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Objective Bayesian Meta-Analysis Based on Generalized Marginal Multivariate Random Effects Model*

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Abstract. Objective Bayesian inference procedures are derived for the parameters of the multivariate random effects model generalized to elliptically contoured distributions. The posterior for the overall mean vector and the between-study covariance matrix is deduced by assigning two noninformative priors to the model parameter, namely the Berger and Bernardo reference prior and the Jeffreys prior, whose analytical expressions are obtained under weak distributional assumptions. It is shown that the only condition needed for the posterior to be proper is that the sample size is larger than the dimension of the data-generating model, independently of the class of elliptically contoured distributions used in the definition of the generalized multivariate random effects model. The theoretical findings of the paper are applied to real data consisting of ten studies about the effectiveness of hypertension treatment for reducing blood pressure where the treatment effects on both the systolic blood pressure and diastolic blood pressure are investigated.

MSC2020 subject classifications: Primary 62F15, 62H10; secondary 62H12.

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1 Introduction

Random effects model is a well-established quantitative tool when the results of several studies are combined in a single value as it is usually done in meta-analysis and interlaboratory comparison studies which are widely spread in medicine, physics, chemistry, and in many other fields of science (see, e.g., Brockwell and Gordon (2001); Ades et al. (2005); Viechtbauer (2005, 2007); Sutton and Higgins (2008); Riley et al. (2010); Strawderman and Rukhin (2010); Cornell et al. (2014); Novianti et al. (2014); Roever (2016); Bodnar et al. (2017); Rukhin (2017a,b); Wynants et al. (2018); Michael et al. (2019); Veroniki et al. (2019); Bodnar and Eriksson (2023)). In most of the applications considered in the literature, the aim is to infer the common mean of the measurement

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results on a single variable, while the inference procedures for the heterogeneity parameter have recently been derived by Rukhin (2013); Langan et al. (2017); Ma et al. (2018); Bodnar (2019) among others. Both methods of the frequentist and Bayesian statistics have been established to deal with the problem and applied in practice (see, Paule and Mandel (1982); DerSimonian and Laird (1986); Lambert et al. (2005); Guolo (2012); Turner et al. (2015); Bodnar et al. (2017)).

Although statistical theory to analyze the univariate random effects model has been developed and successfully implemented in many applications, new challenges arise when several features are measured simultaneously and have to be combined into a single (multivariate) result. One possibility is based on the application of the univariate random effects to each feature separately. However, important information about the dependence structure present in the joint distribution of the features might be lost in this case. Another approach is to generalize the existent univariate methods to the multivariate case by deriving new statistical procedures which can capture the dependencies present between several features and efficiently combine the (multivariate) results of several studies. Moreover, the assumption of normality, which is commonly imposed in meta-analysis or interlaboratory comparison studies, is not obviously fulfilled (see, Baker and Jackson (2008); Lee and Thompson (2008); Bodnar et al. (2016); Jackson and White (2018); Wang and Lee (2020)) and more sophisticated statistical models which take the heavy-tailed behavior into account should be considered in many applications. This makes an additional difficulty in the practical implementation of the random effects model since only a few observations are present in most cases and the advanced asymptotic methods cannot be longer used. For instance, Davey et al. (2011) pointed out that 75 % of meta-analyses reported in the Cochrane Database of Systematic Reviews (CDSR) contained five or fewer studies.

Multivariate random effects model has increased its popularity in the literature recently (see, Gasparrini et al. (2012), Wei and Higgins (2013), Jackson and Riley (2014), Liu et al. (2015), Noma et al. (2019), Negeri and Beyene (2020), Jackson et al. (2020)). Statistical inferences for the model parameters, which are the common mean vector and the heterogeneity matrix, were initially derived from the viewpoint of frequentist statistics. Jackson et al. (2010) extended the DerSimonian and Laird approach to the multivariate data, while Chen et al. (2012) presented the method based on the restricted maximum likelihood approach. These two procedures from frequentist statistics constitute the commonly used methods in the multivariate meta-analysis (see, e.g., Jackson et al. (2013), Schwarzer et al. (2015), Jackson et al. (2020)). Paul et al. (2010) derived Bayesian inference procedures for the parameters of the two-dimensional random effects model based on the Laplace approximation, while Nam et al. (2003) provided results in a multivariate case. Both papers discussed Bayesian inference obtained when informative priors are employed.

Following Bernstein-von Mises theorem (see, Bernardo and Smith (2000)), a prior has a minor impact on the posterior when the sample size is large. When a sample of a small size is available, which is a common situation in practice (cf., Davey et al. (2011)), the application of an incorrectly chosen informative prior can be very influential on the resulting Bayesian inference procedures for the model parameters. This challenge becomes even more pronounced in the case of Bayesian inference for parameters of a multivariate model.

The contribution of this paper to the existent literature on multivariate random effects model and multivariate meta-analysis is present in several directions. First, we develop objective Bayesian inference procedures for the parameters of the multivariate random effects model. In particular, we derive the analytical expression of the Fisher information matrix and the two noninformative priors: Berger and Bernardo reference prior and Jeffreys prior. Employing these two priors, the expressions of the corresponding posterior distributions are obtained and the conditions for their propriety are established. Second, we weaken the assumption of multivariate normal distribution and replace it with a general class of multivariate distributions, the so-called elliptically contoured distributions (see, Gupta et al. (2013)).

The rest of the paper is structured as follows. In Section 2, the generalized multivariate random effects model is introduced and two noninformative priors, Berger and Bernardo reference prior and Jeffreys prior, are derived. The posterior distribution for model parameters is deduced in Section 3. Here, the conditions for posterior propriety are also provided. In Section 4, numerical procedures are developed to draw samples from the derived posterior distributions. Results for two special families of elliptically contoured distributions are provided in Section 5, while an empirical illustration is presented in Section 6. Final remarks are given in Section 7. The proofs of technical results are present in the supplement material (see, Bodnar and Bodnar (2023)).

2 Model and noninformative priors

We consider an extension of the (normal) multivariate random effects model with density function given by

$$p(\mathbf{X}|\boldsymbol{\mu},\boldsymbol{\Psi}) = \frac{1}{\sqrt{\det(\boldsymbol{\Psi}\otimes\mathbf{I}+\mathbf{U})}} f\left(\mathrm{vec}(\mathbf{X}-\boldsymbol{\mu}\mathbf{1}^\top)^\top(\boldsymbol{\Psi}\otimes\mathbf{I}+\mathbf{U})^{-1}\mathrm{vec}(\mathbf{X}-\boldsymbol{\mu}\mathbf{1})\right), \quad (1)$$

where $\mathbf{X}$ is a $(p\times n)$ matrix, $\boldsymbol{\mu}$ is a p-dimensional vector, $\boldsymbol{\Psi}$ is a $(p\times p)$ matrix, $\mathbf{1}$ is a vector of ones, $\mathbf{I}$ is the identity matrix of an appropriate order, and $\mathbf{U}$ is a $(pn\times pn)$ deterministic matrix. The symbol $\otimes$ denotes the Kronecker product, while vec stands for the *vec* operator. The model (1) extends the univariate approach suggested in Bodnar et al. (2016) to the multivariate case and can also be used when several correlated features obtained from different studies should be combined together.

In a special case of $f(z) = \exp(-z/2)/(2\pi)^{pn/2}$ and $\mathbf{U} = \mathrm{diag}(\mathbf{U}_1,\ldots,\mathbf{U}_n)$ with $\mathbf{U}_i$: $p\times p$ for $i=1,\ldots,n$, the model (1) can be written as

$$\mathbf{x}_i = \boldsymbol{\mu}+\boldsymbol{\lambda}_i+\boldsymbol{\varepsilon}_i \quad \text{with} \quad \boldsymbol{\lambda}_i \sim \mathcal{N}_p(\mathbf{0},\boldsymbol{\Psi}) \quad \text{and} \quad \boldsymbol{\varepsilon}_i \sim \mathcal{N}_p(\mathbf{0},\mathbf{U}_i), \quad (2)$$

where $\{\boldsymbol{\lambda}_i\}_{i=1,\ldots,n}$ and $\{\boldsymbol{\varepsilon}_i\}_{i=1,\ldots,n}$ are mutually independent. The symbol $\mathbf{x}_i$ denotes the i-th column of $\mathbf{X}$, while $\boldsymbol{\lambda}_i$ and $\boldsymbol{\varepsilon}_i$ are normally distributed random vectors used in the stochastic representation (2) of $\mathbf{x}_i$. The presentation (2) defines the normal multivariate random effects model. Motivated by the normal multivariate random effects model, it is assumed that $\mathbf{U} = \mathrm{diag}(\mathbf{U}_1, \ldots, \mathbf{U}_n)$ holds in (1).

In many applications in medicine, physics, and chemistry the aim is to infer $\boldsymbol{\mu}$ given observation matrix $\mathbf{X} = (\mathbf{x}_1, \ldots, \mathbf{x}_n)$. In the applications of these fields the information about the scale matrix $\mathbf{U}$ is usually provided by the participating organizations (see, Lambert et al. (2005), Turner et al. (2015), Bodnar and Elster (2014b), Jackson et al. (2020)). As a result, it is assumed to be a known symmetric positive definite matrix. On the other side, the matrix $\boldsymbol{\Psi}$ is treated as an unknown quantity with the aim to capture the additional variability in data when several observations taken at different places and times are pooled together. The matrix $\boldsymbol{\Psi}$ is usually treated as an additional nuisance parameter of the model.

By (1), the conditional distribution of $\mathbf{X}$ given $\boldsymbol{\mu}$ and $\boldsymbol{\Psi}$ belongs to the class of the matrix-variate elliptical contoured distributions (see, e.g., Gupta et al. (2013) for the definition and properties of this matrix-variate family of distributions). This assertion will be denoted by $\mathbf{X}|\boldsymbol{\mu}, \boldsymbol{\Psi} \sim E_{p,n}(\boldsymbol{\mu}\mathbf{1}^\top, \boldsymbol{\Psi} \otimes \mathbf{I} + \mathbf{U}, f)$ ($p \times n$-dimensional matrix-variate elliptically contoured distribution with location matrix $\boldsymbol{\mu}\mathbf{1}^\top$, dispersion matrix $(\boldsymbol{\Psi} \otimes \mathbf{I} + \mathbf{U})$, and density generator $f(.)$. Following the definition of matrix-variate elliptically contoured distributions (see, Gupta et al. (2013, Theorem 2.7)), the function $f(.)$ should be a non-negative Lebesgue measurable function on $[0, \infty)$ such that

$$\int_0^\infty t^{pn-1} f(t^2) dt < \infty.$$

2.1 Noninformative priors: Berger and Bernardo reference prior and Jeffreys prior

In many practical applications, no information or only vague information is available about the model parameters. In such cases, especially when the sample size is small or the model dimension is large in comparison to the sample size, the usage of an informative prior can be questionable. As a possible solution to this problem, noninformative priors were developed and employed in the derivation of Bayesian inference. Historically, the first noninformative prior was suggested by Laplace (1812) who proposed to assign a constant prior to the parameters of the model. This prior is also known in the literature as the constant prior or the uniform prior. Although the uniform prior works well when Bayesian inference is determined for location parameters of a statistical model, its application does not obviously lead to good results for other types of model parameters. One of the most crucial critiques of the uniform prior is that it is not invariant under transformations of parameters.

As a solution, Jeffreys (1946) proposed to compute a noninformative prior as the square root of the determinant of the Fisher information matrix. Although this approach leads to a prior which is invariant under transformations of model parameters, some difficulties arise in the case of multi-parameter statistical models (see, Held and Bové (2014)). The approach of Jeffreys was further extended in Berger and Bernardo (1992) who suggested the so-called reference prior (see, also Berger et al. (2009) for the properties of the reference prior). The idea used in the derivation of the reference prior is based on the sequential maximization of the Shannon mutual information (see, Bodnar and Elster (2014a)) which determines the distance between the prior and posterior.

In Theorem 1 the analytical expression of the Fisher information matrix is provided, which is then used in the derivation of both the Berger and Bernardo reference prior and the Jeffreys prior for the parameters of the generalized multivariate random effects model (1). The proof of Theorem 1 is given in the supplement material (see, Bodnar and Bodnar (2023)).

