Prevalence and Mortality of Triple-Negative Breast Cancer in West Africa: Biologic and Sociocultural Factors

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INTRODUCTION
Africa is the second-largest continent by population.1 With 54 countries across five geographical regions (Northern, Western, Middle, Eastern, and Southern Africa), the continent boasts great geographical, cultural, and population diversity. Breast cancer (BC) exhibits substantial variability across African populations. BC has become a serious health concern globally. According to the Global Cancer Observatory, BC is the second-leading cause of cancer death and the most common cancer type among women worldwide, occurring in 24% of all women (approximately 2.1 million cases in 2018).2 Although relatively low (Fig 1), BC incidence in Africa is rising rapidly, especially in sub-Saharan Africa (SSA).3,4 The 2030 BC burden in SSA is projected to be twice the 2012 BC burden.4 SSA encompasses multiple low- and middle-income countries (LMICs), which have low gross domestic product per capita and human development index; many of these countries are in West Africa (WA) (Table 1).5

TRIPLE-NEGATIVE BREAST CANCER
Triple-negative breast cancer (TNBC) is a BC subtype with high mortality, early and more frequent recurrence, and poor prognosis.6 Comparative data as presented by Gonçalves et al have shown that women with the TNBC phenotype have a 19% lower 5-year overall survival and 18% lower disease-free survival than their non-TNBC counterparts, alluding to the higher aggressiveness of TNBC tumors.7 These tumors are particularly prevalent in the LMICs of WA.4 TNBC lacks expression of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 (HER2) and accounts for 10%-20% of all BCs worldwide.6,8,9 Significant variation exists in the molecular features of TNBC; hence, in 2016, the Lehmann group proposed a refined molecular classification system, subclassifying TNBC into basal-like 1, basal-like 2, mesenchymal, and luminal androgen receptor (AR) subtypes.11 TNBC has aggressive clinical and histopathologic features, including a high risk of distant metastasis,12 high recurrence rates,13 and poor treatment response.8 Despite their clinical success against HER2-positive BC, anti-HER2 therapies are ineffective against TNBC.14 Taxane- and anthracycline-based chemotherapies remain the mainstay of TNBC treatment; however, the long-term survival outcomes of patients with TNBC remain poor.15 Although many agents that fall under this classification are under study in a clinical setting at multiple treatment stages, poly (ADP-ribose) polymerase inhibitors are showing promising therapeutic capabilities among patients with TNBC who are BRCA1 or BRCA2 mutation carriers.16

Mounting evidence suggests that significant racial disparities exist in TNBC. Jiagge et al17 reported that premenopausal women of West African ancestry, African American (AA), and Ghanaian women had a higher TNBC prevalence (34%, and 51%, respectively) than White-American (CA) and East African women (approximately 16% in each case). Subsequent population-based studies confirmed that WA ancestry is associated with a higher TNBC prevalence and worse disease outcomes.17 Biologic and nonbiologic factors may contribute to racial disparities in TNBC.18,19 It is essential that the underpinnings of the observed racialized TNBC burden are fully studied and understood to determine the most effective means to treat WA TNBC tumors and manage cancer in WA, to provide information essential for the improvement of reproductive health, the prevention of cancer, and the amelioration of the cancer burden; and to improve the quality of life of indigenous African female populations and women of African descent who suffer from this disease. In this article, we discuss established and emerging risk and protective factors associated with TNBC in WA women.

BIOLOGIC FACTORS AFFECTING TNBC DEVELOPMENT AND OUTCOMES
Genetic Factors
Profound geographical variations exist in the mutational and protein expression landscapes of TNBC. Although a diverse range of mutations has been detected in European, North American, and North African women with BC,4 little is known about the mutational landscape of TNBC in WA women because of research constraints, paucity of resources, and a
lack of appropriate technologic platforms. Nonetheless, small-scale studies have shown that in WA women, TNBCs possess not only shared but also unique mutations. In Senegalese women with TNBC, Ndiaye et al. identified a 1,400-year-old pathogenic BRCA1 variant containing a 10-nucleotide duplication (c.815_824dupAGCCATGTGG) in exon 11. The same mutation was previously reported in AAs, suggesting a possible founder effect. Of 94 patients with BC from the Komfo Anokye Teaching Hospital in Kumasi (Ghana), 57 (61%) had TNBC and 58 (62%)

**(CONTEXT)**

**Key Objective**
Triple-negative breast cancer (TNBC) is a malignant breast cancer, lacking targeted therapy, which would benefit from further research to understand its nature and the observed variation in its malignancy between women of differing ancestries. This large-scale systematic literature review examines the current and emerging biologic and nonbiologic factors, which have been shown to influence TNBC disease outcomes among indigenous West African (WA) females while discussing some prospective steps that could be adopted by health care systems for the reduction of this burden.

**Knowledge Generated**
WA women are the most burdened populations in relation to TNBC. Biologic and economic factors have been shown to significantly influence the TNBC disease outcomes. Women’s education initiatives, specialist training, and accessible health care are needed in WA countries.

**Relevance**
The determination of WA-specific biologic, cultural, and socioeconomic TNBC factors could align efforts in developing treatment options and physician recommendations to cancer-burdened women.

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FIG 1. Estimated age-standardized BC incidence rates per 100,000 people in countries in WA. All data presented were obtained from 2018 GLOBOCAN reports. BC, breast cancer; GLOBOCAN, Global Cancer Observatory; WA, West Africa.

