Breast Cancer Phenotypes in Africa: A Scoping Review and Meta-Analysis

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ABSTRACT

PURPOSE	Africans have been associated with more aggressive forms of breast cancer (BC).	(
	However, there is a lack of data regarding the incidence and distribution of	
	different subtypes on the basis of phenotypic classification. This scoping review	A
	and meta-analysis was undertaken to determine the distribution pattern of BC	F
	phenotypes (luminal, human epidermal growth factor receptor 2 [HER2]+, and triple-negative breast cancer [TNBC]) across the African region.	
METHODS	Four online databases (PubMed, Scopus, ProQuest, and EBSCOhost) were	
	accessed to identify studies published between 2000 and 2022 reporting the	(
	representation of receptor status (estrogen receptor, progesterone receptor,	(
	and HER2) in African patients with BC. Furthermore, the meta-analysis was	
	carried out using a random-effects model and pooled using the inverse variance	
	method and logit transformation. 95% CI and I ² statistics were calculated using	
	the Clopper-Pearson method to estimate between-study heterogeneity.	
RESULTS	A total of 2,734 records were retrieved, of which 2,133 were retained for further screening. After the screening, 63 studies were finally selected for the scoping	
	review and meta-analysis. The pooled frequency of luminal, HER2-positive	
	(HER2+), and TNBC was estimated at 56.30%, 12.61%, and 28.10%, respectively.	
	Northern Africa had the highest frequency of the luminal subtype, while West	

CONCLUSION Our results highlight the disparity in the representation of molecular subtypes among the people in different regions of Africa. There is a need to incorporate routine molecular subtyping into the management of African patients with BC.

had a representation of only 24 countries in Africa.

Africa showed higher frequencies of HER2+ and TNBC subtypes. The review also

ACCOMPANYING CONTENT

🛽 Data Supplement

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INTRODUCTION

Breast cancer (BC) is the most diagnosed cancer afflicting women globally and accounts for about 11% of all female cancers.¹ In Africa, BC incidence and mortality rates are estimated at 186,598 and 85,787, respectively.¹ This burden, however, varies widely among different African regions.² This disease ranks highest among female cancer-causing deaths in Northern and Western Africa, accounting for 24.7% and 27.1%, respectively. In Middle Africa and Eastern Africa, BC is the second leading cause of cancer death after cervical cancer, estimated at 23.9% and 17.9%, respectively. The lowest mortality of BC occurs in Southern African countries, where it accounts for about 15% of cancer death, ranking as the second leading cause of cancer death in that region.¹ The high mortality of BC in lower-income continents such as Africa is attributed to the lack of education and awareness, late diagnosis and treatment, poverty, and aggressive tumor subtypes, resulting in worse disease progression in the region.³

BC is a heterogeneous disease showing varied characteristics, progression, and response to therapy.⁴ The subtypes of BC are derived based on the ASCO/College of American Pathologists recommendation that posits that immunohistochemical testing of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) be incorporated into routine BC treatment protocols.^{5,6} Understanding the subtype of BC helps identify patients who could benefit from personalized treatments. Perou et al⁷ further delineated BC on the basis of the variation of gene expression patterns into four molecular subtypes: luminal A (Lum A), luminal B (Lum B), HER2-positive, and triple-negative breast cancer (TNBC). The molecular

subtyping of BC is therefore based on the expression pattern of these receptors.8 The preferred method of choice for molecular subtyping is the use of molecular techniques such as in situ hybridization, fluorescence in situ hybridization (FISH), polymerase chain reaction, or surrogate immunohistochemical methods.⁸ However, classical subtyping with immunohistochemistry (IHC) is commonly used because of the high cost of other molecular techniques.⁷ The molecular subtypes that individuals present with have prognostic implications and influence clinical outcomes and overall survival.⁹ The Lum A and Lum B molecular subtypes are associated with a better prognosis and long-term survival estimated at 80%-85% for 5 years.¹⁰ The HER2 subtype overly expressed in 20%-25% of BC cases has adverse survival outcomes.^{4,11} The TNBC, which is predicted to be the dominant subtype in the African population and associated with African ancestry,12 has the highest mortality rate compared with other molecular subtypes. It accounts for about 15%-20% of all cancers and a mortality rate of 40% within a 5-year diagnostic period.13 The TNBC subtype tumor, which lacks the expression of the three receptors, is characterized by aggressiveness and higher resistance to therapies, and it is generally difficult to manage.¹⁴ The role of racial and ethnic disparities in the incidences and distribution of BC subtypes has been documented.¹⁵ However, the exact distribution of BC subtypes in Africa remains largely unknown.¹⁶

This scoping review and meta-analysis was carried out to identify the distribution of molecular subtypes of BC in the African region. The following research questions were formulated for the review: (1) To what extent has research on BC molecular subtypes been undertaken in Africa? (2) Are all African countries/populations represented in these studies? (3) What is the distribution pattern of BC molecular subtypes in Africa? (4) Are there regional patterns of BC molecular subtypes?

