insight POLICY RESEARCH

Health

Causal Inference Methodology and Its Application in Evaluating Efficacy and Safety of Drugs

Client: U.S. Department of Health and Human Services, Food and Drug Administration

Overview

Causal inference, originally developed for epidemiology studies, considers statistical methods for estimation and inference related to causal effects; it applies to both observational and randomized studies. Insight directed the research, analysis, and training on statistical issues related to establishing a causal link between reported adverse events and prior treatment with an HIV drug/medical device. Although certain methods such as inverse probability of treatment weighting and propensity score stratification are used regularly, optimal robust methods have not been exploited. A recent advance, targeting maximum likelihood estimation, helps to determine the causal effect of drug regimens on both efficacy and toxicity.

The principal objective of this study was to provide statistical consultation and training to staff at the Food and Drug Administration (FDA on exploring the causal inference methodologies and their properties to improve efficacy and safety analyses of HIV clinical trials. Insight led the development of causal inference methodologies to analyze safety data in HIV trials. Insight also provided expertise in statistical programming, data analyses, and training for FDA staff.

The project had two core components:

- HIV safety analyses: Improve the statistical problem of HIV clinical trials that involve deterministic dropout according to rules based on biomarker; implementation of maximum likelihood estimation models
- Data analysis and simulation study of drug, Tygacil: Design and implementation to demonstrate effects of missingness on estimator performance in safety analysis with rare outcomes

For this project, Insight provided statistical consultation and training on causal inference methodologies; developed methodologies for analyzing safety data in HIV trials; provided comparison of methods; conducted trainings; advised, facilitated, and assisted in providing consultation, statistical programming, and data analyses applicable to HIV data; and drafted a technical report on the statistical methods and analysis results.

Products

Final report, *Causal Inference Methodology and Its Application in Evaluation Efficacy and Safety of Drugs* (July 2010)