

# **bnma: Bayesian Network Meta-Analysis using 'JAGS'**

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# Bayesian Network Meta-Analysis R packages

Recently, there has been many developments of Bayesian network meta-analysis (NMA) packages in R.

- ✓ gemtc (van Valkenhoef et al., 2012)
- ✓ pcnetmeta (Lin et al., 2017)
- ✓ BUGSnet (Béliveau et al., 2019)
- ✓ bnma (Seo and Schmid, 2020)
- ✓ multinma (Phillippo et al., 2020)

The goal of this presentation is not to compare different packages, but to go over the package we developed.

- **bnma** implements models described in the National Institute for Health and Care Excellence (NICE) Decision Support Unit Technical Support Documents (Dias et al., 2013a)
- This document provides detailed description of the Bayesian NMA model (Lu and Ades, 2009).
- **bnma** models normal, binomial, and multinomial outcomes.

## bnma package(2)

- Required input includes: outcomes, study indicator, treatment indicator, total number of observations (for binomial or multinomial outcomes) or standard error (for normal outcomes).
- Based on the specified input, bnma creates **JAGS code** and **initial values** and automatically runs Bayesian NMA model.

## Example dataset

- We demonstrate our package using the **smoking cessation counseling programs** dataset
- Twenty-four studies, including 2 three-arm trials, compared **4 smoking cessation counseling programs** and recorded the number of individuals with successful smoking cessation.
- Counseling programs include 1 = no intervention, 2 = self-help, 3 = individual counseling, and 4 = group counseling.

## Example dataset(2)

Here is the first five studies of the smoking dataset.

```
lapply(smoking, head, n = 12)
$Outcomes
[1] 9 23 10 11 12 29 75 363 2 9 58 237
$N
[1] 140 140 138 78 85 170 731 714 106 205 549 1561
$Study
[1] 1 1 1 2 2 2 3 3 4 4 5 5
$Treat
[1] 1 3 4 2 3 4 1 3 1 3 1 3
```

## Model specification

Defining  $r_{ik}$  as the number of events, out of the total number of patients in each arm,  $n_{ik}$ , for arm  $k$  of trial  $i$ ,

$$r_{ik} \sim \text{Binomial}(p_{ik}, n_{ik})$$

$$\text{logit}(p_{ik}) = \eta_i + \delta_{i,1k} I_{\{k \neq 1\}}$$

where  $\eta_i$  are trial-specific baselines and  $\delta_{i,1k}$  are the trial-specific log odds ratios of death on the treatment group ( $k$  vs. 1). For a random effects model,

$$\delta_{i,1k} \sim N(d_{1k}, \sigma_{1k}^2)$$

## Bayesian NMA(2)

### Model specification

Furthermore, NMA requires the consistency equations to hold

$$d_{23} = d_{13} - d_{12}$$

$$d_{24} = d_{14} - d_{12}$$

$$d_{(s-1),s} = d_{1s} - d_{1(s-1)}$$

and equal variances are assumed, i.e.  $\sigma_{12}^2 = \sigma_{13}^2 = \sigma_{23}^2 = \sigma^2$

This model can be fitted using **bnma** as follows:

```
1 network <- with(smoking, network.data(Outcomes =  
    Outcomes, Study = Study, Treat = Treat, N = N,  
    response = "binomial", type = "random"))  
2 result <- network.run(network)
```



## Model summary

```
> summary(result)
```

```
$summary.samples
```

```
...
```

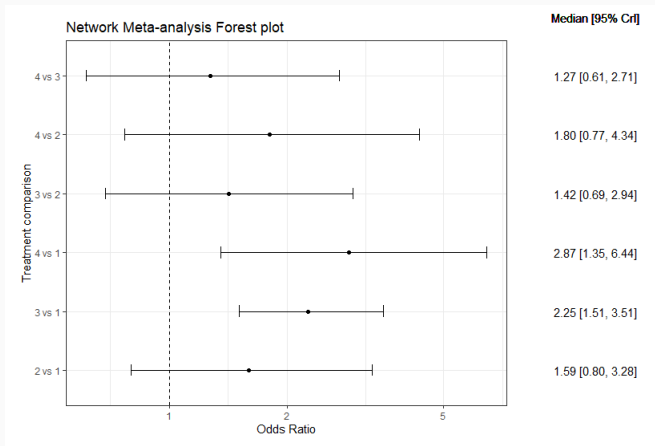
1. Empirical mean and standard deviation for each variable, plus standard error of the mean:

	Mean	SD	Naive SE	Time-series SE
d[1]	0.0000	0.0000	0.0000000	0.000000
d[2]	0.4935	0.4015	0.0010368	0.001943
d[3]	0.8443	0.2388	0.0006166	0.001468
d[4]	1.1028	0.4396	0.0011351	0.002622
sd	0.8410	0.1872	0.0004833	0.001847

The odds ratio for Treatment 4 (group counseling) is  $\exp(1.1028) = 3.01$ . The model estimated a 201% increase in the odds of quitting smoking for group counseling compared to no intervention.

