StanCon 2018: Causal inference with the g-formula in Stan

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9/7/2017

Causal inference

In the Rubin Causal Model, causal inference relies on contrasts of counterfactuals, also called potential outcomes. Say we have an outcome of interest Y, and changing the distribution of some treatment or exposure A causally affects the distribution of Y. The directed acyclic graph depicting this scenario is shown in Figure 1.

Figure 1: The simplest causal model

We call the value that Y_a would take the *potential outcome* under the regime $A = a$. If A is binary, $\mathbb{E}[Y_1 - Y_0]$ is the population average treatment effect (ATE) of changing A from 0 to 1 for every individual in the population. From a data set of size n, we might choose to model this with a logistic regression:

$$\text{logit}\left(P(Y_i = 1|A_i)\right) = \alpha_0 + \alpha_A A_i$$

This corresponds to a model for the potential outcomes Y_a for $a \in \{0, 1\}$:

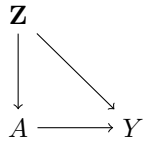
$$\mathbb{E}[Y_a] = \text{logit}^{-1}\left(\alpha_0 + \alpha_A a\right)$$

Then

$$\widehat{ATE} = \widehat{\mathbb{E}}[Y_1 - Y_0] = \text{logit}^{-1}\left(\hat{\alpha}_0 + \hat{\alpha}_A\right) - \text{logit}^{-1}\left(\hat{\alpha}_0\right)$$

Suppose we have measured counfounders $\mathbf{Z}$ and the true causal diagram looks like the one in Figure 2 below.

Figure 2: A simple causal model with exposure-outcome confounders



In the case of confounding by a vector of covariates $\mathbf{Z}$, we can add the confounders to the regression model, in which case the estimated average treatment effect depends on the distribution of $\mathbf{Z}$.

$$\widehat{ATE} = \widehat{\mathbb{E}}[Y_1 - Y_0] = \frac{1}{n}\sum_{i=1}^{n}\left[\text{logit}^{-1}\left(\hat{\alpha}_0 + \hat{\alpha}_A + \hat{\boldsymbol{\alpha}}_Z'\mathbf{Z}_i\right) - \text{logit}^{-1}\left(\hat{\alpha}_0 + \hat{\boldsymbol{\alpha}}_Z'\mathbf{Z}_i\right)\right]$$

Written another way, we can view this as a standardization over the distribution of Z. In epidemiology, this standardization procedure is known as the g-formula. For discrete $\mathbf{Z}$, this formula can be written as a

$$\widehat{ATE} = \sum_z \left(\hat{P}(Y = 1|A = 1, Z = z) - \hat{P}(Y = 0|A = 1, Z = z)\right)\hat{P}(Z = z)$$

In the Bayesian framework, posterior draws of α_0, α_A, and $\boldsymbol{\alpha}_Z$ may be substituted for frequentist point estimates. To account for uncertainty regarding the distribution of the confounders, one could use a classical or Bayesian bootstrap. Using the classical bootstrap, n new values of $\mathbf{Z}$ would be sampled with replacement from the observed $\mathbf{Z}$ distribution during iteration b of the Markov Chain Monte Carlo. Denoting these resampled values as $\mathbf{Z}^{(1,b)}, \ldots, \mathbf{Z}^{(n,b)}$ and the parameter draws as $\alpha_0^{(b)}$, $\alpha_A^{(b)}$, and $\boldsymbol{\alpha}_0^{(b)}$, we can obtain a posterior draw of the ATE as

$$ATE^{(b)} = \frac{1}{n}\sum_{i=1}^{n}\left[\text{logit}^{-1}\left(\alpha_0^{(b)} + \alpha_A^{(b)} + \boldsymbol{\alpha}^{(b)\prime}\mathbf{Z}^{(i,b)}\right) - \text{logit}^{-1}\left(\alpha_0^{(b)} + \boldsymbol{\alpha}^{(b)\prime}\mathbf{Z}^{(i,b)}\right)\right]$$

Posterior summaries of the ATE can be obtained by taking the mean or quantiles of the $ATE^{(b)}$.

Simulating some data

```
# Simulate simple binary data with confounders situation
simulate_simple <- function(n){
  Z1 <- rbinom(n = n, size = 1, prob = 0.3)
  Z2 <- rbinom(n = n, size = 1, prob = plogis(0 + 0.2*Z1))
  A  <- rbinom(n = n, size = 1, prob = plogis(-1 + 0.7*Z1 + 0.8*Z2))
  Y  <- rbinom(n = n, size = 1, prob = plogis(-0.5 + 1*Z1 + 0.7*Z2 + 1.3*A))
  return(data.frame(Z1, Z2, A, Y))
}

# Simulate a data set
set.seed(456)
simple_df <- simulate_simple(n = 5000)

# Package data for Stan
stan_dat <- list(N = nrow(simple_df),
                 P = 3,
                 X = cbind(1, simple_df$Z1, simple_df$Z2),
                 A = simple_df$A,
                 Y = simple_df$Y)
```

The frequentist point estimate of the ATE in this data set would be 0.27.

```
# Calculate frequentist ATE
ffit1 <- glm(Y ~ 1 + Z1 + Z2 + A, family = binomial(link = "logit"), data = simple_df)
fcoef <- coef(ffit1)
fATE <- mean(plogis(cbind(1, simple_df$Z1, simple_df$Z2, 1) %*% fcoef) -
             plogis(cbind(1, simple_df$Z1, simple_df$Z2, 0) %*% fcoef))
```

