REPORTS

The Lifetime Risk of Developing Breast Cancer

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Background: **The lifetime risk of developing breast cancer in U.S. women, often quoted as one in nine, is a commonly cited cancer statistic. However, many estimates have used cancer rates derived from total rather than the cancer-free population and have not properly accounted for multiple cancers in the same individual.** ***Purpose:*** **Our purpose was to provide a revised method for calculating estimates of the lifetime risk of developing breast cancer and to aid in interpretation of the estimates.** ***Methods:*** **A multiple decrement life table was derived by applying age-specific incidence and mortality rates from cross-sectional data to a hypothetical cohort of women. Incidence, mortality, and population data from 1975-1988 were used, representing the geographic areas of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program. The incidence rates reflected only the first breast primary cancer; mortality rates reflected causes other than breast cancer. The population denominator used in calculating incidence rates was adjusted to reflect only those women without previously diagnosed breast cancers in the hypothetical cohort.** ***Results:*** **Our calculations showed an overall lifetime risk for developing invasive breast cancer of approximately one in eight with use of 1987-1988 SEER data, although up to age 85, it was still the commonly quoted one in nine.** ***Conclusion:*** **Our estimate was calculated assuming constant age-specific rates derived from 1987-1988 SEER data. Because incidence and mortality rates change over time, conditional risk estimates over the short term (10 or 20 years) may be more reliable. A large portion of the rise in the lifetime risk of breast cancer estimated using 1975-1977 data (one in 10.6) to an estimate using 1987-1988 data (one in eight) may be attributed to 1) early detection of prevalent cases due to increased use of mammographic screening and 2) lower mortality due to causes other than breast cancer. A common misperception is that the lifetime risk estimate assumes that all women live to a particular age (e.g., 85 or 95). In fact, the calculation assumes that women can die from causes other than breast cancer at any possible age. Cutting off the lifetime risk calculation at age 85 assumes that no women develop breast cancer after that age. While the lifetime risk of developing breast cancer rose over the period 1976-1977 to 1987-1988, the lifetime risk of dying of breast cancer increased from one in 30 to one in 28, reflecting generally flat mortality trends. [J Natl Cancer Inst 85:892-897, 1993]**

The lifetime risk of developing cancer and the risk of developing cancer during certain age intervals are widely cited statistics used to communicate risk estimates to the general population and to provide background risk estimates for comparisons with population subgroups. The term "developing cancer" is taken here to mean "diagnosed cancer" and does not include the development of undiagnosed cancer. Almost no cancer statistic is quoted more often in the popular press than the lifetime risk of developing breast cancer. Dr. Bernadine Healy, director of the National Institutes of Health, stated in a recent *Los Angeles Times* article that "One out of nine women [born today] will be found to have the disease in her lifetime compared wit one out of 20 in 1940" *(1).* Breast cancer activists have used this increas as a rallying point to press for more funds aimed at breast cancer prevention and treatment studies *(2).* Ironically, a recent New *York Times* article *(3)* stated that misperceptions of this number by many women (e.g., thinking it is the risk in the next year) are unnecessarily heightening public fears far beyond reasonable expectations. In contrast, a subsequent *Washington Post* editorial *(4)* argues that the one in nine figure, when interpreted appropriately, could be used to prompt more women to obtain clinical breast examinations and mammograms and to perform periodic breast self-examinations.

The methodology for calculating the general population risk of developing cancer has been discussed by several authors *(5-7).* Historically, this methodology has been applied in areas other than cancer *(8).* A recent paper by Bender et al. *(9)* derived an alternative measure of risk termed the "person years" estimate, which may be useful in certain situations. The authors criticized current lifetime risk assessmer methodologies for failing to account fo prevalent cases of cancer (i.e.. patients who had breast cancer diagnosed at an earlier age and who are still alive) and the presence of multiple cancers in the same individual. The person years approach estimates the risk of cancer (including a second cancer) among the

*See 'Notes' section following "'References. "

total population instead of the cancer-free population and thus avoids these problems. The purpose of our report is to present a revision of the existing methodology *(5-7)* for calculating estimates of the general population risk of developing cancer by addressing these criticisms more directly. We also provide some aid in interpretation. In this study, we apply this revised method using breast cancer incidence data from the nine standard registries of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER)[1] program from 1975 through 1988 as well as mortality data from the National Center for Health Statistics and population data from the Bureau of the Census, both from the SEER geographic areas in the same time periods.

