

REVIEW ARTICLE

Prostate and breast cancers in Africa: Prevalence, risk factors, and molecular overview against the background of the world population

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Abstract

Currently, cancer represents an escalating public health crisis in Africa, ranking as the continent's fifth leading cause of mortality. According to recent GLOBOCAN 2022 estimates, approximately 1.15 million new cancer cases and 754,500 deaths occurred across Africa in that year alone. On a global scale, there were an estimated 20 million new cases and 9.7 million deaths in 2022, with a disproportionate burden falling on underserved regions. Low- and middle-income countries are projected to account for nearly 75% of global cancer deaths, highlighting a stark geographical inequity in access to timely diagnosis and comprehensive care. This review provides an inclusive presentation of the two most prevalent reproductive malignancies in Africa: prostate cancer in men and breast cancer in women. Set against the backdrop of the continent's unique socioeconomic landscape, the article explores the complex interplay of prevalence and risk factors, ranging from genetic and phenotypic predispositions to environmental and epigenetic influences. Recognizing the diverse healthcare landscape in Africa, this work addresses the accessibility of conventional medicine while evaluating the supervised integration of potential herbal agents as complementary therapies. This review identifies barriers to effective disease management and discusses the current and future cancer burden across the African continent for non-specialist readers and those seeking to understand oncological care in Africa. Ultimately, the findings underscore an urgent need for targeted policy-making and strategic investment in prevention. Prioritizing timely screening and strengthening treatment infrastructure are essential steps for authorities to mitigate the surging cancer burden and maintain the health of African populations.

Keywords: Africa; Breast cancer; Sex hormone signaling; Unconventional cancer medicine; Prostate cancer

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1. Introduction

Prostate cancer (PCa) and breast cancer (BCa) are among the most common cancers in humans. They are hormone-dependent cancers due to the involvement of androgens and estrogens in their initiation and growth.¹ In terms of prevalence, PCa and BCa represent the leading reproductive system-related cancers in men and women, respectively.^{2,3} Across the entire global population, BCa^{2,3} is the leading cause of cancer mortality in women⁴, while PCa is the second most diagnosed cancer and the sixth primary cause of death among men worldwide.⁵

In addition to the well-known genetic, epigenetic, and infectious carcinogenesis background of the different organs of the reproductive system, a growing body of evidence highlights a hormonal and environmental etiology related to aberrant expression of hormone receptors.⁶ Sex steroid signaling via specific receptors controls the normal development and function of the reproductive system. However, when specific cell receptors are overexpressed or inactive, cell-autonomous behaviors are promoted through enhanced cell-cycle progression, altered differentiation, increased migration, and decreased apoptosis, which lead to carcinogenesis.⁷ Primary studies have shown that deregulated androgen and/or estrogen signaling pathways contribute to reproductive organ malignancies. Subsequent studies have expanded our knowledge on specific causes of hormone signaling deregulation driven by endocrine-disrupting chemicals present in the environment. This review provides information on the recent global trends in the incidence of PCa and BCa, with comparison to the highly affected African populations.⁵ This review aims to elucidate the association between observed clinical parameters and their underlying etiological causes. Furthermore, it examines the demographic shift contributing to the rising incidence of BCa and PCa, with the ultimate objective of informing prevention and control strategies. Moreover, as cancer morbidity in Africa has emerged as a critical economic crisis, and cancer-related mortality in 2030 is expected to surpass deaths from malaria, tuberculosis, and HIV/AIDS combined, the diagnosis and treatment need to be urgently improved.⁸ By addressing these critical factors, this review aims to support the development of a coherent framework for improving reproductive health outcomes and reducing the burden of these malignancies.

2. Global perspective

Cancer is the principal cause of mortality in 177 out of the 183 countries in the world, according to reports by the International Agency for Research on Cancer (IARC) and GLOBOCAN 2022.^{9,10} There were an estimated 20 million

new cancer cases worldwide in 2022. Approximately one in every nine men and one in every twelve women die from different types of cancers, including non-melanoma skin cancers.¹¹ Of these, 56% of cases and 64% of deaths were reported in less developed countries. Further, it is noteworthy that for most age-adjusted cancers, mortality rates are reportedly higher among males. Also, cancer-specific survival for most cancers is worse for males than for females.^{12,13}

Rates of cancer incidence among females continue to be higher in high-income countries (HICs) compared to low- and middle-income countries (LMICs).⁴ As of 2012, the highest estimated incidence rates (per 100,000) were concentrated in HICs across North America, Europe, Oceania, and parts of Asia. Specifically, the highest rates were recorded in Denmark (329), the United States (297), South Korea (294), the Netherlands (290), and Belgium (289).¹¹ Conversely, the lowest incidence rates for BCa were observed in South-Central Asia (e.g., Maldives, Bhutan; <100), South-Eastern Asia (e.g., Laos, Vietnam; <125), and Africa (e.g., Niger, The Gambia; <100). It is essential to recognize that these incidence rates are indicative not only of underlying biological risk but also of public health awareness and the availability of diagnostic screening services. In contrast, mortality trends present a different geographic profile. Overall, female cancer mortality is highest in LMICs across Oceania, sub-Saharan Africa, and Asia. In 2012, the highest estimated mortality rates were documented in Zimbabwe (147), Malawi (138), Kenya (133), Mongolia (127), and Papua New Guinea (125).¹¹ Moreover, recent estimates indicate that cancer mortality rates remain alarming in many of the countries previously identified, e.g., Zimbabwe, Malawi, and Kenya. Africa currently exhibits the highest overall mortality rate relative to its population, with an age-standardized mortality rate of roughly 19.16 per 100,000 for BCa alone, significantly higher than in North America (12.32).¹⁴

Breast cancer remains the primary cause of cancer-related mortality among women globally. Incidence rates exhibit more than a tenfold variation across international registries, with the highest prevalence observed in Western Europe and the United States, and the lowest in Africa and Asia.¹⁵ This cancer shares the highest diagnostic burden with cervical cancer in Latin America, the Caribbean, Africa, and much of Asia.¹⁵ The elevated incidence in HICs, including specific demographics such as Black women in the United States¹⁵, is attributed to both widespread screening practices and a higher prevalence of established risk factors.¹⁶ These factors include weight gain during sexual maturity, obesity, menopausal hormone therapy, physical inactivity, and excessive alcohol consumption.

Furthermore, reproductive and hormonal status based on an extended menstrual history, recent oral contraceptive use, nulliparity, or advanced age at first childbirth significantly contribute to BCa risk.^{17,18} Conversely, breastfeeding has been identified as a protective factor.¹⁸ Although BCa incidence is rising in LMICs, the underlying drivers remain partially understood. Shifting reproductive patterns and increased diagnostic awareness are considered key contributors.^{16,18} Public health strategies emphasize that BCa risk can be mitigated through weight management, abstinence from alcohol, and regular physical activity.¹⁵ Studies by Michou *et al.*¹⁹ provide the first epidemiological evidence showing that exercise interventions are currently recognized as effective non-pharmacological strategies to improve clinical outcomes in patients with BCa (risk reduction, disease progression, and survivorship). The protective molecular mechanisms involve modulation of sex hormones, metabolic hormones, systemic inflammation, oxidative stress, circulating microRNAs, and BCa-related DNA methylation. Moreover, the synergistic potential of exercise with conventional cancer treatments and bioactive dietary components (polyphenols) is suggested to be beneficial.

Of note, effective mammography screening is also prone to the challenges of false positives, undetected cancers, and even overdiagnosis.²⁰ In such cases, awareness of early signs and symptoms of BCa and clinical examination are recommended.²¹

Prostate cancer is ranked as the second most common malignancy and the sixth leading cause of cancer-related mortality among men worldwide, with an estimated annual burden of 1.1 million cases and 300,000 deaths.^{11,22} In sub-Saharan Africa, both mortality and disability-adjusted life years attributable to PCa doubled between 1990 and 2010.^{23,24} The number of new cases of PCa in sub-Saharan Africa is estimated to increase from approximately 94,000 per year (in 2020) to over 158,000 in 2040. This represents an increase of nearly 70% in just two decades, a rate significantly higher than in developed countries. Epidemiological data show that the highest incidence rates are among the Black population in the United States, followed by France and Australia. Conversely, the highest mortality rates are documented in Trinidad and Tobago, the United States Black population, and South Africa, while Asia reports the lowest incidence and mortality figures.¹⁶ Geographic variations in incidence are largely attributed to the prevalence of prostate-specific antigen (PSA) testing.²⁵ However, the disproportionately high rates observed in populations of African descent suggest that genetic susceptibility also plays a significant role.^{26,27} Although the precise etiology of PCa remains partially understood,

the rising incidence is increasingly linked to risk factors associated with economic transition, including higher consumption of animal-based products.^{26,27} While routine early screening via PSA testing is widely recommended, clinicians must remain cautious of the high potential for overdiagnosis in men at average risk.²⁸ Further detailed understanding of these complex epidemiological and lifestyle factors is imperative for optimizing diagnostic and preventive strategies.

