Spatial Survival Analysis of Stroke Hospitalizations: A Bayesian Approach

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ABSTRACT – Survival analysis encompasses a range of statistical techniques used to evaluate data where the outcome variable represents the time until a specific event occurs. When such data is collected across different spatial regions, integrating spatial information into survival models can enhance their interpretive power. A widely adopted method involves applying an intrinsic conditional autoregressive (CAR) prior to an area-level frailty term, accounting for spatial correlations between regions. In this study, we extend the Bayesian Cox semiparametric model by incorporating a spatial frailty term using the Leroux CAR prior. This approach aims to enhance the model's capacity to analyze stroke hospitalizations at Labuang Baji Hospital in Makassar, with a particular focus on exploring the geographic distribution of hospitalizations, length of stay (LOS), and factors influencing patient outcomes. The dataset, derived from the medical records of stroke patients admitted to Labuang Baji Hospital between January 2022 and June 2024, included variables such as LOS, discharge outcomes, sex, age, stroke type, hypertension, hypercholesterolemia, and diabetes mellitus. The analysis revealed that stroke type was a significant determinant of hospitalization outcomes. Specifically, ischemic stroke patients exhibited faster recovery times than those with hemorrhagic strokes, with a hazard ratio of 1.892, representing an 89% greater likelihood of recovery. Additionally, stroke patients across all districts treated at Labuang Baji Hospital demonstrated similar average recovery rates and discharge durations.

Keywords– Bayesian, Spatial, Survival Analysis, Semiparametric Cox, CAR Leroux

1. INTRODUCTION

Survival analysis, often referred to as time-to-event analysis, involves a collection of statistical methods designed to evaluate data where the primary outcome is the duration until a specific event occurs. In biostatistics, such events may include outcomes like death, recovery, or disease onset, with survival time commonly expressed in units such as days, weeks, or years. A common challenge in this field arises when some individuals do not experience the event within the study period, leading to censored data—a well-recognized and extensively studied issue in the literature [1, 2]. Geographic variations in event distributions necessitate the inclusion of spatial data in analyses. A prominent example is the Bayesian hierarchical spatial survival model developed by Banerjee, Wall, and Carlin [3], which incorporates conditionally autoregressive (CAR) frailty effects into a Weibull baseline hazard. Building on this, we adapted and extended the Bayesian framework proposed by Osnes and Aalen [4] for semiparametric Cox proportional hazards models to investigate stroke hospitalizations in Makassar, Indonesia. Stroke, a cerebrovascular disease, ranks as the second leading cause of death globally after heart disease, accounting for 5.8 million fatalities annually [5]. It is also a major contributor to disability worldwide globally [6], with the Global Burden of Disease Study reporting that 80.1 million people are affected by stroke each year, of whom 6.2 million die [7-9]. In Indonesia, stroke mortality rates are similarly high [10], with prevalence increasing from 7 per 1,000 individuals in 2013 to 10.9 per 1,000 in 2018. The financial burden of stroke is significant, ranking third in healthcare expenditures after heart disease and cancer, with costs reaching 3.23 trillion rupiah in 2022, up from 1.91 trillion rupiah in 2021 [11]. Stroke risk factors are generally categorized into modifiable factors, which can be mitigated through lifestyle changes or medical intervention, and non-modifiable factors, which are linked to genetic predisposition [12, 13]. To reduce the adverse impacts of stroke, it is crucial to analyze modifiable risk factors influencing clinical recovery among stroke patients.

Survival models are frequently employed to examine various aspects of stroke outcomes. Cox proportional hazards models, for example, have been used to explore relationships between stroke risk factors and hospitalization frequency [14], recurrence and recurrence-free survival [15], and mortality [16]. Additionally, parametric and flexible parametric survival models have assessed stroke recurrence, associated risk factors, and long-term survival [17-20]. Despite significant research on stroke outcomes and the critical role of timely treatment, spatial effects are seldom incorporated. One study employed a Bayesian log-logistic proportional odds model with a Gaussian random field to evaluate spatial effects on in-hospital stroke mortality [21]. Bayesian methods are widely utilized in disease mapping due to their ability to integrate prior information, enhancing result precision and interpretability [22]. The conditional autoregressive (CAR) prior is particularly popular for modeling spatial effects [1] and has been applied in survival analyses for diseases such as cancer [23] and dengue fever [24, 25]. However, its application in stroke research remains limited. This study addresses this gap by employing a Bayesian spatial survival Cox-Leroux model to analyze recovery rates among hospitalized stroke patients, explicitly incorporating geographic data to evaluate spatial influences on clinical outcomes. A novel aspect of this study is its assessment of how geographic factors interact with modifiable risk factors to affect stroke progression and recovery. This study aims to enhance the modeling of stroke hospitalizations at a Labuang Baji Hospital in Makassar by focusing on the geographic distribution of hospitalizations, LOS, and the factors that influence patient outcomes.

