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Prostate Cancer Genomics Research Disparities in Africa: Advancing Knowledge in Resource Constrained Settings

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Abstract

Prostate cancer disproportionately affects men of African descent and it is estimated that Africa will bear the highest disease burden in the next decade. Underlying genomic factors may contribute to prostate cancer disparities; however, it is unclear whether Africa has prioritised genomics research toward addressing these disparities. A Pubmed review was performed of publications spanning a 15-year period, with specific focus on prostate cancer genomics research that included samples from Africa and investigators in Africa. Data are presented on research publications from Africa relative to similar publications from different geographical regions, and more specifically, the extent of disparities and the contributions to prostate cancer knowledge as a result of genomics research that included African samples and African institutions. Limited publication output may reflect the infrastructure and funding challenges in Africa. Widespread cooperation should be fostered by sharing capacity and leveraging existing expertise to address the growing cancer burden facing the continent.

Keywords

Prostate cancer, genomics, Africa, African descent, disparities

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Introduction

Prostate cancer (CaP) is the most commonly diagnosed cancer in men,[1] with men of African descent suffering disproportionately from the disease compared to men of other ethnicities.[2] In the United States of America (USA), African American men have a higher risk of developing CaP, and are at increased risk of dying from CaP compared to men of European or Asian descent.[3,4] In the United Kingdom (UK), men of African descent have an increased risk of being diagnosed and dying from CaP.[5] Data from GLOBOCAN 2008 showed the CaP age-adjusted mortality rate in Caribbean men of African descent was 26.3 per 100 000,[6] while a more recent study reported a higher age-adjusted mortality rate of 33.8 per 100 000, second only to the rate observed in African American men (33.8 vs 41.0 per 100 000, respectively).[4]

For African men, the CaP age-adjusted incidence per 100 000 population ranges from 10.6 in Northern Africa to 61.7 in Southern Africa.[7] In a recent study, the age-standardised incidence rate (ASIR) in South African Black men was shown to increase from 44.9 to 57.3 per 100 000 for the period between 2006 and 2016.[8] In Sub-Saharan Africa (SSA) for the period 1990–2010, disability-adjusted life years (DALYs) and mortality from CaP increased from 100 200 to 219 700 and 5600 to 12 300, respectively.[7] Moreover, the International Agency for Research on Cancer (IARC) estimated that CaP deaths in Africa would increase from approximately 28 000 deaths in 2010 to more than 57 000 deaths by 2030.[6] Pinheiro and colleagues observed CaP age-adjusted mortality rates of 32.7 vs 27.3 vs 17.3 per 100 000 for men from West-and-Central Africa vs African men not from West-Central Africa vs East African men.[4] However, the true CaP incidence and mortality rates in Africa is known to be significantly underestimated due to

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underdiagnoses, under treatment, inadequate health management information systems, limited cancer registry data and lack of screening.[2,5]

Worldwide, African American men are more likely to develop CaP compared with European American men, and are generally younger at diagnosis, present with more aggressive disease and are up to 4.2-fold more likely of dying from the disease.[9] Furthermore, CaP disproportionately affects individuals of African ancestry, regardless of their country of residence; consequently, it has thus been suggested that the disproportionality might involve complex interplay between biological, environmental and genetic factors.[10] Although the underlying causes of CaP largely remain inconclusive, the only well-established risk factors for disease are age, ethnicity and family history.[11]

Prostate cancer exhibits the highest reported heritability of any major cancer, with a genetic contribution of approximately 58%.[12,13] Additionally, individuals with a family history of CaP have a 2.5-fold increased risk of developing lethal CaP if they had a single affected first-degree relative, the risk increased to 5.3-fold for individuals with 3 or more affected first-degree relatives.[14] Prostate cancer is generally considered to be a complex disease with several genes that play a role in disease onset and severity; several susceptibility genes are also known to contribute to disease risk. Early family-based linkage studies identified causal loci with rare high-penetrance variants that increase CaP risk; however, these studies were mainly carried out in populations of European descent. These loci, responsible for hereditary CaP, include HOXB13,[15] HPC1 (1q24-25),[16] HPCX (Xq27-28),[17] HPC20 (20q13),[18] PCAP (1q42-43)[19] and CAPB (1p36).[20] Only a few studies were subsequently able to replicate these finding in men of African ancestry, more specifically, in African American men, for HPC1, PCAP, HPC20, and HPCX.[21-23] Importantly, these hereditary CaP risk loci have not been replicated in African men, although it is unclear whether similar linkage-replication investigations were in fact performed in African populations.

