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Long-term Predictors of Stroke Severity among Patients on Secondary Prevention in Northern Ghana

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Abstract

This paper sort to establish some risk factors of stroke and to estimate the effect of the covariates at different levels of disease states. A review of the literature on stroke risk factors did not reveal any article that estimate possible covariate effect of transition. To fill this gap, we incorporate the covariates in a Continuous Time Markov Model in multi-state models to observe the transition rates of the patients at two-monthly intervals for two years. Patient variables are age, sex, location of the patient, local treatment, smoking, alcohol intake, and hemiparesis. Secondary data from stroke patients under rehabilitation at the Tamale Teaching Hospital from 2014 to 2019 was used. It is observed that males recover earlier in all states compared to females. Old and Older patient groups have some probability of transiting to less severe states; and they have similar probabilities of transiting from mild to a more severe states. The youth are better off in the severe state than the two older groups. In severe state, a patient without local treatment lives less than two months before

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death, whiles patients who seek local treatment may remain with severe stroke for at least two months before transiting to a less severe state. Thus left hemiparesis patients are about twice less likely (0.06738) to transit to the severe state than right hemiparesis patients (0.1207).

Keywords: Stroke predictors; secondary prevention; stroke severity; Ghana; long-term and state.

1 Introduction

Globally, stroke is one of the primary roots of morbidity and death and the principal cause of disability [1]. The Global Burden of Disease 2002 to 2030 shows rather unwelcoming projections of the worldwide burden of stroke. Community-based studies in Sub-Saharan Africa (SSA) show that stroke is the cause of five to ten percent (5% to 10%) of all deaths [2]. In Ghana, stroke was the second most deadly disease after malaria, with a mortality rate of 26 percent between 1990 and 2010 [3]. Approximately 87 percent of deaths due to stroke occurred in the middle-lower income countries, including Ghana [3]. These statistics show that the incidence of stroke in high-income countries is low compared to the middle-lower income countries. This could have resulted from extensive stroke prevention strategies, including public education on stroke risk factors and hypertension management at the population level [4]. Secondary stroke prevention is one of the most successful goals for all stroke managers and modern medicine. Before looking for direct treatment for stroke symptoms, the majority of people turn to general care physicians or local treatment. Though the incidence of stroke has decreased significantly in some industrialized countries because of population-wide high blood pressure control initiatives, stroke incidence has increased in underdeveloped nations like Ghana [5]. Ghana has implemented prophylactic measures to control the disease, but the complexity of stroke treatment and recovery is growing due to many morbidities and socioeconomic problems [6].

The incidence of stroke and its associated mortality rate is reduced in the high-income countries compared to the middle-lower income countries due to the availability of quality and evidence-based care [3]. According to [3], stroke care in middle-income countries is characterized by a lack of knowledge and skills in stroke care among health providers and other caregivers. Other characteristics of stroke care in middle-income countries are a lack of medical equipment to handle strokes and the extremely high cost of stroke treatment [3]. This can be attributed to higher cases of stroke death and stroke-related disability in most developing countries or middle-lower income countries [2,3]. Although secondary preventive measures are on the rise, patients still face different time points after stroke [7]. The ability for a patient to recover from a stroke depends on the severity and how quickly the patient gets medical attention.