A demonstration of the Bayesian g-formula in Stan

The Stan code to obtain the ATE is shown below.

```
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];
}

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

parameters {
  // regression coefficients
  vector[P] alpha;
  real alphaA;
}

model {
  // no priors -> use Stan defaults
  // likelihood
  Y ~ bernoulli_logit(X * alpha + A * alphaA);
}

generated quantities {
  // weights for the bootstrap
  int<lower=0> counts[N] = multinomial_rng(boot_probs, N);

  // calculate ATE in the bootstrapped sample
  real ATE = 0;
  vector[N] Y_a1;
  vector[N] Y_a0;
  for (n in 1:N) {
    // sample Ya where a = 1 and a = 0
    Y_a1[n] = bernoulli_logit_rng(X[n] * alpha + alphaA);
    Y_a0[n] = bernoulli_logit_rng(X[n] * alpha);

    // add this observation's contribution to the bootstrapped ATE
    ATE = ATE + (counts[n] * (Y_a1[n] - Y_a0[n]))/N;
  }
}
```

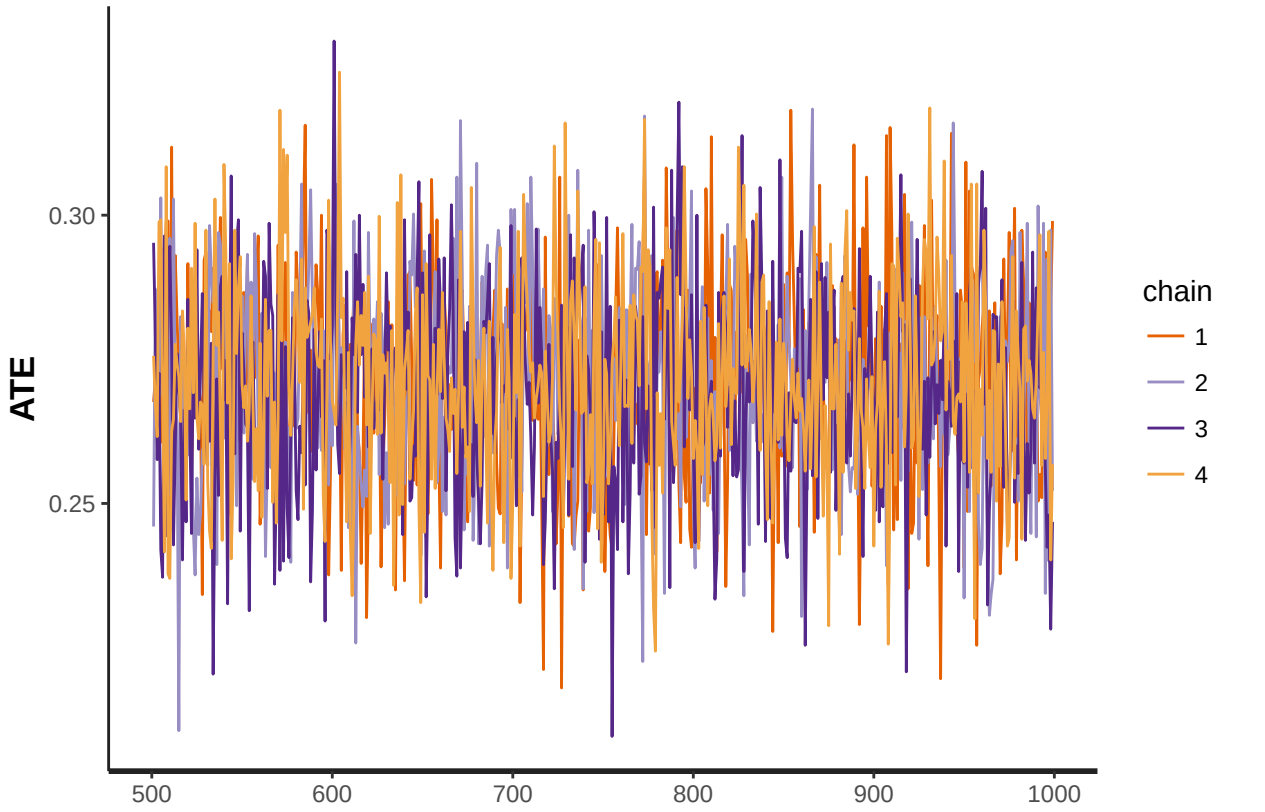
```
# Fit model
suppressPackageStartupMessages(library("rstan"))
rstan_options(auto_write = TRUE, mc.cores = parallel::detectCores())
fit1 <- stan(file = "simple_mc.stan", data = stan_dat, iter = 1000)
```

```
##
## SAMPLING FOR MODEL 'simple_mc' NOW (CHAIN 1).
##
## Gradient evaluation took 0.000779 seconds
## 1000 transitions using 10 leapfrog steps per transition would take 7.79 seconds.
```

```
## Adjust your expectations accordingly!
##
##
## Iteration:   1 / 1000 [  0%]  (Warmup)
## Iteration: 100 / 1000 [ 10%]  (Warmup)
## Iteration: 200 / 1000 [ 20%]  (Warmup)
## Iteration: 300 / 1000 [ 30%]  (Warmup)
## Iteration: 400 / 1000 [ 40%]  (Warmup)
## Iteration: 500 / 1000 [ 50%]  (Warmup)
## Iteration: 501 / 1000 [ 50%]  (Sampling)
## Iteration: 600 / 1000 [ 60%]  (Sampling)
## Iteration: 700 / 1000 [ 70%]  (Sampling)
## Iteration: 800 / 1000 [ 80%]  (Sampling)
## Iteration: 900 / 1000 [ 90%]  (Sampling)
## Iteration: 1000 / 1000 [100%]  (Sampling)
##
##  Elapsed Time: 3.33217 seconds (Warm-up)
##                3.334 seconds (Sampling)
##                6.66618 seconds (Total)
##
##
## SAMPLING FOR MODEL 'simple_mc' NOW (CHAIN 2).
##
## Gradient evaluation took 0.000483 seconds
## 1000 transitions using 10 leapfrog steps per transition would take 4.83 seconds.
## Adjust your expectations accordingly!
##
##
## Iteration:   1 / 1000 [  0%]  (Warmup)
## Iteration: 100 / 1000 [ 10%]  (Warmup)
## Iteration: 200 / 1000 [ 20%]  (Warmup)
## Iteration: 300 / 1000 [ 30%]  (Warmup)
## Iteration: 400 / 1000 [ 40%]  (Warmup)
## Iteration: 500 / 1000 [ 50%]  (Warmup)
## Iteration: 501 / 1000 [ 50%]  (Sampling)
## Iteration: 600 / 1000 [ 60%]  (Sampling)
## Iteration: 700 / 1000 [ 70%]  (Sampling)
## Iteration: 800 / 1000 [ 80%]  (Sampling)
## Iteration: 900 / 1000 [ 90%]  (Sampling)
## Iteration: 1000 / 1000 [100%]  (Sampling)
##
##  Elapsed Time: 3.48222 seconds (Warm-up)
##                3.36602 seconds (Sampling)
##                6.84825 seconds (Total)
##
##
## SAMPLING FOR MODEL 'simple_mc' NOW (CHAIN 3).
##
## Gradient evaluation took 0.000498 seconds
## 1000 transitions using 10 leapfrog steps per transition would take 4.98 seconds.
## Adjust your expectations accordingly!
##
##
## Iteration:   1 / 1000 [  0%]  (Warmup)
```

```
## Iteration: 100 / 1000 [ 10%]  (Warmup)
## Iteration: 200 / 1000 [ 20%]  (Warmup)
## Iteration: 300 / 1000 [ 30%]  (Warmup)
## Iteration: 400 / 1000 [ 40%]  (Warmup)
## Iteration: 500 / 1000 [ 50%]  (Warmup)
## Iteration: 501 / 1000 [ 50%]  (Sampling)
## Iteration: 600 / 1000 [ 60%]  (Sampling)
## Iteration: 700 / 1000 [ 70%]  (Sampling)
## Iteration: 800 / 1000 [ 80%]  (Sampling)
## Iteration: 900 / 1000 [ 90%]  (Sampling)
## Iteration: 1000 / 1000 [100%]  (Sampling)
##
##  Elapsed Time: 3.11816 seconds (Warm-up)
##                3.00939 seconds (Sampling)
##                6.12755 seconds (Total)
##
##
## SAMPLING FOR MODEL 'simple_mc' NOW (CHAIN 4).
##
## Gradient evaluation took 0.000503 seconds
## 1000 transitions using 10 leapfrog steps per transition would take 5.03 seconds.
## Adjust your expectations accordingly!
##
##
## Iteration:   1 / 1000 [  0%]  (Warmup)
## Iteration: 100 / 1000 [ 10%]  (Warmup)
## Iteration: 200 / 1000 [ 20%]  (Warmup)
## Iteration: 300 / 1000 [ 30%]  (Warmup)
## Iteration: 400 / 1000 [ 40%]  (Warmup)
## Iteration: 500 / 1000 [ 50%]  (Warmup)
## Iteration: 501 / 1000 [ 50%]  (Sampling)
## Iteration: 600 / 1000 [ 60%]  (Sampling)
## Iteration: 700 / 1000 [ 70%]  (Sampling)
## Iteration: 800 / 1000 [ 80%]  (Sampling)
## Iteration: 900 / 1000 [ 90%]  (Sampling)
## Iteration: 1000 / 1000 [100%]  (Sampling)
##
##  Elapsed Time: 3.37845 seconds (Warm-up)
##                3.57669 seconds (Sampling)
##                6.95514 seconds (Total)
```

```r
# Traceplot of ATE
traceplot(fit1, pars=c("ATE"))
```




```
# Posterior summary of ATE
summary(extract(fit1)[["ATE"]])
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##  0.2096  0.2592  0.2708  0.2707  0.2828  0.3302
```

