

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

Gift C. Nwagu, HSD<sup>1</sup>; Shristi Bhattarai, PhD<sup>1</sup>; Monica Swahn, PhD<sup>2,3</sup>; Saad Ahmed, PhD<sup>2,4</sup>; and Ritu Aneja, PhD<sup>1,2</sup>

## INTRODUCTION

Africa is the second-largest continent by population.<sup>1</sup> 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).<sup>2</sup> Although relatively low (Fig 1), BC incidence in Africa is rising rapidly, especially in sub-Saharan Africa (SSA).<sup>3,4</sup> The 2030 BC burden in SSA is projected to be twice the 2012 BC burden.<sup>4</sup> 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).<sup>5</sup>

## TRIPLE-NEGATIVE BREAST CANCER

Triple-negative breast cancer (TNBC) is a BC subtype with high mortality, early and more frequent recurrence, and poor prognosis.<sup>6</sup> 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.<sup>7</sup> These tumors are particularly prevalent in the LMICs of WA.<sup>4</sup> 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.<sup>6,8,9</sup> Significant variation exists in the molecular features of TNBC<sup>10</sup>; 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.<sup>11</sup> TNBC has aggressive clinical and histopathologic features, including a high risk of distant metastasis,<sup>12</sup> high recurrence rates,<sup>13</sup> and poor treatment response.<sup>6</sup> Despite their clinical success against HER2-positive BC, anti-HER2 therapies

are ineffective against TNBC.<sup>14</sup> Taxane- and anthracycline-based chemotherapies remain the mainstay of TNBC treatment; however, the long-term survival outcomes of patients with TNBC remain poor.<sup>15</sup> 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.<sup>16</sup>

Mounting evidence suggests that significant racial disparities exist in TNBC. Jagge et al<sup>17</sup> 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.<sup>17</sup> Biologic and nonbiologic factors may contribute to racial disparities in TNBC.<sup>18,19</sup>

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,<sup>4</sup> little is known about the mutational landscape of TNBC in WA women because of research constraints, paucity of resources, and a

Author affiliations and support information (if applicable) appear at the end of this article.

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## 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

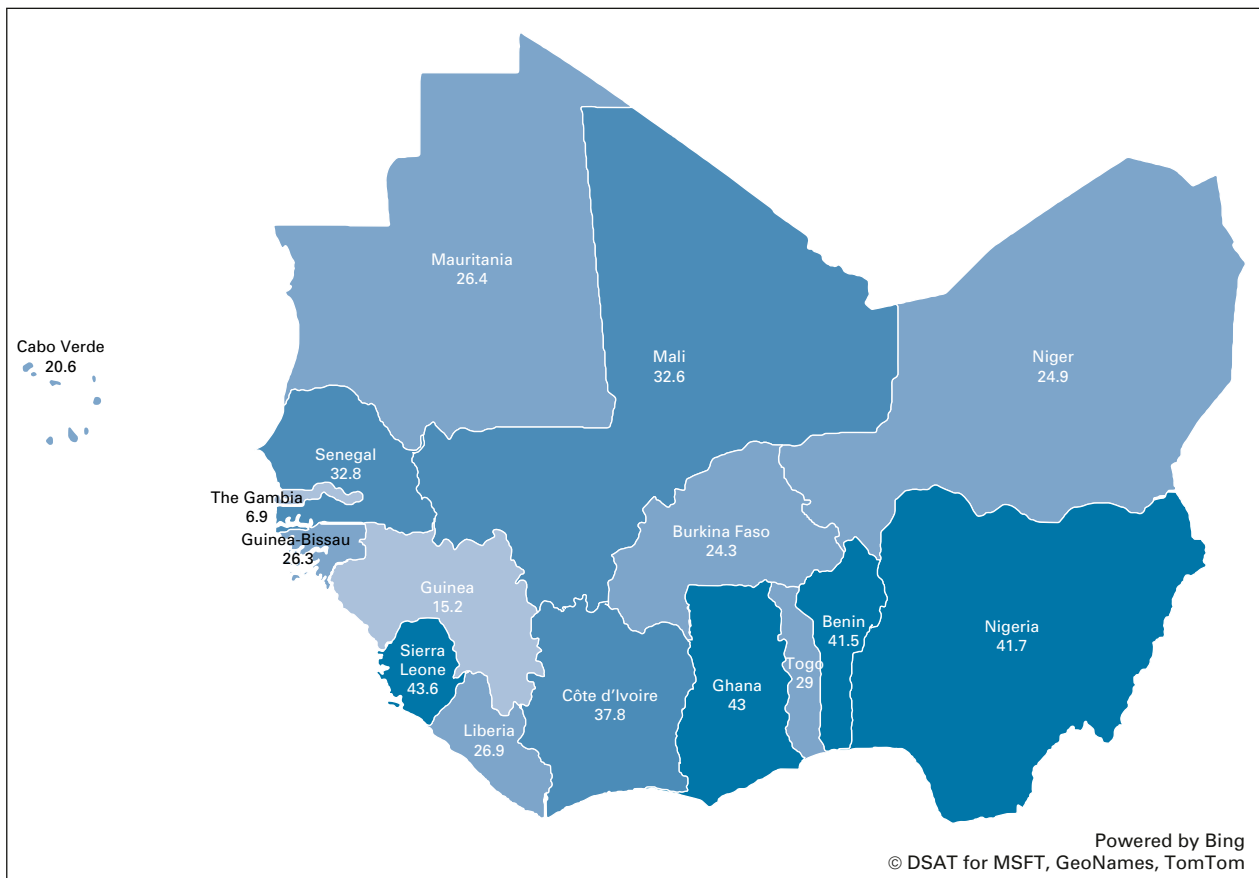
WA women are the most burdened populations in relation to TNBC. Biologic and economic factors have been shown to significantly influence the TNBC disease outcomes. Women's education initiatives, specialist training, and accessible health care are needed in WA countries.

