Practical Meta-analysis in R

Saskia le Cessie Katerina Papadimitropoulou

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R and R-studio

- R is a programming language, originally 'written' in 1992 by Ross Ihaka and Robert Gentleman (yes, "R" stems from the first letter of their first names), inspired by another programming language called S.
- Throughout this practical you'll be encouraged to use R-studio. R-studio is a free, open-source "Integrated Development Environment" (IDE) for R (for Windows, Mac and Linux).
- Installing R-studio requires only two steps:
  - Download and install "base R" from the R project website: `https://cloud.r-project.org/`.
  - Download and install R-studio from the R-studio website `https://www.rstudio.com/products/rstudio/download/`.

Install and load libraries

```
# load libraries
install.packages(c("foreign", "metafor", "meta"))

library(foreign)
library(metafor)
library(meta)

# set your working directory
setwd("D:/Meta-analysis course LUMC")
```

EXERCISE I - Diuretic dataset

```r
# Load the dataset
diuretic = read.dta("diuretic.dta")

# Take a look at the data
View(diuretic)
```

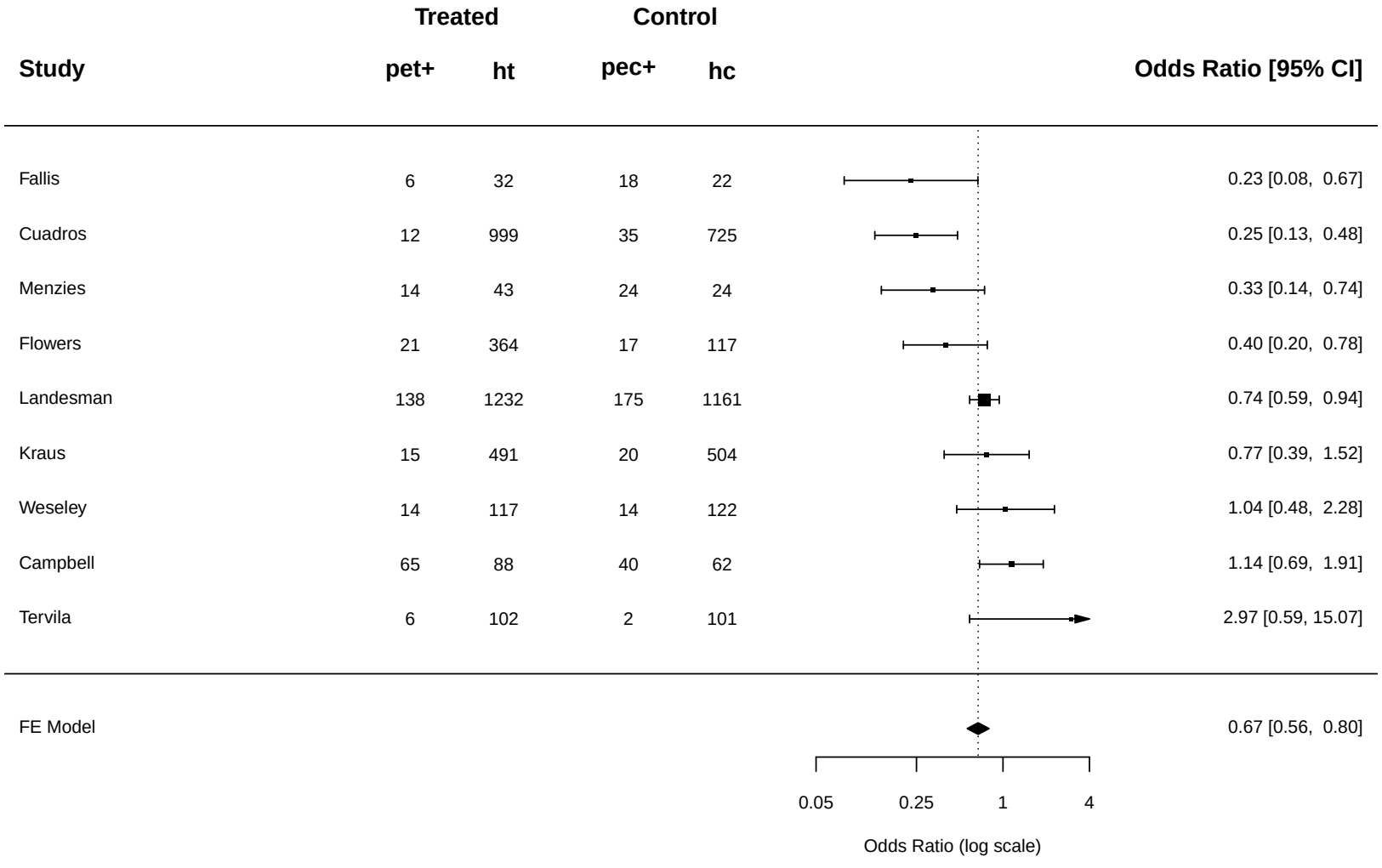
- There are two ways to calculate the (log) odds ratios
  - Manually; fist calculating the number of healthy subjects (without pre-eclampsia)
  - Using “escalc” function in R

