Simulation study of estimating between-study variance and overall effect in meta-analyses of log-response-ratio for lognormal data

Ilyas Bakbergenuly, David C. Hoaglin, and Elena Kulinskaya

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Abstract

Methods for random-effects meta-analysis require an estimate of the between-study variance, $\tau^2$. The performance of estimators of $\tau^2$ (measured by bias and coverage) affects their usefulness in assessing heterogeneity of study-level effects, and also the performance of related estimators of the overall effect. For the effect measure log-response-ratio (LRR, also known as the logarithm of the ratio of means, RoM), we review four point estimators of $\tau^2$ (the popular methods of DerSimonian-Laird (DL), restricted maximum likelihood, and Mandel and Paule (MP), and the less-familiar method of Jackson), four interval estimators for $\tau^2$ (profile likelihood, Q-profile, Biggerstaff and Jackson, and Jackson), five point estimators of the overall effect (the four related to the point estimators of $\tau^2$ and an estimator whose weights use only study-level sample sizes), and seven interval estimators for the overall effect (four based on the point estimators for $\tau^2$, the Hartung-Knapp-Sidik-Jonkman (HKSJ) interval, a modification of HKSJ that uses the MP estimator of $\tau^2$ instead of the DL estimator, and an interval based on the sample-size-weighted estimator). We obtain empirical evidence from extensive simulations of data from lognormal distributions.

Keywords between-study variance, heterogeneity, random-effects model, meta-analysis, log-response-ratio, ratio of means
1 Introduction

Meta-analysis is a statistical methodology for combining estimated effects from several studies in order to assess their heterogeneity and obtain an overall estimate. In this paper we focus on the log-response-ratio (LRR, also known as the logarithm of the ratio of means, RoM) as the effect measure. In ecology almost half of all meta-analyses use this outcome measure [Koricheva and Gurevitch 2014, Nakagawa and Santos 2012].

The LRR was introduced by Hedges et al. 1999 and rediscovered as RoM by Friedrich et al. 2008. Both publications assumed underlying normality of the raw data. However, the LRR is not defined for negative values of the study means, and Lajeunesse 2015 modeled the data by lognormal distributions. We explore the meta-analysis of LRR under the lognormal distribution in this report. Our results under normality constitute a companion report.

If the studies can be assumed to have the same true effect, a meta-analysis can use a fixed-effect (FE) model (common-effect model) to combine the estimates. Otherwise, the studies’ true effects can depart from homogeneity in a variety of ways. Most commonly, a random-effects (RE) model regards those effects as a sample from a distribution and summarizes their heterogeneity via its variance, usually denoted by $\tau^2$. The between-studies variance, $\tau^2$, has a key role in estimates of the mean of the distribution of random effects; but it is also important as a quantitative indication of heterogeneity [Higgins et al., 2009]. In studying estimation for meta-analysis of LRR, we focus first on $\tau^2$ and then proceed to the overall effect.

Veroniki et al. 2016 provide a comprehensive overview and recommendations on methods of estimating $\tau^2$ and its uncertainty. Their review, however, has two important limitations. First, the authors study only “methods that can be applied for any type of outcome data.” However, as we show elsewhere, the performance of the methods varies widely among effect measures. Second, any review of the topic, such as Veroniki et al. 2016, currently can draw on only limited empirical information on the comparative performance of the methods. We address both issues for the effect measure LRR.

Veroniki et al. 2016 (Appendix Table 1) cite no previous simulation studies on the comparative performance of estimates of $\tau^2$ for LRR.

Several studies have considered the quality of estimation of LRR itself. Friedrich et al. 2008 report extensive simulations for LRR under normality, but they use
only the DerSimonian-Laird (DL) method to estimate \( \tau^2 \) and do not report on its quality. Lajeunesse [2015] discusses bias correction for LRR and its variance, and provides some simulation results for lognormal distributions, but only under the fixed-effect model. Doncaster and Spake [2018] provide some limited simulation results for accuracy of estimation of the heterogeneity variance \( \tau^2 \), the overall LRR, and its variance, using the DL and restricted maximum-likelihood (REML) methods to estimate \( \tau^2 \) under normality. To assess bias of the estimators of LRR, they use mean absolute error, which is not a measure of bias; it is the linear counterpart of mean squared error.

To address this gap in information on methods of estimating the heterogeneity variance for LRR, we use simulation to study four methods recommended by Veroniki et al. [2016]. These are the well-established methods of DerSimonian and Laird [1986], restricted maximum likelihood, and Mandel and Paule [1970] (MP), and the less-familiar method of Jackson [2013]. We also study coverage of confidence intervals for \( \tau^2 \) achieved by four methods: the Q-profile method of Viechtbauer [2007], the methods of Biggerstaff and Jackson [2008] and Jackson [2013], and the profile-likelihood-based interval.

For each estimator of \( \tau^2 \), we also study bias of the corresponding inverse-variance-weighted estimator of the overall effect. However, it is well known that these inverse-variance-weighted estimators have unacceptable bias for some other effect measures, as Bakbergenuly et al. [2018] and Hamman et al. [2018] show for the standardized mean difference. Therefore, we added an estimator (SSW) whose weights depend only on the sample sizes of the Treatment and Control arms. We study the coverage of the confidence intervals associated with the inverse-variance-weighted estimators, and also the HKSJ interval (Hartung and Knapp [2001], Sidik and Jonkman [2002]), a modification of the HKSJ interval that uses the MP estimator of \( \tau^2 \) instead of the DL estimator, and an interval centered at SSW that uses the MP estimator of \( \tau^2 \) in estimating its variance and bases its half-width on a \( t \) distribution.

## 2 Study-level estimation of log-response-ratio

We assume that each of the \( K \) studies in the meta-analysis consists of two arms, Treatment and Control, with sample sizes \( n_{iT} \) and \( n_{iC} \). The total sample size in Study \( i \) is \( n_i = n_{iT} + n_{iC} \). The subject-level data in each arm are assumed to be
lognormally distributed with means $\mu_{iT}$ and $\mu_{iC}$ and variances $\sigma_{iT}^2$ and $\sigma_{iC}^2$. The sample means are $\bar{X}_{ij}$, and the sample variances are $s_{ij}^2$, for $i = 1, \ldots, K$ and $j = C$ or $T$.

The response ratio is usually meta-analyzed on a log scale, where the effect measure is $\lambda_i = \log(\mu_{iT}/\mu_{iC})$, estimated by $\hat{\lambda}_i = \log(\bar{X}_{iT}/\bar{X}_{iC})$, and the population and sample means are assumed to be positive. The within-study variance estimate of $\hat{\lambda}_i$, obtained by the delta method, is [Hedges et al., 1999]

$$v_i^2 = \frac{s_{iT}^2}{n_{iT}X_{iT}^2} + \frac{s_{iC}^2}{n_{iC}X_{iC}^2} = \frac{\hat{V}_{iT}^2}{n_{iT}} + \frac{\hat{V}_{iC}^2}{n_{iC}}, \tag{2.1}$$

where $\hat{V}_{ij}$ is the sample coefficient of variation (CV).

The log transformation introduces bias (as discussed by Bakbergenuly et al. [2016]): the expected value of $\hat{\lambda}_i$ is not equal to $\lambda_i$. To eliminate this bias in small samples, Lajeunesse [2015] proposed two bias-corrected modifications, and he recommended

$$\hat{\lambda}_i^\Delta = \hat{\lambda}_i + \frac{1}{2} \left[ \frac{s_{iT}^4}{n_{iT}^2X_{iT}^4} - \frac{s_{iC}^4}{n_{iC}^2X_{iC}^4} \right], \tag{2.2}$$

and estimated its variance by

$$\overline{\text{Var}}(\hat{\lambda}_i^\Delta) = v_i^2 + \frac{1}{2} \left[ \frac{s_{iT}^4}{n_{iT}^2X_{iT}^4} - \frac{s_{iC}^4}{n_{iC}^2X_{iC}^4} \right]. \tag{2.3}$$

Because $\hat{\lambda}$ is not defined for negative values of the study means, and dropping negative findings would introduce a bias, Lajeunesse [2015] modeled the data by lognormal distributions. In principle, log-normal distributions often make sense for non-negative data. This choice would eliminate the restricted-range bias, but not the transformation bias of LRR. Of course, the choice of model should be based on the properties of the data and not on the perceived ease of statistical modeling.

Even though sample means and variances are unbiased estimators of the population means and variances for lognormal distributions, they are very inefficient, especially as far as variance estimation is concerned [Johnson et al., 1994, Section 14.4.1, p. 220–222]. If the data are assumed to come from lognormal distributions, a much more straightforward approach would be to log-transform the individual observations, which would reduce the problem to meta-analysis of mean difference. This would provide much better inference. However, when individual-level data are not available, meta-analyses must work with the sample means and variances.

