Journal of Mathematics and Statistics Studies (JMSS)
ISSN: 2709-4200
Journal hompage: www. al-kindipublisher.com/index.php/jmss

Bayesian Test of Efficiency in a Two-arm Meta-analysis by the Savage-Dickey Density Ratio

Hamimes Ahmed[1]* & Benamirouche Rachid [2]
[1]*Phd student, National Higher School of statistics and applied economics, Tipaza,Algeria, Assistant Professor at the Faculty of Medicine, University of Constantine3, Algeria*
[2]*Professor, National Higher School of statistics and applied economics, Tipaza, Algeria*
***Corresponding Author:** ABDU, Bello Magaji (PhD), E-mail: ahmedhamimes@yahoo.com*

ARTICLE INFORMATION

Received: October 15, 2020
Accepted: December 01, 2020
Volume: 1
Issue: 2

KEYWORDS

Bayes factor, meta-analysis, MCMC, Savage-Dickey density ratio

ABSTRACT

Meta-analysis offers a rational and useful way of dealing with a number of practices with difficulties; affects anyone trying to make sense of the search for efficiency. The relationship with the bayes factor constitutes an important tool in the detection of efficacy, through this factor we find a decision scale related to the importance of the treatment. In this contribution, the Savage-Dickey density ratio (Dickey, 1971, Dickey & Lientz, 1970) is used in the two-armed meta-analysis. The advantage of this method is the possibility of implementing the test with Monte Carlo sampling by Markov Chains.

1. Introduction

In making a decision, the doctor (practitioner or researcher) is often confronted with a multiplicity of information. When choosing a therapy for a disease, he often has the results of many contradictory therapeutic trials. Before putting this information into practice, he must sort and synthesize it. The meta-analysis technique makes it possible to agglomerate, under certain conditions and hypotheses, different test data relating to identical treatments to answer a question asked. The aim of systematic reviews is to present a balanced and unbiased synthesis of current research, allowing decisions on efficacy to be based on all relevant studies of adequate quality. Meta-analysis This is a systematic technique, as it involves as exhaustive a search as possible of all published and unpublished trials. It is quantified because it is based on statistical calculations allowing a precise estimate of the size of a common effect. Meta-analysis is a systematic approach summarizing the findings of a collection of independently conducted studies on a specific research problem. In Meta-analysis, statistical analyzes are performed on the published results of empirical studies on a specific research question, in many medical specialties it is common to find that several trials have attempted to answer similar questions on the clinical efficacy; for example: Does the new treatment confer significant advantages over conventional treatment? Often many of the individual tests will fail to show a difference; statistically significant between the two treatments. However, when the results of studies are aggregated using appropriate techniques (meta-analysis), significant treatment benefits can be shown. A good example of this is a retrospective review of the evidence for the effectiveness of "thombolytic" therapy for the prevention of myocardial infarction. The study showed that the meta-analysis was performed at an early stage, it would have demonstrated the benefits of thombolytic therapy. Meta-analyzes are now a hallmark of evidence-based medicine. In meta-analysis methodologies, so-called fixed-effect (or common-effect model) methods allow data from several studies to be "pooled" by assuming a common fixed effect for all studies. This method does not assume the existence of variability in the effect studied between studies. In contrast, random-effects meta-analysis techniques take into account heterogeneity between studies on the same parameter.

In a term, the p-value is ubiquitous. But just because a metric is ubiquitous doesn't automatically mean it's the best metric. Alternative statistical methods have long been discussed (e.g., Edwards, Lindman and Savage, 1963), and there has recently

been a growing trend towards alternative analyzes that overcome some shortcomings of null hypothesis significance tests (NHST) and p- values (Dienes, 2011; Gallistel, 2009; Johnson, 2013; Nuzzo, 2014). Bayesian methods in particular, and Bayes variables, have been proposed as an excellent alternative (see Wagenmakers, 2007 for a detailed review of this alternative), in the same vein as Masson (2011). Bayesian statistics have undergone significant progress over the past thirty years, with the development of computational methods and iterative algorithms with Markovian properties that make it possible to overcome complexity obstacles.The Bayesian method makes it possible to use all the information available (both past and present) for a given technology. In addition, the Bayesian approach is particularly interesting in situations where the number of subjects is low. Finally, by using informative a priori information, it can reduce the number of staff and thus reduce the time and resources required for a clinical trial. The concept of Bayes differs from the classical concept whose meaning where the parameter is a random variable whose behavior is assumed to be known, by associating it with a probability distribution on the space Θ called a priori distribution and noted $\pi\ (\theta)$ describes this that we know and what we do not know before observing X, through this design the statistical analysis makes it possible to consider all the qualitative and quantitative information on the uncertainty in the model. Then, if we use Bayes' rule which allows to reverse the probabilities, we can deduce the a posteriori distribution $\pi\ (\theta\ /\ x)$ which allows us to construct inferential procedures in the most natural way possible, which also explains the persistence of this paradigm, against all odds for 250 years.

