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Bayesian Hierarchical Modeling of the Individual Hypoglycaemic Symptoms' Reporting Consistency

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Abstract*:Hypoglycaemia symptoms vary between individual and across episodes making it difficult for the patients to realize if they are having a hypoglycaemia. Therefore, the ability to detect the onset of hypoglycaemia is important for quick corrective action. In this paper, we describe a Bayesian hierarchical model which is able to quantify the consistency of reporting symptoms by individual patient and simultaneously investigate patient-specific covariates affecting the consistency. The model is developed within a Bayesian framework using Markov chain Monte Carlo methodology where the consistency parameter is estimated via Gibbs sampling. The association between patient-specific covariates and consistency is investigated using generalized linear model before implementing the stepwise regression to identify the best predictive model. The results obtained show that symptoms classified as autonomic and neuroglycopenic are prominent in detecting the onset of hypoglycaemia. No patient-specific covariate appears to be significantly affecting patients reporting' consistency. However, the best predictive model obtained contains covariates gender, type of diabetes, retinopathy, serum angiotensin converting enzyme and C-peptide.The hierarchical model developed allows researchers to estimate patient's consistency in reporting symptoms and identify factors affecting it under one setting.

Keywords* : Bayesian modeling, Hierarchical modeling, Stepwise regression, Predictive model, Markov chain Monte Carlo.

I. INTRODUCTION

Hypoglycaemia is a problem of glucose deprivation in the brain when the blood glucose level in the body become abnormally low. It is very important for patients to be able to detect the onset of hypoglycaemia so that necessary action can be taken to bring the declining glucose level back to normal. Symptoms of hypoglycaemia differ significantly between patients [1] and vary accross espisodes of an adult patient [2]. Variability both within and between individual patients makes it difficult for patients to precisely detect the onset of hypoglycaemia episodes, with between-variability hindering the precise identification of a condition-specific set of symptoms. Patients should be able to identify a sufficient number of typical symptoms and understand that it is possible to experince different sets of symptoms in diferent episodes.

Symptoms of hypoglycemia can be categorized into different groups based on what cause them, e.g. neuroglycopenic and autonomic [3] and general malaise [4]. The individual consistency of hypoglycaemic symptom reporting can be modeled by categorizing all the symptoms into six distinct groups; autonomic, neuroglycopenic, general malaise, and autonomic/neuroglycopenic other symptom and no symptom [5]. This allows the model to have additional source of variation to symptoms' reporting. Table 1 summarizes 26 symptoms considered in this study together with their groupings [5].

To help diabetic patients recognise their hypoglycaemic episodes efficiently, it is vital to educate them about factors that may cause variation in their symptoms. The effect of ten patient-specific covariates on consistency was investigaetd using GLM methodology [2]. This paper build on work in [5] by formulating a hierarchical model which can address two objectives; estimate consistency and identify significant factors affecting consistency.

II. DATA

The data used in this analysis were symptoms reported by 66 diabetic patients during hypoglycaemia episodes provided by the UK Hypoglycaemia Study Group [6]. Every subject participated in this survey was given a form to record each of the hypoglycaemia episodes experienced, and was asked to return the forms on a monthly basis for 12 months. Subjects were asked to monitor their blood glucose using a Medisense G glucose meter (Abbott Laboratories, Abbott Park, IL). Episodes with capillary glucose reading < 3.0 mmol/L (< 54 mg/dL) or when there was no blood glucose measurement available and the symptoms resolved on taking carbohydrate are considered valid, while episodes with capillary glucose > 4.0 mmol/L are not considered as valid hypoglycaemic episodes [2].

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Besides blood glucose level, the forms collected data of date, time and duration of the hypoglycaemic episodes, treatments received during the episodes, and symptoms experienced. The data also contain information on 10 patient specific characteristics which are used as covariates in this analysis. The identity of each subject in the study is confidential. Therefore, a unique four-digit code is assigned to each of them.

