

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

Project Overview

Insight directed the research, analysis, and training on the statistical issues surrounding establishing a causal link between reported adverse events and prior treatment with an HIV drug/medical device.

Causal inference, originally developed for epidemiology studies, considers statistical methods for estimation and inference related to causal effects and applies to both observational and randomized studies. 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 principle objective of this study was to provide statistical consultation and training to FDA review staff 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 provided expertise with respect to statistical programming, data analyses, and training for FDA staff.



Two core components included:

- **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
- **Tyagacil data analysis and simulation study:** Design and implementation to demonstrate effects of missingness on estimator performance in safety analysis with rare outcomes

This project involved providing statistical consultation and training on causal inference methodologies; developing methodologies for analyzing safety data in HIV trials; providing comparison of methods; conducting trainings; advising, facilitating, and assisting in providing consultation, statistical programming, and data analyses applicable to HIV data; and drafting a technical report on the statistical methods and analysis results.

Core Activities

Secondary Data Analysis and Simulations

Products

The final report is entitled "Causal Inference Methodology and Its Application in Evaluation Efficacy and Safety of Drugs." (July 2010)