# Recent Trends in U.S. Breast Cancer Incidence, Survival, and Mortality Rates

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***Background:*** **Clinical trials have demonstrated that use of mammographic screening and advances in therapy can improve prognosis for women with breast cancer.** ***Purpose:*** **We determined the trends in breast cancer mortality rates, as well as incidence and survival rates by extent of disease at diagnosis, for white women in the United States and considered whether these trends are consistent with widespread use of such beneficial medical interventions.** ***Methods:*** **We examined mortality data from the National Center for Health Statistics and incidence and survival data by extent of disease from the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute, all stratified by patient age, using statistical-regression techniques to determine changes in the slope of trends over time.** ***Results:*** **The age-adjusted breast cancer mortality rate for U.S. white females dropped 6.8% from 1989 through 1993. A significant decrease in the slope of the mortality trend of approximately 2% per year was observed in every decade of age from 40 to 79 years of age. Trends in incidence rates were also similar among these age groups: localized disease rates increased rapidly from 1982 through 1987 and stabilized or increased more slowly thereafter; regional disease rates decreased after 1987; and distant disease rates have remained level over the past 20 years. Three-year relative survival rates increased steadily and significantly for both localized and regional disease from 1980 through 1989 in all ages, with no evidence of an increase in slope in the late 1980s.** ***Implications:*** **The decrease in the diagnosis of regional disease in the late 1980s in women over the age of 40 years likely reflects the increased use of mammography earlier in the 1980s. The increase in survival rates, particularly for regional disease, likely reflects improvements in systemic adjuvant therapy. Statistical modeling indicates that the recent drop in breast cancer mortality is too rapid to be explained only by the increased use of mammography; likewise, there has been no equivalent dramatic increase in survival rates that would implicate therapy alone. Thus, indications are that both are involved in the recent rapid decline in breast cancer mortality rates in the United States. [J Natl Cancer Inst 1996;88:1571-9]**

The past two decades have seen advances in the detection, diagnosis, and treatment of breast cancer. Mammography was shown to be beneficial in reducing breast cancer mortality in randomized clinical trials in the early 1980s (*1,2*). Recommendations to use screening mammography beginning at age 40 years resulted in dramatic increases in the number and usage of screening mammography machines (*3-6*). Subsequent clinical trial results have further demonstrated the benefits of mammography (*7,8*). The benefits of adjuvant therapy for both premenopausal and postmenopausal women were demonstrated in randomized clinical trials in the late 1970s and early 1980s (*9,10*), resulting in recommendations to the oncology community regarding the use of adjuvant therapy (*11,12*). Results (*13*) have affirmed the benefits of adjuvant therapy. If the benefits demonstrated in clinical trials extend to community medical practice, then increased use of mammography should affect both the magnitude of breast cancer incidence rates and the distribution of cases by extent of disease at diagnosis, and improved treatment regimens should result in increases in breast cancer survival rates, particularly for regional disease. Furthermore, if these medical interventions are both beneficial and widely employed, then they should eventually result in declining breast cancer mortality rates.

Marked drops in breast cancer mortality rates since 1990 have been reported in the United States (*14*), England and Wales (*15,16*), and Canada (*17*), and these abrupt declines may provide evidence of improved medical interventions. Evaluation of trends in breast cancer mortality rates, however, is not straightforward. Because of existing birth cohort trends in breast cancer mortality for white females (*18,19*), care must be taken in evaluating trends in breast cancer mortality for evidence of a benefit due to screening or treatment. Since mortality decreases are expected in certain age groups because of existing birth cohort patterns, unanticipated or accelerated mortality decreases are required for evidence of screening and/or treatment benefits (*19*). Examination of trends in breast cancer mortality using age-adjusted rates for all ages, or even for broad age groups, such as ages less than 65 years and ages 65 or greater, also makes interpretation difficult (*19*). Accordingly, relatively narrow age groupings must be used in evaluating breast cancer trends.

In the current investigation, breast cancer incidence rates and survival rates, both by extent of disease and age at diagnosis, and breast cancer mortality rates by decade of age at death are examined for white females in the United States. The incidence,

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

survival, and mortality trends are analyzed for significant changes, and the extent to which such changes are consistent with early detection and successful treatment of breast cancer is discussed.

## Materials and Methods

Incidence and survival rates were obtained from population-based data collected by the Surveillance, Epidemiology, and End Results (SEER) Program[1] of the National Cancer Institute (*20,21*). These rates are based on all white female breast cancer cases diagnosed from 1973 through 1993 (*22*) among residents of nine geographic areas: Connecticut, Hawaii, Iowa, New Mexico, Utah, Atlanta, Detroit, Seattle-Puget Sound, and San Francisco-Oakland. Annual incidence rates are age standardized to the 1970 U.S. population by direct standardization (*23*). On the basis of past SEER experience, the incidence rates currently reported for the most recent year (i.e., 1993) are 3%-4% lower than the actual incidence rates because of incomplete ascertainment (*24*). Investigations into survival are based on 3-year relative survival rates (*25,26*) by tumor extent at diagnosis.