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harbored BRCA mutations, including BRCA1185delAG (47%), BRCA1 5382insC (44%), and BRCA2 6174delT (47%).21 Consistently, numerous BRCA1 mutations were identified among Burkina Faso women with suspected BC.22 Mutations in TP53 and PALB2 have been associated with a higher TNBC incidence in certain WA populations. A genomic study of 209 Nigerian patients revealed that mutations in TP53 and PALB2 were common among inherited and invasive BCs, such as TNBC.23 Genetic screening for germline mutations may help reduce the TNBC burden in high-risk WA women through both preventive (eg, mastectomy) and treatment health care. Although genetic screening, genetic counseling, and preventive treatments have proved to be effective mitigation strategies in high-income African countries, these practices are not widespread in LMICs in WA because of their high costs.24 Risk stratification on the basis of well-established BC risk factors has been proposed as an alternative cost-effective means to identify high-risk individuals requiring genetic screening.24 Genetic screening can subsequently be used as a means to determine individuals with deleterious BRCA1/2 mutations that would ideally benefit from the incorporation of novel international government–approved poly (ADP-ribose) polymerase inhibitors into their treatment regimens. These drugs are not widespread in LMICs, and access to these drugs in WA is significantly hindered, possibly because of its high cost in most markets.25 Differences in protein expression levels have also been implicated in racial disparities in TNBC. The transcription factor Kaiso was found to be upregulated in TNBCs of WA (Nigerian), Barbadian, and AA women compared with those of CA women.26 Jiagge et al27 reported that Ghanaian women had a higher TNBC incidence, higher ALDH1 positivity (36%), and lower AR levels than their CA, AA, and Ethiopian counterparts. In indigenous Nigerian women, the levels of PIASγ were associated with the clinicopathologic characteristics of TNBC.28 Interestingly, melatonin MT1 receptors, which have been associated with favorable outcomes, were found to be expressed in lower levels in AA women than in CA women with TNBC.29 Differences in protein expression levels may contribute to the more aggressive TNBC clinical course in WA women. WA women might benefit from the use of immunotherapeutic agents as the protein, programmed death ligand-1 is considered to be highly expressed in TNBCs, but more research is needed to ascertain that this remains the case or is possibly amplified among WA women.30

Viral Infections

Viral infections play a critical role in TNBC development.31 Human papillomavirus, Epstein-Barr virus, and HIV are of great interest when considering TNBC in WA because of their high frequency of occurrence. Among women with normal cytology, HPV positivity has been recorded to be as

TABLE 1. General and Female Population Health, Wellness, and Wealth Metrics

| Country      | Population (2019) | Female Population (2019) | Female Life Expectancy at Birth | Percent of Adult Female Literacy Rate | Female Unemployment Rate* | GDP Per Capita (PPP) (2017) | Per Capita Health Expenditure (PPP) | HDI Values (2019) |
|--------------|-------------------|--------------------------|--------------------------------|--------------------------------------|--------------------------|-------------------------------|-------------------------------------|-------------------|
| Benin        | 11,801,151        | 5,910,016                | 63                             | 31                                   | 2.9                      | 3,423.6                       | 84.65                               | 0.520             |
| Burkina Faso | 20,321,378        | 10,172,882               | 62                             | 33                                   | 4.6                      | 2,280.4                       | 129.06                              | 0.434             |
| Cabo Verde   | 549,953           | 273,932                  | 76                             | 82                                   | 12.1                     | 7,469.1                       | 357.07                              | 0.651             |
| Côte D'Ivoire| 25,716,544        | 12,742,548               | 59                             | 40                                   | 3.9                      | 5,455.4                       | 175.66                              | 0.516             |
| The Gambia   | 2,347,706         | 1,183,244                | 63                             | 42                                   | 12.4                     | 2,298.4                       | 55.77                               | 0.466             |
| Ghana        | 30,417,856        | 15,002,087               | 65                             | 74                                   | 4.4                      | 5,637.0                       | 146.87                              | 0.596             |
| Guinea       | 12,771,246        | 6,605,288                | 62                             | 22                                   | 3.6                      | 2,670.3                       | 89.17                               | 0.466             |
| Guinea-Bissau| 1,920,922         | 981,975                  | 60                             | 31                                   | -                        | 2,071.8                       | 123.29                              | 0.461             |
| Liberia      | 4,937,374         | 2,456,344                | 65                             | 34                                   | 2.4                      | 1,487.0                       | 104.67                              | 0.465             |
| Mali         | 19,658,031        | 9,813,289                | 60                             | 26                                   | 1.6                      | 2,423.8                       | 84.16                               | 0.427             |
| Mauritania   | 4,525,696         | 2,253,797                | 66                             | 43                                   | 11.4                     | 5,412.4                       | 170.15                              | 0.527             |
| Niger        | 23,310,715        | 11,597,081               | 63                             | 27                                   | 7.8                      | 1,269.6                       | 78.85                               | 0.377             |
| Nigeria      | 200,963,599       | 99,135,343               | 55                             | 53                                   | 7.5                      | 5,348.3                       | 221.10                              | 0.534             |
| Senegal      | 16,296,364        | 8,350,257                | 70                             | 40                                   | 7.3                      | 3,535.6                       | 143.09                              | 0.514             |
| Sierra Leone | 7,813,215         | 3,915,202                | 55                             | 35                                   | 3.9                      | 1,789.6                       | 205.36                              | 0.438             |
| Togo         | 8,082,366         | 4,061,389                | 62                             | 51                                   | 2.8                      | 1,662.1                       | 103.73                              | 0.513             |

NOTE. Source: The World Bank (2002-2019) and Human Development Reports (2019). Abbreviations: GDP, gross domestic product; HDI, human development index; PPP, purchasing power parity; WA, West Africa.

