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THRESHOLD SELECTION FOR THE BAYESIAN LOGISTIC LATENT VARIABLE MODEL OF HYPOGLYCEMIA SYMPTOM REPORTING CONSISTENCY

(*Pemilihan Ambang untuk Model Logistik Bayesian Berpemboleh Ubah Laten bagi Konsistensi Pelaporan Gejala Hipoglikemia*)

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ABSTRACT

Individual symptom patterns are unique, and consistent reporting of hypoglycemia symptoms is crucial for early detection and swift action. Symptoms occur when an individual's propensity combined with episode intensity exceeds a patient-specific threshold. Selecting an appropriate threshold form for consistency modeling is vital, as different forms can affect reporting patterns significantly. This study explores variations in symptom reporting consistency and precision using various threshold types and distributions within a logistic-type latent variable Bayesian model. The optimal threshold form is determined through analysis of real and simulated data, providing posterior estimates of consistency and precision values, along with Bayesian intervals and MCMC errors. This study examines five threshold forms: product, summation, interaction, sum of squared and square of product, along with two threshold distributions: Log-normal and Weibull. The square product threshold with a Log-normal threshold distribution proved most effective for modeling hypoglycemia symptom reporting consistency, achieving high specificity (83.76%) and strong negative predictive value (94.03%), but with moderate sensitivity (56.25%).

Keywords: hypoglycemia; symptom; Log-normal; Weibull; latent variable.

ABSTRAK

Corak simptom individu adalah unik, dan pelaporan simptom hipoglikemia yang konsisten adalah penting untuk pengesanan awal dan tindakan pantas. Gejala berlaku apabila kecenderungan individu digabungkan dengan intensiti episod melebihi ambang khusus pesakit. Memilih bentuk ambang yang sesuai untuk pemodelan konsisten adalah penting, kerana bentuk yang berbeza boleh menjejaskan corak pelaporan dengan ketara. Kajian ini meneroka variasi dalam konsistensi dan ketepatan pelaporan gejala menggunakan pelbagai jenis ambang dan taburan dalam model Bayesan pembolehubah pendam jenis logistik. Bentuk ambang optimum ditentukan melalui analisis data sebenar dan simulasi, memberikan anggaran posterior nilai ketekalan dan ketepatan, bersama-sama dengan selang Bayesian dan ralat MCMC. Kajian ini mengkaji lima bentuk ambang—hasil, penjumlahan, interaksi, jumlah kuasa dua dan kuasa dua produk—dan dua taburan ambang: Log-normal dan Weibull. Pemodelan konsistensi simptom hipoglikemia ditunjukkan sebagai paling berkesan apabila menggunakan bentuk ambang hasil darab ambang kuasa dua dengan taburan ambang Log-normal.

Kata kunci: hipoglikemia; gejala; Log-normal; Weibull; pembolehubah terpendam.

1. Introduction

Diabetes results from high glucose levels in the blood, while hypoglycemia occurs when blood glucose drops below 4mmol/L, causing glucose deprivation in the brain (Yale *et al*. 2018). Prompt detection of hypoglycemia is crucial to prevent medical emergencies, cognitive decline,

or more severe outcomes (Paluchamy 2019). Symptoms of hypoglycemia exhibit variability, both among individuals and within the same individual (Cox *et al*. 1993; McAulay *et al*. 2001), making identification challenging (Zammitt *et al*. 2011; Zulkafli *et al*. 2020). These fluctuations pose difficulties for patients in recognizing the onset of hypoglycemic episodes. Hence, timely recognition of hypoglycemia is crucial for prompt corrective action. Being consistent in reporting hypoglycemia symptoms is crucial for quickly detecting them and taking necessary corrective measures (Al Sharmin *et al*. 2024; Zulkafli *et al*. 2016).

Since consistency is not directly observable, a latent variable model is used. A logistic-type latent variable model developed by Zammit *et al*. (2011) within a parametric framework, assuming random thresholds for symptom reporting adhere to a Log-normal distribution to assess intra-individual consistency in reporting symptoms of hypoglycemia.

The study aims to comprehensively explore how symptom reporting consistency and precision vary across different threshold forms and threshold distributions. It identifies the optimal threshold form by analyzing real and simulated data. The exploration of alternative threshold forms in the context of symptom reporting, as examined by Zammit *et al*. (2011) and further developed by Zulkafli *et al*. (2016), highlights the potential for various mathematical formulations to better capture the dynamics of symptom experiences. To assess sensitivity to the distribution of thresholds, the thresholds random variable alternatively be drawn from a Weibull family instead of a Log-normal distribution. The Weibull distribution is chosen for modeling threshold variability because it offers flexibility in capturing a wide range of behaviors, including increasing or decreasing hazard rates. Unlike the Log-normal distribution, which assumes a constant hazard, the Weibull can model varying frequencies of hypoglycemic symptoms (Grover & Sabharwal 2012). It is well-suited for survival and reliability data, making it effective for understanding time-to-event scenarios in medical contexts like hypoglycemia (DeVries 2013).

Moreover, individuals differ in sensitivity to blood sugar changes, affecting symptom-reporting frequency (Zammit *et al*. 2011). Individuals who report more symptoms might be sensitive to both small and large physiological changes. This means they notice and report symptoms at different levels of blood sugar fluctuations, reflecting a wider band of response (Malkani & Kotwal 2017). More precisely, a higher frequency of symptom reporting indicates that individuals have a broader range of response levels for experiencing symptoms. This variability necessitates a more flexible modeling approach to accurately reflect the underlying distribution of symptom reporting (Zhou *et al*. 2020). The Weibull distribution is particularly suited for modeling data that exhibit non-homogeneous behaviors, such as those seen in symptom reporting related to blood sugar levels (Zulkafli 2017). In contrast, the Log-normal distribution assumes a symmetrical behavior which may not be appropriate given the skewness observed in symptom reporting data (Sauenram *et al*. 2023). Hence, exploring Weibull threshold distributions instead of Log-normal is crucial for assessing the robustness of the analysis regarding threshold distribution choice.

