POSITIVE ESTIMATION OF THE BETWEEN-GROUP VARIANCE COMPONENT IN ONE-WAY ANOVA AND META-ANALYSIS

JOACHIM HARTUNG[1] & KEPHER H. MAKAMBI

University of Dortmund, Dortmund, Germany & Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya

Summary

Positive estimators of the between-group (between-study) variance are proposed. Explicit variance formulae for the estimators are given and approximate confidence intervals for the between-group variance are constructed, as our proposal to a long outstanding problem. By Monte Carlo simulation, the bias and standard deviation of the proposed estimators are compared with the truncated versions of the maximum likelihood (ML) estimator, restricted maximum likelihood (REML) estimator and a (lately) standard estimator in meta-analysis. Attained confidence coefficients of the constructed confidence intervals are also presented.

Key words: random effects model; positive estimates of the between-group variance; confidence intervals on the between-group variance; Patnaik's approximation.

1. Introduction

In the usual random effects ANOVA model, the problem of variance component estimation is widely documented. The traditional one-way ANOVA estimator of the between-group variance component, also called the between-study variance in meta-analysis, is unbiased but can assume negative values, Thompson (1962) and Wang (1967). Even the maximum likelihood (ML) and restricted maximum likeli-

[1] **Correspondence Address:** Prof. Dr. Joachim Hartung, Department of Statistics, University of Dortmund, Vogelpothsweg 87, D-44221 Dortmund, Germany.

Research partly supported by the German Academic Exchange Service (DAAD) and the German Research Community, DFG (SFB 475).

hood (REML) procedure can give negative estimates which have to be truncated at zero, cf: Herbach (1959) and Thompson (1962), respectively. In practice, whenever unbiased estimators become negative, they are truncated at zero, thus making them biased and have now a positive probability to take on the value zero which, in most applications, is not a very useful value and contradicts practical understanding. Such estimators have also a further disadvantage that in concrete situations their estimates of precision cannot be computed, meaning that confidence bounds on the variance components cannot be constructed.
In meta–analysis, the same problem is encountered by using, for example, the DerSimonian and Laird (1986) estimator, which of late may be regarded as the standard estimator of the between-study variance. In fact Hardy and Thompson (1996) observe that since the DerSimonian-Laird estimator is truncated, there is no possibility of obtaining confidence intervals on the between-study variance. For work on confidence intervals on the between-group variance component for the unbalanced case but with homogeneous error variances, see for instance, Thomas and Hultquist (1978), Burdick and Eickman (1986), and Hartung and Knapp (2000). The REML approach has also been advocated for use in meta-analysis by, cf: for example, Brown and Kempton (1994) and Normand (1999). However, REML together with ML procedures are iterative methods and by Searle's (1988) remarks that nothing is unbiased after iteration (referring specifically to REML). For more insightful discussions refer, for instance, to Hartley and Rao (1967), and Harville (1977) for ML; and Corbeil and Searle (1976) for REML.

In this paper, we propose finite positive (almost everywhere) estimators of the between-study variance in a one-way random effects ANOVA and meta–analysis model. In section 2, we present our working model together with the moments estimator of the between-study variance by DerSimonian and Laird (1986). In section 3, we derive two positive estimators of the between-study variance and give their explicit variance formulae. Confidence limits on the between-study variance are also presented in section 3. Section 4 presents simulation results on the biases and standard deviations of the two proposed positive estimators, and the truncated versions of the DerSimonian-Laird estimator, the ML estimator and the REML estimator. Reported also in section 4 are results on the attained confidence coefficients of the constructed confidence bounds.

2. Model

Consider a situation where K studies are available, with the ith study having n_i observations, $i = 1, \ldots, K$,which follow the model

$$y_{ij} = \mu + a_i + e_{ij},\ i = 1, \ldots, K \geq 2,\ j = 1, \ldots, n_i \geq 2. \tag{1}$$

The variables $a_1, \ldots, a_K, e_{11}, \ldots, e_{Kn_K}$ are mutually independent and normally distributed with $a_i \sim (0, \sigma_a^2)$, $e_{ij} \sim (0, \sigma_{e_i}^2)$, $\sigma_a^2 \geq 0$, $\sigma_{e_i}^2 > 0$, and μ is the common mean. In the ith study, the estimate of the common mean is given by $\hat{\mu}_i = \bar{y}_{i.} = \sum_{j=1}^{n_i} y_{ij}/n_i, i = 1, \ldots, K$.These estimates are also normally distributed with mean μ and variance $\tau_i^2 = \sigma_a^2 + \sigma_{e_i}^2/n_i = \sigma_a^2 + \sigma_i^2$. The error variances are estimated unbiasedly by $\hat{\sigma}_{e_i}^2 = s_{e_i}^2 = \sum_{j=1}^{n_i}(y_{ij} - \bar{y}_{i.})^2/(n_i - 1), i = 1, \ldots, K$.
Let $\hat{\sigma}_i^2 = s_{e_i}^2/n_i = \xi_i$ and define $\omega_\Sigma = \sum_{i=1}^{K} \omega_i$, $\omega_i = 1/\xi_i$ $i = 1, \ldots, K$.For $var(\xi_i) = 2 \cdot \sigma_i^4/(n_i - 1)$, we can take $\widehat{var}(\xi_i) = 2 \cdot \xi_i^2/(n_i - 1)$ as its estimate or the best invariant unbiased estimator $\widehat{var}(\xi_i) = 2 \cdot \xi_i^2/(n_i + 1)$,cf: Hartung and Voet (1986). The standard estimate of σ_a^2 in meta–analysis is a moment estimator suggested by DerSimonian and Laird (1986), namely,

