RE: “ADJUSTING SURVIVAL CURVES FOR CONFOUNDERS: A REVIEW AND A NEW METHOD”

Nieto and Coresh (1) are reviewing alternative methods for presenting adjusted survival curves. The proposed new method is a special case of the Ederer II method currently used at cancer registries worldwide. In addition, there are other frequently used methods for adjusting for deaths and censorings that are not mentioned.

It is important to state the context in which any adjusted survival curves are to be used. Age-adjusted survival curves are analogous to directly standardized incidence rates (2). These rates may be expressed as the weighted average of the age-specific survival curve for each study group, where the weights are chosen to be proportional to the age distribution of some external standard population. A term that helps to distinguish this type of adjustment from others and emphasizes that covariates other than age may be adjusted is externally covariate-adjusted survival curves.

Adjusted survival curves may also be used to provide a graphic representation of survival obtained from a fitted regression model of survival such as the Cox model or Aalen’s additive risk model (3). This curve describes survival for individuals with a particular set of covariates. A term that describes this type of adjustment is internally covariate-adjusted survival curve.

Another type of adjusted survival curves is one that describes the survival probability of a randomly selected individual in the study group. It is obtained as the average of the individual survival curves where the individual survival curves are obtained from the fitted regression model. These survival curves are usually called directly adjusted survival curves. This adjusted survival curve is, in mathematical terms, similar to the method used in cancer survival analysis to evaluate expected survival curves (4). It is evaluated as the average of the individual survival curves where the individual survival curves are obtained from population mortality tables.

Ederer et al. (5) noted that it might be reasonable to adjust the expected survival curve for deaths in the study group. The Ederer II definition of expected survival is

\[
S(t) = \exp \left[ - \int_0^t \sum_{i=1}^n Y_i(s) \mu_i(s) ds \right],
\]

where \( \mu_i(t) \) is the population mortality rate for the \( i \)th individual, \( Y_i(t) \) is an indicator variable that is one if the \( i \)th individual is at risk just prior to time \( t \) and zero elsewhere, and \( Y(t) = \sum_{i=1}^n Y_i(t) \). This definition may also be derived from the additive hazard model discussed by Andersen and Vaeth (6). The adjusted hazard rate in equation 1 is equal to adjust the conditional survival probability. One may adjust for multiple covariates simultaneously by aggregating over several covariates. A small difference is that \( \mu_i(t) \) is taken from population mortality tables in the Ederer II method, while Nieto and Coresh (1) estimate \( \mu_i(t) \) from the population under study. However, the method of adjusting for deaths is similar.

Another class of estimators of survival curves that take the observed censoring into account was suggested by Hakulinen (7). With this method, survival curves predict that the mortality patients would be observed to have given the observed censoring. This estimator was proposed in order not to make assumption about mortality in future time. The same type of correction has also been proposed by Bonsel et al. (8).

Adjustment for deaths and censorings is frequently used in medical statistics as well as in cancer survival analysis (8, 9). To summarize, I think that adjusted conditional survival curves should not be presented without reference to Ederer et al. (5). Furthermore, it should always be stated whether externally, internally, or directly adjusted survival curves are used and how individual survival curves are evaluated.

REFERENCES

The Authors Reply

We thank Dr. Zahl for his letter (1) regarding our paper on methods to obtain adjusted survival curves (2). We agree with Dr. Zahl that some of the procedures we discussed in our review as well as the new method we proposed are analogous to the methods for obtaining relative survival estimates proposed by Ederer et al. (3) and others (4–6). As Dr. Zahl points out, the latter methods have been widely