From a statistical point of view, the objective is to make the best use of the data available in the meta-analysis. There are analytical instruments and statistical tests available to determine the effect of bias and methods to assess the sensitivity of bias effects (Rothstein, Sutton et al. 2005). A number of statistical methods have been proposed to detect bias in a meta-analysis (Sterne, Sutton et al. 2011). Most of them consistently measure the degree of skewness in the funnel diagram as an indication of the impact of small studies, i.e. the propensity of small studies to give larger estimates of the effect. treatment, regardless of the reasons for this effect (Begg and Mazumdar 1994; Egger, Davey Smith et al. 1997; Macaskill, Walter et al. 2001; Schwarzer, Antes et al. 2002; Harbord, Egger et al. 2006; Peters, Sutton et al. 2006). In addition, several approaches have been developed to assess the sensitivity of results to bias (Sutton, Song et al., 2000). There is a distinction between selection models, the so-called “cut and substitute” approach (in English, trim and fill), and approaches based on meta-regression. Briefly, weighting functions are used in selection models to model the selection process for the trial (Iyengar and Greenhouse 1988; Hedges 1992; Vevea and Hedges 1995; Givens, Smith et al. 1997; Silliman 1997; Vevea and Woods 2005; Rufibach 2011).

In this article the relationship with bayes factor is used in the detection of the efficacy of treatments in clinical trials performed with a two-arm (two-treatment) meta-analysis.

From this factor it is possible to directly and accurately measure the relationship between two treatments in terms of efficacy and according to a decision scale and to overcome the problems of comparison based on classical methods. In this contribution we use the Savage-Dickey density ratio (Dickey, 1971, Dickey & Lientz, 1970). The advantage of this method is the possibility of implementing the test with Monte Carlo sampling by Markov Chains.

2. The Bayesian approach in statistics

Bayesian statistical analysis makes it possible to combine several sources of information on uncertainty in the model, also it provides results of interpretation that are more direct (less complicated) and richer than those of classical statistics, this approach respects the principle likelihood which means that all the information from a data set is contained in the likelihood function.

A posteriori distribution is defined by

$$\pi(\theta/x) = \frac{f(x/\theta) \times \pi(\theta)}{\int_{\Theta} f(x/\theta) \times \pi(\theta) d\theta} = \quad \frac{f(x/\theta) \times \pi(\theta)}{m(x)} \qquad (1)$$

This a posteriori distribution is the combination of:

- $f(x/\theta)$the density function of x knowing the value of the random variable θ.
- $\pi(\theta)$models the density function a priori on θ.
- $m(x)$ the marginal distribution of x.
-

Expression (1) represents what is known about the parameter considering the observed data; it is also the update of $\pi\ (\theta)$ after observing our sample.

Once we have the data, the quantity $m\ (x)$ is a normalization constant which guarantees that π (θ⁄x) is indeed a probability distribution. We can write :

$$\pi(\theta/x) \propto f(x/\theta) \times \pi(\theta) \qquad (2)$$

Expression (2) shows that Bayesian inference satisfies the likelihood principle: a posteriori, the information from the data comes exclusively from the likelihood $f\ (x\ /\ \theta)$ (see Begin, J .F. (2010)) .Un estimateur $\delta^*(x)$est un estimateur de Bayes sous le coût $L(\theta, \delta)$ s'il minimise le risque bayésien c'est-à-dire :

$$\delta^* = arg\ \min_{\delta} \int_{\Theta} \int_{\chi} L\left(\theta, \delta(x)\right) f(x/\theta)\pi(\theta)dx\ d\theta \qquad (3)$$

For the cost L^2 (the quadratic loss) defined by $L(\theta, \delta) = (\theta - \delta)^2$, the expectation of the posterior distribution is a Bayes estimator:

$$\hat{\theta} = E(\theta/X) = \int_{\Theta} \theta\ \pi(\theta/x)\ d\theta = \frac{\int_{\Theta} \theta f(x/\theta) \times \pi(\theta)d\theta}{\int_{\Theta} f(x/\theta) \times \pi(\theta)d\theta} \qquad (4)$$

If no specific loss function is available, estimator (4) is often used as a default estimator, although alternative solutions are also available. For example, The posterior maximum estimator (the posterior mode) defined by:

$$\hat{\theta} = arg\ \max_{\theta} \pi(\theta/x) = arg\ \max_{\theta} f(x/\theta)\pi(\theta) \qquad (5)$$

We can calculate the posterior distribution directly in the simple case or we do the calculation by MCMC simulation in the case where the calculation of the integral is very complex.

In this article we use this approach in the framework of multiprocessing meta-analysis, we mainly rely on Gibbs sampling as a tool for solving complex posterior equations. The important role of the integration of published trial synthesis tools via multi-treatment meta-analysis is investigated in three treatments plus placebo for people with bipolar disorder. The Bayesian approach was first described and is the most frequently used in meta-analysis methods (Higgins and Whitehead 1996; Whitehead 2002; Lu and Ades 2004). This approach and within this framework is based on the calculation of the posterior distributions of all the parameters on the stochastic algorithm MCMC (Gibbs sampling algorithm).

3. The Bayesian approach to meta-analysis

The Bayesian random effects model of Smith et al. (1995) developed for binary data, on trials comparing two types of treatment: T (treatment) and C (control). The principle is to model the number of successes in the test (noted r_i) by a binomial distribution of parameters $(n_i\ ;\ p_i)$ (respectively number of patients and probability of success in test i; with by exponent T or C according to whether it is the experimental or control arm):

$$r_i^T \sim bin(p_i^T, n_i^T)$$
$$r_i^C \sim bin(p_i^C, n_i^C)$$

We then ask:

$$logit(p_i^T) = \mu_i + \delta_i$$
$$logit(p_i^C) = \mu_i$$
$$\delta_i \sim \mathcal{N}(\delta; \tau^2)$$

Or

μ_i : the mean of the event rate of trial i in the logit scale.

and

$$\delta_i = logit(p_i^T) - logit(p_i^C) = logOR_i^{TC}$$

LogORs approximately follow a normal distribution. We can therefore write that these δ_i follow a normal distribution centered on the true difference δ of the effect of the T and C treatments in the logit scale.