According to [8], smoking is a deep-rooted risk factor of stroke and cessation of smoking has been recommended for stroke prevention. Patients who survived a stroke were signed on and followed by the Nanjing Stroke Registry Program (NSRP). Their smoking status was measured at starting point and reassessed at the first follow-up. After three months from the index stroke, the primary end point was defined as a severe or nonfatal recurrent stroke. A multivariate Cox regression model was used to establish the relationship between smoking and the risk of stroke recurrence. The hazard ratio for stroke recurrence using non-smokers as the reference group were 1.16 in former smokers, 1.31 in quitters, and 1.93 in persistent smokers. The criteria for assessment for stroke recurrence among long-term smokers varied from 1.68 for individuals who smoked 1 to 20 cigarettes per day to 2.72 for those who smoked more than 40 cigarettes per day. According to studies on alcohol use conducted in 2018 by [9], there is little evidence linking alcohol consumption to outcome measures following a stroke. The study used a prospective cohort study with twenty-one thousand, eight hundred and sixty-two men who participated in the Physicians' Health Study, gave baseline data on alcohol intake, and had no history of stroke or transient ischemic attack (TIA). Multinomial logistic regression was employed to assess the association between alcohol consumption levels and functional. According to the findings, there were seven hundred and sixty-seven TIAs and one thousand, three hundred and ninety-three out of one thousand, three hundred and ninety-three strokes (1157 ischemic, 222 hemorrhagic, and 14 of uncertain kind) throughout the course of a mean 21.6-year follow-up. Men who drank one drink per week had the lowest probabilities for any result compared to men who consumed but did not have a TIA or stroke [10]. Predicted outcomes in stroke with acute stroke on baseline severity and improvement in the first twenty-four hours after the index event. The author hypothesized that the change in NIHSS in the first 24 hours after stroke improved stroke outcome prediction. Records of three hundred and sixty-nine patients were retrieved from Leuven Genetic Study. NIHSS scores were calculated over ninety days of admission. Multiple logistic regression models were used to independently predict outcome measures. The results revealed that NIHSS was associated with functional outcomes. One hundred and thirty-one participants with moderate to severe stroke, the predictive model was more accurate including the NIHSS to the model which included NIHSS, age, and ischemic heart disease. In conclusion, NIHSS is a predictor of stroke outcome. In predicting three-month mortality among patients hospitalized for first-ever acute ischemic stroke, [11] investigated factors related to three months mortality at admission in patients with first-ever acute ischemic stroke at Taiwan medical center within forty-eight hours after the index event. Multivariate logistic regression was used to identify the major predictors of acute stroke following three months after the index event. The severity of the stroke was assessed using the National Institutes of Health Stroke Scale (NIHSS) score. The stroke subtype was split into anterior circulation and posterior circulation in order to investigate any potential links between posterior circulation ischemic stroke and fatality rates. The 360 patients recruited had a 7.8% in-hospital mortality rate (28 deaths), and a 9.7% three-month mortality rate (35deaths). 27 deaths, or 77% of all fatalities, were due to stroke. Long-term predictors of activity limitation of stroke outcomes were investigated [12]. That was to determine factors at index stroke and predict the level of activity participation and limitation. One hundred and thirty-nine participants admitted at the Sheba Medical center in Israel were prospectively followed-up for four years. The Barthel Index (BI) (activity limitation; BI<95) and Frenchay Activities Index (FAI) (participation restriction; FAI<30) were the outcome measures. Perception of recovery was assessed using two simple questions. At the end of the four years, nine patients (6.4%) were lost to follow-up, 71 (54.1%) participants had survived; 42.3% with activity limitation, 28.2% were categorized as restricted in participation, and 78.1% think that they were not fully recovered. Activity limitation is significantly predicted by the age at the initial stroke and the acute phase disability. Participation restriction was not indicated by any demographic factor or clinical baseline characteristics. Four years after a stroke, there was a positive correlation between activity restriction and participation restriction [12].

All the articles reviewed concentrated on estimating the risk factors on stroke severity based on different designs and modeling concepts. These researchers did not consider the effects of the covariates as the diseases progress. The studies reviewed undertook a cross-sectional study and employed multiple variables at a given time, however they did not provide any information on the influence of time on the variables they measured. According to [13], a longitudinal study is used in studying the relationship between risk factors and the development of diseases. In our research, we looked into the effectiveness of secondary prevention therapies on the severity of stroke among survivors over time and to discover the prevalence of some stroke risk factors and examine their predictive transition rates at the various disease states.

2 Methodology

2.1 Data set

We retrospectively obtained secondary stroke data from the Medical Unit of the Tamale Teaching Hospital (TTH). The Hospital serves all the five northern regions of Ghana. Selection criteria included those patients who had an initial or were referred for hospitalization for stroke from January 2014 to December 2019. Thirty-eight patients who survived the stroke were given rehabilitation therapy under the Medical Unit in the Hospital. Monitoring of patients was done by the Stroke Unit. Disease progression was recorded at different two month-time intervals using the Modified Barthel Index (MBI). MBI measures the Functional Independence (FI) of the patients. It has ten items on Activity of Daily living (ADL). The total score of 20 indicates full independence in the ADL; a higher score represents a higher level of independence (mild stroke). $MBI < 15$ usually represent moderate disability and MBI<10 indicates severe disability [14]. Some patients were lost to follow-up, some withdrew and some died.