3. African perspective

The socioeconomic repercussions of cancer are profound in all LMICs, being particularly acute in Africa. Without targeted interventions, rising incidence rates will continue to undermine the public health and socioeconomic stability of sub-Saharan Africa.^{29,30} A complex interplay of demographic and lifestyle shifts drives this increasing problem. As these regions undergo economic transition and globalization, average life expectancy is rising due to public health successes in controlling infectious diseases and reducing maternal and infant mortality.^{30,31} However, this longevity is accompanied by a higher prevalence of various non-communicable diseases, including cancers. Furthermore, changing reproductive patterns characterized by delayed childbearing and reduced parity have contributed to the rising prevalence of malignancies that were previously more common in HICs. Consequently, the epidemiological landscape of LMICs is rapidly converging with that of developed countries, necessitating urgent strengthening of healthcare systems (also see [Table 1](#)).

Table 1. Regional divergence in genetic, environmental, and healthcare landscapes

Genetic	Environmental	Healthcare systems
West: <i>BRCA1</i> and triple-negative breast cancer	North: metabolic	South: national care
East: <i>BRCA2</i>	West: pesticides	East/West: out-of-pocket
South: high admixture	Rural: biomass	Conflict zones: crisis

While PCa incidence and mortality rates in Africa remain lower than in several other global regions¹³, mortality is disproportionately higher among predominantly Black African populations compared to other ethnic groups.³² African ancestry has been identified as a significant risk factor, with mortality rates across sub-Saharan Africa being 2.7 times higher than the global average.³³ This disparity is attributed to a complex interplay of systemic and biological

factors, including pervasive poverty, dietary patterns, genetic predispositions, and the high prevalence of co-existing infectious diseases.³⁴ Furthermore, significant barriers to effective PCa management contribute to these elevated mortality rates, such as the lack of affordable, community-based screening and health promotion initiatives for early diagnosis.³⁵ Additionally, deeply rooted social norms and cultural beliefs continue to influence health-seeking behaviors and treatment outcomes in the region.^{35,36}

The incidence of BCa has steadily increased over the past few decades. According to recent estimates, the age-standardized incidence rate (ASR) for BCa in East Africa ranges from 30 to 50 per 100,000 women, with variations observed between urban and rural areas. Countries such as Kenya, Uganda, and Tanzania are witnessing significant rises in BCa cases driven by factors such as urbanization, changes in reproductive behavior, and lifestyle alterations associated with economic development.³⁷ In Kenya, for example, BCa has become the most common cancer among women with an ASR of approximately 40 per 100,000.³ Similarly, Uganda and Tanzania have reported increasing BCa incidence with ASRs of around 30 and 35 per 100,000, respectively.³ This rise in incidence is partly attributed to improved diagnostic capabilities in urban centers, while rural areas still experience significant underreporting due to limited access to healthcare services.³⁸ Mortality rates for BCa in East Africa remain alarmingly high, with the region's mortality-to-incidence ratio estimated between 0.50 and 0.70. This metric underscores a critical disparity: a substantial proportion of women diagnosed with BCa succumb to the disease, a stark contrast to outcomes in HICs.³⁹ In Tanzania, approximately 70% of BCa cases are diagnosed at advanced stages, often when curative interventions are no longer feasible.⁴⁰ Comparable patterns of late-stage diagnosis are prevalent in Uganda and Kenya. Consequently, the five-year survival rates in these countries remain significantly lower than those observed in HICs.^{41,42}

4. The economic burden of cancer in African countries

Rising rates of cervical cancer, PCa, and BCa are imposing a substantial economic burden across Africa. Public costs of operating already inefficient healthcare systems and individual and social costs are increasing.⁴³ The latter are mainly related to direct medical expenses, reduced productivity of those affected by the disease, and their premature deaths. The types of cancer mentioned above are particularly important in Africa as they affect an increasingly younger portion of the population and represent one of the greatest financial and organizational

challenges for public care and societies. The high cost of BCa in African countries is due to treatment at an advanced stage, which is often the result of late detection of the disease. In regions with a lower level of development, such as many African countries, the limited infrastructure for early detection can lead to particularly high treatment costs relative to the country's gross domestic product. The increased cost of treatment in advanced cases makes prevention and early detection crucial. This situation is also due to the lack of universal screening. Using human papillomavirus (HPV) vaccination as an example, universal HPV vaccination programs have been shown to have the potential to prevent huge medical costs and economic losses in the future, as they effectively protect against high-risk strains, reducing the risk of cervical cancer.⁴⁴

The cost of medical care for aging patients with PCa, including surgery, radiotherapy, and hormone therapy, is very high. Furthermore, in many African countries, late diagnosis increases these costs due to the need for more intensive and long-term treatment.⁴⁵ Moreover, aggressive phenotypes of BCa and PCa that are often present in the African population also require more expensive treatment strategies.

While cutting-edge oncological technologies and innovations are continuously evolving globally, they remain largely inaccessible across the African continent. Bridging this gap by integrating modern innovations into African healthcare systems is essential to mitigating the region's disproportionately high cancer mortality rates (Table 1). To effectively address this escalating crisis, emerging cancer control techniques must be made widely available. Furthermore, a multidisciplinary framework is required to navigate the complex challenges associated with the development, adaptation, and implementation of advanced oncological solutions within the African context.⁴⁶

5. Risk factors: Genetic, phenotypic, environmental, epigenetic

Both BCa and PCa are influenced by a complex interplay of various factors. A comprehensive understanding of these factors is essential for developing targeted interventions focusing on prevention and treatment strategies that address the uniqueness of any given population. This also opens avenues for personalized medicine and targeted therapies. For instance, genetic screening for the BCa mutations can guide preventive measures and treatment decisions for BCa. In PCa, recognizing unique genetic and epigenetic profiles of men in regional populations may lead to personalized and effective treatments (see in detail in Table 2).

Table 2. Key risk factors for breast and prostate cancer in African populations

Risk Factor	Breast cancer	Prostate cancer
Genetic	Unique <i>BRCA1</i> & <i>BRCA2</i> gene mutations: West and South Africa	Homeobox 13 (<i>HOXB13</i>) and <i>BRCA2</i> mutations: principally West Africa
Epigenomic factors	Specific epigenetic profiles linked to more aggressive forms of breast cancer	Unique African epigenomic profiles
Molecular	Estrogen, progesterone, and human epidermal growth factor-2 receptors	Prostate-specific antigen levels
Phenotype	Higher breast density	More aggressive type
Hormonal factors	Increased estrogen exposure (early menstruation, late menopause, hormonal replacement therapy)	Higher testosterone levels, hormonal imbalances
Lifestyle factors	Increased urbanization, physical inactivity, dietary changes (high-fat, low-fiber diets), increased alcohol consumption, and obesity	Increased urbanization, physical inactivity, dietary changes (high-fat, low-fiber diets), increased alcohol consumption, and obesity
Socioeconomic	Limited screening programs contribute to late-stage diagnoses	Limited screening programs contribute to late-stage diagnoses
Environmental factors	Urbanization, industrialization, and modernized farming increase exposure to endocrine-disrupting chemicals, pesticides, and pollutants	Urbanization, industrialization, and modernized farming increase exposure to endocrine-disrupting chemicals, pesticides, and pollutants

5.1. Genetic factors

Understanding genetic and genomic alterations that predispose individuals to cancer is essential for identifying predictive molecular risk markers and guiding appropriate treatment selection. Elucidating the role of *BRCA* proteins in the pathogenesis of BCa has fundamentally transformed therapeutic paradigms, particularly through the implementation of poly(ADP-ribose) polymerase (PARP) inhibitors for patients harboring deleterious germline mutations.⁴⁷ Pathogenic variants in the *BRCA1* and *BRCA2* tumor suppressor genes are established drivers of hereditary susceptibility, significantly elevating the lifetime risk for both breast and ovarian malignancies.

