Course EPIB-683 - Intermediate Bayesian Analysis for the Health Sciences

Assignment 5

In this assignment we will analyze data for a meta-analysis. In question 1, we will use a very simple meta-analysis model that assumes that the effects are identical across all trials. In the second we will use a hierarchical (random effects) model, that assumes that the effects across studies are not identical, but follow a common distribution. In the third we will create a forest plot corresponding to the analyses carried out in question 2. In question 4 we will continue to use a random effects model, but we will try to see if some of the variations in effects between studies can be explained by study-level covariates, by adding a regression component to the meta-analytic hierarchical model. Finally, we will discuss some assumptions behind meta-analysis.

The basic setup for all five questions is as follows: Fifteen trials have been carried out to see if inserting stents are useful following heart attacks. Each of the 15 trials has a treatment (stent) group, and a control (placebo) group. In addition, each trial either used a plastic or a metal stent. The primary objective is to see whether subjects who receive stents have fewer future events (i.e., further heart attacks).

1. Download the data set meta.txt from the course web page. It is already in WinBUGS format. WinBUGS comes with an example called Blocker, which we have discussed in class. We will use the Blocker example in question 2 below, but here we want to use a simpler meta-analysis model, without random effects. Starting from the Blocker model, therefore, we wish to change delta[i] to a single effect delta, which also means that the line giving a normal distribution to delta should move outside of the "loop" over i, and "d" and "tau" should be constants (such as 0, and 0.001) rather than variables. The rest of the program can remain as it is, but add a line that provides an odds ratio for the overall effect, i.e., add a line like:

```
or <- exp(delta)
```

Run this meta-analytic model using the meta.txt data set, monitor all unknown parameters (including *pc* and *pt*), and report the results. Does there seem to be an effect of the stents?

2. Now, using the same data set, run the blocker model, but as it was originally. Again, add a line that gets the overall odds ratio, now using delta.new rather than delta. That is, add a line like:

```
or <- exp(delta.new)
```

Compare the odds ratio for stents in the two models. Are their means similar? What about their variances? Looking at the parameter for the SD of the effect of delta (i.e., looking at sigma), does a random effects model seem warranted (i.e., does there seem to be variations in effects across the 15 studies)?

3. The course web page contains a link to an R program called `forest.plot.or` which creates forest plots. This program has its own web page which explains how to run it, here:

`http://www.medicine.mcgill.ca/epidemiology/Joseph/PBelisle/forest-plot.html`

There are a large number of options, and the look of the program is highly customizable, but you can ignore all of these optional arguments and just create a basic plot. required fields are: m0, n0, m1, n1, authors (just call them "Paper 1", Paper 2", etc), group.labels ("stent" and "no stent" and meta.ci, which contains the results from WinBUGS. See program web page for full details.

Using the original data set and your output from question 2, create a forest plot for your results.

4. Again using the blocker model, now switch to the meta.reg.txt data set. This data set is identical to the one used in the first two questions, except that is adds a variable to indicate whether the coating was plastic or metal. We will see if some of the variability in study-to-study effect can be explained by the stent type by adding a regression term to the prior distribution of delta[i]. To do this, remove the three lines in blocker (note that they are not consecutive lines in the program)

```
delta[i] ~ dnorm(d, tau)
d ~ dnorm(0.0,1.0E-6)
delta.new ~ dnorm(d, tau)
```

and replace them with:

```
delta.mean[i] <- alpha + beta*coating[i]
delta[i] ~ dnorm(delta.mean[i], tau)
alpha ~ dnorm(0.0,0.001)
beta ~ dnorm(0.0,0.001)
mean.plastic <- alpha
mean.metal <- alpha + beta
delta.plastic ~ dnorm(mean.plastic, tau)
delta.metal ~ dnorm(mean.metal, tau)
or.plastic <- exp(delta.plastic)
or.metal <- exp(delta.metal)
or.diff <- or.plastic - or.metal
```

Lines with [i]'s in them (first two lines above) go inside the loop, other lines (all the rest) go outside the loop. The last line calculates the difference in odds ratios between the two stent types.

Run this model, and report results from all parameters. Does it appear that stent type explains some of the variability in the effectiveness of stents across studies?

5. It has become standard practice in some meta-analytic circles (such as the Cochrane project) to run a test of heterogeneity of effects, and if the null hypothesis is not rejected, then to run a fixed effects model rather than a random effects model.

In other words, one first considers this test of homogeneity (assume M studies):

$$\begin{aligned} H_0: &\quad OR_1 = OR_2 = \cdots = OR_m \\ H_A: &\quad \text{At least one OR is different from the rest} \end{aligned}$$

Discuss advantages and disadvantages of such a method of proceeding.