

STATISTICS 536B, Lecture #7

March 19, 2015

Network Meta-Analysis? Indirect Comparisons?

trial #	Treatment Success		
	Drug A	Drug B	Drug C
1	10/200	15/100	
2	20/200	20/100	
3	30/200	25/100	
4		10/100	55/200
5		20/100	60/200
6		30/100	70/200

How much better is Drug C than Drug A?

As before represent i -th trial data via sample log-OR and SE:

(y_i, σ_i)

(But keep track of which pair of treatments are being compared in each trial.)

Random effect structure - in i-th trial

Generically, think of $\delta_{i,RS}$ as being the log-odds-ratio for treatment S compared to treatment R, in the i-th study population.

In fact, with three treatments (A,B,C) we assume the following random effects structure

$$\delta_i = \begin{pmatrix} \delta_{i,AB} \\ \delta_{i,AC} \end{pmatrix} \sim N \left(\begin{pmatrix} d_{AB} \\ d_{AC} \end{pmatrix}, \tau^2 \begin{pmatrix} 1 & 0.5 \\ 0.5 & 1 \end{pmatrix} \right)$$

with the implicit **consistency assumption** that

$\delta_{i,BC} = \delta_{i,AC} - \delta_{i,AB}$, and similarly $d_{BC} = d_{AC} - d_{AB}$.

Why correlation 0.5???

So can think about $(Y_{i,RS} | \delta_i) \sim N(\delta_{i,RS}, \sigma_i^2)$

So marginally (with random effects integrated away...)

$$Y \sim N(Xd, D),$$

And we know how to handle linear models

$$Y \sim N(Xd, D),$$

leads to

$$\hat{d} = (X^T D^{-1} X)^{-1} X^T D^{-1} Y$$

and

$$\text{Var}(\hat{d}) = (X^T D^{-1} X)^{-1}$$

Back to our toy example

```
> y
[1] 1.21 0.81 0.64 1.23 0.54 0.23

> sqrt(sig2)
[1] 0.43 0.34 0.30 0.37 0.29 0.26

> dsgn
      [,1] [,2]
[1,]     1     0
[2,]     1     0
[3,]     1     0
[4,]    -1     1
[5,]    -1     1
[6,]    -1     1

> tau2 <- .15^2
```

```
vr <- solve(t(dsgn) %*% solve(diag(sig2+tau2)) %*% dsgn)

est <- vr%*%t(dsgn)%*%solve(diag(sig2+tau2))%*%y

### drug B versus drug A
> c(est[1],sqrt(vr[1,1]))
[1] 0.83  0.22

### drug C versus drug A
> c(est[2], sqrt(vr[2,2]))
[1] 1.41  0.29

### drug C versus drug B
> cntrst <- c(-1,1)
> c( sum(cntrst*est), sqrt(t(cntrst)%*%vr%*%cntrst)) )
[1] 0.58  0.19
```

How would our toy example **actually** be analyzed?

Success counts for (A,B) trial:

$$Z_{i,A} \sim \text{Binomial}(n_i, \text{expit}(\mu_i))$$

$$Z_{i,B} \sim \text{Binomial}(n_i, \text{expit}(\mu_i + \delta_{i,AB}))$$

Or for (B,C) trial:

$$Z_{i,B} \sim \text{Binomial}(n_i, \text{expit}(\mu_i + \delta_{i,AB}))$$

$$Z_{i,C} \sim \text{Binomial}(n_i, \text{expit}(\mu_i + \delta_{i,AC}))$$

Then $\mu_i \sim N(0, \kappa^2)$ and, as before,

$$\delta_i = \begin{pmatrix} \delta_{i,AB} \\ \delta_{i,AC} \end{pmatrix} \sim N \left(\begin{pmatrix} d_{AB} \\ d_{AC} \end{pmatrix}, \tau^2 \begin{pmatrix} 1 & 0.5 \\ 0.5 & 1 \end{pmatrix} \right)$$

In fact, typically interpreted/fit as a Bayesian hierarchical model, say using WinBUGS

	network meta-analysis	all other biostat. apps.
Bayesian	rule	exception
non-Bayesian	exception	rule