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Is the Peak in Breast Cancer Incidence in Sight? A Study Conducted in the Southeastern Netherlands

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Breast cancer is the most frequent malignancy in the western world, and increases in the incidence have been observed worldwide. We investigated temporal trends in breast cancer incidence in the southeastern Netherlands between 1960 and 1989 by birth cohort analysis, using data of the Eindhoven Cancer Registry. An overall time-trend in incidence rate was estimated, based on age and year of diagnosis. Rate ratios were calculated, as the ratio of the observed versus the expected incidence rates, which was based on the estimated time-trend. In this unscreened population the age-specific incidence increased for every successive birth cohort in the period 1880–1949. Women born between 1940 and 1949 had the highest age-specific incidence rates with an excess of 10% (relative risk 1.10, 95% confidence interval 1.01–1.22). The incidence rates in women born after 1949 declined and were 21% lower than expected by the estimated secular trend (relative risk 0.79, 95% confidence interval 0.64–0.96). This decrease in incidence for women aged under 40 suggests that the peak in incidence of female breast cancer may be in sight. It remains unclear which risk factors are responsible for this changing trend.
Key words: breast cancer, cancer registry, incidence, birth cohort
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INTRODUCTION

BREAST CANCER is the most common form of cancer in women in industrialised countries [1], and an increasing incidence has been reported in both industrialised and developing countries [2–5]. In the Netherlands the incidence rate is among the highest in western Europe [1]. Temporal changes in the incidence of breast cancer, and especially birth cohort-related changes in incidence may point to aetiologic factors that affect a specific age-group at a certain period and indicate future trends. Using data of the Eindhoven Cancer Registry, we investigated trends in breast cancer incidence rates by a birth cohort analysis in the southeastern Netherlands, over the period 1960–1989.

MATERIALS AND METHODS

The population-based Eindhoven Cancer Registry has collected data of all cancer patients in the southeastern Netherlands since 1955. We analysed trends in the incidence rates of first primary invasive female breast cancer diagnosed between 1960 and 1989 by a birth cohort analysis. Age-specific incidence rates were calculated by year of diagnosis and by 10- and 20-year birth cohort since 1880. There is no consensus whether, in analysing temporal trends, the linear effects of the variables age, period and cohort are identifiable [6–11] and, therefore, we estimated an overall time-trend in the incidence. Observed incidence rates by birth cohort were compared with predicted rates, based on the estimated time-trend in the whole study period.

Registry

Data on first primary breast cancers were obtained from the Eindhoven Cancer Registry [1], which was founded as a hospital-based registry in 1955, and became population-based in 1960. From 1960 to 1969 the area of registration was the southeastern part of the Dutch province of North Brabant, and it has been extended to the northern part of the adjacent province of Limburg since 1970, now covering about 1 million residents. The registry is routinely informed of newly diagnosed cases of cancer by pathology laboratories, the regional radiotherapy department and hospital medical archives in the community hospitals. Data are collected from medical records by the registry staff during regular visits to the hospitals. Referrals to specialised clinics outside the region are traced.

The present material comprises 7106 cases of first primary breast cancer diagnosed in women aged 20–89 years during the period 1960–1989. All histological types are included, with the exception of precancerous or *in situ* lesions. The composition of the population, subdivided into calendar year, 5-year age groups and municipality, was derived from the Department of Population Statistics of the Netherlands Central Bureau of Statistics.

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Data analysis

Poisson regression analysis was used to study trends in incidence, with the observed number of patients taken as a Poisson variate. The expected number of patients was considered as a log-linear function of a number of potential predictors, calculated from year and age at diagnosis. In this function the logarithm of the number of women at risk served as offset. The relevant predictors were forwardly selected by means of likelihood ratio tests in a maximum likelihood estimation procedure. For each year of diagnosis and age, residuals were calculated as the difference between the observed and predicted number of cases. These values were checked for overdispersion with respect to the Poisson variation around the predicted number of cases. We examined whether the residuals showed a systematic pattern with the predictors, indicating that some alternative model could provide a better data description. Model parameters were selected on the basis of the significance of their contribution to the model and on the basis of residual analyses. Dummy variables were defined to indicate birth cohorts (of 10 and 20 years) between 1880 and 1969, and tested for their contribution to the selected model by means of likelihood ratio tests. In this way a time-trend in incidence rate was assessed and expected incidence rates by birth cohort were estimated. Rate ratios between the observed and expected rates for every birth cohort were calculated. A separate analysis was performed on data of women under 50 years.