METHODS

Protocol

This scoping review was carried out using the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.¹⁷

Eligibility Criteria

Four online databases (PubMed, Scopus, ProQuest, and EBSCOhost) were accessed to identify studies published between January 2000 and December 2022. The search strategy used for PubMed was modified for the other databases (Data Supplement, Table S1). The search keywords used were terms such as "Molecular subtypes," "luminal," and "TNBC" (Data Supplement, Table S1) and names of African countries ("Africa" and names of the 54 African countries). All articles found during the searches were saved into a reference manager software (EndNote, X9) and duplicates across the four databases were removed. Three reviewers participated in the review process. Two of the three

reviewers independently read the titles and abstracts of the articles, and irrelevant articles were removed, leaving 89 articles for the full review. Before this, a calibration exercise was performed to ensure a standardized review of the papers by the reviewers. For standardization, two of the three reviewers screened each paper independently from the searches and compared it until a consensus was reached. All conflicts generated during the screening stages between the reviewers were discussed and 88% agreement was reached on the articles included in the review. Three studies in the French language¹⁸⁻²⁰ were translated using Google Translate before inclusion in the review. The inclusion criteria for selected studies were studies done in Africa, or of African origin where the sample location could be identified, studies where the location of the sample in Africa can be identified, studies limited to BC molecular subtypes in women, otherwise, the majority of the sample population (98%) must be women, and studies with qualitative or quantitative reports indicating receptor status ER, PR, and HER2.

The following exclusion criteria were used: nondisclosure of sample country/city of origin, studies on populations outside Africa, studies that were written in other languages where a translation could not be obtained, studies where the full text cannot be accessed, studies on other cancers apart from BC, as well as studies on animals and cell lines. Review articles, book chapters, and conference proceedings were also excluded from the list.

The electronic database search retrieved 2,734 citation records. After removing duplicates, 2,136 articles were retained. Further screening of titles and abstracts resulted in the removal of 2,133 articles and a total of 113 articles were selected for full-text screening. Finally, 63 articles were included in the scoping review, while 50 articles were excluded from the screening process as they did not meet the inclusion criteria (Fig 1). The included studies were reviewed by three different reviewers and a consensus was reached on 63 eligible studies that met the criteria for the scoping review.

Quality Assessment

The systematic quality assessment of studies was not performed as it is not required in a scoping review.

Patient and public involvement: None.

Synthesis of Results

To organize data from the selected articles, we used a Microsoft Excel spreadsheet to extract relevant data on the basis of the research questions. Two reviewers extracted and charted the data independently, while the third reviewer validated them for accuracy. The following data were recorded in the spreadsheet: author(s), the title of publication, publication year, the country where the study was conducted, study design, analytical method, and outcomes measured (Data Supplement, Table S2).

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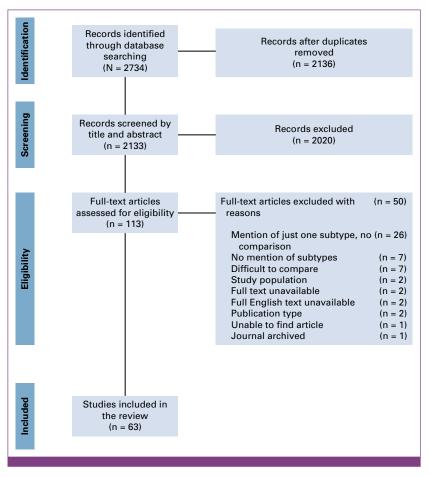


FIG 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses flowchart for studies included in the scoping review and meta-analysis.

Data Analysis

From the list of eligible studies, a heatmap of Africa was designed to show the represented countries and the proportion of BC molecular subtypes in each country using Tableau (2021-2-1). The meta-analysis was completed using R (V4.2.1).²¹ The analysis of Luminal, HER2-positive (HER2+), and TNBC frequencies was carried out for African women, stratified by region and individual country, using the meta and metafor packages in R. A random-effects model pooled using the inverse variance method and logit transformation was used. 95% CI and I² statistics were calculated using the Clopper-Pearson method to estimate betweenstudy heterogeneity. Between-study heterogeneity was assessed with Cochrane's Q, I², and H statistics as described previously by Hercules et al.²

RESULTS

The review had representations from 24 countries in Africa (Fig 2). The highest number of articles were from Nigeria (n = 10), followed by Egypt and Morocco (n = 7), Tunisia and South Africa (n = 4), Algeria, Ghana, Kenya, Uganda (n = 3), Ethiopia, Mali, Ivory Coast, Tanzania (n = 2), Angola,

Cameroon, Democratic Republic of Congo, Eritrea, Guinea, Malawi, Mozambique, Republic of Congo, Rwanda, and Togo (n = 1). A particular study also combined participants from two countries: Sudan and Eritrea (n = 1; Data Supplement, Table S2).

