Trends in Breast Cancer in Younger Women in Contrast to Older Women

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Using data from the Surveillance, Epidemiology, and End Results (SEER) Program and the National Center for Health Statistics, trends in female breast cancer rates were examined for the time period 1973-1989 for the age group 20-39 and contrasted with those for older ages. Only about 7% of breast cancers occur by the age of 40; the risk of developing breast cancer prior to the age of 40 is less than 1%. The incidence trends for women in the 20-39 age group have been essentially stable. whereas for women 40 and older the rates increased steeply during the 1980s (at a faster rate than anticipated based on historical trends) and then leveled off beginning in 1987. Breast cancer mortality has been much more stable over time than incidence. Up to age 40, blacks have a higher incidence than whites. Over age 40, white rates exceed those for blacks, and the absolute and relative differences in incidence increase with advancing age. For whites, 5-year relative survival rates improved with advancing age up to age 50. Blacks under the age of 30 had survival rates similar to whites, whereas, in the older age groups, whites had somewhat better survival rates overall and by stage. The occurrence of second cancers was also analyzed in women with a first invasive breast cancer. Cancers found to occur at higher than expected rates included leukemia and cancers of the breast, ovary, and lung. [Monogr Natl Cancer Inst 16:7-14, 1994]

Summary statistics on breast cancer incidence and mortality. e.g., the age-adjusted rate. are heavily weighted by the higher rates in older age groups. Since breast cancer rates in younger women display patterns that are different from those in older women. it is important to review rates by age group to discern patterns that are hidden by the summary measures.

Data Sources

Data on newly diagnosed cancer cases. including patient follow-up. were collected through the Surveillance. Epidemiology, and End Results (SEER) Program. The SEER Program began in 1973 as part of the National Cancer Program and is administered by the Surveillance Program in the Division of Cancer Prevention and Control at the National Cancer Institute (NCI). The mission of the SEER Program is to provide a basis for assessing progress in reducing the burden of cancer in the general population *(1).*

The SEER Program currently consists of 11 population-based registries under contract with the NCI to provide data on all cancers diagnosed in residents of their coverage areas. Data collected include cancer site/type, morphology, extent of disease. first course of cancer-directed therapy, and patient follow-up, including cause of death. Data are submitted to the NCI annually. The coverage areas of the 11 registries are the entire states of Hawaii, New Mexico, Iowa. Utah, and Connecticut and the metropolitan areas of San Francisco, Seattle, Detroit, and Atlanta. The county of Los Angeles and the San Jose-Monterey area of California, which is adjacent to the five-county San Francisco area, have been recently added to the SEER Program; however, data from these registries are not included in the analysis presented here.

Mortality data were obtained from the National Center for Health Statistics for the entire United States and population estimates by county from the Census Bureau, the latter being required for the calculation of cancer incidence and mortality rates.

In calculating incidence/mortality rates for age ranges, e.g.. 20-39, the rates are age-adjusted within the designated range using weights from the 1970 United States Standard population for the 5-year age groups included in the range.

Results

Proportion of Breast Cancers Diagnosed at Younger Ages

Fig. 1 presents the cumulative distribution of breast cancers occurring in women during the period 1987-1989 by age at diagnosis in the SEER areas. Only 6.5% of the breast cancers were diagnosed in women under age 40. and 21.8% were diagnosed before the age of 50. Applying the 6.5% to the 183 000 breast cancers expected to be diagnosed in women in the United States during 1993 *(2)* indicates that approximately 12 000 breast cancers will be diagnosed in women under the age of 40.

Probability of Developing Breast Cancer

The probability of developing cancer can be calculated up to a specified age or for an entire lifetime. It is a useful statistic to consider, particularly in regard to the study of a rare event like

