Panoptic Overview of Triple-Negative Breast Cancer in Nigeria: Current Challenges and Promising Global Initiatives

abstract

Purpose Triple-negative breast cancer (TNBC) is the most deadly form of breast cancer (BC) today. TNBC treatment is fraught with challenges because of the extensive interpatient heterogeneity in clinical behavior and scarcity of stratifying biomarkers and actionable targets. Women of African ancestry face a disproportionate burden resulting from this disease, which affects them earlier and more aggressively and has a higher propensity to spread and resist conventional treatments. A much higher proportion of Nigerian patients with BC have TNBC compared with patients with BC in the United States and Europe.

Methods This article spotlights Nigeria as an example of a nation wherein genetic and nongenetic spheres of influence intersect to affect the prevalence of this disease, the scale of its challenge, and its toll.

Results Studies have illuminated the inherently different tumor biology of Nigerian TNBCs, which show distinct genetic variants and gene expression patterns compared with European or European-American TNBCs. Parallels are apparent between TNBC phenotypes among African Americans and Nigerians, implicating the common thread of shared genetic ancestry between these populations. Reproductive, lifestyle, socioeconomic, and cultural factors also shape TNBC outcomes in Nigeria, as do resource constraints in Nigerian health care and research sectors.

Conclusion Increasing our understanding of how these factors contribute to poorer outcomes among Nigerian women may uncover valuable insights and strategies in alleviating the TNBC burden in many countries of the world and help reduce the racial disparity in BC-related outcomes here in the United States. Importantly, this review also highlights collaborative global and local initiatives that converge expertise and resources to advance research on effective management of TNBC in diverse populations.

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TRIPLE-NEGATIVE BREAST CANCER: A CONFLUENCE OF COMPLEX CHALLENGES

Triple-negative breast cancer (TNBC) accounts for 20% (approximately 0.17 million) of breast cancer (BC) cases worldwide but remains the most deadly subgroup of BCs.[1] Defined by the absence of therapeutically targetable estrogen receptor (ER), progesterone receptor, and human epidermal growth factor receptor 2 overexpression, TNBCs often present with more aggressive clinicopathologic features (eg, basal-like phenotype, higher grade and stage, greater proliferation) than luminal tumors.[1,2] Currently, no targeted therapies are approved for TNBC; thus, surgery, anthracycline- and taxane-based chemotherapy, and radiation therapy are the primary treatment options for patients with TNBC. Despite these treatments, TNBCs run a high risk of progression, especially within the first 5 years after diagnosis.[3] Rampant interpatient and intratumor heterogeneity render management of this disease complex and warrant deeper dissection of the molecular landscape of TNBC.[4] Nongenetic factors such as health care facilities, resource constraints in patients' countries, and lifestyle, epidemiologic, and cultural factors all collude and contribute to the burden that TNBC imposes on patients and families, as the disease takes away years from life and life from years. Thus, enhancing our understanding of tumor

Table 1. Potential Biomarkers Underlying Nigerian TNBC

Genetic Variant	Detection Technique	Biomarker Description	TNBC Risk Association	Potential Therapeutic Agents
Ancestry informative markers	Genome-wide admixture mapping	SNPs associated with European and African ancestry	ER-positive/PR-positive and early-stage BC associated with European AIMs[13]	
TERT rs10069690 SNP in 5p15	Genome-wide association study	Low-penetrance genetic variant; higher frequency of the allele in women of African ancestry	Strongly associated with ER-negative/PR-negative BC and TNBC[13]	
BRCA1 mutation	Whole-genome sequence analysis	Tumor suppressor gene involved in DNA damage repair; associated with poor prognosis in BC and increased sensitivity to DNA damage agents	Associated with a 50% increased risk for TNBC; prevalence is only approximately 1.4% in AAs but approximately 7% among Nigerian patients with BC[15]	Platinum-based DNA damage agents (eg, cisplatin, carboplatin), PARP inhibitors
Mutant *p53*	IHC	Tumor suppressor gene involved in DNA damage repair; associated with poor survival, metastasis, and chemotherapy resistance in BC	Higher expression in Nigerian BC cases compared with grade-matched BC specimens from United Kingdom; positively correlated with ER-negative/PR-negative BC, TNBC, basal-like phenotype, premenopausal status, younger age at diagnosis, larger tumor size, and LVI; more frequent in Nigerian patients than in UK patients[17]	p53 induction of massive apoptosis (PRIMA-1), WEE1 or CHK1 inhibition, and *p53* mutant–specific inhibitors
Aurora A	IHC	Tumor suppressor and regulator of stem-cell renewal	Overexpression associated with ER-negative/PR-negative status, TNBC, basal-like BC; expression correlated with downregulation of E-cadherin and upregulation of CK5/6 and Ki67 among Nigerian patients with BC[18]	Aurora kinase inhibitors
Ku 70/80	IHC	NHEJ regulator; associated with higher grade, LVI, ER-negative status, and basal-like phenotype among patients with BC	Expression positively correlated with TNBC and basal-like phenotype, metastatic disease, and downregulation of *BRCA1* and *p53*; expression prognostic in Nigerian patients[19]	
Ki67	IHC	Cell proliferation biomarker; expressed higher in AA compared with EA patients with BC	Higher expression in Nigerian patients with BC compared with grade-matched UK patients with BC; expression positively correlated with TNBC status and/or basal-like tumor biology, downregulation of E-cadherin, *BRCA1* mutation, and upregulation of *p53*, CK5/6, and CK16[20]	
PARP1	IHC	Repairs DNA damage (ie, single-strand DNA breaks) through poly-ADP ribosylation to promote cell survival	Expression positively correlated with ER-negative/PR-negative and TNBC status, basal-like BC, higher grade, CK5/6 and CK14 expression, p53, EGFR, Ki67, and PI3KCA expression; poor prognosis biomarker in Nigerian patients with BC[21]	PARP1 inhibitors
PIASγ	IHC	Inhibitor of STAT signaling pathway; E3 SUMO protein ligase; implicated in BRCA1 deficiency and TNBC status	Expression positively correlated with high grade, expression of basal-like biomarkers, ER-negative/PR-negative status, TNBC, basal-like phenotype; poor prognosis biomarker in Nigerian patients with BC[22]	

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Table 1. Potential Biomarkers Underlying Nigerian TNBC (Continued)

Genetic Variant	Detection Technique	Biomarker Description	TNBC Risk Association	Potential Therapeutic Agents
ALDH1	IHC	Cancer stem- and progenitor-cell marker	Higher expression in Ghanian patients with BC; expression associated with TNBC[23]	ALDH1 inhibitors
EZH2	IHC	Oncogene involved in transcriptional repression; strongly association with ER-negative/PR-negative and metastatic BC and poorer clinical outcomes	Overexpression positively correlated with high tumor grade and basal-like phenotype; cytoplasmic EZH2 expression associated with TNBC among Ghanian patients with BC[24]	EZH2 and HMT inhibitors

Abbreviations: AA, African American; AIM, ancestry informative marker; BC, breast cancer; EA, European American; EGFR, epidermal growth factor receptor; ER, estrogen receptor; HMT, histone methyltransferase; IHC, immunohistochemistry; LVI, lymphovascular invasion; NHEJ, nonhomologous end joining; PARP, poly (ADP-ribose) polymerase; PI3K, phosphatidylinositol 3-kinase; PR, progesterone receptor; SNP, single-nucleotide polymorphism; STAT, signal transducer and activator of transcription; TNBC, triple-negative breast cancer.

biology and modifiable factors that influence clinical outcomes, identifying better biomarkers for patient stratification, and developing newer, more effective targeted therapies are critical for improving TNBC management globally.

Several studies have suggested that biogeographic ancestry might be a key driver of aggressive BC. Women of African ancestry are disproportionately affected by TNBC, with poorer clinical outcomes compared with patients with BC of other ethnicities. In the United States, African American (AA) women are two to three times more likely to be diagnosed with TNBC compared with European Americans (EAs).[5] Among patients with TNBC, AAs are more likely to experience rapid disease progression and shorter survival times than EAs. Furthermore, TNBC is significantly more prevalent and presents with higher grade and earlier onset among West African (WA) women compared with AA women.[6] Thus, clearer understanding of the interplay between genetic and nongenetic causes of higher TNBC prevalence in WA women, who share a common ancestry with AAs because of the trans-Atlantic colonial slave trade, may allow us to design better strategies (health care guidelines and policies, preventative measures, strategic investment in infrastructure) to ameliorate global TNBC burden and racial disparity in BC outcomes in the United States. Essentially, this review aims to dissect the complex landscape of Nigerian TNBC to understand drivers of the disproportionate burden of TNBC in WA women and racial disparity in outcomes in the United States and to highlight concerted global and local initiatives and collaborative interventions across multiple stakeholders that aim to drive sustainable change and reduce the devastating footprint of this disease.