*Although the unemployment rates in WA are low, underemployment rates (which have not been meticulously measured) remain an issue, as indicated by the relatively low GDP per capita values. The high underemployment rates have rendered many women incapable of seeking health care.
high as 48% in Guinea, with HPV16 commonest variant, and EBV is a highly prevalent virus group, infecting more than 90% of the human population worldwide. In addition to oropharyngeal cancer, HPV has also been linked to cervical cancer, a common malignancy among SSA women. Piana et al. found that 15% of Italian women with TNBC were infected with HPV. In a recent study, the HPV genome was detected in 44% of TNBC and HER2+ BCs. However, the relationship between HPV and TNBC in WA patients remains unclear. EBV is another widespread oncovirus associated with Burkitt lymphoma, the most common pediatric cancer in SSA. EBV may increase malignancy in BC, and a strong correlation between EBV infection and BC development has been reported.

HIV is also common in WA, especially among women in SSA (approximately 2.8 million in West and Central Africa). The Joint United Nations Program on HIV and AIDS identified Cameroon, Ivory Coast, and Nigeria as epicenters for the HIV epidemic, accounting for 60% of new infections and 54% of AIDS-related deaths every year. This remains the case even as the HIV burden is gradually reducing in Africa. Although HIV is not a typical oncovirus, BC incidence is high among HIV-infected women in SSA. Interestingly, HIV infection has been associated with treatment toxicity and poor BC outcomes; however, the relationship between HIV and TNBC incidence and outcomes in WA remains elusive. Identification of viruses significant to TNBC occurrence could aid in the identification of antiviral vaccines suitable for African populations that once administered could serve as added cancer prevention.

ENVIRONMENTAL AND SOCIAL RISK DETERMINANTS OF TNBC IN WA

Sociocultural Factors

Reproductive factors. Epidemiologic studies have shown that in women of African ancestry, age at first pregnancy, age of menarche, and oral contraceptive use did not significantly affect TNBC risk. The results on the influence of nulliparity on TNBC are conflicting. Breastfeeding appears to have a protective effect against TNBC. Compared with parous AA women age between 20 and 44 years who never breastfed, their counterparts who breastfed for at least 6 months had an 82% decreased TNBC risk. John et al. identified a significant association between the duration of breastfeeding over a lifetime among young parous women and a reduced TNBC risk. Although breastfeeding is common in WA, exclusive breastfeeding for extended periods is relatively uncommon, and children are typically weaned at early ages. This is likely due to the lack of education on exclusive breastfeeding practices, fear of disease transmission, changing perceptions of womanhood, and deep-rooted cultural practices. Moreover, breastfeeding is often initiated late in WA, possibly contributing to the high TNBC burden among WA women. The relationship between long-term breastfeeding and TNBC in WA women should be further investigated as breastfeeding could serve as a cost-effective strategy to prevent TNBC.

Culture, social norms, and religious aspects of BC in WA. Cultural and social factors in WA pose unique challenges and opportunities for BC management. In WA, long-held social concepts of the ideal body type often hinder women from seeking surgical treatment. Women often fear that surgery would tarnish their femininity and may lead to rejection by their spouses, friends, and families. These fears, however, are not unfounded. Despite this, many women associate a BC diagnosis with unavoidable death.

Many women with BC are not well-received by their communities because of the widespread misinformation on the nature of the disease. Members of these communities often believe that BC is caused by sexual promiscuity. Therefore, women frequently relegate health concerns, attributing their pain and discomfort to their roles as family caretakers. Those who eventually seek treatment often do so without emotional support and because of the patriarchal structure of most WA societies, they would require constant permission and funds from husbands or male community leaders who lack awareness of BC and reproductive health. For example, women in rural North Ghana often have to obtain approval from a Baga (a male community leader) before seeking medical care. Such societal constraints may delay TNBC diagnosis and result in treatment discontinuation, leading to poor long-term survival outcomes.

Another barrier to seeking treatment is cultural taboos. In some WA communities, it is believed that women should not touch their breasts, which may significantly delay BC diagnosis. Similarly, allowing a man other than a spouse to touch or look at women’s breasts is considered shameful in WA, hindering women from seeking BC screening. Hence, many WA women prefer traditional healers and herbal medicines over established screening and treatment methods. Alternative BC therapies are commonly used among Ghanaian, Malian, Ivorian, and Sierra Leonean women. Grosse Frie et al. found that 38% of Northwestern Nigerian women had been divorced or separated within the first 3 years of their surgery. Additionally, many women associate a BC diagnosis with unavoidable death.
treatment are often kept a secret from patients by family and religious leaders and patients have no part in treatment decisions. Knowledge gaps remain in the intersection between religion and treatment adherence. Sociocultural and religious beliefs and patient mentality were found to be critical reasons for the delayed diagnosis and treatment of TNBC, contributing to the poor TNBC outcomes among WA communities; thus, it is paramount to understand how these factors influence patient decisions, specifically in WA, where TNBCs are often diagnosed at a late stage.

