

Breast cancer incidence and mortality in a Caribbean population: Comparisons with African-Americans

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on behalf of the Barbados National Cancer Study Group

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We describe breast cancer incidence and mortality in the predominantly African-origin population of Barbados, which shares an ancestral origin with African-Americans. Age-standardized incidence rates were calculated from histologically confirmed breast cancer cases identified during a 45-month period (July 2002–March 2006). Mortality rates were estimated from death registrations over 10-years starting January 1995. There were 396 incident cases of breast cancer for an incidence rate of 78.1 (95% confidence interval (CI) 70.5–86.3), standardized to the US population. Breast cancer incidence in African-Americans between 2000 and 2004 was 143.7 (142.0–145.5) per 100,000. Incidence peaked at 226.6 (174.5–289.4) per 100,000 among Barbadian women aged 50–54 years, and declined thereafter, a pattern in marked contrast to trends in African-American women, whose rates continued to increase to a peak of 483.5 per 100,000 in those aged 75–79 years. Incidence rate ratios comparing Barbadian and African-American women showed no statistically significant differences among women aged ≤ 39 years, marginal statistical differences among women 40–54 years and strongly significant differences among women aged ≥ 55 years ($p \leq 0.001$ at all older ages). The age-standardized mortality rate in Barbados was 32.9 (29.9–36.0) per 100,000; similar to reported US rates. The pattern of diverging breast cancer incidence between Barbadian and African-American women may suggest a greater contribution from genetic factors in younger women, and from environmental factors in older women. Studies in intermediate risk populations, such as Barbados, may assist the understanding of racial disparities in breast cancer.

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Key words: breast cancer; African-origin; incidence; mortality

Although breast cancer incidence rates are lower in African-American women than comparable White populations, their morbidity and mortality rates are higher.^{1–3} African-American women tend to present with late stage disease, which may reflect poor access to or utilization of health services, or indeed more aggressive forms of the disease.^{4–7} Insight into reasons for these differences may be gained by studying breast cancer patterns in other populations across the African diaspora. Of particular interest are comparisons with African-Caribbean populations, which share a common heredity with African-Americans and West Africans.⁸ As Caribbean countries undergo developmental changes consistent with the latter stages of the epidemiological transition,⁹ high rates of lifestyle-related chronic diseases are now prevalent,^{10–12} underpinning the similar health profiles in African-Caribbean and African-American populations. There remains, however, a dearth of relevant epidemiological data about breast cancer, reported to be the principal malignancy affecting women in the region.¹³

The aim of this report is to provide the first population-based data of breast cancer incidence and trends in mortality for women in Barbados, West Indies. Barbados is an independent Caribbean island nation in the western Atlantic Ocean, with an estimated population of about 270,000. At the 2000 household census, over 90% of all Barbadians were of African descent, approximately 4% were of European origin, while South Asian and other ethnic groups accounted for less than 2% of the population.¹⁴ The geographic features of the island, its comprehensive publicly-funded healthcare system, centralized pathology, radiology and other clinical specialist services, as well as cooperation of clinical col-

leagues, have facilitated the development of a comprehensive epidemiologic study of breast and prostate cancer. The Barbados National Cancer Study commenced in 2002 with the aim of describing the incidence and risk factors (environmental and genetic) for breast and prostate cancer. Our study provided infrastructure and allowed data collection for this report.

Material and methods

The Barbados National Cancer Study (BNCS) centers are the Clinical Center (Ministry of Health and The University of the West Indies, Bridgetown, Barbados, West Indies), the Local Laboratory Center (The University of the West Indies), the Coordinating Center (University Medical Center, Stony Brook, NY), the National Human Genome Research Institute (NHGRI) Center (Bethesda, MD) and the Gene Discovery Center (Translational Genomics Research Institute, Phoenix, AZ). The BNCS is funded by the NHGRI, with contribution from the Office for Minority Health.

All histologically confirmed cases of breast cancer occurring for the first time (*in situ* and invasive disease) were ascertained from records held at the Pathology Department of the Queen Elizabeth Hospital, Bridgetown. This is the sole public tertiary care hospital and all pathological samples in the country are evaluated in the department. Other data sources such as patient charts and pathology reports were reviewed and cases of recurrent breast cancer or disease occurring in nonresidents (*i.e.*, domiciled for less

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Received 8 April 2008; Accepted after revision 10 July 2008

DOI 10.1002/ijc.23889

Published online 9 October 2008 in Wiley InterScience (www.interscience.wiley.com).

