Non-iterative t-distribution Based Tests for Meta-Analysis[1]

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Summary: The estimator of the variance of the optimal estimator of the overall mean in a heteroscedastic one-way fixed and random ANOVA model is dominated by positive semi-definite quadratic functions. This makes it possible to develop closely related tests on the nullity of the overall mean parameter, in one-way fixed and random effects ANOVA models, which make use of the quantiles of the t-distribution. These tests are founded on the convexity arguments similar to Hartung (1976). Simulation results indicate that the proposed tests attain type I error rates which are far more acceptable than those of the commonly used tests.

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1. Introduction

Combining results from different experiments (or studies) has become common in many fields of scientific inquiry. One has, for example, balanced or unbalanced, homoscedastic or heteroscedastic samples to assess the overall treatment effect. With treatment-by-centre interaction in such samples, we get a random effects model, otherwise we have a fixed effects model.

The possibility of many false positives in meta-analysis due to the underestimate of the variance of the estimate of the overall treatment effect cannot be overemphasized as indicated by Li et al. (1994) and Boeckenhoff and Hartung (1998). This observation has also been made elsewhere in the context of mixed linear models, for example, Kackar and Harville (1984), and Kenward and Roger (1997). Suggested corrections for the fixed effects model with the resulting test statistics being normally distributed do not extend naturally to the random effects model.

As would be expected, there already exists some test procedures for the overall-treatment effect, for example, those based on the Maximum Likelihood (ML) as well as on the Restricted Maximum Likelihood (REML), cf: for instance, Brown and Kempton (1994), and Kenward and Roger (1997). In meta-analysis, inference is usually based on summary statistics reported from, say, trials in a multicentre study. Such summaries may be some mean treatment differences together with their standard errors, see Cochran (1954). In such absence of original data, efficient estimates of the overall treatment effect and variance components cannot be obtained via REML analysis, observes Brown and Kempton (1994). In addition, convergence of the estimates when using REML (as well as ML) is not assured and one has to change to more time consuming procedures, Kenward and Roger (1997).

By noting that the estimate of the variance of the estimate of the overall treatment effect is dominated by a positive semi-definite quadratic form and approximating its distribution by a χ^2-distribution by equating its first two moments, we obtain tests of significance for the overall treatment effect which are based on the t-distribution. Two related tests, cf. section 2, for the fixed effects model are suggested and one test, cf. section 3, for the random effects model. Accompanying simulation results, cf. Tables I and II, indicate that our suggested test statistics improve greatly the attained type I error rates compared with the commonly used test.

The procedures we suggest, being non-iterative, will be easier to apply and this will make them more appealing for practical purposes, especially in medical and epidemiological applications where meta-analysis is common place.

2. Fixed Effects Model

For $K \geq 2$ independent experiments, let y_{ij} be the observation on the $j-th$ subject of the $i-th$ experiment, $i = 1, \ldots, K$ and $j = 1, \ldots, n_i$, such that

$$y_{ij} \;=\; \mu + e_{ij},\; i = 1, \ldots, K,\; j = 1, \ldots, n_i, \qquad (1)$$

where μ is the common mean for all the K homogeneous experiments, e_{ij} are error terms which are assumed to be mutually stochastically independent and normally distributed, that is, $e_{ij} \sim N(0, \sigma_i^2);\; i = 1, \ldots, K,\; j = 1, \ldots, n_i$. The best estimate for μ in each study (experiment) is the individual sample mean $\hat{\mu}_i = \sum_{j=1}^{n_i} y_{ij}/n_i = \bar{y}_{i.}$ with variance $\sigma_i^2/n_i,\; i = 1, \ldots, K$. This means that we have a fixed effects combinations model such that $\hat{\mu}_i \sim N(\mu, \sigma_i^2/n_i),\; i = 1, \ldots, K$.

Our interest is in testing the hypothesis $H_0 : \mu = 0$ against $H_1 : \mu \neq 0$ at some type I error rate, α. We emphasize here that in a typical meta-analysis situation, what is usually available from the $i-th$ trial is just the set of values $(\bar{y}_{i.}, \hat{\sigma}_i^2/n_i),\; i = 1, \ldots, K$.

