## ESTIMATION OF TREATMENT EFFECT ADJUSTING FOR NON-COMPLIANCE USING THE INTENSITY SCORE METHOD - AN APPLICATION TO A LARGE PRIMARY PREVENTION STUDY FOR CORONARY EVENTS -

Y. Tanaka, Y. Matsuyama, and Y. Ohashi

University of Tokyo, Tokyo, Japan

Email: y\_tanaka@epistat.m.u-tokyo.ac.jp

Recently, there has been much interest in methods for analyzing clinical trials of treatments that are subject to non-compliance. In this talk, we propose the intensity score methods to estimate the causal effect of treatment changes in a clinical trial with time-to-event outcomes. The intensity score is the cumulative differences over time between treatment actually received and treatment predicted by prior medical history. The approach was originally proposed by Brumback et al. for adjusting for time-dependent confounding. We extend their approach to the survival analysis. We compared the performance of the proposed method with other analysis methods (as treated analysis, intention-to-treat analysis, and g-estimation proposed by Robins) through simulation studies, which showed that the intensity score based estimator was unbiased and more efficient in the presence of non-random non-compliance. The proposed methods are applied to data from a large randomized primary prevention study for coronary events (MEGA study), in which pravastatin treatment was compared with the usual treatment. The results of our analysis showed that the treatment effect of pravastatin by the intensity score approach was larger (hazard ratio = 0.65, 95% confidence interval: 0.44, 0.97) than that of intention-to-treat analysis, while the g-estimation could not give the valid confidence intervals due to the small numbers of events.