$$\hat{\sigma}_{a,DL}^2 = max\ \{0, \hat{\sigma}_{a,1}^2\},$$

where

$$\hat{\sigma}_{a,1}^2 = \frac{\omega_\Sigma}{\omega_\Sigma^2 - \sum_{i=1}^{K} \omega_i^2} \left\{ \sum_{i=1}^{K} \omega_i \left(\bar{y}_{i.} - \sum_{j=1}^{K} \frac{\omega_j}{\omega_\Sigma} \bar{y}_{j.} \right)^2 - K + 1 \right\}, \tag{2}$$

cf: also Mengersen, Tweendie and Biggerstaff (1995), Biggerstaff and Tweendie (1997). Other authors have also suggested the ML and the REML estimators.

However, these estimators are iterative in nature and their difficulties are well documented in, for example, Brown and Kempton (1994).

3. Proposed Positive Estimators and Confidence Bounds on σ_a^2

Now, let $b = (b_1, \ldots, b_K)'$ be weights such that $\sum_{i=1}^K b_i = 1$, $b_i < 1/2$, $i = 1, \ldots, K$. Define an unbiased estimate of μ by $\hat{\mu}(b) = \sum_{i=1}^K b_i\, \hat{\mu}_i$ with $var\{\hat{\mu}(b)\} = \sum_{i=1}^K b_i^2\, \tau_i^2$; and a quadratic form $Q(b)$ by $Q(b) = \sum_{i=1}^K \gamma_i \{\hat{\mu}_i - \hat{\mu}(b)\}^2$, where $\gamma_i = b_i^2/\{(1-2b_i) \cdot \sum_{j=1}^K b_j(1-b_j)/(1-2b_j)\}$.

Lemma 1

The estimator

$$\hat{\sigma}_{a,2}^2 = \frac{1}{\sum_{j=1}^K b_j^2} \cdot \{\, Q(b) - \sum_{i=1}^K b_i^2 \xi_i\} \qquad (3)$$

is unbiased for σ_a^2.

Proof

Using Rao et al. (1981),

$$\begin{aligned} E\{Q(b)\} &= \sum_{i=1}^K \gamma_i \{(1-2b_i)\tau_i^2 + \sum_{i=1}^K b_i^2 \tau_i^2\} \\ &= \frac{1 + \sum_{i=1}^K b_i^2/(1-2b_i)}{\sum_{i=1}^K b_i(1-b_i)/(1-2b_i)} \cdot \sum_{i=1}^K b_i^2 \tau_i^2 \\ &= \sum_{i=1}^K b_i^2 \tau_i^2. \qquad (4) \end{aligned}$$

Therefore,

$$\begin{aligned} E(\hat{\sigma}_{a,2}^2) &= \frac{1}{\sum_{j=1}^K b_j^2} \cdot E\{Q(b) - \sum_{i=1}^K b_i^2 \xi_i\} \\ &= \sigma_a^2. \end{aligned}$$

Now, $E(\hat{\sigma}_{a,2}^2) = [\, E\{Q(b)\} - E(\sum_{i=1}^K b_i^2 \xi_i)]/\sum_{j=1}^K b_j^2$, implying that

$$E\left\{\frac{Q(b)}{\sum_{j=1}^K b_j^2}\right\} = E(\hat{\sigma}_{a,2}^2) + E\left(\frac{\sum_{i=1}^K b_i^2 \xi_i}{\sum_{j=1}^K b_j^2}\right) > E\left(\frac{\sum_{i=1}^K b_i^2 \xi_i}{\sum_{j=1}^K b_j^2}\right). \qquad (5)$$

However, after a realization from a random experiment, $E\{Q(b)\}$ and $E(\sum_{i=1}^{K} b_i^2\xi_i)$ are, respectively, replaced by, say, $Q(b)$ and $\sum_{i=1}^{K} b_i^2\xi_i$. This may lead to $Q(b) < \sum_{i=1}^{K} b_i^2\xi_i$, meaning that the estimate of σ_a^2 is negative. This is a problem which restricts the use of most unbiased estimators of variance components. Usually solutions are given in the name of truncated estimators, cf: Herbach (1959). By using truncated estimators, apart from losing the desirable property of unbiasedness, in many applications, it sometimes becomes difficulty to accept zero as an estimate of the between-study variance when it is well known that there is variation among groups under consideration. For example, in genetics we know that genetic variation exists among, say, bulls whose sperms are used for insemination. This and many other similar situations beg for a positive estimate of the between-group variance. Instead of using complicated numerical algorithms, cf: Hartung (1981, sec. 5), we will proceed as follows:

Interpret $Q_1(b) = Q(b)/\sum_{j=1}^{K} b_j^2$ as a positive estimate of σ_a^2 which requires some correction and define an estimator of σ_a^2 by $\hat{\sigma}_a^2(b) = \delta \cdot Q_1(b),\ \delta > 0$. For $r_i = b_i^2/\sum_{j=1}^{K} b_j^2$, the magnitude of the bias of $\hat{\sigma}_a^2(b)$ is given by

$$\begin{aligned}
|Bias\{\hat{\sigma}_a^2(b)\}| &= |E\{\delta \cdot Q_1(b)\} - \sigma_a^2| \\
&= |\delta \cdot \sigma_a^2 + \delta \cdot \sum_{i=1}^{K} r_i\sigma_i^2 - \sigma_a^2| \\
&= \left\| \begin{pmatrix} \delta - 1 \\ \delta \end{pmatrix} \cdot \begin{pmatrix} \sigma_a^2 \\ \sum_{i=1}^{K} r_i\sigma_i^2 \end{pmatrix} \right\| \\
&\leq \left\| \begin{pmatrix} \delta - 1 \\ \delta \end{pmatrix} \right\| \cdot \left\| \begin{pmatrix} \sigma_a^2 \\ \sum_{i=1}^{K} r_i\sigma_i^2 \end{pmatrix} \right\| \qquad (6)
\end{aligned}$$

by the Cauchy-Schwarz inequality, where $\|(.)\|$ represents the euclidean norm of (.). According to the uniformly minimum bias principle, cf: Hartung (1981), we have to minimize $(\delta - 1)^2 + \delta^2$ for $\delta > 0$, giving $\delta = \frac{1}{2}$.

Now, to adjust for bias, let $\hat{\sigma}_a^2(\eta) = \eta \cdot \frac{1}{2} \cdot Q_1(b) = \eta \cdot \hat{\sigma}_a^2(b)$ such that

$$E\left\{\eta \cdot \hat{\sigma}_a^2(b) + \eta \cdot \sum_{i=1}^{K} r_i \xi_i \right\} = E\{Q_1(b)\}, \tag{7}$$

giving

$$\eta = \frac{E\{Q_1(b)\}}{(1/2) \cdot E\{Q_1(b)\} + \sum_{i=1}^{K} r_i \sigma_i^2},$$

which can be estimated by

$$\eta^* = \frac{2 \cdot Q_1(b)}{Q_1(b) + 2 \cdot \sum_{i=1}^{K} r_i \xi_i}$$

and henceforth regarded as fixed. The above arguments lead us to a positive estimator of σ_a^2 which is given by

$$\hat{\sigma}_a^2(\eta) = \eta^* \cdot \frac{1}{2} \cdot Q_1(b) = \frac{Q_1(b)}{Q_1(b) + 2 \cdot \sum_{i=1}^{K} r_i \xi_i} \cdot Q_1(b), \;\; \eta^* \leq 1. \tag{8}$$

Lemma 2

The variance of $\hat{\sigma}_a^2(\eta)$ is given by

$$\begin{aligned} var\{\hat{\sigma}_a^2(\eta)\} \;\; = \;\; & \frac{\lambda_1^2}{(\sum_{j=1}^{K} b_j^2)^2} \cdot \left[\sum_{i=1}^{K} \gamma_i^2 \{(1-2b_i)\tau_i^2 + var(\hat{\mu}(b))\}^2 \right. \\ & \left. + \sum_{i=1}^{K} \sum_{j \neq i=1}^{K} \gamma_i \gamma_j \{var(\hat{\mu}(b)) - b_i^2 \tau_i^2 - b_j^2 \tau_j^2\}^2 \right], \end{aligned} \tag{9}$$

for $\lambda_1 = Q_1(b)/\{Q_1(b) + 2 \cdot \sum_{i=1}^{K} r_i \xi_i\}$.

The proof of the above lemma is straight forward by using equation (30) of Rao et al. (1981).

We see that the proposed estimator of σ_a^2, apart from being finite and positive, has an explicit variance formula which can be used, for example, in the construction of confidence intervals.

Consider once again the quadratic form $Q(b)$ and define $\nu_Q = 2 \cdot [E\{Q(b)\}]^2 / var\{Q(b)\}$. By Patnaik's approximation, cf: Patnaik (1949), the variable $\nu_Q \cdot Q(b)/E\{Q(b)\}$ is distributed approximately as a $\chi^2_{\nu_Q}$. From equation (4) above,

$$E\{Q(b)\} = \sum_{i=1}^{K} b_i^2 \tau_i^2 = \sigma_a^2 \cdot \sum_{i=1}^{K} b_i^2 + \sum_{i=1}^{K} b_i^2 \sigma_i^2 ,$$

so that the approximate probability statement

$$P\left[\chi^2_{\nu_Q;\kappa/2} \le \nu_Q \cdot \frac{Q(b)}{E\{Q(b)\}} \le \chi^2_{\nu_Q;1-\kappa/2}\right] \approx 1 - \kappa \tag{10}$$

results in an approximate $(1-\kappa)100\%-$confidence interval on σ_a^2 which is given by

$$CI_1(\sigma_a^2) : \left[\frac{\hat{\nu}_Q \cdot Q_1(b)}{\chi^2_{\hat{\nu}_Q;1-\kappa/2}} - \sum_{i=1}^{K} r_i \xi_i \, , \; \frac{\hat{\nu}_Q \cdot Q_1(b)}{\chi^2_{\hat{\nu}_Q;\kappa/2}} - \sum_{i=1}^{K} r_i \xi_i\right] , \tag{11}$$

where $\chi^2_{\hat{\nu}_Q;\kappa/2}$ and $\chi^2_{\hat{\nu}_Q;1-\kappa/2}$ are, respectively, the lower and upper points of $\chi^2_{\hat{\nu}_Q}$, and $\hat{\nu}_Q = 2 \cdot Q^2(b)/\widehat{var}\{Q(b)\}$; with $\widehat{var}\{Q(b)\}$ obtained by replacing τ_i^2 by $\hat{\tau}_i^2 = \hat{\sigma}_a^2(\eta) + \xi_i$, $i = 1 \, , \ldots , K$.Note that if the limits takes on negative values, they are truncated at zero.

