

# Dissecting the journey to breast cancer diagnosis in sub-Saharan Africa: Findings from the multicountry ABC-DO cohort study

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## Abstract

Most breast cancer patients in sub-Saharan Africa are diagnosed at advanced stages after prolonged symptomatic periods. In the multicountry African Breast Cancer-Disparities in Outcomes cohort, we dissected the diagnostic journey to inform downstaging interventions. At hospital presentation for breast cancer, women recalled their diagnostic journey, including dates of first noticing symptoms and health-care provider (HCP) visits. Negative binomial regression models were used to identify correlates of the length of the diagnostic journey. Among 1429 women, the median (inter-quartile range) length (months) of the diagnostic journey ranged from 11.3 (5.7-21.2) in Ugandan, 8.2 (3.4-16.4) in Zambian, 6.5 (2.4-15.7) in Namibian-black to 5.6 (2.3-13.1) in Nigerian and 2.4 (0.6-5.5) in Namibian-non-black women. Time from first HCP contact to diagnosis represented, on average, 58% to 79% of the diagnostic journey in each setting except Nigeria where most women presented directly to the diagnostic hospital with advanced disease. The median number of HCPs visited was 1 to 4 per woman, but time intervals between visits were long. Women who attributed their initial symptoms to cancer had a 4.1 months (absolute) reduced diagnostic journey than those who did not, while less-educated (none/primary) women had a 3.6 months longer journey than more educated women. In most settings the long journey to breast cancer diagnosis was not primarily due to late first presentation but to prolonged delays after first presentation to diagnosis. Promotion of breast cancer awareness and implementation of accelerated referral pathways for women with suspicious symptoms are vital to downstaging the disease in the region.

## KEYWORDS

Africa, breast cancer, cancer diagnosis, early diagnosis

**Abbreviations:** ABC-DO, African Breast Cancer - Disparities in Outcomes (study); AD, absolute difference; BC, breast cancer; CI, confidence interval; HCP, health-care provider; HIC, high-income country; HIV, human immunodeficiency virus; IQR, inter-quartile range; IRR, incidence rate ratio; LMIC, low- and middle-income county; SEP, socioeconomic position; SSA, sub-Saharan Africa.

Milena Foerster and Fiona McKenzie contributed equally to this study.

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## 1 | INTRODUCTION

In high-income countries (HICs), most breast cancer (BC) patients are diagnosed at an early stage,<sup>1</sup> when the disease is potentially curable.<sup>2</sup> In contrast, in sub-Saharan Africa (SSA), most BC women are diagnosed at advanced stages.<sup>3</sup> Delays in seeking care, and in getting a definitive diagnosis, are the major drivers of advanced stage at diagnosis, with studies in HICs having shown that a time interval greater than 3 months between symptom discovery and diagnosis is associated with advanced-stage disease and poor outcomes.<sup>4</sup> The Breast Health Global Initiative has emphasized the need for downstaging interventions which promote early diagnosis and timely access to appropriate treatment in low- and middle-income countries (LMICs).<sup>5</sup> However, to implement those in SSA, it is vital to understand the array of personal, sociocultural, and economic barriers on a woman's journey from symptom onset to cancer diagnosis. During this diagnostic period, "delays" may occur either before or after the first contact with a health-care provider (HCP), hereafter referred to as the pre-contact and post-contact intervals. Few SSA studies have examined the diagnostic period, and they involved small numbers of patients, no standardized collection of data on key events along the diagnostic journey and limited data on potential correlates.<sup>6</sup>

The African Breast Cancer-Disparities in Outcomes (ABC-DO) study is a multicountry prospective cohort of BC patients in SSA,<sup>7</sup> which obtained recalled information on the navigational pathway to BC diagnosis. In a previous ABC-DO analysis, poor BC awareness, low educational level and unskilled employment were identified as drivers of late-stage diagnosis with their mediating pathway being mainly through prolonged time to diagnosis.<sup>8,9</sup> The main aims of the present analysis are to characterize and dissect the navigational path to BC diagnosis and to identify the main drivers of its length to inform cancer control policies in the region.

## 2 | MATERIALS AND METHODS

### 2.1 | Study participants and data collection

A detailed protocol of the ABC-DO study has been published.<sup>7</sup> Briefly, women aged  $\geq 18$  years with histologically confirmed or suspected BC were recruited between September 2014 and September 2017, through hospitals located in five SSA countries: Namibia (Windhoek Central Hospital, Windhoek), Uganda (Mulago Hospital and the Uganda Cancer Institute, Kampala), Nigeria (Abia State University Teaching Hospital and the Maranatha private clinic, Aba, and the Federal Medical Centre, Owerri), Zambia (Cancer Diseases Hospital and University Teaching Hospital, Lusaka, and Kabwe General Hospital, Kabwe) and South Africa (Chris Hani Baragwanath Academic Hospital, Soweto). The overall response rate was 99%. The present analysis excludes data from South Africa (as this site used a different baseline questionnaire) and from Kabwe General Hospital (as recruitment was not clinic/hospital-based). The study populations will be referred to hereafter as Nigerian, Ugandan, Zambian, Namibian-black and Namibian-non-black women.

### What's new?

In sub-Saharan Africa, most women with breast cancer are diagnosed long after symptoms first arise. Here, the authors studied the diagnostic journey for breast cancer among the African Breast Cancer-Disparities in Outcome cohort. This is the largest study to quantify the length of the diagnostic journey across various settings in sub-Saharan Africa. Time to final diagnosis decreased substantially when a woman recognized her symptoms as cancer. Most delays, they found, were due to extended time between first examination and final diagnosis. Promotion of breast cancer awareness among both women and healthcare providers could help reduce these delays.

ABC-DO study implementation, management and data collection were enabled via a specifically tailored m-health mobile phone application. Participants completed a face-to-face baseline interview at, or near, the time of the first visit to the participating hospital for possible BC diagnosis. This interview captured information on sociodemographic variables as well as recalled information on the diagnostic journey (eg, nature and date of first symptom, dates of all HCP visits) as detailed in Tables 1 and 2. Information on TNM BC stage at diagnosis was extracted from clinical records.

