁴³ Equally, the available data from Nigeria show lower prostate cancer incidence rates (2%–16% and 4.2%–37.1% for the pre-PSA and post-PSA era, respectively) for patients aged younger than 50 years. The observation that a subset of patients with prostate cancer present at a younger age is consistent with the universal pattern whereby only few prostate cancer cases in the population have a genetic predisposition leading to early onset of the disease.^{29,46,47} Close scrutiny of the age distribution of prostate cancer cases from the zonal registries in Nigeria revealed the disease burden in a number of patients whose ages ranged from (slightly less than) 50 years and above. This justifies the sensitivity of PSA as a tumor marker, and also demonstrates its benefit in detecting previously undiagnosed cases that might only present in old age. Data obtained from prospective cross-sectional studies on the age distribution of prostate cancer in the PSA era reveal a narrowing of the incidence of the disease from the age group 60–79 years to that >50 years or 50–59 years.²⁴ This finding strengthens the evidence for an earlier age of disease prevalence in the Nigerian population, but weakens the argument for use of hospital-based registry reports to demonstrate the incidence of prostate cancer in Nigeria. Given that hospital-based incidence records do not reflect the true nature of the disease in Nigeria, the observation of advanced disease in these patients points strongly to the need for cross-sectional or population-based surveys that

would uncover latent and asymptomatic cases, especially in the middle-aged population. Currently, the influence of the environment, including dietary risk factors, in early onset of disease is being emphasized.^{48,49} Nonetheless, the reliability and significance of the different ages quoted in these data have previously been questioned considering the literacy level of the parents of some of these patients and unreliability of some of their birth records.⁵⁰ This concern seems genuine, considering that reliable birth recording was not mandatory in some remote parts of the country until 50 years ago.

Indeed, the sources of data for this report made calculation of a nationwide age-standardized incidence of prostate cancer almost impossible. A reason for this is that the exact population sizes encompassed by the different tertiary hospitals within the geopolitical zones are indeterminate. This is associated with the imprecise and overlapping character of the surrounding states and towns served by these hospitals. In such cases, census figures for calculating persons at risk in a defined area are based on guesswork. These figures could be so large as to reduce the expected age standardized incidence rates of the disease following a measure of the quotient obtained from the number of reported cases versus the product of the standard world population of persons at risk. Furthermore, the futility of calculating an age-standardized incidence rate is also associated with the reliance on hospital-based data in a society with little health education, poor health care, and inadequate screening programs. Overall, inadequacy in health education and the lack of effective screening programs could be a factor in the presentation of very severe

Table 8 Clinical stages of prostate cancer reported in different zones of Nigeria

Geopolitical zones		
Clinical stages (TNM)	SS ²⁹ n (%)	SE ⁶⁰ n (%)
T1	8 (5.5)	–
T2	13 (9.0)	5* (18.5)
T3	28 (19.3)	22 (81.5)
T4	90 (62.1)	–
Not stated	6 (4.1)	
Period	(1984–1999)	(1993–1998)
Total	145 (100)	27 (100)

Note: Figures in superscript denote citation references. *Indicates that tumor stage was not specified as T1 or T2, and is only referred to as early disease.

Abbreviations: SS, South-South; SE, South-East; TNM, tumor, node, metastasis.

cases in hospitals, therefore skewing the actual prevalence of the disease against the age-standardized incidence rates. The overall impact of this shortcoming could be inaccuracy of locally obtained hospital-based data on age-standardized incidence rates when compared with data obtained around the world. Notwithstanding these shortcomings, the crude and average annual age-standardized incidence rates for prostate cancer in all the zones were calculated to draw attention to the exact nationwide character of the disease. The pre-PSA data for the SW and NC zones showed the highest crude and age-standardized rates, but were surpassed by the SS zonal studies in the PSA period. In addition to the disparity in health care that occasionally causes regional differences in the incidence of the disease, other factors like lower screening rates, cultural factors, and less aggressive therapy, could account for the differences observed in the regional crude and age-standardized rates obtained in this study. The reliability of data from such settings should be investigated in either a series of cross-sectional studies or, better still, a countrywide population-based screening program.

