Bayesian Analysis of Factors Associated with Fibromyalgia Syndrome Subjects

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**Abstract.** Factors contributing to movement-related fear were assessed by Russek, et al. 2014 for subjects with Fibromyalgia (FM) based on the collected data by a national internet survey of community-based individuals. The study focused on the variables, Activities-Specific Balance Confidence scale (ABC), Primary Care Post-Traumatic Stress Disorder screen (PC-PTSD), Tampa Scale of Kinesiophobia (TSK), a Joint Hypermobility Syndrome screen (JHS), Vertigo Symptom Scale (VSS-SF), Obsessive-Compulsive Personality Disorder (OCPD), Pain, work status and physical activity dependent from the “Revised Fibromyalgia Impact Questionnaire” (FIQR). The study presented in this paper revisits same data with a Bayesian analysis where appropriate priors were introduced for variables selected in the Russek’s paper.

**Keywords:** Bayes, Bayesian, Priors, Least Squares, Fibromyalgia, FIQR, FIQ, pain, movement

**INTRODUCTION**

Fibromyalgia syndrome (FM) is a condition of chronic widespread pain in the muscles with symptoms such as fatigue, balance disorders, sleep disturbance, headaches, cognitive difficulties, anxiety, morning stiffness, burning skin and depression [1, 2]. Of those diagnosed with FM, 85% are women with age between 16-68 years [3].

The factors contributing to movement-related fear were assessed for subjects with FM in a previous study by [4]. Based on the collected data, the contribution of Pain, Activity Balance Confidence (ABC), Vertigo Symptoms Scale (VSS) and Tampa Scale of Kinesiophobia (TSK) towards the Revised Fibromyalgia Impact Questionnaire (FIQR) [4] was shown using linear regression.

The current study applies a Bayesian methodology to the data set used in [4] using a linear model (similar to linear regression) and compares it with the results for the linear coefficients found in the previous work. Three cases for both non-standardized and standardized data are examined. Using a student-t likelihood with uniform priors, a Gaussian likelihood with uniform priors, and a Gaussian likelihood with a combination of Jeffreys and Gaussian priors. These were used to highlight the similarities and the differences of the parameter estimates (coefficients) in the current work with those in the previous work.
RELATED WORK

The data was collected using the Survey Monkey, and the Clinical Trials page of the National Fibromyalgia Association (NFA) website which consisted of valid questionnaires related to Fibromyalgia Impact Questionnaire-Revised (FIQR) [5], demographic and work status information [4], Activity Balance Confidence (ABC) [6], work and leisure activity level [4], Vertigo Symptoms Scale short form (VSS) [7], Tampa Scale of Kinesiophobia (TSK) [8], Joint Hypermobility Questionnaire (JHS) [9], Obsessive Compulsive Personality Disorder screen (OCPD) [10], Primary Care Post-Traumatic Stress Disorder screen (PC-PTSD) [11], and Pain [4] over a period of 24 months. This survey identified 1125 individuals having FM diagnosed by a health care provider from the 1363 that responded.

The same factors (Pain, ABC, VSS and TSK) as in [4], were considered in the Bayesian analysis in order to maintain consistency. The Multivariate regression analysis for FIQR with non-standardized and standardized coefficients are given in eq. (1) and (2) respectively from [4], which shows the variable Pain has the highest importance and should be concerned more when treating the patients.

\[
FIQR = 17.149 + 4.902(Pain) - 0.143(ABC) + 0.274(VSS) + 0.386(TSK) \quad (1)
\]

\[
FIQR = 4.014 \times 10^{-17} + 0.517(Pain) - 0.210(ABC) + 0.192(VSS) + 0.167(TSK) \quad (2)
\]

METHODOLOGY

Bayes’ theorem is an expression for the conditional probability of \( \theta \) given \( D \), which is equal to

\[
P(\theta|D) = \frac{P(\theta)P(D|\theta)}{P(D)}
\]

For the current study, \( \theta \) will be the set of parameters related to the assumed linear model and \( D \) is a set of observations. In this study, the maximum of the posterior (MAP) will be used as the estimates for the parameters. It should be noted that the posterior will be symmetric and unimodal because of the Gaussian likelihood that is used. Therefore, the MAP is equivalent to the mean and median.