2.2 Model formation

We incorporated the covariates into the CTMC modelling as described in [15]. In order to support regression modeling, the Markov model can be easily extended. According to the assumption that the proportional intensities can be stated as

$$q_{ij}(z) = q_{ij}\exp\{\mathrm{B}'_{ij} z(t)\} \qquad i \neq j \tag{1}$$

where Z is the S dimensional vector of covariate; B_{ij} is a vector of S regression parameters linking the instantaneous rate of changes from state i to state j to the covariate and $q_{ij}(\boldsymbol{z})$ denotes the baseline intensity relating to the transition from state i to state j. The change that follows $q_{ij}(\boldsymbol{z})$ intensity matrix $Q(\boldsymbol{z})$ with regard to a subject and a set of covariates z using elements is possible in Equations (1) and (2) the transition probability matrix $P(t\,|\boldsymbol{z})$: must be calculated. The elements $p_{ij}(t\,|\boldsymbol{z})$ of this transition probability matrix represents the likelihood function's contribution from each observation

$$q_{ij}(z) = q_{ij0}\exp\{\mathrm{B}'_{ij} z(t)\} \qquad i \neq j \tag{2}$$

A log-linear Markov rate model $\boldsymbol{q_{ij}}(\boldsymbol{z})$ is mainly chosen for analytical ease, and this model has the appealing property of providing nonnegative transition intensities for any $\boldsymbol{Z}$ and $\boldsymbol{B_{ij}'s}$. In some instances, alternate parameterizations might be a better fit. Additionally, it is feasible to explore how factors affect the baseline probability by modeling on comparable scales like log-hazard. The value of the coefficient B_{ijk} can be conveniently interpreted using the log-linear model, which is not always the case with other models. Consider the fact that if the number of covariates increases, the algorithm may become too complex to implement. In transition from $i \to j$, more data must be included in the analysis and more computing power must be available as the number of covariates (or regression coefficients) rises because it becomes highly challenging to calculate the likelihood. Using a Cox proportional regression model, $q_{ij}(t)$ models the effect of covariate vector $\boldsymbol{Z}$ on transition for a stroke patient, and the transition hazard is given by

$$q_{ij}(t\,|\,z) = q_{ij0}(\mathrm{t})\exp\{\mathrm{B}_{ij}^{T} z\} \qquad i \neq j \tag{3}$$

where $q_{ij0}(\mathrm{t})$ is the baseline hazard of transition i and j, and B_{ij} is the vector of the regression coefficients that describe Z the effect on transition i and j. An alternative way of writing this model is

$$q_{ij}(t\,|\,z) = q_{ij0}(\mathrm{t})\exp\{\mathrm{B}_{ij}^{T} z_{ij}\} \qquad i \neq j$$

where z_{ij} is a vector covariates specific to transition $i \to j$, defined for the patient base on his or her covariates The estimates $\hat{B}$ can be obtained by maximizing the partial likelihood function is given by

$$L(\beta) = \prod_{k=l}^{n} \frac{\exp\{\mathrm{B}_{ij}^{T} z_{ij}\}}{\sum_{l \in R(t_{ij,k})} \exp\{\mathrm{B}_{ij}^{T} z_{ij,l}\}} \tag{4}$$

where $z_{ij,k}$, the covariate vector is for patient k and $R(t_{ijk})$ is the risk set a time for making transition from $i \to j$ [15].

Using a proportional intensities model, we predicted how the independent factors affected the pace of transition. If we have an intensity matrix Q (z) which depend on the covariate vector Z , the transition intensity for patient i at observation time j is

$$q_{rs}\left(z_{ij}\right)=q_{ij}^{(0)}\exp\left(\beta_{rs}^{T}z_{ij}\right).$$

2.3 Transition rate

This shows the transitions over the two-year time period (t=1, 2, 3, …, 12) described by our CTMC. The model contains both backward and forward transitions. This model is essential because it will help us understand how quickly participants transition into new states and how quickly they will transition into different states in the future based on how long they spent in their present states. Non adherence to treatment may result to transition to a more severe state, while patients who adhere to treatment may experience early recovery. An array of numbers indicating the instantaneous rate at which a CTMC transit between states is referred to as a transition rate matrix, also known as an intensity matrix or an infinitesimal generator matrix. In a infinitesimal generator matrix with element q_{ij} for $i \neq j$ represents the rate Q departing from i and entering in state j . The transverse elements q_{ij} can be well-defined as

$$q_{ii}=-\sum_{j\neq i}q_{ii}$$

and satisfied the following conditions:

$$0 \leq -q_{ii} \leq \infty$$
$$0 \leq q_{ij} : \text{for}\, i \neq j$$
$$\sum_{j\neq i}q_{ij} = 0 : \text{for}\, all\, i$$