2. LITERATURE REVIEW

2.1. Survival Analysis

Survival analysis is a set of statistical procedures used to analyze data where the response variable is the time until the occurrence of a specific event. Survival time can be measured in years, months, weeks, or days from the start of an individual's follow-up period until the event occurs [26]. In survival analysis, both censored and uncensored data are utilized to estimate survival probabilities, hazard rates, and to model the relationship between covariates and survival times. Censoring occurs when the event of interest has not yet been observed or is only partially observed for some individuals within the study. In contrast, uncensored data refers to cases where the event of interest has been precisely recorded, occurring within the study period.

2.2. Bayesian Spatial Semiparametric Cox-Leroux Model

The semiparametric Cox model [27] is a widely used technique for analyzing time-to-event data due to its flexibility, as it does not require specifying a parametric baseline hazard function. In this study, we extend the semiparametric Cox proportional hazards model by building on the methodology proposed by Osnes and Aalen [4]. Specifically, we model the LOS using a proportional hazards function, also referred to as the intensity function, for patients k = 1, 2, …, K incorporating the covariate X_k [4]. The hazard function for patient k is defined as

$$h(t_k; x_k) = h_{kj} = h_0(t_k)\exp\{\beta^T X_k\} \quad (1)$$

where $h_0(t_k)$ represents the unknown baseline hazard rate, modeled nonparametrically. The vector β contains regression parameters, and both β and X_k are assumed to remain constant over time, with $j = t_k$.

Counting process data, such as survival data, are typically analyzed using intensity models. For a given patient k = 1, 2, …, K, the intensity function (or hazard function) is denoted as I_{kj}, while Y_{kj} indicates whether the patient is at risk during the j-th time interval. The observation time within this interval is denoted by t_k, and the number of events (failures) occurring up to time j is represented by $\mathrm{N}(t_k; X_k) = N_{kj}$. The increment of events over the small interval $[j, j + d_j]$ is given by dN_{kj}, where:

$$dN_{kj} = \begin{cases} 1 & \text{if patient k is discharged during interval j} \\ 0 & \text{otherwise} \end{cases}$$

The increment dN_{kj} follows a Poisson distribution with a mean equal to $I_{kj} = Y_{kj}h_{kj}$

$$dN_{kj} \sim \mathrm{Poisson}(I_{kj}) \quad (2)$$

The multiplicative intensity model is expressed as:

$$I_{kj} = Y_{kj}\exp\{\beta^T X_k\}h_0(t_k) \quad (3)$$

where the baseline hazard function, $h_0(t_k)$. To extend this model, we incorporate a spatial frailty term u_i, which follows a Leroux conditional autoregressive (CAR) prior. The extended model is expressed as

$$I_{kj} = Y_{kj}\exp\{\beta^T X_k + u_i\}h_0(t_k) \quad (4)$$

Here, the baseline hazard function $h_0(t_k)$ is assigned a Gamma prior distribution, $\mathrm{Gamma}(ch_0^*(t_k), c)$, where c = 0.001, $h_0^*(t_k)$ is the prior estimate of the hazard function, and c reflects the confidence in that estimate. The regression coefficients β are modeled using a normal prior distribution, β ~ N(0,100).

The spatial frailty term u_i, is modeled using the Leroux CAR prior prior [28], which introduces a single frailty term to capture spatial autocorrelation among neighboring regions. The degree of spatial autocorrelation is controlled by the parameter ρ, which is estimated and constrained to the interval [0,1]. The conditional distribution of u_i, given u_j for $i \neq j$, is defined as:

$$(u_i | u_j, i \neq j, \sigma_u^2) \sim \mathrm{N}\left(\frac{\rho \sum_j u_j \omega_{ij}}{\rho \sum_j \omega_{ij} + 1 - \rho}, \frac{\sigma_u^2}{\rho \sum_j \omega_{ij} + 1 - \rho}\right)$$

