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Letters to the Editor

RE: "STATISTICAL MODELLING OF LUNG CANCER AND LARYNGEAL CANCER INCIDENCE IN SCOTLAND, 1960–1979"

I read Boyle and Robertson's recent article (1) with interest, especially since their approach to help overcome the nonidentifiability of age-period-cohort models by using data from individual records has already been proposed in my paper (2). However, I would like to comment here that this approach does not solve the identification problem because this model is derived by linking (or imposing constraints on) two separate age-period-cohort models.

The ordinary, unidentifiable age-period-cohort model is usually applied to data tabulated in the form of a two-way (age × period) contingency table in which the width of age is equal to the length of period, and is assumed to be a Poisson regression of the form:

$$\log E(d_{ij}/N_{ij}) = \mu + \alpha_i + \beta_j + \gamma_k, \quad (1)$$
$$i = 1, \ldots, I; j = 1, \ldots, J; k = I - i + j,$$

where α_i, β_j, and γ_k represent parameters of effects due to age, period, and cohort, respectively, and d_{ij} and N_{ij} denote the number of cases and the population at risk in the (i,j) cell, respectively. In this model, cohorts defined as diagonal cells are overlapping.

When individual records are available, we can divide the cell (i,j) into two right-angled triangular cells indexed $(i,j;s)$, $s = 0, 1$, so that the cells $(i,j;0)$ and $(i,j;1)$ constitute two successive nonoverlapping cohorts. Then, by introducing nonoverlapping cohort effects γ_k^* instead of overlapping cohort effects γ_k, we can suggest an alternative age-period-cohort model:

$$\log E(d_{ij}^{(s)}/N_{ij}^{(s)}) = \mu + \alpha_i + \beta_j + \gamma_k^*,$$
$$k = I - i + j + s, \quad (2)$$

where $d_{ij}^{(s)}$ and $N_{ij}^{(s)}$ denote the number of cases and the population at risk in the $(i,j;s)$ triangular cell. This model is easily shown to be fully identifiable, which is exactly the model proposed by Tango (2) and by Boyle and Robertson (1).

However, if one examines closely the data structure comprising two IJ triangular cells, it is easily revealed that the more appropriate but unidentifiable age-period-cohort model can be, for each s,

$$\log E(d_{ij}^{(s)}/N_{ij}^{(s)}) = \mu^{(s)} + \alpha_i^{(s)} + \beta_j^{(s)} + \gamma_k^{(s)},$$
$$k = I - i + j, \quad (3)$$

where $\alpha_i^{(s)}$, $\beta_j^{(s)}$, and $\gamma_k^{(s)}$ denote the parameters of effects relating to the triangular cells $(i,j;s)$. The reason

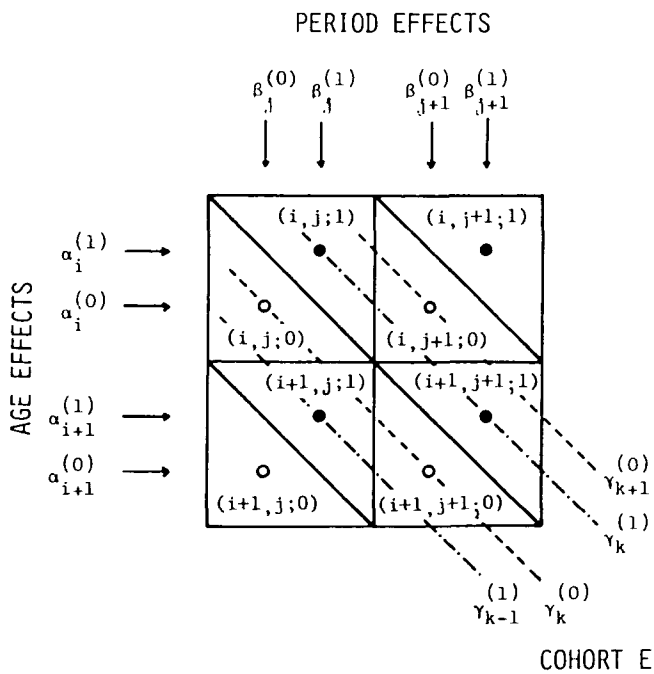

FIGURE 1. Relation between the centers of gravity of triangular cells (○ for lower triangles and ● for upper triangles) and three kinds of time effects.

for this is illustrated in figure 1, which indicates the centers of gravity of the triangular cells. For example, $\alpha_i^{(0)}$ and $\alpha_i^{(1)}$ are generally not equal since the lower triangle $(i,j;0)$ and the upper triangle $(i,j;1)$ in the same age category have different age distributions, leading to different "mean" ages. Similarly, the lower triangle $(i,j;0)$ and the upper triangle $(i+1, j;1)$ in the same nonoverlapping cohort of model 2 also have different "mean" birth periods.

However, if we can reasonably assume that for all i, j, k,

$$\alpha_i^{(0)} = \alpha_i^{(1)},\ \beta_j^{(0)} = \beta_j^{(1)},\ \gamma_k^{(0)} = \gamma_{k-1}^{(1)},$$

then model 2 is derived. Therefore, the truth of the conclusion to which one is led by using model 2 depends entirely upon the validity of the constraints given above. Because age is the single most important factor of cancer risk, a reduced model 3′ having only $\alpha_i^{(0)} \neq \alpha_i^{(1)}$ should also be more valid than model 2, but it is also unidentifiable. Identifiability comes about only when all three factors are constrained. Namely, model 2 can be considered one of procedures which impose some constraints on the model parameters whether or not they are reasonable.

Boyle and Robertson (1) stated that the analysis using model 2 "can proceed without arbitrarily setting two cohort effects to be equal, or any other such scheme" (p. 735). This statement is, however, clearly false.

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Editor's note: The response to this letter by Drs. Boyle and Robertson was received too late for publication in this issue and is therefore scheduled for an upcoming issue.

RE: "DIET IN THE ETIOLOGY OF BREAST CANCER"

Rohan and Bain (1) are to be commended for their excellent review of dietary factors in the etiology of breast cancer. However, they have omitted several important references to animal experiments, as well as epidemiologic and clinical studies concerning the possible relation of methylxanthine consumption to breast cancer and benign breast disease.

At least four animal studies produced negative results (2–5). Three important epidemiologic papers have been published that were likewise negative (6–8). Finally, a recent clinical trial did not point to any relation between caffeine consumption and benign proliferative disease (9).

Taken together, all of these negative studies make it very unlikely that there is any relation between methylxanthine consumption and benign breast disease or breast cancer.

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THE AUTHORS REPLY

We thank Dr. Grossman (1) for bringing to our attention extra evidence relating to the association between methylxanthine consumption and risk of breast disease. Undoubtedly, the extra references will be of use to those who are interested in further study of this relation (although the article by Snowdon and Phillips (2) appears in our review as reference 144). However, several of the references that he provides relate to benign breast disease, and it was not our intention to review this area in detail. With regard to the disease under review (i.e., breast cancer), his conclusions, while similar to ours, are stated somewhat more strongly.

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