The denominator, \( P(D) \), which is sometimes called the “evidence”, is a constant and so does not influence the estimates. Therefore, eq. (3) can be rewritten as,

\[
P(\theta|D) \propto P(\theta)P(D|\theta)
\]

The MAP estimate was determined for the posterior by taking the log of the posterior, which is the sum of logarithm of the priors and logarithm of the likelihood (shown in eq. (5)) to estimate the parameters of the model.

\[
\log P = \log(P(\theta|D)) = \log(P(\theta)) + \log(P(D|\theta)) + \text{proportionality constant}
\]

The study assumed the error associated with measurements was linear and Gaussian distributed. Therefore, a Gaussian likelihood was used as the model of the noise in the
measurements.

$$\text{error} = FIQR - (\theta_0 + \theta_1(Pain) + \theta_2(ABC) + \theta_3(VSS) + \theta_4(TSK)) \quad (6)$$

The uncertainties of the estimates (error bars) were computed by taking the square root of the diagonals of the covariance matrix, calculated by the negative inverse of the Hessian matrix $H$, which is the second derivatives of the log posterior function taken about the mean. Also the normalized uncertainties were computed by taking the uncertainties over its estimated parameter to compare the different methods.

$$\text{cov} = \begin{pmatrix}
\sigma^2_{\theta_0} & \sigma^2_{\theta_0,\theta_1} & \cdots & \sigma^2_{\theta_0,\theta_4} \\
\sigma^2_{\theta_0,\theta_1} & \sigma^2_{\theta_1} & \cdots & \sigma^2_{\theta_1,\theta_4} \\
\vdots & \vdots & \ddots & \vdots \\
\sigma^2_{\theta_0,\theta_4} & \sigma^2_{\theta_1,\theta_4} & \cdots & \sigma^2_{\theta_4}
\end{pmatrix} = -H^{-1} = - \begin{pmatrix}
\frac{\partial^2 \log P}{\partial \theta_0^2} & \frac{\partial^2 \log P}{\partial \theta_0 \partial \theta_1} & \cdots & \frac{\partial^2 \log P}{\partial \theta_0 \partial \theta_4} \\
\frac{\partial^2 \log P}{\partial \theta_0 \partial \theta_1} & \frac{\partial^2 \log P}{\partial \theta_1^2} & \cdots & \frac{\partial^2 \log P}{\partial \theta_1 \partial \theta_4} \\
\vdots & \vdots & \ddots & \vdots \\
\frac{\partial^2 \log P}{\partial \theta_0 \partial \theta_4} & \frac{\partial^2 \log P}{\partial \theta_1 \partial \theta_4} & \cdots & \frac{\partial^2 \log P}{\partial \theta_4^2}
\end{pmatrix}^{-1}
$$

Three different distributions for the priors and the likelihoods for non-standardized and standardized data were examined: Student-t likelihood with uniform priors, Gaussian likelihood with uniform priors, and Gaussian likelihood with a combination of Jeffreys and Gaussian priors. These were selected to compare and contrast the Bayesian analysis with that of the linear regression used in the previous work and are discussed below.

**Student-t Likelihood with Uniform Priors**

For this case, uniform (flat) priors were assumed. Since the uncertainty ($\sigma$) of the linear model was not specified, the Gaussian distribution is marginalized over all possible uncertainties to get a student-t distribution which was used for the likelihood.

$$P(D|\theta) \propto \left( \sum \text{error}^2 \right)^{-n/2} \quad (7)$$

where $n$ is the number of independent observations, which was 1125. Because of the uniform priors the posterior is proportional to the likelihood.

$$P(\theta|D) \propto \left( \sum \text{error}^2 \right)^{-n/2} \quad (8)$$

Thus, the logarithm of posterior function is a function of the logarithm of the model.

$$\log P = \log(P(\theta|D)) = -\frac{n}{2} \log \left( \sum \text{error}^2 \right) + \text{constant} \quad (9)$$

**Gaussian Likelihood with Uniform Priors**

For this case, it was assumed that the likelihood was Gaussian with uniform priors. The uncertainty in the Gaussian function, $\sigma$, is the model uncertainty, and was calculated
by \( \sqrt{\frac{\Sigma \text{error}^2}{n}} = 9.6496 \), which turns out to be the maximum likelihood estimate of \( \sigma \) for non-standardized data, and 0.592 for standardized data. Considering these facts, the likelihood for \( n \) independent observations can be written as,

\[
P(D|\theta) \propto \frac{1}{(2\pi\sigma^2)^{n/2}} e^{-\frac{1}{2\sigma^2} \sum \text{error}^2} \quad (10)
\]

This gives a logarithm of the posterior function as a relationship of the error term.

\[
\log P = \sum \frac{-\text{error}^2}{2\sigma^2} + \text{constant} \quad (11)
\]

**Gaussian Likelihood with a Combination of Jeffreys and Gaussian Priors**

For this case, the assumption made earlier that the priors are a constant was relaxed. Now Jeffreys priors are assumed for variables VSS and TSK, and Gaussian priors (from previous work) for variables Pain and ABC.