Categories of tumor extent at diagnosis used in this report are in situ, localized, regional, and distant disease. The total invasive incidence rates include all staged cancers as well as unstaged cancers, but exclude in situ cases. In situ lesions have not penetrated the basement membrane. Localized disease refers to invasive neoplasms confined entirely to the breast. Regional disease refers to a neoplasm that extends beyond the limits of the breast directly into surrounding tissues/organs or involves regional lymph nodes. Distant disease refers to a neoplasm that has metastasized to remote sites of the body. Unstaged disease denotes cases for which insufficient information was available to permit the accurate assignment of a stage (*24*).

Breast cancer mortality data from 1969 through 1993 were from the National Center for Health Statistics (NCHS). The NCHS receives death certificates for all 50 states and compiles mortality rates by race, sex, age, year of death, and cause of death. The current study includes all deaths of white females in the United States, with breast cancer listed as the underlying cause of death (*27*). Mortality rates are age adjusted by direct standardization to the 1970 U.S. population. Breast cancer mortality rates for white females in the SEER areas follow the same general trend seen in total U.S. rates but with considerably greater variability.

Linear regression analyses of log-transformed rates were used to quantify the direction and magnitude of trends in breast cancer survival and mortality rates; all reported $P$ values are two-tailed. Piecewise regression analyses were used to test for a sudden change in the slope of the linear trend in rates (Appendix). For mortality rates, the trend for all ages was analyzed first, and then the trends by decade of age were examined to determine the consistency of the change in the slope identified for all ages. With the exception of the 30-39- and 60-69-year age groups, all regression analyses started with the year 1980. Mortality curves for women 30-39 years of age and 60-69 years of age were not linear from 1980 through 1990 due to downturns beginning in the mid-1980s. As a result, piecewise regression analyses for the 30-39- and 60-69-year age groups beginning in 1980 would give exaggerated estimates of the magnitude of the downturn in the 1990s. Accordingly, the piecewise regression analyses for these age groups started in 1984 for the 30-39-year group and 1985 for the 60-69-year group, so that recent changes in mortality rates could be evaluated relative to previously existing decreasing trends.

For the survival rates, trends in 3-year relative survival rates from 1975 through 1989 were evaluated for all cases, for localized disease, for regional disease, and for distant disease; to obtain stable rates for each extent of disease classification by age, trends were evaluated in three broad age groups (i.e., <50 years of age, 50-69 years of age, and ≥70 years of age at diagnosis).

## Results

The age-adjusted breast cancer mortality rates for white females of all ages from 1969 through 1993 are shown in Fig. 1. While breast cancer mortality increased slightly in the 1980s, there was a sharp decrease in breast cancer mortality after 1989. Piecewise regression indicates a significant ($P<10^{-4}$) decrease in