Methods

The methods described in this section can be applied to any specified cancer, although the results are described for breast cancer only. The probability of developing breast cancer was computed by applying age-specific incidence and mortality rates from the cross-sectional experience of a population in a specified year (or group of years) to a hypothetical cohort of 10 million live births. This hypothetical cohort is considered at risk for two mutually exclusive events: 1) being diagnosed with breast cancer for the first time and 2) death due to other causes without ever having developed breast cancer. Thus, we derived a standard multiple decrement life table (10) (in 5-year age intervals up to age 94 and a 95+ interval) using these two types of events. The general approach to calculating the probability of developing cancer has been previously described by Goldberg et al. (5), Zdeb (6), and Seidman et al. (7), and results of these calculations have been reported by Seidman et al. (7,11).

The method of calculation used in this paper follows the basic methodology of previous authors (5-7) with the following five modifications:

1) Both incidence and mortality from the nine standard SEER areas (Connecticut, Hawaii, Utah, Metropolitan Atlanta, Metropolitan Detroit, Iowa, New Mexico, San Francisco/Oakland, and Seattle [Puget Sound]) are used, rather than SEER incidence and U.S. mortality. SEER registries represent a nonrandomly selected 10% of the U.S. population, and differences in mortality rates between SEER and the entire U.S. populations have been noted (12).

2) The incidence rates associated with developing breast cancer were based on cancers diagnosed in a specific year (or group of years) and count only the first occurrence of breast cancer for each individual during the entire history of the SEER registry (1973-1988). The cancer of interest may have been preceded by cancer of some other site. Caaes of this type were ascertained by having the computer select only those breast cancer cases where any prior records for that registry case number (a unique person identifier) did not identify any prior history of breast cancer since registry collection began in 1973. In the past, either all incident breast primaries were selected (allowing for multiple entries for a single individual), or only the first primary cancer was selected (eliminating a case if they had another type of cancer prior to a later breast primary).

3) The denominator in the standard calculation of age-specific incidence rates includes prevalent cases from earlier ages, but this factor is inappropriate for these calculations. An adjustment based on age-specific prevalence was used to estimate the probability of developing cancer in each 5-year interval among the cancer-free population. More specifically, in each 5-year age interval, the probability of developing breast cancer among the total population was estimated on the basis of the usual incidence rates. This estimate was then adjusted by multiplying by a ratio R, where

$$R = \left[\frac{\text{No. alive at age } x}{\text{No. alive and free of breast cancer at age } x}\right].$$

The proportion of prevalent cases of breast cancer at age x is related to R since prevalence equals 1 - (1/R). The estimate of the number of individuals alive at age x was calculated by using cross-sectional estimates of mortality attributable to all causes to successively decrement the hypothetical cohort of 10 million. In a similar manner, the number alive and free of breast cancer at age x was estimated by using cross-sectional estimates of age-specific breast cancer incidence rates and mortality attributable to causes other than breast cancer to successively decrement the hypothetical cohort. The adjustment factor, R, produces higher probabilities of developing cancer in older age groups, especially for sites where the incidence rate is high and survival is long (i.e., high prevalence).

4) We assumed a constant incidence and mortality rate for each age interval, which implies an exponential occurrence of events during the age interval instead of a uniform occurrence of events as assumed by Seidman et al. (7). The results using either assumption are similar; however, our assumption greatly simplifies calculations in the final open-ended age interval.

5) The population figures for SEER areas are available only up to age 85+. To include older age groups in these calculations, populations for the 85-89, 90-94, and 95+ age groups were obtained by partitioning the 85+ figure from SEER areas in accordance with their distribution in the U.S. as enumerated in the 1980 decennial census. Estimates produced in this manner may lack precision; however, the sensitivity of lifetime risk estimates to changes in mortality and incidence rates for individuals over age 85 is likely to be small.

