METRUM INSTITUTE

MI260: Homework 2

Metrum Institute

Spring 2013

Problem statement

Because we found there to be significant between-study variability in the Atorvastatin data, we will attempt to describe the variability using meta-regression.

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

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`.

Questions

1. Read the data, derive the mean difference from placebo, and corresponding standard error. Re-use the code you wrote for Homework 1 or in the file *IntroductionToMetafor.r*, posted on the course website.
2. Using the functions `funnel` and `radial` in the `rma` package, make funnel and radial plots of the difference from placebo. Do the plots look symmetric to you? Do you think there is any evidence of small study bias?
3. Plot the observed mean difference from placebo against the baseline LDL using a scatterplot. Make a forest plot of the difference from placebo, adding the baseline LDL as data (using the `ilab` option). Which plot do you prefer? Does this variable seem promising to explain some of the heterogeneity? Try making the same plots using the change from baseline in the placebo group.
4. Fit random-effects meta-regression model using both covariates. First fit the models with one covariate, then fit a model with both covariates. How would you interpret the coefficients in this meta-regression? Is there a statistically significant effect of either or both covariates? Is the estimated effect clinically meaningful? What might we conclude about the impact of the covariates on the drug effect? Is there additional residual heterogeneity after including the covariates?
5. Plot the results from one or more of your models using a forest plot. Add prediction intervals for placebo responses of -4%, -2%, 0%, and 2%.
6. Try fitting one of your meta-regression models using WinBUGS. Example code for setting up and running the models using the `R2WinBUGS` package can be found in the Homework 1 solutions. How do the posterior mean and standard deviations compare to maximum likelihood estimates?