Table 9 Clinical stages of prostate cancer reported in different zones of Nigeria

Clinical stages (Whitmore-Jewett)	Geopolitical zones		
	SE ^{32,*} no. (%)	SW ⁴³ no. (%)	SW ³³ no. (%)
A	21 (2.5)	11 (5.8)	3 (2.4)
B	78 (9.2)	–	14 (11.2)
C	242 (28.6)	81 (42.9)	34 (27.2)
D	506 (59.7)	97 (51.3)	74 (59.2)
Period	(1989–1998)	(1991–2007)	(1988–1993)
Total	847 (100)	189 (100)	125 (100)

Notes: Figures in superscript denote citation references. *Indicate data are from combined reports of carcinoma of the prostate after previous prostatectomy for BPH and cases with carcinoma in intact prostate.

Abbreviations: SS, South-South; SW, South-West.

Table 10 Histological scoring of prostate cancer reported in different zones of Nigeria

Scheme of histologic features	Geopolitical zones		
	NC ⁵⁶ n (%)	NW ²⁵ n (%)	NW ³¹ n (%)
Well differentiated	79 (67)		36 (37.9)
Moderately differentiated	15 (13)	27* (73)	12 (12.6)
Poorly differentiated	24 (20)	10 (27)	47 (49.5)
Period	(2001–2004)	(2000–2002)	(1993–1998)
Total	118 (100)	37 (100)	95 (100)

Note: Figures in superscript denote citation references. *Indicates that tumor stage was not specified and figures include well differentiated and moderately differentiated types.

Abbreviations: NC, North-Central; NW, North-West.

It is to be expected that the age-specific incidence of prostate cancer among Nigerian men aged 59 years or younger increased during the PSA period as opposed to the pre-PSA era. A reason for this, as shown by reports from the SS^{1,24}, SW^{2,43} and NW²⁵ zones is adherence to existing methods for diagnosis of prostate cancer and risk assessment. Annual DRE and measurement of serum PSA are currently recommended beginning at age 50 years and advocated to start at age 45 years in those whose first-degree relatives had the disease.^{51,52} The increase in the number of diagnosed prostate cancer cases among Nigerian age cohorts that previously showed moderate cases confirm that, most men are now diagnosed with the disease in its early stages (localized disease) because of the detection of elevated or rising serum PSA detected during screening.⁵¹ A parallel may be drawn with the younger age at onset of prostate cancer among Nigerian and African-American patients as opposed to Caucasians.⁵³ Reasons for such differences have been suggested to be genetic, pathologic, molecular, and/or socio-economic.⁵³ Nevertheless, age is still universally accepted as an important risk factor for prostate cancer, which is rarely seen in men younger than 40 years of age. The increased use of PSA as a screening test for Nigerian men, in addition to the increase in cross-sectional or population-based surveys, has led to detection of a significant number of latent cases, as has been observed in other places, which may potentially lead to a dramatic reduction in the number of patients with metastatic disease at the time of diagnosis.⁵¹

The rapidity with which the calculated annual incidence of prostate cancer per 100,000 for defined age groups in the corresponding zonal populations progressed beyond 50 years of age is similar to previously reported US data on age-specific incidence curves.⁵⁴ However, this upsurge in incidence of prostate cancer from 50 years of age onwards contrasts with the steady rise observed in China and the Middle East.⁵⁵ The

