METRUM INSTITUTE

MI260: Homework 1

Metrum Institute

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Problem 1: Problem statement

The dataset *MI260/FixedEffectsHandsOn/AtorvastatinStudies.csv* presents data from controlled clinical trials of atorvastatin. For this analysis we will obtain fixed- and random-effects estimates of the mean difference between 80 mg atorvastatin and placebo on the percent change from baseline LDL.

This analysis parallels what we did during the lecture for comparing 10 mg atorvastatin vs. placeo. These data will also be used later in the course to demonstrate several MBMA models.

Sample R code for data manipulation and use of the `forest` and `rma` functions is in the file *IntroductionToMetafor.r*, posted on the course website.

The variables of interest are `ldlPcfb` (mean percent change from baseline LDL) and `seLdlPcfb` (the associated standard error). The corresponding sample size in in the variable `n`.

Problem 1: Questions

1. Read the data, derive the mean difference from placebo, and corresponding standard error. Code for this step can be found in *IntroductionToMetafor.r*.
2. Make a forest plot of the data. Explore various options to make your plot look the way you'd like. You can find the options in the help files for `forest`. Looking at the forest plot, do you think there is substantial beween study variability in the difference from placebo?
3. Calculate the fixed effects estimate using the `rma` function. How can you see what the weights are for each of these studies? Are there any studies that are having a large effect on the estimated mean difference from placebo. What is the estimate of Q? Would you conlcude that there is statistically significant heterogeneity?
4. Calculate the random effects estimate using the `rma` function. Try using both the DerSimonian and Laird (`method="DL"`) and restricted maximum likelihood (`method="REML"`) estimators of τ^2. How do the estimates compare?
5. Look at the estimated values for Q and I^2. What do you conclude about heterogeneity of effect? Do you prefer the fixed or random effects model?
6. Using the `forest` and `addpoly` functions, make a forest plot overlaying the data, the fixed effect estimate and a random effects estimate of the mean difference from placebo.
7. EXTRA: If you're comfortable with Bayesian modeling, fit the random effects model using WinBUGS and your choice of prior distributions for θ and τ^2. How do your results compare to the results you obtained using `rma`?

Problem 2: Problem statement

The dataset *MI260/FixedEffectsHandsOn/CochranePancreaticData12months.csv* presents 12 month mortality data from 15 controlled clinical comparing gemcitabine+chemotherapy (GC) with gemcitabine (G) with in pancreatic cancer (Yip et al. 2006). For this analysis we will obtain meta-analysis estimates of the odds of death.

The variables of interest are `d.GC` (# deaths on GC), `N.GC` (# randomized to GC), `d.G` (# deaths on G), and `N.G` (# randomized to G). The variables `chemo` and `baseORR` will be used later in the course.

The odds ratio comparing GC to G is $OR = \frac{d.GC \times (N.G - d.G)}{(N.GC - d.GC) \times d.G}$.

For the likelihood-based methods (using `rma`), we will approximate variance of the log odds ratio using the formula

$$Var(logOR) = \frac{1}{d.GC} + \frac{1}{N.GC - d.GC} + \frac{1}{d.G} + \frac{1}{N.G - d.G}$$

Problem 2: Questions

1. Read the data, derive the log odds ratio comparing GC to G and corresponding standard error.
2. Make a forest plot of the log odds ratio values. Explore the effects of the `transf` and `atransf` options. (You can find descriptions of these in the help file for `forest.default`.) Looking at the forest plot, do you think there is substantial beween study variability in the difference from placebo?
3. Calculate the random effects estimate using the `rma` function. What do you conclude about heterogeneity of effect? Based on your answer, would you prefer a fixed or random effects model?
4. Using the `forest` and `addpoly` functions, make a forest plot overlaying the data, the fixed effect estimate and a random effects estimate of the odds ratio.
5. EXTRA: If you're comfortable with Bayesian modeling, fit the random effects model using WinBUGS and your choice of prior distributions for θ and τ^2. How do your results compare to the results you obtained using `rma`?