EPIDEMIOLOGY

Breast Cancer Patterns and Lifetime Risk of Developing Breast Cancer Among Puerto Rican Females.

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Objectives. **The purpose of this study was to evaluate the epidemiologic patterns of breast cancer and to estimate the lifetime risk probability of developing breast cancer among Hispanic females using cancer data from Puerto Rico.**

Background. **The age-adjusted breast cancer incidence rate (per 100,000) in Puerto Rico increased from 15.3 in 1960-1964 to 43.3 in 1985-1989. The age-adjusted breast cancer mortality rate (per 100,000) increased from 5.7 to 10.6 comparing the same two time periods (1960-1964 vs 1985-1989). Nevertheless, in 1985-1989 breast cancer incidence rate was higher in US White females (110.8 per 100,000) compared to Puerto Rican females (51.4 per 100,000; age-adjusted to the 1970 US standard population). The breast cancer mortality rate was also higher in US White females (27.4 per 100,000) than in Puerto Rican females (15.1 per 100,000; age-adjusted to the 1970 US standard population) during 1985-1989.**

Methods. **A multiple decrement life table was constructed applying age-specific incidence and mortality rates from cross-sectional data sets (1980-1984 and 1985-1989 data for Puerto Rican females and 1987-1989 SEER data sets for US White and Black females) to a hypothetical cohort of 10,000,000 women. The probability of developing invasive breast cancer was computed for the three groups using the long version of DEVCAN: Probability of DEVeloping CANcer software, version 3.3.**

Results. **The lifetime risk of developing breast cancer was 5.4% for Puerto Rican females, compared to 8.8% for US Black females and 13.0% for US White females. Lifetime risk for Puerto Rican females increased from 4.5% in 1980-1984 to 5.4% in 1985-1989.**

Conclusions. **Lifetime risk of breast cancer appears to be increasing in Puerto Rico, but remains lower than the probability for US White females. Therefore, the application of lifetime probability of developing invasive breast cancer estimated for the US female population will overestimate the risk for the Puerto Rican female population.** *Key words: Breast carcinoma, Breast cancer incidence, Breast cancer mortality, Hispanics, Lifetime risk, Puerto Rico.*

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death among females living in Puerto Rico (1). It is also an important cancer site among White and Black females in the United States (2). Breast cancer incidence and mortality have been increasing steadily in Puerto Rico since 1950 (Figure 1). The age-adjusted breast cancer incidence rate increased from 15.3 per 100,000 females (1960-1964) to 43.3 per 100,000 females (1985-1989) (1). The age-adjusted breast cancer mortality rate increased from 5.7 per 100,000 females (1960-1964) to 10.6 per 100,000 females (1985-1989) (1).

Age-adjusted rates for Puerto Rico were re-calculated using the 1970 United States standard population to control for differences in age-structure and to obtain comparable rates for Puerto Rico and the United States. Standardized breast cancer incidence rates were higher for US White females (110.8 per 100,000) followed by US Black females (92.5 per 100,000) compared to Puerto Rican females (51.4 per 100,000) during the 1985-1989 time period (3). The age-adjusted mortality rates per 100,000 for the same time period was 27.4 for US White, 30.3 for US Black and 15.1 for Puerto Rican females.

The average annual age-adjusted invasive breast cancer incidence rate for Hispanics in the United States was 69.8 per 100,000 during the 1988-1992 time period, an intermediate rate between US Black females and Puerto Rican females (4). Even though breast cancer incidence and mortality rates are lower for Puerto Rican females, their risk of developing and dying of breast cancer is