After analysis of the results, the pooled luminal frequency was 56.30% (95% CI, 51.88 to 60.67; $I^2 = 98\%$). When pooled by region, North Africa (n = 21) had the highest frequency of 63.42 (95% CI, 58.57 to 68.13; $I^2 = 97$). Central Africa also showed a high frequency of 81.89% but had representation from just two studies. The frequency of the luminal subtype was lowest in West Africa (n = 15) with 41.04% (95% CI, 31.27 to 51.17; $I^2 = 97$; Fig 3). Pooling by individual countries showed Kenya (n = 3) had the highest frequency (68.44%; 95% CI, 62.65 to 73.96; $I^2 = 63\%$). Luminal frequency was lowest in Ghana (n = 2) with 27.46% (95% CI, 10.88 to 48.09; $I^2 = 94\%$; Data Supplement, Table S3). The level of between-study heterogeneity (I^2) was found to be high at 94% (Data Supplement, Fig S1).

The pooled HER2+ frequency was 12.61% (95% CI, 11.37 to 13.91; $I^2 = 86\%$). When pooled by region, West Africa (n = 19) had the highest frequency of 14.87 (95% CI, 11.52 to 18.56;

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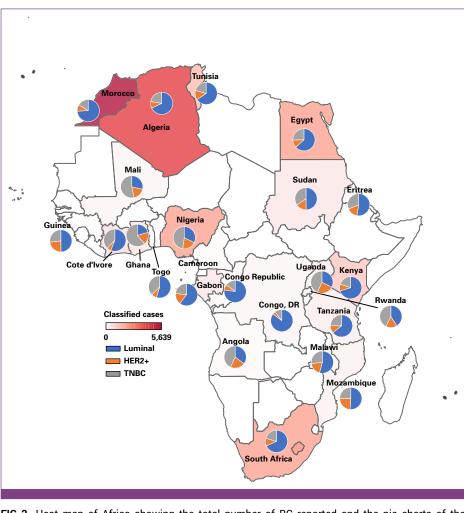


FIG 2. Heat map of Africa showing the total number of BC reported and the pie charts of the proportion of BC subtypes reported for each country. BC, breast cancer; HER2+, human epidermal growth factor receptor 2–positive; TNBC, triple-negative breast cancer.

I² = 88%). It was lowest in Central Africa (n = 3) with 8.05% (95% CI, 2.33 to 116.31; I² = 72; Fig 4). Pooling by individual countries showed that Uganda (n = 3) had the highest HER2+ frequency (18.72%; 95% CI, 13.67 to 24.33; I² = 34%). It was lowest in Kenya (n = 3) with 9.45% (95% CI, 7.81 to 11.23; I² = 0%; Data Supplement, Table S4). The level of between-study heterogeneity (I²) was found to be high at 86% (Data Supplement, Fig S1).

The pooled TNBC frequency was 28.10% (95% CI, 24.77 to 31.55; I² = 97%). When pooled by region, West Africa (n = 19) had the highest frequency of 42.36 (95% CI, 35.88 to 48.97; I² = 94%). It was lowest in Central Africa (n = 3) with 18.25% (95% CI, 7.53 to 32.08; I² = 83; Fig 5). Pooling by individual countries showed that Ghana (n = 3) had the highest TNBC frequency of 56.17% (95% CI, 49.77 to 62.47; I² = 54%). It was lowest in Morocco (n = 7) with 15.52% (95% CI, 12.32 to 19.01; I² = 91%; Data Supplement, Table S5). The level of between-study heterogeneity (I²) was found to be high at 97% (Data Supplement, Fig S1).

DISCUSSION

BC remains the leading cause of cancer deaths among women in Africa.^{1,22,23} Despite a lower incidence than the Western population, its mortality has continued to surge in the Black population.¹ The lack of consideration for an individualized approach according to molecular BC subtypes or IHC phenotypes, rather than a holistic approach, worsens BC prognosis in the region.²⁴ Studies have shown that even within the African population, BC inter-regional variability exists.²⁵ To our knowledge, this study provides evidence as the first scoping review and meta-analysis assessing the distribution of BC phenotypes in Africa.

This study examined 63 publications that reported the subtypes of BC across African countries. Our results confirm that variability exists in the distribution of phenotypes of BC in African regions and countries (Fig 2). The method of choice used in most of the studies analyzed for molecular subtyping was classical IHC. Only four studies²⁶⁻²⁹ incorporated FISH

