Exact confidence intervals in meta-analysis

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1 Meta-analysis

- Meta-analysis: statistical analysis that combines the results of multiple studies.
- Meta-analysis of randomized clinical trial is a powerful tool for evidence-based medicine.
- A random effect model is often used.

2 Univariate Meta-analysis

We assume that there are n clinical trials and that $y_i, i = 1, \ldots, n$ is the estimated treatment effect in the ith trial. We consider the random-effect model:

$$y_i = \theta_i + e_i, \quad \theta_i = \mu + \varepsilon_i, \quad i = 1, \ldots, n,$$

where θ_i is the true effect size of the ith study, and μ is the average treatment effect. Here e_i and ε_i are mutually independent and distributed as $e_i \sim N(0, \sigma_i^2)$ and $\varepsilon_i \sim N(0, \tau^2)$, where σ_i^2 are assumed known and fixed to their valid estimates calculated from each study.

Under the model, the likelihood function is given by

$$L(\mu, \tau^2) = -\frac{n}{2}\log(2\pi) - \frac{1}{2}\sum_{i=1}^{n}\log(\tau^2 + \sigma_i^2) - \frac{1}{2}\sum_{i=1}^{n}\frac{(y_i - \mu)^2}{\tau^2 + \sigma_i^2}.$$

The likelihood ratio statistic for testing $\mathrm{H}_0 : \mu = \mu_0$ is given by

$$T_{\mu_0}(Y) = \max_{\mu, \tau^2} L(\mu, \tau^2) - \max_{\tau^2} L(\mu_0, \tau^2),$$

with $Y = (y_1, \ldots, y_m)^t$, and its asymptotic distribution is χ_1^2. Then, the confidence interval of μ is obtained by inverting the likelihood ratio test.

However, the asymptotic approximation error is unacceptable when the number of study n is small or moderate, which leads to the short-coverage property of the confidence interval. To solve this problem, we propose a Monte Carlo method to compute exact p-values of the likelihood ratio test and obtain the exact confidence interval of μ. We will report some numerical results on the day.

3 Multivariate Meta-nalysis

The proposed Monte Carlo algorithm can also be used for deriving exact confided intervals of parameters of interest in multivariate meta-analysis including diagnostic meta-analysis and network meta-analysis. We will report details with some results from real data analysis on the day.