

SELECTING AN EXPOSURE LAG: IS THE MODEL WITH THE LARGEST EXPOSURE EFFECT THE BEST MODEL?

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In epidemiology, we are generally inclined to consider more credible those associations showing a stronger exposure-response relation, such as higher relative risks or rate ratios. Higher parameter estimates look particularly credible, because one usually exercises care to avoid sources of upward bias, such as bias from selection or misclassification or confounding. Higher relative risks or rate ratios are often emphasized as a criterion to choose among various hypothesized exposure-lag values. The purpose of exposure lagging, or in general of exposure weighting, is to discount exposures which are thought not to be relevant for the outcome under study. Whereas this "highest estimate" approach may often work in practice, the validity of such a criterion is not demonstrated. The purpose of this presentation is to compare exposure-lag choices based on the highest estimate approach vs. those based on a statistical goodness-of-fit criterion (likelihood ratio test). It seems likely that many epidemiologists believe that the two criteria are equivalent i.e., they would lead to the same choice of exposure-lag parameter estimates or they may at the most show trivial differences. The examples shown are based on both previously published studies and hypothetical data, in which an exposure-lag parameter is estimated by trial-and-error fitting: the behavior of the goodness of fit statistic obtained over the assigned values of the parameter is compared with that of the relative risk. The examples show that the magnitude of the point estimate and goodness-of-fit criteria based on the likelihood may disagree. In particular, it is possible to generate examples in which for different hypothesized lags one obtains: 1) an unchanging goodness-of-fit statistic accompanied by a wide variation in relative risk, or 2) an unchanging relative risk accompanied by a wide variation in goodness-of-fit statistic, or 3) a strong disagreement between the exposure lag at which the highest relative risk is obtained and the lag at which the goodness-of-fit statistic is maximized. In summary, the examples built on hypothetical data

indicate the possibility of major discrepancies between these two criteria; these discrepancies can be substantial even with real data. Additionally, situations may exist in which the highest estimate is a biased estimate: the lag may be correlated with the exposure (e.g., duration or cumulative exposure) and it may be a determinant of the outcome (more cases may be counted in the unexposed category as the lag increases). Small-sample bias may also play a role in determining an upwardly biased estimate, since the more extreme lags are often associated with very few observations in the exposed categories. In conclusion, it is suggested that the highest-estimate criterion should not be used for the estimation of exposure-lag or exposure-weighting parameters. A priori biological knowledge and/or goodness-of-fit criteria should be relied upon.



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