## Model summary(2)

We can use a forest plot to visualize the results.



```
1 network.forest.plot(result)
```

## Checking convergence

- Disperse initial values are generated i.e. treatment effect estimated through simple regression of log odds ratio against treatments assigned.
- We use Gelman-Rubin diagnostics to test convergence of parameters  $\eta_i$ ,  $d_{1k}$ ,  $\log\sigma^2$ .
- We check convergence every **setsize** iterations. Once the samples converged, it keeps the last half of the converged sequence. User specifies the final sample size through parameter **n.run**; more samples are drawn if needed.

```
1 result <- network.run(network, n.run = 100000,  
    setsize = 10000)
```

## Contrast-based model with random study intercept

- Assume that the baseline risk across trials is drawn from a normal distribution with common mean and between-study variance i.e.  $\eta_{i1} \sim N(E, \sigma_E^2)$ .
- Note that we have added 1 in the subscript in  $\eta_{i1}$ . Baseline risk (i.e. study intercepts) now all refer to treatment 1, even if treatment 1 is not included in a trial.
- Although treatment in arm 1 will not always be treatment 1 (the reference treatment), the fundamental assumption on exchangeability means that treatment arms can be assumed to be missing at random without loss to efficacy (Achana et al., 2013).

## Contrast-based model with random study intercept(2)

- The extra assumption of random intercepts should lead to greater precision. However, this comes at the price of using **between-study information**, meaning that the treatment effect estimated across the network is informed not only by the usual differences within studies but also by differences between studies (White et al., 2019).

```
1 network <- with(smoking, network.data(Outcomes =  
    Outcomes, Study = Study, Treat = Treat, N = N,  
    response = "binomial", type = "random", baseline.  
    risk = "exchangeable"))
```

## Contrast-based model with random study intercept(3)

```
> summary(result)
```

```
...
```

	Mean	SD	Naive SE	Time-series SE
E	-2.4912	0.1280	0.0003304	0.0010630
d[1]	0.0000	0.0000	0.0000000	0.0000000
d[2]	0.5315	0.3264	0.0008428	0.0018280
d[3]	0.7817	0.1926	0.0004973	0.0011850
d[4]	1.0513	0.3367	0.0008695	0.0022016
sd	0.7213	0.1295	0.0003345	0.0008852
sdE	0.4624	0.1069	0.0002761	0.0008865

Common mean for the baseline risk is estimated to be -2.4912, which is equivalent to a baseline probability of quitting of 0.076.

## Model specification

$$\delta_{i,1k} \sim N(d_{1k} + \beta_{1k}(\eta_{i1} - \bar{\eta}), \sigma_{1k}^2)$$

where we centered the baseline risk on  $\bar{\eta}$ , the observed mean log odds in the non-active control group (Treatment 1), to improve convergence.

- Using the 'true' but unobserved non-active control log odds  $\eta_{i1}$  in trial  $i$  as a measure of the baseline risk, we can extend the NMA to include a covariate for the baseline risk as a possible source of heterogeneity (Dias et al., 2013b).

## Network Meta-regression on baseline risk(2)

Can specify three different assumptions on the regression terms

1. Common:  $\beta_{1k} = \beta$
2. Exchangeable:  $\beta_{1k} \sim N(B, \sigma_B^2)$
3. Independent:  $\beta_{1k}$

For instance to assume **common** effect treatment x covariate interactions, we use the following code:

```
1 network <- with(smoking, network.data(Outcomes =  
    Outcomes, Study = Study, Treat = Treat, N = N,  
    response = "binomial", type = "random", baseline.  
    risk = "exchangeable", baseline = "common"))
```



## Network Meta-regression on baseline risk(3)

```
> summary(result)
```

```
...
```

	Mean	SD	Naive SE	Time-series SE
b_bl [1]	0.0000	0.0000	0.0000000	0.0000000
b_bl [2]	-0.4148	0.5315	0.0013723	0.0065083
b_bl [3]	-0.4148	0.5315	0.0013723	0.0065083
b_bl [4]	-0.4148	0.5315	0.0013723	0.0065083
d [1]	0.0000	0.0000	0.0000000	0.0000000
d [2]	0.6204	0.3511	0.0009066	0.0023820
d [3]	0.8988	0.2502	0.0006460	0.0025149
d [4]	1.1543	0.3637	0.0009392	0.0028476
sd	0.7524	0.1324	0.0003418	0.0009809

Odds ratio  $\exp(1.1543)=3.17$  is now the treatment effect of group counseling for patients with a baseline logit probability of quitting of  $\bar{\eta} = -2.745$  (i.e. a baseline probability of quitting of 0.06)

# Summary

- We showed how to fit a simple Bayesian NMA using smoking dataset with **bnma**
- We demonstrated how to incorporate baseline risk (i.e. via a exchangeable assumption or as a meta-regression)
- The following slide is uploaded in my private website:  
<https://mikejseo.github.io/conferences/>

# References i

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## References ii

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