**TABLE 1** Characteristics of the ABC-DO study participants at the time of cohort recruitment (not including South Africa)

	N = 1429	Percent <sup>a</sup>
ABC-DO population group		
Namibia-black women	371	25.9
Namibia-non-black women	96	6.7
Nigeria	397	27.8
Uganda	400	28.0
Zambia	165	11.6
Sociodemographic		
Age at diagnosis: mean (SD)	50.1	(13.9)
Low SEP (vs medium/high) <sup>b</sup>	810	56.7
Not married (vs married) <sup>c</sup>	710	49.7
Having any children living at home (vs none)	1096	76.7
Primary/no education (vs secondary/higher)	628	44.0
Working in unskilled employment (vs skilled)	1007	70.5
Health-related		
Recent birth (<3 years prior to BC diagnosis)	176	12.3
Having a personal or family history of BC (vs no)	174	12.2
Positive HIV status (vs negative)	136	9.5

(Continues)

**TABLE 1** (Continued)

	N = 1429	Percent <sup>a</sup>
Having ever had other chronic comorbidities (vs never) <sup>d</sup>	740	51.8
Knowledge and beliefs		
Heard previously about BC (vs no/don't know)	1176	82.3
Know someone with BC (vs no/don't know)	663	46.4
Thinks BC is common (vs no/don't know)	577	40.3
Thinks BC is curable (vs no/don't know)	754	52.8
Attributed first symptom(s) to cancer (vs no/don't know)	144	10.1
Belief in traditional medicine/healing (vs no/don't know)	346	24.2
Belief in spiritual/faith healing (vs no/don't know)	1010	70.7
Being Muslim (vs no) <sup>e</sup>	54	13.5
Breast symptom and final diagnosis		
Self-recognition of symptoms (vs screen/CBE detection) <sup>f</sup>	1399	97.9
First change noticed: breast lump (vs no)	1230	86.1
Final diagnosis: Benign condition	33	2.3
Final diagnosis: BC	1396	97.7
Presenting with advanced BC stage (TNM III/IV; vs TNM I/II) <sup>g</sup>	831	63.2

Abbreviations: BC, breast cancer; CBE, clinical breast examination; HCP, health-care provider; SEP, socioeconomic position.

<sup>a</sup>Column percentages unless stated otherwise.

<sup>b</sup>Calculated as setting-specific tertiles (low, medium and high) of the distribution of a SEP score (range: 0-9) based on the following self-reported possessions and facilities: home ownership; indoor water; flush toilet; electricity; vehicle; refrigerator; landline; gas or electric stove; and a bed.

<sup>c</sup>Marital status at enrolment defined as married or not married (ie, single, divorced or widowed).

<sup>d</sup>Having ever suffered from one of the following non-HIV chronic conditions: hypertension, heart disease, diabetes, chronic anemia, chronic obstructive pulmonary disease (COPD, eg, chronic bronchitis, emphysema), asthma, hepatitis B or C, tuberculosis, other chronic infection, other cancer, other chronic disease.

<sup>e</sup>Percentage restricted to the Ugandan setting, the only with a sizeable Muslim population.

<sup>f</sup>For 30 women (including 15 Namibian-non-black and 8 Namibian-black women) the breast abnormality was first detected through mammographic/ultrasound screening or a routine CBE.

<sup>g</sup>Percentage out of all women with a final BC diagnosis and with known stage (n = 1314; information on stage was missing for 81 women: 32 from Uganda, 23 from Zambia and 26 from Nigeria).

The term “patient delay” is often used in HICs with universal access to free health care to refer to the time interval from symptom recognition to presentation to a HCP, as its length is essentially driven by patient-mediated factors. In contrast, the terms “provider delay,” “health-system delay” or “diagnostic delay” are often used to refer to the time interval from presentation to definitive diagnosis, as its length is driven predominantly by health system-mediated factors.

However, these terms may not properly capture conditions in most SSA settings—that is, without free access to health care, the length of each interval is likely to be the result of a complex interplay between patient and health system drivers. For instance, a woman may delay presentation not only because of patient-related factors (eg, lack of BC awareness) but also because of lack of a HCP in her area of residence. Similarly, a woman who first presents with a suspicious cancer may delay final diagnosis due to fear of its consequences (eg, mastectomy, death) or desire to try first an informal HCP (eg, traditional healer). Hence, to avoid any a priori judgement on the reasons underlying the length of these time intervals, the diagnostic journey of a woman with a suspicious BC was divided into a *pre-contact interval* (date of symptom discovery to date of first HCP visit) and a *post-contact interval* (date of first HCP visit to date of diagnosis). HCP contacts included those with either the *formal* or the *informal health system* (Table 2). The date of final diagnosis was defined according to the European Network of Cancer Registries guidelines,<sup>10</sup> that is, prioritizing date of biopsy/cytology or date of hospital admission. If histological confirmation was not available (12.7% [n = 182]), diagnosis was based on the clinical history or imaging examinations (eg, mammography).

Women were excluded from this analysis if: their first reported symptom occurred >5 years (n = 70) previously (likely related to a previous condition); the date of symptom discovery was missing (n = 6); or, due to errors, the recorded date of symptom discovery was later than the date of diagnosis (n = 7). A further 43 women were excluded from the post-contact interval analyses because the date of diagnosis preceded the self-reported date of the first HCP visit.

## 2.2 | Statistical methods

The primary outcomes were the lengths (in months) of the diagnostic journey, and of its two components: the pre- and post-contact intervals. As the distributions of these lengths were positively skewed, medians (inter-quartile ranges [IQR]) are reported. The cumulative probability of obtaining a diagnosis by time since symptom recognition, and time since first HCP contact, were estimated using Kaplan-Meier. Negative binomial regression models were fitted to identify woman-level correlates of interval lengths. These models yielded incidence rate ratios (IRRs) which can be interpreted as an estimate of the ratio of interval lengths. Variables within groups of sociodemographic, health-related, knowledge and belief factors (Table 1) were highly correlated. Hence, *minimally adjusted* models, which adjusted for study population and age, were fitted first to identify the variable within each group with the strongest association with interval lengths. Thereafter, *fully adjusted* models were fitted which further controlled for the variables identified by the minimally adjusted models, that is, educational level, ever-suffering from a non-human immunodeficiency virus (HIV) comorbidity, and attributing the initial symptom(s) to cancer. Odds ratio (OR) for the association between advanced-stage (III/IV) relative to early stage (I/II) at diagnosis and length of the diagnostic journey were estimated using logistic regression models. Analyses were conducted in Stata version 14.2.

