COHORT FERTILITY PATTERNS AND BREAST CANCER MORTALITY AMONG U.S. WOMEN*

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ABSTRACT

Epidemiological research has shown that women who have early births and numerous births have reduced risks of being diagnosed with breast cancer. We examine whether cohort fertility patterns are associated with breast cancer mortality rates in the US. We use negative binomial age-period-cohort models, and data from US Vital Statistics and the US Census to examine the relationship between breast cancer mortality rates among women aged 40 and older (in five year age groups), and age-specific cumulative first birth rates, age-specific cumulative second birth rates, and completed birth rates at ages 35 to 39. Our results show that cohorts marked by higher rates of childlessness at ages 15 through 24, and lower cumulative second birth rates at ages 20 through 29, have higher rates of breast cancer mortality. Further, cohort fertility patterns appear to dampen the rise in breast cancer mortality rates in the 1970s through the 1990s.

BACKGROUND

Prospective and case-control studies have shown that reproductive factors—including early childbearing, frequent childbearing, and total number of children born to women—reduce the risk of breast cancer and breast cancer mortality (Kelsey et al. 1993; Russo et al. 2005).But those studies focus on single cohorts and do not examine whether or to what extent fertility patterns account for differential breast cancer mortality rates over time and across cohorts. Some scholars use age-period-cohort models to examine trends in breast cancer mortality, and suggest that cohort fertility patterns may partially account for fluctuations in breast-cancer mortality over time (Chu et al. 1996; Tarone et al. 1997). But those scholars do not directly include measures of cohort fertility. We examine the relationship between breast cancer mortality rates and three salient measures of cohort fertility—age specific rates of childlessness, age specific cumulative second birth rates, and total cumulative birth rates at ages 35-39.

DATA AND METHODS

The dependent variable for out analysis is the age-specific breast-cancer mortality rate for women aged 40-44 to 85 and older, for every fifth calendar year from 1948 to 2003. By using five-year age groups, every fifth calendar year, we can uniquely identify birth cohorts as they pass through life. The numerators of the breast-cancer mortality rates come from vital statistics data, and the denominators come from U.S. Census data.[1]

We use a series of measures to capture cohort fertility patterns among women. We include the age-specific rate of childlessness (number of women who have never had a live birth at ages x to x+5/number of women aged x to x+5)*1,000 at ages 15-19 through ages 35-40. The age specific rate of childlessness is simply the inverse of the age-specific cumulative first birth rate. We include the age-specific cumulative second birth rate (number of women who have had a second live birth at ages x to x+5/number of women aged x to x+5)*1,000 at ages 15-19 through 35-40. The age-specific rate of childlessness and the age-specific second birth rate help us to assess the timing of early births across cohorts. Finally, we include the total cumulative fertility rate for women aged 34 to 40: (total number of live births to women aged 35 to 40/ total number of women aged 35 to 40)*1,000. This indicates the completed family size by ages 35 to 40 across cohorts. Although some women may go on to have additional births, most women have completed most of their childbearing by these ages, and by limiting completed family size to the ages of 35-40, we can use this variable to predict subsequent breast-cancer mortality rates among women aged 40 and older. The cohort fertility measures come from US vital statistics data.[2]

Up to 30% of the values on some of the cohort fertility measures are missing. In most instances, we have fertility measures for cohorts when they were aged 35-40, but we are missing data about their fertility at younger ages due to incomplete historical data. Fortunately, we can readily assume that the cohort fertility measures are missing random (due to lapses in the collection of historical fertility data) rather than due to unobserved mechanisms. That is, we can assume that the process that generates these missing values is “ignorable” (Rubin 1987) after conditioning on observed age and calendar year variables. Further, because we often have fertility data on cohorts at older ages, but not younger ages, we have fairly good information about a cohort’s likely fertility patterns at younger ages.

