Original Article

# Determination of Hazard State of Non-Communicable Diseases Using Semi-Markov Model

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## Abstract

**Background:** The developed Semi-Markov model with Kumaraswamy Exponentiated Inverse Rayleigh distribution examined patients with hypertension, heart diseases, smoking habits and Stroke, is measured from one state to another.

**Materials and Methods:** Patients with Non-Communicable disease described through Kumaraswamy Exponentiated Inverse Rayleigh distribution.

**Results:** The estimated parameters of Semi-Markov model with this distribution predicted by the maximum likelihood estimation for each successive state observed significant abnormality. The data noted predicts established model is a good fit for many attributes that prevailed in studied data. The developed Semi-Markov model is a best fit for non-Communicable disease in the long run of patient's data. Through different Exponential family distribution, one can look at for further perfect fit of patient data, which is to be estimated.

**Conclusion:** This model can be an alternative method to estimate the effect of patient in survival analysis, where it will be effective in time consumption in medical field.

**Keywords:** heart diseases, hypertension, Semi-Markov processes, smoking, stroke

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## Introduction

The World Health Organization (WHO) has predicted that Non-Communicable Diseases (NCDs) get about 40 million individuals worldwide each year [1]. Four major syndromes, the essential focus of worldwide NCDs response has been; cancer, chronic respiratory infections, diabetes and heart disease. The NCDs response also concentrates on four key risk issues; harmful practice of liquor, physical lethargy, tobacco usage and unhealthy diet are the issues perceived by the WHO as significant elements leading to NCDs. In this article, through Semi-Markov Process (SMP) the four major NCDs are depicted with real-life data to find out the survival probability of patients.

Stroke in the human body immune system reveals the identical manner as a heart disease, but this stroke happens in brain (blood flow gets interrupted) which lead to damage. Worldwide, heart diseases cause approximately one third deaths [2]. 15 million people worldwide suffer from stroke each year, with the amount of stroke deaths increases every year [3]. This stroke could even raise for the next upcoming 20 years, specifically in the developing countries [4]. Examining effectiveness in human body and health fitness is an urgent proposal to lesser the burden. Hypertension is a leading risk factor for cardiovascular disease, and randomized cases have determined that antihypertensive drug therapy reduces risks of stroke, cardiovascular disease, heart failure and total mortality [5].

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Some experimental investigations have showed that relationship of blood pressure to cardiovascular risk is not linear, with no better devaluation in risk or perhaps indeed an extended risk identified with low blood pressure.

Getting blood pressure control (BP) in victims with hypertension reduces the risk of stroke and ischemic heart disease [6, 7, 8]. Barriers to hypertension control take place at the stages of the patient, physician and health system, and comprise inadequate approach to high-quality care, physician and patient unwillingness to enhance therapy for uncontrollable BP (i.e., inertia), and treatment non-adherence [9]. The relative influence of these various obstacles is recognized and is not focused on by Joint national committee [10]. The increased incidence of hypertension is due to a combination of behavioral risk factors, age, and population expansion, including recurrent stress, being overweight, a lack of physical activity, hazardous alcohol use, and an unhealthful diet [11].

## Materials and Methods:

### Semi – Markov Model:

This methodology used for the study are elucidated as follows. In Stochastic process, the theory of Semi-Markov Model (SMP) is an area which develops rapidly in the past few decades. The fact is that SMP provide a natural useful model in real life systems of examining, standby systems, stochastic mechanisms and many others. P. Levy the author who individually and instantaneously introduced the SMP[10]. Derivation of SMP starts from the Markov renewal process with special case of 2-dimensional Markov sequence. SMP concept is a normal derivation from the Markov chains [12].

A standardized regular Markov chain, with discrete set of states denotes; $E$= 0, 1, 2, 3… is simplified by a matrix $Q = q_{ij}\,;\ i,j\ \in E$ where;

$$q_{ij} = -q_i = -\sum_{j\in E,\ i\neq j} q_{ij}$$

Markov chain derives; the $i^{th}$state of a particular system having a random time $\theta_i$ distributed by the exponential family law with, parameter $q_i$ and by the system passing the $j^{th}$ state with a probability $p_{ij} = \frac{q_{ij}}{q_i}\ i,j\ \in E$.