Remark 1

The condition that $b_i < 1/2$, $i = 1 \, , \ldots , K$,helps to avoid the tendency of one of the studies dominating the estimation process, an observation already made by Cochran (1954).

Corollary 1

Let $\beta_i = w_i/w_\Sigma$, $w_\Sigma = \sum_{i=1}^K w_i$, $w_i = 1 \, /\hat{\sigma}_i^2$, see also $\hat{\sigma}^2_{a,1}$ in equation (2) above. Another positive estimator of σ_a^2 is given by

$$\hat{\sigma}_a^2(\lambda_2) = \frac{\lambda_2}{1 - \sum_{i=1}^K \beta_i^2} \cdot \sum_{i=1}^{K} \beta_i \left(\bar{y}_{i.} - \sum_{j=1}^{K} \beta_j \bar{y}_{j.}\right)^2 , \tag{12}$$

where

$$\lambda_2 = \frac{\sum_{i=1}^K \omega_i \left(\bar{y}_{i.} - \sum_{j=1}^K b_j^* \bar{y}_{j.}\right)^2}{2(K-1) + \sum_{i=1}^K \omega_i \left(\bar{y}_{i.} - \sum_{j=1}^K b_j^* \, \bar{y}_{j.}\right)^2}, \quad b_i^* = \frac{\omega_i}{\omega_\Sigma}.$$

This estimator is obtained by using arguments similar to those that lead to $\hat{\sigma}_a^2(\eta)$ above.

Corollary 2

The variance of $\hat{\sigma}_a^2(\lambda_2)$ is given by

$$\begin{aligned} var\{\hat{\sigma}_a^2(\lambda_2)\} \quad = \quad & \frac{\lambda_2^2}{(1-\sum_{i=1}^K \beta_i^2)^2} \cdot \left[\sum_{i=1}^K \beta_i^2 \left\{ (1-2\beta_i)\tau_i^2 + \sum_{i=1}^K \beta_i^2 \tau_i^2 \right\}^2 \right. \\ & \left. + \sum_{i=1}^K \sum_{j \neq i=1}^K \beta_i \beta_j \left(\sum_{i=1}^K \beta_i^2 \tau_i^2 - \beta_i^2 \tau_i^2 - \beta_j^2 \tau_j^2 \right)^2 \right]. \end{aligned} \qquad (13)$$

This corollary follows from considerations similar to those of lemma 2 above.

If we now set $Q(\beta) = \sum_{i=1}^K \beta_i \left(\bar{y}_{i.} - \sum_{j=1}^K \beta_j \bar{y}_{j.} \right)^2$, then it can be shown that

$$E\{Q(\beta)\} = \sigma_a^2 \cdot (1 - \sum_{i=1}^K \beta_i^2) + \sum_{i=1}^K (\beta_i - \beta_i^2) \cdot \sigma_i^2.$$

Therefore, an approximate $(1-\kappa)100\%-$confidence interval on σ_a^2 can be constructed along the lines of $CI_1(\sigma_a^2)$. That is, for $r_i^* = (b_i^* - b_i^{*2})/(1 - \sum_{i=1}^K b_i^{*2})$,

$$CI_2(\sigma_a^2) : \left[\frac{\hat{\nu}_{Q^*} \cdot Q(b^*)}{(1-\sum_{i=1}^K b_i^{*2}) \cdot \chi^2_{\hat{\nu}_{Q^*};1-\kappa/2}} - \sum_{i=1}^K r_i^* \xi_i \, , \, \frac{\hat{\nu}_{Q^*} \cdot Q(b^*)}{(1-\sum_{i=1}^K b_i^{*2}) \cdot \chi^2_{\hat{\nu}_{Q^*};\kappa/2}} - \sum_{i=1}^K r_i^* \xi_i \right], \qquad (14)$$

where $Q(b^*) = \sum_{i=1}^K b_i^* \left(\bar{y}_{i.} - \sum_{j=1}^K b_j^* \bar{y}_{j.} \right)^2$ and $\hat{\nu}_{Q^*} = 2 \cdot Q^2(b^*)/\widehat{var}\{Q(\beta)\}$, and $\widehat{var}\{Q(\beta)\}$ is obtained by replacing τ_i^2 by $\hat{\tau}_i^2 = \hat{\sigma}_a^2(\lambda_2) + \xi_i$, $i = 1, \ldots, K$.Here also, the limits are truncated at zero if they takes on negative values.

4. Simulation Results and Discussion

A simulation study, with patterns shown in Table I below, was used to judge the performance of the proposed positive estimators of the between-study variance with respect to their bias and standard deviation. For comparison we have also included the corresponding results of the bias and standard deviation of the DerSimonian-Laird, ML and REML estimator in their truncated form (see Table II and III). The simulations are conducted using S-Plus 4.5 under windows NT with the procedure

VARCOMP used to obtain ML and REML estimates. For groups of size $K = 3$, Table II, and $K = 6$,Table III, 1,000 runs were made for each pattern in Table I with the between-group variances set at $\sigma_a^2 = 0$ .0,0.05, 0.5, 1.0, 5.0, and 10.0.

