

# Access to Radiation Therapy and Related Clinical Outcomes in Patients With Cervical and Breast Cancer Across Sub-Saharan Africa: A Systematic Review

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**PURPOSE** To better understand the barriers to accessing standard-of-care radiation therapy (RT) for breast and cervical cancer in sub-Saharan Africa and their impact on outcomes.

**METHODS** A comprehensive literature search was completed with a medical librarian. Articles were screened by title, abstract, and full text. Included publications were analyzed for data describing barriers to RT access, available technology, and disease-related outcomes, and further grouped into subcategories and graded according to predefined criteria.

**RESULTS** A total of 96 articles were included: 37 discussed breast cancer, 51 discussed cervical cancer, and eight discussed both. Financial access was affected by health care system payment models and combined burdens of treatment-related costs and lost wages. Staffing and technology shortages limit the ability to expand service locations and/or increase capacity within existing centers. Patient factors including use of traditional healers, fear of stigma, and low health literacy decrease the likelihood of early presentation and completion of therapies. Survival outcomes are worse than most high- and middle-income countries and are affected by many factors. Side effects are similar to other regions, but these findings are limited by poor documentation capabilities. Access to palliative RT is more expeditious than definitive management. RT was noted to lead to feelings of burden, lower self-esteem, and worsened quality of life.

**CONCLUSION** Sub-Saharan Africa represents a diverse region with barriers to RT that differ on the basis of funding, available technology and staff, and community populations. Although long-term solutions must focus on building capacity by increasing the number of treatment machines and providers, short-term improvements should be implemented, such as interim housing for traveling patients, increased community education to reduce late-stage diagnoses, and use of virtual visits to avoid travel.

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## INTRODUCTION

Breast cancer (BC) and cervical cancer (CC) represent the first and fourth most common cancers in women worldwide and first and second in sub-Saharan Africa (SSA), respectively.<sup>1-4</sup> Nineteen of 20 countries with the highest incidence of CC are in Africa, and 90% of CC deaths in 2020 occurred in less-developed nations.<sup>5,6</sup> BC 5-year overall survival (OS) in SSA is below 50%, far lower than high-income (90%) or middle-income countries (66%).<sup>4,7</sup> Poor survival outcomes are related to tremendous disparities in access to preventative services and screening, leading to late-stage diagnoses.<sup>8-11</sup>

Additionally, because of advances in prevention and treatment of infectious agents, the average lifespan in SSA has increased, leading to higher cancer burdens.<sup>12</sup> Increased incidence necessitates a heightened focus on

expanding access to quality cancer care.<sup>13</sup> Treatments for locally advanced BC and CC involve chemotherapy and radiation therapy (RT), both with limited access in SSA.<sup>14-17</sup>

Compounding access, factors such as location, treatment length, and alignment of cultural beliefs represent challenges to providing curative treatments to all indicated patients.<sup>18,19</sup> These factors, along with clinical outcomes, are often described as isolated barriers or single-institutional outcomes and are rarely RT-specific. In this review, we aim to better understand the barriers to accessing standard-of-care RT for BC and CC across SSA and their impact on cancer outcomes.

## METHODS

The PRISMA Extension for Scoping Reviews checklist was used as a reporting guide.<sup>20</sup> The protocol was

## 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

What is the current status of radiation therapy access and outcomes for breast and cervical cancers in sub-Saharan Africa?

### Knowledge Generated

Sub-Saharan Africa is a diverse region with varying radiation offerings. Barriers to care include financial toxicities of treatment, prolonged travel to regional clinics and lack of local care opportunities, health literacy, staffing shortages, and unreliable technology, among others. Overall survival for both breast and cervical cancer are poor compared with high-income countries, and understandings of impacts on quality of life and mental health are understudied.

### Relevance

The cancer burden in sub-Saharan African continues to grow. As such, it is imperative that an accurate understanding of radiation therapy capacity and treatment outcomes is available to allow for focused discussion of resource allocation.

registered with PROSPERO (ID: CRD42021246847) and reported using PRISMA 2020 guidelines.

### Literature Search

A comprehensive literature search was developed with a medical librarian and peer reviewed using Peer Review of Electronic Search Strategies guidelines.<sup>21</sup> Searches were conducted on December 30, 2021, in MEDLINE (Ovid), Scopus, Web of Science, and African Index Medicus, and limited to English language articles. Searches were limited to 2016-present to ensure presentation of the current state of RT.

Search strategies were created using medical subject headings and keywords combined with database-specific advanced techniques. Medical subject headings and keywords were identified to represent RT, BC, CC, and SSA. The full search strategy from Ovid Medline is detailed in the Data Supplement. Citations were downloaded into EndNote, deduplicated, and uploaded into Rayyan for screening.

### Study Selection/Screening

Articles were screened by two independent reviewers (S.E.B.P. and S.A.A. or J.C.B.) to determine eligibility including title, abstract, and full-text review. Blinded screening was conducted in Rayyan with conflicts resolved by group consensus. Full selection is presented in [Figure 1](#).

### Eligibility Criteria

Included studies were original studies or summaries of national/regional interventions that assessed the use of RT, including external-beam radiation therapy (EBRT) and brachytherapy, or RT-related outcomes, including survival, toxicities, mental health, palliation, and quality of life (QoL), for BC and CC. There were no exclusions on the basis of patient or tumor characteristics. Additional criteria included human studies, full-text availability, publication after 2015, and from/describing SSA.

### Data Extraction/Synthesis

Included studies were analyzed for discussion of RT access and RT-related outcomes. Access was divided into subcategories of financial, location, staff, technology, and patient factors. Technology was specified by type including 2D, 3D conformal

(3DCRT), intensity-modulated RT (IMRT), brachytherapy, and other. Outcomes included survival, side effects, QoL, palliation, and mental health. Subcategory data were systematically extracted from the text and categorized as poor, intermediate, or good according to [Table 1](#).

### Quality Assessment

No randomized controlled trials were identified. Most included studies were retrospective studies or qualitative interviews. By the nature of these designs, risk of bias is elevated. Each article was systematically assessed for bias types, funding sources, and conflicts of interest. A minority of studies were case control or cohort studies, which were analyzed using their respective Newcastle-Ottawa Quality Assessment Scales. Assessments are provided in the Data Supplement.

