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Bayesian Approach to Three-Arm Non Inferiority Trials

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Bayesian Approach

to

Three-Arm Non-inferiority trials

By

Marcus Chenier Britton

Under the direction of Pulak Ghosh

Abstract

In non-inferiority trials, the goal is to show how an experimental treatment is statistically and clinically not inferior to the active control. The three-arm clinical trial usually recommended for non-inferiority trials by the FDA. The three-arm trial consists of a placebo, reference, and an experimental treatment. The three-arm trial shows the superiority of the reference over the placebo and comparison of the reference to an experimental treatment. In this paper, I will assess a non-inferiority trial with Bayesian methods. By employing Bayesian analysis, the parameters are random and assign vague prior distributions. I will compare the models involving different prior distributions to assess the best fit model.

Keywords: Bayesian methods; Gold Standard Design: Markov Chain Monte Carlo; non-inferiority; WINBUGS

Bayesian Approach To Three-Arm Non-inferiority trials

by

Marcus Britton

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Master of Science

In the College of Arts and Sciences

Georgia State University

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Bayesian Approach To Three-Arm Non-inferiority trials

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Introduction

Non-inferiority trial is a trial with the objective of showing how an experimental treatment is statistically and clinically not inferior to the active control (Agostion, 173). Clinical trial for establishment of non-inferiority of a test therapy as compared to an active control agent has become very popular in drug research and development (Chow, 2005). Non-inferiority studies are typically confirmatory trials that employ a randomized parallel group design with an active control group. Some trials also include a placebo control group. The placebo is used to validate the study and to demonstrate superiority of the test treatment to the placebo (Garrett, 2003). Non-inferiority methods are frequently used in more serious, acute, and sometimes life-threatening indications such as oncology and infectious diseases (Garrett, 2003). In these cases the primary endpoint is often a binary outcome measure and in some cases the trials objective will incorporate a time to event evaluation (Garrett, 2003)

Placebo controlled trials are ideal for evaluating medical treatment efficacy. These trials allow for control of the placebo effect. Also they require the smallest number of patients to detect a treatment effect (D'Agostino 200). In the absence of effective treatments, placebo-controlled Randomized Clinical Trials are uncontroversial.

Gold Standard design

Three-arm trial includes placebo, active control, and the new treatment referred to as gold standard design. Non-inferiority implies that a patient who has previously been treated with the reference can be switched to the new experimental treatment without a relevant loss in efficacy. Second, given that the treatment effect of the reference (comparator) is of clinical relevance, non-inferiority with an adequately chosen margin results in clinically relevant efficacy over placebo. The three arm trial has the ability to show substantial superiority of the comparator over the placebo can be assessed prior to the comparison of reference and new experiment treatment (Hauschke and Pigeot, 2005).

In dealing with a three arm clinical trail, the investigation on the efficacy of a new experimental treatment relative to an active control is the main focus. For this type of trial, there are two clinical settings considered when evaluating relative efficacy. In the first setting, non-inferiority implies that a patient who has previously been treated with the reference can be switched to the new experimental treatment without a relevant loss in efficacy. The second setting, given that the treatment effect of the reference is of clinical relevance, non-inferiority with an adequately chosen margin results in clinical relevant efficacy over the placebo. In this setting, the three arm trial is recommended because of assay sensitivity. Assay sensitivity is the ability of the study to show substantial superiority of the reference over the placebo can be assessed prior to the comparison of the reference and the new experimental treatment (Hauschke and Pigeot, 2005).

Margins

In a placebo-controlled clinical trial, it is not sufficient to just demonstrate a statistically significant treatment difference. The choice of non-inferiority margin requires that in order to demonstrate superiority of a new product over a placebo, not only does it has to be statistical significance but also clinical relevance have to be shown.

The consideration of the margin in a non-inferiority test is important. A different choice of non-inferiority margin may affect the method of analyzing clinical data and the conclusion of the clinical study. The guidelines of the International Conference on Harmonization, the determination of non-inferiority margins should be based on both statistical reasoning and clinical judgment. The non-inferiority margin should be chosen to satisfy at least the following two criteria (D'Agostion, 2003):

Criterion1: We want the ability to claim that the test therapy is non-inferior to the active control agent and is superior to the placebo (even though the placebo is not considered in the active control trial).

Criterion2: The non-inferiority margin should be suitably conservative and variability should be taken into account.

A fixed margin that does not depend on any parameter is rarely suitable under criterion1.

Let us define some notation.

θ_T unknown test therapy population efficacy

θ_A unknown active control agent population efficacy

θ_p unknown placebo population efficacy

$\Delta \geq 0$ a non-inferiority margin

Let $\delta > 0$ be a superiority margin if a placebo-controlled trial is conducted to establish the superiority of the test therapy over a placebo control. Since the active control is an established therapy, we may assume that

$$\theta_A - \theta_p > \delta$$

However, when

$$\theta_T - \theta_A > -\Delta$$

The test therapy is non-inferior to the active control. For a fixed τ we can not ensure that

$$\theta_T - \theta_p > \delta$$

The test therapy is superior to the placebo unless $\Delta = 0$

Thus, it is reasonable to consider non-inferiority margins depending on unknown parameters.

In a fequentist view for non-inferiority trial, it is necessary to pre-specify a fixed margin. This is important because the margin determines the null hypothesis. For a margin to properly represent the maximal acceptable loss in a known beneficial effect, the subject assessment must account for the factors other than the effectiveness (Hung 2005). Other factors involved such as, benefit versus risk or price to be paid with the experimental treatment. IF there is not a universally accepted metric for the benefit/risk assessment, the fixed margin is almost impossible to determine just on assessment (Hung, 2005).

The non-inferiority margin should be selected to provide a sufficient cushion to protect the test from possibly being seriously biased.

The FDA has considered non-inferiority margins dependent upon the highest of the two observed response percentage being compared (The FDA is now in the process of reviewing this recommendation) The CPMP has fixed the non-inferiority margin at about 10 per cent. For many non-serious infections (Garrett , 2003)

The International Conference on Harmonisation offers 2 guidelines

1. The determination of the margin in non-inferiority trials is based on both statistical reasoning and clinical judgment and should reflect uncertainties in the evidence on which the choice is based and should be suitably conservative.

2. This non-inferiority margin cannot be greater than the smallest effect size that the active drug would be reliably expected to have compared with placebo in the setting of a placebo controlled trial.

D'Agostino (2003) states that he has never seen a case where criteria 1 have been employed. Some researchers feel the active control treatment and the new treatment should be within some percent of each other. The ICH feels the control and new treatment should be 20 percent while the FDA says 10 percent. From general guidelines, there are only concrete suggestions on the choice of non inferiority margin for specific indications (Lange and Freitag, 2005).

Assay Sensitivity

Assay sensitivity means the ability within a trial to detect any difference between groups. With respect to clinical trials, detect differences between effective, less effective, and ineffective therapies.

Assay sensitivity is an important issue for non-inferiority trials. The International Conference on Harmonization states that assay sensitivity is inherent in superiority trails. This occurs because rejection of the null hypothesis is concluded when there is a significant difference in the endpoint for the two arms and the difference validates the assay. In non-inferiority trials, rejection of the null hypothesis is concluded when the endpoints for the two arms are close to each other (Aras, 2001). There is a concern with this evaluation. Both arms may not have performed as intended. In particular, we could have proved that a placebo is not inferior to a placebo. In order not to make this mistake, in addition to showing non-inferiority, we must establish the assay sensitivity

external to the trials. We can establish this by including historic evidence or by including a small placebo arm in the trial and performing secondary comparisons with respect to it. With a small placebo arm, there may not be adequate power to separate treatments from the placebo. However, a trend in the right direction for comparison of treatments with the placebo combined with historic data on the control arm my help to argue assay sensitivity (Aras 2001).

Placebo-Controlled trials

An appropriate control group is always essential and when feasible, a placebo control is optional. An active control with the test treatment indicates that the two treatments are similar. Now, if a placebo group is not included in the study, we can never be sure if the new treatment is better than the placebo. Placebo control group was the usual optional control group for establishing efficacy of an experimental treatment. Now with the large array of proven effective treatment, ethical considerations cast doubts on the appropriateness of using a placebo control. Dose response trials are possible alternatives but they also raise ethical problems since the low dose may not be any different than the placebo. Ellenberg says that placebo controls are ethical when delaying or omitting available treatment has no permanent adverse consequence for the patient and as long as the patient are fully informed about the alternative.

An active control may be included in the RCT, but the active control is there for reasons such as assay sensitivity (D'Agostino, 2005).

Non-inferiority placebo controlled trials are the ideal trails for evaluating medical treatment efficacy. They allow for control of the placebo effect and require the smallest

number of patients to detect a treatment effect. A placebo control is ethically justified if no standard treatment exists. If the standard treatment has not been proven efficiency, then there are no risks associated with delaying treatment and escape clauses are included in the protocol (D'Agostino, 2005).

Problems with Placebo-Control trials

Using a placebo control clinical trials can occur problems in non-inferiority trials. In some clinical studies, there are a small number of available historical placebo-controlled studies. For many indications, there is only one historical placebo-controlled trial that exist. The estimate of a control and placebo trial from only one study is sometimes questioned by regulatory agencies. These agencies feel there is not an adequate estimate of the variability for estimation of control versus placebo. Variability is the estimate across previous clinical trials that involve the same entities. The variability of control versus placebo is important for determine the margin error M for the non-inferiority trial. In some studies, a placebo controlled study is not available. In these situations, researchers may try to work with previous dose response studies of the active control. In these studies, the marketed dose of the active control is compared with a low dose. The low dose effect may or may not be an adequate substitute for a placebo effect (D'Agostino et al 2005).

An example of a no available placebo-controlled trial is the study in vancomycin-resistant-enterococcal (VRE) infection. In VRE studies, the cure of the infection is defined as a success. The product linezolid is often used as the active control comparator. There are no published placebo-controlled studies of linezolid. The results of the study

compares high dose of linezolid versus low does of linezolid. The results show a difference in success rate of 14 percent. This approach is considered conservative and may underestimate the true control versus placebo. But, this process is better then simple guessing the control versus placebo. The best value to use for M the margin of error is also unclear (D'Agostino et al 2005) .