### 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.

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<sup>20</sup> 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%)



**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.

**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 <sup>a</sup>	GDP Per Capita (PPP)	Per Capita Health Expenditure (PPP) (2017)	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.

<sup>a</sup>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.

harbored *BRCA* mutations, including *BRCA1185delAG* (47%), *BRCA1 5382insC* (44%), and *BRCA2 6174delT* (47%).<sup>21</sup> Consistently, numerous *BRCA1* mutations were identified among Burkina Faso women with suspected BC.<sup>22</sup> 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.<sup>23</sup> 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.<sup>24</sup> 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.<sup>24</sup> 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.<sup>25</sup>

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.<sup>26</sup> Jiagge et al<sup>27</sup> 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 PIASy were associated with the clinicopathologic characteristics of TNBC.<sup>28</sup> 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.<sup>29</sup> 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.<sup>30</sup>

### Viral Infections

Viral infections play a critical role in TNBC development.<sup>31</sup> 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

high as 48% in Guinea, with HPV16 commonest variant,<sup>32</sup> and EBV is a highly prevalent virus group, infecting more than 90% of the human population worldwide.<sup>33</sup> In addition to oropharyngeal cancer,<sup>34</sup> HPV has also been linked to cervical cancer,<sup>31</sup> a common malignancy among SSA women. Piana et al<sup>35</sup> 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.<sup>36</sup> 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.<sup>37</sup> EBV may increase malignancy in BC,<sup>38</sup> and a strong correlation between EBV infection and BC development has been reported.<sup>39</sup>

HIV is also common in WA, especially among women in SSA (approximately 2.8 million in West and Central Africa).<sup>40</sup> 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.<sup>41</sup> This remains the case even as the HIV burden is gradually reducing in Africa.<sup>42</sup> Although HIV is not a typical oncovirus, BC incidence is high among HIV-infected women in SSA.<sup>43</sup> 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.<sup>44</sup> The 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.<sup>45-47</sup> 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.<sup>45</sup> John et al<sup>47</sup> 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.<sup>48</sup> This is likely due to a lack of education on exclusive breastfeeding practices, fear of disease transmission,<sup>49</sup> changing perceptions of womanhood,<sup>50</sup> and deep-rooted cultural practices.<sup>49</sup> Moreover, breastfeeding is often initiated late in WA,<sup>51</sup> 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.<sup>52</sup> Women often fear that surgery would tarnish their femininity<sup>53</sup> and may lead to rejection by their spouses,<sup>3</sup> friends, and families.<sup>52,54,55</sup> These fears, however, are not unfounded. Odigie et al<sup>56</sup> 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.<sup>53,57</sup>

