

## LETTERS TO THE EDITOR

### A COMPARISON OF TWO METHODS FOR CALCULATING EXPECTED MORTALITY

by A. J. Hartz, E. E. Giefer and R. G. Hoffmann, *Statistics in Medicine*, **2**, 381-386 (1983)

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The authors conclude that the traditional person-years method used in occupational mortality studies cannot be justified. They contend that expected mortality should not take into account the survival experience of the study group. Although this proposal has a certain intuitive appeal, we submit that this approach is inappropriate and that their presentation is inconsistent.

Hartz *et al.* present an alternative method to the person-years method, which they call the 'prospective' method, and which we will here call the 'actuarial method'. The proposed actuarial method of calculating expected mortality is simply a sum of individual risks, with risk defined in the usual sense as the conditional probability of dying during the period of study. This method results in a cumulative estimate of expected deaths at the end of follow-up. In this way the expected mortality is a function of the length of the study period. The basis for the person-years method, on the other hand, is the calculation of rates (as opposed to risks) per person-time. This method therefore takes into account instantaneous changes in the survival experience of the study group relative to the standard over the entire period of study. We, along with other commentators, believe that such a method is preferable when examining long-term mortality data.<sup>1</sup>

Hartz *et al.*'s example 3 actually illustrates the problem quite well. In a cohort where all 50 individuals in the study group die in the first year of a 20 year follow-up, use of the actuarial method virtually ignores this unusual situation and results in 16.6 expected deaths. Use of the person-years method, on the other hand, results in an expectation of only one death, compared to the observed value of 50, a result more descriptive of the dramatic excess mortality rate in this example.

Inconsistencies in the paper occur with an attempt to explain the differences between the expected mortality calculated according to the two methods. The authors state that the person-years method results in estimates of expected mortality that are 'too low' when the mortality rates in the study group are less than the standard rates. Actually, in general, the person-years method produces higher expected mortality than the actuarial method when the study group has lower mortality rates compared to the standard population, whereas the reverse is true when the study group has higher mortality rates. The situation becomes more complicated for cause-specific mortality, not considered by Hartz *et al.* Their example 2 as well as their calculations from actual data on page 384 illustrate this point.

In summary, there is no 'bias' in the person-years method of calculating expected mortality, compared to the actuarial method. Each method estimates a different parameter, one based on rates per person-time and the other based on cumulative risks. We believe that the person-years method (or some other method based on rates) generally constitutes the appropriate technique for long-term occupational mortality studies.

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The authors state that the person-years method of 'expected death' calculation in prospective studies cannot be justified. We wish to suggest that the method can be justified and that this justification follows logically from the prospective model suggested by Hartz and his colleagues, although the term 'exposure to death' is preferable to 'expected death'.

Consider a theoretical control group, as suggested by Hartz. Let the probability of theoretical individual  $i$  surviving to an age sufficient to enter the  $k$ th element of the person-years matrix be  $x_{ki}$ . This probability will be a function of the death rates to which the individual has been exposed since ascertainment. The probability of his survival to exit from the  $k$ th element will be

$$x' = x_{ki} e^{-pt}$$

where  $p$  is the death rate within the  $k$ th element and  $t$  is the time that the individual spent within the element. This individual's contribution to the expected death rate for this element will be

$$d_{ki} = x_{ki} - x' = x_{ki}(1 - e^{-pt})$$

His contribution to the years at risk in the element will be

$$y_{ki} = \int_0^t x_{ki} e^{-pt} dt$$

$$y_{ki} = x_{ki} \frac{(1 - e^{-pt})}{p} = \frac{d_{ki}}{p}$$

Therefore the total expected deaths in the element, including all individuals, will be

$$D_k = \sum_i d_{ki} = p \sum_i y_{ki} = pY_k$$

where  $Y_k$  is the total years at risk.

