PROBABILISTIC ANALYSIS OF DEPRESSIVE EPISODES: APPLICATION OF RENEWAL THEORY UNDER UNIFORM PROBABILITY LAW.

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Abstract: The renewal process has been formulated on the basis of hazard rate of time between two consecutive occurrences of depressive episodes. The probabilistic analysis of depressive episodes can be performed under various forms of hazard rate viz. constant, linear etc. In this paper we are considering a particular form of hazard rate which is $h(x)=(b-x)^{-}$ where b is a constant, x is the time between two consecutive episodes of depression. As a result time between two consecutive occurrences of depressive episodes follows uniform distribution in (a,b)

The distribution of range i.e. the difference between the longest and the shortest occurrence time to a depressive episode, and the expected number of depressive episodes in a random interval of time are obtained for the distribution under consideration. If the closed form of expression for the waiting time distribution is not available, then the Laplace transformation is used for the study of probabilistic analysis. Hazard rate of occurrence and expected number of depressive episodes have been presented graphically.

Key words: Hazard rate, Major Depressive Disorder, Recurrent episodic disorder, Uniform distribution, Laplace transformation

1.1 Introduction

Psychiatric disorders have proved to be a major health problem in the recent years. Kasper, et al. (2008) mentioned psychiatric disorders affect about 10% of the population in general.

Major depressive disorder is a syndrome characterized by recurrent episodes of low mood manifested by persistent alteration of mood for more than two weeks with profound sadness, decreased psychomotor activity, guilt feeling, self blaming, also feeling of hopelessness, helplessness and worthlessness, suicidal ideas, poor sleep and loss of appetite (Freedman 2002).

It can be stated that Major depressive disorder is a recurrent episodic disorder. After a

single episode of depression, about 85% of patients experience recurrent episodes (Gelder et al. 2009). After a single major depressive episode, the risk of a second episode is about 50%, after a third episode the risk of a fourth is 90% (Thase 1990). First episode of depression is often provoked by events like death of dear one, loss of job, retirement, marital separation or divorce. Subsequent episodes are often unprecipitated. Any depressive episode should be treated as completely as possible. Discontinuation of effecting treatment often leads to relapse, especially if medications are withdrawn rapidly. The greater the number of previous recurrence, the higher is the risk of future recurrence (Mueller and Leon 1996). Depressive episodes typically increase in frequency and duration as they recur (Goodwin et al. 2007). This recurrence will take place with respect to time which cannot be specified exactly.

The hazard rate of occurrence plays a pivotal role in diagnosing a depressive episode as a disease. With time it is observed that both the severity and the rate of occurrence increases and the time interval between subsequent episodes decrease (Freedman et al. 2002)

1.2 Review of literature

Renewal theory in discrete time has been thoroughly discussed by Feller (1957). Cox (1962), Ross (1989) and Medhi (1994) concentrated on renewal theory in continuous time. Heyde (1967) suggested some renewal theorem in discrete time for a sequence of independent and identically distributed random variables. Smith (1958) has given an excellent

account of the general mathematical theorems of renewal theory, and has given a number of advanced developments, especially concerning problems about electronic counters. According to Feller (1949) renewal theory is important for studying wide class of stochastic processes. Skellam and Shenton (1957) gave many exact results for the distribution of number of renewals for a fixed interval of time. Cox (1960) has considered the number of renewals in a random time interval. Feller (1941) gave the first rigorous proof of the convergence of the renewal density to a limit. Smith (1960) has given a remarkable necessary and sufficient condition for convergence. Recurrence time problems which are generally important in stochastic processes were discussed by Bartlett (1955). Cox and Smith (1953b) and Smith (1961) have studied renewal theory when the failure-times, although independent, are not identically distributed. Chow and Robbins (1963) have suggested a renewal theorem for dependent and non-identically distributed random variables for continuous time. Renewal process is also a particular case of counting process. Counting process methodology has been applied in survival analysis. The

$$P(E) = P(x \leq X_{(i)} \leq x + dx)$$

The sampling distribution of Y_n , the largest value in the random value of size n , is given by

$$g_n(y_n) = n \cdot \left[\int_{-\infty}^{y_n} f(x) dx \right]^{n-1} f(y_n), \text{ for } -\infty < y_n < \infty \quad \dots (2)$$

