A new measure of between-studies heterogeneity in meta-analysis

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Conclusions

• We recommend the use of $R_b$, as the preferred measure for quantifying the impact of heterogeneity
• Its validity does not require the specification of a $\sigma^2$ term
• $R_b$ can be interpreted as the proportion of the variance of the pooled random effect estimate due to between-studies heterogeneity
• The proposed measure is implemented in the dosresmeta R package and %metaanal SAS macro

Introduction

Measures of heterogeneity, $I^2$ and $R_b$, relates the heterogeneity, $\tau^2$, to the total variance of the effect estimate, $\tau^2 + \sigma^2$, where $\sigma^2$ is a summary of the observed within-study error variances, $\nu_i$. The latter term, however, may substantially vary across studies (Table I). A measure that relaxes the hypothesis of homogeneity of within-studies variances is desirable.

Aims

To propose a new measure of heterogeneity, $R_b$, which does not depend upon the definition of $\sigma^2$. Performances of the proposed measure are evaluated through simulations studies.

A new measure of heterogeneity, $R_b$

The new measure quantifies the contribution of $\tau^2$ relative to the variance of the pooled random-effects estimate, $\hat{\beta}_{re}$:

$$R_b = \frac{\hat{\tau}^2}{K \hat{V}ar(\hat{\beta}_{re})} = \frac{1}{K} \sum_{i=1}^{K} \frac{\hat{\tau}^2}{\nu_i + \hat{\tau}^2}$$

$K$ equal to the number of studies and $\hat{\tau}^2$ being the moment based estimate of heterogeneity. $R_b$ satisfies the properties for a measure of heterogeneity. $R_b$ is a consistent and asymptotically normal distributed estimator. It coincides with $I^2$ and $R_I$ when $\nu_i = 0, \forall i = 1, ..., K$

Table I. Example of two hypothetical meta-analyses of 10 studies

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Effect Size</th>
<th>$p$ Value for Q test</th>
<th>$CV_{\nu_i}$</th>
<th>$\sigma^2 (I^2)$</th>
<th>$\sigma^2 (R_I)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gibson, 2002</td>
<td>SMD</td>
<td>0.008</td>
<td>0.67</td>
<td>51 (17, 85)</td>
<td>56 (19, 94)</td>
</tr>
<tr>
<td>Codd, 1994</td>
<td>logRR</td>
<td>0.001</td>
<td>1.14</td>
<td>74 (53, 96)</td>
<td>94 (85, 100)</td>
</tr>
<tr>
<td>Millett, 2008</td>
<td>LogOR</td>
<td>0.05</td>
<td>0.53</td>
<td>1.78</td>
<td>77 (44, 100)</td>
</tr>
</tbody>
</table>

Table II. Heterogeneity assessment in a re-analysis of 3 meta-analyses

Simulation study

Different scenario simulations: true heterogeneity measure = 0.1, 0.5, 0.7; effect size $\beta_{re} = 1, 2, 4$; coefficient of variation of $\nu_i$, $CV_{\nu_i} = 0.5, 1, 2$; coefficient of variation of $\hat{\beta}_{re}$, $CV_{\hat{\beta}} = 1, 3$; $K = 5, 20, 50, 100$.

• No specific pattern in the bias for $R_b$ according to $CV_{\nu_i}$ and $CV_{\hat{\beta}}$ values
• $I^2$ and $R_I$ overestimated the impact of heterogeneity
• The coverage was good for confidence intervals based upon $R_b$
• Bias and coverage for $I^2$ and $R_I$ worsened as $CV_{\nu_i}$ increased

Figure 1. Percent relative bias for $R_b$, $I^2$ and $R_I$ as a function of within-study variances ($CV_{\nu_i}$) for simulated meta-analyses of ($K = 50$ and true heterogeneity = 0.5) studies, averaged over different values of between-studies coefficient of variations ($CV_{\nu_b}$).