For the choice of weights b_i, $i = 1, \ldots, K$,to avoid domination of a single study (in line with remark 1 above), we used the following procedure: Let $c_i = \omega_i/\omega_\Sigma > 0$ be a positive estimate of b_i, $i = 1, \ldots, K$,and φ a constant such that $0 < \varphi < \frac{1}{2} - \frac{1}{K}$, then

$$b_i = \begin{cases} c_i, & \text{if } c_i \leq \frac{1}{2} - \varphi,\ i = 1, \ldots, K, \\ \frac{1}{2} - \varphi, & \text{for } i = i_0 \text{ with } c_{i_0} = max\{c_j : c_j > \frac{1}{2} - \varphi\}, \\ (\frac{1}{2} + \varphi) \cdot c_i / \sum\limits_{i_0 \neq i=1}^{K} c_i, & i_0 \neq i = 1, \ldots, K. \end{cases} \tag{15}$$

If (15) gives $b_i \leq \frac{1}{2} - \varphi$, $i = 1, \ldots, K$,then stop, otherwise, put $\varphi = \varphi/2$ and start (15) once again, etc.. In our simulations, we have chosen $\varphi = K^{-3}$.

Table IV reports results on attained confidence coefficients for the confidence bounds $CI_1(\sigma_a^2)$ and $CI_2(\sigma_a^2)$ in section 3 above for $K = 3$ and $K = 6$ with 10,000 runs for each pattern. These results are for a two-sided confidence interval with $\kappa = 0$ .05.

Table I: Sample designs for $K = 3$,6 for the simulation results in Table II, III and IV.

	Study	$K=3$			$K=6$					
	i	1	2	3	1	2	3	4	5	6
	n_i	20	20	20	20	20	20	20	20	20
A1	$\sigma_{e_i}^2$	4	4	4	4	4	4	4	4	4
	n_i	20	20	20	20	20	20	20	20	20
A2	$\sigma_{e_i}^2$	1	3	5	1	3	5	1	3	5
	n_i	10	20	30	10	20	30	10	20	30
B1	$\sigma_{e_i}^2$	4	4	4	4	4	4	4	4	4
	n_i	10	20	30	10	20	30	10	20	30
B2	$\sigma_{e_i}^2$	1	3	5	1	3	5	1	3	5
	n_i	10	20	30	10	20	30	10	20	30
B3	$\sigma_{e_i}^2$	5	3	1	5	3	1	5	3	1

Table II: Bias (B) and Standard Deviation (SD) for the five betwen-study variance estimators, $K = 3$.

$K = 3$											
		$\hat{\sigma}_a^2(\eta)$		$\hat{\sigma}_a^2(\lambda_2)$		$\hat{\sigma}_{a,DL}^2$		MLE		$REML$	
σ_a^2	Plan	B	SD	B	SD	B	SD	B	SD	B	SD
0.00	A1	0.099	0.17	0.089	0.13	0.074	0.15	0.033	0.28	0.081	0.16
	A2	0.053	0.09	0.061	0.09	0.052	0.11	0.028	0.08	0.063	0.14
	B1	0.093	0.18	0.096	0.15	0.081	0.17	0.031	0.10	0.081	0.19
	B2	0.062	0.11	0.060	0.09	0.051	0.10	0.014	0.05	0.038	0.09
	B3	0.061	0.12	0.078	0.13	0.069	0.14	0.052	0.14	0.115	0.23
0.05	A1	0.086	0.23	0.076	0.19	0.065	0.22	0.007	0.13	0.076	0.22
	A2	0.034	0.14	0.043	0.13	0.039	0.15	-0.009	0.10	0.039	0.17
	B1	0.082	0.25	0.085	0.21	0.075	0.24	0.009	0.15	0.091	0.26
	B2	0.051	0.16	0.050	0.14	0.045	0.16	-0.019	0.08	0.024	0.15
	B3	0.051	0.18	0.059	0.17	0.054	0.19	0.024	0.15	0.101	0.26
0.50	A1	0.031	0.73	0.012	0.64	0.044	0.69	-0.197	0.43	0.025	0.66
	A2	0.002	0.78	0.000	0.66	0.031	0.69	-0.199	0.41	0.007	0.62
	B1	0.012	0.76	-0.001	0.64	0.027	0.69	-0.184	0.45	0.060	0.71
	B2	-0.022	0.73	-0.030	0.61	-0.002	0.64	-0.225	0.42	-0.012	0.65
	B3	-0.014	0.76	-0.014	0.67	0.014	0.70	-0.161	0.44	0.070	0.67
1.00	A1	-0.086	1.21	-0.056	1.10	0.004	1.16	-0.386	0.80	0.004	1.22
	A2	0.032	1.47	0.001	1.21	0.053	1.25	-0.413	0.73	-0.057	1.11
	B1	-0.030	1.49	-0.061	1.21	-0.002	1.26	-0.362	0.85	0.056	1.30
	B2	-0.040	1.13	-0.045	1.10	0.008	1.14	-0.449	0.73	-0.086	1.11
	B3	-0.079	1.41	-0.081	1.23	-0.033	1.27	-0.304	0.84	0.108	1.27
5.00	A1	0.114	6.53	-0.005	5.65	0.014	5.69	-1.760	3.43	-0.046	5.15
	A2	-0.284	6.20	-0.207	5.26	-0.115	5.28	-1.687	3.42	0.041	5.12
	B1	-0.286	5.71	-0.256	4.91	-0.120	4.95	-1.748	3.42	-0.006	5.13
	B2	-0.199	6.20	-0.172	5.24	-0.076	5.27	-1.829	3.22	-0.132	4.87
	B3	-0.465	6.40	-0.402	5.57	-0.308	5.60	-1.672	3.35	0.063	5.03
10.00	A1	-0.119	12.96	-0.364	10.75	-0.215	10.78	-3.628	6.38	-0.345	9.57
	A2	0.259	12.43	0.260	10.33	0.366	10.35	-3.218	7.20	0.247	10.79
	B1	-0.104	12.94	-0.415	10.46	-0.255	10.49	-3.279	6.71	0.206	10.07
	B2	-0.037	12.29	0.195	10.83	0.306	10.84	-3.638	6.47	-0.346	9.70
	B3	0.152	14.21	0.250	12.47	0.361	12.49	-3.678	7.20	-0.447	10.80