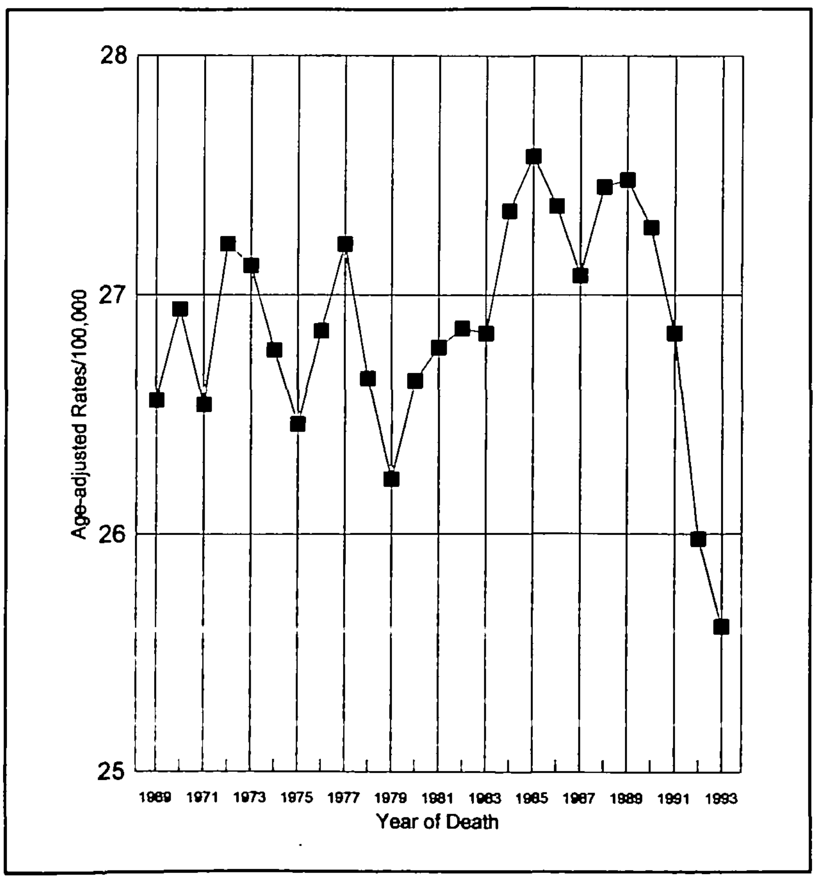


**Fig. 1.** Age-adjusted breast cancer mortality rates for U.S. white females of all ages, standardized to the 1970 U.S. population.

the slope of the mortality curve for all ages (Table 1), with the change in slope after 1989. Breast cancer mortality curves by decade of age are shown in Fig. 2. The results of the piecewise regression analyses for each age group assuming a change in slope after 1989 are summarized in Table 1. The slope decreased significantly by about 2% per year after 1989 in the 40-49-, 50-59-, 60-69-, and 70-79-year age groups. The 30-39-year age group had a nonsignificant decrease of 2.9% per year in the slope, but this was due primarily to a sharp 1-year decline in 1993.

The age-adjusted breast cancer incidence rates for all ages by extent of disease at diagnosis are shown in Fig. 3, A. The stage-specific incidence rates for age groups 40-49, 50-59, 60-69, 70-79, and 80 years or older all had patterns very similar to that observed for all ages. Incidence rates by stage at diagnosis are shown in Fig. 3, B, for the 40-49-year age group. As with the rates for all ages, total invasive breast cancer incidence rates stabilized after 1987. All age groups aged 40 years or more also showed the marked increase in localized and in situ disease rates following 1982. The increase in localized disease abated only slightly following 1987 in the 50-59-year and 80 years or more age groups, but subsided considerably, showing only slight increases following 1987 in the 40-49-, 60-69-, and 70-79-year age groups. All age groups over age 40 years also showed decreasing regional disease rates after 1987, with stable distant disease rates over the entire period from 1973 through 1993. The stage-specific incidence rates for invasive disease in the 30-39-year age group differed from those in older women (Fig. 3, C); invasive cancer rates were level or slightly declining for each stage during the 1980s.

Breast cancer 3-year relative survival rates for all invasive cancer and for localized and regional disease by age groups from 1975 through 1989 are shown in Fig. 4. Piecewise regression indicated a significant improvement in survival around 1980, particularly in women under the age of 70 years. Thus, analyses were restricted to survival rates after 1980. The slopes of the survival curves for all invasive disease, localized disease, regional disease, and distant disease by age group are given in Table 2. Survival rates increased significantly in all age groups for localized and regional disease. The slopes increased with age for both localized and regional disease, and there was no significant change in survival trends in the 1980s.

**Table 1.** Annual percentage change in breast cancer mortality rates from 1980 through 1993 estimated by piecewise regression analysis with a change in slope from 1989 through 1993

| Age, y | Slope of trend from 1980 through 1989* | Change in slope after 1989*,† |
|---|---|---|
| All ages | 0.4 ± 0.1 ($P$ = .0005) | −2.2 ± 0.2 ($P<10^{-4}$) |
| 30-39‡ | −2.3 ± 0.8 ($P$ = .018) | −2.9 ± 1.5 ($P$ = .11) |
| 40-49 | −0.0 ± 0.2 ($P$ = .90) | −2.4 ± 0.7 ($P$ = .007) |
| 50-59 | −0.7 ± 0.1 ($P$ = .0003) | −2.0 ± 0.4 ($P$ = .0007) |
| 60-69‡ | −0.3 ± 0.3 ($P$ = .39) | −1.7 ± 0.5 ($P$ = .013) |
| 70-79 | 1.4 ± 0.1 ($P<10^{-4}$) | −2.2 ± 0.3 ($P<10^{-4}$) |
| ≥80 | 1.3 ± 0.1 ($P<10^{-4}$) | −0.5 ± 0.4 ($P$ = .20) |

*Values = least-squares estimate of slope ± standard error.

†Measures the amount the slope changed after 1989; the slope of the mortality curve following 1989 is the sum of the slope from 1980 through 1989 and this change in slope.

‡Regression analysis begins in 1984 for the 30-39-year age group and in 1985 for the 60-69-year age group because their mortality curves are not linear over the entire period from 1980 through 1990.

