

# Assessment of Breast Cancer Management in Sub-Saharan Africa

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**PURPOSE** To document progress and bottlenecks in breast cancer management in sub-Saharan Africa, subsequent to a 2013 pilot survey conducted through the African Organization for Research and Treatment in Cancer (AORTIC) network.

**METHODS** An anonymous survey of breast cancer management was conducted in 2018 among AORTIC members. Results concerning respondent specialty, access to tumor boards, treatment accessibility, diagnostic services, and factors influencing treatment outcomes were compared with the 2013 findings.

**RESULTS** Thirty-seven respondents from 30 facilities in 21 sub-Saharan Africa countries responded. The majority (92%) were clinical oncologists. Radiotherapy facilities were available in 70% of facilities. Seventy-eight percent of these had linear accelerators, and 42% had cobalt<sup>60</sup> machines. Eighty percent of facilities had multidisciplinary tumor boards. Immunohistochemistry was routinely performed in 74% of facilities, computed tomography scan in 90%, bone scan in 16%, and positron emission tomography scans in 5%. Anthracyclines, taxanes, tamoxifen, letrozole, anastrozole, and zoledronic acid were available in the majority; trastuzumab, fertility, and genetic counseling were available in 66%, 58%, and 16%, respectively. There were a 50% increase in oncologist respondents over 2013 and a > 50% increase in radiotherapy facilities, particularly linear accelerators. Availability of trastuzumab, aromatase inhibitors, and taxanes increased. Immunohistochemistry capacity remained the same, whereas facilities harvesting at least 10 axillary lymph nodes increased. Bone scan facilities decreased. Responses suggested improved diagnostic services, systemic therapies, and radiotherapy. Sociocultural and economic barriers, system delays, and advanced stage at presentation remain.

**CONCLUSION** Clinicians in sub-Saharan Africa have basic tools to improve breast cancer outcomes, recording positive strides in domains such as radiotherapy and systemic therapy. Socioeconomic and cultural barriers and system delays persist. Workforce expansion must be prioritized to improve quality of care to improve outcomes.

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## BACKGROUND

Breast cancer is the most common cancer in women worldwide.<sup>1</sup> In low- to middle-income countries (LMIC), 50%-70% of patients present with advanced-stage disease, contributing to high mortality rates.<sup>2</sup> More than half of sub-Saharan Africa (SSA) patients with breast cancer will die from their disease compared with less than a quarter in developed countries.<sup>1</sup> Black Africans have lagged behind in breast cancer survival rates (33% in 2000 and 40% in 2018) in comparison with Black Americans (76% in 2015).<sup>3</sup> This is attributed primarily to limitations in early detection programs and delayed access to effective treatment. Other factors are lack of skilled manpower, functional surgical equipment, systemic therapy, and radiation facilities.<sup>4</sup> In 2020, only 23 of 52 countries in Africa had radiotherapy facilities, of which 60% were located in South Africa and Northern

Africa.<sup>5</sup> A recent update indicates some progress. Nine additional countries have radiotherapy facilities.<sup>6</sup>

Advanced breast cancer has few cost-effective treatment options in LMIC, resulting in poorer treatment outcomes. In a study from Taiwan, the 5-year survival rate was 85% for those receiving timely treatment versus 45% for those with delayed or no treatment.<sup>7</sup> Diagnosis and treatment delays in LMIC are partly blamed on weak health systems. Namibia and South Africa, both upper-middle-income countries with comparatively stronger health systems, report higher survival rates among Blacks, compared with other SSA countries.<sup>8</sup>

Establishment of effective multidisciplinary tumor boards (MDTs) in Africa is hindered by health system insufficiencies, including few tertiary institutions with the necessary organizational infrastructure, insufficient

## ASSOCIATED CONTENT

### Data Supplement

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

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## CONTEXT

### Key Objective

To document advancements and gaps in the management of breast cancer in sub-Saharan Africa.