Data is presented in a $J \times K$ matrix in order to assess the individual reporting consistency across episodes. For patient i, J correspond to the number of symptoms and $K_i$correspond to the number of episodes for patient i, see for example Fig. 1(a) for Subject 6058 with $K = 20$ episodes. In Fig. 1(b) from the top-left corner, symptoms and episodes are arranged in descending order, from more frequent to less frequent symptom and from more intense to less intense episode. Propensity of a symptom is represented by the rate of the symptom's reporting across the episodes whereas the intensity of an episode is represented by how many symptoms are reported in the episode.

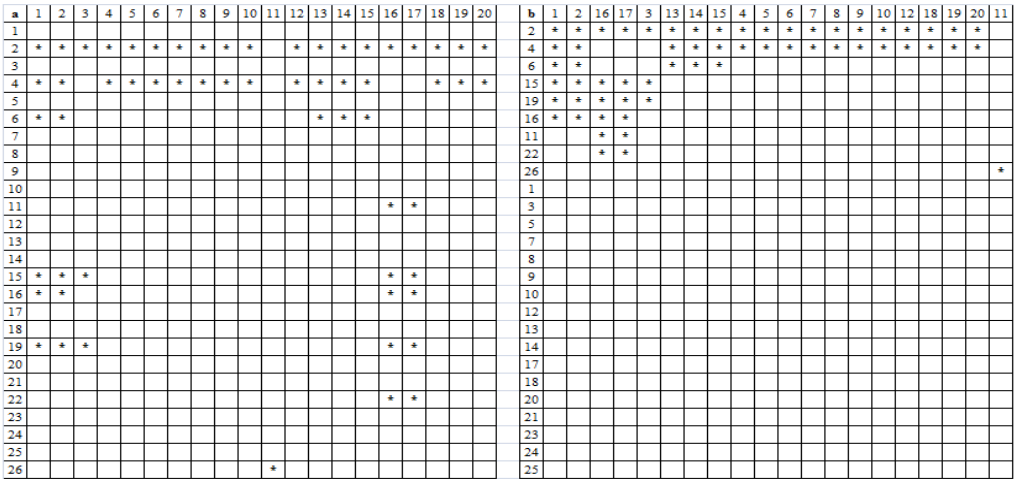

Fig. 1: (a): Illustration of the indicator variables matrix with dimension J xK for patient 6058. J is the number of symptoms (1-26) and K is the number of episodes. Every reported symptom is marked with a dot. (b) The matrix after rearrangement in descending order with respect to the rows and columns according to the frequency with which symptoms are experienced and columns according to the number of symptoms per episode.

Table I:List of symptoms on patients' report forms and their category.

Symptom	Description	Category
1	Confusion	Neuroglycopenic
2	Sweating	Autonomic
3	Drowsiness	Neuroglycopenic
4	Weakness	Neuroglycopenic
5	Dizziness	Neuroglycopenic
6	Feeling warm	Autonomic/ Neuroglycopenic
7	Difficulty speaking	Neuroglycopenic
8	Pounding heart	Autonomic
9	Impaired concentration	Neuroglycopenic
10	Shivering	Autonomic
11	Unsteady	Neuroglycopenic
12	Nonspecific awareness	Other
13	Double vision	Neuroglycopenic
14	Blurred vision	Neuroglycopenic
15	Hunger	Autonomic
16	Thirst	Autonomic
17	Nausea	General malaise
18	Anxiety	Autonomic
19	Tiredness	Neuroglycopenic
20	Tingling	Autonomic
21	Trembling	Autonomic
22	Headache	General malaise
23	Malaise	General malaise
24	Irritability	Autonomic/ Neuroglycopenic
25	Other	Other
26	None	No symptom

Note. Adapted from "*Bayesian Modelling of the Consistency of Symptoms Reported During Hypoglycaemia for Individual Patients*", by Zulkafli et al., 2016, *Malaysian Journal of Mathematical Sciences, 10(s)*, 27-39. Copyright 2016 by Universiti Putra Malaysia Press.

III. METHODOLOGY

A. Bayesian hierarchical modeling

The indicator random variable is defined such that $Y_{ijk} = 1$ if subject i reports symptom j at episode k and $Y_{ijk} = 0$ if otherwise.

Assume

$$Y_{ijk} \sim \text{Bernoulli}\,(p_{ijk}) \qquad (1)$$

for individual $i = 1,\ldots,\text{I}$, symptom $j = 1,\ldots,J$ and episode $k = 1,\ldots,K$. p_{ijk} is the probability of patient i reporting symptom j at episode k.