Molecular Subtypes of Breast Cancer in Africa

Study	Luminal	Total	Events per 100 Observations	Luminal Frequency (%)	95% CI	Weigh
Region = Central Africa			:			
Luyeye G et al 2015	67	87		77.00	67.52 to 85.30	1.79
Maseb'a et al 2022	162	190	· · · · · · · · · · · · · · · · · · ·	85.26	79.84 to 89.98	1.89
Random-effects model		277	: 🗢	81.89	73.13 to 89.27	3.59
Heterogeneity: / ² = 64% [0% to 92%], τ ²		:			
Region = East Africa			<u>_</u>			
Tesfamariam et al 2013	12	20		60.00	37.48 to 80.65	1.39
Galukande et al 2014	99	226	- <u></u>	44.00	37.58 to 50.53	1.89
Rambau et al 2014	27	52		51.90	38.23 to 65.44	1.69
Sayed et al 2014	206	286	_: ""	72.00	66.64 to 77.06	1.89
Sawe et al 2017	27	49	_	55.00	40.85 to 68.77	1.69
Sengal et al 2017	339	678	••••••••••••••••••••••••••••••••••••••	50.00	46.24 to 53.76	1.99
Hadgu et al 2018	75	114		66.00	57.02 to 74.44	1.79
Uyisenga et al 2020	50	138		36.30	28.46 to 44.52	1.89
Sayed et al 2021	580	838	: 💻	69.21	66.04 to 72.29	1.99
Rweyemamu et al 2021	176	263	: 🖶	66.92	61.11 to 72.49	1.89
Desalegn et al 2022	195	334		58.38	53.05 to 63.62	1.89
Random-effects model		2998	~	57.57	50.19 to 64.78	19.19
Heterogeneity: / ² = 93% [89% to 95%],	² = 0.0131, <i>P</i> < .01	:			
Region = North Africa						
Abdelkrim et al 2010	131	194	: 	67.50	60.73 to 73.93	1.89
Salhia et al 2011	131	194	· · · · · · · · · · · · · · · · · · ·	69.10	62.47 to 75.36	1.8
Bennis et al 2012	256	366		70.00	65.20 to 74.59	1.8
Chaher et al 2012	250	176		51.60	44.20 to 58.97	1.8
El A et al 2012	151	274		55.10	49.17 to 60.96	1.8
El A et al 2012 Elnashar et al 2012	48	255		18.80	49.17 to 60.96 14.22 to 23.84	1.8
Fouad et al 2012	48 236	335		70.30	65.29 to 75.08	1.8
Aiad et al 2014	40	51	: <u>"</u>	78.00	65.48 to 88.44	1.6
Azim et al 2014	803					
		1096 125		73.27	70.61 to 75.85	1.9
Elesawy et al 2014	67			53.60	44.79 to 62.30	1.8
Fourati et al 2014	620	966		64.20	61.15 to 67.20	1.9
Cherbal et al 2015	2119	3014		70.30	68.66 to 71.92	1.9
Khalil et al 2016	661	1277	.	51.80	49.06 to 54.54	1.9
Samaka et al 2016	46	81		56.70	45.74 to 67.35	1.7
Bakkach et al 2017 Elidrissi M et al 2017	54	82		66.20	55.56 to 76.09	1.7
	1745	2260		77.20	75.45 to 78.91	1.9
Sahraoui et al 2017	86	116		74.40	66.03 to 81.97	1.8
Aznag et al 2018	1080	1559		69.30	66.99 to 71.57	1.9
Slaoui et al 2018	146	219		66.60	60.20 to 72.71	1.8
Mejri et al 2020	103	160		64.40	56.80 to 71.66	1.89
Belhadj et al 2021 Random-effects model	695	1140 13944	:	61.00 63.42	58.15 to 63.81	1.99 38.0 9
Heterogeneity: $I^2 = 97\%$ [!	96% to 97%], τ		Ĩ	03.42	58.57 to 68.13	30.0
Region = South Africa			:			
McCormack et al 2013	831	1216		68.30	65.66 to 70.89	1.99
Miguel et al 2017	36	140		25.70	18.77 to 33.29	1.8
Ruff et al 2018	345	554	;	62.20	58.12 to 66.20	1.9
Brandao et al 2020	107	210		51.00	44.23 to 57.76	1.8
Youngblood et al 2020	50	100		50.00	40.19 to 59.81	1.7
Kakudji et al 2021	83	116		71.50	62.91 to 79.38	1.8
Mthembu et al 2021	158	222		71.50		1.8
Random-effects model	158	2558		57.49	65.02 to 76.96	12.6
Heterogeneity: / ² = 95% [92% to 97%], τ		\sim	57.49	47.50 to 67.18	12.0
Pagion - Wast Africa						
Region = West Africa Adebamowo et al 2008	154	192		80.20	74.24 to 85.56	1.8
Agboola et al 2012	97	308		80.20 31.50	26.42 to 36.81	1.8
Ly et al 2012	97 19	114	- -	17.00	10.61 to 24.50	1.0
Der et al 2015	41	223	— :	18.40	13.57 to 23.77	1.7
Seshie et al 2015	59	156		37.80	30.33 to 45.57	1.8
Adeniji et al 2016	59 54	156		37.80	24.83 to 38.78	1.8
Effi et al 2016	54 186	302		61.60	24.83 to 38.78 56.04 to 67.01	1.8
Titloye et al 2016	172	835	•	20.60	17.92 to 23.41	1.0
Jkah et al 2017	60	123		48.40	39.59 to 57.26	1.9
keri et al 2018	55	125		37.90	30.15 to 45.96	1.8
Fraore et al 2018	28	58		48.30	30.15 to 45.96 35.47 to 61.24	1.8
Dembele et al 2019	28	58 98		48.30 35.70	26.47 to 45.48	1.0
Adani A et al 2019	35 64	98 117		35.70 54.70	45.59 to 63.65	1.7
Adani A et al 2020 Akinyemiju et al 2021	64 80			47.34	39.83 to 54.90	
Akinyemiju et al 2021 Aka et al 2021	171	169 335		47.34 51.04		1.8º 1.8º
Aka et al 2021 Random-effects model	171	335 3346		51.04 41.04	45.68 to 56.39 31.27 to 51.17	1.8 26.8
Heterogeneity: I^2 = 97% [!	96% to 98%], τ		~	41.04	31.27 10 31.17	20.8
Random-effects model		23123	\$	56.30	51.88 to 60.67	100.0
Heterogeneity: I ² = 98% [97% to 98%], τ	² = 0.0267, <i>P</i> = 0	0 20 40 60 80			
est for subgroup differer	$\chi_4 = 30.4$	L, UI = 4 \F < .U1)				
			Luminal Prevalence (%	6)		