RESULTS

There was a fairly consistent secular trend towards a higher incidence of breast cancer in every successive birth cohort between 1880–1989 and 1940–1949 (Fig. 1). Age-specific incidence increased more markedly in birth cohort 1940–1949 as compared to all previous cohorts, with a rate ratio of 1.10 [95% confidence interval (CI) 1.01–1.22], suggesting a higher risk of developing breast cancer than predicted. A decrease in incidence was observed in birth cohort 1950–1959, continuing in birth cohort 1960–1969, with a rate ratio significantly lower than one [Relative risk (RR) 0.43, 95% CI 0.20–0.96]. Birth cohorts

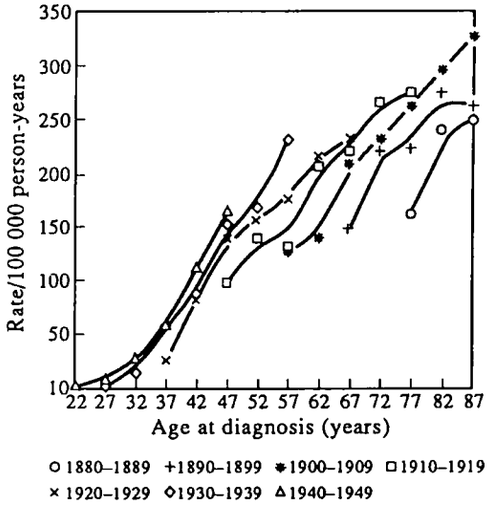

Fig. 1. Age-specific incidence according to 10-year birth cohort of breast cancer in the southeastern Netherlands diagnosed between 1960 and 1989. The rates are the means of 5-year age groups, being indicated by their mid-ages.

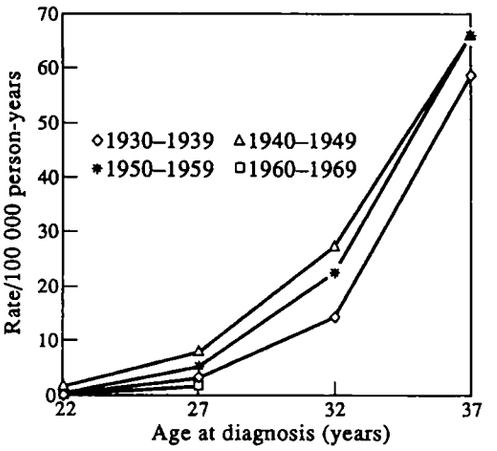

Fig. 2. Age-specific incidence rates of breast cancer according to 10-year birth cohort, in the youngest birth cohorts in the southeastern Netherlands diagnosed between 1960 and 1989. The rates are the means of 5-year age groups, being indicated by their mid-ages.

1950–1959 and 1960–1969 combined also had a rate ratio significantly lower than one (RR 0.79, 95% CI 0.64–0.96) (Fig. 2). Rate ratios based on an analysis comprising women under 50 years were very similar to those based on the total group, albeit with larger confidence intervals.

DISCUSSION

The steady increase in incidence is in line with the rise in incidence in many industrialised countries [2–5]. These results also confirm the reports from Washington state [12] and Sweden [13] on an increased risk for women born between 1940 and 1949. However, in our population this increase does not continue in women born after 1949 and actually turns into a decrease.

A decrease in the incidence rates has been reported only in the U.S.A. in women of 50 years and older. This was explained as the end stage of a transitory rise in incidence caused by temporary increased detection of tumours by screening mammography [14]. In the southeastern Netherlands the decrease in incidence appeared in women under 40 years, who did not undergo screening. Although alterations in detection modalities, such as increased use of mammography, can produce short-term changes in incidence, it is unlikely that this affected especially the youngest women in our study region. On the contrary, we may be observing the first signs that the increase in incidence during the last few decades is coming to an end.

The observed overall increase in incidence can probably not be explained by a more accurate registry over time, because close cooperation with pathologists, surgeons and radiotherapists has always existed and no major changes in the methods of registration occurred during the study period. In the 1970s the introduction of new diagnostic techniques such as mammography, cytology and echography resulted in earlier detection. While incidence rates can rise temporarily due to earlier detection, this cannot be the sole cause of the fairly continuous increase [15], even if some otherwise dormant disease may be detected.

This leads to the probability of changes in aetiologic factors over time, such as earlier menarche [16], later menopause [17] and increases in the energy intake in early life [18], all of them

relevant in this population. As incidence rates are generally higher in women having fewer children at a later age [19–21], the increase may in part be attributed to a marked decrease in family size since 1965. However, this would primarily affect women born after 1930, but would not be in concordance with the decrease in women born after 1949.

Although the exact reasons for the changes are unknown, two risk factors may be related to the increased incidence in birth cohort 1940–1949. Women aged 20–30 years received high doses of oral oestrogens and progestagens in the early 1970s [22–26]; additionally, this group had a high exposure to X-rays [27, 28], because women aged 10–20 years were regularly screened by X-ray for tuberculosis in the 1950s and 1960s. Which risk factors might explain the decrease in the youngest birth cohorts remains unclear.

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