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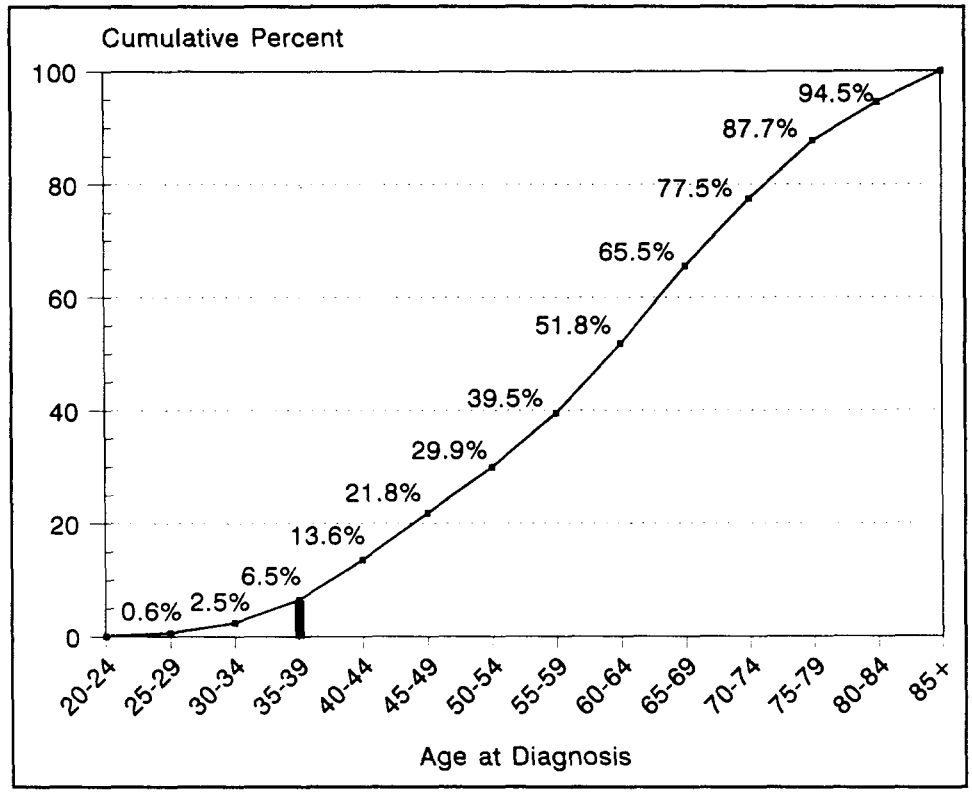

Fig. 1. Cumulative distribution of breast cancer diagnoses by age for the period 1987-1989.

the diagnosis of breast cancer in young women, because it puts the occurrence of such an event in a proper perspective. The method used here to calculate the probability of developing breast cancer was developed by Feuer et al. *(3).*

The lifetime probability of developing breast cancer varies somewhat by race, being .13 in white women, i.e., 13 of 100 women followed from birth develop breast cancer over their lifetime versus .09 in black women. Prior to age 50, these probabilities do not differ appreciably by race. The probability of developing breast cancer prior to age 50 is .02 and prior to age 40 is less than .01.

Incidence/Mortality Trends

Breast cancer incidence trends by age are presented in Fig. 2. The log scale is used here and in some subsequent graphs, meaning that lines which are Parallel have the same proportional

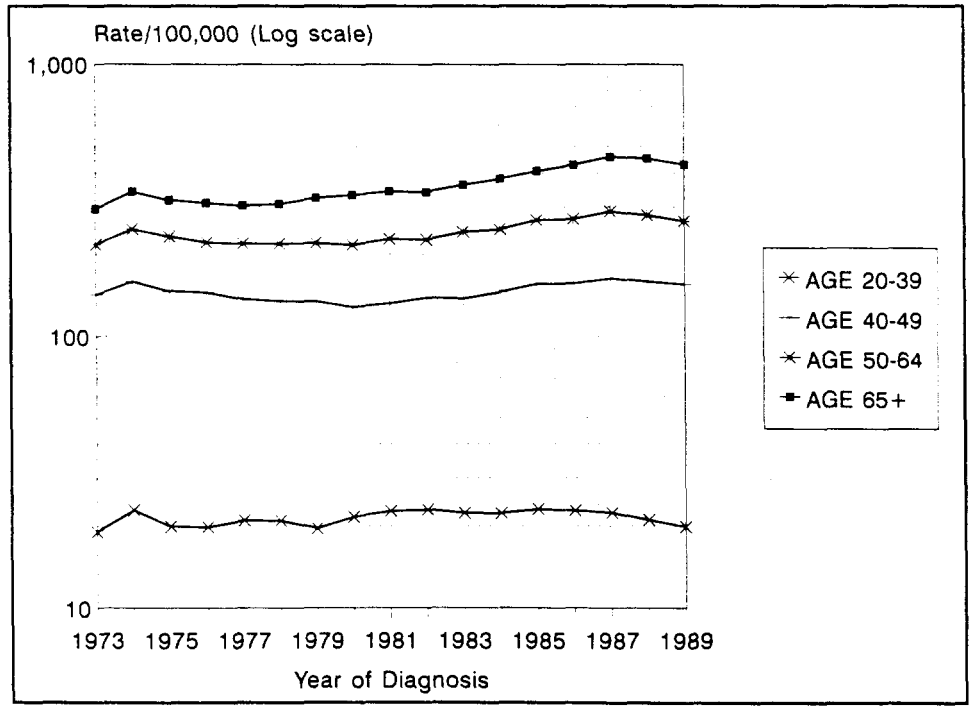

Fig. 2. Trends in invasive breast cancer incidence rates for following age groups: 20-39, 40-49.50-64, 65+.

rate of change over the X axis, which is calendar year in this case. It is of interest to note that the effect of increased public awareness associated with the diagnosis of breast cancer in 1974 in two prominent public figures, Happy Rockefeller and Betty Ford, had roughly the same proportional impact in all of the age groups, i.e., the lines connecting the 1973 and 1974 rates appear to be parallel across all of the age groups, except for the youngest age group where the line appears to be steeper. The trends of the rates in the three age groups 40 and older have an increasing slope for the period 1982-1987, with the slope for the oldest age group appearing to be the steepest, indicating a faster annual rate of increase as compared to the other two groups. Beginning in 1987, there appears to be a leveling off, if not a decrease, for the rates in these age groups. This recent change in the incidence trend is not likely due to chance variation.