We provide simulations from lognormal distributions in Section 6. Simulations from normal distributions are in a separate arXiv report.
3 Standard random-effects model

The standard random-effects model assumes that within- and between-study variabilities are accounted for by approximately normal distributions of within- and between-study effects. For a generic measure of effect,

\[ \hat{\theta}_i \sim N(\theta_i, \sigma_i^2) \quad \text{and} \quad \theta_i \sim N(\theta, \tau^2), \]  

resulting in the marginal distribution \( \hat{\theta}_i \sim N(\theta, \sigma_i^2 + \tau^2) \). \( \hat{\theta}_i \) is the estimate of the effect in Study \( i \), and its within-study variance is \( \sigma_i^2 \), estimated by \( \hat{\sigma}_i^2 \), \( i = 1, \ldots, K \). The between-study variance, \( \tau^2 \), is estimated by \( \hat{\tau}^2 \). The overall effect, \( \theta \), is customarily estimated by the weighted mean

\[ \hat{\theta}_{RE} = \frac{\sum_{i=1}^{K} \hat{w}_i(\hat{\tau}^2)\hat{\theta}_i}{\sum_{i=1}^{K} \hat{w}_i(\hat{\tau}^2)}, \]  

where the \( \hat{w}_i(\hat{\tau}^2) = (\hat{\sigma}_i^2 + \hat{\tau}^2)^{-1} \) are inverse-variance weights. The FE estimate \( \hat{\theta} \) uses weights \( \hat{w}_i = \hat{w}_i(0) \).

If \( w_i = 1/\text{Var}(\hat{\theta}_i) \), the variance of the weighted mean of the \( \hat{\theta}_i \) is \( 1/\sum w_i \). Thus, many authors estimate the variance of \( \hat{\theta}_{RE} \) by \( \left[ \sum_{i=1}^{K} \hat{w}_i(\hat{\tau}^2) \right]^{-1} \). In practice, however, this estimate may not be satisfactory (Sidik and Jonkman [2006], Li et al. [1994], Rukhin [2009]).

4 Methods of estimating between-study variance

In this section we briefly list the point and interval estimators of the between-studies variance (\( \tau^2 \)) used in our study.

4.1 Point estimators

The most popular, but rather biased, estimator of \( \tau^2 \) is the method-of-moments estimator of DerSimonian and Laird [1986] (DL), denoted by \( \hat{\tau}_{DL}^2 \).

Assuming that the \( \hat{\theta}_i \) are distributed as \( N(\theta_i, \hat{\sigma}_i^2 + \tau^2) \), the restricted-maximum-likelihood (REML) estimator \( \hat{\tau}_{REML}^2 \) maximizes the restricted (or residual) log-likelihood function \( l_R(\theta, \tau^2) \). REML is superior to DL because of its balance between unbiasedness and efficiency Viechtbauer, 2005.
The Mandel-Paule (MP) estimator \( \hat{\tau}^2_{MP} \), is another moment-based estimator of the between-study variance. It is estimated iteratively. It is known to be superior to DL \( \text{[Veroniki et al. 2016]} \), but no simulations for LRR have been performed so far.

DerSimonian and Kacker \( \text{[2007]} \) generalized DL, replacing the weights \( \hat{w}_i \) by arbitrary fixed positive constants, \( a_i \). As an option when there is little a priori knowledge about the extent of heterogeneity, but some is anticipated, \( \text{[Jackson 2013]} \) proposed the estimator of \( \tau^2 \) with \( a_i = 1/\hat{\sigma}_i^2 \). We refer to this method as J.

### 4.2 Interval estimators

The 95% profile-likelihood (PL) confidence interval for \( \tau^2 \) consists of the values that are not rejected by the likelihood-ratio test with \( \tau^2 \) as the null hypothesis. This interval is usually used with \( \hat{\tau}^2_{RE,ML} \).

Similarly, the Q-profile (QP) confidence interval for \( \tau^2 \) consists of the values that are not rejected by the usual test for heterogeneity based on Cochran’s \( Q \) \( \text{[Cochran 1954]} \). The distribution of \( Q \) is assumed (incorrectly) to be the chi-squared distribution with \( K - 1 \) degrees of freedom.

For a generic effect measure, Biggerstaff and Jackson \( \text{[2008]} \) derived the exact distribution of a \( Q \) statistic with constant weights \( a_i \). That distribution yielded a generalized Q-profile confidence interval. We refer to this interval with \( a_i = 1/\hat{\sigma}_i^2 \) as the BJ confidence interval.

Jackson \( \text{[2013]} \) proposed another generalized Q-profile confidence interval (J) for \( \tau^2 \). The approach is the same as for the BJ interval, but with \( a_i = 1/\hat{\sigma}_i \).

### 5 Methods of estimating overall effect

Most of the point estimators of the overall effect have corresponding interval estimators, but some do not. Therefore, we describe point estimators and interval estimators in separate sections.

#### 5.1 Point estimators

A random-effects method that estimates \( \theta \) by a weighted mean with inverse-variance weights, as in Equation (3.2), is determined by the particular \( \hat{\tau}^2 \) that it uses in \( \hat{w}_i(\hat{\tau}^2) \). Because the study-level effects and their variances are related (as in Equation (2.1)}
for LRR), all inverse-variance-weighted estimators of \( \hat{\lambda} \) may have considerable bias. For completeness, we studied DL, REML, MP, and J.

To reduce this bias in estimating \( \lambda \), our experience with the bias of inverse-variance-weighted estimators for standardized mean difference (Bakbergenuly et al. 2018) led us to include a point estimator whose weights depend only on the studies’ sample sizes (Hedges and Olkin 1985, Hunter and Schmidt 1990). For this estimator (SSW), \( w_i = \tilde{n}_i = n_i T n_i C / (n_i T + n_i C) \); that is, \( w_i \) substitutes 1 for the estimated CVs in Equation (2.1); \( \tilde{n}_i \) is the effective sample size in Study \( i \). The estimator of the variance of SSW is

\[
\hat{\text{Var}}(\hat{\theta}_{SSW}) = \frac{\sum \tilde{n}_i^2 (v_i^2 + \hat{\tau}^2)}{\left(\sum \tilde{n}_i\right)^2},
\]

in which \( v_i^2 \) comes from Equation (2.1) and \( \hat{\tau}^2 = \hat{\tau}^2_{MP} \).

We also study the behavior of the bias-corrected estimator \( \hat{\lambda}^\Delta \), Equation (2.2), in lognormal data.

### 5.2 Interval estimators

The point estimators DL, REML, MP, and J have companion interval estimators of \( \theta \). The customary approach estimates the variance of \( \hat{\theta}_{RE} \) by

\[
\sum_{i=1}^{K} \tilde{w}_i (\hat{\tau}^2)
\]

bases the half-width of the interval on the normal distribution. These intervals are usually too narrow.

Hartung and Knapp 2001 and, independently, Sidik and Jonkman 2002 developed an improved estimator for the variance of \( \hat{\theta}_{RE} \). The Hartung-Knapp-Sidik-Jonkman (HKSJ) confidence interval uses this estimator together with critical values from the \( t \) distribution on \( K - 1 \) degrees of freedom. A potential weakness is that the HKSJ interval uses \( \hat{\theta}_{DL} \) as its midpoint, so it will have any bias that is present in \( \hat{\theta}_{DL} \). We studied a modification of the HKSJ confidence interval that uses \( \hat{\tau}^2_{MP} \) and \( \hat{\theta}_{MP} \); we refer to this interval as the HKSJ(MP) confidence interval.

The interval estimator corresponding to SSW (SSW MP) uses the SSW point estimator as its center, and its half-width equals the estimated standard deviation of SSW under the random-effects model times the critical value from the \( t \) distribution on \( K - 1 \) degrees of freedom.
6 Simulation study

As mentioned in Section 1, a few studies have used simulation to examine estimators of the overall effect for LRR, but no studies have examined estimators of $\tau^2$.

The range of values of RR may be rather wide. The empirical study by Senior et al. [2016] reports values of RR up to 3.72, though the second largest value is 1.46. The simulations by Friedrich et al. [2008] used values up to 1.56 (LRR = 0.445). Lajeunesse [2015] used means between 0 and 8 in both arms and small sample sizes, starting from $n_T + n_C = 4$. Our simulation study for LRR uses an interval of $0 \leq \lambda \leq 2$ (or $0 \leq \text{RR} \leq 7.39$) as realistic for a range of applications. Unfortunately, no information is available on the accompanying range of $\tau^2$ values. In their simulations for SMD, Hamman et al. [2018] consider the range from 0 to 2.5 as typical for ecology.

6.1 Design of the simulations

Our simulation study assesses the performance of four methods for point estimation of the between-studies variance, $\tau^2$ (DL, REML, J, and MP) and four methods of interval estimation of $\tau^2$ (the Q-profile interval, the generalized Q-profile intervals of Biggerstaff and Jackson [2008] and Jackson [2013], and the profile-likelihood confidence interval based on REML).