Now, the best linear unbiased estimator of μ which traces back to Cochran

(1954) (see also Whitehead and Whitehead, 1991) is:

$$\tilde{\mu} = \frac{\sum_{i=1}^{K} \frac{n_i}{\sigma_i^2} \cdot \hat{\mu}_i}{\sum_{i=1}^{K} n_i/\sigma_i^2} \tag{2}$$

with variance $\sigma_{\tilde{\mu}}^2 = \left(\sum_{i=1}^{K} n_i/\sigma_i^2\right)^{-1}$. Under H_0 the statistic

$$T = \frac{\tilde{\mu}}{\sqrt{\sigma_{\tilde{\mu}}^2}} \sim N(0,1). \tag{3}$$

In most practical situations, however, the individual error variances, σ_i^2, are unknown and are estimated in the $i-th$ trial by their unbiased estimators, $s_i^2 = \sum_{j=1}^{n_i}(y_{ij} - \bar{y}_{i.})^2/(n_i - 1)$, so that $\hat{\sigma}_i^2/n_i = s_i^2/n_i$ is made available for a meta-analysis. Consequently we have the estimate of the overall mean to be

$$\hat{\mu} = \frac{\sum_{i=1}^{K} \frac{n_i}{\hat{\sigma}_i^2} \cdot \hat{\mu}_i}{\sum_{i=1}^{K} n_i/\hat{\sigma}_i^2}, \tag{4}$$

so that when $\mu = 0$, the test statistic

$$T_1 = \frac{\hat{\mu}}{\sqrt{\hat{\sigma}_{\tilde{\mu}}^2}} \overset{approx}{\sim} N(0,1), \tag{5}$$

cf: for example, Normand (1999).

The test in (5) above attains type I error rates which are much greater than the nominal level, α, see Li et al. (1994) and Boeckenhoff and Hartung (1998).

Now, consider a positive discrete random variable d taking on realizations $d_i = 1/x_i$ with probabilities ω_i, for $i = 1, \ldots, K$, and the convex function $g(d) = 1/d$, then Jensen's inequality

$$g\{E(d)\} = \frac{1}{\sum_{i=1}^{K} \omega_i \cdot d_i} \leq E\{g(d)\} = \sum_{i=1}^{K} \omega_i \cdot \frac{1}{d_i}$$

provides us with the well known inequality between the harmonic and arithmetic means.

Lemma 1

For $x_i > 0,\ \omega_i \geq 0,\ i = 1, \ldots, K,\ \sum_{i=1}^K \omega_i = 1$, there holds

$$\bar{x}_{\omega,h} = \frac{1}{\sum_{i=1}^K \omega_i \cdot \frac{1}{x_i}} \leq \sum_{i=1}^K \omega_i \cdot x_i = \bar{x}_{\omega,a}.$$

Next, let

$$f_{\hat{\mu},h}(s^2) = \hat{\sigma}^2_{\tilde{\mu}} = \frac{1}{\sum_{i=1}^K n_i/s_i^2} = \frac{1}{N} \cdot \frac{1}{\sum_{i=1}^K \frac{n_i/N}{s_i^2}}, \tag{6}$$

Using Lemma 1 above and setting $\omega_i = n_i/N$ we get

$$f_{\hat{\mu},h}(s^2) = \frac{1}{N} \cdot \frac{1}{\sum_{i=1}^K \omega_i/s_i^2} \leq \frac{1}{N} \cdot \sum_{i=1}^K \omega_i\, s_i^2 =: f_{\hat{\mu},a}(s^2) \tag{7}$$

with $x_i = s_i^2$. Clearly $f_{\hat{\mu},a}(s^2)$ is a positive semi-definite quadratic form in the random variables, which dominates the function $f_{\hat{\mu},h}(s^2)$. Thus, the approximate distribution of $f_{\hat{\mu},h}(s^2)$ can be obtained as follows:
Let

$$Q(f_{\hat{\mu},h}) = \nu \cdot \frac{1}{E\{f_{\hat{\mu},h}(s^2)\}} \cdot f_{\hat{\mu},h}(s^2),$$

then $Q(f_{\hat{\mu},h}) \overset{approx}{\sim} \chi^2_\nu$, where according to Patnaik (1949)

$$\nu = 2 \cdot \frac{[E\{f_{\hat{\mu},h}(s^2)\}]^2}{Var\{f_{\hat{\mu},h}(s^2)\}}$$

Remember that in our considerations above, we have used Patnaik's approximation to estimate the degrees of freedom. This approximation is a generalization of Satterthwaite's method which requires that the statistic under consideration be a linear function (or can be expressed as) of mean squares; the statistic $\hat{\sigma}^2_{\tilde{\mu}}$ is not an explicit linear function of mean squares.