**Diet and anthropometric measures.** Studies have linked increased polyunsaturated fatty acids level, fruit consumption, decreased saturated fat levels, and low-refined carbohydrate consumption with a lower risk of BC occurrence. People in countries in Africa where the incidence of TNBC is low (eg, Northern African countries) tend to adhere to diets that possess these anti-BC properties. Donovan et al reported that adherence to a Mediterranean diet rich in vegetables, fruits, fish, and olive oil (with the latter two being primary sources of polyunsaturated fatty acids) was inversely correlated with TNBC incidence. WA diet consists of mainly leafy vegetables; carbohydrates from yam (Dioscorea rotunda), cassava, and African rice (Oryza glaberrima); saturated fats from oil palm (Elaeis guineensis); and to a lesser extent, animal proteins, which have only recently been incorporated from Western diets. This combination of carbohydrates and saturated fats may contribute to the high TNBC occurrence in WA.

The role of obesity in TNBC development merits further investigation, as emerging data suggest that obesity may be a significant TNBC risk factor. The Carolina Breast Cancer Study identified an increased TNBC incidence among premenopausal and postmenopausal AA women with high waist-to-hip ratios. Notably, both obesity (high body mass index) and waist-to-hip ratios are indicators of body fatness, and high adiposity has been linked to TNBC occurrence. The relevance of obesity and metabolic disorders in TNBC should be further studied among WA cohorts, in which metabolic disorders show an increasing prevalence because of westernization and high-calorie intake.

**Lifestyle factors.** Lifestyle factors, such as alcohol consumption and smoking, need to be further studied as potential risk factors for TNBC in WA, especially given the recent trends of westernization and increase in access to alcohol and tobacco. Although some studies reported no significant relationship between alcohol intake and TNBC, others suggested that alcohol promotes TNBC cell migration and invasion. Recent studies have also shown that smoking was not significantly associated with TNBC. The value of smoking and alcohol consumption as risk factors for BC is conflicting, and more data need to be collected from WA cohorts.

The common use of personal care products (eg, hair relaxers and skin lighteners) among women of African descent may increase the risk of TNBC because of the presence of phthalates and other toxic compounds (eg, mercury). Brinton et al found an increased BC risk among women with prior use of non-lye hair relaxers. Mosquito insecticides necessary in this predominantly tropical area may have carcinogenic effects.

**Economic Factors**

**Income and education.** BC incidence and mortality in LMICs in Africa are rising, especially in WA, where many developing countries with low human development indexes are found. The financial constraints at the governmental, organizational, and individual levels may prevent patients with BC from seeking medical care. Grosse Frie et al identified economic hardship as a primary reason for delays in BC diagnosis and treatment among women in Bamako, Mali. Because of the lack of means, many women forgo routine check-ups, delaying tumor detection. Frequently, women with suspected BC refrain from seeking medical care because they cannot afford the costs of screening and treatment. Instead, they may use low-quality and outdated medicines. Only a small fraction of WA women with BC begin treatment, and an even smaller portion, is able to complete treatment because of financial instability. Many essential chemotherapeutic and palliative drugs registered on the Essential Medicines List of the WHO remain inaccessible to many patients with BC in SSA. As chemotherapeutic drugs, surgery, and radiation therapy are the basis for TNBC treatment, it is necessary that solutions are proffered on how their costs might be minimized.

At the governmental level, only a small portion of funds can be allocated to BC research and management because of the lack of financial resources. Federal funding is essential for the encouragement of innovation, training of local scientists, the establishment of sustainable population-based cancer registries, the building of infrastructure, development of region-tailored treatment solutions, and further understanding of TNBC biology and etiology in WA. Sufficient funding would also mitigate the over-reliance of WA scientists on foreign institutions in North America and Europe because of the lack of facilities and instrumentation in countries in WA.

Furthermore, the lack of formal education and BC awareness poses significant barriers to BC research and management. Lack of education has prevented many women, especially those in rural areas, from adopting health care–seeking behavior. Education and language barriers hamper research efforts and render health care inaccessible to patients who only speak indigenous languages. Although certain progress has been made in reproductive health awareness, it is crucial to boost efforts to provide BC-specific education. Educating women on BC risk factors, self-examination practices, national health insurance programs, and treatment options may facilitate
early BC detection and help women adhere to complex treatment regimens. Improving BC awareness will also help combat ignorance and misinformation on BC, which delays BC diagnosis and treatment in WA.58,62

Treatment access and care. Patients with BC in WA are insufficiently serviced by their health care systems.3,81 Most hospitals in WA lack access to trained professionals, health care coverage,61 screening technologies, and treatment facilities.84 In the developing world, it is common for clinical oncologists to perform both radiation and medical oncology.85 As these oncologists may not be able to gain sufficient expertise in both fields, patients with cancer may not receive optimal care.85 Similarly, the outcomes of surgical tumor excision are poor, possibly because surgeries are performed by general surgeons who lack training in surgical oncology.85 Therefore, there is a dire need for highly specialized oncologists, which could be achieved by providing appropriate training to general practitioners.52,53,85

