
Birth Cohort and Calendar Period Trends in Breast Cancer Mortality in the United States and Canada

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Background: Previous studies of regional and temporal variation in U.S. breast cancer mortality rates have been confined largely to analyses of rates for white women. **Purpose:** Breast cancer mortality rates from 1969 through 1992 for white women and black women in four regions of the United States and for all women throughout Canada were compared to identify racial, regional, and temporal differences. Differences and trends in the rates were evaluated in view of breast cancer risk factors and relevant medical interventions. **Methods:** Age-period-cohort models were fit to the data, and changes in birth cohort trends (suggesting a change in a breast cancer risk factor or protective factor) and calendar period trends (suggesting, in part, the impact of new or improved medical interventions) were examined. **Results:** Breast cancer mortality rates for white women were significantly higher in the Northeast than in any other region of the United States (two-sided *t* tests; $P < .005$); the rates for black women were not. Birth cohort trends for all women were similar until about 1940, with a moderation of mortality risk beginning around 1924. A marked moderation of risk by 4-year birth cohorts was observed for U.S. white women born after 1950, whereas stable or slightly decreasing trends were observed for U.S. black women and Canadian women. For women born from 1924 to around 1938, fertility rates increased for all three groups; after 1950, they declined uniformly. Looking at temporal effects, we found that the slope of the mortality calendar period trend increased in the 1980s compared with the 1970s for all women. In the last calendar period, 1991-1992, a trend of

decreasing mortality rates was found for white women in the United States and for Canadian women. **Implications:** Widespread environmental exposures are unlikely to explain the higher relative breast cancer mortality rates observed for U.S. white women in the Northeast, since the rates for black women in this region were not higher than in other regions. The moderation of breast cancer mortality rates for women born between 1924 and 1938 coincides with increased fertility rates following World War II. Stable or decreasing mortality rates for U.S. women and Canadian women born after 1950 were not expected in view of declining fertility rates, suggesting a change in a breast cancer risk factor or protective factor. The increase in calendar period trend slope in the 1980s likely reflects the coincident rise in breast cancer diagnosis via mammography. The recent decline in calendar period trend for white women in the United States and for Canadian women may be the result of earlier detection and increased use of adjuvant therapy. [J Natl Cancer Inst 1997;89:251-6]

Considerable geographic variation in breast cancer mortality rates within the United States has been reported (1-4), with high rates found in the Northeast and low rates found in the South (1,4). Breast cancer mortality rates are slightly higher in Canada than in the entire United States (5), but the relationship between Canadian rates and U.S. regional rates has not been investigated. Previous reports of geographic variation in U.S. breast cancer mortality rates have been based largely on studies of white women. In view of racial variability in breast cancer risk (3,6), an examination of geographic variation according to race would seem warranted.

Breast cancer mortality risk increased for U.S. women who were born during the period from before the turn of the century until around 1920 (7-12). An increase in breast cancer incidence rates over this same period was identified in Canada (13). Breast cancer mortality risk then moderated for U.S. women born between 1925 and 1940 (9,11,12). During the past two decades, these two birth cohort trends have led to increasing U.S. breast cancer mortality rates for older women and de-

creasing or stable mortality rates for younger women (11). This discordance in breast cancer mortality trends according to age has also been observed in Canada (14).

Previous studies of U.S. birth cohort patterns of breast cancer mortality risk were based on analyses of rates for all women or for white women only. In this study, we compared breast cancer mortality rates for white and black women in four U.S. regions (the Northeast, the Midwest, the South, and the West) and Canadian women. Breast cancer mortality data were evaluated by fitting age-period-cohort models for both black women and white women in each U.S. region and for all Canadian women. Mortality risk patterns were examined according to race and region, and the implications of changes in birth cohort and calendar period trends with regard to breast cancer risk factors and medical interventions were explored.

Materials and Methods

U.S. breast cancer mortality data for white and black women from 1969 through 1992 were obtained from the Division of Vital Statistics of the National Center for Health Statistics (Hyattsville, MD). Canadian breast cancer mortality data for the same period were obtained from the Health Statistics Division, Statistics Canada (Ottawa, ON). Race is not indicated for Canadian deaths, but 1991 census data showed that only 9.2% of the Canadian population is of non-European ethnic origin.