In the African situation, the prevalence and genomic landscape of *BRCA* mutations exhibit considerable heterogeneity.⁴⁸ Evidence suggests that specific populations, notably in Nigeria and South Africa, possess unique and distinct mutation spectra. For instance, studies have identified that up to 20% of inherited invasive BCa cases among Nigerian women are associated with germline mutations in *BRCA1*, *BRCA2*, *PALB2*, or *TP53*.⁴⁹ These findings corroborate earlier reports of an exceptionally high frequency of *BRCA* mutations within this cohort. Furthermore, such mutations have been linked to increased structural genomic variation and a more aggressive disease phenotype, specifically in Nigerian women with hormone receptor-positive/human epidermal growth factor receptor 2-positive (HR⁺/HER2⁺) tumors and Black South African women presenting with epithelial ovarian malignancies.

Understanding these population-related genetic profiles is crucial for optimizing risk assessment and personalizing oncological management in the region.^{50,51}

Research conducted in Tunisia by Mahfoudh *et al.*⁵² indicates that the *BRCA1* mutation significantly contributes to the development of triple-negative BCa (TNBC). The elevated prevalence of the TNBC phenotype is a primary driver of the higher BCa mortality rates observed in women of West African ancestry compared to white populations on the continent. This genetic landscape underscores the poor prognosis across various BCa subtypes in the region. Consequently, implementing *BRCA* screening programs in Africa is essential to identifying candidates for PARP inhibitor therapy, which could substantially improve clinical outcomes.⁵³ Genomic studies focused on the Afrikaner population in South Africa have characterized *BRCA1* mutations that mirror those reported in the Netherlands and among Ashkenazi Jews, reflecting the European ancestral origins of this cohort.⁵³ Furthermore, variants of *PALB2*, a critical partner and localizer of *BRCA2*, have been associated with early-onset BCa in both South African patients and women of European descent.⁵⁴ Given these findings, it is imperative to integrate data on population-specific founder mutations into screening, diagnostic, and therapeutic frameworks across Africa. Such a targeted approach is vital for optimizing precision oncology and addressing the unique genetic drivers of the disease within diverse African populations.

Prostate cancer frequently presents with a notably aggressive phenotype among men of African descent.⁵⁵

Like BCa, this cancer is a hormone-responsive malignancy, with its risk significantly modulated by genetic factors (most notably family history and pathogenic variants in genes such as *HOXB13* and *BRCA2*). Men of West African ancestry exhibit the highest global incidence rates of PCa, a disparity that strongly suggests a robust hereditary component.²⁶ Extensive genomic research within African populations has implicated several other genetic variants in the onset and pathogenesis of PCa. Notable among these are polymorphisms in the cytochrome P450 gene family (involved in sex steroid biosynthesis), specifically *CYP3A4*, *CYP3A5*, *CYP1A1*, and *CYP17*, which have been documented in cohorts across Morocco, Tunisia, Nigeria, South Africa, and Senegal.⁵⁶⁻⁶⁰ There is also strong evidence of *ATM*, *BRCA2*, *HOXB13*, *CHEK2*, and *PALB2* as candidate genes impacting risk of aggressive and/or metastatic PCa in men of African ancestry.⁶¹ Furthermore, variations in the androgen receptor (*AR*) gene, specifically alterations in the CAG (polyglutamine) and GGN (polyglycine) repeat lengths, have been identified as significant risk factors in North Africa, the Ivory Coast, and Nigeria.^{62,63} Interestingly, PCa cases among sub-Saharan African populations and North African Berbers exhibit a high frequency of short-length alleles, typically characterized by fewer than 18 CAG repeats and fewer than 15 GGC repeats. These findings suggest that population-specific *AR* polymorphisms may play a critical role in the distinct epidemiological profile of PCa across the continent.⁶³

Furthermore, genetic variations affecting the detoxification and metabolic pathways involving glutathione S-transferase mu 1 (*GSTM1*), glutathione S-transferase theta 1 (*GSTT1*), UDP-glucuronosyltransferase (*UGT*) genes, and sulfotransferase (*SULT*) genes have been documented in Tunisia and Algeria. These polymorphisms are increasingly recognized as significant contributors to the heightened susceptibility to PCa observed across diverse African populations.⁶³⁻⁶⁷

5.2. Phenotypic factors

Breast malignancies can originate within diverse anatomical regions of the breast, including the ducts, lobules, or the intervening stroma. Within the broader classification of BCa, they are further categorized based on their invasiveness relative to the primary site. Distinguishing between these molecular and histological subtypes is critical, as they dictate divergent clinical prognoses and therapeutic strategies.⁶⁸ Current research indicates that BCa diagnosed in African women frequently exhibits a disproportionately high prevalence of poor-prognosis phenotypes, including TNBC and core basal-like tumors.^{69,70} Notably, West African ancestry demonstrates a significant correlation with the TNBC subtype, highlighting

the role of genetic lineage in disease presentation.⁷¹ It is noteworthy that there is disparity in the representation of molecular subtypes among the people in different regions of Africa. For example, the luminal subtype appears more frequent in Northern Africa, whereas HER2⁺ and TNBC subtypes appear more frequent in West Africa.⁷²

Phenotypic factors, specifically breast density and receptor expression profiles including estrogen receptor (ER), progesterone receptor (PR), and HER2, play a critical role in the pathogenesis and progression of BCa. Elevated breast density is a well-established and significant risk factor, with studies indicating a higher prevalence of this phenotype among women of African descent. Understanding these phenotypic variations is essential for risk stratification and the development of targeted screening protocols within this population.⁴⁸

Prostate cancer is a markedly heterogeneous disease across clinical, morphological, and molecular dimensions. Primary PCa is frequently multifocal, characterized by topographically and morphologically distinct tumor foci within the same gland. While metastatic lesions typically arise from a single clonal lineage of a primary focus, they often exhibit significant subclonal heterogeneity. This complex biological landscape presents substantial challenges for accurate diagnosis and the selection of effective therapeutic strategies. Clinical assessment of PCa risk and progression relies on established parameters, including prostate volume, PSA levels, and histological grading via the Gleason score. Notably, men of African descent frequently present with more aggressive disease phenotypes, characterized by advanced stage at diagnosis and higher-grade tumors.⁷³ Addressing this heterogeneity and its population-specific manifestations remains a critical priority for optimizing oncological outcomes in this demographic.⁷⁴

5.3. Environmental factors

Escalating urbanization and rapid industrial expansion across the African continent are suspected to be primary drivers of rising cancer incidence. Specifically, deteriorating outdoor air quality and increased occupational exposure to carcinogenic contaminants resulting from intensified industrial production and waste imported from other parts of the world represent significant environmental risk factors.⁷⁵ It is currently well-known that environmental chemical substances interfere with estrogen and androgen signaling, either through interacting with receptors or by influencing steroid metabolism and altering hormone levels within the body.⁷ Considering the above, stringent regulatory frameworks and public health interventions need to be provided. Of note, constant exposure to chemicals

with estrogen-like properties, such as polychlorinated biphenyls, may contribute to BCa occurrence.⁷⁶ In men, epidemiologic evidence has also linked polychlorinated bisphenyls and inorganic arsenic exposures to elevated PCa risk.

5.4. Epigenomic factors

A lack of national regulations on the use of pesticides and other chemical agents, as well as waste utilization, allows for chronic exposure of African citizens to these substances, which can affect gene expression.⁷⁷ Moreover, infectious diseases such as HIV affect immune function, which may contribute to the development of cancers. The action of the above results in epigenetic alterations, including aberrant DNA methylation, histone modifications, and the dysregulation of microRNA expression, which significantly modulate gene activity and induce BCa.⁷⁸ In BCa, hypermethylation of tumor suppressor gene promoters silences critical regulatory pathways, thereby promoting uncontrolled cellular proliferation and subsequent metastasis.⁷⁹ Consequently, these hypermethylation profiles serve as potential biomarkers for both diagnostic stratification and therapeutic monitoring. A prominent example is the superoxide dismutase 3 (*SOD3*) gene, which is downregulated in BCa and inversely correlated with promoter CpG island methylation, a state significantly associated with poor clinical outcomes. Furthermore, evidence suggests that African women exhibit distinct epigenetic signatures linked to more aggressive disease phenotypes.⁸⁰ Characterizing these population-specific epigenetic profiles is essential for advancing precision medicine and improving prognostic accuracy within this demographic.⁸¹

Analyses of PCa genomic data have revealed an enrichment of African ancestry-specific drivers, many of which are novel in PCa, including several putative therapeutic targets: chromodomain helicase DNA-binding protein 7 (*CHD7*), double PHD fingers 3 (*DPF3*), RNA polymerase I subunit B (*POLR1B*), SET domain-containing 1B histone lysine methyltransferase (*SETD1B*), upstream binding transcription factor (*UBTF*), and vacuolar protein sorting 72 homolog (*VPS72*).⁸² Such distinct genomic profiles may also help explain the aggressive nature of the disease in this population.