We study bias of the inverse-variance-weighted estimator of the overall effect corresponding to each of the estimators of $\tau^2$ (DL, REML, J, and MP), as well as bias of SSW, whose weights depend only on the sample sizes of the Treatment and Control arms.

We also study coverage of the confidence intervals associated with those inverse-variance-weighted estimators, and also the HKSJ interval (Hartung and Knapp [2001], Sidik and Jonkman [2002]), a modification of the HKSJ interval that uses the MP estimator of $\tau^2$ instead of the DL estimator, and an interval centered at SSW that uses the MP estimator of $\tau^2$ in estimating its variance and uses critical values from a $t$ distribution.

Two basic distributions may serve as the source of the data in the Treatment and Control arms: the lognormal distribution (the subject of the present report) and the normal distribution (the subject of a separate report). We generate $\lambda_i$ from $N(\lambda, \tau^2)$ and set $\mu_{iT} = \exp(\lambda_i)\mu_{iC}$. Then we generate $n_{ij}$ independent observations...
from the lognormal distributions with means $\mu_{ij}$ and variances $\sigma_{ij}^2$. We obtain the sample means $\bar{X}_{ij}$ and the sample variances $s_{ij}^2$ and calculate the sample LRR $\hat{\lambda}_i = \log(\bar{X}_{iT}/\bar{X}_{iC})$ and their variances $\hat{\nu}_i^2$ as in Equation (2.1). We also calculate the bias-corrected estimate, $\hat{\lambda}_i^\Delta$, Equation (2.2), and its variance, Equation (2.3) [Lajeunesse, 2015].

For the overall value of LRR, we chose $\lambda = (0, 0.2, 0.5, 1, 2)$ (corresponding to $0 \leq \text{RR} \leq 7.39$), as realistic for a range of applications.

When the data are lognormal, proximity to zero does not affect data generation or inferences. Therefore, as the mean of the Control arm we take $\mu_{iC} = 1$.

All simulations use the same numbers of studies, small ($K = 5, 10, 30$) and large ($K = 50, 100, 125$) and, for each combination of parameters, the same vector of total sample sizes $n = (n_1, \ldots, n_K)$ and equal numbers of observations in the Control and Treatment arms.

We study only meta-analyses in which the study size is the same in all $K$ studies. The study sizes, $n_i$, start from 4, because some studies in ecology have such small sample sizes, and they extend to 1000. By using the same patterns of sample sizes for each combination of the other parameters, we avoid the additional variability in the results that would arise from choosing sample sizes at random (e.g., uniformly between 100 and 250).

In summary, we vary four parameters: the overall true LRR ($\lambda$), the between-studies variance ($\tau^2$), the number of studies ($K$), and the total sample size ($n$). We set $\sigma_{C}^2 = \sigma_{T}^2 = 1$. Table 1 lists the configurations.

We use a total of 10,000 repetitions for each combination of parameters. Thus, the simulation standard error for estimated coverage of $\tau^2$ or $\lambda$ at the 95% confidence level is roughly $\sqrt{0.95 \times 0.05/10,000} = 0.00218$.

The simulations were programmed in R version 3.3.2 using the University of East Anglia 140-computer-node High Performance Computing (HPC) Cluster, providing a total of 2560 CPU cores, including parallel processing and large memory resources. For each configuration, we divided the 10,000 replications into 10 parallel sets of 1000 replications.

6.2 Results

Bias and coverage in estimation of $\tau^2$ (Appendices A1–A4 and C1–C4)
Table 1: Configurations of parameters in the simulations for LRR.

| Parameter                                      | Equal study sizes                        | Full results in Appendix |
|------------------------------------------------|------------------------------------------|--------------------------|
| $K$ (number of studies: small/large)           | (5, 10, 30) & (50, 100, 125)             | A & B - small n          |
| $n$ (total study size: small/large)            | (4, 10, 20, 40) & (100, 250, 640, 1000)  | C & D - large n          |
| $\sigma^2_2$ & $\sigma^2_C$ (within-study variances) | 1 & 1                                    |                          |
| $\lambda$ (overall value of the LRR)           | 0, 0.2, 0.5, 1, 2                         |                          |
| $\tau^2$ (variance of random effect)           | 0(0.1)1                                   |                          |
| Lognormal distribution $\mu_C$ (mean in Control arm) | 1                                        |                          |
| estimation of $\tau^2$                        |                                          | A & C                    |
| estimation of $\lambda$                       |                                          | B & D                    |

**Bias.** When $n$ is very small (Figures A1.1.1–A1.1.5), all four estimators of $\tau^2$ have substantial positive bias, increasing linearly with $\tau^2$ (when $\lambda = 0$ and $n = 4$, the intercept is around 0.4, and the slope is around 0.9). This pattern persists for $\lambda \leq 1$; but when $\lambda = 2$, the slope is essentially 0. As $n$ increases to 40, the intercept and slope decrease; but the trace for DL begins to diverge from the others, followed by the trace for J, and increasingly as $\lambda$ increases. $K$ has little effect. MP and REML have similar, reasonably small, bias when $n \geq 40$ (Figures C1.1.1–C1.1.5). When $n \geq 100$, the traces for DL and J bend toward increasingly negative bias as $\tau^2$ increases; their bias becomes worse as $n$ increases and slightly worse as $K$ increases (for example, when $\lambda = 0$, $n = 1000$, and $K \geq 50$, the bias of DL is $-0.28$ at $\tau^2 = 1$). The bias correction for $\hat{\lambda}_i$ does not reduce the bias (Appendices A2, A4, C2, and C4).

**Coverage.** When $n < 40$ and $K = 5$, the coverage of all four intervals for $\tau^2$ is below the nominal 95%, especially when $n = 4$ and $\tau^2 < 0.4$; increasing $K$ to 10 and 30 reduces coverage substantially and makes this pattern worse (Figure A1.2.1), and increasing $\lambda$ has little effect (Figures A1.2.2–A1.2.5). Increasing $K$ to 50 and beyond reduces coverage further, even to 0 when $n = 4$ and $\tau^2 = 0$ (Figure A3.2.1). When $n \geq 40$ and $K = 5$ or 10, BJ and J generally provide nominal or slightly higher coverage, and QP and PL are slightly lower. Situations with $K \geq 30$ are often quite challenging; BJ has low coverage for $K \geq 30$ (Figure C1.2.4), and for larger $n$ and $K$, coverage of J deteriorates similarly to BJ, but QP and PL provide good coverage.
Bias and coverage in estimation of $\lambda$ (Appendices B1–B4 and D1–D4)

**Bias.** All five estimators of $\lambda$ have bias that shows little dependence on $K$. When $\lambda = 0$ and $\tau^2 = 0$, they all have essentially no bias. When $\tau^2 > 0$, the bias is very roughly linear in $\tau^2$, with negative slope but a non-negative intercept for the IV-weighted estimators and a negative intercept for SSW. The intercept for the IV-weighted estimators is positive for $n \geq 10$, so their bias is positive for smaller $\tau^2$ and negative for larger $\tau^2$; but the traces flatten as $n$ increases, and by $n = 40$ their bias is positive for $0.1 \leq \tau^2 \leq 1$. The trace for SSW flattens similarly; and when $n = 40$, its bias has smaller magnitude than the IV-weighted estimators when $0.1 \leq \tau^2 \leq 0.5$ and larger magnitude when $0.6 \leq \tau^2 \leq 1$. When $\lambda > 0$, the biases of all five estimators at $\tau^2 = 0$ and the intercepts (i.e., biases) at $\tau^2 = 0.1$ increase; for a given $\lambda$ both the intercepts and the slopes decrease as $n$ increases. As a result, when $\lambda \geq 0.5$, the bias of SSW usually has smaller magnitude than the IV-weighted estimators. In relative terms, when $n < 40$, the biases are substantial: as much as 10% of $\lambda$ in some cases. Here SSW has the least bias, about 10% for $\lambda \geq 1$ and $n = 10$, declining to 5% for $\lambda \geq 1$ and $n = 20$ (Figure B1.1.4). The bias correction for $\hat{\lambda}_i$ reduces the bias (Figure B2.1.4) and should be used.

**Coverage.** $t$-intervals centered at SSW provide the best coverage of $\lambda$, and that coverage is satisfactory when $n \geq 20$ and $K \leq 30$. Those intervals may have coverage greater than 97% (primarily when $\tau^2 = 0$ and $K = 5$ or 10 and in a few cases where $\tau^2 = 0.1$, $K = 5$, $n = 20$ or 40, and $\lambda \leq 0.5$) or coverage less than 93% (mainly when $\tau^2$ is small, $K \geq 50$, $n = 20$ or 40, and $\lambda \geq 0.5$). All other methods have inferior coverage and are not recommended. Coverage of the intervals centered at SSW is better when the bias correction is used for $\hat{\lambda}_i$; then it is good when $n \geq 10$ (Figure B2.2.5). When $n$ is small, $K \geq 50$, and $\lambda = 0$, coverage of the standard methods improves somewhat, whereas coverage of SSW MP becomes less than 93% when $K > 50$, especially for large $\tau^2$ (Figure B3.2.1). When the bias correction is used, coverage of SSW MP is the best, and it is good overall for small $\lambda$, but it is much below 95% for $n = 4$, $\lambda \geq 0.5$ and small $\tau^2$, where it worsens for larger $K$ (Fig-
ure [B3.2.4]. For large $K$ and large $n$, coverage of SSW MP is still the best, especially at $\tau^2 = 0$, and the bias correction still produces better results (Figure [D4.2.4]).