FIG 3. Pooled luminal frequency stratified by regions.

for molecular subtype analysis (Data Supplement, Table S2). Africa still lags in integrating genomic markers for BC care and management.³⁰ Thus, IHC, which combines ER, PR, HER2, and Ki-67 (a human nuclear antigen proliferative marker), has become the surrogate method in most African countries.³¹ From our results, the combined luminal subtype frequency was highest in Northern Africa (63.42%) compared with other regions (41.04%–63.42%). This corroborates the report of El Fatemi et al³² suggesting a dominant Lum B subtype in this region. When pooled by individual countries

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Study	HER_2	Total	Events per 100 Observations	HER2+ Frequency (%)	95% CI	Weigl
Region = Central Africa			÷			
Kemfang J et al 2015	5	25		20.00	6.25 to 38.28	0.7
uyeye G et al 2015	7	87	- B ÷	8.10	3.14 to 14.90	1.3
Vaseb'a et al 2022	8	190	-	4.21	1.74 to 7.60	1.7
Random-effects model	-	302	$\overline{\diamond}$	8.05	2.33 to 16.31	3.7
Heterogeneity: $I^2 = 72\%$ [:	3% to 92%], ·		Ť	0.00	2.33 to 10.31	3.7
Region = East Africa Roy et al 2011	5	45	————————————————————————————————————	11.00	3.23 to 22.08	1.0
Fesfamariam et al 2013	1	20		5.00	0.00 to 20.22	0.6
Galukande et al 2014	50	226	- : 	22.00	16.82 to 27.65	1.8
Rambau et al 2014	5	52		9.60	2.82 to 19.35	1.0
	22	286		7.70		
Sayed et al 2014	4	49			4.87 to 11.10	1.8
Sawe et al 2017				8.00	1.73 to 17.56	1.0
Sengal et al 2017	108	678	_=	16.00	13.33 to 18.86	2.0
Hadgu et al 2018	11	114	<u> </u>	10.00	5.08 to 16.26	1.5
Vlole et al 2020	19	103		18.50	11.53 to 26.64	1.4
Jyisenga et al 2020	20	138		14.50	9.07 to 20.91	1.5
Sayed et al 2021	88	838	-	10.50	8.51 to 12.67	2.1
Rweyemamu et al 2021	29	263		11.03	7.50 to 15.12	1.8
Desalegn et al 2022	62	334	: 0	18.56	14.56 to 22.92	1.9
Random-effects model Heterogeneity: <i>I</i> ² = 74% [5	i5% to 85%],	3146 τ ² = 0.0032, <i>P</i> < .01	*	12.86	10.31 to 15.64	19.4
Region = North Africa			:			
Abdelkrim et al 2010	28	194	<u>-</u>	14.50	9.87 to 19.83	1.7
Salhia et al 2011	23	198	B	11.60	7.48 to 16.47	1.7
Bennis et al 2012	46	366	—	12.60	9.38 to 16.21	1.9
Chaher et al 2012	16	176	B	9.00	5.17 to 13.72	1.7
I A et al 2012	45	274	: 20 -	16.40	12.24 to 21.03	1.8
Inashar et al 2012	11	255		4.30	2.11 to 7.18	1.8
ouad et al 2012	38	335	E	11.30	8.12 to 14.93	1.9
Viad et al 2014	7	51		14.00	5.62 to 25.06	1.0
Azim et al 2014	116	1096		10.58	8.83 to 12.47	2.1
lesawy et al 2014	17	125		13.60	8.09 to 20.22	1.5
ourati et al 2014	129	966		13.40	11.32 to 15.62	2.1