5.5. Regional variability and interactions of genetic, environmental, and epigenetic factors

Overall, genetic factors, environmental exposures, and healthcare infrastructure vary across West, East, North, and Southern Africa (summarized in Table 1). However, the etiology of BCa and PCa in Africa is increasingly conceptualized as a multi-layered, synergistic confluence of unique genomic background, distinct epigenetic modifications, and a rapidly changing environment⁸³ (Table 1). These new environmental exposures act on specific biological mechanisms within genomes, leading to the acceleration of carcinogenesis (summarized in Table 3). In contemporary oncology research and precision therapeutics, focusing on the paradigm of gene-environment interactions must be prioritized. Such approaches are necessary to understand how these interactions affect population-specific genetic susceptibilities that modulate an individual's physiological and molecular responses to exogenous chemical, dietary, metabolic, and lifestyle exposures.

Table 3. Synthesis of core gene-environment interactions

Locus/pathway	Genetic susceptibility	Environmental trigger	Carcinogenic outcome and mechanism
<i>BRCA1/BRCA2</i>	Inherited loss-of-function variants	Folate-deficient, ultra-processed diets	Accelerated second-hit inactivation via gene promoter hypermethylation.
Triple-negative breast cancer risk loci	Chromosome 19p13.1 risk alleles	Elevated body mass index and obesity	Chronic inflammation activates NF-κB, fueling estrogen-independent tumor growth.
8q24 region	African-specific SNPs (rs114798100)	High intake of red meat/high-heat cooking	Dietary mutagens interact with the locus to heavily upregulate proto-oncogene (MYC family) expression.
AR	Shorter polymorphic CAG repeat sequences	Metabolic syndromes	Elevated IGF-1 signaling works together with sensitive AR to drive early metastatic growth.
Xenobiotic pathway	Polymorphisms in <i>CYP1A1</i> , <i>CYP19A1</i>	Exposure to endocrine-disrupting chemicals	Hyperactivation of toxic chemical intermediates leads to tissue damage and higher local estrogen levels.

Abbreviations: AR: Androgen receptor; CAG: Cytosine-adenine-guanine; IGF-1: Insulin-like growth factor 1; MYC: MYC proto-oncogene; NF-κB: Nuclear factor kappa B; SNPs: Single-nucleotide polymorphisms.

6. Molecular pathogenesis: Breast and prostate cancer

6.1. Reproductive hormones

Physiological regulation of the reproductive system organs is primarily mediated by the hypothalamic–pituitary–gonadal (HPG) axis. This neuroendocrine cascade initiates with the pulsatile release of gonadotropin-releasing hormone (GnRH) from the hypothalamus, which stimulates the anterior pituitary to secrete the gonadotropins: follicle-stimulating hormone and luteinizing hormone. Gonadotropins subsequently control the synthesis and secretion of sex steroid hormones, principally androgens and estrogens, within the gonads, supplemented by a minor pool of adrenal androgens.⁸⁴ While these steroid hormones act as the primary regulators of reproductive tissue homeostasis under physiological conditions, their dysregulation is equally central to pathological states such as PCa and BCa in both females and males.

6.2. Hormone receptors

Nuclear hormone receptors constitute a prominent superfamily of evolutionarily conserved, DNA-binding proteins that function primarily as ligand-dependent transcription factors.⁸³ Beyond their fundamental roles in regulating cellular differentiation, metabolism, and inflammatory responses, these receptors are key drivers of carcinogenesis, promoting tumor initiation, proliferation, and survival. The AR serves as the primary driver of carcinogenesis in the prostate, while ER and PR facilitate the growth of numerous BCa subtypes.^{85,86} Consequently, the pharmacological inhibition of nuclear hormone receptor activity has remained a cornerstone of the standard of care for the management of metastatic breast and prostate malignancies for decades.

6.2.1. Androgen receptors in prostate cancer and breast cancer

Under physiological conditions, the AR orchestrates male sexual development and differentiation by binding to its endogenous ligands, testosterone and 5 α -dihydrotestosterone (DHT) (Figure 1)⁸⁷

Within the normal prostate, AR expression in both the epithelium and stroma is essential for maintaining homeostasis. However, AR dysregulation can lead to the recruitment of oncogenic cofactors, thereby initiating tumorigenesis through aberrant cellular proliferation and increased migration. Clinically, diminished stromal AR expression is often associated with advanced-stage disease and suboptimal prognoses, although its precise role in promoting or inhibiting progression remains a subject of debate⁸⁸ (Figure 2).

The transition to androgen-independent PCa is frequently driven by AR gene mutations, splice variants, and *de novo* intracrine androgen synthesis.^{89,90} Notably, the first exon of the AR gene, which encodes the N-terminal transactivation domain, exhibits significant CAG and GGN polymorphisms. While excessive CAG repeat expansions may result in reduced AR transactivation and transcriptional activity (despite a theoretically higher binding affinity for DHT), shorter CAG polymorphisms are hypothesized to elevate the risk of PCa development. The precise correlation between repeat length and age at disease onset or clinical severity remains incompletely elucidated. Shorter CAG segments are observed with markedly higher frequency among African American populations, potentially contributing to the distinct disease profile.⁹¹

In healthy breast tissue, the AR is predominantly localized within luminal mammary epithelial cells. However, immunoreactive AR is also evident in stromal fibroblasts and adipocytes (Figure 2).^{88,92} Androgenic signaling is thought to counteract and modulate estrogen-induced proliferation in the mammary epithelium (a mechanism essential for normal breast development and homeostatic maintenance).⁹³ Despite its physiological role, the AR is increasingly recognized as a pivotal factor in the pathogenesis of BCa.⁹⁴ The high concordance rate (exceeding 70%) of AR expression between primary and metastatic lesions suggests its potential utility as both a diagnostic biomarker and a therapeutic target for AR-positive BCa patients.⁹⁵ Biological insights into these malignancies reveal that the AR engages in significant crosstalk with various oncogenic signaling pathways and molecular receptors. Consequently, the functional role of the AR varies considerably across different BCa subtypes, exhibiting divergent biological behaviors depending on the molecular context (Figure 3). It is important to add here that some membrane ARs (G-protein-coupled receptors ZIP9, GPRC6A, and OXER1) trigger rapid cytoplasmic signaling through pathways such as mitogen-activated protein kinase/extracellular signal-regulated kinase (MAPK/ERK).⁹⁶ Some studies show that activating these receptors might induce apoptosis in certain cancer cells of the prostate, while other studies suggest that inhibiting these pathways could prevent resistance.⁸⁷

6.2.2. Estrogen receptors in prostate cancer and breast cancer

Estrogens occur naturally in three different forms: estradiol, estrinol, and estrone. They exert their action through the ER, which belongs to the steroid hormone superfamily of nuclear receptors. There are two types of ER involved