### Knowledge Generated

There are improvements in clinical practice linked with increasing availability of basic inputs such as radiotherapy and chemotherapy drugs. Confounding patient factors such as fertility concerns are being addressed. Networking between oncologists and other clinical disciplines and the application of treatment guidelines set the stage for standardization of treatments even in weaker health care systems. Despite the gains realized, sub-Saharan Africa continues to battle less than optimal: (1) comprehensive diagnostic capacity to guide breast cancer management, (2) access to life-saving targeted therapies for breast cancer, (3) health literacy levels resulting in late stage at initial presentation, and (4) comprehensive universal health coverage.

### Relevance

This study highlights successes of breast cancer management, in line with the African Organization for Research and Treatment in Cancer goal to improve cancer outcomes in Africa. A call to address the persistent barriers outlined here is warranted.

oncology workforce, and inadequate pathology, imaging, and genetic counseling services.<sup>9</sup> In many LMIC, patient factors, such as access to rehabilitation, financial toxicity, and fertility concerns, that influence quality of life and treatment compliance are often ignored.<sup>10,11</sup> Strengthening health systems, as a means of addressing disparities in cancer outcomes and mortality, should be a priority.<sup>12</sup>

The African Organization for Research and Treatment of Cancer (AORTIC) is a network of cancer clinicians and researchers, representing 35 of the 46 SSA countries. AORTIC goals include improving cancer outcomes promoting advocacy and research on the continent. A 2013 pilot survey of SSA care providers in the AORTIC database indicated gains in overall breast cancer management.<sup>13</sup> Inadequate pathology services, low radiotherapy access with frequent equipment breakdowns, poor access to trastuzumab, scarcity of multidisciplinary cancer teams, high out-of-pocket payments, and sociocultural factors were limitations to optimizing care. Here, we report on a follow-up survey, 5 years on, to evaluate the current state of breast cancer management in SSA. The results provide a benchmark for future evaluation of milestones and persistent bottlenecks.

## METHODS

AORTIC members from 21 countries participated in an anonymous online survey. Ethical approval for the study was granted by Korle-bu Teaching Hospital, Accra, Ghana. Respondents gave consent to have data published. We used a 40-item structured questionnaire in English, Portuguese, and French, developed using AppSheet,<sup>14</sup> to query respondent specialty, access to tumor boards, treatment accessibility, levels of diagnostic services, and factors influencing treatment outcomes. Further questions addressed current management recommendations, prioritizing breast cancer drugs listed in the WHO's essential medicines list (WHO-EML). The questionnaire included

open-ended and dichotomous questions; however, the majority were closed-ended. Snowball sampling via professional networks yielded a convenience sample. Responses were collated in a spreadsheet, and descriptive statistics was used to compare the results with those of a 2013 pilot study by longitudinal data analysis for overlapping variables.

## RESULTS

### Respondents and Practice

There were 37 respondents from 30 institutions in 21 SSA countries (Table 1). The majority (92%) were oncology specialists, of whom 30% were medical oncologists. National breast cancer treatment guidelines were available in 13 countries. The majority (90%) of institutions have oncologist-led, weekly breast MDT, and consult treatment guidelines, with the National Comprehensive Cancer Network (NCCN) guidelines being the most popular.

### Radiotherapy

Fifteen countries (71%) had radiotherapy equipment in 19 institutions (64%; Fig 1). Six countries, Burundi, Malawi, Cape Verde, Democratic Republic Congo, Seychelles, and Eritrea, recorded no radiotherapy facilities. Linear accelerators were available in 78% of institutions, and cobalt<sup>60</sup> teletherapy machines in 42%. Three-dimensional treatment planning was available in 60% of facilities. Four (22%) institutions implemented intensity-modulated radiotherapy planning. Frequent machine downtimes were reported in fewer than 25% (Fig 2). Interval to receipt of adjuvant radiotherapy was 8 weeks in 10 institutions (33%), 8-12 weeks in nine institutions (29%), and more than 12 weeks in seven institutions (23%).