Theorem 1. *The Fisher information matrix for model (1) with* $\mathbf{U} = diag(\mathbf{U}_1, \ldots, \mathbf{U}_n)$ *is given by*

$$\mathbf{F} = \begin{pmatrix} \mathbf{F}_{11} & \mathbf{O} \\ \mathbf{O} & \mathbf{F}_{22} \end{pmatrix} \tag{3}$$

where

$$\mathbf{F}_{11} = \frac{4J_1}{pn} \sum_{i=1}^{n} (\mathbf{\Psi} + \mathbf{U}_i)^{-1}, \tag{4}$$

$$\begin{aligned} \mathbf{F}_{22} &= \mathbf{G}_p^\top \Bigg[\left(\frac{J_2}{2pn + p^2n^2} - \frac{1}{4} \right) vec\left(\sum_{i=1}^{n} (\mathbf{\Psi} + \mathbf{U}_i)^{-1} \right) vec\left(\sum_{j=1}^{n} (\mathbf{\Psi} + \mathbf{U}_j)^{-1} \right)^\top \\ &+ \frac{2J_2}{2pn + p^2n^2} \sum_{i=1}^{n} \left((\mathbf{\Psi} + \mathbf{U}_i)^{-1} \otimes (\mathbf{\Psi} + \mathbf{U}_i)^{-1} \right) \Bigg] \mathbf{G}_p \end{aligned} \tag{5}$$

with

$$J_i = \mathbb{E}\left((R^2)^i \left(\frac{f'(R^2)}{f(R^2)} \right)^2 \right), \tag{6}$$

where $R^2 = vec(\mathbf{Z})^\top vec(\mathbf{Z})$ *with* $\mathbf{Z} \sim E_{p,n}(\mathbf{O}_{p,n}, \mathbf{I}_{p\times n}, f)$ *standard matrix-variate elliptically contoured distribution with density generator* $f(.)$ *and* $\mathbf{G}_p$ *stands for the duplication matrix.*

The results of Theorem 1 show that the Fisher information matrix depends on the type of elliptical distribution only over the two univariate constants J_1 and J_2 which are fully determined by density generator $f(.)$. Moreover, the Fisher information matrix $\mathbf{F}$ is finite if $J_1 < \infty$ and $J_2 < \infty$. Thus, it is assumed throughout the paper that the density generator $f(.)$ is chosen such that these two conditions are fulfilled. Although the expectations in the definition of J_1 and J_2 cannot always be analytically computed, they can easily be approximated via simulations by drawing samples from the corresponding standard elliptically contoured distribution. Finally, J_1 is present in $\mathbf{F}_{11}$ as a multiplicative constant. Thus, both the Berger and Bernardo reference prior and the Jeffreys prior depend on J_2 only as shown below.

Since $\mathbf{F}$ is block-diagonal and it does not depend on $\boldsymbol{\mu}$, the Jeffreys prior for $\boldsymbol{\mu}$ and $\boldsymbol{\Psi}$ depends on $\boldsymbol{\Psi}$ only and it is given by

$$\pi_J(\boldsymbol{\mu},\boldsymbol{\Psi}) = \pi_J(\boldsymbol{\Psi}) \propto \sqrt{\det(\mathbf{F})} = \sqrt{\det(\mathbf{F}_{11})}\sqrt{\det(\mathbf{F}_{22})}, \tag{7}$$

where $\mathbf{F}_{11}$ and $\mathbf{F}_{22}$ are given in (4) and (5), respectively.

Moreover, using the block-diagonal structure of $\mathbf{F}$ and the fact that $\mathbf{F}$ does not depend on $\boldsymbol{\mu}$, we immediately obtain the Berger and Bernardo reference prior $\pi_R(\boldsymbol{\mu},\boldsymbol{\Psi})$ for the generalized multivariate random effects model (1) from the corollary to Proposition 5.29 in Bernardo and Smith (2000). This result is summarized in Theorem 2.

Theorem 2. *For model (1) with $\mathbf{U} = diag(\mathbf{U}_1,\dots,\mathbf{U}_n)$ and grouping $\{\boldsymbol{\mu},\boldsymbol{\Psi}\}$ (i.e., with $\boldsymbol{\Psi}$ as the nuisance parameter), the Berger and Bernardo reference prior is given by*

$$\pi_R(\boldsymbol{\mu},\boldsymbol{\Psi}) = \pi_R(\boldsymbol{\Psi}) \propto \sqrt{\det(\mathbf{F}_{22})}, \tag{8}$$

where $\mathbf{F}_{22}$ is given in (5).

The following remark links the results obtained in Theorem 2 and in (7) to those derived for $p = 1$ by Bodnar et al. (2016) and Bodnar (2019):

Remark 1. *From Theorem 1, denoting $\boldsymbol{\Psi}$ by τ^2 and $\mathbf{U}_i$ by u_i^2 and using that $\mathbf{G}_p = 1$ for $p = 1$, we get the Fisher information matrix in the (μ,τ^2)-parametrization expressed as*

$$\mathbf{F}_{11} = \frac{4J_1}{n}\sum_{i=1}^{n}(\tau^2+u_i^2)^{-1} = \frac{4J_1}{n} tr\left(\left(\mathbf{V}+\tau^2\mathbf{I}\right)^{-1}\right), \tag{9}$$

$$\begin{aligned}\mathbf{F}_{22} &= \left(\frac{J_2}{2n+n^2}-\frac{1}{4}\right)\left(\sum_{i=1}^{n}(\tau^2+u_i^2)^{-1}\right)^2 + \frac{2J_2}{2n+n^2}\sum_{i=1}^{n}(\tau^2+u_i^2)^{-2}\\ &= \left(\frac{J_2}{2n+n^2}-\frac{1}{4}\right)\left(tr\left(\left(\mathbf{V}+\tau^2\mathbf{I}\right)^{-1}\right)\right)^2 + \frac{2J_2}{2n+n^2} tr\left(\left(\mathbf{V}+\tau^2\mathbf{I}\right)^{-2}\right),\end{aligned} \tag{10}$$

where $\mathbf{V} = diag(u_1^2,\dots,u_n^2)$ and

$$J_i = \mathbb{E}\left((R^2)^i\left(\frac{f'(R^2)}{f(R^2)}\right)^2\right),\ R^2 = vec(\mathbf{z})^\top vec(\mathbf{z}) \text{ with } \mathbf{z}\sim E_n(\mathbf{0}_n,\mathbf{I}_n,f). \tag{11}$$

The application of the reparametrization lemma (see, Proposition 3.14 in Sundberg (2019)) leads the Fisher information matrix in the (μ,τ)-parametrization given by

$$\tilde{\mathbf{F}} = \begin{pmatrix} \tilde{\mathbf{F}}_{11} & \mathbf{O}\\ \mathbf{O} & \tilde{\mathbf{F}}_{22}\end{pmatrix} \tag{12}$$

where

$$\tilde{\mathbf{F}}_{11} = \frac{4J_1}{n} tr\left(\left(\mathbf{V}+\tau^2\mathbf{I}\right)^{-1}\right), \tag{13}$$

$$\tilde{\mathbf{F}}_{22} = \tau^2\left(\frac{4J_2}{2n+n^2}-1\right)\left(tr\left(\left(\mathbf{V}+\tau^2\mathbf{I}\right)^{-1}\right)\right)^2+\frac{8\tau^2J_2}{2n+n^2}tr\left(\left(\mathbf{V}+\tau^2\mathbf{I}\right)^{-2}\right), \quad (14)$$

which are the same expressions as those provided in Theorem 1 of Bodnar (2019). As a result, we get the Berger and Bernardo reference prior and the Jeffreys prior as given in Section 2.2 of Bodnar (2019).

Under additional restrictions imposed on matrix $\mathbf{U}$ and density generator $f(.)$, several simplifications of the expressions of both the Berger and Bernardo reference prior and the Jeffreys prior are obtained. The results are presented in Corollary 1 and Corollary 2. For example, when the normal multivariate random effects model (2) is assumed, then we get

Corollary 1. *For model (2) and grouping $\{\boldsymbol{\mu}, \mathbf{\Psi}\}$ (i.e., with $\mathbf{\Psi}$ as the nuisance parameter), the following results hold:*

(i) the Berger and Bernardo reference prior is given by

$$\pi_R(\boldsymbol{\mu}, \mathbf{\Psi}) = \pi_R(\mathbf{\Psi}) \propto \sqrt{\det\left(\mathbf{G}_p^\top\left[\sum_{i=1}^n((\mathbf{\Psi}+\mathbf{U}_i)^{-1}\otimes(\mathbf{\Psi}+\mathbf{U}_i)^{-1})\right]\mathbf{G}_p\right)}, \quad (15)$$

(ii) the Jeffreys prior is given by

$$\pi_J(\boldsymbol{\mu}, \mathbf{\Psi}) = \pi_J(\mathbf{\Psi}) \propto \pi_R(\mathbf{\Psi})\sqrt{\det\left(\sum_{i=1}^n(\mathbf{\Psi}+\mathbf{U}_i)^{-1}\right)}. \quad (16)$$

If the generalized multivariate random effects model is assumed to be homoscedastic, that is the equality $\mathbf{U}_1 = \ldots = \mathbf{U}_n = \mathbf{V}$ holds, then the Berger and Bernardo reference prior and the Jeffreys prior are given by

Corollary 2. *Under the assumption of Theorem 2, assume that $\mathbf{U}_1 = \ldots = \mathbf{U}_n = \mathbf{V}$. Then*

(i) the Berger & Bernardo reference prior is given by

$$\pi_R(\boldsymbol{\mu}, \mathbf{\Psi}) = \pi_R(\mathbf{\Psi}) \propto \det\left(\mathbf{\Psi}+\mathbf{V}\right)^{-(p+1)/2}, \quad (17)$$

(ii) the Jeffreys prior is given by

$$\pi_J(\boldsymbol{\mu}, \mathbf{\Psi}) = \pi_J(\mathbf{\Psi}) \propto \det\left(\mathbf{\Psi}+\mathbf{V}\right)^{-(p+2)/2}. \quad (18)$$

The proofs of both corollaries are provided in the supplement material. It is remarkable that both the Berger and Bernardo reference prior and the Jeffreys prior under the assumption of homoscedasticity do not depend on the type of elliptically contoured distribution. In particular, the formulas from Corollary 2 can be used for the normal multivariate random effects model (2) as well as for the t multivariate random effect model introduced in Section 5.2.

3 Posterior

In the derivation of the posterior we consider a prior for $\boldsymbol{\mu}$ and $\boldsymbol{\Psi}$ which is a function of $\boldsymbol{\Psi}$ only, that is $\pi(\boldsymbol{\Psi})$. Such a prior is an extension of both the Berger and Bernardo reference prior and the Jeffreys prior and, consequently, the derived posterior can be used to deduce the posteriors obtained when the Berger and Bernardo reference prior and the Jeffreys prior are employed as important special cases.

Under such a general prior the joint posterior for $\boldsymbol{\mu}$ and $\boldsymbol{\Psi}$ is obtained from (1) and it is given by

$$\begin{aligned}\pi(\boldsymbol{\mu}, \boldsymbol{\Psi}|\mathbf{X}) &\propto \pi(\boldsymbol{\Psi}) p(\mathbf{X}|\boldsymbol{\mu}, \boldsymbol{\Psi}) \\ &= \frac{\pi(\boldsymbol{\Psi})}{\sqrt{\det(\boldsymbol{\Psi} \otimes \mathbf{I} + \mathbf{U})}} f\left(\text{vec}(\mathbf{X} - \boldsymbol{\mu}\mathbf{1}^\top)^\top (\boldsymbol{\Psi} \otimes \mathbf{I} + \mathbf{U})^{-1} \text{vec}(\mathbf{X} - \boldsymbol{\mu}\mathbf{1})\right), \end{aligned} \tag{19}$$

with $\mathbf{U} = \text{diag}(\mathbf{U}_1, \ldots, \mathbf{U}_n)$. In Theorem 3, whose proof is given in the supplement material (see, Bodnar and Bodnar (2023)), it is shown that the conditional reference posterior for $\boldsymbol{\mu}$ belongs to the family of elliptically contoured distributions.

Theorem 3. *Under the generalized multivariate random effects model (1) with* $\mathbf{U} =$ *diag*$(\mathbf{U}_1, \ldots, \mathbf{U}_n)$, *the conditional posterior* $\pi(\boldsymbol{\mu}|\boldsymbol{\Psi}, \mathbf{X})$ *is given by*

$$\pi(\boldsymbol{\mu}|\boldsymbol{\Psi}, \mathbf{X}) \propto f_{\boldsymbol{\Psi},\mathbf{X}}\left((\boldsymbol{\mu} - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))^\top \left(\sum_{i=1}^n (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1}\right) (\boldsymbol{\mu} - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))\right), \tag{20}$$

where

$$f_{\boldsymbol{\Psi},\mathbf{X}}(u) = f\left(\sum_{i=1}^n (\mathbf{x}_i - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))^\top (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1} (\mathbf{x}_i - \tilde{\mathbf{x}}(\boldsymbol{\Psi})) + u\right) \qquad u \geq 0, \tag{21}$$

with

$$\tilde{\mathbf{x}}(\boldsymbol{\Psi}) = \left(\sum_{i=1}^n (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1}\right)^{-1} \sum_{i=1}^n (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1} \mathbf{x}_i. \tag{22}$$

From the results of Theorem 3 we get that the conditional posterior of $\boldsymbol{\mu}$ given $\boldsymbol{\Psi}$ belongs again to the family of elliptically contoured distribution. Moreover, using (20) the location parameter of the conditional posterior $\tilde{\mathbf{x}}(\boldsymbol{\Psi})$ is given by (22), while its dispersion matrix is $\left(\sum_{i=1}^n (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1}\right)^{-1}$. These two results appear to be very useful. If the first moment of the conditional posterior exists, then it is equal to $\tilde{\mathbf{x}}(\boldsymbol{\Psi})$. The existence of the second moment ensures that the covariance matrix of the conditional posterior is proportional to the dispersion parameter. The coefficient of proportionality is expressed as

$$C(\boldsymbol{\Psi}) = \mathbb{E}\left(R^2_{\boldsymbol{\Psi},\mathbf{X}}\right) \quad \text{with} \quad R^2_{\boldsymbol{\Psi},\mathbf{X}} = \mathbf{z}^\top_{\boldsymbol{\Psi},\mathbf{X}} \mathbf{z}_{\boldsymbol{\Psi},\mathbf{X}}, \tag{23}$$

where $\mathbf{z}_{\boldsymbol{\Psi},\mathbf{X}} \sim E_p(\mathbf{0}_p, \mathbf{I}_p, f_{\boldsymbol{\Psi},\mathbf{X}})$. The density generator $f_{\boldsymbol{\Psi},\mathbf{X}}$ is connected to the density generator f, as described in (21).