With the advent of MCMC techniques for analyzing the posterior distribution of complex hierarchical models, the a priori information is presented in a more complex way, since there are several levels of parameters. One such example is taken from volume 1 of the support part of WinBUGS version 1.4 and is based on a review by Carlin (1992), who considered a Bayesian approach to meta-analysis, and provides the following example of 22 trials of beta-blockers to prevent death from myocardial infarction (Table 1). Here are the program statements (See A1 in the appendices):

Openbugs code (1)

```
model
{
for( i in 1 : N ) {
rc[i] ~ dbin(pc[i], nc[i])
rt[i] ~ dbin(pt[i], nt[i])
logit(pc[i]) <- m[i]
logit(pt[i]) <- m[i] + d[i]
m[i] ~ dnorm(0.0,1.0E-5)
d[i] ~ dnorm(delta, tau)
}
delta ~ dnorm(0.0,1.0E-6)
tau ~ dgamma(0.001,0.001)
delta.new ~ dnorm(d, tau)
sigma <- 1 / sqrt(tau)
}
```

For each trial, a different probability of success is given for the control and treatment classes, and the probabilities are converted to the logit scale, then the logit parameters are given standard, non-informative priors. Thus, the $m\ (i)$ receive independent normal distributions with a mean of 0.0 and a precision of 0.00001. The $d\ (i)$ has a normal distribution (delta, tau) and the delta has a normal distribution (0.0, .000001). In this example, three parameter rates are involved. The performance probabilities, the logit parameters, namely the $m\ (i)$ and $d\ (i)$, and finally the usual distribution (0.0, .000001) for delta at the third point, which is the average of the parameters of the second level d.

Another third level parameter is the tau precision of the delta parameters, which receives an uninformative gamma distribution (0.001, 0.001). The parameter tau is the variance vice versa. The most interesting parameter is the delta, because there is no difference in mortality between the control and treated groups if it is negative. In the discussion of Gibbs sampling, we'll come back to this example.

4. Bayesian test of effectiveness of a two-armed meta-analysis

We pose the following hypothesis test

$$H_0: \theta \in \Theta_0 \quad , \quad H_0: \theta \in \Theta_0$$

If Θ_0 and Θ_1 are the same dimension, the most popular method in Bayesian statistics is to use the odds ratio a posteriori. This method poses some problems, when the prior distribution $\pi(\Theta_i)$ is improper the a posteriori distributions are undefined, so in the proper case it is possible that these distributions are chosen incorrectly. Moreover, the automatic choice of weights a_0 and a_1 which is not based on utility considerations can be a drawback in Bayesian decision procedures. This last point is at the origin of the Bayes factor and which in their objective is to limit the importance of the a priori choice of the parameters a_0 and a_1. Consequently, the Bayes factor is the posterior odds ratio on the a priori odds ratio, defined by:

$$BF_{01} = \frac{P(\theta \in \Theta_0/x)}{P(\theta \in \Theta_1/x)} \Big/ \frac{\pi(\theta \in \Theta_0)}{\pi(\theta \in \Theta_1)} \tag{6}$$

In the discrete case

$$B_{01} = \frac{odds\ a\ posterior}{odds\ a\ prior} = \frac{\alpha_0/\alpha_1}{\pi_0/\pi_1} = \frac{f(x/\theta_0)}{f(x/\theta_1)},$$

In the continuous case, the Bayes factor of H_0 relating to $H_1$is defined by

$$BF_{01} = \frac{\int_{\Theta_0} f(x/\theta)\pi_0(\theta)d\theta}{\int_{\Theta_1} f(x/\theta)\pi_1(\theta)d\theta} \tag{7}$$

Jeffreys developed an "absolute" scale to assess the degree of certainty in favor or against H_0 provided by the data, in the absence of a real decision framework. According to Raftery (1995), the Bayes factor can be interpreted as follows:

Table 1: the scale of interpretation of the bayes factor.

Interpretation	$\boldsymbol{B_{AB}}$	$\boldsymbol{log(B_{AB})}$	$\boldsymbol{P(\mathcal{M}_A/D)}$
$\mathcal{M}_B$ decisively acceptable.	< 0.0067	< -5	< -0.1
$\mathcal{M}_B$ is highly acceptable.	$0.0067\ to\ 0.05$	$-5\ to\ -3$	$0.01\ to\ 0.05$
$\mathcal{M}_B$ is substantially acceptable.	$0.05\ to\ 0.33$	$-3\ to\ -1$	$0.025\ to\ 0.25$
$\mathcal{M}_B$ is weakly acceptable.	$0.33\ to\ 1$	$-1\ to\ 0$	$0.25\ to\ 0.5$
No model is accepted	1	0	0.5
$\mathcal{M}_A$ is weakly acceptable.	$1\ to\ 3$	$0\ to\ 1$	$0.5\ to\ 0.75$
$\mathcal{M}_A$ is substantially acceptable.	$3\ to\ 20$	$1\ to\ 3$	$0.75\ to\ 0.95$
$\mathcal{M}_A$ is highly acceptable.	$20\ to\ 150$	$3\ to\ 5$	$0.95\ to\ 0.99$
$\mathcal{M}_A$ decisively acceptable.	> 150	> 5	> 0.99