Individual i reports symptom j at episode k when $\alpha_{ij}\beta_{ik}$ exceeds a random threshold associated with each patient, where α_{ij} represents the propensity ofsymptom j for individual i, β_{ik} represents the intensity of episode k for individual i. The random threshold for each symptom $j = 1,\ldots,J$ experienced at episode $k = 1,\ldots,K_i$ by individual $i = 1,\ldots,I$ denoted by τ_{ijk}, is assumed to follow a log-normal distribution;

$$\tau_{ijk} \sim \text{Log-Normal}\,(0,\sigma_i^2) \qquad (2)$$

$$p_{ijk} = \Pr(\tau_{ijk} \le \alpha_{ij}\beta_{ik}), \\ = \Phi\left\{\frac{\log(\alpha_{ij}\beta_{ik})}{\sigma_i}\right\}, \quad (3)$$

There is no loss of generality when the mean of the log-normal distribution is set to 0 for all subjects i, because here the mean of the logarithm of the threshold $\mathrm{E}\{\log(\tau_{ijk})\}$ is not of interest and inestimable. Thus, the probability of patient i reporting symptom j at episode k, is given by where $\Phi(\cdot)$ is the cumulative distribution function of a standard normal variable.

Parameter σ_i measures the symptom reporting consistency of a patient. A rescaled consistency parameter, $c_i = 100/(1+\sigma_i^2)$, is used for easier interpretation where $c_i \in (0; 100]$. A large c_i value indicates high consistency. For large c_i (i.e. small σ_i^2) the thresholds get highly concentrated around constant reporting of symptoms associated with latent symptom propensity α_{ij} and episode intensity β_{ik} such that $\alpha_{ij}\beta_{ik} > \tau*_{ijk}$, with $\tau*_{ijk}$ approaching a constant value as σ_i tends to zero (or c_i tends to 1). Therefore, consistent reporting is associated with high concentration of the threshold distribution, corresponding to increased values of the consistency parameter c_i.

Under a Bayesian framework [7,8], appropriate prior distributions for the model parameters α_{ij}, β_{ik} and σ_i are specified. To allow for group effects, each symptom is being assigned to a specific group. Therefore we have α_{ijl}, where $l = 1,\ldots,6$ indicates group and we assume the following hierarchical prior:

$$\alpha_{ijl} \sim \text{Gamma}\left(\theta, \frac{\theta}{u_l}\right), l = 1,\ldots,6,$$

giving

$$\mathrm{E}(\alpha_{ijl}) = u_l, l = 1,\ldots,6,$$

and

$$\mathrm{Var}(\alpha_{ijl}) = \frac{u_l^2}{\theta}, l = 1,\ldots,6,$$

with

$$\theta \sim \text{Gamma}(a_\theta, b_\theta), \\ u_l \sim \text{Gamma}(a_{ul}, b_{ul}).$$

Here, θ is set equal to 1 since the information in the data at this level of hierarchy is limited, and also to expedite the Markov chain Monte Carlo (MCMC) convergence. This effectively corresponds to an exponential prior with mean u_l for α_{ijl}. For similar reasons, a_{ul} and b_{ul} are also set equal to 1.

The prior distribution given to latent variable β_{ik} is

$$\beta_{ik} \sim \text{Gamma}(a_\beta, b_\beta)$$

with $a_\beta = 1$ and $b_\beta = 0.1$.

To estimate c_i, the latent variables α_{ijl} and β_{ik} need to be estimated first. Estimation of α_{ijl} and β_{ik} is informed by the frequency with which a symptom is reported throughout all episodes and the number of symptoms per particular episode. A Bayesian approach is implemented to estimate the posterior distribution of the unobserved latent factors and the variability of the thresholds. MCMC is carried out to estimate the posterior distribution of the latent variables [9,10] which sample from the posterior distribution [11] iteratively [12]. MCMC allows simpler evaluation of complex integrated function especially for multi-parameter model [13] by avoiding the calculation of the marginal distribution [14]. Here, Metropolis Hastings algorithm is used to perform the MCMC [15].