When considering priors for the coefficients for Pain and ABC, Gaussian priors were chosen since data relating to these parameters were found from a previous analysis [12] and [13]. Since it was difficult to get previous information on the exact relationship of interest, the search criteria was narrowed down into any linear regression of Fibromyalgia Impact Questionnaire (FIQ) that had any of the variables in the model. From a previous analysis, relationships for FIQ with Pain [12] and FIQ with ABC [13] were found. However, no previous data was found for VSS and TSK so they were assumed to have Jeffreys priors, a non-informative invariant prior, which for this case are constants [14].

For non-standardized data, Karsdorp and Vlaeyen discussed a correlation coefficient of 0.4 for FIQ with Pain having standard deviations of 1.82 and 2.02, respectively for 409 patients [12]. Jones et al. had a correlation coefficient of -0.64 between FIQ and ABC with standard deviations of 17.85 and 24.02, respectively for 32 patients with FM [13]. These results were incorporated into this study by assuming a simple linear regression for FIQ with Pain and ABC that lead to determine the coefficients of Pain and ABC as 0.3604 and -0.4756 respectively using the relationship of correlation coefficient (\( r \)) with covariance (\( \text{cov} \)) and standard deviations (\( s \)), and regression coefficients (\( \beta \)) as in eq. (12).

\[
r = \frac{\text{cov}(x,y)}{s_x s_y} \quad \text{and} \quad \beta = \frac{\text{cov}(x,y)}{s_x^2} \quad (12)
\]

where \( x \) = independent variable, \( y \) = dependent variable.

For standardized data, each calculated \( \beta \) was converted into standardized regression coefficients, \( \beta’ \), using eq. (13). The results were 0.4 and -0.64 for Pain and ABC respectively.

\[
\beta’ = \frac{s_x}{s_y} \beta \quad (13)
\]

Using these calculated regression coefficients \( \beta’ \)’s as the means of the Gaussian priors and the standard deviations (\( s \)) for the uncertainty in the Gaussian priors, the posterior is...
now shown to be proportional to these Gaussian priors for Pain and ABC, and a Gaussian
likelihood,
\begin{align*}
P(\theta | D) & \propto \frac{1}{\sqrt{2\pi \sigma_{\text{Pain}}^2}} e^{-\frac{(\theta_1 - \beta_{\text{Pain}})^2}{2\sigma_{\text{Pain}}^2}} \frac{1}{\sqrt{2\pi \sigma_{\text{ABC}}^2}} e^{-\frac{(\theta_2 - \beta_{\text{ABC}})^2}{2\sigma_{\text{ABC}}^2}} e^{-\frac{\sum - \text{error}^2}{2\sigma^2}}
\end{align*}

(14)

where \( \theta_1 \) and \( \theta_2 \) are the coefficients of Pain and ABC, and uncertainties of these
prior coefficients are \( \sigma_{\text{Pain}}^2 \) and \( \sigma_{\text{ABC}}^2 \), respectively. Based on the amount of prior data,
standard deviations for the priors were determined to be \( \ll 10 \) resulting in a much lower
total uncertainty. Uncertainties for both of the priors were assumed to be 10 to make
the model more robust. Thus, the logarithm of the posterior function becomes the sum of all
the exponential terms,
\begin{align*}
\log P &= -\frac{(\theta_1 - \beta_{\text{Pain}})^2}{2\sigma_{\text{Pain}}^2} - \frac{(\theta_2 - \beta_{\text{ABC}})^2}{2\sigma_{\text{ABC}}^2} + \sum - \frac{\text{error}^2}{2\sigma^2} + \text{constant}
\end{align*}

(15)

**RESULTS AND DISCUSSION**

Parameter estimates of the linear model using different analysis methods for a sample
of 1125 data points are shown in Table 1 for non-standardized data and Table 2 for stan-
dardized data, with standard deviations for each parameter estimate with the percentage
of the normalized uncertainties below the calculated value. To compare the uncertain-
ties occurred in the parameters, the total uncertainties were calculated summing all the
standard deviations of the parameters, and the total normalized uncertainty percentage
by summing all the percentages for the Bayesian analysis methods as shown in Table 1.