The methods and designing of transition probabilities of SMP defined as: Firstly, considering a model with $k$ states belonging to finite state space $E = \{1, 2, \ldots, k\}$; where,$(X_0, X_1, X_2, \ldots, X_n) \in E$; be the sequential states where the $n$ visits a random process, when $(0 = T_0 < T_1 < \ldots < T_n)$ are the sequential time to enter into each of these five states. Therefore, the probability of n transitions from the first state to fifth state, denoted by $i\ to\ j$, the model fixed is been defined as in **eqn. (1).**

$$P_{ij} = P(X_{n+1} = j/X_n = i) \quad \ldots\ldots\ (1)$$

Transition probability, $P_{ij}$ satisfy the conditions, as $P_{ij} \geq 0$, $\sum P_{ij} = 1$ for all $j$. As the Marko process does not deal with the population sizes of region at time of the state transitions the random process, esteems the transition population size of region at

$(T_{n+1} - T_n)$ in a SMP and distribution that satisfies:

$$Q_{ij}\,(t) = P(X_{n+1} = j,\ T_{n+1} - T_n \leq t/X_n = i) \ldots\ldots (2)$$

The Kumaraswamy Exponentiated Inverse Rayleigh (KEIR) [16] probability density function (pdf) of population size of region time in a particular state 'i' before passing to state 'j' given in **eqn. (2)**

$$\mathrm{f_{ij}\,(t)} = \frac{2\mathrm{ab}\alpha\theta}{\mathrm{x}^3}\left(\mathrm{e}^{-\frac{\theta}{\mathrm{x}^2}}\right)^{\mathrm{a}\alpha}\left[1-\left(\mathrm{e}^{-\frac{\theta}{\mathrm{x}^2}}\right)^{\mathrm{a}\alpha}\right]^{(\mathrm{b}-1)}$$

$$\mathrm{x} \geq 0; \mathrm{a}, \mathrm{b}, \alpha, \theta > 0 \quad \ldots\ldots (3)$$

The cumulative density function (CDF) $F_{ij}\,(t)$, along with corresponding survival function (SF) eqn. (4); of waiting time in state $i$, $S_i(t)$ observed in **eqn. (5)**

$$F_{ij}\,(t) = 1 - \left[1-\left(\mathrm{e}^{-\frac{\theta}{\mathrm{x}^2}}\right)^{\mathrm{a}\alpha}\right]^{\mathrm{b}} \quad \ldots (4)$$

Where $F_{ij}$ is the historical frequency of transition from state$i$ to state$j$.

$$S_{ij}(t) = \left[1-\left(\mathrm{e}^{-\frac{\theta}{\mathrm{x}^2}}\right)^{\mathrm{a}\alpha}\right]^{\mathrm{b}} \quad \ldots (5)$$

The parameters of the KEIR distribution are predicted through the maximum likelihood estimation (MLE) method.

Log likelihood function is observed in eqn. (6)

$$l = nlog(2) + nlog(a) + nlog(b) + nlog(\alpha) + nlog(\theta) - \sum_{i=1}^{n} lnx_i^3 - \sum_{i-1}^{n} \frac{a\alpha\theta}{x_i^2} + (b-1)\sum_{i=1}^{n} ln\left[1 - e^{\frac{\theta a\alpha}{x_i^2}}\right] \ldots (6)$$

The MLE obtained by solving the above non-linear system of eqn. (6). In **eqn. (6)** we do not have the exact solution, from the large sample property of ML Estimates; MLE $\hat{\theta}$ can be treated as being approximately normal with mean $\theta$ and variance covariance matrix equal to the inverse of the expected information matrix.