## Discussion

The decrease in breast cancer mortality from 1989 through 1993 represents a highly significant departure from the slight increase in breast cancer mortality in the 1980s (Table 1). The 6.1% drop from 1990 through 1993 and the 6.8% drop from 1989 through 1993 are the largest short-term decreases in the age-standardized (to the 1970 U.S. population) breast cancer mortality rate for all ages since 1950. The previous largest decline over a 3-year period was 3.7% from 1955 through 1958, while the previous largest decline over a 4-year period was 4.1% from 1955 through 1959. Breast cancer mortality rates are declining in every decade of age under 80 years of age, and the age-adjusted breast cancer mortality rate is lower in 1993 than it has been at any time since 1950. The final provisional breast cancer mortality rates (based on 10% samples of death certificates, and age adjusted to the 1940 U.S. population) for men and women combined were 11.9 and 11.5 per 100 000 in 1993 and 1994, respectively (*28*). Thus, there is no indication that the recent marked decrease in breast cancer mortality will abate.

A 2% per year decline in the slope of the breast cancer mortality curve after 1989 is seen in every age group from 40 to 79 years (Fig. 2, Table 1). In the 70-79-year age group, the decrease in slope was of sufficient magnitude to cause a decrease in rates after 1989, despite anticipated steady increases resulting from an increasing birth cohort trend in risk (*19*). The recent decrease in women 30-39 years of age is largely due to decreasing birth cohort risks for women born after 1946 (Tarone RE, Chu KC, Gaudette LA: submitted for publication). When changes in mortality occur simultaneously across several age groups, the most likely explanation is either a change in coding or ascertainment or the introduction of improvements in medical interventions. There have been no recent coding changes affecting breast cancer, and examination of recent mortality trends for causes of death other than breast cancer indicate no systematic problems with ascertainment after 1989. Thus, medical interventions, such as early detection and successful treatment, are the most probable sources for the declines in breast cancer mortality.

Evidence for a role for mammography in the recent mortality declines comes from the increased incidence of localized disease and subsequent declining incidence of regional disease in each age group over 40 years. These changes suggest that mammography has led to stage shifts from regional to localized disease as cancers are detected through screening before they can progress to higher stages (*29-31*). Declining regional disease should eventually result in lower mortality, because about 50% of breast cancer deaths occur in women diagnosed with regional disease (*32*). Women under the age of 40 years show little change in localized disease incidence rates in the 1980s, consistent with the minimal amount of breast cancer screening in this age group (*3,4*). The increase in in situ breast cancer rates in the mid-1980s in women 30-39 years of age indicates some increase in the use of mammography in younger women, perhaps due to

