

広島統計談話会
Hiroshima Statistics Study Group

第 303 回談話会を下記のように開催致しますので御参集下さいますようご案内申し上げます。

You are cordially invited to the 303rd meeting as scheduled below.

日 時 : 2017 年 4 月 21 日 (金) 15:00 –

Date : April 21, 2017 (Fri) 15:00 –

場 所 : 放射線影響研究所 E-205 会議室

Place : RERF Conference Room E-205

演 者 : ジョン B. コローン (放射線影響研究所 統計部 主任研究員)

Speaker : John B. Cologne, Ph.D.

Senior Scientist

Department of Statistics, RERF

演 題 : 「潜在中間因子としてバイオマーカーを伴う肝がん因果モデルの共同開発:
複雑なコホートに基づくサンプリング・デザインを用いた多重代入法による構造方程式」

Title : “Collaborative Development of a Causal Model of Liver Cancer with Biomarkers of Intermediate Latent Factors: Structural Equations with Multiple Imputation under a Complex Cohort-based Sampling Design”

要 約 :

Summary:

The juxtaposition of biostatistics and clinical epidemiology is effecting a research-paradigm shift away from the black-box inference of standard cause-and-effect regression modeling towards hypothesis-driven analyses of complex causal mechanisms. In this new paradigm, researchers seek to explain relationships between risk factors and outcomes rather than merely test and estimate associations. However, such causal modeling with observational data requires thoughtful assessment—through subject-matter knowledge—of assumptions that cannot be tested directly using the data. This necessitates close collaboration between clinical-epidemiological researchers and statisticians to enable the formulation, fitting, and interpretation of plausible causal models.

We present an example of such a collaboration in a study of atomic-bomb radiation exposure and risk of liver cancer (hepatocellular carcinoma, HCC), in which we used stored sera to measure biomarkers of several intermediate stages of liver disease that were of particular interest. A key element of the causal model is possible mediation of radiation risk by viral hepatitis, which in turn is related to chronic inflammation, insulin resistance, and liver fibrosis, all three of which are latent constructs. After we developed a latent-factor measurement model (with factor analysis) by striking a compromise between statistical criteria and clinical judgment, we fit causal models using MIMIC (multiple indicators, multiple causes) models and assessed risk of HCC for radiation with the latent constructs as intermediates and HCC as a dichotomous endpoint. The model also allowed for effects of other risk factors—such as BMI and smoking and drinking behavior—and one of our aims was to test for interaction of these risk factors with the radiation and viral-hepatitis pathways to HCC.

We encountered several challenges in applying existing causal-modeling approaches to this study. One challenge was due to the fact that the data were collected under a nested case-control (NCC) design with counter matching on radiation dose. The NCC design is typically analyzed with conditional binary regression, and counter matching requires the use of sampling weights as offsets; however, there is no facility for fitting conditional binary regression models in standard structural equation analysis software, such as Mplus. Another challenge was the need to deal in a principled manner with missing data; this requires using multiple imputation in a way that takes account of the complex sampling design both at the imputation stage and at the analysis stage. We dealt with these challenges in an ad hoc fashion, by incorporating the sampling design variables in the imputation models and by analyzing the data as if it arose through retrospective sampling, using unconditional binary regression with sampling weights. These approaches are not rigorous: their statistical properties need to be examined and, if necessary, more appropriate approaches need to be developed.

In this presentation I will describe the study and the analyses in progress as a practical illustration of the aims and potential pitfalls of complex causal modeling in an observational clinical research setting. I will focus on the iterative, collaborative model-building process. Some preliminary results will be presented to facilitate the illustration, and some open methodological research questions will be posed.