i.e., $\sqrt{n}(\hat{\theta} - \theta) \rightarrow N(0, nI^{-1}(\theta).I(\theta)$is the information matrix then its inverse of matrix is $I^{-1}(\theta)$ provides the variances and covariance's.

$$\hat{a} \pm Z_{\frac{\alpha}{2}}\sqrt{I_{a\hat{a}}^{-1}(\hat{\theta})},\ \ \hat{\alpha} \pm Z_{\frac{\alpha}{2}}\sqrt{I_{\alpha\hat{\alpha}}^{-1}(\hat{\theta})},\ \hat{b} \pm Z_{\frac{\alpha}{2}}\sqrt{I_{b\hat{b}}^{-1}(\hat{\theta})},\ \hat{\theta} \pm Z_{\frac{\alpha}{2}}\sqrt{I_{\theta\hat{\theta}}^{-1}(\hat{\theta})} \ldots \quad (7)$$

The significance providing by iterations as observed in equation (7), with likelihood functions as the ideal solution to the parameters.

**Table-1**, is a typical Markov chain state consistent to transition matrix *P* with the interactive population size of region transition probabilities change from the first state observation, as observed in **eqn. (3)**

$$Pij\,(t) = \begin{bmatrix} 1-a & b & \alpha & \theta \\ \alpha & 1-b & \theta & a \\ b & \theta & 1-\alpha & a \\ \theta & \alpha & b & 1-\theta \end{bmatrix} \quad \ldots(8)$$

**Table 1. The transitions between the phases of the process occur at regular intervals.**

| Patients has Hypertension | Patients has Heart Diseases | Patients has Smoking Habits | Patients had a Stroke |
|---|---|---|---|
| 498 | 276 | 1674 | 249 |
| 214 | 36 | 214 | 66 |
| 36 | 138 | 138 | 27 |
| 214 | 138 | 1674 | 112 |
| 66 | 47 | 112 | 249 |

The rows of eqn. (8), signifies the present four states of the model use withdrawal and renormalization, of Stroke processes and long-term process, the columns represent the four statuses (S2, S3, S4 and S5) on the state. The records in the first row access the probabilities of hypertension will stay to stroke (1 – a) or leave (a), and thus move into the second state b. Following the first row, the second row provides probability an individual in b will be in the next observation, having heart diseases in state (1 – b). The third row gives the probability of smoking habits $(1-\alpha)$ and forth state had a stroke process $(1-\theta)$. [13]

## Results and Discussion

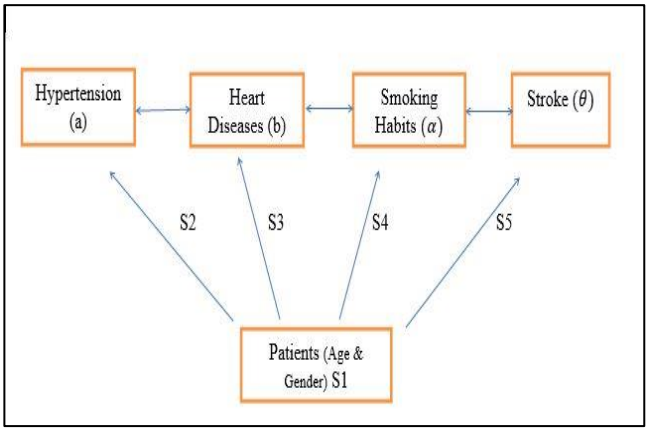
For the taken dataset [14], with the utilization of information factors like segment attributes and various sicknesses, the dataset might be used to foresee whether a patient is probably going to experience the ill effects of stroke. Every section in the dataset contains data about the patient that is pertinent to that segment.