The consistency parameter for each patient was estimated using a Bayesian approach (Berger 1985). The study presents posterior estimates of consistency and precision values, including 95% Bayesian intervals (BI) and MCMC errors. A total of 5,000 MCMC iterations were conducted, with the initial 1,000 iterations removed during the burn-in period, using the MCMC methodology in WinBUGS.

2. Literature Review

The assessment of consistency in reporting hypoglycemia symptoms is crucial for effective management of diabetes and prevention of adverse health outcomes. Logistic-type latent variable models have emerged as a powerful tool for evaluating symptom reporting consistency

by estimating unobservable constructs from observed data (Zammit *et al*. 2011). A key aspect of these models is the choice of threshold forms and threshold distribution, which determines how symptoms are perceived and reported by individuals.

Logistic latent variable models provide a flexible framework for analyzing binary and ordinal data, making them well suited for assessing hypoglycemia symptom reporting consistency. These models assume the existence of an underlying latent variable that influences the observed symptom data (Cai 2012; Kristensen & Bibby 2020). By relating the latent variable to the observed variables through a logistic function, the model can estimate individual-specific consistency parameters and symptom-specific thresholds.

Zammit *et al*. (2011) pioneered the use of logistic latent variable models in hypoglycemia research by developing a model that assumes random thresholds follow a Log-normal distribution. This approach allowed for the quantification of intra-individual consistency in symptom reporting, revealing significant individual differences influenced by factors such as age, sex, and diabetes type. The Log-normal distribution has been widely used in biostatistics due to its ability to model positively skewed data (Fabrizi & Trivisano 2012), making it a natural choice for modeling symptom reporting thresholds.

While the Log-normal distribution has proven useful in modeling symptom reporting thresholds, exploring alternative threshold distributions can provide additional insights into the underlying mechanisms of symptom reporting consistency. The Weibull distribution, in particular, has gained attention due to its flexibility in modeling various types of data (Zichuan *et al*. 2021).

The Weibull distribution has been successfully applied in fields such as survival analysis and reliability engineering, where it has been used to model time-to-event data and failure rates (Kundu & Mitra 2016). Its versatility in modeling different types of data makes it a promising candidate for modeling symptom reporting thresholds in a logistic latent variable framework.

By comparing the performance of Weibull and Log-normal threshold distributions within a Bayesian logistic latent variable model, researchers can assess the robustness of their analyses and gain insights into the optimal threshold form for modeling hypoglycemia symptom reporting consistency. Bayesian inference, in particular, allows for the incorporation of prior knowledge and uncertainty, making it well suited for medical research where data may be limited or noisy (Berger 1985).

Consistency models play a crucial role in understanding and improving patient outcomes in diabetes management. The variability in symptom perception and reporting can lead to delays in treatment and increased health risks (Al Sharmin *et al*. 2024). By quantifying symptom reporting consistency, clinicians can identify patients who may benefit from targeted interventions and develop personalized treatment strategies.

Moreover, consistency models can inform the development of clinical decision support systems that assist healthcare providers in managing hypoglycemia more effectively. These systems can leverage the insights gained from consistency models to provide real-time feedback on symptom reporting patterns and guide treatment decisions (Pichardo-Lowden *et al*. 2021). As computing technology and software tools continue to advance, the application of these models in medical research is expected to grow, leading to improved patient outcomes and enhanced quality of care.

3. Materials and Methods

Graphically, the symptoms and episodes of each patient are displayed in a J × K matrix (Figure 1), where J is the number of symptoms and K is the number of episodes. A symptom's frequency indicates its propensity, and the intensity of an episode is shown by the number of symptoms in that episode. Each reported symptom is marked in a cell. The rows are arranged by symptom

frequency, and the columns by the number of symptoms per episode. The clustering of marked cells in this representation indicates the consistency of symptom reporting.

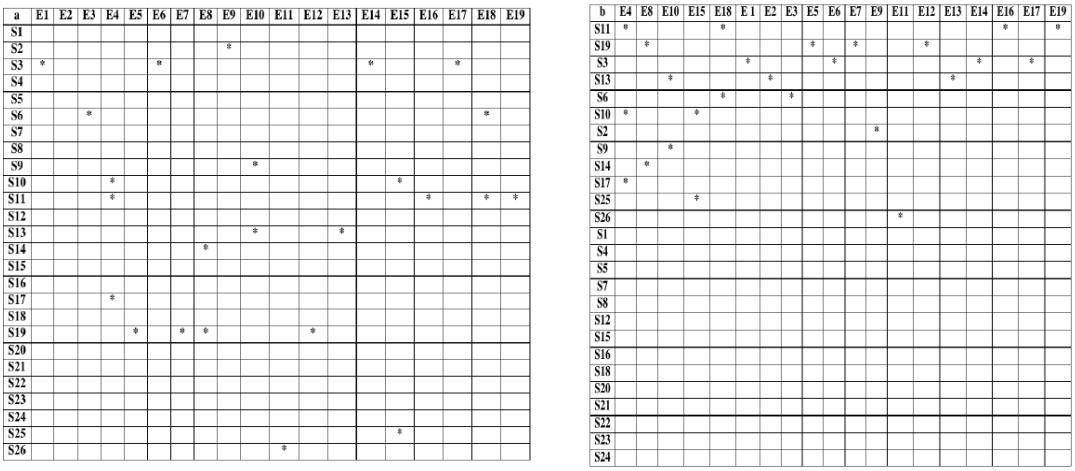


Figure 1: Blank cell to see consistency for patient 3015 (a), the matrix shows each reported symptom with a square. In part (b), the rows and columns of the matrix are rearranged based on symptom frequency and the number of symptoms per episode, with both arranged in descending order from the top-left corner.