To compare the two observed groups with the theoretical control group, we follow Mantel's concept of exposure to death.<sup>1,2</sup> Hence, if in the observed group the number of deaths in the element was  $D'_k$  and the years at risk  $Y'_k$ , the exposure to death of the observed group will be

$$E'_k = (D'_k + D_k) \frac{Y'_k}{Y_k + Y'_k}$$

Since we can take theoretical group as arbitrarily large, we can state that

$$D_k \gg D'_k$$

and

$$Y_k \gg Y'_k$$

and so

$$E'_k \rightarrow \frac{D'_k}{Y_k} Y'_k$$

$$E'_k \rightarrow pY'_k$$

which is the value which would have been produced had the person-years method been used directly. Comparison then results from the standard formula

$$\chi^2 = \frac{(D'_k - E'_k)^2}{E'_k}$$

This approach has the considerable advantage of allowing the quantification of any difference merely by increasing the 'exposure to death' by any constant and retesting or by use of formulae suggested by Liddel.<sup>3</sup>

Compared with the method suggested by Hartz and colleagues, the person-years method has the considerable advantage of computational simplicity and should produce the same conclusion.

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The authors compare two methods for evaluating mortality for follow-up studies of occupational mortality, the standard person-years (PY) method and the prospective model (PM) method. They claim that the expected mortality obtained from the PY method has no theoretical basis and lacks justification. They propose the PM method of computing expected mortality based on the standard mortality rates and individuals 'potential follow-up' under study. Their results on expectations are correct, but other justification for the PY method suggests not only that it is an appropriate statistic, but that it is more powerful than the PM method.

The type of study considered has individuals followed over a period of time. One records the time each individual spends in a stratum (e.g. age group) for each of  $K$  strata. Calculations in both the PY and PM methods are obtained from formulae of the form

$$Z = \Sigma (O_j - E_j) / (\Sigma V_j)^{1/2} \quad (1)$$

where  $O_j$  is an observed number of deaths, and  $E_j$  and  $V_j$  are appropriate normalizing constants. The methods differ in the determination of  $E_j$  and  $V_j$  as well as in the domain of summation.

We describe the PY method as follows: we consider a process whereby for each stratum  $j$  we observe individuals in sequence at risk  $\lambda_{oj}$  of failure (if the standard rates apply) for period  $t_{ij}$  and whether or not they fail. The assumption of follow-up of individuals until the total follow-up time observed in stratum  $j$  was  $T_j$ , leads to an approximate Poisson distribution for the observed number of deaths in stratum  $j$  ( $O_j$ ) with mean and variance  $\lambda_{oj}T_j$ . By letting

$$E_j = V_j = \lambda_{oj}T_j \quad (2)$$

we compute the statistic  $Z_{PY}$  by substituting these values into (1) and summing over strata. The argument above provides an easy way to remember how to do the calculation, but it is not a theoretical justification of the procedure. Breslow<sup>1</sup> studied the PY method and showed that, although the PY expected number of deaths is a random variable, under the null hypothesis one can justify the conventional interpretation on the grounds that its expected value equals the actual expected number of deaths. He also derives the person-years test statistic as a score statistic using the parameterization  $\lambda_j = \lambda_{oj} \exp(\beta)$ .

The PM method assumes that the  $n$  individuals under study have fixed, known 'potential' contributions,  $y_{ij}$ , to stratum  $j$ ,  $j = 1, \dots, K$ ;  $i = 1, \dots, n$ . By letting  $O_i = 1$  if the  $i$ th individual dies and zero otherwise,  $O_i$  is then Bernoulli ( $p_i$ ) where  $p_i = 1 - \exp\left(-\sum_{j=1}^K \lambda_{oj} y_{ij}\right)$  if the standard rates apply. Thus, the expected value and variance of  $O_i$  are

$$E_i = p_i \quad \text{and} \quad V_i = p_i(1 - p_i) \quad (3)$$

respectively. Substitution of these values into (1) and summation over individuals yield the value of  $Z_{PM}$ .

The authors compare the 'variances' from the two approaches and note that 'for studies with long follow-up and therefore high values of  $p_i$  the binomial variance may be much smaller' than the Poisson variance. They conclude from this that 'tests using . . . [the binomial] . . . variance are more sensitive to deviations from expected mortality'.

However, the smaller variance is an inherent characteristic of the method for calculating the expected number of deaths with the PM model, and not indicative of any power advantage for the model. With increasing patient follow-up, the observed and expected numbers of deaths will both converge to the number of study subjects and the variance will decrease appropriately. In fact, with sufficiently long 'potential follow-up', the observed number of deaths will equal that expected (namely  $n$ , the number of study subjects) and the variance will be zero, irrespective of the relationship of mortality rates between the study and standard populations.<sup>2</sup>

The advantage that the PY method has over the PM method stems from the fact that in the computations for the PY method one compares mortality rates; in the PM method one compares number of deaths.