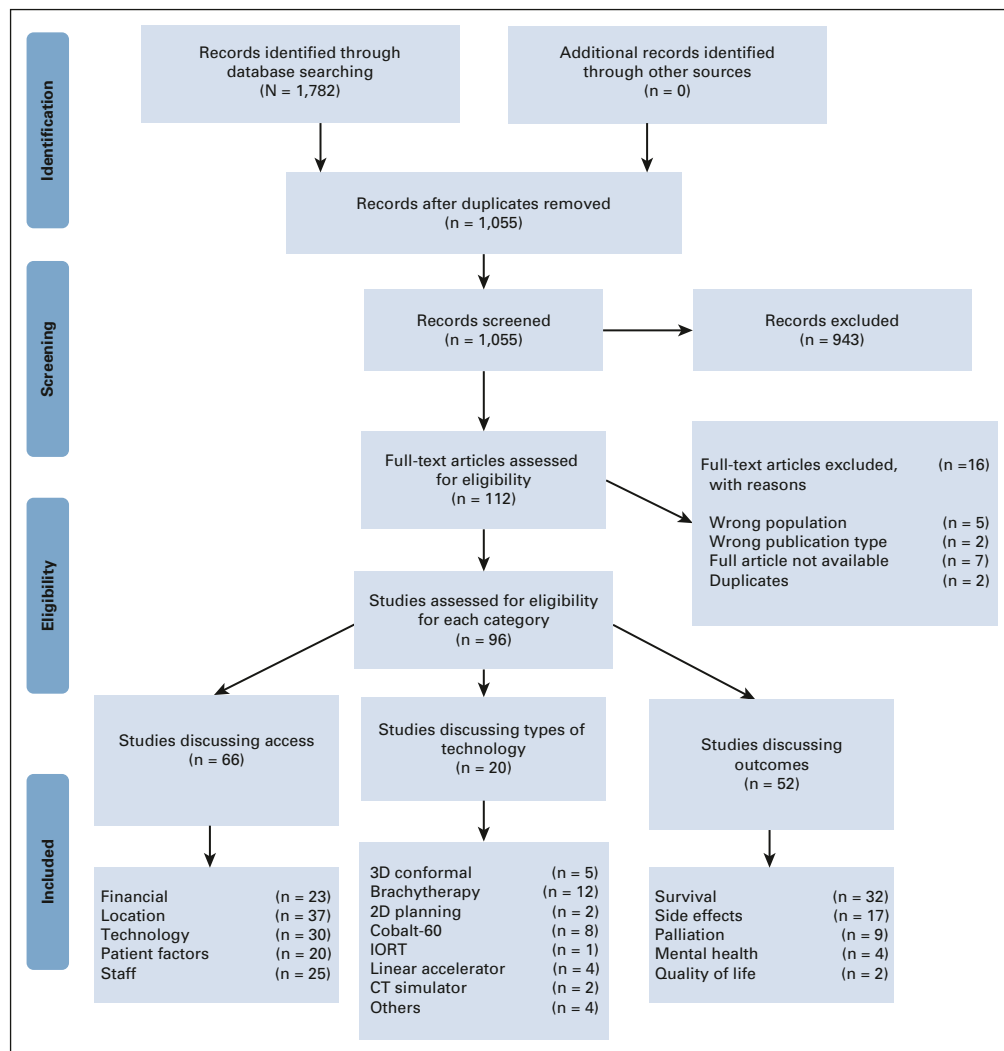
## RESULTS

The number of articles in each category can be found in [Figure 1](#), with trends for themes and grading in [Figure 2](#). A total of 96 articles were included: 37 BC, 51 CC, and eight discussed both. An article breakdown of categories and grades is provided in the Data Supplement.

### Access: Financial

Financial payment models differ throughout SSA. Most frequently, out-of-pocket (OOP) payment methods are used.<sup>22,23</sup> In this model, treatment poses too great a financial burden, even with insurance, to allow for adequate care. Additionally, costs varied substantially. For example, while living on approximately 1 US dollar (USD) per day, the cost of RT was 1,200 USD in Kenya compared with 1.5-25 USD in Ethiopia, a burdensome but less debilitating cost.<sup>22,23</sup> Furthermore, Ethiopia developed a mixed model with government, private, and NGO contributions; 70% of patients may still require OOP payments.<sup>23,24</sup> In Gabon, patient costs decreased from 51% to 22% of health spending from 2008 to 2020 because of increased government healthcare allocations, improving access for low-income patients.<sup>25</sup> Similarly, in Botswana, government subsidies comprise a significant portion of low-income patient coverage.<sup>26</sup> National insurance covers just 5% of Nigerians; because of financial constraints,

**FIG 1.** PRISMA flow-chart. CT, computed tomography; IORT, intra-operative radiation therapy. From Moher D, Liberati A, Tetzlaff J, et al: *Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement*. *PLoS Med* 6:e1000097, 2009. For more information, visit [www.prisma-statement.org](http://www.prisma-statement.org).



only 22 of 66 patients for whom breast RT was recommended were referred, and only five completed treatment.<sup>27</sup> Without additional subsidies, RT remains inaccessible.<sup>28</sup> In Tanzania, care is free if patients pay for biopsies; although less expensive, this often remains unaffordable.<sup>29</sup> Treatment length affects costs as some hospitals charge for entire RT courses, while others charge per fraction, potentially leading to incomplete treatments on the basis of inability to continue paying.<sup>30</sup>

Payment models affect treatment completion rates. In comparing one Ugandan, one Namibian, and two Nigerian hospitals, rates of treatment initiation within the first year after diagnosis ranged from 38% to 82% in facilities with largely OOP payments compared with 98.7%-100% in a free center.<sup>31</sup> Financial burdens lead to delays, unplanned breaks, or nonstandard treatments.<sup>32-37</sup> They affect treatment options, particularly with new technologies such as intraoperative RT (IORT), which are ineligible for aid and, therefore, only available for wealthy South Africans.<sup>38</sup> Insurance may help offset impacts, increasing RT utilization.<sup>39</sup>