This graphical representation is expressed within a parametric framework using a logistic-type latent variable model. In logistic-type latent variable Bayesian model, the observed variable Y_{ijk} takes a value of 1 if symptom j is reported by patient i in episode k, otherwise, Y_{ijk} takes the value 0:

$$y_{ijk} \sim Bernoulli(\theta_{ijk})$$

where, $i = 1, \dots, n; j = 1, \dots, J; k = 1, \dots, K_i$ *and* θ_{ijk} is the probability that i^{th} patient reports j^{th} symptom in k^{th} episode , and it depends on whether the function $h(\eta_{ij}, \phi_{ik})$, which combines the propensity of symptom j for patient i (η_{ij}) and the intensity of episode k for patient i (ϕ_{ik}), exceeds a random threshold (τ_{ijk}) assigned to each instance and $h()$ is an appropriate functional for:

$$\theta_{ijk} = Pr\left(\tau_{ijk} \leq h(\eta_{ij}, \phi_{ik})\right) = \Phi\left(\frac{\log(\eta_{ij}.\phi_{ik})}{\sigma_i}\right). \quad (1)$$

where $\Phi()$ denotes the cumulative distribution function of a standard normal variable, $\eta_{ij} \sim Gamma(\alpha_\eta, \beta_\eta)$, $\phi_{ik} \sim Gamma(\alpha_\phi, \beta_\phi)$, $\tau_{ijk} \sim Log - normal(0, \sigma_i^2)$ and $\sigma_i^2 \sim Inv - Gamma(\alpha_\sigma, \beta_\sigma)$. Adopting a Bayesian approach, independent prior distributions are assigned to the latent variables η_{ij} and ϕ_{ik} with $\alpha_\eta = \alpha_\phi = \alpha_\sigma = 1$ and $\beta_\eta = \beta_\phi = \beta_\sigma = 0.1$ to reflect relative prior ignorance. In the assumed Log-normal model, the variance of τ_{ijk} is $e^{\sigma_i^2}(e^{\sigma_i^2} - 1)$, and as σ_i approaches 0, the variance of τ_{ijk} approaches 0 as well. To simplify interpretation, the precision parameter σ_i^{-2} is transformed into a consistency parameter $c_i = 100/(1 + \sigma_i^2)$, ranging from 0 to 100. Higher values indicate greater symptom consistency. A model with thresholds following a Weibull distribution can also be fitted: $\tau_{ijk} \sim Weibull(\upsilon_i, \lambda_i)$, where, υ_i and λ_i represent the shape and scale parameters, respectively, and υ_i represents the parameter associated with the variation in symptoms reported by patient i,and it is simulated from an Inverse-Gamma distribution: $\upsilon_i \sim Inv - Gamma(\alpha_\upsilon, \beta_\upsilon)$. As υ_i approaches infinity, the

variance of τ_{ijk}, $var(\tau_{ijk}) = \Gamma\left(1+\frac{2}{\upsilon_i}\right) - \{\Gamma\left(1+\frac{1}{\upsilon_i}\right)\}^2$, tends to zero, indicating highly consistent symptom reporting. Parameter values can be rescaled for convenience, $c_i = \frac{100}{1+\upsilon_i{}^{-1}}$.

Moreover, in previous research by Zammit *et al*. (2011), assumed that individual i experienced symptom j during episode k when $\tau_{ijk} \leq h(\eta_{ij}, \phi_{ik}) = \eta_{ij}.\phi_{ik}$. Subsequently, Zulkafli *et al*. (2016), following Zammitts' approach, explored two other threshold forms for this model: (i) summation form $(h(\eta_{ij}, \phi_{ik}) = \eta_{ij} + \phi_{ik})$, and (ii) interaction form $(h(\eta_{ij}, \phi_{ik}) = \eta_{ij} + \phi_{ik} + \eta_{ij}.\phi_{ik})$. Nevertheless, there remains potential for further exploration of alternative threshold forms: sum of squared $(h(\eta_{ij}, \phi_{ik}) = \eta_{ij}^2 + \phi_{ik}^2)$, and square of product $(h(\eta_{ij}, \phi_{ik}) = (\eta_{ij}.\phi_{ik})^2)$. Similarly, for Weibull threshold distribution, the probability θ_{ijk} for patient i reporting symptom j during episode k, is

$$\theta_{ijk} = Pr\left(\tau_{ijk} \leq h(\eta_{ij}, \phi_{ik})\right) = 1 - exp[-\lambda_i h(\eta_{ij}, \phi_{ik})^{\upsilon_i}]. \quad (2)$$

where υ_i is the shape parameter and λ_i is the scale parameter and and set to λ_i =1 for this study. This θ_{ijk} can also be applied to the five threshold forms mentioned above.

The study utilized survey data from the UK Hypoglycemia Study Group focusing on symptoms reported during hypoglycemic episodes by individuals with diabetes aged 22 to 72. It covered 26 symptoms experienced by both Type 1 and Type 2 diabetes patients. Information included episode details such as time, date, duration, symptoms, treatment, and blood glucose levels. Episodes within 24 hours of a preceding one were excluded to avoid repetition. The dataset includes information on various parameters for a set of 58 patients across different episodes and insulin therapy types: type 1 diabetes with <5 years' duration (T1 Ins<5), type 1 diabetes with >15 years' duration (T1 Ins>15); type 2 diabetes treated with insulin for <2 years (T2 Ins<2), type 2 diabetes treated with insulin for >5 years (T2 Ins>5). Each patient was assigned a unique identification number. Over a period of 9 to 12 months, patients recorded their symptoms during each hypoglycemic episode they experienced. In total 2671 episodes of 58 patients experiencing at least two episodes monthly are considered in this study, which is the strength too of this study and data (UK Hypoglycemia Study Group 2007).

4. Result and Discussion

The distribution of posterior estimate of symptom precision ($\tilde{\sigma}_i^{-2}$) and consistency ($\tilde{c}_i$) for Log-normal and Weibull threshold distributions are visualized from Figure 2 to Figure 5 for all patients. Distribution of $\tilde{\sigma}_i^{-2}$ appears skewed for all types of threshold, with most patients showing low consistency. The left red line on the graph indicates the lowest consistency value, while the right red line shows the value of the highest consistency value. On average, the consistency scores, $\tilde{c}_i$, amount to 50.07, with a standard deviation of 16.59.