As a direct consequence of the result in Theorem 3 by substituting $\pi(\mathbf{\Psi})$ with $\pi_R(\mathbf{\Psi})$ and $\pi_J(\mathbf{\Psi})$ from (8) and (7) respectively, we get the conditional reference posterior $\pi(\boldsymbol{\mu}|\mathbf{\Psi}, \mathbf{x})$ for the generalized multivariate random effects model (1) and the conditional posterior when the Jeffreys prior is used. Moreover, from the proof of Theorem 3 we also get the marginal posterior for $\mathbf{\Psi}$ as presented in Corollary 3 with the proof given in the supplement material (see, Bodnar and Bodnar (2023)).

Corollary 3. *Under the generalized multivariate random effects model (1) with* $\mathbf{U} =$ *diag*$(\mathbf{U}_1, \ldots, \mathbf{U}_n)$*, the marginal posterior* $\pi(\mathbf{\Psi}|\mathbf{X})$ *is given by*

$$\begin{aligned} \pi(\mathbf{\Psi}|\mathbf{X}) &\propto \frac{\pi(\mathbf{\Psi})}{\sqrt{\det(\sum_{i=1}^n (\mathbf{\Psi}+\mathbf{U}_i)^{-1})} \prod_{i=1}^n \sqrt{\det(\mathbf{\Psi}+\mathbf{U}_i)}} \\ &\times \int_0^\infty u^{p-1} f\left(u^2 + \sum_{i=1}^n (\mathbf{x}_i - \tilde{\mathbf{x}}(\mathbf{\Psi}))^\top (\mathbf{\Psi}+\mathbf{U}_i)^{-1} (\mathbf{x}_i - \tilde{\mathbf{x}}(\mathbf{\Psi}))\right) \mathbf{d}u. \end{aligned} \tag{24}$$

The posterior mean vector and the posterior covariance matrix of $\boldsymbol{\mu}$ are derived from Theorem 3 by using the rule of iterated expectations. They are given by

$$\begin{aligned} \mathbb{E}\,(\boldsymbol{\mu}|\mathbf{X}) &= \mathbb{E}(\mathbb{E}(\boldsymbol{\mu}|\mathbf{\Psi}, \mathbf{X})|\mathbf{X}) = \mathbb{E}(\tilde{\mathbf{x}}(\mathbf{\Psi})|\mathbf{X}) \\ &= \mathbb{E}\left(\left(\sum_{i=1}^n (\mathbf{\Psi}+\mathbf{U}_i)^{-1}\right)^{-1} \sum_{i=1}^n (\mathbf{\Psi}+\mathbf{U}_i)^{-1}\mathbf{x}_i \middle| \mathbf{X}\right) \end{aligned} \tag{25}$$

and

$$\begin{aligned} \mathbb{V}ar\,(\boldsymbol{\mu}|\mathbf{X}) &= \mathbb{E}(\mathbb{V}ar(\boldsymbol{\mu}|\mathbf{\Psi}, \mathbf{X})|\mathbf{X}) + \mathbb{V}ar(\mathbb{E}(\boldsymbol{\mu}|\mathbf{\Psi}, \mathbf{X})|\mathbf{X}) \\ &= \mathbb{E}\left(C(\mathbf{\Psi})\left(\sum_{i=1}^n (\mathbf{\Psi}+\mathbf{U}_i)^{-1}\right)^{-1} \middle| \mathbf{X}\right) \\ &+ \mathbb{V}ar\left(\left(\sum_{i=1}^n (\mathbf{\Psi}+\mathbf{U}_i)^{-1}\right)^{-1} \sum_{i=1}^n (\mathbf{\Psi}+\mathbf{U}_i)^{-1}\mathbf{x}_i \middle| \mathbf{X}\right), \end{aligned} \tag{26}$$

where $C(\mathbf{\Psi})$ is given in (23).

In Theorem 4 we formulate the conditions required for the propriety of the posterior.

Theorem 4. *Consider the generalized multivariate random effects model (1) with* $\mathbf{U} =$ *diag*$(\mathbf{U}_1, \ldots, \mathbf{U}_n)$*. Let* $f(u)$ *be a non-increasing function in* $u \geq 0$ *and* $\frac{J_2}{2pn+p^2n^2} - \frac{1}{4} \leq 0$ *where* J_2 *is defined in* (6)*.*

1. *If* $n \geq p$*, then the posterior* $\pi(\boldsymbol{\mu}, \mathbf{\Psi}|\mathbf{X})$ *derived under the Jeffreys prior* $\pi_J(\mathbf{\Psi})$ *is proper.*
2. *If* $n \geq p+1$*, then the posterior* $\pi(\boldsymbol{\mu}, \mathbf{\Psi}|\mathbf{X})$ *derived under the Berger and Bernardo reference prior* $\pi_R(\mathbf{\Psi})$ *is proper.*

The proof of Theorem 4 is provided in the supplement material (see, Bodnar and Bodnar (2023)).

4 Drawing samples from the posterior distribution: Metropolis-Hastings algorithm

In this section we develop algorithms to draw samples $(\boldsymbol{\mu}^{(b)}, \boldsymbol{\Psi}^{(b)})$ from the posterior derived under the Berger and Bernardo reference prior and the Jeffreys prior. The idea is based on the application of the Markov chain Monte Carlo based on the Metropolis-Hastings algorithm, a popular approach is Bayesian statistics (see, e.g., Givens and Hoeting (2012)). Recently, Hill and Spall (2019) provided a comprehensive discussion of the stationarity and convergence of the algorithm, that depends on the chosen proposal from which the samples are generated. A good proposal distribution should have the support which covers the support of the target distribution, i.e., of the posterior for $\boldsymbol{\mu}$ and $\boldsymbol{\Psi}$. Also, it should ensure that the constructed Markov chain has good mixing properties and it will not stack in a single point.

As a proposal, we suggest to use the special case of the posterior distribution derived under each of the considered priors in the case $\mathbf{U}_1 = \ldots = \mathbf{U}_n = \mathbf{O}$. The two proposals are then defined for all positive semi-definite matrices, thus having the same supports as the two posteriors derived under the Berger and Bernardo reference prior and the Jeffreys prior. More precisely, ignoring the normalizing constants the proposal under the Berger and Bernardo reference prior is given by

$$q_R(\boldsymbol{\mu}, \boldsymbol{\Psi}|\mathbf{X}) \quad = \quad \det(\boldsymbol{\Psi})^{-(n+p+1)/2} f\left(\operatorname{tr}\left(\boldsymbol{\Psi}^{-1}\sum_{i=1}^{n}(\mathbf{x}_i-\boldsymbol{\mu})(\mathbf{x}_i-\boldsymbol{\mu})^\top\right)\right),$$

and it is expressed as

$$q_J(\boldsymbol{\mu}, \boldsymbol{\Psi}|\mathbf{X}) \quad = \quad \det(\boldsymbol{\Psi})^{-(n+p+2)/2} f\left(\operatorname{tr}\left(\boldsymbol{\Psi}^{-1}\sum_{i=1}^{n}(\mathbf{x}_i-\boldsymbol{\mu})(\mathbf{x}_i-\boldsymbol{\mu})^\top\right)\right)$$

under the Jeffreys prior.

Let

$$\bar{\mathbf{x}} = \frac{1}{n}\sum_{i=1}^{n}\mathbf{x}_i \quad \text{and} \quad \mathbf{S} = \frac{1}{n-1}\sum_{i=1}^{n}(\mathbf{x}_i-\bar{\mathbf{x}})(\mathbf{x}_i-\bar{\mathbf{x}})^\top, \tag{27}$$

In using that

$$\sum_{i=1}^{n}(\mathbf{x}_i-\boldsymbol{\mu})(\mathbf{x}_i-\boldsymbol{\mu})^\top = (n-1)\mathbf{S} + n(\boldsymbol{\mu}-\bar{\mathbf{x}})(\boldsymbol{\mu}-\bar{\mathbf{x}})^\top, \tag{28}$$

which implies

$$\det\left(\sum_{i=1}^{n}(\mathbf{x}_i-\boldsymbol{\mu})(\mathbf{x}_i-\boldsymbol{\mu})^\top\right) = \det((n-1)\mathbf{S})\left(1+\frac{n}{n-1}(\boldsymbol{\mu}-\bar{\mathbf{x}})^\top\mathbf{S}^{-1}(\boldsymbol{\mu}-\bar{\mathbf{x}})\right)$$

we get

$$q_R(\boldsymbol{\mu}, \boldsymbol{\Psi}|\mathbf{X}) \quad \propto \quad \left(1+\frac{1}{n-p}\frac{n(n-p)}{n-1}(\boldsymbol{\mu}-\bar{\mathbf{x}})^\top\mathbf{S}^{-1}(\boldsymbol{\mu}-\bar{\mathbf{x}})\right)^{-n/2}$$

$$\times \quad \det(\boldsymbol{\Psi})^{-(n+p+1)/2}\det\left(\sum_{i=1}^{n}(\mathbf{x}_i-\boldsymbol{\mu})(\mathbf{x}_i-\boldsymbol{\mu})^\top\right)^{n/2}$$
$$\times \quad f\left(\mathrm{tr}\left(\boldsymbol{\Psi}^{-1}\sum_{i=1}^{n}(\mathbf{x}_i-\boldsymbol{\mu})(\mathbf{x}_i-\boldsymbol{\mu})^\top\right)\right) \tag{29}$$

and

$$\begin{aligned} q_J(\boldsymbol{\mu},\boldsymbol{\Psi}|\mathbf{X}) \quad &\propto \quad \left(1+\frac{1}{n-p+1}\frac{n(n-p+1)}{n-1}(\boldsymbol{\mu}-\bar{\mathbf{x}})^\top\mathbf{S}^{-1}(\boldsymbol{\mu}-\bar{\mathbf{x}})\right)^{-(n+1)/2} \\ &\times \quad \det(\boldsymbol{\Psi})^{-(n+p+2)/2}\det\left(\sum_{i=1}^{n}(\mathbf{x}_i-\boldsymbol{\mu})(\mathbf{x}_i-\boldsymbol{\mu})^\top\right)^{(n+1)/2} \\ &\times \quad f\left(\mathrm{tr}\left(\boldsymbol{\Psi}^{-1}\sum_{i=1}^{n}(\mathbf{x}_i-\boldsymbol{\mu})(\mathbf{x}_i-\boldsymbol{\mu})^\top\right)\right). \end{aligned} \tag{30}$$

The expression of the proposal $q_R(\boldsymbol{\mu},\boldsymbol{\Psi}|\mathbf{X})$ derived under the Berger and Bernardo reference prior is proportional to the joint density function of $\boldsymbol{\mu}$ and $\boldsymbol{\Psi}$ with $\boldsymbol{\Psi}|\boldsymbol{\mu},\mathbf{X}\sim GIW_p(n+p+1,\sum_{i=1}^n(\mathbf{x}_i-\boldsymbol{\mu})(\mathbf{x}_i-\boldsymbol{\mu})^\top,f)$ (generalized p-dimensional inverse Wishart distribution with $n+p+1$ degrees of freedom, scale matrix $\sum_{i=1}^n(\mathbf{x}_i-\boldsymbol{\mu})(\mathbf{x}_i-\boldsymbol{\mu})^\top$ and density generator f, see, Sutradhar and Ali (1989)) and $\boldsymbol{\mu}|\mathbf{X}\sim t_p\left(n-p,\bar{\mathbf{x}},\dfrac{(n-1)\mathbf{S}}{n(n-p)}\right)$ (p-dimensional multivariate t-distribution with $n-p$ degrees of freedom, location vector $\bar{\mathbf{x}}$, and scale matrix $\dfrac{(n-1)\mathbf{S}}{n(n-p)}$). Similarly, we get that the proposal under the Jeffreys prior is proportional to the joint density function of $\boldsymbol{\mu}$ and $\boldsymbol{\Psi}$ with $\boldsymbol{\Psi}|\boldsymbol{\mu},\mathbf{X}\sim GIW_p(n+p+2,\sum_{i=1}^n(\mathbf{x}_i-\boldsymbol{\mu})(\mathbf{x}_i-\boldsymbol{\mu})^\top,f)$ and $\boldsymbol{\mu}|\mathbf{X}\sim t_p\left(n-p+1,\bar{\mathbf{x}},\dfrac{(n-1)\mathbf{S}}{n(n-p+1)}\right)$.

