Probabilistic analysis of depressive episodes:
Renewal Theoretic approach

5.1 Introduction
It has been mentioned in Chapter 1 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 un-precipitated.

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 Discontinuation of effecting treatment often leads to relapse, especially if medications are withdrawn rapidly.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.

To study this phenomenon depression is taken as a system dependent on time. This chapter deals with probabilistic analysis of depressive episodes as an ordinary renewal process

5.1.1 Importance of hazard rate of occurrence
The hazard rate of occurrence plays a pivotal role in diagnosing a depressive episode as a disease. As already mentioned in Chapter 1, depression can be termed as a disease if it lasts more than two weeks at a stretch. Normal depression waxes and wanes over time and generally lasts for short duration. Since it is an episodic disorder it tends to recur at different time interval with varying intensities. 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)
5.2 Materials and methods

The renewal theory which is to be applied in this chapter has been formulated on the basis of \( F(x) \), where \( F(x) \) is the distribution function of time between two consecutive occurrences of depressive episodes. The form of \( F(x) \) is dependent on hazard rate.

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

\[
h(x) = \frac{dF(x)}{1 - F(x)}, \quad \ldots (5.1)
\]

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

This rate of occurrence is unique to every distribution function. It may be noted that, probabilistic behaviour of random variables differs depending on the structure of the hazard rate. A distribution may be characterized by \( h(x) \) as increasing hazard rate (I.H.R) and decreasing hazard rate (D.H.R) distribution. A hazard rate is said to be I.H.R if \( h(x) \) increases as \( x \) increases and D.H.R if \( h(x) \) decreases as \( x \) increases (Barlow and Proschan 1965). Order statistics plays a very important role in describing the characteristics of depressive episodes which can be defined as

**Order Statistics:** Let \( X_1, X_2, \ldots, X_n \) be a random sample from a p.d.f \( f_x(x, \theta) \).

Suppose that the \( n \) observations are arranged in ascending order so that

\[ X_{(1)} \leq X_{(2)} \leq \ldots \leq X_{(n)} \]

where \( X_{(1)} \) is the smallest observation and \( X_{(n)} \) is the largest observation. Clearly \( X_{(1)} \) can be any of the \( n \) \( X_i \)‘s. Then \( X_{(1)} \) is called the first order statistic, whereas \( X_{(n)} \) is called the \( n \)\(^{th}\) order statistic. In general \( X_{(i)} \) is called the \( i \)\(^{th}\) order statistic, and it has \((i-1)\) observations preceding it.

**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 –
\[ P(E) = P(x \leq X_i \leq x + dx) \]

\[
g_i(y_i) = \frac{n!}{(i-1)!(n-i)!} \left[ \int_{-\infty}^{y_i} f(x)dx \right]^{i-1} \left[ \int_{y_i}^{\infty} f(x)dx \right]^{n-i}, \text{ for } -\infty < y_i < \infty \ldots (5.2)\]

In particular, the sampling distribution of \( Y_n \), the largest value in the random value of size \( n \), is given by

\[
g_n(y_n) = n \left[ \int_{-\infty}^{y_n} f(x)dx \right]^{n-1} f(y_n), \text{ for } -\infty < y_n < \infty \ldots (5.3)\]

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

\[
g_1(y_1) = n \left[ \int_{y_1}^{\infty} f(x)dx \right]^{n-1} f(y_1), \text{ for } -\infty < y_1 < \infty \ldots (5.4)\]

### 5.3 Depressive episodes as a renewal process

It has been mentioned earlier that depressive episodes are random functions of time. 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). So here it can be said that depression is a function of time

For a normal person, let \( X_i \) be the time epoch at which depressive episode is registered for the \( i^{th} \) time. Now there is a sequence of random variables viz. \( X_1, X_2, \ldots, X_n \) representing time corresponding to \( 1^{st}, 2^{nd}, \ldots, n^{th} \) occurrence of depressive episodes.
The number of depressive episodes $N(t)$ in a random interval of time $(0,t]$ results a renewal process where $X_1, X_2, ..., X_n$ 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. The next section of this chapter presents the distribution of depressive episodes $N(t)$ under different structures of hazard rate of occurrence.