7 Discussion

The results of our simulations provide a rather disappointing picture of the current state of meta-analysis of LRR. For such effect measures as LRR and SMD, also popular in ecology, the relation between the studies’ estimated effects and their estimated variances has several undesirable results: dependence of the performance of all inverse-variance-based methods on the effect sizes, biased estimation of overall effects, and below-nominal coverage of their confidence intervals, especially for small sample sizes. Our simulations show this clearly.

We show that, for a lognormal underlying distribution, the between-studies variance $\tau^2$ cannot be estimated reliably for sample sizes less than 100.

Arguably, the main purpose of a meta-analysis is to provide point and interval estimates of an overall effect. For general use, the estimate of overall effect should be unbiased, and the confidence interval should have nominal coverage.

Usually, after estimating the between-study variance $\tau^2$, an inverse-variance-weighted approach is used to estimate the overall effect (and, often, its variance). The origin of the IV approach lies in the fact that, for known variances, and given unbiased estimates of the within-study effects, it provides a uniformly minimum-variance unbiased estimate (UMVUE) of $\theta$. However, in practice, the within-study variances are unknown, and using estimates for them leads to bias in the IV estimate of the overall effect and below-nominal coverage of the confidence interval. Thus, the IV approach is misguided; for most measures of effect, it cannot avoid these shortcomings.

The gaps in evidence include the possibility that the variances in the two arms may differ, which is rarely, if ever, reflected in simulations. Due to sheer volume of our simulations, we did not attempt to fill this gap. However, we do not expect the performance of the IV methods to improve under more challenging scenarios.

A pragmatic solution to unbiased estimation of $\theta$ uses weights that do not involve estimated variances (for example, weights proportional to the studies’ sample sizes...
n_i). Our point estimator SSW uses weights proportional to an effective sample size, \( \tilde{n}_i = n_iCN/n_i \). Then, the estimate of the overall effect is \( \hat{\lambda}_{SSW} = \sum \tilde{n}_i \hat{\lambda}_i / \sum \tilde{n}_i \), and the estimate of its variance comes from Equation (5.1). Finally, the t-based confidence interval for \( \lambda \) is centered at \( \hat{\lambda}_{SSW} \).

SSW, combined with the bias-corrected estimator of \( \lambda_i \), works reasonably well for sample sizes as low as 10 in interval estimation of \( \lambda \), and for \( n \geq 40 \) in point estimation. We recommend this method for further use in applications.

8 Methods of estimation of \( \tau^2 \) and \( \lambda \) used in simulations

Point estimators of \( \tau^2 \)

- DL - method of [DerSimonian and Laird 1986]
- J - method of [Jackson 2013]
- MP - method of [Mandel and Paule 1970]
- REML - restricted maximum-likelihood method

Interval estimators of \( \tau^2 \)

- BJ - method of [Biggerstaff and Jackson 2008]
- J - method of [Jackson 2013]
- PL - profile-likelihood confidence interval based on \( \hat{\tau}^2_{REML} \)
- QP - Q-profile confidence interval of [Viechtbauer 2007]

Point estimators of \( \lambda \)

Inverse-variance-weighted methods with \( \tau^2 \) estimated by:

- DL
- J
- MP
- REML

and

- SSW - weighted mean with weights that depend only on studies’ sample sizes
Interval estimators of $\lambda$

Inverse-variance-weighted methods using normal quantiles, with $\tau^2$ estimated by:

- DL
- J
- MP
- REML

Inverse-variance-weighted methods with modified variance of $\hat{\lambda}$ and t-quantiles as in [Hartung and Knapp 2001] and [Sidik and Jonkman 2002]

- HKSJ (DL) - $\tau^2$ estimated by DL
- HKSJ (MP) - $\tau^2$ estimated by MP

and

- SSW MP - SSW point estimator of $\lambda$ with estimated variance given by Equation (5.1) and t-quantiles

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Appendices

A: Plots of bias and coverage of estimators of $\tau^2$, small $n$

- A1. Lognormal model, usual estimator of $\lambda_i$, $K = 5, 10, 30$
- A2. Lognormal model, bias-corrected estimator of $\lambda_i$, $K = 5, 10, 30$
- A3. Lognormal model, usual estimator of $\lambda_i$, $K = 50, 100, 125$
- A4. Lognormal model, bias-corrected estimator of $\lambda_i$, $K = 50, 100, 125$
A1. Lognormal model, usual estimator of $\lambda_i$

$n = 4, 10, 20, 40, K = 5, 10, 30$

A1.1 Bias of point estimators of $\tau^2$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 4, 10, 20, 40)$, and a set of values of $K (= 5, 10, 30)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The point estimators of $\tau^2$ are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
Figure A1.1.1: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$. 
Figure A1.1.2: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0.2$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$. 
Figure A1.1.3: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0.5$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$
Figure A1.1.4: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 1$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$.
Figure A1.1.5: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 2$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$.
A1.2 Coverage of interval estimators of $\tau^2$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 4, 10, 20, 40)$, and a set of values of $K (= 5, 10, 30)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The interval estimators of $\tau^2$ are

- QP (Q-profile confidence interval)
- BJ (Biggerstaff and Jackson interval)
- PL (Profile-likelihood interval)
- J (Jackson interval)
Figure A1.2.1: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0, n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$
Figure A1.2.2: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0.2$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$. 
Figure A1.2.3: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0.5$, $n = 4$, 10, 20, 40, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$.
Figure A1.2.4: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 1$, $n = 4$, 10, 20, 40, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$
Figure A1.2.5: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$
when $\lambda = 2$, $n = 4$, 10, 20, 40, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$
A2. Lognormal model, bias-corrected estimator of $\lambda_i$, $n = 4, 10, 20, 40$, $K = 5, 10, 30$

A2.1 Bias of point estimators of $\tau^2$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 4, 10, 20, 40)$, and a set of values of $K (= 5, 10, 30)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The point estimators of $\tau^2$ are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
Figure A2.1.1: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$
Figure A2.1.2: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0.2$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$. 
Figure A2.1.3: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0.5$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$. 


Figure A2.1.4: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 1$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$
Figure A2.1.5: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 2$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$. 
A2.2 Coverage of interval estimators of $\tau^2$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 4, 10, 20, 40)$, and a set of values of $K (= 5, 10, 30)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The interval estimators of $\tau^2$ are

- QP (Q-profile confidence interval)
- BJ (Biggerstaff and Jackson interval)
- PL (Profile-likelihood interval)
- J (Jackson interval)
Figure A2.2.1: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$
Figure A2.2.2: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0.2$, $n = 4$, 10, 20, 40, and $K = 5$, 10, 30. Bias-corrected estimate of $\lambda_i$. 

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Figure A2.2.3: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0.5$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda$. 
Figure A2.2.4: Coverage of 95% confidence intervals for the between-studies variance \( \tau^2 \) when \( \lambda = 1, n = 4, 10, 20, 40, \) and \( K = 5, 10, 30. \) Bias-corrected estimate of \( \lambda_i \)
Figure A2.2.5: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 2, n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$
A3. Lognormal model, usual estimator of $\lambda_i$,

$n = 4, 10, 20, 40, \ K = 50, 100, 125$

A3.1 Bias of point estimators of $\tau^2$

Each figure corresponds to a value of $\lambda$ ( = 0, 0.2, 0.5, 1, 2), a set of values of $n$ ( = 4, 10, 20, 40), and a set of values of $K$ ( = 50, 100, 125).

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The point estimators of $\tau^2$ are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
Figure A3.1.1: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$
Figure A3.1.2: Bias of estimators of between-studies variance \( \tau^2 \) for \( \lambda = 0.2, n = 4, 10, 20, 40, \) and \( K = 50, 100, 125. \) Usual estimate of \( \lambda_i \)
Figure A3.1.3: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0.5$, $n = 4$, 10, 20, 40, and $K = 50$, 100, 125. Usual estimate of $\lambda_i$.
Figure A3.1.4: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 1$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$. 
Figure A3.1.5: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 2$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$
A3.2 Coverage of interval estimators of $\tau^2$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 4, 10, 20, 40)$, and a set of values of $K (= 50, 100, 125)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0(0.1)1.0$ on the horizontal axis.