We finally note that both proposals (29) and (30) are proper under the conditions $n\geq p+1$ and $n\geq p$, respectively, which coincides with the conditions needed for the propriety of the posteriors derived under the Berger and Bernardo reference prior and the Jeffreys prior in Theorem 4. As a result, the suggested proposals possess the similar tail behaviour as the corresponding posteriors and, thus, they are good candidates for the construction of the Markov chains.

The Metropolis-Hastings algorithm for generating a draw from $\pi(\boldsymbol{\mu},\boldsymbol{\Psi}|\mathbf{X})$ derived under the Berger and Bernardo reference prior is given in Algorithm 1. A similar algorithm with minor changes is constructed to draw a sample from the posterior $\pi(\boldsymbol{\mu},\boldsymbol{\Psi}|\mathbf{X})$ derived under the Jeffreys prior. It is summarized in Algorithm 2.

5 Two families of elliptical distributions

In this section we apply the obtained theoretical results in case of two special families of elliptically contoured distribution: normal distribution and t-distribution.

Algorithm 1 Metropolis-Hastings algorithm for drawing realizations from $\pi(\boldsymbol{\mu}, \boldsymbol{\Psi}|\mathbf{X})$ as in (19) under the Berger and Bernardo reference prior (8).

(1) **Initialization:** Choose the initial values $\boldsymbol{\mu}^{(0)}$ and $\boldsymbol{\Psi}^{(0)}$ for $\boldsymbol{\mu}$ and $\boldsymbol{\Psi}$ and set $b = 0$.

(2) **Generating new values of $\boldsymbol{\mu}^{(w)}$ and $\boldsymbol{\Psi}^{(w)}$ from the proposal:**

   (i) For given data $\mathbf{X} = (\mathbf{x}_1, \dots, \mathbf{x}_n)$, generate $\boldsymbol{\mu}^{(w)}$ from $t_p\left(n-p, \bar{\mathbf{x}}, \dfrac{(n-1)\mathbf{S}}{n(n-p)}\right)$ with $\bar{\mathbf{x}}$ and $\mathbf{S}$ as in (27);

   (ii) Using data $\mathbf{X}$ and the drawn in step (i) $\boldsymbol{\mu}^{(w)}$, generate $\boldsymbol{\Psi}^{(w)}$ from $\boldsymbol{\Psi}|\boldsymbol{\mu} = \boldsymbol{\mu}^{(w)}, \mathbf{X} \sim GIW_p(n+p+1, \sum_{i=1}^n (\mathbf{x}_i - \boldsymbol{\mu}^{(w)})(\mathbf{x}_i - \boldsymbol{\mu}^{(w)})^\top, f)$.

(3) **Computation of the Metropolis-Hastings ratio:**

$$MH^{(b)} = \frac{\pi(\boldsymbol{\mu}^{(w)}, \boldsymbol{\Psi}^{(w)}|\mathbf{X}) q_R(\boldsymbol{\mu}^{(b-1)}, \boldsymbol{\Psi}^{(b-1)}|\mathbf{X})}{\pi(\boldsymbol{\mu}^{(b-1)}, \boldsymbol{\Psi}^{(b-1)}|\mathbf{X}) q_R(\boldsymbol{\mu}^{(w)}, \boldsymbol{\Psi}^{(w)}|\mathbf{X})}.$$

(4) **Moving to the next state of the Markov chain:**

   (i) Generate $U^{(b)}$ from the uniform distribution on $[0, 1]$;

   (ii) If $U^b < \min\left\{1, MH^{(b)}\right\}$, then set $\boldsymbol{\mu}^{(b)} = \boldsymbol{\mu}^{(w)}$ and $\boldsymbol{\Psi}^{(b)} = \boldsymbol{\Psi}^{(w)}$ (Markov chain moves to the new state). Otherwise, set $\boldsymbol{\mu}^{(b)} = \boldsymbol{\mu}^{(b-1)}$ and $\boldsymbol{\Psi}^{(b)} = \boldsymbol{\Psi}^{(b-1)}$ (Markov chain stays in the previous state).

(5) Return to step (2), increase b by 1, and repeat until the sample of size B is accumulated.

5.1 Normal multivariate random effects model

In the case of the normal multivariate random effects model (2), we have

$$f(u) = K_{p,n} \exp(-u/2) \quad \text{with} \quad K_{p,n} = (2\pi)^{-pn/2}, \tag{31}$$

which directly yields

$$f_{\boldsymbol{\Psi},\mathbf{X}}(u) = \frac{1}{(2\pi)^{pn/2}} \exp\left(-\frac{u}{2}\right) \exp\left(-\frac{1}{2}\sum_{i=1}^n (\mathbf{x}_i - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))^\top (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1} (\mathbf{x}_i - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))\right).$$

The last equality leads to the conclusion that the conditional posterior for $\boldsymbol{\mu}$ given $\boldsymbol{\Psi}$ is a multivariate normal distribution expressed as

$$\boldsymbol{\mu}|\boldsymbol{\Psi}, \mathbf{X} \sim \mathcal{N}\left(\left(\sum_{i=1}^n (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1}\right)^{-1} \sum_{i=1}^n (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1} \mathbf{x}_i, \left(\sum_{i=1}^n (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1}\right)^{-1}\right), \tag{32}$$

while the marginal posterior for $\boldsymbol{\Psi}$ is given by

$$\pi(\boldsymbol{\Psi}|\mathbf{X}) \quad \propto \quad \frac{\pi(\boldsymbol{\Psi})}{\sqrt{\det(\sum_{i=1}^n (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1})} \prod_{i=1}^n \sqrt{\det(\boldsymbol{\Psi} + \mathbf{U}_i)}}$$

Algorithm 2 Metropolis-Hastings algorithm for drawing realizations from $\pi(\boldsymbol{\mu}, \boldsymbol{\Psi}|\mathbf{X})$ as in (19) under the Jeffreys prior (7).

(1) **Initialization:** Choose the initial values $\boldsymbol{\mu}^{(0)}$ and $\boldsymbol{\Psi}^{(0)}$ for $\boldsymbol{\mu}$ and $\boldsymbol{\Psi}$ and set $b = 0$.

(2) **Generating new values of $\boldsymbol{\mu}^{(w)}$ and $\boldsymbol{\Psi}^{(w)}$ from the proposal:**

  (i) For given data $\mathbf{X} = (\mathbf{x}_1, \dots, \mathbf{x}_n)$, generate $\boldsymbol{\mu}^{(w)}$ from $t_p\left(n-p+1, \bar{\mathbf{x}}, \dfrac{(n-1)\mathbf{S}}{n(n-p+1)}\right)$ with $\bar{\mathbf{x}}$ and $\mathbf{S}$ as in (27);

  (ii) Using data $\mathbf{X}$ and the drawn in step (i) $\boldsymbol{\mu}^{(w)}$, generate $\boldsymbol{\Psi}^{(w)}$ from $\boldsymbol{\Psi}|\boldsymbol{\mu} = \boldsymbol{\mu}^{(w)}, \mathbf{X} \sim GIW_p(n+p+2, \sum_{i=1}^n(\mathbf{x}_i - \boldsymbol{\mu}^{(w)})(\mathbf{x}_i - \boldsymbol{\mu}^{(w)})^\top, f)$.

(3) **Computation of the Metropolis-Hastings ratio:**

$$MH^{(b)} = \frac{\pi(\boldsymbol{\mu}^{(w)}, \boldsymbol{\Psi}^{(w)}|\mathbf{X}) q_J(\boldsymbol{\mu}^{(b-1)}, \boldsymbol{\Psi}^{(b-1)}|\mathbf{X})}{\pi(\boldsymbol{\mu}^{(b-1)}, \boldsymbol{\Psi}^{(b-1)}|\mathbf{X}) q_J(\boldsymbol{\mu}^{(w)}, \boldsymbol{\Psi}^{(w)}|\mathbf{X})}.$$

(4) **Moving to the next state of the Markov chain:**

  (i) Generate $U^{(b)}$ from the uniform distribution on $[0, 1]$;

  (ii) If $U^b < \min\left\{1, MH^{(b)}\right\}$, then set $\boldsymbol{\mu}^{(b)} = \boldsymbol{\mu}^{(w)}$ and $\boldsymbol{\Psi}^{(b)} = \boldsymbol{\Psi}^{(w)}$ (Markov chain moves to the new state). Otherwise, set $\boldsymbol{\mu}^{(b)} = \boldsymbol{\mu}^{(b-1)}$ and $\boldsymbol{\Psi}^{(b)} = \boldsymbol{\Psi}^{(b-1)}$ (Markov chain stays in the previous state).

(5) Return to step (2), increase b by 1, and repeat until the sample of size B is accumulated.

$$\times \quad \exp\left(-\frac{1}{2}\sum_{i=1}^n (\mathbf{x}_i - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))^\top (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1} (\mathbf{x}_i - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))\right). \tag{33}$$

The posterior mean vector and the posterior covariance matrix of $\boldsymbol{\mu}$ are obtained as in (25) and (26) with $C(\boldsymbol{\Psi}) = 1$. Finally, we note that the posterior $\pi(\boldsymbol{\mu}, \boldsymbol{\Psi}|\mathbf{X})$ is proper for $n \geq p+1$ for the Berger and Bernardo reference prior and for $n \geq p$ for the Jeffreys prior following Theorem 4, since $\exp(-u/2)$ is a decreasing function in u and $\frac{J_2}{2pn+p^2n^2} - \frac{1}{4} = 0$.

All the derived expressions for the normal multivariate random effects model, like conditional posterior for $\boldsymbol{\mu}$, posterior mean vector, etc., depend on the marginal posterior for $\boldsymbol{\Psi}$ and thus cannot be computed analytically. In the univariate case, Bodnar et al. (2016) suggested a numerical procedure for the computation of such quantities based on the evaluation of one-dimensional integral. In the multivariate case $\boldsymbol{\Psi}$ is a matrix and since it should be positive semidefinite it imposes further complications on the numerical integration. For that reason we opt for the simulation-based approach as described in Section 4.

For generating samples from the posterior $\pi(\boldsymbol{\mu}, \boldsymbol{\Psi}|\mathbf{X})$ we apply Algorithm 1 under the Berger and Bernardo reference prior and Algorithm 2 under the Jeffreys prior where the inverse generalized Wishart distribution becomes the inverse Wishart distribution with $n+p+1$ and $n+p+2$ degrees of freedom, respectively. Other parts of the algorithms remain the same without changes.

To draw sample from the joint posterior distribution of $\boldsymbol{\mu}$ and $\boldsymbol{\Psi}$ following Algorithms 1 and 2, first the realization of $\boldsymbol{\mu}$ is draw from the marginal posterior of $\boldsymbol{\mu}$ following the draw of $\boldsymbol{\Psi}$ from the conditional posterior of $\boldsymbol{\Psi}$ given $\boldsymbol{\mu}$. Alternatively, one can modify these two algorithms using the properties of the normal distribution, which allow to obtain the scheme where $\boldsymbol{\Psi}$ is generated from the marginal posterior and $\boldsymbol{\mu}$ from the corresponding conditional posterior. Under the Berger and Bernardo reference prior, another proposal distribution can be constructed by using (29) with (31). Namely, from (27) and (28) we get

$$\begin{aligned} & \exp\left(-\frac{1}{2}\mathrm{tr}\left(\boldsymbol{\Psi}^{-1}\sum_{i=1}^{n}(\mathbf{x}_i-\boldsymbol{\mu})(\mathbf{x}_i-\boldsymbol{\mu})^\top\right)\right) \\ = \quad & \exp\left(-\frac{n-1}{2}\mathrm{tr}\left(\boldsymbol{\Psi}^{-1}\mathbf{S}\right)\right)\exp\left(-\frac{n}{2}(\boldsymbol{\mu}-\bar{\mathbf{x}})^\top\boldsymbol{\Psi}^{-1}(\boldsymbol{\mu}-\bar{\mathbf{x}})\right). \end{aligned}$$

This leads to the algorithm derived under the Berger and Bernardo reference prior, which is summarized in Algorithm S.1 in the supplement material (see, Bodnar and Bodnar (2023)). A similar approach can also be used when the Jeffreys prior is employed with the only change in step (2) of Algorithm S.1, where $\boldsymbol{\Psi}^{(w)}|\mathbf{X} \sim IW_p(n+p,(n-1)\mathbf{S})$ should be replaced by $\boldsymbol{\Psi}^{(w)}|\mathbf{X} \sim IW_p(n+p+1,(n-1)\mathbf{S})$.