More recently, genome-wide association studies (GWAS) had identified 170 single nucleotide polymorphisms (SNPs) (or risk variants) associated with CaP risk, predominantly in populations of European and Asian ancestry.[24] A few studies were able to replicate previous CaP GWAS findings in African American men[25-27]; however, it was also noted in each of these studies that a number of the previously reported SNP associations could not be replicated in African American men.[27] Similarly, in African men (who are resident in Africa), Tindall and colleagues demonstrated that a significant percentage of GWAS identified risk variants failed replication within a Black South African cohort.[28] A GWAS study in Ghanaian men that tested 81 previously associated SNPs, was only able to replicate associations with 10 SNPs.[29] In a small GWAS replication study, Fernandez and colleagues were only able to demonstrate associations with variants on chromosome 8q24 and 10q11, although these authors noted that their study may have been significantly underpowered and their African descent study population was admixed.[30] A notable consequence of studies in African descent men was the identification and subsequent replication of novel loci associated with CaP risk, associations that were not observed in European or Asian populations. Two studies identified novel risk loci in African American men and were able to replicate these associations in Ghanaian and Ugandan men.[31,32] Another study identified novel associations with variants on chromosomes 13q24 and 22q12 in Ghanaian and Ugandan men.[33] A recent trans-ancestry GWAS identified 1 novel variant associated with CaP risk, the association was only observed in men of African ancestry.[34]

Advancements in high-throughput genomics technologies such as array-based analyses and next generation sequencing (NGS) have increasingly enabled large genomic studies to provide insights into the CaP genome, transcriptome and epigenome.[35-38] However, men of African ancestry, and particularly African men resident on the African continent, are often underrepresented in these large genomic studies.[39] It has be suggested that this underrepresentation may be due to insufficient number of available biological or clinical specimens from African Ancestry men, and as a result, it has been difficult to generalize genomic findings across all populations, which in turn, may contribute to the continued health disparity observed in African descent populations globally.[13,40]

Prostate cancer has the highest heritability of all major cancers. Moreover, African ancestry is a major risk factor for CaP, and disease-associated mortality is disproportionality higher in men of African ancestry. There is substantial evidence suggesting that underlying genomic factors may play a role in CaP disparity in men of African descent, but it is unclear whether CaP genomics research has been prioritised in Africa in order to address these disparities. In this review, the aim was to describe the extent of disparities and the novel contributions to CaP knowledge of genomics research with African involvement. A literature review was undertaken of publication output over a 15-year period, in order to catalogue CaP genomics research across the African continent with a specific focus on research on biological or clinical samples from Africa by investigators in Africa. The goal was to demonstrate existing CaP genomics knowledge, and to identify gaps that may need to be addressed in order to challenge the growing cancer burden in Africa.

Materials and methods

Publications included in this review were extracted from PubMed and covered a 15-year period, with a custom range of publications set between 01 January 2006 and 28 February 2021. Pubmed searches were performed in an alphabetical order by country name, and was initiated by entering the terms ‘CaP genomics AND Algeria’ (medical subject headings (MeSH) terms incorporated several terms including ‘prostatic neoplasms’, ‘prostate’ OR ‘cancer’, ‘genomes’ OR ‘genomic’ OR ‘genomically’ and ‘Algeria’). All returned publication

abstracts for Algeria were then saved in a spreadsheet. Subsequently, the process was repeated to retrieve publication abstracts linked to each of the other 53 African countries, and were saved per country in separate spreadsheets. In addition, to compare published genomics research abstracts from Africa to abstracts from other geographical regions, a similar approach was employed for Asia, Europe, North America, Oceania and South America, respectively. For Asia: the terms 'CaP genomics and Asia' followed by the same term but entering different Asian country names, for Europe: 'CaP AND Europe' followed by the same term but entering different European country names, for North America: 'CaP genomics AND USA' and 'CaP genomics AND Canada', for Oceania: 'CaP genomics AND Australia' and 'CaP genomics AND New Zealand', and for South America: 'CaP genomics AND South America' followed by the same term but entering different South American country names, also included was "CaP genomics AND Caribbean" (for this study the Caribbean was grouped with South America). Countries in Central America and Central Europe were not included, this approach is a limitation as it underestimates the total number of abstracts. The non-African abstracts were not individually read.

Each of the African-specific abstracts were individually read. Abstracts were excluded if (i) there was no full English text freely available online, (ii) the article was a review of published works, (iii) the abstract only detailed proceedings of meetings or conferences, (iv) an author surname matched an African country name (1 case was identified), or (v) no African institution was listed in the author affiliations. This review was purposefully targeted toward investigating genomics research with active involvement of African investigators at African institutions. Article access charges for certain publications are a hindrance particularly to institutions in lower-resourced settings; therefore, at the onset of this study it was decided to only include freely available full-text articles. The author concedes that these inclusion criteria are notable study limitations because (i) African investigators based at non-African institutions and (ii) relevant information in the excluded articles, could be missed.