TABLE I – AGE-SPECIFIC AND AGE-STANDARDIZED INCIDENCE OF FEMALE BREAST CANCER IN BARBADOS BETWEEN JULY 1, 2002 AND MARCH 30, 2006 PER 100,000 PERSON-YEARS OF OBSERVATION

Age group	Number of cases	Person years ¹	Age specific rate	95% CI
0–4	0	33,891	0	0–10.9
5–9	0	36,670	0	0–10.1
10–14	0	36,535	0	0–10.1
15–19	0	37,676	0	0–9.8
20–24	0	35,767	0	0–10.3
25–29	3	40,035	7.5	1.6–21.9
30–34	15	40,166	37.3	20.9–61.6
35–39	25	44,333	56.4	36.5–83.2
40–44	45	41,959	107.3	78.2–143.5
45–49	50	35,028	142.7	106.0–188.2
50–54	64	28,239	226.6	174.5–289.4
55–59	43	20,730	207.4	150.1–279.4
60–64	25	19,894	125.7	81.3–185.5
65–69	34	18,780	181.1	125.4–253.0
70–74	25	17,973	139.1	90.0–205.3
75–79	26	13,799	188.4	123.1–276.1
80–84	19	11,068	171.7	103.4–268.1
85+	17	10,974	154.9	90.2–248.0
Unknown age	5	–	–	–
Crude rate	396	523,517	75.6	68.4–83.5
Age standardized rates (US)	–	–	78.1	70.5–86.3
Age standardized rates (Europe)	–	–	78.6	70.7–87.2
Age standardized rates (World)	–	–	58.4	52.5–65.0

¹85+ age group rounded down to 10,974 to maintain correct person-year total.

than 6 months a year) were excluded. To ascertain mortality from breast cancer, we reviewed all death certificates held at the offices of the Registrar General for the 10-year period commencing January 1, 1995. These data were collected independently of the standard data gathering activities of the BNCS.

Statistical methods

We calculated crude incidence rate per 100,000 years of observation by dividing the number of incident cases by the number of women in the Barbados population and multiplying by 100,000. We calculated age specific incidence rates in 18 age groups (0–4 years, 5–9 years, 10–14 years, . . . , 85 years and older). The incidence of breast cancer is known to increase with age: to allow comparisons independent of age, we calculated age-standardized rates (with 95% confidence intervals), using the direct method, applied to 3 standard populations: the 2000 US standard population¹⁵ and the IARC European and World standard million populations.¹⁶ Age-standardized data (using the 2000 US standard population) were compared to the US breast cancer incidence rates from the Surveillance Epidemiology and End Results (SEER) reports for the period of 2000–2004.¹⁷ The same techniques were used to calculate age-stratified and age-standardized death rates for the 10-year study period of 1995–2004. For crude and age-stratified rates we calculated exact Poisson confidence intervals, and for age-standardized confidence intervals we used a Gamma approximation, which has improved properties when the number of cases is small.¹⁸ We compared Barbados and SEER incidence rates by age and year of diagnosis using incidence rate ratios, calculated from a log-linear model. We performed all analyses using Stata (Version 10, StataCorp LP, College Station, TX).

Results

During the study period, 396 women were diagnosed with histologically confirmed breast cancer. Table I presents age-specific incidence of female breast cancer in Barbados. The age at presentation ranged from 26 to 100 years, with a median age of 54 years (interquartile range of 45–68 years). Crude breast cancer incidence increased from 7.5 (95% CI 1.6–21.9) per 100,000 in women aged 25–29 years, to a peak at 226.6 (95% CI: 174.5–289.4) per 100,000 in women aged 50–54 years, declining thereafter in

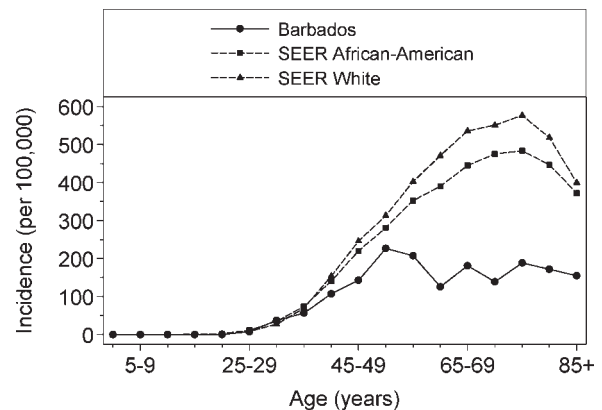


FIGURE 1 – Age-specific incidence of female breast cancer in Barbados (2002–2006) and the United States (2000–2004).