### Fertility and Genetic Counseling and Screening

Discussion of fertility options and genetic counseling was mentioned by 16% and 58% of respondents, respectively. No genetic screening was available in any facility.

**TABLE 1.** Geographical Distribution of Respondents

Subregion	Countries
East Africa	Rwanda, Eritrea, Uganda, Seychelles, Kenya, Ethiopia, and Burundi
West Africa	Cabo Verde, Nigeria, Ghana, Mali, and Senegal
Southern Africa	Zimbabwe, Namibia, Malawi, Zambia, Mozambique, and South Africa
Central Africa	Republic of Congo, Demographic Republic of Congo, and Angola

### Systemic Therapy

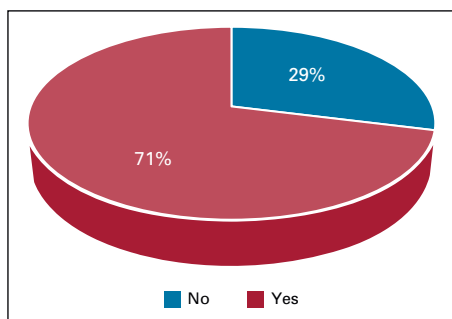
Anthracyclines and taxanes are available to the majority of respondents (Fig 3). Tamoxifen is widely available. Letrozole and anastrozole are the most available aromatase inhibitors (Fig 4). Trastuzumab is available in 66% of facilities. Human epidermal growth factor receptor 2 (HER2)-targeted therapies were unavailable in 17% (Fig 5). Zoledronic acid is available in 90%, and denosumab in 6.7% (two institutions). Immunohistochemistry (IHC) for estrogen, progesterone, and HER neu receptors influenced management for 85% of respondents. IHC for recurrent lesions is performed in 27% of facilities. Treatment response assessment was reported by 90% of respondents.

### Surgery

The majority of institutions performed upfront surgery for early disease, whereas 10% implemented neoadjuvant chemotherapy. For locally advanced breast cancer, 95% implemented neoadjuvant chemotherapy, whereas one institution used neoadjuvant hormonal therapy. Axillary node dissection was regularly performed in 74% of institutions. More than 50% harvested 10 lymph nodes. Sentinel node biopsy was performed in 4 institutions. The interval between surgery and chemotherapy was up to 8 weeks in 80% of institutions and more than 8 weeks in 20%.

### Pathology Services

Core biopsy was performed in 80% of institutions. The report turnaround was up to 3 weeks in 80% and 1 week in 5%. Tumor size, number of lymph nodes retrieved, and grade were reported in 95%, margin status in 85%, IHC and lymphovascular invasion (LVI) in 68%, intraductal

**FIG 1.** Radiotherapy availability in 21 countries.

component in 52%, ki67 in 53%, EGFR in 10%, and Oncotype DX testing in one institution. IHC testing was available locally to 74% of institutions.

### Imaging

Plain x-rays, ultrasound, mammogram, computed tomography scan, and magnetic resonance imaging were available in at least 75% of institutions. Bone scans, positron emission tomography (PET) scans, and bone density scans were available for 16%, 5%, and 5% of respondents, respectively.

### Treatment Financing

Government financing of treatment was available for 64% of institutions, with 30% benefiting from comprehensive coverage. Private insurance was available to another 30%. In 17%, the patient was solely responsible for treatment cost. Out-of-pocket payment for trastuzumab is affordable to < 20% of patients. Two institutions used 9 weeks and 6 months of trastuzumab, respectively, whereas the majority implemented the 1-year protocol.

### Factors Affecting Outcome

More than 50% of patients presented with advanced disease in 78% of institutions. Other factors affecting treatment outcome included culture, cost and logistics (system delays and access to care), and socioeconomic status (Fig 6). Suggestions for improving breast cancer care included early detection, political will, skilled human resources, pathology services, and regular supply of medicines.

