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### Abstract

Meta-analysis can be presented in the Frequentist or Bayesian framework. Based on the model of DuMouchel, a simulation study is conducted which fixes the overall mean and variance-covariance matrix to generate estimates of the true mean effect. These estimates will be compared to the true effect to assess bias. A sensitivity analysis, to measure the robustness of results to the selection of prior distributions, is conducted by employing Uniform and Pareto distributions for the variance components, the  $t$ -distribution for the overall mean component and a combination of priors for both variance and mean components respectively. Results were more sensitive when the prior was changed only on the overall mean component.

### Keywords

Sensitivity analysis, hierarchical Bayesian model, meta-analysis

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# Prior Sensitivity Analysis for a Hierarchical Model

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## Abstract

Meta-analysis can be presented in the Frequentist or Bayesian framework. Based on the model of DuMouchel, a simulation study is conducted which fixes the overall mean and variance-covariance matrix to generate estimates of the true mean effect. These estimates will be compared to the true effect to assess bias. A sensitivity analysis, to measure the robustness of results to the selection of prior distributions, is conducted by employing Uniform and Pareto distributions for the variance components, the  $t$ -distribution for the overall mean component and a combination of priors for both variance and mean components respectively. Results were more sensitive when the prior was changed only on the overall mean component.

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## 1. Introduction

Meta analysis is a statistical method used to obtain an overall estimate by combining results from several individual related studies [10]. Combining results of comparable studies to obtain an overall estimate of treatment effect (e.g. odds ratio, relative risk, risks ratio) can reduce uncertainty and can be useful when the sample size used in each study is small in an attempt to increase power [16].

Meta-analyses can be presented in the Frequentist or Bayesian framework. Within the Frequentist framework, hypotheses are based on information presented within studies and results are often presented in term of 95% confidence intervals to estimate parameters [7]. Weighted averages tend to be used as the overall treatment effect from individual study estimates. One of the more common models used is the inverse of the within-study variances ([2], [11]). Frequentist can be differentiated into fixed-effect and random-effect approaches. The sources of variation due to differences study estimates (sampling error) not due to systematic differences can be accommodated by fixed-effect thus this allows only for within study variability. However, systematic differences can be accommodated by random-effect which assumes a true effect in each study to be a random realisation from a common distribution of population effect thus this allows for within and between study variability.

Bayesian methods combine prior probability distributions that reflect a prior belief of the possible values, with the (likelihood) distributions based on the observed data, to produce the posterior probability distributions. The methods are based on the Bayesian rule for probability and can be considered an alternative approach to statistical inference. By multiplying the prior probability with the likelihood, information about the parameters which come from the observed data can be combined with information from the prior distribution that is external to the data ([2], [3]). The posterior distribution can be explained in terms of probabilities and can be considered as borrowing strength from the other studies.

## 2. Methods

### Hierarchical Bayesian Model

A variety of Bayesian methods have been developed in meta-analysis which include those developed by DuMouchel ([13], [14], [15]). The standard hierarchical Bayesian model proposed by DuMouchel [13] provides the following distributional assumptions:

$$Y_i \sim N(\theta_i, \sigma_Y^2 W_Y) \quad i = 1, 2, \dots, n \quad (1)$$
$$\sigma_Y^2 \sim \frac{\chi_{\nu_Y}^2}{\nu_Y}$$

$$\theta_i \sim N(\mu, \sigma_\theta^2 W_\theta) \quad (2)$$

$$\sigma_\theta^2 \sim \frac{\chi_{V_\theta}^2}{V_\theta}$$

$$\mu \sim N(0, D \rightarrow \infty) \quad (3)$$

The Model has 3 levels, level one indicates data from the studies, the next level refers to study-specific parameters, and level three represents hyper-parameters which indicate the overall mean and corresponding variance.