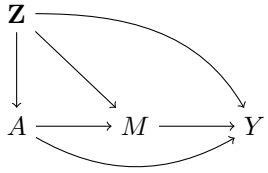
```
# Posterior mean
bATE <- mean(extract(fit1)[["ATE"]])
```

The posterior mean ATE is 0.2707398, which is compatible with the frequentist estimate of 0.2701615.

Another demonstration: the g-formula applied to mediation

Mediators are intermediate variables on the causal path between the exposure and the outcome. Figure 3 shows a causal diagram with an exposure A, a mediator M, outcome Y, and baseline confounders $\mathbf{Z}$.

Figure 3: Basic mediation model with exposure-mediator and exposure-outcome confounders



One potential question in causal inference is the degree to which an effect would remain if we somehow intervened upon part of the downstream causal pathway. This estimand is typically referred to as a natural direct effect (NDE). We simulate data from this scenario below using logistic link models for binary M and Y:

```r
# Function to simulate data for mediation
simulate_simple_med <- function(n){
  Z1 <- rbinom(n = n, size = 1, prob = 0.3)
  Z2 <- rbinom(n = n, size = 1, prob = plogis(0 + 0.2*Z1))
  A  <- rbinom(n = n, size = 1, prob = plogis(-1 + 0.7*Z1 + 0.8*Z2))
  M  <- rbinom(n = n, size = 1, prob = plogis(-2 + 0.3*Z1 + 0.5*Z2 + 1*A))
  Y  <- rbinom(n = n, size = 1, prob = plogis(-2 + 0.4*Z1 + 0.3*Z2 + 0.9*A + 0.9*M))
  return(data.frame(Z1, Z2, A, M, Y))
}

med_df <- simulate_simple_med(n = 5000)

# Package data for Stan
med_dat <- list(N = nrow(med_df),
                P = 3,
                X = cbind(1, med_df$Z1, med_df$Z2),
                A = med_df$A,
                M = med_df$M,
                Y = med_df$Y)
```

The mediator gets added to the outcome model:

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

In addition to the Y model, we also adopt a logistic model for M.