2.4 Data visualization and analysis

Patient variables included in the study data are *patient number*, *age*, *sex*, *location of patient*, *local treatment*, *smoking*, *alcohol intake*, and *hemiparesis* (defect on right side or left side). Patients with less than three visits were excluded from the study. Each patient's number of visits to the facility was recorded. The state of each patient at a particular time was indicated by the medical officer. The multi-state model in the *R* package was used to model the transition rates. We coded the data and imported it into the package. The ages of the patients were grouped as *youth* (15-45 years), *Old* (46-60 years) and *Older* (61 years or more). Thus, age was coded as

$$\text{Age} = \begin{cases} \text{Youth } (15-45 \text{ years}), & 0 \\ \text{Old } (46-60 \text{ years}), & 1 \\ \text{Older } (61 \text{ years and over}), & 2 \end{cases}$$

Coding for sex was as follows:

$$\text{Sex} = \begin{cases} \text{Male}, & 0 \\ \text{Female}, & 1 \end{cases}$$

Some patients received local treatment prior to their first visit and during rehabilitation, whereas others only received hospital rehabilitation:

$$\text{Treatment} = \begin{cases} \text{Combined with local Treatment}, & 0 \\ \text{Only Hospital rehabilitation}, & 1 \end{cases}$$

The TTH is a referral unit in northern Ghana, and patients were referred to this facility from different locations in the north. On record, we have the following:

$$\text{Location} = \begin{cases} \text{Upper East}, & 0 \\ \text{Northern}, & 1 \\ \text{North East}, & 2 \\ \text{Savanna}, & 3 \\ \text{Upper West}, & 4 \end{cases}$$

Patients' alcohol intake is coded as

$$\text{Alcohol intake} = \begin{cases} \text{No Alcohol}, & 0 \\ \text{Addicted to Alcohol}, & 1 \end{cases}$$

Patients who were into smoking were advised to quit smoking in order to improve rehabilitation. Patient's severity status was recorded on arrival. We considered coding disease state as free, mild, moderate, severe, and death.

$$\text{Disease state} = \begin{cases} \text{Free}, & 1 \\ \text{Mild}, & 2 \\ \text{Moderate}, & 3 \\ \text{Severe}, & 4 \\ \text{Death}, & 5 \end{cases}$$

In preparing the data for analysis, we installed the MSM package from the CRAN archive in the console (version 4.1.0) on a computer through the internet. Data in an excel sheet was put in a long format (data frame) to enable the package to run it. The time of observations and the observed states for the process were: state 1 (disease-free), state 2 (patients with mild stroke), state 3 (patients with moderate stroke), state 4 (patients with severe stroke), and state 5 (patients who die during the study period or withdrawal from the study). The excel file was saved in CSV format to enable reading of the data by console. Our next analysis was estimates of the model (model 1 = illness-to-death). This result shows the baseline transition intensities among the various states. To determine the effect of the covariates on the transition rates, we ran the data for each covariate. We first compare the model 1 transition rate with the baseline rates of the covariate. If the covariate baseline rates indicate some effects (with transition rates less than 1), we go ahead and estimate the rates for each level of the factors. When the baseline rates of the covariates are greater than or equal to 1 (indicating no contribution of the covariate), all the rates for the levels of that factor will be estimated at rates greater than or equal to 1 [16]. We conclude that the covariate has no significant effect on the transition rates of the stroke patient.

3 Results

The values in the various tables are the transition matrices which represent the probability of transition from one state to the other and their respective 95% confident interval estimates in the parenthesis. Larger size of some of the hazard ratios' confidence intervals indicates that there may be no information about the covariate effect in the data, which results in a probability that is a flat function of the characteristics [16].

