Evaluation of statistical methods for meta-analysis

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Evidence to inform statistical methods

- Statistical theory
- Empirical data
  - impact of different methods on results
  - context of implementation
- Simulation studies

- Interpretation
  - by users of methods
  - by readers

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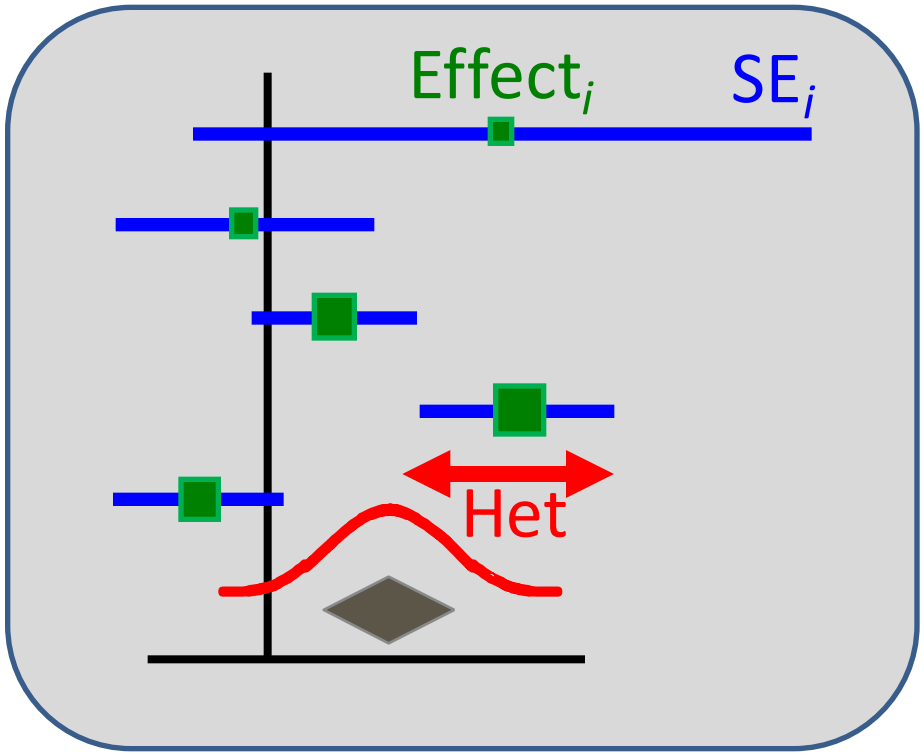
Random-effects meta-analysis

$$\frac{\sum \text{Effect}_i \Big/ \left(\text{SE}_i^2 + \text{Het}\right)}{\sum 1 \Big/ \left(\text{SE}_i^2 + \text{Het}\right)}$$

$$\frac{\sum y_i w_i^*}{\sum w_i^*}$$



Some issues

- Choice of effect measure y_i
- Choice of estimator y_i
- Error in estimated SE_i
- Validity of normal distribution
- *Choice of heterogeneity estimator*

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Review of available methods

Invited Review

Research Synthesis Methods

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Methods to estimate the between-study variance and its uncertainty in meta-analysis

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Meta-analyses are typically used to estimate the overall/mean of an outcome of interest. However, inference about between-study variability, which is typically modelled using a between-study variance parameter, is usually an additional aim. The DerSimonian and Laird method, currently widely used by default to estimate the between-study variance, has been long challenged. Our aim is to identify known methods for estimation of the between-study variance and its corresponding uncertainty, and to summarise the simulation and empirical evidence that compares them. We identified 16 estimators for the between-study variance, seven methods to calculate confidence intervals, and several comparative studies. Simulation studies suggest that for both dichotomous and continuous data the estimator proposed by Paule and Mandel and for continuous data the restricted maximum likelihood estimator are better alternatives to estimate the between-study variance. Based on the scenarios and results presented in the published studies, we recommend the Q-profile method and the alternative approach based on a 'generalised Cochran between-study variance statistic' to compute corresponding confidence intervals around the resulting estimates. Our recommendations are based on a qualitative evaluation of the existing literature and expert consensus. Evidence-based recommendations require an extensive simulation study where all methods would be compared under the same scenarios.