For the Log-normal threshold distribution, patient 1028, with over 15 years of Type 1 diabetes, shows the highest precision at 34.78 (MCMC error: 0.2703, Bayesian interval: 12.85, 71.87) and consistency at 96.64 (MCMC error: 0.02378, Bayesian interval: 92.78, 98.63) for $\tau_{ijk} \leq \eta_{ij}.\phi_{ik}$, based on 42 recorded hypoglycemia episodes. In contrast, patient 2013, also with over 15 years of Type 1 diabetes, has the lowest consistency score at 17.75 with a Bayesian interval of 13.21 to 23.12 and MCMC error 0.1197 and reported the most episodes (138). Similarly, for other types of threshold, patient 1028 exhibits the highest posterior estimate for both consistency and precision parameters across all categories. Conversely, patient 2013 exhibits the lowest estimates for both consistency and precision across three threshold types:

product, square of product, and summation threshold forms. For the sum of square threshold, patient 5009 displays the lowest consistency (67.1, MCMC error: 0.217, Bayesian interval: 67.48, 79.29) and precision (2.178, MCMC error: 0.02175, Bayesian interval: 1.12, 3.83). While patient 2013 exhibits the lowest precision, patient 5009 shows the lowest consistency but not precision for interaction threshold (see Figure 2 and 3).

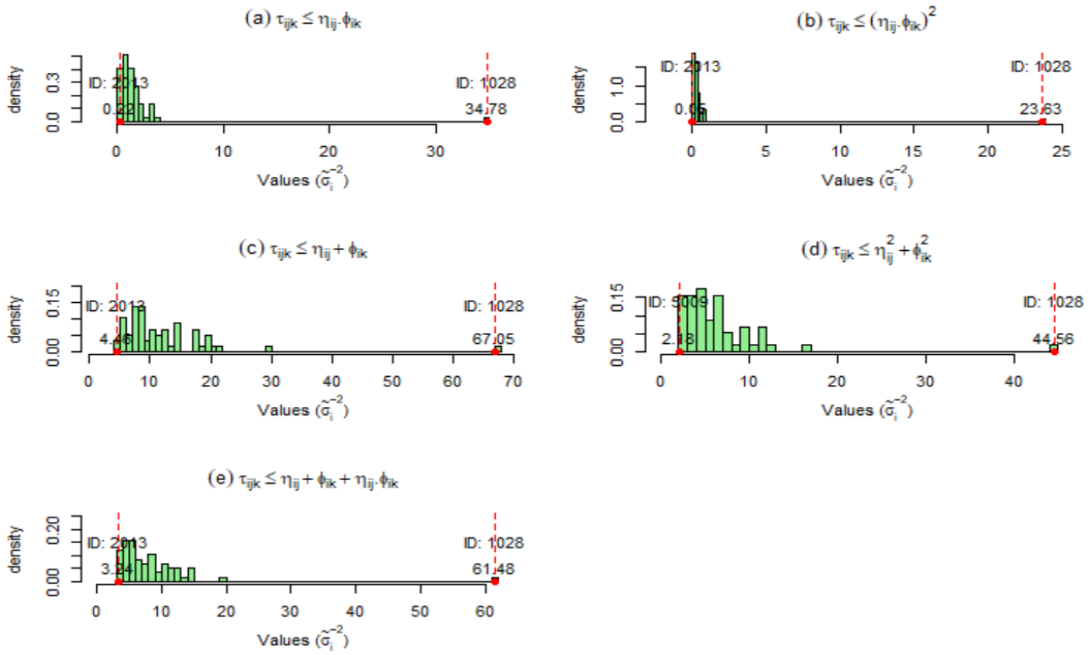


Figure 2: Posterior estimate of symptom precision across five threshold forms with Log-normal threshold distribution.

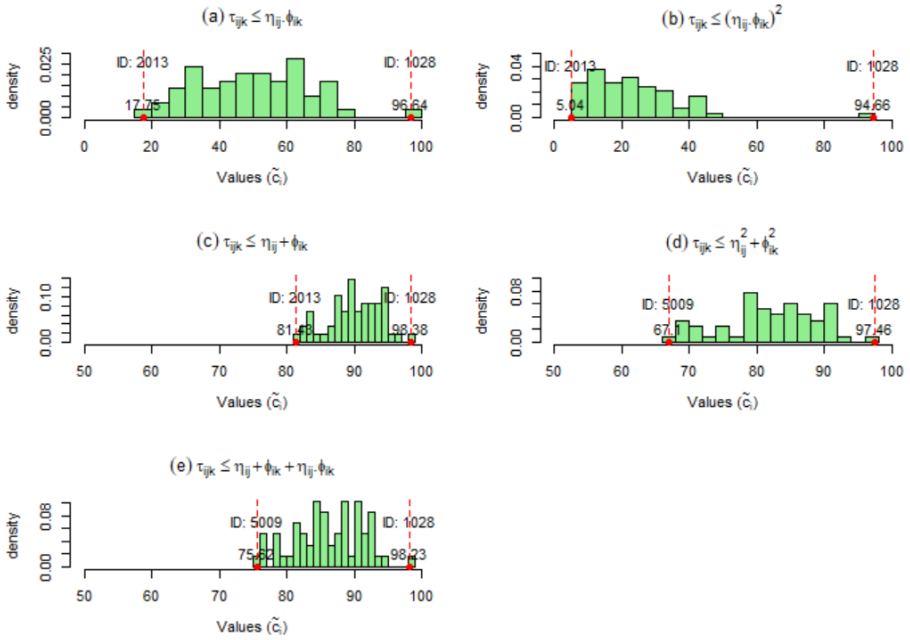


Figure 3: Posterior estimate of symptom consistency across five threshold forms with Log-normal threshold distribution.