During the 1980s up to 1987 when the incidence was rising in the older age groups, there was little change in the age group 20-39 after a small jump at the beginning of the decade (Fig. 2). Since 1987 the trend has either not changed or is decreasing.

During the conference, a number of individuals indicated that it was their feeling that there has been an increase in the number of young women getting breast cancer because doctors were reporting more diagnoses in younger women. Since any increase in reported breast cancer diagnoses in younger women was not likely due to an increase in the incidence rates, it was of interest to assess the change in the size of the young female population over time. Fig. 3 presents estimates of the total female population by age for calendar years 1970, 1980, and 1990. It can be seen that, over this 20-year period, there has been a dramatic increase in the number of women in the 20-39-year-old age range. Applying the age-specific female breast cancer incidence rates from the SEER Program to the 5-year age groups in the age range 20-39 for the three calendar years yields the following numbers of cancers diagnosed in this age range: 5120 diagnosed in 1970; 7800 diagnosed in 1980: and 10 050 diagnosed in 1990. For 1970, 1973 SEER rates were used, since the SEER Program was not established until 1973. Clearly, there has been a large increase in the *number* of women diagnosed with breast cancer at ages 20-39. However, the increase in numbers is primarily due to the increase in the size of the young female population, since the incidence rates have remained relatively constant over the period (Fig. 2).

Reasons for the Increase in Incidence at Older Ages

While the focus here is on breast cancer in younger women, it is of interest to consider possible reasons for the increase in incidence in the older age groups that occurred during the 1980s. Based on survey data, the rate for the use of mammography for breast cancer screening, i.e., the percent of women without symptoms who had had a mammogram within the last year, has increased from 5% to 10% at the beginning of the decade to more than 20% in 1987 in women aged 40 and above *(4)*.

If is assumed that in situ breast cancers, as well as localized invasive cancers <2 cm in diameter, are on the average slower growing than other breast cancers, then, due to a phenomenon known as length-biased sampling *(5)*, these early cancers should be preferentially detected at screening and diagnosed at an earlier point in their natural history. The interval between the time at which a cancer is detected at screening and the time at which it would have been diagnosed clinically is referred to as lead time (5). Over the period that the use of mammography was increasing, the incidence of breast cancer in a given calendar year would include all those cancers expected to be diagnosed in the absence of early detection plus those cancers diagnosed early that would have otherwise been diagnosed at a later time. Eventually, the increase in incidence should begin to wane because of the number of cancers removed from the total pool of breast cancers in a given calendar year due to an earlier diagnosis in a previous calendar year. The dynamics of such a change in incidence would be governed by such things as the rate of increase