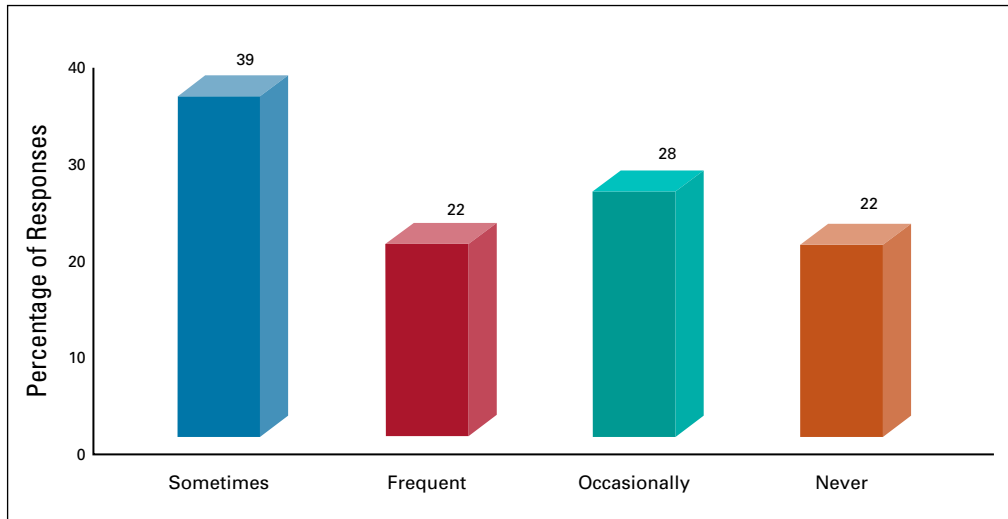
### Comparison With 2013 Survey

The current survey added 7 countries and 11 facilities to the 2013 survey's counts. Ninety two percent of respondents were oncologists versus 54% (30% were medical oncologists compared with 5%). We document a 50% increase in radiotherapy facilities and a surge in linear accelerators. The machine downtime of fewer than once per week is 66% versus 50%. MDT meetings increased by 34%. The number harvesting at least 10 axillary lymph nodes increased from 15% to 52%. Trastuzumab availability increased by 34%. There was a large increase in anthracycline, aromatase inhibitor, and taxane availability. Pertuzumab and denosumab were available in few institutions. Pathology reporting time, IHC capacity, and use in decision making remained the same. Bone scan facilities decreased from 47% to 16%. Factors contributing to poor outcomes increased compared with the 2013 survey (Fig 6).

### DISCUSSION

There is a paucity of data on the progress of breast cancer management in SSA. Nor is there an evolving database of cancer treatment facilities.<sup>15</sup> We have attempted to elucidate current resources available for breast cancer management by surveying members of the AORTIC network, representing 75% of SSA countries.

An increase in the number of cancer specialists (notably, medical oncologists) compared with the 2013 survey has likely



**FIG 2.** Radiotherapy machine breakdown.

improved the accuracy of this survey and may indicate an increase in cancer specialists in SSA. Our results contradict earlier reports indicating limited uptake of breast treatment guidelines in SSA.<sup>16</sup> Interestingly, international treatment guidelines are prioritized over national guidelines. Reasons for this could include a preference for treatment options from high-resource regions, ease of accessibility, or lack of buy-in from local oncologists in the development of national guidelines. An increase in guidelines use and in oncology-led MDT is a laudable quality improvement indicator. Patient, health system, and workforce factors could subvert the full implementation of MDT recommendations, negating the expected benefit.<sup>17</sup>

Despite the International Atomic Energy Commission commitment to improve radiotherapy resources in Africa, none of the countries surveyed reached the minimum target of 250,000 persons per radiotherapy machine.<sup>18</sup> Several factors aside from income level account for the deficiency.<sup>19</sup>