**TABLE 2** Navigation-related features of the journey to breast cancer diagnosis in the ABC-DO cohort, by study population group

Variable	Study population group											
	Namibia, black (n = 371)		Namibia, non-black (n = 96)		Nigeria (n = 397)		Uganda (n = 400)		Zambia (n = 165)		All (n = 1429)	
	n <sup>a</sup>	% <sup>a</sup>	n <sup>a</sup>	% <sup>a</sup>	n <sup>a</sup>	% <sup>a</sup>	n <sup>a</sup>	% <sup>a</sup>	n <sup>a</sup>	% <sup>a</sup>	n <sup>a</sup>	% <sup>a</sup>
Urban (vs rural) residence <sup>b</sup>	207	55.8	85	88.5	262	66.0	108	27	111	67.3	773	54.1
First person told												
Relative/friend	297	80.1	67	69.8	313	78.8	343	85.8	157	95.2	1177	82.4
Formal HCP <sup>c</sup>	60	16.2	28	29.2	76	19.1	34	8.5	5	3.03	203	14.2
Informal HCP <sup>d</sup>	2	0.5	0	0	6	1.5	8	2.0	1	0.6	17	1.2
Other	12	3.2	1	1.0	2	0.5	15	3.8	2	1.2	32	2.2
First HCP visited <sup>e</sup>												
Type of first HCP												
Primary <sup>f</sup>	208	56.1	82	85.4	20	5.0	97	24.3	58	35.2	465	32.5
Secondary/tertiary <sup>g</sup>	160	43.1	13	13.5	362	91.2	249	62.3	97	58.8	881	61.7
Informal <sup>h</sup>	3	0.8	1	1.0	15	3.8	54	13.5	10	6.1	83	5.8
Barriers to first HCP visit <sup>i</sup>												
No transport available	81	21.8	0	0	6	1.5	48	12	4	2.4	139	9.7
Transport/treatment costs	68	18.3	2	2.1	35	8.8	77	19.3	11	6.7	193	13.5
Pain and/or fear	15	4.04	2	2.1	45	11.3	37	9.3	29	17.6	128	9.0
Other <sup>l</sup>	39	10.5	9	9.4	46	11.6	115	28.8	17	10.3	226	17.6
None	250	67.4	87	90.1	274	69.0	237	59.3	117	70.9	965	67.5
Outcome of first HCP visited												
Appropriate diagnosis/referral <sup>k</sup>	257	69.4 <sup>k</sup>	80	83.3 <sup>k</sup>	95	55.2 <sup>k</sup>	144	42.9 <sup>k</sup>	103	64.0 <sup>k</sup>	679	59.9 <sup>k</sup>
Inappropriate diagnosis/referral <sup>kl</sup>	112	30.4 <sup>k</sup>	16	16.7 <sup>k</sup>	77	44.8 <sup>k</sup>	192	57.1 <sup>k</sup>	58	36.0 <sup>k</sup>	455	40.1 <sup>k</sup>
Not applicable <sup>m</sup>	2	—	0	—	225	—	64	—	4	—	295	—
No. HCPs visited <sup>e</sup>												
1	5	1.4	2	2.1	238	60.0	69	17.3	6	3.6	320	22.4
2	55	14.8	11	11.5	117	29.5	5	1.3	78	47.3	266	18.6
3	122	32.9	38	39.6	40	10.1	89	22.3	65	39.4	354	24.8
4	104	28.0	24	25.0	2	0.5	83	20.8	15	9.09	228	16.0
≥5	85	22.9	21	21.9	0	0	154	38.5	1	0.6	261	18.3

(Continues)

**TABLE 2** (Continued)

Variable	Study population group																	
	Namibia, black (n = 371)			Namibia, non-black (n = 96)			Nigeria (n = 397)			Uganda (n = 400)			Zambia (n = 165)			All (n = 1429)		
	n <sup>a</sup>	% <sup>a</sup>	(3-4)	n <sup>a</sup>	% <sup>a</sup>	(3-4)	n <sup>a</sup>	% <sup>a</sup>	(1-2)	n <sup>a</sup>	% <sup>a</sup>	(3-5)	n <sup>a</sup>	% <sup>a</sup>	(2-3)	n <sup>a</sup>	% <sup>a</sup>	(2-4)
Median (IQR)	4	(3-4)		3	(3-4)		1	(1-2)		4	(3-5)		2	(2-3)		3	(2-4)	
Median (IQR) time (months) between HCP contacts <sup>b</sup>																		
1-2	1.4	(0.5-4.0)		0.6	(0.2-1.2)		5.0	(1.7-12.1)		2.0	(0.6-5.9)		3.0	(1.2-7.9)		1.1	(0.1-4.3)	
2-3	1.1	(0.5-2.7)		0.7	(0.2-1.9)		3.2	(1.2-7.9)		1.2	(0.3-3.5)		2.1	(1.1-5.0)		1.2	(0.4-3.3)	
3-4	0.8	(0.3-1.6)		0.9	(0.5-1.4)		7.1	(6.0-8.3)		0.8	(0.2-2.0)		0.8	(0.2-2.0)		1.6	(0.2-3.0)	
Length of the post-contact interval as % of the length of the diagnostic journey																		
All women, median (IQR)	60.6%	(12.1%-96.2%)		77.8%	(15.7%-96.4%)		10.6%	(0.9%-66.7%)		63.7%	(24.6%-87.0%)		78.3%	(18.0%-98.2%)		51.5%	(7.8%-89.1%)	
Symptomatic women, median (IQR) <sup>c</sup>	57.6%	(11.8%-95.3%)		69.6%	(9.5%-90.9%)		10.5%	(0.9%-66.6%)		63.6%	(24.6%-87.0%)		78.6%	(18.9%-98.2%)		50.2%	(7.3%-88.7%)	

Abbreviations: HCP, health-care provider; IQR, inter-quartile range.

<sup>a</sup>Unless otherwise specified.

<sup>b</sup>Usual place of residence defined as urban (ie, city/town) or rural (ie, village/rural).

<sup>c</sup>Includes doctors, nurses and midwives.

<sup>d</sup>Includes other health-related professionals (eg, chemists/pharmacists), church pastors, elders and traditional and spiritual healers.

<sup>e</sup>Including the study hospital. HCP either part of the formal health system (primary/secondary/tertiary): medical facilities including private doctors/general practitioners, hospitals, community and outreach clinics—or the informal health system: other non-medically trained health professionals (eg, chemist/pharmacist), traditional and spiritual healers or church leaders.

<sup>f</sup>Includes private doctors, community clinics, pharmacists and community health-care workers.

<sup>g</sup>Includes both public and private secondary and tertiary hospitals.

<sup>h</sup>Includes traditional and spiritual healers as well as other informal HCPs.

<sup>i</sup>Women could select more than one answer.

<sup>j</sup>Include barriers selected by less than 5% of the participants—for example, could not get time off from job; lack of childcare; fear of being unwell or dying; felt that treatment would not help; fear of rejection by husband/family; preference for traditional or spiritual medicine; could not get an appointment.