The Savage - Dickey density ratio (Dickey and Lientz, 1970) provides a conceptually simple approach to calculate the Bayes factor. The idea of the Savage-Dickey ratio (Dickey, 1971) is to use only the posterior distribution under the alternative hypothesis. According to this method the Bayes factor can be obtained by dividing the height of the posterior distribution of θ by the height of the a priori distribution of θ, at the point of interest. We set x the observed data and θ the parameter of interest. Also we set two models $\mathcal{M}_0, \mathcal{M}_1$ denote respectively the restrictions $\theta = \theta_0$ and $\theta = \theta_1$, where θ_0 and θ_1 are each points. If the marginal probability of the data under H_0can be expressed as a restriction of the model $\mathcal{M}_1$ as follows

$$f(\ x/\theta = \ \theta_0, \mathcal{M}_1),$$

we can use the Savage-Dickey method and we write

$$B_{01} = \frac{f(x/\mathcal{M}_0)}{f(x/\mathcal{M}_1)} = \frac{f(\ x/\theta = \ \theta_0, \mathcal{M}_1)}{f(x/\mathcal{M}_1)} \tag{8}$$

we divide the two ratios on the function $f(\mathcal{M}_1)$, we find that

$$B_{01} = \frac{f(\ x/\theta = \ \theta_0)}{f(x)} \tag{9}$$

from the bayes rule we know that

$$f(\ x/\theta = \ \theta_0) = \frac{f(\ \theta = \ \theta_0/x) f(x)}{f(\theta = \ \theta_0)} \tag{10}$$

we replace (9) in (10) and we find

$$B_{01} = \frac{f(\ x/\theta = \ \theta_0)}{f(x)} = \frac{f(\ \theta = \ \theta_0/x)}{f(\theta = \ \theta_0)} \tag{11}$$

In this part we use the random effects model for the set of two equations:

$$r_i^T \sim bin(p_i^T, n_i^T)$$
$$r_i^c \sim bin(p_i^c, n_i^c)$$

we use the probit transformation represents the quantile function associated with the standard normal distribution. Mathematically the probit transformation is the inverse cumulative distribution function of the standard normal distribution. We use the probit scale as Figure (1) goes up, to determine the probabilities φ_1 and φ_2 for the means of p_1 et p_2, respectively and as follows

$$\Phi^{-1}(\varphi_i^c) = p_i^c \tag{12}$$

and

$$\Phi^{-1}(\varphi_i^T) = p_i^T \tag{13}$$

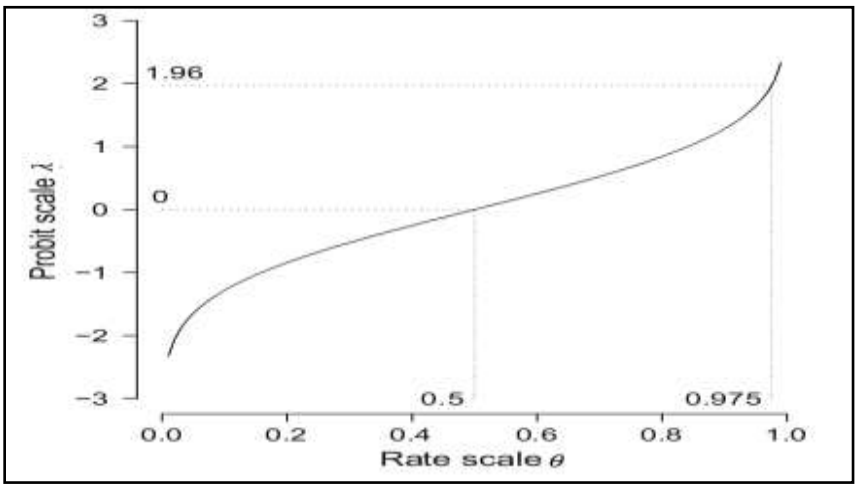

Figure 1: The probit transformation.

therefore:

$$\varphi_i^T = \varphi_i^c + \alpha_i$$

Log odds ratio of this study is α_i.
and

$$\alpha_i \sim \mathcal{N}(\mu_\alpha, 1/\sigma_\alpha^2)$$

μ_α and the true effects of the treatment in a random effects model. For programming reasons, only one distribution is used for the parameters φ_i^T, φ_i^c.
and

$$\varphi_i^c \sim \mathcal{N}(\mu, 1/\sigma^2)$$

we pose

$$\mu \sim Gaussian\ (0,1)_{I(0,\infty)}$$
$$\sigma \sim Uniform(0,10)$$

For the Dicky-Savage test and in a similar way to the frequentist test, it is possible to parameterize by $\delta_{test} = \mu_\alpha / \sigma_\alpha^2$. In order to generalize the test, we assume a prior distribution for δ represents the standardized effect size. Rouder et al. (2009) used Cauchy's distribution (0.1) for the parameter δ. The Cauchy distribution (see figure 2) used is a student distribution with 1 degree of freedom. The size of the effect is a quantity without proportions, which makes it reasonably straightforward to describe an earlier theory. The Cauchy distribution (i.e. a student distribution with one degree of freedom) and the regular normal distribution (e.g. Gönen, Johnson, Lu, & Westfall, 2005; Rouder et al., 2009) are the appropriate default choices for effect size priors. As it contains as much information as a single observation (Kass & Wasserman, 1995), the latter a priori is known under the name of "unit information prior". The normative normal distribution is the prior distribution of impact size that we will use in this article. We pose

$$\mu_\alpha = \delta_{test} * \sigma_\alpha^2$$

and

$$\delta_{test} \sim Gaussian\ (0,1)_{I(0,\infty)}$$
$$\sigma_\alpha^2 \sim Uniform(0,10)$$

we define δ_{test}, as the measure or scale of difference between the parameters of binomial distributions, respectively. We write the test this way

$$H_0 : \delta_{test} = 0,$$
$$H_1 : \delta_{test} \neq 0,$$

Mathematically, the Savage-Dickey density ratio is written as

$$BF_{01} = \frac{f(\delta_{test} = 0/\mathcal{D}, \mathcal{H}_1)}{f(\delta_{test} = 0/\mathcal{H}_1)} \tag{14}$$