From the two tables (Table 1 & Table 2), it is evident that the parameter estimates
from student-t likelihood method are slightly different (a few decimal places) from the
Gaussian with uniform priors since these were marginalized over for the student-t model
from \( 0 \) to \( \infty \). It is clear that the student-t likelihood method is the least successful out
of all three, as it has the highest total uncertainty even though it is not a considerable
difference.

Parameter estimates using a Gaussian likelihood with uniform priors gave the same
outcome as the original linear regression method except the intercept for standardized
data. The reason for this is the errors were assumed to be Gaussian in linear regression,
and it followed the same as in Bayesian with constant priors. When comparing estimates
of student-t and Gaussian likelihood with uniform priors individually, uncertainties and
normalized uncertainties are small, except for the normalized uncertainty of the TSK
estimate for non-standardized data. The intercept parameter using a Gaussian likelihood
with uniform priors is much larger than the one calculated from student-t. There is a
considerable amount of change in the estimates with priors versus using a Student-t
likelihood or a Gaussian likelihood with uniform priors.

For non-standardized data, Gaussian likelihood with Gaussian priors for Pain and
ABC resulted in reducing the uncertainties of the intercept and Pain, while the rest re-
mained the same as in the Gaussian likelihood with Uniform priors case. The normalized
TABLE 1. Performance of regression analysis using different methods for parameter estimates for non-standardized data (N=1125 participants)

<table>
<thead>
<tr>
<th>Estimate</th>
<th>Method</th>
<th>Linear Regression</th>
<th>Student-t Likelihood</th>
<th>Gaussian Likelihood with Uniform Priors</th>
<th>Gaussian Likelihood with Gaussian Priors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>17.149</td>
<td>17.08390</td>
<td>17.14890</td>
<td>17.1566</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(2.37450)</td>
<td>(13.8626%)</td>
<td>(13.8395%)</td>
<td>(2.37440)</td>
</tr>
<tr>
<td>θ₀</td>
<td></td>
<td>(13.8995%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.902</td>
<td>4.85220</td>
<td>4.90240</td>
<td>4.9008</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.18699)</td>
<td>(3.8537%)</td>
<td>(3.8141%)</td>
<td>(0.18695)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(9.6716%)</td>
<td></td>
<td></td>
<td>(3.8147%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-0.143</td>
<td>-0.14184</td>
<td>-0.14285</td>
<td>-0.14287</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.01372)</td>
<td>(9.6027%)</td>
<td>(9.6013%)</td>
<td>(0.01372)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.274</td>
<td>0.27358</td>
<td>0.27374</td>
<td>0.27379</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.02940)</td>
<td>(10.7475%)</td>
<td>(10.7406%)</td>
<td>(0.02940)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(10.4548%)</td>
<td></td>
<td></td>
<td>(10.7389%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.386</td>
<td>0.39499</td>
<td>0.38620</td>
<td>0.38629</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.04547)</td>
<td>(11.7747%)</td>
<td>(11.7719%)</td>
<td>(0.04547)</td>
</tr>
<tr>
<td>θ₆</td>
<td></td>
<td>0.274</td>
<td>0.27358</td>
<td>0.27374</td>
<td>0.27379</td>
</tr>
<tr>
<td></td>
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<td>(0.02940)</td>
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<td>(0.02940)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(10.4548%)</td>
<td></td>
<td></td>
<td>(10.7389%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>2.65019</td>
<td>2.65007</td>
<td>2.64994</td>
<td></td>
</tr>
<tr>
<td>Uncertainty (%)</td>
<td>59.6854%</td>
<td>49.7783%</td>
<td>49.7663%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: θ₀, θ₁, θ₂, θ₃ and θ₄ are parameter estimates of intercept and variables Pain, ABC, VSS and TSK, respectively. Standard deviations of the estimates and percentages of normalized uncertainties are given in the top and bottom parenthesis, respectively in columns 3, 4 and 5.

Uncertainties were reduced when a Gaussian likelihood with Gaussian priors was used except for the estimate of Pain, regardless of having a prior. However, these results depend on the selection of values for \( \sigma^2_{\beta_{\text{Pain}}} \) and \( \sigma^2_{\beta_{\text{ABC}}} \).

For the standardized data, uncertainties for the estimates for the Gaussian likelihood with uniform priors are the same as in the Gaussian likelihood with Gaussian priors except for the intercept. The normalized uncertainties were reduced for the intercept and ABC. The intercept parameter for the Gaussian likelihood with Gaussian priors is about four hundred times larger than the intercept using a Gaussian likelihood with uniform priors.