A detailed technical description of the methodology and a computer program for performing these calculations, using SEER data since 1975 for over 20 different cancers categorized by race and sex, are available by writing to the first author.

In addition to the lifetime risk of developing breast cancer, estimates of the tifetime risk of dying of breast cancer were included. These calculations were performed using a standard multiple decrement life table (10) in which a woman is exposed to the risk of dying of breast cancer and to all other causes based on mortality data from the SEER registry geographic areas.

Results

The life table for invasive breast cancer (Table 1) summarizes results for all races using incidence and mortality data from SEER areas in 1987-1988. The total number of individuals alive and cancer free at the beginning of each interval (column two) decreases in each interval starting with a cohort of 10 million live births. The number who develop cancer (column three), though initially low, rises through middle age before decreasing. The number of new cases decreases after age 69 even though the breast cancer incidence rates rise steadily up through age 79; this apparent contradiction can be explained by the fact that these higher rates are applied to successively smaller age-specific populations. The number of nonbreast cancer deaths among those who are cancer free (column four) rises and falls much like the number of incident cancer cases, except for the large number of infant deaths. The cumulative probability of developing cancer from birth, shown in the last column, is calculated by cumulatively summing the number of those who develop cancer and then dividing by 10 million.

Table 2 shows the percentage of women developing invasive breast cancer before a specified age (Z), given that a woman is cancer free at a current age (Y) as derived from Table 1. For example, for a 50-year-old woman who is currently cancer free, there is a 5.74% chance of developing invasive breast cancer prior to age 70. This calculation is performed using the same basic method as the lifetime probability of developing breast cancer; however, only those cases over the age intervals from 50 *(Y)* up to 70 *(Z)* (i.e., 50-54, 55-59, 60-64, and 65-69) are summed

Table 1. Probability of developing invasive breast cancer in SEER areas, women, all races, 1987-1988

Age	Total No. alive and cancer free at beginning of interval	No. that developed cancer this interval	No. that died of other causes this interval*	Cumulative probability of developing cancer from birth†
0-4	10000000	59	107510	.000006
5-9	9892431	0	9137	.000006
10-14	9883294	0	9484	.000006
15-19	9873810	0	24344	.000006
20-24	9849466	450	24967	.000051
25-29	9824049	3449	28665	.000396
30-34	9791935	12116	36133	.001607
35-39	9743686	29912	48245	.004599
40-44	9665529	61967	68852	.010795
45-49	9534710	91069	109308	.019902
50-54	9334333	103830	174980	.030285
55-59	9055523	120721	267754	.042357
60-64	8667048	151118	413587	.057469
65-69	8102343	160288	571101	.073498
70-74	7370954	154016	809216	.088900
75-79	6407722	150217	1083758	.103921
80-84	5173747	110820	1413174	.115003
85-89	3649753	60041	1423203	.121008
90-94	2166509	35570	1323699	.124565
95+	807240	11287	795953	.125693

*Among cancer-free population at beginning of the interval who did not develop cancer during the interval.

†Until the end of the interval.

and then divided by the number alive and cancer free at age 50 (i.e., 9334333).

Table 3 presents the probability of women eventually developing invasive and in situ breast cancer by race using incidence and mortality rates from groups of years. The lifetime probability of developing breast cancer has risen steadily since 1975-1977 in both Blacks and Whites. However, it has risen faster since 1981-1983, with the probability of developing in situ breast cancer rising faster than the probability of developing invasive breast cancer. The higher lifetime risk of developing breast cancer for Whites versus Blacks is associated with the higher age-specific incidence rates among Whites and with the higher mortality due to other causes among Blacks, which implies that a smaller proportion of the cohort reaches older ages where the incidence rates become very high. If Blacks in 1987-1988 had the same mortality from other causes as Whites and the incidence rates for Blacks remain the same, the lifetime risk of invasive breast cancer would be 10.60% instead of 8.98%. The remaining difference (i.e., 10.6070 compared with 13. 18%) is attributable to differences in incidence.