By convexity arguments similar to those of Hartung (1976, sec. 1), cf: also Boeckenhoff and Hartung (1998), we have

$$E\{f_{\hat{\mu},h}(s^2)\} \leq \sigma^2_{\tilde{\mu}}.$$

Further, it can be shown that

$$Var\{f_{\hat{\mu},h}(s^2)\} \;\leq\; E\left\{\left(\sum_{i=1}^{K}\frac{n_i}{s_i^2}\right)^{-2} - \left(\sum_{i=1}^{K}\frac{\sqrt{n_i^2-1}}{n_i-3}\cdot\frac{n_i}{s_i^2}\right)^{-2}\right\} = E(\hat{V}_1) \quad (8)$$

$$Var\{f_{\hat{\mu},h}(s^2)\} \;\leq\; \left(\sum_{i=1}^{K}\sqrt{\frac{n_i-1}{n_i+1}}\cdot\frac{n_i}{\sigma_i^2}\right)^{-2} - \left(\sum_{i=1}^{K}\frac{n_i-1}{n_i-3}\cdot\frac{n_i}{\sigma_i^2}\right)^{-2} = V_2 \quad (9)$$

For the estimated degrees of freedom, ν, we will make use of $\hat{V}_j,\ j = 1, 2$, as given in (8) and (9) above with the parameters $\sigma_i^2/n_i,\ i = 1, \ldots, K$, in V_2 replaced by their estimators, s_i^2/n_i, to obtain $\hat{V}_2$. That is,

$$\hat{\nu}_j = 2\cdot\frac{\{f_{\hat{\mu},h}(s^2)\}^2}{\hat{V}_j},\ j = 1, 2.$$

In the following, however, we propose to introduce some compensation to the numerator of $\nu_j,\ j = 1, 2$, which is an upper bound of the variance of $f_{\hat{\mu},h}(s^2)$, to avoid adverse underestimation. This can be done by adding some amount of the standard deviation, say, $\delta_j = \kappa\cdot\sqrt{\hat{V}_j},\ j = 1, 2,\ 0 < \kappa < 1$. Thus we have the modified operational $\nu_j,\ j = 1, 2$, given by

$$\hat{\nu}_j(\kappa) = 2\cdot\frac{\{f_{\hat{\mu},h}(s^2)+\delta_j\}^2}{\hat{V}_j},\ j = 1, 2.$$

We now summarise the above considerations to formulate the following theorem.

Theorem 1:

The test statistics $T_{1,t}$, $t = 1, 2$, under $H_0 : \mu = 0$, are such that:

a)

$$T_{1,1} = \frac{\hat{\mu}}{\sqrt{f_{\hat{\mu},h}(s^2)}} \overset{approx}{\sim} t_{\hat{\nu}_1(\kappa)}$$

b)

$$T_{1,2} = \frac{\hat{\mu}}{\sqrt{f_{\hat{\mu},h}(s^2)}} \overset{approx}{\sim} t_{\hat{\nu}_2(\kappa)}$$

Using $T_{1,1}$ and $T_{1,2}$ with $\kappa = 0.5$, we now demonstrate through a simulation study that the two proposed tests attains type I error rates which are closer to the nominal level than the commonly used test, T_1, which attains levels well above the prescribed level, α, especially for small sample sizes. For comparison, we have also considered in our simulations $T_{1,0} = \hat{\mu}/(\sum_{i=1}^{K} n_i/\sigma_i^2)^{-1/2}$ with the true σ_i^2 in the variance term of T_1, and the critical values are taken from the standard normal distribution.

Table I: Actual type I error rates (10 000 runs) for $K = 3$ and $K = 6$ for the fixed effects model.