### 5.4 Constant hazard rate

Let the occurrence rate of depressive episodes be $\lambda$ which implies

$$F(x) = 1 - e^{-\lambda x}, \quad x \geq 0, \lambda > 0 \quad \cdots (5.5)$$

The corresponding density function is given by

$$f(x) = \lambda e^{-\lambda x} \quad \cdots (5.6)$$

The process $\{N(t), t \geq 0\}$ results in an ordinary renewal process with

$$\Pr\{N(t) = n\} = e^{-\lambda t} \frac{(\lambda t)^n}{n!}, \quad \text{for } n = 0, 1, 2\ldots \text{ and } t > 0. \quad \cdots (5.7)$$

In this case the process $\{N(t), t \geq 0\}$ results a Poisson process.
The episode function \( E \{N (t)\} = \lambda t = M (t) \) \hspace{1cm} \ldots (5.8)

and episode density \( m (t) = \frac{d}{dt} M (t) \) \hspace{1cm} \ldots (5.9)

are the main operating characteristics of depressive episodes.

The Poisson process reveals some interesting properties regarding the behaviour of depressive episodes.

**Properties related to hazard rate**-

1. Though hazard rate of occurrence of depressive episodes are constant, the expected number of depressive episodes in a random interval of length \( t \), monotonically increases in \( t \).

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

   (i) \( \Pr \{M = x\} = n \lambda \left(1 - e^{-\lambda x}\right)^{n-1} e^{-\lambda x} \)

   (ii) \( \Pr \{m = x\} = n \lambda e^{-n\lambda x} \)

Proof:

\[ \Pr \{M = x\} = n \lambda \left(1 - e^{-\lambda x}\right)^{n-1} e^{-\lambda x} \]

From equation (5.2)

\[ g_n(y_n) = n \left[ \int_{-\infty}^{y_n} f(x)dx \right]^{n-1} f(y_n) \], \hspace{1cm} \text{for} \hspace{0.1cm} -\infty < y_n < \infty \hspace{1cm} \ldots (5.10) \]

\[ \therefore \Pr[M = x] = n[F(x)]^{n-1} f(x) = n \lambda (1 - e^{-\lambda x})^{n-1} e^{-\lambda x} \hspace{1cm} \ldots (5.11) \]

\[ \Pr \{m = x\} = n \lambda e^{-n\lambda x} \]
From equation (5.3)

\[ g_i(y_1) = n \left[ \int_{y_1}^{\infty} f(x) \, dx \right]^{n-1} f(y_1) \quad \text{for} \ -\infty < y_1 < \infty \quad \ldots (5.12) \]

\[ \therefore \Pr\{m=x\} = n[1-F(x)]^{n-1} f(x) = n\lambda e^{-\lambda x} \quad \ldots (5.13) \]

(3) The conditional probability of occurrence of \(i^{th}\) depressive episode, given the probability of waiting time to \(n^{th}\) depressive episode follows binomial law and is independent of the parameter of exponential distribution.

**Proof:**

Assume \(S_n = X_1 + X_2 + \ldots + X_n\) be the waiting time to nth re-occurrence of depressive episode. Clearly, \(S_j = S_{j-1} + X_j\) i.e. \(S_j\) is dependent on \(S_{j-1}\) for \(j = 2, 3, \ldots, n\).

The joint density of \(S_1, S_2, \ldots, S_n\) may be obtained by using Jacobian of transformation denoted by ‘J’

Now we have \(S_1 = X_1, S_2 = X_1 + X_2, S_3 = X_1 + X_2 + X_3, \ldots, S_n = X_1 + X_2 + X_3 + \ldots + X_n\) so ‘J’ is as follows

\[
J = \begin{pmatrix}
1 & 0 & 0 & \ldots & 0 & \ldots & 0 \\
1 & 1 & 0 & \ldots & 0 & \ldots & 0 \\
1 & 1 & 1 & \ldots & 0 & \ldots & 0 \\
\vdots & \vdots & \vdots & \ddots & \vdots & \ddots & \vdots \\
1 & 1 & 1 & \ldots & 1 & \ldots & 1
\end{pmatrix}
\]

\[ \Rightarrow \det J = 1 \quad \ldots (5.14) \]