Compounding costs of workup and treatment, patients are often paying for transportation and temporary housing because

of distance from treatment facilities.<sup>35,36,40,41</sup> Travel needs limit employment, increasing financial toxicity.<sup>42</sup> Bearing these consequences in mind, the choice of treatment options in BC, mastectomy or lumpectomy and RT, are affected by the ramifications of travel logistics and lost wages.<sup>43</sup> After completion of therapy, early recurrences may be missed because of unaffordability of surveillance imaging.<sup>44</sup> Financial barriers affect all aspects of care from initial presentation through long-term follow-up and contribute to lack of survivorship care.<sup>45</sup>

### Access: Location

Approximately 90% of African RT capacity is concentrated in Northern and Southern Africa, with nearly 60% within Egypt and South Africa alone.<sup>44,46</sup> In one study, only 2% of patients with CC and no patient with BC completed RT despite this being standard of care.<sup>47</sup> As of the writing of included publications (2016-2021), 26 of 54 African countries had no RT, including Malawi, Chad, Cameroon, Guinea, Burundi, Cape Verde, the Democratic Republic of Congo, Seychelles, Eritrea, and Niger; some may have increased capacity since publication.<sup>48-55</sup> In countries with RT, access is often limited to poorly maintained tertiary centers or cost-prohibitive private

**TABLE 1.** Definitions for Poor, Intermediate, and Good Access, Technology, and Outcomes

Subcategory	Poor	Intermediate	Good
Access: financial	All patients struggle to pay for services	Neither poor nor good	Payment did not inhibit access
Access: location	No radiotherapy machine in a country or region	Neither poor nor good	No needs for travel to access radiotherapy
Access: staff	Significant needs for increased staff	Some aspects of clinical staff are adequate while others are not	Well-staffed clinics
Access: technology	Lack of machines, routinely unreliable machines	Mixed opinions, have one type of technology and not others	Adequate number of machines and consistent power supply
Access: patient factors	Decreased likelihood that patient would pursue SOC	Some factors increased the likelihood that patient would pursue SOC, while others decreased	Increased likelihood that patient would pursue SOC
Technology: type	Available, but regularly broken or inaccessible	Available, but not adequate for patient volume	Available
Outcomes: OS	> 20% worse than SEER stage predictions or if 1-3 years' survival was equal to or worse than SEER 5-year survival <sup>110,119</sup>	10%-20% worse than SEER stage predictions or if 1-3 years' survival was better than 5-year survival but within 10%	< 10% worse than SEER stage predictions or if 1-3 years' survival was better than 5 year by > 10%
Outcomes: survival (DFS, only seen in BC data)	> 15% worse than EBCTCG LRR or any recurrence <sup>120</sup>	5%-15% worse than EBCTCG LRR or any recurrence	< 5% worse than EBCTCG LRR or any recurrence
Outcomes: palliation	Noted underutilization, unexpected toxicities	Neither poor nor good	Palliative radiation used and well tolerated
Outcomes: side effects	Unexpected or unusually severe and poorly controlled	Either unexpected, unusually severe, or poorly controlled	Expected and well controlled
Outcomes: mental health and QoL	Negative outcomes or experiences	Mixed outcomes or experiences	Positive outcomes or experiences

NOTE. NA was used for survival if discussed factors affecting survival without defining percentages OR if no time interval was specified; NA was used for side effects if severity or category of effects not detailed.

Abbreviations: BC, breast cancer; DFS, disease-free survival; EBCTCG, Early Breast Cancer Trialists' Collaborative Group; LRR, locoregional recurrence; OS, overall survival; QoL, quality of life; SOC, standard-of-care treatments.

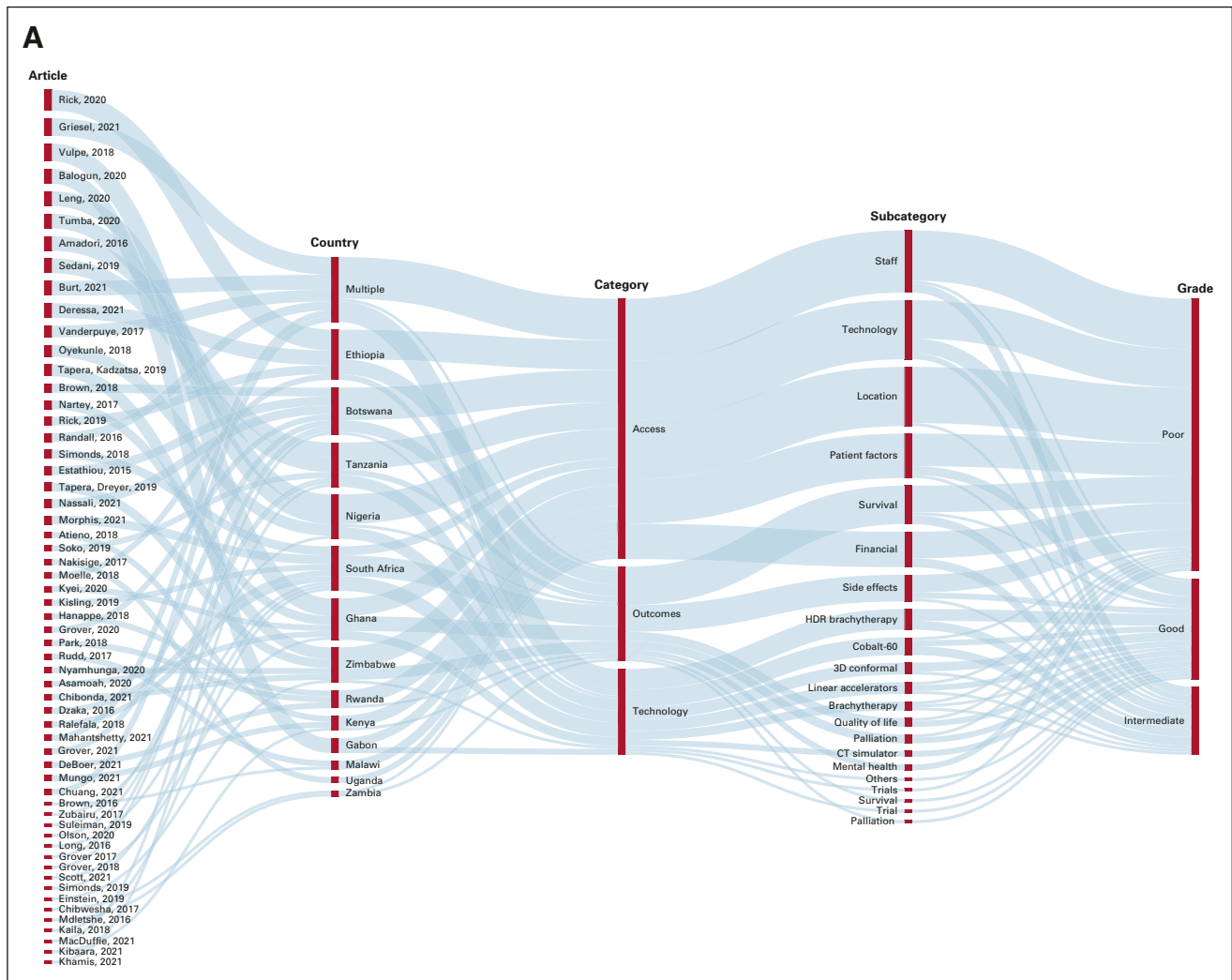
hospitals.<sup>50</sup> In Botswana, RT is available at one private hospital serving 1.3 million residents.<sup>26,56,57</sup> It is not uncommon to find a single RT center within a country; this was noted in Zimbabwe, Zambia, Uganda, and Ethiopia.<sup>23,58-60</sup> Having single national centers leads to delays; while awaiting RT for CC, an Ethiopian cohort noted 16 deaths and 44.4% progression to a higher stage if waiting for more than 60 days.<sup>24</sup> Ethiopia, however, is actively working to expand RT access to six regional centers.<sup>23</sup> Ghana and Sudan have two centers each, and, within Ghana, 78% of patients live within 45 km of a RT center.<sup>44,61,62</sup> Access is improved in South Africa with 86.4% of referred postmastectomy patients and 78.6% of breast-conserving surgery patients completing adjuvant RT because of proximity.<sup>63</sup>