Table 1 compares the transition rates between male and female patients. The table displays the estimated transition ratios (together with 95% confidence intervals, in parenthesis) for the period. The results reveal that female patients in mild states have a higher probability (0.08538) of total recovery than their male counterparts (0.07732). They also indicate less probability of transiting to higher state (moderate) state (0.05783) as compared to the rate of 0.09802 for males. While male patients in a severe state indicate no information of recovery (1.133) to moderate state, their female counterparts have a better recovery rate of transition (0.863). Female patients stay longer at a severe state ($\frac{1}{0.985} \times 2 = 2\, months$) than males ($\frac{1}{1.186} \times 2 = 1.68\, months$). Also, female patients indicated higher probabilities of dying at states 2 and state 4 (state 2 = 0.05483, and state 4 = 0.1355) compared to males (state 2 = 0.02161, and state 4 = 0.0523) but very similar at state three (3).

Table 1. Covariates effect of male compared with female

	State 1	State 2	State 3	State 4	State 5
	Male				
State 2	0.077 (0.04, 0.15)	-0.197 (-0.31, 0.12)	0.098 (0.05, 0.18)	0	0.021 (0.02, 0.12)
State 3	0.0000001	0.494 (0.13, 0.62)	-0.81 (-1.2, -0.54)	0.313(0.15, 0.69)	0.0034 (0.00, inf)
State 4	0.000001	0.00002	1.133 (0.64, 2.01)	-1.186(-2.03,0.68)	0.052 (0.002, 0.68)
State 5	0	0	0	0	0
	Female				
	State 1	**State 2**	**State 3**	**State 4**	**State 5**
State 2	0.085 (0.03, 0.13)	-0.198 (-0.40, -0.09)	0.057 (0.01, 0.23)	0	0.054 (0.03, 0.30)
State 3	0.0009	0.341 (0.18, 0.68)	-0.57 (-0.99,-0.32)	0.22 (0.07, 0.69)	0.003 (0.00, inf)
State 4	0.0000023	0.0000021	0.863 (0.42, 1.75)	-0.99 (-1.8, -0.5)	0.13 (0.01, 4.71)
State 5	0	0	0	0	0

Table 2. Transition intensities for age (youth compared with old)

	State 1	State 2	State 3	State 4	State 5
Youth					
State 2	0.052 (0.02, 0.2)	-0.29 (-0.5, -0.2)	0.0978 (0.01, 0.3)	0	0.1448 (0.06, 0.3)
State 3	0.00012 (0.0, inf)	0.643 (0.3, 1.1)	-0.655 (-1.1, -0.4)	0.01 (0.001, 0.2)	0.00042(0.0, inf)
State 4	0	0	0.83 (0.08, 0.2)	-0.83 (-1.6,-0.4)	0.00000002 (0.0, inf)
State 5	0	0	0	0	0
Old					
State 2	0.067(0.03, 0.1)	-0.21 (-0.3,-0.1)	0.085 (0.03, 0.2)	0	0.058 (0.005, 0.1)
State 3	0.00001 (0.0, inf)	0.46 (0.2, 0.54)	-0.548 (-1.6,-0.5)	0.08 (0.03, 0.3)	0.00002 (0.00, inf)
State 4	0	0.00009 (0.0, inf)	1.01(0.6, 1.6)	-1.01 (-1.6, -0.6)	0.0002 (0.0, inf)
State 5	0	0	0	0	0
Older					
State 1	0	0	0	0	0
State 2	0.086 (0.03, 0.19)	-0.185 (-0.3,-0.1)	0.075 (0.02, 0.2)	0	0.024 (0.005, 0.1)
State 3	0	0.33 (0.2, 0.54)	-0.94 (-1.68,-0.52)	0.612 (0.2, 1.4)	0.000002 (0.00, inf)
State 4	0	0.00000 (0.0, inf)	1.24 (0.6, 2.5)	-1.38 (-2.6, -0.7)	0.149 (0.05, 0.4)

Table 2 shows the hazard rates of transition among the age factor levels: youth, old and older groups. The older and old age have a better recovery rate at mild stroke, i.e. state 2 (0.086 and 0.067) than the youth (0.052). While the old and older age group have a less and similar probability of moving from mild to moderate state (0.075, 0.085), the youth is more likely (0.0978) to transit to a more severe state than these two groups. At state 2, the youth have more than twice (0.1448/0.0588) probability of transiting into the absorbing state than the old age and about six (6) times (0.1448/0.024) entering into the absorbent state than the older aged group. At moderate state, the youth have about double the chance (0.6434/0.3303) and (0.6434/0.46) of transiting to a less severe state than both old and older. Similarly, old and older age patients with moderate stroke have no chance of recovering. Finally, a patient with severe stroke has zero chance of transiting to a less severe state, thus older patients with a severe stroke stand a higher probability (0.1491) of moving to the absorbing (death) state than both old and youth (0.00000002, 0.000002).