For the included abstracts, full text articles were retrieved and each article individually read (at this stage publications were still separated per country). Subsequently, publications were excluded if they only involved analyses on commercially obtained cell lines, that is, the publication did not include African samples under any of the categories: biological, clinical, tissue, saliva, urine, deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) (here collectively termed biosamples), or genomic data directly derived from analyses of African biosamples. The author acknowledges the excellent work done by many colleagues on the continent using commercially obtained cell lines. However, this conservative exclusion was chosen because in many cases commercially obtained cell lines are derived from non-African donors.

All prioritised publications were then pooled without separation per country. Each article was reviewed, with particular note made of (i) the institution of the first (lead) author (ii) African biosample representation, compared to non-African samples for multi-national studies and (iii) novel findings/contributions as a result of African inclusion. Funding sources were also observed, although this was primarily done to assess the level of private funding (non-federal and/or non-academic institution) for African CaP genomics research.

Results

For the abstract searches, 32 of the 54 African countries returned at least 1 abstract, and combined, African countries produced a total of 347 abstracts (Figure 1). Abstract counts were low from most countries, only 12 of the 32 countries returning 5 or more abstracts (Figure 1), and only 5 countries, Egypt (n = 92) and South Africa (n = 79), Nigeria (n = 29), Ghana (n = 28) and Tunisia (n = 25), each returning more than 20 abstracts. The abstract comparison against all geographical regions produced a combined total of 11 777 abstracts (Figure 2). The African abstracts accounted for 347 of 11 777 (2.9%) of the total abstracts. Most published abstracts were from North America (4480 of 11 777; 38.0%), followed by Europe (3902 of 11 777; 33.1%), Asia (2379 of 11 777; 20.2%), and Oceania (476 of 11 777; 4.0%), with only South America (193 of 11 777; 1.6%) producing fewer abstracts than Africa (Figure 2).

After reviewing each of the 347 African abstract, 170 abstracts were excluded based on (i) free availability, (ii) article type, (iii) meeting or conference proceedings, (iv) an author-country name match and (v) no African institution in the authorship list, resulting in 177 full text publications being retrieved. Reading each full text publication (separately per country) using the inclusion criteria that the research must include African biosamples, or data directly derived from analyses of African biosamples, resulted in 52 publications being further prioritised. At this point, all the publications were pooled and further assessed to determine if any of the studies overlapped. A final total of 37 individual publications fulfilled the conservative inclusion criteria set for this study (Table 1).

More than 60% of the CaP genomics research that included African samples was published recently, within the last 6 years (23 of 37; 62.2%) (Table 1). The majority of studies were multi-national research collaborations. These collaboration tended to follow specific patterns with West and East African institutions primarily partnering with collaborators in the USA, North African institutions generally partnered with collaborators in Europe, while South African institutions tended to publish on their own or partner with Australian collaborators (Table 1). Only Cameroon, Egypt, Ghana, South Africa and Tunisia generated studies on African samples without non-African collaborations (Table 1); for most of these self-generated studies, a national-federal agency in that country provided all- or part-of the funding support.

In 10 of 37 studies (27.0%), the first author listed had an affiliation at an African institution (Table 1). Association studies and biomarker analyses comprised the majority of