The general model is written this way:

$$r_i^T \sim bin(p_i^T, n_i^T)$$

$$r_i^c \sim bin(p_i^c, n_i^c)$$
$$\Phi^{-1}(\varphi_i^c) = p_i^c$$
$$\Phi^{-1}(\varphi_i^T) = p_i^T$$
$$\varphi_i^T = \varphi_i^c + \alpha_i$$
$$\alpha_i \sim \mathcal{N}(\mu_\alpha, 1/\sigma_\alpha^2)$$
$$\varphi_i^c \sim \mathcal{N}(\mu, 1/\sigma^2)$$
$$\mu \sim Gaussian\ (0,1)_{I(0,\infty)}$$
$$\sigma \sim Uniform(0,10)$$
$$\mu_\alpha = \delta_{test} * \sigma_\alpha^2$$

and

$$\delta_{test} \sim Gaussian\ (0,1)_{I(0,\infty)}$$
$$\sigma_\alpha^2 \sim Uniform(0,10)$$

4. Application

The example of 22 beta-blocker trials is used to prevent mortality after myocardial infarction, see the following table:

Table 2 : Results of 22 clinical trials of beta-blockers for reducing mortality after myocardial infarction, from Yusuf et al.(1985).

	Basic data (deaths/total)	
study number	**Treated**	**Control**
1	3/38	3/39
2	7/114	14/116
3	5/69	11/93
4	102/1533	127/1520
5	28/355	27/365
6	4/59	6/52
7	98/945	152/939
8	60/632	48/471
9	25/278	37/282
10	138/1916	188/1921
11	64/873	52/583
12	45/363	47/266
13	9/291	16/293
14	57/858	45/883
15	25/154	31/213
16	33/207	38/213
17	28/251	12/122
18	8/151	6/154
19	6/174	3/134
20	32/209	40/218
21	27/391	43/364
22	22/680	39/674

Analyzes are run with 50,000 generated values of the posterior distribution of delta and sigma. The parameter delta is the mean of the parameters of $d\ (i)$ as much as sigma is the standard deviation, and both parameters were given from the uninformative prior distributions. The characteristics of the a posteriori distribution of delta and tau are given in the following table (according to the OpenBUGS code (A.2)):

Table 3 : the estimation of the delta and sigma parameters.

	mean	**SD**	**MC_error**	**val2.5pc**	**median**	**val97.5pc**
delta	-0.2502	0.06183	8.045E-4	-0.3694	-0.2508	-0.1268
sigma	0.1147	0.06713	8.257E-4	0.02677	0.102	0.2743

The analyzes also generate the graph of the posterior density, for the graph of the posterior distribution of delta: Are there any effect treatments? The mass of the posterior distribution is to the left of zero where the lower point is -0.36, and the upper point is -0.1268 (see Figure (3)), so the posterior evidence suggests that delta is different to zero on scale, and B-blockers a lower the mortality of a heart attack.

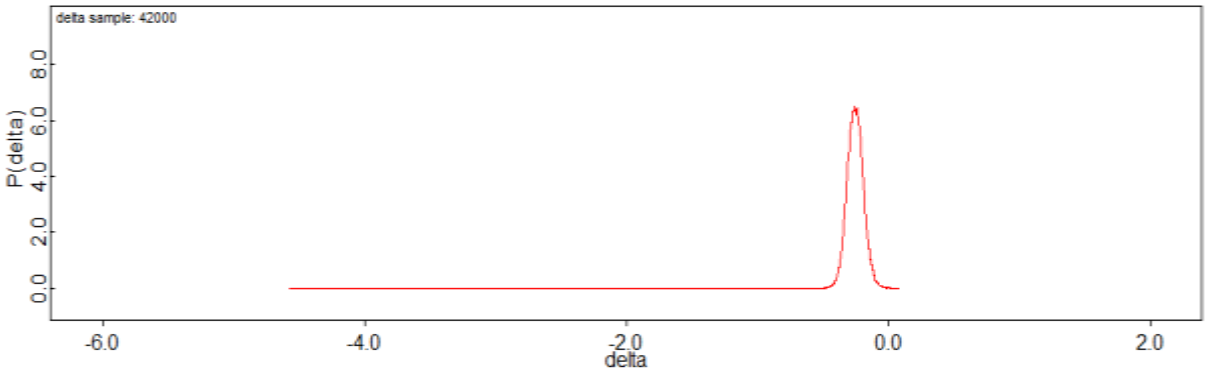

Figure2 : The Kernel kernel estimator for the marginal delta density.