Nulliparity data for U.S. women were obtained from annual reports on natality by the National Center for Health Statistics. Nulliparity data for Canadian women were provided by the Health Statistics Division, Statistics Canada.

Age-adjusted breast cancer mortality rates were calculated on the basis of year of death for women in Canada and in each of the four U.S. regions (regions defined by the U.S. Census Bureau independent of breast cancer risk) using the 1970 U.S. census population as the standard. Averages of these age-adjusted rates were calculated to summarize the rates in two decades (1972-1981 and 1982-1991), and two-sided *t* tests were employed to compare

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See "Notes" following "References."

rates between races, decades, and regions. Because of the number of comparisons made, a nominal level of .005 was used to determine statistical significance in preliminary analyses.

Age-period-cohort models were fit to the breast cancer mortality data with the use of 2-year age and calendar intervals (12,15,16). There were 30 age intervals (ranging from 24-25 to 82-83 years of age), 12 calendar period intervals (ranging from 1969-1970 to 1991-1992), and 41 4-year birth cohort intervals (ranging from 1885-1888 to 1965-1968). Each birth cohort will be identified in the text by the second year in the interval. For example, the 1950 birth cohort will include women born from 1949 through 1952, with 75% of the women in this cohort having been born in 1950 and 1951.

Changes in the slope of linear trends in birth cohort and calendar period effects were examined by use of identifiable differences in linear contrasts (12,15,16). A significant change in the birth cohort trend usually indicates a change in an etiologic factor, resulting in increasing or decreasing risk. A significant change in the calendar period trend usually indicates the impact of new or improved medical interventions or a change in ascertainment or coding of cause of death. Standard errors of the linear contrasts were adjusted for possible overdispersion when the deviance for the full age-period-cohort fit exceeded the number of residual degrees of freedom (17).

Results

For white U.S. women, breast cancer mortality was significantly (i.e., $P < .005$) higher in the Northeast than in any other region and significantly lower in the South than in any other region in each decade (1972-1981 and 1982-1991; Table 1). Canadian rates in both decades were slightly higher than white Midwest rates but significantly lower than white Northeast rates. For black women, rates in the

Table 1. Average age-adjusted breast cancer mortality rates* (U.S. 1970 population as standard) for white women and black women according to region of the United States and for Canadian women

Country/region†	1972-1981		1982-1991	
	White	Black	White	Black
United States				
NE	30.54 ± 0.15	28.76 ± 0.37	30.64 ± 0.18	30.43 ± 0.47
MW	27.38 ± 0.12	28.29 ± 0.55	27.78 ± 0.12	32.20 ± 0.23
SO	23.23 ± 0.11	24.57 ± 0.27	24.53 ± 0.20	29.06 ± 0.64
WE	26.47 ± 0.11	27.75 ± 0.51	26.77 ± 0.11	31.74 ± 0.33
Canada‡	28.09 ± 0.18		28.52 ± 0.21	

*Mean number of breast cancer deaths per 100 000 women per year ± standard error of the mean.

†NE = Northeast: Maine, Vermont, New Hampshire, Massachusetts, Connecticut, Rhode Island, New York, New Jersey, and Pennsylvania; MW = Midwest: Ohio, Illinois, Indiana, Michigan, Wisconsin, Minnesota, Iowa, Missouri, North Dakota, South Dakota, Nebraska, and Kansas; SO = South: Delaware, Maryland, District of Columbia, West Virginia, Virginia, Kentucky, Tennessee, North Carolina, South Carolina, Georgia, Florida, Alabama, Mississippi, Louisiana, Oklahoma, Arkansas, and Texas; and WE = West: Washington, Oregon, California, Nevada, New Mexico, Arizona, Idaho, Utah, Colorado, Montana, Wyoming, Alaska, and Hawaii.

‡More than 90% of Canadian women are of European ethnic origin.

South were significantly lower than those in any other region from 1972 through 1981 and significantly lower than those in the Midwest and the West from 1982 through 1991. The rates for black women in the Northeast were not significantly higher from 1972 through 1981 than those in the Midwest or the West and were not significantly higher from 1982 through 1991 than even the low rates in the South. Only in the Northeast was breast cancer mortality higher for whites than for blacks. The increase in rates in 1982-1991 compared with 1972-1981 was significantly greater for black women than for U.S. white or Canadian women.