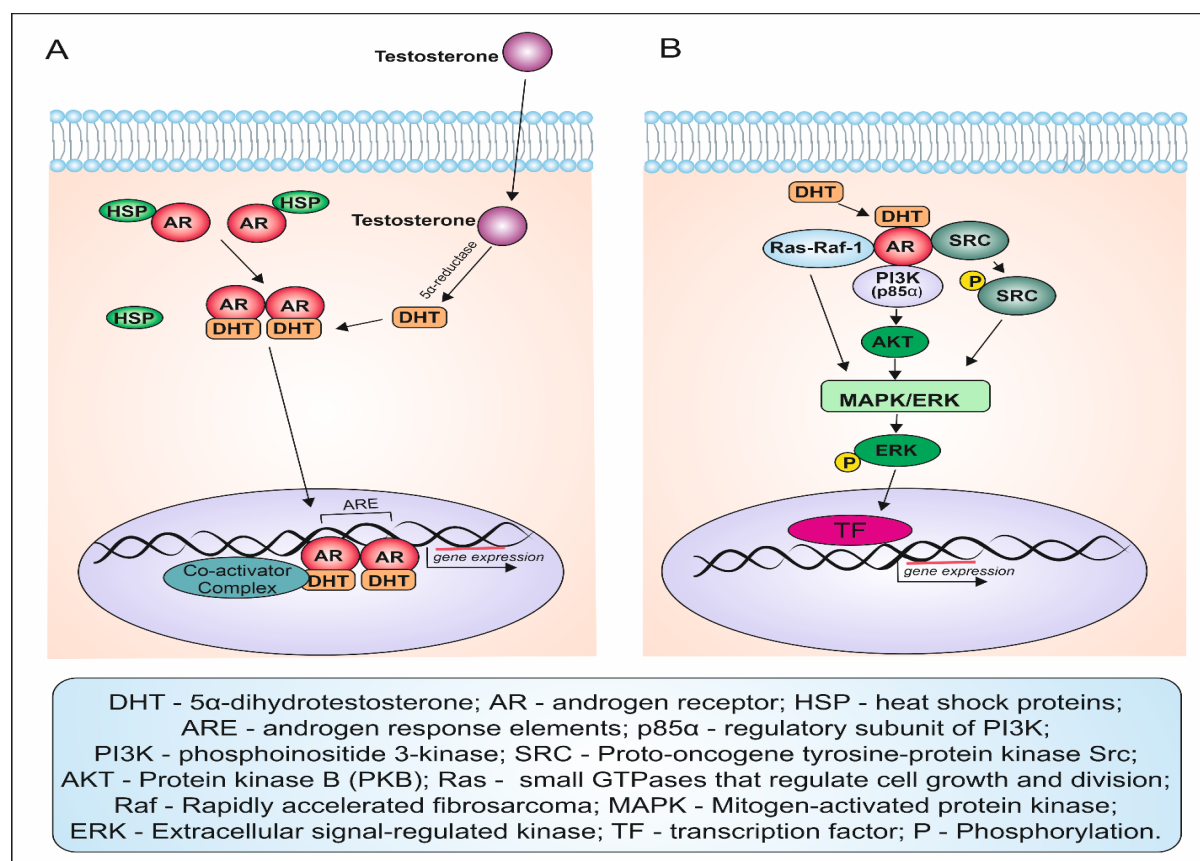


Figure 1. AR signaling pathway. (A) Canonical genomic AR signaling in the prostate is initiated by the intracellular entry of testosterone, which is subsequently converted into its more potent metabolite, DHT, by the enzyme 5 α -reductase. (B) Non-genomic AR signaling in the prostate is characterized by rapid, transcription-independent interactions with various cytoplasmic signaling effectors. These non-genomic pathways bypass classical nuclear translocation to rapidly drive cellular proliferation and survival, underscoring the multifaceted nature of AR-mediated carcinogenesis in the prostate. Illustration based on Bader *et al.*⁸⁷

Abbreviations: AKT: Protein kinase B; AR: Androgen receptor; ARE: Androgen response element; DHT: 5 α -dihydrotestosterone; ERK: Extracellular signal-regulated kinase; HSP: Heat shock protein; MAPK: Mitogen-activated protein kinase; P: Phosphorylation; p85 α : Regulatory subunit of PI3K; PI3K: Phosphoinositide 3-kinase; Raf-1: Rapidly accelerated fibrosarcoma kinase 1; Ras: Rat sarcoma small GTPase; Src: Proto-oncogene tyrosine-protein kinase Src; TF: Transcription factor.

in carcinogenesis: classical nuclear ERs (ER α , ER β) and membrane receptors, G protein-coupled (Figure 4).

Estrogen receptors α and β have been identified as key modulators in the pathogenesis of PCa, exerting divergent carcinogenic and anti-carcinogenic effects, respectively. Furthermore, the aberrant expression of enzymes critical to steroid biosynthesis and metabolism, specifically aromatase and 5 α -reductase, has been significantly implicated in the development and progression of PCa.⁹⁷ These enzymes are expressed in steroidogenic cells in the steroid biosynthetic pathway leading to sex steroid production. However, their aberrant expression may contribute to PCa development by altering local androgen production.

Estrogen signaling is fundamental to normal mammary gland development and function. Luminal cells express ER α , which serves as the primary mediator of estrogenic function, whereas ER β is widely distributed across basal and luminal epithelial cells, as well as fibroblasts, adipocytes, lymphocytes, and endothelial cells^{98,99} (Figure 2). ER α activation induces cell cycle progression and stimulates growth, which may lead to carcinogenic initiation and progression. Clinically, assessing ER α expression in BCa specimens is a critical diagnostic standard for guiding therapeutic strategies. Nevertheless, ER α expression alone is not an absolute predictor of response to endocrine therapy. In experimental models, such as the BCa cell line (MCF-7), estradiol enhanced proliferation and drove tumor

formation in mouse xenografts.¹⁰⁰ Conversely, exogenous ER β overexpression in MCF-7 cells has been shown to inhibit proliferation *in vitro* and prevent estradiol-induced tumor formation. These findings underscore the divergent roles of ER isoforms, with ER β potentially acting as a tumor suppressor that counteracts the proliferative effects of ER α . In recent therapeutic approaches, upregulation and sensitization of ER β receptors are favored.

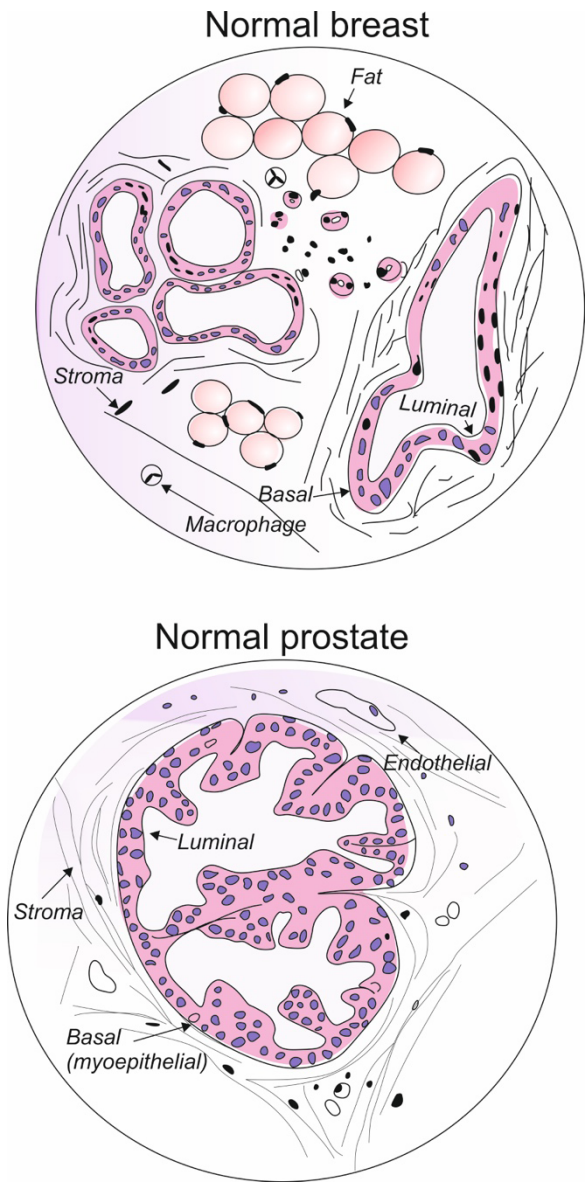


Figure 2. Distribution of estrogen receptor α (ER α), estrogen receptor β (ER β), and androgen receptor (AR) in normal breast and prostate tissues. In normal breast tissue: ER α , luminal epithelial cells; ER β , luminal and basal epithelial cells, stromal cells, adipocytes, endothelial cells, and macrophages; AR, luminal epithelial cells. In normal prostate tissue: AR, luminal epithelial cells; ER β , basal/myoepithelial and luminal epithelial cells, stromal cells, endothelial cells, and macrophages. Illustration based on Omoto and Iwase.¹

It is worth noting here that besides environmental endocrine disruptor chemicals, other chemical factors, such as toxic heavy metals, promote cancer initiation and development, thus disrupting natural endocrine pathways, driving early-onset and aggressive tumor phenotypes. Recent studies by Njale *et al.*¹⁰¹ reported the positive association between the risk of BCa in Tanzanian women and exposure to metals (aluminum, arsenic, nickel, cadmium, and lead). In addition, elevated blood molybdenum was associated with an increased risk of ovarian cancer in *BRCA1* mutation carriers¹⁰² (for more information, see [Table 4](#)).