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

These two models can be estimated simultaneously with Stan. Using the resampling of $\mathbf{Z}$ as described earlier, we can draw samples from the distributions of the counterfactuals M_a for $a \in \{0, 1\}$. At the b^{th} MCMC iteration and for $i = 1, \ldots, n$,

$$M_a^{(i,b)} \sim \text{Bernoulli}\left(\text{logit}^{-1}\left(\beta_0^{(b)} + \boldsymbol{\beta}_Z^{(b)}\mathbf{Z}^{(i,b)} + \beta_A a\right)\right)$$

The outcome counterfactuals Y_{aM_a} and $Y_{aM_{a^*}}$ represent the potential outcome values under regime $A = a$ when the mediator M is set to the value it would naturally take under either a or a^*. For example, we may be interested in the hypothetical outcomes if the population were exposed (i.e., all $A = 1$) while the path through M is somehow disabled $M = M_{a=0}$. This contrast is sometimes referred to as a natural direct effect because it captures the effect of A on Y that is "direct" – that is, the effect *not* through the mediator.

$$M_a^{(i,b)} \sim \text{Bernoulli}\left(\text{logit}^{-1}\left(\beta_0^{(b)} + \boldsymbol{\beta}_Z^{(b)}\mathbf{Z}^{(i,b)} + \beta_A a\right)\right)$$

Stan code to fit these models is shown below.

```
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;
```

```
  // observed mediator
  int<lower=0,upper=1> M[N];
  // outcome
  int<lower=0,upper=1> Y[N];
}

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

  // make vector version of M
  vector[N] Mv = to_vector(M);
}

parameters {
  // regression coefficients (outcome model)
  vector[P] alpha;
  real alphaA;
  real alphaM;

  // regression coefficients (mediator model)
  vector[P] beta;
  real betaA;
}

model {
  // no priors -> use Stan defaults
  // likelihoods
  M ~ bernoulli_logit(X * beta + A * betaA);
  Y ~ bernoulli_logit(X * alpha + A * alphaA + Mv * alphaM);
}

generated quantities {
  // weights for the bootstrap
  int<lower=0> counts[N] = multinomial_rng(boot_probs, N);

  // calculate NDE in the bootstrapped sample
  real NDE = 0;
  vector[N] M_a0;
  vector[N] Y_a1Ma0;
  vector[N] Y_a0Ma0;
  for (n in 1:N) {
    // sample Ma where a = 0
    M_a0[n] = bernoulli_logit_rng(X[n] * beta);

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

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

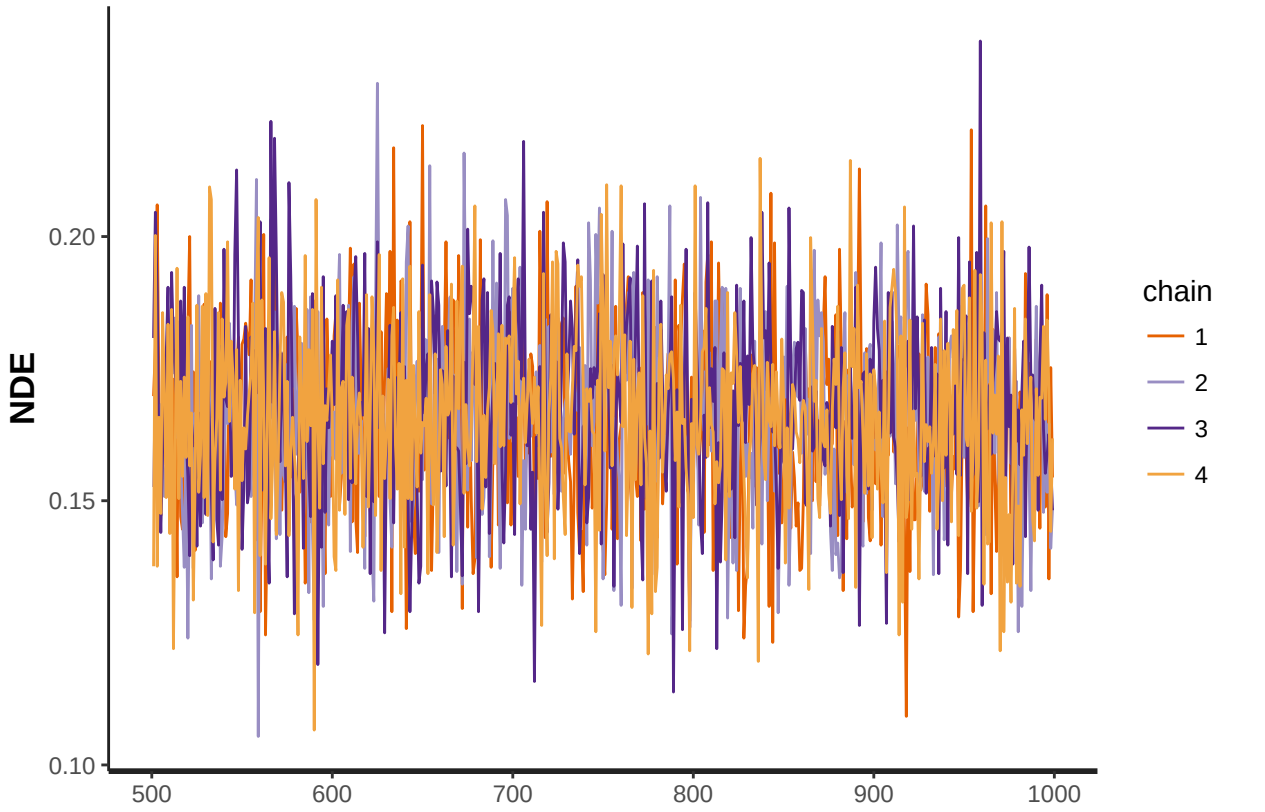
```
}
```