The breast cancer mortality birth cohort effects for white women and black

women in the United States and for Canadian women (Fig. 1) all show a moderation of risk beginning around 1924. U.S. white women also show a marked moderation in birth cohort risk after 1950; the curves for black and Canadian women show stable or slightly decreasing trends after this time. The magnitude of these changes in birth cohort trend is summarized in Table 2. The moderation in breast cancer mortality risk beginning after the 1924 birth cohort was significant for both black women and white women in the United States and for Canadian women; the magnitude of this change in slope was greater for U.S. white women and Canadian women than for U.S. black women, and it was significant for white women in each region.

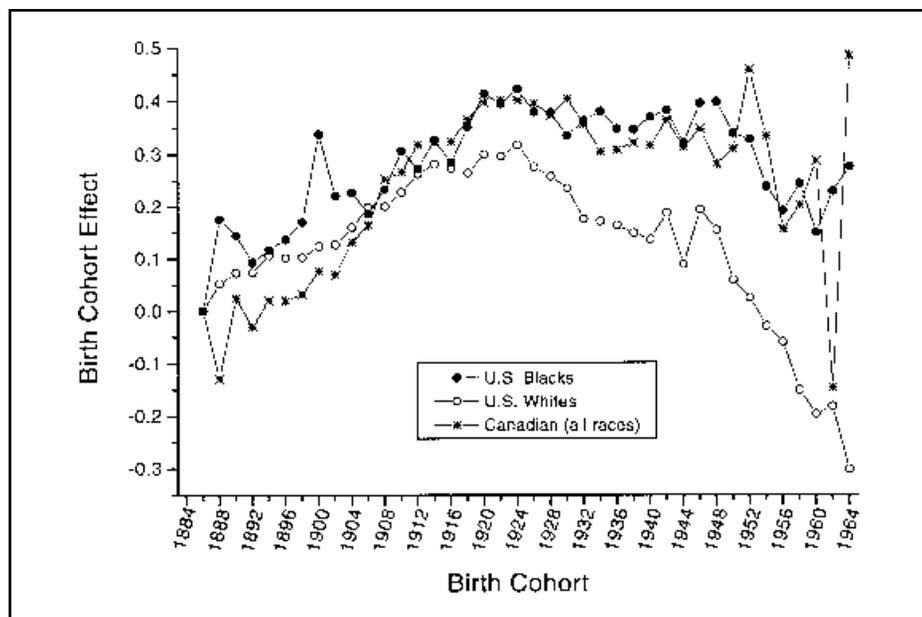


Fig. 1. Maximum likelihood estimates of birth cohort effects for an age-period-cohort model fit to breast cancer mortality data for white women and black women in the United States and for all Canadian women. Because of the linear relationship between year of birth, year of death, and age at death (i.e., if any two of these quantities are known, then the third can be calculated), a constraint must be imposed on the parameters of the age-period-cohort model to obtain parameter estimates. Different estimates will be obtained under different constraints, and, thus, the individual birth cohort effects do not necessarily have an interpretation in terms of relative risk. Changes in the slope of the birth cohort effect curves are, however, independent of the constraint employed and, thus, can be identified unequivocally, indicating changes in birth cohort risk. The estimates plotted were obtained under the constraint that the final birth cohort effect (i.e., for the 1966 birth cohort) is zero. The final constrained birth cohort effect is not plotted.

Table 2. Changes in the birth cohort and calendar period trends from age-period-cohort analyses of breast cancer mortality

Population*	Birth cohort trends†	
	1924-1939 versus 1900-1915	1950-1965 versus 1934-1949
United States		
White	-4.05 (±0.13)‡	-4.04 (±1.04)‡
Black	-1.13 (±0.39)§	-1.45 (±1.54)
NE		
White	-3.95 (±0.26)‡	1.10 (±1.98)
Black	-0.73 (±0.85)	0.78 (±3.54)
MW		
White	-3.68 (±0.26)‡	-3.82 (±2.04)
Black	-1.06 (±0.85)	2.02 (±3.29)
SO		
White	-4.28 (±0.25)‡	-4.67 (±1.81)§
Black	-1.34 (±0.52)§	-2.41 (±2.13)
WE		
White	-4.29 (±0.32)‡	-3.60 (±2.33)
Black	0.62 (±1.43)	-13.64 (±7.96)
Canada, all races	-4.72 (±0.39)‡	-1.94 (±2.57)
Population*	Calendar period trends†	
	1980-1990 versus 1970-1980	1991-1992 versus 1990-1991
United States		
White	0.57 (±0.07)‡	-0.040 (±0.009)‡
Black	1.20 (±0.18)‡	0.026 (±0.027)
NE		
White	0.52 (±0.13)‡	0.002 (±0.018)
Black	0.54 (±0.40)	0.080 (±0.059)
MW		
White	0.50 (±0.13)‡	-0.051 (±0.019)§
Black	1.40 (±0.40)‡	0.015 (±0.060)
SO		
White	0.87 (±0.12)‡	-0.045 (±0.017)§
Black	1.45 (±0.25)‡	0.030 (±0.038)
WE		
White	0.06 (±0.14)	-0.020 (±0.022)
Black	0.83 (±0.65)	-0.092 (±0.092)
Canada, all races	0.91 (±0.18)‡	-0.027 (±0.027)