<sup>k</sup>Percentages out of those women who visited at least one formal or informal HCP prior to visiting the study hospital.

<sup>l</sup>Inappropriate outcome includes women who were reassured, and told not to worry (no. across all population groups [n] = 161); women who underwent tests, but were not informed of their results (n = 65); women who were told they had something else, and treatment was offered (n = 211); and those who were told they had something else, but no treatment was offered (n = 18).

<sup>m</sup>Not applicable if women did not visit any formal or informal HCP prior to visiting the study hospital.

<sup>n</sup>Time interval between first visits to consecutive HCP, that is, between first and second, second and third, and third and fourth HCP visited among women who visited at least a total of two, three and four HCPs, respectively. A breakdown in the length of these intervals by total number of HCP visited is shown in Figure 2.

<sup>o</sup>Excluding 30 women with screen-detected cancers.

### 3 | RESULTS

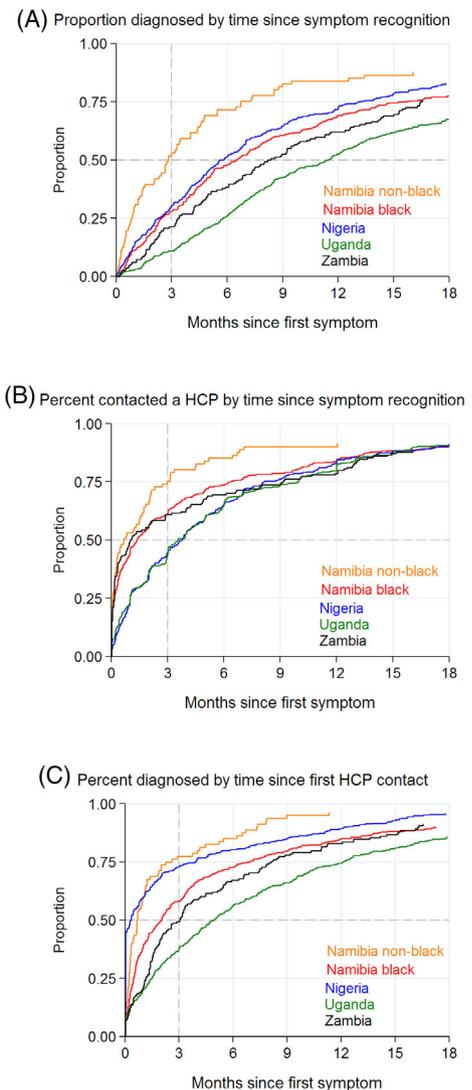
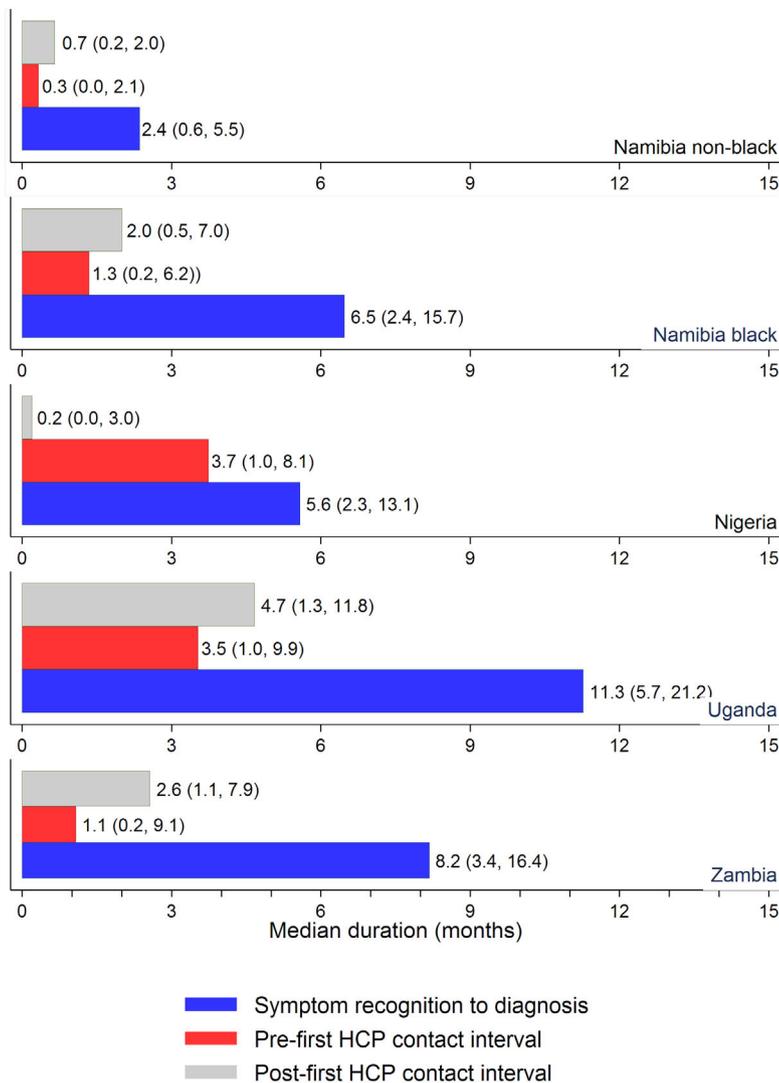
#### 3.1 | Study participants

In all, 1429 women were included in the analysis (Table 1). Mean age at diagnosis was 50.1 years, 44% reported low education, 71% believed in spiritual or faith healing (range: 50% in Uganda to 96% in Zambia) and 24% believed in traditional medicine (12% in Namibia to 38% in Uganda). A breast lump was the first symptom noticed by 86% of the participants. Only 10% attributed their symptoms to cancer (3% in Nigeria to 14% in Namibian-black and 33% in

Namibian-non-black women). In all, 98% of BCs were symptomatic detections.