upsurge in incidence after 50 years of age in the US had been attributed to its increased detection in these age cohorts.⁵⁵ Also, higher life expectancy in the US could have caused the sharp rise in incidence rate in men aged over 50 years, because most men in the US live long enough to develop this “disease of the elderly”. In contrast, the sharp rise in prostate cancer among Nigerian men aged 50–79 years could be attributed to the survival of these men into the period of life when prostate cancer manifests clinically and is detected. The peak annual incidence at 70–79 years accounted for a third of all hospital-based prostate cancer cases observed in Nigeria. There may be a number of reasons for the decline in annual incidence rate for men aged 80 years and older in all the zones. To begin with, life expectancy in Nigeria is far less than 80 years, and as such, very few men live to this age,⁵⁶ thus skewing the number of hospital cases. This could be compounded by the fact that 50%–81% of Nigerian patients present with clinically obvious and advanced disease,^{29,56} ie, higher rates of palpable disease with adverse prognostic features. The influence of life expectancy on the incidence of prostate cancer in the elderly is well known from data generated in the Western world.^{57,58} Again, the decline in incidence rate after 80 years of age in Nigeria could relate directly to the low socioeconomic status of the majority of the population, poor access to health care, and poor health awareness nationwide. In such a scenario, these men are unlikely to undergo prostate cancer screening, and could have impalpable and undetectable prostate cancer, which might only be detected as an incidental finding or on biopsy. Lastly, the dramatic deviation in annual incidence of prostate cancer recorded in the SW^{26,43} in favor of much higher incidence rates as compared with other geopolitical zones could be explained by the historic location of the cancer registries serving the tertiary university teaching hospitals at Ibadan and Ile-Ife. The main cancer registry at Ibadan is the only population-based registry in Nigeria, serving a population of 1.22 million (1991 census) or more (2001 census) with a defined area of 70 square kilometers in Ibadan, Oyo state, SW Nigeria.⁵⁹ Data for UCH Ibadan is regularly obtained from all the hospitals and health facilities (public, mission, and private) in the local government counties subserving the registry.⁵⁹ In addition, the UCH is the National Headquarters for Cancer Registries in Nigeria, which coordinates the training programs and establishment of other zonal registries throughout the country. In this respect, data from this registry could be more precise, better managed, and its specific population boundaries better defined to enhance its apparent recording of higher incidence rates. Traditionally, UCH Ibadan, which is the nation’s leading tertiary health institution, remains the

last referral option for most Nigerians, irrespective of their regions of domicile, and this may have contributed to the higher than average incidence of prostate cancer recorded by its registry. On the other hand, the urbanized nature of Ibadan, its environs, and its outer reaches, like Ile-Ife, could have been ideal for an increased culture of cancer screening, and health care access provided by the tertiary hospitals in the SW zone of Nigeria. The highly skewed incidence rates of disease in this region could thus be explained, at least in part, by its early adoption of the PSA test, and the level of health awareness of its population.

Prostate cancer stage of T3, C or greater, recorded for the vast majority of patients from one of the tertiary hospitals in the SE zone of Nigeria, has been attributed to the late presentation of prostate cancer among these patients.⁶⁰ The greater than 80% presentation of advanced disease in these patients may not have appropriately represented the demographic characteristics of the disease in this zone. One reason for the poor demographic representation of data in this zone was the very low number of cases seen ($n = 27$) over a 5 year period, indicating that these were hospital-referred symptomatic cases at the time of presentation. Again, the presence of a major tertiary hospital (ie, University of Nigeria Teaching Hospital, Enugu) within 200 km of the source of these data suggests that case loads might have been lifted off the smaller registries. Whereas a lower percentage (19.3%) of advanced disease was reported in a SS zonal study, a much worse staging of T4 (62.1%) was reported for patients in this zone at the time of presentation to hospital. Although there were only two comprehensive zonal representative reports available on TNM staging of prostate cancer in Nigeria, the uncovering of advanced disease here does not deviate from countrywide reports of the advanced stages of disease seen in hospitals.^{21,43} The staging of close to one third or more of tumors in the southern zones, such as those extending through the capsule (stage C) using Whitmore-Jewett criteria agrees closely with the TNM staging scheme reported earlier. Tumor staging in the geopolitical zones by the Whitmore-Jewett criteria also revealed that more than half of the patients had tumors that had spread to other organs (stage D). This also closely resembled the tumor grading found in the SS zone by the TNM scheme. To estimate the destructive potential and ultimate prognosis of the disease, pathologists from the SS, NC, and NW zones used the histologic scoring system to show the profile of surgical and biopsy specimens.^{25,31,61} Based on histologic scoring of NC and NW specimens, 20% and 49%, respectively, were considered to be high-grade or poorly differentiated. This suggests that these patients had an

