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« Instrumental Variable in a Survival Context »

Eric Tchetgen Tchetgen, Ph.D.
Professeur agrégé
Dép. de biostatistiques & Dép. d'épidémiologie
Harvard School of Public Health, Boston

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À l'invitation du professeur Mireille Schnitzer

Bias due to unobserved confounding can seldom be ruled out with certainty when estimating the causal effect of a nonradomized treatment. The instrumental variable (IV) design offers, under certain assumptions, the opportunity to tame confounding bias, without directly observing all confounders. The IV approach is very well developed in the context of linear regression and also for certain generalized linear models with a non-linear link function. However, IV methods are not as well developed for regression analysis with a censored survival outcome. In this talk, we will discuss the instrumental variable approach for regression analysis in a survival context, primarily under an additive hazards model, for which we describe two simple methods for estimating causal effects. The first method is a straightforward two-stage regression approach analogous to two-stage least squares commonly used for IV analysis in linear regression. In this approach, the fitted value from a first -stage regression of the exposure on the IV is entered in place of the exposure in the second-stage hazard model to recover a valid estimate of the treatment effect of interest. The second method is a so-called control function approach, which entails adding to the additive hazards outcome model, the residual from a first-stage regression of the exposure on the IV. Formal conditions will be given justifying each strategy, and the methods are illustrated in a novel application to a Mendelian randomization study to evaluate the effect of diabetes on mortality using data from the Health and Retirement Study. We also establish that analogous strategies can also be used under a proportional hazards model specification provided the outcome is rare over the entire follow-up.