*See Table 1 for region definitions. Average population size in millions: NE = 29.0 white, 3.1 black; MW = 32.7 white, 3.0 black; SO = 38.7 white, 7.9 black; WE = 23.6 white, 1.3 black; and Canada = 14.9. Ratios of the deviance to the residual degrees of freedom: U.S. white 1.37, black 1.36; NE = white 1.36, black 1.03; MW = white 1.25, black 1.04; SO = white 1.11, black 0.90; WE = white 1.04, black 0.91; and Canada = 0.96.

†Linear contrasts (± standard error) of birth cohort or calendar period effects testing for changes in the slopes for the two eras indicated (14).

‡Significant change, $P < .001$.

§Significant change, $P < .01$.

The decrease in the slope of the birth cohort mortality risk after 1950 for U.S. white women was significant, despite the variability inherent in estimates of recent birth cohort effects (see the Canadian curve in Fig. 1). Estimates of recent birth cohort effects are based on a few age-specific rates from the youngest age groups, and, therefore, they should be interpreted cautiously, particularly for smaller populations. Nonetheless, there is some evidence of geographic heterogeneity in the recent birth cohort trends for white women in the United States and Canada, with decreases of similar magni-

tude in the Midwest, the South, and the West but little or no evidence of a decrease in Canada or the Northeast. The recent birth cohort effects for U.S. black women are quite variable, but only in the Northeast is there no evidence for a decrease in birth cohort effects after 1950 (the positive contrast for the Midwest is a result of a single high estimate for the 1964 birth cohort).

To document the recent decrease in birth cohort risk among U.S. white women in greater detail, age-specific breast cancer mortality rates were plotted against birth cohort according to 5-year

age intervals for ages 20-49 years (Fig. 2). A decrease in mortality rates after 1946 is evident for each age group under 40 years of age, showing that the decrease in birth cohort effects after 1950 (Fig. 1) is not an artifact of statistical modeling.

The proportion of nulliparous women 20-24 years of age has been used to document changes in fertility patterns, and a high concordance between trends in this value and breast cancer mortality has been noted previously for white females (9,11). These proportions are plotted against birth cohort in Fig. 3 for white women and nonwhite women in the United States and for Canadian women, and each curve indicates decreasing fertility rates after 1950.

The calendar period effects for U.S. white women and black women and for Canadian women all show an increase in slope in the 1980s relative to the 1970s (Fig. 4). The curves for U.S. white women and Canadian women also show a decrease in the last calendar period (1991-1992). The increased slope in the 1980s was significant in all three curves, and the abrupt change in slope for U.S. white women in the last calendar period was also significant (Table 2). In regional analyses, a significant increase in slope in the 1980s compared with the 1970s was observed for U.S. white women in every region except the West. The increases in slope in the 1980s for black women are of comparable magnitude in all regions and are larger than the corresponding increases for white women. There is evidence of a decrease in risk in the last calendar period for Canadian women and for U.S. white women in every region, except the Northeast.