RETURNING TO OUR ROOTS: DIGGING DEEP INTO THE LANDSCAPE OF TNBC IN NIGERIA TO BETTER MANAGE TNBC WORLDWIDE

"The roots of education are bitter, but the fruit is sweet." —Aristotle

Ancestry genotyping studies show that the AA population predominantly harbors West or West-Central African ancestry, presumably because of the colonial slave trade.[7] Mortality rates have been reported to be much lower among East African compared with WA patients with BC, suggesting that WA ancestry may explain, at least in part, poorer clinical outcomes between AA and EA patients.[8] Nigeria, the largest and most populous developing country in Africa, exemplifies the current dismal state of BC in WA. There are more than 27,000 new cases of BC annually in Nigeria; roughly 70% to 80% of these patients present with locally advanced or metastatic BC, and nine of 10 of these women die within the first 5 years.[9] The mean age at presentation for Nigerian patients with BC is approximately 43 years, with 74% identified as premenopausal and 12% younger than age 30 years.[10] A large percentage of Nigerian BC cases are often classified as TNBC, although it has been suggested that many of these cases are false negatives, resulting from suboptimal tissue fixation and pathology practices.[11,12] Over the next few sections, we discuss contributions of genetic and nongenetic factors to the etiology and prognosis of TNBC in Nigeria and explore how this knowledge could inform clinicians
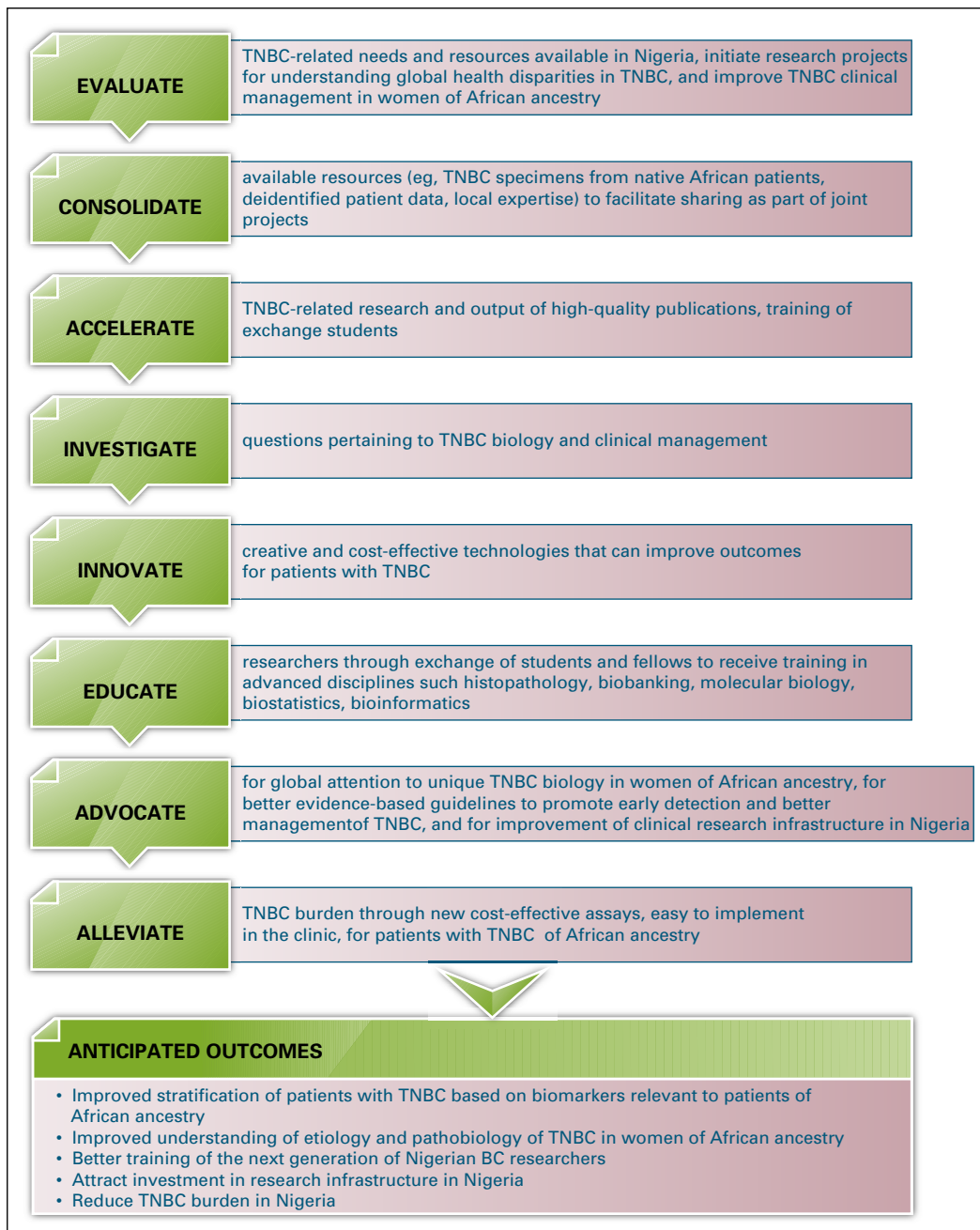
Fig 1. International Consortium for Advancing Research on Triple-Negative Breast Cancer (TNBC) strategic action plan for Nigeria. BC, breast cancer.

EVALUATE TNBC-related needs and resources available in Nigeria, initiate research projects for understanding global health disparities in TNBC, and improve TNBC clinical management in women of African ancestry

CONSOLIDATE available resources (eg, TNBC specimens from native African patients, deidentified patient data, local expertise) to facilitate sharing as part of joint projects

ACCELERATE TNBC-related research and output of high-quality publications, training of exchange students

INVESTIGATE questions pertaining to TNBC biology and clinical management

INNOVATE creative and cost-effective technologies that can improve outcomes for patients with TNBC

EDUCATE researchers through exchange of students and fellows to receive training in advanced disciplines such histopathology, biobanking, molecular biology, biostatistics, bioinformatics

ADVOCATE for global attention to unique TNBC biology in women of African ancestry, for better evidence-based guidelines to promote early detection and better managementof TNBC, and for improvement of clinical research infrastructure in Nigeria

ALLEVIATE TNBC burden through new cost-effective assays, easy to implement in the clinic, for patients with TNBC of African ancestry

ANTICIPATED OUTCOMES
- Improved stratification of patients with TNBC based on biomarkers relevant to patients of African ancestry
- Improved understanding of etiology and pathobiology of TNBC in women of African ancestry
- Better training of the next generation of Nigerian BC researchers
- Attract investment in research infrastructure in Nigeria
- Reduce TNBC burden in Nigeria

about strategies to more effectively overcome the disease.

WE CANNOT HELP WHAT WE ARE BORN WITH: GENETIC RISK FACTORS IN NIGERIAN TNBC

"We can't choose where we come from, but we can choose where we go from there." —Steven Chbosky

The stark disparity in TNBC prevalence and mortality between WA women and women of other ancestral backgrounds has spurred efforts to elucidate its genetic basis, as summarized in Table 1. Studies have identified an association of African ancestry as well as genetic variants, more prevalent among women of African descent, with increased risk for more aggressive BC phenotypes and advanced stage.[13,14] Mutations in tumor suppressor genes such as *BRCA1* have also been implicated in the higher TNBC incidence rate in Nigeria.[15,16] Furthermore, studies have uncovered multiple biomarkers that are generally overexpressed in Nigerian and WA patients with BC and are associated with TNBC

Table 2. Comparison of Breast Clinicopathologic Variables Between Lymph Node–Matched Patients With BC in Nigeria and the United Kingdom

Characteristic	No. (%)		
	United Kingdom[†]	Nigeria[‡]	P[*]
Age, years			< .001
≤ 50	108 (35.1)	187 (60.7)	
> 50	200 (64.9)	121 (39.3)	
Menopausal status			< .001
Pre	128 (41.6)	208 (67.5)	
Post	180 (58.4)	100 (32.5)	
Tumor grade			< .001
1	28 (9.1)	8 (2.6)	
2	98 (31.8)	196 (63.6)	
3	182 (59.1)	104 (33.8)	
Tumor size, cm			< .001
≤ 2	118 (38.3)	27 (8.8)	
> 2	190 (61.7)	281 (91.2)	
Tumor histologic type			< .001
Ductal/NST	199 (64.6)	268 (87.0)	
Tubular mixed	44 (14.3)	17 (5.5)	
Tubular	9 (2.9)	4 (1.3)	
Lobular	22 (7.1)	4 (1.3)	
Mucinous	0 (0.0)	5 (1.6)	
Atypical medullary	5 (1.6)	5 (1.6)	
Mixed NST	5 (1.6)	3 (1.0)	
Tubulolobular	2 (0.7)	1 (0.3)	
Typical medullary	0 (0.0)	1 (0.3)	
Lobular mixed	13 (4.2)	0 (0.0)	
Other	9 (2.9)	0 (0.0)	
Vascular invasion			< .001
Negative	116 (37.7)	76 (24.7)	
Positive	192 (62.3)	232 (75.3)	

Abbreviations: BC, breast cancer; NST, no special type.

