Causal Inference
in
Biomedical Research

BSTA 790

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Tuesday and Thursday 10:30AM - 12:00 PM

This course will consider approaches to defining and estimating causal effects in a variety of settings. The potential outcomes approach will provide the conceptual framework for the concepts of causality developed here, although we will briefly consider alternatives. Topics to be considered include: the definition of effects of scalar or point treatments, nonparametric bounds on effects, identifying assumptions and estimation in simple randomized trials, simple observational studies and alternative methods of inference and controlling confounding, propensity scores, sensitivity analysis for unmeasured confounding, graphical models, instrumental variables estimation, joint effects of multiple treatments, direct and indirect effects, intermediate variables and effect modification, randomized trials with simple noncompliance, principal stratification, effects of time-varying treatments, time-varying confounding in observational studies and randomized trials, nonparametric inference for joint effects of treatments, marginal structural models, structural nested models, and surrogate outcomes.

There is no required text to purchase; readings will come largely from journal articles in the statistics, biostatistics, and epidemiology literature, as well as from the book Hernan and Robins (HR), 2009, Causal Inference, Chapman and Hall/CRC.

There will be weekly homeworks, a final project, and possibly a final exam. Class participation is expected and will be part of the grade.

Outline of causality course:

Introduction/Goals of course

I. The effects of a single treatment: definition and estimation

A. Potential outcomes and the definition of effects of scalar or point treatments

1. Required reading:
   a. Holland P. Statistics and causal inference (with discussion). Journal of the American Statistical Association 1986;81:945-70.
   b. HR, Chapter 1.

B. Nonparametric bounds on treatment effects

1. Required reading:
   a. Manski CF. Nonparametric bounds on treatment effects. American Economic Review Papers and Proceedings 1990;80:319-23.

C. Simple randomized trials: identifying assumptions and estimation

1. Required reading
   a. Holland P. Statistics and causal inference (with discussion). Journal of the American Statistical Association 1986;81:945-70.

D. Simple observational studies: ignorability and confounding

1. Required reading
   a. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. Biometrika 1983;70:41-55.

   b. Greenland S, Robins JM. Identifiability, exchangeability, and epidemiological confounding. International Journal of Epidemiology 1986;15:412-8.

E. Standard approaches to controlling confounding
1. Standard modeling/stratified methods
   a. Required reading
2. Confounding, collapsibility, and effect modification
   a. Required reading:
      (1) Greenland S, Robins JM. Identifiability, exchangeability, and epidemiological confounding. International Journal of Epidemiology 1986;15:412-8.

F. Propensity score-based methods for controlling confounding

1. The propensity score and its properties
   a. Required reading
      (1) Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. Biometrika 1983;70:41-55.
2. Propensity scores: standard adjustment
   a. Required reading
      (1) Rosenbaum PR, Rubin DB. Reducing bias in observational studies using subclassification on the propensity score. Journal of the American Statistical Association 1984;79:516-24.
   b. Suggested reading
      (1) Joffe M, Rosenbaum P. Propensity Scores. American Journal of Epidemiology 1999;150:327-33.
3. Weighted estimation/marginal structural models
   a. Required reading:
      (1) Rosenbaum PR. Model-based direct adjustment. Journal of the American Statistical Association 1987;82:387-94.
      (2) Joffe MM et al. Model Selection, Confounder Control, and Marginal Structural Models: Review and New Applications. American Statistician 2004.
   b. Suggested reading
      (1) Hirano and Imbens, 04
4. Semiparametric models for treatment effect/testing ignorability
   a. Required reading:
      (1) Rosenbaum PR. From association to causation in observational studies: the role of tests of strongly ignorable treatment assignment. Journal of the American Statistical Association 1984;79:41-8.
   b. Suggested reading:
      (1) Joffe MM, Brensinger C. Administrative and Artificial Censoring in Censored Regression Models. Statistics in Medicine 2001;20:2287-304.

G. Sensitivity analysis for unmeasured confounding

1. Required reading:
   a. Rosenbaum (suggest reference)
   b. Cornfield J et al. Smoking and lung cancer: recent evidence and a discussion of some questions. Journal of the National Cancer Institute 1959;22:173-203.
   c. Greenland S. Basic methods for sensitivity analysis of biases.

International Journal of Epidemiology 1996;25:1107-16.