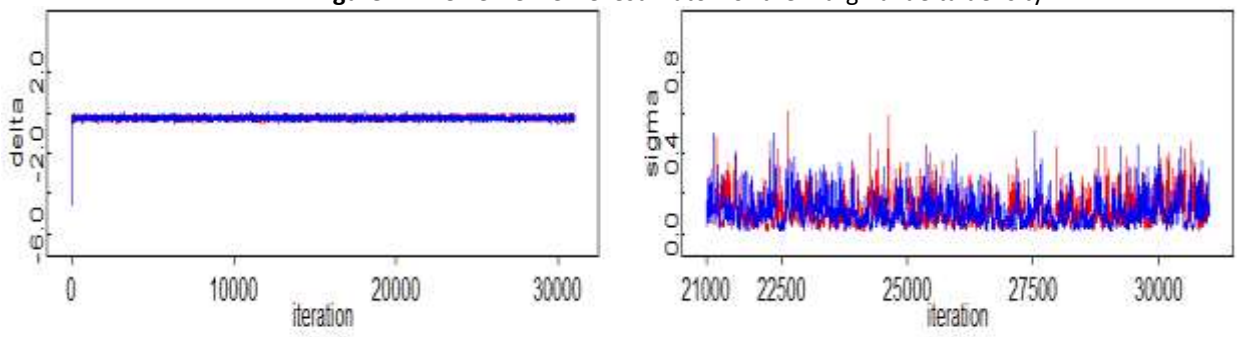

Figure 3 : The trace of the posterior distribution for the parameters delta and sigma.

In Figure 4, each color denotes an MCMC chain. The chains mix well: convergence is achieved.

This time we estimate the model in code (A3) written in the form probit. Table (3) shows that the interval of the effect size parameter does not contain the value "0", so it is clear that β-blockers a lower heart attack mortality.

Table 3: the estimate of the parameters delta.test (the size of the effect) and sigma.

	mean	sd	MC_error	val2.5pc	median	val97.5pc
delta.test	1.161	0.509	0.006087	0.307	1.11	2.302
sigma	1.587	0.2719	8.348E-4	1.159	1.552	2.218

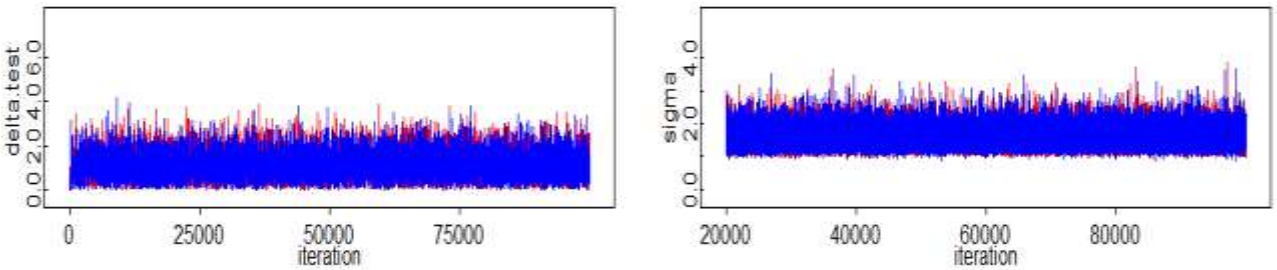

Figure 4 : The trace of the posterior distribution for the delta parameters. test and sigma.

In Figure 5, each color denotes an MCMC chain. The chains mix well: convergence is achieved.

The Bayesian test of efficiency in a two-armed meta-analysis by the Savage-Dickey density ratio reinforces the results found previously. Sometimes we are not able to determine the test graphically or by the interval, so we need to know the exact relationship in the form of a scale to quantify the relationship.
In equation (14), the Savage-Dickey density ratio is written as:

$$BF_{01} = \frac{f(\delta_{test} = 0/\mathcal{D}, \mathcal{H}_1)}{f(\delta_{test} = 0/\mathcal{H}_1)} \quad (15)$$

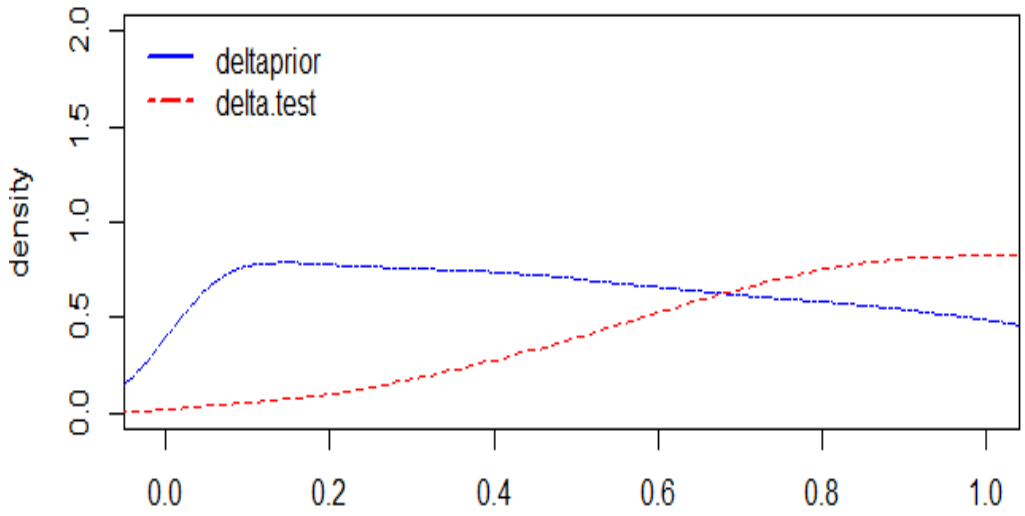

Figure 5: The distribution of δ_{test} and δ^{prior} for calculate the ratio of Dickey – Savage.