For the Weibull threshold distribution, patient 5009 shows minimum consistency value at 74.29 (MCMC error: 0.0625, Bayesian Interval: 69.69, 78.63) for $\tau_{ijk} \leq \eta_{ij} + \phi_{ik} + \eta_{ij}.\phi_{ik}$. Similarly, patient ID 6018 exhibits a consistency value of 75.69 (MCMC error: 0.0972, Bayesian Interval: 71.52, 79.71), and patient ID 2013 registers a consistency value of 75.14 (MCMC error: 0.0397, Bayesian Interval: 72.64, 77.62). Notably, these three patients demonstrate nearly identical consistency levels. Patient ID 2013 also showcasing the minimum consistency and precision for $\tau_{ijk} \leq \eta_{ij}.\phi_{ik}$, $\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$, $\tau_{ijk} \leq \eta_{ij} + \phi_{ik}$. Conversely, patient ID 1028 displays the maximum consistency value of 97.27 (MCMC error: 0.0135, Bayesian Interval: 95.01, 98.7). Though, ID 5009 shows the minimum precision value of 2.92 (MCMC error: 0.0097, Bayesian Interval: 2.30, 3.68) for $\tau_{ijk} \leq \eta_{ij} + \phi_{ik} + \eta_{ij}.\phi_{ik}$, it is close to the value for ID 2013 at 3.03 (MCMC error: 0.0065, Bayesian Interval: 2.66, 3.47) (Figure 4 and 5).

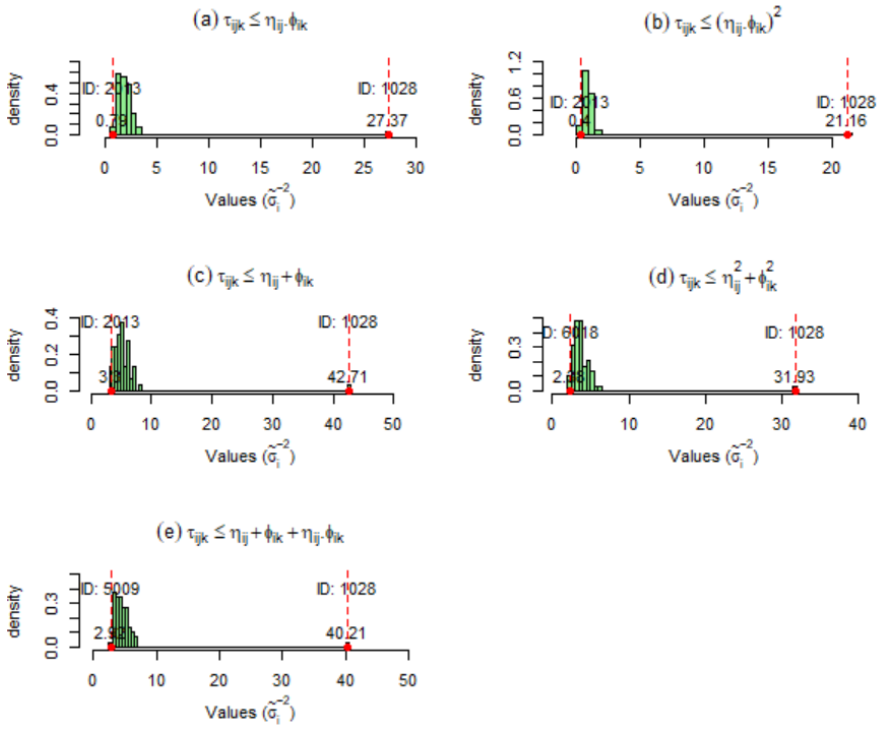


Figure 4: Posterior estimate of symptom precision across five threshold forms with Weibull threshold distribution.

Table 1 provides the values of Deviance, DIC (Deviance Information Criterion), and BIC (Bayesian Information Criterion) among five threshold forms for both Log-normal and Weibull threshold distributions to determine the best models.

Initially it was assumed that a Weibull distribution with a fixed scale parameter might be advantageous compared to the Log-normal distribution. However, results indicated that the Log-normal distribution is actually the better option. Specifically, the Log-normal with $\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$ threshold demonstrated the best fit, with the lowest values for Deviance (26544.1), DIC (28765.9), and BIC (26577.5). In contrast, for the Weibull distribution, the model with $\tau_{ijk} \leq \eta_{ij}.\phi_{ik}$ was identified as the best choice, yielding higher Deviance (26679.5), DIC (29224.1), and BIC (26724.1). Ultimately, the Log-normal model with $\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$ is preferred due to its superior overall fit for the data compared to the Weibull model.

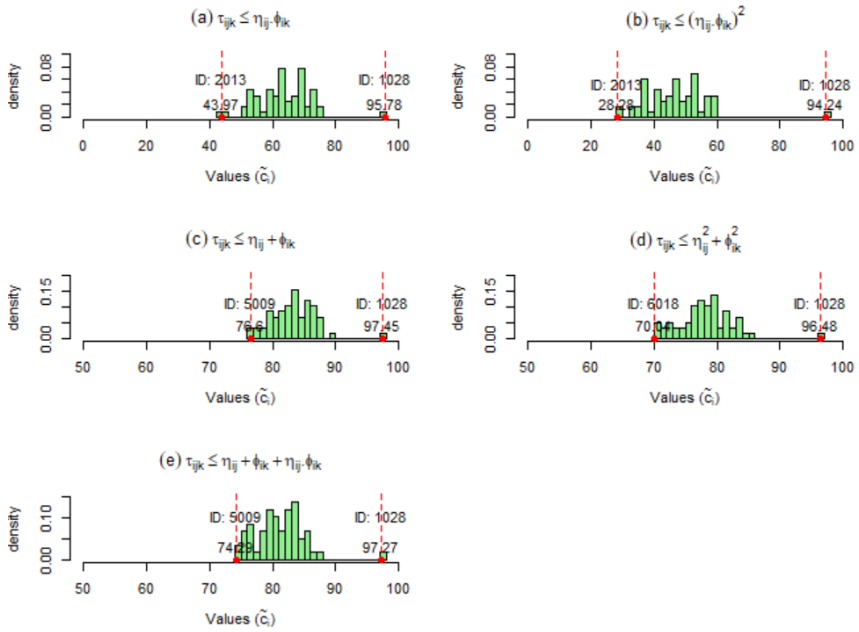


Figure 5: Posterior estimate of symptom consistency across five threshold forms with Weibull threshold distribution.