nominal level, α=5%		Attained type I error rates, $\hat{\alpha}$%							
Sample sizes	Error variances	$K = 3$				$K = 6$ (1 Replication of K=3)			
(n_1, n_2, n_3)	$(\sigma_1^2, \sigma_2^2, \sigma_3^2)$	$T_{1,0}$	T_1	$T_{1,1}$	$T_{1,2}$	$T_{1,0}$	T_1	$T_{1,1}$	$T_{1,2}$
(5,5,5)	(1,3,5)	9.2	18.2	8.0	11.7	10.1	23.4	13.6	10.8
	(4,4,4)	8.3	18.6	10.5	8.2	11.4	23.6	13.7	10.9
(10,10,10)	(1,3,5)	6.6	10.0	5.4	4.9	7.0	11.0	6.0	5.4
	(4,4,4)	6.9	10.8	6.0	5.4	7.3	11.7	6.5	5.9
(20,20,20)	(1,3,5)	5.7	7.0	4.5	4.4	6.0	7.5	4.9	4.7
	(4,4,4)	5.9	7.2	4.8	4.5	6.0	7.5	4.8	4.6
(5,10,15)	(1,3,5)	7.3	13.3	6.9	5.9	9.5	16.8	9.0	7.6
	(4,4,4)	8.0	13.1	7.2	6.4	8.8	13.4	7.6	6.8
	(5,3,1)	7.2	10.1	6.0	5.6	8.4	12.3	6.8	6.3
(10,20,30)	(1,3,5)	6.5	9.3	5.2	4.8	6.5	9.4	5.4	5.0
	(4,4,4)	6.2	7.6	5.0	4.8	6.2	8.1	5.0	4.8
	(5,3,1)	5.9	6.9	4.8	4.7	6.0	7.2	5.0	4.9

We consider first $K = 3$ with various combinings of sample sizes and error variances (see Table I below). In order to see the effect of increasing the number of experiments with all the other factors held constant, we make one independent replication of $K = 3$ to obtain $K = 6$. The results given are for testing $H_0 : \mu = 0$ against a two-sided alternative $H_1 : \mu \neq 0$.

We notice that the attained type I error rates in column 4 and 8 of Table I are far much greater than the nominal level of 5.0 percent . For small sample sizes, this liberality of T_1 is relatively higher for balanced samples and increases with the number of experiments (studies), that is, the attained levels are greater for $K = 6$ than for $K = 3$. The proposed tests, $T_{1,1}$ and $T_{1,2}$, improve the attained levels appreciably, despite showing traces of liberality in small sample cases. For balanced samples greater than 10, the proposed tests attain reasonable stability with respect to increase in the number of experiments. This is also conspicuous for unbalanced samples in cases where the smallest sample size is equal to 10.

3 Random Effects Model

For the one-way random effects model we add a random effect $a_i \sim N(0, \sigma_a^2),\ i = 1, \ldots, K$, to model (1), see section 2 above, to obtain

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

with $a_1, \ldots, a_K, e_{11}, \ldots, e_{Kn_K}$ being mutually stochastically independent, so that $\hat{\mu}_i \sim N(\mu, \sigma_a^2 + \sigma_i^2/n_i)$. Then the estimator of μ equivalent to (4) is given by

$$\hat{\mu} = \frac{\sum_{i=1}^K \frac{1}{v_i} \cdot \hat{\mu}_i}{\sum_{i=1}^K 1/v_i}, \tag{10}$$

where $v_i = \hat{\sigma}_a^2 + \hat{\sigma}_i^2/n_i = \hat{\sigma}_a^2 + \xi_i,\ i = 1, \ldots, K$. Therefore, we have the commonly used test statistic

$$T_1^r = \frac{\hat{\mu}}{(\sum_{i=1}^K 1/v_i)^{-1/2}} \overset{approx}{\sim} N(0, 1) \tag{11}$$

This test suffers from the same weaknesses as its fixed effects counterpart, with the situation here being compounded by the estimation of the variance of the random effect, σ_a^2.

Let $\tau_i^2 = \sigma_a^2 + \sigma_i^2/n_i$, and define the quadratic form $Q = \sum_{i=1}^K h_i(\hat{\mu}_i - \sum_{j=1}^K b_j\,\hat{\mu}_j)^2$, where $h_i > 0$ and $b_i > 0$ with $\sum_{i=1}^K b_i = 1,\ i = 1, \ldots, K$. By a somewhat lengthy derivation, it can be shown that, Hartung (1999), (cf: also Hartung, 1981; Mathai and Provost, 1992)

$$E(Q) = \sum_{i=1}^K h_i(1-2b_i)\tau_i^2 + (\sum_{i=1}^K h_i)(\sum_{i=1}^K b_i^2\tau_i^2), \tag{12}$$

$$Var(Q) = 2 \cdot \left(\sum_{i=1}^K h_i^2 D_i^2 + \sum_{i=1}^K \sum_{i \neq j=1}^K h_i h_j C_{ij}^2 \right), \tag{13}$$