Table 3 also presents the lifetime risk of women dying of breast cancer by year for all races combined. In 1987-1988, the lifetime risk of dying of breast cancer was 3.7% for Whites and 3.5% for Blacks. These probabilities are rather small compared with the risk of developing cancer, indicating that many who develop breast cancer eventually die of other causes. Also, the risk of dying of breast cancer has climbed only slightly since 1975.

The trend in the lifetime risk of developing invasive breast cancer since 1975 is shown in Fig. 1 by the asterisks and the thick solid line. The large increase in the probability of developing cancer since 1981-1983 is associated with a recent rise in incidence that is substantially greater than a long-term background rise in incidence. This rise in incidence has been studied extensively (13-16), and a large portion of the recent rise above the secular trend seems to be attributable to early detection associated with a sharp increase in mammographic screening. Miller et al. *(14)* estimated that the long-term rise in incidence (observed since 1940 in the Connecticut tumor registry) is about 1.16% per year across all age groups prior to 1982. No change in the population prevalence of putative risk factors has been firmly linked to this long-term increase. From 1982 to 1987, incidence has been increasing at an average rate of 4.02% per year, with larger increases in older age groups (60 and over) and smaller increases in younger age groups (under 60). To assess the suspected impact of the recent rise in screening on lifetime breast cancer risk, we recalculated these estimates on the basis of lower breast cancer rates that would have occurred if the annual 1.16% secular trend increase had persisted. Thus, our

Table 2. Percent developing invasive breast cancer before a specified age (*Z*) given free of invasive breast cancer at current age (*Y*) in SEER areas, women, all races, 1987-1988

Current age (*Y*), y	Develop cancer by age (*Z*), %									
	10	20	30	40	50	60	70	80	90	Eventually
0	0.00	0.00	0.04	0.46	1.99	4.24	7.35	10.39	12.10	12.57
10		0.00	0.04	0.46	2.01	4.29	7.44	10.51	12.24	12.72
20			0.04	0.47	2.02	4.30	7.46	10.55	12.29	12.76
30				0.43	1.99	4.29	7.47	10.57	12.32	12.80
40					1.58	3.91	7.13	10.28	12.04	12.53
50						2.41	5.74	9.01	10.83	11.33
60							3.59	7.10	9.07	9.62
70								4.13	6.45	7.08

Table 3. Percent of women in SEER areas developing and dying of breast cancer from birth by race and year

Year	Developing						Dying
	All races		Whites		Blacks		All races
	Invasive only	Invasive and in situ	Invasive only	Invasive and in situ	Invasive only	Invasive and in situ	
1975-1977	9.43	9.81	9.76	10.14	6.92	7.15	3.33
1978-1980	9.46	9.78	9.82	10.16	6.89	7.13	3.31
1981-1983	10.14	10.53	10.55	10.94	7.75	8.09	3.45
1984-1986	11.44	12.27	11.90	12.77	8.67	9.24	3.50
1987-1988	12.57	13.91	13.18	14.58	8.98	9.89	3.61