Table 1: Comparison of Deviance, DIC, and BIC values among five threshold forms

Types of threshold distributions		Types of threshold				
		$\tau_{ijk} \leq \eta_{ij}.\phi_{ik}$	$\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$	$\tau_{ijk} \leq \eta_{ij} + \phi_{ik}$	$\tau_{ijk} \leq \eta_{ij}^2 + \phi_{ik}^2$	$\tau_{ijk} \leq \eta_{ij} + \phi_{ik} + \eta_{ij}.\phi_{ik}$
Log-normal	Deviance	26556.6	**26544.1**	34911.2	26945.0	35480.1
	DIC	30142.8	**28765.9**	37520.9	29058.0	38168.0
	BIC	26590.1	**26577.5**	34944.7	29091.4	35513.5
Weibull	Deviance	**26679.5**	28120.2	90619.6	44127.6	95791.4
	DIC	**29224.1**	30720.1	91678.0	45782.6	96980.5
	BIC	**26724.1**	28164.8	90664.2	44172.2	95835.9

To test the Log-normal with $\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$ model adequacy, stochastic latent residuals approach is used. The stochastic latent residuals approach is now frequently used to test the adequacy of models with latent variables (Zulkafli *et al*. 2020). If the model is adequate, the latent residuals should follow a uniform distribution. The adequacy of this uniform distribution can be tested using the p-value of Kolmogorov-Smirnov goodness-of-fit test. For this model the Kolmogorov-Smirnov test for uniformity of the latent residuals yielded a p-value of 0.9826. This high p-value indicates that we do not reject the null hypothesis that the latent residuals follow a uniform distribution. This result suggests that the model's assumptions about the distribution of latent residuals are valid, as the observed data aligns well with the theoretical uniform distribution (Figure 6).

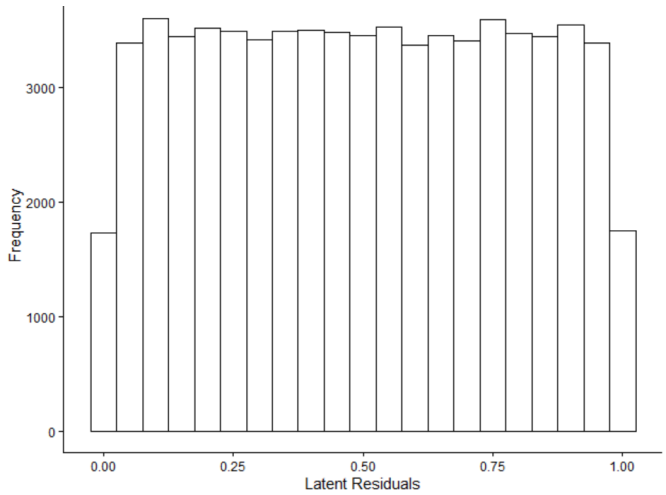


Figure 6: Distribution of stochastic latent residuals for the Log-normal threshold with $\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$ model

Moreover, the model demonstrated a high specificity of 83.76%, indicating that it correctly identified a significant proportion of patients who did not report symptoms of hypoglycemia. Additionally, the model exhibited a high negative predictive value (NPV) of 94.03%, suggesting strong reliability in predicting the absence of symptoms. However, the model's sensitivity, or true positive rate (TPR), was moderate at 56.25%, reflecting that it correctly identified just over half of the patients who reported symptoms. The precision, or positive predictive value (PPV), was notably low at 29.65%, indicating a high rate of false positives where many patients identified as reporting symptoms did not actually report them. These results highlight the model's strength in identifying non-reports but reveal a need for improvement in accurately detecting true reports of symptoms and reducing false positives.

As outlined in Al Sharmin *et al*. (2024), following the approach utilizing the regularized incomplete beta function (Pearson & Johnson 1968) for the estimated consistency values (Table 2) for Log-normal $\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$ type threshold model, cutoff points of hypoglycemia symptom consistency can be established as: $0 \leq \tilde{c}_i \leq 15.13$ for low consistency, $15.13 < \tilde{c}_i \leq 27.76$ for medium consistency, and $27.76 < \tilde{c}_i \leq 100$ for high consistency.

Table 2: Posterior estimate of symptom reporting consistency for Log-normal threshold distribution with $\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$

Serial no.	Patient ID	No. of hypoglycemia episodes	Consistency	SE	MCMC error	95% Bayesian interval 2.5%	97.5%
			T1 Ins<5				
1	1009	74	22.75	4.17	0.14	15.26	22.55
2	1021	43	19.83	4.72	0.19	12.09	19.32
3	1036	24	21.81	5.99	0.23	12.21	21
4	2012	37	9.83	2.71	0.11	5.688	9.48
5	2027	22	36.56	9.12	0.35	21.06	35.77
6	3001	31	25.81	6.73	0.28	15.07	24.99
7	3024	27	22.06	5.72	0.21	12.77	21.35
8	3029	69	32.25	6.13	0.20	21.49	31.83
9	3050	44	19.53	4.44	0.18	12.06	19.15
10	4023	134	6.714	1.10	0.05	4.831	6.621
11	4034	55	27.79	5.57	0.22	18.34	27.25

Table 2 (Continued)