Another problem with Placebo- control trials is Biocreep. Biocreep is when a slightly inferior treatment becomes the active control for the next generation of non-inferiority trials and so on until the active controls become no better than a placebo (D'Agostino et al 2005).

Model Specification

μ_E Mean treatment effect under the experiment

μ_R Mean treatment effect under reference drug

μ_P Mean treatment effect under the placebo

X_{E_i} Experimental treatment quantitative measure of efficacy

X_{R_i} Reference treatment quantitative measure of efficacy

X_{p_i} Placebo quantitative measure of efficacy

n_E Sample size of the Experimental

n_R Sample size of the reference

n_p Sample size of the placebo

The non-inferiority trial for this study involves mildly asthmatic patients. The primary outcome FVC (forced vital capacity) was measured after a treatment period of six weeks for three groups of patients. Since the experimental treatment is under review, I can no give further details. The data set consist of 74 patients. The summary for the measures are given (Pigeot et. al, 2003)

	Experimental	Reference	Placebo
Mean	4.32	4.86	3.14
Standard deviation	1.16	1.03	0.97
Minimum	1.8	2.94	1.41
Maximum	6.52	6.90	4.99

Summary measures for the data set on mildly asthmatic patients

For the non-inferiority trials, let X_E and X_R denote quantitative measures of efficacy under experimental and reference treatments. We can symbolize the problem of non-inferiority by

$$H_o : \mu_E - \mu_R \leq \delta$$

Versus

$$H_o : \mu_E - \mu_R > \delta$$

This two sample design with an active control and an experimental group gives rises to a major problem. The study does not account for assay sensitivity. To take care of this problem, we can use a placebo group for internal validation. Once we include the placebo, we have now changed to a three-arm study (Pigeot et. al, 2003). The three arm study consists of a placebo, an active reference, and the experimental treatment. Now, are quantitative measures of efficacy are

$$X_{E_i} \sim \mathrm{N}(\mu_E, \sigma^2)\text{ , I=1,}\ldots\ldots\ldots n_E$$

$$X_{p_i} \sim \mathrm{N}(\mu_P, \sigma^2)\text{, I=1,}\ldots\ldots\ldots n_p$$

$$X_{R_i} \sim \mathrm{N}(\mu_R, \sigma^2)\text{, I=1,}\ldots\ldots\ldots n_R$$

The statistical testing problem is

$$H_o : \mu_E - \mu_R \leq \delta$$

Versus

$$H_o : \mu_E - \mu_R > \delta$$

δ can be chosen as a fraction f of the difference in population means μ_R and μ_P such that

$$\delta = f(\mu_R - \mu_p)$$

Therefore we get

$$H_o : \mu_E - \mu_R \leq f(\mu_R - \mu_P)$$

Versus

$$H_1 : \mu_E - \mu_R > f(\mu_R - \mu_P)$$

For the choice of δ, there often is a difference of 20 percent that is clinically unimportant. To handle this case, we choose a value $f = \frac{-1}{5}$

Now, since

$$\mu_R - \mu_P > 0$$

And

$$\theta = 1 + f$$

$$H_0 : \frac{\mu_E - \mu_P}{\mu_R - \mu_P} \leq \theta$$

Versus

$$H_1 : \frac{\mu_E - \mu_P}{\mu_R - \mu_P} > \theta$$

Prior Distribution

The distribution for the parameter is called your prior distribution. It represents the distribution of your degree of belief about the parameter prior to your observing any data. Bayesian methods gives a procedure for updating your prior belief about the value of the parameter to produce a posterior distribution for the parameter, one determined subsequent to having observed the outcome of an experiment bearing on the value of the unknown parameter.

Within Bayesian analysis, prior distribution for the unknown parameters needs to be specified. In many situations involving vague prior, distribution are chosen with the intention that they have little or no impact. However, naïve use of vague prior distribution may lead to them having an influence on any inference made.

The purpose of a reference prior is to be uniform over the range of interest and be considered the possible values of the unknown parameter to be equally likely. The problem is such prior distribution is that uniformity is sensitive to transformation. Therefore, a prior distribution that is uniform on the variance will not be uniform on the standard deviation. Since standard deviation $= \sqrt{\text{var}\,iance} = \sqrt{1/\,percision}$, the prior distribution for the scale parameters of the random effects in the Bayesian models can be put on the variance, standard deviation, or precision. I used the prior distributions illustration in Lambert et al (2005) paper as followed:

Prior 1

$$\frac{1}{\sigma^2} \sim \text{Gamma}(0.001,0.001)$$

This is the most common used prior distribution for variance parameters. This prior distribution is approximately uniform for most of the range but has a spike of probability mass close to zero.

Prior 2

$$\frac{1}{\sigma^2} \sim \text{Gamma}(0.1,0.1)$$

This is of the same distributional form as prior 1, but with the two parameters set to 0.1. This provides a simple assessment of the sensitivity to the choice of these parameter values

Prior 3

$$\text{Log}(\sigma^2) \sim \text{Uniform}(-10,10)$$

This prior distribution is uniform on the log variance scale between two specified parameters.

Prior 4

$$\text{Log}(\sigma^2) \sim \text{Uniform}(-10,1.386)$$

This prior distribution is uniform on the log variance scale between two specified parameters. This is a weakly informative prior distribution because it gives zero density to large values. The maximum value between-study variance can be is 4

Prior 5

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

This prior distribution is uniform on the variance.

Prior 6

$$\sigma^2 \sim \text{Uniform}(1/1000,4)$$

This is a weakly informative version of Prior 5. The maximum value between-study variance can be is 4.

Prior 7

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

When using a Pareto Distribution with parameters α and c a uniform prior distribution for τ^k on the range (0,r) can be expressed by setting α =k/2 and c= r^{-2}/k . The values of k=2,1 and -2 give uniform prior distributions on the variance, standard deviation and precision scales.

Prior 8

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

This is the weakly informative version of prior 7 and is equivalent to a uniform prior distribution for the variance in the range (0,4)

Prior 9

$$\sigma \sim \text{Uniform}(0,100)$$

This is a uniform prior distribution on the standard deviation. The scale for the range is (0,100)

Prior 10

σ ~Uniform(0,2)

This is the weakly informative version of prior 9 and is a uniform distribution on the standard deviation with a range (0,2)

Prior 11

σ ~N(0,100) for τ >0

This is a half normal distribution truncated at zero placed on the standard deviation scale.

Prior 12

σ ~N(0,1) for τ >0

This is the weakly informative version of prior 11. This prior gives a smaller variance and a low probability to values greater than 4 for the between-study variance.

DIC

For model comparison, we examine the deviance information criterion (DIC). To compare between various models, we need a Bayesian model selection technique. There

are many Bayesian approaches to model selection. Some examples are posterior model probabilities, Bayes factor, and posterior predictive checks. However, some of these methods are not well defined with vague prior while the others are not automatic nor easily reduced to a unique, single number summary. I used the recently developed DIC which is a hierarchical model generalization of AIC. The structure of DIC allows for automatic computation using WINBUGS.

DIC consists of two components, a term that measures goodness-of-fit and a penalty term for increasing model complexity:

$$\text{DIC}= \overline{D}+ p_D$$

The first term, $\overline{D}$, is defined as the posterior expectation of the deviance:

$$\overline{D} = E_{\theta|y}[D(\overline{\theta})] = E_{\theta|y}[-2\ln f(y\,|\,\overline{\theta})]$$

The better the model fits the data, the smaller is the value of $\overline{D}$.

The second component, p_D, measures the complexity of the model by the effective number of parameters and is defined as the difference between the posterior mean of the deviance and the deviance evaluated at the posterior mean of the deviance and the deviance evaluated at the posterior mean $\overline{\theta}$ of the parameters.

$$p_D = \overline{D} - D(\overline{\theta}) = E_{\theta|y}[D(\theta)] - D(E_{\theta|y}[\theta]) = E_{\theta|y}[-2\ln f(y\,|\,\theta)] + 2\ln f(y\,|\,\overline{\theta})$$

The above expression shows that p_D can be regarded as the expected excess of the true over the estimated residual information in data y conditional on θ. Hence, p_D can be interpret as the expected reduction in uncertainty due to estimation. Rearranging

$$p_D = \overline{D} - D(\overline{\theta}) = E_{\theta|y}[D(\theta)] - D(E_{\theta|y}[\theta]) = E_{\theta|y}[-2\ln f(y\,|\,\theta)] + 2\ln f(y\,|\,\overline{\theta})$$

Give

$$\overline{D} = D(\overline{\theta}) + p_D$$

As a result, DIC can be represented as

$$\overline{D} = D(\overline{\theta}) + 2p_D$$

DIC can be computed based on the MCMC sample, and is reported automatically by WINBUGS. The interpretation of DIC is similar to that of the AIC., as a single-number summary of the relative fit between the model and the 'true model' generating the data, from the perspective of prediction, conditional on the clusters in the hierarchy. The smaller the DIC the better the fit and in analogy with AIC, a difference larger than 10 is overwhelming evidence in favor of the better model. The effective number of parameters p_D in effect counts the random effects as a fraction, and comparing them between different models gives a sense of how strongly are they 'shrunk' by the hierarchical distribution assumption.

Results

The scale parameters of the non-inferiority clinical trial in the Bayesian Model are tested on the prior distributions presented by Lambert et al (2005). The data set is from a non-inferiority trial on mildly asthmatic patients given by Pigeot et al (2003).

Tables 1 through 12 shows the estimated values for the parameters of the experimental, reference and placebo treatment. Figure 1 through figure 12 shows the

posterior distributions for the parameters of the experimental, reference, and placebo treatment.