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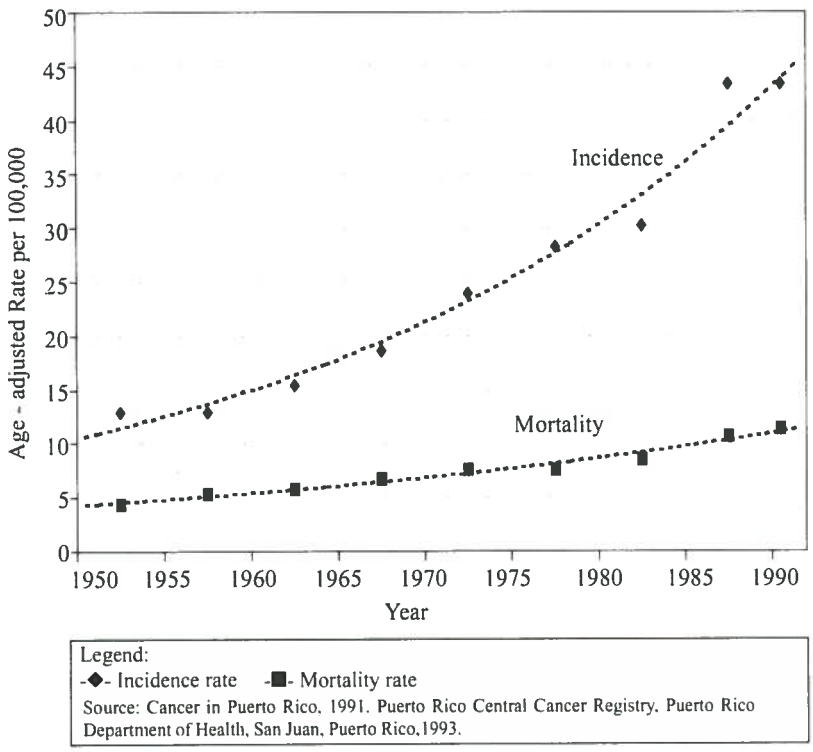

Figure 1. Annual average age-adjusted breast cancer incidence and mortality rates per 100,000 females, Puerto Rico, 1950-1990.

increasing at a faster pace than for US females. The estimated annual percent change (1970-1974 to 1985-1989) in the age-adjusted incidence rate was +4.1% per year for Puerto Rican females (1). This increase is three times greater than the estimated annual percent change for a comparable time period (1973 to 1989) for US White (+1.4% per year) and 2.6 times greater than the percent change for US Black females (+1.6% per year) (3). Likewise, the estimated annual percent change in the age-adjusted mortality rate was +1.98% for Puerto Rican females (1970-1974 to 1985-1989) compared to +0.12% for US White females and +1.04% for US Black females (1973 to 1989) (1, 3).

A woman's lifetime risk of developing breast cancer is a frequently, but sometimes incorrectly, cited statistic (5). Applying the probability for the US White population of being diagnosed with breast cancer to other race/ethnic groups with lower risks, such as the Hispanic population, will produce an overestimation of the actual lifetime risk for a Hispanic female. The derivation of age-conditional and lifetime risks of developing breast cancer used in this paper are based on the methodology presented by Wun et al. (1993) (6). Incidence rates are commonly used to indicate risk of developing a disease, but the numerator usually include multiple diagnosed cases of the cancer in the same person and the denominator may include persons not at risk of developing (for the first time) the disease. Feuer's method addresses the criticism of the standard lifetime risk methodology based on incidence rates that could include more than the first instance of cancer and which reflects rates among the total population rather than the population free of cancer. Even though this method do not take into account individual behaviors and risk factos, it is grounded on population-based data. The risks estimates of developing breast cancer are derived using a three stochastic process with transient state representing the women alive and free of breast cancer and two absorbing states representing the person developing breast cancer and death from other causes in the absence of breast cancer.

The main purpose of this paper is to present the estimated lifetime and age-conditional risk of being diagnosed with invasive breast cancer among Puerto Rican females using the appropriate incidence and mortality statistics. The estimated lifetime risk probabilities for Puerto Rican females are compared to the probabilities for US White and Black females published by the National Cancer Institute (3). The change in risk over time as well as probable explanations, justifications, determinants for these changes are also discussed.

Methods

Age-specific breast cancer incidence rates were calculated for women living in Puerto Rico. The numerator for these rates were cases with a first time diagnosis of invasive breast cancer (excluding *in situ*) in females residing in Puerto Rico during 1985-1989. The cases were obtained from the Puerto Rico Central Cancer Registry, a SEER registry until 1989. The denominator for the incidence rate was the mean population of women for the 1985-1989 period in each specific age group, as provided by the Puerto Rico Health Statistics Office. Age-specific breast cancer mortality rates and age-specific mortality rates from other causes were also obtained from the Puerto Rico Health Statistics Office for the same time periods. Nearly all (98.8%) breast cancer cases diagnosed during 1985-1989 had microscopic confirmation of diagnosis (7).

