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Breast Cancer Incidence, Mortality, and Survival in North Carolina

by

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ABSTRACT

The objective of this study is to examine incidence, death rates, and survival from breast cancer in North Carolina as influenced by the stage of cancer, age at diagnosis, and minority status. Breast cancer cases from 1995 were used to examine incidence distributions. Data for North Carolina female resident deaths between 1986 through 1995 were used to examine death rates and trends. The Cancer Registry files between 1987 and 1990 were used for the survival analyses.

The overall age-adjusted incidence rate was higher for majority women (112.1) than for their minority counterparts (92.2), but the proportion of regional and distant cancers was higher for minority women (29.2% for majority women vs 35.5% for minority women). Women under 50 years of age had a higher percentage of late-stage cancers than women 65 and older (37.5% vs 26.1%).

The overall breast cancer death rate declined 11 percent between 1986 and 1995, a trend evident only among majority women between ages 50 and 65. The death rate for minority women 65 years of age and older increased sharply. Five-year, age-adjusted death rates were 20.2 and 26.5 per 100,000 for majority and minority women, respectively.

All three variables—stage, age at diagnosis, and minority status—significantly influenced five-year survival of breast cancer. The stage of cancer was the most predictive of survival. Five-year survival fractions were 94 percent, 79 percent and 35 percent for localized, regional, and distant cancers, respectively.

After controlling for stage and age, minority women had a higher risk of dying from breast cancer. Both later stage and younger age at diagnosis contributed to a higher risk of dying from breast cancer for minority women.

The average age at death from breast cancer as well as for all causes of death for women between 1986 and 1995 increased, suggesting that the decline in breast cancer mortality was a part of overall improvement in women's health status in North Carolina. Higher rates of late stage cancers for women under 50 years of age were indicative of the lower rates of mammogram screening. The survival of minority women could be improved substantially by early detection alone.

Introduction

Breast cancer has received the much-needed attention of researchers and public policy makers. This attention has generated a wealth of research leading to improved early detection, diagnostic methods, and treatments and has increased public awareness of breast cancer risk factors. For early detection, mammography screening has been proven effective and its use increased greatly in the early 1980's. As a result, early stage breast cancer cases rose sharply in the United States in the late 1980's and regional cancer cases declined in the early 1990's (Hankey et al. 1994; Sondik 1994; Garfinkel et al. 1994).

This decline is expected to reduce future breast cancer death rates. A recent study showed that the US breast cancer mortality rate declined 8 percent between 1989 and 1993 (Chu et al. 1996). Improvements in diagnostic methods, treatments, and possible changes in risk factors along with early detection may have contributed to declining mortality rates in the 1990's in the United States and several other countries (Chu et al. 1996; Beral et al. 1995) . Currently, breast cancer still ranks as the second leading cause of cancer deaths, with an estimated 44,000 deaths nationally and as the leading cancer, with an estimated 184,300 new breast cancer cases each year for women in the United States.

In addition to incidence and mortality, survival time after diagnosis is also affected by advances in breast cancer management. Many factors affect breast cancer survival–stage of cancer, tumor size and biology, type of surgery or treatment, nulliparity, age at diagnosis, and minority status. In this study, cancer stage, age at diagnosis, and minority status were chosen to examine their association with survival. These data are reliable and readily available from the North Carolina Central Cancer Registry.

Cancer stage has been proven to be highly predictive of breast cancer survival. Many studies reported higher mortality and lower survival rates for minority women. (Simon and Severson 1996; Roach and Alexander 1995; Eley et al. 1994; Muss et al. 1992; Ragland et al. 1991). Examination of survival in relation to minority status is especially important in North Carolina, due to a large minority population and higher rates of death among minorities. Survival differences from breast cancer based on age at diagnosis appear to be small, however, most studies have shown a survival advantage for women over age 50 (Hankey et al. 1994, Nixon et al. 1994, Ewertz 1993; Lethaby et al. 1992).

The objective of this study is to examine recent breast cancer incidence, death rates and trends, and survival from breast cancer as influenced by the stage of cancer, age at diagnosis, and minority status in North Carolina.

Methods

For this study, data for female resident deaths between 1986 and 1995 were used to examine the trend in breast cancer mortality. For incidence data, the Central Cancer Registry file of resident female breast cancer cases in 1995 was used. Both death and incidence rates were age-adjusted by direct standardization to the 1940 United States population. Stage and minority group specific rates were age-adjusted in a similar fashion.

Breast cancer incidence data from 1987 through 1990 were used in the survival analyses. These years were chosen to maximize the number of cases for a five-year survival analysis. At the time of this analysis, the last available death file was from 1995. After removing duplicates and non-resident cases, there were 8,570 breast cancer cases reported to the Central Cancer Registry in 1987-1990. These cases were matched with the North Carolina death files to determine the vital status of the cases at five years following diagnosis.