Discussion

Regional Variation

Geographic variability in U.S. breast cancer mortality rates is evident for both black women and white women. The most consistent finding is that breast cancer mortality rates are lowest in the South, which for white women appears to be explained, at least in part, by an earlier average age at first childbirth (a protective factor for breast cancer incidence) in the South (4). For white women, breast cancer mortality rates are highest in the Northeast, and, although some of the ex-

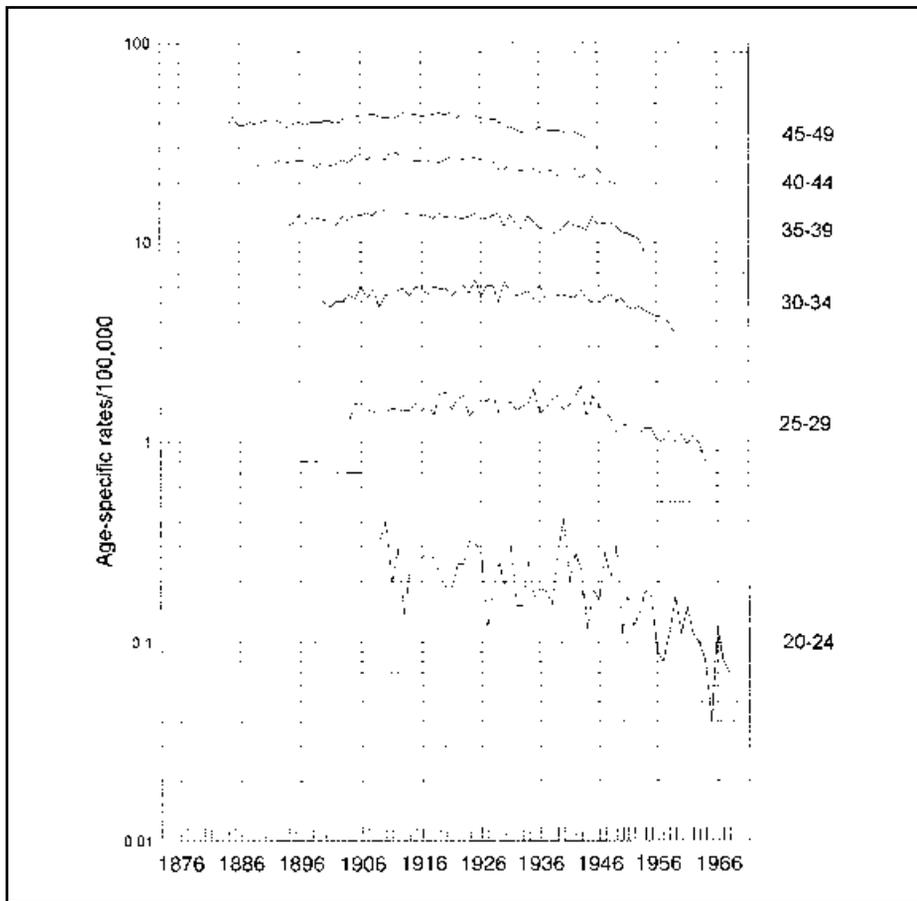


Fig. 2. Age-specific breast cancer mortality rates for white women under the age of 50 years in the United States plotted on a logarithmic scale against birth cohort; bottom curve = 20-24 years of age; top curve = 45-49 years of age.

