Causal inference using the g-formula in Stan

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# Presentation information

https://github.com/lcomm/stancon2018

You'll find:

- These slides
- A document with more details on motivation and implementation
- Stan code files for all models shown here

Crash course on causal inference

- Goal: learn about causal mechanisms using observational data
- Why?
  - Useful for identifying targets for policy intervention
  - Can create projections for what *would* occur after some policy change
  - Need to make decisions even when conclusive data are not available
- Caveats:
  - Correlation still $\neq$ causation; more about formalizing *what would be necessary* for that to hold
  - Not going to be very rigorous today

The potential outcomes framework
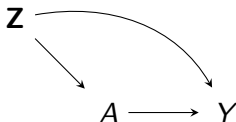
- ▶ Some treatment or exposure A
- ▶ Outcome of interest is Y
- ▶ Under some assumptions, the **potential outcome** Y_a is the value Y would take on if A were set to a
- ▶ For binary A:
    - ▶ Average treatment effect: $\mathbb{E}[Y_1 - Y_0]$
    - ▶ Average treatment effect on treated: $\mathbb{E}[Y_1 - Y_0 | A = 1]$
- ▶ Often need to adjust for a set of baseline confounders $\mathbf{Z}$

The g-formula for standardization

$$\textbf{g-formula:} \quad \mathbb{E}\left[Y_a\right] = \sum_{\mathbf{z}} \mathbb{E}\left[Y | A = a, \mathbf{Z} = \mathbf{z}\right] P(\mathbf{Z} = \mathbf{z})$$

- This requires no unmeasured confounding given $\mathbf{Z}$: $Y_a \perp\!\!\!\perp A | \mathbf{Z}$
- Average treatment effect of changing A from a to a^* for whole population: $\mathbb{E}\left[Y_{a^*}\right] - \mathbb{E}\left[Y_a\right]$
- Common (frequentist) approach is to adopt parametric models for $Y | A, \mathbf{Z}$ and use empirical distribution of $\mathbf{Z}$ for $P(\mathbf{Z} = \mathbf{z})$
- Frequentist bootstrap used for inference

A Bayesian version of the g-formula

Adopting parametric models indexed by $\boldsymbol{\theta}$, the Bayesian g-formula is:

$$p(\tilde{y}_a|o) = \int \int p(\tilde{y}|a, \tilde{\mathbf{z}}, \theta) p(\tilde{\mathbf{z}}|\boldsymbol{\theta}) p(\boldsymbol{\theta}|o) d\boldsymbol{\theta} d\tilde{\mathbf{z}}$$

- $p(\tilde{y}_a|o)$
    - Distribution of Y we would expect to see if A were set to a in some population with same:
        - Underlying confounder distribution (comparability)
        - Data-generating parameters (causal transportability)
- This integrates over uncertainty in $\boldsymbol{\theta}$
- Causal estimands usually compare means of $p(\tilde{y}_1|o)$ and $p(\tilde{y}_0|o)$
- See paper by Keil et al for more details (Keil et al. 2015)

Causal inference with Stan

Two components to Bayesian causal inference with the g-formula:

- ▶ Get posterior samples of parameters θ
  - ▶ Learn from data in `data` block
  - ▶ Fit parametric models in `model` block

- ▶ Do causal inference using posterior predictive draws of potential outcomes
  - ▶ Use confounder distribution from `data` block (may or may not be same data used to fit the model)
  - ▶ Sample potential outcomes in the `generated quantities` block

A simple example
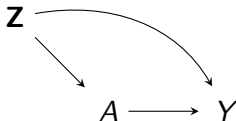
- Nothing in particular assumed about distribution of **Z**
- Binary A
- Binary Y

Simple example: model

Assume Y is generated according to logistic model:

$$\mathrm{logit}\left(P(Y_i = 1 | A_i, Z_i)\right) = \alpha_0 + \alpha_A A_i + \boldsymbol{\alpha}'_Z \mathbf{Z}_i$$

Simple example: code

```
data {
  // number of observations
  int<lower=0> N;
  // number of columns in design matrix excluding A
  int<lower=0> P;
  // design matrix, excluding treatment A
  matrix[N, P] X;
  // observed treatment
  vector[N] A;
  // outcome
  int<lower=0,upper=1> Y[N];
}
```

Simple example: code

```
transformed data {
  // make vector of 1/N for (classical) bootstrapping
  vector[N] boot_probs = rep_vector(1.0/N, N);
}
```