Table 3 compares the effect of alcohol in stroke patients to patients who do not take alcohol while on rehabilitation. The table indicated that patients with no history of alcohol at state two (2) have a better probability (0.4055) of transiting to stroke free than patients with a history of alcohol intake (0.07475). Also, patients with alcohol history retire recovery about ten (10) times (0.087) more than patients with no alcohol history in transiting to a more severe state with probabilities (0.000005). Unfortunately, patients with moderate stroke and who take alcohol could do better (0.4544) than patients without alcohol (0.00000002). Alcohol-based patients are also less likely to transit to a more severe state (0.2534) as compare to patients without alcohol history (0.3848). Meanwhile, severe rated patients with a history of alcohol have no information (1.671) of transiting to a less severe state, unlike their counterparts who are likely to transit to a less severe state (0.4945).

Table 4 indicate the baseline transition rates among patients who sort to smoke in the various states. The rate of transition suggest that smoking has no information as to whether the patients may recover or transit to a more severe or less state or die.

Table 3. Hazard rate for alcohol compared with no alcohol

	State 1	State 2	State 3	State 4	State 5
Alcohol					
State 2	0.0747 (0.04, 0.1)	-0.1916 (-0.2, -0.1)	0.087 (0.04, 0.16)	0	0.0293(0.01, 0.08)
State 3	0.00004 (0.0, Inf)	0.4589 (0.32, 0.63)	-0.7109 (-0.9, -0.51)	0.262 (0.13, 0.5)	0.000002 (0.00, Inf)
State 4	0	0.000006 (0.00, Inf)	1.047 (0.68, 1.7)	-1.134 (-1.7, -0.7)	0.0862 (0.02, 0.3)
No Alcohol					
State 2	0.4055 (0.1, 2.9)	-0.4055 (-2.9, -0.1)	0.000005 (0.000, Inf)	0	0.000002 (0.00, Inf)
State 3	0.000004 (0.0, Inf)	0.000001 (0.00, Inf)	-0.6389 (-3.1, -0.1)	0.3848 (0.04, 3.6)	0.254 (0.03, 0.8)
State 4	0	0.0000001 (0.00, Inf)	0.4945 (0.05, 4.3)	-0.494 (-4.3, -0.1)	0.000003 (0.0, Inf)

Table 5 compares the transition rates of patients who combined local treatment and hospital with patients who had only hospital rehabilitation. At state 2 (mild), patients who combined the two-treatment achieved similar total recovery (0.0799) as against patients who did not seek local treatment (0.08075). Patients who combine local treatment are also less likely to transit to a more severe state (0.07897) compared with none local treatment (0.09458). A patient seeking local treatment may remain at a mild state for about (10 months), 5 visits (1/0.2038) before death with probability (0.045) whereas none local treatment may stay alive at (a mild) state for about (9 months) 4 visits for (1/0.2255) before transiting to death at the rate of (0.05017). Moderately rated patients with or without local treatment history may move to a less severe state with similar transition rates (0.4279, 0.4487). In a severe state, a patient without local treatment will live less than two months (1/1.242) before death (0.2150) whiles local treatment may remain with severe stroke for at least two months (1/0.9721) before transiting to a less severe state.

Table 6 compares the hazard rates of transition between patients who had hemiparesis (arm or leg paralyzed), patients who were paralyzed with right or left side. The table indicated that, at mild state, patients with left hemiparesis or right hemiparesis have a similar probability of total recovery (0.08011 or 0.0788). The table also shown that right hemiparesis has higher probability of transiting to a higher state; (at state 3, a probability of 0.3011 to state 4 and at state 4, a probability of 0.0944 to state 5) as compare to left hemiparesis (at state 3, a probability of 0.224 to state 4 and at state 4, a probability of 0.000002 to state 5).