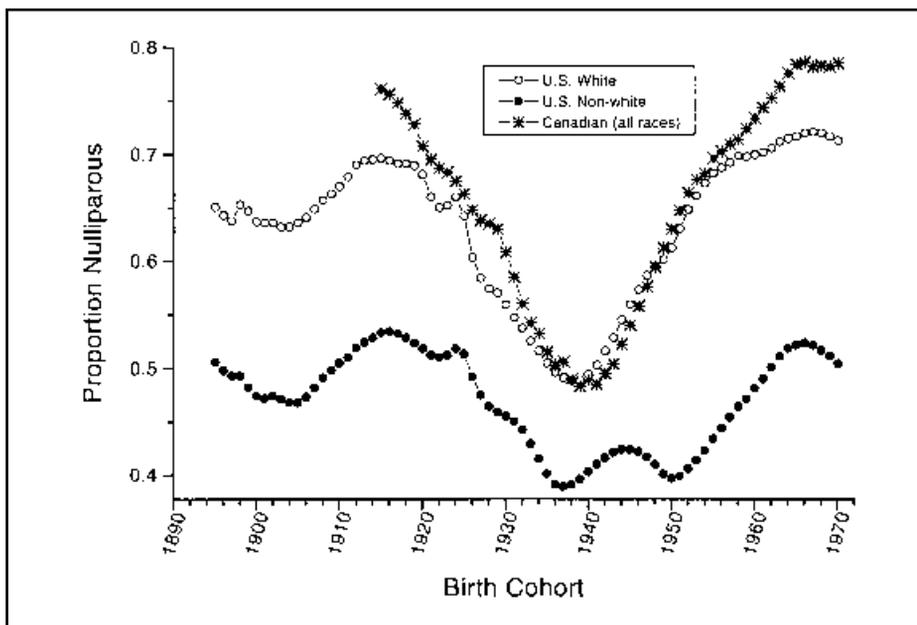


Fig. 3. Proportion of nulliparous women 20-24 years of age for white and nonwhite women in the United States and for all Canadian women, plotted against birth cohort. Examination of census counts for black women according to year of birth indicates that the nonwhite curve closely reflects black fertility patterns.

cess in the Northeast may be explained by known breast cancer risk factors (4), it appears that much of the excess risk may remain unexplained (18). There is no evidence of higher breast cancer mortality rates for black women in the Northeast. Thus, any environmental factors contributing to the Northeast excess for white

women (1,4) must be concentrated in areas with predominantly white residents.

Birth Cohort Trend in Mothers of Baby Boomers

The patterns of birth cohort risk for U.S. and Canadian women show remarkable consistency until the late 1940s. In

particular, the marked moderation in breast cancer mortality risk noted for all U.S. white women beginning around 1925 (9,11,12) is evident in each region of the United States and in Canada. It is also observed, although to a lesser extent, for U.S. black women in every region, except the West. Possible explanations for

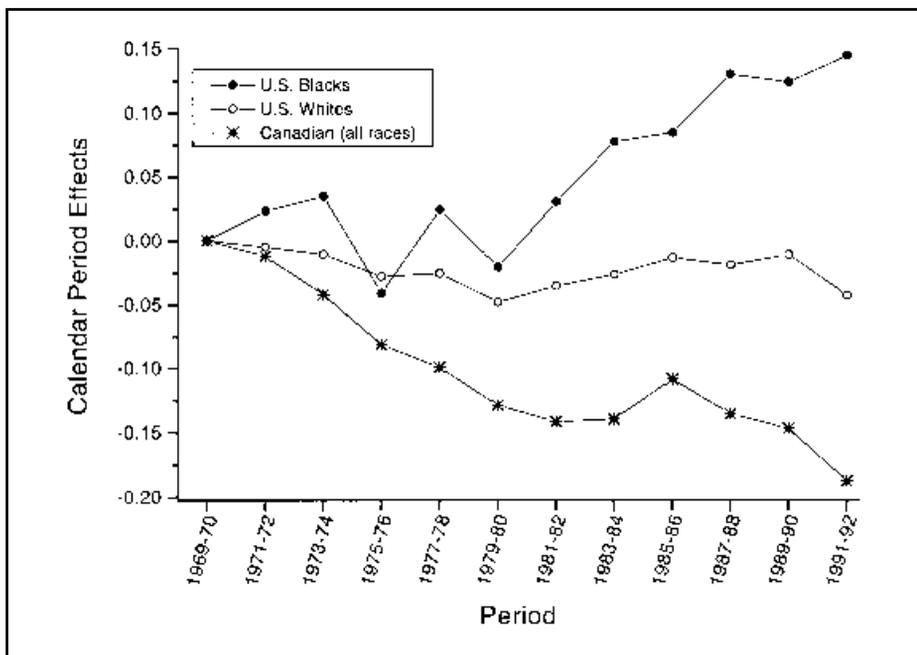


Fig. 4. Maximum likelihood estimates of calendar period effects for an age-period-cohort model fit to breast cancer mortality data for white women and black women in the United States and for all Canadian women. Estimates were obtained under the constraint that the final birth cohort effect is zero. As was the case for birth cohort effects (Fig. 1), the individual calendar period effects do not necessarily have an interpretation in terms of relative risk; however, changes in the slope of the calendar period effect curves can be identified unequivocally, indicating changes in calendar period risk.

the moderation in birth cohort risk beginning in the mid-1920s include changes in childbearing practices following World War II and dietary restriction early in life because of the Great Depression (11,12). Increased fertility rates for women born from 1924 to 1938 are indicated by all three curves in Fig. 3.