Table 4. Toxic heavy metals/metalloestrogens: Mechanisms involved in carcinogenesis

heavy metal/ metalloestrogen	Mechanism
Cadmium	Mimics estrogen, blocks selenium
Arsenic	Upregulates proto-oncogenes (MYC), causes double-strand breaks
Zinc and selenium	Deficiencies: loss of antioxidant defense

7. Treatment approaches: Conventional and clinically controlled potential alternative therapy

The optimization of clinical outcomes and patient health-related quality of life depends highly on the deployment of highly cost-effective, evidence-based therapeutic strategies. Therefore, additional potentially alternative pharmacological treatments controlled by clinicians and used for specific patient phenotypes may be used in specific cases. Based on the constantly used traditional herbal medicine by the African population, the subsequent analysis that delineates their pharmacological mechanisms of action and clinical efficacy is urgently needed for strategic assessment and/or integration with conventional treatments for comprehensive, resource-stratified care models.

7.1. Conventional therapies

The contemporary standard of care for reproductive system malignancies relies on multimodal therapeutic protocols. These strategies integrate surgical resection, high-energy ionizing radiation, and systemic cytotoxic chemotherapy to optimize local control and systemic eradication. Surgical intervention is often the first line of standard care treatment. For BCa, operative strategies are dictated by clinical staging, anatomical distribution, and tumor-to-breast ratio. Procedures range from breast-conserving

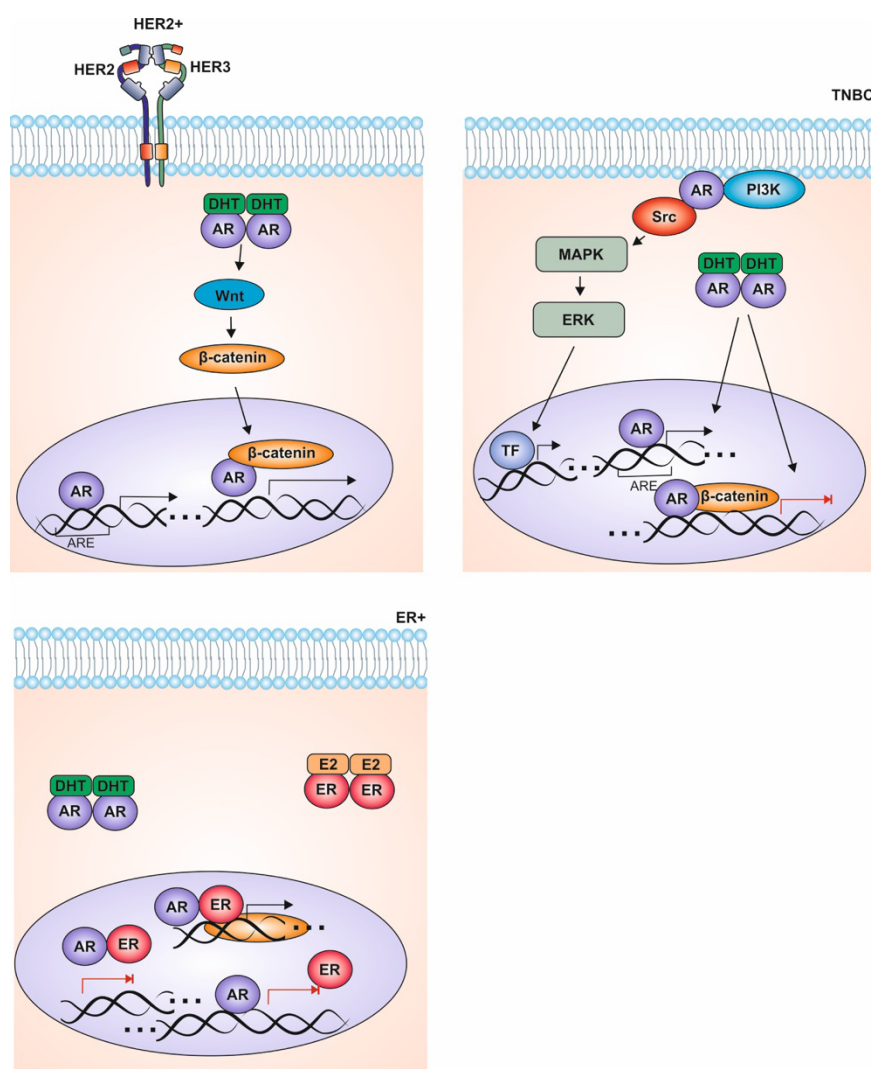


Figure 3. Mechanisms of AR-mediated gene transcription in different subtypes of breast cancer. In ER α ⁻/HER2⁺ BCa, the Wnt/ β -catenin signaling pathway is frequently implicated in facilitating the transcriptional activity of AR, thereby driving tumor progression. Within the TNBC subtype, androgenic signaling appears to initiate secondary messenger cascades that often establish a positive feedback loop, further accelerating malignancy. Conversely, in ER-positive BCa, a dynamic and complex interplay exists between ER and AR. Illustration based on Anestis *et al.*⁹⁵

Abbreviations: AKT: Protein kinase B; AR: Androgen receptor; ARE: Androgen response element; DHT: 5 α -dihydrotestosterone; E2: Estradiol; ER: Estrogen receptor; ER+: Estrogen receptor-positive; ERK: Extracellular signal-regulated kinase; GPER: G protein-coupled estrogen receptor 1; HER2: Human epidermal growth factor receptor 2; HER2⁺: Human epidermal growth factor receptor 2-positive; HER3: Human epidermal growth factor receptor 3; MAPK: Mitogen-activated protein kinase; PI3K: Phosphoinositide 3-kinase; Src: Proto-oncogene tyrosine-protein kinase Src; TF: Transcription factor; TNBC: Triple-negative breast cancer; Wnt: Wingless-related integration site.

surgery, such as localized lumpectomy, to radical or modified radical mastectomy in cases characterized by multicentricity or advanced local progression.^{103,104} In prostate-confined disease, radical prostatectomy serves as a cornerstone intervention. Clinical data demonstrate that definitive surgical excision significantly improves overall survival and cancer-specific survival by ensuring local oncological control and enabling pelvic lymph node

dissection for precise risk stratification.¹⁰⁵ Radiotherapy uses high-energy radiation to destroy cancer cells. Following BCa staging, external beam radiation therapy targeting the whole breast (whole-breast irradiation) is standard clinical practice. This adjuvant intervention is critical for eradicating occult subclinical residual disease, thereby reducing local recurrence rates.¹⁰³ For localized and locally advanced PCa, both external beam radiation

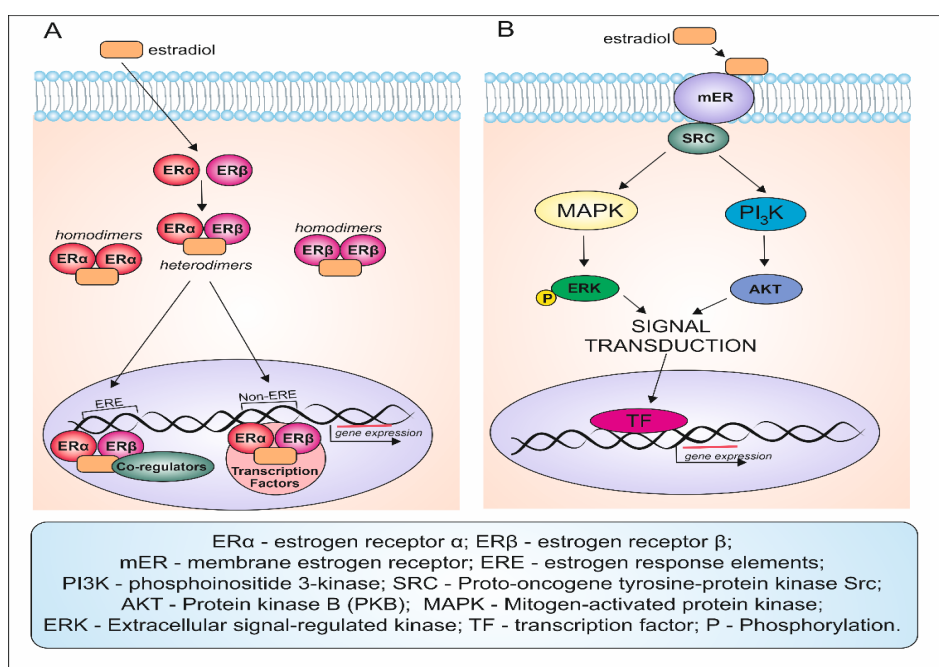


Figure 4. ER signaling pathway. (A) Classical genomic signaling pathway in breast cancer. Beyond this direct DNA-binding mechanism, ERs also regulate gene expression by serving as co-regulators for other transcription factors, thereby exerting a broader influence on the oncogenic transcriptome. (B) Non-classical genomic signaling pathway. ER on the plasma membrane may also activate the PI3K signaling pathway. Estrogen not only regulates gene transcription but also binds to the ER on the cell membrane to activate the non-genomic signaling pathway. Illustration based on Feng *et al.*⁶⁸ Abbreviations: AKT: Protein kinase B; ERα: Estrogen receptor alpha; ERβ: Estrogen receptor beta; ERE: Estrogen response element; ERK: Extracellular signal-regulated kinase; MAPK: Mitogen-activated protein kinase; mER: Membrane estrogen receptor; Non-ERE: Non-estrogen response element; P: Phosphorylation; PI3K: Phosphoinositide 3-kinase; Src: Proto-oncogene tyrosine-protein kinase Src; TF: Transcription factor.