EXERCISE I - Perform the MA

```
res1 = rma(yi, vi, data = diuretic, method = "FE",
    measure = "OR")
res1
```

```
##
## Fixed-Effects Model (k = 9)
##
## Test for Heterogeneity:
## Q(df = 8) = 27.2649, p-val = 0.0006
##
## Model Results:
##
## estimate      se     zval    pval    ci.lb    ci.ub
##  -0.3980  0.0893  -4.4548  <.0001  -0.5731  -0.2229  ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' '
```

Forestplot - Fixed effects analysis



Random effects meta-analysis

```
res2 = rma(yi, vi, data = diuretic, method = "REML",
    measure = "OR")   # default
```

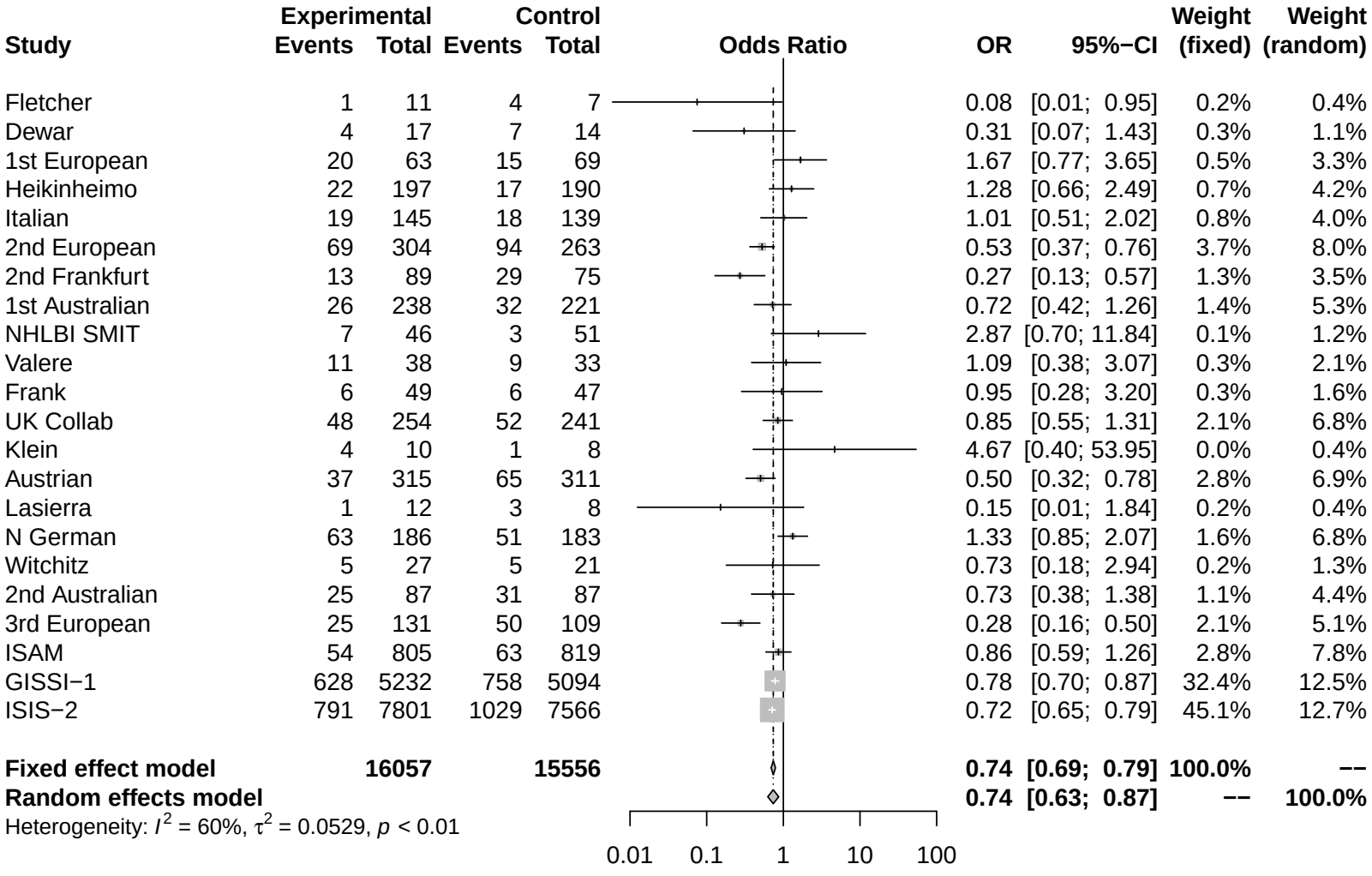
Many iterarive and non-iterative approaches to estimate τ^2:

$$Y_i = \theta + \theta_i + \epsilon_i$$
$$\theta_i \sim N(0, \tau^2)$$
$$\epsilon_i \sim N(0, V_i)$$

- DL: DerSimonian-Laird (most commonly used)
- EB: Empirical Bayes
- HE: Hedges
- Hs: Hunter-Schmidt
- ML: Maximum-likelihood
- REML: Restricted maximum-likelihood (default)
- SJ: Sidik-Jonkman

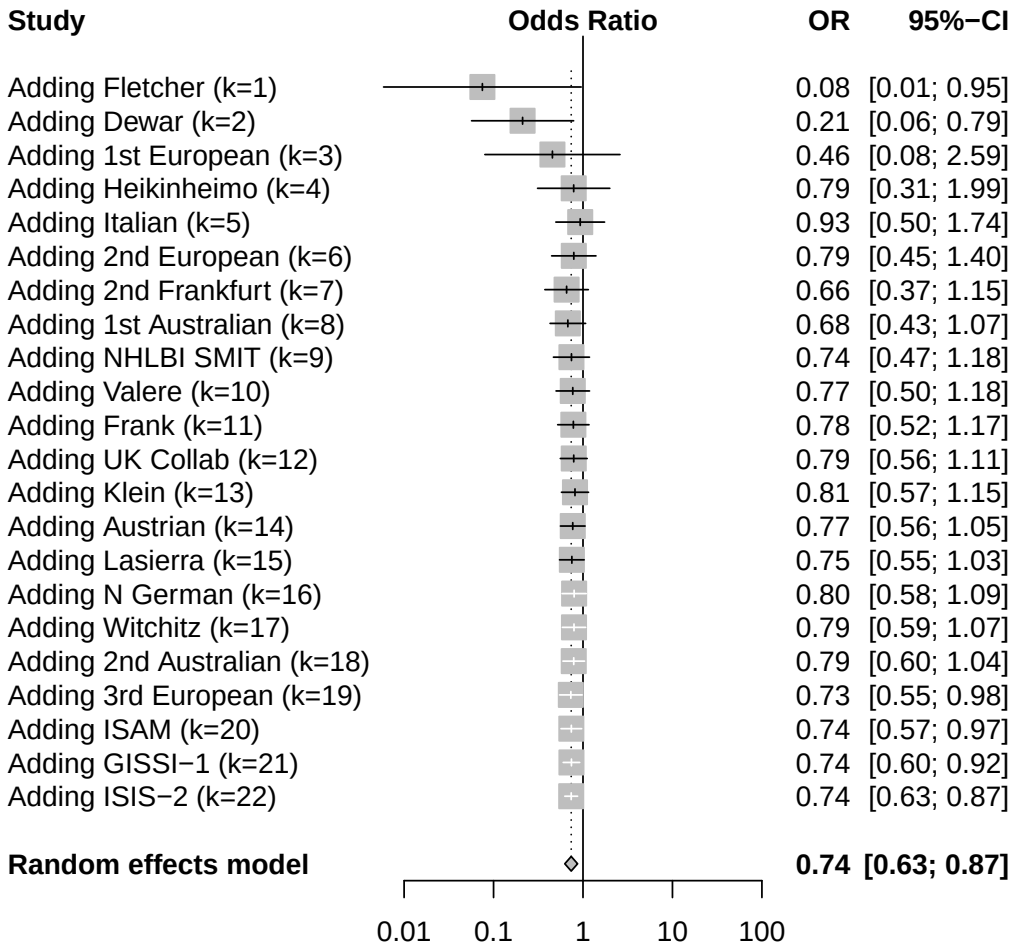
EXERCISE II - Streptokinase dataset

Odds ratio as outcome - using function "metabin" from package meta



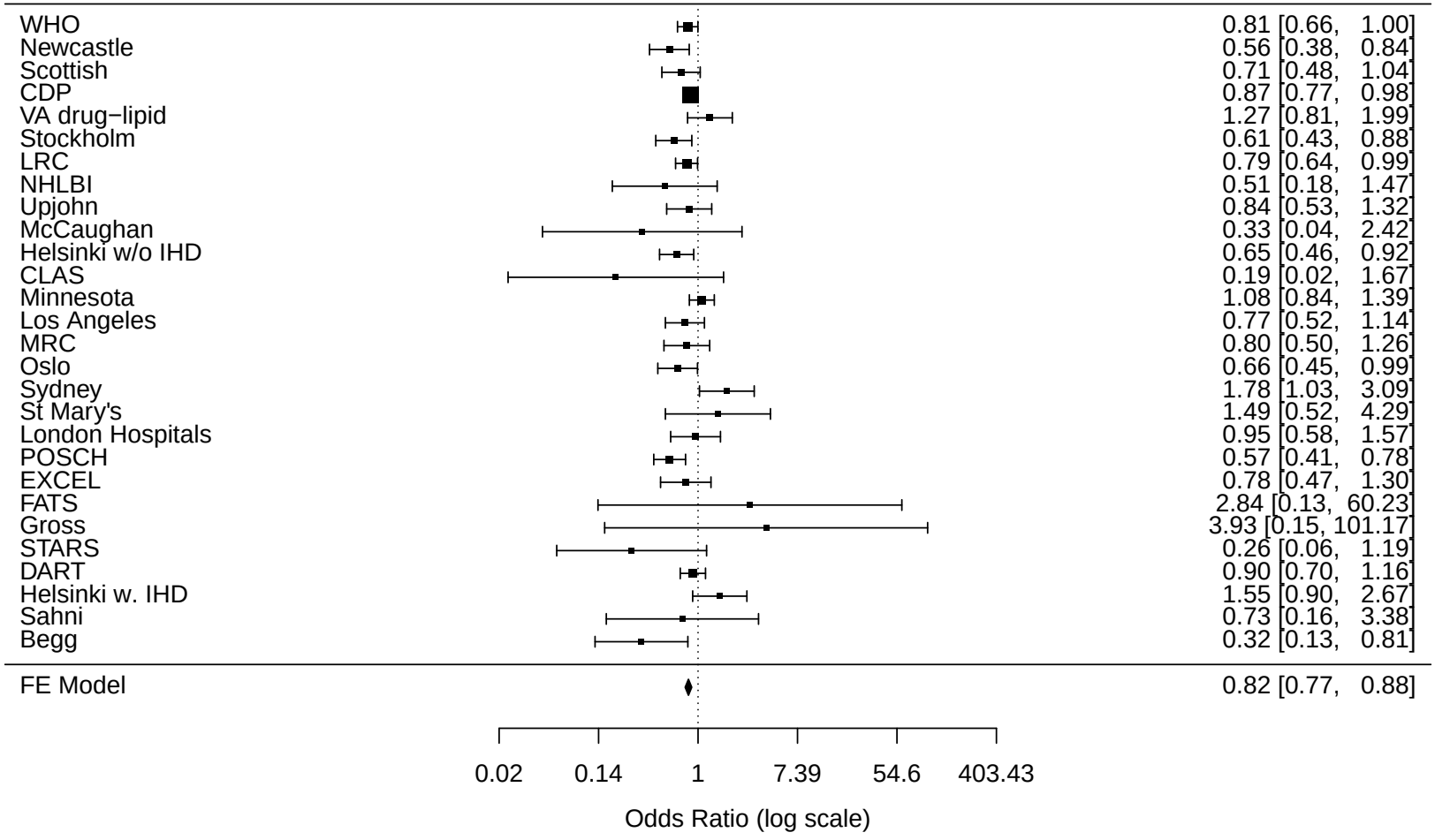
Cumulative meta-analysis

```
res4 = metacum(res1, sortvar = year, pooled = "random")
forest(res4)
```