We document an increase in linear accelerators and less equipment downtime compared with the 2013 survey. The

acquisition of modern equipment could explain the reduction in downtimes experienced. Treatment interruptions beyond 2-7 days reduce the efficacy of radiation treatments.<sup>20,21</sup> The uptake of conformal techniques suggests improvement in radiotherapy delivery. However, low utilization rates, underfunding, and poor maintenance contracts prevail.<sup>22</sup>

Long radiotherapy waiting times are not uncommon in SSA. Waiting times beyond 3 months are reported in some facilities. Recommendations for waiting time run from 4 to 8 weeks. Waiting times of more than 3 months result in poor outcomes.<sup>23</sup> Extended radiotherapy waiting times in addition to other treatment pathway delays as experienced by several LMIC in SSA negatively affect survival.<sup>12,24</sup> A multipronged approach led by governments is required to reduce waiting times and ensure timely cancer management.

The current survey reveals a wider availability of systemic cancer drugs (Figs 3–5). The majority of these drugs are beyond the basic WHO-EML 2018 and NCCN-harmonized guidelines for SSA recommendations for breast cancer.<sup>25</sup>

**FIG 3.** Chemotherapy availability. CTX, cyclophosphamide; FU, fluorouracil; MTX, methotrexate.

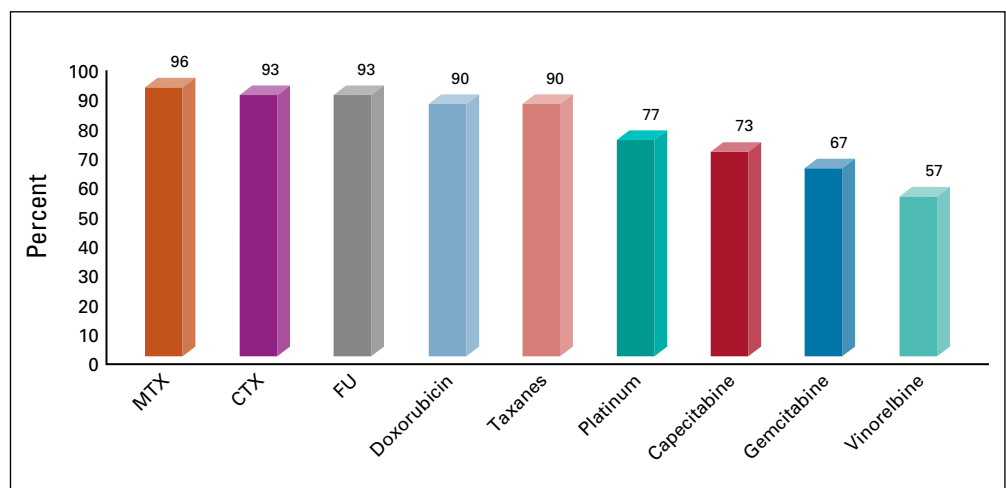
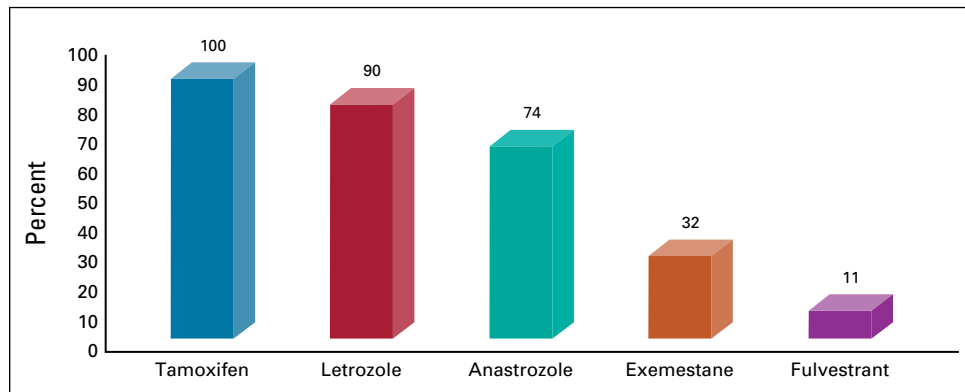


FIG 4. Hormonal therapy availability.