therapy and brachytherapy (interstitial radiation) represent highly effective modalities. Longitudinal comparative trials indicate that radiation therapies yield oncological outcomes and biochemical progression-free survival rates equivalent to radical surgery in appropriately stratified risk cohorts.¹⁰⁶ Chemotherapy is a fundamental component of BCa management. It is mandatory for advanced metastatic disease and highly aggressive molecular subtypes, including TNBC and HER2⁺ tumors.¹⁰⁷

Therapeutic management of hormone-sensitive reproductive malignancies requires targeted endocrine intervention to disrupt systemic signaling pathways, which is highly effective for BCa and PCa. For hormone-positive BCa, competitive antagonism of the ER is clinically achieved using selective estrogen receptor modulators, most notably tamoxifen. This agent exerts tissue-specific antagonist effects in mammary tissue, blocking estrogen-stimulated transcription cascades required for cellular replication.¹⁰³ In postmenopausal cohorts where peripheral adipose tissue is the primary site of steroidogenesis, new-generation aromatase inhibitors such as anastrozole are employed. These agents selectively inhibit aromatase, the

enzyme encoded by *CYP19A1*, preventing the peripheral conversion of derived from adrenals androgens into bioactive estrogens.¹⁰³ For PCa in which cells rely heavily on AR signaling, suppression of the HPG axis is a primary therapeutic target. PCa is less responsive to chemotherapy, but drugs like docetaxel are used in advanced hormone-refractory cases.¹⁰⁸ Surgical or medical castration serves as the cornerstone of PCa management. Therapeutic suppression is frequently achieved using GnRH agonists such as leuprolide acetate, which induce pituitary receptor desensitization and downregulate luteinizing hormone release, decreasing serum testosterone to castrate levels.¹⁰⁹ In advanced or metastatic castration-resistant PCa, complete androgen blockade requires new-generation agents. The selective AR inhibitor enzalutamide competitively blocks androgen binding, nuclear translocation, and DNA binding.¹¹⁰ Upon progression to castration-resistant phenotypes, the therapeutic index shifts toward taxane (*Taxus* genus derivatives)-based chemotherapy regimens. The microtubule-stabilizing agent docetaxel is widely utilized as a standard systemic therapy in advanced hormone-refractory states, promoting mitotic arrest and

apoptosis in independent cell populations.⁹³

Personalized, genotype-directed therapies in the management of metastatic PCa use PARP inhibitors, a family of enzymes characterized by their ability to catalyze the transfer of ADP-ribose moieties to target proteins.¹¹¹ These agents are pivotal in various fundamental cellular processes, including the modulation of chromatin architecture, transcription, replication, recombination, and DNA repair, which are dysregulated in PCa.¹¹² Of clinical significance is the role of PARP in the DNA damage response in BCa cells with homologous recombination deficiencies, such as those harboring *BRCA1/2* mutations, may become dependent on PARP-mediated DNA repair.¹¹¹

Targeted therapeutics based on monoclonal antibodies exploit specific genetic aberrations and overexpressed surface proteins unique to neoplastic cells, minimizing off-target systemic toxicity while maximizing cancerogenic efficacy. In approximately 15–20% of BCa, the amplification of the *ERBB2* gene results in the overexpression of HER2. This aberrant receptor density triggers continuous downstream pro-survival signaling *via* the phosphoinositide 3-kinase/protein kinase B/mammalian target of rapamycin and mitogen-activated protein kinase pathways. Trastuzumab, a recombinant monoclonal antibody, selectively binds the HER2 protein and alters the trajectory of this aggressive phenotype.¹¹³ In metastatic castration-resistant PCa, the development of sipuleucel-T represents a major milestone. Sipuleucel-T is an autologous cellular immunotherapy consisting of peripheral blood mononuclear cells, including antigen-presenting cells, that have been harvested via leukapheresis.¹¹⁴ These cells are *ex vivo* activated and matured with a recombinant fusion protein that consists of prostatic acid phosphatase (highly expressed in PCa) fused to granulocyte-macrophage colony-stimulating factor. Upon re-infusion into the patient, these primed, antigen-presenting cells induce a robust, T-cell-mediated immune response specifically directed against the antigen in cancer cells.

For African PCa patients, interventions such as GnRH analogs, oral antiandrogens (e.g., bicalutamide and flutamide), or docetaxel chemotherapy are occasionally utilized, because their application is restricted to select clinical settings.^{115–118} In metastatic PCa, androgen deprivation therapy is essential for symptomatic relief and improved survival, and in Africa, therefore surgical castration remains the primary treatment strategy.¹¹⁸ However, the emergence of castration-resistant PCa remains a critical challenge. New-generation oral hormonal therapies hold the potential for an expanded role in managing both castration-sensitive and castration-resistant disease states within African populations.

Given these regional constraints, there is an urgent need to develop novel, context-specific approaches to PCa management that diverge from the standard protocols employed in HICs and upper-middle-income countries.¹¹⁹ Designing strategies for the specific socioeconomic and clinical realities of the African continent is paramount for improving oncological outcomes in this demographic.¹²⁰

In the management of BCa, HER2-targeted therapy with trastuzumab remains largely inaccessible in sub-Saharan Africa because of cost-prohibitive barriers, despite the need for multidisciplinary treatment approaches.^{42,121,122,123}

For patients with hormone receptor-positive malignancies, endocrine therapy comprising tamoxifen and aromatase inhibitors is the standard of care. While access to aromatase inhibitors remains constrained in many regions, tamoxifen's low cost and availability (often provided free of charge) make it the most accessible oncological medication across the African continent. This high accessibility frequently leads to the empirical administration of tamoxifen in patients whose hormone receptor status remains undetermined.^{124,125} Although hormone receptor-positive patients derive significant therapeutic benefit from tamoxifen, this empirical approach carries substantial potential adverse effects without gaining any clinical advantage. This situation underscores the critical necessity for a standardized diagnostic infrastructure to prevent unnecessary toxicity and to ensure that endocrine interventions are directed only toward those who will benefit.^{126,127} The immune checkpoint inhibitors, specifically atezolizumab and pembrolizumab in combination with chemotherapy, are first-line treatments for TNBC patients. Furthermore, pembrolizumab is indicated in both neoadjuvant and adjuvant settings for early-stage TNBC. Despite these therapeutic advancements, their implementation in sub-Saharan Africa is hindered by the limited availability of the predictive biomarker testing essential for identifying high levels of programmed death ligand 1 expression.^{120,128} Beyond diagnostic barriers, immunotherapy is associated with rare but potentially severe immune-related adverse events, which necessitate rigorous routine monitoring and specialized clinical management. Consequently, expanding the use of these highly effective agents in the African context requires significant funding investment.