The accompanying five state boundaries were set up for the model turn of events, as displayed in **Figure-1**, for the accompanying reasons:

The accompanying five state boundaries were set up for the model turn of events, as displayed in **Figure-1**, for the accompanying reasons:

S1: Patients Age and Gender
S2: Patients with Hypertension
S3: Patients with Heart Diseases
S4: Patients with Smoking Habits
S5: Patients with Stroke

**Figure – 1 A five-state model data from the Hepatitis C Prediction Dataset**




In the Assembled Realm, the Clinical Exploration Gathering Malignancy Family Appraisal Exploration (MRC CFAS) is an enormous size multi-focus longitudinal glance. [15]

The examinations, what began inside the late 1980s and covered a specialist example of thirteen 004 individuals from the more seasoned organization, transformed into intended to explore dementia and intellectual decrease inside the matured people. The realities have also been utilized to concentrate on various afflictions along with sadness [16] and actual debilitation [9], notwithstanding to view the solid energetic future [2] of the members. The meetings with people have been acted in extra of 46 000 cases to far. There are more insights on the gander plan close by on the web (www.Cfas.Ac.United realm). To take a gander at getting more seasoned inside the more established people, the creators utilized a three-country variant with the conditions of "healthy," "records of stroke," and "death." The conditions of "refreshing," "history of stroke," and "death toll" have been totally addressed through change powers in a three-state model (country three).

In **Figure–2**, you could see an illustration of the multi-state model. It very well may be energizing to look how the amount of time that elapses following a stroke impacts the charge of downfall. We concentrate on a subset of the MRC CFAS data, explicitly records from the Newcastle place. This data set may be known as the MRC CFAS for the length of this paper. This subset conveys data on 2316 individuals who had been 65 years or more established at the time

in their meeting, which occurred among 1991 and 2003. These individuals have been exposed to however much nine meetings throughout which they have been mentioned on the off chance that they had a stroke for the explanation that their past visit, and their age at the hour of the meetings changed into noted. Even after the conviction of the subsequent period, the exact dates of death are all things considered close by. At pattern, the people's stroke history became explored, and they gave measurements on their age (A), sexual orientation (G; 0 for women and 1 for folks), long periods of tutoring (E; zero for under 10 years and 1 for a considerable length of time or extra), and smoking distinction at 60 years old years (S; zero for non-smokers or ex-smokers and 1 for current individuals who smoke). By characterizing smoking along these lines, it's miles less potentially that people could give up due to disease.

After the age of 60, smoking conduct won't change. The yearly report on smoking-related direct and perspectives distributed in 2005 [6] saw that the people who smoke after the age of 65 years are the most un-plausible of all to need to stop, and the individuals who do wish to stop are significantly more liable to have accomplished so before the age of 65 years. People contrasted in expressions of the number of meetings they had and the measure of time they spent among interviews. **Figures 2(a)** and a couple of **2(b)** portray the wide assortment of meetings finished through anyone, just as a dispersion of the time of follow-up spans, separately.

**Figure – 2(a) Unmistakable information on the quantity of meetings per individual**

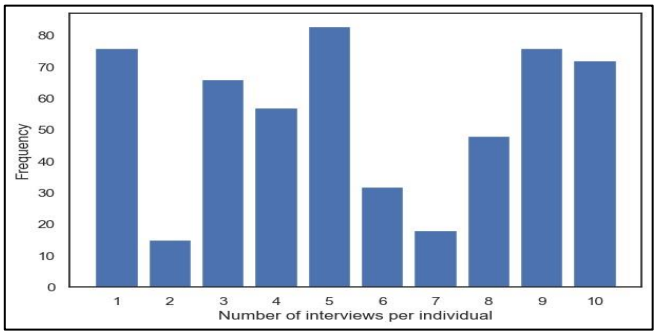
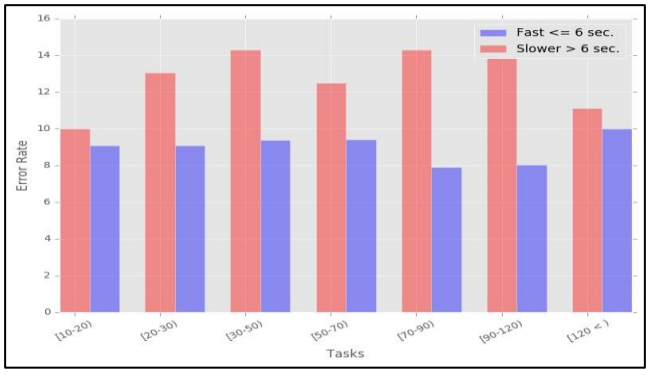
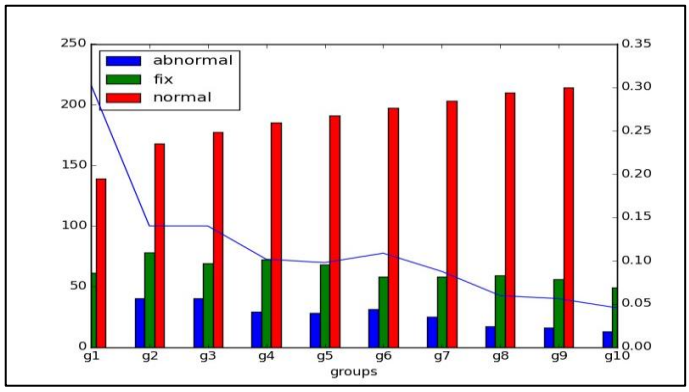