Many LMIC are less likely to include HER2-targeted therapies, taxanes, and aromatase inhibitors in their essential medicine lists.<sup>26</sup>

Neoadjuvant endocrine therapy for locally advanced, hormone receptor-positive disease is an underutilized, although a potentially cost-effective, management option, especially for LMIC.<sup>27</sup> Access to capecitabine in SSA could further improve outcomes for patients with triple-negative breast cancer after incomplete response to neoadjuvant chemotherapy.<sup>28</sup> Drug availability does not translate into improved access in situations where low health literacy, high out-of-pocket payments, poor geographical distribution, and frequent drug stock outages are the norm.<sup>29</sup> Further widening existing inequities, the cost of anticancer medicines is higher in Africa than in regions with similar gross national incomes.<sup>30</sup> The equivalence of shorter versus longer durations of trastuzumab for early breast cancer is debated.<sup>31,32</sup> Abbreviated duration of trastuzumab could expand access to this life-saving drug in LMIC. South Africa and Botswana, both upper-middle-income countries, battle deficits in their health budgets caused by trastuzumab access.<sup>33</sup> Other HER2-targeting drugs such as pertuzumab and lapatinib were rarely available in SSA. Pertuzumab and trastuzumab combination offers significant clinical benefits in metastatic breast cancer but could result in financial fallout and fail to be a cost-effective option without drug pricing interventions.<sup>34</sup> Zoledronic acid is

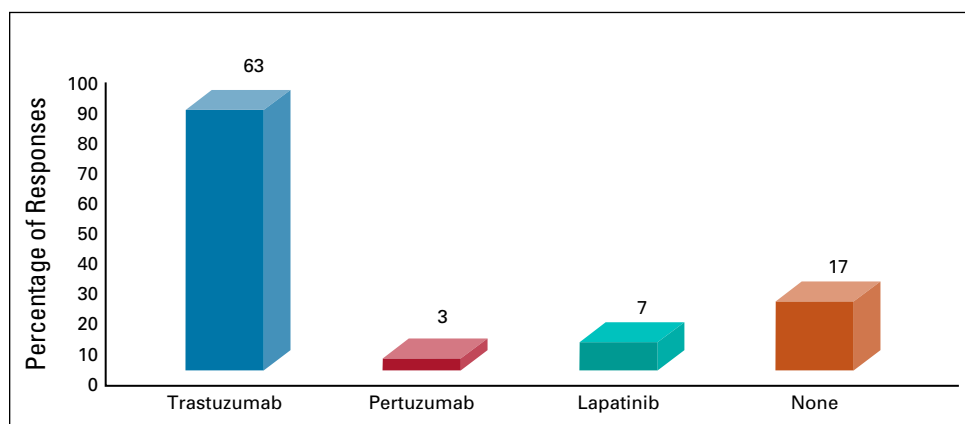
widely available to manage bone metastases. Guidelines recommend that IHC results dictate breast cancer management. However, some facilities experience lack of, or substantial delays in, reporting, limiting its usefulness and application.<sup>35</sup> IHC testing is not routinely repeated in recurrent disease, indicating a missed opportunity for personalized care.