The matching of the 1987-1990 cancer incidence and 1987-1995 death records was done using a SAS-SQL program that allowed the comparison of every possible record combination from each file. After preliminary testing, each cancer incidence record was compared with every death record for social security number, first and last name, birth date, middle initial, minority status, county of residence, year of death/diagnosis, and zip code of residence.

After manual examination of questionable matches, 31 initial matches were deleted. Initial survival analyses showed nearly 100 percent cancer survival of *in situ* cancer in five years. That made odds ratios for other stages relative to *in situ* cancer extremely large and uninterpretable. For this reason, 834 *in situ* cases were excluded from the survival analyses, leaving a total of 7,736 cases of which 2,320 were matched with death records. Of these deaths, 710 could not be attributed to breast cancer on the death certificate.

The remaining 1,610 deaths had breast cancer recorded either as the underlying cause of death (n=1,542) or as a mentioned condition with another type of cancer listed as the underlying cause (n=32), or were deaths possibly due to distant breast cancers (n=36).

Variables were organized for survival analyses in the following fashion:

- Age at diagnosis was grouped into three categories: under 50, 50 to 64, and 65 and older.
- Cancer stages were localized, regional, distant, and unknown at the time of diagnosis. Three stages, localized, regional, and distant were compared for survival and unknown stage was set to missing.
- Declared or reported race or ethnicity of women was grouped into two categories: "white" (or majority) and other race categories (or minority). This variable is important because of social, economic, and political factors that affect the health status and use of health services of minority women.

A proportional hazard regression analysis that included all interaction combinations was performed to examine interactions among these three variables (Cox 1973). No interaction term was significant at the p=0.1 level, indicating homogeneity across comparison groups. Thus, proportional hazard regressions were performed on single and multiple variables for survival analyses. The life table approach was used to estimate survival fractions.

Results

Breast Cancer Incidence

There were 5,378 new breast cancer cases reported in North Carolina in 1995. The rates and distributions in 1995 are summarized in Tables 1 and 2. The overall age-adjusted rate was 108.3 per 100,000, but was higher for majority women (112.1) than their minority counterparts (92.2) . The stage-specific, age-adjusted rates showed a similar pattern between the groups with the exception of the rate of distant cancer. Unadjusted age-specific rates also indicated higher incidence for majority women with the exception of the oldest age group (Table 2). The unadjusted incidence rates increased by age groups. Overall, 195.3 women per 100,000 over 19 years of age were diagnosed with breast cancer in 1995.

Breast cancer stage distributions for age and minority status groups varied greatly (Table 2). For example, women under 50 years of age with cancer were much more likely to be diagnosed with later stage diseases (regional plus distant) than women 65 and older (37.5% vs 26.1%). Stage distributions were similar between minority status groups among women under 50 years of age, while they differed between the two groups for older women.

Table 1
Age-adjusted stage and minority status specific breast cancer incidence rates in North Carolina, 1995

Socio-Political Status	Rate/100,000				
	In situ	Localized	Regional	Distant	All Cases
Majority	15.9	57.5	29.3	5.1	112.1
Minority	11.1	42.8	26.9	5.8	92.2
All	15.0	54.8	28.8	5.2	108.3

Table 2
Percent distribution and rate of breast cancer cases by stage, age, and minority status groups in 1995

Age Groups	Stages				Unadjusted Rate* (per 100,000)
	In-situ (%)	**Localized** (%)	**Regional** (%)	**Distant** (%)	
20 through 49					
Majority	14.7	44.3	32.5	5.5	91.8
Minority	12.4	46.3	32.4	3.2	73.6
All	14.2	44.7	32.5	5.0	87.2
50 through 64					
Majority	15.3	52.9	24.1	4.0	344.4
Minority	12.6	44.8	28.7	8.8	185.4
All	14.9	51.7	24.8	4.7	326.7
65 and Older					
Majority	11.5	58.3	20.3	4.3	405.5
Minority	10.5	46.9	26.3	7.7	411.6
All	11.2	56.5	21.3	4.8	396.3
All Age groups					
Majority	13.6	52.9	24.7	4.5	209.6
Minority	11.6	46.1	29.0	6.5	141.7
All	13.2	51.8	25.5	4.8	195.3

*Unadjusted rates based on women population age 20 and older.
Note: Percentages do not add across to 100.0 due to missing information on stage for some incidence records.