The interval estimators of $\tau^2$ are

- QP (Q-profile confidence interval)
- BJ (Biggerstaff and Jackson interval)
- PL (Profile-likelihood interval)
- J (Jackson interval)
Figure A3.2.1: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$
Figure A3.2.2: Coverage of 95% confidence intervals for the between-studies variance \( \tau^2 \) when \( \lambda = 0.2, n = 4, 10, 20, 40, \) and \( K = 50, 100, 125. \) Usual estimate of \( \lambda_i \)
Figure A3.2.3: Coverage of 95% confidence intervals for the between-studies variance \( \tau^2 \) when \( \lambda = 0.5, n = 4, 10, 20, 40, \) and \( K = 50, 100, 125. \) Usual estimate of \( \lambda_i \)
Figure A3.2.4: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 1$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$.
Figure A3.2.5: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$
when $\lambda = 2$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$. 

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A4. Lognormal model, bias-corrected estimator of $\lambda_i$, $n = 4, 10, 20, 40$, $K = 50, 100, 125$

A4.1 Bias of point estimators of $\tau^2$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 4, 10, 20, 40)$, and a set of values of $K (= 50, 100, 125)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The point estimators of $\tau^2$ are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
Figure A4.1.1: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$. 

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Figure A4.1.2: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0.2$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$. 

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Figure A4.1.3: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0.5$, $n = 4$, 10, 20, 40, and $K = 50$, 100, 125. Bias-corrected estimate of $\lambda_i$
Figure A4.1.4: Bias of estimators of between-studies variance \( \tau^2 \) for \( \lambda = 1 \), \( n = 4, 10, 20, 40 \), and \( K = 50, 100, 125 \). Bias-corrected estimate of \( \lambda_i \).
Figure A4.1.5: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 2$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$. 

λ = 2, n = 4, K = 50

λ = 2, n = 4, K = 100

λ = 2, n = 4, K = 125

λ = 2, n = 10, K = 50

λ = 2, n = 10, K = 100

λ = 2, n = 10, K = 125

λ = 2, n = 20, K = 50

λ = 2, n = 20, K = 100

λ = 2, n = 20, K = 125

λ = 2, n = 40, K = 50

λ = 2, n = 40, K = 100

λ = 2, n = 40, K = 125
A4.2 Coverage of interval estimators of $\tau^2$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 4, 10, 20, 40)$, and a set of values of $K (= 50, 100, 125)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0(0.1)1.0$ on the horizontal axis.

The interval estimators of $\tau^2$ are

- QP (Q-profile confidence interval)
- BJ (Biggerstaff and Jackson interval)
- PL (Profile-likelihood interval)
- J (Jackson interval)
Figure A4.2.1: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$.
Figure A4.2.2: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0.2$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$. 
Figure A4.2.3: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0.5$, $n = 4$, 10, 20, 40, and $K = 50$, 100, 125. Bias-corrected estimate of $\lambda_i$
Figure A4.2.4: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 1, n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$. 


Figure A4.2.5: Coverage of 95\% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 2$, $n = 4$, 10, 20, 40, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$. 
B: Plots of bias and coverage of estimators of $\lambda$, small $n$

- B1. Lognormal model, usual estimator of $\lambda_i$, $K = 5, 10, 30$
- B2. Lognormal model, bias-corrected estimator of $\lambda_i$, $K = 5, 10, 30$
- B3. Lognormal model, usual estimator of $\lambda_i$, $K = 50, 100, 125$
- B4. Lognormal model, bias-corrected estimator of $\lambda_i$, $K = 50, 100, 125$
B1. Lognormal model, usual estimator of $\lambda_i$,

$n = 4, 10, 20, 40, \ K = 5, 10, 30$

B1.1 Bias of point estimators of $\lambda$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 4, 10, 20, 40)$, and a set of values of $K (= 5, 10, 30)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The point estimators of $\lambda$ are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
- SSW (sample-size-weighted)
Figure B1.1.1: Bias of estimators of $\lambda$ for $\lambda = 0$, $n = 4$, 10, 20, 40, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$
Figure B1.1.2: Bias of estimators of $\lambda$ for $\lambda = 0.2$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$
Figure B1.3: Bias of estimators of $\lambda$ for $\lambda = 0.5$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$. 

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Figure B1.1.4: Bias of estimators of $\lambda$ for $\lambda = 1$, $n = 4$, 10, 20, 40, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$
Figure B1.1.5: Bias of estimators of $\lambda$ for $\lambda = 2$, $n = 4$, 10, 20, 40, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$
B1.2 Coverage of interval estimators of $\lambda$

Each figure corresponds to a value of $\lambda$ ($= 0, 0.2, 0.5, 1, 2$), a set of values of $n$ ($= 4, 10, 20, 40$), and a set of values of $K$ ($= 5, 10, 30$).

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The interval estimators of $\lambda$ are the companions to the inverse-variance-weighted point estimators

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)

and

- HKSJ (Hartung-Knapp-Sidik-Jonkman)
- HKSJ MP (HKSJ with MP estimator of $\tau^2$)
- SSW MP (SSW as center and half-width equal to critical value from $t_{K-1}$ times estimated standard deviation of SSW with $\hat{\tau}^2 = \hat{\tau}^2_{MP}$)
Figure B1.2.1: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 0$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$
Figure B1.2.2: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 0.2$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$
Figure B1.2.3: Coverage of 95% confidence intervals for \( \tau^2 \) when \( \lambda = 0.5, n = 4, 10, 20, 40, \) and \( K = 5, 10, 30 \). Usual estimate of \( \lambda_i \)
Figure B1.2.4: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 1$, $n = 4$, 10, 20, 40, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$
Figure B1.2.5: Coverage of 95% confidence intervals for $\tau^2$ when $\lambda = 2$, $n = 4$, 10, 20, 40, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$
B2. Lognormal model, bias-corrected estimator of $\lambda_i$, $n = 4, 10, 20, 40$, $K = 5, 10, 30$

B2.1 Bias of point estimators of $\lambda$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 4, 10, 20, 40)$, and a set of values of $K (= 5, 10, 30)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The point estimators of $\lambda$ are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
- SSW (sample-size-weighted)
Figure B2.1.1: Bias of estimators of $\lambda$ for $\lambda = 0$, $n = 4$, 10, 20, 40, and $K = 5$, 10, 30. Bias-corrected estimate of $\lambda_i$
Figure B2.1.2: Bias of estimators of $\tau^2$ for $\lambda = 0.2$, $n = 4$, 10, 20, 40, and $K = 5$, 10, 30.

Bias-corrected estimate of $\lambda_i$
Figure B2.1.3: Bias of estimators of $\lambda$ for $\lambda = 0.5$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$
Figure B2.1.4: Bias of estimators of $\lambda$ for $\lambda = 1$, $n = 4, 10, 20, 40$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$. 

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Figure B2.1.5: Bias of estimators of $\lambda$ for $\lambda = 2$, $n = 4$, 10, 20, 40, and $K = 5$, 10, 30.

Bias-corrected estimate of $\lambda_i$
B2.2 Coverage of interval estimators of $\lambda$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 4, 10, 20, 40)$, and a set of values of $K (= 5, 10, 30)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The interval estimators of $\lambda$ are the companions to the inverse-variance-weighted point estimators

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)

and

- HKSJ (Hartung-Knapp-Sidik-Jonkman)
- HKSJ MP (HKSJ with MP estimator of $\tau^2$)
- SSW MP (SSW as center and half-width equal to critical value from $t_{K-1}$ times estimated standard deviation of SSW with $\hat{\tau}^2 = \hat{\tau}^2_{MP}$)
Figure B2.2.1: Coverage of 95% confidence intervals for $\tau_2$ when $\lambda = 0$, $n = 4$, 10, 20, 40, and $K = 5$, 10, 30. Bias-corrected estimate of $\lambda_i$. 
Figure B2.2.2: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 0.2$, $n = 4$, 10, 20, 40, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$. 
Figure B2.2.3: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 0.5$, $n = 4$, 10, 20, 40, and $K = 5$, 10, 30. Bias-corrected estimate of $\lambda_i$
Figure B2.2.4: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 1$, $n = 4$, 10, 20, 40, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$. 