Keywords: heterogeneity; mean squared error; bias; coverage probability; confidence interval

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Empirical examination of differences in results

Original Article

Research Synthesis Methods

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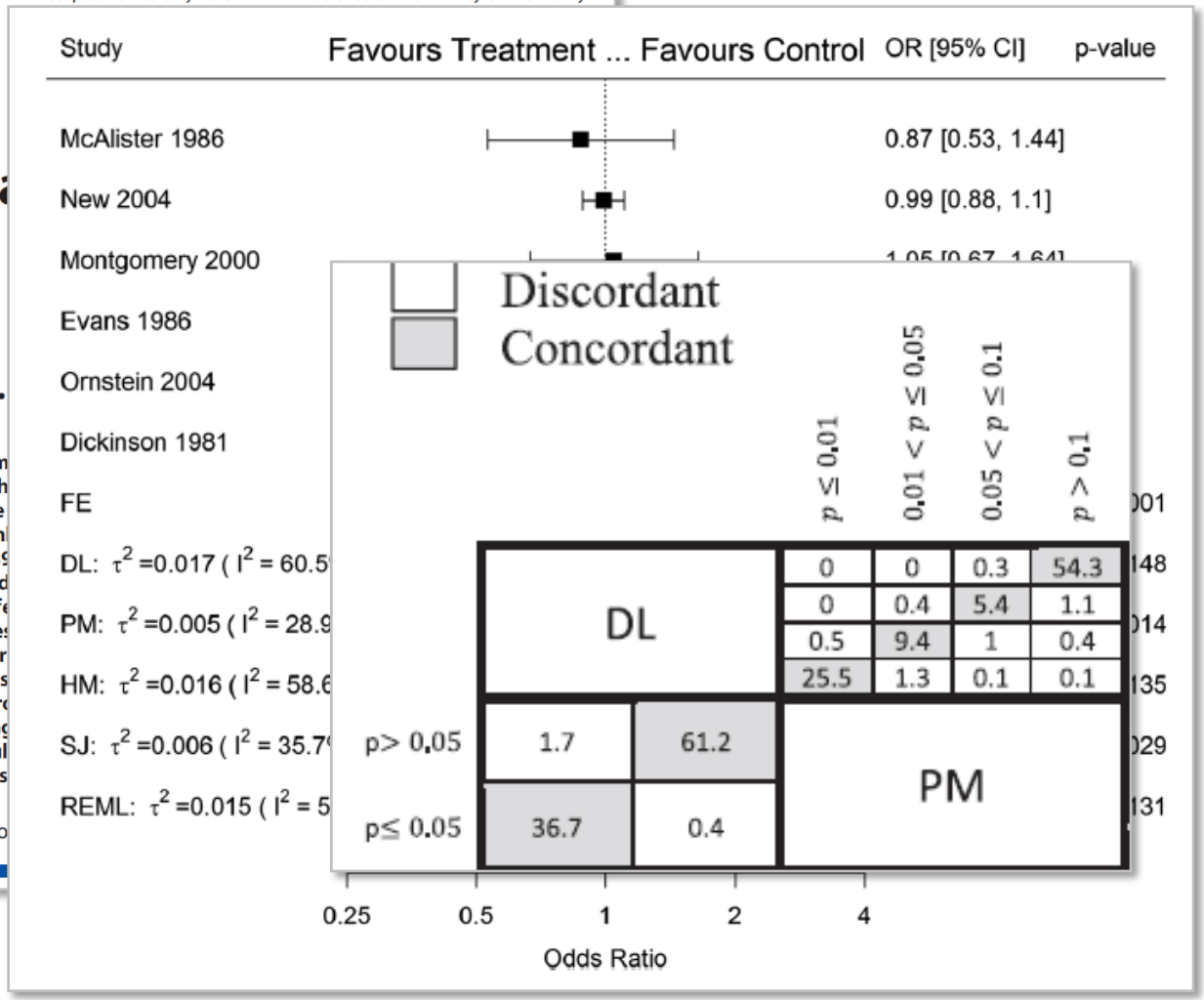
An empirica heterogeneity in 12894

Dean Langan,[a*†] Julian P.

Heterogeneity in meta-analysis is most comm by DerSimonian and Laird. However, this meth methods to estimate heterogeneity include proposed by Paule and Mandel, Sidik and Jon of these five methods on the results of 12,89 *Systematic Reviews*. We compared the method expressed as an I^2 statistic; (2) the overall effe and (4) *p*-values testing the no effect hypothes differ by more than 50% when different heter statistical significance (at a 5% level) were dis analyses, indicating that the choice of heter analysis. These findings imply that using a sing in some meta-analyses, and researchers shoul method. Copyright © 2015 John Wiley & Sons

Keywords: meta-analysis; heterogeneity; rando



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Systematic review of simulation studies

Comparative performance of heterogeneity variance estimators in meta-analysis: a review of simulation studies