The probability of developing invasive breast cancer was computed using DEVCAN, Probability of

DEVeloping CANcer software, version 3.0, based on average age-specific incidence and mortality rates for the Puerto Rican females and US females (8). The invasive breast cancer incidence rate and the mortality rate from all other causes were then applied to a hypothetical cohort of 10,000,000 live births subjected to two mutually exclusive probabilities: being diagnosed with invasive breast cancer and dying from other diseases without developing breast cancer. A multiple decrement life table was derived using these two events for each 5-year age-interval from 0-4 years of age up to 90-94 years of age and a last open-ended interval of 95+ years of age. This analysis followed the recommended procedures described by Feuer *et al* (1993) and using the long version of DEVCAN software (5). The lifetime and age-conditional risks were calculated applying age-specific incidence and mortality rates from cross-sectional data sets (1980-1984 and 1985-1989 data for Puerto Rican females and 1987-1989 SEER data sets for US White and Black females). This method was used to estimate comparable breast cancer lifetime risks for the US White, US Black and the Puerto Rican female population. DEVCAN software includes SEER data sets for US White and Black populations, but it does not include a data set for Hispanics. By applying Feuer *et al* (1993) method to appropriate data sets we were able to estimate and compare the lifetime risk probabilities for the three ethnic groups.

Results

During 1985-1989, the Puerto Rico Department of Health reported 4,289 new breast cancer cases. The mean population for this time period was estimated as 1,767,829 females. The lifetime risk of developing invasive breast cancer for Puerto Rican females calculated from 1985-1989 is presented in Table 1. The same detailed information was obtained with DEVCAN for US Whites and Blacks, but only a summary is presented on Table 2 for these two groups

Assuming an initial hypothetical population of 10 million, the total number of women alive and free of cancer at the beginning of each age interval is shown in the second column as the number decreases through each age-interval. The number of women who would be expected to develop breast cancer using the Puerto Rico age-specific incidence rates, are shown in column three. The expected number of cases increases reaching a peak at age 60-64 and decreases thereafter. Column four presents the number of women who died of causes other than breast cancer in each age interval. After the initial peak in the 0-4 years age group, the number of females who would have died of causes other than breast cancer, increases steadily. The last column presents the cumulative risk of being diagnosed with invasive breast cancer from birth for Puerto Rican females. Based on the 1985-1989 incidence and mortality rates, the lifetime risk of eventually developing breast cancer was estimated as 5.4%; one in nineteen women born in Puerto Rico will develop breast cancer in their lifetime. We must note that the lifetime risk of developing invasive breast cancer in Puerto Rico for time periods beyond 1985-1989 were not estimated due to the unavailability of recent cancer incidence data. But if breast cancer risk continues the increasing trend observed in Puerto Rico since 1960 (Figure1), recent incidence and mortality rates would probably be higher than the rates used in this analysis to estimate lifetime risk. Thus, the actual lifetime risk of developing invasive breast cancer in Puerto Rico might also be greater than the estimate presented in this article.

The lifetime risk of 5.4% (1 in 19) for Puerto Rican females is lower than the lifetime risk calculated from

Table 1. Lifetime risk of developing invasive breast cancer for Puerto Rican females, using age-specific incidence and mortality rates for the time period 1985-1989.

Age (yrs)	Total no. alive and cancer free at beginning of interval	Number who developed cancer in this interval	Number who died of other causes in this interval*	Cumulative probability of developing cancer from birth
0-4	10000000	0	143838	0.000000
5-9	9856162	0	9031	0.000000
10-14	9847131	59	9986	0.000006
15-19	9837086	0	18188	0.000006
20-24	9818898	270	28053	0.000033
25-29	9790575	3278	39977	0.000361
30-34	9747320	9384	48605	0.001299
35-39	9689331	19931	63040	0.003292
40-44	9606360	35618	80471	0.006854
45-49	9490271	48660	110012	0.011720
50-54	9331599	51705	178786	0.016890
55-59	9101108	57575	271022	0.022648
60-64	8772511	64190	432615	0.029067
65-69	8275706	59932	617174	0.035060
70-74	7598600	61169	940934	0.041177
75-79	6596497	51317	1204823	0.046309
80-84	5340357	39492	1558856	0.050258
85-89	3742009	22663	1542220	0.052524
90-94	2177126	11476	1232887	0.053672
95+	932763	2975	929788	0.053969

* Among cancer-free women at the beginning of the interval who did not develop invasive breast cancer during the interval.
Until the end of the interval.

