國 立 中 央 大 學

統 計 研 究 所

學 術 演 講

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講　　題：**Surrogate marker assessment using mediation and instrumental variable analyses in a case-cohort design**

時　　間：**110 年 12 月 21 日（星期二）上午 11：00 ～ 12：00**

地　　點：中央大學鴻經館 **M-429** 室

茶　　會：**上午 10：30 ～ 11：00**　　地　點：鴻經館 **M510** 室

ABSTRACT

The identification of surrogate markers for gold standard outcomes in clinical trials enables future cost-effective trials that target the identified markers. Due to resource limitations, these surrogate markers may be collected only for cases and for a subset of the trial cohort, giving rise to what is termed the case-cohort design. Motivated by a COVID-19 vaccine trial, we propose methods of assessing the surrogate markers for a time-to-event outcome in a case-cohort design by using mediation and instrumental variable (IV) analyses. In the mediation analysis, we decomposed the vaccine effect on disease risk into an indirect effect (the effect mediated through the surrogate marker), and a direct effect (the effect not mediated by the marker), and we propose that the mediation proportions are surrogacy indices. In the IV analysis, we aimed to quantify the causal effect of the surrogate marker on disease risk in the presence of surrogate--disease confounding, which is unavoidable even in randomized trials. We employed weighted estimating equations derived from nonparametric maximum likelihood estimators (NPMLEs) under semiparametric probit models for the time-to-disease outcome. We plugged in the weighted NPMLEs to construct estimators for the aforementioned causal effects and surrogacy indices, and we determined the asymptotic properties of the proposed estimators. Finite sample performance was evaluated in numerical simulations. We illustrated the utility of the proposed mediation and IV analyses using two data sets from an influenza vaccine trial and from a mock COVID-19 vaccine trial.

關鍵詞：Causal mediation model; Case-cohort study; Clinical trials; Instrumental variable; Surrogate endpoint; Survival analysis

◎敬請張貼　　歡迎參加◎