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Abstract. Coronary artery disease (CAD) continues to be one of the leading causes of morbidity and mortality globally. Of particular relevance for this issue is that major efforts should be focused on understanding the risk factor involved. In this study, three types of Bayesian models, each with different prior distribution were considered to identify associated risk factors in CAD among Malaysian male patients presenting with ST-Elevation Myocardial Infarction (STEMI) and to obtain a feasible model to fit the data. The results of the three models were compared to find the best model. A total of 7180 STEMI male patients from the National Cardiovascular Disease Database-Acute Coronary Syndrome (NCVD-ACS) registry year 2006-2013 were analysed. Univariate and multivariate analyses for the three models were performed using one of the Bayesian Markov Chain Monte Carlo (MCMC) simulation approach known as Gibbs sampling. Models' performances are evaluated through overall model fit. Bayesian model C which used both Beta and Dirichlet prior distributions, consisted of six significant variables namely diabetes mellitus, family history of cardiovascular disease, chronic lung disease, renal disease, Killip class and age group was considered as the best model. The same set of variables that were observed to be significant in the Bayesian model C was also found to be significant in models A and B which used single prior distribution, respectively. Model C has a better fit than models A and B as the deviance value produced was the smallest. This study showed that posterior estimation was mostly influenced by the existing prior knowledge. Though applying the non-informative prior which were both Beta and Dirichlet distribution priors, model C can minimise uncertainty in making effective clinical decisions and provides better parameters estimates of the posterior distribution.

1. Introduction

Coronary artery disease (CAD) continues to be one of the leading causes of morbidity and mortality among men and women globally [1,2] and the figure of these deaths is predicted to grow to 23.6 million in the next 20 years [3,4]. CAD is caused by plaque build-up in the walls of the arteries that supply blood to the heart and other parts of the body [5]. The diagnosis of CAD was based on existing imaging reports

or on the cardiologist's estimation of CAD, if no imaging was performed. In patients referred for imaging, a significant stenosis (>50%) was considered to indicate CAD [6].

Males had a greater risk of suffering CAD and they also had attacks earlier in life [7,8]. Even worse, males with CAD are more likely to present with ST-Elevation Myocardial Infarction (STEMI) than unstable angina or non-ST-Elevation Myocardial Infarction (NSTEMI) [9,10]. Since CAD often develops over decades, males might not notice a problem until they have a significant blockage or a heart attack [11]. Sometimes a heart attack occurs without any apparent signs or symptoms. Chest pain or also known as angina remains the most ordinary symptom among males [12]. In medical treatments, physicians extremely often have to make numerous complicated and crucial decisions during the diagnosis of the patients. In fact, these decisions are filled of uncertainty and unpredictability. Of particular relevance for this issue is that major efforts should be focused on helping the physicians identifying and understanding the risk factor involved in CAD.

In order to identify the risk factor, Bayesian approach is applied. This approach has become a popular tool for meta-analysis of clinical data [13,14] and keeps statistics in the realm of the self-in light of new data [15]. Bayesian approach involves learning from evidence as it accumulates. This approach uses Bayes' Theorem to formally combine prior information (prior) with current information on a quantity of interest to make decisions about the future (posterior) [16,17]. When good prior information on medical use of a device exists, the Bayesian approach may allow this information to be included into the statistical analysis of a trial [18,19]. Therefore, choice of prior is very important in the development of Bayesian model.

In this study, three types of Bayesian models each with different prior were developed, only Beta prior with shape parameters $\alpha = \beta = 0.5$ [20–22] was assigned for the first Bayesian model (Model A). While only Dirichlet prior with $\alpha = (\alpha_i, \ldots, \alpha_K)$ [23] was assigned for the second Bayesian model (Model B) and both Beta and Dirichlet priors were assigned for the third Bayesian model (Model C). The reason of using various type of prior for each model is to see how this affects the risk factors in CAD among male patients presenting with STEMI and how does this improve the prediction of the proposed Bayesian model. The results of the three models were compared to obtain robust conclusions.

The organisation of this study is as such; it begins with an overview of the CAD, Bayesian approach and prior selection in Section 1, followed by materials and methods in Section 2. Next, is the results of proposed models in Section 3 and followed by a discussion of the findings of the analysis in Section 4. Finally, conclusion is given in Section 5.