Centralized RT limits access because of encumbrances of travel. This places a larger burden on community clinics to diagnose oncologic processes, posing a risk for misdiagnoses by nurses who manage rural facilities without physician oversight, loss of documents as they shuffle between centers, and limited communication in referrals.<sup>23,26</sup> Despite referring to the closest center, in a Nigerian cohort, 41.9% and 12.4% of patients traveled more than 3 and 8 hours, respectively, for care, with distances up to 800 miles.<sup>29,32</sup> The closest center may be out of the country, leading to sharp decreases in the percentage of successful referrals and a need for caregivers to

accompany patients, increasing the burden of lost wages.<sup>45,51</sup> In Botswana, interim housing is available but always at capacity, leading to hospital admissions in overburdened wards.<sup>60</sup> Living near RT centers increases the likelihood of guideline compliance, improves follow-up, and expands the number of treatment options.<sup>33,36-38,64,65</sup> In patients with BC, 66% completed RT in a Namibian center, 15% in Uganda, and < 5% in a Nigerian hospital without on-site RT.<sup>31</sup>

#### Access: Staff

Staff volume varies greatly between countries and centers. In Kenyatta National Hospital, lack of staff is postulated to negatively affect outcomes with only four practicing radiation oncologists within the country managing care for approximately 82,000 new cancer cases annually.<sup>22</sup> Because of lack of trained staff, a Botswana center rejected a cobalt-60 machine with the potential to significantly increase treatment volumes.<sup>60</sup> Some centers are forced to turn away patients because of long lines, high patient volumes, or limited physician presence.<sup>26,35</sup> Low staffing, accompanied by physician/staff strikes and clinic closures, lengthens wait times. In a center with five oncologists and a machine operating 8 hours a day, median wait time for consultations was 40 days and time from consultation to treatment was 130.5



**FIG 2.** Depictions of trends in the literature regarding radiation access and outcomes throughout SSA. Beginning with specific articles, these outline the most common countries, types of access/outcomes and technology discussed, and the grade given in each article (on the basis of Table 1): (A) cervical cancer and (B) breast cancer. CT, computed tomography; HDR, high dose rate; IORT, intraoperative radiation therapy; LDR, low dose rate; SSA, sub-Saharan Africa. (continued on following page)

days.<sup>29,32,42,49,58,66</sup> Additionally, there is a shortage of pathologists in SSA. Although some patients underwent surgery without a pathologic cancer diagnosis, they were less likely to accept recommended adjuvant therapies.<sup>37,42,62,66,67</sup> Specific to CC, a shortage of gynecologic oncologists places more pressure on RT services for early-stage patients who may be surgical candidates.<sup>33,42,44,50,68,69</sup> The use of multidisciplinary clinics may help improve staffing, referral systems, and delays as patients only need one visit to arrange care.<sup>70</sup>

Limited training capacity poses an additional barrier. A Gabonese clinic recently converted to 3DCRT with help from Moroccan staff who spent 18 months facilitating the transition, leading to an appropriately staffed clinic.<sup>25</sup> Ethiopia has started a dual radiation/medical oncology training program for 7-10 trainees each year.<sup>23</sup> Partly because of government-sponsored education requiring trainees to practice locally, this has tripled the number of oncologists in the country between 2017 and

2020.<sup>23</sup> Dual training, however, is challenging as more advanced radiation technologies and complex systemic options become available as mastering the progressively expanding toolbox of treatment options and techniques is difficult for any one individual.<sup>71</sup> Staffing concerns extend beyond providers and lead to struggles with managing a vast referral network and recordkeeping, limiting provision adequate survivorship care with incomplete documentation.<sup>24,42,67,72</sup>

### Access: Technology and Technology Type

SSA has just 0.115 radiation machines per one million people, far less than the recommended 4, and many oncology facilities are without RT.<sup>25,33,45,54,62,71,72</sup> Even in areas with a growing RT capacity such as Botswana, the growth in cancer incidences outpaces that of RT services.<sup>60</sup> In other areas, issues surround the lack of brachytherapy, affecting CC outcomes despite adequate access to EBRT.<sup>35</sup> In a