Table 2. Cumulative probability of developing invasive breast cancer from birth until the end of the age interval, given cancer free at the beginning of the age interval, for US White and Black females (SEER: 1987-1989).

Age (yrs)	US White* SEER: 1987-1989	US Black* SEER: 1987-1989	Puerto Rico PR:1980-1984	Puerto Rico PR:1985-1989
0-4	0.000000	0.000000	0.000000	0.000000
5-9	0.000000	0.000000	0.000000	0.000000
10-14	0.000000	0.000000	0.000006	0.000006
15-19	0.000000	0.000015	0.000018	0.000006
20-24	0.000037	0.000082	0.000079	0.000033
25-29	0.000425	0.000615	0.000419	0.000361
30-34	0.001621	0.002036	0.001272	0.001299
35-39	0.004575	0.005125	0.002954	0.003292
40-44	0.010695	0.010500	0.005831	0.006854
45-49	0.019888	0.017781	0.010311	0.011720
50-54	0.030516	0.026466	0.014536	0.016890
55-59	0.043182	0.035709	0.019691	0.022648
60-64	0.058542	0.046515	0.024435	0.029067
65-69	0.075545	0.057220	0.028852	0.035060
70-74	0.091859	0.066691	0.033978	0.041177
75-79	0.107204	0.075130	0.038251	0.046309
80-84	0.118701	0.081608	0.041689	0.050258
85-89	0.012579	0.085072	0.043511	0.052524
90-94	0.129239	0.087211	0.044408	0.053672
95+	0.130361	0.087860	0.044752	0.053969
	1 in 7.7 US White	1 in 11.4 US Black	1 in 22.3 PR:1980-84	1 in 18.5 PR:1985-89

* Calculated with DEVCAN 3.3 software using the 1987-1989 SEER data set for invasive breast cancer provided with the program.
Calculated with DEVCAN 3.3 software using data from Puerto Rico for invasive breast cancer for 1980-1984 and 1985-1989.

SEER data for US Black females (8.8% or 1 in 11) or the US White females (13.0% or 1 in 8) for a similar time period (Table 2). A lifetime risk of 5.4% for Puerto Rican females for the 1985-1989 period represents an increase from 4.5% in 1980-1984. The cumulative probability for each current age group is also higher for US White and Black females than it is for Puerto Rican females (Figure 2).

The risk of developing invasive breast cancer before a specified age (Z), conditioned that they were free of breast cancer at the current age (Y) is presented in Table 3 for Puerto Rican females, US White and Black females. Using this data we can estimate that in Puerto Rico, only 1.42% (1 in 70) of females who were cancer free at age 40 years would be diagnosed with breast cancer by age 50, a very low risk. The lifetime risk probability for females free of breast cancer by age 70 (Z=70 years) in the three ethnic groups is as follows: 2.49% (1 in 40) for Puerto Rican females, 4.92% (1 in 20) for US Black females and 7.31% (1 in 14) for US White females.

Discussion

Lifetime risk of developing breast cancer is lower for Puerto Rican females compared to US females. Therefore, the application of lifetime probability of developing invasive breast cancer estimated for the US female population to the Hispanic Puerto Rican population will overestimate their risk. When the risk status for Hispanic women is assessed, for example to evaluate their eligibility for clinical trials, accurate risks should be used. Hispanic women should know their true risk.

The lower breast cancer incidence rates among Hispanic females could be explained by the presence of strong protective factors and/or lower exposure to recognized risk factors. However, as Hispanics acquire Western lifestyles, risk factors for breast cancer are modified and incidence rates are likely to follow the trend of industrialized societies (9). Although risk is lower in Hispanics and they may be protected from breast cancer, the data also suggest that Hispanics are rapidly losing protection as the rate of change is much greater in this population. The lifetime risk for invasive breast cancer increased from 1 in 22 (using 1980-1984 data) to 1 in 19 Puerto Rican females (using 1985-1989 data). Furthermore, the age-adjusted (1970 Puerto Rican population) breast cancer incidence rate increased from 15.3 to 43.3 per 100,000, a +183% change when the average rates of 1960-1964 are compared to 1985-1989 (1). Based on the observed trend, we have considered that the estimated lifetime risk probabilities could probably be greater than 5.4%, if recent cancer incidence data would be available for further analysis.