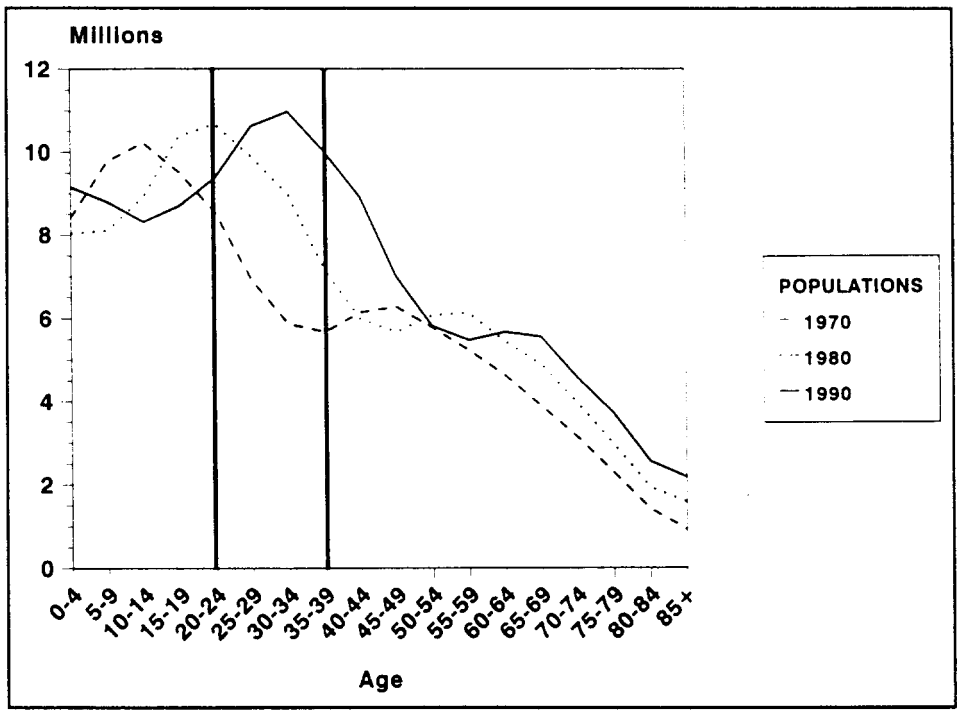

Fig. 3. Total U.S. female population by age and calendar year.

in early detection and the amount of lead time associated with the cancers diagnosed early.

Fig. 4 presents trends in the incidence rates by age for in situ and localized invasive tumors <2 cm in diameter for the period 1983-1989. As expected, rates increase for these two groups in patients 40 years and older at diagnosis, although only through 1987. After 1987, the rates level off. For women 20-39 years of age, there is little change in the rates for localized invasive cancers <2 cm in diameter and a smaller increase in the rate for in situs. Rates for all other invasive cancers (not shown) in all age groups changed very little during this period. It is of interest to note that the incidence of in situ cancers does not increase with age the way the rate for small invasive cancers does; in fact, there is no increase by age in the incidence of in situ cancers above age 50.

These observations provide indirect evidence that early detection played a major role in the increase of breast cancer incidence that occurred during the early 1980s. An alternative possibility is that temporal changes in risk factors selectively affected the incidence of early-stage breast cancers, We are not aware of evidence supporting this possibility.

Subsequent to 1987, it is of interest to note that in conjunction with the leveling off of the incidence rates in the older age groups, the reported proportion of women who had had a mammogram within the last 12 months roughly doubled between 1987 and 1990. These data were collected as part of the National Health Interview Survey that is conducted annually by the National Center for Health Statistics. Thus, trends in mammography utilization and breast cancer incidence during the period 1987-1990 present something of a conundrum. Efforts to understand why breast cancer incidence did not continue to increase are currently underway *(6)*. Part of the explanation rests with the dynamics of the interrelationships between lead time, screening rates. and baseline incidence trends as described by Feuer and Wun *(7)*.

Incidence/Mortality Patterns by Race

There are some interesting contrasts between breast cancer incidence and mortality patterns for blacks and whites. Mortality rates given here are for the total United States. Fig. 5 presents black/white differences in incidence and mortality by age for the period 1987-1989. The incidence of breast cancer is higher in blacks up to age 40, and breast cancer mortality is higher in blacks up to age 65. Differences in incidence and mortality by race have existed for several years among younger women (Fig. 6).

Stage at Diagnosis and Survival Patterns by Race

The staging system used by the SEER Program to classify cancers consists of the following categories along with their definitions: localized—invasive malignant neoplasm confined entirely to the organ of origin: regional—malignant neoplasm that has extended beyond the limits of the organ of origin directly into surrounding organs or tissues, involves lymph nodes by way of the lymphatic system, or has both regional involvement and involvement of regional lymph nodes; distant—malignant neoplasm that has spread to parts of the body remote from the primary tumor either by direct extension or by discontinuous metastasis (e.g.. implantation or seeding) to distant organs, tissues. or via the lymphatic system to distant lymph nodes: and unstaged—insufficient information for staging purposes. This system can be applied to patients diagnosed in all years since the beginning of the SEER Program.

Fig. 7-presents the percent of tumors that were localized to the site of origin at diagnosis by age and race. For breast cancers diagnosed in women under the age of 40, there is very little difference in this percent by race or age group. The percent localized decreases for blacks in the older age groups, which is somewhat surprising since screening recommendations apply primarily to women 50 and older. However, other factors could

