

Letter to the Editor

Age and Breast Cancer Incidence

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IN 1979 we concluded on the basis of the best available evidence that, whereas the overall incidence rates of female breast cancer were very different in different parts of the world, the shapes of the age-specific incidence curves were remarkably similar [1]. Specifically, we concluded that the fall in the rates after menopause seen in cross-sectional curves in Osaka was due to a strong cohort effect. On the basis of this analysis, we suggested that the difference in the shape of the incidence curves from Eastern and Western populations might be artefactual, and cautioned against the use of cross-sectional curves to draw inferences.

Recently, our conclusions have been challenged by de Waard [2]. First, de Waard claims that there are populations in which the fall in rates after menopause is not an artefact of cohort effects. He is evidently unwilling to abandon conclusions originally drawn from cross-sectional data. Second, de Waard calls into question the validity of what he calls our mathematical model.

We would like to address the second issue first. The conclusions in our 1979 paper were based on a rather simple statistical analysis, which could be considered a quantification of the graphical technique of cohort analysis familiar to most epidemiologists. These statistical techniques were extensions of those originally used by Bjarnason *et al.* [3] and Breslow and Day [4] for the analysis of breast cancer data in Iceland. de Waard questions the validity of these techniques by plotting breast cancer incidence data from Denmark (de Waard's Fig. 6). He concludes from this figure that there is a fall in post-menopausal incidence rates in the cohorts of women born before 1893. He states, "Apparently the

mathematical model was insensitive to this phenomenon."

The trouble with de Waard's argument is that his Fig. 6 is incorrect. We have plotted the Danish incidence data in Fig. 1. The data are those from Table 1 of our paper [1] with two more periods of observation included. The ultimate source of all the data is the set of volumes brought out by Clemmesen and the Danish Cancer Registry [5-9]. The reader has simply to check these volumes to see that our Fig. 1 is correct. This figure clearly demonstrates an increase in rates with age in every birth cohort. Thus de Waard's criticism of our method is based on a false graphical representation of the data.

Now to get to de Waard's first point. He states that there are populations, such as the Japanese migrants in Hawaii and the female populations of Bombay and rural Warsaw, in which the early

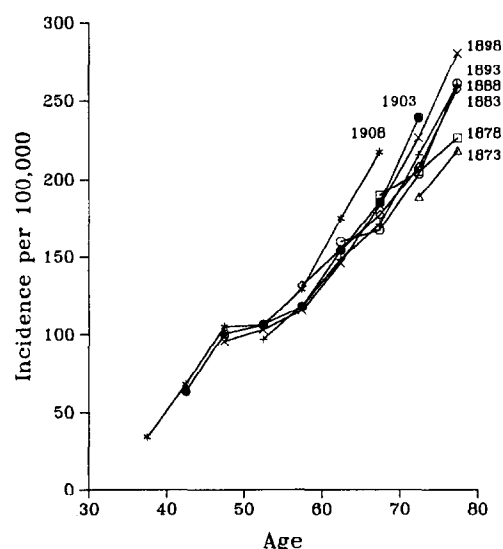


Fig. 1. Age-specific incidence rates for female breast cancer in Denmark by birth cohorts. Note that the rates are increasing with age in every birth cohort, contrary to de Waard's claim [2].

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birth cohorts do not show an increase in rates after menopause. We would like to make two points about this. First, the rates in these populations are based on small numbers and thus subject to great statistical fluctuations. Moreover, inaccuracies in the data are most likely to be present in the earliest cohorts. Thus we do not believe that these data support de Waard's contention. Second, we did not suggest in our 1979 paper that a fall in rates after menopause did not occur in any population. In fact, we were careful to limit our conclusions to only those populations we had analyzed. In a later

paper [10] we suggested that among very lean women, in whom there is little peripheral conversion of androstenedione into estrogen after menopause, we might expect to see a fall in rates after menopause. Thus we did not, as de Waard states, "draw inferences from their model that go far beyond their data."

In summary, statistical methods have an indispensable role to play in epidemiology. The epidemiologist who does not use these methods deprives himself of powerful tools.

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Dr Moolgavkar's letter has been forwarded to Prof. de Waard, who offers the following reply:

Dr Moolgavkar is correct that we have made mistakes in our Fig. 6. I am sorry for this and I apologise for any conclusions from the Danish data which seemed to question the sensitivity of his mathematical model.

I am glad for the modification of Dr Moolgavkar's opinion expressed in his reference [10] that a fall of incidence after menopause is indeed possible. Future volumes of *Cancer Incidence in Five Continents* will tell us with

greater certainty if it does so in some populations.

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