

Breast Cancer Early Detection in Eswatini: Evaluation of a Training Curriculum and Patient Receipt of Recommended Follow-Up Care

Daniel S. O'Neil, MD, MPH¹; Sifiso Nxumalo, RN, BNS²; Cebisile Ngcamphalala, MPH²; G Tharp, BS²; Judith S. Jacobson, DrPH, MBA³; Harriet Nuwagaba-Biribonwoha, MbChB, PhD²; Xolisile Dlamini, MPH⁴; Lydia E. Pace, MD, MPH⁵; Alfred I. Neugut, MD, PhD^{3,6}; and Tiffany G. Harris, PhD, MS²

PURPOSE Breast cancer (BC) is detected at late stages in sub-Saharan Africa. We piloted a BC early-detection program in Eswatini aimed at increasing breast health knowledge and clinical skills. We also aimed to determine the proportion of patients with breast abnormalities who completed referral to breast specialty clinics.

METHODS Nurses and counselors from five human immunodeficiency virus and/or antiretroviral therapy clinics underwent training in BC and clinical breast examination (CBE). We compared knowledge and skill examinations completed before, immediately after, and 90 days after training. Nurses then screened female clinic patients ≥ 18 years for breast symptoms, examined those with symptoms, and referred women with CBE abnormalities to a surgeon or the national breast clinic. Consenting women were contacted at 30 and 60 days after screening to determine if they had completed referral.

RESULTS In 2019, 44 nurses underwent training. Median scores (interquartile range) on pretraining, immediate post-training, and 90-day post-training knowledge examinations were 17.5 (16-19), 20 (19-21), and 20 (19-21), respectively. Median scores (interquartile range) on pretraining, immediate post-training, and 90-day post-training skills examinations were 10 (7-11), 23 (21.5-25), and 23 (22-24), respectively. Compared with pretraining scores, post-training scores were significantly improved ($P < .0001$ for all comparisons). From June 2019 to April 2020, a total of 9,502 clinic patients were screened for breast symptoms: 150 (2%) underwent CBE, 93 (62%) were referred for further evaluation, and 88 (97%) were included in the study. Of those, 54 (61%) completed referral. Referral completion was not associated with age, employment, relationship status, or prior experiences related to BC.

CONCLUSION The program's training curriculum improved breast health knowledge and clinical skills. Efforts are needed to improve patients' receipt of recommended evaluation for breast abnormalities.

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BACKGROUND

Breast cancer (BC) is the most common malignancy diagnosed in women globally.¹ In sub-Saharan Africa (SSA), approximately 75% of Black patients have stage III or IV BC at diagnosis, more than double the comparable proportion in the United States.^{2,3} No country in SSA provides population-level mammographic screening, and few health care providers (HCPs) are trained to recognize or manage breast abnormalities.^{4,5} In both Rwanda and South Africa, patients with BC have reported that HCPs failed to recognize their early BC symptoms.^{6,7}

In countries where mammographic screening is available, clinical breast examinations (CBEs) have not been shown to decrease BC mortality.⁸ In countries where mammography is *not* widely available, investigators have explored using CBE as a stand-alone BC screening or early-detection technique.⁹⁻¹⁶ Recent

data from India suggest that CBE screening decreases BC stage at diagnosis and may decrease BC mortality in women > 50 years old.¹⁷ However, there is consensus that before any screening program can be implemented, health systems must have the capacity to facilitate early diagnosis of symptomatic disease by building community awareness, enhancing providers' ability to evaluate abnormal findings, and ensuring robust referral systems to facilitate timely diagnosis.¹⁸ In Rwanda, Pace et al developed a BC early-diagnosis program that trained nurses from primary health centers to address breast complaints and to perform CBE. Nurses learned about BC symptoms and received hands-on training in CBE skills. Over 2 years, 127 nurses evaluated 1,560 women who presented with breast complaints at primary health centers. Of these women, 18 were diagnosed with BC.¹¹

In SSA, 4.5 million people living with HIV are > 50 years old; that number is expected to triple over the next 25

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

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CONTEXT

Key Objective

Can a breast cancer (BC) early-detection program in Eswatini improve HIV clinic nurses' breast evaluation skills and improve evaluation of their patients' breast symptoms?