increased tumor burden that was associated with a higher risk of metastatic disease, an increased chance of post-treatment failure, and a worse overall prognosis.^{62–64} Using this prostatic adenocarcinoma classification scheme, between 13% and 73% of tumor specimens were considered moderately differentiated or generally low-grade tumors. The 73% outlier value reported from the NW₁ derives from the summing of well and moderately differentiated carcinoma as a group.²⁵ Furthermore, 38%–67% of tumor specimens analyzed from these zones were well differentiated or low grade tumors. Based on the Gleason grading system, regarded as the “gold standard” for classifying prostatic adenocarcinoma,⁶⁵ an average of one third of the northern zonal cases were high grade, corroborating the TNM and the Whitmore-Jewett staging reported earlier from the southern zones.

Evaluation of the significance of race on prostate cancer presentation and progression revealed a correspondence between the 52% rate of stage D disease found in African-American men⁶⁶ and the observation that more than 50% of patients in this study presented with the disease in the southern zones of Nigeria. The 52% rate of stage D disease observed in African-American men was far higher than the 26% rate observed in Caucasians with access to the same military health care system.⁶⁶ The biological difference that could account for the different stages of prostate cancer among African-Americans and Caucasians provided with the same standard of health care is yet to be elucidated.⁵³ In addition, African-American men have been reported to present with a higher incidence (16.1%) of advanced disease or distant metastasis (from combined categories T3/T4, N1, or M1) than Caucasians (3.8%).⁵³ More disturbing is the observation of a worse scenario in which 62.1% of Nigerian men from the SS zone presented with T4 disease. On the Gleason grading system, a comparable number of African-American men (35%) and Nigerian men (30%) from the northern geopolitical zones had high grade tumor scores when viewed against data for Caucasians (25%).⁵³ The reasons for presentation of advanced disease by most inner city African-Americans and most likely Nigerians, in contrast with Caucasians, could be attributed to rare screening or hospital visitation by the former, except during symptomatic and aggressive disease.⁶⁷

Limitations of this study include the dominance of its data by hospital-based registry reports and its substantially retrospective nature, both leading to an underestimation of the definite number of prostate cancer cases in the studied populations. The reasons for these low cases could be associated with exclusion of latent and symptom-free subjects

from hospital reports, and the incomplete documentation and retrieval systems used by most of the registries. Another limitation of this study is the discordant research strategy and data presentation, causing overlap and divergence of the study periods, leading to great difficulty in harmonizing the data. Finally, most of the data presented are limited by the exclusion of specific histologic subtyping of cases, which would have had significant prognostic and therapeutic implications.

Conclusion and recommendations

This study suggests that the incidence of prostate cancer among Nigerian men is higher at a younger age than in Western countries. Reasons for such early disease occurrence may include behavior, biology, or both. This early age of disease prevalence in Nigeria weakens the rationale for use of hospital-based registry data to demonstrate the incidence of prostate cancer in Nigeria. The finding of advanced disease in more than one-third of hospital-based cases seen in all the zones, regardless of the tumor grading scheme used, is an indication that the reported cases are mostly for symptomatic patients. This justifies funding of quality, controlled, population-based screening programs in all the regions. The data also suggest the need to investigate closeness of incidence of disease in the Nigerian and African-American populations as opposed to Caucasian populations. This is particularly relevant, given that our study population accounted for a highly significant proportion of the African diaspora, indicating that both populations may harbor similar inherited genetic predispositions that trigger alterations associated with increased risk of prostate cancer. Considering the inconsistent pattern of reported findings for each study, we recommend the formation of a national study group on prostate cancer, which would formulate national guidelines for a research strategy and presentation of study protocols. Such an arrangement would enhance the harmonization of these diverse investigations into coherent demographic and health reports of prostate cancer. We also recommend the formation of collaborative study programs on population-based screening of Nigerian men and African-American men, in addition to examining genetic variants predisposing to prostate cancer that may be common in these populations. Elucidation of such common genetic variants may unmask common pathways in prostate carcinogenesis and reveal a universal etiology of prostate cancer. Moreover, identification of specific histologic subtypes of cancer in pathology reports may lead to significant prognosis of the cases and enable development of suitable therapeutic interventions.

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Disclosure

The authors report no conflicts of interest in this work.

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