From equation (15), the Savage - Dickey density ratio (Dickey and Lientz, 1970) provides a conceptually simple approach to calculate the Bayes factor. The idea of the Savage-Dickey ratio (Dickey, 1971) is to use only the posterior distribution under the alternative hypothesis. According to this method, the Bayes factor can be obtained by dividing the height of the a posteriori distribution of the parameter of interest δ_test by the height of the a priori distribution of ^ prior at point "0".
The Bayes factor and Dickey-Savage ratio is BF≃ (0.0068 / 1) = 0.0068, which means that the hypothesis that beta-blockers a lower the mortality of a heart attack is highly acceptable

5. Conclusion

In this article on the use of the bayes factor relationship in the identification of the effectiveness of clinical trial treatments conducted with a two-bras meta-analysis (two treatments). From this factor, the relationship between two treatments can be calculated explicitly and objectively in terms of efficacy and a decision-making scale and resolve comparative problems based on traditional methods.

A Bayesian approach to test efficiency in a two-arm meta-analysis based on the Dickey method - Savage offers practical, simple and relatively easy solutions for the direct use of the results of Monte Carlo sampling by Markov chains the limit of this method is the number of arms used and the latter represents the future work.

References

[1] Begg, C. B., & Mazumdar, M. (1994). Operating characteristics of a rank correlation test for publication bias. *Biometrics*, 1088-1101.
[2] Carlin, J. B. (1992). Meta-analysis for 2× 2 tables: a Bayesian approach. *Statistics in medicine*, *11*(2), 141-158.
[3] Dickey, J. M. (1971). The weighted likelihood ratio, linear hypotheses on normal location parameters. *The Annals of Mathematical Statistics*, *42*(1), 204–223.
[4] Dickey, J.M., Lientz,B.P. (1970). The weighted likelihood ratio, sharp hypotheses about chances, the order of a Markov chain. *The Annals of Mathematical Statistics*, *41*(1), 214-226.

[5] Dienes, Z. (2011). Bayesian versus orthodox statistics: Which side are you on? *Perspectives on Psychological Science*, *6*(3), 274–290. http://dx.doi.org/10.1177/1745691611406920.
[6] Edwards, W., Lindman, H., & Savage, L. J. (1963). Bayesian sta -tistical inference for psychological research. *Psychological Review*, *70* (3), 193–242. http://dx.doi.org/10.1037/h0044139.
[7] Egger, M., G. Davey Smith, et al. (1997). Bias in meta -analysis detected by a simple, *graphical test*. BMJ, *315* (7109): 629 -634.
[8] Gallistel, C. R. (2009). The importance of proving the null. *Psychological Review*, *116*(2), 439–453. http://dx.doi.org /10.1037/a0015251.
[9] Givens, G. H., D. D. Smith, et al. (1997). Publication bias in meta-analysis:a Bayesian data-augmentation approach to account for issues exemplified in the passive smoking debate. *Statist Sci*, *12*, 221-250.
[10] Harbord, R. M., M. Egger, et al. (2006). A modified test for small-study effects in meta -analyses of controlled trials with binary endpoints. *Stat Med*, *25*(20), 3443-3457.
[11] Hedges, L. V. (1992). Modeling publication selection effects in meta-analysis. *Stat Sci*, *7*(2), 246-255.
[12] Higgins, J. P. and A. Whitehead (1996). Borrowing strength from external trials in a meta-analysis. *Stat Med*, *15*(24): 2733-2749.
[13] Iyengar, S. and J. B. Greenhouse (1988). Selection Models and the File Drawer Problem. *Statist Sci, 3*(1), 109-117.
[14] Johnson, V. E. (2013). Revised standards for statistical evidence. *Proceedings of the National Academy of Sciences of the United States of America*, *110*(48) , 19313–19317. http://dx.doi.org/10.1073/pnas.1313476110.
[15] Lu, G. and A. E. Ades (2004). Combination of direct and indirect evidence in mixed treatment comparisons. *Stat Med, 23*(20), 3105-3124.
[16] Macaskill, P., S. D. Walter, et al. (2001). A comparison of methods to detect publication bias in meta -analysis. *Stat Med*, *20*(4), 641-654.
[17] Masson, M. E. J. (2011). A tutorial on a practical Bayesian alternative to null-hypothesis significance testing. *Behav-ior Research, 43*(3), 679–690. http://dx.doi.org/10.3758 /s13428-010-0049-5.
[18] Nuzzo, R. (2014). Statistical errors. Nature, 506 , 150–152.
[19] Peters, J. L., A. J. Sutton, et al. (2006). Comparison of two methods to detect publication bias in meta -analysis. *JAMA, 295* (6): 676-680.
[20] Rothstein, H. R., A. J. Sutton, et al. (2005). Publication bias in meta-analysis: prevention, assessment and adjustments . Chichester, UK, John Wiley & Sons Ltd.
[21] Rufibach, K. (2011). Selection models with monotone weight functions in meta analysis. *Biom J, 53*(4), 689-704.
[22] Schwarzer, G., G. Antes, et al. (2002). Inflation of type I error rate in two statistical tests for the detectio n of publication bias in meta -analyses with binary outcomes. *Stat Med, 21*(17), 2465-2477.
[23] Silliman, N. P. (1997). Hierarchical Selection Models With Applications in Meta- Analysis. *JASA, 92*(439), 926 -936.
[24] Smith TC, Spiegelhalter DJ, Thomas A. (1995). Bayesian approaches to random-effects meta-analysis: a comparative study. *Statistics in Medicine*, 4, 2685–2699.
[25] Sterne, J., M. Egger, et al. (2011). Chapter 10: Addressing reporting biases. Cochrane Handbook for Systematic Reviews of Interventions. J. P. Higgins and S. Green, The Cochrane Collaboration.
[26] Sutton, A. J., F. Song, et al. (2000).Modelling publication bias in meta-analysis: a review. *Stat Methods Med Res, 9*(5), 421-445.
[27] Vevea, J. L. and C. M. Woods. (2005). Publication bias in research synthesis: sensitivity analysis using a priori weight functions. *Psychol Methods, 10*, 428-443.
[28] Vevea, J. L. and L. V. Hedges (1995). A general linear model for estimating effect size in the presence of publication bias. *Psychometrika, 60*, 419-435.
[29] Wagenmakers, E. J. (2007). A practical solution to the perva-sive problems of p values. *Psychonomic Bulletin and Review, 14*(5), 779–804. http://dx.doi.org/10.3758/BF03194105.
[30] Whitehead, A. (2002). Meta-analysis of Controlled Clinical Trials. Chichester, UK, John Wiley & Sons, Ltd. World Health Organization International Clinical Trials Registry Platform.
[31] Yusuf, S., Peto, R., Lewis, J., Collins, R. and Sleight, P. (1985). Beta blockade during and after myocardial infarction: an overview of the randomized trials', *Progress in Cardiovascular Diseases*, XXVII, 335-371