Knowledge Generated

Following a 2-day training, nurses demonstrated significantly improved breast health knowledge and clinical breast examination skills. Those improvements were durable as well, with practically no deterioration at 90 days after training. However, when these nurses put their skills to use in the clinic, only 61% of patients with abnormal breast examinations completed their referral for further testing, reducing the program's potential for early BC detection.

Relevance

Successful efforts to decrease the stage of BC diagnosis in resource-limited health systems will require both effective detection strategies and accessible services for timely diagnosis.

years.^{19,20} As women living with HIV (WLHIV) age, their risk of developing BC increases, as does that of other women. Among patients with BC in both the United States and SSA, mortality is higher among WLHIV than among HIV-negative individuals.²¹⁻²⁵ Integration of HIV care with other non-communicable diseases services is recommended, but has been limited.

In collaboration with the Ministry of Health of Eswatini (MOH), we piloted an adapted version of the program of Pace et al in five HIV and/or antiretroviral therapy (ART) clinics in Eswatini. We aimed to evaluate the pilot program's effectiveness in improving breast health knowledge and clinical skills of HIV and/or ART clinic nurses and HIV counselors. We also aimed to determine the volume of clinic patients who would be referred, because of breast abnormalities, by the trained nurses and the proportion of patients who would complete referrals.

METHODS

Context

The Kingdom of Eswatini (formerly Swaziland) is a small country in Southern Africa with a population of 1.3 million people. Eswatini has the world's highest prevalence of HIV in adults (27%), but > 90% of PLHIV use ART.²⁰ Eswatini's Essential Health Care Package, issued by the MOH, specifies that routine BC screening by CBE should be offered at every facility in the public health care system, but screening breast examinations are rarely performed.²⁶

This study included high-volume HIV and/or ART clinics at four regional hospitals and one national referral hospital located in the four regions of the country. The national referral hospital has a breast specialty clinic where women with breast abnormalities can be referred for further evaluation. At the regional hospitals, women can also be referred to onsite surgical clinics.

Study Design and Participants

We conducted a prospective, two-phase pilot study of a training program for the early detection of BC in WLHIV and

receiving care at a study clinic. First, we evaluated the impact of this training on breast health knowledge and clinical skills among nurses and HIV counselors working in the clinics. We subsequently evaluated the proportion of patients who completed follow-up care for an identified breast abnormality.

Nurses and HIV counselors were eligible for the study if they were ≥ 18 years old, were employed at a study clinic, attended the training session, were not planning to leave the clinic within 3 months of the planned training, and provided written, informed consent.

Patients were eligible for screening if they were female, ≥ 18 years old, diagnosed with HIV, and receiving care at a study clinic. They were eligible for the study if they had a CBE-detected breast abnormality, had at least one working telephone number, and provided verbal, informed consent.

Procedures

In May and June 2019, participating nurses and counselors underwent a 2-day BC early-detection training program conducted by the MOH and study staff, with a curriculum adapted from the aforementioned Rwandan program.¹¹ Content included normal breast physiology, benign pathology, and BC. Substantial time was devoted to CBE skills, including practice on silicone training mannequins.²⁷ Nurses were trained in a clinical algorithm that emphasized referring women with abnormal breast examination to a surgeon or the national breast clinic. The curriculum included standardized patient simulations to allow trainees to practice these skills. Following the training, study staff visited study clinics monthly to reinforce breast evaluation skills and monitor study activities.

