

```

library(simstudy)
library(rstan)
library(data.table)

defS <- defData(varname = "a.k", formula = 3, variance = 2, id = "study")
defS <- defData(defS, varname = "d.0", formula = 3, dist = "nonrandom")
defS <- defData(defS, varname = "v.k", formula = 0, variance = 6, dist =
"normal")
defS <- defData(defS, varname = "s2.k", formula = 16, variance = .2, dist =
"gamma")
defS <- defData(defS, varname = "size.study", formula = ".3;.5;.2", dist =
"categorical")
defS <- defData(defS, varname = "n.study",
  formula = "(size.study==1) * 20 + (size.study==2) * 40 + (size.study==3) *
60",
  dist = "poisson")

defI <- defDataAdd(varname = "y", formula = "a.k + x * (d.0 + v.k)", variance =
"s2.k")

RNGkind(kind = "L'Ecuyer-CMRG")
set.seed(12764)

ds <- genData(12, defS)

dc <- genCluster(ds, "study", "n.study", "id", )
dc <- trtAssign(dc, strata = "study", grpName = "x")
dc <- addColumns(defI, dc)

d.obs <- dc[, .(study, id, x, y)]

```

Build the Stan model

There are multiple ways to estimate a Stan model in R, but I choose to build the Stan code directly rather than using the `brms` or `rstanarm` packages. In the Stan code, we need to define the data structure, specify the parameters, specify any transformed parameters (which are just a function of the parameters), and then build the model – which includes laying out the prior distributions as well as the likelihood.

In this case, the model is slightly different from what was presented in the context of a mixed effects model. This is the mixed effects model:

```

\[\ y_{ik} = \alpha_k + \delta_k x_{ik} + e_{ik} \\\
\\
\delta_k = \delta_0 + v_k \\\
e_{ik} \sim N(0, \sigma_k^2), v_k \sim N(0, \tau^2)
\]
```

In this Bayesian model, things are pretty much the same:

```

\[\ y_{ik} \sim N(\alpha_k + \delta_k x_{ik}, \sigma_k^2) \\\
\\
\delta_k \sim N(\Delta, \tau^2)
\]
```

The key difference is that there are prior distributions on Δ and τ , introducing an additional level of uncertainty into the estimate. I would expect that the estimate of the overall treatment effect Δ will have a wider 95% CI (credible interval in this context) than the 95% CI (confidence interval) for δ_0 in the mixed effects model. This added measure of uncertainty is a strength of the Bayesian approach.

```

data {
  int N;                // number of observations
  int K;                // number of studies
  real y[N];            // vector of continuous outcomes
  int kk[N];           // study for individual
  int x[N];            // treatment arm for individual
}

parameters {
  vector[K] beta;       // study-specific intercept
  vector[K] delta;      // study effects
  real sigma[K];        // sd of outcome dist - study specific
  real Delta;           // average treatment effect
  real tau;             // variation of treatment effects
}

transformed parameters{

  vector[N] yhat;

  for (i in 1:N)
    yhat[i] = beta[kk[i]] + x[i] * delta[kk[i]];
}

model {

  // priors

  sigma ~ normal(0, 2.5);
  beta ~ normal(0, 10);

  tau ~ normal(0, 2.5);
  Delta ~ normal(0, 10);
  delta ~ normal(Delta, tau);

  // outcome model

  for (i in 1:N)
    y[i] ~ normal(yhat[i], sigma[kk[i]]);
}

```

Generate the posterior distributions

With the model in place, we transform the data into a list so that Stan can make sense of it:

```

N <- nrow(d.obs)                ## number of observations
K <- dc[, length(unique(study))] ## number of studies
y <- d.obs$y                    ## vector of continuous outcomes
kk <- d.obs$study               ## study for individual
x <- d.obs$x                    ## treatment arm for individual

ddata <- list(N = N, K = K, y = y, kk = kk, x = x)

```

And then we compile the Stan code:

```

rt <- stanc("model.stan")
sm <- stan_model(stanc_ret = rt, verbose=FALSE)

```

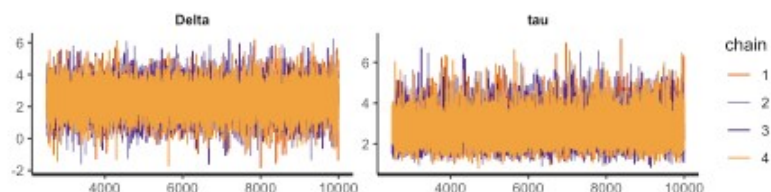
Finally, we can sample data from the posterior distribution:

```
fit <- sampling(sm, data=ddata, seed = 3327, iter = 10000, warmup = 2500,
               control=list(adapt_delta=0.9))
```