The second level of the hierarchical model is to investigate which factors affect the consistency of symptom reporting of individual patients. The covariates under consideration are age (x_1), duration of diabetes (x_2), body mass index (BMI, x_3), stimulated C-peptide (x_4), haemoglobin A1c (Hba, x_5), angiotensin-converting enzyme (ACE, x_6), hypoglycaemia awareness score (1 to 7, with higher scores corresponding to weaker awareness of hypoglycaemia, x_7), gender (x_8), diabetes type (x_9), and retinopathy (x_{10}).

All covariates have numerical values except for gender, awareness of hypoglycaemia, type of diabetes and retinopathy which are considered as categorical factors in the model. For the categorical factors gender and type of diabetes, each factor has one coefficient in the model with male and Type 1 as the baseline. As for retinopathy, it has three coefficients and a sum-to-zero constraint is set for comparing effects to a mean level. The missing values of the covariates are treated as random variables allowing their posterior distributions of the incomplete data given the observed data to be estimated by the model using MCMC techniques [16].

To allow for hierarchical estimation, the variance parameter, σ_i^2 follows a hierarchical inverse-gamma distribution:

$$\sigma_i^2 \sim \text{Inv-Gamma}\left(\delta, \frac{\delta}{m_i}\right), \quad (2)$$

where

$$\delta \sim \text{Inv-Gamma}(a_\delta, b_\delta).$$

To facilitate the MCMC algorithm's convergence, we set $a_\delta = b_\delta = 1$ as it reduces the variability of hyper-parameter δ. To link estimates of the posterior estimate of the consistency parameter σ_i^{-2} with thecovariates, a generalized linear model with gamma errors is used, with linear predictor:

$$\log\{E(\sigma_i^{-2})\} = b_0 + \sum_{l=1}^{7} b_l z_{il} + b_8 \text{GEN}_i \\ + b_9 \text{TYPE}_i + b_{10,1}\text{RET}_1 \\ + b_{10,2}\text{RET}_2 + b_{10,2}\text{RET}_3$$

for $i = 1,\ldots,66$, GEN stands for gender, TYPE stands for type of diabetes, RET1, RET2 and RET3 stand for no retinopathy, background retinopathy and proliferative retinopathy respectively. The standardized observations of covariates $x_1,\ldots,x_7$ are denoted by z_{il} with x_{il} being the original observation Therefore, $z_{il} = (x_{il} - \bar{x}_l)/\ sd(x_l)$. b_0 is the standardised intercept term and coefficients $b_1,\ldots,b_7$ are the standardized coefficients for $x_1,\ldots,x_7$, whereas b_8 and b_9 correspond to covariate gender and type of diabetes respectively, and b_{10} represents different levels of retinopathy factors.

To simplify notation, we use $w_i = \sigma_i^{-2}$. The generalised linear model response variable is the estimated posterior mean of the precision parameter, $\widetilde{w}_i = E(w_i|y_i)$. Assume

$$\widetilde{w}_i \sim \text{Gamma}\left(\lambda, \frac{\lambda}{m_i}\right) \text{ for } i = 1, \dots, 66,$$

so we have $E(\widetilde{w}_i) = m_i$ and $Var(\widetilde{w}_i) = m_i^2/\lambda$.

Parameter m_i is the mean consistency response and linked to all patient-specific covariates through function

$$m_i = \exp(\boldsymbol{Z}^* b) \text{ where } i = 1, \dots, I. \quad (4)$$

$\boldsymbol{b} = (b_0, b_1, \dots, b_{10,1}, b_{10,2}, b_{10,3})^T$ is a coefficients vector corresponds to the covariates vector with $b_{10,1}, b_{10,2}, b_{10,3}$ are the parameters correspond to RET1, RET2 and RET3 respectively and

$\boldsymbol{Z}^* =$
$(1, z_1, z_2, z_3, z_4, z_5, z_6, z_7, \text{GEN}, \text{TYPE}, \text{RET1}, \text{RET2}, \text{RET3})$.
All $b_l, l = 1,2, \dots, 12$ are assumed to have Normal prior distributions and the prior for λ is inverse-gamma:

$$b_l \sim \text{Normal}(\mu_{\beta l}, \sigma_{\beta l}^2),$$
$$\lambda \sim \text{Inverse-Gamma}(\gamma_\lambda, \delta_\lambda).$$

where $\mu_{\beta l} = 0, \sigma_{\beta l}^2 = 10^4$ and $\gamma_\lambda = \delta_\lambda = 10^{-3}$.