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.<sup>58</sup> 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<sup>59</sup> 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.<sup>60</sup> For example, women in rural North Ghana often have to obtain approval from a *Baga* (a male community leader) before seeking medical care.<sup>54</sup> 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 busts is considered shameful in WA, hindering women from seeking BC screening.<sup>52</sup> Hence, many WA women prefer traditional healers and herbal medicines over established screening and treatment methods. Alternative BC therapies are commonly used among Ghanaian,<sup>53</sup> Malian,<sup>61</sup> Ivorian,<sup>62</sup> and Sierra Leonean<sup>63</sup> women. Grosse Frie et al<sup>61</sup> found that Malian women with large tumors (characteristic of TNBC) and who used traditional medicine in tandem with Western medicine had poor survival.

The use of traditional and spiritual healing is linked to polytheistic West African religions.<sup>54</sup> Nevertheless, their efficacy remains controversial.<sup>64</sup> Religious women may view their BC diagnosis as a result of their offending ancestors or divine spirits and would likely go to healers, pastors, imams, or prayer camps for help instead of seeking medical treatment.<sup>57</sup> In Mauritania, BC diagnosis and

treatment are often kept a secret from patients by family and religious leaders and patients have no part in treatment decisions.<sup>65</sup> 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<sup>66</sup>; 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 acid levels, fruit consumption, decreased saturated fat levels, and low-refined carbohydrate consumption with a lower risk of BC occurrence.<sup>67</sup> 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<sup>68</sup> 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.<sup>69</sup> 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.<sup>19</sup> The Carolina Breast Cancer Study identified an increased TNBC incidence among premenopausal and postmenopausal AA women with high waist-to-hip ratios.<sup>70</sup> 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.<sup>71</sup> 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.<sup>69</sup>

**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.<sup>72,73</sup> Although some studies reported no significant relationship between alcohol intake and TNBC,<sup>5,13</sup> others suggested that alcohol promotes TNBC cell migration and invasion.<sup>74</sup> Recent studies have also shown that smoking was not significantly associated with TNBC.<sup>13,75,76</sup> 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).<sup>77</sup> Brinton et al<sup>77</sup> 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.<sup>8</sup>

## Economic Factors

**Income and education.** BC incidence and mortality in LMICs in Africa are rising, especially in WA,<sup>78</sup> where many developing countries with low human development indexes are found.<sup>79</sup> The financial constraints at the governmental, organizational, and individual levels may prevent patients with BC from seeking medical care. Grosse Frie et al<sup>59</sup> 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.<sup>55</sup> Instead, they may use low-quality and outdated medicines.<sup>80</sup> 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.<sup>3,81</sup> Many essential chemotherapeutic and palliative drugs registered on the Essential Medicines List of the WHO remain inaccessible to many patients with BC in SSA.<sup>78,82</sup> As chemotherapeutic drugs, surgery, and radiation therapy are the basis for TNBC treatment,<sup>6</sup> 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.<sup>83</sup>

Furthermore, the lack of formal education and BC awareness poses significant barriers to BC research and management.<sup>3,52</sup> Lack of education has prevented many women, especially those in rural areas, from adopting health care-seeking behavior.<sup>61</sup> Education and language barriers hamper research efforts and render health care inaccessible to patients who only speak indigenous languages.<sup>54</sup> Although certain progress has been made in reproductive health awareness, it is crucial to boost efforts to provide BC-specific education.<sup>52,58</sup> Educating women on BC risk factors, self-examination practices, national health insurance programs,<sup>53</sup> 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.<sup>58,62</sup>

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

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.<sup>54</sup> 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.<sup>52</sup>

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.<sup>3,86</sup> 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.<sup>14</sup>

### 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.<sup>87,88</sup> Typically, QNBCs are chemoresistant<sup>89</sup> and have a poor prognosis.<sup>90</sup> QNBCs are more likely to exhibit aggressive phenotypes than TNBCs,<sup>91</sup> and AR expression is associated with favorable survival outcomes.<sup>92</sup> QNBCs constitute a significant portion of TNBCs in WA.<sup>92</sup> Bhattarai 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.<sup>27</sup> Significant differences in QNBC biology between WA and CA women have also been reported. For instance, Angajala et al<sup>93</sup> 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.<sup>92</sup> In WA women, TNBCs display QNBC-like clinical features (eg, large tumor size and high tumor grade at diagnosis)<sup>91</sup>; hence, QNBC, and not TNBC, may be the bigger challenge among WA women with BC.