To assess the performance of  $Z_{PM}$  and  $Z_{PY}$ , we computed the asymptotic relative efficiency (ARE, Pitman efficiency)<sup>3</sup> of  $Z_{PM}$  relative to  $Z_{PY}$ . The form of the alternative hypotheses we employed is that for each stratum  $j$ ,  $\lambda_j = \lambda_{oj}^{(1+\theta/n^{1.2})}$ .

$$\text{ARE} = \lim_{n \rightarrow \infty} \frac{\left[ \sum_{i=1}^n (1-p_i) \{-\ln(1-p_i)\} \right]^2}{\left\{ \sum_{i=1}^n p_i(1-p_i) \right\} \left\{ \sum_{j=1}^K \lambda_{oj} T_j \right\}}$$

We consider a simple situation, in which there is a single stratum for which the standard population survival distribution is exponential ( $\lambda$ ) and we follow  $n$  individuals, each with a potential follow-up of  $T$  years. Then

$$\text{ARE} = (\lambda T) e^{-\lambda T} / (1 - e^{-\lambda T})$$

and Table I displays the ARE for various value of  $\lambda T$ .

Table I. ARE for various values of  $\lambda T$

$\lambda T$	Prob. (death)	ARE
0.10	0.095	0.95
0.25	0.221	0.88
0.70	0.503	0.69
1.40	0.753	0.46
2.30	0.900	0.26

In this case, contrary to the claims of the authors, the PM method is only nearly as efficient as the PY method when the vast majority of subjects are expected to survive the follow-up period. Its performance relative to the PY method is quite poor as the follow-up becomes more complete.

Often, the risk of death for the standard population can reasonably be assumed to be constant within strata, but varying across strata. If the risk of death in the study group is proportional to that in the standard population, asymptotically the PM method will never be more powerful than the PY method.<sup>2</sup> Berry provides additional details of the analysis of mortality by the person-years method.<sup>4</sup>

#### ACKNOWLEDGEMENT

This investigation was supported by Grants CA-33601 and CA-23415, awarded by the National Cancer Institute, and ES-02709 awarded by the National Institute for Environmental Health Sciences.

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## AUTHORS' REPLY

Anderson and Anderson's asymptomatic results for the exponential distribution suggest that the person-years method is more powerful than the prospective method for significance testing in mortality studies. Other research found that the person-years method can be used to estimate the relative hazard rates of the standard and study populations.<sup>1</sup> These findings suggest that the potential utility of the prospective method in mortality studies is less than we indicated in our paper.<sup>2</sup>

The advantage of the prospective method compared to the person-years method is that the prospective method can be used to determine the expected mortality. It can also be used to determine cause-specific expected mortality by computing for each year of follow-up the joint probability that the subject will die from a specific cause and has not died from any cause prior to this time. On the other hand, the person-years method can only be used to estimate expected mortality, and this estimate is biased unless the hazard rates for the study population and the standard population are equal.

The prospective expected mortality and expected mortality rates have several uses: One use is to compare the cumulative expected mortality to the cumulative observed mortality. This comparison may demonstrate a healthy worker effect or a lag effect that would be missed with one significance test at the end of the study. Using the person-years method to estimate cumulative expected mortality may give inaccurate estimates of expected mortality either because of bias or random variation.

A second use of the prospective method is to derive the baseline mortality so that the mortality rate from the study sample can be expressed as a percentage above the standard. The increase in mortality may have more practical implications than the relative hazard rate. For example, knowing that the increase in the 20 year cancer mortality rate was 1 per cent may be more informative than knowing that the standardized mortality ratio (SMR) was 3. The SMR corresponds to the relative risk, and the increase in mortality rate corresponds to the attributable risk.

A third use of the prospective method is to assist in the design of studies. Before follow-up is attempted the prospective method can be used to determine the expected mortality for any given length of follow-up and the approximate power for detecting a given increase in the mortality rate.

Our claim that the person-years method was inappropriate for calculating expected mortality was not meant to imply that we believe that it is not a useful technique. Based on recent research we believe that the person-years method will continue to be the most useful statistic for mortality studies without a control group. However, the prospective method may provide useful information for some studies.

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