STA 790 (Fall 2022) — Bayesian Causal Inference

Chapter 5: Sensitivity Analysis

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Assessing Assumptions

- Two key assumptions in causal inference with observational data: overlap (a.k.a. positivity) and unconfoundedness
- Overlap is on the observed data, testable
- Unconfoundedness is inherently untestable
- Prudent to perform some sensitivity analysis to assess how sensitive the causal analysis if unconfoundedness is violated
- Balance is not an assumption, but closed related to both overlap and unconfoundedness, should always be checked

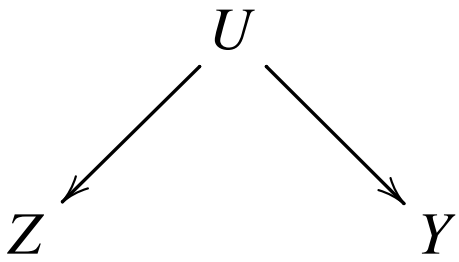
Sensitivity analysis

- Sensitivity analysis aims at assessing how sensitive the causal effect estimates when the unconfoundedness assumption is assumed to fail in some specific and meaningful ways
- Sensitivity is not testing – unconfoundedness is intrinsically non-testable, more of a "insurance" check
- Sensitivity analysis in causal inference dates back to the Hill-Fisher debate on causation between smoking and lung cancer, and first formalized in Cornfield (1959, JNCI)

Smoking and Lung Cancer: Revisited

Cornfield et al. (1959 JNCI)

Common cause hypothesis



- Smoking Z
- Lung cancer Y
- Genetic factor U

- Fisher argued the association between smoking and lung cancer may be due to a common gene that causes both
- Cornfield showed: assuming Fisher is right, the smoking-gene association must satisfy:

$$\mathrm{RR}_{ZU} \geq \mathrm{RR}_{ZY}^{\mathrm{obs}} \approx 9$$

- Such a genetic confounder is too strong to be realistic
- Thus, association must be causal

Sensitivity Analysis since Cornfield et al. (1959)

An incomplete review

Epidemiology

- Bross (1966, 1967)
- Schlesselman (1978)
- Flanders and Khoury (1990)
- Poole (2010)
- Lee (2011)
- MacLehose et al. (2005, bounds)
- Ding and VanderWeele (2014, 2016, 2016)

Statistics and Econometrics

- Rosenbaum and Rubin (1983, JRSSB)
- Yanagawa (1984)
- Lin et al. (1998)
- Rosenbaum (2002, book)
- Imbens (2003 AER)
- Ichino et al. (2008, JAE)
- Manski (1990 AER, bounds)

Sensitivity analysis

Rosenbaum and Rubin (1983, JRSS-B)

- Fundamental idea: check what would happen had there was one unmeasured confounder?
- Central assumption: the assignment to treatment is not unconfounded given the set of observed covariates X, i.e.,

$$\Pr(Z|Y(0), Y(1), X) \neq \Pr(Z|X)$$

but uncounfoundedness holds given X and an unobserved binary covariate U (latent unconfoundedness)

$$\Pr(Z|Y(0), Y(1), X, U) = \Pr(Z|X, U)$$

Model-based sensitivity analysis

Rosenbaum and Rubin (1983, JRSS-B)

- Given these assumptions, specify a set of parameters characterizing the distribution of U and the association of U with Z, $Y(1)$ and $Y(0)$ given observed covariates
- Binary outcome Y, binary treatment Z, and one binary unmeasured confounder U
- One categorical covariate X ($x = 1, \ldots, k$) - think of subclass of propensity score
- Decompose the joint distribution:

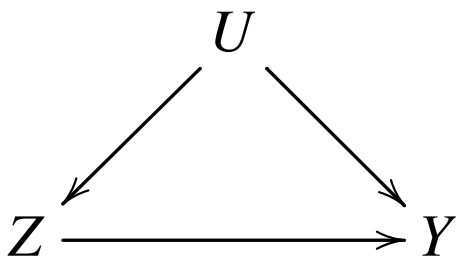
$$\Pr(Y(1), Y(0), Z, X, U) = \Pr(Y(1), Y(0) | X, U) \Pr(Z | X, U) \Pr(U | X) \Pr(X)$$

Model-based sensitivity analysis

Rosenbaum and Rubin (1983, JRSS-B)