Under these conditions, multiple imputation is an ideal method of dealing with missing data. There are several good summaries of multiple imputation methods elsewhere (Allison 2002; Rubin 1987; Schafer 1997, 1999), but in general, the process entails creating multiple imputed data sets, each with a slightly different pattern of likely values. Then, we estimate a given model in each data set, take the mean of the coefficient across them, and calculate standard errors that adjust for the variation within and between the data sets to account for our uncertainty in the imputed values (Rubin [1987] provides the formulae for calculating the coefficients and standard errors). We use Royston's (2005) programs for Stata to create and analyze our multiple imputed data.

Statistically identifying the distinct impacts of age, period, and cohort effects on a given outcome can be problematic because each variable is a linear combination of the other two variables. Many scholars resolve this issue by introducing some constraints, although those constraints are often arbitrary, and the estimates can be quite sensitive to the restrictions employed. In our models, rather than including a series of dummy variables to indicate the birth cohort, we include variables to assess the cohort's fertility patterns. We use negative binomial regression to predict the rate of breast-cancer mortality, with a set of dummy variables that indicate five-year age groups and calendar periods. Then we sequentially add and then remove cohort fertility measures (co-linearity precludes including many fertility measures simultaneously) to assess their impact on breast-cancer mortality rates. Negative binomial regression accounts for the over-dispersion in the rates of breast-cancer mortality. All of our models include weights to adjust for the size of the population at each age and time period.

RESULTS

Table 1 presents descriptive statistics for the cohort fertility measures we use in our analyses. As expected, the rate of childlessness declines with age. In the cohorts studied here, an average of 942 out of 1,000 women aged 15-19 were childless at ages 15-19, a rate that declines to 190 per 1,000 women aged 35-39. The cumulative second birth rate increases with age. On average, only 9 out of 1,000 women aged 15-19 have had a second live birth, whereas 625 out of 1,000 are women aged 35-39 have had a second live birth. The total cumulative birth rate for ages 35-39 shows that, on average, there have been 2,471 live births per 1,000 women.

(Table 1 about here)

Table 2 presents the negative binomial regression coefficients for the relationship between age-specific rates of childlessness and breast cancer mortality rates. Model 1 includes the rate of childlessness when women of each cohort were 15 to 19 years old, and shows that a one unit increase in the rate of childlessness is associated with a 0.36% increase in the rate of breast cancer (incidence risk ratio [IRR]=exp$^{.0036}$=1.0036). To put this in perspective, a one standard deviation (shown on Table 1) increase in the age-specific rate of childlessness at ages 15-19 would increase the breast cancer mortality rate by 5%. Alternately, we could conceptually translate our results to the case of an individual woman by comparing a situation in which all women have their first child at ages 15-19, to a situation in which all women remain childless from ages 15-19: this would result in an increase in the rate of breast cancer by 360%.

Model 2 finds a positive relationship between the rate of childlessness at ages 20-24 and the breast cancer mortality rate. Although the coefficient for the rate of childlessness is smaller for ages 20-24 than for ages 15-19, the standard deviation is greater (see Table 1); thus, a one standard deviation increase in the rate of childlessness at ages 20-24 is associated with a 5% increase in the breast cancer mortality rate. To extend the comparison used above, if we went from a population where all women had a first birth by ages 20-24 to a population where no women had a first birth by the ages 20 to 24, we would expect to see a 70% increase in the breast cancer mortality rate. The rates of childlessness at ages 25 and older are unassociated with the breast cancer mortality rate (see Models 3 through 5). Cohorts marked by high rates of childlessness at ages 15-24 have increased rates of breast cancer mortality at ages 40 and older.