Before the training, nurses and counselors completed a survey on demographics and prior breast health experience. Before and immediately after the training, all participants took a written examination to evaluate knowledge about breast health and BC. Before and after training, nurses also completed a case-based practical skills examination on evaluating a breast complaint, including

performance of a CBE on the anatomical model and execution of the referral algorithm. Approximately 90 days after the training, nurses completed the knowledge and skills examinations for a third time.

Following training, nurses were instructed to screen all female patients ≥ 18 years for five specific breast symptoms: a breast mass, breast pain, breast skin or nipple changes, nipple discharge, and swelling in the armpit. Patients who reported breast symptoms underwent CBE. If an abnormality was found, referral to a surgeon or specialty breast clinic was provided. Nurses also asked referred patients for permission for a study coordinator to contact them. If the patient agreed, a study coordinator contacted them via telephone within 7 days and, if the patient provided verbal, informed consent, administered a questionnaire on demographics, BC risk factors, and knowledge of other women diagnosed with BC. Patient participants were phoned 30 days after enrollment to complete a questionnaire on whether they had completed the referral visit and the reasons for not completing the referral or the clinical outcome, as appropriate. Participants who had not completed referral at 30 days were phoned again at 60 days and completed the same questionnaire. Nurses logged counts of all women who were screened for breast symptoms and who were referred for clinical follow-up. Clinic charts were flagged postscreening to prevent rescreening at subsequent visits to the ART clinic. This phase of the pilot was planned for 1 year, but participant enrollment was ended 2 months early because of the COVID-19 pandemic.

Statistical Analysis

Among trainees, we used counts and percentages to describe demographics and experience with HIV and BC. To evaluate the impact of training curriculum on breast-related knowledge and clinical skills, pretraining, immediate post-training, and 90-day post-training examination scores were compared using Wilcoxon signed-rank tests. Among referred WLHIV, we determined the percentage completing referral and reported barriers to doing so. To explore factors associated with referral completion, demographic information and BC-related knowledge were compared between patients who did and did not undergo further evaluation using Z-score testing, chi-squared testing, and Wilcoxon-Mann-Whitney tests, as appropriate.

Ethical Considerations

The study was approved and monitored by the Eswatini Human and Health Research Review Board and the Columbia University Institutional Review Board. All participants provided written or verbal informed consent.

RESULTS

Trainees and Curriculum Evaluation

A total of 44 nurses and 36 counselors were trained in May-June 2019. The median age of the nurses was 35 years (interquartile range [IQR] 31-42), and 34 (78%) were

female (Table 1). The median age of the counselors was 38 years (IQR 32-42), and 33 (92%) were female. Nurses reported a median of 10 years (IQR 7-16) of total work experience. Few had on-the-job experience or training related to BC. Just 10 nurses (23%) reported having cared for someone with BC, and five (11%) reported formal training related to BC. Four counselors (11%) reported having cared for a patient with BC.

All 44 nurses and 36 counselors completed the pretraining and immediate post-training knowledge examinations. Of 23 possible points, nurses scored a median of 18 (IQR 16-19) points on the pretraining examination (Fig 1A). On the immediate post-training examination, nurses scored a median of 20 (IQR 19-21) points, a significant improvement ($P < .0001$). Thirty-eight nurses (86%) completed the 90-day post-training examination, with a mean actual time from the training of 105 (range: 92-105) days. On the 90-day examination, nurses scored a median of 20 (IQR 19-21) on the written examination, also an improvement compared with pretraining examination scores ($P < .0001$). Among counselors, the median pretraining examination score was 16 (IQR 14-18) and the immediate post-training score was 18 (IQR 17-20), a significant improvement ($P < .0001$; Fig 1B).

The nurses' scores on the practical skills examination also improved after training. Of 28 possible points, median scores were 10 points (IQR 7-11) before training, 24 points (IQR 22-25) immediately after training, and 23 points (IQR 22-24) at 90 days after training (Fig 1C). Both post-training scores were improvements over the pretraining scores ($P < .0001$).