women of postmenopausal age. The overall crude incidence rate was 75.6 (95% CI: 68.4–83.5) per 100,000, with rates of 78.1 (70.5–86.3), 78.6 (70.7–87.2) and 58.4 (52.5–65.0) per 100,000 standardized to the US, European and World populations, respectively. Comparable US rates varied according to ethnic group, such that overall breast cancer incidence in White and African-American women was 162.7 (95% CI: 162.1–163.4) per 100,000 and 143.7 (95% CI: 142.0–145.5) per 100,000, respectively.

Figure 1 presents breast cancer incidence in Barbadian women and data from the US. Rates were similar in Barbadian and African-American until age 40–44 years, when the incidence among Barbadians was 107.3 (95% CI: 78.2–143.5), compared to 140.6 (135.1–146.2) among African-Americans (log linear model comparison, $p = 0.07$). Thereafter, breast cancer incidence rates among African-American women rose faster and into later life than in Barbadians. The highest incidence among African-Americans was 483.5 (95% CI: 461.7–505.9) among women aged 75–79; over 250 per 100,000 higher and 25 years later than the peak incidence among Barbadian women. Incidence rates among White

TABLE II – SHORT-TERM SECULAR CHANGE IN BREAST CANCER INCIDENCE IN BARBADOS AND IN AFRICAN-AMERICANS

Year	Follow-up months (days)	Cases	Person-years exposure	Age-standardized incidence rate (2000 US standard population)	
				Barbados	African-Americans
2002	6 (183)	55	69,981	79.2 (59.3–103.7)	143.3 (139.5–147.3)
2003	12 (365)	107	139,579	80.6 (65.8–97.8)	143.0 (139.1–146.9)
2004	12 (365)	93	139,961	67.9 (54.7–83.5)	143.7 (139.9–147.6)
2005	12 (365)	107	139,579	79.5 (65.0–96.5)	n/a ¹
2006	3 (91)	34	34,417	101.1 (69.4–143.1)	n/a ¹
2002–2006	45 (1,369)	396	523,517	75.6 (68.4–83.5)	–

All rates based on invasive and *in-situ* disease.

¹SEER data for 2005 and 2006 not available (n/a).

TABLE III – INCIDENCE RATE RATIOS (IRRS) COMPARING AGE-STRATIFIED INCIDENCE RATES, AND SECULAR INCIDENCE RATES BETWEEN BARBADOS AND AFRICAN-AMERICANS (2002–2004)¹⁷

Characteristic	IRR	95% CI	p Value
Age			
25–29	1.49	0.48–4.67	0.49
30–34	0.94	0.56–1.57	0.81
35–39	1.31	0.89–1.95	0.18
40–44	1.31	0.98–1.76	0.07
45–49	1.54	1.17–2.04	0.002
50–54	1.24	0.97–1.59	0.09
55–59	1.70	1.26–2.30	0.001
60–64	3.10	2.09–4.60	<0.001
65–69	2.46	1.75–3.45	<0.001
70–74	3.42	2.30–5.07	<0.001
75–79	2.57	1.74–3.78	<0.001
80–84	2.60	1.65–4.09	<0.001
85+	2.40	1.49–3.88	<0.001
All ages	1.59	1.44–1.76	<0.001
Year			
2002	1.51	1.16–1.97	0.002
2003	1.59	1.31–1.93	<0.001
2004	1.84	1.50–2.26	<0.001

Americans diverged even earlier and reached a peak at 576.8 (95% CI: 569.7–583.9) per 100,000.

Table II presents secular trends in incident breast cancer in Barbadian and African-American women during the period from 2002 to 2006. Rates in African-Americans were consistently around 143 per 100,000 between 2002 and 2004 in contrast to an age-standardized rate of 75.4 (95% CI: 65.9–86.2) per 100,000 in Barbadians during this period.