```
library("rstan")
fit2 <- stan(file = "mediation_mc.stan", data = med_dat, iter = 1000)
```

```
##
## SAMPLING FOR MODEL 'mediation_mc' NOW (CHAIN 1).
##
## Gradient evaluation took 0.005179 seconds
## 1000 transitions using 10 leapfrog steps per transition would take 51.79 seconds.
## Adjust your expectations accordingly!
##
##
## Iteration:   1 / 1000 [  0%]  (Warmup)
## Iteration: 100 / 1000 [ 10%]  (Warmup)
## Iteration: 200 / 1000 [ 20%]  (Warmup)
## Iteration: 300 / 1000 [ 30%]  (Warmup)
## Iteration: 400 / 1000 [ 40%]  (Warmup)
## Iteration: 500 / 1000 [ 50%]  (Warmup)
## Iteration: 501 / 1000 [ 50%]  (Sampling)
## Iteration: 600 / 1000 [ 60%]  (Sampling)
## Iteration: 700 / 1000 [ 70%]  (Sampling)
## Iteration: 800 / 1000 [ 80%]  (Sampling)
## Iteration: 900 / 1000 [ 90%]  (Sampling)
## Iteration: 1000 / 1000 [100%]  (Sampling)
##
##  Elapsed Time: 10.8832 seconds (Warm-up)
##                12.0493 seconds (Sampling)
##                22.9325 seconds (Total)
##
##
## SAMPLING FOR MODEL 'mediation_mc' NOW (CHAIN 2).
##
## Gradient evaluation took 0.001364 seconds
## 1000 transitions using 10 leapfrog steps per transition would take 13.64 seconds.
## Adjust your expectations accordingly!
##
##
## Iteration:   1 / 1000 [  0%]  (Warmup)
## Iteration: 100 / 1000 [ 10%]  (Warmup)
## Iteration: 200 / 1000 [ 20%]  (Warmup)
## Iteration: 300 / 1000 [ 30%]  (Warmup)
## Iteration: 400 / 1000 [ 40%]  (Warmup)
## Iteration: 500 / 1000 [ 50%]  (Warmup)
## Iteration: 501 / 1000 [ 50%]  (Sampling)
## Iteration: 600 / 1000 [ 60%]  (Sampling)
## Iteration: 700 / 1000 [ 70%]  (Sampling)
## Iteration: 800 / 1000 [ 80%]  (Sampling)
## Iteration: 900 / 1000 [ 90%]  (Sampling)
## Iteration: 1000 / 1000 [100%]  (Sampling)
##
##  Elapsed Time: 10.5019 seconds (Warm-up)
##                9.42161 seconds (Sampling)
##                19.9235 seconds (Total)
```

```
##
##
## SAMPLING FOR MODEL 'mediation_mc' NOW (CHAIN 3).
##
## Gradient evaluation took 0.001131 seconds
## 1000 transitions using 10 leapfrog steps per transition would take 11.31 seconds.
## Adjust your expectations accordingly!
##
##
## Iteration:   1 / 1000 [  0%]  (Warmup)
## Iteration: 100 / 1000 [ 10%]  (Warmup)
## Iteration: 200 / 1000 [ 20%]  (Warmup)
## Iteration: 300 / 1000 [ 30%]  (Warmup)
## Iteration: 400 / 1000 [ 40%]  (Warmup)
## Iteration: 500 / 1000 [ 50%]  (Warmup)
## Iteration: 501 / 1000 [ 50%]  (Sampling)
## Iteration: 600 / 1000 [ 60%]  (Sampling)
## Iteration: 700 / 1000 [ 70%]  (Sampling)
## Iteration: 800 / 1000 [ 80%]  (Sampling)
## Iteration: 900 / 1000 [ 90%]  (Sampling)
## Iteration: 1000 / 1000 [100%]  (Sampling)
##
##  Elapsed Time: 10.0504 seconds (Warm-up)
##                9.22312 seconds (Sampling)
##                19.2735 seconds (Total)
##
##
## SAMPLING FOR MODEL 'mediation_mc' NOW (CHAIN 4).
##
## Gradient evaluation took 0.001116 seconds
## 1000 transitions using 10 leapfrog steps per transition would take 11.16 seconds.
## Adjust your expectations accordingly!
##
##
## Iteration:   1 / 1000 [  0%]  (Warmup)
## Iteration: 100 / 1000 [ 10%]  (Warmup)
## Iteration: 200 / 1000 [ 20%]  (Warmup)
## Iteration: 300 / 1000 [ 30%]  (Warmup)
## Iteration: 400 / 1000 [ 40%]  (Warmup)
## Iteration: 500 / 1000 [ 50%]  (Warmup)
## Iteration: 501 / 1000 [ 50%]  (Sampling)
## Iteration: 600 / 1000 [ 60%]  (Sampling)
## Iteration: 700 / 1000 [ 70%]  (Sampling)
## Iteration: 800 / 1000 [ 80%]  (Sampling)
## Iteration: 900 / 1000 [ 90%]  (Sampling)
## Iteration: 1000 / 1000 [100%]  (Sampling)
##
##  Elapsed Time: 10.0708 seconds (Warm-up)
##                9.3878 seconds (Sampling)
##                19.4586 seconds (Total)
```