Table III: Bias (B) and Standard Deviation (SD) of five betwen-study variance estimators, $K = 6$.

$K=6$											
		$\hat{\sigma}_a^2(\eta)$		$\hat{\sigma}_a^2(\lambda_2)$		$\hat{\sigma}_{a,DL}^2$		MLE		$REML$	
σ_a^2	Plan	B	SD	B	SD	B	SD	B	SD	B	SD
0.00	A1	0.092	0.12	0.082	0.09	0.058	0.10	0.014	0.03	0.036	0.07
	A2	0.034	0.05	0.045	0.04	0.032	0.05	0.013	0.03	0.031	0.06
	B1	0.085	0.12	0.088	0.09	0.065	0.11	0.015	0.04	0.041	0.09
	B2	0.058	0.08	0.052	0.05	0.035	0.06	0.008	0.03	0.021	0.05
	B3	0.022	0.03	0.042	0.04	0.031	0.05	0.023	0.06	0.052	0.11
0.05	A1	0.122	0.18	0.112	0.14	0.053	0.14	-0.023	0.06	0.009	0.10
	A2	0.041	0.12	0.057	0.09	0.0256	0.10	-0.028	0.05	-0.002	0.09
	B1	0.102	0.19	0.108	0.13	0.068	0.16	-0.024	0.06	0.013	0.11
	B2	0.062	0.13	0.062	0.10	0.024	0.10	-0.034	0.04	-0.013	0.08
	B3	0.022	0.10	0.050	0.09	0.022	0.09	-0.013	0.08	0.028	0.14
0.50	A1	0.011	0.50	-0.014	0.41	0.026	0.46	-0.197	0.22	0.025	0.33
	A2	-0.041	0.62	-0.040	0.42	-0.003	0.63	-0.348	0.21	-0.243	0.33
	B1	-0.031	0.50	-0.035	0.4	-0.0003	0.45	-0.357	0.22	-0.240	0.35
	B2	-0.001	0.58	-0.026	0.42	0.033	0.60	-0.366	0.22	-0.261	0.34
	B3	-0.017	0.68	-0.016	0.46	0.019	0.48	-0.320	0.24	-0.196	0.37
1.00	A1	-0.042	0.89	-0.066	0.74	0.028	0.78	-0.689	0.39	-0.490	0.60
	A2	0.046	1.29	-0.016	0.81	0.082	1.50	-0.690	0.38	-0.499	0.58
	B1	-0.079	0.95	-0.084	0.75	-0.009	0.99	-0.710	0.38	-0.510	0.58
	B2	-0.036	1.04	-0.065	0.74	0.016	1.06	-0.743	0.32	-0.563	0.49
	B3	0.016	1.32	-0.037	0.88	0.015	0.89	-0.655	0.41	-0.442	0.62
5.00	A1	-0.124	3.81	-0.111	3.37	0.038	3.39	-3.447	1.70	-2.600	2.56
	A2	0.092	6.29	-0.023	4.16	0.065	4.17	-3.360	1.77	-2.476	2.65
	B1	-0.254	4.28	-0.212	3.42	-0.060	3.44	-3.403	1.79	-2.509	2.70
	B2	-0.026	4.93	-0.088	3.52	0.017	3.56	-3.458	1.70	-2.599	2.56
	B3	0.166	5.76	-0.027	4.43	0.051	4.44	-3.421	1.66	-2.558	2.49
10.00	A1	-0.135	7.33	-0.213	6.16	-0.047	6.18	-6.859	3.32	-5.181	4.99
	A2	-0.344	10.39	-0.249	7.18	-0.156	7.19	-6.638	3.57	-4.859	5.37
	B1	0.032	9.10	-0.039	6.95	0.131	5.97	-7.010	3.31	-5.385	4.98
	B2	0.089	9.99	-0.133	6.87	-0.020	6.88	-6.714	3.42	-4.949	5.14
	B3	-0.386	11.94	-0.246	8.18	-0.164	11.95	-6.873	3.27	-5.200	4.91