Using available SEER data published in 1984 by ethnic groups, we calculated the percent change in the age-adjusted (1970 US Standard population) breast cancer incidence rate from 1973-1977 to 1978-1981 for White, Black, and Hispanic females from New Mexico and Puerto Rico (10). The percent change was as follows: -1.95% for US White females; +1.13% for US Black females; 14.38% for Hispanics in New Mexico and 13.87% for Puerto Rican females (10). In 1992, Miller, et al. reported the percent change from 1973 to 1989 as +23.1% for US White and +26.6% for US Blacks (3). There was no information for Hispanics or Puerto Rican females in that publication. We estimated the percent change for Puerto Rican females using available data from a comparable time period (1970-1974 to 1985-1989) as +81.2% (7). Another NCI report published in 1996 presented age-adjusted

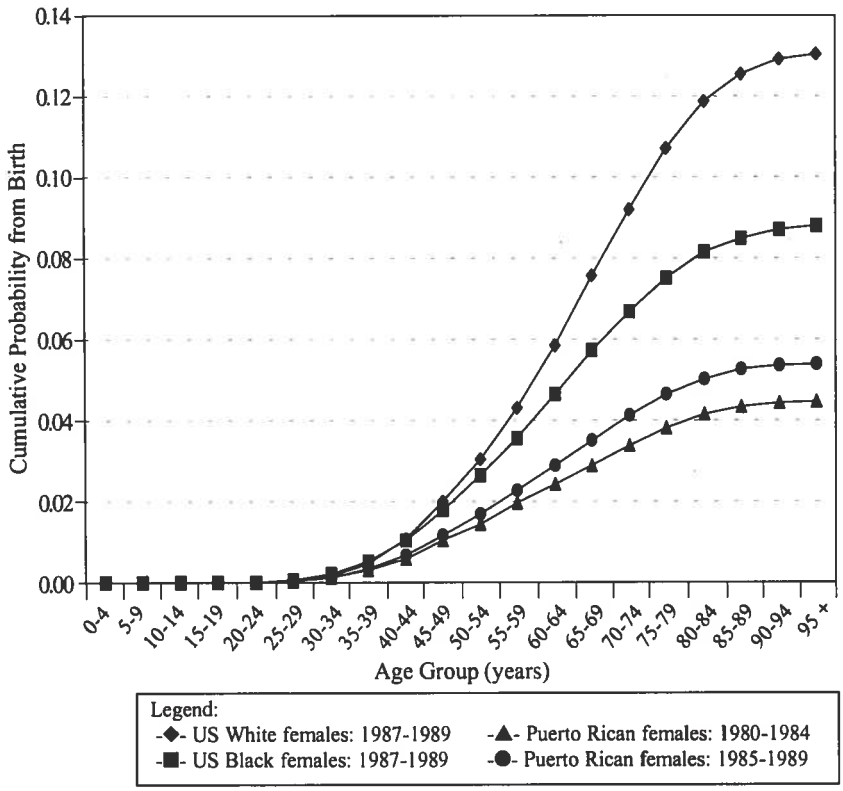

Figure 2. Cumulative probability of developing invasive breast cancer from birth until the end of the age interval, given cancer free at the beginning of age interval.

(1970 US Standard population) breast cancer incidence rates by ethnic groups including Hispanics, but excluding Puerto Rico (4). The monograph presented the percent change from 1988 to 1992. Unfortunately, the rates for Hispanics in that NCI report are not comparable to their previous report, since it only included Hispanics from New Mexico.