*P values were calculated using the χ^2 test.

†British cohort: 308 formalin-fixed, paraffin-embedded (FFPE) specimens from patients with BC presenting between 1986 and 1993 from the Nottingham-Tenovus Primary Breast Carcinoma Series.

‡Nigerian cohort: 308 FFPE specimens from patients with BC presenting from January 2002 to December 2008 at Olabisi University Teaching Hospital in Sagamu and Histopathology Specialist Laboratory Hospital in Idi-Araba, Lagos, Nigeria.

status and aggressive clinicopathologic characteristics (Table 1).[17-24] However, additional research is necessary to uncover selectively targetable inherent tumor biologic characteristics in Nigerian women to improve their disease outcomes. In the United States, the AA population is highly admixed and typically harbors 14% to 21% European ancestry and approximately 1% to 3% Native American ancestry.[25]

Thus, ancestry genotyping, which has hitherto received scant consideration, has to be more firmly embedded in biomarker and drug discovery and development studies and clinical trial designs so that the personal can be more fully reinstated in personalized medicine for TNBC.

NATURE VERSUS NURTURE: WHAT WE KNOW AND NEED TO KNOW ABOUT NONGENETIC RISK FACTORS FOR TNBC IN NIGERIA

"You inherit your environment as much as your genes." —Johnny Rich

Studies are increasingly showing that behavioral and social factors profoundly influence disease risk, and TNBC is no exception. Because these are modifiable via appropriate interventions, their due consideration via a life course approach could affect TNBC diagnoses, prevalence rates, management strategies, and outcomes in Nigeria.

Epidemiologic Risk Factors

Reproductive factors. A positive association between higher parity and increased likelihood of developing TNBC and a negative association between breastfeeding duration and risk of developing TNBC have been detected in AA women.[26,27] Furthermore, one study reported that the use of oral hormonal contraceptives is associated with a 2.9 times greater risk of TNBC in women age between 45 and 64 years.[28] Thus, these associations warrant further study in the Nigerian population.

Anthropometric factors. Obesity has been linked to increased risk for developing TNBC in women of all ethnic backgrounds.[29] Obesity is increasing in Nigeria because of increased consumption of calorie-dense foods.[30] A high hip-to-waist ratio, more prevalent among women of African descent, has been linked to increased risk for developing TNBC or ER-negative/progesterone receptor–negative BC in women of African descent.[27] Furthermore, a study conducted in Nigeria reported that height is significantly linked to increased risk for developing BC; thus, it may be interesting to investigate if height is associated with increased risk of TNBC in Nigeria.[31]

Lifestyle. Diet and nutrition may play a critical role, according to one study, which found that there is an inverse association between a diet high in fruits and vegetables and risk of

Table 3. Comparison of BC Biomarker Status Between Lymph Node–Matched Patients With BC in Nigeria and the United Kingdom

Biomarker	No. (%)		
	United Kingdom[†]	Nigeria[‡]	P[*]
BRCA1			< .001
Negative	29 (11.0)	194 (81.5)	
Positive	235 (89.0)	44 (18.5)	
CK5/8			< .001
Negative	265 (86.9)	166 (64.3)	
Positive	40 (13.1)	92 (35.7)	
CK7/8			< .001
Negative	21 (6.9)	263 (91.0)	
Positive	285 (93.1)	26 (9.0)	
CK14			< .001
Negative	274 (91.3)	132 (58.9)	
Positive	26 (8.7)	92 (41.1)	
CK18			< .001
Negative	63 (21.7)	242 (85.5)	
Positive	227 (78.3)	41 (14.5)	
E-cadherin			< .001
Negative	109 (35.6)	160 (70.8)	
Positive	197 (64.4)	66 (29.2)	
ER			< .001
Negative	82 (27.0)	215 (78.5)	
Positive	222 (73.0)	59 (21.5)	
EGFR			< .001
Negative	228 (82.3)	157 (66.8)	
Positive	49 (17.7)	78 (33.2)	
KI67			.02
Negative	66 (25.7)	46 (17.4)	
Positive	191 (74.3)	218 (82.6)	
MDM2			< .001
Negative	1 (1.1)	205 (82.0)	
Positive	87 (98.9)	45 (18.0)	
P-cadherin			.27
Negative	140 (51.3)	124 (46.6)	
Positive	133 (48.7)	142 (53.4)	
PR			< .001
Negative	125 (40.7)	160 (72.4)	
Positive	182 (59.3)	61 (27.6)	
p21			< .001
Negative	105 (51.2)	157 (71.7)	
Positive	100 (48.8)	62 (28.3)	
p27			.005
Negative	72 (41.6)	119 (56.1)	
Positive	101 (58.4)	93 (43.9)	

(Continued on following page)

developing ER-negative BC.[32-34] Alcohol consumption, smoking, and physical inactivity have all been linked to increased BC risk in Nigeria; thus, it may be worthwhile to investigate their effects on TNBC risk in Nigeria.[35-37]

Socioeconomic status. Irrespective of ancestral background, living in poor socioeconomic conditions can increase a woman's chances of being diagnosed with TNBC over other BC subtypes.[38] Nigeria ranks among the poorest nations in the world, with a population of more than 150 million but a gross domestic product of only US$2,000 per capita annually.[39] A study conducted in a Nigerian tertiary hospital found that almost 45% of the patients declined treatments in the middle of their chemotherapy regimens because of financial instability.[39] Thus, the poor, marginalized, and rural women of the country bear the most acute brunt of the burden of TNBC.

Health literacy and education. A clinical study conducted at the University College Hospital in Ibadan, Nigeria, found that approximately 85% of Nigerian patients with BC presented at an advanced stage.[40] Lack of knowledge of BC signs and symptoms are serious barriers to Nigerian patients receiving timely and adequate treatment. Although some studies report approximately 80% to 92% of Nigerian women are aware of mammography screening, only 3% to 10% are reported to have actually undergone the screening.[41] Studies have revealed that Nigerian women with a higher level of education exhibit more knowledge about breast self-examination (BSE), tend to believe that early BC detection leads to better survival rates, and are more likely to practice BSE compared with those with a lower level of education.[42-44] Studies have also revealed that most Nigerian health care providers lack sufficient knowledge of BC risk factors and the procedure for BSE.[45] Also, single marital status, premenopausal status, fear of discovering a lump, and residing in rural or remote areas have been associated with delay in seeking medical attention in Nigeria.[41,45-49] A majority of Nigerian women obtain their BC information from television (31%), clinics (31%), and health professionals as well as from their elders, friends, and neighbors among rural women according to one study; thus, disparities in socioeconomic status may underlie differences in awareness and stage at presentation between semiurban and rural Nigerian communities.[48,50-52] These studies

Table 3. Comparison of BC Biomarker Status Between Lymph Node–Matched Patients With BC in Nigeria and the United Kingdom (Continued)

Biomarker	No. (%)		
	United Kingdom[†]	Nigeria[‡]	P[*]
p53			< .001
Negative	222 (72.1)	80 (26.0)	
Positive	81 (26.3)	138 (44.8)	
HER2			.08
Negative	265 (86.9)	208 (81.6)	
Positive	40 (13.1)	47 (18.4)	
Triple negative			< .001
No	218 (78.1)	108 (53.5)	
Yes	61 (21.9)	94 (46.5)	
Molecular classification			< .001
Luminal A	211 (70.3)	48 (26.1)	
Luminal B	17 (5.7)	10 (5.4)	
Basal	30 (10.0)	69 (37.5)	
HER2	23 (7.7)	34 (18.5)	

Abbreviations: BC, breast cancer; EGFR, epidermal growth factor receptor; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor.
*P values were calculated using the χ^2 test.
†British cohort: 308 formalin-fixed, paraffin-embedded (FFPE) specimens from patients with BC presenting between 1986 and 1993 from the Nottingham-Tenovus Primary Breast Carcinoma Series.
‡Nigerian cohort: 308 FFPE specimens from patients with BC presenting from January 2002 to December 2008 at Olabisi University Teaching Hospital in Sagamu and Histopathology Specialist Laboratory Hospital in Idi-Araba, Lagos, Nigeria.

highlight a need for continuing medical and health education programs to improve awareness among the Nigerian adult population and health care professionals of early detection to improve outcomes. Several nonprofit organizations or nongovernmental societies and community outreach programs have been established in Nigeria to improve BC awareness to eventually reduce societal, financial, emotional, and health burdens resulting from TNBC.