The performance of two algorithms for drawing samples from the posterior distribution is studied in Figure 1 for the normal multivariate random effects model when the Berger and Bernardo reference prior and the Jeffreys prior are employed. The notation 'Algorithm A' corresponds to the case where $\boldsymbol{\mu}$ is drawn from the marginal distribution and $\boldsymbol{\Psi}$ is generated from the conditional distribution as in Algorithms 1 and 2 with density generator $f(.)$ as in (31), while the notation 'Algorithm B' corresponds to the case when $\boldsymbol{\Psi}$ is generated from the marginal distribution and $\boldsymbol{\mu}$ is obtained from the conditional distribution as in Algorithm S.1 in the supplement material (see, Bodnar and Bodnar (2023)).

As a performance measure, we use the empirical coverage probability of the credible interval constructed for μ_1, which is computed based on 5000 independent repetitions. In each simulation run, the data matrix $\mathbf{X}$ is drawn from the normal multivariate random effects model (2) with the same $\boldsymbol{\mu}$, $\boldsymbol{\Psi} = \tau^2\boldsymbol{\Xi}$, and $\mathbf{U} = diag(\mathbf{U}_1, \dots, \mathbf{U}_p)$. The elements of $\boldsymbol{\mu}$ are generated from the uniform distribution on $[1,5]$. The eigenvalues of $\boldsymbol{\Xi}$, $\mathbf{U}_1$, …, $\mathbf{U}_{p-1}$, and $\mathbf{U}_p$ are generated from the uniform distribution on $[1,4]$, while the eigenvectors are simulated from the Haar distribution. The results in Figure 1 are obtained for $p \in \{2,5\}$, $n \in \{10,20\}$, and $\tau^2 \in \{0.25, 0.5, 0.75, 1, 2\}$.

Figure 1 depicts the coverage probabilities of the constructed credible intervals at 95% significance level. For comparison purposes, the coverage probabilities of the 95% confidence intervals obtained by the three approaches of conventional statistics, namely, the maximum likelihood (ML) of Gasparrini et al. (2012), the restrictive maximum likelihood (REML) of Gasparrini et al. (2012), and the methods of moments (MM) of Jackson et al. (2013) are presented in Figure 1 as well. The computation is performed

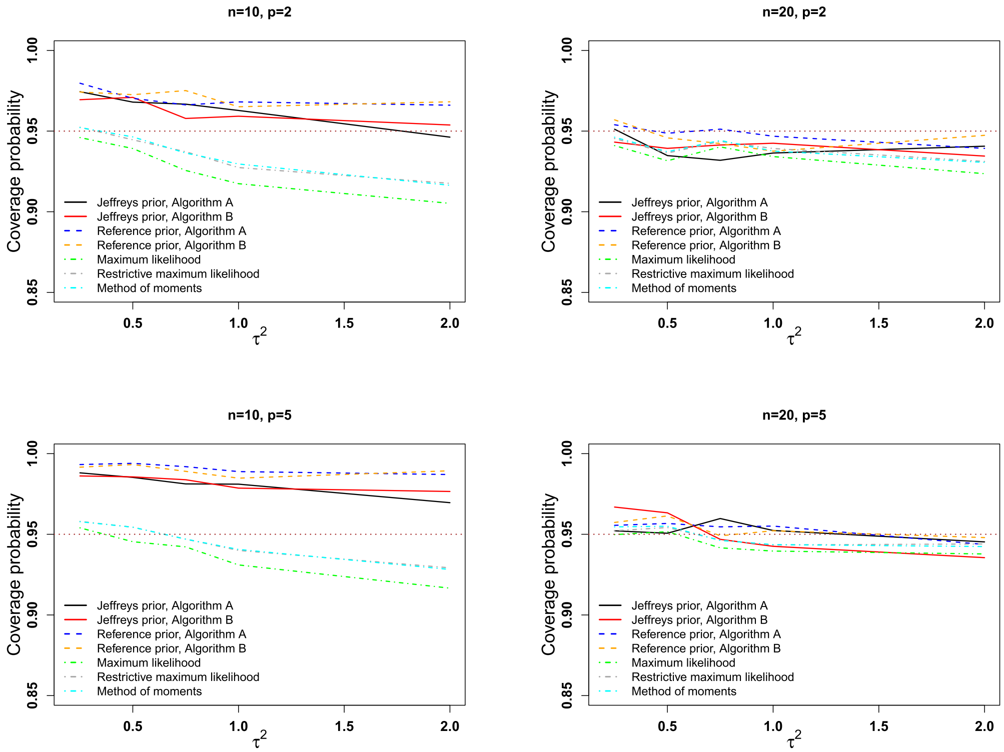

Figure 1: Coverage probabilities of the 95% credible intervals for the first component of $\boldsymbol{\mu}$ as a function of τ^2 under the assumption of the normal multivariate random effects model when the Berger and Bernardo reference prior and the Jeffreys prior are employed and when three methods of conventional statistics, namely, the maximum likelihood, the restrictive maximum likelihood, and the method of moment, are used. We set $p \in \{2, 5\}$ and $n \in \{10, 20\}$.

by using the R-package *mvmeta* (Multivariate and Univariate Meta-Analysis and Meta-Regression, Gasparrini (2019)) for the frequentist methods and the R-package *BayesMultMeta* (Bayesian Multivariate Meta-Analysis, Bodnar et al. (2022)) for the Bayesian approaches.

The computation of the empirical coverage probability is based on the sequence of 5000 independent Bernoulli random variable. As such, the upper bound of the Monte Carlo standard error can be assessed by

$$\frac{1}{\sqrt{5000}} \max_{\pi \in [0,1]} \sqrt{\pi(1-\pi)} = \frac{1}{2\sqrt{5000}} \approx 0.007.$$

and in the case of the pairwise comparison, we get the upper bound of 0.01. As such, the values of the empirical coverage probability which lie outside the interval $[0.9384, 0.9616]$

are deemed to be statistically significant at 5% level, while for the pairwise comparison one gets that the differences in the absolute values larger than 0.02 can be considered to be statistically significant at 5% level.

In Figure 1 we observe that the credible intervals obtained by employing the Berger and Bernardo reference prior possess larger coverage probabilities than those obtained by using the Jeffreys prior in most of the considered cases when $n = 10$, although the differences between the two non-informative priors are not large when $n = 20$. The empirical coverage probabilities computed by using the two numerical procedures of drawing samples from the posterior distribution are above the chosen significance level of 95% in almost all of the considered cases when $n = 10$, while they are slowly below the target value of 95% when $n = 20$. Moreover, only for $n = 10$, $p = 5$, and large values of τ^2 the empirical coverage probabilities obtained under the Berger and Bernardo reference prior and under the Jeffreys prior can be deemed to deviate significantly from the target value of 95% at 5% level. The resulting empirical coverage probabilities obtained by the three frequentist approach are below 95% almost in all cases. Moreover, they are significantly smaller than 95% at significance level of 5% for $\tau^2 \geq 1$ when $n = 10$ and $p = 2$ and for $\tau^2 \geq 1.5$ when $n = 10$ and $p = 5$. When $n = 20$ and $p = 5$ all considered approaches perform similarly and no significant deviation from the target value of 95% is observed in this case.

5.2 t multivariate random effects model

In the case of the t multivariate random effects model, it holds that

$$f(u) = K_{p,n,d}(1 + u/d)^{-(pn+d)/2} \quad \text{with} \quad K_{p,n,d} = (\pi d)^{-pn/2} \frac{\Gamma\left((d + pn)/2\right)}{\Gamma\left(d/2\right)}. \tag{34}$$

Hence,

$$\begin{aligned}
&\pi(\boldsymbol{\mu}, \boldsymbol{\Psi}|\mathbf{X}) \\
&\quad\propto \frac{\pi(\boldsymbol{\Psi})}{\sqrt{\prod_{i=1}^n \det(\boldsymbol{\Psi} + \mathbf{U}_i)}} \Bigg(1 + \frac{1}{d}(\boldsymbol{\mu} - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))^\top \left(\sum_{i=1}^n (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1}\right)(\boldsymbol{\mu} - \tilde{\mathbf{x}}(\boldsymbol{\Psi})) \\
&\qquad + \frac{1}{d}\sum_{i=1}^n (\mathbf{x}_i - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))^\top (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1} (\mathbf{x}_i - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))\Bigg)^{-(pn+d)/2} \\
&\quad= \frac{\pi(\boldsymbol{\Psi})}{\sqrt{\prod_{i=1}^n \det(\boldsymbol{\Psi} + \mathbf{U}_i)}} \left(1 + \frac{1}{d}\sum_{i=1}^n (\mathbf{x}_i - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))^\top (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1} (\mathbf{x}_i - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))\right)^{-(pn+d)/2} \\
&\qquad \times \Bigg(1 + \frac{1}{pn + d - p} \frac{pn + d - p}{d + \sum_{i=1}^n (\mathbf{x}_i - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))^\top (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1} (\mathbf{x}_i - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))} \\
&\qquad \times (\boldsymbol{\mu} - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))^\top \left(\sum_{i=1}^n (\boldsymbol{\Psi} + \mathbf{U}_i)^{-1}\right)(\boldsymbol{\mu} - \tilde{\mathbf{x}}(\boldsymbol{\Psi}))\Bigg)^{-(pn+d)/2},
\end{aligned}$$

which shows that the conditional posterior of $\boldsymbol{\mu}$ given $\boldsymbol{\Psi}$ is

$$\pi(\boldsymbol{\mu}|\boldsymbol{\Psi},\mathbf{X}) \propto \left(1+\frac{1}{pn+d-p}\frac{pn+d-p}{d+\sum_{i=1}^n(\mathbf{x}_i-\tilde{\mathbf{x}}(\boldsymbol{\Psi}))^\top(\boldsymbol{\Psi}+\mathbf{U}_i)^{-1}(\mathbf{x}_i-\tilde{\mathbf{x}}(\boldsymbol{\Psi}))}\right.$$
$$\times \left.(\boldsymbol{\mu}-\tilde{\mathbf{x}}(\boldsymbol{\Psi}))^\top\left(\sum_{i=1}^n(\boldsymbol{\Psi}+\mathbf{U}_i)^{-1}\right)(\boldsymbol{\mu}-\tilde{\mathbf{x}}(\boldsymbol{\Psi}))\right)^{-(pn+d)/2}, \tag{35}$$

i.e., $\boldsymbol{\mu}$ conditionally on $\boldsymbol{\Psi}$ and $\mathbf{X}$ has a p-dimensional t-distribution with $pn+d-p$ degrees of freedom, location parameter $\tilde{\mathbf{x}}(\boldsymbol{\Psi})$ and dispersion matrix

$$\frac{d+\sum_{i=1}^n(\mathbf{x}_i-\tilde{\mathbf{x}}(\boldsymbol{\Psi}))^\top(\boldsymbol{\Psi}+\mathbf{U}_i)^{-1}(\mathbf{x}_i-\tilde{\mathbf{x}}(\boldsymbol{\Psi}))}{pn+d-p}\left(\sum_{i=1}^n(\boldsymbol{\Psi}+\mathbf{U}_i)^{-1}\right)^{-1}.$$

Moreover, the marginal posterior for $\boldsymbol{\Psi}$ can also be deduced and it is expressed as

$$\pi(\boldsymbol{\Psi}|\mathbf{X}) \propto \frac{\pi(\boldsymbol{\Psi})}{\sqrt{\det(\sum_{i=1}^n(\boldsymbol{\Psi}+\mathbf{U}_i)^{-1})}\prod_{i=1}^n\sqrt{\det(\boldsymbol{\Psi}+\mathbf{U}_i)}}$$
$$\times \left(1+\frac{1}{d}\sum_{i=1}^n(\mathbf{x}_i-\tilde{\mathbf{x}}(\boldsymbol{\Psi}))^\top(\boldsymbol{\Psi}+\mathbf{U}_i)^{-1}(\mathbf{x}_i-\tilde{\mathbf{x}}(\boldsymbol{\Psi}))\right)^{-(pn+d)/2}. \tag{36}$$

To this end, the posterior mean vector and the covariance matrix of $\boldsymbol{\mu}$ are obtained as in (25) and (26) with

$$C(\boldsymbol{\Psi})=\frac{d+\sum_{i=1}^n(\mathbf{x}_i-\tilde{\mathbf{x}}(\boldsymbol{\Psi}))^\top(\boldsymbol{\Psi}+\mathbf{U}_i)^{-1}(\mathbf{x}_i-\tilde{\mathbf{x}}(\boldsymbol{\Psi}))}{pn+d-p-2}.$$

Finally, we note that the constant J_2 can analytically be computed in the case of the t multivariate random effects model and it is expressed as (see, Bodnar (2019, Section 3.2))

$$J_2=\frac{pn(pn+2)(pn+d)}{4(pn+2+d)}$$

The application of the last expression leads to the following formulas of the Berger and Bernardo reference prior

$$\pi_R(\boldsymbol{\Psi}) \propto \left(\det\left\{\mathbf{G}_p^\top\left[\frac{pn+d}{2(pn+2+d)}\sum_{i=1}^n\left((\boldsymbol{\Psi}+\mathbf{U}_i)^{-1}\otimes(\boldsymbol{\Psi}+\mathbf{U}_i)^{-1}\right)\right.\right.\right. \tag{37}$$
$$\left.\left.\left.-\frac{1}{2(pn+2+d)}\text{vec}\left(\sum_{i=1}^n(\boldsymbol{\Psi}+\mathbf{U}_i)^{-1}\right)\text{vec}\left(\sum_{j=1}^n(\boldsymbol{\Psi}+\mathbf{U}_j)^{-1}\right)^\top\right]\mathbf{G}_p\right\}\right)^{1/2},$$

while the Jeffreys prior is given by (7) with $\pi_R(\boldsymbol{\Psi})$ as in (37). Furthermore, since $(1+u/d)^{-(pn+d)/2}$ is a decreasing function in u and

$$\frac{J_2}{2pn+p^2n^2}-\frac{1}{4}=\frac{1}{4}\left(\frac{pn+d}{pn+d+2}-1\right)<0,$$

the posterior $\pi(\boldsymbol{\mu}, \boldsymbol{\Psi}|\mathbf{X})$ is proper for $n \geq p+1$ for the Berger and Bernardo reference prior and for $n \geq p$ for the Jeffreys prior due to Theorem 4.