All the five estimators have nonnegative bias for $\sigma_a^2 = 0$ which decreases with increasing K, see Table II and III. For $\sigma_a^2 = 0\ .05$,$\hat{\sigma}_a^2(\eta)$, $\hat{\sigma}_a^2(\lambda_2)$ and $\hat{\sigma}_{a,DL}^2$ have nonnegative bias whereas the REML estimator has nonnegative bias for $K = 3$ which sometimes becomes negative for $K = 6$ .The ML estimator has, largely, negative bias. In general, all the five estimators seem to underestimate σ_a^2 for $\sigma_a^2 \geq 0.5$. For example, for $K = 6$ and $\sigma_a^2 = 10\ .0$,the underestimation is between 1.5% and 4% for $\hat{\sigma}_a^2(\eta)$, between 0.4% and 2.5% for $\hat{\sigma}_a^2(\lambda_2)$, between 0.2% and 2% for $\hat{\sigma}_{a,DL}^2$, between 66% and 71% for ML estimator and between 48% and 54% for REML estimator. In other words, the underestimation is more pronounced for the ML estimator followed by the REML estimator. A similar trend is true for $K = 3$ with lower levels of underestimation for ML and REML estimator.

The standard deviations of the five estimators increase with σ_a^2 and decrease with K. The ML estimator has smaller standard deviation than the other four estimators. However, it can generally be said that the differences in magnitude of the standard deviations of the five estimates is not dramatic.

The results in Table IV above indicate that for $K = 3$, $CI_1(\sigma_a^2)$ sometimes overstates the nominal confidence coefficient but, in general this interval can be regarded as attaining acceptable confidence coefficients. An almost similar trend is manifested for $K = 6$ .Notice that for $K = 6$ in the unbalanced case when smaller sample sizes are paired with larger variances (Plan B3), the interval always attains confidence coefficients of over 96.0% .

For $K = 3$,the interval $CI_2(\sigma_a^2)$ attains confidence coefficients which are always $\leq 95\%$, except plan A1 for $\sigma_a^2 = 1\ .0$.However, the confidence coefficients are generally close to 95%. For $K = 6$,the interval attains confidence coefficients near the nominal confidence coefficient.

On comparing $CI_1(\sigma_a^2)$ and $CI_2(\sigma_a^2)$, it can be said that both intervals attains acceptable confidence coefficients but $CI_1(\sigma_a^2)$ tends towards being more conservative when the value of σ_a^2 become large.

Table IV: Attained confidence coefficients for the confidence intervals of the between-study variance for $K = 3$,6 and $\kappa = 0$ .05.

		Estimates of $(1-\kappa)100\%$			
		$K = 3$		$K = 6$	
σ_a^2	Plan	$CI_1(\sigma_a^2)$	$CI_2(\sigma_a^2)$	$CI_1(\sigma_a^2)$	$CI_2(\sigma_a^2)$
0.00	A1	94.3	94.1	94.4	94.3
	A2	95.6	94.0	95.9	94.3
	B1	95.0	94.2	94.6	94.5
	B2	94.8	94.0	94.1	94.3
	B3	94.7	94.2	96.2	95.3
0.05	A1	94.9	94.3	94.8	94.6
	A2	96.1	94.7	96.0	94.5
	B1	95.1	94.4	95.4	94.8
	B2	95.1	94.6	95.8	94.3
	B3	95.7	94.0	96.3	94.0
0.50	A1	94.6	94.5	95.6	94.8
	A2	96.0	95.0	96.2	95.4
	B1	96.1	94.7	95.2	94.8
	B2	95.7	94.9	95.6	94.7
	B3	95.9	94.7	96.5	94.9
1.00	A1	95.8	95.1	95.1	94.7
	A2	96.3	94.9	96.3	94.7
	B1	96.3	95.0	95.6	94.8
	B2	96.0	94.5	95.2	94.8
	B3	95.8	94.4	96.6	94.8
5.00	A1	96.0	94.9	95.6	95.2
	A2	96.1	94.8	96.5	95.4
	B1	95.6	95.0	95.8	95.8
	B2	96.4	94.8	96.6	95.4
	B3	96.0	94.8	97.0	95.6
10.00	A1	95.8	94.8	96.1	95.2
	A2	96.3	95.0	97.0	95.8
	B1	95.9	94.4	96.4	95.3
	B2	95.7	94.9	97.4	95.3
	B3	96.1	94.8	96.5	96.0

5. Example

To demonstrate how the methods we have presented in the preceding sections can be used in practical situations, we take a classical example from Snedecor and Cochran (1967, p. 290), the data are presented in Table V below. In research on artificial insemination of cows, a series of semen samples from a bull are sent out and tested for their viability. The data show the percentages of conceptions obtained from samples of six bulls.

From the data above we calculated the weights as $b_1 = 0.153$, $b_2 = 0.178$, $b_3 = 0.283$, $b_4 = 0.053$, $b_5 = 0.139$, $b_6 = 0.194$; so that $c_i = b_i < \frac{1}{2} - \varphi = 0.495$, $i = 1, \ldots, 6$. That is, no single group (bull) can be said to be dominating the others. The estimators and their estimates are given in Table VI. The confidence intervals at a confidence coefficient of 95% are obtained as:

$$CI_1(\sigma_a^2) : [-0.424, 189.875] \triangleq [0, 189.875], \quad \text{and} \quad CI_2(\sigma_a^2) : [17.518, 230.479].$$

We see that all the estimates given in Table VI lie within the two confidence bounds, $CI_1(\sigma_a^2)$ and $CI_2(\sigma_a^2)$.