Cultural Norms and Beliefs

Cultural traditions and spiritual beliefs in Nigeria can influence a patient's decision to seek timely medical treatment. Some Nigerian women believe that unless the swelling or lump in the breast is painful, it is unlikely to be malignant, and they do not need medical attention.[53] Another study found that 17.5% of Nigerian patients with BC initially consulted with traditional healers for treatment, which was associated with a more than 3-month delay until presentation.[54] Also, in some African cultures, people believe that BC is caused by social misconduct, such as oral or nipple contact, or a woman wearing unclean garments.[55] Fear of being divorced by her husband or of being ostracized by the community, fear of disfigurement by surgery, fear of pain or embarrassment during medical examinations (especially if the medical practitioner is of the opposite sex), fear of ineffective treatment, lack of confidence in physicians, belief that surgery accelerates metastasis, fear of death, and other factors, including lack of family support, may also deter a woman from seeking medical help immediately.[55] Thus, to reduce the TNBC burden in Nigeria, there is a critical unmet need to develop a more nuanced understanding of the wider social context of the human lives it affects and develop focused interventions to address all exacerbating factors.

Other Potential Risk Factors

Infectious agents or environmental estrogens such as insecticides and dichlorodiphenyltrichloroethane, used for preventing insect-borne diseases like malaria, are postulated to elevate risk for developing hormonal-related diseases, because they can alter hormone levels.[43] Cosmetic products frequently used among African women, such as hair relaxers and skin lighteners, may also be contributing to increased risk for TNBC among Nigerian women, because these contain dangerous carcinogens and/or hormonally active compounds.[43] Their potential influence on TNBC risk in Nigeria merits further study.

ADDING FUEL TO THE FIRE: CHALLENGES IN TNBC CARE AND TREATMENT IN NIGERIA

"Access to healthcare shouldn't depend on your postcode." —Richard Di Natale

The resource-constrained Nigerian health care system, lack of education and empowerment, poverty, shortage of well-trained health care personnel, and inadequate research infrastructure, as compared with other countries in the world such as the United States, have had significant adverse impacts on TNBC outcomes among the Nigerian population.
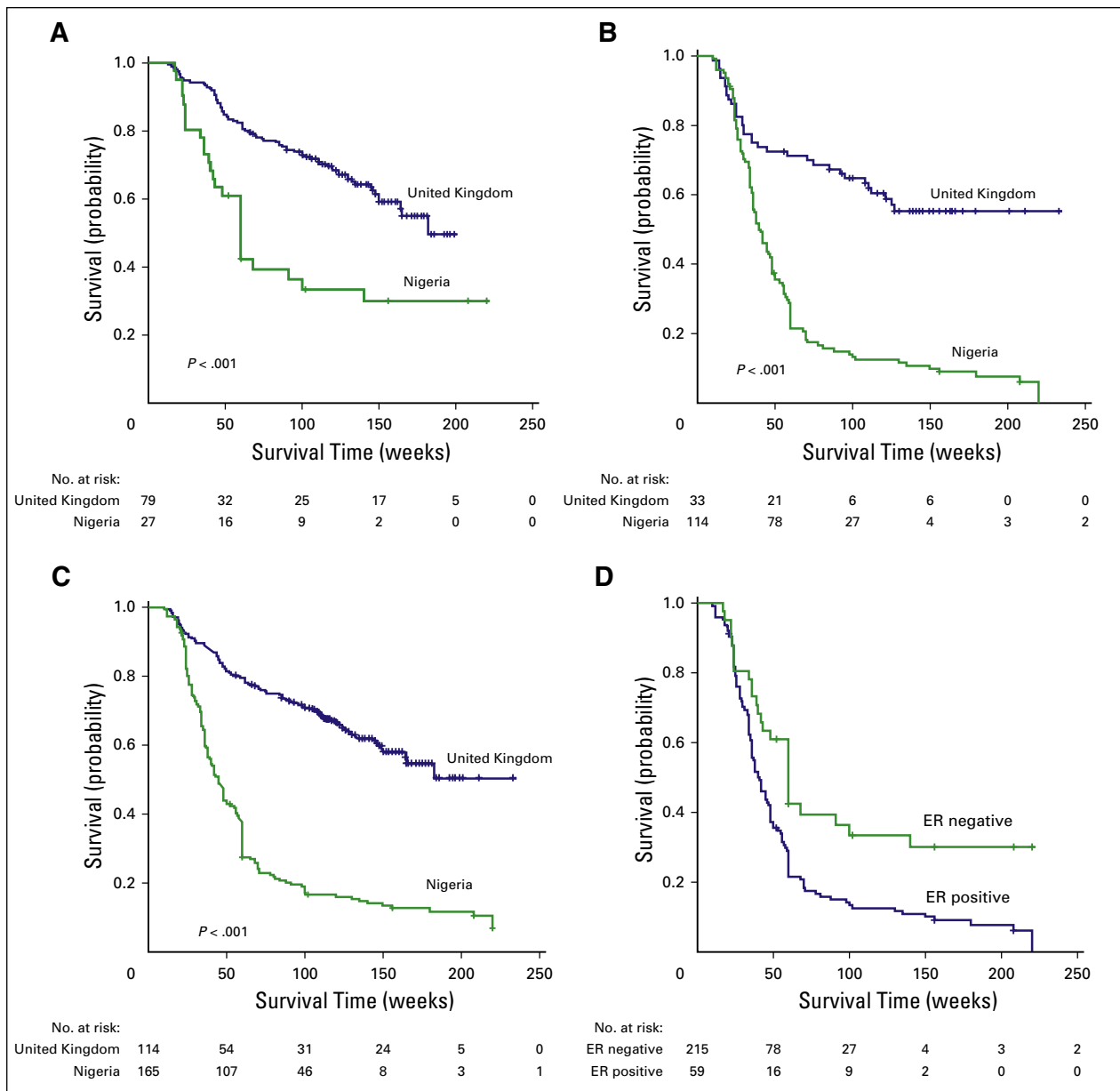
Fig 2. Overall survival comparison between patients with breast cancer (BC) in Nigeria and the United Kingdom. Overall survival of lymph node–matched patients with BC in Nigeria (n = 308) and the United Kingdom (n = 308) observed at Olabisi University Teaching Hospital in Sagamu, Nigeria, and the Nottingham-Tenuous Primary Breast Carcinoma Series, respectively, among (A) estrogen receptor (ER) –positive, (B) ER-negative, and (C) all cases. (D) Overall survival among Nigerian patients with ER-negative and ER-positive disease. Nigerian patients presented between January 2002 and December 2008, and UK patients presented between 1986 and 1993.