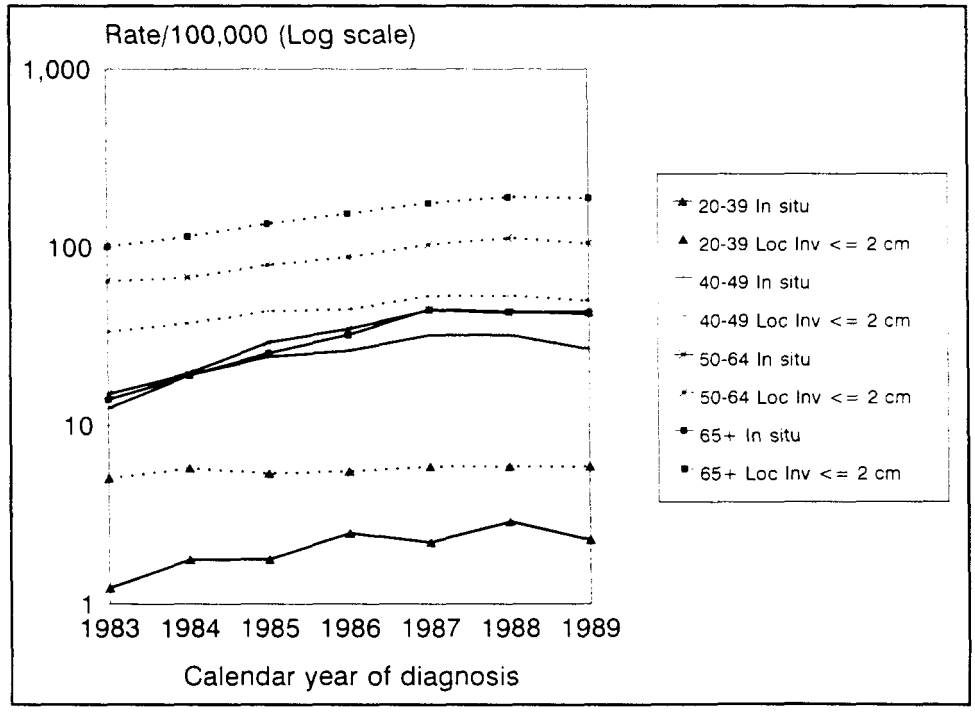

Fig. 4. Trends in breast cancer incidence rates for in situ and localized invasive tumors <=2 cm in diameter for the following age groups: 20-39.40-49.50-64, 65+.

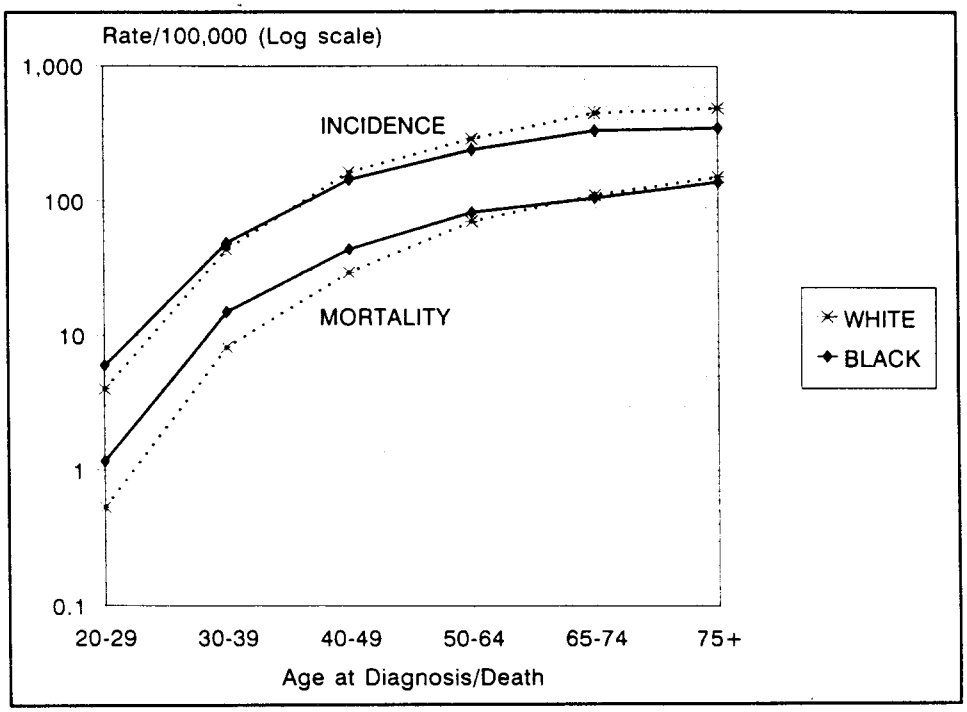

Fig. 5. Age-specific female invasive breast cancer incidence rates and age-specific female breast cancer mortality rates (total, United States) by race.