EXERCISE III - cholesterol dataset

Fixed effects meta-analysis - Forestplot

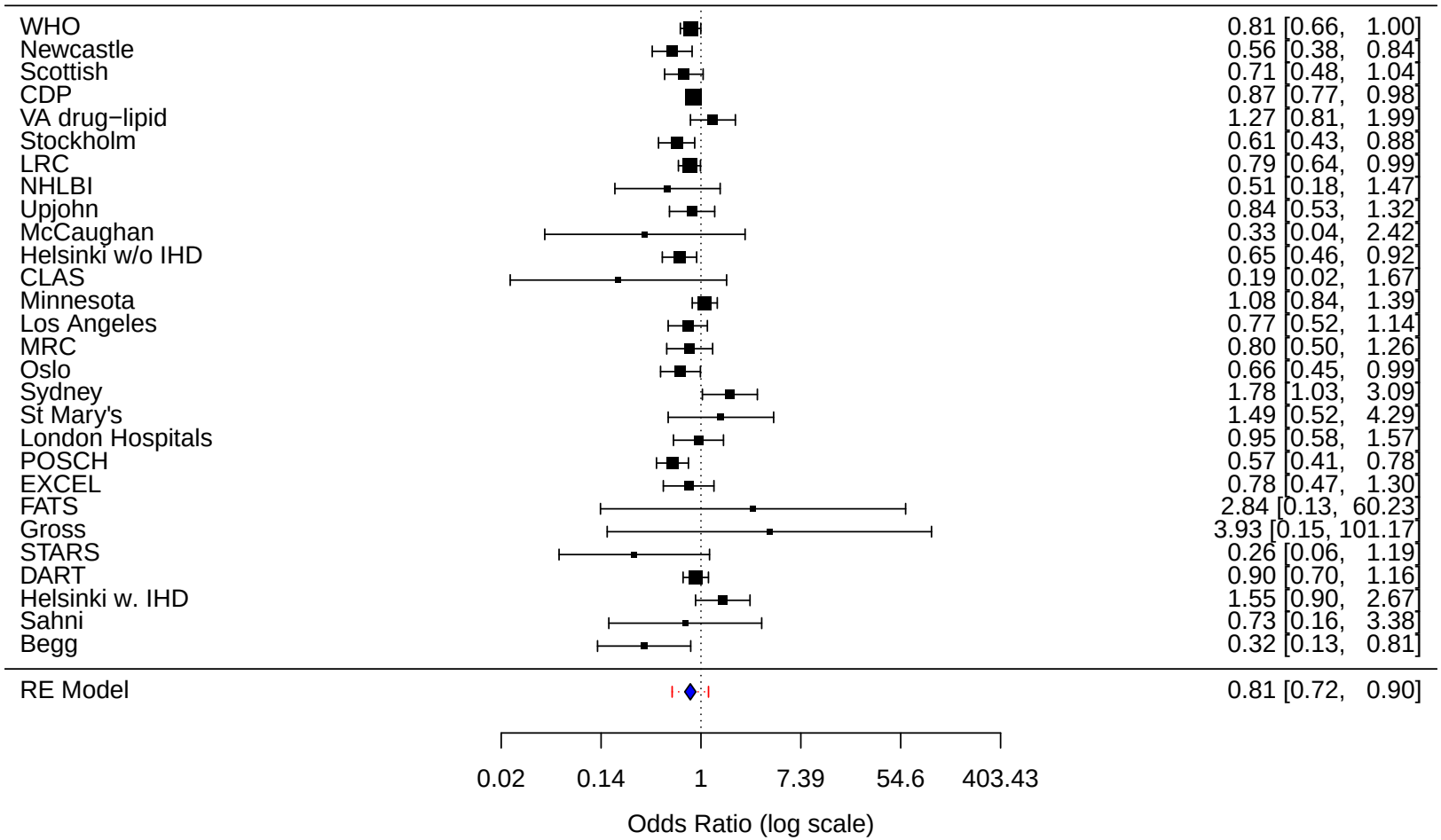


Random effects meta-analysis

```
##
## Random-Effects Model (k = 28; tau^2 estimator: REML)
##
## tau^2 (estimated amount of total heterogeneity): 0.0313 (SE =
## tau (square root of estimated tau^2 value):      0.1770
## I^2 (total heterogeneity / total variability):   47.24%
## H^2 (total variability / sampling variability):  1.90
##
## Test for Heterogeneity:
## Q(df = 27) = 49.6904, p-val = 0.0049
##
## Model Results:
##
## estimate      se     zval    pval    ci.lb    ci.ub
##  -0.2128  0.0567  -3.7530  0.0002  -0.3240  -0.1017  ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' '
```