The latest published cancer data from the Puerto Rico Central Cancer Registry reports cases diagnosed during 1991. The age-adjusted (1970 Puerto Rico, census population) breast cancer incidence rate for Puerto Rico during 1991 is lower (40.3 per 100,000) than the incidence rate for the previous year (43.3 per 100,000) or the previous 5-year average (43.3 per 100,000), thus requiring cautious use of the 1991 breast cancer data until more recent population rates are published to confirm if the apparent change in trend is due to random single-year variability or to reporting bias (1). However, this analysis suggests that females in Puerto Rico are experiencing an increasing breast cancer risk and the rate of increase is faster in this population than in US White or Black women. The increase in incidence among Puerto Rican women over the past three decades suggests that the risk factors of Puerto Rican women are beginning to resemble that of industrialized societies.

Researchers and public health officials interested in breast cancer have studied the effect of screening campaigns on the observed increasing trend of breast cancer (11-14). The effect of early detection commonly reduces breast cancer mortality and increases the proportion of *in situ* breast cancer cases. Therefore, the effect of early detection on the rising trend of breast cancer in Puerto Rico was also evaluated. An average of 3.75% of breast cancer were diagnosed as *in situ* cases during 1975-1979 in Puerto Rico (15). Ten years later (1985-1989), an average of 4.10 % of the breast cancer cases were diagnosed as *in situ* cases. The percent of *in situ* cases in Puerto Rico only increased 1.2 times in a ten year time period. In contrast, the Seattle-Puget Sound (SEER) Registry reported a three to five fold increase in the incidence of *in situ* breast tumors between 1974-1978 to 1986-1987, almost all of the increases occurring after the initiation of breast cancer screening (16).

The impact of screening campaigns could also present peaks in the incidence rate trends. In Puerto Rico, breast cancer reflects a +56.2% change, an increase from 15.3 to 23.9 per 100,000 (comparing 1960-1964 to 1970-1974), at a time when almost no screening campaigns were conducted. Breast cancer incidence increased from 28.2 to 43.3 per 100,000 (comparing 1975-1979 to 1985-1989) once breast cancer screening was available, a +53.6% change. Thus, these two time period have similar rate of change (+56.2% change vs +53.6% change). Also, effective early detection of breast cancer should lower the mortality rate of this disease. An increasing trend (+39.4%) in breast cancer mortality is evident in Puerto Rico when comparing the same time periods (1975-1979 vs 1985-1989). These analyses suggest that the increase in risk for Puerto Rican females is real and not due to screening programs.

Unfortunately, there is no published data regarding the prevalence of screening mammograms in Puerto Rico. Nevertheless, during 1994-1995, the rate of women who

Table 3. Percent developing invasive breast cancer before a specified age (Z), conditioned to be free of invasive cancer at current age (Y)

Current age-yrs (Y)	Percent developing Invasive breast cancer by age (Z) for Puerto Rican Females*							
	30	40	50	60	70	80	90	Eventually
20	0.13	0.70	1.72	2.96	4.19	5.12	5.47	5.50
30		0.67	1.70	2.95	4.19	5.12	5.47	5.50
40			1.42	2.68	3.94	4.89	5.24	5.28
50				1.86	3.16	4.13	4.50	4.53
60					2.11	3.15	3.54	3.57
70						2.00	2.45	2.49
Current age/yrs (Y)	Percent developing invasive breast cancer by age (Z) for US white females							
	30	40	50	60	70	80	90	Eventually
20	0.16	1.08	3.09	5.93	9.31	12.02	13.09	13.21
30		1.05	3.06	5.92	9.31	12.04	13.12	13.23
40			2.67	5.56	8.99	11.75	12.84	12.95
50				4.11	7.65	10.51	11.63	11.75
60					5.55	8.61	9.81	9.94
70						5.76	7.16	7.31
Current age-yrs (Y)	Percent developing invasive breast cancer by age (Z) for US black females							
	30	40	50	60	70	80	90	Eventually
20	0.21	1.08	2.72	4.78	6.86	8.39	8.97	9.04
30		1.03	2.69	4.78	6.88	8.43	9.01	9.08
40			2.28	4.43	6.59	8.18	8.78	8.85
50				3.24	5.52	7.21	7.84	7.91
60					3.93	5.82	6.53	6.61
70						3.92	4.82	4.92

* Calculated with DEVCAN 3.3 software using the 1985-1989 data from Puerto Rico.
Calculated with DEVCAN 3.3 software using the 1987-1989 SEER data set for invasive breast cancer provided with the program.

received mammography services (which includes both screening and diagnostic mammograms) paid by Medicare (Part B) to non-HMO beneficiaries was reported as 23.7% for Puerto Rico compared to 40.2% for US females (17). We suspect that screening for breast cancer is not reaching a considerable proportion of the at risk population in Puerto Rico, which may explain the lack of a strong screening effect in the Puerto Rico incidence data.