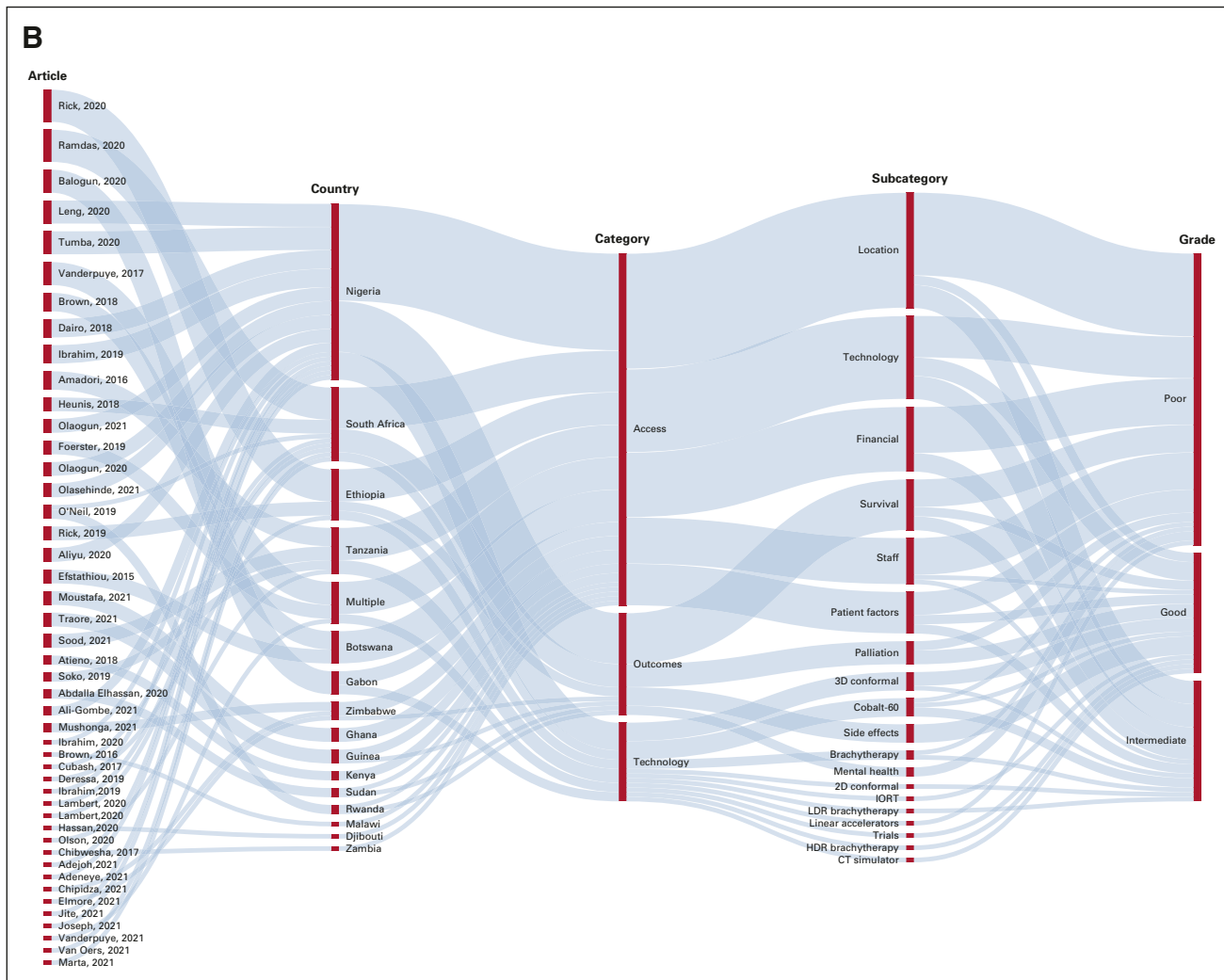


FIG 2. (Continued)

survey of health care providers from 23 countries, 44.8% were without EBRT and 52.5% lacked brachytherapy.<sup>69</sup> In a second survey, 70% of facilities had RT access with 78% of these having linear accelerators (linacs), 42% having cobalt-60 machines, 60% using 3DCRT, and 22% using IMRT.<sup>55</sup> Reviews of available technologies can be found in Table 2.

In addition to equipment, access to technology is affected by unreliable power grids, the cost of exchanging cobalt sources, unstable supplies of concurrent chemotherapy, and broken-down equipment.<sup>14,23,27,32,58,60,73</sup> In one survey, four of seven RT facilities noted downtime at least weekly.<sup>71</sup> These challenges lead to delays and decrease the number of patients treated in a given period. Capacity could increase with additional and/or more reliable machines.<sup>29,32,71</sup> The ability to obtain generators or purchase linacs with built-in generators helps decrease delays by increasing machine reliability.<sup>23</sup> Unreliable equipment leads to non-standard-of-care treatments and/or the need to travel long distances.<sup>36,74</sup> Some institutions have increased capacity and are participating in research.<sup>75,76</sup> Only 4% of surveyed centers noted participation

in clinical trials; reasons included limited funding, high workload, and inability to meet trial requirements at their center.<sup>14</sup>

Innovative technologies may increase capacity. An RT planning assistant with automated plan generation from computed tomography scans led to all plans being subsequently approved by treating physicians in one study.<sup>77</sup> Certain technologies, such as IORT, may increase access by allowing for single treatments; patients presenting with advanced disease do not qualify for this option, limiting utility.<sup>38</sup> International partnerships can also help train physicians, physicists, and others in using new technologies as they become available.<sup>78</sup> In planning any expansions, it is essential to first understand the demographics, cancer incidences, and availability of therapies to ensure resources are used efficiently.<sup>60</sup>

**Access: Patient Factors**

Social and cultural beliefs, health literacy, and other patient-specific factors affect care utilization positively and

**TABLE 2.** Breakdown of Technology by Country

Country	Technology Type Discussed
Gabon	Linear accelerators, CT simulator, 3D conformal, no brachytherapy <sup>25</sup>
Ethiopia	Linear accelerators <sup>a</sup> , CT simulator, 2D and 3D conformal, HDR brachytherapy <sup>23</sup>
Ghana	External beam radiation (machine not specified), brachytherapy (type not specified) <sup>44</sup>
South Africa	Linear accelerators, 3D conformal, HDR brachytherapy, IORT <sup>38,84</sup>
Uganda	External-beam radiation (machine not specified) <sup>68</sup>
Tanzania	Cobalt-60 machines, CT simulator, HDR brachytherapy, orthovoltage, linear accelerator <sup>78</sup>
South Africa	2D and 3D conformal, cobalt-60 machines <sup>121</sup>
Nigeria	Cobalt-60 machines, LDR brachytherapy <sup>49,101</sup>
Zimbabwe	HDR brachytherapy, cobalt-60 machines <sup>94</sup>

Abbreviations: CT, computed tomography; HDR, high dose rate; IORT, intraoperative radiation therapy; LDR, low dose rate.