(Table 2 about here)

Table 3 follows the same modeling strategy to examine the relationship between age-specific cumulative second birth rates and breast cancer mortality among women. Model 1 finds a negative but non-significant relationship between the cumulative second birth rate when women in a cohort were aged 15-19 and breast cancer mortality. This non-significant finding likely reflects the relative rarity of second births among women aged 15-19, as indicated on Table 1. Models 2 and 3 show that a one unit increase in the cumulative second birth rate when women in a cohort were aged 20-24 is associated with a .09% reduction, and a one unit increase in the cumulative birth rate when women in a cohort were aged 25-29 is associated with a .03% reduction in the breast cancer mortality rate, respectively. If we compared a population where no women had their second live births by ages 20-24 and 25-30, to a population where all women had second live births by ages 20-24 and 25-30, we would expect the breast cancer mortality rate to decline by 90% and 30%, respectively. The cumulative second birth rates at ages 30 and older are marginally (Model 4) or non-significantly (Model 5) related to breast cancer mortality rates among women in those cohorts. Cohorts that have increased cumulative second birth rates at ages 20-29 exhibit lower rates of breast cancer mortality at ages 40 and older.

(Table 3 about here)

Table 4 examines the relationship between the total cumulative fertility rate at ages 35-39, that is, the completed fertility level among women aged 35-39, to ascertain whether total parity levels in cohorts are associated with breast cancer mortality rates. Model 1 shows that the cumulative fertility rate among women aged 35-39 is unassociated with cohort breast cancer mortality rates.

(Table 4 about here)

Figure 1 graphs the first differences in the coefficients for the relationship between the calendar year and breast cancer mortality rates. The solid black line comes from a model that includes variables for age and calendar year only (model not tabled, results available from the authors), and shows a level or possibly slightly increasing trend from the early 1950s until the mid-1980s or early 1990s, where breast cancer rates begin to decline. This general pattern has been documented previously (Chu et al. 1996; Tarone et al. 1997). When adjusting for either the rate of childlessness at ages 20-24 (the line with long dashes) or the cumulative second birth rates at ages 20-24 (the line with alternating long and short dashes), a slightly different pattern emerges. From the early 1950s to the mid-1980s we document a clear increase in breast cancer rates, with the divergence from the unadjusted breast cancer rates increasing until the early 1990s. In the mid-1980s the breast cancer rate begins to fall, first slowly, then more quickly after the early 1990s. The divergence between the adjusted and unadjusted coefficients suggests that cohort fertility patterns dramatically dampened the increasing rate of breast cancer mortality in the 1970 through 1990 calendar years.

CONCLUSION

In general, we find that cohorts marked by high levels of fertility at young ages have lower breast cancer mortality rates than cohorts marked by low levels of fertility at the younger ages. Specifically, cohorts of women who lower rates of childlessness between the ages of 15 and 25, or increased rates of progression to the second live birth between ages 20 and 29, had significantly and substantially lower rates of breast cancer mortality later in life. These findings are consistent with epidemiological studies that show that early parity is associated with reduced risks of breast cancer (Kelsey et al. 1993; Russo et al. 2005), and we demonstrate that this pattern is evident in national data for cohorts of women born between 1863 and 1963, and aged 40 and older. But some epidemiological studies find that the total fertility levels of individual women are associated with breast cancer rates (Hinkula et al. 2005)—a pattern that does not manifest in our cohort data.

We contribute to prior work by documenting that cohort fertility patterns have tended to dampen calendar year increases in breast cancer rates, especially in the 1970s through 1990s. Prior work has suggested that cohort fertility might shape period breast cancer mortality rates, but did not empirically document that relationship. Regardless of cohort fertility patterns, however, we document a substantial decrease in breast cancer mortality rates in recent decades. Other researchers suggest that these trends may result from improved breast cancer screening technologies and more effective treatments for those women who are diagnosed (Chu et al. 1999; Jatoi and Miller 2005; Wingo et al. 1998).

Our study examines breast cancer mortality rates for the total population. However, prior research has shown that blacks and whites have markedly different trends in breast cancer diagnosis across calendar years (Chu et al. 1999; Tarone and Chu 2000). Future work might overcome this limitation in our work by examining the relationship between cohort fertility patterns and breast cancer mortality rates separately for blacks and whites. Nevertheless, we have shown a persistent connection between breast cancer mortality rates and cohort fertility patterns.