The posterior Probability is

$P(H_1) = \frac{1}{M}\sum_{i=1}^{M} I(\mu_{E_i} - \mu_{R_i} > f(\mu_{R_i} - \mu_{P_i}))$ where i=1,……..1100 is the MCMC sample. From the WINBUG model, pho symbolize the posterior probability for all twelve models.

Discussion

In this paper, the evaluation of a non-inferiority trial involving three arms was performed. I used twelve different prior distributions for the variance parameters. One data set was involved in non-inferiority model. The data was from a trial involving mildly asthmatic patients. The model that involved prior 9 is considered an outlier. The data obtained for the experimental standard deviation, experimental variance, placebo standard deviation, placebo variance, reference standard deviation, and reference variance is inconsistent with the other prior distribution data. The posterior distribution for all twelve models is 1. The Deviance Information Criterion (DIC) gives use an indication of which model is the best fit. The model with the lowest DIC is the best overall fit for the data. From the DIC printout, the model involving prior 4 has the lowest DIC total 229.351

Table 1: Table 1 shows the estimated values, standard deviation, Monte Carlo error median, and 97.5% credible interval for the experimental mean.

emu	mean	sd	MC error	2.5%	Median	97.5 %	Start	Sample
Prior1	4.321	0.2019	0.001991	3.919	4.321	4.72	1	11000
Prior2	4.32	0.2012	0.001971	3.92	4.32	4.718	1	11000
Prior3	4.32	0.2032	0.001759	3.921	4.319	4.722	1	11000
Prior4	4.32	0.201	0.001858	3.932	4.321	4.715	1	11000
Prior5	4.32	0.2095	0.002037	3.912	4.316	4.733	1	11000
Prior6	4.32	0.2109	0.002042	3.898	4.319	4.74	1	11000
Prior7	4.319	0.2112	0.001913	3.9	4.32	4.729	1	11000
Prior8	4.321	0.2092	0.001963	3.904	4.323	4.73	1	11000
Prior9	4.319	0.2009	0.001916	3.924	4.316	4.717	1	11000
Prior10	4.32	0.2053	0.001906	3.912	4.32	4.729	1	11000
Prior11	4.323	0.2052	0.002114	3.91	4.321	4.733	1	11000
Prior12	4.32	0.2043	0.002057	3.914	4.32	4.722	1	11000

Table 2: Table 2 shows the estimated values, standard deviation, Monte Carlo error median, and 97.5% credible interval for the experimental standard deviation.

esd	Mean	SD	MCerror	2.5%	Median	97.5%	Start	Sample
Prior1	1.186	0.1488	0.001695	0.9388	1.171	1.516	1	11000
Prior2	1.185	0.1481	0.001653	0.9388	1.17	1.514	1	11000
Prior3	1.187	0.1492	0.001422	0.9377	1.171	1.521	1	11000
Prior4	1.1186	0.1483	0.001442	0.9398	1.172	1.518	1	11000
Prior5	1.224	0.1583	0.001614	0.9605	1.207	1.587	1	11000
Prior6	1.227	0.1595	0.001755	0.9597	1.21	1.588	1	11000
Prior7	1.225	0.1596	0.001542	0.9624	1.208	1.585	1	11000
Prior8	1.1225	0.1579	0.00158	0.9631	1.209	1.584	1	11000
Prior9	50.21	28.98	0.2753	2.365	50.48	97.57	1	11000
Prior10	1.204	0.1515	0.001603	0.9496	1.19	1.541	1	11000
Prior11	1.205	0.153	0.001542	0.9488	1.189	1.545	1	11000
Prior12	1.2	0.1519	0.001582	0.9475	1.186	1.542	1	11000

Table 3: Table 3 shows the estimated values, standard deviation, Monte Carlo error median, and 97.5% credible interval for the experimental tau.

etau	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
Prior1	0.7435	0.1816	0.002099	0.4354	0.7298	1.135	1	11000
Prior2	0.7446	0.1814	0.002069	0.4366	0.7304	1.135	1	11000
Prior3	0.7422	0.1796	0.00156	0.4322	0.729	1.137	1	11000
Prior4	0.7435	0.1803	0.001653	0.4347	0.7286	1.132	1	11000
Prior5	0.7001	0.1751	0.00166	0.397	0.6861	1.084	1	11000
Prior6	0.6973	0.1756	0.001737	0.3968	0.6828	1.086	1	11000
Prior7	0.699	0.1751	0.001714	0.3979	0.6852	1.08	1	11000
Prior8	0.6993	0.1747	0.001736	0.3986	0.6847	1.0781	1	11000
Prior9	0.7422	0.1802	0.001595	0.4295	0.7291	1.141	1	11000
Prior10	0.7215	0.1767	0.001777	0.4213	0.7066	1.109	1	11000
Prior11	0.7218	0.1778	0.001763	0.4193	0.7077	1.111	1	11000
Prior12	0.7267	0.1789	0.001769	0.4208	0.7107	1.114	1	11000

Table 4: Table 4 shows the estimated values, standard deviation, Monte Carlo error median, and 97.5% credible interval for the experimental variance.

evar	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
Prior1	1.429	0.3675	0.004133	0.8814	1.37	2.297	1	11000
Prior2	1.427	0.3654	0.004016	0.8814	1.369	2.291	1	11000
Prior3	1.432	0.3706	0.003727	0.8793	1.372	2.315	1	11000
Prior4	1.429	0.3664	0.003668	0.8832	1.373	2.304	1	11000
Prior5	1.523	0.4058	0.00425	0.9225	1.458	2.52	1	11000
Prior6	1.531	0.4092	0.004679	0.921	1.465	2.521	1	11000
Prior7	1.527	0.4132	0.003969	0.9262	1.459	2.514	1	11000
Prior8	1.525	0.4038	0.004041	0.9275	1.461	2.51	1	11000
Prior9	3361.0	2996.0	28.33	5.591	2549.0	9529.0	1	11000
Prior10	1.473	0.3805	0.004114	0.9017	1.415	2.374	1	11000
Prior11	1.474	0.385	0.003957	0.9002	1.413	2.386	1	11000
Prior12	1.469	0.3845	0.003767	0.8894	1.409	2.386	1	11000

Table 5: Table 5 shows the estimated values, standard deviation, Monte Carlo error median, and 97.5% credible interval for the proportion of Ho:.

p	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
Prior1	3.977	0.2124	0.002094	3.56	3.977	4.397	1	11000
Prior2	3.976	0.2117	0.002091	3.561	3.976	4.396	1	11000
Prior3	3.976	0.2153	0.001944	3.551	3.974	4.399	1	11000
Prior4	3.975	0.2121	0.001964	3.562	3.976	4.392	1	11000
Prior5	3.974	0.2212	0.002166	3.541	3.975	4.405	1	11000
Prior6	3.976	0.2223	0.002085	3.533	3.975	4.412	1	11000
Prior7	3.975	0.2233	0.002045	3.536	3.977	4.407	1	11000
Prior8	3.977	0.2209	0.002099	3.539	3.978	4.407	1	11000
Prior9	3.974	0.2123	0.002088	3.555	3.974	4.395	1	11000
Prior10	3.975	0.2162	0.002027	3.544	3.976	4.392	1	11000
Prior11	3.979	0.2179	0.002148	3.545	3.978	4.41	1	11000
Prior12	3.974	0.2156	0.002059	3.556	3.976	4.398	1	11000

Table 6: Table 6 shows the estimated values, standard deviation, Monte Carlo error median, and 97.5% credible interval for the posterior probability.

pho	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
Prior1	1	0	9.535E-10	1	1	1	1	11000
Prior2	1	0	9.535E-10	1	1	1	1	11000
Prior3	1	0	9.535E-13	1	1	1	1	11000
Prior4	1	0	9.535E-13	1	1	1	1	11000
Prior5	1	0	9.535E-13	1	1	1	1	11000
Prior6	1	0	9.535E-13	1	1	1	1	11000
Prior7	1	0	9.535E-13	1	1	1	1	11000
Prior8	1	0	9.535E-13	1	1	1	1	11000
Prior9	1	0	9.535E-13	1	1	1	1	11000
Prior10	1	0	9.535E-13	1	1	1	1	11000
Prior11	1	0	9.535E-13	1	1	1	1	11000
Prior12	1	0	9.535E-13	1	1	1	1	11000

Table 7: Table 7 shows the estimated values, standard deviation, Monte Carlo error median, and 97.5% credible interval for the placebo mean

pmu	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
Prior1	3.135	0.2286	0.002334	2.677	3.133	3.596	1	11000
Prior2	3.136	0.229	0.002255	2.677	3.135	3.598	1	11000
Prior3	3.134	0.2318	0.002156	2.671	3.134	3.6	1	11000
Prior4	3.131	0.2261	0.002152	2.675	3.131	3.5714	1	11000
Prior5	3.136	0.2451	0.002368	2.656	3.137	3.632	1	11000
Prior6	3.136	0.2434	0.002319	2.654	3.135	3.624	1	11000
Prior7	3.133	0.2471	0.002125	2.654	3.131	3.632	1	11000
Prior8	3.133	0.2431	0.002144	2.654	3.13	3.628	1	11000
Prior9	3.135	0.229	0.002188	2.68	3.135	3.582	1	11000
Prior10	3.136	0.234	0.002018	2.68	3.133	3.593	1	11000
Prior11	3.137	0.2399	0.002049	2.666	3.139	3.619	1	11000
Prior12	3.132	0.2338	0.002052	2.67	3.131	3.607	1	11000

Table 8: Table 8 shows the estimated values, standard deviation, Monte Carlo error median, and 97.5% credible interval for the placebo standard deviation

psd	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
Prior1	1.012	0.1751	0.001763	0.7376	0.99	1.421	1	11000
Prior2	1.011	0.1734	0.001786	0.7391	0.9891	1.415	1	11000
Prior3	1.009	0.17	0.00178	0.741	0.9862	1.409	1	11000
Prior4	1.013	0.1722	0.001884	0.7408	0.9902	1.415	1	11000
Prior5	1.075	0.1966	0.002516	0.769	1.049	1.546	1	11000
Prior6	1.075	0.1948	0.002425	0.7651	1.048	1.533	1	11000
Prior7	1.077	0.2008	0.002115	0.7723	1.049	1.548	1	11000
Prior8	1.076	0.1962	0.002195	0.7722	1.049	1.539	1	11000
Prior9	50.2	28.9	0.278	2.698	50.17	97.36	1	11000
Prior10	1.036	0.1787	0.00179	0.753	1.015	1.451	1	11000
Prior11	1.042	0.1831	0.002173	0.7498	1.017	1.468	1	11000
Prior12	1.035	0.1837	0.002284	0.7518	1.009	1.454	1	11000