<sup>a</sup>Transition from cobalt-60 to linear accelerators in progress as of 2020 when the article cited was published.

negatively. These factors are outlined in Table 3. Expanding on the theme of misinformation, a survey on RT-specific beliefs noted that 83% of respondents felt RT would decrease their lifespan and over half believed RT was poison,

**TABLE 3.** Factors Impacting Care Seeking Behaviors

Factors Increasing Likelihood of Seeking Care	Factors Decreasing Likelihood of Seeking Care
Positive awareness of cancer/family history <sup>26</sup>	Lack of awareness of cancer/education <sup>23,24,29,33,40-42,66,89,122</sup>
Strong support system <sup>26,123</sup>	Lack of health-seeking behaviors at symptom onset/underreporting initial symptoms <sup>23,33,67</sup>
Protestant affiliation <sup>40</sup>	Preference to seek treatment from traditional or religious healers <sup>23,31,40,41,66,89</sup>
	Stigma, discrimination, and fear of ostracization from community <sup>23,40,42,123</sup>
	Fear of treatment itself <sup>49</sup>
	Low SES <sup>24,31,66,89,122</sup>
	HIV-positive status <sup>a,31</sup>
	Challenging referral system <sup>72</sup>
	Previous bad experiences in hospitals/health care <sup>32</sup>

NOTE. On the basis of these factors, initial presentation was either hastened or delayed at the time of presentation or time of specialist referral.

Abbreviations: PET, positron emission tomography; SES, socioeconomic status.

<sup>a</sup>Although HIV status affected care-seeking behavior, there was no difference in PET-positive lymph nodes or treatment recommendations in cervical cancer on the basis of HIV status after presenting for consultation.<sup>124</sup>

would cause their cancer to spread, or would make them radioactive.<sup>46</sup> Although this decreased care-seeking, one analysis noted that education, use of traditional healers, and low socioeconomic status did not affect initiation of treatment after consultations were completed.<sup>32</sup> The COVID-19 pandemic altered treatment decisions secondary to increased delays, fear of exposures, and generalized unease<sup>38</sup>; once treated, patients were more likely to be lost to follow-up if they were older or had advanced presentations.<sup>45</sup>

### Outcomes: Survival

Numerical survival data, including overall and progression-free survival, can be seen in Table 4 along with data on locoregional and distant recurrences. Factors that improve survival include curative-intent treatments, higher parity, no previous medical history, and guideline adherence.<sup>33,35,41,79-81</sup> Despite the importance of guideline compliance, only 5.2% of patients received guideline-compliant treatment with curative intent, while 2.4% received curative-intent treatment with minor deviations and 8.2% received curative-intent treatment with major deviations.<sup>33</sup> Factors that decrease survival include late-stage presentations, treatment breaks, loss to follow-up, poor performance status, undifferentiated tumors, older age, poor nutrition, and long wait times.<sup>24,34,36,41,43,61,79-83</sup> In one series, compared with wait times of < 60 days, all-cause mortality was three times higher for waits between 120 and 179 days and 5.8 times higher if > 180 days.<sup>24</sup> Some patients with CC were given chemotherapy while awaiting RT availability; within this cohort, survival was similar to those given upfront chemoradiation.<sup>51</sup> HIV status was shown in separate studies to negatively affect survival or have no impact, a finding that may be mediated by CD4 count.<sup>34,56,79,84-86</sup>

Specific to CC, use of concurrent chemotherapy and brachytherapy improved survival, the type of brachytherapy (low v high dose rate) had no impact, and baseline anemia worsened survival.<sup>36,56,79,81,83,85-88</sup> One multinational study notes nearly identical survival compared with 20 years before.<sup>33</sup> Specific to BC, a lack of human epidermal growth factor receptor 2-targeted agents, large subset of triple-negative and/or undifferentiated tumors, and expensive chemotherapy worsened survival.<sup>53,89</sup> Survival data, however, are challenging to obtain because of low socioeconomic status and long distances traveled for treatments leading to decreased ability to access and afford survivorship care; one study noted 40.3% of patients lost to follow-up by 5 years, with another noting 91.2% of patients lost by 3 years.<sup>33,61,73,84</sup>

### Outcomes: Side Effects

Ninety-four percent of patients, including all cancers, were noted to complete treatment uninterrupted in an Ethiopian series, alluding to limited severe acute toxicities.<sup>90</sup> Within CC, studies reported differing rates of toxicities; one noted 27% of patients with adverse effects, while another noted 18% grade 3+ toxicities.<sup>34,74</sup> In two series with EBRT alone, acute side effects included radiation dermatitis (9%),