Completion of Referrals

From June 2019 through April 2020, a total of 15,408 women ≥ 18 years old visited a participating ART clinic at least once. Trained nurses screened 9,502 WLHIV for breast symptoms. Of women screened, 150 (2%) reported symptoms and underwent a documented CBE, and 93 (1%) had an abnormal CBE, which prompted referral for further evaluation. Ninety (97%) of the referred women consented to participate in this study. Two consenting women could not be reached for any further follow-up; information on the remaining 88 women is reported here.

The median age of the referred patients was 39 years (IQR 33-46; Table 2). The largest group of patients came from the Hhohho region ($n = 40$; 45%), which contains the capital city of Mbabane.

At the 30-day follow-up, 38 of 88 patients (43%) reported completing the referral; 38 patients (43%) had not done so, and 12 (14%) could not be contacted. At the 60-day follow-up, among the 50 patients not known to have completed a referral at 30 days, 16 (32%) had completed the referral and 31 (62%) had not. Patients who did and did not complete referral did not differ in age, region, employment status, or relationship status (Table 2). The reasons most

TABLE 1. Characteristics of Nurses and Counselors Undergoing BC Early-Detection Training, Eswatini, 2019

Characteristic	Nurses (n = 44)	Counselors (n = 36)
Age, years, median (IQR)	35 (31-42)	38 (32-42)
Years working as a nurse or counselor, median (IQR)	10 (7.0-16.5)	4 (3.0-6.5)
Years working with PLHIV, median (IQR)	4 (2.0-7.0)	4 (3.0-6.5)
Sex, No. (%)		
Female	34 (77)	33 (92)
Male	10 (23)	3 (8)
Highest level of education, No. (%)		
University degree	38 (91)	0 (0)
Nursing school	4 (10)	30 (91)
Secondary school	0 (0)	3 (9)
Missing or declined	2	3
Reported having heard of BC, No. (%)	42 (96)	33 (92)
Reported having cared for someone with BC, No. (%)	10 (23)	4 (11)
Reported having received training in breast health, No. (%)	9 (21)	0 (0)
Reported having received training in BC, No. (%)	5 (11)	1 (3)

Abbreviations: BC, breast cancer; IQR, interquartile range.

frequently cited by the patients for not yet having completed follow-up were the costs of transportation and follow-up care, non-work-related time constraints, and not being convinced that further evaluation of their breast complaint was needed (Table 3). Only three patients mentioned COVID-19 precautions as a reason for not completing the referral; however, enrollment stopped in April 2020, early in the pandemic.

Nearly all referred patients (n = 80; 91%) had heard of BC (Table 4). Only 44 (50%) reported having known a woman with BC personally, and 22 (25%) reported knowing a woman who had been cured of BC. Although 54 women (61%) reported having ever performed a breast self-examination, only 31 (35%) reported having ever undergone CBE. Patients who did and did not complete referral by 60 days did not differ in BC knowledge or exposure (all $P > .05$). Women completing referral reported a median of 4 months of symptoms before their CBE, whereas women who did not complete referral reported a median of 6 months; the difference was not statistically significant.

Of the 54 women who completed referral, 42 (81%) self-reported not being diagnosed with any specific illness, six women (11%) reported that they were still undergoing evaluation with additional imaging or a biopsy to determine their diagnosis, one (2%) reported being diagnosed with a breast abscess, and three (6%) reported being newly diagnosed with BC.

