Bimodality of the likelihood function of the random-effects model in meta-analysis

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Context: One of the objectives of a meta-analysis is to synthesize multiple estimates of some common phenomenon of interest (e.g., a treatment effect, the association between two variables, the central tendency of a variable). A random-effects model is typically used for this purpose, accounting not only for differences in the precision of the estimates, but also for potential heterogeneity in the parameter being estimated.

Objectives: The random-effects model can be fitted using various procedures, including maximum likelihood (ML) and restricted maximum likelihood (REML) estimation. The ML and REML estimates must be obtained using iterative algorithms (e.g., Fisher scoring). If the (restricted) likelihood function is not unimodal, the algorithm may converge to a local optimum instead of the global one. The objectives of this talk are to examine whether the (restricted) likelihood function of the random-effects model can exhibit this behavior and to discuss the consequences if this should occur.

Methods: Using 1991 meta-analyses extracted from the Cochrane Database of Systematic Reviews, we checked for non-unimodality by profiling the (restricted) likelihood functions and searching for multiple peaks in an automated manner. Analyses were conducted using different outcome measures (i.e., odds ratios, risk ratios, and risk differences).

Results: Several cases of non-unimodality of the (restricted) likelihood function were found, but overall occurrence of this phenomenon was rare (i.e., $< 1\%$ of cases). Only bimodal cases occurred, with one peak arising at an estimate of zero for the heterogeneity variance component and another peak at a larger variance estimate. Either the former or the latter could be the global optimum and hence the true ML/REML estimate of the variance component. A meta-analysis on the effectiveness of intravenous immunoglobulin for preventing sepsis in preterm / low birth weight infants will be examined in detail.

Conclusions: The possibility of local maxima in the likelihood function has been documented for various types of models (e.g., Barnett, 1966; Henn & Hodges, 1989; Hoeschele, 2014; Small et al., 2000). The meta-analytic random-effects model can also exhibit this behavior. Estimates obtained using iterative algorithms may therefore not reflect the true ML/REML estimates. The consequences of this possibility will be discussed.