**Level 1:**  $Y_i \sim N(\theta_i, \sigma_Y^2 W_Y)$

In the Model,  $n$  denotes the number of studies ( $i = 1, 2, \dots, n$ ).  $Y_i$  indicates the observed statistics which follows the normal distribution with mean ( $\theta_i$ ) and covariance matrix ( $\sigma_Y^2 W_Y$ ). Furthermore,  $W_Y$  indicates the observed precision matrices (inverse observed variance-covariance matrix) describing within-study variation. If studies are assumed independent,  $W_Y$  is to be a diagonal matrix with the individual estimates of the variance of  $Y_i$  on the diagonal.  $\sigma_Y^2$  indicates the degree of uncertainty around the observed precision matrix, as expressed through the respective degree of freedom  $V_Y$  which denotes set to the average number of cases of studies (df =  $n-1$ ). The chi-square distribution is defined by parameter  $V_Y$  denoting how well known the variance structure  $W_Y$ .

**Level 2:**  $\theta_i \sim N(\mu, \sigma_\theta^2 W_\theta)$

$\theta_i$  denotes study-specific parameters following the normal distribution with mean ( $\mu =$  an overall mean) and covariance matrix ( $\sigma_\theta^2 W_\theta$ ).  $W_\theta$  is the prior precision matrix describing between-study variation. Independence is assumed between studies, so the precision matrices are all diagonal.  $\sigma_\theta^2$  indicates the degree of uncertainty around the prior precision matrix, as expressed through the respective degree of freedom  $V_\theta$  denoting set to equal to the number of studies (df =  $n - 1$ ). The chi-square distribution is defined by parameter  $V_\theta$  denoting how well known the variance structure  $W_\theta$ .

**Level 3:**  $\mu \sim N(0, D \rightarrow \infty)$

$\mu$  is an overall mean following the normal distribution with mean (0) and variance ( $D \rightarrow \infty$ ).  $D \rightarrow \infty$  indicates that elements of  $D$  are very large and tend to infinity.

Following statistical theory, the chi-squared distribution is imposed on  $\sigma_Y^2$  and  $\sigma_\theta^2$  which, when divided by their degrees of freedom has an expected

value equal of one or alternatively, the degree of freedom can be chosen subjectively accordance with the uncertainty around  $W_Y$  or  $W_\theta$ , respectively.

### Prior Sensitivity Analysis

The prior distribution plays a crucial role in Bayesian analysis. The conclusion obtained using the Bayesian approach is dependent on the prior distributions. The choice of prior(s) distribution must be determined with care, particularly, when the likelihood doesn't dominate the posterior. If the likelihood dominates the posterior, the posterior distribution will essentially be invariant over a wide range of priors. When the number of studies is large, the prior distribution will be less important. The non-informative prior distribution will be very useful in the situation when prior information, expectations and beliefs are minimal or not available. In a multi-parameter setting, the specification or elicitation of prior beliefs is not an easy task. Uniform priors or Jeffrey's prior are assumed non-informative priors. A vague prior is also non-informative that can be a standard choice for parameters with large variance. The use of vague priors can be problematic due to small amount of data. Hence choosing a vague prior distribution is heavily dependent on the situation [12]. Discussion about different priors is conducted in ([5], [12]).

DuMouchel [15], stated that results can be affected by different specifications of prior distributions. Sensitivity analysis, to measure the robustness of results regarding selection of prior distributions, should always be carried out. The final results in terms of posterior distributions in meta-analysis will be more robust if the results obtained are unchanged via a sensitivity analysis [12].

Using different prior distributions, for variance components for the within and between studies standard deviation  $\sigma$ , were specified on the Model. However it should be realized that specification of a prior distribution on the standard deviation scale, implies a distribution on the variance and precision scales. Moreover, different prior distribution was imposed on overall mean should be done with careful to summarise results. The parameterisations for the different prior distributions are described in the WinBugs. The prior distributions are employed presented in Table 2.1.

