Marginal Structural Cox Models for Dynamic Treatment Regimes

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In the absence of unmeasured confounding and model misspecification, inverse probability (IP) weighting of marginal structural Cox models can be used to estimate the causal effect of time-varying treatments on mortality. Unlike standard estimation methods, IP weighting can appropriately adjust for confounding due to time-varying covariates that are affected by prior treatment. As a result, IP weighting of marginal structural Cox models is being increasingly used in pharmacoepidemiologic studies with time-varying confounding by indication. However, most applications of the method have focused on static (nondyanmic) treatment regimes. For example, several published papers compare the AIDS-free survival of HIV-infected patients under the static regimes "initiate highly active antiretroviral therapy (HAART) at baseline" vs "never initiate HAART during the follow-up". IP weighting can also be used to compare dynamic treatment regimes. For example, Hernán et al (2006) used IP weighting of a marginal structural Cox model to compare the AIDS-free survival of HIV-infected patients under the dynamic regimes "initiate HAART when CD4 cell count drops below 500" vs "initiate HAART when CD4 cell count drops below 200." However, applications of IP weighting that are agnostic about the relative effects of each dynamic regime, like that by Hernán et al, will typically lead to unstable effect estimates (e.g., wide confidence intervals). Dynamic marginal structural models, proposed by Orellana et al (2007), reduce the variance of the estimator via parametric assumptions about the relative effects of the dynamic regimes. This presentation applies this idea to marginal structural Cox models, and estimates the causal effect of HAART on AIDS-free survival under several dynamic regimes.