The scarcity of health care professionals has unintended consequences for patients and their families, especially those in remote areas. Patients are often referred to several different doctors, possibly far from their homes, inadvertently delaying treatment and increasing transportation costs. Patients might also be transferred to different hospitals because of a lack of infrastructure.54 Ultrasonography, a cheaper alternative to mammography, is becoming increasingly popular among WA hospitals. As ultrasonography does not have any imposed age limitations, and the ultrasound technology could be used for other purposes, ultrasonography might become a prominent diagnostic tool in WA.82

Several limitations in pathology services have been identified in WA, where the accuracy of tumor identification is limited by poor laboratory practices and specimen handling, lack of quality assurance, delays in tissue fixation, and a lack of standardized diagnostic evaluation methods.3,86 These problems could be mitigated by providing frequent training to pathologists. Moreover, the adoption of appropriate collection, fixation, storage, and evaluation practices is required. Immunohistochemistry has become one of the predominant methods to identify and characterize TNBCs; however, lack of access to immunohistochemistry reagents and facilities impedes the widespread use of immunohistochemistry in WA.14

Prevalence of Quadruple-negative breast cancer in West Africa

TNBCs lacking AR expression are known as quadruple-negative breast cancers (QNBCs), which account for 75%-80% of all TNBCs.87,88 Typically, QNBCs are chemoresistant27 and have a poor prognosis.27 QNBCs are more likely to exhibit aggressive phenotypes than TNBCs91 and AR expression is associated with favorable survival outcomes.92 QNBCs constitute a significant portion of TNBCs in WA.92 Bhattacharai et al showed that most TNBCs in Nigeria have no AR expression, associated with worse clinical outcomes. Racial disparities are apparent in QNBC, with women of West African ancestry being at a particularly high risk of QNBC. Notably, women from WA (Ghanaians) have lower AR levels than AA, CA, and EA women.27 Significant differences in QNBC biology between WA and CA women have also been reported. For instance, Angajala et al93 reported a lower expression of hsa-mir-190b among AA patients with QNBC. There are limited data on QNBC in WA as AR expression analysis is uncommon. Yet, data from AA women suggest that AR negativity is frequent among specific WA populations.92 In WA women, TNBCs display QNBC-like clinical features (eg, large tumor size and high tumor grade at diagnosis)91; hence, QNBC, and not TNBC, may be the bigger challenge among WA women with BC.

Future Perspectives

To improve BC management in WA, health care establishments must revamp their operational infrastructure, standards, practices, training programs, and methods to communicate information to patients and families. Significant efforts have already been undertaken to improve BC screening through the introduction of ultrasonography and new cost-effective radiation technologies.94 Governments should strive to commercialize such technologies to lower cancer treatment costs.95 Choosing Wisely Africa, a task force convened by the African Organization for Research and Training in Cancer, aims to eliminate harmful, low-quality, and resource-consuming practices in African health care establishments. Choosing Wisely Africa identified that palliative care in patients with advanced disease improved treatment outcomes and reduced treatment costs in the long run.96

Access to chemotherapy equipment and associated drugs in WA also hinder effective management of cases. Chemotherapeutic agents are generally costly and make treatment compliance difficult, warranting government action. Nigeria, in 2019, launched an innovative partnership between Clinton Health Access Initiative Inc, Pfizer, American Cancer Society, Worldwide Healthcare, and EMGE Resources Limited. The aim is to deliver lifesaving chemotherapies for cancer treatment to seven teaching hospitals throughout the country. It is expected that patients could save up to 50% of their treatment costs and have access to high-quality drugs. This initiative can be extended to other West African regions.

Additionally, cancer control programs,97 hospitals, health care professionals, and trained local volunteers52 should maximize efforts to spread BC awareness in rural villages, where cultural and social hindrance factors are more prevalent. In urban areas, women should be informed on the potential effects of westernization on TNBC risk. Innovative cancer advocacy programs by the Sebeccly Cancer Care and Support Center in Nigeria have prioritized the education of media professionals, enabling them to
broadcast simple, inexpensive, and easily accessible cancer care tips. The use of mass media to spread BC awareness should be adopted in other countries in WA. Several programs have been created to educate cancer education advocates and professionals to disseminate accurate BC information in WA. The Africa Cancer Advocacy Toolkit was established as an easily accessible means to offer guidelines on how to effectively manage innovative advocacy programs, share resources, and secure funding under resource-constrained conditions. African Organization for Research and Training in Cancer serves as a central body offering training opportunities to health care professionals, especially oncologists. The International Atomic Energy Agency and the WHO also provide radiation technology training to African health care professionals.

It is also essential to tailor solutions to the unique cultural and social landscape of WA by establishing culturally sensitive treatments and education programs for male spouses and leaders. Policies are required to encourage the inclusion of healers into health care systems and foster the establishment of referral systems for cancer screening (Fig 2). A healer-to-hospital referral system is already in place in Ghana but could be improved by more opportunities for dialogue between Western physicians and healers. Razali proposed regular retreats as a means for dialogue and exchange of knowledge and recommended that governments treat traditional healers as primary care providers, providing them with necessary facilities to improve initial patient care.