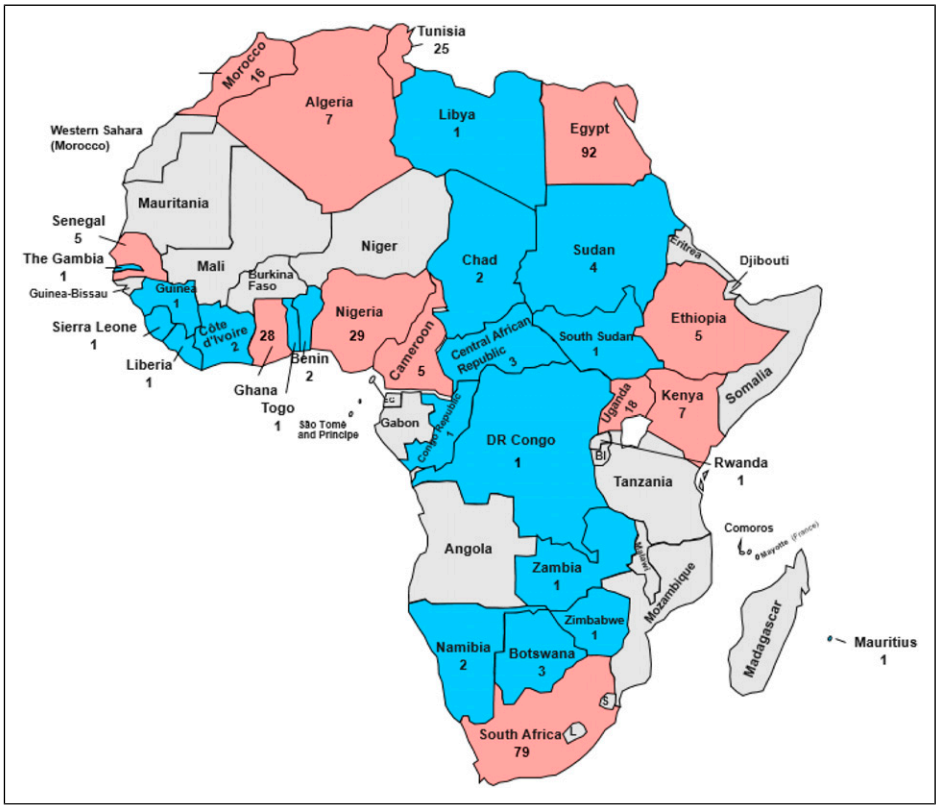

Figure 1. Published prostate cancer genomics abstracts for Africa (2006–2021).

genomics investigations undertaken. Four studies detailed the use of next generation genomics technologies on analyses of African samples (Table 1). Two studies from the same group described refining genomic sample collection and storage protocols, and genotype analyses in a multi-centred African setting, and subsequently the development of a custom African-specific (Pan-African) cancer genotyping array (Table 1). The number of African samples were generally low to moderate when compared to samples from other geographical regions on large multi-national studies, with most of the CaP genomics research being undertaken on samples from West Africa (Ghana), East Africa (Uganda) and Southern Africa (South Africa) (Table 1).

Discussion

The present study undertook a literature review of Pubmed publications to catalogue CaP genomics research across the African continent. Taken as a whole, CaP genomics research was uniformly carried out across Africa, as evidenced by the distribution of returned abstracts per country. However, there was clear disparity in the number of abstract outputs per country. Five African countries (Egypt, Ghana, Nigeria, South Africa and Tunisia) generated a combined total of 253 of 347 abstracts (72.9%), the remaining 27 countries combined only accounted for 94 of 347 abstracts (27.1%). Interestingly, for these 5 countries there is somewhat of a discordance between the CaP genomic research output and their cancer burden. In Nigeria and South Africa, CaP is the most common cancer in males, however, liver cancer is the most common in men in Egypt and Ghana, while lung cancer in the most common in men in Tunisia.[1] When published abstract comparisons were made to other geographical regions, returned abstracts for Africa accounted for almost 3% of the global total. However, this proportional percentage may be less because not all regions were included in this study. Men of African descent are disproportionately affected by CaP, underlying genomic factors may influence disease disparity and increasing evidence suggests that the CaP burden might in fact be higher in African men residing on the continent.[2,13] Intuitively, it would be assumed that genomics research output would mostly match the cancer burden. However, in Africa there is a large deficit in infrastructure and funding required to carry out necessary genomics research, with only South Africa having dedicated government-sponsored grants for genomic research.[41] Rotimi and colleagues highlighted this deficit by demonstrating that all African cancer genomics research publications only represented 0.061% of total publications on cancer globally.[42] Additionally, for their CaP specific analyses, 14 of 375 (3.7%) relevant publications were found, this is fairly close to the percentage observed in this study (2.9% vs 3.7%).