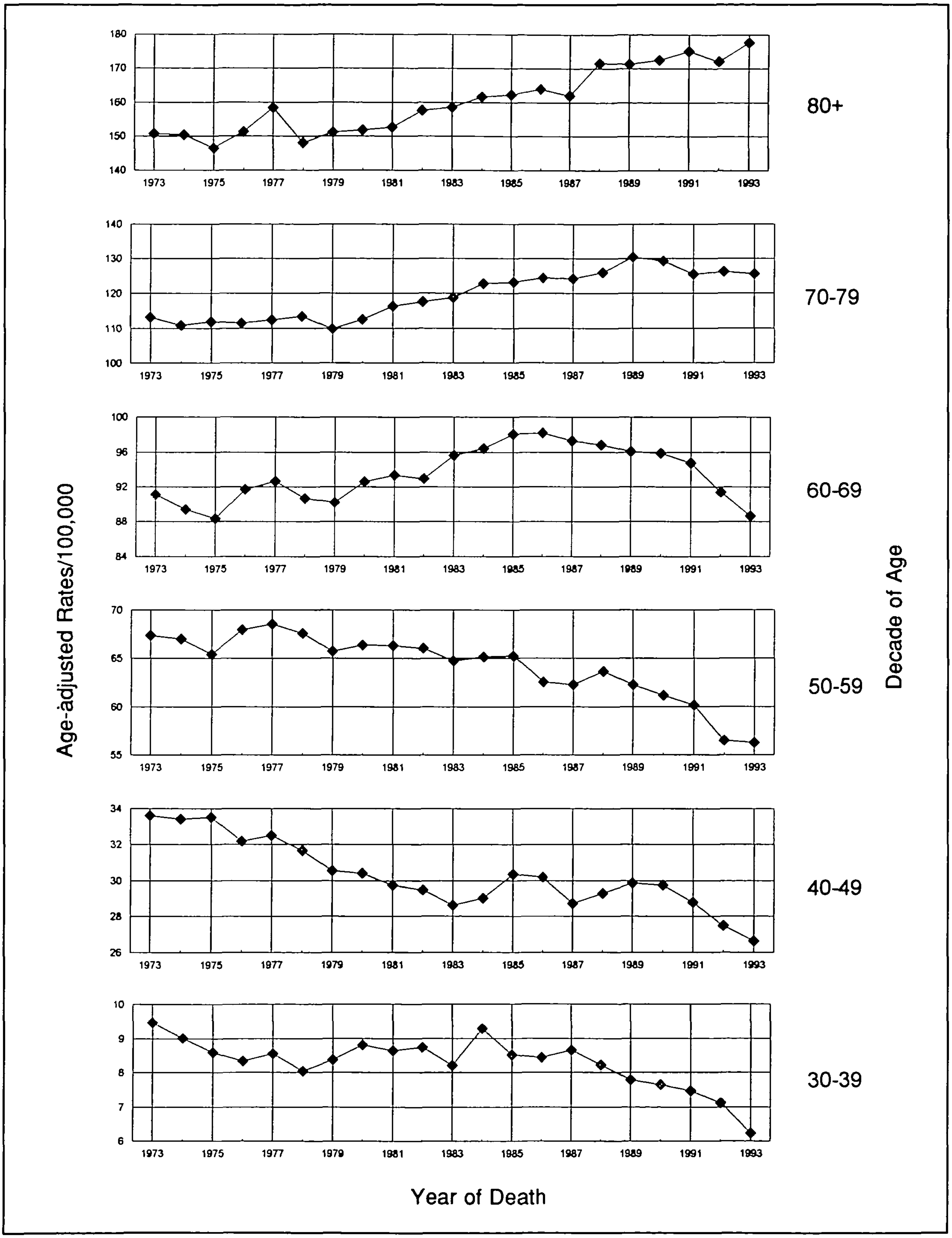


Fig. 2. Age-adjusted breast cancer mortality rates per 100 000 for U.S. white females by decade of age, standardized to the 1970 U.S. population.