The sampling distribution of Y_1 , the smallest value of size n , is given by

$$g_1(y_1) = n \cdot \left[\int_{y_1}^{\infty} f(x) dx \right]^{n-1} f(y_1), \text{ for } -\infty < y_1 < \infty \quad \dots\dots\dots (3)$$

1.4 Depressive episodes as a renewal process

Depressive episodes have a tendency to recur even after treatment (Thase 1992). This recurrence will take place with respect to time which cannot be specified exactly (Freedman et al. 2002). It may be worth mentioning that depression is a function of time. For a normal person, let X_i be the time epoch at which

approach first developed by Allen (1975) and later on it was well exploited by Andersen et al. (1993), Fleming and Harrington (1991). Barthakur and Sarmah (2007) have considered a renewal process in discrete time in a dependent and non-identical set up. In this paper, a renewal process in continuous time in an independent and identical set up is considered.

1.3 Materials and methods

The rate of occurrence in this context means the Hazard Rate defined by

$$h(x) = \frac{dF(x)}{1 - F(x)}, \quad \dots (1)$$

where x is the time to occurrence between two consecutive depressive episodes.

Order Statistics:

Distribution of i^{th} order statistic:

Let E denote the event that i^{th} ordered observation $X_{(i)}$ lies between x , $x+dx$. This implies that $(i-1)$ observations occur before x and $(n-1)$ observations after $x+dx$. Using multinomial probability mass function –

depressive episode is registered for the i^{th} time. Now there is a sequence of random variables viz. $X_1, X_2, \dots, X_n$ representing time corresponding to 1st, 2nd, ..., n^{th} occurrence of depressive episodes.

The number of depressive episodes $N(t)$ in a random interval of time $(0, t]$ results a renewal process where $X_1, X_2, \dots, X_n$ are independent and identically distributed (i.i.d) random variables with distribution function $F(x)$.

The numbers of depressive episodes mainly dependent on its occurrence rate are of different forms. Here we are considering a particular form of hazard rate $h(x) = (b-x)^{-1}$ where b is a constant, x is the time between two consecutive

$$h(x) = (b-x)^{-1} = \frac{\left[1 + \frac{x}{b} + \frac{x^2}{b^2} + \dots\right]}{b}, \quad \text{for}$$

$$a \leq x \leq b$$

Hence the sequence of random variable $\{X_i\}$, $i=1,2,\dots$ follows uniform distribution with distribution function

The distribution of time to n th reoccurrence of depressive episode is obtained as follows.

Here $S_n = X_1 + X_2 + X_3 + \dots + X_n$ represents the waiting time to n th re occurrence of depressive episode.

Clearly $S_j = S_{j-1} + X_j$ i.e. S_j is dependent on S_{j-1} for $j=2,3,\dots,n$

The joint density of $X_1, X_2, X_3, \dots, X_n$ is

$$\Rightarrow f(X_1, X_2, \dots, X_n) = \frac{1}{(b-a)^n}$$

for $a \leq x \leq b$ (4)

$$\Rightarrow f(S_1, S_2, S_3, \dots, S_n) = \frac{1}{(b-a)^n}$$

$$\text{for } a \leq S_1 < S_2 < \dots < S_n \leq nb$$

To obtain the marginal density of S_n , it is required to integrate one variable at a time.

$$\therefore f(S_2, S_3, \dots, S_n) = \int \frac{1}{(b-a)^n} ds_1,$$

$$\text{for } a \leq s_1 < s_2$$

$$= \frac{(s_2 - a)}{(b-a)^n} \quad \dots (5)$$

Similarly

$$f(S_3, S_4, \dots, S_n) = (s_2 - a) \int \frac{1}{(b-a)^n} ds_2,$$

$$= \frac{(s_2 - a)(s_3 - a)}{(b-a)^n} \quad \dots (6)$$

episodes of depression. As a result time between two consecutive occurrences of depressive episodes follows uniform distribution in (a,b)

1.5 The occurrence rate of depression is given by

$$F(x) = \frac{(x-a)}{(b-a)}, a \leq x \leq b$$

$$1 - F(x) = \frac{(b-a-x+a)}{(b-a)} = \frac{(b-x)}{(b-a)}$$

$$f(x) = \frac{1}{(b-a)}, a \leq x \leq b$$

= 0, otherwise

$$f(S_n) = (s_2 - a)(s_3 - a) \dots (s_{n-1} - a) \int \frac{1}{(b-a)^n} ds_{n-1}$$

$$= \frac{(s_2 - a)(s_3 - a) \dots (nb - a)}{(b-a)^n} \quad \dots (7)$$

If $X_1, X_2, \dots, X_n$ are i.i.d random variables, such that $M = \max(X_i)$ and $m = \min(X_i)$, then