where ω_{ij} = 1 if areas i and j are adjacent, and ω_{ij} = 0 otherwise. The prior distribution for ρ is uniform on [0,1], $\rho \sim$ Unif(0,1), and the variance σ_u^2 follows an Inverse Gamma distribution:

$$\sigma_u^2 \sim \mathrm{IG}(1, 0.1)$$

A sensitivity analysis was performed to assess the influence of different prior distributions on the posterior estimates. Specifically, we evaluated three prior distributions for the variance of the spatial frailty term, σ_u^2, for Cox–Leroux models: IG(1, 0.1), IG(0.5, 0.05), and IG(2,0.2) [25]. These priors were selected to provide a range of options, from highly concentrated to highly diffuse, in relation to the data and posterior distribution. Model performance was evaluated by comparing predictive accuracy across models using the Watanabe-Akaike Information Criterion (WAIC) [29], where lower WAIC values indicated better model fit. In the selected model, covariates were deemed significant if the 95% posterior credible interval (CI) for the untransformed coefficient excluded zero, or equivalently, if the 95% CI for the exponentiated coefficient excluded one. Parameter estimation was performed using the R2WinBUGS package in R (version 3.6.1) [30]. Posterior parameter estimates were obtained from 5,000 Markov Chain Monte Carlo (MCMC) samples following a burn-in period of 5,000 samples. Both the data and the R code used for the analysis are available upon request.

2.3. *Hazard Ratio (HR)*

The hazard ratio is the exponentiated mean value exp(mean) and represents the relative hazard of an event occurring in a particular district compared to a baseline (often the district with zero effect or the average hazard).

- HR > 1 indicates a higher hazard (increased risk) relative to the baseline.
- HR < 1 indicates a lower hazard (decreased risk) relative to the baseline.
- HR = 1 suggests no difference in hazard compared to the baseline.

3. METHODOLOGY

3.1. *Data*

The stroke patient data were obtained from medical records at Labuang Baji Hospital, Makassar City. The dataset includes stroke patients admitted between January 2022 and June 2024. Study participants were individuals consistently recorded during their treatment at Labuang Baji Hospital for stroke. The research variables included the length of hospital stay (in days), discharge status (recovered/improved, not recovered, deceased, or transferred to another hospital), age, sex, history of hypertension, hypercholesterolemia, diabetes mellitus, type of stroke, and residential address. Patients' residential addresses at the time of diagnosis were geocoded and categorized into one of the 15 districts in Makassar City as of 2024. Patients with hospital stays of less than one day were excluded from the study.

The initial dataset comprised 220 stroke patients. Of these, 63 patients (28.64%) resided outside Makassar City, 18 patients (8.18%) had incomplete clinical data, and 78 patients (35.45%) lacked recorded residential address information. After data cleaning, the final dataset used for analysis consisted of 61 patients. The response variable in this study was the length of hospital stay for stroke patients treated during the study period, defined as follows:

- For patients discharged after recovery or improvement, the length of hospital stay was treated as uncensored survival data since the expected event—discharge—had occurred.
- For patients who died, were transferred to another hospital, remained hospitalized at the end of the study period (June 30, 2024), or self-discharged, their length of stay was treated as censored data.

Censoring also applied when the exact recovery time could not be recorded, such as for patients who left the hospital before recovery or were still hospitalized at the end of the study period. The data underwent cleaning and accuracy verification through cross-referencing with hospital medical record staff. Written consent was obtained from the hospital for the use of these data.

3.2. *Research Variables*

The variables utilized in this study are detailed in Table 1.

Table 1 The variables utilized in this study

Variables	Variable Names	Descriptions
Y	Survival Time	Represents the duration, in days, that a stroke patient undergoes hospital treatment until recovery or improvement.
X1	Age	The age of the stroke patient at the time of hospital admission, measured in years.
X2	Sex	The gender of the stroke patient, coded as: 0 = Female 1 = Male
X3	hypertension	Indicates the presence of hypertension, coded as: 0 = No hypertension 1= Hypertension present
X4	Diabetes	Indicates the presence of diabetes, coded as: 0 = No diabetes 1 = Diabetes present
X5	hypercholesterolemia	Indicates the presence of hypercholesterolemia, coded as: 0 = No hypercholesterolemia 1= Hypercholesterolemia present
X6	stroke types	Specifies the type of stroke, coded as: 0= haemorrhagic 1= ischemic
S	Status	The clinical outcome of the stroke patient, coded as 0 = No event (not recovered/deceased) 1 = Event occurrence (recovery/improvement)

IV. RESULTS AND DISCUSSIONS

4.1. *Descriptive Analysis*

Labuang Baji Hospital is located in the Mamajang District. Table 2 presents the distribution of stroke patients by residential district. The highest proportion of patients originated from the Rappocini District (18.03%), followed by the Mariso District (14.75%). Of the total stroke patients, 61% were female.