Appendices

A1. BUGS project definition

BUGS is a software package for performing Bayesian inference using Gibbs Sampling. The project started in Cambridge in 1989. BUGS made Bayesian analysis accessible to everyone using a laptop. Bayesian analysis could only be applied in the pre-BUGS era in situations where solutions could be obtained in closed form in so-called conjugate analyzes, or by an ingenious but limited application of numerical integration methods. Therefore, BUGS has helped to educate academic and business communities about Bayesian modeling.

A2. The OpenBUGS code

model
{

```
for( i in 1 : N ) {
rc[i] ~ dbin(pc[i], nc[i])
rt[i] ~ dbin(pt[i], nt[i])
logit(pc[i]) <- m[i]
logit(pt[i]) <- m[i] + d[i]
m[i] ~ dnorm(0.0,1.0E-5)
d[i] ~ dnorm(delta, tau)
}
delta ~ dnorm(0.0,1.0E-6)
tau ~ dgamma(0.001,0.001)
sigma <- 1 / sqrt(tau)
}

list(rt = c(3,  7,  5,  102,  28, 4,  98,  60, 25, 138, 64, 45,  9, 57, 25, 33, 28, 8, 6, 32, 27, 22 ),
nt = c(38, 114, 69, 1533, 355, 59, 945, 632, 278,1916, 873, 263, 291, 858, 154, 207, 251, 151, 174, 209, 391, 680),rc = c(3, 14,
11, 127, 27, 6, 152, 48, 37, 188, 52, 47, 16, 45, 31, 38, 12, 6, 3, 40, 43, 39),nc = c(39, 116, 93, 1520, 365, 52, 939, 471, 282,
1921, 583, 266, 293, 883, 147, 213, 122, 154, 134, 218, 364, 674), N = 22)
list(delta = 0, tau=1, m = c(0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0),
d = c(0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0))
list(delta = 2, tau=0.1, m = c(2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2),d = c(2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2,
2, 2, 2, 2, 2, 2))
```

A3. The OpenBUGS code

```
model{
for (i in 1:N){
# Data
rc[i] ~ dbin(pc[i], nc[i])
rt[i] ~ dbin(pt[i], nt[i])
# Probit Transformation
pc[i] <- phi(phib[i])
pt[i] <- phi(phin[i])
phin[i] ~ dnorm(mu,lambda)
alpha[i] ~ dnorm(mualpha,lambdaalpha)
phib[i] <- phin[i]+alpha[i]
}
# Priors
mu ~ dnorm(0,1)I(0,)
sigma ~ dunif(0,10)
lambda <- pow(sigma,-2)
# Priming Effect
sigmaalpha ~ dunif(0,10)
lambdaalpha <- pow(sigmaalpha,-2)
delta.test ~ dnorm(0,1)I(0,)
mualpha <- delta.test*sigmaalpha
# Sampling from Prior Distribution for Delta
deltaprior ~ dnorm(0,1)I(0,)
}
list(rt = c(3,  7,  5,  102,  28, 4,  98,  60, 25, 138, 64, 45,  9, 57, 25, 33, 28, 8, 6, 32, 27, 22 ),
nt = c(38, 114, 69, 1533, 355, 59, 945, 632, 278,1916, 873, 263, 291, 858, 154, 207, 251, 151, 174, 209, 391, 680),rc = c(3, 14,
11, 127, 27, 6, 152, 48, 37, 188, 52, 47, 16, 45, 31, 38, 12, 6, 3, 40, 43, 39),nc = c(39, 116, 93, 1520, 365, 52, 939, 471, 282,
1921, 583, 266, 293, 883, 147, 213, 122, 154, 134, 218, 364, 674), N = 22)
list(delta.test = 0, deltaprior = 0, mu=2, sigma=3)
list(delta.test = 0.5, deltaprior = 0.5, mu=1, sigma=1)
```