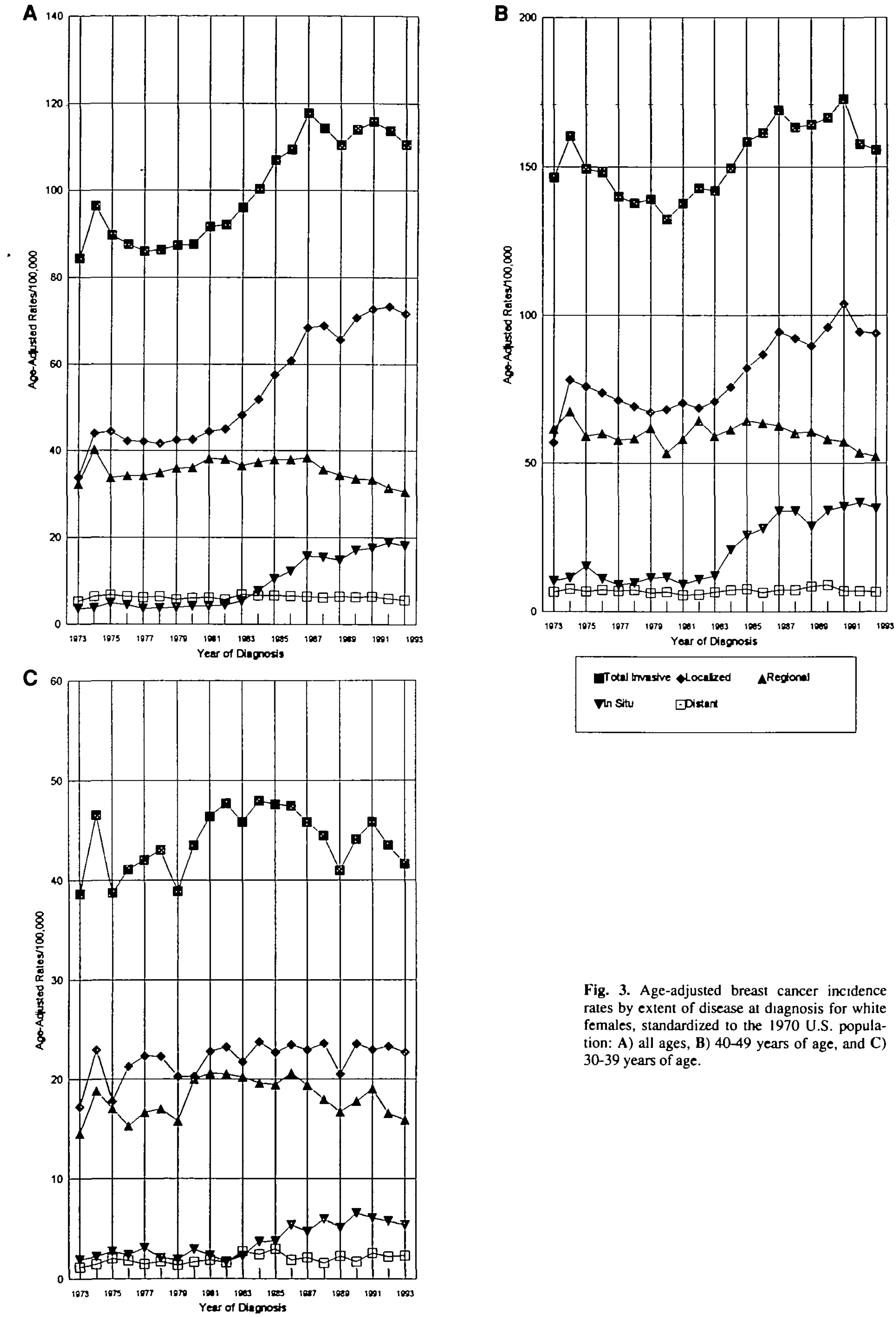


**Fig. 3.** Age-adjusted breast cancer incidence rates by extent of disease at diagnosis for white females, standardized to the 1970 U.S. population: **A**) all ages, **B**) 40-49 years of age, and **C**) 30-39 years of age.

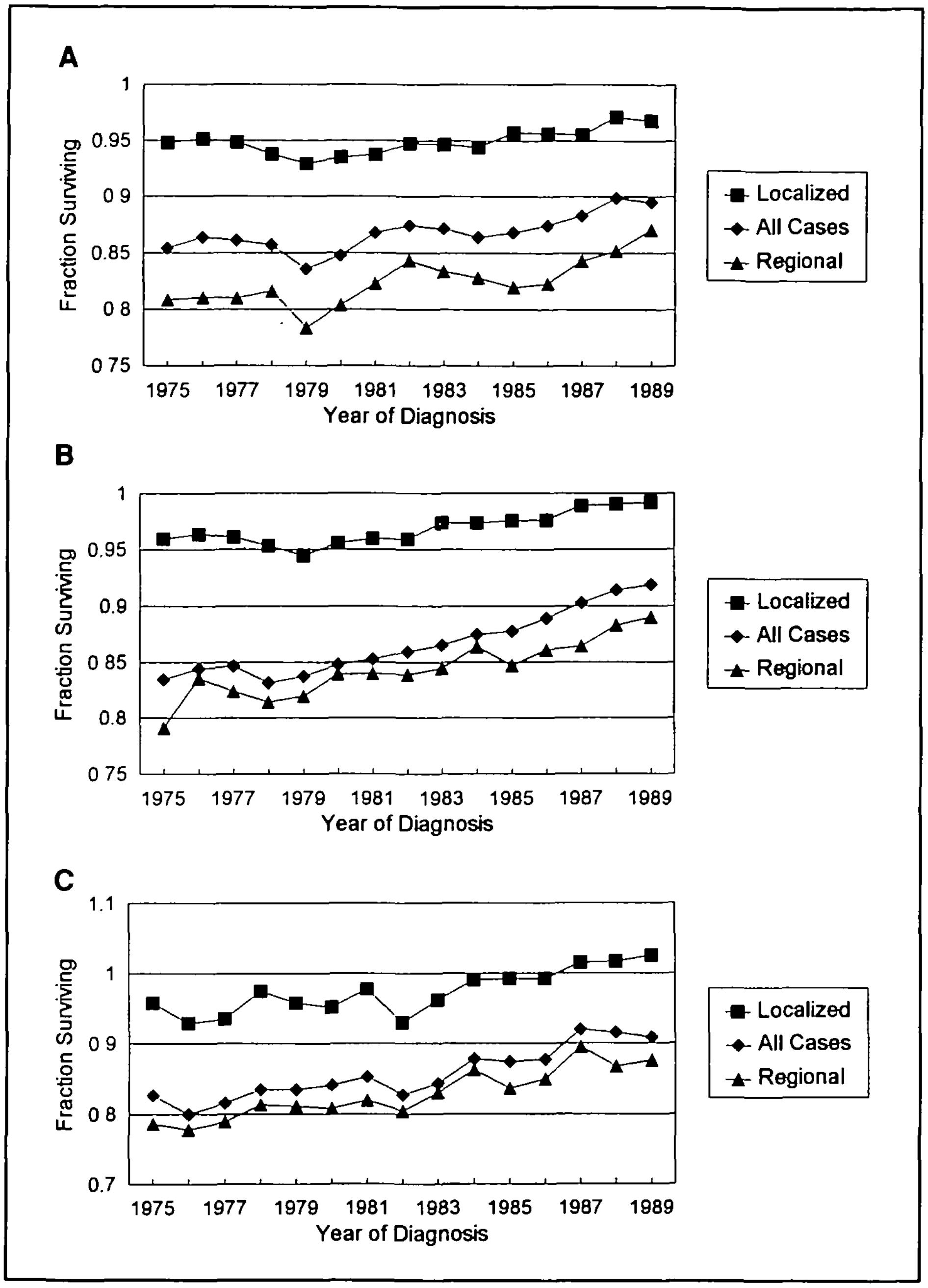


**Fig. 4.** Breast cancer 3-year relative survival rates by stage at diagnosis from 1975 through 1989 for **A)** women less than 50 years of age at diagnosis, **B)** women ages 50-69 years, and **C)** women ages 70 years or more.

base-line mammograms. The decrease in invasive breast cancer incidence rates in women 30-39 years of age in the 1980s, despite increasing use of diagnostic technology, reflects a marked decrease in birth cohort risk in women born during the baby boom (Tarone RE, Chu KC, Gaudette LA: submitted for publication).