FIG 2. Potential patient treatment pathway integrating traditional healers into West African health care systems.
TABLE 2. Organizations Aiming to Improve Global and West African TNBC Detection and Management

| Organization                                      | Specific Program or Suborganization | Region of Influence | Organization or Program | Target(s)                                                                 | Action(s)                                                                                                                                 |
|---------------------------------------------------|-------------------------------------|---------------------|-------------------------|-----------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| Africa Oxford Cancer Foundation (AfroX)           | —                                   | Africa              | Oncology specialists    | Provides training in population-based cancer registration and data use       | Establishes cancer specialist groups and networks                                                                                       |
| African Cancer Registry Network (AFCRN)           | —                                   | SSA                 | African health care systems | Provides technical support to health workers                               | Creates international cancer research projects and networks                                                                          |
| African Organization for Research and Training in Cancer (AORTIC) | —                                   | Africa              | General public          | Supports oncology training programs for health care workers                 | Conducts international cancer conferences and workshops for health care providers                                                      |
| African Women’s Cancer Awareness Association (AWCAA) | AWCAA Medical Missions              | Africa              | Women in African         | Educates locals on breast health (ie, self-examination and early detection) | Establishes cancer specialist groups and networks                                                                                       |
| BIO Ventures for Global Health (BVGH)             | African Access Initiative            | Africa              | Clinics                 | Improves access to cancer medicines and treatment technologies              | Conducts international cancer conferences and workshops for health care providers                                                      |
| Choosing Wisely Africa (CWA)                      | —                                   | Africa              | African health care systems | Evaluates African health care systems and eliminates low-quality practices   |                                                                                                                                 |
| International Atomic Energy Agency (IAEA)         | Program of Action for Cancer Therapy (PACT) | LMICs               | Health professionals    | Provides technical advisory services                                         | Partners with other cancer aid organizations and networks                                                                        |
| International Cancer Control Partnership (ICCP)    | —                                   | Globally            | Health care systems     | Creation and implementation of cancer control plans                          |                                                                                                                                 |
| International Consortium for Advancing Research on TNBC (ICART) | —                                   | Globally            | Researchers              | Conducts high-quality research in TNBC biology, disparities, and clinical management | Maintains international networks among TNBC researchers and consolidates data with the use of available resources and trains exchange students in advanced research areas and bioinformatics |                                                                |
| National Cancer Institute (NCI)                    | Center for Global Health             | Globally            | Researchers              | Coordinates cancer research initiatives and technology for patients with TNBC | Creates research networks among LMICs, facilitates access to cancer medicines and treatment technologies and enhances training, peer review, diagnosis, and treatment |
**TABLE 2.** Organizations Aiming to Improve Global and West African TNBC Detection and Management (Continued)

| Organization | Specific Program or Suborganization | Region of Influence | Organization or Program Target(s) | Action(s) |
|--------------|-------------------------------------|---------------------|-----------------------------------|-----------|
| Union for International Cancer Control (UICC) | SPARC MBC program | Globally | Advocacy groups, Hospital networks, NGOs | Influences national policy in various African countries; Offers financial support (grants) to key organizations to improve health care systems; Provides training, mentoring, and networking opportunities; Performs patient data consolidation |
| WHO | WHO-PACT Joint Program on Cancer Control | LMICs | Oncology specialists, BC management organizations | Creates global public-private partnerships between oncology specialists and organizations; Provides funding for cancer management; Aids the implementation of national cancer control programs |
| WHO | International Agency for Research on Cancer (IARC) | Globally | Researchers | Organizes and promotes international collaboration for oncology research with a special interest in LMIC partnerships |

Abbreviations: BC, breast cancer; LMICs, low- and middle-income countries; MBC, metastatic breast cancer; NGO, nongovernmental organization; SPARC, seeding progress and resources for the cancer community; SSA, sub-Saharan Africa; TNBC, triple-negative breast cancer.

Because of the increasing incidence of cancer and other noncommunicable diseases,[103,104] governments, faith-based organizations, and nonprofit organizations in WA, with the consult of budgeting experts, should commit more funds to allow for the sufficient support of oncology research, cancer registries, treatment facilities, and health care coverage. The long-term improved cancer health of the WA populace can also be assured by various governments contributing funds to the improvement of health amenities and the establishment of initiatives that advocate for healthy food consumption, improved living conditions, reduced health care costs, and widespread formal education. Health insurance schemes should be made to cover all aspects of cancer prevention, diagnosis, and treatment across WA; advocacy through the Economic Community for West African States is encouraged.

More emphasis should be placed on national and international collaborations.[104] In 2016, we created the International Consortium for Advancing Research on TNBC (ICART), a prime example of a global collaborative effort to better understand TNBC and its disparities by leveraging experts across 12 different research groups in nine countries and four continents.[8] Apart from hosting international symposiums and obtaining viable TNBC tumor samples, the ICART has also championed novel studies such as the NeoAdjuvant ChemoTherapy Response in Nigerian patients with TNBC: Biologic and Social Determinants (NACTRENT-BIS) study currently being conducted in Nigeria, with the long-term aim of elucidating the biologic, dietary, social, and reproductive determinants of chemotherapy response. The ICART and other similar efforts (Table 2) can help reduce the TNBC burden and improve BC management in WA.

**RESEARCH PRIORITIES**

It is increasingly essential that all aspects of TNBC etiology and management in WA are comprehensively studied to fill gaps in knowledge and improve BC diagnosis and treatment within the West African cultural and financial climate. These research efforts will provide the knowledge required for policy making, governmental action, and educational and advocacy program establishment.

The biologic factors potentially increasing TNBC risk among West Africans should be further investigated as therapeutic targets. The role of psychologic and behavioral factors in TNBC development and outcomes also merits further investigation. What goes on in the minds of women who refuse to seek diagnosis or opt out of treatment programs? How can health care facilities encourage health-seeking behaviors among high-risk WA populations? Do maladaptive behaviors (eg, smoking, tobacco use, and poor diet) affect TNBC treatment outcomes? The potential utilization of established positive health behaviors (eg, breastfeeding) as inexpensive strategies to prevent TNBC should also be further assessed.