#### 3.2 | Navigational nodes to BC diagnosis

Most women reported first approaching a close relative/friend before visiting a HCP. Few women first visited an informal HCP except in Uganda (14%) (Table 2). Half of the participants reported having experienced barriers to first visiting a HCP (multiple answers possible); the most common for Namibian-black and Ugandan women were lack of



**FIGURE 1** Left panel: Median (IQR) length (in months) of the diagnostic journey from symptom discovery to diagnosis (breast cancer or other), and of its pre- and post-contact components, in the ABC-DO study, by population group. Right Panel: Cumulative probabilities of: A, a definitive diagnosis by time since self-recognition of a suspicious symptom (diagnostic interval); B, a first visit to a HCP by time since discovery of a suspicious symptom (pre-contact interval); and C, a definitive diagnosis by time since first visit to a HCP (post-contact interval) [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.com)]

transport (22% and 12%, respectively) and treatment/transport costs (18% and 19%, respectively), while in Zambia and Nigeria the most common were pain and/or fear (18% and 11%, respectively). Of the 1134 participants who had visited other HCPs prior to the study hospital, 40% reported inappropriate outcomes (eg, told not to worry, wrong diagnosis) of their first visit (range: 57% in Uganda to 17% in Namibian-non-black women). The median number of HCP visited per woman ranged from 1 in Nigeria to 4 in Uganda and Namibian-black women.

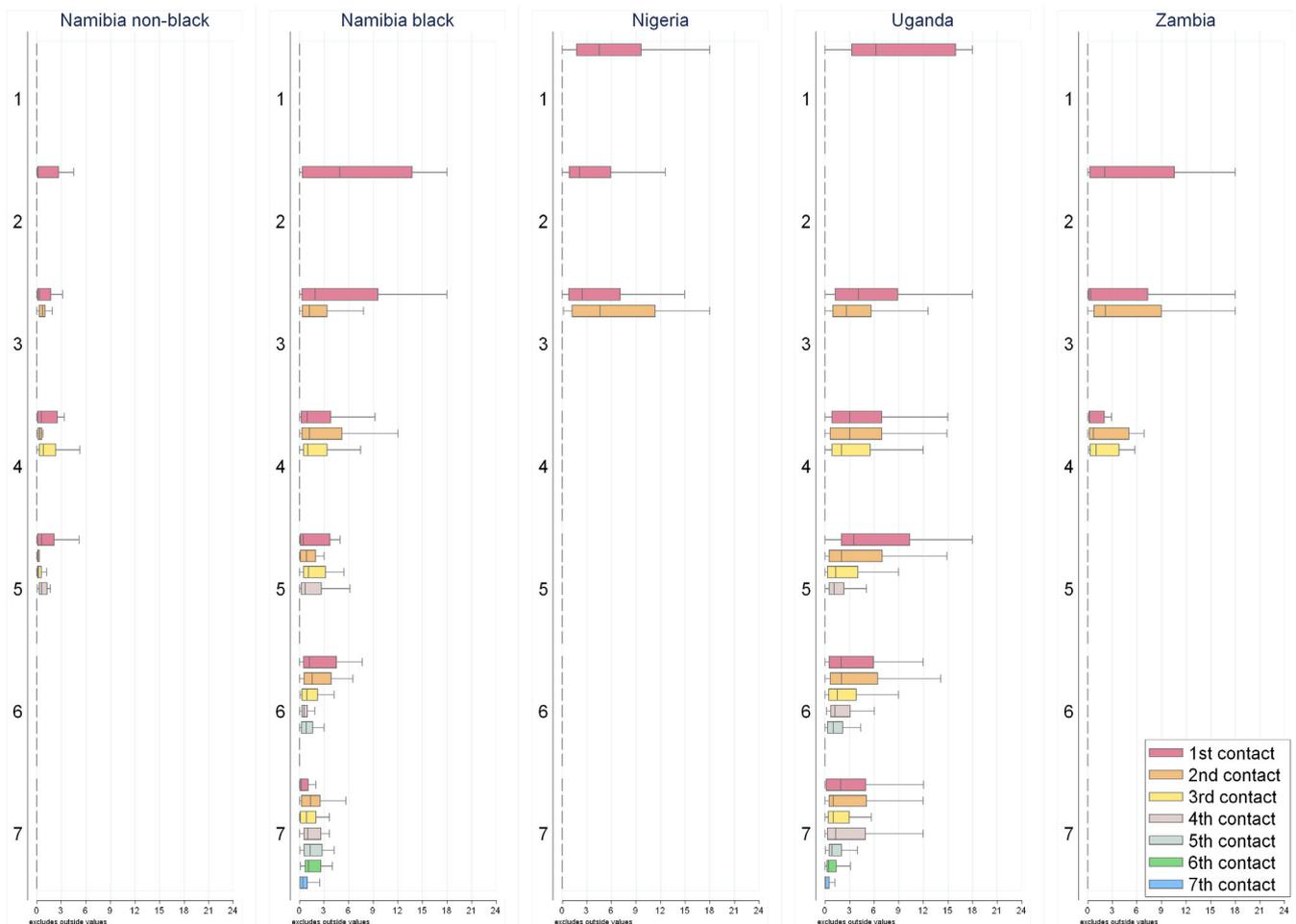
### 3.3 | Length of the diagnostic journey

Lengths of the diagnostic journey (Figure 1, left panel) were shortest for Namibia-non-blacks (median [months]: 2.4) and longest in Uganda (11.3). Consequently, the percent of women diagnosed within 3 months of symptom recognition ranged from 59% in Namibia-non-black women to 11% in Uganda (Figure 1, right panel). The diagnostic journey was much shorter for women whose breast abnormality was

first detected during a routine hospital visit (screen-detected/CBE, 30 women including 15 Namibian-non-black and 8 Namibian-black) than for symptomatic women, with medians (IQR) of 1.6 (0.3-5.9) and 7.3 (3.1-16.7) months, respectively.

### 3.4 | Length of the diagnostic journey and BC stage at diagnosis

Among women with malignant BC, 65% had advanced disease (Stages III/IV), with this percent being highest in Nigerian women (76%) and lowest in Namibian-non-black women (26%). Excluding screen-detected women, the odds of being diagnosed with Stage III/IV BC increased with increasing length of the diagnostic journey (age-population-adjusted OR (95% confidence interval [CI]): 1 (reference), 1.32 (0.93-1.86), 1.75 (1.25-2.45) and 1.98 (1.45-2.70) for <3, 3 to <6, 6 to <12 and ≥12 months, respectively; *P*-for-trend <.001), with no clear evidence of between-population group heterogeneity.