DISCUSSION

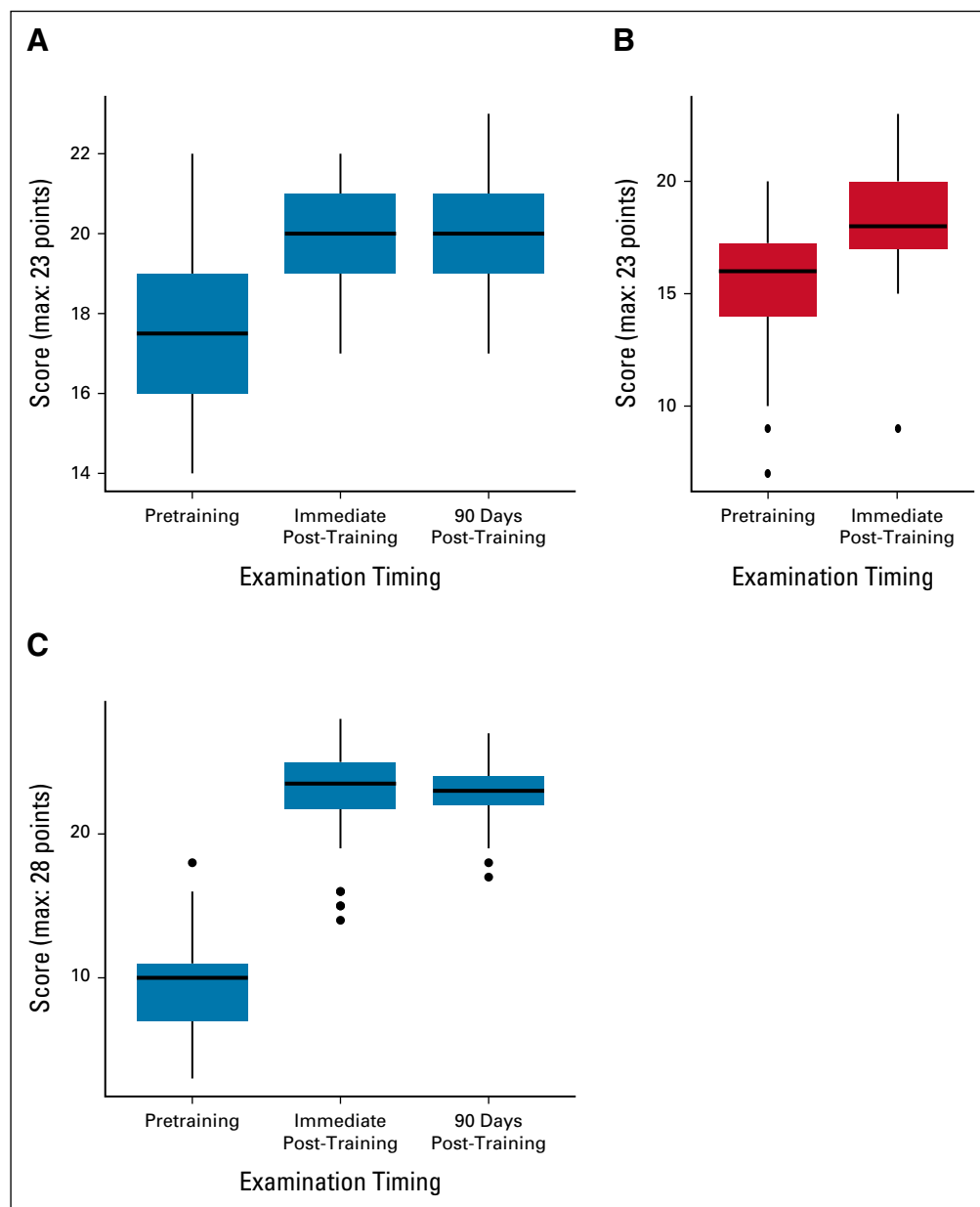
We describe early findings from a BC early-detection pilot program conducted in five HIV and/or ART clinics in Eswatini. The program's training curriculum successfully improved nurse and counselor breast health knowledge,

and nurses maintained that improvement for at least 90 days. Nurses also showed a large and durable improvement in their breast evaluation clinical skills. The program had substantial reach: over 10 months, these trained nurses screened more than 9,500 women for breast symptoms and referred 93 for breast abnormalities. However, referral completion was suboptimal. Of the 88 referred women who enrolled in the study, 54 (61.4%) self-reported having completed their referral within 60 days of enrollment. Participants who did not complete referral frequently cited the costs or time required as reasons. On the basis of self-report, three new BCs were diagnosed.

