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Brief Communication

Prostate cancer clinicopathological presentation in South-East Africa during the 2010 decade

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Abstract

Prostate cancer is the leading cause of cancer-associated death among men across Sub-Saharan Africa, with Southern and East Africa ranking first and fifth globally. However, lack of coordinated national cancer registries has biased data toward single-sourced, averaged, or model estimates. Here, our retrospective study included 8634 South-East African patients diagnosed between 2010 and 2019, which when compared with 71 694 Black and 322 356 White period-matched American men, were over threefold more likely to present with aggressive disease (International Society of Urological Pathology grade groups ≥4: 45.38% vs 21.22% and 21.05%; prostate-specific antigen ≥20 ng/mL: 62.04% vs 17.29% and 11.17%, respectively; all 2-sided $P < .0001$). East over Southern African men are 1.5 times more likely to present with advanced disease, however, age was not a confounder. Supporting prostate cancer as a major health concern for Africa, our data suggest underestimation in East Africa, while highlighting the need for accurate monitoring, increased awareness, and tailored screening criteria.

Prostate cancer is the leading cause of cancer-related deaths among men of African ancestry and/or from Africa. Besides the Caribbean (ranked second globally), all regions of Sub-Saharan Africa are notably impacted (Figure 1, A), with Southern Africa having the highest (29.7 age-standardized rate per 100 000 males) and East Africa the lowest (16.8 per 100 000) mortality rates.[1] However, the true clinical impact across Africa remains poorly appreciated, requiring country and regional validations. To address this gap, the US Department of Defense–funded Health Equity Research and Outcomes Improvement Consortium Prostate Cancer Precision Health Africa1K consortium, via the Southern African Prostate Cancer Study and the East African Prostate Cancer Study, is endeavoring to build a clearer regional perspective.[2] Using the National Comprehensive Cancer Network clinicaopathological definition for high-risk and very high-risk prostate cancer at presentation,[3] we previously reported that Black South Africa men have a 2.1-fold increased risk for International Society of Urological Pathology (ISUP) and at least 4- and 4.8-fold for prostate-specific antigen (PSA) at least 20 ng/mL at presentation than Black American men.[4]

Here, using complete sampling, we reviewed histopathological (South Africa) or hospital (Kenya) records retrieved for men diagnosed from January 1, 2010, to December 31, 2019, for age, PSA levels, and ISUP group grading from primary and secondary Gleason scores. The study was approved by the National Health Laboratory Service (PR2223713) and University of Pretoria Faculty of Health Sciences research ethics committee (393/2021) in South Africa and Kenyatta National Hospital University of Nairobi ethics and research committee (P425/05/2019) in Kenya, with additional review and approval granted by the Human Research Protection Office of the US Army Medical Research and Development Command as part of the US Department of Defense Health Equity Research and Outcomes Improvement Consortium Prostate Cancer Precision Health Africa1K–funded research (E03333). Patients included 6 500 Black South African men from Steve Biko Academic ($n = 5271$) and Kalafong tertiary

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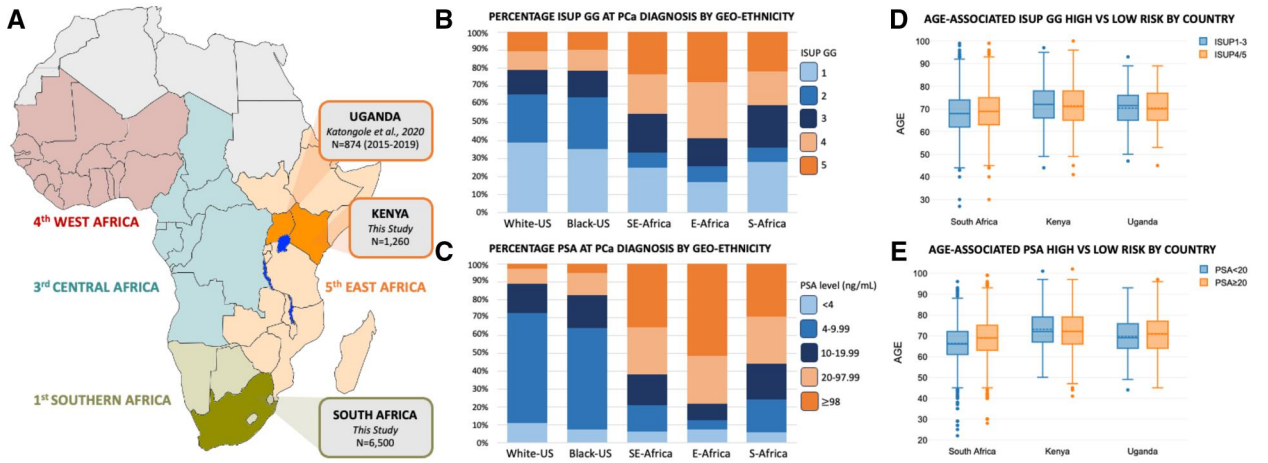

