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Some tests based on the profile likelihood estimator for testing homogeneity of diagnostic odds ratios in meta-analysis

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Abstract

This research aims to propose some modified tests “ χ^2_{PLE1} ” and “ χ^2_{PLE2} ” based on the profile likelihood estimator for testing homogeneity of diagnostic odds ratios in meta-analysis and compare their performances with the conventional tests of Q_{WLS} , Q_{MH} and χ^2_{Con} . According to the performance in terms of type I error rates under H_0 and power of tests under H_1 , Monte Carlo simulation with R language was applied. The results found that all of tests cannot control type I error rates when sample sizes are small ($n_i^D, n_i^H \leq 5$), regardless of study size (k). However, for $k \geq 16$ in combination with $n_i^D, n_i^H \geq 50$, three tests (χ^2_{PLE1} , Q_{WLS} , χ^2_{Con}) can control type I error rates in almost all situations. In addition, the profile test (χ^2_{PLE1}) performs best with highest power when $n_i^D, n_i^H = 50, 100$ for $k \geq 16$, while conventional tests of Q_{WLS} and χ^2_{Con} perform well with the same power as the profile test (χ^2_{PLE1}) when $n_i^D, n_i^H = 500$ for $k \geq 16$. Therefore, the χ^2_{PLE1} is recommended to be used when $k \geq 16$ in combination with $n_i^D, n_i^H \geq 50$.

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1. Introduction

Let diagnostic odds ratio estimate as an effect size be defined as $\hat{\theta} = \hat{q}^D / \hat{q}^H$ where $\hat{q}^D = \hat{p}^D / (1 - \hat{p}^D)$ and $\hat{q}^H = \hat{p}^H / (1 - \hat{p}^H)$ are the estimated odds of positive risks $\hat{p}^D = x^D / n^D$ and $\hat{p}^H = x^H / n^H$ in the disease and healthy

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groups, where x^D and x^H are the number of positive data out of the total number of subjects n^D and n^H , respectively. Mostly the point estimator $\hat{\theta}$ is derived by a maximum likelihood method. But in this study, we are interested to seek an alternative estimate $\hat{\theta}$ from the profile likelihood approach which widely used to eliminate a nuisance parameter and it also has an invariant property¹. Usually, meta-analysis is a statistical technique for combining results of different studies into a summarizing result. However, before combining the diagnostic odds ratios of different studies to obtain an overall effect, the hypothesis testing is requested to evaluate whether there is true heterogeneity occurrence, or not. Cochran's Q test is conventionally popular for testing the null hypothesis: $H_0: \theta_1 = \dots = \theta_k = \theta$ where θ is a true diagnostic odds ratio over across study i ($i=1, \dots, k$)². However, Cochran's Q test might have been low in the power of test when the number of studies (k) included in the meta-analysis is small. The low power of test implies that a statistically non-significant test can occur even though the genuine heterogeneity of population effects is present. Many scientists try to increase the power of Q test with several methods. We also have an attempt to modify some tests by replacing the profile likelihood estimator into the variance of logarithm of diagnostic odds ratio. A comparison of the performance of tests in terms of type I error and the power is applied via a simulation study.

2. Methodology

The methods are divided into two parts: (1) providing the idea of creating modified tests for homogeneity of diagnostic odds ratios in meta-analysis and (2) comparing the efficiency between two new proposed tests (χ^2_{PMLE1} , χ^2_{PMLE2}) based on the profile likelihood estimator (PLE) and the conventional tests by simulation with R language in different situations.

Part 1: We followed the work of Böhning et al.³ who had already provided the estimate of the diagnostic odds ratios based on the profile likelihood method and the pooled diagnostic odds ratio estimator under homogeneity is obtained as:

$$\hat{\theta}_{PMLE} = \frac{\sum_{i=1}^k \frac{(n_i^H - x_i^H)x_i^D}{\sqrt{r_i(\hat{\theta}_{PMLE})}}}{\sum_{i=1}^k t_i(\hat{\theta}_{PMLE})} \quad \text{where } q_i^H[\hat{\theta}] = \frac{-(x_i^D + x_i^H - n_i^H + (x_i^D + x_i^H - n_i^D)\hat{\theta}) - \sqrt{r_i(\hat{\theta})}}{2(x_i^D + x_i^H - n_i^H - n_i^D)\hat{\theta}}$$

$$r_i(\hat{\theta}) = -4(x_i^D + x_i^H)(x_i^D + x_i^H - n_i^H - n_i^D)\hat{\theta} + [(x_i^D + x_i^H - n_i^H) + (x_i^D + x_i^H - n_i^D)\hat{\theta}]^2$$

$$t_i(\hat{\theta}) = \frac{n_i^D(\hat{\theta} \times (q_i^H)'[\hat{\theta}] + q_i^H[\hat{\theta}])}{1 + \hat{\theta} \times q_i^H[\hat{\theta}]} - \frac{(x_i^D + x_i^H)(q_i^H)'[\hat{\theta}]}{q_i^H[\hat{\theta}]} + \frac{n_i^H(q_i^H)'[\hat{\theta}]}{1 + q_i^H[\hat{\theta}]} + \frac{(n_i^H - x_i^H)x_i^D - x_i^D\sqrt{r_i(\hat{\theta})}}{\hat{\theta}\sqrt{r_i(\hat{\theta})}}$$

To obtain the modified tests for testing homogeneity of diagnostic odds ratios over k studies in meta-analysis, we replace the profile likelihood estimator $\hat{\theta}_{PMLE}$ into the variance formula of logarithmic diagnostic odds ratio $\hat{v}ar(\hat{\theta}_i)$ on the form of the below χ^2 :

$$\chi^2 = \sum_{i=1}^k \frac{(\hat{\theta}_i - \hat{\theta}_{PMLE})^2}{\hat{v}ar(\hat{\theta}_i)} \quad \text{where } \hat{\theta}_i = \log \hat{\theta}_i = \log\left(\frac{\hat{p}_i^D}{1 - \hat{p}_i^D}\right) - \log\left(\frac{\hat{p}_i^H}{1 - \hat{p}_i^H}\right) \quad \text{and } \hat{\theta}_{PMLE} = \log \hat{\theta}_{PMLE}$$

1. Conventional variance estimate from the delta's method for χ^2_{Con}

$$\hat{v}ar(\hat{\theta}_i) = \frac{1}{n_i^D \hat{p}_i^D (1 - \hat{p}_i^D)} + \frac{1}{n_i^H \hat{p}_i^H (1 - \hat{p}_i^H)} = \frac{1}{x_i^D} + \frac{1}{n_i^D - x_i^D} + \frac{1}{x_i^H} + \frac{1}{n_i^H - x_i^H}$$

2. Modification of variance estimate for χ^2_{PMLE1} when $\hat{p}_i^H = x_i^H / n_i^H$ and $\hat{p}_i^D = \frac{\hat{\theta}_{PMLE} \hat{p}_i^H}{(1 - \hat{p}_i^H + \hat{\theta}_{PMLE} \hat{p}_i^H)}$

$$\hat{v}ar(\hat{\theta}_i) = \frac{1}{n_i^D \left(\frac{\hat{\theta}_{PMLE} \hat{p}_i^H}{1 - \hat{p}_i^H + \hat{\theta}_{PMLE} \hat{p}_i^H} \right) \left(1 - \frac{\hat{\theta}_{PMLE} \hat{p}_i^H}{1 - \hat{p}_i^H + \hat{\theta}_{PMLE} \hat{p}_i^H} \right)} + \frac{1}{n_i^H \hat{p}_i^H (1 - \hat{p}_i^H)}$$

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