

# Birth cohort trends for breast cancer among women in Europe and North America

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## ABSTRACT

Age-period-cohort analyses have demonstrated a decrease in the birth cohort risk of breast cancer in Europe and in North America for women born after World War II. The interpretation of age-period-cohort analyses can be difficult, and is sometimes controversial. Using breast cancer mortality rates from 1950 through 2013 for United States women from 20 through 49 years of age at death, it is demonstrated that the decrease in birth cohort risk is evident for every five-year age-specific mortality rate curve, without the application of age-period-cohort methods. The demonstration that the birth cohort decrease is evident even among women in their twenties indicates that etiologic factors responsible for the decrease in birth cohort risk must occur early in life and affect a relatively high percentage of the female population.

A recent comprehensive report on age-period-cohort analyses of cancer mortality rates among European men and women for 18 major cancer types provides a valuable resource for identification of possible risk or protective factors, and of evidence for improvements in medical treatment or management, for different types of cancer [1]. As with all ecologic analyses, it is not possible to make firm inferences regarding specific etiologic factors or improvements in treatment for any given cancer, but certain patterns in parameter estimates, in particular, a change in the slope of the trend for the calendar period effects or the birth cohort effects, can provide valuable clues [2]. The purpose of this commentary is to highlight one particular birth cohort pattern of risk observed in European women, namely, the decreasing birth cohort risk of breast cancer beginning with women born after World War II. As will be documented, this birth cohort pattern of risk, for which there is currently no plausible explanation, has also been observed in North America, and has been found in analyses of breast cancer incidence rates as well as mortality rates. It appears that there was a change in exposure to some risk or protective factor that led to decreasing risk of breast cancer among Western women born after World War II, and the identification of the factor or factors responsible for this declining risk pattern should be a priority in epidemiologic research.

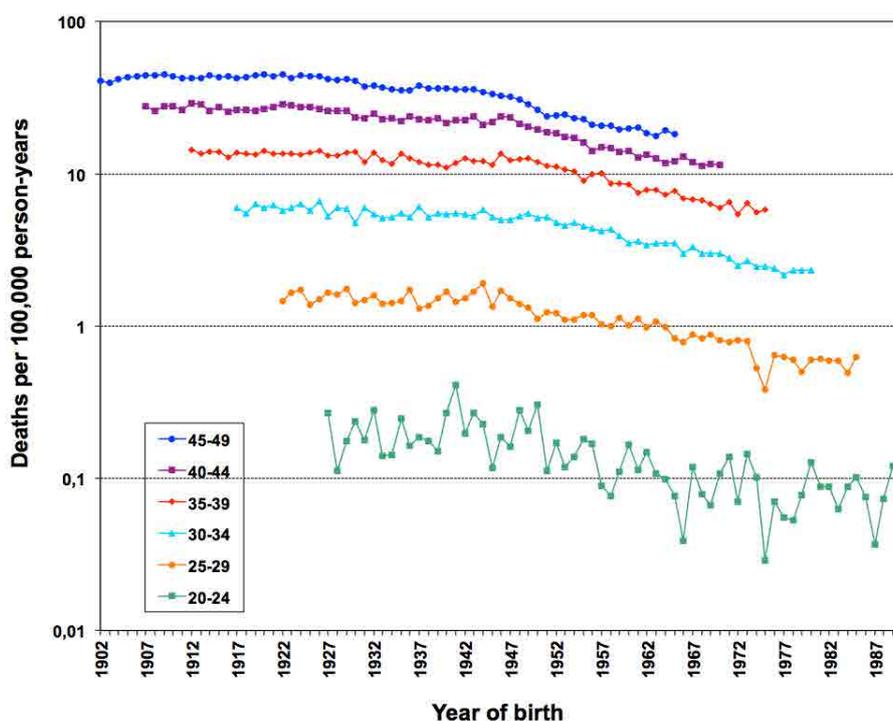
The age-period-cohort analysis of breast cancer mortality rates in European women demonstrated a decrease in the slope of birth cohort effects trend around 1945 [1, Supplementary Figure 1]. A similar decrease in the slope of the birth cohort effects trend was observed in over half of the sixteen European countries included in separate age-period-cohort analyses [1, Supplementary Figure 2], which shows remarkable consistency in view of the relatively small population sizes for some individual countries. The most common birth cohort pattern of risk in European countries not showing the slope decrease around 1945 was an even longer decrease in birth cohort effects, usually beginning around 1920. Thus nearly all individual countries showed a recent favorable birth cohort trend in breast cancer mortality over a period of three decades or longer.

The birth cohort pattern of risk observed in analyses of breast cancer mortality rates in the United States is remarkably similar to that observed in the overall analysis for Europe [1]. Birth cohort effects were increasing at the beginning of the twentieth century, subsequently moderated, and then began decreasing sharply after 1945 [3,4]. A similar pattern of birth cohort risk was observed for Canadian women and for both black and white women in the United States [3,5]. The age-period-cohort analyses of breast cancer mortality rates in both Europe and North America also indicate a sharp decline in the slope of the calendar period effects curve beginning around 1990, reflecting well documented improvements in the detection, treatment, and management of breast cancer over the past twenty-five years. The birth cohort decrease in breast cancer mortality risk after World War II, however, almost certainly reflects the impact of changes in some risk or protective factor (or factors) [2,4], a conclusion supported by the observation of a similar decrease in the birth cohort effects slope in analyses of breast cancer incidence rates in the United States [6,7]. Indeed, the first indication for the presence of this unexpected trend in birth cohort risk after World War II came from an early analysis of Scottish breast cancer incidence rates [8].

Figure 1 shows age-specific breast cancer mortality rates among young white women in the United States dying from 1950 through 2013, plotted against year of birth [9]. Remarkably, the decrease in breast cancer mortality rates for women born after World War II is apparent even in women under the age of 35. The decline in rates for the three youngest age groups began with women dying prior to 1980, which is well before improvements in cancer detection and treatment had a measurable impact on population mortality rates. The declines began with women born around 1945 and continued for about three decades, after which rates were relatively flat.

There is currently no plausible explanation for the decrease in birth cohort risk of breast cancer after World War II. Trends in some known risk factors for breast cancer would, in fact, predict increasing breast cancer rates among these women. For example, these women had fewer babies than prior generations, were taller than prior generations, and had access to oral contraceptives early in life and for long duration, unlike prior generations [4,5]. Thus the decreasing breast cancer trend for women born after World War II has been observed in spite of the fact that an increasing trend might be expected based on some risk factors. It is noteworthy that a decrease in birth cohort risk of ovarian cancer mortality is also observed in both Europe and North America for women born after World War II, in spite of decreasing parity [1,4]; access to oral contraceptives almost certainly plays a major role in this trend [1,4,10]. The demonstration of the decreasing birth cohort trend for breast cancer in women under the age of 35 (Figure 1) shows the strength of the unknown risk or protective factor(s), and indicates that exposure to the etiologic factor(s) responsible for the declining risk must have occurred early in life and been fairly widespread.

**FIGURE 1. Age-specific breast cancer mortality rates by 5-year age intervals among United States white women between the ages of 20 through 49 dying in the calendar years 1950 through 2013; plotted against year of birth.**



The unexpected and puzzling decrease in breast cancer risk beginning for United States women born around 1945 has been largely overlooked or ignored by cancer researchers. Now that the presence of this trend has been documented in European women [1], increased priority would seem warranted for investigations into possible explanations for the enigmatic and unexplained decrease in breast cancer risk for Western women born after World War II.

### Conflict of Interest

The author declares that there is no conflict of interest.

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