

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

Alessio Crippa,¹ Polyna Khudyakov,² Molin Wang,^{2,3} Nicola Orsini,¹ Donna Spiegelman^{2,3}

¹Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden

²Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA

³Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA, USA

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 σ^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

<https://alecri.shinyapps.io/bias/>

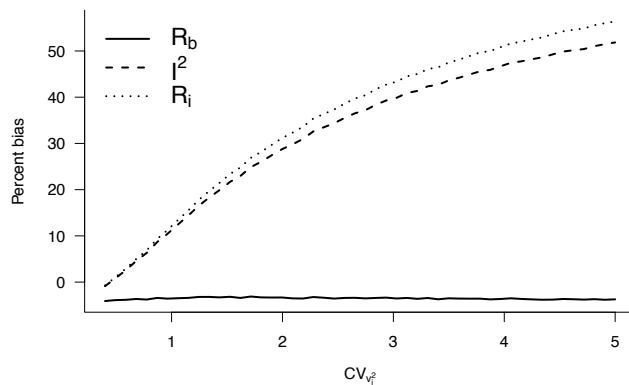


Figure 1. Percent relative bias for R_b , I^2 and R_I as a function of within-study variances (CV_{v_i}) for simulated meta-analyses of ($K = 50$ and true heterogeneity = 0.5) studies, averaged over different values of between-studies coefficient of variations (CV_B).

Introduction

Measures of heterogeneity, I^2 and R_I , relates the heterogeneity, τ^2 , to the total variance of the effect estimate, $\tau^2 + \sigma^2$, where σ^2 is a summary of the observed within-study error variances, v_i . The latter term, however, may substantially varies 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 σ^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 τ^2 relative to the variance of the pooled random-effects estimate, $\bar{\beta}_{re}$

$$\hat{R}_b = \frac{\hat{\tau}^2}{K \text{Var}(\bar{\beta}_{re})} = \frac{1}{K} \sum_{i=1}^K \frac{\hat{\tau}^2}{v_i + \hat{\tau}^2}$$

K equal to the number of studies and $\hat{\tau}^2$ being the moment based estimate of heterogeneity.

R_b satisfied 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 $v_i = 0, \forall i = 1, \dots, K$

Analysis	v_1, \dots, v_{10}	CV_{v_i}	$\sigma^2 (I^2)$	$\sigma^2 (R_I)$
A	6, 6.1, 6.2, 5.9, 6, 5.9, 6.1, 5.8, 6, 6.2	0.022	6.018	6.017
B	5, 19, 3, 15, 6, 23, 4, 17, 2, 8.8	0.736	6.017	5.602

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

Author, Year	K	Effect Size	β_{re} (95% CI)	p value for Q test	CV_{v_i}	\hat{R}_b (95% CI)	I^2 (95% CI)	R_I (95% CI)
Gibson, 2002	13	SMD	-0.19 (-0.35, -0.04)	0.008	0.67	51 (17, 85)	55 (11, 85)	56 (19, 94)
Colditz, 1994	13	logRR	-0.71 (-1.06, -0.36)	< 0.001	1.14	74 (53, 96)	92 (82, 98)	94 (85, 100)
Millett, 2008	15	LogOR	-0.05 (-0.20, -0.11)	0.53	1.78	39 (9, 68)	61 (16, 100)	77 (44, 100)

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 $\bar{\beta}_{re} = 1, 2, 4$; coefficient of variation of v_i , $CV_{v_i} = 0.5, 1, 2$; coefficient of variation of $\bar{\beta}_{re}$, $CV_B = 0.5, 1, 3$; $K = 5, 20, 50, 100$.

- No specific pattern in the bias for R_b according to CV_{v_i} and CV_B 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_{v_i} increased



Karolinska Institutet
Alessio Crippa
Department of Public Health Sciences
Tomtebodavägen 18A
SE-171 77, Stockholm

E-mail: alessio.crippa@ki.se
Website: <http://ki.se/en/people/alecri>

