Seminar Series: Research Colloquium  
Date: Friday, September 15, 2017  
Time: 10:30 – 11:20 a.m.  
Location: GRIS 103  
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Modeling Survival Distribution as a Function of Time to Treatment Discontinuation: a Dynamic Treatment Regime Approach

Abstract: We consider estimating the effect that discontinuing a beneficial treatment will have on the distribution of a time to event clinical outcome. In particular, we are interested in assessing whether there is a period of time over which the beneficial effect may continue after discontinuation and if so how long does such a "legacy" effect last. There are two major challenges. The first is to make a distinction between mandatory discontinuation, where by necessity treatment has to be terminated and optional discontinuation which is decided by the preference of the patient or physician. If we view treatment discontinuation as an intervention, then it only makes sense to consider optional treatment discontinuation where either choice of continuing treatment or not could have been made. The innovation in this article is to cast the intervention in the form of a dynamic regime "terminate treatment optionally at time v unless a mandatory treatment-terminating event occurs prior to v" and consider estimating the distribution of time to event as a function of treatment regime v. The second challenge arises from biases associated with the nonrandom assignment of treatment regimes, because, naturally, optional treatment discontinuation is left to the patient and physician, and so time to discontinuation may depend on the patient's disease status. To address this issue, we develop dynamic-regime Marginal Structural Models (dr-MSMs) and use inverse probability of treatment weighting to estimate the impact of time to treatment discontinuation on a time to event outcome, compared to the effect of not discontinuing treatment. We illustrate our methods using the IMProved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT) data on cardiovascular disease.