Bayesian Methods for Salvaging Uninformative Studies

Most clinical studies, including clinical trials, are famously uninformative, usually a result of poor design and/or execution; in particular, most studies do not have sufficient statistical power to detect clinically useful effects. A random effects meta-analysis of an ensemble of such trials is usually proposed as one remedy. However, the random effects grand mean, which assumes that the between-studies variation is not zero, can be irrelevant to the individual patient. Moreover, investigators often make inappropriate inferences from those under-powered studies in which the point estimate suggests a clinically useful effect but the null hypothesis cannot be rejected. Finally, clinical trials and meta-analyses are currently designed and interpreted on the Neyman-Pearson model, which permits neither inclusion of prior information nor estimation of the predictive probabilities of future observations (e.g., the probability that a given patient will respond to a given treatment).

We present two Bayesian models that solve these, as well as several other refractory problems in design, estimation, and inference. These are the Hierarchical Bayes and the Empirical Bayes models of meta-analysis. The former provides for incorporation of prior information in parameter estimates and for estimation of predictive probabilities in the individual case. The latter takes advantage of the Stein effect to produce more accurate and precise study-specific parameter estimates.

The methods are illustrated with a small set of clinical data in infectious disease, but can obviously be generalized to almost any sort of data.