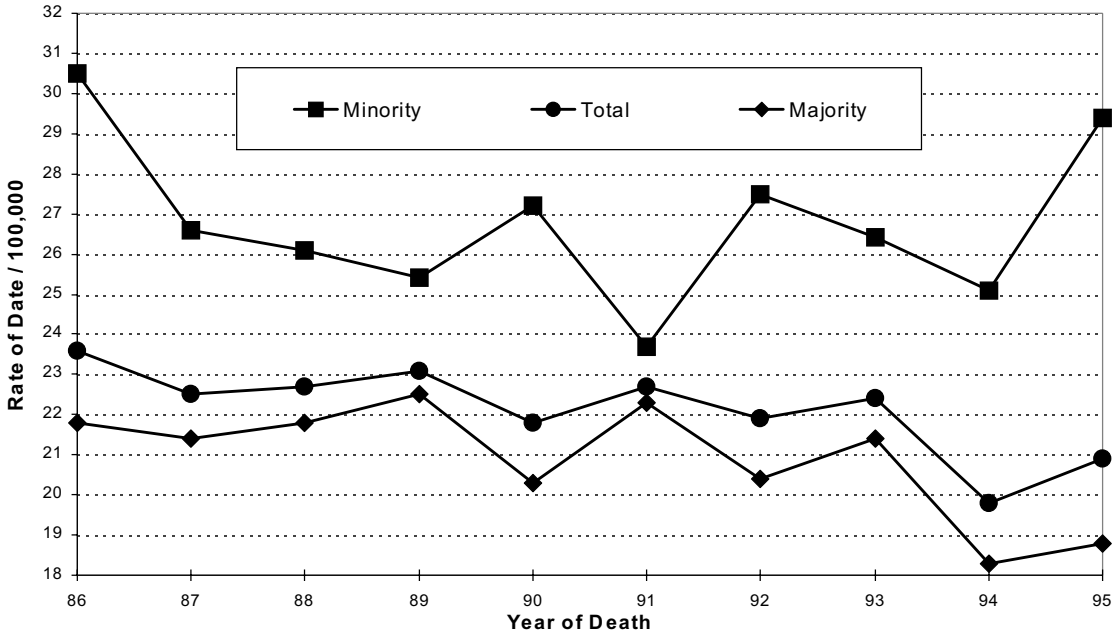
For example, regional cancer proportions were similar between majority and minority women under age 50. Among women 50 years of age and older, a high percentage of minority women had regional cancer. Proportions of late stage cancers (regional plus distant) were 35.5% and 29.2% for minority and majority women, respectively. Minority women were more often diagnosed with breast cancer at earlier ages than their majority counterparts. Unstaged cancers were more frequent for older and minority women than for younger and majority women.

Breast Cancer Mortality

It is encouraging that breast cancer mortality rates have declined between 1986-1995. On the average, 1,107 North Carolina women died from breast cancer each year, based on data from 1986 to 1995. Even though the number of deaths has increased steadily (1.3% a year, from 1,037 in 1986 to 1,187 in 1995), this increase was mainly due to a population increase among women in North Carolina (Table 3). The age-adjusted death rate, which takes population growth into account, was down from 23.6 per 100,000 in 1986 to 20.9 per 100,000 in 1995. Figure 1 shows a downward trend (an average of 1.1% a year) in the death rates.

The decline in cancer mortality rates differed among age groups. During 1986-1995, the percentages of total breast cancer deaths by age groups were 17.5%, 30.2% and 52.3% for women under 50, ages 50 to 64, and 65 and older, respectively. The age-specific rate among women ages 50 to 64 decreased 15.8% (Table 4). Meanwhile, an increasing number of women died from breast cancer at

Figure 1
Breast Cancer Death Rates by Minority Status in North Carolina between 1986 and 1995



older ages in North Carolina. The increase in deaths among women 65 and older was almost entirely due to the female population increase in this age group during the same time span. The age-specific rates for women 65 and older remained constant during 1986-1995.

Women who died from breast cancer in the 1990's had lived longer compared to women who died from breast cancer in the 1980's. The average age at death from breast cancer increased from 63.2 to 65.1 years between 1986 and 1995, with an overall average of 64.4 years. Between 1986 and 1995, the average age at death for all women from all causes also increased, from 72.4 to 74.4 years in North Carolina. In contrast to the overall decline in mortality and increase in the age at death, age-specific breast cancer death rates for women under age 50 did not show any decrease.