Although Eswatini's national guidelines call for use of CBE in routine screening, nurses lacked practical skills for assessing a breast complaint, performing a CBE, and escalating care when appropriate. Our program adapted a training curriculum that has previously shown success in Rwanda.¹¹ The training combined didactic presentations, hands-on examination practice with training mannequins, and practical case studies. Nurse trainees immediately put their skills to use in the clinic. This combination of multimodal training techniques and routine real-world practice likely contributed to the excellent retention seen 3 months after training. Our findings were consistent with the experience of Pace et al in Rwanda, where median knowledge examination scores improved from 73.9% to 91.3% and practical examination scores improved from 24.0% to 88.0%, also with near total retention at 3-6 months.¹¹

The curriculum's success in two different health care systems suggests that it could similarly improve knowledge and skills in any setting where HCPs lack skills in basic breast health. The curriculum is inexpensive, short, and

FIG 1. Change in BC knowledge and practical skills examination scores with training, Eswatini, 2019. (A) BC knowledge examination scores among nurses. Immediate post-training and 90-day post-training scores both significantly improved, compared with pretesting scores ($P < .0001$ for both). (B) BC knowledge examination scores among counselors: pretraining and immediate post-training. Immediate post-training scores significantly improved, compared with pretesting scores ($P < .0001$). (C) BC practical skills examination scores among nurses: pretraining, immediate post-training, and 90-day post-training. Immediate post-training and 90-day post-training scores both significantly improved, compared with pretesting scores ($P < .0001$ for both). Wilcoxon signed-rank tests used for all comparisons. BC, breast cancer.



scalable. If implemented widely, training group size would be limited only by the number of mannequins on hand for CBE practice. For countries aiming to offer universally available CBE, we would recommend broad implementation of our curriculum among HCPs. The Rwanda program included mentorship for nurses in the months after training, whereas our nurses were visited monthly by a trained study coordinator, which may have contributed to skill retention. Refresher trainings and ongoing supervision therefore might also be beneficial.

The major challenge our program faced was patient retention following abnormal examination. Fewer than two in three women obtained further evaluation after their abnormal breast examination. If women who did and did not complete referral had similar BC prevalence, then two of the 34 women

who did not complete referral had BC and went undiagnosed. Poor follow-up undermines the potential of early-detection programs to reduce mortality. A CBE screening program in Manila, Philippines, was discontinued after 1 year when only 35% of referred women completed follow-up, reducing that program's CBE sensitivity for BC from 53% to 26%.¹² Participants in our study cited associated costs—both financial and time—as the greatest barrier to completing follow-up. The time and money needed to obtain follow-up care could be reduced by offering those services at the hospitals where participants already receive HIV care. Breast ultrasound and fine-needle aspiration may be feasible outside tertiary referral hospitals. Experience from Rwanda suggests that general practitioners and nurses can be trained in breast ultrasound.²⁸

TABLE 2. Demographic Characteristics of Referred Patients, Eswatini, 2019-2020

Characteristic	Patients Who Completed Referral by 60 Days, n = 54	Patients Who Did Not Complete Referral, n = 34	Total ^a , N = 88	P
Age, years, median (IQR)	41 (33-48)	38 (33-42)	39 (33-46)	.51 ^b
Region, No. (%)				.10 ^c
Shiselweni	4 (5)	5 (6)	9 (10)	
Hhohho	30 (34)	10 (11)	40 (45)	
Manzini	14 (16)	15 (17)	29 (33)	
Lubombo	6 (7)	4 (5)	10 (11)	
Employment status, No. (%)				.91 ^c
Employed	29 (33)	19 (22)	48 (55)	
Unemployed	24 (27)	14 (16)	38 (43)	
Student	1 (1)	1 (1)	2 (2)	
Relationship status, No. (%)				.37 ^c
Married	13 (15)	14 (16)	27 (31)	
Single or never married	18 (20)	12 (14)	30 (34)	
Divorced or separated	5 (6)	2 (2)	7 (8)	
Widowed	8 (9)	3 (3)	11 (13)	
Cohabiting	10 (11)	3 (3)	13 (15)	

Abbreviation: IQR, interquartile range.