```r
# Traceplot of NDE
traceplot(fit2, pars=c("NDE"))
```




```
# Posterior summary of NDE
summary(extract(fit2)[["NDE"]])
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##  0.1054  0.1542  0.1658  0.1660  0.1780  0.2370
```

Application: data integration in unmeasured confounding

While the above models demonstrate application of the parametric g-formula for mediation in a Bayesian framework, they offer little advantage over existing frequentist methods. However, this need not be true. Suppose that one variable of $\mathbf{Z}$ is not measured in the analysis data set but is measured in a smaller, secondary data source. Denoting this variable with U, we can fit maximum likelihood regression models for U, M, and Y in the secondary data set. The point estimates and variance-covariance matrices from the maximum likelihood fits can serve as the mean and variance of multivariate normal priors.

We can simulate data using the same function as the previous mediation example, renaming Z_2 to U because it is unmeasured. (In our simulated data, $\mathbf{Z}$ will no longer be a vector of covariates, but we keep the more general notation since $\mathbf{Z}$ may be vector-valued.) We also add a model for U, giving model equations

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

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

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

Informative prior distributions are derived from the maximum likelihood point estimates and variance-covariance matrices from the secondary data source. For example, the prior for $\boldsymbol{\gamma} = (\gamma_0, \boldsymbol{\gamma}_Z)'$ would be

$$\boldsymbol{\gamma} \sim \mathcal{MVN}\left(\hat{\boldsymbol{\gamma}}_{MLE}, \widehat{\boldsymbol{\Sigma}}_{MLE}\right)$$

where $\hat{\boldsymbol{\gamma}}_{MLE}$ and $\widehat{\boldsymbol{\Sigma}}_{MLE}$ are the frequentist point estimate and variance-covariance matrix. Analogous priors are adopted for $\boldsymbol{\beta} = (\beta_0, \boldsymbol{\beta}_Z, \beta_U, \beta_A)'$ and $\boldsymbol{\alpha} = (\alpha_0, \boldsymbol{\alpha}_Z, \alpha_U, \alpha_A, \alpha_M)'$.

```r
# Simulate small and big mediation data sets from same data generating parameters
small_df <- simulate_simple_med(n = 200)
big_df   <- simulate_simple_med(n = 5000)

# Rename Z2 to U (because it is unmeasured)
names(small_df)[names(small_df) == "Z2"] <- "U"
names(big_df)[names(big_df) == "Z2"] <- "U"

# Frequentist model fits for prior information
fitU <- glm(U ~ Z1, data = small_df)
fitM <- glm(M ~ Z1 + U + A, data = small_df)
fitY <- glm(Y ~ Z1 + U + A + M, data = small_df)

# Prior means for coefficients
gamma_m <- unname(coef(fitU))
beta_m  <- unname(coef(fitM))
alpha_m <- unname(coef(fitY))

# Prior variance-covariance matrices
gamma_vcv <- unname(vcov(fitU))
beta_vcv  <- unname(vcov(fitM))
alpha_vcv <- unname(vcov(fitY))

# Package data for Stan
medU_dat <- list(N = nrow(big_df),
                 P = 2,
                 X = cbind(1, big_df$Z1),
                 A = big_df$A,
                 M = big_df$M,
                 Y = big_df$Y,
                 alpha_m = alpha_m,
                 beta_m = beta_m,
                 gamma_m = gamma_m,
                 alpha_vcv = alpha_vcv,
                 beta_vcv = beta_vcv,
                 gamma_vcv = gamma_vcv)
```

The Stan code to fit these models is shown below.

```
data {
  // number of observations
  int<lower=0> N;
  // number of columns in design matrix excluding A
  int<lower=0> P;
  // design matrix, excluding A, M, U
  matrix[N, P] X;
```

```
  // observed treatment
  vector[N] A;
  // observed mediator
  int<lower=0,upper=1> M[N];
  // outcome
  int<lower=0,upper=1> Y[N];
  // mean of regression priors
  vector[P + 3] alpha_m;
  vector[P + 2] beta_m;
  vector[P] gamma_m;
  // variance-covariance of regression priors
  cov_matrix[P + 3] alpha_vcv;
  cov_matrix[P + 2] beta_vcv;
  cov_matrix[P] gamma_vcv;
}

transformed data {
  // vectors of ones and zeros
  vector[N] all_ones = rep_vector(1, N);
  vector[N] all_zeros = rep_vector(0, N);

  // make vector of 1/N for (classical) bootstrapping
  real one = 1;
  vector[N] boot_probs = rep_vector(one/N, N);

  // make vector version of M
  vector[N] Mv = to_vector(M);
}

parameters {
  // regression coefficients (confounder model)
  vector[P] gamma;

  // regression coefficients (outcome model)
  vector[P + 3] alpha;

  // regression coefficients (mediator model)
  vector[P + 2] beta;
}

transformed parameters {
  // P(U = 1) for mixture weights
  vector[N] pU1 = inv_logit(X * gamma);

  // partial M coefficient parameters
  vector[P] betaZ = head(beta, P);
  real betaU = beta[P + 1];
  real betaA = beta[P + 2];