Cherbal et al 2015	268	3014	F	8.90	7.91 to 9.94	2.1
Chalil et al 2016	200	1277		6.30	5.03 to 7.70	2.2
Samaka et al 2016	16	81		19.80	11.76 to 29.26	
						1.3
Bakkach et al 2017	9	82		10.80	4.87 to 18.56	1.3
lidrissi M et al 2017	194	2260		8.60	7.48 to 9.79	2.2
Sahraoui et al 2017	10	116		9.00	4.38 to 14.97	1.5
Aznag et al 2018	162	1559		10.40	8.93 to 11.97	2.1
Vejri et al 2020	31	160		19.20	13.44 to 25.70	1.6
Belhadj et al 2021 Random-effects model	137	1140 13725	• •	12.00 10.98	10.18 to 13.95 9.61 to 12.43	2.1 35.5
Heterogeneity: $I^2 = 81\%$ [7	'2% to 87%],			10.00		0010
Region = South Africa			<u>.</u>			
McCormack et al 2013	137	1216	<u> </u>	11.30	9.58 to 13.14	2.1
Viguel et al 2017	22	140		15.70	10.10 to 22.24	1.6
Ruff et al 2018	64	554		11.60	9.06 to 14.41	2.0
Brandao et al 2020	50	210	:	24.00	18.45 to 30.03	1.7
Youngblood et al 2020	17	100	- .	17.00	10.21 to 25.05	1.4
Kakudji et al 2021	7	116		6.00	2.29 to 11.17	1.5
Athembu et al 2021	26	222	÷.	11.71	7.78 to 16.30	1.7
Random-effects model leterogeneity: I ² = 80% [5	i9% to 90%],	2558 τ ² = 0.0033, <i>P</i> < .01	*	13.40	10.15 to 17.00	12.0
Region = West Africa						
Adebamowo et al 2008	8	192	= :	4.00	1.61 to 7.31	1.7
Adisa et al 2012	2	17		12.00	0.31 to 32.60	0.5
Agboola et al 2012	57	308	. 🔂	18.50	14.35 to 23.04	1.9
y et al 2012	21	114	- -	18.00	11.44 to 25.64	1.5
, Jer et al 2015	52	223	:	23.30	17.97 to 29.09	1.7
roctor et al 2015	15	147	-B-	10.00	5.61 to 15.43	1.6
eshie et al 2015	20	156	-	12.80	7.97 to 18.54	1.6
deniji et al 2016	33	171		19.30	13.70 to 25.58	1.6
ffi et al 2016	19	302	E	6.30	3.81 to 9.35	1.9
itloye et al 2016	164	835	: 📼	19.60	16.98 to 22.36	2.1
labi et al 2017	51	240	: 🖶	21.30	16.34 to 26.72	1.8
Jkah et al 2017	13	123		10.60	5.70 to 16.73	1.5
keri et al 2018	29	145		20.00	13.86 to 26.94	1.6
animowo et al 2019	20	61		32.80	21.51 to 45.16	1.1
raore et al 2019	13	58		22.40	12.48 to 34.13	1.1
raore et al 2019 Jembele et al 2019						
dani A et al 2019	14	98 117		14.30	7.99 to 22.00	1.4
	9	117		7.70	3.46 to 13.32	1.5
kinyemiju et al 2021	37	169		21.89	15.96 to 28.47	1.6
ka et al 2021	19	335	■ :	5.67	3.42 to 8.43	1.9
andom-effects model leterogeneity: I ² = 88% [8	3% to 92%1	3811 τ ² = 0.0097, <i>P</i> < .01	◇	14.87	11.52 to 18.56	29.4
	/0 (O UZ /0]/				44.0-	
Random-effects model leterogeneity: / ² = 86% [8	13% to 89%],	23542 τ ² = 0.0041, <i>P</i> < .01		12.61	11.37 to 13.91	100.0
	annu 2 7 2	2, df = 4 (<i>P</i> = .12)	0 20 40 60 80	100		

FIG 4. Pooled HER2+ frequency stratified by regions. HER2+, human epidermal growth factor receptor 2– positive.