B. Model selection: stepwise regression

Model selection is performed using stepwise regression to determine the most suitable predictive model for consistency prediction. The stepwise selection method adds in or removes one predictor at each stage, given that the predictor meets a selection criterion for entry or removal, until there is no new predictor that can be added or deleted [17]. The selection criterion used in this analysis is the Deviance Information Criterion (DIC)[18]. Every time a new predictor is added ordropped from the model, the significance of each of the predictor already in the model is re-examined and compared sequentially. To run the stepwise regression, a binary vector $\gamma = (\gamma_1, \dots, \gamma_{10})$ is incorporated to the linear predictor in Equation (4)[19]. Therefore,

$$\log\{m_i\} = b_0 + \sum_{q=1}^{p} b_q \gamma_q x_{iq},$$

where $m_i = \text{E}(\sigma_i^{-2})$ [20].

In each step, p candidate models were fitted and best model was selected based on their DIC estimates. The procedure stops when it gets to a stable set of predictors.

IV. RESULTS AND DISCUSSION

Consistency estimates for all patients obtained from this model are comparable with what obtained with the non-hierarchical consistency estimate model. Fig. 2 (left) gives the distribution of the posterior mean estimates of the consistency parameter, $\tilde{c}_i$, for all 66 patients in the hierarchical model, whereas Fig. 2 (right) shows the estimates of $\log(\sigma_i^2)$. Subject 6064 was the most consistent patient in reporting consistency with $\tilde{c}_i = 82.79$ with 95% credible interval (71.62, 91.20). The least consistent patient among all is subject 2013, $\tilde{c}_i =$ 11.53 with 95% credible interval (9.09, 14.36). Fig. 3 gives the rank of consistency estimates for this hierarchical model versus the non-hierarchical model. Patients are ranked such that the patient with the highest consistency is ranked first and patient with the lowest consistency is ranked last. This plot shows a decent correspondence suggesting that the estimations obtained from the hierarchical and non-hierarchical model are similar.

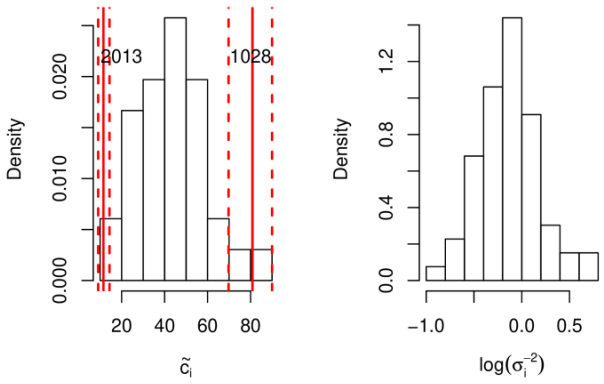

Fig. 2.Histograms shows the estimated posterior consistency parameter, $\tilde{c}_i$, and the estimated posterior precision parameter, σ_i^{-2}.

Fig. 4 shows the distribution of the posterior mean propensity of each group, u_l andTable 2 provides the posterior estimates of the propensity of each group. Autonomic and neuroglycopenic groups have the highest propensity suggesting their importance in detecting the onset of hypoglycaemia with $u_1 =$ 0.0420 and $u_2 =$ 0.0377 respectively.

The analysis on covariates' effect suggests that there is no significant covariate affecting consistency measure. Fig. 5 shows the caterpillar plots for coefficients $\boldsymbol{b}$ corresponding to each covariate.