Since \(X_1, X_2, \ldots, X_n\) are independent, the joint density of \(X_1, X_2, \ldots, X_n\) is

\[ f(x_1, x_2, \ldots, x_n) = \lambda^n e^{-\lambda \sum x} \quad \ldots (5.15) \]
Hence the preceding transformation yields that

\[ S_n = X_1 + X_2 + X_3 + \ldots + X_n \quad \text{where} \]

\[ X_1 = S_1, \quad X_2 = S_2 - S_1, \quad X_3 = S_3 - S_2, \ldots, \quad X_n = S_n - S_{n-1}. \]

Hence, the joint density of \( S_1, S_2, S_3, \ldots, S_n \) is

\[
f(s_1, s_2, \ldots, s_n) = \lambda^e \left( \sum_{i=1}^{n} X_i \right) e^{-\lambda s_n}, \quad 0 < s_1 < s_2 < \cdots < s_n \quad \ldots (5.16)
\]

The marginal density of \( S_n \), may be obtained by integrating out other variables one at a time.

This gives

\[
f\left( s_n \right) = \lambda^e \left( s_n \right)^{n-1} \frac{e^{-\lambda s_n}}{(n-1)!} \quad s_n > 0, \quad n = 1, 2, 3, \ldots \quad \ldots (5.17)
\]

Equation (5.17) follows Gamma distribution with parameters \((n, \lambda)\).

Conditional probability of occurrence of \(i\)th depressive episode, given the probability of waiting time to \(n\)th depressive episode may be obtained as follows

We have \( X_i = S_i - S_{i-1} \)

\[
\Pr(X_i = x_i \mid S_n = s_n) = \Pr(X_i = x_i, S_n = s_n) \Pr(S_n = s_n)
\]

\[
= \Pr(X_i = x_i, S_n = \sum X_i = s_n) \Pr(S_n = s_n)
\]

\[
= \Pr(X_i = x_i \mid S_{n-1} = \sum X_i - X_i = s_{n-1}) \Pr(S_n = s_n)
\]

\[
= \Pr(X_i = x_i) \Pr(S_{n-1} = \sum X_i - X_i = s_{n-1}) \Pr(S_n = s_n)
\]
\begin{align*}
= & \Pr(X_i = s_i - s_{i-1}) \Pr(S_{n-1} = S_n - S_i + S_{i-1} = s_{n-1}) \Pr(S_n = s_n) \\
= & \frac{\lambda e^{-\lambda (s_i - s_{i-1})} \lambda^{-1} (s_i - s_{i-1}) (s_{n-1})^{n-2} e^{-\lambda s_{n-1}} / (n-2)!}{\lambda^n (s_n)^{n-1} e^{-\lambda s_n} / (n-1)!} \\
= & \frac{\lambda e^{-\lambda (s_i - s_{i-1})} \lambda (s_i - s_{i-1}) (s_{n-1})^{n-2} e^{-\lambda (s_n - s_i + s_{i-1})} / (n-2)!}{\lambda^n (s_n)^{n-1} e^{-\lambda s_n} / (n-1)!} \\
= & \frac{(n-1)(s_i - s_{i-1}) (s_{n-1})^{n-2}}{(s_n)^{n-1}} \\
= & (n-1)(s_i - s_{i-1}) (s_{n-1})^{-1} \left\{ \frac{(S_n - S_i + S_{i-1})}{S_n} \right\}^{n-2} \\
= & (n-1) \left( \frac{X_i}{S_n} \right) \left( \frac{S_n - S_i + S_{i-1}}{S_n} \right)^{n-2} \\
= & (n-1) \left( \frac{X_i}{S_n} \right) \left( 1 - \frac{X_i}{S_n} \right)^{n-2} ... (5.18)
\end{align*}

Which is independent of occurrence rate \( \lambda \) of depressive episode and follows binomial distribution with parameters \( \left\{ n, \left( \frac{X_i}{S_n} \right) \right\} \).
and \((i-1)\)th occurrence is free from the parameter which is going to be helpful to estimate certain character of depressive episodes based on time between the consecutive episodes.

(4) If \(X_1, X_2, \ldots, X_n\) are i.i.d random variables, the distribution of range i.e., the difference between the longest and the shortest occurrence time to a depressive episode is an interesting characteristic and may be clinically important.