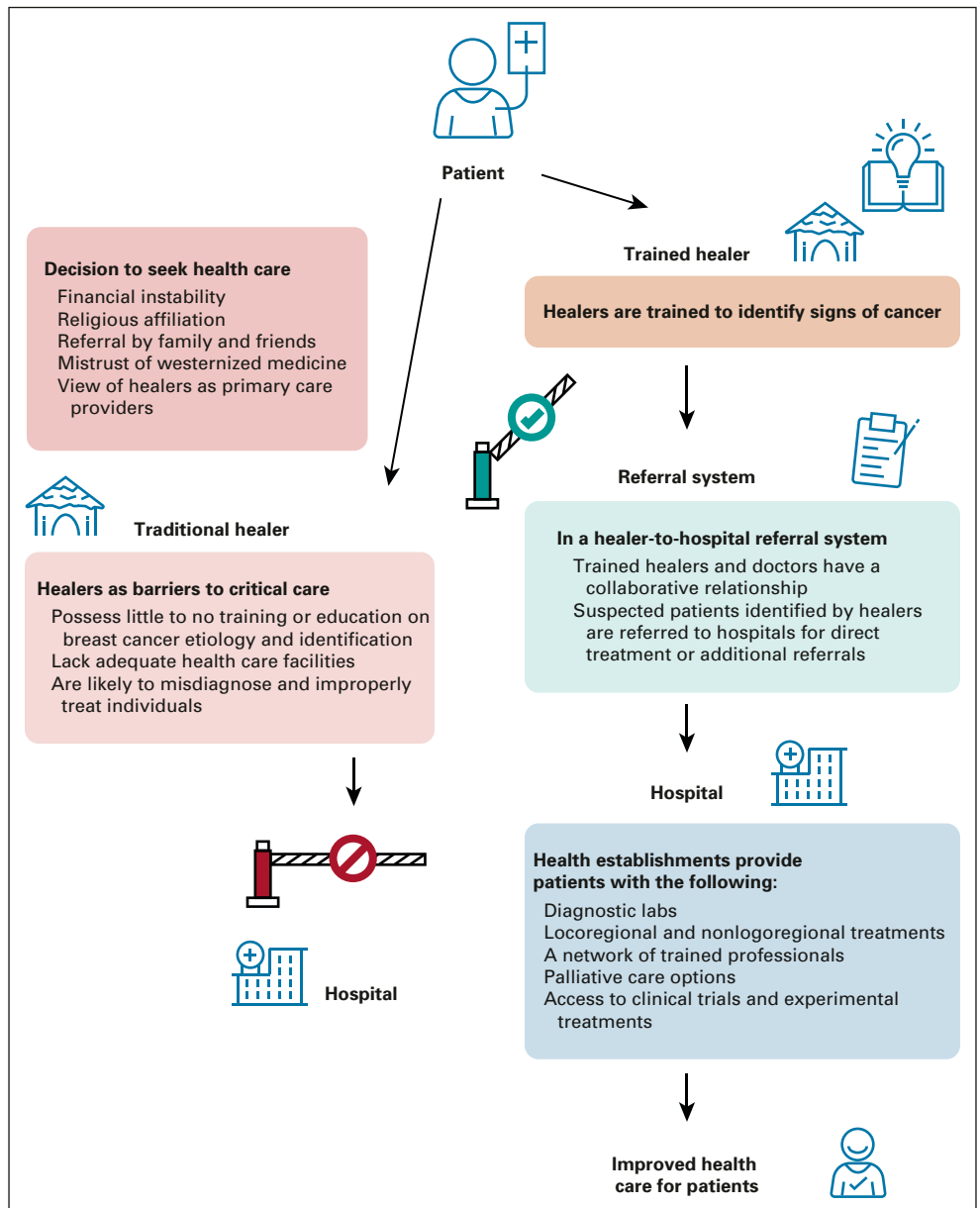
### FUTURE PERSPECTIVES

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.<sup>94</sup> Governments should strive to commercialize such technologies to lower cancer treatment costs.<sup>95</sup> 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.<sup>96</sup>

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,<sup>97</sup> hospitals, health care professionals, and trained local volunteers<sup>52</sup> 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 Sebecly Cancer Care and Support Center in Nigeria have prioritized the education of media professionals, enabling them to