2. Materials and Methods

2.1. Source of data

A total of 7180 male patients who were diagnosed with ST-Elevation Myocardial Infarction (STEMI) were selected from the National Cardiovascular Disease Database-Acute Coronary Syndrome (NCVD-ACS) registry for the years 2006 to 2013. Data was collected from the time the male patient with STEMI was admitted to the hospital till 30 days post discharge. Variables were categorized into demographic, risk factors, comorbidities, clinical presentation, and treatment. Killip classification in the clinical presentation predicts the chances of survival within 30 days in patients, in which Killip class IV having a higher possibility of dying [24].

2.2. Ethical approval

This NCVD registry study was approved by the Medical Review & Ethics Committee (MREC), Ministry of Health (MOH) Malaysia in 2007 (Approval Code: NMRR-07-20-250). MREC waived informed consent for NCVD.

2.3. Statistical methods

For the Bayesian analysis purpose, the data were split up into training and test dataset with the ratio of 70:30. The training dataset was used in model development while the test dataset was used for model validation. At first, to identify significant variables individually, univariate logit models were developed and followed by multivariate model to obtain the estimate posterior mean of parameters. Specifically, there are two things need to be assigned in any Bayesian analysis namely, the likelihood for the outcome variable and the prior. Here, data are kept as a likelihood function, which defined the strength of support gained from the observations for the numerous probable values of the parameter. Therefore, in this study, the likelihood function is assigned as Bernoulli distribution with the parameter μ, described as a logistic.

In the Bayesian model, the prior information about the unknown parameter of the statistical model plays a very important role, which requires to be identified and expressed in the form of a prior distribution [25]. In this study, non-informative priors were used because of a lack of information on the regression parameters. Beta distribution with shape parameters $\alpha = \beta = 0.5$ which is also known as Jeffreys prior Beta [20–22] and Dirichlet distribution with $\alpha = (\alpha_i, \ldots, \alpha_K)$ [23] were selected as priors. Three types of Bayesian models were developed, for the first Bayesian model (Model A), only Beta prior with shape parameters $\alpha = \beta = 0.5$ [20–22] was assigned. Whereas only Dirichlet prior with $\alpha = (\alpha_i, \ldots, \alpha_K)$ [23] was assigned for the second Bayesian model (Model B) and for the third Bayesian model (Model C), both Beta and Dirichlet priors were assigned.

This information gained from the prior distribution, $p(\theta)$ is multiplied by a likelihood function, $p(y|\theta)$ and then divided by the distribution of the data to produce posterior distribution, $p(\theta|y)$ which expresses the enhancement in the knowledge about the parameter after obtaining the data. This Bayesian methodology can be mathematically formulated through Bayes' theorem as in equation (1).

$$p(\theta|y) = \frac{p(\theta)p(y|\theta)}{p(y)} \tag{1}$$

The denominator is usually ignored as it does not have any parameters and it is constant. Thus, Bayes' theorem is re-expressed as

$$p(\theta|y) \propto p(\theta)p(y|\theta) \tag{2}$$

In this study, Beta prior, $p(\theta)$ is given by

$$p(\theta) = \frac{1}{\mathrm{B}(\alpha,\beta)}\theta^{\alpha-1}(1-\theta)^{\beta-1} \tag{3}$$

where $\mathrm{B}(\alpha,\beta) = \frac{\Gamma(\alpha)\Gamma(\beta)}{\Gamma(\alpha+\beta)}$, Γ is the Gamma function and $\alpha > 0$ and $\beta > 0$.

While Dirichlet prior, $p(\theta)$ is given by

$$p(\theta) = \mathrm{Dir}(\theta|\alpha) = \frac{1}{\mathrm{B}(\alpha)}\prod_{i=1}^{K}\theta_i^{\alpha_i-1} \tag{4}$$

Markov chain Monte Carlo (MCMC) method is then applied to estimate the posterior distribution. In short, MCMC is a method for simulating from the distributions of random quantities [16]. One of the MCMC algorithm known as Gibbs sampling is used. Three multiple parallel chains with different initial points were applied in the simulation work. The three Bayesian models each with different prior were then compared to obtain the best model. As for the performance measure of the proposed models, Brier score and deviance were utilised.