**FIGURE 2** Median (IQR) time intervals between first visits to consecutive HCP, by total number of HCPs visited, among ABC-DO symptomatic women. Total number of HCP visited includes the study hospital. Outlier values were excluded and estimates for categories with <10 women were omitted [Color figure can be viewed at wileyonlinelibrary.com]

**TABLE 3** Associations between woman-level factors and length of the diagnostic journey to breast cancer, and its pre-contact and post-contact intervals, among symptomatic women in the ABC-DO cohort

Variable	Study population group	Pre-diagnostic interval		$P_{\text{het}}^b$	Pre-contact interval		Post-contact interval	
		IRR (95% CI) <sup>a</sup>			IRR (95% CI) <sup>a</sup>		IRR (95% CI) <sup>a</sup>	
		Overall (n = 1399) <sup>c</sup>	Group-specific		Overall (n = 1399) <sup>c</sup>	Group-specific	Overall (n = 1356) <sup>c,d</sup>	Group-specific
<b>Sociodemographic</b>								
Age (10 years increase)		1.32 (1.02, 1.69)		.148	1.26 (0.89, 1.79)		1.35 (0.94, 1.93)	
Low SEP (vs medium/high)		1.12 (1.00, 1.25)		.306	1.10 (0.93, 1.30)		1.22 (1.03, 1.43)	
Not married (vs married)		1.07 (0.96, 1.20)		<.001	1.06 (0.91, 1.24)		1.11 (0.95, 1.31)	
	Namibia-non-blacks		2.21 (1.23, 4.00)			2.63 (1.22, 5.64)		1.96 (0.85, 4.52)
	Namibia-blacks		1.39 (1.10, 1.74)			1.28 (0.90, 1.80)		1.50 (1.10, 2.05)
	Nigeria		0.75 (0.60, 0.94)			0.70 (0.54, 0.91)		0.91 (0.60, 1.36)
	Uganda		1.04 (0.88, 1.23)			1.15 (0.91, 1.47)		0.96 (0.75, 1.21)
	Zambia		1.07 (0.79, 1.44)			1.09 (0.63, 1.87)		1.04 (0.70, 1.54)
Any children living at home (yes vs no)		0.97 (0.86, 1.10)		.86	1.01 (0.85, 1.19)		0.92 (0.77, 1.11)	
Primary/no education (vs secondary/higher)		1.24 (1.10, 1.40)		.037	1.16 (0.98, 1.37)		1.35 (1.13, 1.61)	
	Namibia-non-blacks		0.89 (0.40, 1.98)			0.75 (0.27, 2.07)		0.90 (0.31, 2.65)
	Namibia-blacks		1.47 (1.16, 1.86)			1.83 (1.30, 2.57)		1.21 (0.86, 1.69)
	Nigeria		1.16 (0.89, 1.53)			1.12 (0.81, 1.55)		1.33 (0.80, 2.20)
	Uganda		1.20 (1.00, 1.45)			0.91 (0.70, 1.18)		1.45 (1.13, 1.88)
	Zambia		1.37 (1.00, 1.87)			1.00 (0.56, 1.80)		1.71 (1.13, 2.57)
Working in unskilled employment (yes vs no)		1.10 (0.96, 1.26)		.302	1.22 (1.01, 1.47)		1.06 (0.86, 1.29)	
<b>Knowledge and beliefs</b>								
Ever heard about BC (yes vs no)		1.05 (0.92, 1.21)		.015	0.89 (0.74, 1.08)		1.28 (1.04, 1.57)	
	Namibia-non-blacks		—			—		—
	Namibia-blacks		1.06 (0.79, 1.43)			1.01 (0.64, 1.60)		1.20 (0.81, 1.79)
	Nigeria		1.08 (0.83, 1.40)			0.93 (0.68, 1.26)		1.30 (0.82, 2.06)
	Uganda		1.19 (0.97, 1.46)			0.99 (0.74, 1.33)		1.40 (1.04, 1.89)
	Zambia		0.85 (0.54, 1.33)			0.92 (0.40, 2.10)		0.95 (0.51, 1.76)
Know someone with BC		1.03 (0.92, 1.14)		.916	0.93 (0.81, 1.08)		1.12 (0.96, 1.32)	
Thinks BC is common		0.98 (0.87, 1.10)		<.001	0.78 (0.67, 0.92)		1.14 (0.97, 1.36)	
	Namibia-non-blacks		0.31 (0.14, 0.65)			0.35 (0.13, 0.95)		0.19 (0.06, 0.58)
	Namibia-blacks		1.10 (0.88, 1.39)			0.91 (0.64, 1.27)		1.32 (0.97, 1.80)
	Nigeria		0.88 (0.67, 1.16)			0.89 (0.65, 1.22)		0.75 (0.45, 1.26)
	Uganda		1.15 (0.96, 1.37)			0.82 (0.64, 1.05)		1.50 (1.17, 1.93)
	Zambia		0.97 (0.71, 1.33)			0.78 (0.44, 1.39)		1.04 (0.70, 1.57)
Thinks BC is curable		0.96 (0.86, 1.08)		.174	0.93 (0.80, 1.09)		0.96 (0.81, 1.14)	
Attributed symptom(s) to cancer		0.56 (0.47, 0.67)		.115	0.50 (0.39, 0.64)		0.62 (0.47, 0.80)	

(Continues)