Table 9: Table 9 shows the estimated values, standard deviation, Monte Carlo error median, and 97.5% credible interval for the placebo tau.

ptau	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
Prior1	1.061	0.3477	0.003442	0.4953	1.02	1.839	1	11000
Prior2	1.062	0.3455	0.00343	0.5	1.022	1.831	1	11000
Prior3	1.062	0.337	0.003204	0.5037	1.028	1.822	1	11000
Prior4	1.056	0.3412	0.003412	0.003685	1.02	1.824	1	11000
Prior5	0.9478	0.3275	0.003873	0.4187	0.9082	1.691	1	11000
Prior6	0.9479	0.3276	0.003485	0.4257	0.9105	1.708	1	11000
Prior7	0.9461	0.3256	0.003301	0.418	0.9094	1.677	1	11000
Prior8	0.9473	0.3254	0.003455	0.4224	0.9095	1.679	1	11000
Prior9	1.057	0.3401	0.003132	0.5098	1.018	1.817	1	11000
Prior10	1.012	0.3325	0.003123	0.4753	0.9714	1.764	1	11000
Prior11	1.004	0.3351	0.003466	0.4641	0.9669	1.779	1	11000
Prior12	1.016	0.3353	0.003856	0.4728	0.9821	1.77	1	11000

Table 10: Table 10 shows the estimated values, standard deviation, Monte Carlo error median, and 97.5% credible interval for the placebo variance.

pvar	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
Prior1	1.054	0.3834	0.003899	0.544	0.9801	2.019	1	11000
Prior2	1.052	0.3783	0.003958	0.5463	0.9783	2.001	1	11000
Prior3	1.047	0.3708	0.004056	0.5491	0.9725	1.985	1	11000
Prior4	1.056	0.3763	0.00417	0.5488	0.9805	2.001	1	11000
Prior5	1.195	0.4614	0.006013	0.5914	1.101	2.39	1	11000
Prior6	1.194	0.4522	0.005885	0.5854	1.098	2.35	1	11000
Prior7	1.2	0.4921	0.005244	0.5964	1.1	2.396	1	11000
Prior8	1.195	0.4581	0.005187	0.5962	1.1	2.368	1	11000
Prior9	3356.0	2993	28.17	7.281	2517.0	9479.0	1	11000
Prior10	1.106	0.3992	0.004107	0.567	1.03	2.105	1	11000
Prior11	1.118	0.4126	0.005079	0.5622	1.034	2.155	1	11000
Prior12	1.106	0.4204	0.005398	0.5652	1.018	2.115	1	11000

Table 11: Table 11 shows the estimated values, standard deviation, Monte Carlo error median, and 97.5% credible interval for the reference mean.

rmu	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
Prior1	4.853	0.2497	0.002543	4.363	4.85	5.358	1	11000
Prior2	4.853	0.2495	0.002511	4.361	4.849	5.359	1	11000
Prior3	4.858	0.2479	0.002588	4.364	4.855	5.353	1	11000
Prior4	4.855	0.2503	0.002179	4.35	4.855	5.355	1	11000
Prior5	4.862	0.2578	0.003147	4.324	4.865	5.392	1	11000
Prior6	4.858	0.2688	0.002477	4.323	4.857	5.385	1	11000
Prior7	4.853	0.2642	0.002466	4.326	4.851	5.376	1	11000
Prior8	4.853	0.2632	0.00257	4.329	4.852	5.38	1	11000
Prior9	4.862	0.2493	0.002666	4.368	4.861	5.355	1	11000
Prior10	4.86	0.2568	0.002336	4.347	4.861	5.369	1	11000
Prior11	4.858	0.2572	0.00253	4.355	4.854	5.366	1	11000
Prior12	4.862	0.259	0.002509	4.345	4.863	5.378	1	11000

Table 12: Table 12 shows the estimated values, standard deviation, Monte Carlo error median, and 97.5% credible interval for the reference standard deviation.

rsd	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
Prior1	1.072	0.1888	0.001673	0.7793	1.048	1.509	1	11000
Prior2	1.072	0.1879	0.001584	0.7806	1.047	1.514	1	11000
Prior3	1.078	0.1934	0.002206	0.7801	1.053	1.53	1	11000
Prior4	1.078	0.1872	0.00172	0.783	1.054	1.515	1	11000
Prior5	1.145	0.2151	0.003134	0.8122	1.114	1.646	1	11000
Prior6	1.149	0.2149	0.00281	0.8111	1.12	1.661	1	11000
Prior7	1.143	0.2149	0.002218	0.8128	1.113	1.643	1	11000
Prior8	1.141	0.2093	0.002305	0.8128	1.112	1.632	1	11000
Prior9	50.29	28.84	0.2448	2.556	50.29	97.73	1	11000
Prior10	1.107	0.199	0.00209	0.8004	1.08	1.581	1	11000
Prior11	1.107	0.1979	0.00231	0.7995	1.081	1.565	1	11000
Prior12	1.106	0.2027	0.002113	0.797	1.075	1.58	1	11000

Table 13: Table 13 shows the estimated values, standard deviation, Monte Carlo error median, and 97.5% credible interval for the reference tau.

rtau	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
Prior1	0.9478	0.3138	0.002776	0.4393	0.9113	1.647	1	11000
Prior2	0.9475	0.312	0.00264	0.4366	0.9125	1.642	1	11000
Prior3	0.9391	0.3134	0.0032	0.4273	0.9028	1.643	1	11000
Prior4	0.9362	0.31	0.002754	0.4359	0.9004	1.632	1	11000
Prior5	0.8394	0.2944	0.00374	0.3693	0.8054	1.516	1	11000
Prior6	0.8344	0.2973	0.003506	0.3627	0.7978	1.52	1	11000
Prior7	0.842	0.2961	0.003166	0.3703	0.807	1.515	1	11000
Prior8	0.8435	0.295	0.003234	0.3755	0.8086	1.515	1	11000
Prior9	0.9409	0.3141	0.003177	0.4285	0.9058	1.646	1	11000
Prior10	0.8916	0.3002	0.002709	0.4001	0.857	1.561	1	11000
Prior11	0.8911	0.3005	0.003038	0.4088	0.8556	1.565	1	11000
Prior12	0.8938	0.3022	0.002741	0.4008	0.8648	1.576	1	11000

Table 14: Table 14 shows the estimated values, standard deviation, Monte Carlo error median, and 97.5% credible interval for the reference variance.

rvar	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
Prior1	1.185	0.4406	0.00391	0.6074	1.097	2.278	1	11000
Prior2	1.184	0.4386	0.003725	0.6093	1.096	2.292	1	11000
Prior3	1.199	0.4646	0.005623	0.6086	1.108	2.341	1	11000
Prior4	1.197	0.434	0.004069	0.6131	1.111	2.295	1	11000
Prior5	1.357	0.5478	0.008286	0.6596	1.242	2.709	1	11000
Prior6	1.367	0.5328	0.007129	0.6578	1.254	2.76	1	11000
Prior7	1.354	0.5397	0.005413	0.6607	1.239	2.7	1	11000
Prior8	1.346	0.5156	0.005622	0.6607	1.237	2.664	1	11000
Prior9	3361.0	2991	25.35	6.535	2529.0	9551	1	11000
Prior10	1.265	0.4796	0.00536	0.6406	1.167	2.5	1	11000
Prior11	1.265	0.4751	0.005815	0.6391	1.169	2.449	1	11000
Prior12	1.265	0.5008	0.005573	0.6352	1.156	2.496	1	11000

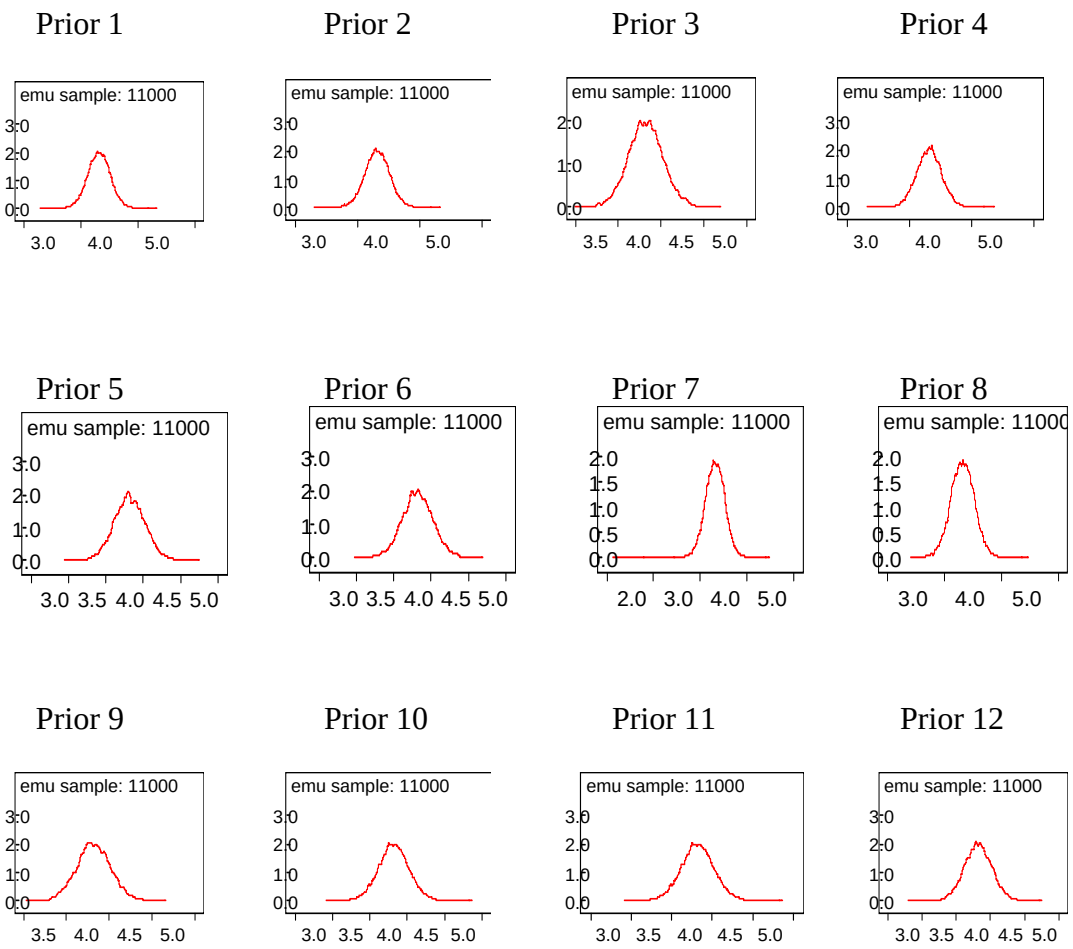

Figure 1: Figure 1 above shows posterior distributions of the experimental mean.