Table 3
Age-adjusted breast cancer death rates (100,000) and number of deaths in North Carolina, 1986 to 1995

	Majority		Minority		All	
Year	Rate	Number	Rate	Number	Rate	Number
86	21.8	795	30.5	242	23.6	1037
87	21.4	790	26.6	227	22.5	1017
88	21.8	862	26.1	231	22.7	1093
89	22.5	866	25.4	233	23.1	1099
90	20.3	817	27.2	250	21.8	1067
91	22.3	899	23.7	230	22.7	1129
92	20.4	862	27.5	265	21.9	1127
93	21.4	927	26.4	271	22.4	1198
94	18.3	850	25.1	267	19.8	1117
95	18.8	867	29.4	320	20.9	1187
91-95	**20.2**	**4405**	**26.5**	**1353**	**21.5**	**5758**

Table 4
Age-specific breast cancer mortality rates by minority status in North Carolina, 1986-1995

	Majority			Minority			All		
Year	Under 50	50-64	65 and Older	Under 50	50-64	65 and Older	Under 50	50-64	65 and Older
86	10.1	69.8	117.1	18.7	94.9	105.8	12.2	74.7	115.0
87	11.0	70.2	108.4	15.3	66.4	117.7	12.1	73.7	107.9
88	11.0	69.7	123.9	13.2	67.6	128.3	11.6	73.8	122.0
89	12.2	71.1	116.0	15.0	49.6	147.5	12.9	70.3	118.4
90	10.9	63.2	111.1	17.9	57.9	138.2	12.6	66.1	112.7
91	12.5	71.5	114.7	14.7	44.4	144.2	13.1	69.4	116.5
92	11.7	59.7	115.5	15.3	68.5	144.0	12.6	66.1	116.9
93	13.3	62.3	119.4	14.5	55.5	170.9	13.6	64.7	124.0
94	8.7	54.8	116.9	15.9	56.2	150.6	10.5	58.9	118.9
95	12.1	54.5	107.0	15.7	71.8	178.7	13.0	62.9	115.4
86-95	**11.4**	**64.5**	**114.9**	**15.6**	**62.4**	**143.0**	**12.4**	**67.9**	**116.9**

*Age Specific rate for women under 50 based on women population between age 20 and 49.

On average for each year from 1986-95, 194 of 1,107, or 18 percent of breast cancer deaths were among women under 50 years of age. This makes breast cancer one of the costliest diseases in terms of number of years of life lost.

Breast cancer death rates differed between majority and minority women. Five-year, age-adjusted death rates were 20.2 and 26.5 per 100,000 for majority and minority women, respectively (Table 3). Between 1986 and 1995, the overall decline in breast cancer mortality rates did not benefit minority women. The adjusted rates declined for majority women at an average of 1.4% a year, while there was no apparent trend in minority rates. The difference between minority and majority mortality was consistently present in age-adjusted rates in the last 10 years, and was increasing. Age-specific rates (Table 4) showed similar majority/minority mortality differences across all age groups. Age-specific rates increased dramatically for minority women 65 and older, from 105.8 in 1986 to 178.7 per 100,000 in 1995.

Minority women died at an earlier age and had a higher rate of breast cancer death than majority women. The average age at death during 1986-95 was 65.3 and 61.6 years for majority and minority women, respectively. This gap has been narrowing in recent years due to the increase in the age at death for minority women. The difference in the average age at death between majority and minority women for breast cancer was less when compared to the average age at death for all causes of female deaths between the two groups during the same period (74.4 and 66.2 years for majority and minority women, respectively). One in three women who died from breast cancer under the age of 50 was minority; among women 65 years of age or older, one out of five breast cancer deaths was to minority women.

Breast Cancer Survival

Survival analyses revealed that all three variables – age at diagnosis, stage at diagnosis, and minority status significantly influenced five-year survival of breast cancer (Table 5). Stage of cancer was by far the most predictive variable influencing breast cancer prognosis. At the end of five years, survival fraction estimates from the survival analysis were 94 percent, 79 percent and 35 percent for localized, regional, and distant cancers, respectively (Figure 2). Odds of death from regional and distant cancers were 3.6 and 14.3 times higher than that for localized cancer. This result shows the importance of early detection for survival from breast cancer.

Survival differences between stages were statistically significant and consistent across age and minority status groups. The level of significance and odds ratios for stage changed little after controlling for age and minority status group. There were 4,286 women with localized, 2,605 with regional, and 564 with distant breast cancer cases reported in 1987-1990. Of these women, 377 with localized cancers, 759 with regional cancers and 378 with distant cancers died within five years. Survival differences between distant and other cancers were well established a few months after diagnosis, with an immediate decline of distant cancer survival (Figure 2).

The age at diagnosis was not as strong a prognostic factor as the stage of cancer. There were 1,896, 2,462 and 3,378 women ages under 50, 50 to 64, and 65 and older, respectively, who had breast cancer reported in 1987-1990. A significantly higher proportion of women under 50 years of age died from breast cancer than women ages 65 years and older.