Figure 1. Prostate cancer presentation in Sub-Saharan Africa. **A)** Map of Africa depicting regional Sub-Saharan Africa GLOBOCAN 2022 prostate cancer–associated worldwide mortality rankings as well as South-East African patient resources targeted in this study. **B)** Distribution (percentage) of prostate cancer International Society of Urological Pathology (ISUP) grade grouping across the study's geo-ancestral identifiers, with further distinction using National Comprehensive Cancer Network criteria as high-/very high-risk (ISUP ≥4, orange) vs low-risk prostate cancer (ISUP <4, blue). **C)** Distribution (percentage) of prostate-specific antigen (PSA) levels (ng/mL) at diagnosis across the study's geo-ancestral identifiers, with further National Comprehensive Cancer Network categorization as high-/very high-risk (PSA ≥20 ng/mL, orange) vs low-risk prostate cancer (PSA <20 ng/mL, blue). **D)** Box plots depicting age distribution for high-/very high-risk (ISUP ≥4, orange) vs low-risk (ISUP <4, blue) prostate cancer cases at diagnosis by South-East African country. **E)** Box plots depicting age distribution for high-/very high-risk (PSA ≥20 ng/mL, orange) vs low-risk (PSA <20 ng/mL, blue) prostate cancer cases at diagnosis by South-East African country. Abbreviations: E = East; GG = grade grouping; PCa = prostate cancer; S = South; SE = South-East.

hospitals ($n = 1229$) in Pretoria, while the 1260 Kenyan men were sourced from central Kenyatta National hospital in Nairobi ($n = 966$) and 2 regionally located Meru ($n = 231$) and Nyeri tertiary hospitals ($n = 63$). For the South African case series, self-identification as non-African men led to case exclusion, while additional pathological features of benign prostatic hyperplasia and/or prostatitis were reviewed.

Although retrospective prostate cancer studies across Sub-Saharan Africa are scarce, 1 study out of Uganda ($n = 874$) met our requirement as a regional neighbor, with data type matching and period overlap (2015-2019 restricted),[5] for a total of 2134 East African men. Furthermore, US Surveillance, Epidemiology, and End Results (US-SEER) data including 17.6 million patients (November 2023 update) spanning 17 registries (2000-2021) allow for global comparative analyses. After filtering for primary cancer site (prostate gland), year of diagnosis (2010-2019), and race (non-Hispanic Black and White), data were assessed for age, PSA level, and first and second primary and secondary Gleason scores (converted to ISUP group grading) at diagnosis. Further exclusion for "all" missing data or nonconfirmed diagnosis and "unknown" first and second Gleason score (White men only) allowed for 71 694 Black and 322 356 White American men.

Generating 5 categorical variables each (4 degrees of freedom) for age, PSA, and ISUP, statistical significance was calculated using a 2-sided χ^2 with Cramer V strength statistic after accounting for missing data. Whereas South-East African data had no upper limit cutoffs, the US-SEER data were capped for age (90 years and older) and PSA (≥98 or 98+ ng/mL). Bonferroni test for post hoc analysis was used to determine if age is a confounder for aggressive disease by country within South-East Africa. Cutoff for statistical significance is a P value less than .05.

For South-East Africa, the age distribution ranged from 22 to 102 years, with a mean (68.6 years) more closely reflecting White (66.8 years) over Black (63.6 years) American men, and delayed diagnosis in East over Southern Africa (3.4-4.8 years) (Table 1). Notably, 59% of East African men present with a statistically significant advanced ISUP grade of at least 4 compared with 41% of Black South African and 21% of American men (Figure 1, B; all $P < .0001$). The latter was even more evident when considering PSA at diagnosis (Figure 1, C). Although levels of at least 1000 ng/mL are not uncommon in South-East African men (8.4% South Africa, 7.3% Kenya, 14.5% Uganda), when considering the US-SEER capped at 98 ng/mL (upper limit), this increased to 30%, 49%, and 55%, respectively, contrasting with statistical significance to Black (5%) and White (2.7%) American men (all $P < .0001$). Using National Comprehensive Cancer Network PSA screening criteria, 62% of South-East African men would have been classified as high-risk or very high-risk (≥20 ng/mL) compared with Black (17%) and White (11%) American men. Conversely, American men most commonly presented in the 4-9.99 ng/mL range (57% Black and 62% White patients). Although age is a well-established prostate cancer risk factor, surprisingly, we found age not to be a confounder for advanced pathology in South-East Africa (Figure 1, D; Table S1), while statistical significance was only reached in South Africa for PSA levels (Figure 1, E, Table S1). Observing an elevated presence of benign prostatic hyperplasia (41.0%, 2665 of 6500) and prostatitis (33.9%, 2204 of 6500) in our South African patients, one cannot rule out the contribution of these co-pathologies to the elevated PSA levels observed.