where

$$D_i = (1-2b_i)\tau_i^2 + \sum_{k=1}^K b_k^2 \tau_k^2, \tag{14}$$

$$C_{ij} = \sum_{k=1}^K b_k^2\tau_k^2 - b_i\tau_i^2 - b_j\tau_j^2,\ i,j = 1, \ldots, K, \tag{15}$$

which are also estimated by replacing parameters by their estimates. Set $\gamma_\Sigma = \sum_{i=1}^K \gamma_i,\ \ \gamma_i = n_i/\sigma_i^2$. Then for fixed weights

$$b_i = \frac{\gamma_i}{\gamma_\Sigma},\quad h_i = \frac{b_i}{1 - \sum_{i=1}^K b_i^2}$$

we obtain the so-called DerSimonian-Laird estimator for meta-analysis, cf: DerSimonian and Laird (1986), and Whitehead and Whitehead (1991),

$$\tilde{\sigma}_a^2 = \frac{\gamma_\Sigma}{\gamma_\Sigma^2 - \sum_{i=1}^K \gamma_i^2} \left\{ \sum_{i=1}^K \gamma_i(\hat{\mu}_i - \sum_{j=1}^K b_j\,\hat{\mu}_j)^2 - K + 1 \right\}, \tag{16}$$

which is an unbiased estimator of σ_a^2 with variance, $Var(\tilde{\sigma}_a^2) = Var(Q)$. As in section 2 above, $Var(\xi_i) = 2 \cdot \sigma_i^4/\{n_i^2(n_i-1)\}$ and its best invariant unbiased estimator is given by $\widehat{Var}(\xi_i) = 2 \cdot \xi_i^2/(n_i+1)$, Hartung and Voet (1986). Note that $\tilde{\sigma}_a^2$ has a positive probability of taking negative values. For a realization the parameter σ_i^2/n_i in b_i is replaced by ξ_i so that $\tilde{\sigma}_a^2$ becomes the estimator

$\hat{\sigma}_a^2$.

Making use now of Lemma 1 again, we have

$$\frac{1}{\sum_{i=1}^K 1/v_i} \leq \frac{1}{K} \cdot \sum_{i=1}^K \frac{1}{K} \cdot v_i = \frac{1}{K^2} \sum_{i=1}^K (\tilde{\sigma}_a^2 + \xi_i), \tag{17}$$

and therefore,

$$\frac{1}{\sum_{i=1}^K 1/v_i} = \Delta \cdot (\tilde{\sigma}_a^2 + \frac{1}{K} \sum_{i=1}^K \xi_i),$$

where Δ is a positive random variable. Next,

$$\begin{aligned} \nu_r \cdot \left\{ E\left(\frac{1}{\sum_{i=1}^K 1/v_i} \right) \right\}^{-1} \cdot \frac{1}{\sum_{i=1}^K 1/v_i} &= \nu_r \cdot \frac{\Delta \cdot (\tilde{\sigma}_a^2 + \frac{1}{K} \sum_{i=1}^K \xi_i)}{E\left\{ \Delta \cdot (\tilde{\sigma}_a^2 + \frac{1}{K} \sum_{i=1}^K \xi_i) \right\}} \\ &\approx \nu_r \cdot \frac{(\tilde{\sigma}_a^2 + \frac{1}{K} \sum_{i=1}^K \xi_i)}{E(\tilde{\sigma}_a^2 + \frac{1}{K} \sum_{i=1}^K \xi_i)} \overset{approx}{\sim} \chi^2_{\nu_r}, \end{aligned}$$

and by the independence of Q and $\xi_i,\ i = 1, \ldots, K$, ν_r is given by

$$\begin{aligned} \nu_r &= 2 \cdot \frac{\left[E\left\{ \Delta \cdot (\tilde{\sigma}_a^2 + \frac{1}{K} \sum_{i=1}^K \xi_i) \right\} \right]^2}{Var\left\{ \Delta \cdot (\tilde{\sigma}_a^2 + \frac{1}{K} \sum_{i=1}^K \xi_i) \right\}} \\ &\approx 2 \cdot \frac{\left\{ E(\tilde{\sigma}_a^2 + \frac{1}{K} \sum_{i=1}^K \xi_i) \right\}^2}{Var\left(\tilde{\sigma}_a^2 + \frac{1}{K} \sum_{i=1}^K \xi_i \right)} \\ &= 2 \cdot \frac{\left\{ E(\tilde{\sigma}_a^2 + \frac{1}{K} \sum_{i=1}^K \xi_i) \right\}^2}{Var(Q) + \frac{2}{K^2} \sum_{i=1}^K \sigma_i^4 / \{ n_i^2 (n_i - 1) \}}. \end{aligned}$$