The odds of survival for women between 50 and 64 years of age were not significantly different than the odds for women 65 years of age and older. In the first two years after diagnosis, survival differences were small and younger women survived slightly better than older counterparts (Figure 3).

Minority status appears to be a strong determinant of breast cancer survival and these differences remained apparent after stratifying by stage and age at diagnosis (Figures 4, 5 and 6). Controlling for stage and age, minority women had a higher risk of dying from breast cancer. Both later stage and younger age at diagnosis contributed to a higher risk of dying from breast cancer for minority women. After including both variables in the survival model (Table 5), the mortality odds for minority women was 44 percent higher than for majority women.

Table 5
Risk ratios from analyses of breast cancer survival using proportional hazard model for breast cancer cases from 1987-1990

Variable	Multivariate Model Risk Ratios	Multivariate Model p-value	Univariate Model Risk Ratios	Univariate Model p-value
Stage-at-diagnosis				
Localized	1.00		1.00	
Regional	3.56	0.0001	3.67	0.0001
Distant	14.34	0.0001	14.86	0.0001
Age-at-diagnosis				
65 and Older	1.00		1.00	
50-64	1.04	0.4786	1.07	0.2491
Under 50	1.14	0.0402	1.26	0.0002
Minority Status				
Majority	1.00		1.00	
Minority	1.44	0.0001	1.71	0.0001