**FIG 2.** Potential patient treatment pathway integrating traditional healers into West African health care systems.



broadcast simple, inexpensive, and easily accessible cancer care tips.<sup>98</sup> 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.<sup>99</sup> The International Atomic Energy Agency and the WHO also provide radiation technology training to African health care professionals.<sup>98</sup>

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.<sup>60</sup> Policies are required to encourage the inclusion of healers into health care systems and foster the establishment of referral systems for cancer screening<sup>100</sup> (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.<sup>101</sup> Razali proposed regular retreats as a means for dialogue and exchange of knowledge<sup>102</sup> and recommended that governments treat traditional healers as primary care providers,<sup>102</sup> providing them with necessary facilities to improve initial patient care.

**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 NGOs Governments	Creates alliances between individuals, NGOs, and governments to educate and provide financial support Aims to reduce global cancer care disparities
African Cancer Registry Network (AFCRN)	—	SSA	African health care systems	Provides training in population-based cancer registration and data use Provides technical support to health workers Improves cancer surveillance in SSA Creates international cancer research projects and networks
African Organization for Research and Training in Cancer (AORTIC)	—	Africa	General public Researchers Clinicians Students	Promotes research on Africa-prevalent cancers Supports oncology training programs for health care workers Conducts international cancer conferences Establishes cancer specialist groups Raises public cancer awareness
African Women's Cancer Awareness Association (AWCAA)	AWCAA Medical Missions	Africa	Women in African communities with limited access to health care Local health institutions	Educates locals on breast health (ie, self-examination and early detection) Trains local health care institutions on community outreach strategies
BIO Ventures for Global Health (BVGH)	African Access Initiative	Africa	Clinics Oncology infrastructure industry	Consolidates data through clinical trials Improves health care infrastructure and clinical oncology capacity Increases access to cancer medicines and treatment technologies
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 Radiation personnel	Educates and trains radiation personnel Provides technical advisory services Provides health care centers with equipment and tools Encourages radiation safety and quality checks Partners with other cancer aid organizations
International Cancer Control Partnership (ICCP)	—	Globally	Health care systems	Creation and implementation of cancer control plans Leverages international networks to maximize collective resources
International Consortium for Advancing Research on TNBC (ICART)	-	Globally	Researchers Exchange students Clinics	Conducts high-quality research in TNBC biology, disparities, and clinical management Maintains international networks among TNBC researchers Consolidates data with the use of available resources Trains exchange students in advanced research areas (eg, histopathology and bioinformatics) Equips clinics with cost-effective assays and technologies for patients with TNBC
National Cancer Institute (NCI)	Center for Global Health	Globally	Researchers Health care systems	Coordinates cancer research initiatives Creates research networks among LMICs Engages in grant provision in low-resource settings Enhances training, peer review, diagnosis, and treatment

(Continued on following page)



**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,<sup>103,104</sup> 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.<sup>104</sup> 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.<sup>8</sup> 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.

## AFFILIATIONS

<sup>1</sup>Department of Biology, Georgia State University, Atlanta, GA

<sup>2</sup>International Consortium for Advancing Research on Triple Negative Breast Cancer, Georgia State University, Atlanta, GA

<sup>3</sup>Department of Population Health Sciences, Georgia State University, Atlanta, GA

<sup>4</sup>Department of Pathology, Ahmadu Bello University, Zaria, Nigeria

## CORRESPONDING AUTHOR

Ritu Aneja, PhD, Department of Biology, Georgia State University, 614 Petit Science Center, 100 Piedmont Ave, Atlanta, GA 30303; e-mail: raneja@gsu.edu.

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## AUTHOR CONTRIBUTIONS

**Conception and design:** Gift C. Nwagu, Shristi Bhattarai, Saad Ahmed, Ritu Aneja

**Administrative support:** Saad Ahmed

**Provision of study materials or patients:** Saad Ahmed

**Collection and assembly of data:** Gift C. Nwagu, Saad Ahmed, Ritu Aneja

**Data analysis and interpretation:** Gift C. Nwagu, Shristi Bhattarai, Monica Swahn, Ritu Aneja

**Manuscript writing:** All authors

**Final approval of manuscript:** All authors

**Accountable for all aspects of the work:** All authors

## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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