Given the role of traditional medicine in WA, studies should be conducted to investigate the reasons behind patients’ decision to seek health care from traditional healers instead of Western health care establishments. Similarly, studies are required to explore possible ways to enhance the inclusion of traditional healers in health care systems and build relationships between healers and Western physicians. Given the financial condition of many countries in WA, it is worth exploring possible low-cost diagnostic and treatment strategies to render health care more accessible to women across WA.
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REFERENCES
1. Bray F, Ferlay J, Soerjomataram I, et al: Global cancer statistics 2018. GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68:394-424, 2018
2. GLOBOCAN: World Fact Sheet Lyon, France, International Research Agency for Research on Cancer, World Health Organization, 2018
3. Brinton LA, Figueroa JD, Awuah B, et al: Breast cancer in sub-Saharan Africa: Opportunities for prevention. Breast Cancer Res Treat 144:467-478, 2014
4. Lukong KE, Ogbonjule Y, Kamdem JP: Breast cancer in Africa: Prevalence, treatment options, herbal medicines, and socioeconomic determinants. Breast Cancer Res Treat 165:365-367, 2017
5. Aderinji AA, Dawudo OU, Habeebu MY, et al: Distribution of breast cancer subtypes among Nigerian women and correlation to the risk factors and clinicopathological characteristics. World J Oncol 11:165-172, 2020
6. Kumar P, Aggarwal R: An overview of triple-negative breast cancer. Arch Gynecol Obstet 293:247-269, 2016
7. Gonçalves H Jr, Guerra MR, Duarte Cintra JR, et al: Survival study of triple-negative and non-triple-negative breast cancer in a Brazilian cohort. Clin Med Insights Oncol 12:1179554918790563, 2018
8. Wright N, Rida P, Raikha E, et al: Panoptic overview of triple-negative breast cancer in Nigeria: Current challenges and promising global initiatives. JCO Glob Oncol 4:1-20, 2018
9. Jouali F, Marchoudi N, Talbi S, et al: Detection of PIK3/AKT pathway in Moroccan population with triple negative breast cancer. BMC Cancer 18:900, 2018
10. Sagna T, Bonora E, Ouedraogo MNL, et al: Identification of BRCA1/2 p.Ser1613Gly, p.Pro871Leu, p.Lys1183Arg, p.Glu1038Gly, p.Ser1140Gly, p.Leu1246Val, p.His2440Arg variants in women under 45 years old with breast nodules suspected of having breast cancer in Burkina Faso. Biometr Concepts 10:120-127, 2019
11. Zheng Y, Walsh T, Gulsuner S, et al: Inherited breast cancer in Nigerian women. J Clin Oncol 36:2820-2825, 2018
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24. Silverstein A, Sood R, Costas-Chavarri A: Breast cancer in Africa: Limitations and opportunities for application of genomic medicine. Int J Breast Cancer 2016:4792865, 2016
25. Goldsberry WN, Summerlin SS, Guayton A, et al: The financial burden of PARP inhibitors on patients, payors, and financial assistance programs: Who bears the cost? Gynecol Oncol 160:800-804, 2021
26. Bassey-Archibong Bi, Hercules SM, Rayner LGA, et al: Kaiso is highly expressed in TNBC tissues of women of African ancestry compared to Caucasian women. Cancer Causes Control 28:1295-1304, 2017
27. Jiaggé E, Jibril AS, Davis M, et al: Androgen receptor and ALDH1 expression among internationally diverse patient populations. JCO Glob Oncol 4:1-8, 2018
28. Aghoolla A, Musa A, Banjo A, et al: PIASy expression in relation to clinico-pathological, tumour factors and survival in indigenous black breast cancer women. J Clin Pathol 67:301-306, 2014
29. Oprea-Ilies G, Haus E, Sackett-Lundeen L, et al: Expression of melatonin receptors in triple negative breast cancer (TNBC) in African American and Caucasian women: Relation to survival. Breast Cancer Res Treat 137:667-687, 2013
30. Cyprian FS, Akhtar S, Gatalica Z, et al: Targeted immunotherapy with a checkpoint inhibitor in combination with chemotherapy: A new clinical paradigm in the treatment of triple-negative breast cancer. Bosn J Basic Med Sci 19:227-233, 2019
31. Horakova D, Boucharova K, Cwierkta K, et al: Risks and protective factors for triple negative breast cancer with a focus on micronutrients and infections. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 162:83-89, 2018
32. De Vuyst H, Alemany L, Lacey C, et al: The burden of human papillomavirus infections and related diseases in sub-Saharan Africa. Vaccine 31:F32-F46, 2013 (suppl 9)
33. Smatti MK, Al-Sadeq DW, Ali NH, et al: Epstein-Barr virus epidemiology, serology, and genetic variability of LMP-1 oncogene among healthy population: An update. Front Oncol 8:211, 2018
34. de Martel C, Plummer M, Vignat J, et al: Worldwide burden of cancer attributable to HPV by site, country and HPV type. Int J Cancer 141:664-670, 2017