12	4049	22	29.53	7.45	0.29	17.18	28.8
13	4063	42	12.09	2.98	0.12	7.331	11.72
14	5029	45	30.33	6.23	0.23	19.48	29.89
15	5044	69	14.83	2.89	0.11	9.928	14.57
16	5045	68	19.01	3.75	0.13	12.62	18.74
17	5088	87	15.96	4.47	0.16	8.908	15.47
18	6010	19	33.08	8.51	0.25	18.86	32.17
19	6019	64	13.47	2.76	0.10	8.85	13.22
20	6038	79	8.983	1.70	0.07	6.066	8.852
21	6065	39	20.77	4.98	0.18	12.58	20.22
			T1 Ins>15				
22	1008	95	9.755	1.71	0.07	6.768	9.626
23	1015	27	15.81	4.32	0.16	8.974	15.26
24	1025	25	31.21	7.72	0.28	17.97	30.48
25	1028	42	94.66	3.05	0.04	86.67	95.44
26	1039	43	10.09	2.48	0.10	6.03	9.79
27	1086	67	14.48	3.03	0.12	9.61	14.13
28	2009	86	9.941	1.83	0.07	6.865	9.776
29	2010	89	11.28	2.07	0.10	7.684	11.11
30	2013	138	5.038	0.80	0.03	3.631	4.982
31	2015	32	23.04	5.47	0.21	13.87	22.48
32	2021	24	26.5	6.93	0.26	15.13	25.85
33	2022	36	16.56	4.29	0.17	9.745	15.98
34	3015	19	27.4	7.89	0.27	14.92	26.47
35	3022	20	34.27	8.23	0.27	20.24	33.55
36	4003	23	45.95	9.32	0.30	29.01	45.64
37	4008	59	10.26	2.01	0.07	6.938	10.05
38	4013	39	20.38	4.84	0.18	12.41	19.84
39	4043	35	13.91	3.58	0.13	8.344	13.47
40	4045	38	19.29	4.67	0.17	11.57	18.79
41	5004	26	29.53	7.41	0.27	16.85	29
42	5023	20	42.16	9.95	0.29	24.59	41.37
43	5026	24	43.96	9.65	0.35	26.64	43.38
44	6018	39	9.604	2.40	0.10	5.73	9.312
45	6023	59	10.93	2.24	0.08	7.136	10.75
			T2 Ins<2				
46	3016	22	41.25	9.36	0.30	24.88	40.66
47	6002	34	14.95	3.84	0.14	8.933	14.43
48	6056	28	32.41	7.64	0.28	19.52	31.81
49	6058	20	43.67	9.40	0.35	26.61	43.19
			T2 Ins>5				
50	1055	25	44.06	9.49	0.30	26.91	43.59
51	3048	31	35.33	8.18	0.28	21.23	34.67
52	3052	105	20.15	3.41	0.12	14.05	19.91
53	3057	51	14.55	3.31	0.14	9.18	14.2
54	3065	26	24.69	6.54	0.23	13.82	24.1
55	3067	26	16.15	4.60	0.19	9.059	15.46
56	4072	39	25.59	5.70	0.17	15.87	25.04
57	4076	29	22.73	6.06	0.24	13.03	21.99
58	5009	36	8.25	2.00	0.07	5.08	8.017

Table 3 categorizes patients by their level of consistency according to the $\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$ model, considering the Log-normal threshold distribution. Analyzing Table 3, both ID 2013 and ID 5009 fall into the low consistency category, which aligns with the results shown in Figures 2 and 3. Not only is that, ID 3015 that is fall into middle consistency category shown in Figure 1. Where Figure 1 (b) shows not much clustering of marked cells i.e. remain emmeded empty cell that which represent the middle consistency of symptom reporting.

Table 3. Grouping of patients by consistency level for the Log-normal threshold distribution with $\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$

Low consistency (0 to 15.13)		Middle consistency (15.13 to 27.76)		High consistency (27.76 to 100)	
1008	5044	1009	3067	1025	5029
1039	6002	1015	4013	1028	6010
1086	6018	1021	4034	1055	6056
2009	6019	1036	4045	2027	6058
2010	6023	2015	4072	3016	
2012	6038	2021	4076	3022	
2013		2022	5045	3029	
3057		3001	5088	3048	
4008		3015	6065	4003	
4023		3024		4049	
4043		3050		5004	
4063		3052		5023	
5009		3065		5026	

A simulation study is carried out to assess the performance of different forms of threshold for Log-normal thesholdhold distribution. The simulation is conducted using the R statistical package for sample sizes n = 50, 100, and 150. Each patient is assigned 26 symptoms, and there are 19 episodes for each patient. The algorithm of generating simulated data is given below:

(1) For each threshold form, random 0s and 1s are generated using a Bernoulli distribution to create the response variable, with θ_{ijk} being generated for each type of the cumulative distribution function (Eq. (1) and Eq. (2)) of the threshold variable, τ_{ijk}:

$$y_{ijk} \sim Bernoulli(\theta_{ijk}), \quad \text{where, } \theta_{ijk} = Pr(\tau_{ijk} \leq h(\eta_{ij}, \phi_{ik}))$$

(2) Each latent parameter, η_{ij} and ϕ_{ik} are sampled from Gamma distributions:

$$\eta_{ij} \sim Gamma(\alpha_\eta, \beta_\eta) \quad \text{and} \quad \phi_{ik} \sim Gamma(\alpha_\phi, \beta_\phi)$$

(3) The threshold random variables τ_{ijk} are generated from two different probability distributions:

(i) For the Log-normal distribution: $\tau_{ijk} \sim Log-normal(0, \sigma_i^2)$ with $\sigma_i^2 \sim Inv-Gamma(\alpha_\sigma, \beta_\sigma)$, and associated with the variability of symptoms reported by individual patient i.

(ii) For the Weibull distribution: $\tau_{ijk} \sim Weibull(\upsilon_i, \lambda_i)$ with $\lambda_i = 1$ and $\upsilon_i \sim Inv-Gamma(\alpha_\upsilon, \beta_\upsilon)$. The shape parameter, υ_i of weibull distribution is the parameter associated with the variability of symptoms reported by individual patient i and and follows Gamma with $\alpha_\upsilon = 1$ and $\beta_\upsilon = 0.1$.