Within strata of

- covariates
- propensity scores



- Confounder $U \sim \text{Bern}(\pi)$
- Assignment mechanism model:

$$\text{logit}\ \Pr(Z = 1 \mid u) = \gamma + \alpha u$$

- Outcome model:

$$\text{logit}\ P\{Y(z) = 1 \mid u\} = \beta_z + \delta_z u$$

- Sensitivity parameters:

$$(\pi, \alpha, \delta_1, \delta_0)$$

Model-based sensitivity analysis

Rosenbaum and Rubin (1983, JRSS-B)

- Interpret the parameters:
  - $\alpha = \log\left[\frac{\Pr(Z=1|U=1)/\Pr(Z=0|U=1)}{\Pr(Z=1|U=0/\Pr(Z=0|U=0)}\right]$: log odds ratio between Z and U
  - $\delta_z = \log\left[\frac{\Pr(Y(z)=1|U=1)/\Pr(Y(z)=0|U=1)}{\Pr(Y(z)=1|U=1)/\Pr(Y(z)=0|U=1)}\right]$: log odds ratio between $Y(z)$ and U
- In practice, the the parameters is all conditioning on X or propensity scores
- For parsimony, often assume the parameters α, δ are constant across strata of X or PS

Model-based sensitivity analysis

Rosenbaum and Rubin (1983, JRSS-B)

Sensitivity parameters

- U is not observed, the above models are not identifiable
- The parameters $\pi, \alpha, \delta_0, \delta_1$ can be viewed as sensitivity parameters
- Treatment effects can still be estimated by fixing the values of $\pi, \alpha, \delta_0, \delta_1$
- Rosenbaum and Rubin maximized the full likelihood of the two logistic models given the fixed sensitivity parameters (integration bridges observed likelihood and likelihood of full data)

Sensitivity analysis: Procedure

Rosenbaum and Rubin (1983, JRSS-B)

1. Set $\pi, \alpha, \delta_0, \delta_1$ to a grid of possible values (boundary are the most extreme values deemed plausible substantively)
2. Estimate treatment effect for each grid point
3. Assess the variability of these values: If conclusions are relatively insensitive over a range of plausible assumptions about U, causal inference is more defensible

One can also identify the boundary of the sensitivity parameters where the treatment effect reduces to null (explained away)

Bayesian sensitivity analysis

Dorie et al. (2016, Stat Med)

- Dorie et al. (2016) extended Rosenbaum and Rubin's model-based SA: same factorization
  - Instead of integrating U out in estimation, generate U for all units $U \sim Bern(\pi)$
  - A logistic model for $Z|X, U \sim Bern(\Phi(\beta X + \delta_z U))$
  - Assume a BART model for the outcome $\Pr(Y|Z, X, U)$

$$Y|Z, X, U \sim N(\mu_{xz} + \delta_y U, \sigma^2), \quad \mu_{xz} \sim BART(X, Z)$$

  - Draw the posterior of the model parameters and thus causal estimates given fixed value of the sensitivity parameters $(\delta_y, \delta_z, \pi)$ and simulated U
  - Repeat for a grid of sensitivity parameters

Bayesian sensitivity analysis

- Without unconfoundedness, two strategies
  - Model $\Pr\{Z_i \mid Y_i(0), Y_i(1), X_i; \theta_Z\}$, or
  - Assume $\Pr(Z_i \mid Y_i(0), Y_i(1), X_i, U_i\} = \Pr(Z_i \mid X_i, U_i)$ for some unmeasured U_i, and model $\Pr(Z_i \mid X_i, U_i; \theta_Z)$ (e.g. RR83, Dorie et al.)

