Speaker: Bharati Kumar (University of Bath)

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Title: Weighted hazard ratio estimation for delayed and diminishing treatment effect

Abstract:
Non proportional hazards (NPH) have been observed in confirmatory clinical trials with time to event outcomes. Under NPH, the hazard ratio does not stay constant over time and the log rank test is no longer the most powerful test. The weighted log rank test (WLRT) has been introduced to deal with the presence of non-proportionality. In this talk, we focus our attention on the WLRT and the complementary Cox model based on time varying treatment effect proposed by Lin and León (2017) (doi: 10.1016/j.conctc.2017.09.004). We conduct a simulation study which investigates whether the proposed weighted hazard ratio (WHR) approach is unbiased in scenarios where the WLRT statistic is the most powerful test. In the diminishing treatment effect scenario where the WLRT statistic would be most optimal, the time varying treatment effect estimated by the Cox model estimates the treatment effect very close to the true one. However, when the true hazard ratio is large we note that the proposed model overestimates the treatment effect and the treatment profile over time. However, in the delayed treatment scenario, the estimated treatment effect profile over time is typically close to the true profile. For both scenarios, we have demonstrated analytically that the hazard ratio functions are approximately equal under certain constraints. In conclusion, our results illustrates that in certain scenarios where a given WLRT would be most powerful, we observe that the WHR from the corresponding Cox model is estimating the treatment effect close to the true one.