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						-
egion = Central Africa			:			
emfang J et al 2015	10	25		40.00	21.46 to 60.04	1.2
uyeye G et al 2015	13	87		14.90	8.10 to 23.24	1.5
laseb'a et al 2022	20	190	•	10.53	6.52 to 15.33	1.6
andom-effects model eterogeneity: 1 ² = 83% [47	7% to 9.4%1 a	302 ² = 0.0152 <i>P</i> < 01		18.25	7.53 to 32.08	4.3
eterogeneity. 7 = 65% [47	76 LU 3476], 1	= 0.0152, r < .01	•			
egion = East Africa	16	45	:	36.00	22 E1 to E0 67	1.4
oy et al 2011 esfamariam et al 2013	2	45 20		10.00	22.51 to 50.67	1.4
					0.20 to 27.83	
alukande et al 2014	77	226		34.00	27.95 to 40.32	1.6
ambau et al 2014	20	52		38.50	25.66 to 52.18	1.4
ayed et al 2014	58	286		20.30	15.83 to 25.17	1.7
awe et al 2017	18	49		37.00	23.94 to 51.07	1.4
engal et al 2017	231	678	: 5	34.00	30.48 to 37.61	1.7
adgu et al 2018	27	114		24.00	16.56 to 32.31	1.6
llole et al 2020	39	103		37.90	28.74 to 47.51	1.6
yisenga et al 2020	52	138		37.70	29.77 to 45.97	1.6
ayed et al 2021	153	838	— _:	18.26	15.71 to 20.95	1.7
weyemamu et al 2021	58	263		22.05	17.24 to 27.28	1.7
esalegn et al 2022	77	334		23.05	18.68 to 27.73	1.7
andom-effects model eterogeneity: 1 ² = 87% [80)% to 92%], t	3146 ² = 0.0076, <i>P</i> < .01	\$	28.21	23.40 to 33.27	20.0
egion = North Africa						
egion = North Africa bdelkrim et al 2010	35	194		18.00	12.89 to 23.74	1.6
alhia et al 2011	22	198	B	11.30	7.23 to 16.12	1.6
ennis et al 2012	46	366		12.60	9.38 to 16.21	1.7
haher et al 2012	24	176	T i	13.60	8.90 to 19.09	1.6
A et al 2012	78	274		28.50	23.30 to 34.00	1.7
Inashar et al 2012	196	255	_ : 🖶	76.90	71.51 to 81.88	1.7
ouad et al 2012	38	335	-	11.30	8.12 to 14.93	1.7
iad et al 2014	4	51	- 	8.00	1.83 to 17.33	1.4
zim et al 2014	177	1096	:	16.15	14.03 to 18.39	1.7
lesawy et al 2014	21	125		16.80	10.71 to 23.91	1.6
ourati et al 2014	216	966		22.40	19.82 to 25.09	1.7
herbal et al 2015	627	3014	_ = :	20.80	19.37 to 22.27	1.7
halil et al 2016	143	1277	■ _;	11.20	9.53 to 12.99	1.7
amaka et al 2016	19	81		23.50	14.84 to 33.41	1.5
akkach et al 2017	19	82		23.00	14.46 to 32.79	1.5
lidrissi M et al 2017	321	2260	Image: 1	14.20	12.79 to 15.67	1.7
ahraoui et al 2017	19	116		16.60	10.33 to 23.97	1.6
znag et al 2018	316	1559	-	20.30	18.34 to 22.33	1.7
laoui et al 2018	47	219		21.60	16.38 to 27.31	1.6
lejri et al 2020	26	160		16.40	11.03 to 22.57	1.6
elhadj et al 2021	308	1140		27.00	24.46 to 29.62	1.7
andom-effects model eterogeneity: 1 ² = 97% [96	5% to 97%], a	13944 ² = 0.0120, <i>P</i> < .01	~	19.81	16.02 to 23.89	34.4
egion = South Africa						
cCormack et al 2013	248	1216		20.40	18.18 to 22.71	1.7
liguel et al 2017	44	140		31.40	23.95 to 39.36	1.6
uff et al 2018	114	554	<u> </u>	20.60	17.33 to 24.07	1.7
randao et al 2020	52	210		25.00	19.36 to 31.10	1.6
oungblood et al 2020	25	100	-8-	25.00	16.95 to 34.00	1.5
akudji et al 2021	26	116	- 🖬 ÷	22.50	15.32 to 30.59	1.6
Ithembu et al 2021	38	222		17.12	12.43 to 22.37	1.6
andom-effects model eterogeneity: $I^2 = 55\%$ [0		2558	~	22.20	19.44 to 25.09	11.4
	,o to o i /oj, 't	- 5.0010, 1 = .04				
egion = West Africa debamowo et al 2008	30	192	-	15.80	10.96 to 21.33	1.6
disa et al 2012	11	17		64.70	40.19 to 86.00	1.0
gboola et al 2012		308		37.50	32.17 to 42.99	1.7
	116					
/ et al 2012	52	114		46.00	36.91 to 55.22	1.6
er et al 2015	130	223	: "	58.30	51.75 to 64.70	1.6
roctor et al 2015	89	147	: _ _	60.50	52.45 to 68.27	1.6
eshie et al 2015	77	156	_: -8-	49.40	41.56 to 57.26	1.6
deniji et al 2016	43	171		25.10	18.86 to 31.89	1.6
ffi et al 2016	97	302	÷ -	32.10	26.94 to 37.48	1.7
tloye et al 2016	499	835	: 🔤	59.80	56.45 to 63.10	1.7
labi et al 2017	92	240	÷	38.30	32.24 to 44.55	1.6
kah et al 2017	50	123	÷	41.00	32.44 to 49.84	1.6
eri et al 2018	61	125	÷ _	41.00	34.16 to 50.25	1.6
animowo et al 2019	38	61	: •	42.10 62.30	49.72 to 74.11	1.4
aore et al 2019	15	58		25.90	15.34 to 38.04	1.4
embele et al 2019	49	98		50.00	40.09 to 59.91	1.5
dani A et al 2020	44	117	<u>_</u>	37.60	29.01 to 46.59	1.6
kinyemiju et al 2021	52	169		30.77	24.02 to 37.96	1.6
ka et al 2021	145	335		43.28	38.01 to 48.63	1.7
andom-effects model eterogeneity: / ² = 94% [91		3811	\$	42.36	35.88 to 48.97	29.9
	i /0 to 3070], 1				A	
andom-effects model eterogeneity: / ² = 97% [96	5% to 97%], t	23761 ² = 0.0210, P = 0		28.10	24.77 to 31.55	100.0
est for subgroup difference	es: $\chi_4^2 = 42.6$	6, df = 4 ($P < .01$)	0 20 40 60 80	100 (o)		

FIG 5. Pooled TNBC frequency stratified by regions. TNBC, triple-negative breast cancer.