Figure 2
Five-year Breast Cancer Survival by Stage at Diagnosis

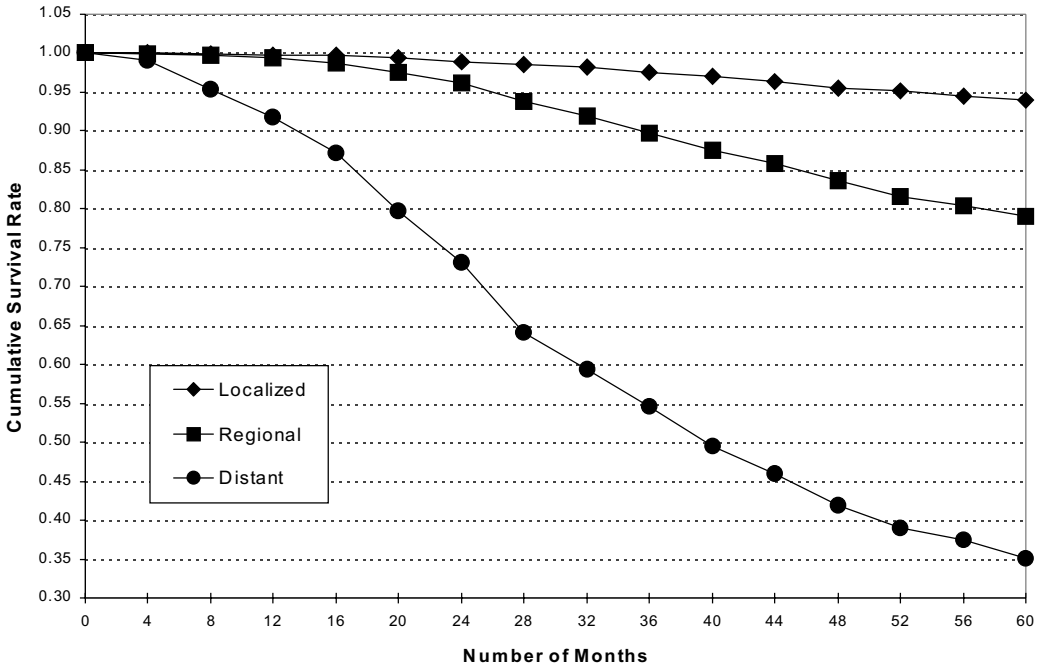


Figure 3
Five-year Breast Cancer Survival among Age Groups

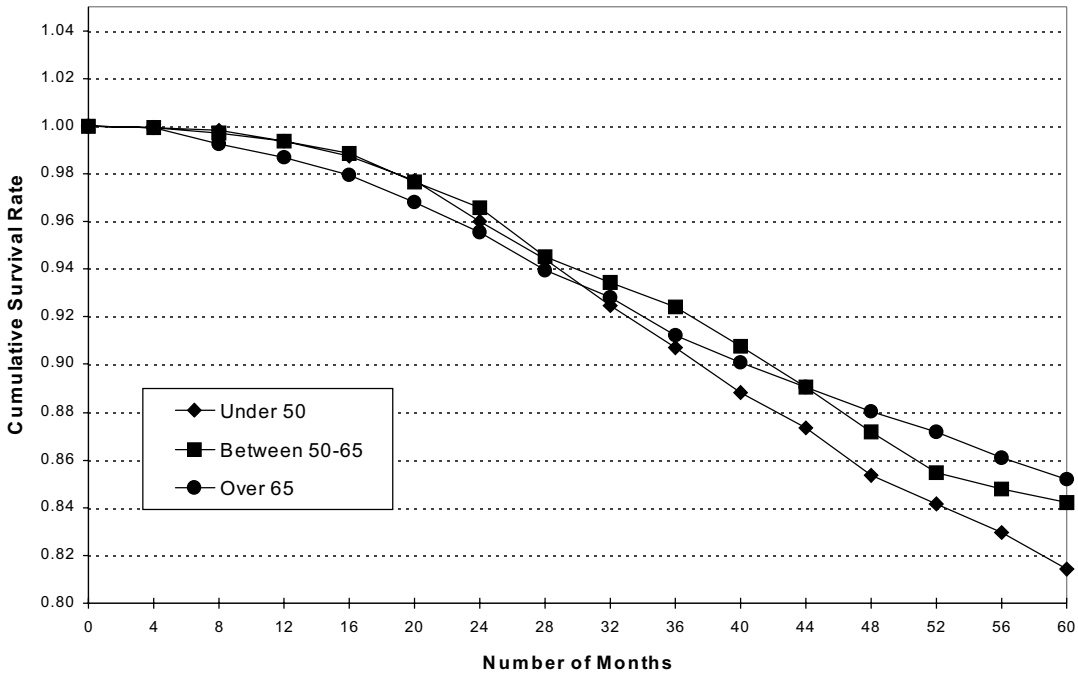


Figure 4
Five-year Breast Cancer Survival between Minority Status Groups

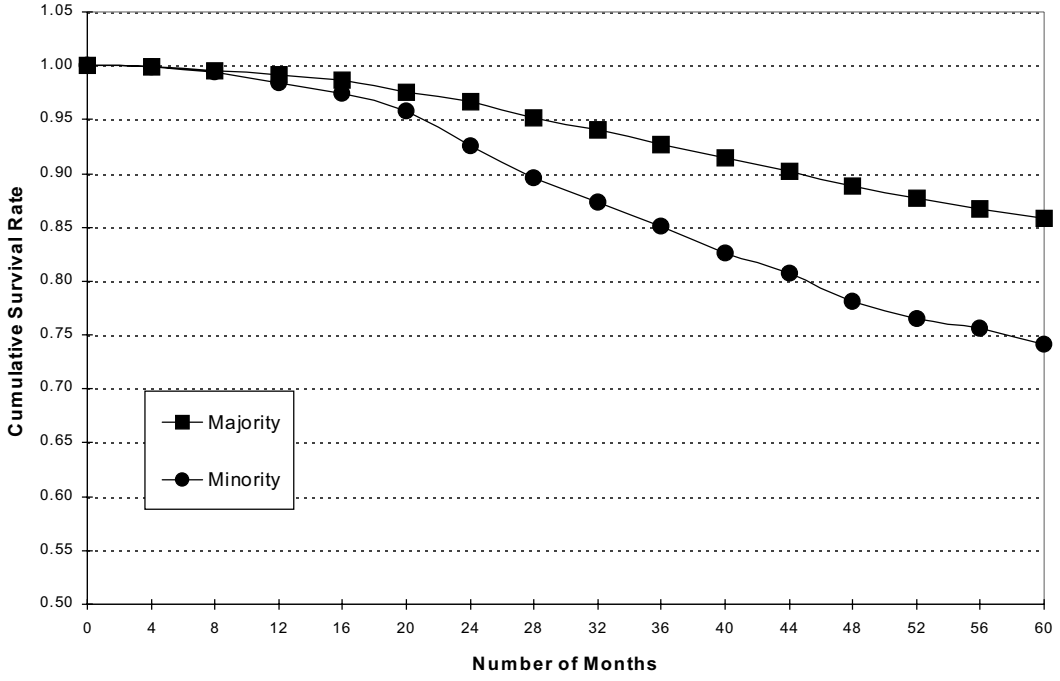


Figure 5
Five-year Breast Cancer Survival by Minority Status Group and Stage-at-diagnosis