35. Piana AF, Sotgiu G, Muroni MR, et al: HPV infection and triple-negative breast cancers: An Italian case-control study. Virol J 11:190, 2014
36. Di Martino N, Alzetta G, Di Sciliprandi C, et al: HPV DNA associates with breast cancer malignancy and it is transferred to breast cancer stromal cells by extracellular vesicles. Front Oncol 9:12, 2019
37. Gopal S, Gross TG: How I treat Burkitt lymphoma in children, adolescents, and young adults in sub-Saharan Africa. Blood 132:254-263, 2018
38. Kanda T: EBV-encoded latent genes. Adv Exp Med Biol 1045:377-394, 2018
39. Cyprian FS, Al-Farsi HF, Vranic S, et al: Epstein-Barr virus and human papillomaviruses interactions and their roles in the initiation of epithelial-mesenchymal transition and cancer progression. Front Oncol 8:111, 2018
40. Avert: HIV and AIDS in West and Central Africa Overview. Brighton, United Kingdom, Avert, 2019
41. UNAIDS: UNAIDS Data 2019. Geneva, Switzerland, Joint United Nations Programme on HIV/AIDS (UNAIDS), 2019
42. Djomand G, Quaye S, Sullivan PS: HIV epidemic among key populations in West Africa. Curr Opin HIV AIDS 9:506-513, 2014
43. Chirkut S: Breast cancer, human immunodeficiency virus and highly active antiretroviral treatment; implications for a high-rate seropositive region. Oncol Rev 13:376, 2019
44. Grover S, Martei YM, Puri P, et al: Breast cancer and HIV in sub-Saharan Africa: A complex relationship. JCO Glob Oncol 4:1-11, 2018
45. Ma H, Ursin G, Xu X, et al: Reproductive factors and the risk of triple-negative breast cancer in white women and African-American women: A pooled analysis. Breast Cancer Res 19:6, 2017
46. Lorona NC, Cook LS, Tang MC, et al: Recent use of oral contraceptive and risk of luminal B, triple-negative, and HER2-overexpressing breast cancer. Horm Cancer 10:71-76, 2019
47. John EM, Hines LM, Phipps AI, et al: Reproductive history, breast-feeding and risk of triple negative breast cancer: The Breast Cancer Etiology in Minorities (BEM) study. Int J Cancer 142:2273-2285, 2018
48. Nukpezah RN, Nuovor SV, Nimnioni J: Knowledge and practice of exclusive breastfeeding among mothers in the tamale metropolis of Ghana. Reprod Health 15:140, 2018
49. Engebretsen IMS, Doherty T, Horwood C, et al: Development and challenges to breastfeeding in sub-Saharan Africa (in German). Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 61:937-944, 2018
50. Nikrumah J, Gbogbo FY: Institutional support for breastfeeding in Ghana: A case study of University of Education, Winneba. BMC Res Notes 11:501, 2018
51. Ezech OK, Ogbo FA, Stevens GJ, et al: Factors associated with the early initiation of breastfeeding in Western African States (ECOWAS). Nutrients 11:2765, 2019
52. Tetteh DA, Faulkner SL: Sociocultural factors and breast cancer in sub-Saharan Africa: Implications for diagnosis and management. Womens Health (Lond) 12:147-156, 2016
53. Obrist M, Osei-Bonsu E, Awuah B, et al: Factors related to incomplete treatment of breast cancer in Kumasi, Ghana. Breast 23:821-828, 2014
54. Asobayire A, Alley R: Women's cultural perceptions and attitudes towards breast cancer: Northern Ghana. Health Promot Int 30:647-657, 2015
55. Martei YM, Vanderpuye V, Jones BA: Fear of mastectomy associated with delayed breast cancer presentation among Ghanaian women. Oncologist 23:1446-1452, 2018
56. Odige VI, Tanaka R, Yusufo LM, et al: Psychosocial effects of mastectomy on married African women in Northwestern Nigeria. Psychooncology 19:893-897, 2010
57. Clegg-Lamptey JN, Dakubo JC, Attobra YN: Psychosocial aspects of breast cancer treatment in Accra, Ghana. East Afr Med J 86:348-353, 2009
58. Akukwo CP, Armah E, Sarpong T, et al: Barriers to early presentation and diagnosis of breast cancer among African women living in sub-Saharan Africa. PLoS One 12:e0171024, 2017
59. Grosse Frie K, Samoura H, Diop S, et al: Why do women with breast cancer get diagnosed and treated late in sub-Saharan Africa? Perspectives from women and patients in Bamako, Mali. Breast Care (Basel) 13:39-43, 2018
60. Amadeo EP, Amalba A, Kudjo T, et al: Reducing the breast cancer menace: The role of the male partner in Ghana. Asian Pac J Cancer Prev 15:8115-8119, 2014
61. Grosse Frie K, Karnaté B, Traoré CB, et al: Factors associated with time to first healthcare visit, diagnosis and treatment, and their impact on survival among breast cancer patients in Mali. PLoS One 13:e0207928, 2018
62. Toure M, Nguesann E, Bambara AT, et al: Factors linked to late diagnosis of breast cancer in sub-Saharan Africa: Case of Côte d’Ivoire (in French). Gynecol Obstet Fertil 41:696-700, 2013
63. Nitenganya F, Petroze RT, Kamara TB, et al: Prevalence of breast masses and barriers to care: Results from a population-based survey in Rwanda and Sierra Leone. J Surg Oncol 110:903-906, 2014
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