Let, \(R=X_{(n)} - X_{(1)}\), where \(X_{(n)} = \max \{ X_1, X_2, \ldots, X_n \} \), \(X_{(1)} = \min \{ X_1, X_2, \ldots, X_n \} \)

\[
\Pr(R \leq r) = n\int[F(x_i + r) - F(x_i)]^{n-1}f(x_i)dx_i, \quad 0 \leq x_i \leq r \quad \ldots \quad (5.19)
\]

For \(X_1, X_2, \ldots, X_n\) i.i.d exponential random variables

\[
\Pr(R \leq r) = n\int\left[ e^{-\lambda x_1} - e^{-\lambda (x_1 + r)} \right]^{n-1}\lambda e^{-\lambda x_1}dx_1, \quad 0 \leq x_i \leq r \quad \ldots \quad (5.20)
\]

\[
= n\lambda\int\left[ e^{-\lambda x_1} (1 - e^{-\lambda r}) \right]^{n-1} e^{-\lambda x_1}dx_1
\]

\[
= n\lambda\int e^{-n\lambda x_1} (1 - e^{-\lambda r})^{n-1} e^{-\lambda x_1}dx_1
\]

\[
= \left(1 - e^{-\lambda r}\right)^{n-1} n\lambda\int e^{-\lambda (n+1) x_1}dx_1
\]

\[
= \left(1 - e^{-\lambda r}\right)^{n-1} n\lambda\int e^{-\lambda (n+1) x_1}dx_1 / (n+1)
\]

\[
= \frac{n}{(n+1)} \left(1 - e^{-\lambda r}\right)^{n-1} \quad \ldots \quad (5.21)
\]
M(t), the expected number of depressive episodes in a random interval of time may be obtained easily when counting process is a Poisson process.

We have

\[ M(s) = LM(t) = \frac{f(s)}{s[1 - f(s)]} \]  \hspace{1cm} \text{… (5.22)}

where \( f(s) \) is the Laplace transformation of

\[ f(t) = \lambda e^{-\lambda t}, \quad x \geq 0, \lambda > 0 \]  \hspace{1cm} \text{… (5.23)}

and \( f(s) = \frac{\lambda}{\lambda + s} \)  \hspace{1cm} \text{… (5.24)}

\[ M(s) = L\{M(t)\} = \frac{\lambda}{s^2} \]  \hspace{1cm} \text{… (5.25)}

\[ \Rightarrow M(t) = \lambda t \]  \hspace{1cm} \text{… (5.26)}

Thus property (1) mentioned in the beginning of this section is proved.

**5.5 The hazard rate**  \( h(x) = \lambda x \)

When the occurrence rate is \( \lambda x \) (i.e. when the hazard rate is linearly increasing in \( x \)), the sequence of random variables \( \{X_i\} \) \( i=1,2,... \) follows Rayleigh distribution with distribution function

\[ F(x) = 1 - e^{-\lambda^2 / 2} \quad \text{where} \quad x \geq 0, \lambda > 0 \]  \hspace{1cm} \text{… (5.27)}

The corresponding density function is

\[ f(x) = \lambda x e^{-\lambda^2 / 2} \quad \text{where} \quad x \geq 0, \lambda > 0 \]  \hspace{1cm} \text{… (5.28)}
If \(X_1, X_2, \ldots, X_n\) are i.i.d random variables, such that \(M=\max (X_i)\) and \(m=\min (X_i)\), then

(i) \(\Pr\{M = x\} = n[F(x)]^{n-1} f(x)\)

where \(F(x) = \int_0^x \lambda u e^{-\lambda u^2/2} du\) \(\ldots (5.29)\)

\begin{align*}
&= n\left[1-e^{-\lambda x^2/2}\right]^{n-1} \lambda x e^{-\lambda x^2/2} = n\lambda \left(1-e^{-\lambda x^2/2}\right)^{n-1} e^{-\lambda x^2/2} \\
& \quad \ldots (5.30)
\end{align*}

(ii) \(\Pr\{m = x\} = n[1 - F(x)]^{n-1} f(x)\)

\begin{align*}
&= n\left[1-e^{\lambda x^2/2}\right]^{n-1} \lambda x e^{\lambda x^2/2} = n\lambda x e^{\lambda x^2/2} \\
& \quad \ldots (5.31)
\end{align*}