From equation 2 and 3

$$\Pr\{M = x\} =$$

$$n \left[\frac{(x-a)}{(b-a)} \right]^{n-1} \frac{1}{(b-a)}$$

$$= \frac{n}{(b-a)^n} (x-a)^{n-1} \quad \dots (8)$$

$$(ii) \Pr\{m = x\} = n \left[1 - \frac{(x-a)}{(b-a)} \right]^{n-1} \frac{1}{(b-a)}$$

$$= \frac{n}{(b-a)^n} (b-x)^{n-1} \quad \dots (9)$$

The distribution of range i.e. the difference between the longest and shortest occurrence time to depressive episode is given by

$$\Pr(R \leq r) = n \int [F(x_1 + r) - F(x_1)]^{n-1} f(x_1) dx_1$$

, $a \leq x_1 \leq b$

...(10)

$$\begin{aligned}
 &= \\
 n \int &\left[\frac{x_1 + r - a}{b - a} - \frac{x_1 - a}{b - a} \right]^{n-1} \frac{1}{(b - a)} dx_1 \\
 &= n \int \left[\frac{r}{b - a} \right]^{n-1} \frac{1}{b - a} dx_1 \\
 &= n \left[\frac{r}{(b - a)} \right]^n \left[1 - \frac{a}{r} \right] \quad \dots (11)
 \end{aligned}$$

$M(t)$, the expected number of depressive episodes which is defined in the interval $(0, t]$ may be obtained by using renewal equation (J. Medhi).

$$M(t) = \frac{(t - a)}{(b - a)} + \frac{1}{(b - a)} \int_a^t M(t - x) dx, \quad a \leq x \leq t \leq b \quad \dots (12)$$

$$M'(t) = \frac{-a}{(b - a)} + \frac{1}{(b - a)} M(t) \quad \dots (13)$$

$$= -ac + cM(t), \quad \text{where } c = \frac{1}{(b - a)}$$

$$\text{Let } r(t) = -ac + cM(t)$$

$$\text{Hence } r'(t) = cM'(t)$$

$$= c[-ac + cM(t)] = cr(t)$$

$$\Rightarrow \frac{r'(t)}{r(t)} = c$$

$$d\{\log r(t)\} = c$$

$$\log r(t) = ct + \text{const}$$

$$\Rightarrow r(t) = e^{ct} + K \quad \dots (14)$$

Where K may be determined by the initial condition $M(0) = 0$

$$\Rightarrow -ac + cM(t) = e^{ct} + K$$

$$\Rightarrow M(t) = a + (c)^{-1} e^{ct} + K$$

$$= a + \left[(b - a) e^{(b-a)^{-1}t} \right] + K$$

$$M(0) = 0, \text{ gives } K = -b$$

$$\Rightarrow M(t) = (b - a) \left[e^{(b-a)^{-1}t} - 1 \right] \quad \dots (15)$$

The expected number of depressive episodes per unit of time converges to $[E(X)]^{-1}$,

$$\text{where } E(X) = \frac{(b + a)}{2} \quad \dots (16)$$

1.6 Discussion:

Hazard rate of occurrence and expected number of depressive episodes have been presented graphically. The average hazard rate is obtained from data collected from records of the Out Patients Department (OPD) of the department of Psychiatry of Gauhati Medical College Hospital (Assam, North East India) by random sampling for a period of 10 years from 2000-2009 (Phookun and Sarmah, 2010). Therefore the average hazard rate $\lambda = 0.25$, is the estimated occurrence rate of depressive episodes from the collected data. The graph of $h(x)$ for Uniform, distribution is presented below.

Fig: 1. Hazard rate of uniform distribution

The graph shown above explains the nature of the hazard rate. Here $h(x)$ shows an increasing trend. The hazard rate plays a pivotal role in determining the nature of the different operating characteristics which may be helpful in the treatment process. The waiting time to n^{th} depressive episode and the range of depressive episode in a particular period of time may play a crucial role in the treatment process.

The graph showing the behaviour of $M(t)$ corresponding to uniform distribution is as follows

Fig: 2 M (t) of Uniform distribution

From the above graphs it is clear that M(t) is also increasing.

Thus the above graph can exhibit the expected number of renewals of depressive episodes.

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