The large increases in breast cancer incidence rates in the 1980s have been tied to the dramatic increase in mammography use (*33-38*). Few national mammography utilization data of high quality are available prior to 1987, but it appears that breast cancer screening had reached perhaps 10%-20% of women over the age of 40 years by the early 1980s (*39*). National data on the use of mammography, obtained from three supplements to the National Health Interview Survey (NHIS) for the years 1987, 1990, and 1992, are shown in Table 3 (*6*). The percentages in Table 3 are for mammograms obtained for any reason; however, data collected regarding the most recent mammogram indicate that more than 70% of such mammograms were reported to be screening mammograms in each age group. Usage of mammography was greatest among women ages 40-79 years, with those 35-39 years old having about the same levels of mammography as those 80 years or older.

Using the NHIS data for 1987 and 1992, a projection model called CAN_TROL (*40*) was used to examine the effect of recent screening trends on the overall age-adjusted breast cancer mortality rates. Details of the model have been reported (*41*). CAN_TROL projects cancer mortality rates on the basis of trends in cancer prevention, screening, and treatment activities. Using NHIS screening data, the model predicted that the increase in mammography use would lead to decreasing mortality starting in the late 1980s, but the predicted declines are not as abrupt as those actually observed following 1990. Thus, factors

Table 2. Annual percentage changes in 3-year relative survival rates from 1980 through 1989

| | Womens' age, y | | |
|---|---|---|---|
| | <50* | 50-69* | ≥70* |
| All cases | 0.49 ± 0.10† | 0.93 ± 0.05† | 1.11 ± 0.19† |
| Localized | 0.39 ± 0.05† | 0.43 ± 0.04† | 0.89 ± 0.18† |
| Regional | 0.55 ± 0.18‡ | 0.64 ± 0.10† | 1.02 ± 0.20† |
| Distant | 1.88 ± 1.80 | 2.05 ± 0.66‡ | −1.00 ± 1.09 |

*Values = least-squares estimate of slope ± standard error.
†$P<.005$.
‡$P<.05$.

other than mammography must be contributing to the observed mortality declines.

Significant increases in the survival rates were observed for localized and regional disease in the 1980s. The increases in localized disease survival rates may be influenced by the ability of mammography to detect smaller, better prognosis, localized lesions (*36*) as well as the increased use of breast-conserving surgery, such as lumpectomy (*42*). The increase in localized disease survival largely offsets the increase in localized disease incidence rates in the 1980s, so that the contribution of localized disease to mortality remained relatively constant during the mid- and late-1980s (*32,43*).

The increase in regional-disease survival rates would suggest a gradual improvement in the treatment of regional disease. Regional-disease cases were prime candidates for the initial use of adjuvant therapy, chemotherapy for premenopausal women, or tamoxifen therapy for postmenopausal women. The first randomized clinical trials of chemotherapy as adjuvant therapy were begun in 1972-1973, and the initial finding of benefit was reported in 1976 (*9*). The first randomized trials for tamoxifen as adjuvant therapy were begun in 1977, with positive findings reported in 1983 (*10*). A 1985 National Institutes of Health consensus conference recommended the use of tamoxifen for postmenopausal, node-positive women with positive estrogen receptor status and the use of chemotherapy for premenopausal, node-positive women (*11*). An international meeting on adjuvant therapies in early 1988 reported survival benefits for node-negative patients (*44*), and in mid-1988, the National Cancer Institute released a Clinical Alert to physicians recommending adjuvant therapy for node-negative patients (*12*). The gradual improvement in survival rates is consistent with the progressively wider use of adjuvant therapy in the 1980s. Although no abrupt increases in 3-year survival rates were observed for cases diagnosed through 1989, evaluation of longer-term survival rates, or short-term survival rates for cases diagnosed after 1989, may eventually show a survival pattern more consistent with the observed sharp decrease in breast cancer mortality rates after 1989.

