STATISTICS 536B, Lecture #5

March 10, 2015

Meta-Analysis: Synthesizing evidence from different studies of the same relationship

y_i: Estimated 'effect size' from i-th study.

σ_i: standard error for this effect size.

A typical abstract...

```
Med Sci Monit. 2002 Aug;8(8):CR558-65.
Meta-analysis of 20 case-control studies on the N-acetyltransferase
2 acetylation status and colorectal cancer risk.

Abstract
BACKGROUND: Rapid NAT2 acetylation has been considered as a risk factor for
developing colon cancer in a number of studies, however the overall results
of such studies are inconsistent. To clarify the influence of NAT2 rapid
acetylation status on colon cancer risk, we have performed a meta-analysis
of 20 published case-control studies (4431 cases, 4547 controls).

MATERIAL/METHODS:...

RESULTS: The pooling of studies based on phenotyping methods indicated that
the overall odds ratio of colon cancer risk associated with rapid
acetylator was 1.51 (95%CI: 1.07-2.12).  However, the risk of colon cancer
associated with rapid acetylator from the studies based on genotyping
method was lower with a calculated overall odds ratio of 1.06
(95%CI: 0.971.15)...
```

The data

```
> library(mmeta)
> data(colorectal)
> colorectal
    y1  y2  n1  n2 studynames
1   10  27  41  49      Ilett
2   19  27  45  49     Ilett1
3   13  23  41  43    Wohlleb
4   40  49  96 109     Ladero
5   13  20  28  44  Rodriguez
6   92  14 205  34       Lang
7   33  33  36  36        Oda
8  151 112 329 234    Shibuta
9   50  96 112 202       Bell
10  34  32  96 103      Spurr
11 140 100 343 275    Hubbard
12  74  73 174 174    Welfare
13  68  44 201 114        Gil
...
19 119  60 258 120    Agundez
20 162 156 209 200     Butler
```

E.g., one of the 20 studies

	cases	controls
X=1	23	13
X=0	20	28

Fixed effect meta-analysis

$Y_i \sim N(\theta, \sigma_i^2),\ i = 1, \ldots m.$

Random effect meta-analysis

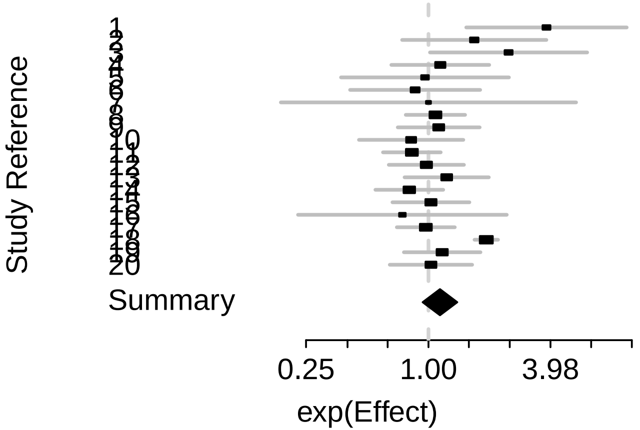
$Y_i \mid \theta_i \sim N(\theta_i, \sigma_i^2)$, $i = 1, \ldots, m$.

$\theta_i \sim N(\mu, \tau^2)$

Implement random effect meta analysis

```
y <- log(colo$y2/(colo$n2-colo$y2))-
     log(colo$y1/(colo$n1-colo$y1))

sg <- sqrt(1/colo$y1 + 1/(colo$n1-colo$y1) + 1/colo$y2 + 1/(colo$n2-colo$y2))

library(rmeta)

> meta.summaries(y,sg, method="random")
Random-effects meta-analysis
Call: meta.summaries(d = y, se = sg, method = "random")
Summary effect=0.13   95% CI (-0.0661, 0.327)
Estimated heterogeneity variance: 0.12  p= 0

> plot(meta.summaries(y,sg, method="random"),log=T)
```

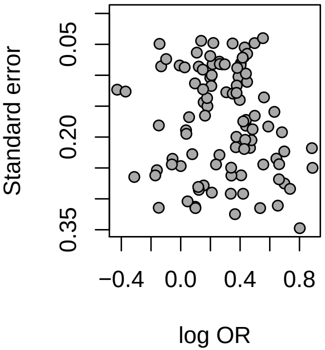
Forest plot

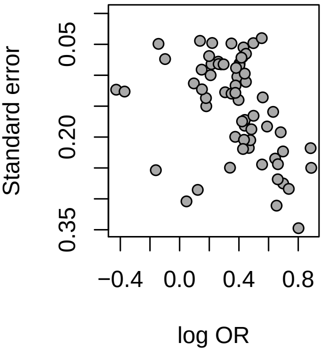

Study Reference
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
Summary
0.25
1.00
3.98
exp(Effect)

Quick simulation

```
m.orig <- 100

##### variety of sample sizes
n <- round(1/runif(m.orig, sqrt(1/8000), sqrt(1/100))^2)

##### distribution of actual effects
theta <- rnorm(m.orig, mean=log(1.3),  sd=((log(1.3)-log(.9))/2) )

##### simulate the studies
y <- sg <- rep(NA, m.orig); pub <- rep(T, m.orig)
for (i in 1:m.orig)  {
  ### simulate exposure status for controls and cases
  tmp.cn <- rbinom(1, size=n[i], prob=.25)
  tmp.cs <- rbinom(1, size=n[i], prob=expit(logit(.25)+theta[i]))
  ###  effect estimate
  y[i] <- log(tmp.cs/(n[i]-tmp.cs)) - log(tmp.cn/(n[i]-tmp.cn))
  ### SE
  sg[i] <- sqrt(1/tmp.cs + 1/(n[i]-tmp.cs) + 1/tmp.cn + 1/(n[i]-tmp.cn))
  ### gets published ?
  if (abs(y[i])<(2*sg[i])) { if (runif(1)<.67) {pub[i] <- F} }
}
```

```
> sum(pub)
[1] 66

> library("meta")
> funnel(y,       sg,       xlab="log OR")
> funnel(y[pub], sg[pub], xlab="log OR")
```


Standard error
0.05
0.20
0.35
−0.4
0.0
0.4
0.8
log OR


Standard error
0.05
0.20
0.35
−0.4
0.0
0.4
0.8
log OR

```
> library(rmeta)

> meta.summaries(y, sg, method="fixed")
Fixed-effects meta-analysis
Call: meta.summaries(d = y, se = sg, method = "fixed")
Summary effect=0.271   95% CI (0.25, 0.292)
Estimated heterogeneity variance: 0.039  p= 0


> meta.summaries(y, sg, method="random")
Random-effects meta-analysis
Call: meta.summaries(d = y, se = sg, method = "random")
Summary effect=0.276   95% CI (0.226, 0.326)
Estimated heterogeneity variance: 0.039  p= 0
```

```
> meta.summaries(y[pub], sg[pub], method="fixed")
Fixed-effects meta-analysis
Call: meta.summaries(d = y[pub], se = sg[pub], method = "fixed")
Summary effect=0.309   95% CI (0.286, 0.332)
Estimated heterogeneity variance: 0.04  p= 0


> meta.summaries(y[pub], sg[pub], method="random")
Random-effects meta-analysis
Call: meta.summaries(d = y[pub], se = sg[pub], method = "random")
Summary effect=0.342   95% CI (0.282, 0.401)
Estimated heterogeneity variance: 0.04  p= 0
```