Delays in receiving neoadjuvant or adjuvant chemotherapy involve an interplay of sociocultural elements and resource constraints even within a single SSA country.<sup>36</sup> Improving access through regulatory mechanisms, improved quality of imports, compulsory licensing, and implementation of universal health care would likely improve outcomes.<sup>37</sup>

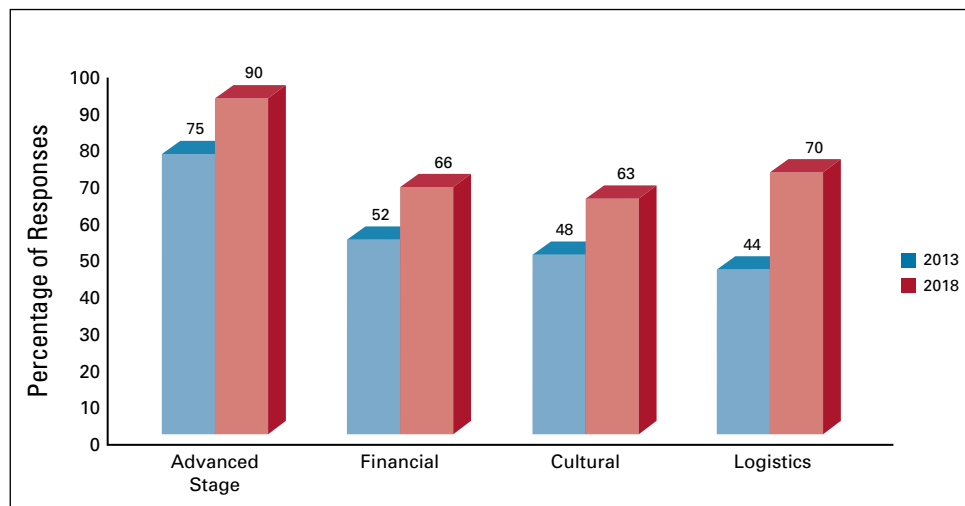
A majority of facilities performed primary surgery for early disease and neoadjuvant chemotherapy for locally advanced disease in line with treatment guidelines. Updated guidelines recommend the use of neoadjuvant chemotherapy for early stage (triple-negative breast cancer), underscoring the importance of presurgical MDT in management.<sup>5</sup>

The results of this survey reveal an increase in facilities harvesting at least 10 axillary lymph nodes, in line with the standard practice.<sup>38</sup> Substandard axillary dissections continue in almost half of the SSA institutions surveyed. The low utilization of sentinel node biopsy in SSA could be explained by the scarcity of eligible patients, limited expertise, and logistics. The average surgical waiting time

FIG 5. Targeted therapy availability.



**FIG 6.** Factors affecting treatment outcome (2013 v 2018).



of < 3 months in our survey is considered acceptable. A Nigerian study reported a 3% and 31% hazard of progressing from early to locally advanced breast cancer within 30 days of diagnosis versus 31% within 90 days, respectively.<sup>39</sup> Surgical delays would further worsen outcomes. An inherent desire of patients with cancer in SSA to seek complementary interventions further worsens treatment delays and the patients' plight.<sup>8,24,40,41</sup>

Positive strides in cancer diagnosis in SSA are attributed to north-south collaboration.<sup>42</sup> Lack of pathologists, logistical support, and standardization of tests continue, however, to hinder quality cancer management and research output.<sup>43,44</sup> Core biopsy utilization and improved reporting turnaround in SSA indicate attempts at standardization. The mean turnaround time for pathology reporting in high-income countries, South Africa, and Botswana is 4, 16 ( $\pm$  11), and up to 57 days, respectively.<sup>45</sup> Further input is required to improve figures in SSA. Breast cancers in Africa were earlier presumed to be predominantly estrogen receptor–negative as poor handling of specimens resulted in false-negative IHC results.<sup>46</sup> Skill transfer and improved quality assurance have shown that, in fact, at least half of breast cancers in Africa are estrogen receptor–positive. Although Ki67, a predictive biomarker for breast cancer, is increasingly applied in SSA facilities, there is no standardization in cutoff points for accurate interpretation.<sup>47</sup> LVI is a marker of aggressive cell migration and indicative of increased risk of metastases. However, LVI is underutilized in SSA for unknown reasons.<sup>45</sup> LVI expression in hormone receptor–positive and HER2-positive early breast cancer exhibits unfavorable outcomes and may require more aggressive management.<sup>48</sup> Concordance with the standard pathology reporting format should improve practice.