Table III compares age-specific and secular breast cancer incidence in African-American and Barbadian women. Incidence rate ratios (IRR) showed no statistically significant differences among women aged 39 or less, marginal statistical differences among women aged 40–54, and strongly significant differences among women aged 55 years and older. At ages 60 years and older, incidence rates among African-American women were consistently between 2 and 4 times greater than in Barbadian women ($p < 0.001$ in all cases).

Table IV presents age-stratified and age-standardized death rates in Barbados from breast cancer between 1995 and 2004, per 100,000 person years of observation. In this 10-year period, there were 469 death certifications citing breast cancer as a principal cause of death. The number of deaths from breast cancer progressively increased with older age, with the distribution by 10-year age-groups being: aged 39 or less (33 or 7.0%), 40–49 (79 or 16.8%), 50–59 (78 or 16.6%), 60–69 (83 or 17.7%), 70–79 (86 or 18.3%), 80+ (110 or 23.5%). The crude death rate was 33.6 (95% CI: 30.6–36.8) per 100,000, whereas the age-standardized rate (using the US standard 2,000 population) was 32.9 (95% CI: 29.9–36.0) deaths per 100,000 person years.

Figure 2 and Table V present data comparing mortality from breast cancer in the Barbadian and US populations between 1995 and 2004. Despite the lower breast cancer incidence among older

TABLE IV – AGE-STRATIFIED AND AGE-STANDARDIZED DEATH RATES FROM BREAST CANCER IN BARBADOS BETWEEN JANUARY 1, 1995 AND DECEMBER 31, 2004 PER 100,000 PERSON-YEARS OF OBSERVATION

Age group	Number of cases	Person years	Age specific rate	95% CI
0–4	0	90,360	0	0–4.1
5–9	0	97,770	0	0–3.8
10–14	0	97,410	0	0–3.8
15–19	0	100,450	0	0–3.7
20–24	0	95,360	0	0–3.9
25–29	4	106,740	3.8	1.0–9.6
30–34	13	107,090	12.1	6.5–20.8
35–39	16	118,200	13.5	7.7–22.0
40–44	38	111,870	34.0	24.0–46.6
45–49	41	93,390	43.9	31.5–59.6
50–54	33	75,290	43.8	30.2–61.6
55–59	45	55,270	81.4	59.4–108.9
60–64	47	53,040	88.6	65.1–117.8
65–69	36	50,070	71.9	50.4–99.5
70–74	48	47,920	100.2	73.9–132.8
75–79	38	36,790	103.3	73.1–141.8
80–84	43	29,510	145.7	105.5–196.3
85+	67	29,260	229.0	177.5–290.8
Crude rate	469	1,395,790	33.6	(30.6–36.8)
Age standardized rates (US)	–	–	32.9	(29.9–36.0)
Age standardized rates (Europe)	–	–	31.6	(28.6–34.8)
Age standardized rates (World)	–	–	22.6	(20.4–25.0)

Barbadians (standardized to the US population), we note the similar age-stratified death rates in the Barbadian, African-American and White American populations. In Barbados, breast cancer mortality ranged from 28.7 to 37.8 per 100,000, and among African-Americans rates ranged from 32.3 to 38.2 per 100,000.

Discussion

Breast cancer incidence was lower in the predominantly African ancestry population of Barbados, compared to rates in African and White Americans (78.1 vs. 143.7 and 162.7 per 100,000, respectively). Among Barbadians, age-specific rates reached a peak in the 50–54 year age group and declined thereafter, while rates continued to increase until ages 75–79 in the American populations (Fig. 1). Compared to Barbadian women, overall breast cancer incidence was 1.6 times higher in African-American women (IRR 1.59; 95% CI: 1.44–1.76), with elderly African-Americans (aged 60 years and older) experiencing 2–4 times the breast cancer incidence (Table III). In spite of the lower frequency of disease, Barbadian and African-American women experienced similar breast cancer mortality, with rates of 32.9 and 33.8 per 100,000, respectively (Table V). White American women had slightly lower mortality (25 per 100,000) (Fig. 2).