  // partial Y coefficient parameters
  vector[P] alphaZ = head(alpha, P);
  real alphaU = alpha[P + 1];
  real alphaA = alpha[P + 2];
```

```
  real alphaM = alpha[P + 3];
}

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

  // likelihoods
  M ~ bernoulli(inv_logit(X * betaZ + A * betaA + betaU).*pU1 +
                inv_logit(X * betaZ + A * betaA).*(1-pU1));
  Y ~ bernoulli(inv_logit(X * alphaZ + A * alphaA + Mv * alphaM + alphaU).*pU1 +
                inv_logit(X * alphaZ + A * alphaA + Mv * alphaM).*(1-pU1));
}

generated quantities {
  // weights for the bootstrap
  int<lower=0> counts[N] = multinomial_rng(boot_probs, N);

  // calculate NDE in the bootstrapped sample
  real NDE = 0;
  vector[N] U;
  vector[N] M_a0;
  vector[N] Y_a1Ma0;
  vector[N] Y_a0Ma0;
  for (n in 1:N) {
    // sample U
    U[n] = bernoulli_logit_rng(pU1[n]);

    // sample Ma where a = 0
    M_a0[n] = bernoulli_rng(inv_logit(X[n] * betaZ + A[n] * betaA + betaU)*pU1[n] +
                            inv_logit(X[n] * betaZ + A[n] * betaA)*(1-pU1[n]));

    // sample Y_(a=1, M=M_0) and Y_(a=0, M=M_0)
    Y_a1Ma0[n] = bernoulli_rng(inv_logit(X[n] * alphaZ + alphaA + M[n] * alphaM + alphaU)*pU1[n] +
                               inv_logit(X[n] * alphaZ + alphaA + M[n] * alphaM)*(1-pU1[n]));
    Y_a0Ma0[n] = bernoulli_rng(inv_logit(X[n] * alphaZ + M[n] * alphaM + alphaU)*pU1[n] +
                               inv_logit(X[n] * alphaZ + M[n] * alphaM)*(1-pU1[n]));