Variance components	$\sigma^2 \sim \text{Uniform}(1/1000, 1000)$ $1/\sigma^2 \sim \text{Pareto}(1, 0.25)$ $1/\sigma^2 \sim \text{Pareto}(1, 0.001)$
Overall mean	$\mu \sim t\text{-distribution}$
Combination	$\sigma^2 \sim \text{Uniform}(1/1000, 1000)$ $1/\sigma^2 \sim \text{Pareto}(1, 0.25)$ $\mu \sim t\text{-distribution}$

**Table 2.1.** Prior distributions used on the model due to sensitivity analysis.

### 3. Results

A simulation study for the model is presented. By employing 1,000 random samples in each of 30 studies, the R code program was created to simulate from the multivariate normal distribution. By fixing the overall mean and variance-covariance matrix, we generate estimates of the true mean effect. These estimates will be compared to the true effect to assess the bias. Steps used for the simulation study will be as follow.

*Step 1.* We fix a value overall mean ( $\mu$ ).

*Step 2.* We generate  $\theta_i$  based on the  $\mu$  (where  $n$  be the number of studies,  $i = 1, 2, \dots, n$ );  $\Sigma_\theta$  indicates symmetric, positive definite  $n \times n$  variance-covariance matrix.

*Step 3.* The value of observed statistics ( $Y_i$ ) will be obtained based on  $\theta_i$ .  $\Sigma_Y$  denotes a symmetric, positive definite  $n \times n$  variance-covariance matrix.

Furthermore, by using the risks ratios  $Y_1, Y_2, \dots, Y_{30}$  and weighted matrix (inverse of variance) in WinBugs we obtained an overall mean value of 2.554 associated with credible interval 2.233-2.878 which was close to the fixed true effect (2.560) confirming the setup of the simulation study.

Risks Ratios	Mean	S.D	2.5%	97.5%
$\sigma_Y^2 \sim \text{Uniform}(1/1000, 1000)$				
$\mu$	2.558	0.144	2.283	2.826
$\sigma_\theta^2 \sim \text{Uniform}(1/1000, 1000)$				
$\mu$	2.564	0.089	2.417	2.714
$1/\sigma_\theta^2 \sim \text{Pareto}(1, 0.001)$				
$\mu$	2.568	0.074	2.420	2.712
$1/\sigma_\theta^2 \sim \text{Pareto}(1, 0.25)$				
$\mu$	2.459	0.539	1.406	3.497
$1/\sigma_Y^2 \sim \text{Pareto}(1, 0.25) \ \& \ 1/\sigma_\theta^2 \sim \text{Pareto}(1, 0.25)$				
$\mu$	2.412	0.624	1.173	3.615

**Table 3.1. Summary statistics for overall mean ( $\mu$ ) by changing the prior variance components using Uniform and Pareto distributions on the model.**

Sensitivity analysis, to measure the robustness of results to the selection of prior distributions, is conducted. The DuMouchel model utilised the Chi-square distribution on the variance parameters,  $\sigma_Y^2$  and  $\sigma_\theta^2$ . Based on the methods of Lambert [12], the Uniform and Pareto distribution will also be employed here for the variance parameters of this model. The Normal distribution will be utilised initially for the overall mean ( $\mu$ ), consistent with that used by Dumouchel. This will be compared to the  $t$ -distribution. Simulation data based on 1,000 random samples for 30 studies here will be generated. The true overall mean ( $\mu$ ) used for this demonstration is 2.560.

#### Prior distribution for variance components

Spiegelhalter [6] investigates the uniform prior distribution on the variance.

$$\sigma^2 \sim \text{Uniform}(1/1000, 1000)$$

By using this distribution for parameters  $\sigma_Y^2$  as well as  $\sigma_\theta^2$ , burn-in for 10,000 iterations on the model, the results show an estimated overall mean are 2.558 and 2.564, respectively. These are close to the true effect (2.560). From this preliminary analysis, the use of these others prior distributions on the model do not appear to have a substantial effect on the true study estimate.