Table 4. Transition intensities for smoking

	Baseline	Smoking
State 2- State 1	0.021 (0.000, Inf)	0.2265 (0.0000, Inf)
State 2- State 2	-0.05988 (-Inf, 0.000)	–
State 2- State 3	0.02454 (0.000, Inf)	23700000 (0.00, Inf)
State 2- State 5	0.01450 (0.000, Inf)	2458000000 (0.0, Inf)
State 3- State 1	0.06937 (0.000, Inf)	0.9014 (0.0000, Inf)
State 3- State 2	0.428(0.306, 0.597)	2.423 (0.328,17.883)
State 3- State 3	-0.6864 (-0.943, -0.499)	–
State 3- State 4	0.2584 (0.137, 0.484)	0.9813 (0.1049, 9.179)
State 3- State 5	0.00000076 (0.000, Inf)	0.0018 (0.0000, Inf)
State 4- State 2	0.00000000005 (0.00, Inf)	2.668 (0.0000, Inf)
State 4- State 3	1.019 (0.6546, 1.585)	2.338 (0.2755,19.846)
State 4- State 4	-1.04 (-1.39, 7.735000)	–
State 4- State 5	0.02109 (0.000, Inf)	2.996 (0.0000, Inf)

Table 5. Local treatment compared with no local treatment

	State 1	State 2	State 3	State 4	State 5
Local Treatment					
State 2	0.079 (0.03,0.1)	-0.204 (-0.33, 0.12)	0.07897 (0.03, 0.19)	0	0.045 (0.02, 0.1)
State 3	0.000008 (0.0, inf)	0.4279 (0.28, 0.65)	-0.5887 (-0.8, -0.4)	0.16 (0.06, 0.41)	0.00007 (0.00, Inf)
State 4	0	0.0000001 (0.0, Inf)	0.9721 (0.57, 1.6)	-0.972 (1.61, 0.57)	0.001 (0.0, Inf)
No Local Treatment					
State 2	0.08075 (0.03, 0.2)	-0.2255 (-0.3, 0.1)	0.095 (0.03, 0.23)	0	0.05017 (0.01, 0.14)
State 3	0.000001	0.4487 (0.26, 0.76)	-0.903 (-1.5, -0.54)	0.055 (0.2, 1.1)	0.000005 (0.00, Inf)
State 4	0	0.00002 (0.00, Inf)	1.027 (0.47, 2.2)	-1.24 (-2,- 0.6)	0.215 (0.07, 0.6)

Table 6. Right hemiparesis compared with left hemiparesis

	State 1	State 2	State 3	State 4	State 5
Left Hemiparesis					
State 2	0.08 (0.05, 0.1)	-0.1746 (-0.2, -0.1)	0.0674 (0.03, 0.15)	0	0.02712 (0.01, 0.07)
State 3	0.0000001	0.4058 (0.2, 0.6)	-0.6298 (-0.9, -0.4)	0.224 (0.1, 0.4)	0.0000
State 4	0	0.000007 (0.0, inf)	1.00 (0.62, 1.5)	-1.00 (-1.5, -0.6)	0.000002
Right Hemiparesis					
State 2	0.079 (0.03, 0.2)	-0.2257 (-0.3,-0.1)	0.1207 (0.05, 0.25)	0	0.026 (0.01, 0.1)
State 3	0.000001	0.4631 (0.3, 0.7)	-0.7643 (-1.1, -0.51)	0.3011 (0.1, 0.6)	0.000
State 4	0	0.000000	0.9948 (0.59, 1.67)	-1.089 (-1.7, -0.6)	0.0944 (0.03,0.3)