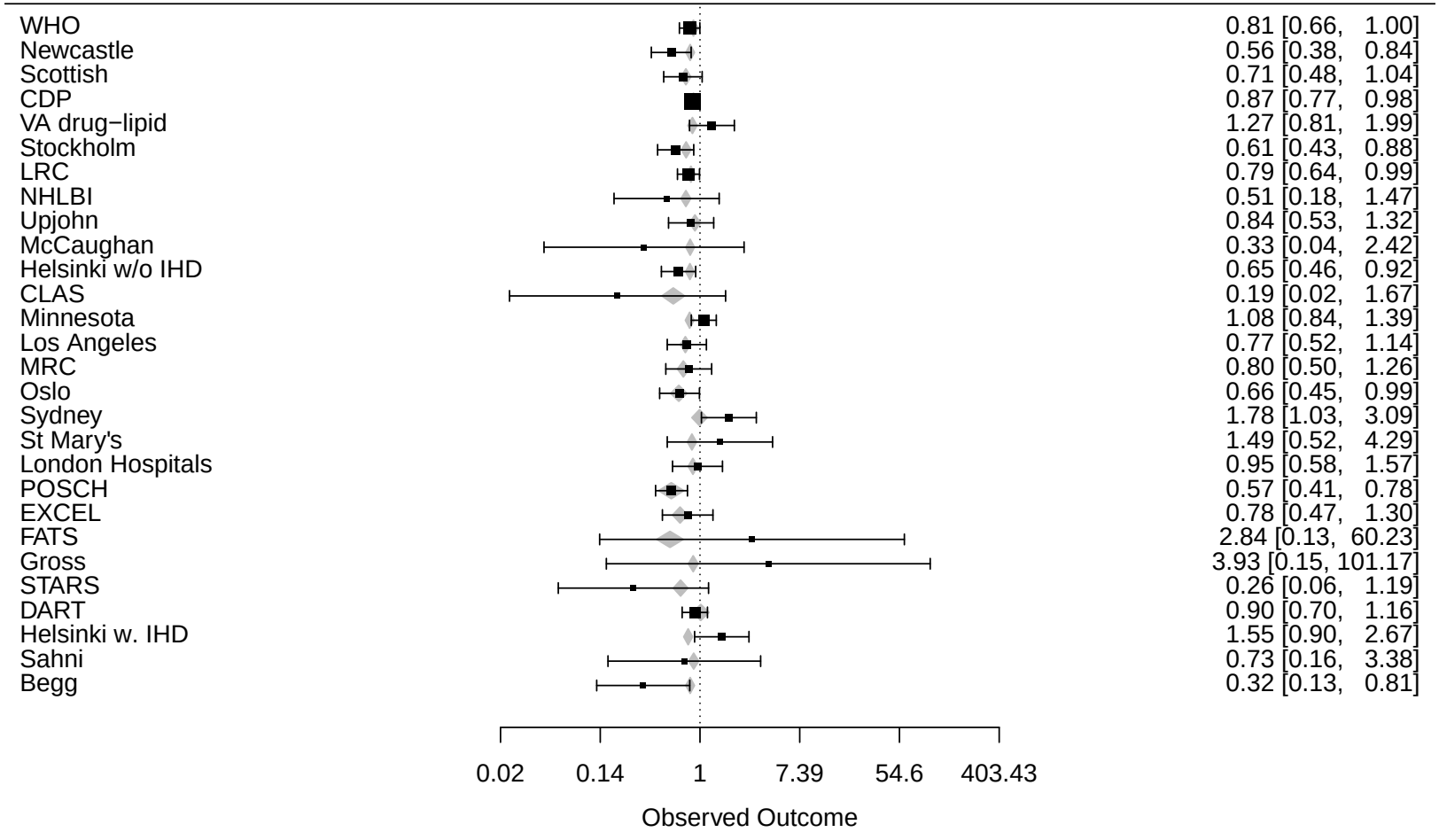
Forestplot with prediction interval

```
forest(res2, atransf = exp, slab = chol$trialname,
    addcred = TRUE, col = c("blue", "red"))
```