Driven by a lack of prostate cancer screening and uptake, perpetuated by reduced prostate cancer awareness, mistrust, and low socioeconomic status across Sub-Saharan Africa,[6] it is not surprising that the mean age at presentation ranged from 67.6 (South Africa) to 72.4 (Kenya) years, with the greatest disparity gap between East African and Black American men (8.8 years). Whereas South-East African men are at 2.1-fold greater risk than American men for an ISUP grade of at least 4 at diagnosis, this risk increased to 2.8-fold for East Africa. The greatest ancestral differences at prostate cancer presentation was noted for the ISUP 2 grade group (or pathological Gleason score 3 + 4), with Black and White American men 3.4-fold and 3.2-fold more likely to receive this generally good prognosis over South-East African men (range = 8.18%-8.86%), respectively. Pathology shortage, estimated at 1 pathologist per million Sub-Saharan Africans, is a

Table 1. Prostate cancer clinicopathological variables (age, PSA and ISUP group grade) at presentation for Southern and East African patients compared with US all-population patients from 2010 to 2019[a]

Variables at diagnosis	South Africa	East Africa				United States[b]		United States[b]	
	South Africa this study, No. (%) (*n* = 6500)	Kenya this study, No. (%) (*n* = 1260)	Uganda published,[a] No. (%) (*n* = 874)	South vs East Africa, *P* (χ2; *df*; φc)	South-East Africa, No. (%) (*n* = 8634)	Black American non-Hispanic men, No. (%) (*n* = 71 694)	South-East African vs Black American men, *P* (χ2; *df*; φc)	White American non-Hispanic, No. (%) (*n* = 322 356)	South-East African vs White American men, *P* (χ2; *df*; φc)
Age, y	(*n* = 6463)	(*n* = 1259)	(*n* = 874)		(*n* = 8596)	(*n* = 71 694)		(*n* = 322 356)	
Younger than 50	137 (2.12)	8 (0.95)	9 (1.03)	<.0001	154 (1.79)	3297 (4.60)	<.0001	5763 (1.79)	<.0001
50-59	951 (14.71)	111 (8.58)	96 (10.98)	(350.97; 4; 0.2021)	1158 (13.47)	19 902 (27.76)	(2730.78; 4;	58 968 (18.29)	(449.25; 4; 0.0368)
60-69	2714 (41.99)	344 (27.32)	280 (32.04)		3338 (38.83)	31 659 (44.16)	0.1844)	140 406 (43.56)	
70-79	2082 (32.21)	490 (38.92)	328 (37.53)		2900 (33.74)	14 265 (19.90)		92 754 (28.77)	
80 and older	579 (8.96)	306 (24.31)	161 (18.42)		1,046 (12.17)	2571 (3.59)		24 465 (7.59)	
Missing data[c]	37	1	0		38	0		0	
Mean	67.6	72.4	71		68.6	63.6		66.8	
Median	68	72	70		69	64		67	
Range	22-99	41-102	44-100		22-102	26 to ≥98		25 to ≥98	
Prostate-specific antigen, ng/mL	(*n* = 5184)	(*n* = 1088)	(*n* = 815)		(*n* = 7087)	(*n* = 63 621)		(*n* = 279 228)	
<4.0	296 (5.71)	78 (7.17)	60 (7.36)	<.0001	434 (6.12)	4712 (7.41)	<.0001	30 834 (11.04)	<.0001
4-9.99	957 (18.46)	52 (4.78)	44 (5.40)	(452.14; 4; 0.2526)	1053 (14.86)	36 089 (56.72)	(10408.89; 4;	172 082 (61.63)	(26 627.75; 4; 0.305)
10-19.99	1028 (19.83)	109 (10.02)	66 (8.10)		1203 (16.97)	11 817 (18.57)	0.3837)	45 116 (16.16)	
20-97.99	1365 (26.33)	316 (29.04)	200 (24.54)		1881 (26.54)	7794 (12.25)		23 768 (8.51)	
98-999.99	1103 (21.28)	454 (41.73)	327 (40.12)		2516 (35.50)	3209 (5.04)		7428 (2.66)	
≥1000	435 (8.39)	79 (7.26)	118 (14.48)		Merged above	Not determined		Not determined	
Missing data[c]	1316	172	59		1547	8073		43 128	
Mean	661	510.8	1951.8		786.5	16.2		12.3	
Median	26	94.295	100		37.8	7.5		6.7	
Range	0.1-606 200	0-99 918	0-99 999.99		0-606200	0.1 to ≥98		0.1 to ≥98	
International Society of Urological Pathology	(*n* = 3483)	(*n* = 869)	(*n* = 386)		(*n* = 4738)	(*n* = 71 060)		(*n* = 322 356)	
1	976 (28.02)	134 (15.42)	81 (20.98)	<.0001	1191 (25.14)	25 161 (35.41)	<.0001	126 005 (39.09)	<.0001
2	285 (8.18)	77 (8.86)	34 (8.81)	(147.55; 4; 0.1765)	396 (8.36)	20 164 (28.38)	(2080.48; 4;	85 373 (26.48)	(2321.93; 4; 0.0843)
3	809 (23.23)	149 (17.15)	43 (11.14)		1001 (21.13)	10 651 (14.99)	0.1657)	43 131 (13.38)	
4	656 (18.83)	224 (25.78)	165 (42.75)		1045 (22.06)	8147 (11.46)		33 972 (10.54)	
5	757 (21.73)	285 (32.80)	63 (16.32)		1105 (23.32)	6937 (9.76)		33 875 (10.51)	
Missing data[c]	3017	391	488		3896	634		0	