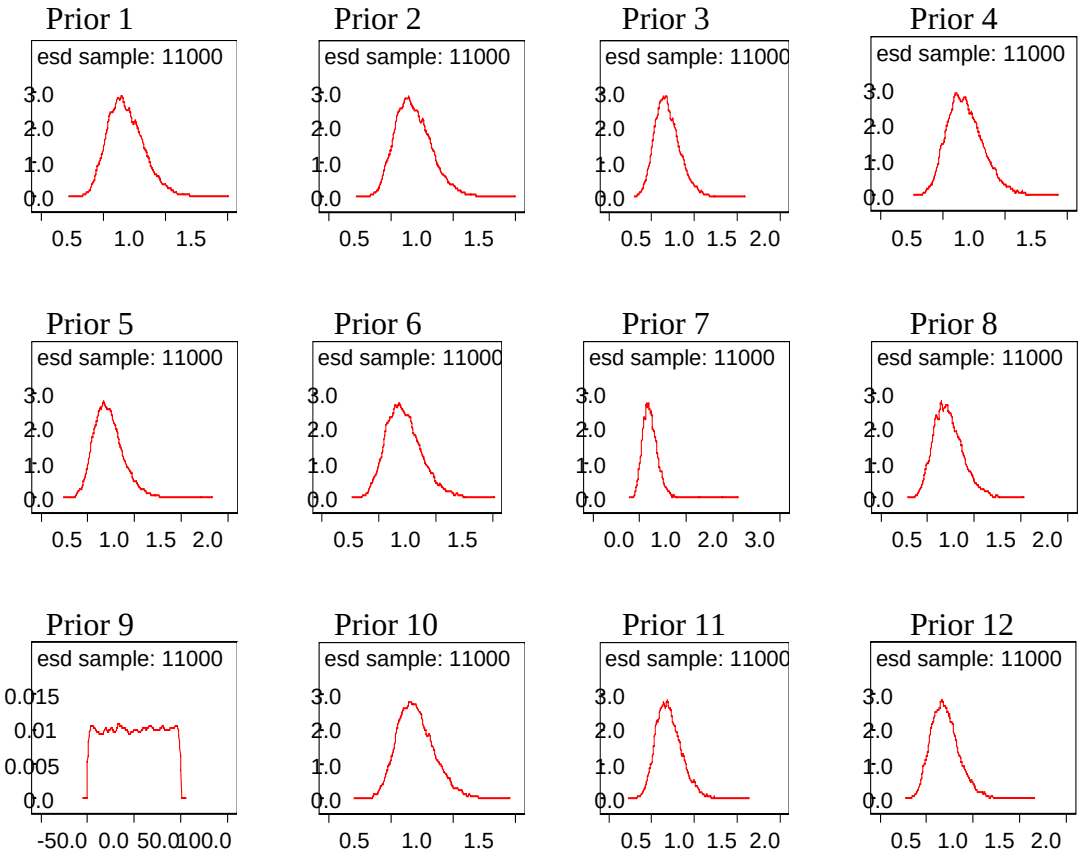

Figure 2: Figure 2 above shows posterior distributions of the experimental standard deviation.

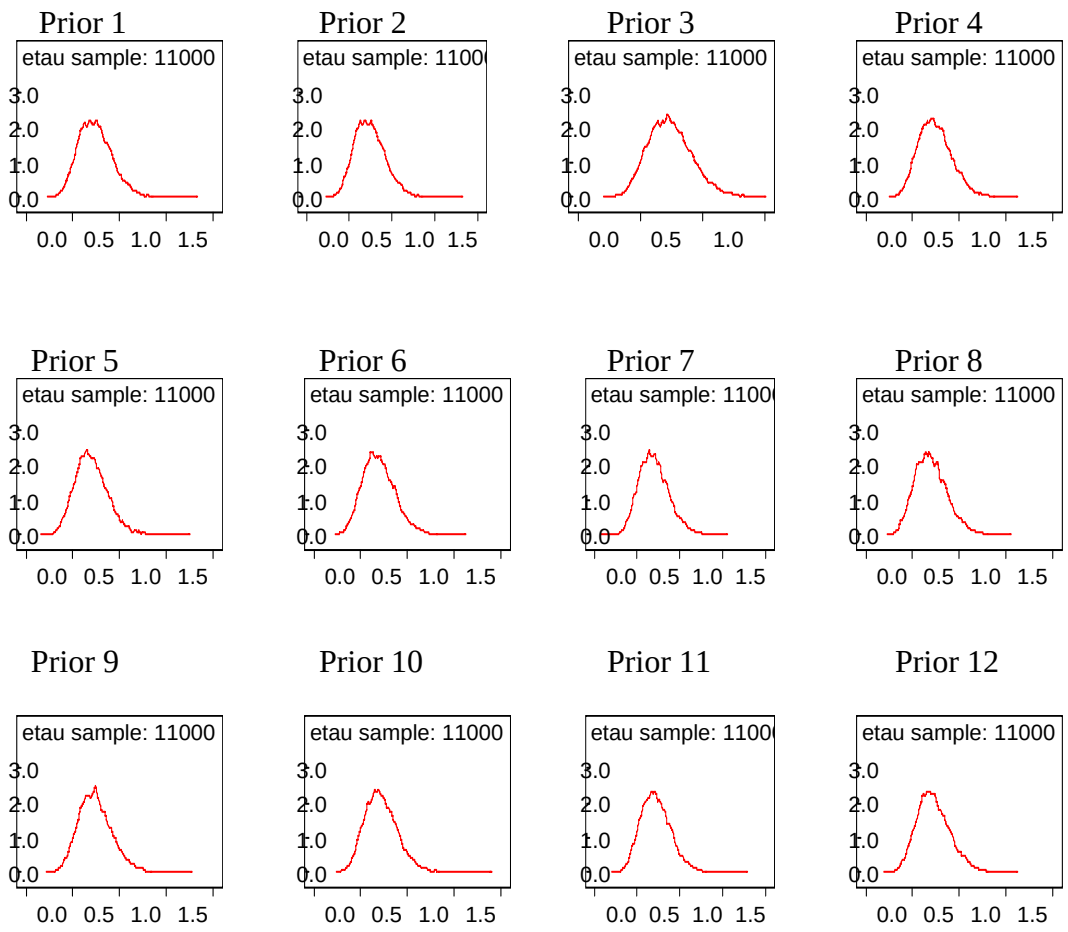

Figure 3: Figure 3 above shows posterior distributions of the experimental tau.