Algorithms 1 and 2 are used to draw samples from the posterior $\pi(\boldsymbol{\mu}, \boldsymbol{\Psi}|\mathbf{X})$ derived by employing the Berger and Bernardo reference prior and the Jeffreys prior, respectively. Under the special case of the t multivariate random effects model, step (ii) of both algorithms is performed by computing $\boldsymbol{\Psi}^{(b)} = \frac{\xi^{(b)}}{d}\boldsymbol{\Omega}^{(b)}$ where $\xi^{(b)}$ and $\boldsymbol{\Omega}^{(b)}$ are simulated independently from χ^2_d-distribution and the inverse Wishart distribution with parameter matrix $(n-1)\sum_{i=1}^n(\mathbf{x}_i - \boldsymbol{\mu}^{(b)})(\mathbf{x}_i - \boldsymbol{\mu}^{(b)})^\top$ and degrees of freedom equal to $n+p+1$ under the Berger and Bernardo reference prior and $n+p+2$ under the Jeffreys prior.

The modification of Algorithms 1 and 2 similar to the one derived for the normal multivariate random effects model can also be obtained under the assumption of the t-distribution. The application of the equality

$$\left(1 + \frac{1}{d}\mathrm{tr}\left(\boldsymbol{\Psi}^{-1}\sum_{i=1}^n(\mathbf{x}_i - \boldsymbol{\mu})(\mathbf{x}_i - \boldsymbol{\mu})^\top\right)\right)^{-(pn+d)/2} = \left(1 + \frac{n-1}{d}\mathrm{tr}\left(\boldsymbol{\Psi}^{-1}\mathbf{S}\right)\right)^{-(pn+d)/2}$$
$$\times\left(1 + \frac{1}{np+d-p}\frac{n(np+d-p)}{d+(n-1)\mathrm{tr}\left(\boldsymbol{\Psi}^{-1}\mathbf{S}\right)}(\boldsymbol{\mu} - \bar{\mathbf{x}})^\top\boldsymbol{\Psi}^{-1}(\boldsymbol{\mu} - \bar{\mathbf{x}})\right)^{-(pn+d)/2}$$

leads to another numerical procedure described in Algorithm S.2 in the supplement material (see, Bodnar and Bodnar (2023)) when the posterior $\pi(\boldsymbol{\mu}, \boldsymbol{\Psi}|\mathbf{X})$ is derived by applying the Berger and Bernardo reference prior. Under the Jeffreys prior the step (2) of Algorithm S.2 should be modified by generating $\boldsymbol{\Omega}^{(w)}$ from $IW_p(n+p+1, (n-1)\mathbf{S})$.

To investigate the properties of the two proposed algorithms, we conduct a simulation study for the t multivariate random effects model designed similarly to the one presented in Section 5.1 for the normal multivariate random effect models. Also, we use the same notations 'Algorithm A' and 'Algorithm B' to distinguish between the two procedures to draw samples from the posterior distributions derived by employing the Berger and Bernardo reference prior and the Jeffreys prior.

We use the empirical coverage probability of the credible interval constructed for μ_1 as a performance measure and compute it based on 5000 independent repetitions. In each simulation run, the data matrix $\mathbf{X}$ is simulated from the t multivariate random effects model, i.e., from the model (1) with $f(.)$ as in (34). The model parameters $\boldsymbol{\mu}$, $\boldsymbol{\Psi} = \tau^2\boldsymbol{\Xi}$, and $\mathbf{U} = diag(\mathbf{U}_1, \ldots, \mathbf{U}_p)$ are chosen in the same way as the corresponding parameters of the normal multivariate random effects model in Section 5.1. Finally, we set $p \in \{2, 5\}$, $n \in \{10, 20\}$, and $\tau^2 \in \{0.25, 0.5, 0.75, 1, 2\}$.

The results of the simulation study are depicted in Figure 2 where the empirical coverage probabilities of the constructed 95% credible intervals are presented. The empirical coverage probabilities are larger than the chosen significance level of 95% in almost all of the considered cases, independently of whether the Markov chains are constructed following Algorithm A or Algorithm B. The application of the Berger and Bernardo reference prior leads to slightly larger values of the empirical coverage probabilities in most of the cases, although the differences are not statistically significant

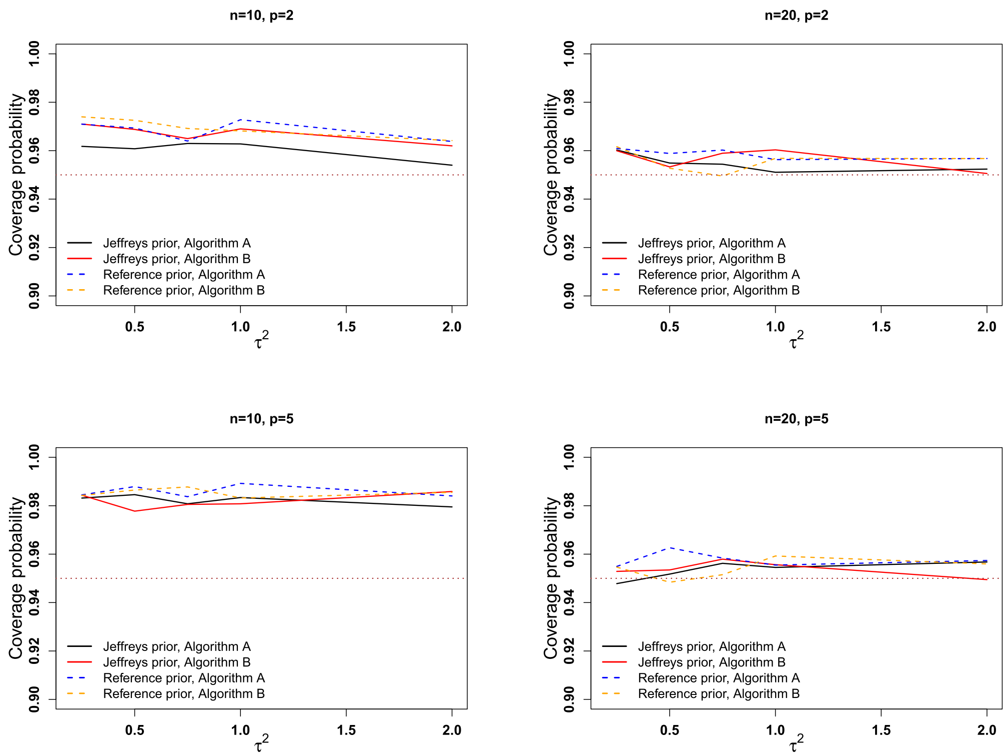

Figure 2: Coverage probabilities of the 95% credible intervals for the first element of $\boldsymbol{\mu}$ as a function of τ^2 under the assumption of the t multivariate random effects model when the Berger and Bernardo reference prior and the Jeffreys prior are employed. We set $p \in \{2, 5\}$ and $n \in \{10, 20\}$.

at 5% level. If $n = 10$, then the empirical coverage probabilities are larger than 95% with the largest values obtained for $p = 5$, similar to the results obtained in the case of the normal multivariate random effects model. Moreover, the deviations of the coverage probabilities from the target value of 95% are statistically significant at 5% in almost all of the considered cases. Finally, the coverage probabilities are close to 95% when the sample size is $n = 20$ independently of the chosen values of $p \in \{2, 5\}$.

6 Empirical illustration

In this section we illustrate the derived theoretical findings on real data consisting of results obtained in ten studies that assess the effectiveness of hypertension treatment for reducing blood pressure. The treatment effects on the systolic blood pressure and diastolic blood pressure are investigated in the studies where the negative values document beneficial effect of the treatment. The data are provided in Table 1 and are taken

Study	$X_{i;1}$ (SBP)	$X_{i;2}$ (DBP)	$\sqrt{U_{i;11}}$ (SBP)	$\rho_{i;12} = \dfrac{U_{i;12}}{\sqrt{U_{i;11}U_{i;22}}}$	$\sqrt{U_{i;22}}$ (DBP)
1	−6.66	−2.99	0.72	0.78	0.27
2	−14.17	−7.87	4.73	0.45	1.44
3	−12.88	−6.01	10.31	0.59	1.77
4	−8.71	−5.11	0.30	0.77	0.10
5	−8.70	−4.64	0.14	0.66	0.05
6	−10.60	−5.56	0.58	0.49	0.18
7	−11.36	−3.98	0.30	0.50	0.27
8	−17.93	−6.54	5.82	0.61	1.31
9	−6.55	−2.08	0.41	0.45	0.11
10	−10.26	−3.49	0.20	0.51	0.04

Table 1: Data collected in 10 studies about the effectiveness of hypertension treatment with the aim to reduce blood pressure. The variables $X_{i;1}$ and $X_{i;2}$ denote the treatment effects on the systolic blood pressure (SBP) and the diastolic blood pressures (DBP) from the ith study, while $\mathbf{U}_i = (U_{i;lj})_{lj=1,2}$ is the corresponding covariance matrix.

from Jackson et al. (2013) where the treatment effects in each study are provided together with the covariance matrices $\mathbf{U}_i$ which are assumed to be known throughout this section.

Multivariate meta-analysis is performed by using data from Table 1 under the assumption of the normal multivariate random effects model (Section 5.1) and the t multivariate random effects model (Section 5.2) when the Berger and Bernardo reference prior and the Jeffreys prior are employed. The samples from the joint posterior distribution $\pi(\boldsymbol{\mu}, \boldsymbol{\Psi}|\mathbf{X})$ are drawn by applying two versions of the Metropolis-Hastings algorithm which are described in Section 5.1 for the normal multivariate random effects model and denoted by Algorithm A and Algorithm B, respectively. For each type of the Metropolis-Hastings algorithm, the distributional class of the multivariate random effects model, and the chosen prior, 10^5 realizations from the posterior distribution $\pi(\boldsymbol{\mu}, \boldsymbol{\Psi}|\mathbf{X})$ are drawn with 10% used as burn-in sample.