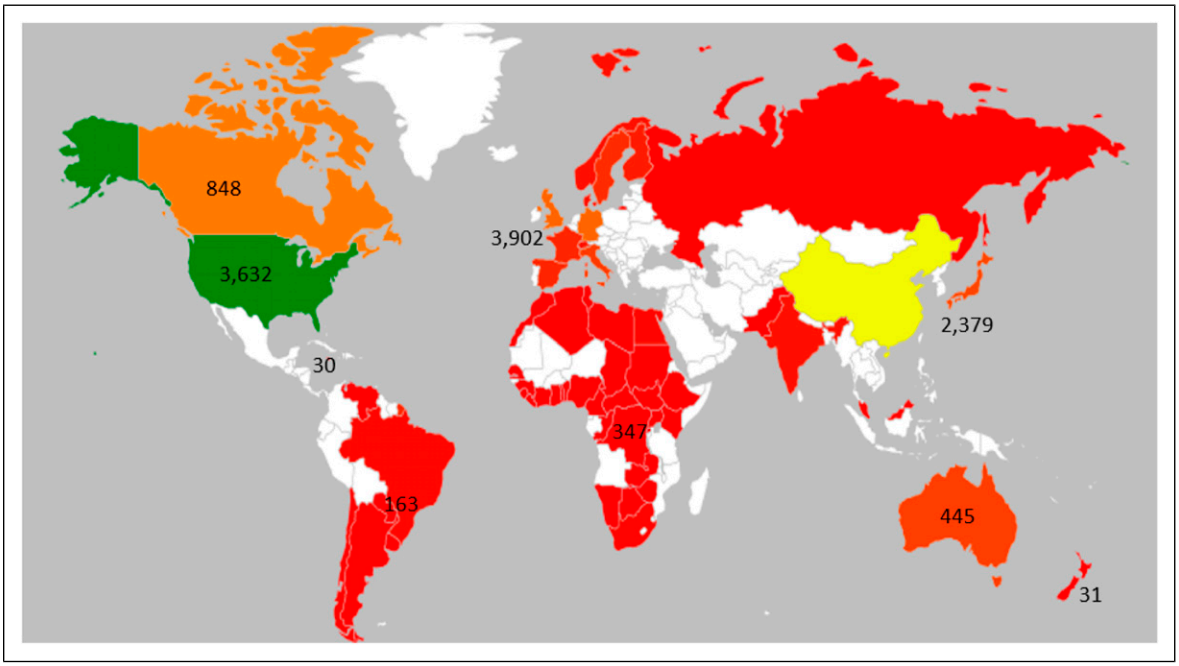

Figure 2. Published prostate cancer genomics abstracts per geographical region (2006–2021).

African-led CaP Genomics Research

Due to the inherent genetic diversity in populations, it has been difficult to generalise genomic findings across populations.[13,40] Additionally, African populations have the greatest amount of genetic diversity, smaller linkage disequilibrium (LD) blocks and a larger proportion of unique population specific alleles,[43,44] but biosamples of individuals of African ancestry are often significantly underrepresented in large genomics studies compared to samples of European or Asian descent.[39,45] Consequently, the present study sought to catalogue CaP genomics research with involvement of African institutions and analyses that specifically included African biosamples, or data directly derived from African biosamples. Although wide-ranging CaP genomics research is generally undertaken on the continent, there was a substantial paucity of publications that involves actual African biosamples and investigators from African institutions. Of more concern, in only 10 of 37 prioritised studies discussed here (Table 1) the first (lead) author was based at an African institution. When separating the studies by North Africa vs SSA, for the 4 studies from North Africa,[46-49] 2 (50%) had the first author affiliated to an African institution (Table 1). For the SSA studies, 8 of 33 studies (24.2%) had a first author affiliated to an African institution (Table 1). Interestingly, a recent study assessing authorship in cancer genomics studies publications also observed a more than 50% first authorship for North African countries, but first authorship for SSA countries ranged between 2.2% and 13.6%.[50] The present study differed from that study as it only focused of CaP genomics studies (not all cancers) and it used a conservative filter that excluded studies that did not include at least 1 African institution in the authorship list. In addition, this study did not assess last authorship, these factors combined may have contributed to the higher SSA first author percentage. Notwithstanding, overall literature disappointingly showing that less than one-third of African cancer genomics research is headed by African-based investigators, should embolden more investigators on the continent to assume a more leading role in the dissemination of genomics research findings.

African Biosample Representation in CaP Genomics Studies

There was also notable disparity in the African biosample numbers, both inter-continentally when compared to biosamples from other geographical regions, and intra-continentally when compared to contributions between African countries (Table 1). Ghana, Uganda and South Africa contributed the most biosamples to genomics analyses either on their own or on collaborative multi-national studies. The sample numbers shown in Table 1 appear to suggest a robust and constant collection of 'new' biosamples from different geographical regions across different studies. However, the numbers should be viewed with some restraint. Twelve studies included biosamples from Ghana,[29,31-34,51-57]; however, 7 of the 12 studies used the same set of biobanked biosamples,[29,31-33,51,52,55] and 2 studies[34,53] used genotype data derived from the biobanked biosamples. Only 3 other studies[54,56,57] presented analyses of newly collected Ghanaian biosamples. Similarly, the Uganda-linked studies all used biosamples and/or data derived from the same set of biosamples.[32,34,53,58,59] Only 6 studies[55,60-64] undertook

Table 1. Prostate Cancer Genomics Publications on African Biosamples Involving African Institutions (2006-2021).