High-end technologies, including PET scans, are not realistic for many LMIC. Bone density scans are scarce, despite the widespread availability of aromatase inhibitors known to affect bone health.<sup>49</sup> A decline in bone scan facilities is not

mitigated by alternative bone imaging options such as PET scans and diffusion-weighted imaging as these are limited in SSA.<sup>50</sup> The high operator cost of advanced imaging techniques and limited access to imported radionuclides may be implicated. To improve staging accuracy, magnetic resonance imaging could be upgraded to diffusion-weighted imaging where PET scans are inaccessible.<sup>51</sup>

In SSA, fertility concerns are considered an important aspect of cancer management, whereas genetic counseling is not. Infertility is a common reason for noncompliance with breast cancer treatments in SSA.<sup>52</sup> Previous reports indicated that premenopausal women in SSA have limited opportunity to discuss the impact of therapies on future fertility plans or available options.<sup>10</sup> Limited awareness of oncofertility interventions among caregivers, cost, culture, and religion may be reasons why fertility preservation is not implemented in many LMIC.<sup>53,54</sup> We expect this trend to change with improved practice. Interventions such as temporary ovarian suppression with hormones during chemotherapy may increase post-treatment pregnancy rates and improve treatment compliance.<sup>54</sup>

Patients and caregivers sometimes erroneously interchange the terms genetic counseling and genetic testing. The latter is often brushed aside as resource-intensive. Health care workers in SSA may not be conversant with genetic counseling recommendations and so avoid the subject. In addition, the influence of culture and religion in understanding the concept of inherited genes as cancer causative renders it a difficult subject to discuss.<sup>55</sup> The increasing prevalence of BRCA1/BRCA2 mutation and other pathogenic variants in SSA highlights the need for genetic risk assessment to save lives.<sup>56-58</sup>

WHO sustainable development goals include global universal health coverage by 2030. The framework to achieve this goal is implemented by few SSA countries. Few facilities report complete financial sheltering from cancer treatment. Others have no or partial access to private or



government finances. East African countries, for instance, Kenya, offer lessons in reducing financial toxicity of cancer treatment.<sup>59</sup> High out-of-pocket payments for care are an impediment to treatment compliance and cancer control in SSA, demanding urgent attention.<sup>59</sup> The spiraling costs of cancer care, dwindling health care budgets, and competition for monetary resources all contribute to the financial burden of cancer treatment in SSA.

Advanced stage at presentation, patient socioeconomic and cultural characteristics, health care financing, and health care system deficiencies remain daunting obstacles to improving breast cancer outcomes in SSA. Reasons for the observed increases should be earnestly investigated and measures implemented if improvements in treatment outcomes are to be realized.

The snowball sampling technique affords little control and might have led to sampling bias. The current survey and

that conducted in 2013 differ in sample size. Respondent's specialty was a source of uncontrolled variation. The differing numbers of oncology versus nononcology specialists might have affected accuracy of responses. Finally, our results may not be representative of SSA, generally, because of the small sample size, nonrandomized sampling, and being confined to the AORTIC network.

In conclusion, clinicians in SSA have basic tools to improve breast cancer outcomes. Progress in domains such as radiotherapy and systemic therapy is proceeding rapidly, whereas in other domains such as imaging, it remains slow. Late-stage presentation and heavy cost burden are persistent obstacles to effective breast cancer management. Opportunities to further expand skilled workforce, including pathology, medical, and surgical oncology specialties, should translate into improved quality of care.

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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless

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Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians ([Open Payments](http://Open Payments)).

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