Simple example: code

```
parameters {
  // regression coefficients
  vector[P + 1] alpha;
}

transformed parameters {
  vector[P] alphaZ = head(alpha, P);
  real alphaA = alpha[P + 1];
}
```

Simple example: code

```
model {
  // priors for regression coefficients
  alpha ~ normal(0, 2.5);

  // likelihood
  Y ~ bernoulli_logit(X * alphaZ + A * alphaA);
}
```

Simple example: code

```
generated quantities {
  // row index to be sampled for bootstrap
  int row_i;

  // calculate ATE in the bootstrapped sample
  real ATE = 0;
  vector[N] Y_a1;
  vector[N] Y_a0;
  for (n in 1:N) {
    // sample baseline covariates
    row_i = categorical_rng(boot_probs);

    // sample Ya where a = 1 and a = 0
    Y_a1[n] = bernoulli_logit_rng(X[row_i] * alphaZ + alphaA);
    Y_a0[n] = bernoulli_logit_rng(X[row_i] * alphaZ);

    // add contribution of this observation to the ATE
    ATE = ATE + (Y_a1[n] - Y_a0[n])/N;
  }
}
```

Simple example: more on the ATE calculation

- Remember: we want $\mathbb{E}[Y_1] - \mathbb{E}[Y_1]$, which marginalizes over **Z**
- Weighted average of causal effects for different **Z** values (like $P(\mathbf{Z} = \mathbf{z})$ in the frequentist g-formula)
- On average, bootstrapped data sets will have same $P(\mathbf{Z} = \mathbf{z})$ as in the main data set

Switching gears: mediation analysis

$$A \longrightarrow M \longrightarrow Y$$
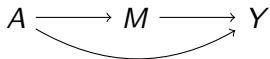
- ▶ Mediation analysis seeks to understand more about causal mechanisms of actions
- ▶ For every causal intermediate ("mediator") M, we can decompose the total effect of an exposure into two parts:
  - ▶ Part mediated by M (natural indirect effect; NIE)
  - ▶ Part enacted through other pathways (natural direct; NDE)
- ▶ Policymakers want to target the causal paths with biggest impact

A mediation example
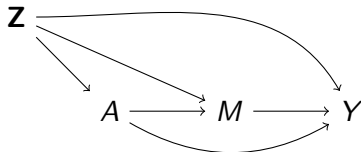
- Nothing in particular assumed about distribution of **Z**
- Binary treatment A
- Binary mediator M
- Binary outcome Y

Mediation: models

Assume M and Y are generated according to logistic models:

$$\text{logit}\left(P(M_i = 1 | A_i, Z_i)\right) = \beta_0 + \boldsymbol{\beta}_Z' \mathbf{Z}_i + \beta_A A_i$$

$$\text{logit}\left(P(Y_i = 1 | A_i, M_i, Z_i)\right) = \alpha_0 + \boldsymbol{\alpha}_Z' \mathbf{Z}_i + \alpha_A A_i + \alpha_M M_i$$

Mediation: code

Changes to data and model blocks are the addition of a model for *M*

```
data {
  ...
  vector[P + 1] beta_m;
  cov_matrix[P + 1] beta_vcv;
  ...
}
...
model {
  ...
  M ~ bernoulli_logit(X * betaZ + A * betaA);
  Y ~ bernoulli_logit(X * alphaZ + A * alphaA + Mv * alphaM);
  ...
}
```

Mediation: code

Calculation of NDE is done in `generated quantities` block:

```
// calculate NDE in the bootstrapped sample
real NDE = 0;
...
for (n in 1:N) {
  ...
  // sample Ma where a = 0
  M_a0[n] = bernoulli_logit_rng(X[row_i] * betaZ);

  // sample Y_(a=1, M=M_0) and Y_(a=0, M=M_0)
  Y_a1Ma0[n] = bernoulli_logit_rng(X[row_i] * alphaZ +
                                   M_a0[n] * alphaM + alphaA);
  Y_a0Ma0[n] = bernoulli_logit_rng(X[row_i] * alphaZ +
                                   M_a0[n] * alphaM);

  // add contribution of this observation to the bootstrapped NDE
  NDE = NDE + (Y_a1Ma0[n] - Y_a0Ma0[n])/N;
}
```

Data integration for unmeasured confounding

- ▶ Policymakers usually have to make decisions based on available data
- ▶ We rarely have the ideal data set $\rightarrow$ often lack important confounders
- ▶ This is problematic for causal inference
- ▶ Analysts may struggle to communicate the additional uncertainty to the decision maker