ENDNOTES

1. The age-specific numbers of deaths for women come from the *Vital Statistics of the United States* for the calendar years 1948 through 1978, and the numbers of deaths from 1983 through 1998 come from the website of the National Center for Health Statistics, Center for Disease Control and Prevention. Unpublished death data for 2003 were supplied by the National Center for Health Statistics. The age-specific number of women at risk for the years 1948 and 1978 come from the U.S. Census Bureau, Current population Reports (Series P-25, No. 311, No. 314, No. 519, No. 870, and Series P-20, No. 441). Population estimates in 2003 are taken from the website of the U.S. Census Bureau.

2. The recent and historical fertility data come from the *Vital Statistics of the United States* (U.S. Department of the Census, various years) and Heuser (1976).

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Table 1: Means and Standard Deviations for Age-Specific Cohort Fertility Measures.

	Mean	Std.Dev.
Age Specific Rate of Childlessness		
Age 15-19	942.65	14.06
Age 20-24	622.86	70.96
Age 25-29	355.74	96.15
Age 30-34	233.98	77.65
Age 35-39	190.38	65.81
Age Specific Cumulative Second Birth Rate		
Age 15-19	9.02	4.69
Age 20-24	153.81	52.14
Age 25-29	397.07	108.59
Age 30-34	557.16	116.42
Age 35-39	625.30	110.79
Completed Fertility		
Age 35-39	2471.05	363.43

N=120

Table 2: Negative binomial regression coefficients for the relationship between breast cancer mortality rates and the age-specific rate of childlessness.

	Model 1	Model 2	Model 3	Model 4	Model 5
Age Specific Rate of Childlessness					
Age 15-19	0.0036**				
Age 20-24		0.0007***			
Age 25-29			0.0002		
Age 30-34				-0.0001	
Age 35-39					-0.0003
Age Groups					
40-44	ref.	ref.	ref.	ref.	ref.
45-49	0.4957***	0.5020***	0.5007***	0.4997***	0.5007***
50-54	0.8387***	0.8531***	0.8514***	0.8500***	0.8520***
55-59	1.0647***	1.0820***	1.0826***	1.0819***	1.0849***
60-64	1.2036***	1.2271***	1.2303***	1.2313***	1.2362***
65-69	1.3214***	1.3496***	1.3610***	1.3655***	1.3729***
70-74	1.4776***	1.5058***	1.5268***	1.5362***	1.5469***
75-79	1.6221***	1.6456***	1.6752***	1.6924***	1.7090***
80-84	1.7789***	1.7982***	1.8373***	1.8599***	1.8803***
85+	2.0300***	2.0520***	2.0841***	2.1143***	2.1404***
Calendar Periods					
1948	ref.	ref.	ref.	ref.	ref.
1953	-0.0419	-0.0409	-0.0604	-0.0661	-0.0665*
1958	-0.0694	-0.0665*	-0.0836**	-0.0937**	-0.1000**
1963	-0.0595	-0.0565	-0.0772*	-0.0913**	-0.1008**
1968	-0.0153	-0.0102	-0.0347	-0.0535	-0.0681
1973	-0.0044	0.0019	-0.0339	-0.0579	-0.0758*
1978	0.0002	0.0045	-0.0381	-0.0667	-0.0881*
1983	0.0069	0.0039	-0.0424	-0.0745	-0.0985**
1988	0.0518	0.0447	-0.0058	-0.0400	-0.0658
1993	0.0132	0.0025	-0.0496	-0.0838*	-0.1109**
1998	-0.1095*	-0.1263***	-0.1774***	-0.2122***	-0.2412***
2003	-0.2047***	-0.2231***	-0.2751***	-0.3116***	-0.3426***
_cons	-11.7134***	-8.7501***	-8.3633***	-8.2674***	-8.2123***
lnalpha	-4.9936***	-5.0602***	-4.9165***	-4.9013***	-4.9209***

* p≤.10; ** p≤.05; ***p≤.01

N=120

Table 3: Negative binomial regression coefficients for the relationship between breast cancer mortality rates and the age-specific cumulative second birth rate.