**TABLE 3** (Continued)

Variable	Study population group	Pre-diagnostic interval			Pre-contact interval		Post-contact interval	
		IRR (95% CI) <sup>a</sup>		<i>P</i> <sub>het</sub> <sup>b</sup>	IRR (95% CI) <sup>a</sup>		IRR (95% CI) <sup>a</sup>	
		Overall (n = 1399) <sup>c</sup>	Group-specific		Overall (n = 1399) <sup>c</sup>	Group-specific	Overall (n = 1356) <sup>c,d</sup>	Group-specific
Belief in spiritual medicine		1.06 (0.94, 1.19)		.346	0.97 (0.82, 1.15)		1.11 (0.93, 1.32)	
Belief in traditional medicine		1.10 (0.98, 1.25)		.007	1.03 (0.87, 1.22)		1.24 (1.03, 1.48)	
	Namibia-non-blacks		0.24 (0.06, 0.91)			0.09 (0.01, 0.75)	0.40 (0.08, 2.12)	
	Namibia-blacks		0.89 (0.65, 1.20)			1.03 (0.65, 1.64)	0.70 (0.46, 1.07)	
	Nigeria		1.42 (1.11, 1.81)			1.20 (0.89, 1.62)	1.92 (1.23, 3.00)	
	Uganda		0.89 (0.65, 1.20)			0.94 (0.74, 1.21)	1.12 (0.88, 1.42)	
	Zambia		1.08 (0.78, 1.49)			0.95 (0.51, 1.75)	1.21 (0.79, 1.85)	
Muslim (vs other religions) <sup>e</sup>		0.76 (0.60, 0.97)		n.a.	0.94 (0.67, 1.32)		0.69 (0.48, 0.97)	
Health related								
Recent birth (<3 years)		1.02 (0.85, 1.21)		.104	1.08 (0.84, 1.38)		0.95 (0.73, 1.22)	
Other chronic comorbidities (ever vs never)		0.91 (0.81, 1.02)		.297	0.83 (0.71, 0.98)		0.99 (0.84, 1.17)	
Personal or known family history of BC		1.09 (0.92, 1.28)		.261	0.88 (0.70, 1.11)		1.33 (1.05, 1.70)	
HIV positive		1.04 (0.87, 1.25)		.022	1.18 (0.92, 1.51)		0.96 (0.74, 1.25)	
	Namibia-non-blacks		—			—	—	
	Namibia-blacks		0.93 (0.68, 1.26)			1.11 (0.70, 1.76)	0.77 (0.50, 1.19)	
	Nigeria		1.14 (0.61, 2.13)			0.64 (0.31, 1.35)	2.16 (0.72, 6.47)	
	Uganda		0.77 (0.60, 1.00)			0.77 (0.53, 1.13)	0.71 (0.49, 1.03)	
	Zambia		1.77 (1.17, 2.68)			2.12 (0.97, 4.62)	1.60 (0.93, 2.75)	
Symptom related								
First symptom recognized was breast lump (yes vs no) <sup>f</sup>		1.16 (0.99, 1.36)		.574	1.42 (1.14, 1.76)		1.04 (0.82, 1.31)	
Navigation-related								
Urban residence		0.99 (0.88, 1.11)		.957	1.09 (0.93, 1.28)		0.95 (0.81, 1.13)	
First contact								
Primary HCP		1 (ref.)		.409	1 (ref.)		1 (ref.)	
Secondary HCP		1.04 (0.92, 1.18)			1.29 (1.08, 1.53)		0.87 (0.73, 1.05)	
Informal HCP		1.27 (1.00, 1.62)			1.07 (0.77, 1.50)		1.49 (1.05, 2.11)	

Abbreviations: BC, breast cancer; HCP, health care provider; n.a., not applicable; ref., reference category; SEP, socioeconomic position; —, estimates based on <10 women omitted.

<sup>a</sup>Incidence rate ratios (IRR), with 95% confidence intervals (CI), adjusted for study population group, age (in four categories: 18-39; 40-49; 50-59; 60+), educational level (primary or none vs secondary or higher), having suffered from a non-HIV chronic comorbidities (ever vs never) and attributing first breast symptom(s) to cancer (yes vs no).

<sup>b</sup>*P*-value for interaction with study population group.

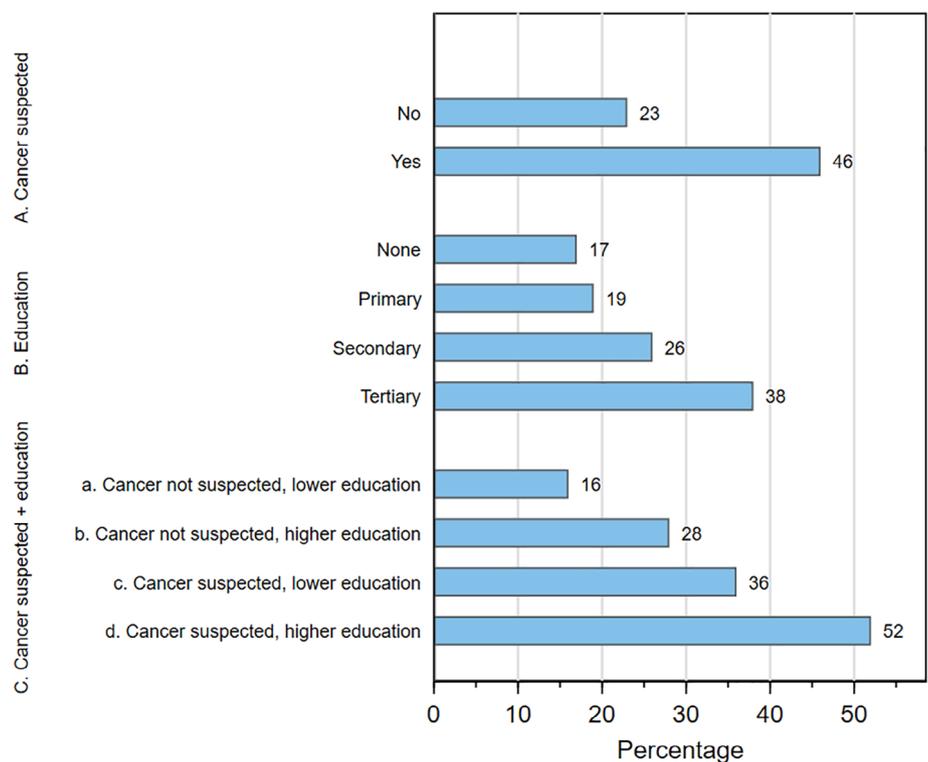
<sup>c</sup>Excludes 30 women whose symptoms were first discovered by a routine clinical breast examination or through screening mammography/ultrasound (see Results section).

<sup>d</sup>Excludes a further 43 women whose date of final diagnosis preceded the self-reported date of their first HCP visit (see Methods section).

<sup>e</sup>IRR (95% CI) estimates for the Ugandan population group only as this is the only one with a sizeable Muslim population (n = 395 for the pre-diagnostic and the pre-contact intervals; n = 386 for the post-contact interval).

<sup>f</sup>Excludes an additional eight women with missing data for this variable.

**FIGURE 3** Percentage of ABC-DO symptomatic women diagnosed within 3 months from the time of their symptom recognition by: A, whether the woman suspected first symptom might be cancer; B, the woman's highest level of formal education; and c, combined education and suspicion of cancer, where lower education is none/primary and higher education is secondary or more [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]



### 3.5 | Partitioning the diagnostic journey into pre- and post-first HCP contact intervals

The median post-contact interval represented at least 60% of the diagnostic journey in all settings except Nigeria, where the pre-contact interval dominated (Table 2). Although the number of HCP visited was not excessive, the time intervals between visits to consecutive HCPs were long (Figure 2). For instance, the median length (in months) between visits to the first and second HCP ranged from 0.6 in Namibian-non-black and 1.4 in Namibian-black women to 3 in Zambia and 5 in Nigeria.