**Figure – 2 (b) Unmistakable information on the length among meetings**




The standard length of notice up spans changed into years, and the middle wide assortment of meetings directed was with regards to member. **Figure 2(c)** portrays the circulation of time between the hour of the last meeting and the hour of destruction or appropriate control, whichever happens first.

**Figure – 2(c) Unmistakable information on the time between the last meeting and either demise or control are likewise accessible**




Frequencies of change are summed up from the dataset. The answers for the change probabilities μ_(ij) (t) at time t utilizing the calculation are gotten with S5 states: T = 6178, progress likelihood matric as given in **Table-1**.

**Table-1** shows the recurrence dispersions of sets of progressive states saw in the records test. These frequencies identify with the number of times a person had an assertion in country I followed through an assertion in country j for every one of the 2 states I and j and for the entirety of individuals in the example. In light of the varieties inside the states' definitions, there have been no advances from country 2 to country 1. An assortment of likely detectable examples of follow-up for each body inside the MRC CFAS longitudinal investigations have been perceived inside the notice. A person can, as an occurrence, be in advantageous wellbeing while the analyze begins off evolved however at that point go through a stroke inside the next years and pass on or stay alive while the examiner closures, or the individual in question can be in superb wellness however at that point experience a stroke and either pass on before the view closes or be legitimate controlled, depending on the cases. Also, if an individual is accounted for to have had a stroke toward the beginning of the exploration, it's miles conceivable that the person might live to tell the story or pass on before the conviction of the investigate.

**Figure-3, 4, 5, 6** portray a graphical portrayal of those various examples, which can be delegated free examples A–F. In styles A, B, E, and F, it is recognized that a shift from country 1 to country 2 has taken region sometime. In any case, on account of examples C and D, the ways of life of oversight makes it hard to decide if or presently not this kind of shift has occurred. As a final product, there are capacity results. It is possible that an individual moved to realm 2 anyway became in no way, shape or form reported on this nation because of restriction, or that a