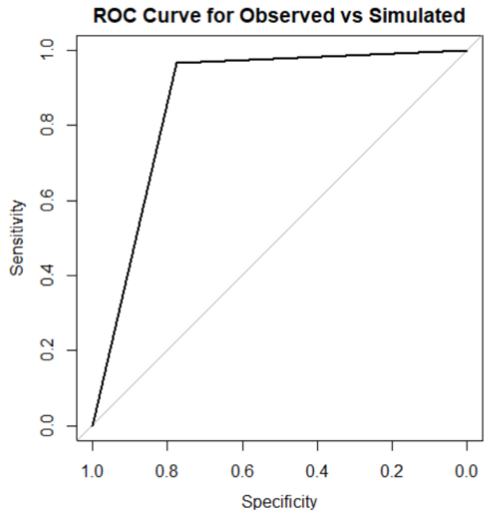
The simulated data is applied to the logistic latent variable model and the consistency and precision parameters are estimated under Bayesian approach. The Markov chain Monte Carlo simulation techniques was performed in WinBUGS with 1,000 burn-in period and the posterior distributions were sampled from 5000 iterations. This study is repeated for multiple sample sizes (n = 50, 100, 150). We used $\alpha_\eta = \alpha_\phi = \alpha_\sigma = \alpha_\upsilon = 1$ and $\beta_\eta = \beta_\phi = \beta_\sigma = \beta_\upsilon = 0.1$ for both data generation and model specification (Zammit *et al*. 2011).

Table 4: Model comparison based on the Log-normal threshold distribution across different sample sizes

Sample size (Total observation, N=n*J*K)		$\tau_{ijk} \leq \eta_{ij}.\phi_{ik}$ (Model 1)	$\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$ (Model 2)	$\tau_{ijk} \leq \eta_{ij} + \phi_{ik}$ (Model 3)	$\tau_{ijk} \leq \eta_{ij}^2 + \phi_{ik}^2$ (Model 4)	$\tau_{ijk} \leq \eta_{ij} + \phi_{ik} + \eta_{ij}.\phi_{ik}$ (Model 5)
n =50 (24700)	DIC	25461.60	**22958.70**	33823.30	30271.20	33442.40
	AUC	0.85	0.87	0.55	0.80	0.56
n =100 (49400)	DIC	51156.70	**46837.20**	67785.80	59797.80	66220.30
	AUC	0.86	0.87	0.59	0.80	0.58
n =150 (74100)	DIC	77171.11	**75838.90**	100979.00	88293.00	94748.70
	AUC	0.86	0.87	0.59	0.81	0.56

While comparing models based on a Log-normal threshold distribution across different sample sizes (Table 4), Model 2, represented by the equation $\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$, consistently demonstrates superior performance. This model achieves the lowest Deviance Information Criterion (DIC) values and the highest area under the curve (AUC) scores, indicating that it provides the best fit and the most robust discriminative power. Conversely, Model 3, defined by $\tau_{ijk} \leq \eta_{ij} + \phi_{ik}$, shows the highest DIC values and some of the lowest AUC scores, reflecting its poor fit and weak classification capability. As the sample size increases, although DIC values rise for all models, the performance ranking remains consistent, with Model 2 retaining its advantage. This suggests that Model 2 is the most reliable option for modeling under a Log-normal threshold distribution, while Model 3, along with Model 5, should be approached with caution due to their consistently suboptimal performance.

Additionally, in Receiver Operating Characteristic (ROC) curve, a model with good performance will have a curve that bows towards the top left corner, indicating high sensitivity and specificity. Figure 7 shows that the model with Log-normal threshold with $\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$, has a high sensitivity of 96.7% and a moderate specificity of 77.4% with an AUC of 0.87 for n=150, confirming that the model is strong in correctly identifying both true positives and true negatives, making it a reliable choice for classification tasks, i.e. the model has a good balance between sensitivity and specificity, effectively separating true positives from true negatives.



Observed	Simulated 0 (Negative)	1(Positive)
0 (Negative)	2255	658
1(Positive)	2323	68864

Here,
True Negatives (TN): 2255 (correctly predicted as negative),
False Positives (FP): 658 (incorrectly predicted as positive),
False Negatives (FN): 2323 (incorrectly predicted as negative) ,
True Positives (TP): 68864 (correctly predicted as positive)

Sensitivity: $\left(\frac{TP}{TP+FN}\right) = \left(\frac{68864}{68864+2323}\right)$=0.967 (96.7%)
Specificity: $\left(\frac{TN}{TN+FP}\right) = \left(\frac{2255}{2255+658}\right)$ =0.774 (77.4%)

Figure 7: ROC curve for the Log-normal threshold model with $\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$ for n=150

Previous studies (Zammitt *et al*. 2011; Zulkafli *et al*. 2016; 2020) have indicated that, for Log-normal threshold distribution with $\tau_{ijk} \leq \eta_{ij}.\phi_{ik}$ model outperforms the models with $\tau_{ijk} \leq \eta_{ij} + \phi_{ik}$ and $\tau_{ijk} \leq \eta_{ij} + \phi_{ik} + \eta_{ij}.\phi_{ik}$. Consistent with these findings, our study yields similar results among these threshold types. However, in prior studies (Zammit *et al*. 2011; Zulkafli *et al*. 2016; 2020), the scale parameter of the Weibull distribution was assumed to be fixed. Without imposing this condition on the scale parameter, the Weibull distribution can still model the threshold variables (Sharmin & Islam 2017; 2018). Hence, further research is needed to assess the sensitivity to the threshold distribution without fixing the scale parameter of the Weibull distribution.

5. Conclusion

The selection of threshold form is considered pivotal, as different forms may exhibit significant associations with symptom reporting patterns. As an extension, two new threshold forms ($\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$ and $\tau_{ijk} \leq \eta_{ij}^2 + \phi_{ik}^2$) are introduced for modeling symptom consistency, and the square product threshold form ($\tau_{ijk} \leq (\eta_{ij}.\phi_{ik})^2$) in conjunction with log-normal threshold distribution demonstrates superior performance compared to others. Furthermore, it is observed that extreme consistency and precision values are not specific to any particular threshold models as well as threshold distribution, as nearly every model identifies the same patient with the highest consistency. This information can assist researchers and practitioners in comprehending the variability in symptom reporting across different conditions, thereby facilitating the design and interpretation of studies concerning symptom assessment and management.

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