Prior information to the rescue

- Thankfully, all is not lost!
- We often have *some* information about the unmeasured confounder in another data source
- We can derive informative priors from the external data source

Revisiting mediation example: new structure
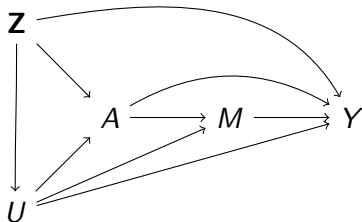
- Now we have an unmeasured binary baseline confounder U

Revisiting mediation example: new models

Assume the following generative models:

$$\text{logit}\left(P(U_i = 1 | \mathbf{Z}_i, A_i)\right) = \gamma_0 + \boldsymbol{\gamma}'_Z \mathbf{Z}_i$$

$$\text{logit}\left(P(M_i = 1 | \mathbf{Z}_i, A_i, U_i)\right) = \beta_0 + \boldsymbol{\beta}'_Z \mathbf{Z}_i + \beta_U U_i + \beta_A A_i$$

$$\text{logit}\left(P(Y_i = 1 | A_i, Z_i, U_i, M_i)\right) = \alpha_0 + \boldsymbol{\alpha}'_Z \mathbf{Z}_i + \alpha_U U_i + \alpha_A A_i + \alpha_M M_i$$

Marginalization over unmeasured confounder

- Full data likelihood (i.e., if U were measured)

$$\prod_{i=1}^{n} f(y_i|\boldsymbol{\alpha}, \mathbf{z}_i, a_i, m_i, u_i) f(m_i|\boldsymbol{\beta}, \mathbf{z}_i, a_i, u_i) f(u_i|\boldsymbol{\gamma}, \mathbf{z}_i)$$

- Marginalizing likelihood over binary U

$$\prod_{i=1}^{n} \left[\sum_{u=0}^{1} f(y_i|\boldsymbol{\alpha}, \mathbf{z}_i, a_i, m_i, u_i = u) f(m_i|\boldsymbol{\beta}, \mathbf{z}_i, a_i, u_i = u) P(U_i = u|\boldsymbol{\gamma}, \mathbf{z}_i) \right]$$

Incorporation of prior information

Obviously, parameters involving U are unidentifiable in the original data set

- ▶ Fit maximum likelihood models in supplemental
- ▶ Use MLE from external data as priors in main analysis
    - ▶ Point estimates as prior means
    - ▶ Variance-covariance matrices as prior variances on parameter vectors
- ▶ Other data integration possibilities exist, but this one:
    - ▶ Sidesteps data privacy concerns that hinder data sharing
    - ▶ Keeps interpretability of confounder distribution

Unmessured confounding in mediation: code

Likelihood in model block becomes a mixture:

```
// likelihood
for (n in 1:N) {
  // contribution if U = 0
  ll_0 = ...;

  // contribution if U = 1
  ll_1 = ...;

  // contribution is summation over U possibilities
  target += log_sum_exp(ll_0, ll_1);
}
```

Unmeasured confounding in mediation: code

Informative priors (based on R model fits) are passed in as data

```
model {
  ...
  // informative priors
  alpha ~ multi_normal(alpha_m, alpha_vcv);
  beta  ~ multi_normal(beta_m, beta_vcv);
  gamma ~ multi_normal(gamma_m, gamma_vcv);
  ...
}
```

Unmeasured confounding in mediation: code

Recreating the data-generating sequence $\mathbf{Z} \to U \to A \to M \to Y$

```
for (n in 1:N) {
  // sample U
  U[n] = bernoulli_logit_rng(pU1[n]);

  // sample M_a where a = 0
  M_a0[n] = bernoulli_logit_rng(X[n] * betaZ + U[n] * betaU);

  // sample Y_(a=0, M=M_0) and Y_(a=1, M=M_0)
  Y_a0Ma0[n] = bernoulli_logit_rng(X[n] * alphaZ + M_a0[n] * alphaM +
                                   U[n] * alphaU);
  Y_a1Ma0[n] = bernoulli_logit_rng(X[n] * alphaZ + M_a0[n] * alphaM +
                                   alphaA + U[n] * alphaU);
  ...
}
```

Summary

- ▶ Bayesian causal inference with the parametric g-formula is a powerful tool
- ▶ The `generated quantities` block allows us to sample potential outcomes for new observations based on model for data
- ▶ Prior information is a nice way to integrate data sources and perform informed sensitivity analyses

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References

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