^aExcludes two referred and enrolled patients who were lost to follow-up without a 30-day or 60-day call.

^bWilcoxon-Mann-Whitney test.

^cChi-square test.

A successful screening or early-diagnosis program also requires downstream diagnostic systems able to accommodate an influx of new patients, as even the best screening tests discover far more false positives than true positives. Six patients reported that their referral clinic was not able to see them when they presented. At the end of the study period, six women who had pursued follow-up care were awaiting further testing to determine their diagnosis. If diagnostic services cannot be offered in a timely fashion, follow-up rates are likely to decrease over time.

Our strategy of examining only women who reported breast symptoms may reduce the diagnostic burden from false-positive CBEs. The program of Pisani et al in the Philippines targeted all women age 35-64 years, and the program of Sankaranarayanan et al offered screening CBE to all women age 30-69 years in the Trivandrum district of India.

In both, CBE had a positive predictive value (PPV) of approximately 1%.^{12,13} Alternatively, the program of Pace et al in Rwanda targeted women who self-presented with a breast complaint and produced a PPV of 6%-7%.¹¹ In Kenya, Botswana, and Tanzania, at discrete BC screening events open to interested women, CBE yielded PPVs of 9%, 3%-4%, and 5%, respectively.^{10,14,15}

BC incidence data would be needed to determine how much examining only symptomatic women affected CBE's sensitivity, but the strategy detected 32 new BC cases per 100,000 women examined. That proportion is similar to those reported by Pisani et al and Sankaranarayanan et al and double that currently documented by Eswatini's cancer registry (32 v 15 per 100,000 person-years).^{1,12,13} Our study was not designed to evaluate this program's impact on BC stage at diagnosis or mortality. However, Rwanda's

TABLE 3. Barriers Cited for Not Completing Referral (multiple answers allowed), Eswatini, 2019-2020

Reason	By 30-Day Follow-Up, n = 38, No. (%)	By 60-Day Follow-Up, n = 31, No. (%)
Costs of transportation or care	15 (39)	14 (45)
Work-related time constraints	10 (26)	3 (10)
Other time constraints	3 (8)	5 (16)
Not convinced of the need for further breast evaluation	5 (13)	4 (13)
Fear of a breast cancer diagnosis	2 (6)	4 (13)
Physical distance to breast specialist	3 (8)	3 (10)
Breast specialist was unable to see patient upon presentation	5 (13)	5 (16)
COVID-19 precautions	2 (5)	1 (3)

TABLE 4. Patient Participants' Breast-Related Knowledge and Referral Completion, Eswatini, 2019-2020

Characteristic	Patients Who Completed Referral, n = 54, No. (%)	Patients Who Did Not Complete Referral, n = 34, No. (%)	Total ^a , N = 88, No. (%)	P
Had heard of BC	50 (93)	30 (88)	80 (91)	.42 ^b
Had known a person with BC	29 (54)	15 (44)	44 (50)	.36 ^b
Had known a family member with BC	11 (20)	6 (18)	17 (19)	.82 ^b
Had known a person whose BC was cured	12 (22)	10 (29)	22 (25)	.46 ^b
Had ever performed a breast self-examination	34 (63)	20 (59)	54 (61)	.70 ^b
Had undergone a clinical breast examination (before study)	19 (35)	12 (35)	31 (35)	1.00 ^b
Had undergone a breast biopsy	6 (11)	2 (6)	8 (9)	.42 ^b
Had visited a traditional healer for breast symptoms	3 (6)	1 (3)	4 (5)	.52 ^b
Currently pregnant	1 (2)	0 (0)	1 (1)	.56 ^b
Currently breastfeeding	1 (2)	1 (3)	2 (2)	.76 ^b
Time since first noticing breast symptoms (months), median (IQR)	4 (1-10)	6 (3-11)		.22 ^c

Abbreviations: BC, breast cancer; IQR, interquartile range.