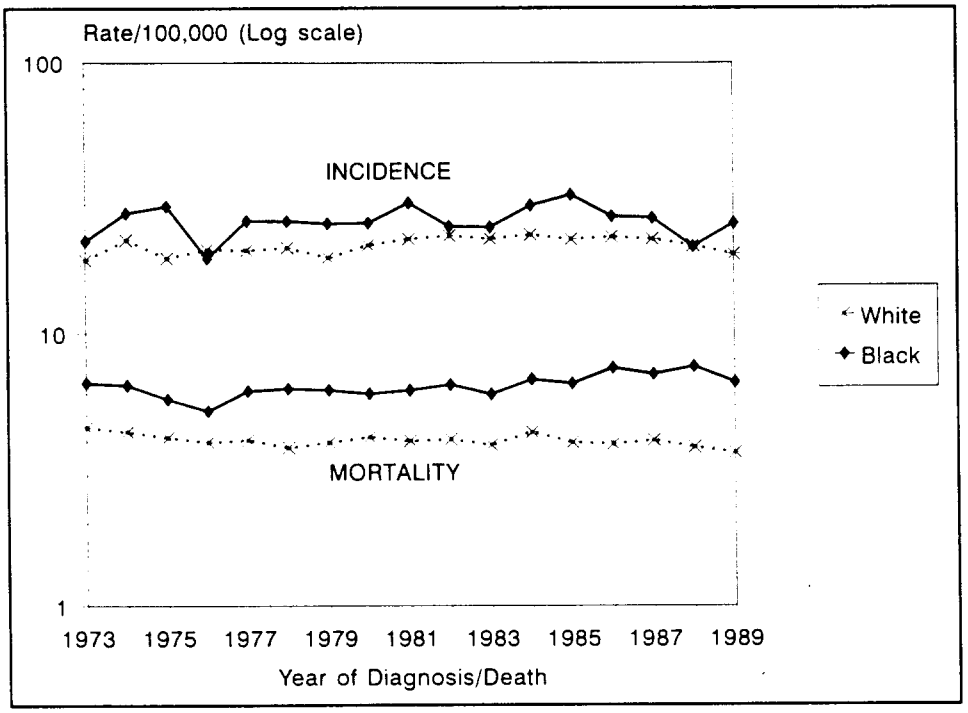

Fig. 6. Female invasive breast cancer incidence rates and female breast cancer mortality rates (total, United States) for the age group 20-39 by race and calendar year.

be operating. e. g., at older ages, breast cancers in black women may be more aggressive than those in whites.

Fig. 8 presents 5-year relative survival rates by race and age for all stages combined. The rates improve somewhat among whites Up to age 50, whereas there is no evidence of an effect of age on survival among blacks. For the age group 20-29, the difference between the rates is not statistically significant and there are no differences in survival by stage (not shown). For women 30 and older, survival for whites by stage was better than that for blacks in all cases. except for patients 40-49 years old at diagnosis with distant disease. in which case survival for blacks was only little better than that for whites; hoever, the difference was not statistically significant (not shown).

Second Cancer Risk (Incidence)

The risk of subsequent cancers in women with a first invasive breast cancer also varies by age at diagnosis of the first breast cancer and, therefore, is considered here. Other reasons for analyzing second cancer risk associated with female breast cancer include 1) obtaining clues about the etiology of selected second cancers since, if they occur in excess, this may indicate the presence of risk factors in common with breast cancer, and

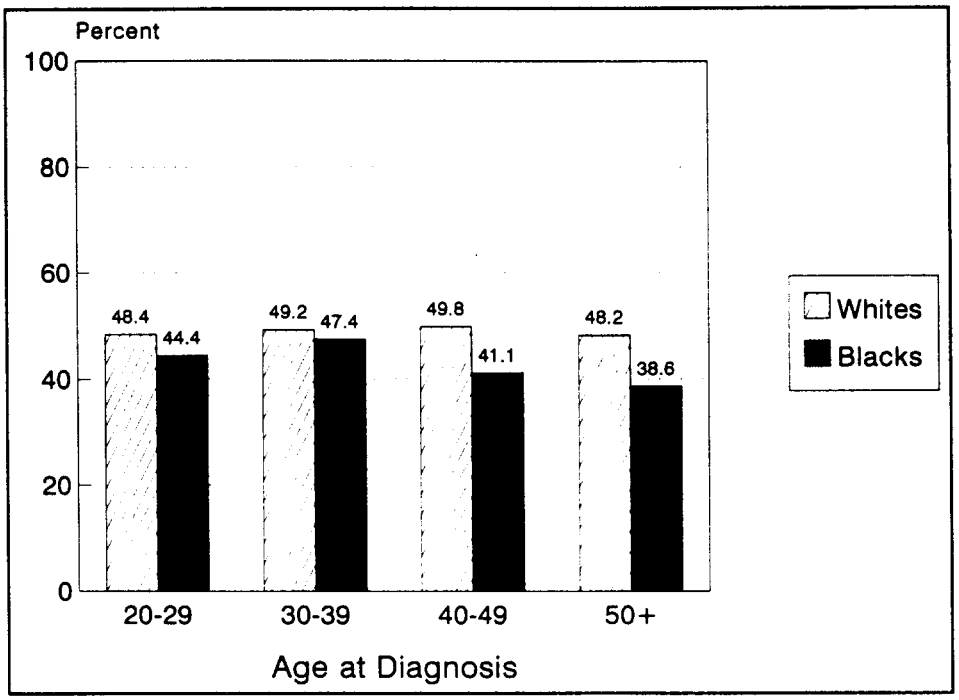

Fig. 7. Percent of invasive breast cancers diagnosed as localized by race and age for the period 1975-1984.