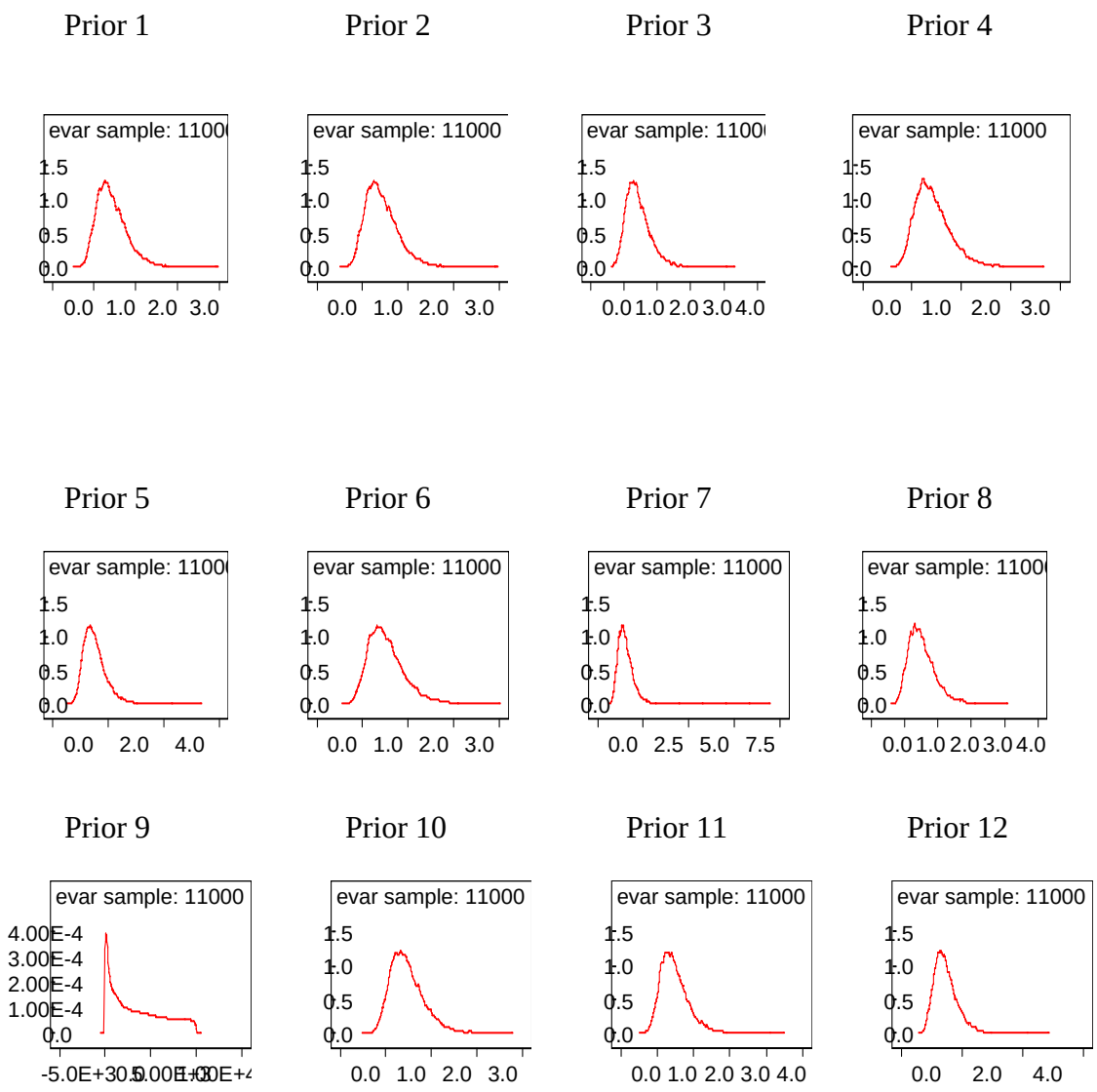

Figure 4: Figure 4 above shows posterior distributions of the experimental variance.

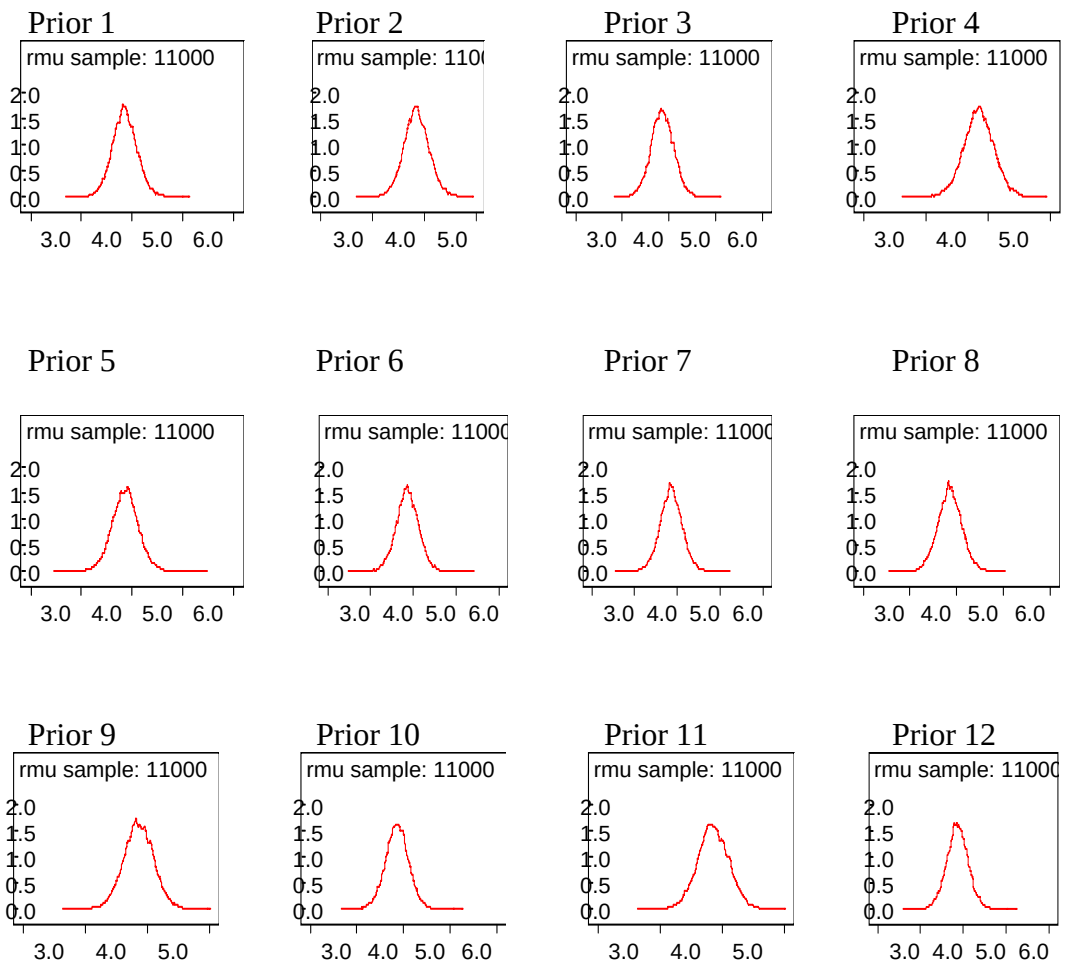

Figure 5: Figure 5 above shows posterior distributions of the reference mean.

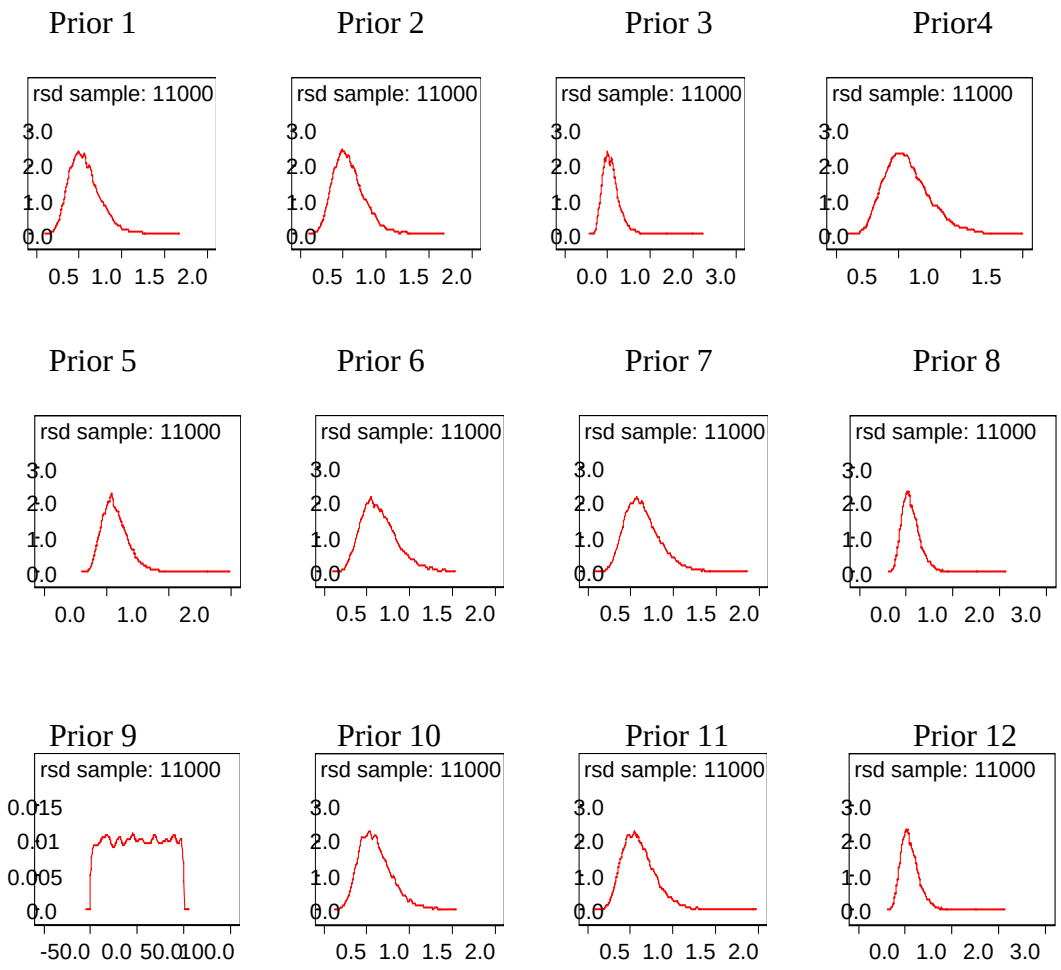

Figure 6: Figure 6 above shows posterior distributions of the reference standard deviation.