H. Graphical models and criteria for confounding
   1. Required reading:
      a. Greenland S, Pearl J, Robins J. Causal Diagrams for Epidemiologic Research. Epidemiology 1999;10:37-48.

   2. Suggested reading:
      a. Pearl J. Causal diagrams for empirical research. Biometrika 1995;83:669-90.

I. Instrumental variables estimation
   1. Required reading:
      a. McClellan M, McNeil BJ, Newhouse JP. Does more intensive treatment of acute myocardial infarction in the elderly reduce mortality. Journal of the American Medical Association 1994;272:859-66.
      b. Suggestion from Dylan

II. The effects of multiple treatments

A. Defining effects
   1. Robins J. A graphical approach to the identification and estimation of causal parameters in mortality studies with sustained exposure periods. J.Chron.Dis. 40:139S-161S, 1987.

B. Direct and indirect effects
   1. Required reading:
      a. Pearl J. Direct and indirect effects. Proceedings of the Seventeenth Conference on Uncertainty in Artificial Intelligence. San Francisco: Morgan Kaufmann, 2001:411-20.

C. Intermediate variables
   1. Required reading:
      a.

D. Randomized trials with simple noncompliance
   1. Required reading:
      a. Angrist JD, Imbens GW, Rubin DB. Identification of causal effects using instrumental variables (with discussion). Journal of the American Statistical Association 1996;91:444-72.
      b. Imbens GW, Rubin DB. Bayesian inference for causal effects in randomized experiments with noncompliance. Annals of Statistics 1997;25:305-27.
      c. Joffe MM, Brensinger C. Weighting in instrumental variables and

G-estimation. Statistics in Medicine 2003;22:1285-303.

E. Principal stratification
   1. Required reading:
      a. Frangakis CE, Rubin DB. Principal stratification in causal inference. Biometrics 2002;58:21-9.
      b. Gilbert et al.

F. Time-varying confounding in observational studies and randomized trials
   1. Required reading:
      a. Robins J. A graphical approach to the identification and estimation of causal parameters in mortality studies with sustained exposure periods. J.Chron.Dis. 40:139S-161S, 1987.

G. Nonparametric inference for joint effects of treatments
   1. Required reading:
      a. Robins J. A graphical approach to the identification and estimation of causal parameters in mortality studies with sustained exposure periods. J.Chron.Dis. 40:139S-161S, 1987.
   2. Suggested reading
      a. Robins J. The control of confounding by intermediate variables. Statistics in Medicine 1989;8:679-701.

H. Marginal structural models
   1. Required reading:
      a. Hernan MA, Brumback B, Robins JM. Marginal structural models to estimate the causal effect of zidovudine on the survival of HIV-positive men. Epidemiology 2000;11:561-70.
   2. Suggested reading:
      a. Robins JM, Hernan MA, Brumback B. Marginal structural models and causal inference in epidemiology. Epidemiology 2000;11:550-60.
      b. Brumback BA et al. Sensitivity analyses for unmeasured confounding assuming a marginal structural model for repeated measures. Statistics in Medicine 2004;23:749-67.

I. Structural nested models
   1. Required reading:
      a. Robins JM et al. G-estimation of the effect of prophylaxis therapy for pneumocystic carinii pneumonia on the survival of AIDS patients. Epidemiology 1992;3:319-36.
      b. Robins JM, Rotnitzky A, Scharfstein DO. Sensitivity analysis for selection bias and unmeasured confounding in missing data and causal inference models. In: Halloran E, Berry D, eds. Statistical Models in Epidemiology. New York: Springer-Verlag, 2000:1-99.

2. Suggested reading:
    a. Joffe MM et al. Estimating the effect of zidovudine on Kaposi's sarcoma using a rank preserving structural failure-time model. Statistics in Medicine 1998;17:1073-102.

J. Optimal dynamic treatment regimes
1. Required reading:
    a. Murphy et al.
2.

III. Suggested reference books:
A. Pearl J. Causality: models, reasoning, and inference. Cambridge University Press, 2000.
B. Rothman KJ, Greenland S. Modern Epidemiology. Philadelphia: Lippincott-Raven, 1998.
C. Rosenbaum PR. Observational Studies. New York: Springer-Verlag, 1995.
D. van der Laan MJ, Robins JM. Unified Methods for Censored Longitudinal Data and Causality. New York: Springer, 2003.

IV. Other books:
A. Shafer G. The art of causal conjecture. Cambridge: The MIT Press, 1996.