**Figure 3: Effect on Patients from State S1 to S2** **Figure 4: Effect on Patients from State S1 to S3**

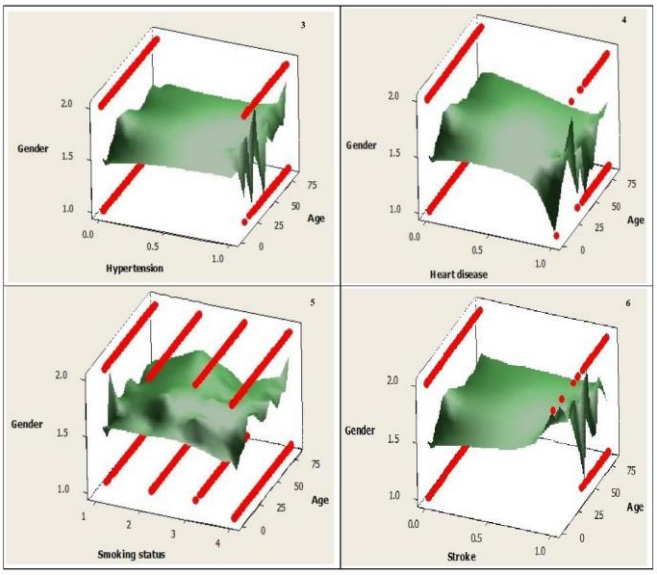



**Figure 5: Effect on Patients from State S1 to S4** **Figure 6: Effect on Patients from State S1 to S5**

a person remained in realm 1 until the person passed on or the state turned out to be pleasantly blue-penciled. The estimated transition intensities for the Semi Markov Model are mentioned in **Table-2.**

**Table: 2. The estimated transition intensities for the Semi Markov model**

| States at time $t_{ij}$ | Patients has Hypertension | Patients has Heart Diseases | Patients has Smoking Habits | Patients had a Stroke |
|---|---|---|---|---|
| State 1 | 0.485 | 0.435 | 0.439 | 0.354 |
| State 2 | 0.208 | 0.056 | 0.056 | 0.095 |
| State 3 | 0.035 | 0.217 | 0.037 | 0.038 |
| State 4 | 0.207 | 0.217 | 0.439 | 0.159 |
| State 5 | 0.065 | 0.075 | 0.029 | 0.354 |

The Semi Markov transitional probabilities through KEIR for the effect of Patient's with age and gender determined by Patient's Hypertension, Patient's Heart Diseases, Patient's Smoking Habits and Patient's with stroke is examined. The threshold for each transition intensities are examined with the conditional probability that the patient will not survive after the time. Among the four non-Communicable diseases the hazard for the Patient's having a Stroke is the first one to look for, as the survival of chance is minimal. The Patient having Stroke the next hazard was heart disease, then with Hypertension and Smoking habits was found.

At the time of the baseline study, the median age of the participants was 74 years. According to the research design, people above the age of 75 were over-sampled in order to obtain an equivalent number of participants as those aged 65–74 years at the beginning of the study. Circling back to every member was booked to happen about like clockwork, as indicated by the review's plan. This present person's specific season of death has been set up. To represent the way that it is hard to build up the specific season of the progress from condition 1 to state-2, the information is exposed to separating on the left, right, and stretch tomahawks, individually. It is conceivable that exchanges from state-1 to state-2 were happened yet were not found preceding demise or right blue penciling toward the finish of the subsequent period, yet this has not been shown. Advances from state-1 to state-2 that happen before the review's beginning date are left edited; else, they are left shortened. For the situation that people are joined up with the exploration, advances from state-1 to state-2 that happen before the review's beginning date are left controlled. Prohibition from the examination might be set off by the passing of a member before to the review's initiation.

Among the five provinces of SMP, the Stroke state S5 is viewed as a retaining state; i.e., when a patient isn't truly in a functioning state, she/he won't ever be in the others states and rather remains there until the end of time. The S5 state stroke is classified Danger state and the others states S1, S2, S3 and S4 moderate states.

## Conclusion

The developed Semi-Markov model is a best fit for non-Communicable disease in the long run of patient's data. Through different Exponential family distribution, one can look at for further perfect fit of patient data, which is to be estimated. There are many more non-Communicable diseases which needs to be estimated in the goodness of fit in the future. This model can be an alternative method to estimate the effect of patient in survival analysis, where it will be effective in time consumption in medical field.

## Authors' contributions:

BR, SKK, and MR: Conception and Study design; BR: Acquisition of Data; BR, SKK, MR: Data processing, Analysis and Interpretation of Data; All authors – BR, SKK, MR were drafting the article, revising it for intellectual content; All authors were checked and approved of the final version of the manuscript.

Here, BR – Balasubramaniam Ramakrishnan; SKK – Senthamarai Kannan; MR – Mahalakshmi Rajendran

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