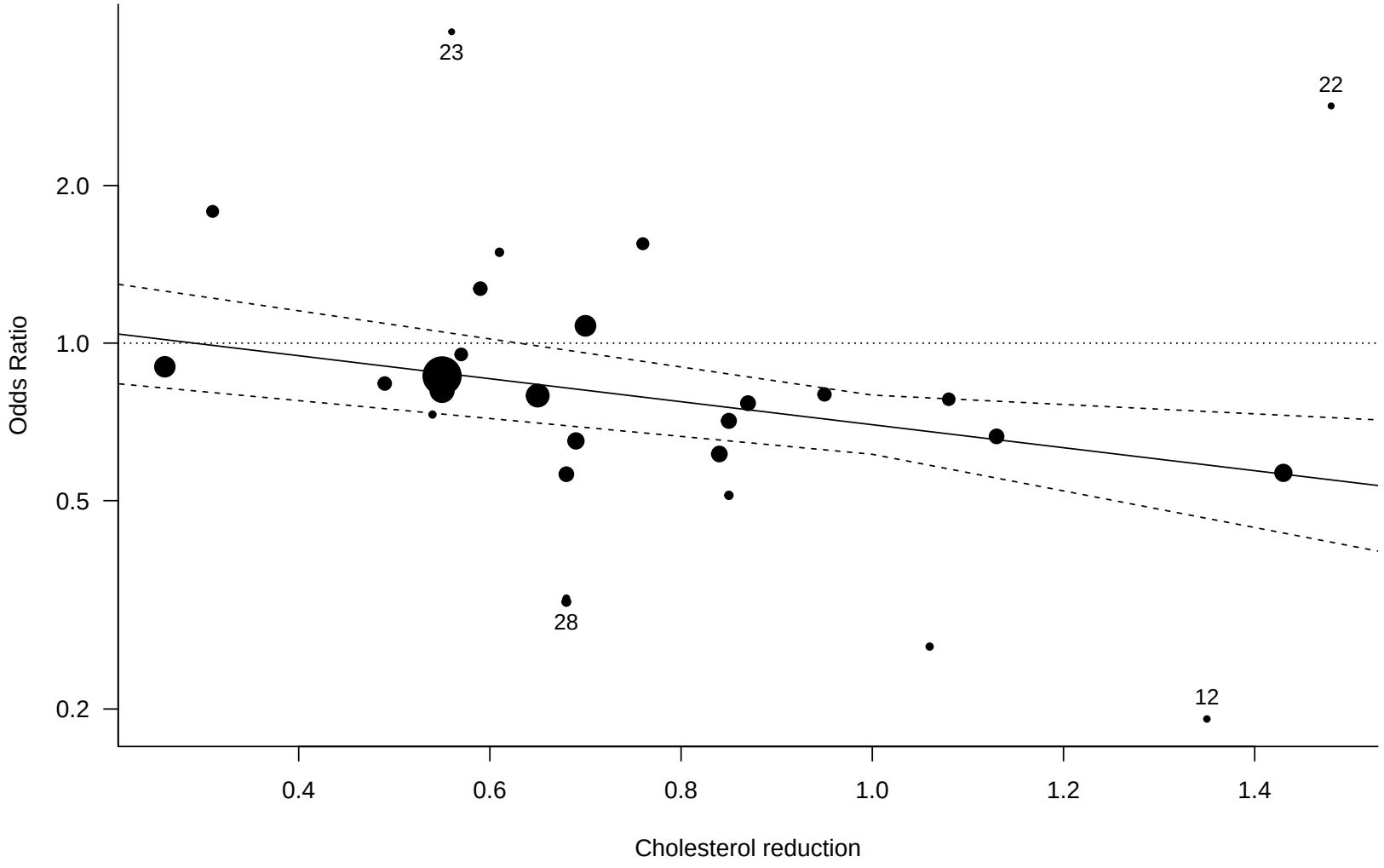
Meta-regression

Cholesterol level reduction as covariate

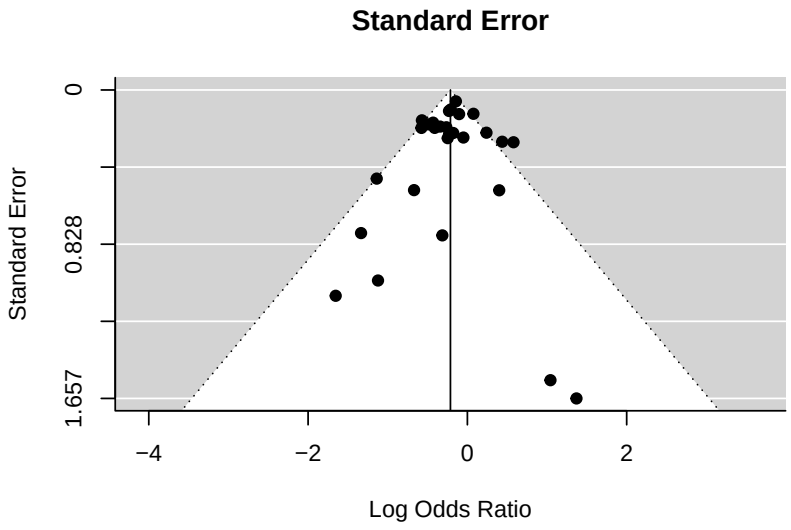


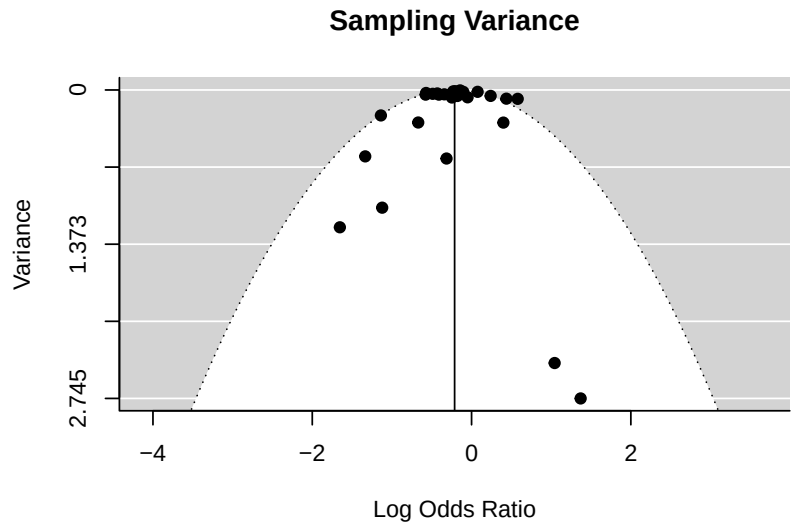
Meta-analytic Scatterplot

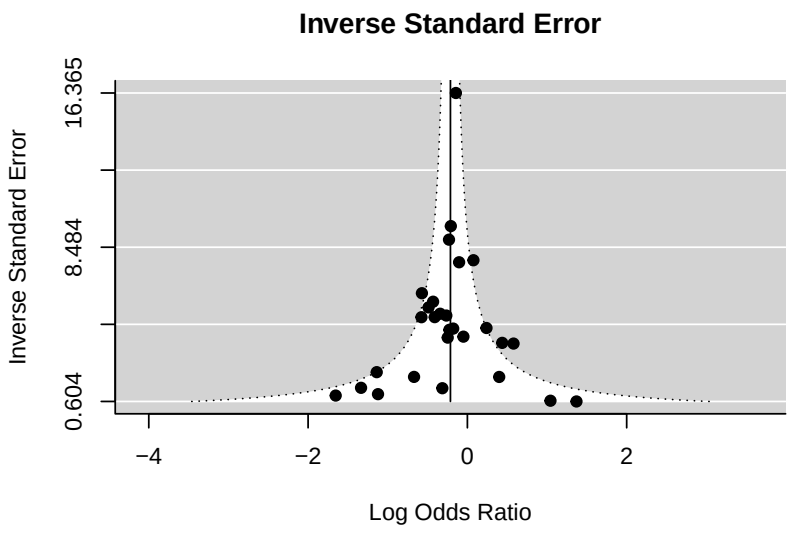
Observed outcomes (ORs) vs individual studies plotted against cholreduc

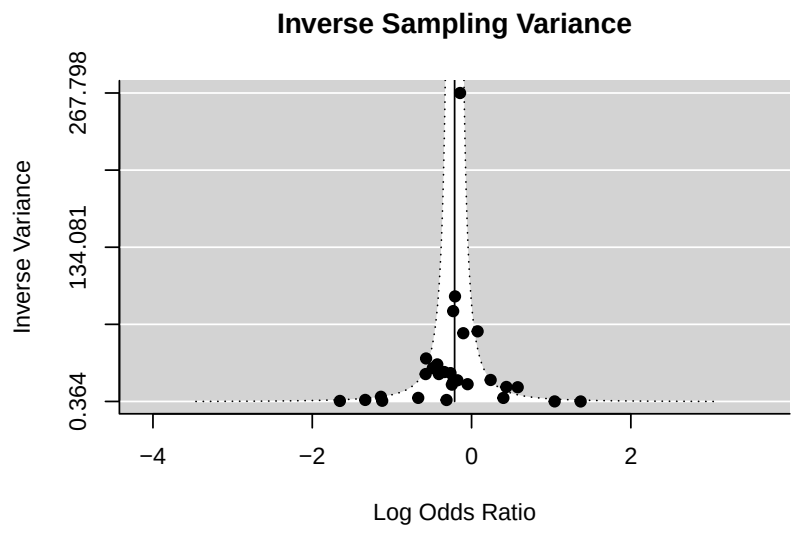


Funnelplot


Standard Error
Standard Error
0
0.828
1.657
−4
−2
0
2
Log Odds Ratio


Sampling Variance
Variance
0
1.373
2.745
−4
−2
0
2
Log Odds Ratio


Inverse Standard Error
Inverse Standard Error
16.365
8.484
0.604
−4
−2
0
2
Log Odds Ratio


Inverse Sampling Variance
Inverse Variance
267.798
134.081
0.364
−4
−2
0
2
Log Odds Ratio