**TABLE 4.** Survival Data

Author, Year	Country	1-Year OS	2-Year OS	5-Year OS	Other (Specified)
Breast					
Heunis, 2018 <sup>21</sup>	South Africa				94.7% (I) 71.3% (IIIC) both 5-year DFS
Olaogun, 2021 <sup>27</sup>	Nigeria				12.5% (1-year LRR) 21% (2-year LRR) 26.8% (3-year LRR)
Abdalla Elhassan, 2020 <sup>61</sup>	Sudan			79.0%	
Lambert, 2020 <sup>43</sup>	South Africa			50.0%	
Olaogun, 2020 <sup>73</sup>	Nigeria	76.8%			
Olasehinde, 2021 <sup>28</sup>	Nigeria				68.5% (with RT) 51.0% (without) No time specified
O'Neil, 2018 <sup>53</sup>	Rwanda		82.1% (early) 53.1% (late) 15.1% (metastatic)		
Ramdas, 2020 <sup>38</sup>					1.9% recurrence No time specified
Ali-Gombe, 2021 <sup>89</sup>	Nigeria		56.1% <sup>a</sup> (all) 100% <sup>a</sup> (O) 80.0% <sup>a</sup> (I) 67.7% <sup>a</sup> (II) 51.4% <sup>a</sup> (III) 37.9% <sup>a</sup> (IV)	37.6% <sup>a</sup> (all) 100% <sup>a</sup> (O) 66.7% <sup>a</sup> (I) 57.6% <sup>a</sup> (II) 27.9% <sup>a</sup> (III) 13.8% <sup>a</sup> (IV)	66.6% (2-year DFS) 60.3% (5-year DFS)
Aliyu, 2020 <sup>75</sup>	Nigeria		90.0%		96.4% (2-year DFS) 3.6% (2-year LRR) 1.2% (2-year DM)
Traore, 2022 <sup>54</sup>	Guinea			60.0% (with RT) 40.0% (surgery alone)	
Cervical					
Simonds, 2018 <sup>84</sup>	South Africa			71.95% (IIB) 49.7% (IIIB)	
Nartey, 2017 <sup>41</sup>	Ghana	62.0%		30%	39% (3-year OS)
Moelle, 2018 <sup>91</sup>	Ethiopia	84.0%	64.0%		
Grover, 2020 <sup>56</sup>	Botswana				MS 550 days with CD4 nadir < 200 and 647 days with nadir > 200 <sup>p</sup>
Grover, 2018 <sup>83</sup>	Botswana		65.5% 65.0% <sup>b</sup>		
Einstein, 2019 <sup>97</sup>	Multiple	76.3% <sup>b,c</sup>			
Asamoah, 2020 <sup>82</sup>	Ghana	86.0% (IA) 100% (IIA) 95.0% (IIB) 90.0% (III)			
Chibonda, 2021 <sup>94</sup>	Zimbabwe	94.0% <sup>a</sup>	95.0% <sup>a</sup>		
Adusei-Poku, 2017 <sup>80</sup>	Ghana			41.0% (all patients) 86.7% (curative) 25.0% (palliative)	
MacDuffie, 2021 <sup>86</sup>	Botswana			56.8% <sup>b</sup> 55.1%	
Khamis, 2021 <sup>81</sup>	Tanzania			26.0%	Mean 33.9 months, MS 19 months
Grover, 2021 <sup>88</sup>	Botswana	68.0% (IIIB)	59.0% (chemoRT) 41.0% (RT alone) 50% (IIIB)		43.0% (IIIB; 3-year OS)
Griesel, 2021 <sup>33</sup>	Multiple	74.0%	51.3%		41.3% (3-year OS)
Deressa, 2021 <sup>35</sup>	Ethiopia	77%	45.3%	28.4%	
Dereje, 2021 <sup>24</sup>	Ethiopia	65.7%	32.6%		MS 21.2 months

(Continued on following page)



**TABLE 4.** Survival Data (Continued)

Author, Year	Country	1-Year OS	2-Year OS	5-Year OS	Other (Specified)
DeBoer, 2022 <sup>51</sup>	Rwanda				All 3-year EFS 38.0% (all) 90.0% (RH) 66.0% (chemoRT) 12.0% (chemo alone)
Morphis, 2021 <sup>102</sup>	South Africa			3.4% (palliative)	

Abbreviations: ART, antiretroviral therapy; chemoRT, chemoradiation; DFS, disease-free survival; DM, distant metastases; EFS, event-free survival; LRR, locoregional recurrence; MS, median survival; OS, overall survival; RH, radical hysterectomy; RT, radiation therapy.

<sup>a</sup>Survival calculated without including patients who were lost to follow-up and/or complete charts only.

<sup>b</sup>HIV+ cohort; stage denoted in ( ) if stage-specific; if no stage specified, cohort included all stages.

<sup>c</sup>Specific to women with high ART adherence and cisplatin-based chemoradiation.

diarrhea (12%), ulcerated sores (52.8%), dysuria (7.5%), thrombocytopenia (5.6%), and anorexia (5.6%).<sup>91,92</sup> One series documented late toxicities with vesicovaginal fistula (18%), radiation proctitis (31%), subcutaneous fibrosis (41%), vaginal strictures (14%), and dysuria (50%).<sup>91</sup> Secondary cancers were discussed, although this risk is low with modern RT.<sup>93</sup> Larger fields had higher rates of severe toxicities.<sup>76</sup>

With brachytherapy, both vesicovaginal and rectovaginal fistulas were noted, but the most common toxicity was vaginal stenosis.<sup>94</sup> One study noted higher bladder and rectum doses than recommended by the American Brachytherapy Society, with maximum doses of 82.5%-95.7% of the prescribed dose compared with a recommended < 80% for bladder and < 65% for rectum.<sup>95</sup> Acutely pain control was poor in brachytherapy procedures, with some women noting they “would’ve rather died from CC.”<sup>96</sup> Aside from increased leukopenia, no differences were noted in toxicities on the basis of HIV status.<sup>83,97,98</sup>

Within BC, toxicities were only discussed in studies assessing a new technology or fractionation.<sup>38,75,99</sup> Within hypofractionated postmastectomy RT, there were no grade 3+ toxicities, 50.6% grade 2 skin toxicities, and 19.2% grade 2 nausea.<sup>75</sup> Postmastectomy RT with IMRT spared higher dose volumes to organs at risk but increased low-dose spillage compared with 3DCRT.<sup>99</sup> Major complications with IORT were rare (2.8%) and included fat necrosis and skin erythema.<sup>38</sup> Notably, side effects are challenging to report because of poor documentation.<sup>81</sup>

### Outcomes: Palliation

Palliative RT is available in many centers with treatments ranging from 1 to 11 fractions and documented responses rates as high as 87%.<sup>58,65,100-102</sup> This was mostly used for bone and brain metastases, but was available for pain, bleeding, obstructive symptoms, vaginal discharge, and neurologic symptoms.<sup>65,90,100,101</sup> In a Nigerian series, palliative RT was offered to 23.2% of patients, with BC and CC comprising 43.5% and 16.1% of this cohort, respectively.<sup>103</sup> In a Zimbabwean series, only 19.7% of patients with metastases were offered palliative RT.<sup>65</sup> Despite performance status improvements and symptom relief, utilization is low

overall. Notably, wait times for palliative RT are significantly less than definitive treatments, decreased from a median of 150 days to 0-15.<sup>90,100-102,104,105</sup>