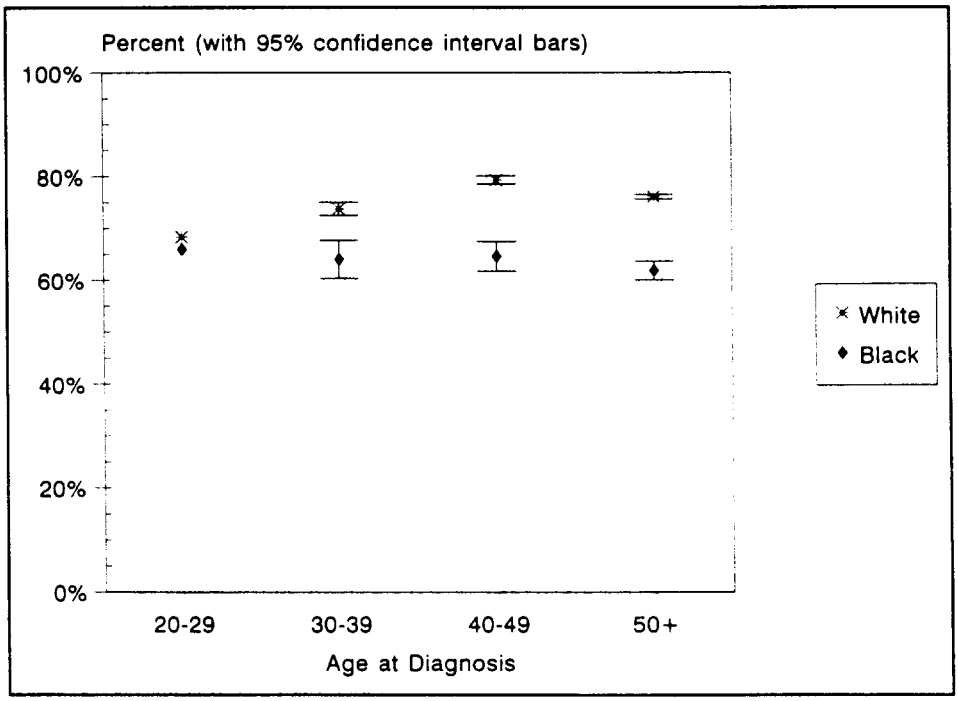

Fig. 8. 5-year relative rates by race and age for the time period 1975-1984. Relative survival rates not significantly different in 20-29-year age group.

2) identifying second cancers that may have been caused by treatment of the first breast cancer. Clinically, it is of interest to know which cancers occur in excess in order that patients be monitored over time for the occurrence of such malignancies.

Excess risk and relative risk of various second cancers per 100 000 person-years were calculated. The person-years at risk for a second cancer is defined to be that time starting 2 months after diagnosis of the breast cancer and extending to the first of the following events: date of diagnosis of any second cancer, date of last follow-up, date of death, or December 31, 1989. Women who survived less than 2 months after diagnosis were excluded from the analysis. The expected numbers of second cancers were calculated by multiplying cancer site–age–calendar year specific incidence rates, as routinely reported by SEER. by the person-years at risk in each cancer site-age-calendar year category. The numbers were then summed to arrive at the total numbers of expected second cancers.

The size of the first breast cancer cohorts by age were as follows; <20 (19 women), 20-29 (1431 women), 30-39 (11 002 women), 40-49 (26 590 women), and 50+ (127 501 women). A factor limiting this analysis is the fact that the more recently diagnosed cases made a lesser contribution to person-years at

risk of second cancers. since they could only be followed through the end of December 1989.

Findings were as follows. Breast cancer patients aged 20-39 at diagnosis were at a significantly increased risk of developing a second invasive cancer of the breast, ovary, and lung. Each of these second cancers showed a consistent pattern of being elevated when the data were analyzed as two cohorts: those patients with a first invasive breast cancer diagnosed during the period 1973-1979. and those patients with a first invasive breast cancer diagnosed during the period 1980-1989. Second leukemias were also found in excess. but have been shown in previous reports *(8,9)* to be related to the radiotherapy and chemotherapy given to treat the initial breast cancer and, therefore, will not be reviewed here.

An excess of second invasive breast cancers is to be expected, but the pattern of increased risk in younger women is of interest. In the age group 20-29, the risk of a second invasive breast cancer was 29.8 and was related to time from diagnosis of the first breast cancer (Table 1). Risk decreased from 79.6 during the first year after diagnosis to 15.4 10+ years after diagnosis. In general, the second breast cancer excess decreased with age and time from diagnosis for women with a first breast cancer diagnosed under the age of 50. For women with a first invasive breast cancer diagnosed after the age of 50, the relative risk was 1.8 and was not related to time from diagnosis.