Inadequate Health Care Infrastructure

A study conducted in a Nigerian teaching hospital in southwestern Nigeria found that the average duration between onset of BC symptoms and presentation was approximately 11.2 months, and approximately 39% of women presented with fungating tumors.[43] In addition to aforementioned cultural and awareness-related factors, the delay in seeking medical attention may also be attributed to prohibitive cost of treatment, lack of transportation or access to radiology and chemotherapy facilities, and hospital overcrowding.[56-60] In Nigeria, out-of-pocket expenditure for health care was an alarming 95.7% in 2014 according to the WHO. WHO reported that Nigeria allocates only $67 per person for health care, and financial constraints were the primary reason for patients with BC discontinuing treatments. Quality of health care also leaves much to be desired, and inappropriate surgeries and biopsy management lead
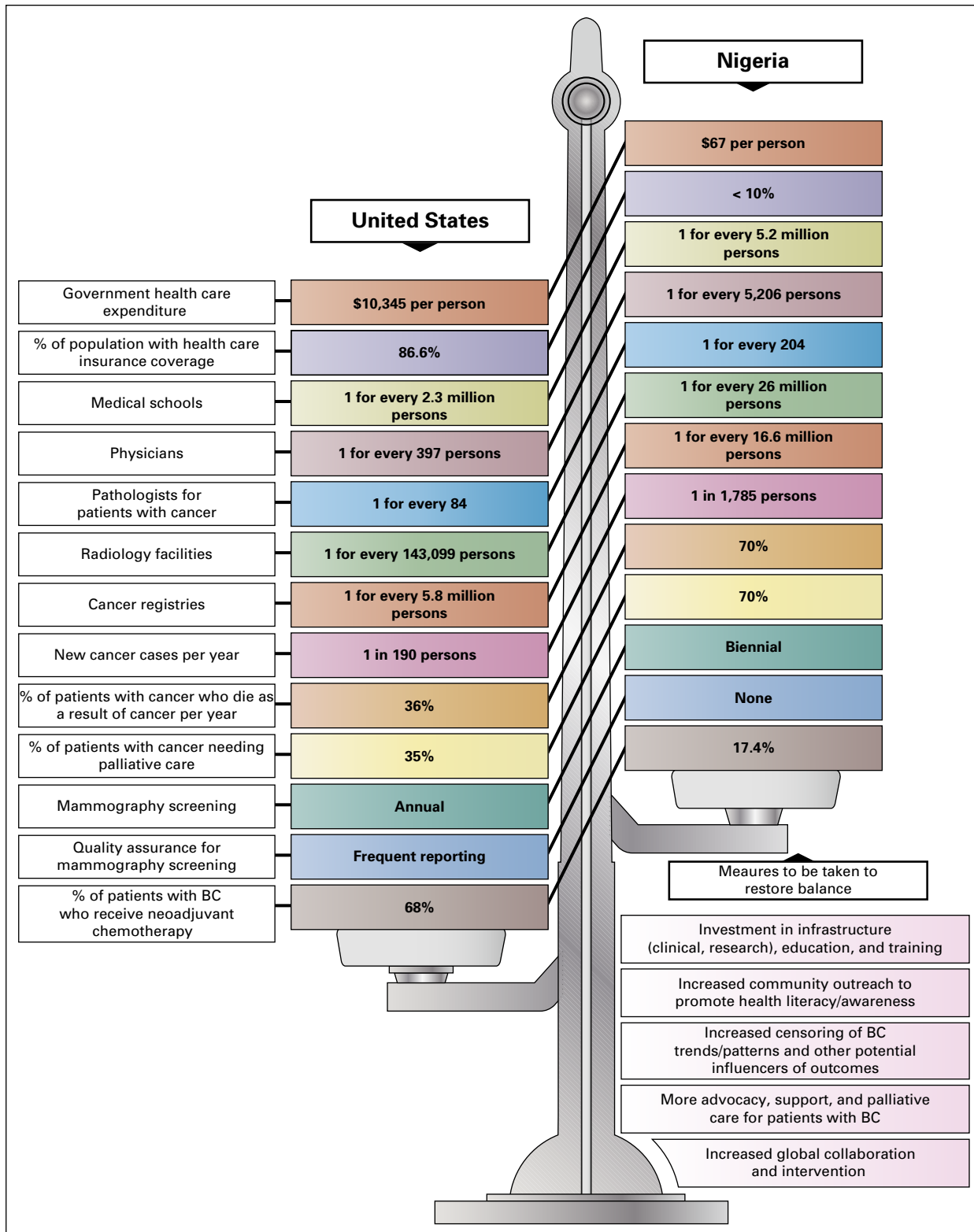
Fig 3. Comparison of health care infrastructure in Nigeria and the United States. BC, breast cancer.

to late-stage presentation.[61] Palliative care is often the only option for patients diagnosed in advanced stages; however, pain medications are often limited or unavailable, especially in rural areas.[62]

Inferior health care infrastructure, especially paucity of facilities for BC detection and treatment, majorly underlies late presentation and poor clinical outcomes among Nigerian patients with TNBC. Nigeria is one of the least developed

countries with regard to oncology services, resources, and radiation therapy facilities.[9] Nigeria houses seven radiotherapy laboratories; however, only 15% of the reported 4 million Nigerians needing radiotherapy have access to these facilities.[63,64] Furthermore, lack of trained personnel to properly operate radiotherapy equipment results in poor maintenance and equipment malfunction.[9] The majority of the radiology equipment at cancer treatment centers is considered nonfunctional because of a lack of qualified personnel who can properly handle the equipment.[65] The frequent breakdown of radiotherapy equipment may be attributed to equipment procurement without consultation or advice from end users, unreliable electricity, high cost of operation, bottlenecks in securing spare parts, absence of maintenance contracts with suppliers, and lack of quick response from foreign engineers when equipment malfunctions.[9] In addition, mammography facilities are scarce in Africa, and they inadequately detect cancer in women with dense breasts.[66] Mammography screening may not detect all tumors in women at the premenopausal age, when the bulkiness of the breast is often an interference in Nigerian women.[11,67] Furthermore, public hospitals are often overcrowded, lack human resources, and require long waiting periods, which stalls screening, diagnosis, and treatment of patients.[68] Also, lack of follow-up and poor patient recordkeeping in clinics interfere with determination of specific factors influencing survival patterns for refinement of treatment plans.[39]

Pathology practices. Subpar pathology practices are prevalent in many centers in Nigeria and often result in inaccurate diagnoses and consequently inappropriate treatment. Incorrect immunohistochemistry results attributable to poor tissue collection or processing, delayed fixation or overfixation, poor-quality reagents, incorrect laboratory techniques, and lack of quality assurance practices are often prime suspects. Records about cause of death are often not notifiable or centrally maintained. Although Nigeria is one of the few African countries that have published guidelines, created by the Nigeria Breast Pathology Working Group in 2010, on standardized pathology reporting, these guidelines have not been adequately circulated or implemented in medical centers. Daramola et al[69] compared histologic parameters in pathology reports from a teaching hospital in Nigeria with the cancer data set of the Royal College of Pathologists in the United Kingdom to verify compliance and concordance. Almost half of the Nigerian BC cases examined were discordant with the Royal College of Pathologists, and roughly half of the cases were either undergraded or overgraded. Poor fixation and exclusion of mitotic count were underlying factors for discordant grading. Thus, proper training and education of Nigerian pathologists are critical to improving accuracy in BC diagnosis and reporting. Templates or proformas have been suggested for use by African pathologists to guide accurate reporting.

Lack of health care personnel. The severe shortage of competent health care providers, including oncologists, radiologists, surgeons, and pathologists, has also contributed to the poor BC-related outcomes in Nigeria. The number of physicians per 100,000 people in Africa is presently 12, which is much lower than the 387 physicians per 100,000 people in Europe.[70,71] The number of physicians per 100,000 people in Nigeria is currently 18.8, which is much lower than the numbers per 100,000 people in most Western nations, including the United States, where there are approximately 148 physicians per 100,000 people.[71,72] Nigeria currently ranks seventh highest among 57 countries in the world facing a health care shortage crisis, according to the Federal Ministry of Health. Adebayo et al[72] reported that there are 33.% and 29.3% gaps in the supply of doctors and nurses, respectively, in Nigeria.[72] The shortage of pathologists in Nigeria is also extreme, with only 6% of practicing specialist physicians certified as pathologists.[73] Furthermore, Nigeria possesses fewer than 40 trained radiation oncologists to provide radiology services and meet the needs of the growing population of patients with cancer.[65] The paucity of practicing clinicians in African countries can be attributed to a significant reduction (6% to 18%) in medical school teaching staff, who have opted to emigrate over the past 5 years (phenomenon known as brain drain).[73,74] Many trainees often leave countries in sub-Saharan Africa for developing countries because of inadequate infrastructure to practice, poor working conditions, and low remuneration.[73] Implementing strategies to attract more African health care personnel, such as raising salaries and improving working conditions, will be crucial to ensuring adequate patient coverage. Fortunately, Nigeria possesses a number of highly skilled, motivated,

and overseas-trained clinicians who can serve as conduits for revamping health care and conquering challenges of TNBC management.