In our study, we recorded 396 incident cases of breast cancer during the period. Since an objective for this first description of breast cancer incidence in Barbados was complete case ascertain-

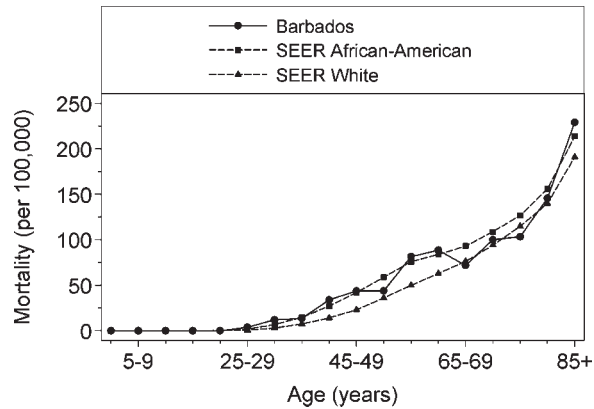


FIGURE 2 – Age-specific death rates of female breast cancer in Barbados (1994–2004) and the United States (2000–2004).

ment, we chose to include combined *in situ* and invasive disease to fulfill this ascertainment goal. Of the total cases, 348 or 88% had basic histology on disease type (*in situ* or invasive disease): 34 (9.8%) were *in situ* and 314 (90.2%) were invasive. The remaining 48 could not be assigned a histology type, and would create an incidence undercount had we chosen to focus on known disease alone. We performed a sensitivity analysis to examine the possible influence of unknown histology on incidence rates. Many of the cases with unknown histology had traveled overseas for histological diagnosis, a decision related to socioeconomic status and thus unlikely to be related to histology type. We therefore assumed that the 48 breast cancers of unknown histology had the same ratio of invasive disease as known cases and assigned 43 (90%) as invasive and 5 (10%) as *in situ*. Restricting to cases with known histology gave incidence rates of 60.0 per 100,000 (95% CI 53.5–67.0) for invasive disease and 6.5 per 100,000 (4.5–9.1) for *in situ* disease. Adding unknown cases increased invasive disease to 68.2 per 100,000 (61.3–75.7) and increased *in situ* disease to 7.5 per 100,000 (5.3–10.2). *In situ* breast cancer therefore accounted for the minority (one-tenth) of cases.

Comparisons of breast cancer incidence across the African diaspora demonstrate a gradient, with rates being lowest in West Africa, higher in the Caribbean and highest among African-Americans.^{13,16,19} Registry-based data, which provide more accurate disease estimates, are available from only 2 of 18 West African countries (Mali and the Gambia, with world standardized breast cancer incidence of 20 and 7 per 100,000, respectively), and 2 Caribbean countries, Martinique and Cuba. Data available from the cancer registry in Martinique, French West Indies documented an incidence rate of 35.8 per 100,000 (1981–2000; standardized to the world population).²⁰ Comparable data from Villa Clara in Cuba estimated breast cancer incidence (1995–1997) at 28.9 per 100,000.¹⁶ From our study, comparable breast cancer incidence in Barbados (standardized to the world population) is 58.4 per 100,000 (Table I). These overall incidences are lower than world standardized rates in African-American women between 2000 and 2004: 104.9 (95% CI: 103.6–106.2) per 100,000. These data have been collected at differing time periods and in populations with varying environmental and other characteristics, such as ancestry and degree of admixture, but they support a gradient in breast cancer incidence across the African diaspora.

Although overall breast cancer incidence is higher in White than African-American women, the latter often present with invasive breast cancer at an earlier age.¹⁷ Similar observations have now been reported in Black British women.²¹ Additionally, breast cancer incidence rates in younger Barbadian and African-American women (aged 50 years and younger) were similar. Biological mechanisms may partly underpin these observations. There are reported racial differences in estrogen and progesterone receptor

TABLE V – ANNUAL AGE-STANDARDIZED DEATH RATES FROM BREAST CANCER IN BARBADOS AND AMONG AFRICAN-AMERICANS BETWEEN JANUARY 1, 1995 AND DECEMBER 31, 2004 PER 100,000 PERSON-YEARS OF OBSERVATION