0.93 0.8 0.93 = 0.95 0.7 0.81 0.99 0.97 = 0.2 0.89 5 0.8 0.99 0.85 0.85 1 = 0.89 0.5 0.81 5 0.3 0.97 = 4 0.89 = 0.99 1 0.1 = 40 1.0 0.9 0.2 0.4 0.9 30 0.77 0.2 0.9 0.3 0.81 0.87 0.95 0.89 0.1 0.83 0.3 = 0.99 0.81 = 0.2 = 0.91 = 0.1 0.93 1 0.93 0.81 0.85 = 0.1 0.4 0.99 1.0 0.6 0.2 0.99 0.5 0.91 0.7 0.95 0.79 0.1 0.7 0.97 0.6 0.83 0.99 1.0 0.3 0.77 1.0 0.99 0.83 1.0 0.1 0.91 1.0 0.85 = 1 0.83 5 0.8 0.9 = 0.83 0.95 0.5 0.9 0.81 0.79 = 0.81 20 0.2 10 = 1.0 0.97 0.91 1.0 0.97 0.79 5 0.3 0.77 0.83 0.79 1.0 10 0.93 1 0.77 0.3 = 0.99 = 0.85 = = 0.87 0.5 0.5 1.0 20 0.89 0.9 0.79 10 0.87 0.6 = 1 10 0.8 0.85 0.83 10 1 0.89 0.9 0.6 0.6 0.77 0.8 0.87 0.91 0.83 0.7 0.95 0.79 0.91 0.5 0.87 0.3 0.89 0.97 0.5 0.7 0.9 = 0.99 0.99 0.81 0.6 0.1 0.4 0.2 0.77 0.81 0.89 0.5 0.4 0.85 4 0.4 0.9 0.77 0.81 40 0.3 0.2 0.3 1 0.79 0.5 4 0.79 0.7 30 0.95 0.9 0.81 0.6 0.1 0.6 = 0.79 0.4 0.8 0.93 1 1 0.79 0.1 0.83 0.9 0.4 0.77 0.8 0.87 0.91 0.83 0.7 0.95 0.79 1 0.87 0.3 0.89 0.97 0.5 0.7 0.9 = 0.99 0.99 0.81 0.6 0.1 0.6 0.77 0.8 0.79 0.4 0.8 0.93 1 1 0.2

Coverage

Coverage

Coverage

0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0

0.75 0.77 0.79 0.81 0.83 0.85 0.87 0.89 0.91 0.93 0.95 0.97 0.99

$\lambda = 1$, $n = 40$, $K = 30$ and $= 5$.
Figure B2.2.5: Coverage of 95% confidence intervals for \( \lambda \) when \( \lambda = 2, n = 4, 10, 20, 40, \) and \( K = 5, 10, 30. \) Bias-corrected estimate of \( \lambda \)
B3. Lognormal model, usual estimator of $\lambda_i$, $n = 4, 10, 20, 40$, $K = 50, 100, 125$

B3.1 Bias of point estimators of $\lambda$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 4, 10, 20, 40)$, and a set of values of $K (= 50, 100, 125)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The point estimators of $\lambda$ are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
- SSW (sample-size-weighted)
Figure B3.1.1: Bias of estimators of $\lambda$ for $\lambda = 0$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$
Figure B3.1.2: Bias of estimators of $\lambda$ for $\lambda = 0.2$, $n = 4$, 10, 20, 40, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$
Figure B3.1.3: Bias of estimators of $\lambda$ for $\lambda = 0.5$, $n = 4$, 10, 20, 40, and $K = 50$, 100, 125. Usual estimate of $\lambda_i$
Figure B3.1.4: Bias of estimators of $\tau^2$ for $\lambda = 1$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$.
Usual estimate of $\lambda_i$
Figure B3.1.5: Bias of estimators of $\theta$ for $\lambda = 2$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$.
B3.2 Coverage of interval estimators of $\lambda$

Each figure corresponds to a value of $\lambda$ ($= 0, 0.2, 0.5, 1, 2$), a set of values of $n$ ($= 4, 10, 20, 40$), and a set of values of $K$ ($= 50, 100, 125$).

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The interval estimators of $\lambda$ are the companions to the inverse-variance-weighted point estimators

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)

and

- HKSJ (Hartung-Knapp-Sidik-Jonkman)
- HKSJ MP (HKSJ with MP estimator of $\tau^2$)
- SSW MP (SSW as center and half-width equal to critical value from $t_{K-1}$ times estimated standard deviation of SSW with $\hat{\tau}^2 = \hat{\tau}^2_{MP}$)
Figure B3.2.1: Coverage of 95% confidence intervals for $\tau^2$ when $\lambda = 0$, $n = 4$, 10, 20, 40, and $K = 50$, 100, 125. Usual estimate of $\lambda_i$. 

$\lambda = 0$, $n = 4$, $K = 50$

$\lambda = 0$, $n = 4$, $K = 100$

$\lambda = 0$, $n = 4$, $K = 125$

$\lambda = 0$, $n = 10$, $K = 50$

$\lambda = 0$, $n = 10$, $K = 100$

$\lambda = 0$, $n = 10$, $K = 125$

$\lambda = 0$, $n = 20$, $K = 50$

$\lambda = 0$, $n = 20$, $K = 100$

$\lambda = 0$, $n = 20$, $K = 125$

$\lambda = 0$, $n = 40$, $K = 50$

$\lambda = 0$, $n = 40$, $K = 100$

$\lambda = 0$, $n = 40$, $K = 125$
Figure B3.2.2: Coverage of 95% confidence intervals for $\tau^2$ when $\lambda = 0.2$, $n = 4$, 10, 20, 40, and $K = 50$, 100, 125. Usual estimate of $\lambda_i$.
Figure B3.2.3: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 0.5$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$.
Figure B3.2.4: Coverage of 95% confidence intervals for \( \lambda \) when \( \lambda = 1, n = 4, 10, 20, 40 \), and \( K = 50, 100, 125 \). Usual estimate of \( \lambda_i \)
Figure B3.2.5: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 2$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$
B4. Lognormal model, bias-corrected estimator of $\lambda_i$, $n = 4, 10, 20, 40$, $K = 50, 100, 125$

B4.1 Bias of point estimators of $\lambda$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 4, 10, 20, 40)$, and a set of values of $K (= 50, 100, 125)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The point estimators of $\lambda$ are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
- SSW (sample-size-weighted)
Figure B4.1.1: Bias of estimators of $\theta$ for $\lambda = 0$, $n = 4$, $10$, $20$, $40$, and $K = 50$, $100$, $125$.

Bias-corrected estimate of $\lambda_i$
Figure B4.1.2: Bias of estimators of $\lambda$ for $\lambda = 0.2$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$
Figure B4.1.3: Bias of estimators of $\lambda$ for $\lambda = 0.5$, $n = 4, 10, 20, 40$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$
Figure B4.1.4: Bias of estimators of \( \theta \) for \( \lambda = 1, n = 4, 10, 20, 40, \) and \( K = 50, 100, 125. \)

Bias-corrected estimate of \( \lambda_i \)
Figure B4.1.5: Bias of estimators of $\lambda$ for $\lambda = 2$, $n = 4$, 10, 20, 40, and $K = 50$, 100, 125.
Bias-corrected estimate of $\lambda_i$
B4.2 Coverage of interval estimators of \( \lambda \)

Each figure corresponds to a value of \( \lambda (= 0, 0.2, 0.5, 1, 2) \), a set of values of \( n (= 4, 10, 20, 40) \), and a set of values of \( K (= 50, 100, 125) \).

Each panel corresponds to a value of \( n \) and a value of \( K \) and has \( \tau^2 = 0.0(0.1)1.0 \) on the horizontal axis.

The interval estimators of \( \lambda \) are the companions to the inverse-variance-weighted point estimators

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)

and

- HKSJ (Hartung-Knapp-Sidik-Jonkman)
- HKSJ MP (HKSJ with MP estimator of \( \tau^2 \))
- SSW MP (SSW as center and half-width equal to critical value from \( t_{K-1} \) times estimated standard deviation of SSW with \( \hat{\tau}^2 = \hat{\tau}^2_{MP} \))
Figure B4.2.1: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 0$, $n = 4$, 10, 20, 40, and $K = 50$, 100, 125. Bias-corrected estimate of $\lambda_i$
Figure B4.2.2: Coverage of 95% confidence intervals for \( \lambda \) when \( \lambda = 0.2, n = 4, 10, 20, 40, \) and \( K = 50, 100, 125 \). Bias-corrected estimate of \( \lambda_i \)
Figure B4.2.3: Coverage of 95% confidence intervals for \( \lambda \) when \( \lambda = 0.5, n = 4, 10, 20, 40, \) and \( K = 50, 100, 125 \). Bias-corrected estimate of \( \lambda_i \).
Figure B4.2.4: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 1$, $n = 4$, 10, 20, 40, and $K = 50$, 100, 125. Bias-corrected estimate of $\lambda_i$
Figure B4.2.5: Coverage of 95% confidence intervals for $\tau^2$ when $\lambda = 2$, $n = 4$, 10, 20, 40, and $K = 50$, 100, 125. Bias-corrected estimate of $\lambda_i$. 
C: Plots of bias and coverage of estimators of $\tau^2$, large $n$

- C1. Lognormal model, usual estimator of $\lambda_i$, $K = 5, 10, 30$
- C2. Lognormal model, bias-corrected estimator of $\lambda_i$, $K = 5, 10, 30$
- C3. Lognormal model, usual estimator of $\lambda_i$, $K = 50, 100, 125$
- C4. Lognormal model, bias-corrected estimator of $\lambda_i$, $K = 50, 100, 125$
C1. Lognormal model, usual estimator of $\lambda_i$, $n = 100, 250, 640, 1000, K = 5, 10, 30$

C1.1 Bias of point estimators of $\tau^2$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 100, 250, 640, 1000)$, and a set of values of $K (= 5, 10, 30)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The point estimators of $\tau^2$ are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
Figure C1.1.1: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Usual estimate of $\lambda$.
Figure C1.1.2: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0.2$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$.
Figure C1.1.3: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0.5$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$. 
Figure C1.1.4: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 1$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$. 
Figure C1.1.5: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 2$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$. 