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

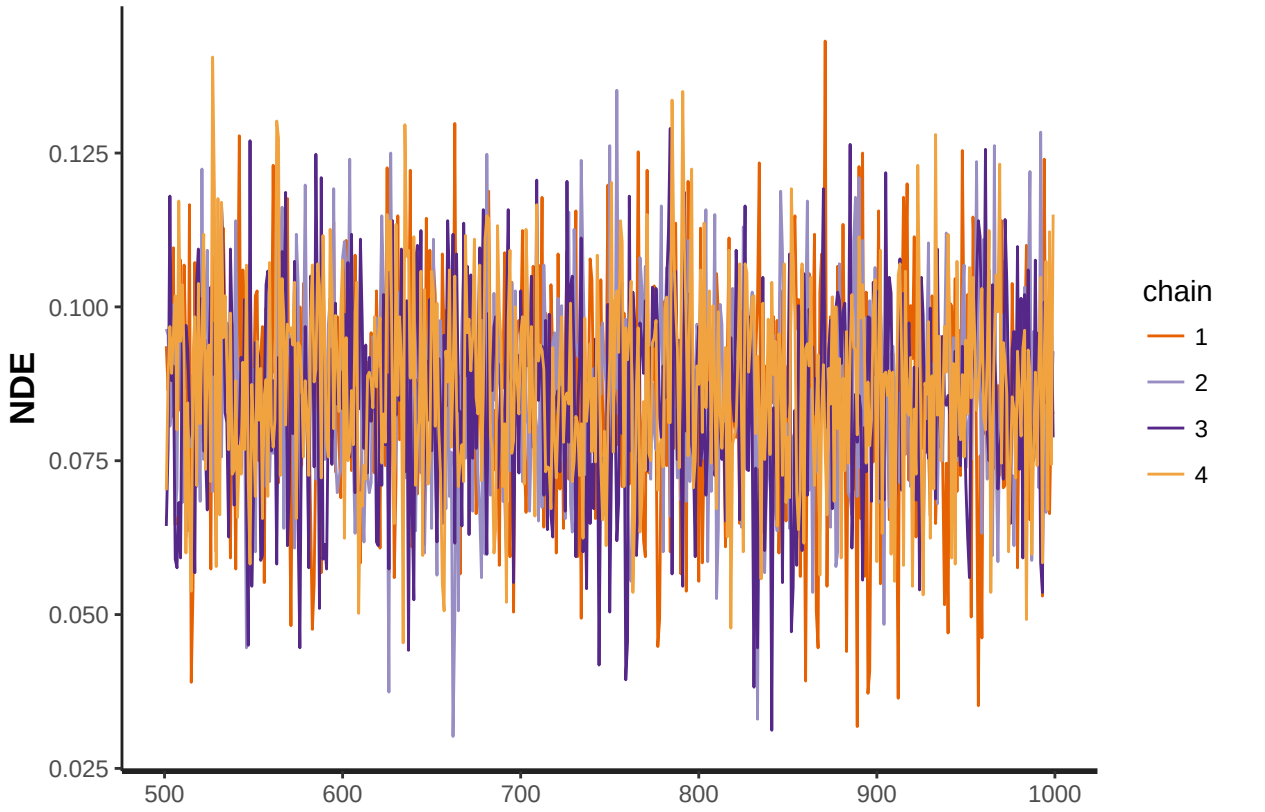
```
# Fit mediation model model with unmeasured confounder
fit3 <- stan(file = "mediation_unmeasured_mc.stan", data = medU_dat, iter = 1000)
```

```
##
## SAMPLING FOR MODEL 'mediation_unmeasured_mc' NOW (CHAIN 1).
##
## Gradient evaluation took 0.007116 seconds
## 1000 transitions using 10 leapfrog steps per transition would take 71.16 seconds.
## Adjust your expectations accordingly!
```

```
##
##
## Iteration:   1 / 1000 [  0%]  (Warmup)
## Iteration: 100 / 1000 [ 10%]  (Warmup)
## Iteration: 200 / 1000 [ 20%]  (Warmup)
## Iteration: 300 / 1000 [ 30%]  (Warmup)
## Iteration: 400 / 1000 [ 40%]  (Warmup)
## Iteration: 500 / 1000 [ 50%]  (Warmup)
## Iteration: 501 / 1000 [ 50%]  (Sampling)
## Iteration: 600 / 1000 [ 60%]  (Sampling)
## Iteration: 700 / 1000 [ 70%]  (Sampling)
## Iteration: 800 / 1000 [ 80%]  (Sampling)
## Iteration: 900 / 1000 [ 90%]  (Sampling)
## Iteration: 1000 / 1000 [100%]  (Sampling)
##
##  Elapsed Time: 30.1606 seconds (Warm-up)
##                28.1886 seconds (Sampling)
##                58.3492 seconds (Total)
##
##
## SAMPLING FOR MODEL 'mediation_unmeasured_mc' NOW (CHAIN 2).
##
## Gradient evaluation took 0.003371 seconds
## 1000 transitions using 10 leapfrog steps per transition would take 33.71 seconds.
## Adjust your expectations accordingly!
##
##
## Iteration:   1 / 1000 [  0%]  (Warmup)
## Iteration: 100 / 1000 [ 10%]  (Warmup)
## Iteration: 200 / 1000 [ 20%]  (Warmup)
## Iteration: 300 / 1000 [ 30%]  (Warmup)
## Iteration: 400 / 1000 [ 40%]  (Warmup)
## Iteration: 500 / 1000 [ 50%]  (Warmup)
## Iteration: 501 / 1000 [ 50%]  (Sampling)
## Iteration: 600 / 1000 [ 60%]  (Sampling)
## Iteration: 700 / 1000 [ 70%]  (Sampling)
## Iteration: 800 / 1000 [ 80%]  (Sampling)
## Iteration: 900 / 1000 [ 90%]  (Sampling)
## Iteration: 1000 / 1000 [100%]  (Sampling)
##
##  Elapsed Time: 29.7486 seconds (Warm-up)
##                28.0236 seconds (Sampling)
##                57.7722 seconds (Total)
##
##
## SAMPLING FOR MODEL 'mediation_unmeasured_mc' NOW (CHAIN 3).
##
## Gradient evaluation took 0.003154 seconds
## 1000 transitions using 10 leapfrog steps per transition would take 31.54 seconds.
## Adjust your expectations accordingly!
##
##
## Iteration:   1 / 1000 [  0%]  (Warmup)
## Iteration: 100 / 1000 [ 10%]  (Warmup)
```

```
## Iteration: 200 / 1000 [ 20%]  (Warmup)
## Iteration: 300 / 1000 [ 30%]  (Warmup)
## Iteration: 400 / 1000 [ 40%]  (Warmup)
## Iteration: 500 / 1000 [ 50%]  (Warmup)
## Iteration: 501 / 1000 [ 50%]  (Sampling)
## Iteration: 600 / 1000 [ 60%]  (Sampling)
## Iteration: 700 / 1000 [ 70%]  (Sampling)
## Iteration: 800 / 1000 [ 80%]  (Sampling)
## Iteration: 900 / 1000 [ 90%]  (Sampling)
## Iteration: 1000 / 1000 [100%]  (Sampling)
##
##  Elapsed Time: 28.9175 seconds (Warm-up)
##                27.8147 seconds (Sampling)
##                56.7321 seconds (Total)
##
##
## SAMPLING FOR MODEL 'mediation_unmeasured_mc' NOW (CHAIN 4).
##
## Gradient evaluation took 0.003183 seconds
## 1000 transitions using 10 leapfrog steps per transition would take 31.83 seconds.
## Adjust your expectations accordingly!
##
##
## Iteration:   1 / 1000 [  0%]  (Warmup)
## Iteration: 100 / 1000 [ 10%]  (Warmup)
## Iteration: 200 / 1000 [ 20%]  (Warmup)
## Iteration: 300 / 1000 [ 30%]  (Warmup)
## Iteration: 400 / 1000 [ 40%]  (Warmup)
## Iteration: 500 / 1000 [ 50%]  (Warmup)
## Iteration: 501 / 1000 [ 50%]  (Sampling)
## Iteration: 600 / 1000 [ 60%]  (Sampling)
## Iteration: 700 / 1000 [ 70%]  (Sampling)
## Iteration: 800 / 1000 [ 80%]  (Sampling)
## Iteration: 900 / 1000 [ 90%]  (Sampling)
## Iteration: 1000 / 1000 [100%]  (Sampling)
##
##  Elapsed Time: 31.4123 seconds (Warm-up)
##                28.397 seconds (Sampling)
##                59.8093 seconds (Total)
```

```r
# Traceplot of NDE
traceplot(fit3, pars=c("NDE"))
```




```
# Posterior summary of NDE
summary(extract(fit3)[["NDE"]])
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
## 0.03020 0.07480 0.08580 0.08599 0.09740 0.14320
```

Summary

Stan's `generated quantities` block offers a straightforward way to apply the g-formula to Bayesian models, including models for mediation. Incorporating prior information from another data source may partially address problems due to unmeasured confounding.