### 3.6 | Woman-level correlates of the diagnostic journey length

Women-level correlates of the diagnostic journey length were analyzed excluding screen-detected/CBE women. Minimally adjusted and fully adjusted analyses yielded similar IRR estimates and hence only findings from the latter are presented (Table 3). The length of the diagnostic journey increased by 32% per every 10-year increase in age at diagnosis (IRR: 1.32, 95% CI: 1.02-1.69). The diagnostic journey was 12% longer (IRR: 1.12, 95% CI: 1.00-1.25) among women of low relative to those of medium/high socioeconomic position (SEP) and 24% longer (1.24, 1.10-1.40) among those with primary/none relative to those with higher education, both driven mainly by longer post-contact intervals. The association with low education was particularly marked in Namibian-black (1.47, 1.16-1.86) and Zambian (1.37, 1.00-1.87) women. Being unmarried was associated with a longer

diagnostic journey in Namibian-black and non-black women, but with a shorter journey in Nigeria.

The length of the diagnostic journey decreased by about half (0.56, 0.47-0.67) if a woman attributed her initial symptom(s) to cancer, reflecting both shorter pre- and post-contact intervals. Belief in traditional medicine was associated with a longer (1.42, 1.11-1.81) diagnostic journey in Nigeria, driven mainly by a longer post-contact interval, but with a shorter (0.24, 0.06-0.91) journey in Namibian-non-black women, reflecting both shorter pre- and post-contact intervals. In Uganda, the only setting with a sizeable Muslim population, Muslim women had a shorter diagnostic journey (0.76, 0.60-0.97), reflecting a shorter post-contact interval. Being HIV-positive was associated with a longer diagnostic journey in Zambia (1.77, 1.17-2.68; HIV prevalence: 15.1%), driven by longer pre- and post-contact intervals, but no association was found for Namibian-black or Ugandan women, who had similar HIV-prevalence (13.2% and 11.8%, respectively). Noticing a breast lump as the first symptom was associated with a longer pre-contact interval. Visiting first an informal HCP was associated with a longer diagnostic journey, reflecting a longer post-contact interval.

The absolute difference (AD) in the median length of the diagnostic journey between women with low vs high education was 3.6 months, and between those who attributed their symptoms to cancer vs those who did not was 4.1 months, translating into AD in the proportion diagnosed  $\leq 3$  months of 20% and 22%, respectively (Figure 3). Hence, the AD in median lengths of the diagnostic journey between higher-educated women who attributed their symptoms to cancer and lower-educated women who did not was 7.2 months, corresponding to a 34% AD in the proportion diagnosed  $\leq 3$  months.

## 4 | DISCUSSION

The diagnostic journey of ABC-DO women was much longer than reported for white and black women in North America,<sup>11-28</sup> stretching back to the 1940 to 1960s, but consistent with those reported for black women in SSA<sup>29-38</sup> (Supplemental Material). The post-contact interval accounted for over 60% of the diagnostic journey in all settings except Nigeria, the sole sites with regional rather than national catchment population, consistent with considerable delays after a woman's first HCP contact and in line with the high proportion of women reporting an inappropriate outcome of their first HCP visit. The prolonged post-contact interval mainly reflected long intervals between visits to a few HCP, rather than visits to multiple HCPs. These findings highlight the importance of educating primary and secondary health-care professionals about BC, and the need for health-system implementation of clear referral pathways to fast-track patients with suspicious breast abnormalities to specialized centers for early diagnosis.

Identified woman-level correlates of prolonged time to diagnosis were consistent with recent literature,<sup>6,39</sup> with higher SEP being associated with shorter diagnostic journeys. Attributing the initial symptom(s) to cancer was associated with shorter time to diagnosis independently of educational level, indicating that improvement of a woman's BC awareness should be a priority, particularly among socioeconomic disadvantaged populations. Contrary to studies in HICs,<sup>40,41</sup> women whose initial symptom was a lump experienced a longer pre-contact interval. Being married was associated with shorter diagnostic journeys in Namibia and Uganda. In contrast, being married and, consistent with the low level of BC awareness, believing in traditional medicine were associated with longer diagnostic journeys in Nigeria.<sup>9</sup> Being HIV+ was associated with a longer diagnostic journey in Zambia, but not in the other two populations with high HIV-prevalence (Namibian-blacks and Uganda), reflecting perhaps between-setting differences in health-care access for HIV+ patients. Treatment and transport costs were the main self-reported barriers to first visiting a HCP in Namibia and Uganda, where women often had to travel long-distances to access health care.

ABC-DO is the largest study yet to quantify the length of the diagnostic journey, and its components, across a range of different SSA settings, and the first to examine their relationship with stage at diagnosis.<sup>8</sup> A major strength was the use of a specifically tailored m-health application to collect time-annotated events through a woman's diagnostic journey and information on potential correlates of its length. Weaknesses include the fact that participants were recruited in public tertiary referral centers and thus might be unrepresentative as not all BC patients are referred to these hospitals or can reach them (eg, lack of resources, early death). Furthermore, the self-reported length of the diagnostic journey might have been affected by between-woman variation in the ability to recognize symptoms (eg, among women with a similar diagnosis journey length mean tumor size was smaller among the more educated than among less-educated women<sup>8</sup>) and across settings (eg, the percent of cancers diagnosed at stages III/IV among women who reported a pre-contact interval of  $\leq 3$  months ranged from 21% in Namibian-non-black women to 54% in Nigerian and Namibian-black women). In particular, the relatively short diagnostic journey in Nigeria seems at odds with the

very high percent of women diagnosed with advanced disease (76%), suggesting later recognition (or admission) of symptoms, perhaps due to poorer BC awareness, greater fear and stigma or faster tumor growth associated with more aggressive tumor subtypes—the lack of immunohistochemistry testing in the Nigerian settings precluded examination of this. Reassuringly, overall, the self-reported length of the diagnostic journey was associated with tumor stage at diagnosis.

In summary, the diagnostic journeys of women with symptoms suspicious of BC, a disease that is a potentially curable if diagnosed and treated early, are unacceptably long in SSA. Priority should be given to promotion of BC awareness among both women and front-line health-care workers and implementation of accelerated mechanisms for referral of women with suspicious abnormalities to specialized centers for early diagnosis and treatment.

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### CONFLICT OF INTEREST

All authors declared no potential conflicts of interest. Where authors are identified as personnel of the International Agency for Research on Cancer/World Health Organization, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy or views of the International Agency for Research on Cancer/World Health Organization.

### ETHICS STATEMENT

The study was approved by all local and institutional ethics committees.<sup>7</sup> Participants provided written informed consent or, if illiterate, a fingerprint.

### DATA AVAILABILITY STATEMENT

Collaborations with ABC-DO at IARC are welcome. Please email [mccormackv@iarc.fr](mailto:mccormackv@iarc.fr)

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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