Research

Research provides the evidence base on which cancer prevention, control, and treatment strategies are built. The numbers of cancer researchers, including epidemiologists, statisticians, scientists, public health experts, health economists, and behavioral scientists, in Africa are limited. Although Nigeria is among the top countries in Africa for publishing research articles on BC, cutting-edge research is still lacking.[75] There is also a significant shortage of cancer registries and trained cancer registry personnel. In 2006, only 11% of the African population was covered by a cancer registry.[76] Nigeria has many population-based cancer registries, such as the Ibadan Cancer Registry located in South West Nigeria and the Abuja Cancer Registry located in North Central Nigeria.[77] Both ensure high-quality cancer data; however, together they cover only 2.5% of the Nigerian population. In addition, the scarcity of data on cancer statistics and trends may be a result of government prioritization of funding of research on communicable diseases, rather than cancer research, infrastructure, or treatment. Furthermore, cancer advocates and trained community health care workers responsible for educating the public and policymakers on cancer are unable to meet the needs of the nation.

TAKING MATTERS INTO OUR OWN HANDS: THE INTERNATIONAL CONSORTIUM FOR ADVANCING RESEARCH ON TNBC

"United we conquer, divided we fall." —Aesop

The increased global awareness of the alarming worldwide BC burden has sparked the launch of several global and local initiatives targeting BC and TNBC globally and in Nigeria (Appendix Table A1). However, global initiatives centered on alleviating the TNBC burden in Nigeria and around the world are almost nonexistent. In view of this unmet need to improve outcomes for patients with TNBC by invigorating multidisciplinary research on the fundamental biology of TNBC in diverse populations, our group, along with a leading BC research group led by Emad Rakha, MD, from Nottingham City Hospital

(Nottingham, United Kingdom), jointly founded the International Consortium for Advancing Research on TNBC (ICART), a global coalition of TNBC researchers from the United States, Europe, Asia, and Africa. The mission of ICART is to consolidate, streamline, and share resources and mobilize and synergize complementary strengths to conduct large-scale multi-institutional and high-impact clinical, translational, and population-based research projects related to TNBC (Fig 1). ICART includes a network of 14 teaching hospitals across the length and breadth of Nigeria, and ICART researchers have already uncovered previously unrecognized disparities in breast clinicopathologic variables (Table 2), biomarker expression (Table 3), and survival (Fig 2) between lymph node–matched Nigerian and UK patients with BC that may underlie the stark disparity in clinical outcomes between these populations. ICART aims to leverage its network of highly skilled and well-qualified Nigerian clinicians and researchers to place Nigeria on the map for excellence in scientific research and health policy among low- to middle-income countries

CHALLENGES OF TNBC: OPPORTUNITIES FOR GROWTH

This review spotlights TNBC in Nigeria, where the disease has reached crisis levels. Insights generated from underlying drivers of this high prevalence would affect our understanding of the etiology and biology of TNBC globally; guide research to improve clinical management of TNBC, especially in women of African ancestry; and help design evidence-based, patient-centered, holistic, and efficacious policy frameworks and health awareness programs that factor in resource constraints while targeting key risk factors and cultural issues that may be exacerbating the burden of TNBC in certain nations or ethnic groups. The stark gap in adequate cancer care between Nigeria and the United States and strategies to reduce this gap are shown in Figure 3. The challenges presented by TNBC worldwide and racial disparity in the United States require multilevel solutions and interventions, because the upstream determinants of outcomes span multiple domains of influence that are complexly intertwined. True impact will require targeted global initiatives like ICART, robust partnerships among governments and implementing

agencies, judicious resource allocation, political will, incentives to promote innovation, team science, and focus on grassroots measures that have both the required reach and efficacy.

"Success is a staircase, not a doorway." —Dottie Walters

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AUTHORS' DISCLOSURES OF
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REFERENCES

1. Boyle P: Triple-negative breast cancer: Epidemiological considerations and recommendations. Ann Oncol 23:vi7-vi12, 2012 (suppl 6)

2. Rhee J, Han SW, Oh DY, et al: The clinicopathologic characteristics and prognostic significance of triple-negativity in node-negative breast cancer. BMC Cancer 8:307, 2008

3. Dent R, Trudeau M, Pritchard KI, et al: Triple-negative breast cancer: Clinical features and patterns of recurrence. Clin Cancer Res 13:4429-4434, 2007

4. Wright N, Rida PCG, Aneja R: Tackling intra- and inter-tumor heterogeneity to combat triple negative breast cancer. Front Biosci 22:1549-1580, 2017

5. Proctor E, Kidwell KM, Jiagge E, et al: Characterizing breast cancer in a population with increased prevalence of triple-negative breast cancer: Androgen receptor and ALDH1 expression in Ghanaian women. Ann Surg Oncol 22:3831-3835, 2015

6. Huo D, Ikpatt F, Khramtsov A, et al: Population differences in breast cancer: Survey in indigenous African women reveals over-representation of triple-negative breast cancer. J Clin Oncol 27:4515-4521, 2009

7. Stefflova K, Dulik MC, Barnholtz-Sloan JS, et al: Dissecting the within-Africa ancestry of populations of African descent in the Americas. PLoS One 6:e14495, 2011

8. Ferlay J, Shin HR, Bray F, et al: Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 127:2893-2917, 2010

9. Adewuyi A: The Current Status of Cancer Care in Nigeria: Stop Breast Cancer From Taking Her Life. http://ceafon.com/wp-content/uploads/2016/05/CEAFON-2015-CONFERENCE-THE-CURRENT-STATUS-OF-CANCER-CARE-IN-NIGERIA-PROF-ADEWUYI-FINAL-october-28.pdf

10. Arowolo OA, Njiaju UO, Ogundiran TO, et al: Neo-adjuvant capecitabine chemotherapy in women with newly diagnosed locally advanced breast cancer in a resource-poor setting (Nigeria): Efficacy and safety in a phase II feasibility study. Breast J 19:470-477, 2013

11. Adisa CA, Eleweke N, Alfred AA, et al: Biology of breast cancer in Nigerian women: A pilot study. Ann Afr Med 11:169-175, 2012

12. Adebamowo CA, Famooto A, Ogundiran TO, et al: Immunohistochemical and molecular subtypes of breast cancer in Nigeria. Breast Cancer Res Treat 110:183-188, 2008

13. Fejerman L, Haiman CA, Reich D, et al: An admixture scan in 1,484 African American women with breast cancer. Cancer Epidemiol Biomarkers Prev 18:3110-3117, 2009

14. Palmer JR, Ruiz-Narvaez EA, Rotimi CN, et al: Genetic susceptibility loci for subtypes of breast cancer in an African American population. Cancer Epidemiol Biomarkers Prev 22:127-134, 2013

15. Fackenthal JD, Zhang J, Zhang B, et al: High prevalence of BRCA1 and BRCA2 mutations in unselected Nigerian breast cancer patients. Int J Cancer 131:1114-1123, 2012

16. Malone KE, Daling JR, Doody DR, et al: Prevalence and predictors of BRCA1 and BRCA2 mutations in a population-based study of breast cancer in white and black American women ages 35 to 64 years. Cancer Res 66:8297-8308, 2006

17. Agboola AO, Banjo AA, Anunobi CC, et al: Molecular profiling of breast cancer in Nigerian women identifies an altered p53 pathway as a major mechanism underlying its poor prognosis compared with British counterpart. Malays J Pathol 36:3-17, 2014

18. Agboola AO, Ayodeji OJ, Ebili E, et al: Aurora A kinase expression in Nigerian breast cancer patients and correlation with clinicopathological, biological and prognostic features. Afri J Sci Nat 2:53-64, 2016

19. Agboola AO, Ebili HO, Iyawe VO, et al: Clinicopathological and molecular characteristics of Ku 70/80 expression in Nigerian breast cancer and its potential therapeutic implications. Pathol Res Pract 213:27-33, 2017

20. Agboola AO, Banjo AA, Anunobi CC, et al: Cell proliferation (KI-67) expression is associated with poorer prognosis in Nigerian compared to British breast cancer women. ISRN Oncol 2013:675051, 2013

21. Agboola AO, Banjo AAF, Anunobi C, et al: Clinical and molecular significance of poly (ADP-ribose) polymerase-1 (PARP-1) in breast cancer of African women and its potential as a targeted therapy. J Cancer Res Treat 2:24-30, 2013

22. Agboola A, Musa A, Banjo A, et al: PIASγ expression in relation to clinicopathological, tumour factors and survival in indigenous black breast cancer women. J Clin Pathol 67:301-306, 2014