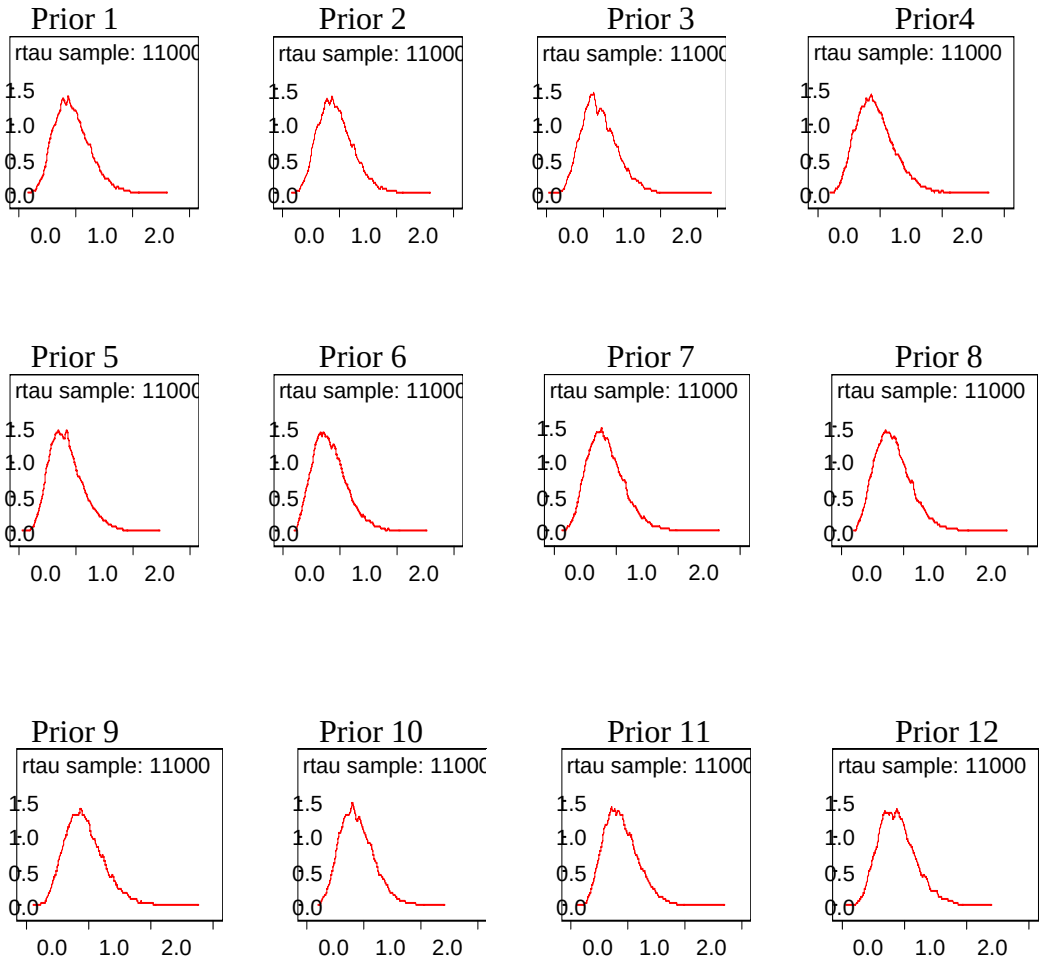

Figure 7: Figure 7 above shows posterior distributions of the reference tau.

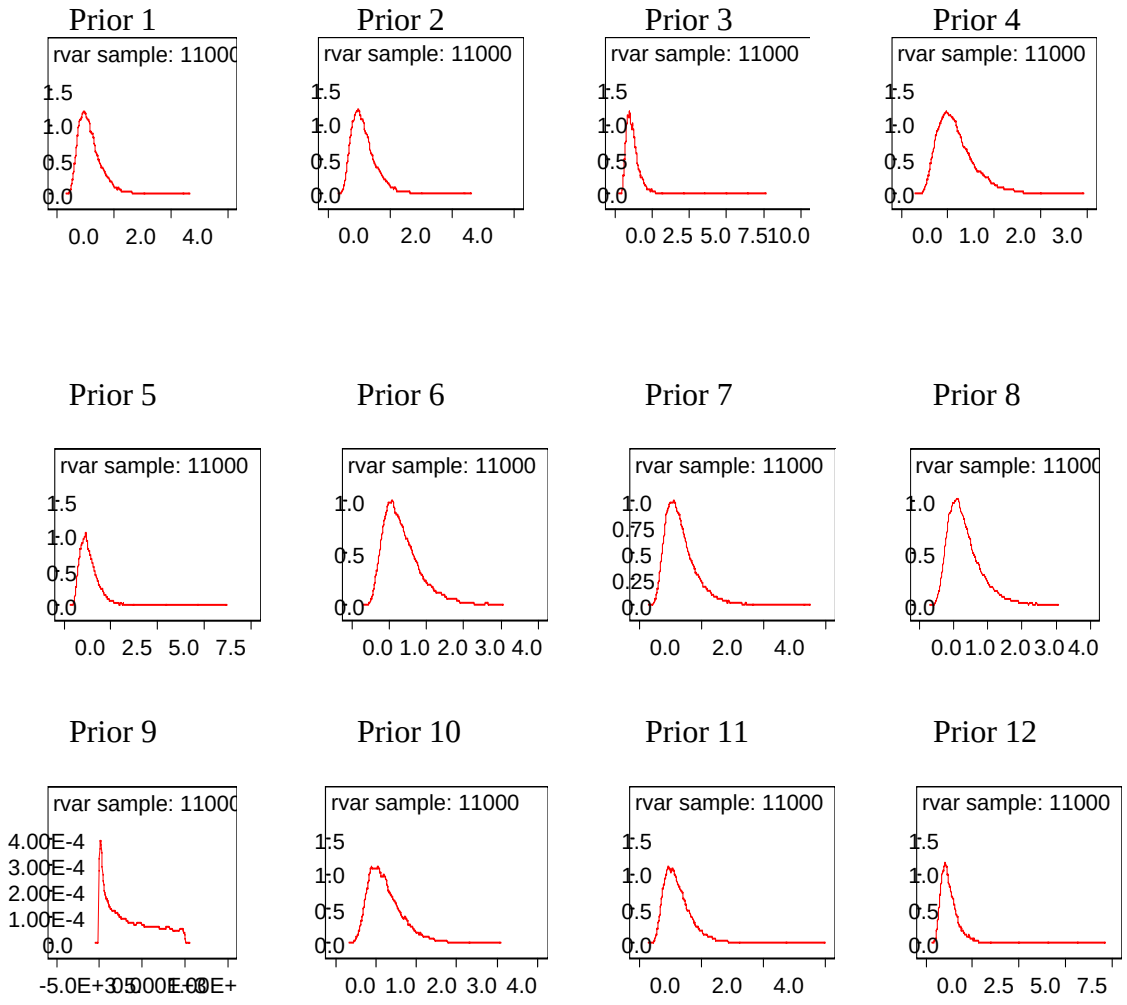

Figure 8: Figure 8 above shows posterior distributions of the reference variance.

Below shows the Deviance Information Criterion (DIC) for each prior distribution on the scale parameters for the model.

ex The experimental unit

px The placebo unit

rx The reference unit

Prior 1

Dbar = post.mean of -2logL; Dhat = -2LogL at post.mean of stochastic nodes

	Dbar	Dhat	pD	DIC
ex	110.782	108.736	2.046	112.828
px	56.651	54.575	2.076	58.728
rx	56.110	54.053	2.057	58.166
total	223.543	217.364	6.179	229.722

Prior 2

Dbar = post.mean of -2logL; Dhat = -2LogL at post.mean of stochastic nodes

	Dbar	Dhat	pD	DIC
ex	110.766	108.735	2.031	112.797
px	56.644	54.574	2.070	58.714
rx	56.099	54.054	2.046	58.145
total	223.509	217.363	6.146	229.656

Prior3

Dbar = post.mean of -2logL; Dhat = -2LogL at post.mean of stochastic nodes

	Dbar	Dhat	pD	DIC
ex	110.782	108.781	2.001	112.783
px	56.614	54.646	1.968	58.581
rx	56.125	54.152	1.973	58.098
total	223.520	217.579	5.942	229.462

Prior 4

Dbar = post.mean of -2logL; Dhat = -2LogL at post.mean of stochastic nodes

	Dbar	Dhat	pD	DIC
ex	110.767	108.777	1.990	112.756
px	56.595	54.661	1.934	58.529
rx	56.110	54.154	1.956	58.066
total	223.472	217.592	5.880	229.351

Prior 5

Dbar = post.mean of -2logL; Dhat = -2LogL at post.mean of stochastic nodes

	Dbar	Dhat	pD	DIC
ex	110.957	109.106	1.851	112.808
px	57.016	55.312	1.704	58.721
rx	56.479	54.809	1.670	58.149
total	224.453	219.228	5.225	229.678

Prior 6

Dbar = post.mean of -2logL; Dhat = -2LogL at post.mean of stochastic nodes

	Dbar	Dhat	pD	DIC
ex	111.011	109.135	1.875	112.886
px	56.985	55.287	1.698	58.683
rx	56.513	54.843	1.670	58.183
total	224.509	219.266	5.243	229.752

Prior 7

Dbar = post.mean of -2logL; Dhat = -2LogL at post.mean of stochastic nodes

	Dbar	Dhat	pD	DIC
ex	110.971	108.859	2.112	113.083
px	57.012	54.809	2.202	59.214
rx	56.454	54.280	2.174	58.628
total	224.437	217.948	6.489	230.926

Prior 8

Dbar = post.mean of -2logL; Dhat = -2LogL at post.mean of stochastic nodes

	Dbar	Dhat	pD	DIC
ex	110.954	108.858	2.096	113.050
px	56.994	54.806	2.189	59.183
rx	56.414	54.274	2.140	58.554
total	224.362	217.937	6.425	230.787

Prior 9

Dbar = post.mean of -2logL; Dhat = -2LogL at post.mean of stochastic nodes

	Dbar	Dhat	pD	DIC
ex	110.758	108.738	2.020	112.778
px	56.625	54.579	2.047	58.672
rx	56.135	54.062	2.072	58.207
total	223.518	217.379	6.139	229.657

Prior 10

Dbar = post.mean of -2logL; Dhat = -2LogL at post.mean of stochastic nodes

	Dbar	Dhat	pD	DIC
ex	110.827	108.905	1.922	112.748
px	56.718	54.859	1.859	58.578
rx	56.228	54.376	1.852	58.080
total	223.773	218.140	5.633	229.406

Prior 11

Dbar = post.mean of -2logL; Dhat = -2LogL at post.mean of stochastic nodes

	Dbar	**Dhat**	**pD**	**DIC**
ex	110.846	108.903	1.943	112.789
px	56.789	54.886	1.903	58.691
rx	56.246	54.380	1.866	58.111
total	223.521	218.169	5.712	229.591

Prior 12

Dbar = post.mean of -2logL; Dhat = -2LogL at post.mean of stochastic nodes

	Dbar	**Dhat**	**pD**	**DIC**
ex	110.826	108.881	1.945	112.771
px	56.751	54.857	1.894	58.645
rx	56.262	54.378	1.884	58.146
total	223.839	218.116	5.723	229.562