^aExcludes two referred and enrolled patients who were lost to follow-up without a 30-day or 60-day call.

^bZ-score testing.

^cWilcoxon-Mann-Whitney.

program appears to have increased the diagnosis of early-stage BC, and population-level CBE screening in India is reported to have reduced BC-related mortality among women > 50 years old.^{17,29} Individual ministries in SSA will need to decide if the suggested benefits and costs of either approach to BC early detection are sufficient for broad implementation. However, our findings demonstrate that, before any widespread early-detection efforts in Eswatini, strategies are needed to ensure that patients can complete recommended evaluation after an abnormal test.

This pilot study has some inherent limitations. The frequency of BC cases detected may shift with multiple rounds of testing as prevalent cancers are diagnosed in the first round. The rate of completed referral might be subject to a

Hawthorne Effect and diminish in real-world practice. Our reliance on patient self-report may have resulted in inaccurate counts of new BC diagnoses.

Much larger studies of CBE as a BC early-detection technique are needed to characterize its impact on BC stage at diagnosis and mortality in SSA. Strategies to improve follow-up—such as patient tracking, patient navigation, transport support, or decentralization of diagnostic services—are critical to the success of early-detection efforts and should be evaluated. However, the sum of work from lower middle-income countries suggests that CBE may be a feasible and effective tool for improving early detection of BC and, possibly, decreasing BC mortality in regions without mammography.

AFFILIATIONS

¹Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL

²ICAP at Columbia University Mailman School of Public Health, New York, NY

³Mailman School of Public Health, Columbia University, New York, NY

⁴Ministry of Health, Mbabane, Eswatini

⁵Brigham and Women's Hospital, Harvard University, Boston, MA

⁶Department of Medicine and Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY

CORRESPONDING AUTHOR

Daniel S. O'Neil, MD, MPH, Sylvester Comprehensive Cancer Center / University of Miami, 1121 NW 14th St, SMOB, Rm 245-B, Miami, FL 33136; e-mail: dso29@miami.edu.

DISCLAIMER

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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AUTHOR CONTRIBUTIONS

Conception and design: Daniel S. O'Neil, Cebisile Ngcamphalala, Judith S. Jacobson, Harriet Nuwagaba-Biribonwoha, Xolisile Dlamini, Lydia E. Pace, Alfred I. Neugut, Tiffany G. Harris

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Administrative support: Daniel S. O'Neil, Xolisile Dlamini

Collection and assembly of data: Daniel S. O'Neil, Sifiso Nxumalo, Cebisile Ngcamphalala, Harriet Nuwagaba-Biribonwoha, Xolisile Dlamini, Tiffany G. Harris

Data analysis and interpretation: Daniel S. O'Neil, Sifiso Nxumalo, G Tharp, Harriet Nuwagaba-Biribonwoha, Xolisile Dlamini, Alfred I. Neugut, Tiffany G. Harris

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Accountable for all aspects of the work: All authors

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Daniel S. O'Neil

Open Payments Link: <https://openpaymentsdata.cms.gov/physician/1272963>

Judith S. Jacobson

Consulting or Advisory Role: Otsuka

Harriet Nuwagaba-Biribonwoha

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Lydia E. Pace

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Alfred I. Neugut

Leadership: EHE International

Stock and Other Ownership Interests: Stemline Therapeutics

Consulting or Advisory Role: Otsuka, United Biosource Corporation, EHE International, Eisai, GlaxoSmithKline

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Tiffany G. Harris

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