23. Schwartz T, Stark A, Pang J, et al: Expression of aldehyde dehydrogenase 1 as a marker of mammary stem cells in benign and malignant breast lesions of Ghanaian women. Cancer 119:488-494, 2013

24. Pang J, Toy KA, Griffith KA, et al: Invasive breast carcinomas in Ghana: High frequency of high grade, basal-like histology and high EZH2 expression. Breast Cancer Res Treat 135:59-66, 2012

25. Baharian S, Barakatt M, Gignoux CR, et al: The great migration and African-American genomic diversity. PLoS Genet 12:e1006059, 2016

26. Brewster AM, Chavez-MacGregor M, Brown P: Epidemiology, biology, and treatment of triple-negative breast cancer in women of African ancestry. Lancet Oncol 15:e625-e634, 2014

27. Millikan RC, Newman B, Tse CK, et al: Epidemiology of basal-like breast cancer. Breast Cancer Res Treat 109:123-139, 2008 [Erratum: Breast Cancer Res Treat 109:141, 2008]

28. Ma H, Wang Y, Sullivan-Halley J, et al: Use of four biomarkers to evaluate the risk of breast cancer subtypes in the women's contraceptive and reproductive experiences study. Cancer Res 70:575-587, 2010

29. Bandera EV, Maskarinec G, Romieu I, et al: Racial and ethnic disparities in the impact of obesity on breast cancer risk and survival: A global perspective. Adv Nutr 6:803-819, 2015

30. Misra A, Ganda OP: Migration and its impact on adiposity and type 2 diabetes. Nutrition 23:696-708, 2007

31. Ogundiran TO, Huo D, Adenipekun A, et al: Case-control study of body size and breast cancer risk in Nigerian women. Am J Epidemiol 172:682-690, 2010

32. Emaus MJ, Peeters PH, Bakker MF, et al: Vegetable and fruit consumption and the risk of hormone receptor-defined breast cancer in the EPIC cohort. Am J Clin Nutr 103:168-177, 2016

33. Jung S, Spiegelman D, Baglietto L, et al: Fruit and vegetable intake and risk of breast cancer by hormone receptor status. J Natl Cancer Inst 105:219-236, 2013

34. Boggs DA, Palmer JR, Wise LA, et al: Fruit and vegetable intake in relation to risk of breast cancer in the Black Women's Health Study. Am J Epidemiol 172:1268-1279, 2010

35. Qian F, Ogundiran T, Hou N, et al: Alcohol consumption and breast cancer risk among women in three sub-Saharan African countries. PLoS One 9:e106908, 2014

36. Okobia MN, Bunker CH, Zmuda JM, et al: Anthropometry and breast cancer risk in Nigerian women. Breast J 12:462-466, 2006

37. Agbo SP, Oboirien M: Risk factors for breast cancer in Sokoto, Nigeria. Merit Res J Med Med Sci 4:465-471, 2016

38. Parise CA, Caggiano V: Risk factors associated with the triple-negative breast cancer subtype within four race/ethnicities. Breast Cancer Res Treat 163:151-158, 2017

39. Adisa AO, Arowolo OA, Akinkuolie AA, et al: Metastatic breast cancer in a Nigerian tertiary hospital. Afr Health Sci 11:279-284, 2011

40. Ntekim A, Nufu FT, Campbell OB: Breast cancer in young women in Ibadan, Nigeria. Afr Health Sci 9:242-246, 2009

41. Ojewusi AA, Obembe T, Arulogun OS, et al: Breast cancer awareness, attitude and screening practices in Nigeria: A systemic review. Clin Rev Opinions 7:11-25, 2016

42. Popoola AO, Wright KO, Igwilo AI, et al: Literacy and breast cancer diagnosis and treatment among patients in a tertiary health institution of Lagos, Nigeria. J Dent Med Sci 5:49-54, 2013

43. 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

44. Isara AR, Ojedokun CI: Knowledge of breast cancer and practice of breast self examination among female senior secondary school students in Abuja, Nigeria. J Prev Med Hyg 52:186-190, 2011

45. Akhigbe AO, Omuemu VO: Knowledge, attitudes and practice of breast cancer screening among female health workers in a Nigerian urban city. BMC Cancer 9:203, 2009

46. Ibrahim NA, Oludara MA: Socio-demographic factors and reasons associated with delay in breast cancer presentation: A study in Nigerian women. Breast 21:416-418, 2012

47. McDonald JT, Sherman A: Determinants of mammography use in rural and urban regions of Canada. Can J Rural Med 15:52-60, 2010

48. Oluwatosin OA, Oladepo O: Knowledge of breast cancer and its early detection measures among rural women in Akinyele Local Government Area, Ibadan, Nigeria. BMC Cancer 6:271, 2006

49. Oluwatosin OA: Assessment of women's risk factors for breast cancer and predictors of the practice of breast examination in two rural areas near Ibadan, Nigeria. Cancer Epidemiol 34:425-428, 2010

50. Okobia MN, Bunker CH, Okonofua FE, et al: Knowledge, attitude and practice of Nigerian women towards breast cancer: A cross-sectional study. World J Surg Oncol 4:11, 2006

51. Maree JE, Wright SC: Cervical cancer: Does our message promote screening? A pilot study in a South African context. Eur J Oncol Nurs 15:118-123, 2011

52. Akuoko 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

53. Pruitt L, Mumuni T, Raikhel E, et al: Social barriers to diagnosis and treatment of breast cancer in patients presenting at a teaching hospital in Ibadan, Nigeria. Glob Public Health 10:331-344, 2015

54. Ezeome ER: Delays in presentation and treatment of breast cancer in Enugu, Nigeria. Niger J Clin Pract 13:311-316, 2010

55. Coughlin SS, Ekwueme DU: Breast cancer as a global health concern. Cancer Epidemiol 33:315-318, 2009

56. Vanderpuye V, Grover S, Hammad N, et al: An update on the management of breast cancer in Africa. Infect Agent Cancer 12:13, 2017

57. Akanbi OO, Adeoti ML, Aremu AA, et al: Financial burden of managing metastatic breast cancer in Sub-Saharan Africa. J Dent Med Sci 15:152-157, 2016

58. Awosusi A, Folaranmi T, Yates R: Nigeria's new government and public financing for universal health coverage. Lancet Glob Health 3:e514-e515, 2015

59. Adisa AO, Gukas ID, Lawal OO, et al: Breast cancer in Nigeria: Is non-adherence to chemotherapy schedules a major factor in the reported poor treatment outcome? Breast J 16:206-207, 2010

60. Donkor A, Lathlean J, Wiafe S, et al: Factors contributing to late presentation of breast cancer in Africa: A systematic literature review. Arch Med 8:1-10, 2015

61. Ukwenya AY, Yusufu LM, Nmadu PT, et al: Delayed treatment of symptomatic breast cancer: The experience from Kaduna, Nigeria. S Afr J Surg 46:106-110, 2008

62. Jemal A, Bray F, Forman D, et al: Cancer burden in Africa and opportunities for prevention. Cancer 118:4372-4384, 2012

63. Cancer: Nigeria has only 7 radiotherapy machines, 5 are faulty. http://www.premiumtimesng.com/news/headlines/193757-cancer-nigeria-has-only-7-radiotherapy-machines-5-are-faulty.html

64. Adetifa F, Ojikutu R: Prevalence and trends in breast cancer in Lagos State, Nigeria. Afri Res Rev 3:1-15, 2009

65. Sunday AA, Oladapo BC, Kingsley KK, et al: Current status of radiation oncology facilities in Nigeria. West Afr J Radiol 20:30-36, 2013

66. Galukande M, Kiguli-Malwadde E: Rethinking breast cancer screening strategies in resource-limited settings. Afr Health Sci 10:89-92, 2010

67. Checka CM, Chun JE, Schnabel FR, et al: The relationship of mammographic density and age: implications for breast cancer screening. AJR Am J Roentgenol 198:W292-5, 2012

68. Busolo DS, Woodgate RL: Cancer prevention in Africa: A review of the literature. Glob Health Promot Educ 22:31-39, 2015

69. Daramola AO, Banjo AA, Bennett A, et al: Breast cancer reporting in Lagos, Nigeria: Implications for training and education in Africa. J Glob Oncol 2:397-402, 2016

70. Ogunbiyi JO, Stefan DC, Rebbeck TR: African Organization for Research and Training in Cancer: Position and vision for cancer research on the African Continent. Infect Agent Cancer 11:63, 2016

71. Population Division, United Nations Department of Economic and Social Affairs: World population prospects: The 2017 revision. https://esa.un.org/unpd/wpp/DataQuery/

72. Adebayo O, Labiran A, Emerenini CF, et al: Health workforce for 2016-2030: Will Nigeria have enough? Int J Innovative Healthcare Res 4:9-16, 2016

73. Adedeji OA: Cancer in Sub-Saharan Africa: Current Practice and Future. Springer International Publishing Company, Cham, Switzerland. 2017., 55 pp.