Author and Year	Listed Author Institutional Affiliations by Country	Number of Biosamples (Country or Region)
Candidate gene, candidate region, genome-wide association studies		
Al Olama et al. 2015[51]	Australia; Bulgaria; Denmark; Finland; Germany; *Ghana*; Italy; Japan; Portugal; *Senegal*; *Uganda*; UK; USA	5327 cases; 5136 controls (*Ghana*, *Senegal*, *Uganda* - no information available on number of sample from each country) 34 379 cases; 33 164 (European) 2563 cases; 4391 (Japanese) 1034 cases; 1046 controls (Latino)
Brureau at al. 2016[80]	*Democratic Republic of Congo*; France; Guadeloupe	162 cases; 144 controls (*Democratic Republic of Congo*) 498 cases; 565 controls (Guadeloupe)
Chung et al. 2014[52]	*Ghana*; USA	39 cases; 39 controls (*Ghana*) 47 controls (USA)
Conti et al. 2017[33]	Barbados; France; *Ghana*; UK; USA	474 cases; 458 controls (*Ghana*) 9728 cases; 10 352 controls (USA)
Conti et al. 2021[34]	Australia; Barbados; Belgium; Bulgaria; Canada; China; Croatia; Denmark; Finland; France; *Ghana*; Germany; Japan; Malaysia; Poland; Portugal; Spain; Sweden; *Uganda*; UK; USA	1586 cases; 1047 controls (*Uganda*) 640 cases; 634 controls (*Ghana* - used available genotype data) 85 554 cases; 91 972 controls (European) 8611 cases; 18 809 controls (East Asia) 2714 cases 5239 controls (USA)
Cook et al. 2014[29]	*Ghana*; USA	474 cases; 458 controls (*Ghana*)
#Djomkam et al. 2019[74]	*Cameroon*	103 cases; 80 controls (*Cameroon*)
Du et al. 2018[81]	*Uganda;* USA	571 cases; 485 controls (*Uganda*)
#Fernandez et al. 2008[73]	*South Africa*	151 cases; 134 controls (*South Africa*)
#Fernandez et al. 2015[30]	*South Africa*	486 cases; 323 controls (*South Africa*)
Haiman et al. 2011[31]	Barbados, *Ghana*; *Senegal*; *Uganda*; USA	271 cases; 968 controls (*Ghana*) 86 cases; 414 controls (*Senegal*) 3425 cases; 3290 controls (USA)
Han et al. 2015[53]	Barbados; China; Finland; Germany; *Ghana*; Japan; UK; USA	474 cases; 458 controls (*Ghana* - used available data) 4852 cases; 4678 controls (USA) 8600 cases; 6946 controls (European) 2563 cases; 4391 controls (Japanese) 1034 cases; 1046 controls (Latino)
Han et al. 2016[32]	Barbados; *Ghana*; USA; *Uganda*	474 cases; 458 controls (*Ghana*) 542 cases; 479 controls (*Uganda*) 3599 cases; 3510 controls (USA) 238 cases; 231 controls (Barbados)
Matejcic et al. 2020[58]	*Uganda*; USA	664 cases; 487 controls (*Uganda*) 1457 cases; 996 controls (USA)
Murphy et al. 2012[82]	*Cameroon*; Jamaica; USA	102 cases; 133 controls (*Cameroon*) 110 cases; 218 controls (*Nigeria*) 380 controls (*Sierra Leone*)
Rand et al. 2016[59]	*Uganda*; USA	332 cases; 235 controls (*Uganda*) 1833 cases; 1799 controls (USA)
#Sfar et al. 2007[49]	*Tunisia*	101 cases; 106 controls (*Tunisia*)
Tindall et al. 2013[28]	Australia; *South Africa*; USA	522 cases; 315 controls (*South Africa*)
Tindall et al. 2014[71]	Australia; *South Africa*; USA	36 controls (*South Africa*) 35 controls (*Kenya* – used available data) 47 controls (*Nigeria* – used available data) 18 controls (*Cameroon* – used available data) 15 controls (*Equatorial Guinea* – used available data) 22 controls (*Guinea* – used available data)

(continued)

Table 1. (continued)