Check the diagnostic plots

Before looking at any of the output, it is imperative to convince ourselves that the MCMC process was a stable one. The *trace* plot is the most basic way to assess this. Here, I am only showing these plots for Δ and τ , but the plots for the other parameters looked similar, which is to say everything looks good:

```
pname <- c("Delta", "tau")
stan_trace(object = fit, pars = pname)
```



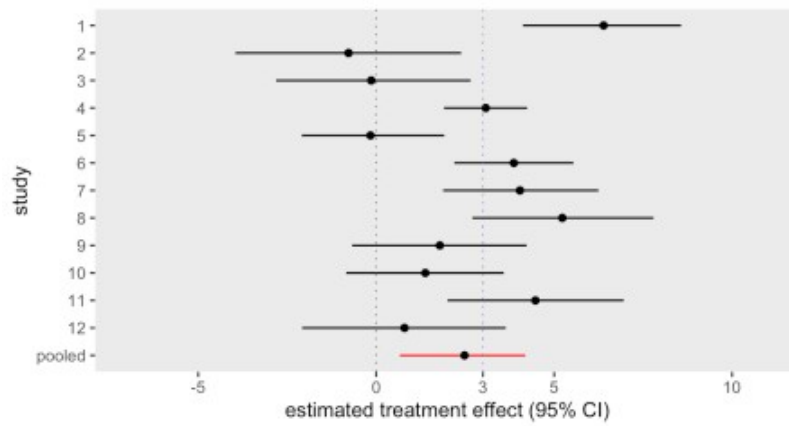
Look at the results

It is possible to look inspect the distribution of any or all parameters. In this case, I am particularly interested in the treatment effects at the study level, and overall. That is, the focus here is on Δ , Δ_k , and τ .

```
pname <- c("delta", "Delta", "tau")
print(fit, pars=pname, probs = c(0.05, 0.5, 0.95))
```

```
## Inference for Stan model: model.
## 4 chains, each with iter=10000; warmup=2500; thin=1;
## post-warmup draws per chain=7500, total post-warmup draws=30000.
##
##               mean se_mean   sd    5%   50%  95% n_eff Rhat
## delta[1]    6.39     0.01 1.13   4.51   6.41  8.22 29562    1
## delta[2]   -0.78     0.01 1.62  -3.45  -0.78  1.85 28188    1
## delta[3]   -0.14     0.01 1.39  -2.37  -0.16  2.18 28909    1
## delta[4]    3.08     0.00 0.59   2.09   3.08  4.05 34277    1
## delta[5]   -0.16     0.01 1.01  -1.77  -0.18  1.52 27491    1
## delta[6]    3.87     0.00 0.86   2.47   3.87  5.27 35079    1
## delta[7]    4.04     0.01 1.11   2.21   4.03  5.87 32913    1
## delta[8]    5.23     0.01 1.29   3.12   5.23  7.36 33503    1
## delta[9]    1.79     0.01 1.25  -0.27   1.78  3.82 30709    1
## delta[10]   1.38     0.01 1.12  -0.46   1.38  3.21 30522    1
## delta[11]   4.47     0.01 1.25   2.43   4.47  6.54 34573    1
## delta[12]   0.79     0.01 1.45  -1.60   0.80  3.16 33422    1
## Delta       2.48     0.00 0.89   1.01   2.50  3.89 31970    1
## tau         2.72     0.00 0.71   1.72   2.64  4.01 24118    1
##
## Samples were drawn using NUTS(diag_e) at Sat Jun 27 15:47:15 2020.
## For each parameter, n_eff is a crude measure of effective sample size,
## and Rhat is the potential scale reduction factor on split chains (at
## convergence, Rhat=1).
```

The forest plot is quite similar to the one based on the mixed effects model, though as predicted, the 95% CI is considerably wider:



As a comparison, here is the plot from the mixed effects model estimated using the `nlme` package in the previous post. The bootstrapped estimates of uncertainty at the study level are quite close to the Bayesian measure of uncertainty; the difference really lies in the uncertainty around the global estimate.