4 Discussion

We incorporated covariates into a continuous-time Markov chain model in multi-state modeling to enable us to estimate the transition rates of the covariates. Studies have shown that when data are equally spaced, both the discrete-time Markov chain model and the continuous-time Markov model can perform well. Thirty-seven (37) patients were monitored at two-monthly intervals for two years. The purpose was to observe the covariate effects of the transition intensities of stroke patients on rehabilitation at some discrete points in time and to determine some risk factors that influence recovery. Table 1 suggest that female patients have a better rate of transiting to a less severe state (0.08538, 0.3418, and 0.863) than their male counterparts (0.07732, 0.4942, and 1.133 (no information about the covariate effect)). These findings are supported by [17] on CD4 cell count that transition from good states to bad states is higher in male patients than their female counterparts. Unfortunately, females are more likely to die (0.05483, 0.0029, and 0.1355) than male patients (0.02161, 0.0043, and 0.0523) in all states. Findings from Table 2 reveal that the age of a stroke patient could retire recovery about ten (10) times than the baseline probability (0.8067/0.08457) and has the same probability of transiting to death state (0.4062/0.03108). While the Old and Older age groups have a less and similar probability of moving from a moderate to severe state (0.0873, 0.6123), the youth is less likely (0.01244) to transmit to a severe state than these two groups. Older age with severe stroke is more likely to die (0.1491) than old age and youth (0.000002, 0.000000002). This result is consistent with the literature [18]. The outcome of Table 3 gives detailed information on the effect of alcohol on stroke survivors. Patients with no history of alcohol may recover more than 5 times (0.4055/0.07475) than patients with a history of alcohol at a mild state. Findings from our study also indicated patients admitted with severe stroke and a history of alcohol intake have no information of becoming less severe (1.047) unlike their counterparts with a 0.4945 probability of moving to a less severe state. This finding is consistent with [9]. Their studies show that the relationship between alcohol consumption and functional outcome from stroke is sparse. The transition intensities in Table 4 indicate that the covariate smoking does not affect stroke severity. The baseline intensity for smoking gives hazard rates to be a positive one or more suggesting the covariate has insufficient information in estimating the covariate effect. Several studies have shown a strong positive relationship between cigarette smoking and the risk of recurrence of stroke [4,8], and [19]. This finding could mean that a stroke patient who previously smokes and quit smoking during rehabilitation may not have any influence on the recovery rate. We also estimated the transition ratios of the covariate therapeutic type (local/traditional and modern rehabilitation) as in Table 5. These estimates predicted that patients who combined local treatment have a similar recovery rate at mild state (0.0799) as compared to patients who never had local treatment (0.08075). Meanwhile, patients in a mild state with a combination of local treatment adhere to treatment and are less likely to transit to a more severe state (0.07897) than patients who never subscribed to local treatment (0.09458). Patients with severe stroke and combined local treatment are more likely to transit to a moderate state (0.9721) than patients with no combination of local treatment (1.027= no sign of recovery). Also, in the severe state with no combination of local treatment are more likely to die (0.05017, 0.2150) compared with patients who combined treatment with non-hospital medication (0.045, 0.000001). These findings are supported by [20] the therapeutic regimen of traditional Chinese Medicine (Acupuncture) combined with modern rehabilitation are effective in improving cognition and has the advantage of being simple, convenient, efficient, and inexpensive without severe adverse effect.

Findings from Table 6 suggested that Right-hemiparesis patients stayed more than 3 times longer (1/0.2257) at a mild state before transiting to a disease free state (1/0.1746). Meanwhile, recovery at a moderate state is faster for right hemiparesis patients (0.4631) as compared to right hemiparesis patients (0.4058). Left or right hemiparesis have similar probabilities of dying at all states except state 4 (0.09447). Thus left hemiparesis patients are about twice less likely (0.06738) to transit to a more severe state than right hemiparesis (0.1207).

5 Conclusion

The objective of this study is to incorporate some covariates into illness-to-death model (CTMC) that will enable us to observe the effects of the covariates on transition intensities of stroke patients on rehabilitation at some discrete points of time. The research reveal that CTMC models best estimate the covariate effects of transition rates of stroke patients on rehabilitation at the TTH. The model estimates transition intensities for all states (i.e. 1, 2, 3, 4, and 5). The transition rate from state 2 to state four (4) is zero (0). Also transition from state 2 to state 5 is higher (0.0581) than transition from state 3 to state 5 (0.0003). It is suggested that older patients have low survival rates. That is, older patients with severe stroke are less likely to transit to a less severe state compared to the youth.

We recommend that stroke patients be advised not to combine orthodox rehabilitation procedures with local treatments. Combination of local treatment with orthodox medicine may only be sufficient on patients with severe stroke. Thus, patients should seek local treatment from only known registered stroke rehabilitation centers. Patients who transit to mild state should be advised to continue to adhere to treatment to speed up total recovery. Public education on risk factors of stroke should be emphasized. Ministry of Health should undertake public education on the risk factors of stroke both at the national and community levels.

Ethical Approval

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Competing Interests

Authors have declared that no competing interests exist.

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