

Causal Assessments of Surrogate Markers when Markers and Outcomes are Multivariate Normal

In many circumstances, medical studies evaluating the efficacy of an intervention need either long follow-up periods or expensive or invasive procedures to obtain the primary outcome. This motivates considerable attention to surrogate evaluation in recent years, which aims to use alternative measures ("surrogate marker(s)") in lieu of the primary outcome to evaluate the efficacy of an intervention. However, conventional surrogate evaluation methods using regression fail to provide a causal interpretation, as surrogate markers are post-randomization variables. Principal surrogacy, defined based on the concept of principal stratification, overcomes such shortcomings (Frangakis and Rubin 2002). We propose a Bayesian estimation strategy for surrogate validation when the joint distribution of potential surrogate and outcome measures is multivariate normal. We model the joint conditional distribution of the potential outcomes of T , given the potential outcomes of S and propose surrogacy validation measures from this model. By conditioning on principal strata of S , the resulting estimates are causal. As the model is not fully identifiable from the data, we propose some reasonable prior distributions and assumptions that can be placed on weakly identified parameters to aid in estimation. We explore the relationship between our surrogacy measures and the traditional surrogacy measures proposed by Prentice (1989) via simulations and applications.