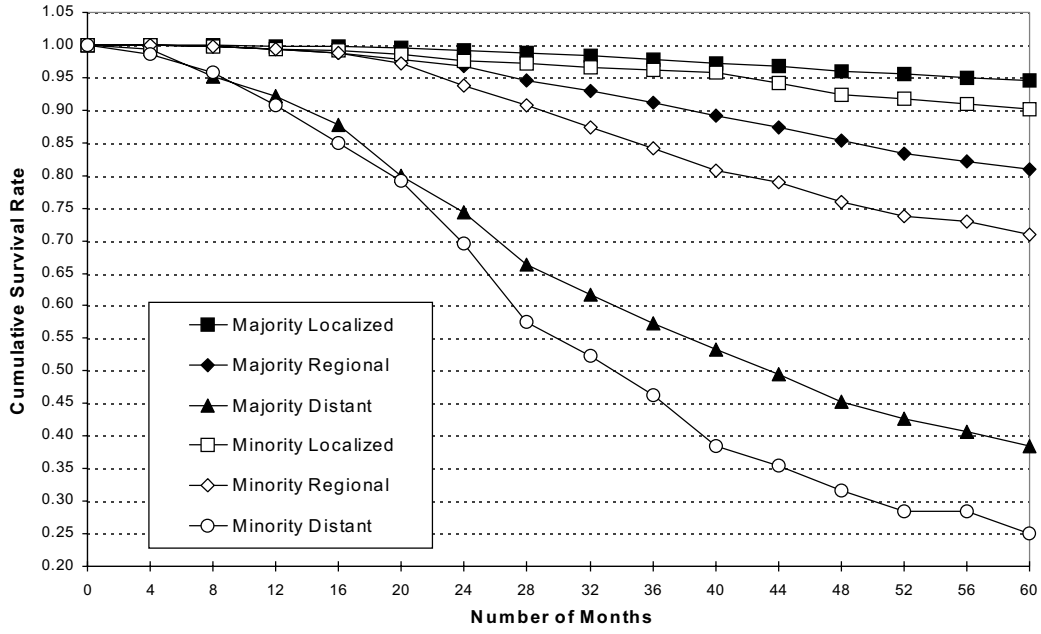
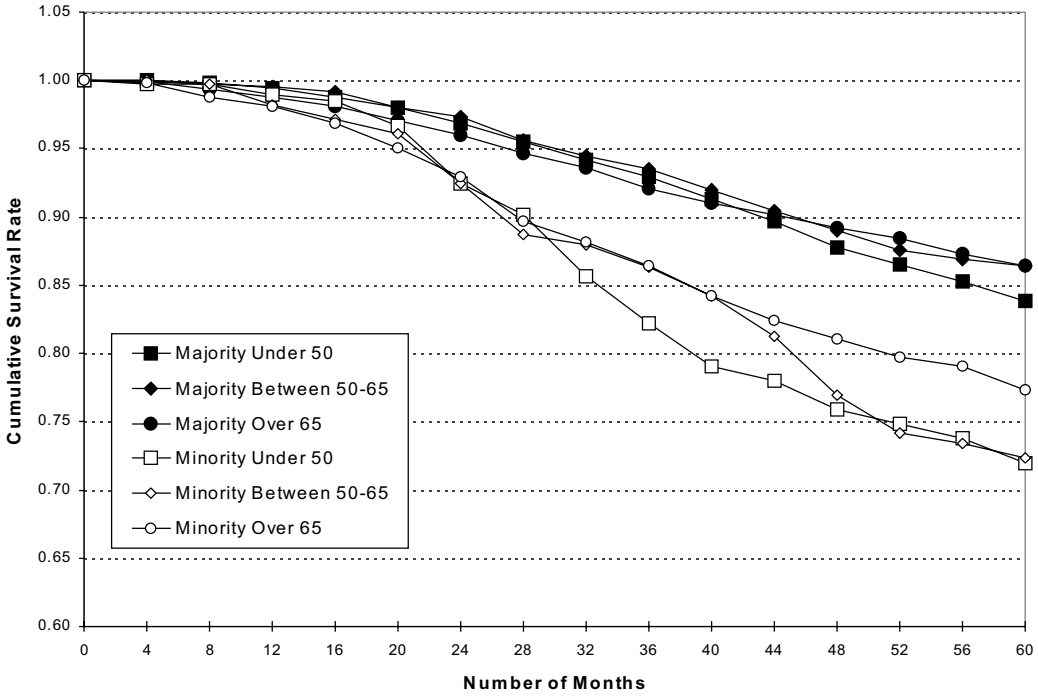


Figure 6
Five-year Breast Cancer Survival by Minority Status Group and Age at Diagnosis



The survival gap between minority status groups decreased little for women ages 65 and older and increased for women ages 50 to 64. The gap increased as the stage at diagnosis advanced. Predictably, the survival gap between minority status groups was maximum for women younger than 50 years of age with distant cancer and minimum for women ages 65 and older with localized cancer.