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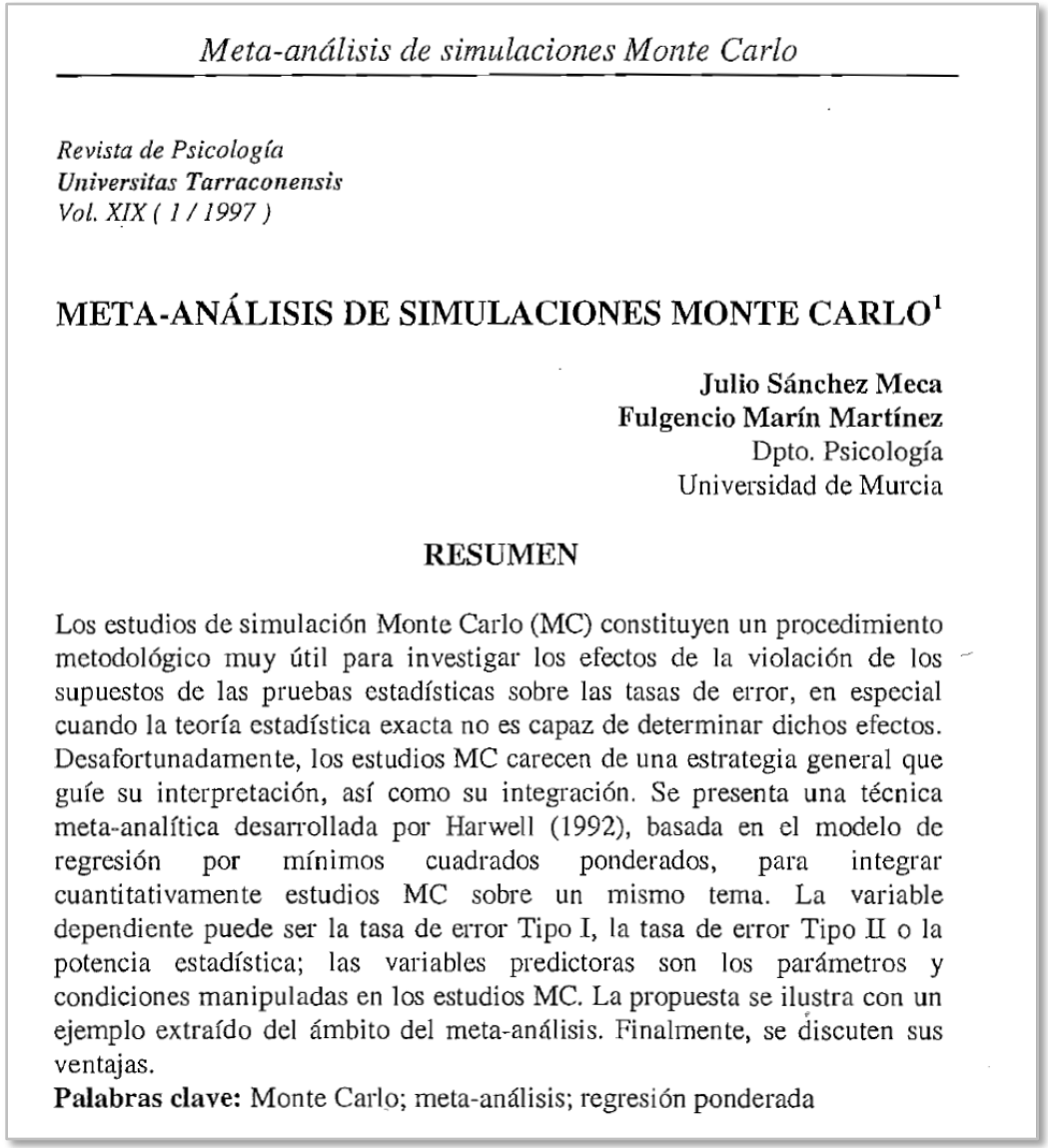
Abstract

Random-effects meta-analysis methods include an estimate of between-study heterogeneity variance. We present a systematic review of simulation studies comparing the performance of different estimation methods for this parameter. We summarise the performance of methods in relation to estimation of heterogeneity and of the overall effect estimate, and of confidence intervals for the latter. Among the twelve included simulation studies, the DerSimonian and Laird method was most commonly evaluated. This estimate is negatively biased when heterogeneity is moderate to high and therefore most studies recommended alternatives. The Paule-Mandel method was recommended by three studies: it is simple to implement, is less biased than DerSimonian and Laird and performs well in meta-analyses with dichotomous and continuous outcomes. In many of the included simulation studies, results were based on data that do not represent meta-analyses observed in practice and only small selections of methods were compared. Furthermore, potential conflicts of interest were present when authors of novel methods interpreted their results. On the basis of current evidence, we provisionally recommend the Paule-Mandel method for estimating the heterogeneity variance, and using this estimate to calculate the mean effect and its 95% confidence interval. However, further simulation studies are required to draw firm conclusions.

"On the basis of current evidence, we provisionally recommend the Paule-Mandel method for estimating the heterogeneity variance, and using this estimate to calculate the mean effect and its 95% confidence interval. However, further simulation studies are required to draw firm conclusions."