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APPENDIX

Prior 1

```
model{
for(i in 1:35){
ex[i]~dnorm(emu,etau);
}
emu~dnorm(0,0.0001);
etau~dgamma(0.001,0.001);
evar<-1/etau
esd<-sqrt(evar)

for(i in 1:19){
rx[i]~dnorm(rmu,rtau);
}
rmu~dnorm(0,0.0001);
rtau~dgamma(0.001,0.001);
rvar<-1/rtau
rsd<-sqrt(rvar)


for(i in 1:20){
px[i]~dnorm(pmu,ptau);
}
pmu~dnorm(0,0.0001);
ptau~dgamma(0.001,0.001);
pvar<-1/ptau
psd<-sqrt(pvar)

p<-emu- (1/5)*(rmu-pmu);
pho<-step(p-0);
}



list(etau=10,rtau=10, ptau=10)
```

Prior 2

```
model{
for(i in 1:35){
ex[i]~dnorm(emu,etau);
}
emu~dnorm(0,0.0001);
etau~dgamma(0.1,0.1);
evar<-1/etau
esd<-sqrt(evar)

for(i in 1:19){
rx[i]~dnorm(rmu,rtau);
}
rmu~dnorm(0,0.0001);
rtau~dgamma(0.1,0.1);
rvar<-1/rtau
rsd<-sqrt(rvar)

for(i in 1:20){
px[i]~dnorm(pmu,ptau);
}
pmu~dnorm(0,0.0001);
ptau~dgamma(0.1,0.1);
pvar<-1/ptau
psd<-sqrt(pvar)

p<-emu- (1/5)*(rmu-pmu);
pho<-step(p-0);
}
```

```
list(etau=10,rtau=10, ptau=10)
```

Prior 3

```
model{
for(i in 1:35){
ex[i]~dnorm(emu,etau);
}
emu~dnorm(0,0.0001);
etau~dgamma(0.1,0.1);
evar<-1/etau
esd<-sqrt(evar)

for(i in 1:19){
rx[i]~dnorm(rmu,rtau);
}
rmu~dnorm(0,0.0001);
rtau~dgamma(0.1,0.1);
rvar<-1/rtau
rsd<-sqrt(rvar)

for(i in 1:20){
px[i]~dnorm(pmu,ptau);
}
pmu~dnorm(0,0.0001);
ptau~dgamma(0.1,0.1);
pvar<-1/ptau
psd<-sqrt(pvar)

p<-emu- (1/5)*(rmu-pmu);
pho<-step(p-0);
}
```

```
list(etau=10,rtau=10, ptau=10)
```

Prior 4

```
model{
for(i in 1:35){
ex[i]~dnorm(emu,etau);
}
emu~dnorm(0,0.0001);
elv~dunif(-10,1.386)
log(evar)<-elv
etau<-1/evar
esd<-sqrt(evar)


for(i in 1:19){
rx[i]~dnorm(rmu,rtau);
}
rmu~dnorm(0,0.0001);
rlv~dunif(-10,1.386)
log(rvar)<-rlv
rtau<-1/rvar
rsd<-sqrt(rvar)


for(i in 1:20){
px[i]~dnorm(pmu,ptau);
}
pmu~dnorm(0,0.0001);
plv~dunif(-10,1.386)
log(pvar)<-plv
ptau<-1/pvar
psd<-sqrt(pvar)


p<-emu- (1/5)*(rmu-pmu);
pho<-step(p-0);
}

list(elv=.1,rlv=.1, plv=.1)
```

Prior 5

```
model{
for(i in 1:35){
ex[i]~dnorm(emu,etau);
}
emu~dnorm(0,0.0001);
evar~dunif(0,1000)
etau<-1/evar
esd<-sqrt(evar)

for(i in 1:19){
rx[i]~dnorm(rmu,rtau);
}
rmu~dnorm(0,0.0001);
rvar~dunif(0,1000)
rtau<-1/rvar
rsd<-sqrt(rvar)

for(i in 1:20){
px[i]~dnorm(pmu,ptau);
}
pmu~dnorm(0,0.0001);
pvar~dunif(0,1000)
ptau<-1/pvar
psd<-sqrt(pvar)

p<-emu- (1/5)*(rmu-pmu);
pho<-step(p-0);
}



list(evar=10,rvar=10, pvar=10)
```

Prior 6

```
model{
for(i in 1:35){
ex[i]~dnorm(emu,etau);
}
emu~dnorm(0,0.0001);
evar~dunif(0,4)
etau<-1/evar
esd<-sqrt(evar)

for(i in 1:19){
rx[i]~dnorm(rmu,rtau);
}
rmu~dnorm(0,0.0001);
rvar~dunif(0,4)
rtau<-1/rvar
rsd<-sqrt(rvar)


for(i in 1:20){
px[i]~dnorm(pmu,ptau);
}
pmu~dnorm(0,0.0001);
pvar~dunif(0,4)
ptau<-1/pvar
psd<-sqrt(pvar)


p<-emu- (1/5)*(rmu-pmu);
pho<-step(p-0);
}



list(evar=.1,rvar=.1, pvar=.1)
```

Prior 7

```
model{
for(i in 1:35){
ex[i]~dnorm(emu,etau);
}
emu~dnorm(0,0.0001);
etau~dpar(1,0.001);
evar<-1/etau
esd<-sqrt(evar)

for(i in 1:19){
rx[i]~dnorm(rmu,rtau);
}
rmu~dnorm(0,0.0001);
rtau~dpar(1,0.001);
rvar<-1/rtau
rsd<-sqrt(rvar)


for(i in 1:20){
px[i]~dnorm(pmu,ptau);
}
pmu~dnorm(0,0.0001);
ptau~dpar(1,0.001);
pvar<-1/ptau
psd<-sqrt(pvar)

p<-emu- (1/5)*(rmu-pmu);
pho<-step(p-0);
}



list(etau=.001,rtau=.001, ptau=.001)
```

Prior 8

```
model{
for(i in 1:35){
ex[i]~dnorm(emu,etau);
}
emu~dnorm(0,0.0001);
etau~dpar(1,0.25);
evar<-1/etau
esd<-sqrt(evar)


for(i in 1:19){
rx[i]~dnorm(rmu,rtau);
}
rmu~dnorm(0,0.0001);
rtau~dpar(1,0.25);
rvar<-1/rtau
rsd<-sqrt(rvar)


for(i in 1:20){
px[i]~dnorm(pmu,ptau);
}
pmu~dnorm(0,0.0001);
ptau~dpar(1,0.25);
pvar<-1/ptau
psd<-sqrt(pvar)


p<-emu- (1/5)*(rmu-pmu);
pho<-step(p-0);
}




list(etau=1,rtau=1,ptau=1)
```

Prior 9

```
model{
for(i in 1:35){
ex[i]~dnorm(emu,etau);
}
emu~dnorm(0,0.0001);
etau~dunif(0,100);
evar<-pow(esd,2)
esd~dunif(0,100)

for(i in 1:19){
rx[i]~dnorm(rmu,rtau);
}
rmu~dnorm(0,0.0001);
rtau~dunif(0,100);
rvar<-pow(rsd,2)
rsd~dunif(0,100)

for(i in 1:20){
px[i]~dnorm(pmu,ptau);
}
pmu~dnorm(0,0.0001);
ptau~dunif(0,100);
pvar<-pow(psd,2)
psd~dunif(0,100)


p<-emu- (1/5)*(rmu-pmu);
pho<-step(p-0);
}




list(etau=10,rtau=10, ptau=10)
```

Prior 10

```
 model{
for(i in 1:35){
ex[i]~dnorm(emu,etau);
}
emu~dnorm(0,0.0001);
etau<-1/evar
evar<-pow(esd,2)
esd~dunif(0,2)

for(i in 1:19){
rx[i]~dnorm(rmu,rtau);
}
rmu~dnorm(0,0.0001);
rtau<-1/rvar
rvar<-pow(rsd,2)
rsd~dunif(0,2)

for(i in 1:20){
px[i]~dnorm(pmu,ptau);
}
pmu~dnorm(0,0.0001);
ptau<-1/pvar
pvar<-pow(psd,2)
psd~dunif(0,2)



p<-emu- (1/5)*(rmu-pmu);
pho<-step(p-0);
}




list(esd=0.1,rsd=0.1, psd=0.1)
```

Prior 11

```
model{
for(i in 1:35){
ex[i]~dnorm(emu,etau);
}
emu~dnorm(0,0.0001);
etau<-1/evar
evar<-pow(esd,2)
esd~dnorm(0,0.01)I(0,)

for(i in 1:19){
rx[i]~dnorm(rmu,rtau);
}
rmu~dnorm(0,0.0001);
rtau<-1/rvar
rvar<-pow(rsd,2)
rsd~dnorm(0,0.01)I(0,)

for(i in 1:20){
px[i]~dnorm(pmu,ptau);
}
pmu~dnorm(0,0.0001);
ptau<-1/pvar
pvar<-pow(psd,2)
psd~dnorm(0,0.01)I(0,)



p<-emu- (1/5)*(rmu-pmu);
pho<-step(p-0);
}
```

```
list(esd=0.1,rsd=0.1, psd=0.1)
```

Prior 12

```
model{
for(i in 1:35){
ex[i]~dnorm(emu,etau);
}
emu~dnorm(0,0.0001);
etau<-1/evar
evar<-pow(esd,2)
esd~dnorm(0,0.1)I(0,)

for(i in 1:19){
rx[i]~dnorm(rmu,rtau);
}
rmu~dnorm(0,0.0001);
rtau<-1/rvar
rvar<-pow(rsd,2)
rsd~dnorm(0,0.1)I(0,)

for(i in 1:20){
px[i]~dnorm(pmu,ptau);
}
pmu~dnorm(0,0.0001);
ptau<-1/pvar
pvar<-pow(psd,2)
psd~dnorm(0,0.1)I(0,)



p<-emu- (1/5)*(rmu-pmu);
pho<-step(p-0);
}




list(esd=0.01,rsd=0.01, psd=0.01
```