74. Mullan F, Frehywot S, Omaswa F, et al: Medical schools in sub-Saharan Africa. Lancet 377:1113-1121, 2011

75. Kantelhardt EJ, Muluken G, Sefonias G, et al: A review on breast cancer care in Africa. Breast Care (Basel) 10:364-370, 2015

76. O'Brien KS, Soliman AS, Awuah B, et al: Establishing effective registration systems in resource-limited settings: Cancer registration in Kumasi Ghana. J Registry Manag 40:70-77, 2013

77. Jedy-Agba E, Curado MP, Ogunbiyi O, et al: Cancer incidence in Nigeria: A report from population-based cancer registries. Cancer Epidemiol 36:e271-e278, 2012

Appendix

Table A1. Initiatives That Aid in Reducing Burden of TNBC in Nigeria

Agency	Level	Initiative Type	Objective or Action	Potential Effect in Nigeria
International Atomic Energy Agency	Global	Governmental	Increase the number of effective and safe radiotherapy treatment centers available in developing African countries	Increased access to radiotherapy for patients with BC or TNBC
International Academy of Pathologists	Global	Health care	Educational exchanges on scientific, technologic, and methodologic advances in pathology practices	Improvement in quality and knowledge of proper pathology practices; more accurate diagnoses and patient record keeping/follow-up
African Organization for Research and Training	Continental	Research	Established the Cancer Plan for the African Continent (2013-2017) to revamp policy and funding for cancer research, increase public awareness and knowledge of the cancer burden in Africa, advance clinical oncology infrastructure and cancer health systems, and improve cancer prevention and control efforts	Development and improvement of regional infrastructure to support basic and translational BC and TNBC research (into areas like surveillance, genetic testing, decision making, propagation of evidence for intervention, epidemiology, and measurement)
International Agency on Cancer Research	Global	Research	Promote the development of cancer registries in multiple countries across Africa	Improved reporting of BC and TNBC trends and patterns
Breast Health Global Initiative	Global	Health care	Revamp health care infrastructure and increase education and awareness of early detection methods and risk factors	Earlier detection of BC and TNBC for timely intervention; improved facilities and treatment
Susan G. Komen for the Cure	Global and national	NGO	Fund international community education and outreach programs; founded the TNBC Foundation	Increased awareness and knowledge of signs and symptoms and risk factors for BC and TNBC
TNBC Foundation	Global	NGO	Increase awareness of TNBC and support the discovery of novel treatments for TNBC	Inspire establishment of more TNBC-focused initiatives globally; increase awareness of TNBC and dissemination of TNBC statistics and trends; advocate to increase resource allocation for alleviating burden of TNBC
American Cancer Society	Global and national	NGO	Established international initiatives for cancer control and prevention	Reduce incidence and mortality rates for BC and TNBC

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Table A1. Initiatives That Aid in Reducing Burden of TNBC in Nigeria (Continued)

Agency	Level	Initiative Type	Objective or Action	Potential Effect in Nigeria
WHO	Global	NGO	Collaborate with Susan G. Komen for the Cure to sponsor lectures and events educating the public on BC and to provide a safe platform for women to have open dialog on the disease	Increased awareness and knowledge of signs, symptoms, and risk factors of BC and TNBC
International Information Service Group	Global	NGO	Network of 50 organizations from 30 LMICs, including Nigeria; partnered with several other organizations to increase awareness of cancer prevention worldwide	Increased awareness and knowledge on signs, symptoms, and risk factors of BC and TNBC
Union for International Cancer Control	Global	NGO	Advocate for worldwide cancer initiatives by encouraging the inclusion of cancer in the global health agenda and development of global cancer burden initiatives and programs	Increase funding for BC and TNBC research and health care infrastructure
Nigerian Health Insurance Scheme by Decree 35 of 1999	National	Governmental	Limit the rise in health care costs, ensure health equity among Nigerian citizens, harness private sector cooperation for provision of health care services, and promote adequate distribution of health care facilities across the country	Increase health care coverage for Nigerian citizens
Nigerian Sovereign Investment Authority	National	Governmental	Establish specialized health care and diagnostic facilities, allocate more public funds to health care, facilitate cooperation between private and federal health care institutions, and improve health care access by boosting the number of primary health care centers	Modernize and expand health care services throughout the private sector; increase availability of specialized and advanced health care services
Nigerian Cancer Society	National	NGO	Support development of cancer treatment and diagnostic facilities, public education on cancer, and cancer research	Increase BC awareness and discovery of novel treatments
Cancer Organization Public Enlightenment	National	NGO	Support BC awareness; provide screening and counseling services	Increased knowledge of signs, symptoms, and risk factors of BC and TNBC and early detection and intervention

(Continued on following page)

Table A1. Initiatives That Aid in Reducing Burden of TNBC in Nigeria (Continued)

Agency	Level	Initiative Type	Objective or Action	Potential Effect in Nigeria
Breast Cancer Association of Nigeria	National	NGO	Increase BC awareness, education, advocacy, and research; established Breast Cancer Awareness Outreach, which encourages women to practice BSE	Increased awareness and knowledge of signs, symptoms, and risk factors of BC and TNBC for early detection and timely intervention
Mama Cancer Foundation of Nigeria	National	NGO	Raise funds for cancer prevention, diagnosis, treatment, research, and support for patients with cancer and their families	Increase funding for health care facilities, BC and TNBC research infrastructure and preventative, diagnostic, and treatment methods and resources
Children Living with Cancer Foundation	National	NGO	Tend to Nigerian children with cancer	Reduce suffering of pediatric patients with BC or TNBC
Preventative Healthcare Initiative	National	NGO	Equip Nigerian women with knowledge, skills, and preventative strategies regarding BC to empower them to become proactive about their own health	Increased awareness of signs, symptoms, and risk factors or BC and TNBC for early detection and timely intervention
Society of Cancer Oncology and Research in Nigeria	National	NGO	Facilitate cancer research and training; secure professional development opportunities for Nigerian health care providers	Improve quality of BC and TNBC research and health care
Research Institute Establishment Act of 1977	National	Governmental	Established Nigerian Institute of Medical Research in Yaba, Lagos, Nigeria, to focus on health concerns in Nigeria	Improve clinical management of BC and TNBC
National Institute for Pharmaceutical Research and Development	National	Government	Advance pharmaceutical research and development	Increased development and commercialization of raw pharmaceutical materials; better access to medications for patients with BC and TNBC
Breast Cancer Clinic Initiative	Local (at Lagos University Teaching Hospital in Lagos, Nigeria)	Health care	Eliminate prolonged waiting times before therapy and improve channeling of patients into specialized treatment facilities to provide quick and optimum patient care	Minimize delays in BC treatment, which can help increase survival rates
Every Drop Counts initiative	Local (at Ahmadu Bello University Teaching Hospital in Zaria, Nigeria)	Health care	Establish an outpatient pharmacy unit in the oncology department to facilitate easier access for patients with cancer to obtain their prescribed medications	Reduced waiting times for receiving medication and reduced drug costs; improved dose precision; reduced contamination of medications

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Table A1. Initiatives That Aid in Reducing Burden of TNBC in Nigeria (Continued)

Agency	Level	Initiative Type	Objective or Action	Potential Effect in Nigeria
Educational workshop with pathologists and laboratory scientists from United Kingdom	Local (at National Hospital Abuja in Abuja, Nigeria)	Health care	Help improve pathology practices, enhance knowledge of IHC, and enable progression to automated IHC in the hospital	Increased accuracy in BC and TNBC diagnosis and screening for prognostic biomarkers
Cancer Registry Project	Local (University of Benin Teaching Hospital in Benin, Nigeria)	Health care	Establish a hospital-based registry to curate cancer incidence and prevalence data	Provide more accurate data pertaining to BC and TNBC burden

Abbreviations: BC, breast cancer; BSE, breast self-examination; IHC, immunohistochemistry; LMIC, low- or middle-income country; NGO, nongovernmental organization; TNBC, triple-negative breast cancer.