Birth Cohort Trend in Baby Boomers

The recent decrease in the breast cancer mortality birth cohort trend among U.S. white women has not been noted previously. Inferences in this report are based on trends in breast cancer mortality rates, which, at least until 1990 (19), have been influenced primarily by changes in etiologic factors (12). A reduction in the risk of developing breast cancer in recent birth cohorts is supported by a decrease in breast cancer incidence rates for U.S. white women 30-39 years of age from 1982 through 1993 (19). A similar non-significant decrease in incidence has been observed for Canadian women 30-39 years of age from 1984 through 1991 (14). In addition, a decrease in breast cancer incidence has been reported for Scottish women in birth cohorts after 1950 (20). These decreases occurred during a period in the United States and Canada in which incidence rates increased sharply in older age groups as the use of mammography expanded rapidly (19; Gaudette LA, Altmayer CA, Nobrega K, Lee JM: unpublished results). The effects of some breast cancer risk factors vary according

to age (21), and, thus, the decrease in breast cancer mortality risk for young women may not continue as these cohorts age.

The decrease in birth cohort mortality risk beginning in the late 1940s among U.S. white women is remarkable, both in its magnitude and because increased, not decreased, breast cancer risk would be expected based on the trends in some known or suspected risk factors for young women. The fertility pattern of the baby boom reversed around 1960 with the introduction of oral contraceptives and the increase in women in the workplace. Early age at first childbirth appears to be an important protective factor for both younger and older women (21). The percentage of nulliparous women 20-24 years of age increased for birth cohorts after 1940 (Fig. 3), reflecting a drop in the frequency of women giving birth for the first time at an early age. Thus, although increases in breast cancer mortality for women born during the baby boom might be expected, no increase was observed for Canadian or U.S. black women, and a significant decrease occurred for U.S. white women.

Baby boomers represent the first generation with the opportunity for early and long-term exposure to oral contraceptives. Oral contraceptive use is not associated with decreased breast cancer incidence (22), and oral contraceptive use at young ages or of long duration may increase breast cancer risk in premenopausal

women (21,23). Thus, the decrease in birth cohort mortality risk after 1950 would not be predicted from the concurrent increase in oral contraceptive use. Breast cancer mortality rates in the U.K. and in Sweden also show no increases with increased oral contraceptive use (24). The possible association between induced abortions and the incidence of breast cancer is controversial (25-27), but there is no evidence of an increase in breast cancer mortality in response to the large increase in abortions that followed liberalization of abortion laws in Canada in 1970 and in the United States in 1973.

The recent birth cohort trends may indicate a change in a risk factor or a protective factor for breast cancer incidence. Examination of known or suspected factors has revealed no trends consistent with a marked decline in breast cancer mortality (data not shown). Although the geographic heterogeneity in the magnitude of the change in the slope of the birth cohort trend after 1950 was not statistically significant, the fact that there was little evidence of the recent decrease in the Northeastern United States or in Canada may be useful in identifying possible explanations. Even the Northeast and the Canadian birth cohort curves show no increase after 1950, again contrary to some trends in risk factors.

Calendar Period Trends

The increase in the mortality calendar period trend slopes in the 1980s coincided

with marked increases in breast cancer incidence rates due to the expanded use of mammography (28-30; Gaudette LA, Alt-mayer CA, Nobrega K, Lee JM, unpublished results). Despite increases in breast cancer survival rates in the United States in the 1980s (6,19), the large increase in the number of women diagnosed with breast cancer apparently resulted in an increase in breast cancer death rates, possibly reflecting, in part, deaths from surgery or chemotherapy that would not have occurred or would have occurred later in the absence of mammography. The larger increase in the mortality calendar period slope for black women than for white women during the 1980s could reflect the higher stage at diagnosis for black women (6). The significant decrease in the most recent calendar period for U.S. white women supports inferences that a recent mortality decrease is due to medical interventions (19). Similar decreases have been observed in the U.K. (31,32) and in Canada (14,19). Increased use of adjuvant therapy, particularly tamoxifen therapy, is likely contributing to recent decreases (31,32), although some benefit from early detection cannot be ruled out (19,32).

Implications

The decreasing birth cohort trend in breast cancer mortality among female baby boomers has important implications with regard to etiology and to projections of future burdens on the health system, particularly if the decrease continues as these cohorts age. The cause of the decrease remains in question, but the magnitude of the decrease suggests that the factor responsible plays a substantial role in determining breast cancer risk. Identification of this factor could increase substantially our understanding of the causes of breast cancer.

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Notes

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