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C1.2 Coverage of interval estimators of $\tau^2$

Each figure corresponds to a value of $\lambda$ (= 0, 0.2, 0.5, 1, 2), a set of values of $n$ (= 100, 250, 640, 1000), and a set of values of $K$ (= 5, 10, 30).

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The interval estimators of $\tau^2$ are

- QP (Q-profile confidence interval)
- BJ (Biggerstaff and Jackson interval)
- PL (Profile-likelihood interval)
- J (Jackson interval)
Figure C1.2.1: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$
Figure C1.2.2: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0.2$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$
Figure C1.2.3: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0.5$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$. 

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Figure C1.2.4: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 1$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$
Figure C1.2.5: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 2$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$. 

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C2. Lognormal model, bias-corrected estimator of $\lambda_i$, $n = 100, 250, 640, 1000$, $K = 5, 10, 30$

C2.1 Bias of point estimators of $\tau^2$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 100, 250, 640, 1000)$, and a set of values of $K (= 5, 10, 30)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The point estimators of $\tau^2$ are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
Figure C2.1.1: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Bias-corrected estimate of $\lambda_i$
Figure C2.1.2: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0.2$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$
Figure C2.1.3: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0.5$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$
Figure C2.1.4: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 1$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$
Figure C2.1.5: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 2$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$. 
C2.2 Coverage of interval estimators of $\tau^2$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 100, 250, 640, 1000)$, and a set of values of $K (= 5, 10, 30)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The interval estimators of $\tau^2$ are

- QP (Q-profile confidence interval)
- BJ (Biggerstaff and Jackson interval)
- PL (Profile-likelihood interval)
- J (Jackson interval)
Figure C2.2.1: Coverage of 95% confidence intervals for the between-studies variance \( \tau^2 \) when \( \lambda = 0, n = 100, 250, 640, 1000, \) and \( K = 5, 10, 30 \). Bias-corrected estimate of \( \lambda_i \).
Figure C2.2.2: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0.2$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Bias-corrected estimate of $\lambda_i$
Figure C2.2.3: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0.5$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Bias-corrected estimate of $\lambda_i$
Figure C2.2.4: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 1$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Bias-corrected estimate of $\lambda_i$.
Figure C2.2.5: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 2$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$
C3. Lognormal model, usual estimator of $\lambda_i$,

$n = 100, 250, 640, 1000, \; K = 50, 100, 125$

C3.1 Bias of point estimators of $\tau^2$

Each figure corresponds to a value of $\lambda$ ($= 0, 0.2, 0.5, 1, 2$), a set of values of $n$ ($= 100, 250, 640, 1000$), and a set of values of $K$ ($= 50, 100, 125$).

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The point estimators of $\tau^2$ are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
Figure C3.1.1: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$
Figure C3.1.2: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0.2$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$. 

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Figure C3.1.3: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0.5$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$
Figure C3.1.4: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 1$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Usual estimate of $\lambda_i$
Figure C3.1.5: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 2$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$
C3.2 Coverage of interval estimators of $\tau^2$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 100, 250, 640, 1000)$, and a set of values of $K (= 50, 100, 125)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The interval estimators of $\tau^2$ are

- QP (Q-profile confidence interval)
- BJ (Biggerstaff and Jackson interval)
- PL (Profile-likelihood interval)
- J (Jackson interval)
Figure C3.2.1: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$
Figure C3.2.2: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0.2$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Usual estimate of $\lambda_i$
Figure C3.2.3: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$
when $\lambda = 0.5$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Usual estimate of $\lambda_i$
Figure C3.2.4: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 1$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Usual estimate of $\lambda_i$
Figure C3.2.5: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 2, n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$.
C4. Lognormal model, bias-corrected estimator of $\lambda_i$, $n = 100, 250, 640, 1000$, $K = 50, 100, 125$

C4.1 Bias of point estimators of $\tau^2$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 100, 250, 640, 1000)$, and a set of values of $K (= 50, 100, 125)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The point estimators of $\tau^2$ are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
Figure C4.1.1: Bias of estimators of between-studies variance \( \tau^2 \) for \( \lambda = 0, n = 100, 250, 640, 1000, \) and \( K = 50, 100, 125. \) Bias-corrected estimate of \( \lambda_i \)
Figure C4.1.2: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0.2$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$.
Figure C4.1.3: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 0.5$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$. 
Figure C4.1.4: Bias of estimators of between-studies variance \( \tau^2 \) for \( \lambda = 1 \), \( n = 100, 250, 640, 1000 \), and \( K = 50, 100, 125 \). Bias-corrected estimate of \( \lambda_i \)
Figure C4.1.5: Bias of estimators of between-studies variance $\tau^2$ for $\lambda = 2$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$.
C4.2 Coverage of interval estimators of $\tau^2$

Each figure corresponds to a value of $\lambda$ ($= 0, 0.2, 0.5, 1, 2$), a set of values of $n$ ($= 100, 250, 640, 1000$), and a set of values of $K$ ($= 50, 100, 125$).

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The interval estimators of $\tau^2$ are

- QP (Q-profile confidence interval)
- BJ (Biggerstaff and Jackson interval)
- PL (Profile-likelihood interval)
- J (Jackson interval)
Figure C4.2.1: Coverage of 95% confidence intervals for the between-studies variance \( \tau^2 \) when \( \lambda = 0, n = 100, 250, 640, 1000, \text{ and } K = 50, 100, 125 \). Bias-corrected estimate of \( \lambda_i \).
Figure C4.2.2: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0.2$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Bias-corrected estimate of $\lambda_i$. 

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Figure C4.2.3: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 0.5$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$.
Figure C4.2.4: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 1$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$. 
Figure C4.2.5: Coverage of 95% confidence intervals for the between-studies variance $\tau^2$ when $\lambda = 2$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Bias-corrected estimate of $\lambda_i$. 
D: Plots of bias and coverage of estimators of $\lambda$, large $n$

- D1. Lognormal model, usual estimator of $\lambda_i$, $K = 5, 10, 30$
- D2. Lognormal model, bias-corrected estimator of $\lambda_i$, $K = 5, 10, 30$
- D3. Lognormal model, usual estimator of $\lambda_i$, $K = 50, 100, 125$
- D4. Lognormal model, bias-corrected estimator of $\lambda_i$, $K = 50, 100, 125$
D1. Lognormal model, usual estimator of $\lambda_i$, 

$n = 100, 250, 640, 1000, \ K = 5, 10, 30$

D1.1 Bias of point estimators of $\lambda$

Each figure corresponds to a value of $\lambda$ (= 0, 0.2, 0.5, 1, 2), a set of values of $n$ (= 100, 250, 640, 1000), and a set of values of $K$ (= 5, 10, 30).

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The point estimators of $\lambda$ are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
- SSW (sample-size-weighted)
Figure D1.1.1: Bias of estimators of $\lambda$ for $\lambda = 0$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$. 

\[ \text{Bias of } \theta \]
Figure D1.1.2: Bias of estimators of $\lambda$ for $\lambda = 0.2$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$
Figure D1.1.3: Bias of estimators of $\lambda$ for $\lambda = 0.5$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Usual estimate of $\lambda_i$. 
Figure D1.1.4: Bias of estimators of $\lambda$ for $\lambda = 1$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$. 
Figure D1.5: Bias of estimators of $\lambda$ for $\lambda = 2$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$. 
D1.2 Coverage of interval estimators of $\lambda$

Each figure corresponds to a value of $\lambda$ (= 0, 0.2, 0.5, 1, 2), a set of values of $n$ (= 100, 250, 640, 1000), and a set of values of $K$ (= 5, 10, 30).