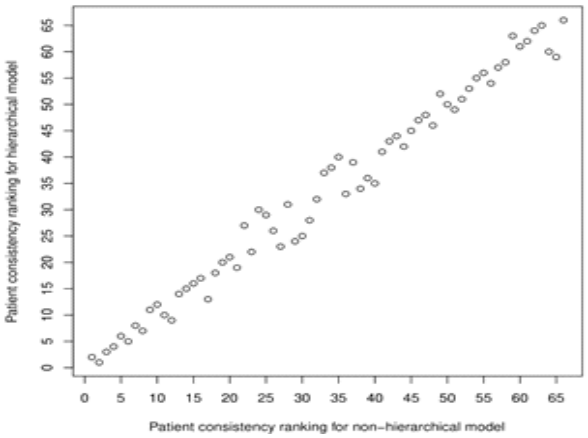

Fig. 3.Graph plots the ranking of consistency estimates, $\tilde{c}_i$ = of 66 individual for hierarchical and non-hierarchical models in ascending order.

To determine the best predictive model, the procedure of stepwise methodology was run with two starting models; a null model and full model. The two starting points used result in the same predictive model which is the model with factorsgender, type of diabetes, retinopathy, C-peptide and serum angiotensin converting enzyme (DIC value = 96.66).

Note that there is no significant covariate affecting consistency. Hence, the option to start from the model with significant covariate indicates that the null model is a good starting point.

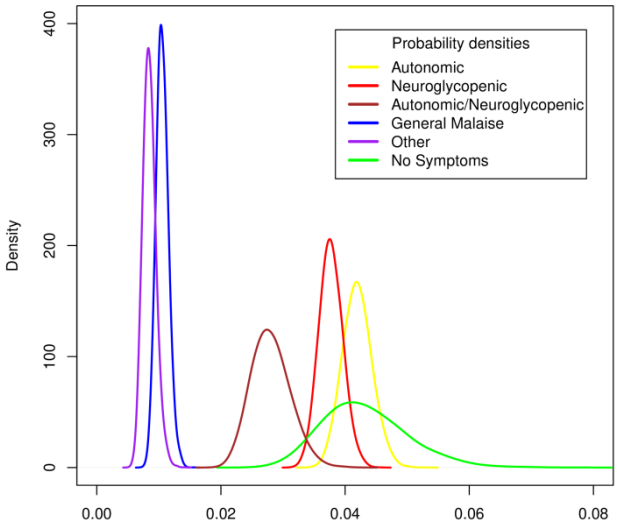

Fig. 4.Posterior distributions of mean group propensity, u_l in hierarchical model.

Table 2:Posterior estimates of the mean, standard deviation (SD) and credible intervals (CI) for the group propensity, u_l.

Group	Mean	SD	2.5% CI	97.5% CI
Autonomic	0.0420	0.0023	0.0376	0.0467
Neuroglycopenic	0.0377	0.0019	0.0341	0.0416
Autonomic/ Neuroglycopenic	0.0280	0.0031	0.0225	0.0347
General malaise	0.0106	0.0010	0.0088	0.0126
Other	0.0085	0.0011	0.0066	0.0108
No symptom	0.0432	0.0068	0.0317	0.0582

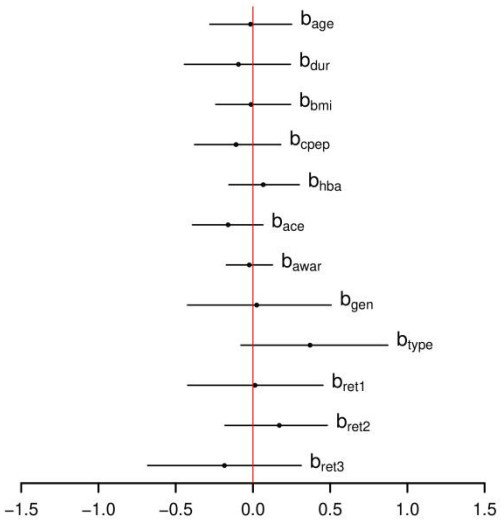

Fig. 5.Posterior means (bullets) and 95% equal-tailed Bayesian intervals (bars) for standardized coefficients of patient-specific covariates.

V. CONCLUSION

In this paper, the Bayesian hierarchical model constructed is able to estimate patients' symptoms reporting consistency and determine which covariates affecting it simultaneously in a single model. Based on this study, individual patients show marked variability in reporting symptoms during hypoglycaemia episodes. The best model identified for predicting consistency include covariates gender, type of diabetes, retinopathy, C-peptide and serum angiotensin converting enzyme.The hierarchical model developed would be beneficial for practitioners to estimate patient's consistency in reporting symptoms and identify factors affecting it when the patients' profile become available.