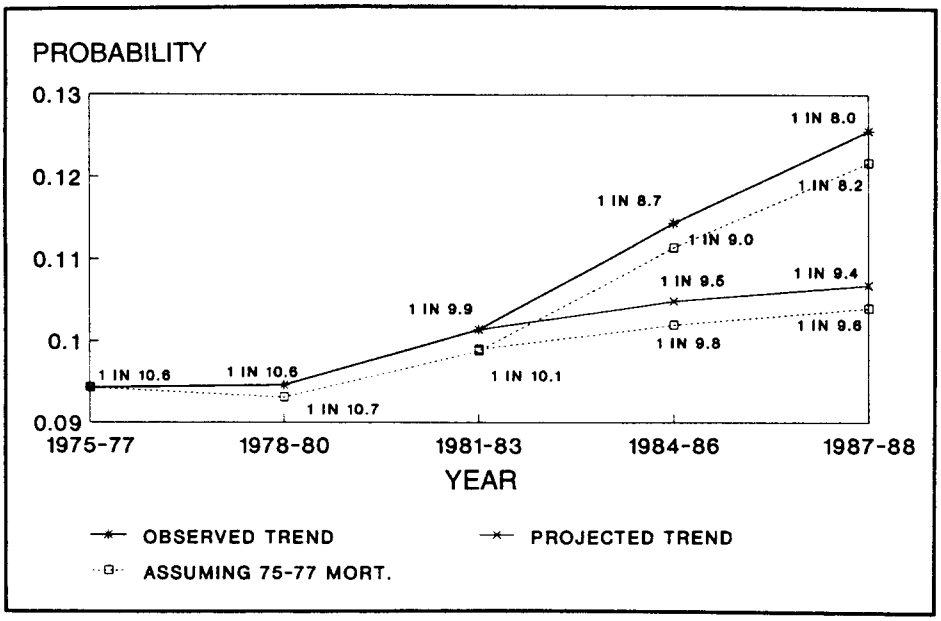

Fig. 1. Lifetime probability of developing invasive breast cancer for women living in SEER areas. The projected trend assumes that increases in screening since 1982, which would inflate the risk of breast cancer, did not occur (*see* text).

new calculations estimate lifetime risk of developing breast cancer that might have occurred in the absence of increases in screening. The Xs and the narrow solid line in Fig. 1 illustrate this projection (e.g., one in 9.4 in 1987- 1988). As the increase in the screening rate begins slowing, incidence rates should start to return to the secular trend (17), and the lifetime risk of developing breast cancer should return close to the projected line in Fig. 1.

An additional factor resulting in a rise of the lifetime risk of developing breast cancer is changes in mortality due to causes other than breast cancer. As mortality rates decrease, more women are living longer and are thus exposed to higher incidence rates. To determine the effect of this decline in mortality due to causes other than breast cancer (mostly associated with declines in cardiovascular mortality) since 1975-1977, we performed calculations for each group of years using the observed rates of breast cancer incidence in those years while holding the mortality due to other causes constant at its 1975-1977 levels. (Modification of all of the previously derived points is shown by the dotted lines in Fig. 1.) This adjustment shows that declining mortality has had a small but evident effect on the lifetime risk of developing breast cancer.

Putting these components together (and assuming independence between breast cancer incidence and mortality due to other causes), we can partition the increase in the lifetime risk of breast cancer into three parts. Using 1975-1977 data, 9.43 of every 100. women born (one in 10.6) were estimated to develop breast cancer during their lifetime; using 1987-1988 data, 12.57 of every 100 women born (one in eight) were projected to develop breast cancer in their lifetime. The increase of 3.14 new breast cancers per 100 women born can be partitioned as follows: 0.27 (9%) of the new cases are attributable to women living longer (lower mortality due to causes other than breast cancer); 0.97 (31 %) of the new cases are attributable to the secular trend rise in incidence (cause unknown); and 1.90 (60%) of the new cases are attributable to the rise in incidence above the secular trend (evidence points to early detection of prevalent cases through screening).

Discussion

Our method for calculating risk estimates that project lifetime probabilities of developing breast cancer in the general female population incorporates several new approaches. Age-specific incidence rates for the first primary breast cancer are used, and a prevalence adjustment to the population at risk has been included. This change serves to decrease the denominator population and thereby increases the age-specific incidence rates, especially in the older age groups where prevalence is high. Conditional probabilities with conditioning starting above age 70 are not calculated because of the instability of incidence and prevalence estimates in the older age groups.

It is important to note that although the lifetime probability of women developing invasive breast cancer, 12.57% (one in eight), appears to be

higher than existing estimates of one in nine *(18)*, there are several important considerations apart from the changes in methodology cited above that must be taken into account. The previous American Cancer Society (ACS) calculation *(18)* used incidence and mortality from 1985-1987 and truncated the estimate at age 85. The probability of developing breast cancer from birth to age 85 estimated in Table 1 is still approximately one in nine.