Author and Year	Listed Author Institutional Affiliations by Country	Number of Biosamples (Country or Region)
Admixture mapping studies		
#Petersen et al. 2019[66]	Australia; *South Africa*	134 cases; 18 controls (*South Africa*)
Biomarker studies		
#Adeola et al. 2015[67]	*South Africa*	15 cases; 15 BPH; 15 controls (*South Africa*)
#Adeola et al. 2016[68]	*South Africa*	15 cases; 15 controls (*South Africa*)
#Adeola et al. 2016[69]	*South Africa*	20 cases; 32 BPH; 15 no uropathy (*South Africa*)
#Arko-Boham et al. 2019[54]	*Ghana*; Netherlands; Switzerland	21 cases; 30 controls (*Ghana*)
Blackburn et al. 2019	Australia; *South Africa*; USA	93 cases; 84 controls (*South Africa*)* 1 case (*Zimbabwe*)*
Esteban at al. 2006[46]	*Egypt*; France; Italy; *Morocco*; Spain	74 controls (*Algeria*) 82 controls (*Egypt*) 88 controls (Cote d'Ivoire) 296 controls (*Morocco*) samples consisted of males and females, no information available on male and female composition
#Fawzy et al. 2016[47]	*Egypt*	50 cases; 25 BPH; 30 controls (*Egypt*)
Haj-Ahmad et al. 2014[48]	Canada; *Egypt*	8 cases; 12 BPH; 10 controls (*Egypt*)
Pal et al. 2019[83]	*Nigeria*; USA	28 cases; 22 controls (*Nigeria*)*
Pal et al. 2020[84]	*Nigeria*; USA	28 cases; 35 BPH; 22 controls (*Nigeria*)*
Zhou et al. 2017[55]	*Ghana*; USA	262 cases (*Ghana*)*
Next generation sequencing, genome mapping and mutational analysis		
Feng at al. 2019[61]	Australia; Canada; China; *South Africa*	6 cases (*South Africa*)* 16 cases (Australia)
Jaratlerdsiri et al. 2017[62]	Australia; *South Africa*; USA	1 case (*South Africa*)*+
Jaratlerdsiri et al. 2018[63]	Australia; *South Africa*	6 cases (*South Africa*)*
McCrow et al. 2016[64]	Australia; *South Africa*; USA	87 cases (*South Africa*)*
Genomics protocols, custom cancer genotype array development		
Andrews et al. 2018[56]	*Ghana*; *Nigeria*; *Senegal*; *South Africa*; UK, USA	311 cases; 218 controls (*Ghana*; *Nigeria*; *Senegal*; *South Africa* - no information available on number per country)
Harlemon et al. 2020[57]	*Ghana*; *Mauritius*; *Nigeria*; *Senegal*; *South Africa*; USA	112 cases; 117 controls (*Ghana*) 112 cases; 113 controls (*Nigeria*) 56 cases; 59 controls (*Senegal*) 129 cases; 114 controls (*South Africa*)

= first author affiliated to an African institution; * = prostate tissue analysed; + = South African male of European ancestry; BPH = benign prostatic hyperplasia. *African country names are written in italics.*

genomic analyses on prostate tissue. Besides funding limitations, there are known shortages of ethics review committee genomics expertise across the continent, this in addition to cultural sensitivity to the use of human biological tissue[65] might have further contributed to the lack of tissue representation on studies. Overall, African biosample numbers were lower compared to biosamples from other geographical regions, this underrepresentation mirrors what has been reported in the literature.[13,39,40] It also has to be noted that although not indicated in Table 1, most of the listed biosamples from the USA did at least include a large percentage of men of African ancestry, namely, African American men; similarly, the biosamples from Barbados and Guadeloupe were all of African ancestry. Moreover, new and unique genomics data can be generated from the same established biosample collections as shown in the Ghanaian and Ugandan studies, and underscores the significant value of establishing well-curated biobanks. This is particularly relevant in Africa where numerous factors such sample acquisition costs, but also administrative barriers and cultural beliefs may limit obtaining large collections of biosamples from the continent's unique and diverse populations.

Contributions to Cap Knowledge

The introduction section of this review presented some of the novel contributions to global understanding of CaP made by

association studies that included biosamples and researchers from Africa.[28-34] Because genomic databases are skewed toward an underrepresentation of African variants, some studies (Table 1) prior to performing association analyses, first undertook genomic sequence analyses to identify unique African variants. Chung and colleagues[52] re-sequenced a 250 kilobase (kb) region on chromosome 8q24.21 and identified 285 novel sequence variants that had not previously been reported in any public database at the time, of these, 135 variants were only observed in Ghanaian samples. Rand and colleagues[59] undertook the first large-scale whole exome sequence (WES) analyses of samples of men of African ancestry (n = 4100) and identified 395 220 coding variants, of which 60% of the rare variants they identified were not in other sequencing project databases. The admixture mapping association study by Petersen and colleagues[66] noted that for studies that sought to identify African ancestral contributions to high risk CaP, the South African mixed ancestry population could serve as an alternative genomic resource to studies that would otherwise focus solely on the African American population (also with known mixed ancestry).