Table V: Data on artificial insemination of cows, taken from Snedecor and Cochran (1967, p. 290).

Bull	Percentages of conceptions to services for successive samples	Sample size	Mean	Variance
1	46, 31, 37, 62, 30	5	41.2	175.7
2	70, 59	2	64.5	60.5
3	52, 44, 57, 40, 67, 64, 70	7	56.3	132.9
4	47, 21, 70, 46, 14	5	39.6	505.3
5	42, 64, 50, 69, 77, 81, 87	7	67.1	270.5
6	35, 68, 59, 38, 57, 76, 57, 29, 60	9	53.2	249.4

Table VI: Estimators and estimates of the between-study variance for the data in Table IV.

Estimator	$\hat{\sigma}^2_{a,DL}$	$\hat{\sigma}^2_{a,2}$	$\hat{\sigma}^2_a(\eta)$	$\hat{\sigma}^2_a(\lambda_2)$	MLE	$REMLE$
Estimate	64.938	31.866	30.834	58.557	54.822	76.746

6. Conclusion

Two positive estimators of the between-group variance component have been derived. Their biases and standard deviations have been shown to be near those of the DerSimonian-Laird estimator, a popular estimator of the between-study variance in meta-analysis. Unlike the ML and REML estimator which have biases which increase at a relatively faster rate with σ^2_a, the proposed estimators have relatively stable biases. Therefore, one is most likely to be closer to the true parameter by using the proposed estimators than by using the ML and REML estimator. More so, given the well documented difficulties in the use of iterative estimators, the proposed estimators are finite and easier to implement.

The new estimators have the advantages associated with the DerSimonian-Laird estimator with one important added advantage, namely, that it is possible to construct explicit confidence intervals, thus contributing in solving a long outstanding problem.

References

BIGGERSTAFF, B. J. & TWEENDIE, R. L. (1997). Incorporating variability in estimates of heterogeneity in the random effects model in meta-analysis: *Statistics in Medicine.* **16,** 753-768.

BROWN, H. K. & KEMPTON, R. A. (1994). The application of REML in clinical trials. *Statistics in Medicine,* **13,** 1601-1617.

BURDICK, R. K. & EICKMAN, J. (1986). Confidence intervals on the among group variance component in the unbalanced one-fold nested design. *Journal of Statistical Computation and Simulation,* **26,** 205-219.

COCHRAN, W. G. (1954): The combination of estimates from different experiments. *Biometrics,* **10,** 101-129.

CORBEIL, R. R. & SEARLE, S. R. (1976). Restricted maximum likelihood (REML) estimation of variance components in the mixed model. *Technometrics,* **18**(1), 31-38.

DERSIMONIAN, R. & LAIRD, N. (1986). Meta-analysis in clinical trials, *Controlled Clinical Trials*, **7,** 177-188.

HARDY, R. J. & THOMPSON, S. G. (1996). A likelihood approach to meta–analysis with random effects. *Statistics in Medicine,* **15,** 619-629.

HARTLEY, H. O. & RAO, J. N. K. (1967). Maximum-likelihood estimation for the mixed analysis of variance model. *Biometrika,* **54,** 93-108.

HARTUNG, J. (1981). Nonnegative minimum biased invariant estimation in variance component models. *Annals of Statistics,* **9,** 278-292.

HARTUNG, J. & KNAPP (2000). Confidence intervals for the between group variance in the one-way random effects model of analysis of variance *Journal of Statistical Computation and Simulation,* **65,** 311-323.

HARTUNG, J. & VOET, B. (1986). Best invariant unbiased estimators for the mean squared error of variance component estimators. *Journal of the American Statistical Association,* **81,** 689-691.

HARVILLE, D. A. (1977). Maximum likelihood approaches to variance component estimation and to related problems. *Journal of the American Statistical Association,* **72,** 320-340.

HERBACH, L. H. (1959). Properties of model–II analysis of variance tests. *Annals of Mathematical Statistics,* **30,** 939-959.

NORMAND, S-L. (1999). Meta–analysis: formulating, evaluating, combining, and reporting. *Statistics in Medicine,* **18,** 321-359.

MENGERSEN, K. L.; TWEENDIE; R. L & BIGGERSTAFF, B. (1995). The impact of method choice on meta-analysis. *Australian Journal of Statistics,* **18**(1), 19-44.

PATNAIK, P. B. (1949). The non-central χ^2- and F-distributions and their aplications. *Biometrika,* **36,** 202-232.

RAO, P. S., KAPLAN, J. & COCHRAN, W. G. (1981). Estimators of the one-way random effects model with unequal error variances. *Journal of the American Statistical Association,* **76,** 89-97.

SEARLE, S. R. (1988). Mixed models and unbalanced data: wherefrom, whereat, and whereto? *Communications in Statistics–Theory and Methods,* **17**(4), 935-968.

SNEDECOR, G. W. & COCHRAN, W. G. (1967). *Statistical Methods,* Sixth ed., Iowa State University Press, Ames.

THOMAS, J. D. & HULTQUIST, R. A. (1978). Interval estimation for the unbalanced case of the one-way random effects model. *Annals of Statistics,* **6,** 582-587.

THOMPSON, W. A. JR. (1962). The problem of negative estimates of variance components. *Annals of Mathematical Statistics,* **33,** 273-289.

WANG, Y. Y. (1967). A comparison of several variance component estimators. *Biometrika,* **54,** 301-305.