3. Results

Descriptive statistics was performed on the training dataset which consisted of 5026 male patients, and the results are shown in table 1. More than 50% of the STEMI male patients were from ethnic Malay (59.3%) followed by Chinese (18.5%) and Indian (17.7%). Majority of male patients were less than 65-year-old (81.2%). Smoking was the most prevalent risk factor for STEMI male patients with more than 75%. This was followed by hypertension and diabetes mellitus. While the most relevant comorbidity was myocardial infarction (MI) followed by renal disease. Most male patients fell into the Killip class I or II on presentation. As for the treatment, cardiac catheterisation was the most common procedure followed by the percutaneous coronary intervention (PCI).

Table 1. Male patients' characteristics.

Characteristic			n = 5026 (%)
Demographic	Ethnicity	Malay	2978 (59.3)
		Chinese	930 (18.5)
		Indian	888 (17.7)
		Others	230 (4.6)
	Age group	<65	4079 (81.2)
		≥65	947 (18.8)
Risk factor	Diabetes Mellitus	No	3241 (64.5)
		Yes	1785 (35.5)
	Hypertension	No	2584 (51.4)
		Yes	2442 (48.6)
	Smoking status	Never	1145(22.8)
		Active/former	3881 (77.2)
	Dyslipidaemia	No	3368 (67.0)
		Yes	1658 (33.0)
	Family history of CVD	No	4312 (85.8)
		Yes	714 (14.2)
Comorbidities	MI history	No	4352 (86.6)
		Yes	674 (13.4)
	Chronic lung disease	No	4923 (98.0)
		Yes	103 (2.0)
	Cerebrovascular disease	No	4893 (97.4)
		Yes	133 (2.6)
	Peripheral vascular disease	No	5014 (99.8)
		Yes	12(0.2)
	Renal disease	No	4870 (96.9)
		Yes	156 (3.1)
Clinical presentation	Killip class	Class I	3364 (66.9)
		Class II	1118 (22.2)
		Class III	184 (3.7)
		Class IV	360 (7.2)
Treatment	PCI	No	3353 (66.7)
		Yes	1673 (33.3)
	Cardiac catheterisation	No	3086 (61.4)
		Yes	1940 (38.6)

Although not presented, at the Bayesian univariate analysis for model A, of the fifteen variables, nine are found to be significant. The nine significant variables were then included into the Bayesian multivariate analysis to determine the prognostic factors. Six variables of the nine were identified to be significantly related with male CAD patient's mortality for model A namely diabetes mellitus, family

history of CVD, chronic lung disease, renal disease, Killip class and age group. Analogous univariate and multivariate analysis were carried out for model B and C.

As for models B and C, the significant variables were found to be similar as in model A for male patients. Comparison between the three Bayesian multivariate models' estimations for STEMI male patients respectively are shown in table 2. Remarkably, similar results were generated by almost all the variables in models B and C for male patients. Moreover, the odds ratios (OR) and the standard errors (SE) for models B and C were a little smaller than model A. Furthermore, the 95% credible intervals for models B and C were slightly narrower than model A which suggested improved precision.

Table 2. Bayesian models' estimations using different priors for STEMI male patients.

Variable	Bayesian model A (Beta prior)			Bayesian model B (Dirichlet prior)			Bayesian model C (Beta and Dirichlet priors)		
	β	SE	OR (95% Credible Interval)	β	SE	OR (95% Credible Interval)	β	SE	OR (95% Credible Interval)
Diabetes Mellitus	0.479	0.013	1.614 (1.251, 2.079)	0.477	0.011	1.612 (1.254, 2.078)	0.477	0.011	1.612 (1.254, 2.078)
Family history of CVD	-0.583	0.022	0.558 (0.354, 0.848)	-0.588	0.020	0.555 (0.356, 0.845)	-0.588	0.020	0.555 (0.356, 0.845)
Chronic lung disease	0.473	0.033	1.604 (1.233, 2.045)	0.472	0.030	1.603 (1.237, 2.043)	0.471	0.029	1.602 (1.239, 2.040)
Renal disease	0.911	0.023	2.487 (1.531, 3.944)	0.910	0.021	2.485 (1.538, 3.938)	0.910	0.021	2.485 (1.538, 3.938)
Killip class II	0.781	0.017	2.184 (1.553, 3.039)	0.779	0.013	2.179 (1.556, 3.037)	0.779	0.013	2.179 (1.556, 3.037)
Killip class III	2.135	0.022	8.457 (5.441, 13.075)	2.134	0.019	8.449 (5.456,13.039)	2.134	0.019	8.449 (5.456,13.039)
Killip class IV	2.893	0.016	18.047 (12.144, 24.993)	2.890	0.012	17.993 (12.480 ,24.661)	2.890	0.012	17.993 (12.480, 24.661)
Age (≥65)	0.886	0.014	2.425 (1.836, 3.190)	0.885	0.011	2.423 (1.840, 3.189)	0.885	0.011	2.423 (1.840, 3.189)

Table 3. Performance indicators of the proposed Bayesian models.