- Challenges arise in both strategies because θ_Z is not fully identifiable due to the unobserved potential outcomes or U_i

- We must conduct SA with respect to weakly identifiable or unidentifiable parameters

- Therefore, in model-based SA, boundary between model checking and sensitivity to unconfoundedness is often blurred (Franks et al. 2018)

Bayesian sensitivity analysis

Franks et al. (2018, JASA)

- Propose to separate the identified and unidentified parts of the sensitivity model
- Used a special parameterization: Tukey's factorization

$$f(Y(z), Z|X;\psi) = f^{obs}(Y(z)|Z=z,X)\, f(Z=z|X)\, \frac{f(Z|Y(z),X;\psi)}{f(Z=z|Y(z),X;\psi)}$$

  - the first two factors constitute the observed data density, nonparametrically identified
  - the final factor is determined by the selection function, unidentified but easily interpreted
- The selection function determines the relationship between the dist of observed outcome vs. missing outcomes

Bayesian sensitivity analysis

Franks et al. (2018, JASA)

- Tukey's factorization implies a (conditional) copula that characterizes the dependence between potential outcomes

$$c(F(f(Y(0)|Z,X), f(Y(1)|Z,X))|Z,X) = \frac{f(Y(1),Y(0)|Z,X)}{f(Y(0)|Z,X)f(Y(1)|Z,X)}$$

  $f(Y(0)|Z,X)$ and $f(Y(1)|Z,X)$ are identifiable, but the copula is not

- Implementation:
  - estimate the two marginal models from observed data
  - use a copula to connect the two marginals and check sensitivity

Model-based sensitivity analysis: Limitations

- To conduct sensitivity analysis, one needs additional un-testable assumptions about confounding:
  - Outcome model: even Bayesian nonparametric models place very strong structures to the data
  - Distribution of the unmeasured confounder: not testable
  - One binary unmeasured confounder, otherwise we have a large number of sensitivity parameters. Justification
    - One confounder: can consider all unmeasured confounders are summarized into one dimension, similar to propensity scores
    - Binary confounder: causal conclusions are more sensitive to unobserved binary covariates than (normal) continuous unobservables (Wang and Krieger, 2005)
- Still, not appealing: fitting is complex, additional assumptions. After all, SA is a secondary analysis

SA without assumptions: Rosenbaum's bounds

Rosenbaum, 2002, Observational Studies

- In a series of papers, Rosenbaum modified RR1983, developed a SA framework based on bounds
- Only one sensitivity parameter – the association between Z and U, i.e. design sensitivity, no assumption on the outcome model
  - Basic idea: assume the odds ratio (OR) between Z and U is bounded with a parameter Γ (recall the logistic model of $Z|U$ in RR1983)

$$\frac{1}{\Gamma} \leq \frac{\Pr(Z=1|U=1)/\Pr(Z=0|U=1)}{\Pr(Z=1|U=0/\Pr(Z=0|U=0)} \leq \Gamma$$

    i.e. $-\log\Gamma \leq \log OR \leq \log\Gamma$

  - For a given estimator, find the lower and upper bound of the estimate given the sensitivity range specified by Γ – an optimization problem

SA without assumptions: Rosenbaum's bounds

Rosenbaum, 2002, Observational Studies

- Key in implementation: starting with a matched sample to mimic a randomized experiment
- The original proposal (Rosenbaum, 1987) was under the Fisher's randomization inference framework:
  - Permute the assignment vector in the matched sample given Γ
  - Calculate the value of a specific estimator (e.g. difference-in-means) under each permutation
  - Repeat this for many Γ values. Answer: "with what Γ value, the p-value of the randomization-based causal conclusions changes from significant to non-significant (or vice versa)?
- Later generalize beyond randomization-based inference: derive bounds for a given estimator given the sensitivity range specified by Γ

Sensitivity Analysis

- To summarize, many sensitivity analysis (SA) techniques often require additional untestable assumptions, e.g. the outcome model, the distribution of U
- Barrier to practice: usually hard to implement, not widely used
- Rosenbaum's bounds framework makes fewer assumptions, but still not easy to implement
- VanderWeele and co-authors since 2014: Sensitivity analysis without assumptions – the E-value. The dominant method in practice now.

Sensitivity Analysis Without Assumptions: the E-value

VanderWeele and Ding (2017; Annals of Internal Medicine)

- Core idea: Sharpen the original Cornfield inequality, free of assumptions on the unmeasured confounder, only one sensitivity parameter
- Main theory and technique built in Ding and VanderWeele (2014, 2016, Biometrika; 2016 Epidemiology)
- Definition of the E-value (2017; Annals of Internal Medicine)
  - *The E-value represents the minimum strength of association, on the RR scale, that an unmeasured confounder would need to have with both the treatment and outcome to fully explain away a specific treatment-outcome association, conditional on the measured covariates*
- Assumption free, clean interpretation and simple calculation

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