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

\[
\Pr(R \leq r) = n\int[F(x_1 + r) - F(x_1)]^{n-1} f(x_1) \, dx_1, \quad 0 \leq x_1 \leq r
\]

\begin{align*}
&= n\int\left[e^{-\lambda x_1^2/2} - e^{-\lambda (x_1+r)^2/2}\right]^{n-1} \lambda x_1 e^{-\lambda x_1^2/2} \, dx_1, \quad 0 \leq x_1 \leq r \\
&= n\int\left[e^{-\frac{\lambda x_1^2}{2}} - e^{-\frac{\lambda (x_1+r)^2}{2}}\right]^{n-1} \lambda x_1 e^{-\frac{\lambda x_1^2}{2}} \, dx_1
\end{align*}
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\[
\frac{\lambda n \int x_1 e^{-\frac{\lambda x_1^2}{2}} \left[ 1 - e^{-\frac{\lambda x_1 r - x_2}{2}} \right]^{n-1} dx_1}{\int f(n\lambda, x_1) \left[ 1 - e^{-\frac{\lambda x_1 r - x_2}{2}} \right]^{n-1} dx_1} \quad \text{(5.32)}
\]

The closed form expression for waiting time distribution of \( n \)-th occurrence of depressive episode is not available, instead a joint distribution of \( S_1, S_2, S_3, \ldots, S_n \) may be obtained as follows:

since \( X_1, X_2, \ldots, X_n \) are independent, the joint density of \( X_1, X_2, \ldots, X_n \) is

\[
f(x_1, x_2, \ldots, x_n) = \lambda^n x^n e^{-\frac{\lambda x^2}{2}} \quad \text{(5.33)}
\]

Hence \( S_n = X_1 + X_2 + X_3 + \ldots + X_n \) gives

\[
X_1 = S_1, \quad X_2 = S_2 - S_1, \quad X_3 = S_3 - S_2, \ldots, \quad X_n = S_n - S_{n-1}.
\]

The joint density of \( S_1, S_2, S_3, \ldots, S_n \) as

\[
f(s_1, s_2, s_3, \ldots, s_n) = \lambda^n (s_1 s_2 s_3 \ldots s_n) e^{-\frac{\lambda \left[ s_1^2 + \sum (s_i - s_{i-1})^2 \right]}{2}} \quad \text{(5.34)}
\]

where \( 0 < s_1 < s_2 < s_3 < \ldots < s_n \)

As the closed form expression for the waiting time distribution under this case is not available, Laplace transform may be used for the study of probabilistic analysis.
The Laplace transform of \( f(x, \lambda) = \lambda x e^{-\lambda x^2 / 2} \) may be obtained as follows

\[
f(s, \lambda) = \int e^{-sx} \lambda x e^{-\lambda x^2 / 2} \, dx
\]

\[
= \int \lambda x e^{-(\lambda x^2 / 2 + sx)} \, dx
\]

\[\ldots (5.35)\]

Let \( \frac{\lambda}{2} x^2 + sx = u \)

\[\Rightarrow (\lambda x + s) dx = du\]

\[\Rightarrow dx = (\lambda x + s)^{-1} du\]

Now \( x \) may be obtained by solving \( \frac{\lambda}{2} x^2 + sx - u = 0 \) as

\[\Rightarrow x = \frac{-s + \sqrt{s^2 + 2\lambda u}}{\lambda}\]

\[\Rightarrow dx = \frac{du}{(s^2 + 2\lambda u)^{1/2}}\]

Hence, \( f(s, \lambda) = \int \lambda \left[ \frac{(s^2 + 2\lambda u)^{1/2} - s}{\lambda} \right] e^{-u} \frac{du}{(s^2 + 2\lambda u)^{1/2}} \)

\[= \int e^{-u} du - \int \frac{s}{(s^2 + 2\lambda u)^{1/2}} e^{-u} du\]
\[ = \left[ 1 - E \left( \frac{s}{(s^2 + 2\lambda u)^{\frac{1}{2}}} \right) \right] \quad \ldots (5.36) \]

Now, \( E \left( \frac{s}{(s^2 + 2\lambda u)^{\frac{1}{2}}} \right) \) may be obtained by expanding the expression \( (s^2 + 2\lambda u)^{\frac{1}{2}} \) and taking expectation where ‘u’ is exponential with parameter 1 (one). It may easily be shown that

\[
f(s, \lambda) = \left[ 1 - \left( \frac{s}{(s^2 + 2\lambda)^{\frac{1}{2}}} \right) \right] = [1 - k(s, \lambda)], \quad \ldots (5.37)\]

where \( \frac{s}{(s^2 + 2\lambda)^{\frac{1}{2}}} = k(s, \lambda) \)

Now \( S_n = X_1 + X_2 + \cdots + X_n \), therefore the Laplace transform of \( f(S_n = s_n) \) is as given below

\[
f(S_n = s_n) = [f(s, \lambda)]^n \]
\[= [1 - K(s, \lambda)]^n \quad \ldots (5.38)\]

Which is the Laplace transform of waiting time distribution to \( n^{th} \) depressive episode and may be obtained upon numerical inversion.