Table 2 The distribution of stroke patients treated at the stroke center during the study period based on their residential districts.

No	Districts	Total Stroke Cases in each district	Percentage
1	Mamajang	4	6.56
2	Manggala	4	6.56
3	Mariso	9	14.75
4	Sangkarrang	0	0.00
5	Rappocini	11	18.03
6	Tamalate	7	11.48
7	Makasar	6	9.84
8	Ujung Pandang	2	3.28
9	Panakukkang	6	9.84
10	Bontoala	1	1.64
11	Wajo	0	0.00
12	Ujung Tanah	1	1.64
13	Tallo	6	9.84
14	Tamalanrea	0	0.00
15	Biringkanaya	4	6.56
Total		61	100.00

The average length of stay for stroke patients was 5 days, as illustrated in Figure 1. The most common length of stay was 3 days (27.87%), followed by 4 days (24.59%) and 5 days (13.11%). The duration of hospital stays ranged from a minimum of 1 day to a maximum of 19 days.

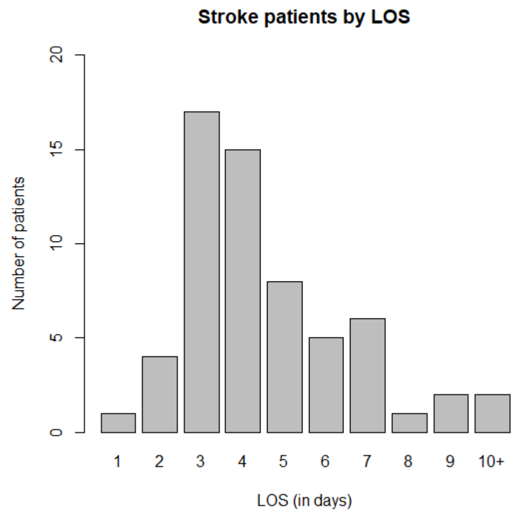

Figure 1. Distribution of stroke patients at Labuang Baji Hospital based on LOS

The majority of stroke patients treated at Labuang Baji Hospital were elderly, with a mean age of 61.46 years and a median age of 61 years, ranging from 38 to 83 years. Most patients were female (61%) (Figure 2.a) and had comorbidities, including diabetes (34.43%) (Figure 2.b), hypercholesterolemia (3.28%) (Figure 2.c) and hypertension (78.69%) (Figure 2.d). Of all stroke cases, 18.03% were diagnosed as hemorrhagic stroke, while the remaining 81.97% were classified as ischemic stroke ((Figure 2.e). Stroke Data Distribution are given in Figure 2.