[a] Ugandan prostate cancer cases recruited from 2015 to 2019 and published in Katongole et al.[5]
[b] Period-matched US Surveillance, Epidemiology, and End Results data downloaded from https://seer.cancer.gov/data/access.html and capped at an upper limit of 90 years for age and 98 ng/mL for prostate-specific antigen levels.
[c] Missing data were excluded from further analyses.

possible co-contributing factor.[7] However, the most dramatic disparity was observed for PSA at diagnosis. Compared with period-matched American men, South-East African men are between 3.3 and 7.3 times more likely to have been classified as high-risk or very high-risk, and 7.1 to 13.3 times more likely to present with a PSA over the US-SEER upper limit (≥98 ng/mL). Although East Africans presented later with more advanced pathology and associated risk, age was not a confounding factor.

Initially championed as the golden standard for cancer screening (mid-1990s), PSA testing guidelines have undergone numerous iterations. Increased incidence rates, with a lack in correlated mortality reduction, led the US Preventive Services Task Force to recommend against PSA screening for men aged older than 75 years in 2008 and adjusting this to men of any age or race in 2012.[8] Consequently, period-matched US-SEER data showed an increase in metastatic disease,[9] resulting in the US Preventive Services Task Force reintroducing in 2018 screening for men aged 55-69 years, while acknowledging lack of sufficient data for Black American men.[10] Our findings escalate these concerns, cautioning against blindly adopting largely European-derived guidelines across Sub-Saharan Africa. Additionally, lack of national screening policies and awareness, perpetuated by underresourced health-care services and associated funding, has inarguably exaggerated mortality rates.[11]

Although the largest study of its kind for Sub-Saharan Africa, we caution that our results are a mere snapshot of the rich geo-ethnic and socioeconomic diversity within South-East Africa, which does not necessarily reflect the entire region or continent. The latter is further evidenced by a smaller 2007-2017 study reporting elevated aggressive prostate cancer presentation for Black Nigerian over South African men.[12] A retrospective case series, our data lack single pathology coordinated review, while records were notably scarce or incomplete in the earlier years. Further limited by extreme age variability, intriguingly, age was largely not a confounding factor. In turn, capping of US-SEER data for age and PSA will have a minimal lowering effect.

Shifting the paradigm from late-stage detection to early intervention, with the goal to reduce mortality across Sub-Saharan Africa, in summary, our findings emphasize the limitations of current prostate cancer screening criteria, while implying the overall burden of aggressive disease has been underestimated, particularly for East Africa. We place urgency in establishing tailored screening guidelines, appreciating the need for regional-specific adjustments. Improving the overall health and well-being of men across Sub-Saharan Africa requires prostate cancer to receive the attention it deserves.

Author contributions

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Supplementary material

Supplementary material is available at *JNCI: Journal of the National Cancer Institute* online.

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Conflicts of interest

V.M.H. is a member of Active Surveillance Movember Committee and received an honorarium from the Korean Urological Oncology Society for Annual Conference guest speaking.

Data availability

All data has been provided in the Supplementary Data Resource file and listed by country and/or ancestry. US-SEER data was downloaded from https://seer.cancer.gov/data/access.html.

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