Meta-analysis of simulation study results



Meta-análisis de simulaciones Monte Carlo

Revista de Psicología
Universitas Tarraconensis
Vol. XIX (1 / 1997)

META-ANÁLISIS DE SIMULACIONES MONTE CARLO[1]

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RESUMEN

Los estudios de simulación Monte Carlo (MC) constituyen un procedimiento metodológico muy útil para investigar los efectos de la violación de los supuestos de las pruebas estadísticas sobre las tasas de error, en especial cuando la teoría estadística exacta no es capaz de determinar dichos efectos. Desafortunadamente, los estudios MC carecen de una estrategia general que guíe su interpretación, así como su integración. Se presenta una técnica meta-analítica desarrollada por Harwell (1992), basada en el modelo de regresión por mínimos cuadrados ponderados, para integrar cuantitativamente estudios MC sobre un mismo tema. La variable dependiente puede ser la tasa de error Tipo I, la tasa de error Tipo II o la potencia estadística; las variables predictoras son los parámetros y condiciones manipuladas en los estudios MC. La propuesta se ilustra con un ejemplo extraído del ámbito del meta-análisis. Finalmente, se discuten sus ventajas.

Palabras clave: Monte Carlo; meta-análisis; regresión ponderada

Meta-regression

Type I error = $\alpha + \beta_1 \times$ no. studies
$+ \beta_2 \times$ study size
$+ \beta_3 \times$ baseline risk
etc

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A comprehensive simulation study

PROTOCOL

A Comprehensive Simulation Study to Compare Methods of Estimating Heterogeneity Variance in Meta-analysis

Version 3.0, 23/12/2014

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Reaching recommendations

- We need to understand the real world implications
- What properties do *meta-analyses* have?

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Davey et al. BMC Medical Research Methodology 2011, 11:160
http://www.biomedcentral.com/1471-2288/11/160

CORRESPONDENCE

Characteristics of meta-

ELSEVIER

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Journal of Clinical Epidemiology 68 (2015) 52–60

Journal of Clinical Epidemiology

Predictive distributions were developed for the extent of heterogeneity in meta-analyses of continuous outcome data

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y heterogeneity is problematic in small meta-analyses. Bayesian meta-analysis is beneficial

Predicting the extent of heterogeneity in meta-analysis, using empirical data from the *Cochrane Database of Systematic Reviews*

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Accepted 22 February 2012

Background Many meta-analyses contain only a small
makes it difficult to estimate the extent
geneity. Bayesian meta-analysis allows
evidence on heterogeneity, and offers adv
random-effects meta-analysis. To assist i
ical evidence on the likely extent of h
areas of health care.

Methods Our analyses included 14 886 meta-ana
Database of Systematic Reviews. We class
according to the type of outcome, type o
and medical specialty. By modelling t
meta-analyses simultaneously, using the
investigated the impact of meta-analys
underlying between-study heterogeneity
butions were obtained for the heteroge
meta-analyses.

Results Between-study heterogeneity variances fo
the outcome was all-cause mortality wer
17% (95% CI 10–26) of variances for
analyses comparing two active pharmaco
erogeneity was on average 75% (95% C
non-pharmacological interventions. Meta
to have only a small effect on heterogenei

Statistics in Medicine

Research Article

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Predictive distributions for between-study heterogeneity and simple methods for their application in Bayesian meta-analysis

Rebecca M. Turner,[a]*† Dan Jackson,[a] Yinghui Wei,[b] Simon G. Thompson[c] and Julian P. T. Higgins[d,e]

Numerous meta-analyses in healthcare research combine results from only a small number of studies, for which the variance representing between-study heterogeneity is estimated imprecisely. A Bayesian approach to estimation allows external evidence on the expected magnitude of heterogeneity to be incorporated.

The aim of this paper is to provide tools that improve the accessibility of Bayesian meta-analysis. We present two methods for implementing Bayesian meta-analysis, using numerical integration and importance sampling techniques. Based on 14 886 binary outcome meta-analyses in the *Cochrane Database of Systematic Reviews*, we

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Combining properties of estimators with prevalence of different scenarios

Combine

- properties of the methods under different scenarios

with

- prevalence of those scenarios

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Concluding remarks

- Recommendations for statistical methods should combine
  - theoretical considerations
  - technical properties as demonstrated through simulation studies
  - empirical data on whether it makes much difference in practice
  - information on which scenarios are most common (if properties of the methods vary by scenario)
- Simulation studies need to be informed by real world scenarios
- In most Cochrane meta-analyses, all methods for estimating between-study variance are poor and likely to be imprecise, with some positive or negative bias
- But confidence intervals for the meta-analysis are reasonably robust if done using Hartung-Knapp correction