For a Pareto distribution with parameters  $\alpha$  and  $c$ , a uniform prior distribution for  $\sigma^k$  on the range  $(0, r)$

$$1/\sigma^2 \sim \text{Pareto}(1, 0.001)$$

can be expressed by setting  $\alpha = k/2$  and  $c = r^{-2}/k$ . Hence values of  $k = 2, 1$  and  $-2$  provide a uniform prior distribution on the variance, standard deviation and precision matrix respectively. This prior is equivalent to a uniform distribution  $(0, 1000)$  on the variance scale. Using this distribution on the model for  $\sigma_\theta^2$  shows the overall mean  $\mu = 2.568$  associated with CI  $(2.420 - 2.712)$  close to the true effect (2.560).

$$1/\sigma^2 \sim \text{Pareto}(1, 0.25)$$

This is the weakly informative version of prior the previous Pareto distribution and is equivalent to a uniform prior distribution for variance in the range  $(0, 4)$ . By changing parameter variance at  $\sigma_\theta^2$ , we obtained the overall mean 2.459  $(1.406 - 3.497)$ . The overall mean 2.412  $(1.173 - 3.615)$  was obtained when  $\sigma_Y^2$  and  $\sigma_\theta^2$  changed using this distribution. Table 3.1 shows summary statistics by changing prior distribution variance components on the Model.

#### Prior distribution for the overall mean

$$\mu \sim t\text{-distribution}(0, k = \text{df})$$

The  $t$ -distribution will be employed for the overall mean of the model. Density of the  $t$ -distribution for degree of freedom 2, 3, 5, 10, 30 and 50 will be compared to the normal distribution ( $\mu = 2.554$ ). The overall estimated mean using the  $t$ -distribution is

Risks ratios	Mean	S.D	2.5%	97.5%
df = 2				
$\mu$	2.556	0.166	2.232	2.875
df = 3				
$\mu$	2.554	0.166	2.226	2.871
df = 5				
$\mu$	2.555	0.165	2.233	2.874
df = 10				
$\mu$	2.554	0.168	2.224	2.874
df = 30				
$\mu$	2.552	0.167	2.228	2.881
df = 50				
$\mu$	2.555	0.167	2.234	2.881

**Table 3.2. Summary statistics the overall mean ( $\mu$ ) by changing the prior of mean using  $t$ -distribution(0,  $k = \text{df}$ ) on the model.**

presented in Table 3.2. This shows the results of overall mean to be very close to the true parameter value.

**Prior distribution for both variance and overall mean**

Prior distributions for both the variance (Uniform and Pareto) and overall mean (*t*-distribution) simultaneously were employed for the model. By changing the overall mean using *t*-distribution (0, *k*=2),  $\sigma_y^2 \sim$  Uniform (1/1000,1000) obtained the overall mean is 2.455 (1.402 – 3.489). When the overall mean was changed using *t*-distribution (0, *k*=2),  $1/\sigma_y^2$  and  $1/\sigma_\theta^2 \sim$  Pareto (1, 0.25) the result was 2.406 (1.164 – 3.598). These show the overall mean to be reasonably close to the true effect. Summary results by changing the priors on the variances and mean can be seen in Table 3.3.

Risks Ratios	Mean	S.D	2.5%	97.5%
$\mu \sim t$ -distribution (0, <i>k</i> = 2) $\sigma_y^2 \sim$ Uniform (1/1000, 1000) $\sigma_\theta^2 \sim \chi^2$				
$\mu$	2.455	0.530	1.402	3.489
$\mu \sim t$ -distribution (0, <i>k</i> = 2) $1/\sigma_y^2 \sim$ Pareto (1, 0.25) $1/\sigma_\theta^2 \sim$ Pareto (1, 0.25)				
$\mu$	2.406	0.618	1.1647	3.5944

**Table 3.3. Summary statistics for  $\mu$  by changing the prior on mean using *t*-distribution and variance components using Uniform/Pareto.**

**4. Conclusions**

The simulation study on the model showed the overall estimated mean to be close to the true effect, indicating the estimator as consistent and unbiased. While the prior distribution was imposed on the overall mean only, a change in prior showed results to be consistent. A change in prior on the variance components only and on the combination of variance and mean components simultaneously are more sensitive compared to when modifying the prior on only the mean component.

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