### Outcomes: Mental Health and Quality of Life

QoL and mental health are affected by complex treatments, toxicities, and changing family relationship dynamics. Qualitative studies noted negative impacts when patients had unmet informational needs, particularly regarding sexual side effects.<sup>96,106</sup> The impact of delays is often underestimated, and those with longer wait times had an increased likelihood of psychiatric hospitalization in the first year of treatment.<sup>67</sup> Survey data demonstrated that early-stage diagnoses, higher education, religiosity, supportive providers, and being married were protective.<sup>96,107</sup> Education was protective in measures of caregiver burnout; however, 72% of respondents noted some burnout.<sup>108</sup>

Specific to brachytherapy, patients noted emotional distress because of fear, pain, and humiliation in regard to multiple providers and staff being present in treatments.<sup>96</sup> In a survey of body image, patients with BC, compared with other cancers, noted higher scores of body dysmorphia, specifically in physical and sexual attractiveness, leading to lower self-esteem, increased tension, and decreased interest in life.<sup>109</sup>

## DISCUSSION

Access to RT affects outcomes in SSA in numerous ways. Clinics are sparse, and obtaining treatment often requires cumbersome travel arrangements that affect financial stability, job security, and availability of socioemotional support. Sociocultural beliefs, such as use of traditional healers and stigmas surrounding cancer diagnoses, cause delayed care-seeking. Compounding limited access, many patients are unable to complete treatments because of financial and social burdens of fractionated RT. These barriers lead SSA to have worse OS in BC and CC compared with high- and middle-income nations.

Five-year OS rates for BC ranged from 38% to 79%, far lower than the United States, where survival is 99% in localized disease and 86% with regional involvement.<sup>43,54,61,89,110</sup> Increased de novo metastatic disease likely drives these rates

lower.<sup>111</sup> High-income countries manage BC like a chronic disease with long-term survivors using indefinite systemic therapies; however, long-term drugs are cost-prohibitive to many in low-income countries. For CC, US all-stage 5-year OS is 66%; SSA cohorts ranged from 3.4% for palliative cases, 26% for all-comers, and 86.7% for localized disease, highlighting that SSA nations vary greatly in outcomes, with some touting cure rates that rival high-income nations, while others lag behind.<sup>35,41,80,81,84,86,102</sup>

Although the presence of barriers is ubiquitous, there is tremendous diversity between countries. Some nations, including Gabon and South Africa, have reasonable technological availability to deliver RT to their populations, while other nations lack RT altogether. Palliative RT had decreased wait times; however, this is likely because of urgency; these patients often present with symptomatic lesions leading to uncontrolled pain or bleeding that require rapid control. Although this speed is necessary, the competition for machine availability poses a risk of further prolonging wait times for definitive cases. Long-term improvements in accessibility for all require increased technology and staffing to allow for more rural centers, increasing regional capacity and reducing current travel burdens. Although large-scale developments take time, strategies should be implemented to increase interim capacity such as temporary lodging, education initiatives, and utilization of hypofractionated regimens and virtual visits.

Systematic initiatives are imperative. Partnerships between governments and outside organizations, such as in Gabon, may help expedite increased RT access by securing funding and providing training for local providers to deliver services, promoting sustainability.<sup>25</sup> Programs to increase the number of trained oncologists and retention strategies are needed, like in Ethiopia; however, careful consideration of dual radiation/medical oncology program development is essential.<sup>23</sup> Additional support staff in existing centers can improve efficiency, allowing for increased patient volume by permitting providers to focus exclusively on treatment planning–related care.

Equitable access requires more facilities within remote regions of SSA. While awaiting large-scale increases in the amount and location of available technologies, several strategies may help improve short-term access. Local lodging and resources can be provided for patients with long-distance traveling to reduce financial burdens, potentially building upon an existing Botswana model.<sup>60</sup> These programs could be government-sponsored in nations that lack RT services to increase the feasibility of their citizens successfully traveling abroad for treatment. Additionally, physicians should be encouraged to adopt hypofractionated schedules, which decrease costs and improve completion rates, particularly as long-term data regarding five-fraction BC regimens become available. In CC, single-insertion brachytherapy procedures could be

considered to decrease travel demands of multifraction courses; however, this increases needs for anesthesia support and inpatient admission that may limit utility.

The COVID-19 pandemic has increased utilization of virtual visits; allowing initial consultations to take place remotely can decrease travel burdens while still permitting necessary treatment-related discussions.<sup>112</sup> Virtual multidisciplinary clinics may be possible as single visits significantly decreased wait times by allowing multiple providers to speak with patients in one encounter, preventing delays caused by referrals.<sup>70</sup> This allows access to subspecialty providers that are otherwise inaccessible in rural clinics. As patients complete oncologic care, regional centers can manage follow-up, offloading the demands of oncologic providers and limiting needs for continued travel while still monitoring long-term toxicities and recurrences.

Additionally, negative impacts of stigma, treatment misconceptions, and fear can be combated with a focus on health literacy to dispel myths, normalize screening and treatment-seeking behaviors, and encourage women to be cognizant of symptoms that warrant medical attention.<sup>9,113-115</sup> Particularly for women from lower educational backgrounds who were more likely to agree with statements about stigmatizing cancer beliefs, these programs can significantly improve screening uptake.<sup>116</sup> A lack of care-seeking behavior leads to delays in presentation, late-stage diagnoses, and worse outcomes. Earlier diagnoses can allow for use of ultrahypofractionation, decreasing treatment lengths. Educational efforts in Ethiopia succeeded in increasing screening rates, which in turn improved survival by allowing timely access to curative treatments.<sup>117</sup> Similarly, increased vaccination programming can, in the long term, lead to a decrease in CC incidence, a shift seen in developed nations, and thus, a decrease in the need for additional RT infrastructure.<sup>118</sup>

Although this review contains a comprehensive summary of the available literature, there are notable limitations. Included studies represent only 15 of 48 SSA countries, which may limit generalizability. Additionally, a significant portion of data was derived from retrospective studies which, though prone to biases, brings to light the significant need for additional research to elucidate barriers, and identify strategies to improve the treatment capacity in SSA.

As SSA's cancer burden increases, infrastructure designed to improve availability of oncologic treatments is essential as poor access directly relates to worse survival. Although long-term improvements require monetary commitments and large-scale national buy-in, small systematic changes such as use of telehealth, locoregional clinic follow-up, and increased availability of low-cost temporary housing can bridge gaps. Additional efforts are needed to determine country-specific solutions, assess technological needs, and expand the pool of qualified physicians and professionals in SSA.

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