The stochastic process \( \{N(t), t \geq 0\} \) of depressive episode in a random interval of time \((0, t]\) may be identified by \( M(t) \), the expected number of episodes at time \( t \). The expression for \( m(t) \) may be obtained in terms of Laplace transform viz.
\[ M(s) = \frac{f(s)}{s \{1 - f(s)\}} \]

\[ m(s) = \frac{f(s)}{\{1 - f(s)\}} \]

These Laplace transformations may be inverted using Post's inversion formula viz.

\[ M(t) = \mathcal{L}^{-1}\{M(s)\} \]

\[ = \lim_{r \to +\infty} \left( \frac{-1}{r!} \right)^{r} \left( \frac{r}{t} \right)^{r+1} M^{(r)}\left( \frac{r}{t} \right) \]

... (5.39)

where \( M^{(r)}\left( \frac{r}{t} \right) \) is the \( r \)th derivative of \( M(s) \) with respect to \( s \) at \( s = \frac{r}{t} \)

The nature of \( M(s) \) may be studied from the expression \( \mathcal{L}^{-1}\{M(s)\} \) where

\[ M(s) = \frac{f(s)}{s \{1 - f(s)\}} \]

\[ = \frac{1 - K(s, \lambda)}{s K(s, \lambda)} \]

\[ = \frac{1}{s} \left[ \frac{1}{K(s, \lambda)} - 1 \right] \]

\[ = \frac{1}{s} \left[ \left( \frac{s^2 + 2\lambda}{s} \right)^\frac{1}{2} - 1 \right] \]

where \( K(s, \lambda) = \frac{S}{(s^2 + 2\lambda)^\frac{1}{2}} \)
\[
\frac{(s^2 + 2\lambda)^{\frac{1}{2}}}{s} - \frac{1}{s} = \left[ \frac{s + (\lambda)s^{-3} + 3!(\lambda)^2 s^{-5} + \cdots}{s^2} \right] - \frac{1}{s} \\
= \left[ (\lambda)s^{-5} + 3!(\lambda^2)s^{-7} + \cdots \right] \\
\Rightarrow \text{Hence } M(t) = (\lambda) \frac{t^4}{4!} + 3!(\lambda)^2 \frac{t^6}{6!} + \cdots \\
= A_0 t^4 + A_1 t^6 + A_2 t^8 + \cdots \\
= t^4 \left( A_0 + A_1 t^2 + A_2 t^4 + \cdots \right) \\
\text{... (5.41)}
\]

where \(A_i\)'s are functions of \(\lambda\) for \(i = 0, 1, 2, \ldots\)

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

where \(E(X) = 3\left( \pi / 2\lambda \right)^{\frac{1}{2}}\) \\
\text{... (5.42)}

\[5.6 \text{ The hazard rate } h(x) = p\lambda^p x^{p-1}, \text{ for } \lambda > 0\]

When the occurrence rate of depressive episode is \(p\lambda^p x^{p-1}\) (i.e. the occurrence time between two depressive episodes is some power of the random variable, this type of hazard rate includes the family of distributions which has both IHR and DHR properties under certain conditions), the sequence of random variables in this case, \(\{X_i\}, i=1,2,\ldots\) follows Weibull distribution with distribution function
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\[ F(x) = \left[ 1 - e^{-\lambda x^p} \right] \] where \( x \geq 0, \lambda > 0. \] \hfill \ldots \ (5.43)

The corresponding density function is

\[ f(x) = p\lambda^p x^{p-1} e^{-\lambda x^p} \] where \( x \geq 0, \lambda > 0 \] \hfill \ldots \ (5.44)

The parameter \( p \) determines nature of rate of occurrence of depressive episode.

If \( p > 1 \), \( h(x) \) is increasing, if \( p = 1 \), \( h(x) \) is constant and if \( p < 1 \), \( h(x) \) is decreasing.