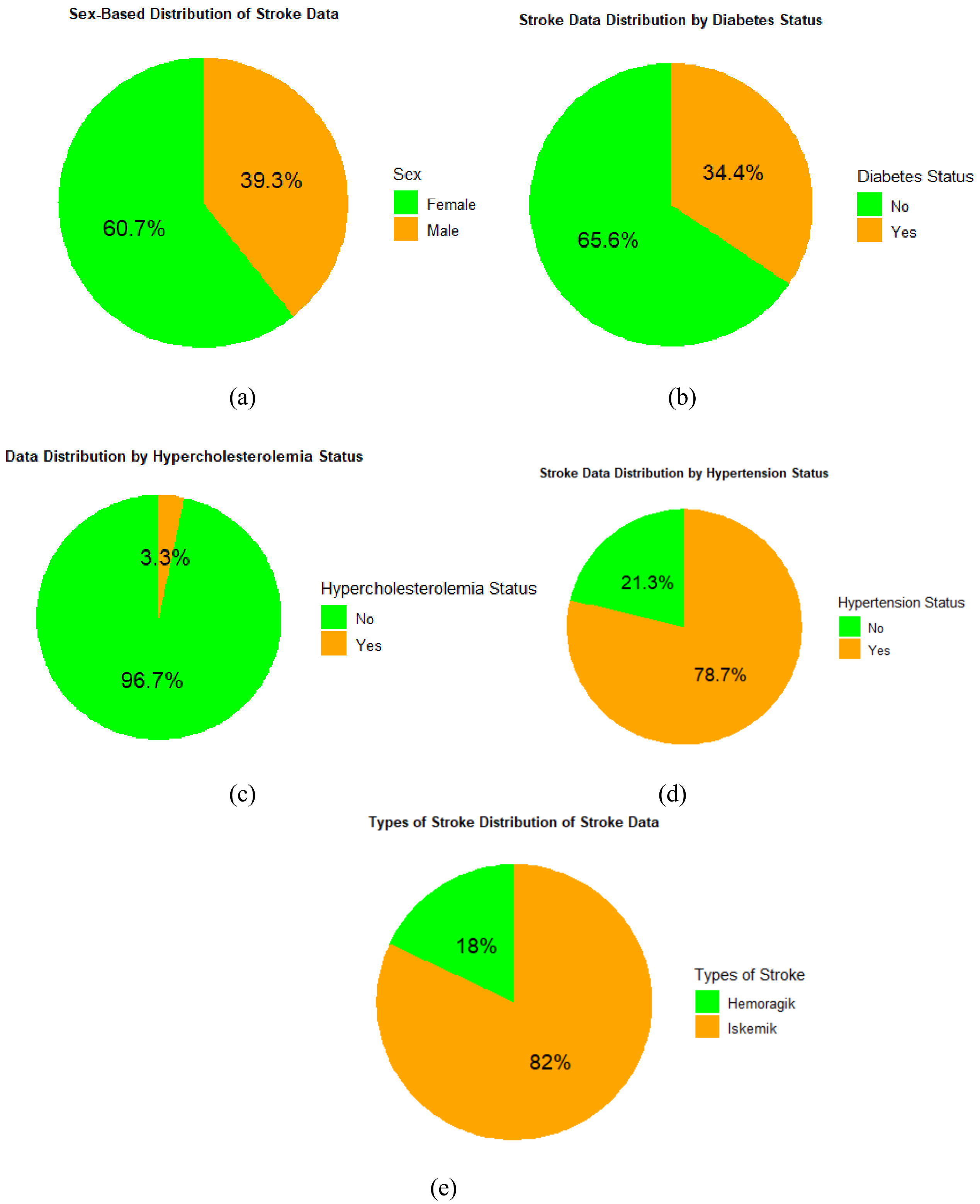

Figure 2. Stroke Data Distribution

4.2. Bayesian Posterior Summaries and Spatial Frailty Estimation in Cox-Leroux Models

A sensitivity analysis was conducted to assess the impact of different prior distributions on posterior estimates. The results indicate that the Cox-Leroux model with a G(1, 0.1) hyperprior yielded the lowest WAIC value (154.29), slightly outperforming the model with a G(2, 0.2) hyperprior (WAIC = 154.38) and the G(0.5, 0.05) hyperprior (WAIC = 154.91). The posterior hazard ratios for the key parameters of the Cox-Leroux model are presented in Table 3.

Table 3. Posterior Hazard Ratios using Cox-Leroux Models.

No	Parameters	Mean	Exp(mean)	95% CI
1	Age	0.298	1.347	0.771; 2.456
2	Sex	0.035	1.036	0.622; 1.733
3	Diabetes mellitus	-0.309	0.735	0.421; 1.258
4	hypertension	-0.271	0.762	0.432; 1.341
5	hypercholesterolemia	0.135	1.144	0.617; 1.886
6	Ischemic vs Hemorrhagic stroke	0.638	1.892	1.032; 4.129
	ρ	0.486	1.626	1.028; 2.644
	σ^2	5.172	176.260	1.341; 58351755.387

The analysis identified stroke type as a significant covariate associated with the LOS, as shown in Table 3. Specifically, patients with ischemic strokes demonstrated faster recovery times than those with haemorrhagic strokes, with a hazard ratio (HR) of 1.892. This indicates that ischemic stroke patients had an 89% higher likelihood of recovery compared to their hemorrhagic counterparts. The spatial dependency parameter, ϱ (HR = 1.63, 95% CI: 1.03–2.64), quantifies the extent of spatial correlation within the dataset. A positive estimate, supported by a confidence interval that excludes 1, highlights a statistically significant spatial dependency in patient outcomes relative to geographic location. This finding underscores the influence of geographic factors on recovery outcomes. The 95% credible intervals for all spatial random effects included 1, suggesting that, on average, stroke patients across all districts admitted to Labuang Baji Hospital experienced similar recovery and discharge times. This regional uniformity, adjusted for covariates, is depicted in Figure 2. The hazard ratios for spatial random effects (spatial frailty) in Cox-Leroux models are provided in Table 4.