Performance Measure	Model A	Model B	Model C
Brier Score	0.048	0.036	0.034
Deviance	1857.693	1849.264	1849.188

Results validation and performance indicators of these three Bayesian models were performed using another 2154 male patients' datasets are shown in table 3. Good overall accuracy is suggested by the Brier score for model C as it has the smallest value. Additionally, model C has a better fit than models A and B as the deviance value produced was the smallest. Thus, Bayesian model C which applied both Beta and Dirichlet prior distributions were considered as the best model for male patients. As all the interaction terms were found to be not significant, only the main effects model C which consisted of the six variables as in table 2 was considered as the final Bayesian model proposed for the STEMI male patients.

4. Discussions

With the advancement of computer technology and Bayesian theory, Bayesian approach has been extensively applied in the practice of medical research [26–29]. This study has shown that Bayesian MCMC approach can be successfully applied in determining the risk factors associated with mortality

among CAD patients. Variables such as diabetes mellitus, family history of CVD, chronic lung disease, renal disease, Killip class and age group were found to be significant risk factors in the mortality of CAD male patients in Malaysia.

While Bayesian approach is steadily growing in popularity and use, priors setting has become an important issue debated as it is an integral part of Bayesian inference [30–33]. As in this study, three types of non-informative priors were assigned to the Bayesian models for male patients; model A which used only Beta prior, model B which used only Dirichlet prior and model C which used both Beta and Dirichlet priors.

It was found that model B which used only Dirichlet prior and model C which used both Beta and Dirichlet priors have produced similar estimations for almost all the variables. This may be explained by that Beta and Dirichlet distributions are identical if the number of categories, K is equal to two, as Beta distribution is a special case of Dirichlet distribution [34,35]. While for the model performances, only minor differences were found in these two models, this could be caused by the constraint of non-informative prior [36]. Model C which used both Beta and Dirichlet priors was chosen as the final Bayesian model for male patients as this model indicated better results than the other two models A and B.

In this study, improvement in results was observed through the use of a non-informative prior which is also supported by other study [37]. A study on the well-being of children in school which also has binary outcome as in this study found out that, the improvement brought upon non or weak informative prior is more particularly important when there is weak variation on the parameters [37]. Similar finding was also found in previous study on Bayesian modelling of 3-component mixture of exponentiated inverted Weibull distribution under non-informative prior [38]. The posterior distribution of the parameters is obtained assuming the non-informative which are Jeffreys and uniform priors [38].

Ideally, a Bayesian inference based on a non-informative prior should have been insensitive to the specific choice of the non-informative prior [39]. However, [39] confirmed that the choice of a non-informative prior can have a substantial influence on the resulting better prediction in the analysis which is also much the same as this study of CAD patients. In addition, selection of prior distribution in this study also in line with previous studies [40,41] which utilized Beta prior distribution in their studies of the prediction of major accidents which have significant consequences for human life and Bayesian modelling for product testing and release respectively. Both studies testified that the precision of posterior estimation mostly depending upon the prior distribution.

5. Conclusion

Three Bayesian models with various prior distribution were developed and compared in this study to provide a predictive approach in finding the risk factors associated with mortality for CAD male patients. The results of the three Bayesian models in this study shown the information from current trial is augmented and the precision can be increased by the incorporation of prior information in a Bayesian analysis. The Bayesian analysis takes to endure the extra, relevant, prior information, which can help in decision making especially in medical. Different choices of prior information or different choices of model can produce different decisions. Thus, it is very important to choose the prior distribution accurately. Though applying the non-informative prior which were both Beta and Dirichlet distribution priors, model C can minimise uncertainty in making effective clinical decisions and provides better parameters estimates of the posterior distribution. A set of six variables were identified to be significant risk factors for male CAD patients namely diabetes mellitus, family history of CVD, chronic lung disease, renal disease, Killip class and age group.

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