	Model 1	Model 2	Model 3	Model 4	Model 5
Age Specific Cumulative Second Birth Rate					
Age 15-19	-0.0054				
Age 20-24		-0.0009***			
Age 25-29			-0.0003***		
Age 30-34				-0.0002*	
Age 35-39					-0.0001
Age Groups					
40-44	ref.	ref.	ref.	ref.	ref.
45-49	0.4986***	0.5012***	0.5009***	0.4995***	0.4991***
50-54	0.8466***	0.8530***	0.8521***	0.8498***	0.8491***
55-59	1.0742***	1.0833***	1.0838***	1.0812***	1.0805***
60-64	1.2169***	1.2271***	1.2311***	1.2291***	1.2289***
65-69	1.3417***	1.3467***	1.3592***	1.3607***	1.3616***
70-74	1.5055***	1.5055***	1.5192***	1.5262***	1.5292***
75-79	1.6565***	1.6472***	1.6618***	1.6737***	1.6799***
80-84	1.8205***	1.8078***	1.8193***	1.8359***	1.8443***
85+	2.0723***	2.0637***	2.0699***	2.0848***	2.0947***
Calendar Periods					
1948	ref.	ref.	ref.	ref.	ref.
1953	-0.0625	-0.0511	-0.0553	-0.0623	-0.0635
1958	-0.0870**	-0.0758**	-0.0782**	-0.0837**	-0.0866**
1963	-0.0817**	-0.0668*	-0.0711*	-0.0780*	-0.0816*
1968	-0.0393	-0.0247	-0.0261	-0.0343	-0.0400
1973	-0.0370	-0.0114	-0.0201	-0.0347	-0.0422
1978	-0.0373	-0.0070	-0.0217	-0.0391	-0.0484
1983	-0.0367	-0.0086	-0.0234	-0.0435	-0.0541
1988	0.0046	0.0312	0.0147	-0.0068	-0.0182
1993	-0.0363	-0.0117	-0.0289	-0.0498	-0.0612
1998	-0.1627***	-0.1402***	-0.1559***	-0.1763***	-0.1882***
2003	-0.2606***	-0.2375***	-0.2521***	-0.2730***	-0.2859***
_cons	-8.2380***	-8.1721***	-8.1737***	-8.2011***	-8.2312***
lnalpha	-4.9216***	-5.0575***	-4.9938***	-4.9225***	-4.9051***

* p≤.10; ** p≤.05; ***p≤.01

N=120

Table 4: Negative binomial regression coefficients for the relationship between breast cancer mortality rates and total cumulative fertility at ages 35-39.

	Model 1
Completed Fertility	
Age 35-39	0.0000
Age Groups	
40-44	ref.
45-49	0.5007***
50-54	0.8525***
55-59	1.0859***
60-64	1.2364***
65-69	1.3711***
70-74	1.5398***
75-79	1.6914***
80-84	1.8572***
85+	2.1096***
Calendar Periods	
1948	ref.
1953	-0.0667*
1958	-0.0920**
1963	-0.0890**
1968	-0.0485
1973	-0.0520
1978	-0.0593
1983	-0.0667*
1988	-0.0326
1993	-0.0776*
1998	-0.2060***
2003	-0.3049***
_cons	-8.2139***
lnalpha	-4.9110***

* p≤.10; ** p≤.05; ***p≤.01

N=120

Figure 1: First Differences in Coefficients for the Relationship between Calendar Year and Breast Cancer Mortality Rates