(Data Supplement, Table S3), Kenya and South Africa showed high frequencies (68.44% and 67.65, respectively) of the luminal subtype. The luminal subtype is associated with a favorable prognosis and a lower risk of metastasis to distant organs.³³ This favorable biology may account for lower mortality in Kenya and South Africa compared with other countries in the 2020 GLOBOCAN data.¹ It is, however, important to note, as suggested by Hamidi et al,³⁴ that the low rate of mortality in Northern Africa is boosted by the more advanced screening, diagnostic, and treatment facilities available to countries in this region.

The reported frequency of HER2+ tumors was generally low in all African regions with an even distribution across all regions. This finding contrasts with observations among African American women who have been shown to have a higher risk of presenting with HER2+ BC.^{15,35} Several factors contribute to this discrepancy, including under-reporting because of the high cost and unavailability of anti-HER2 agents, as well as the misclassification of HER2 status because of the limited use of FISH to confirm equivocal IHC scores.³⁶⁻³⁸ Adani-Ifè et al³⁹ stressed the need for better facilities in Togo as most HER2 tests were obtained using the American Society for Oncology scoring rather than using FISH. Additionally, a review of 20 cancer registries in sub-Saharan African (SSA) countries revealed that only eight centers provided HER2 testing.⁴⁰ Similarly, Olasehinde et al⁴¹ studied an institutional database in Nigeria and found that HER2 testing was performed through staining as facilities for FISH were unavailable. These observations corroborate our finding that only four of the publications reviewed for this article used FISH. These findings underscore the need for capacity and infrastructure development across Africa for proper subtyping of BC, thereby identifying women who can benefit from targeted treatment with anti-HER2/neu agents.

The overall pooled TNBC frequency was 28.10% with regional variations. West Africa had the highest frequency (42.36%) compared with other regions (18.25%–28.21%). These results agree with previous findings of high TNBC prevalence in West Africa.^{2,25,42} Pooling by individual countries showed that Ghana, Mali, and Nigeria had the highest cases of TNBC with 56.17%, 47.85%, and 40.32%, respectively. These results are consistent with previous findings of a higher

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Solomon O. Rotimi, PhD, Department of Biochemistry, Covenant University, Km 10 Idi-Iroko Road, Ota, Ogun State, Nigeria; Twitter: @dapsing; e-mail: ola.rotimi@covenantuniversity.edu.ng. prevalence of TNBC in West Africa, which may account for worse outcomes of BC in this region.^{2,25,42} Newman et al⁴³ found higher TNBC in Ghanaian and African American women than the Whites and noticed a correlation between West African ancestry and the risk of developing the TNBC subtype.

The lack of IHC monitoring is a common challenge in most African countries. A review of 20 registries in SSA showed that only about half of these centers had standby laboratories for IHC testing. Additionally, three of these centers had to rely on obtaining IHC results from other countries, while one center could not obtain IHC results at all.⁴⁰ Furthermore, a review of records from an institutional database in Nigeria showed that of 607 patients diagnosed with BC between 2010 and 2018, only 131 patients had undergone IHC tests.⁴¹ Similarly, in some countries such as Ethiopia and Guinea, IHC is not carried out because of the unavailability of facilities.⁴⁴ A study conducted by Traoré et al⁴⁵ in Guinea revealed that out of 569 breast tumors diagnosed between 2007 and 2016, IHC testing was only carried out on 56 of these cases. In a study that combined data from five SSA countries (Namibia, Nigeria, Uganda, South Africa, and Zambia), it was found that IHC testing is a routined point of care in Namibia and South Africa. However, in Uganda, Nigeria, and Zambia, IHC monitoring is not a standard point of care and when required, it is organized out of pocket. As a consequence, evidence-based decisions are not routinely made for patients with BC in many African countries.⁴⁶

A significant limitation encountered when attempting to stratify the Lum A and B subtypes for this scoping review lies in the inconsistency of biomarkers across various research papers. This necessitated the combination of Lum A and Lum B as luminal for this scoping review.

Overall, our data further support the existing evidence of great variability among the African population. This underscores the need for a genetic and evidence-based approach in stratifying African populations in the studies designed to understand the genetic drivers of disparities in BC burden.^{47,48} A huge disparity exists in BC care and management between developed countries and countries in Africa.

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DATA SHARING STATEMENT

All data used in the analysis are available on request. All relevant data to the study have been included in the article or uploaded as supplementary information.

AUTHOR CONTRIBUTIONS

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I

Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/ rwc or ascopubs.org/go/authors/author-center.

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

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