Several investigations identified potential CaP biomarkers in African men that are unique and differed from European and Asian men. Four studies demonstrated the use of non-invasively collected urine to identify potential CaP biomarkers.[48,67-69] These preliminary findings are noteworthy given that diagnostic sample collection in low-resource settings is often constrained due to the cost of blood draws and inadequate capacity to transport and store blood. Blackburn and colleagues[60] demonstrated that transmembrane protease serine 2:v-ets erythroblastosis virus E26 oncogene (*TMPRSS2-ERG*) fusions are significantly less common in driving CaP tumorigenesis in African men compared to European men. Moreover, Jaratlerdsiri and colleagues[63] employed whole genome sequencing (WGS) on CaP tissue samples from South African men and observed a 1.8-fold increase in small somatic variants in African men vs European men. A recent NGS analyses of samples from 87 South African men demonstrated that mitochondrial genome mutational load is associated with aggressive CaP in men of African ancestry.[64] Furthermore, they observed that a large mitochondrial deletion identified in a European population was absent in the African men. Another study that analysed the bacterial genera composition in CaP tissue, noted a 1.6-fold increase in bacterial burden and higher abundance of anaerobic bacteria in South African vs Australian biosamples, the authors suggested that bacterially driven oncogenic transformation contributed to the aggressive CaP presentation often observed in men of African ancestry.[61]

Funding and Genomics Capacity in Africa

Genomics research in Africa is severely underfunded compared to other continents. Stark and colleagues highlighted this global genomics funding disparity,[70] by showing that since 2013, government funded National Genomic Medicine Initiatives, with cost ranging between US$1.6 million to US$9.2 billion, have been launched on all continents except for the African continent. The present study did not aim to establish the extent of funding, but rather sought to determine if alternative funding sources have contributed to African-linked CaP genomics research initiatives. From the sparse information provided, 6 studies[28,60,62,64,66,71] had private entity co-funding partners, while another study had received funds raised through an institutional fundraiser.[63] Interestingly, for the full text articles that were excluded because they did not include African biosamples and/or data, 9 studies were identified with clear indications of some form of private co-funder partners, Biopharmaceutical support was declared in 2 of these studies (data not shown). A recent report from the Inaugural African Organisation for Research and Training in Cancer (AORTIC) Cancer Genomics Conference, stated the need for Africa to develop private sector funded data centres, and encourage public-private partnerships, including biobanking, while exercising caution against biospecimen commercialisation and profit-making by private partners.[72] Given the increasing global trend of shrinking federal research funding budgets, particularly affecting low-to-middle income countries, public-private partnerships might offer a feasible model to drive future genomics research on the African continent.

Africa has the expertise but is severely underserved in terms of genomics research capacity and infrastructure.[41] Besides the self-driven studies from South Africa,[30,67-69,73] Cameroon,[74] Egypt[47] and Tunisia,[49] for all the other studies the laboratory-based genomics analyses were performed at a collaborating non-African centre (Table 1). For 2 additional studies, dual analyses were performed on genomics platforms in Africa and the USA.[56,57] There has been an increased acknowledgement of population-based disparities in cancer research, unequal distribution of biomedical funding and the shortcomings of not including more diverse populations in genomics research.[10,39,70,75] To this end, the American Association for Cancer Research (AACR), the American Cancer Society (ACS), the American Society of Clinical Oncology (ASCO) and the National Cancer Institute (NCI) released a position statement with comprehensive recommendations to address these disparities, including reforms to address biomedical research funding for developing and under-resourced countries.[76] In Africa, several large initiatives such as the Southern African Human Genome Programme,[77] the Human Hereditary and Health (H3Africa) Consortium,[78] and the African Genome Variation Project (AGVP)[79] have been established to drive genomics research on the continent. Prostate cancer genomics research on the continent is primarily being led by the Men of African Descent and Carcinoma of the Prostate (MADCaP) Consortium[2,56,57] and the African Ancestry CaP GWAS Consortium (AAPC GWAS).[29,31-34,51,53] Several joint collaborations are already in existence between the 2 consortia. However, given that the burden of CaP in Africa is expected to increase significantly, cooperation should

additionally be fostered with other non-cancer focused consortia on the continent in order share expertise and resources.

Conclusion

This study sought to catalogue CaP genomics research specifically by African investigators on African biosamples. The number of the published studies were low, but this may be due to a combination of the genomics capacity, infrastructure and funding challenges that are a reality in Africa, as well as the conservative filtering criteria used in this study. It was noted with some optimism that there was a steady increase in the number of recent CaP genomics publications within the last 5 years, as compared to the previous decade, in addition to a number of significant and novel contributions as a result of African involvement. However, concerted efforts need to be made to increase (i) African biosample representation/numbers on studies, (ii) African investigator involvement on studies and (iii) African investigators as first authors on genomics studies. Funding for genomics research should be prioritised with more emphasis given to increasing public–private partnerships. The diverse genomic architecture in Africa could provide important insights to the global understanding of CaP biology, this contribution can only be fostered by more widespread cooperation and leveraging existing expertise across the continent.

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