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REFERENCES

1. Cox, D. J., Gonder-Frederick, L., Antoun, B.,Cryer, P. E., and Clarke, W. L. (1993). Perceived symptoms in the recognition of hypoglycemia. Diabetes Care, 16(2):519-527.
2. Zammitt, N., Streftaris, G., Gibson, G., Deary,I., and Frier, B. (2011). Modeling the consistency of hypoglycemic symptoms: high variability in diabetes. Diabetes Technology & Therapeutics, 13(5):571-578
3. Hepburn, D., Deary, I., and Frier, B. (1992). Classification of symptoms of hypoglycaemia in insulin-treated diabetic patients using factor analysis: Relationship to hypoglycaemia unawareness. Diabetic Medicine, 9(1):70-75.
4. Deary, I., Hepburn, D., MacLeod, K., and Frier, B. (1993). Partitioning the symptoms of hypoglycaemia using multi-sample confirmatory factor analysis. Diabetologia, 36(8):771-777.
5. Zulkafli, H., Streftaris, G., Gibson, G., and Zammitt, N. (2016). Bayesian modelling of the consistency of symptoms reported during hypoglycaemia for individual patients. Malaysian Journal of Mathematical Sciences, 10(S):27-39.
6. UK Hypoglycaemia Study Group: Risks of hypoglycaemia in types 1 and 2 diabetes: effects of treatment modalities and their duration. Diabetologia 2007;50:1140–1147.
7. Berger, J. O. (1985). Statistical decision theory and Bayesian analysis. Springer.
8. Bernardo, J. M., and A. F. M. Smith, Bayesian Theory, John Wiley, NewYork, 1994.
9. Arminger, G. and Muthen, B. (1998). A bayesian approach to nonlinear latent variable models using the gibbs sampler and the metropolis-hastings algorithm. Psychome-trika, 63:271-300.
10. Tierney, L. (1994) Markov Chains for Exploring Posterior Distributions. The Annals of Statistics, 22, 1701-1762.
11. Carlin, B. P. and Louis, T. A. Bayesian Method for Data Analysis. 3rd Edition. United States: Chapman and Hall. 2009.
12. Raab, G., Yang, S., Allardice, G., Goldberg, D., and McMenamin, J. (1998). Modelling human immunodefiency virus infection and acquired immune deficiency syndrome cases in Scotland: data sources, prior information and Bayesian estimation. Journal of the Royal Statistical Society: Series A (Statistics in Society),161(3):367-384.
13. Reis Jr, D. S., & Stedinger, J. R. (2005). Bayesian MCMC flood frequency analysis with historical information. Journal of hydrology,313(1-2),97-116.
14. Brooks, S. P. Markov chain monte carlo method and its application. Journal of the Royal Statistical Society. Series D. 1998. 47(1): 69–100.
15. Metropolis, N., Rosenbluth, A. W., Rosenbluth, M. N., Teller, A. H. and Teller, E. Equation of state calculations by fast computing machines. The Journal of Chemical Physics. 1953. 21(6): 1087–1092.
16. Ibrahim, J. G., Chen, M.-H., and Lipsitz, S. R. (2002). Bayesian methods for generalized linear models with covariates missing at random. The Canadian Journal of Statistics/La Revue Canadienne de Statistique, pages 55-78.

17. Harrell Jr, F. E. (2015). Regression modeling strategies: with applications to linear models, logistic and ordinal regression, and survival analysis. Springer.
18. Spiegelhalter, D. J., Best, N. G., Carlin, B. P., and Linde, A. (2014). The deviance information criterion: 12 years on. Journal of the Royal Statistical Society: Series B (Statistical Methodology), 76(3):485-493.
19. George, E. I., & McCulloch, R. E. (1993). Variable selection via Gibbs sampling. Journal of the American Statistical Association, 88(423), 881-889.
20. Ntzoufras, I. (2011). Bayesian modeling using WinBUGS, volume 698, Wiley.

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