Earlier estimates of the lifetime risk of breast cancer *(11)* have sometimes been misunderstood by those [e.g., *(19)]* who believed that "all women are assumed to live to 110," which is the oldest age in standard life tables *(19)*. Also, many have interpreted the truncation of the ACS calculation at age 85 (which is close to the average life expectancy for females) as meaning that everyone is assumed to live to age 85 in the calculation. However, this assumption is incorrect, because each age interval is assigned a weight in the calculations on the basis of the probability of living to that age, and only the small but actual probability of surviving to the very old age intervals is included in the lifetime risk measure. In the current calculation, illustrated in Table 1, the lifetime probability assumes that deaths occur in accordance with a standard mortality distribution, including the final interval of those aged 95 and above.

The lifetime risk of breast cancer is a valid estimate for a newborn today if the rates are stationary over that baby's entire life. The risk estimate is a reflection of risks that prevail in the current population of women. Obviously, it should be noted that many factors will change as a baby born today ages over her lifetime. Neither our understanding of the etiology of breast cancer, nor our ability to make future estimates of the population prevalence of risk factors, are sufficient to make long-term incidence projections credible.

Shorter-term risk estimates (e.g., values near the diagonal in Table 2) are more reliable for a woman alive and cancer free in the population today and are less susceptible to changes in mortality and incidence rates in the future. This report reflects general population risk of developing breast cancer, however, risk is certainly not the same for every woman. Gail et al. (20) present probabilities of developing breast cancer for women being screened once a year given their risk profile.

It has been hypothesized, as illustrated in this report, that increases in mammography utilization in the 1980s have caused an apparent increase in incidence rates and therefore a rise in lifetime risk. A projection model by Kessler et al. *(17)* estimated that the "bubble" of increased incidence due to increased screening will have passed through the system by 1991 or 1992, approximately 10 years after it started in 1982. This reversal in incidence rates has conceivably already begun, as SEER incidence rates reported for 1988 and 1989 are lower than those in 1987 (age-adjusted rates of 112.4, 109.4, and 104.6 cases per 100000 women for 1987, 1988, and 1989, respectively). However, a substantial number of women have still not been served by screening programs or do not follow regular screening regimens. As these groups are targeted by new public health initiatives, such as the Medicare coverage of screening mammography that started in 1991, new short-term increases in incidence rates—and therefore, lifetime risk-may be observed,

To attribute changes in the lifetime risk of breast cancer only to changes in breast cancer incidence while holding mortality due to other causes constant, we should base risk estimates on a standard mortality distribution (shown by the broken lines in Fig. 1). This concept is similar to the one of age-adjusting incidence and mortality rates to a standard age distribution so that changes in the age structure of the population will not influence the comparison of rates over time.

While the lifetime risk of developing cancer increased sharply from one in 10.6 to one in eight from 1975-1977 to 1987-1988, the risk of dying of breast cancer rose from only one in 30 to only one in 28. The small rise in the risk of dying of breast cancer is associated with the relatively small increase in breast cancer mortality over this period, as well as the decline in mortality from causes other than breast cancer. One would expect generally flat mortality early on as screening rates just start to increase, because the deaths in a particular year are derived from cases from many prior years even before screening became prevalent in the population. Of course, in the long run, if the screening program is successful, mortality should fall along with the lifetime risk of dying of breast cancer.

Increases in the lifetime risk of breast cancer are better understood in light of two factors associated with this increase: First, women are living longer and dying less often of other causes, factors that tend to increase the lifetime risk of breast cancer. Secondly, increases in screening have led to cases being detected earlier, which (if treated properly) results in improved survival. However, additional research to address the underlying causes for the long-term increases in breast cancer, as well as a means to better identify the basic etiologic mechanisms of the disease, is needed. In the meantime, these risk estimates provide a valuable measure of "background" rates to aid researchers in study planning, as well as to aid in the positive aspects of breast cancer awareness such as encouraging increased use of mammography and clinical breast exams.

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Notes

[1]Ed. Note: SEER is a set of geographically defined, population-based central tumor rsgistri~ in the United Statss, operated by local nonprofit organisations under contract to the National Cancer Institute (NCI). Each registry annually submits its cases to the NCI on a computer tape. These computer tapes are then edited by the NCI and made available for analysis.

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Manuscript received June 3, 1992 revised February 26. 1993; accepted March 2, 1993.