With all parameters replaced by their suitable estimates, ν_r can be estimated by

$$\hat{\nu}_r = 2 \cdot \frac{\left(\hat{\sigma}_a^2 + \frac{1}{K} \sum_{i=1}^K \xi_i \right)^2}{\widehat{Var}(\hat{Q}) + \frac{2}{K^2} \sum_{i=1}^K \xi_i^2 / (n_i + 1)} \tag{18}$$

if $\hat{\sigma}_a^2 > 0$ and for $\hat{\sigma}_a^2 \leq 0$,

$$\hat{\nu}_r = \frac{\left(\sum_{i=1}^K \xi_i \right)^2}{\sum_{i=1}^K \xi_i^2 / (n_i + 1)}. \tag{19}$$

So, for testing the hypothesis $H_0 : \mu = 0$ against $H_1 : \mu \neq 0$, we have the following theorem

Theorem 2

Under H_0 there is

$$T_{1,1}^r = \frac{\hat{\mu}}{(\sum_{i=1}^K 1/v_i)^{-1/2}} \tag{20}$$

distributed approximately as a central t-variable with $\hat{\nu}_r$ degrees of freedom.

Now, by a simulation study (see Table II) we compare the attained type I error rates for the commonly used statistic, T_1^r, and the proposed test $T_{1,1}^r$. For comparison, we have also included the statistic $T_0^r = \hat{\mu}/(\sum_{i=1}^K 1/\tau_i^2)^{-1/2}$ with the true values τ_i^2 in the variance term of T_1^r and the critical values are obtained from the standard normal distribution. To obtain $K = 6$ we independently replicated $K = 3$ once for $\sigma_a^2 = 0, 0.5, 5, 25$.

For $\sigma_a^2 = 0.0$, (cf: Table II), the proposed test T_1^r attains acceptable type I error rates, despite being a liberal for $K = 6$, especially, for sample sizes of 5 per experiment. Also for unbalanced samples, when relatively large individual error variances are paired with relatively small sample sizes, the test is too conservative for $K = 3$.

For values of $\sigma_a^2 = 0.5$, 5.0 and 25.0, the proposed test attains levels far more acceptable than those of the commonly used statistic T_1^r, save for some small traces of liberality especially for small sample size combinations.

Table II: Actual type I error rates (10 000 runs) for $K = 3$ and 6 for the random effects model.

Nominal level, α=5%			Attained type I error rates, $\hat{\alpha}$%					
	Sample sizes	Error variances	$K = 3$			$K = 6$ (1 Replication of K=3)		
σ_a^2	(n_1, n_2, n_3)	$(\sigma_1^2, \sigma_2^2, \sigma_3^2)$	T_0^r	T_1^r	$T_{1,1}^r$	T_0^r	T_1^r	$T_{1,1}^r$
0.0	(5,5,5)	(1,3,5)	9.0	10.1	5.5	9.3	9.7	6.5
		(4,4,4)	6.7	10.4	5.7	7.2	10.1	7.0
	(20,20,20)	(1,3,5)	6.9	4.6	3.6	6.4	4.9	4.0
		(4,4,4)	5.4	4.7	3.5	5.5	4.9	3.7
	(5,10,15)	(1,3,5)	5.8	7.4	5.1	6.4	7.9	6.2
		(4,4,4)	6.7	6.7	3.9	7.2	7.1	4.6
		(5,3,1)	12.0	5.5	2.8	10.5	5.4	3.4
	(10,20,30)	(1,3,5)	5.6	5.2	4.0	5.8	5.6	4.4
		(4,4,4)	5.8	4.6	3.4	6.2	5.1	3.6
		(5,3,1)	10.5	4.4	2.8	8.2	4.6	3.5
0.5	(5,5,5)	(1,3,5)	6.3	16.4	9.1	5.9	12.2	8.5
		(4,4,4)	5.6	13.8	7.5	6.3	11.5	7.6
	(20,20,20)	(1,3,5)	5.3	18.3	9.7	4.9	11.5	6.5
		(4,4,4)	5.1	14.3	7.6	5.0	10.2	5.4
	(5,10,15)	(1,3,5)	5.3	14.9	8.3	5.6	11.3	6.9
		(4,4,4)	5.4	13.3	7.2	5.7	10.8	6.5
		(5,3,1)	5.7	19.9	11.6	6.1	13.7	9.4
	(10,20,30)	(1,3,5)	4.6	15.4	7.8	5.0	10.6	5.4
		(4,4,4)	4.9	15.3	8.1	4.8	10.4	5.8
		(5,3,1)	5.8	21.0	13.4	5.3	13.2	8.8
1.0	(5,5,5)	(1,3,5)	5.5	18.4	10.0	5.4	12.8	8.0
		(4,4,4)	5.6	14.6	7.4	5.4	11.2	6.7
	(20,20,20)	(1,3,5)	4.9	19.3	8.6	5.3	12.6	5.9
		(4,4,4)	5.1	15.9	7.2	5.5	10.4	5.1