Another factor that could affect breast cancer trends is the aging effect or the proportion of females surviving to older ages. The life expectancy at birth for women born in Puerto Rico in 1930 was 41.46 years, increasing to 78.06 years in 1993 (18). The general mortality rate has increased from 496.1 to 611.7 per 100,000 females, comparing 1975 to 1989. Although there is no population-based information regarding the prevalence of BRCA-1 and BRCA-2 genes in Puerto Rico, we have no reason to suspect that the penetrance of these genes is greater in the island than in the US population. Likewise, it has been recognized that less than 10% of all breast cancer cases are attributable to inherited genetic mutations (19,20). Thus, changing lifestyles are likely to explain the recent increases in breast cancer risk observed among Hispanics in the mainland and in Puerto Rico (21).

Reproductive and hormonal factors associated with breast cancer risk have changed in Puerto Rico. A reduction in the fertility rate and the average number of children among women of reproductive age has been documented. General fertility was 173.4 per 1,000 women 15-49 years of age during 1930-1939, increasing to 187.6 during 1940-1949 reflecting the post war 'baby-boom' effect, decreasing to 99.2 in 1970-1979 (22). The average number of children born to women 15-49 years of age also decreased from 6.4 children in 1932 to 2.42 children in 1985 (22). The average number of children was estimated as 1.84 children during the 1995-1996 reproductive health survey (23). The median age at menarche has decreased from 13.2 years (for the cohort born in 1935-1939) to 12.7 years (for the cohort born during 1965-1967) (22). Estrogen replacement therapy may increase breast cancer risk among long term users, particularly for women exposed to high estrogen doses at a young age (24). Use of oral contraceptives among Puerto Rican women dates back to clinical trials for the 'pill' that were conducted during 1961 to 1969 (25). During the 1995-1996 reproductive health survey in Puerto Rico, 21.5% of married women 15-24 years of age and 1.8% of married women 35-49 years of age use oral contraceptives (23). Likewise, 8.04% of married women 15-24 years of age and 62.63% of women 35-49 years of age were surgically sterilized. The high prevalence of sterilized women in the reproductive years reduces the probability and the protective effect of pregnancy against breast cancer.

The reduction of protective factors and the increase of noxious exposures could explain the increasing risk of breast cancer in Puerto Rico. Although absolute risk is lower when compared to US females, our population is rapidly losing protection for breast cancer, as evidenced by the large increase in risk over the last decades. Nevertheless, in spite of the increase in risk, we can not apply the estimated risk for the US population to this Hispanic population as it would result in an erroneously overestimation of risk.

Resumen

El propósito de este estudio fue evaluar los patrones epidemiológicos de cáncer de mama y estimar la probabilidad de desarrollar cáncer de mama durante la vida de la mujer puertorriqueña. La incidencia de cáncer de mama durante 1985-1989 fue mayor para las mujeres blancas en EEUU (110.8 por 100,000) comparadas con la incidencia en las mujeres puertorriqueñas (51.4 por 100,000; ajustadas a la población estandard de los EEUU durante 1970). La probabilidad de desarrollar cáncer de mama durante la vida y condicionadas a grupos de edades fueron calculadas aplicando las tasas de incidencia y mortalidad para Puerto Rico al método de tabla de vida desarrollado por Feuer et al. (1993). Estos estimados fueron obtenidos usando la versión larga del programa de computadoras *DEVCAN: Probability of DEVeloping CANcer software*, versión 3.3. El riesgo de desarrollar cáncer de mama durante la vida fue 5.4% en Puerto Rico comparado con 13.0% para las mujeres blancas en Estados Unidos. En Puerto Rico, ese riesgo aumentó de 4.5% en 1980-1984 a 5.4% en 1985-1989. Aunque el riesgo de desarrollar cáncer de mama está aumentando, el uso de las probabilidades estimadas para las mujeres de los Estados Unidos producirá una sobreestimación del riesgo verdadero en las mujeres en Puerto Rico.

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