Year	Breast cancer death rates					
	Barbados			African-Americans		
	All (95% CI)	<50 years	50+ years	All	<50 years	50+ years
1995	28.7 (20.6–39.3)	11.1	74.9	38.2	11.7	107.5
1996	34.6 (25.6–46.0)	10.0	99.0	37.1	11.7	103.6
1997	29.5 (21.3–40.0)	11.7	76.0	37.4	11.0	106.6
1998	33.5 (24.6–44.7)	10.3	94.2	35.5	10.6	100.7
1999	25.6 (17.9–35.6)	7.0	74.3	35.2	10.3	100.5
2000	34.9 (25.8–46.4)	10.2	99.8	34.4	9.9	98.3
2001	37.2 (27.8–49.0)	14.1	97.7	34.5	9.9	99.1
2002	35.9 (26.5–47.6)	13.3	95.0	34.1	10.0	97.2
2003	37.8 (28.2–49.8)	14.0	100.2	34.1	9.7	97.9
2004	31.0 (22.4–42.1)	10.8	83.5	32.3	9.3	92.4

status, linked to differences in age-specific incident disease, tumor aggressiveness and clinical outcomes.^{22–24} The role of estrogen in the pathogenesis of breast cancer has been well established, and progesterone and HER2 receptor status are also known to affect breast tumorigenesis.^{25,26} As such, African-American women younger than 40 years with invasive cancer are more likely than White women to be negative for estrogen, progesterone and HER2 receptors (triple-negative disease), linked to poor survival regardless of disease stage.²⁶ These observations suggest a possible genetic etiology but this area remains poorly understood. African-American women have low rates of confirmed deleterious BRCA1 and BRCA2 mutations, and a spectrum of mutations which differs from those observed in European-origin populations.²⁷ Unique BRCA1 mutations have been described in African-Americans,²⁸ as well as specific founder mutations,²⁹ and recently, genetic variants in the insulin-like growth factor (IGF) signaling pathway have been described, which may partly explain racial differences in disease manifestations.³⁰ Much work, however, is needed to elucidate the genetic basis of breast cancer susceptibility in African-origin populations.

Breast cancer incidence was considerably lower in postmenopausal Barbadian women than among African-American women. A possible explanation may be differences in environmental exposures, including reproductive-related factors. Among BNCS female participants with breast cancer, Nemesure³¹ reported that reproductive profiles were characterized by later menarche, higher parity, earlier age at childbearing and higher frequency of breast feeding relative to African-American women, likely to confer lower disease risk.^{3,13} Given the expected time sequence between environmental exposures and disease manifestation, environmental factors are likely to contribute to the marked differences in breast cancer incidence among older women.

In spite of the lower disease incidence, breast cancer mortality in Barbados was higher than expected, and similar to the experience of African-American women. Clear disparities in survival after breast cancer diagnosis have been described in the latter group^{4,5,17,26} and may exist in Barbadian women as well. In addition to biological factors, higher breast cancer mortality in African-American women has been associated with more advanced and aggressive disease at presentation,³² low uptake of mammographic screening,³³ diagnostic and treatment delays,³⁴ quality of care³⁵ and comorbid conditions.³⁶ Anecdotally, Barbadian women also present with late stage disease, in spite of easy access to free comprehensive public sector health services. More work is therefore needed to elucidate the reasons for the high breast cancer mortality in Barbados, given the relatively low incidence.

Our study has the strengths of providing comprehensive data on breast cancer patterns in the country. Although a national cancer registry is only now being established on the island, all incident breast cancer cases had a histological diagnosis confirmed at a sin-

gle nation-wide Pathology Department. This feature reduces the likelihood of under-ascertainment or reporting errors. Unfortunately, this level of rigor was not possible in establishing breast cancer as the cause of death. In spite of this potential underestimation, breast cancer mortality was at rates comparable to those reported in the United States. One limitation is that it was not possible to clarify the ethnic group of all women with breast cancer. However, over 90% of the Barbados population is of African origin, with lower racial admixture than African-Americans.³⁷

Conclusions

The parallel incidence patterns of breast cancer in African-American and Barbadian women of 50 years of age and younger may suggest a common disease etiology. There remains limited

understanding of the genetic basis of early-onset clinically aggressive breast cancer in African-origin women, and genetic studies will likely be important in contributing to our understanding of this disease presentation. Although the incidence of breast cancer is lower in older Barbadian women, it would be expected to increase with secular changes in lifestyle risk behaviors as populations such as this continue to adopt more "westernized" lifestyles. Studies in intermediate risk populations such as Barbados can assist our understanding of racial disparities in breast cancer among African-Americans, given the similar heredity, and comparable lifestyle-related risk behaviors and disease outcomes. Variations in environmental risk factors and associated gene-environmental interactions across populations of the diaspora, are also likely to provide insight into breast cancer etiology, treatment and prevention.

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