7.2. Herbal therapies

In sub-Saharan African socio-ecological circumstances, ethnopharmacological systems function as a primary component of the healthcare infrastructure. Traditional medical practitioners deploy a diverse compendium of indigenous flora containing bioactive secondary

metabolites characterized by documented antineoplastic, anti-proliferative, and pro-apoptotic properties.¹²⁹ This traditional local medicine is based on over 5,000 species of plants used for healthcare for ages. It is estimated by the World Health Organization that 80% of the population uses herbal therapies before standard oncology admission.¹³⁰ Multiple further studies in experimental systems have identified species of plants that have demonstrated anti-cancer properties at the cellular levels.¹³¹ Studies were based on the use of cell lines, *ex vivo* systems, e.g., mammary tissues, laboratory animal *in vivo* testing, as well as partial clinical observation of patients.¹³² Some of the medicinal plants used to manage or treat cancer include *Sutherlandia frutescens* (cancer bush), a plant traditionally used in Southern Africa for its anti-cancer and immune-boosting properties. Studies suggest it may have anti-proliferative effects on cancer cells, although more clinical research is needed to confirm its efficacy and safety.¹³³ *Hypoxis hemerocallidea* (African potato), also commonly used in South Africa for its presumed enhancement of the immune system, has shown some *in vitro* anti-cancer activity.¹³⁴ *Artemisia annua* (sweet wormwood) is known for its anti-malarial properties. Artemisinin and its derivatives have exhibited potential anti-cancer activity through induction of cell cycle arrest and apoptosis in various cancer cell lines.¹³⁵ Importantly, artemisinin appears not to alter non-cancerous cells. In recent years, artemisinin has passed three phase I clinical trials intended to evaluate its safety profile and optimal dosage to use in patients with solid tumors and metastatic BCa. One of those trials also found that artemisinin's half-life in the bloodstream is only a few hours, so frequent intake may be needed to overcome this limitation.¹³⁶ *Zanthoxylum chalybeum* (knobwood), *Harungana madagascariensis* (blood tree), *Prunus africana* (red stinkwood), and *Bridelia micrantha* (mtutu), used traditionally for cancer intervention in Eastern Africa, demonstrate cytotoxic activity against cancer cell lines.¹³⁷ *Vernonia amygdalina* (bitter leaf), widely used in West Africa, has shown promise in preclinical studies for its ability to inhibit cancer cell growth and induce apoptosis.¹³⁸ This herb has been studied in clinical trials for the treatment of uncomplicated malaria in Africa. Although no significant side effects or drug toxicity were reported, complete parasite eradication (32%) was found to be low compared to modern anti-malarial drugs.¹³⁹ Recognizing the vast pharmacological potential of natural products, recent computational studies have utilized pharmacophore-based virtual screening and molecular dynamics simulations to target key hormonal receptors, e.g., PR in BCa. These *in silico* investigations have successfully identified several promising lead compounds derived from natural sources, offering new avenues for therapeutic intervention and

the development of novel endocrine-targeting agents for oncological care.^{140,141} Notable findings have also been reported for *Prunus africana*.¹⁴² *In vitro* and *in vivo* studies have provided strong pharmacological evidence for anti-PCa activities of *P. africana*-derived phytochemicals. Through synergistic interactions between different effective phytochemicals, *P. africana* extracts have been shown to exhibit very strong antiandrogenic and antiangiogenic activities together with apoptotic activity. However, as for other herbal compounds, further preclinical and clinical studies ought to be done.

7.3. Integrating conventional and herbal therapies

Currently, there are still many challenges and considerations regarding herbal therapy, with urgently needed more advanced research. Although herbal therapies present significant pharmacological potential, their integration into conventional oncological protocols entails substantial challenges.¹³¹ There is an imperative requirement for rigorous, high-quality clinical trials to definitively establish the efficacy and safety profiles of these agents, as well as to identify potential herb-drug interactions (especially altered drug metabolism, reduced therapeutic efficacy, or increased toxicity) with standard-of-care cancer therapies. Furthermore, the inherent variability in the preparation, standardization, and dosing of plant medicines introduces significant complexity, delaying their systematic implementation within extensive evidence-based clinical settings.^{129,143,144} As a potential synergy, some studies suggest that combining ethnopharmacology with conventional treatments may enhance therapeutic efficacy and reduce side effects. For example, combining traditional Chinese medicine with chemotherapy has shown improved outcomes in some cancers.¹⁴⁵ Similar integrative approaches using locally available herbal medicines could be explored in African contexts. Establishing regulatory frameworks and standardizing herbal preparations are essential to safely integrate herbal medicine into cancer care in specific conditions. This includes ensuring quality control, proper identification of active compounds, and monitoring for adverse effects.¹²⁹ Of note, unlike synthetic drugs, the concentrations of active phytochemicals in plants fluctuate dramatically. A biochemical profile of plants is highly dependent on factors such as climate, seasonal variations, soil quality, and the precise time of harvest. Furthermore, different preparation methods, whether raw decoctions, tinctures, or powdered extracts, drastically alter the bioavailability and concentration of active ingredients. Therefore, establishing a precise, safe, and effective dose may be difficult, and a lack of standardization can lead to inconsistent therapeutic effects (underdosing or accidental overdosing). Ethnotherapeutic medicines are not

inherently toxic. Many herbs contain toxic components, e.g., alkaloids or glycosides, that can lead to organ damage. Moreover, there is a risk of serious interactions between herbs and drugs, herbs and food, or herbs.¹⁴⁴ Herbal supplements can inhibit or induce liver enzymes that process conventional medications, dangerously altering the effectiveness of medications such as blood thinners, high blood pressure medications, or statins. For example, phytoestrogens (such as red clover, soy, and genistein) can interfere with the binding of conventional drugs such as tamoxifen and aromatase inhibitors, potentially stimulating tumor growth or reducing treatment efficacy.

8. Prevention and control of breast and prostate cancer

Substantial opportunities to mitigate cancer-related suffering and mortality in Africa must exist across the entire continuum of care, from primary prevention to early detection and therapeutic intervention.¹⁴⁵ Currently, a profound disparity remains: up to 80% of women in sub-Saharan Africa are diagnosed with late-stage BCa (stage III or IV) when compared to 15% in HICs.^{146,147} Consequently, BCa detection relies heavily on breast self-examination and clinical breast examination, with a marked lack of specialized diagnostic imaging infrastructure and highly trained radiological personnel.^{148,149}

Another important barrier to cancer treatment and control is the paucity of population-based breast registry data. Such a database is an important prerequisite to better managing the unacceptably high cancer mortality rate.¹⁵⁰ Only 11% of the African population is covered by population-based cancer registration, even though such a database is essential for assessing the burden of cancer, setting priorities, and planning and evaluating cancer control programs.¹⁵¹

Additionally, overcoming fatalistic religious and cultural beliefs through advocacy, education programs, and national campaigns on breast health awareness could positively impact BCa control and prevention.¹⁵²

There is also inadequate data on the control and prevention of PCa in the African population. Although findings in the literature are often discordant, there is cumulative evidence suggesting that dietary patterns significantly modulate the risk of PCa development. These observations underscore the potential of nutritional interventions as a viable strategy for primary cancer prevention with special emphasis on Africa.¹⁵³

While ethnotherapy in Africa offers a rich source of potential new anti-cancer compounds, their current use in oncology presents distinct challenges.¹⁵⁴ Nowadays, it

is important to build safe healthcare frameworks based on systematic validation. This requires developing strict standardization protocols, building collaborative networks between traditional healers and oncologists, and designing rigorous clinical trials to ensure patient safety and optimize treatment outcomes (summarized in Table 5).

Table 5. Summary of preclinical and clinical findings from traditional herbal medicine

Preclinical evidence	Clinical evidence	Critical translation gaps
<i>In vitro</i> cytotoxicity and apoptosis	Lack of phase II/III randomized trials	Standardization
Fragmented case reports	Well-defined molecular pathways	Herb–drug interactions
Lack of <i>in vivo</i> animal models	Inconclusive human efficacy data	Safety profiling

9. Conclusion and future perspectives

Incidence and mortality rates for BCa and PCa are escalating across Africa, increasingly reflecting global epidemiological trends.⁴⁶ Despite this rising problem, only a limited number of African nations have implemented comprehensive, holistic cancer control policies. Furthermore, the adoption of cost-effective diagnostic, therapeutic, and palliative care protocols is essential, including the clinically supervised assessment of herbal pharmacological approaches where appropriate.¹⁵³ The treatment of reproductive organ-related cancers in Africa, therefore, requires a multifaceted and interdisciplinary approach that may combine the strengths of conventional therapy enriched with herbal treatments when it is justified and not harmful. Rigorous research involving large-scale randomized controlled trials and regulatory oversight is necessary for the use of herbal medicine, which urgently requires further in-depth studies to offer safe (e.g., highly active and less toxic drugs) and successful treatment, and then for its full integration with conventional approaches. Concomitantly, understanding all genetic, phenotypic, environmental, and epigenomic factors influencing BCa and PCa can help design joint medical treatments for individual African patients.

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Conflict of interest

The authors declare that they have no conflict of interest.

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