Marked declines in breast cancer mortality rates after 1989 have also been observed in England and Wales (*15,16*) and in Canada (*17*). To compare the decreases in different countries, we computed age-adjusted breast cancer mortality rates restricted to women 30-74 years of age, all standardized to the U.S. 1970 population. These age-adjusted breast cancer mortality rates fell 9.3% in England and Wales, 9.8% in Canada, and 9.0% in the United States between 1989 and 1993. In England and Wales and in Canada, mass screening with mammography did not begin until the late 1980s (*16,45*). Breast cancer incidence data indicate that incidence rates in England and Wales did not rise sharply until mass screening began, but it appears that the rate of increase in age-specific incidence rates had increased a few years prior to the introduction of mass screening (*16*). In Canada, incidence rates show increases beginning in the early 1980s, similar in timing, but somewhat smaller than those observed in the United States (*45*). It appears that mammography, although not formally offered in a mass screening program in these countries until the late 1980s, may have had an earlier impact on incidence rates, perhaps through increased diagnostic use in the mid-1980s. Thus, although mass screening is not a plausible explanation for the marked mortality decreases in England and Wales or in Canada, earlier diagnosis may be contributing to the recent mortality decreases, as has been suggested regarding England and Wales (*15*).

There can be little doubt that improved treatment is contributing to the recent breast cancer mortality decreases, and increased use of tamoxifen may be playing an important role in England and Wales (*16*). Nearly all patients with breast cancer in southeast England over the age of 50 years were being treated with tamoxifen by as early as 1990 (*16*). It appears that the use of tamoxifen in U.S. patients with breast cancer over the age of 50 years was less than that in England. In 1991 in SEER areas, adjuvant tamoxifen treatment was given to 55% of the women over the age of 50 years who had an initial diagnosis of early stage breast cancer and were not involved in a clinical trial (Harlan L: personal communication). For patients with positive

Table 3. Percentage of U.S. women reporting in 1987, 1990, and 1992 having a mammogram in the past year and ever having a mammogram*

| | 1987 | | 1990 | | 1992 | |
|---|---|---|---|---|---|---|
| Age, y | Past year | Ever | Past year | Ever | Past year | Ever |
| 35-39 | N/A† | N/A† | 23.4 | 39.9 | 23.0 | 46.0 |
| 40-49 | 24.2 | 42.1 | 40.2 | 64.6 | 41.6 | 71.2 |
| 50-59 | 26.3 | 46.3 | 46.6 | 68.4 | 51.8 | 75.9 |
| 60-69 | 21.5 | 39.1 | 42.0 | 62.5 | 48.4 | 69.7 |
| 70-79 | 17.7 | 32.0 | 34.5 | 54.5 | 39.8 | 63.5 |
| ≥80 | 9.9 | 20.4 | 20.9 | 35.1 | 21.6 | 48.5 |

*Source of data: National Health Interview Survey, any mammogram.
†N/A = not available.

nodal status and positive estrogen receptor status, the percentage of women over 50 years treated with tamoxifen increased to about 75% (Harlan L: personal communication). Thus, although the use of mammography was earlier and greater in the United States, the use of adjuvant tamoxifen therapy was earlier and greater in England. Despite such differences, the recent decline in mortality rates in the two countries is remarkably similar.

In conclusion, recent trends in breast cancer incidence, survival, and mortality rates for women over the age of 40 years provide evidence that both earlier detection and better treatment of breast cancer are contributing to the recent marked declines in breast cancer mortality in the United States. Better information on the differences among countries in the time of introduction and the extent of use of mammography and of different adjuvant therapy regimens may allow a determination of the relative contributions of earlier detection and better treatment to the recent declines in breast cancer mortality.

## Appendix

Let calendar year be indexed by $i = 1, 2, \ldots I$ and the rate for the calendar year $i$ be denoted $R_i$. Piecewise regression analyses (*46*) were performed after taking a logarithmic transformation of rates. For each $i_0$ from 3 to $I - 2$, the linear model,

$$\alpha + \beta_1 i + \beta_2 x_i \,(i - i_0),$$

was fit to $\log(R_i)$ using standard multiple regression methods, where $x_i$ is defined as an indicator function taking the value 0 if $i \leq i_0$ and 1 if $i > i_0$. Thus, $\beta_2$ represents the change in slope after year $i_0$. Let $i^*$ denote the value of $i_0$ that maximizes the $R^2$ value for breast cancer mortality data for all ages (i.e., Fig. 2). If the regression coefficient $\beta_2{}^*$ corresponding to $i^*$ was significantly different from 0 based on the usual $t$ test for multiple regression parameters, then the trend in breast cancer mortality was considered to have a change in slope over the period from $i^*$ to $I$ compared with the period 1 to $i^*$. Since a test for changing slope was performed at 10 different years (i.e., 1982 through 1991), a Bonferroni-adjusted significance level of 0.05/10 = 0.005 was employed in the piecewise regression analysis of mortality rates for all ages. Regression analyses using untransformed and log-transformed rates gave very similar results. (The $t$ statistics for testing for a change in slope varied by <2% in every year tested.) Piecewise regression analysis with $i = i^*$ was applied to mortality data for each age group to determine the consistency of the change in trend over age groups.

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## Notes

[1]*Editor's note:* SEER is a set of geographically defined, population-based central tumor registries in the United States, operated by local nonprofit organizations 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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