The first two columns of Table 2 present the results for the normal multivariate random effects model, while the results for the t multivariate random effects model with $d = 3$ degrees of freedom are shown in the third and the fourth columns of the table. For each chosen prior, random effects model, and numerical algorithm to draw a sample from the posterior distribution, we compute the posterior mean and posterior median as two Bayesian point estimators for the overall mean vector together with the posterior standard deviation and 95% probability symmetric credible interval. In the case of the t multivariate random effects model, we multiply $\mathbf{U}_i$ by $\frac{d-2}{d}$ to ensure that the within-study covariance matrix calculated under the assumption of the t multivariate random effects model coincides with the one given in Table 1. Finally, for comparison purposes, we also include the results obtained by three approaches of the frequentist statistics, namely the maximum likelihood estimator and the restrictive maximum likelihood estimator provided in Gasparrini et al. (2012), and the method of moment estimators from Jackson et al. (2013). The three frequentist procedures are available in the R-package

	Normal random effects model		t random effects model	
	μ_1 (SBP)	μ_2 (DBP)	μ_1 (SBP)	μ_2 (DBP)
Jeffreys prior, Algorithm A				
post. mean	−9.79	−4.05	−10.15	−4.67
post. median	−9.60	−4.27	−10.10	−4.66
post. sd.	0.88	0.93	1.08	0.60
cred. inter.	[−11.73, −8.00]	[−5.61, −2.66]	[−12.44,-8.11]	[−5.87,−3.51]
Jeffreys prior, Algorithm B				
post. mean	−9.78	−4.37	−10.03	−4.66
post. median	−9.84	−4.37	−9.97	−4.65
post. sd.	0.74	0.50	1.13	0.61
cred. inter.	[−11.46, −8.39]	[−5.38, −3.38]	[−12.46, −7.99]	[−5.90, −3.51]
Berger and Bernardo reference prior, Algorithm A				
post. mean	−9.81	−4.49	−10.11	−4.67
post. median	−9.87	−4.44	−10.06	−4.66
post. sd.	1.04	0.59	1.16	0.64
cred. inter.	[−12.06, −8.00]	[−5.78, −3.42]	[−12.58, −7.97]	[−5.96, −3.43]
Berger and Bernardo reference prior, Algorithm B				
post. mean	−9.70	−4.51	−10.08	−4.68
post. median	−9.72	−4.53	−10.03	−4.65
post. sd.	1.01	0.58	1.13	0.64
cred. inter.	[−11.88, −8.06]	[−5.67, −3.49]	[−12.50, −7.97]	[−5.94, −3.42]
ML, Gasparrini et al. (2012)				
estimator	−9.47	−4.41	–	–
stand. error	0.68	0.44	–	–
cred. inter.	[−10.79, −8.14]	[−5.26, −3.55]	–	–
REML, Gasparrini et al. (2012)				
estimator	−9.51	−4.43	–	–
stand. error	0.73	0.47	–	–
cred. inter.	[−10.95, −8.07]	[−5.35, −3.51]	–	–
Method of moments, Jackson et al. (2013)				
estimator	−9.17	−4.31	–	–
stand. error	0.55	0.36	–	–
cred. inter.	[−10.26, −8.08]	[−5.02, −3.60]	–	–

Table 2: Results of Bayesian inference (posterior mean, posterior median, posterior standard deviation, 95% credible interval) for the parameter $\boldsymbol{\mu}$ of the multivariate random effects model obtained for the data from Table 1 by employing the Berger and Bernardo reference prior and the Jeffreys prior. The samples from the posterior distributions are drawn by Algorithm A and Algorithm B defined in Section 5.1. The last three panels of the table include the results of the maximum likelihood estimator and the restrictive maximum likelihood estimator described in Gasparrini et al. (2012), and the method of moment estimators from Jackson et al. (2013).

mvmeta (Gasparrini (2019)), while the Bayesian approaches are implemented in the R-package *BayesMultMeta* (Bodnar et al. (2022)).

All Bayesian point estimators derived under the assumption of the normal multivariate random effects model are very similar and they are almost always slightly smaller than those obtained by the frequentist approaches. In contrast, the computed Bayesian standard errors are larger than those computed by the frequentist approaches, especially when the method of moments is used in their computation. These results are in line with statistical theory and reflect the fact that the Bayesian methods in contrast to the frequentist approaches take automatically the uncertainty about the between-study covariance matrix $\mathbf{\Psi}$ into account, while the frequentist methods usually ignore that $\mathbf{\Psi}$ is an unknown nuisance parameter of the model which has to be estimated before the inferences for the overall mean vector are constructed. Finally, we have that the credible intervals obtained by employing the Berger and Bernardo reference prior are wider than those obtained by using the Jeffreys prior. Similar results are also obtained in the simulation study of Section 5.1 (see, Figure 1), where the larger values of the coverage probabilities are documented for the Berger and Bernardo reference prior. Such a result was also documented in the univariate case in Bodnar (2019). Finally, in the case of the t multivariate random effects model, the estimated elements of the overall mean vector $\boldsymbol{\mu}$ become even smaller than those observed under the of the normal multivariate random effects model, while the corresponding Bayesian standard deviations increase reflecting the impact of heavy tails of the t-distribution.

In Table 3 the Bayesian point estimators, posterior mean and posterior median, for parameter matrix $\mathbf{\Psi}$ are presented. In all of the reported cases, the posterior means are considerably larger than the posterior medians indicating that the marginal posterior distributions of the components of $\mathbf{\Psi}$ are skewed to the right. A similar property of the between-study variability is also observed in the univariate case (cf., Bodnar et al. (2020)). Furthermore, similarly to the univariate case, the Bayesian estimates of the between-study variability are larger than those obtained by the frequentist methods (see, e.g., Bodnar et al. (2017)).

The two-dimensional credible regions at significance levels 0.9 (dark blue), 0.95 (light blue), and 0.99 (green) for the elements of the mean vector $\boldsymbol{\mu}$ are depicted in Figure 3 for the normal multivariate random effects model and in Figure 4 for the t multivariate random effects model with $d = 3$ degrees of freedom. The credible regions obtained under the assumption of the t-distribution are very similar, independently of whether the Berger and Bernardo reference prior or the Jeffreys prior is employed, and the chosen algorithm to draw samples from the posterior distribution. That is not longer the case in Figure 3, where the credible regions computed for the normal multivariate random effects model with Jeffreys prior and using Algorithm B appear to be slightly narrower. Finally, the credible intervals obtained under the assumption of the t-distribution are always wider reflecting the influence of heavy tails.

Finally, we present convergence diagnostic for the constructed Markov chains following the recent approaches developed in Vehtari et al. (2021). Figures 5 and 6 depict the ranks plots and Table 4 shows the split-$\hat{\mathrm{R}}$ estimates based on the rank normalization. The computation is performed by generating four Markov chains of length 10000 with the burn-in period of 10000 for each algorithm constructed under the normal and t multivariate random effects models when the model parameters are endowed with the Berger and Bernardo reference prior and the Jeffreys prior. In the graphical presentations of Figures 5 and 6 we observe that the plots created under the assumption of the t multivariate random effects model are closer to the plots, which are expected when a sample from a uniform distribution is drawn. Moreover, a closer analysis of the plots reveals that the plots obtained for the t multivariate random effects model show the best performance in terms of the split-$\hat{\mathrm{R}}$ estimates based on rank normalization. All of the histograms in the first row of Figure 6 are closest to the histograms corresponding to the uniform distribution in comparison to the plots in other rows of Figures 5 and 6. As such, the rank plots suggest that the Markov chains constructed under the t multivariate random effects model possess better convergence properties with the best results achieved when the Jeffreys prior is used. These results are in line with the previous results depicted in Figures 3 and 4, where the credible sets constructed under the t multivariate random effects model show smoother patterns than the ones computed under the assumption of normality.

	Normal random effects model			t random effects model		
	ψ_{11} (SBP)	ψ_{21}	ψ_{22} (DBP)	ψ_{11} (SBP)	ψ_{21}	ψ_{22} (DBP)
Jeffreys prior, Algorithm A						
post. mean	7.45	2.71	3.68	11.56	5.26	3.90
post. median	5.62	2.25	2.95	8.69	3.88	3.01
Jeffreys prior, Algorithm B						
post. mean	6.62	2.82	2.71	10.81	4.92	3.75
post. median	4.29	2.14	2.16	7.99	3.64	2.98
Berger and Bernardo reference prior, Algorithm A						
post. mean	9.32	3.88	3.13	13.13	6.14	4.64
post. median	6.62	2.77	2.57	9.75	4.34	3.39
Berger and Bernardo reference prior, Algorithm B						
post. mean	8.79	3.71	3.12	12.24	5.71	4.39
post. median	7.56	2.97	2.65	8.84	4.12	3.34
ML, Gasparrini et al. (2012)						
estimator	3.29	1.51	1.57	–	–	–
REML, Gasparrini et al. (2012)						
estimator	3.92	1.81	1.83	–	–	–
Method of moments, Jackson et al. (2013)						
estimator	2.03	0.2	1.04	–	–	–

Table 3: Posterior mean and posterior median for the parameter $\mathbf{\Psi}$ of the multivariate random effects model obtained for the data from Table 1 by employing the Berger and Bernardo reference prior and the Jeffreys prior. The samples from the posterior distributions are drawn by Algorithm A and Algorithm B defined in Section 5.1. The last three panels of the table include the results of the maximum likelihood estimator and the restrictive maximum likelihood estimator described in Gasparrini et al. (2012), and the method of moment estimators from Jackson et al. (2013).

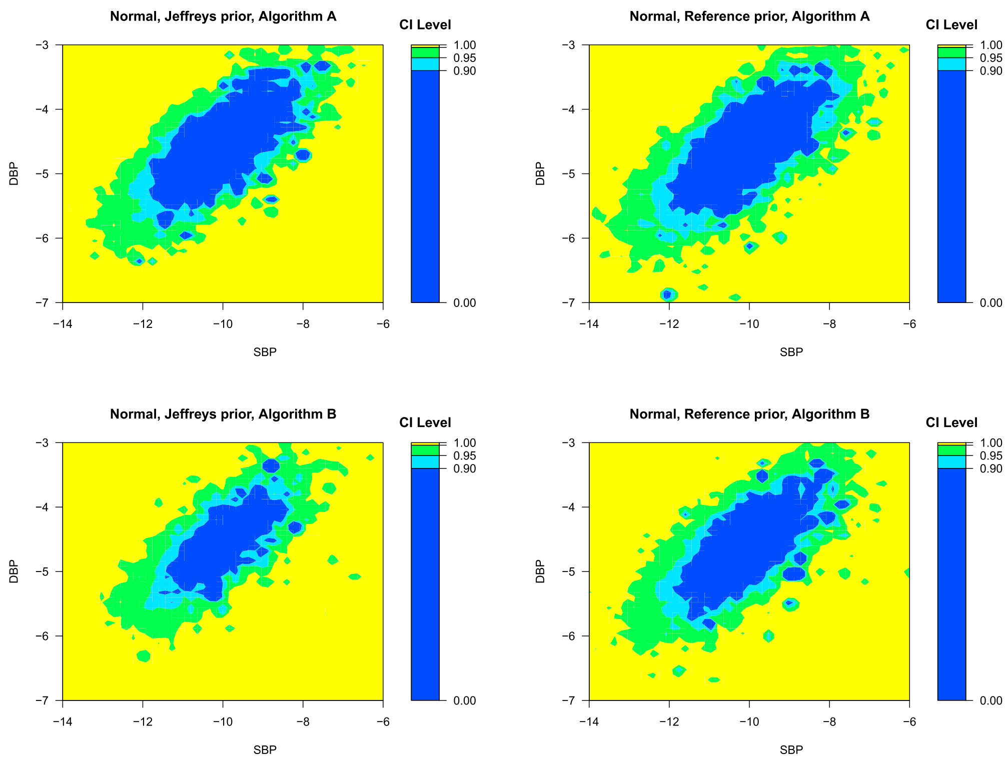

Figure 3: Credible sets for μ_1 (SBP) and μ_2 (DBP) obtained from the posterior distribution $\pi(\boldsymbol{\mu}|\mathbf{X})$ derived for the location parameters of the normal multivariate random effects model by employing the Berger and Bernardo reference prior and the Jeffreys prior and using data from Table 1. The samples from the posterior distributions are drawn by Algorithm A and Algorithm B defined in Section 5.1.

All values of the computed split-$\hat{\mathrm{R}}$ estimates based on the rank normalization are smaller than 1.1 (see, Table 4), the target value recommended in Gelman et al. (2013) for deciding whether the constructed Markov chains possess good mixing properties. Moreover, the values computed under the t multivariate random effects model with the parameters endowed by the Jeffreys prior are all not larger than 1.01, the target value recommended in Vehtari et al. (2021). This result confirms the previous conclusion based on the rank plots, where the Markov chains constructed for the t random effects model with the Jeffreys prior possess good mixing properties, independently of the algorithm used for generating samples from the posterior distribution. Finally, we note that the performance of the constructed Markov chains depends crucially on the way how the samples from the posterior distribution are drawn. In particular, the choice of the proposal distribution can be very important. In this paper, two possible choices of the proposal distribution are considered. Using them, good mixing properties of the constructed Markov chains are documented. However, other choices of the proposal distribution might lead to even better results.