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The interval estimators of $\lambda$ are the companions to the inverse-variance-weighted point estimators

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)

and

- HKSJ (Hartung-Knapp-Sidik-Jonkman)
- HKSJ MP (HKSJ with MP estimator of $\tau^2$)
- SSW MP (SSW as center and half-width equal to critical value from $t_{K-1}$ times estimated standard deviation of SSW with $\hat{\tau}^2 = \hat{\tau}^2_{MP}$)
Figure D1.2.1: Coverage of 95% confidence intervals for \( \lambda \) when \( \lambda = 0 \), \( n = 100, 250, 640, 10000 \), and \( K = 5, 10, 30 \). Usual estimate of \( \lambda_i \)
Figure D1.2.2: Coverage of 95% confidence intervals for $\tau$ when $\lambda = 0.2$, $n = 100, 250, 640, 10000$, and $K = 5, 10, 30$. Usual estimate of $\lambda$.
Figure D1.2.3: Coverage of 95% confidence intervals for \( \lambda \) when \( \lambda = 0.5, \ n = 100, \ 250, \ 640, \ 10000, \) and \( K = 5, \ 10, \ 30 \). Usual estimate of \( \lambda_i \)
Figure D1.2.4: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 1$, $n = 100$, 250, 640, 10000, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$. 
Figure D1.2.5: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 2$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Usual estimate of $\lambda_i$
D2. Lognormal model, bias-corrected estimator of $\lambda_i$, $n = 100, 250, 640, 1000$, $K = 5, 10, 30$

D2.1 Bias of point estimators of $\lambda$

Each figure corresponds to a value of $\lambda$ (= 0, 0.2, 0.5, 1, 2), a set of values of $n$ (= 100, 250, 640, 1000), and a set of values of $K$ (= 5, 10, 30).

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The point estimators of $\lambda$ are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
- SSW (sample-size-weighted)
Figure D2.1.1: Bias of estimators of $\lambda$ for $\lambda = 0$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Bias-corrected estimate of $\lambda_i$
Figure D2.1.2: Bias of estimators of $\lambda$ for $\lambda = 0.2$, $n = 100$, 250, 640, 1000, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$. 


Figure D2.1.3: Bias of estimators of $\lambda$ for $\lambda = 0.5$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Bias-corrected estimate of $\lambda_i$
Figure D2.1.4: Bias of estimators of \( \lambda \) for \( \lambda = 1 \), \( n = 100, 250, 640, 1000 \), and \( K = 5, 10, 30 \). Bias-corrected estimate of \( \lambda_i \)
Figure D2.1.5: Bias of estimators of $\lambda$ for $\lambda = 2$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Bias-corrected estimate of $\lambda_i$
D2.2 Coverage of interval estimators of $\lambda$

Each figure corresponds to a value of $\lambda (= 0, 0.2, 0.5, 1, 2)$, a set of values of $n (= 100, 250, 640, 1000)$, and a set of values of $K (= 5, 10, 30)$.

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The interval estimators of $\lambda$ are the companions to the inverse-variance-weighted point estimators

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)

and

- HKSJ (Hartung-Knapp-Sidik-Jonkman)
- HKSJ MP (HKSJ with MP estimator of $\tau^2$)
- SSW MP (SSW as center and half-width equal to critical value from $t_{K-1}$ times estimated standard deviation of SSW with $\hat{\tau}^2 = \hat{\tau}_{MP}^2$)
Figure D2.2.1: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 0$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$. 

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Figure D2.2.2: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 0.2$, $n = 100$, 250, 640, 1000, and $K = 5$, 10, 30. Bias-corrected estimate of $\lambda$. 


Figure D2.2.3: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 0.5$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$. 
Figure D2.2.4: Coverage of 95% confidence intervals for \( \lambda \) when \( \lambda = 1, n = 100, 250, 640, 1000, \) and \( K = 5, 10, 30. \) Bias-corrected estimate of \( \lambda_i \)
Figure D2.2.5: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 2$, $n = 100, 250, 640, 1000$, and $K = 5, 10, 30$. Bias-corrected estimate of $\lambda_i$. 
D3. Lognormal model, usual estimator of $\lambda_i$,

$n = 100, 250, 640, 1000, K = 50, 100, 125$

D3.1 Bias of point estimators of $\lambda$

Each figure corresponds to a value of $\lambda$ ($= 0, 0.2, 0.5, 1, 2$), a set of values of $n$ ($= 100, 250, 640, 1000$), and a set of values of $K$ ($= 50, 100, 125$).

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The point estimators of $\lambda$ are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
- SSW (sample-size-weighted)
Figure D3.1.1: Bias of estimators of $\lambda$ for $\lambda = 0$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Usual estimate of $\lambda_i$
Figure D3.1.2: Bias of estimators of $\lambda$ for $\lambda = 0.2$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Usual estimate of $\lambda_i$
Figure D3.1.3: Bias of estimators of $\lambda$ for $\lambda = 0.5$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$
Figure D3.1.4: Bias of estimators of $\tau^2$ for $\lambda = 1$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Usual estimate of $\lambda_i$. 
Figure D3.1.5: Bias of estimators of $\theta$ for $\lambda = 2$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Usual estimate of $\lambda_i$
D3.2 Coverage of interval estimators of \( \lambda \)

Each figure corresponds to a value of \( \lambda \) (= 0, 0.2, 0.5, 1, 2), a set of values of \( n \) (= 100, 250, 640, 1000), and a set of values of \( K \) (= 50, 100, 125).

Each panel corresponds to a value of \( n \) and a value of \( K \) and has \( \tau^2 = 0.0(0.1)1.0 \) on the horizontal axis.

The interval estimators of \( \lambda \) are the companions to the inverse-variance-weighted point estimators

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)

and

- HKSJ (Hartung-Knapp-Sidik-Jonkman)
- HKSJ MP (HKSJ with MP estimator of \( \tau^2 \))
- SSW MP (SSW as center and half-width equal to critical value from \( t_{K-1} \) times estimated standard deviation of SSW with \( \hat{\tau}^2 = \hat{\tau}^2_{MP} \))
Figure D3.2.1: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 0$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Usual estimate of $\lambda_i$.
Figure D3.2.2: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 0.2$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$. 

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Figure D3.2.3: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 0.5$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Usual estimate of $\lambda_i$
Figure D3.2.4: Coverage of 95% confidence intervals for $\tau^2$ when $\lambda = 1$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$
Figure D3.2.5: Coverage of 95% confidence intervals for $\tau_2$ when $\lambda = 2$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Usual estimate of $\lambda_i$
D4. Lognormal model, bias-corrected estimator
of \( \lambda_i \), \( n = 100, 250, 640, 1000 \), \( K = 50, 100, 125 \)

D4.1 Bias of point estimators of \( \lambda \)

Each figure corresponds to a value of \( \lambda (= 0, 0.2, 0.5, 1, 2) \), a set of values of \( n (= 100, 250, 640, 1000) \), and a set of values of \( K (= 50, 100, 125) \).
Each panel corresponds to a value of \( n \) and a value of \( K \) and has \( \tau^2 = 0.0(0.1)1.0 \) on the horizontal axis.
The point estimators of \( \lambda \) are

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)
- SSW (sample-size-weighted)
Figure D4.1.1: Bias of estimators of $\lambda$ for $\lambda = 0$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Bias-corrected estimate of $\lambda_i$
Figure D4.1.2: Bias of estimators of $\lambda$ for $\lambda = 0.2$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$.
Figure D4.1.3: Bias of estimators of $\lambda$ for $\lambda = 0.5$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Bias-corrected estimate of $\lambda_i$. 

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Figure D4.1.4: Bias of estimators of $\lambda$ for $\lambda = 1$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$
Figure D4.5: Bias of estimators of $\lambda$ for $\lambda = 2$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Bias-corrected estimate of $\lambda_i$
D4.2 Coverage of interval estimators of $\lambda$

Each figure corresponds to a value of $\lambda$ (= 0, 0.2, 0.5, 1, 2), a set of values of $n$ (= 100, 250, 640, 1000), and a set of values of $K$ (= 50, 100, 125).

Each panel corresponds to a value of $n$ and a value of $K$ and has $\tau^2 = 0.0(0.1)1.0$ on the horizontal axis.

The interval estimators of $\lambda$ are the companions to the inverse-variance-weighted point estimators

- DL (DerSimonian-Laird)
- REML (restricted maximum likelihood)
- MP (Mandel-Paule)
- J (Jackson)

and

- HKSJ (Hartung-Knapp-Sidik-Jonkman)
- HKSJ MP (HKSJ with MP estimator of $\tau^2$)
- SSW MP (SSW as center and half-width equal to critical value from $t_{K-1}$ times estimated standard deviation of SSW with $\hat{\tau}^2 = \hat{\tau}^2_{MP}$)
Figure D4.2.1: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 0$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$. 

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Figure D4.2.2: Coverage of 95% confidence intervals for $\tau^2$ when $\lambda = 0.2$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$
Figure D4.2.3: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 0.5$, $n = 100$, 250, 640, 1000, and $K = 50$, 100, 125. Bias-corrected estimate of $\lambda_i$. 

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Figure D4.2.4: Coverage of 95% confidence intervals for \( \lambda \) when \( \lambda = 1 \), \( n = 100, 250, 640, 1000 \), and \( K = 50, 100, 125 \). Bias-corrected estimate of \( \lambda_i \).
Figure D4.2.5: Coverage of 95% confidence intervals for $\lambda$ when $\lambda = 2$, $n = 100, 250, 640, 1000$, and $K = 50, 100, 125$. Bias-corrected estimate of $\lambda_i$. 