Discussion

Age-adjusted breast cancer death rates have declined 11 percent in North Carolina since 1986, which was parallel to the national decline (Chu et al. 1996). The steady decline may have resulted from medical improvements including early detection, or from changes in underlying risk factors. The average age at death from breast cancer increased and this change was identical to the increase in the average age at death from all causes of death for women between 1986 and 1995. This may suggest that the decline in deaths was a part of overall medical improvements in North Carolina. However, age-specific rates show that the decline was limited primarily to majority women ages 50 to 64. This group of women may have benefited more from new treatments, had fewer co-morbid conditions, or had more reduced risk factors than minority and older women. As compared to women under 50 years of age, they have cancers diagnosed at an earlier stage – resulting in fewer cancer deaths.

Declining mortality rates in North Carolina did not occur among women over 65 and under 50 years of age, and among minorities. The age-adjusted minority death rate for 1991-1995 was 31.2% higher than the majority rate. Minority women were diagnosed with later stages of cancer and at earlier ages than majority women; factors that produced some of the mortality difference between the two groups. Other factors such as access to health care, income, and education level could contribute to the mortality difference. Reporting problems could also bias these comparisons.

In contrast to mortality rates, the age-adjusted breast cancer incidence rate was higher among majority women than for their minority counterparts. The age-specific rates had a similar minority/majority pattern for younger women while they were reversed for the oldest age group. These patterns may be due to differences between the two groups in the mammography screening experience, population distribution, and case reporting. Differences in stage distributions by minority status and age suggest that smaller proportions of minority women have received mammography screening.

In the highest risk population group (women older than 65 years of age), there were proportionally fewer minority women. In the lowest risk group (under 50 years of age), there were proportionally more minority women as compared to their majority counterparts. The younger minority population will tend to decrease the overall unadjusted incidence rate.

The minority status comparisons of incidence rates could be further confounded by selective under-reporting. In the last several years, the age-adjusted rate difference has decreased between minority status groups mainly due to increased reporting of minority cases.

Survival analyses results in this study are in accord with findings in other studies (Simon and Severson 1996; Roach and Alexander 1995; Eley et al. 1994; Hankey et al. 1994; Nixon et al. 1994; Ewertz 1993; Lethaby et al. 1992; Muss et al. 1992; Ragland et al. 1991). The stage at diagnosis was the strongest predictor of breast cancer survival, independent of the other two variables. This finding emphasizes the importance of early detection in breast cancer survival.

The much larger percentage of cancer cases diagnosed at the regional stage for women under age 50, compared to those ages 65 and older, indicates that mammography screening may have helped early cancer detection in the older age group. Expanded mammography screening in all age groups should reduce future breast cancer deaths.

Even though age at diagnosis was not a strong predictor of breast cancer survival, breast cancer survival was significantly lower for women under 50 years of age, regardless of their stage and minority status groups, than for women 65 years of age and older. The poor prognosis of younger women has been reportedly associated with their tumor biology (Peer et al 1996; Nixon et al. 1994). Tumors from younger women were found to have faster metastatic potential, shorter lead time, and a higher recurrence rate than those from older women.

Peer et al. (1996) reported that with the same tumor size, older women had significantly better survival than younger women. They suggested that the detection of a cancer tumor before it reached 10 mm would improve survival among women under 50 years of age. Given the short lead time for young women, the detection of a tumor smaller than 10 mm in size may require diligent mammography screening for women at risk for breast cancer.

The data from this study suggests that younger women have not experienced declining mortality rates and have lower levels of mammography screening in North Carolina. Breast cancer killed more women ages 40-49 than any other disease in North Carolina during 1986-1995. The annual death toll was 194; breast cancer accounted for 13.1% of all female deaths between the ages of 40 and 49 during the period of 1986-1995.

The current mammography recommendation for more frequent screening for women over 40 years of age may improve early detection and thus the survival, eventually reducing mortality for these women.

A significant survival difference exists between minority status groups, with minority women having a higher risk of dying from breast cancer. The odds of dying for minority women with breast cancer compared to majority women decreased from 71 percent greater to 45 percent greater after controlling only for stage at diagnosis. This indicates that the relative survival of minority women could be improved substantially by earlier detection.

The survival for minority women decreased as the stage advanced and increased as they got older. Minority women with distant cancer and under age 50 had the worst survival; ones with localized cancer and 65 years of age or older had the best survival of breast cancer at five years.

It is possible that by age 65, minority women acquired access to health care through Medicare comparable to their majority counterparts and thus their survival improved as compared to younger minority women. However, the persistence of survival differences even for Medicare-eligible women indicates the presence of other factors that affect breast cancer survival unfavorably for minority women. Gornick et al. (1996) reported differences in mammogram use and recommendations between minority and majority women even with the same income levels.

An objective assessment of minority status differences may require partitioning this variable into components such as income, education, access to health care, breast cancer history, diet, and other behavioral risks.

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