Table II: Cont.

Nominal level, α=5%			Attained type I error rates, $\hat{\alpha}$%					
	Sample sizes	Error variances	$K=3$			$K=6$ (1 Replication of K=3)		
σ_a^2	(n_1, n_2, n_3)	$(\sigma_1^2, \sigma_2^2, \sigma_3^2)$	T_0^r	T_1^r	$T_{1,1}^r$	T_0^r	T_1^r	$T_{1,1}^r$
1.0	(5,10,15)	(1,3,5)	5.6	16.9	8.4	5.2	11.4	6.1
		(4,4,4)	5.2	15.6	7.6	5.3	11.4	6.7
		(5,3,1)	6.0	21.0	11.8	5.7	13.8	8.7
	(10,20,30)	(1,3,5)	4.8	17.3	6.8	5.0	10.7	5.4
		(4,4,4)	5.0	17.0	7.9	5.2	11.3	6.0
		(5,3,1)	5.5	21.2	11.8	5.0	12.8	6.8
5.0	(5,5,5)	(1,3,5)	5.4	20.1	8.1	4.8	11.8	5.2
		(4,4,4)	5.0	18.9	7.4	5.0	11.1	5.2
	(20,20,20)	(1,3,5)	5.0	19.1	5.5	5.4	12.3	4.8
		(4,4,4)	4.7	19.2	5.7	4.5	10.4	5.0
	(5,10,15)	(1,3,5)	5.0	18.9	5.7	5.4	11.0	4.7
		(4,4,4)	5.3	19.3	7.0	4.9	10.9	5.2
		(5,3,1)	5.1	21.2	9.0	5.2	12.8	5.8
	(10,20,30)	(1,3,5)	5.0	19.4	5.8	5.3	11.4	5.0
		(4,4,4)	4.9	19.0	6.0	5.3	11.4	5.0
		(5,3,1)	5.1	21.5	7.3	5.1	13.1	4.7
25	(5,5,5)	(1,3,5)	4.8	19.9	5.3	5.3	12.1	4.1
		(4,4,4)	4.9	19.3	5.0	4.9	12.0	4.5
	(20,20,20)	(1,3,5)	4.9	20.9	4.6	4.9	11.8	4.1
		(4,4,4)	5.1	19.4	5.1	4.9	11.1	4.8
	(5,10,15)	(1,3,5)	5.1	19.4	5.1	5.0	11.9	4.6
		(4,4,4)	5.1	19.5	5.2	5.0	11.8	4.7
		(5,3,1)	4.9	20.7	5.5	4.8	13.5	4.2
	(10,20,30)	(1,3,5)	4.8	19.1	4.8	4.9	11.0	4.6
		(4,4,4)	4.9	19.4	5.0	5.0	11.2	4.8
		(5,3,1)	5.1	21.5	4.6	4.5	13.1	4.0

4. Conclusion

The problem of frequent liberal decisions is very common in meta-analysis. In comparison with the commonly used test in meta-analysis, the proposed tests greatly improve the attained type I error rates for both the fixed and random effects model. In the absence of original data from the individual trials, most of the procedures, for example, REML analysis, cannot be efficiently used. The proposed approximate tests being non-iterative, are easier to apply and require no specialist knowledge in programming. We would recommend the use of these tests, especially, in place of the commonly used method.

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