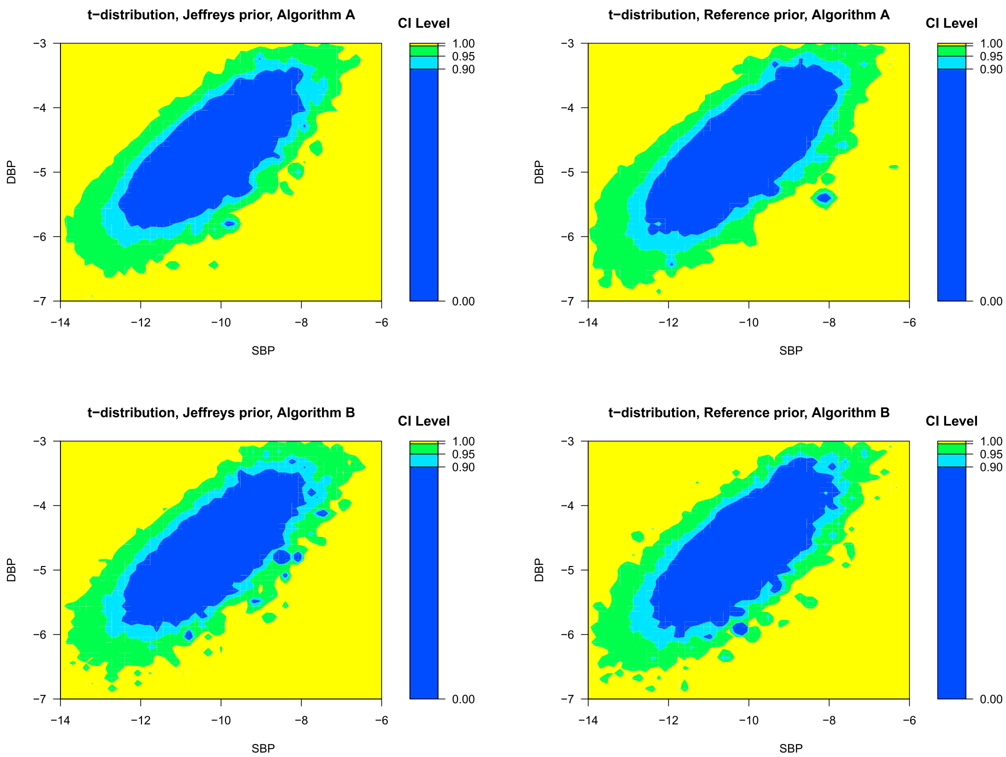

Figure 4: Credible sets for μ_1 (SBP) and μ_2 (DBP) obtained from the posterior distribution $\pi(\boldsymbol{\mu}|\mathbf{X})$ derived for the location parameters of the t multivariate random effects model by employing the Berger and Bernardo reference prior and the Jeffreys prior and using data from Table 1. The samples from the posterior distributions are drawn by Algorithm A and Algorithm B defined in Section 5.2.

7 Summary

Multivariate random effects model is one of the most used statistical tools in multivariate meta-analysis where the aim is to combine multiple values obtained in several studies into a single value. The parameters of the multivariate random effects model are usually estimated from the viewpoint of frequentist statistics, while several subjective Bayesian approaches based on the informative priors exist in the literature. Although both methods provide a good fit of the model to real data when the sample size is relatively large due to the asymptotic theorems in the frequentist statistics and the Bernstein-von-Mises theorem in Bayesian statistics, the results might be different when a sample of small size is present which is the case in the majority of meta-analyses. When the sample size is not large enough the asymptotic approximation might deviate considerably from the exact sample distribution of the estimated parameters or/and the influence of the chosen informative prior might have a significant impact on the

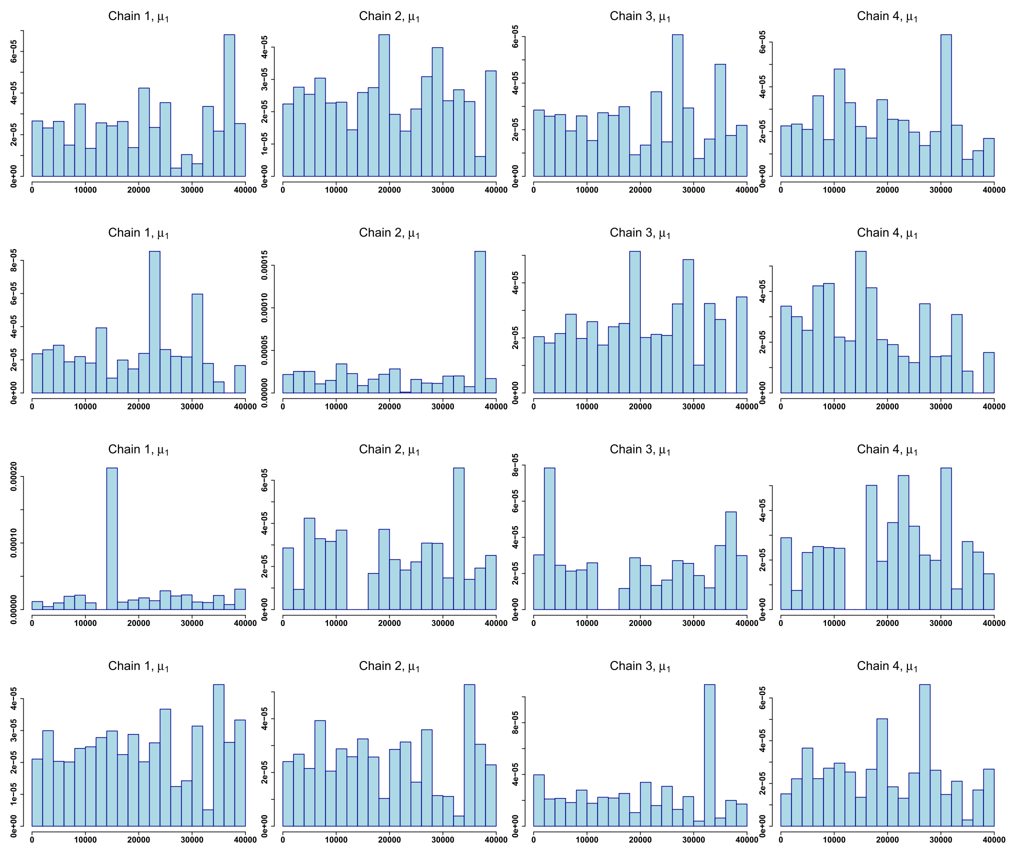

Figure 5: Rank plots of posterior draws from four chains in the case of the parameter μ_1 (SBP) of the normal multivariate random effects model by employing the Jeffreys prior (first and second rows) and the Berger and Bernardo reference prior (third and fourth rows), and by using data from Table 1. The samples from the posterior distributions are drawn by Algorithm A (first and third rows) and Algorithm B (second and fourth rows) defined in Section 5.1.

posterior. Methods of the objective Bayesian statistics propose a solution to the challenges related to the insufficient sample size by providing the model parameters with noninformative prior. In particular, the Berger and Bernardo reference prior is derived by maximizing the Shannon mutual information, i.e. by choosing the prior with the smallest impact on the posterior.

Flexible objective Bayesian procedures for the parameters of the multivariate random effects model are developed by employing two noninformative priors, the Berger and Bernardo reference prior and the Jeffreys prior. The analytical expressions of both the priors are obtained and the corresponding posteriors are derived. The results are established for a general class of multivariate random effects models which include the

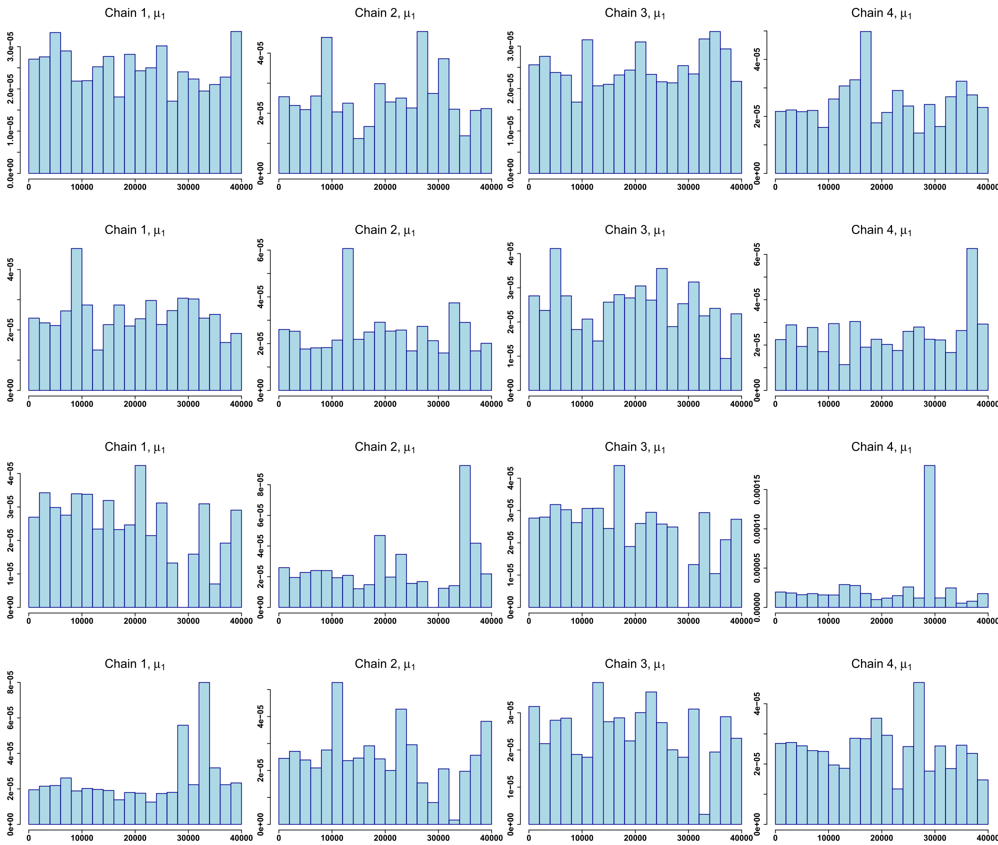

Figure 6: Rank plots of posterior draws from four chains in the case of the parameter μ_1 (SBP) of the t multivariate random effects model by employing the Jeffreys prior (first and second rows) and the Berger and Bernardo reference prior (third and fourth rows), and by using data from Table 1. The samples from the posterior distributions are drawn by Algorithm A (first and third rows) and Algorithm B (second and fourth rows) defined in Section 5.1.

normal multivariate random effects model as a special case. Moreover, the propriety of the posteriors is proved under a weak condition, which requires that the sample size is larger than the dimension of the data-generating model only, independently of the specific class of the multivariate random effects model. Finally, the Metropolis-Hastings algorithm has been developed in the paper to draw samples from the posterior derived for the parameters of the model. Via simulations, it is shown that the considered numerical procedures lead to similar results in the case of the normal multivariate random effects model and the t multivariate random effects model. In an empirical illustration based on data consisting of ten studies about the effectiveness of hypertension treatment for reducing blood pressure, a beneficial effect of the treatments on both systolic blood pressure and diastolic blood pressure is found.

	μ_1 (SBP)	μ_2 (DBP)	ψ_{11} (SBP)	ψ_{21}	ψ_{22} (DBP)
Jeffreys prior, Algorithm A					
normal	1.006	1.010	1.007	1.002	1.003
t-dist.	1.003	1.004	1.005	1.001	1.004
Jeffreys prior, Algorithm B					
normal	1.078	1.044	1.025	1.017	1.026
t-dist.	1.010	1.008	1.006	1.007	1.005
Berger and Bernardo reference prior, Algorithm A					
normal	1.006	1.013	1.095	1.068	1.108
t-dist.	1.049	1.026	1.021	1.017	1.033
Berger and Bernardo reference prior, Algorithm B					
normal	1.020	1.031	1.046	1.020	1.031
t-dist.	1.014	1.010	1.051	1.032	1.023

Table 4: Split-$\hat{\mathrm{R}}$ estimates based on the rank normalization (see, Vehtari et al. (2021)) and computed for the normal multivariate random effects model and for the t multivariate random effects model by employing the Berger and Bernardo reference prior and the Jeffreys prior and by using data from Table 1. The samples from the posterior distributions are drawn by Algorithm A and Algorithm B defined in Section 5.1.

Using the convergence diagnostics, recently proposed in Vehtari et al. (2021), good mixing properties are documented when the Markov chains are constructed under the t multivariate random effects model with the Jeffreys prior, independently of the algorithm used to generate samples from the posterior distribution. These findings might be considered as a justification of the t multivariate random effects model to analyze the effectiveness of hypertension treatment for reducing blood pressure. On the other side, the convergence diagnostic presents only one of many aspects of performing Bayesian inference procedures. A detailed analysis based on the Bayesian model selection is required to provide general recommendations about the choice of an elliptically contoured distribution to be used in practice. This challenging problem is not treated in the present paper and is left for future research.

The proposed multivariate approach is designed for meta-analysis whose outcomes can be described by continuous random variables. Vázquez-Polo et al. (2015) pointed out that the meta-analysis methods proposed for continuous outcomes can be used with caution only for performing meta-analysis in the case of sparse discrete data. In the univariate case, several approaches both from the frequentist and Bayesian statistics have been developed how to pool the results of the studies with discrete outcomes together (see, e.g., Liu et al. (2014); Moreno et al. (2014); Bender et al. (2018); Quaife et al. (2018)). Recently, Jain et al. (2022) discusses the application of the copula modeling for the multivariate meta-analysis with discrete outcomes from both viewpoints of the frequentist and Bayesian statistics. Since the family of elliptically contoured distributions includes also discrete distributions, the multivariate approach considered in the paper can lead to new methods how to combine the results of studies with discrete outcomes. Further investigation in this direction is left for future research.

Supplementary Material

Supplement to "Objective Bayesian meta-analysis based on generalized marginal multivariate random effects model" (DOI: 10.1214/23-BA1363SUPP; .pdf). Supplement A: The proofs of the theoretical results are provided. Supplement B: Metropolis-Hastings algorithms are provided for drawing samples from the posterior distribution when the samples are generated first from the marginal posterior of $\mathbf{\Psi}$ and then from the conditional posterior of $\boldsymbol{\mu}$ given $\mathbf{\Psi}$.

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