The certainty of the priors changed the results of Gaussian likelihood with Gaussian priors case for non-standardized data. The high uncertainty of the priors resulted in similar estimations to the Gaussian likelihood with flat priors case. Having less uncertainty on the prior of Pain compared to ABC (\( \sigma^2_{\beta_{\text{Pain}}} < \sigma^2_{\beta_{\text{ABC}}} \)), resulted in a smaller total uncertainty by affecting the parameter estimates of Pain and the intercept. Similarly, for \( \sigma^2_{\beta_{\text{Pain}}} > \sigma^2_{\beta_{\text{ABC}}} \), a smaller total uncertainty attained for the parameter estimates ABC and the intercept. The total effect was small in this case \( \sigma^2_{\beta_{\text{Pain}}} < \sigma^2_{\beta_{\text{ABC}}} \) as compared to Pain because the uncertainty of the intercept parameter estimate has decreased. However, for the standardized data, the above changes did not effect the parameter estimates except for the intercept.
<table>
<thead>
<tr>
<th>Method</th>
<th>Linear Regression</th>
<th>Student-t Likelihood</th>
<th>Gaussian Likelihood with Uniform Priors</th>
<th>Gaussian Likelihood with Gaussian Priors</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \theta_0' )</td>
<td>4.014e-17</td>
<td>2.7829c-11 (0.01869) (6.717e10%)</td>
<td>-2.4505c-6 (0.01765) (72024%)</td>
<td>9.916e-4 (0.01765) (1779.9%)</td>
</tr>
<tr>
<td>( \theta_1' )</td>
<td>0.517</td>
<td>0.46279 (0.02086) (4.5084%)</td>
<td>0.51655 (0.01970) (3.8139%)</td>
<td>0.51652 (0.01970) (3.8141%)</td>
</tr>
<tr>
<td>( \theta_2' )</td>
<td>-0.210</td>
<td>-0.14704 (0.02136) (14.5238%)</td>
<td>-0.20997 (0.02016) (9.6038%)</td>
<td>-0.21001 (0.02016) (9.6017%)</td>
</tr>
<tr>
<td>( \theta_3' )</td>
<td>0.192</td>
<td>0.10272 (0.02181) (21.2302%)</td>
<td>0.19175 (0.02059) (10.7388%)</td>
<td>0.19173 (0.02059) (10.7402%)</td>
</tr>
<tr>
<td>( \theta_4' )</td>
<td>0.167</td>
<td>0.08604 (0.02083) (24.2107%)</td>
<td>0.16706 (0.01967) (11.7727%)</td>
<td>0.16706 (0.01967) (11.7727%)</td>
</tr>
<tr>
<td>Total Uncertainty</td>
<td></td>
<td>0.10355</td>
<td>0.09777</td>
<td>0.09777</td>
</tr>
<tr>
<td>Percentage of Total Normalized Uncertainty</td>
<td>6.7171e10%</td>
<td>720310%</td>
<td>1815.88%</td>
<td></td>
</tr>
</tbody>
</table>

Note: \( \theta_0', \theta_1', \theta_2', \theta_3' \) and \( \theta_4' \) are parameter estimates of intercept and variables Pain, ABC, VSS and TSK, respectively for standardized data. Standard deviations of the estimates and percentages of normalized uncertainties are given in the top and bottom parenthesis in columns 3, 4 and 5.

The total uncertainty is decreasing for non-standardized data with few assumptions, while it remains the same for Gaussian likelihood with uniform priors and Gaussian priors for standardized data. The percentage of total normalized uncertainty decreases for methods using few assumptions, and it makes a significant difference from Student-t likelihood to Gaussian likelihood for standardized data due to the impact of the intercept parameter.

Assumption of a Gaussian error for the model tends to give a sensible estimation because, a particular value was assigned for \( \sigma \) rather than taking all the possible values; Gaussian likelihood methods give better estimations than Student-t. In general, including a prior makes the estimation less uncertain. However, this observation was not noticed in this study when a large sample (n=1125) was considered, but if it was small, the results would have changed drastically.

**CONCLUSION**

Use of prior information demonstrates that the Bayesian solution reduces uncertainty in the estimations when compared to Gaussian likelihood with Uniform priors. For standardized data, the results follow the same as non-standardized except for intercept. The standard deviations for the priors were determined to be \(< 10 \) resulting in a much
lower total uncertainty based on the availability of prior information. A much higher standard deviation was used to demonstrate that even with a very high uncertain prior would result in better estimates.

Future work includes using the evidence to examine other models, both linear and nonlinear.

REFERENCES