Second cancers of the ovary and lung were found to be elevated in women with a first invasive breast cancer diagnosed

Table 1. Risk of second *invasive* cancer following a first *invasive* breast cancer diagnosed during the period 1973-1989 by age at diagnosis of the first breast cancer *

		Time from diagnosis, y									
		Total		<1		1-4.9		5-9.9		10+	
Second cancer site	Age at diagnosis	O/E	O	O/E	O	O/E	O	O/E	O	O/E	O
Breast											
	20-29	29.8	67†	79.6	10†	45.9	33†	18.1	16†	15.4	8†
	30-39	7.4	403†	10.9	55†	10.4	233†	5.2	97†	2.1	18†
	40-49	3.1	869†	4.3	138†	3.5	417†	2.5	217†	2.2	97†
	50+	1.8	3645†	1.7	525†	1.9	1890†	1.6	919†	1.6	311†
Ovary (including tubes)	30-39	4.3	25†	3.5	2	3.3	8†	5.4	11†	3.9	4†
	40-49	2.1	80†	2.3	9	2.2	35†	2.3	28†	1.3	8
	50+	1.2	344†	1.4	63†	1.1	165	1.2	93	0.9	23
Lung											
	30-39	2.1	16†	2.2	1	3.2	8†	1.7	5	1.0	2
	40-49	1.6	128†	0.9	5	1.6	45†	1.5	42†	1.9	36†
	50+	0.9	781	0.7	83†	1.0	382	0.9	211	1.3	105†

*Observed number of second cancers (O) divided by the expected number (E) with the observed number given in parentheses. Included in the calculation of the risks were women who survived 2 months or more following the diagnosis of their first invasive breast cancer.

†Risk significantly different from 1.0 ($P<.05$).

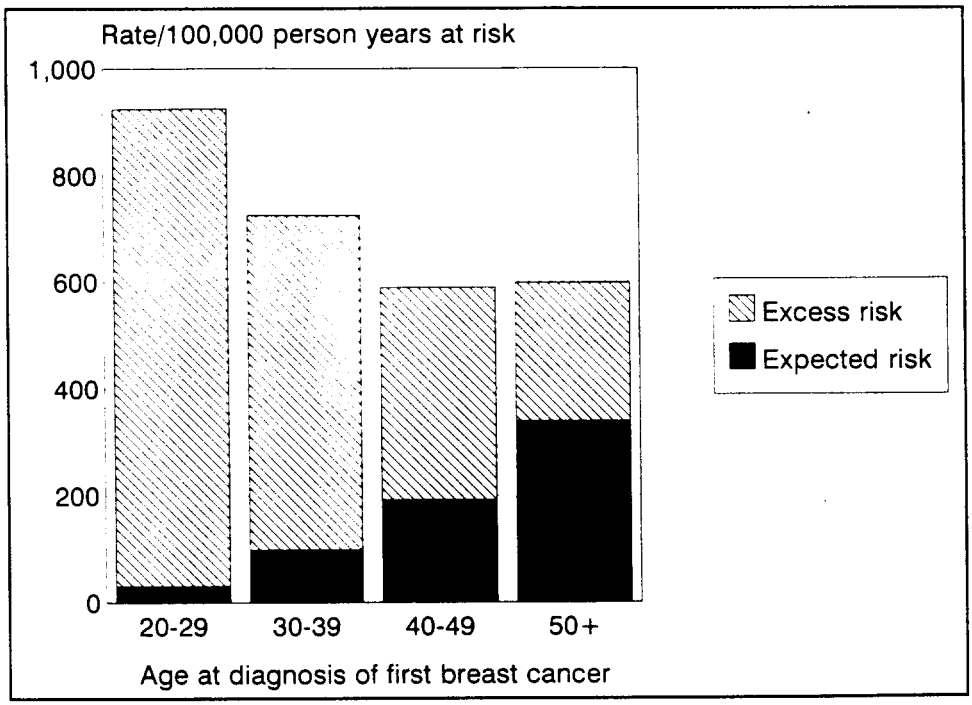

Fig. 9. Expected risk and excess risk of a second invasive breast cancer following a first invasive breast cancer diagnosed during the period 1973-1989.

at ages 30-49 (Table 1). The risk of a second ovarian cancer was highest in the age group 30-39. The relative risks for both cancers were not related to time from diagnosis. The finding of elevated risks for second breast and ovarian cancers in young women with a first breast cancer is consistent with the identification of a genetic marker, which has been reported to be associated with the occurrence of breast and ovarian cancers at a very young age *(10).*

Excess risk (absolute risk) of developing a second invasive breast cancer was calculated by age at diagnosis of the first invasive breast cancer (Fig. 9). This risk was quite high in the 20-29 age group (893.8 per 100 000 person years at risk). The rate decreased with increasing age at diagnosis of the first breast cancer, but remained high relative to the expected rate.

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