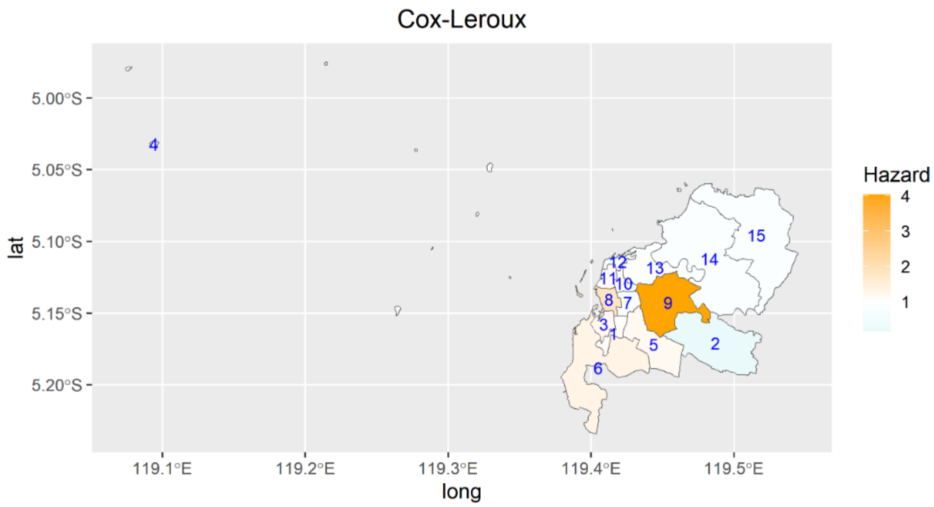

Figure 2. District-Level Spatial Hazard Ratios in the Cox-Leroux Model

Table 4. Estimation of hazard ratios for spatial random effects (spatial frailty) in Cox-Leroux models

No	District	Mean	Exp(mean)	95% CI
1	Mamajang	0.054	1.056	0.105; 10.299
2	Manggala	-1.879	0.153	0.004; 2.031
3	Mariso	0.169	1.185	0.140; 11.908
4	Sangkarrang	0.136	1.145	0.046; 35.208
5	Rappocini	0.170	1.185	0.148; 10.282
6	Tamalate	0.306	1.358	0.141; 16.333
7	Makasar	-0.289	0.749	0.070; 7.325
8	Ujung Pandang	0.616	1.851	0.172; 27.253
9	Panakukkang	1.395	4.035	0.545; 55.052
10	Bontoala	-0.138	0.871	0.040; 13.197
11	Wajo	0.085	1.089	0.031; 35.839
12	Ujung Tanah	-0.181	0.834	0.024; 16.710
13	Tallo	-0.074	0.929	0.094; 9.403
14	Tamalanrea	-0.153	0.858	0.021; 27.496
15	Biringkanaya	-0.161	0.852	0.045; 13.281

Table 4 shows that most districts show wide confidence intervals, reflecting high uncertainty in the estimates. Panakukkang exhibits the highest hazard ratio (HR = 4.035), suggesting a much higher risk in this district, followed by Tamalate (HR= 1.358). The variability in hazard ratios may indicate spatial heterogeneity in risks, but further investigation with more data or refined modeling might be necessary to draw definitive conclusions.

4. CONCLUSIONS AND SUGGESTIONS

In summary, this study identified the Bayesian spatial survival Cox-Leroux model with a G(1, 0.1) hyperprior as the most effective model. The findings indicated that stroke type was a significant predictor of hospitalization outcomes. Patients with ischemic stroke demonstrated faster recovery compared to those with hemorrhagic stroke, with a hazard ratio of 1.892, indicating an 89% higher likelihood of recovery. Furthermore, stroke patients from all districts treated at Labuang Baji Hospital showed comparable recovery rates and discharge durations on average. Future studies could extend this analysis by incorporating data from additional hospitals and comparing length of stay across healthcare facilities.

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