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

(i) \( \Pr\{M = x\} = n[F(x)]^{p-1} f(x) \) where \( F(x) = \int_0^x p\lambda^p u^{p-1} e^{-\lambda u^p} du \)

\[ = n\left[1 - e^{-\lambda x^p}\right]^{p-1} p\lambda^p x^{p-1} e^{-\lambda x^p} = n\lambda^p p x^{p-1} \left[ \lambda^{-1} \left(1 - e^{-\lambda x^p}\right) \right]^{p-1} e^{-\lambda x^p} \]

\[ = n \lambda^p x^{p-1} \left[1 - e^{-\lambda x^p}\right]^{p-1} e^{-\lambda x^p} \] \hfill \ldots \ (5.45)

(ii) \( \Pr\{m = x\} = n\left[1 - F(x]\right]^{p-1} f(x) \)

\[ = n\left[1 - \left(1 - e^{-\lambda x^p}\right)\right]^{p-1} p\lambda^p x^{p-1} e^{-\lambda x^p} \]

\[ = n \lambda^p x^{p-1} \left[1 - \left(1 - e^{-\lambda x^p}\right)\right]^{p-1} e^{-\lambda x^p} \] \hfill \ldots \ (5.46)

The distribution of range i.e. the difference between the longest and shortest occurrence time to depressive episode is given by
\[ \Pr(R \leq r) = n \int \left[ F(x_i + r) - F(x_i) \right]^{p-1} f(x_i) \, dx_i, \quad 0 < x_i < r \]

\[ = n \int \left[ e^{-\lambda x_i^p} - e^{-\lambda (x_i + r)^p} \right]^{p-1} \lambda x_i^{p-1} e^{-\lambda x_i^p} \, dx_i, \quad 0 < x_i < r \]

\[ = np\lambda^p \int \left[ e^{-\lambda x_i^p} - e^{-\lambda (x_i + r)^p} \right]^{p-1} x_i^{p-1} e^{-\lambda x_i^p} \, dx_i \]

\[ = \int f(n\lambda, p, x_i) \left[ e^{-\lambda x_i^p} - e^{-\lambda (x_i + r)^p} \right]^{p-1} \, dx_i \quad \ldots (5.47) \]

Since Weibull Distribution represents both IHR and DHR distributions it may be useful to describe time to occurrence of depressive episode.

The distribution of total time to \( n \)th depressive episode is not available in closed form and hence it may be obtained in terms of Laplace transformation.

In this case

\[ f(x, p, \lambda) = p\lambda x^{p-1} e^{-(\lambda x)^p}, \quad \text{where} \quad x > 0, \lambda > 0, p > 0 \]

\[ = p\lambda x^{p-1} \left[ 1 - (\lambda x)^p + \frac{(\lambda x)^{2p}}{2!} - \frac{(\lambda x)^{3p}}{3!} + \ldots \right] \]

\[ = p\lambda \left[ x^{p-1} - \lambda^p x^{2p-1} + \left( \frac{\lambda^{2p}}{2!} \right) x^{3p-1} - \left( \frac{\lambda^{3p}}{3!} \right) x^{4p-1} + \ldots \right] \quad \ldots (5.48) \]

The Laplace transform of \( f(x, p, \lambda) \) is given by

\[ f(s, p, \lambda) = p\lambda \left[ \frac{(p-1)!}{s^{p-1}} - \lambda^p \frac{(2p-1)!}{s^{2p-1}} + \left( \frac{\lambda^{2p}}{2!} \right) \frac{(3p-1)!}{s^{3p-1}} - \left( \frac{\lambda^{3p}}{3!} \right) \frac{(4p-1)!}{s^{4p-1}} + \ldots \right] \quad \ldots (5.49) \]
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\[ = p \lambda \sum (-1)^i \frac{\left( \lambda^p \right)^i}{i!} \frac{(ip-1)!}{s^{ip-1}} \]

\[ = p \lambda \sum \frac{G_i}{s^{ip-1}} \text{ where } G = \sum (-1)^i \frac{\left( \lambda^p \right)^i}{i!} \frac{(ip-1)!}{s^{ip-1}} \]

\[ ... (5.50) \]

The Laplace transform of renewal function and renewal density is

\[ M(s) = \frac{f(s)}{s[1 - f(s)]} \]

\[ = \left[ \frac{p \lambda \sum (G_i)/s^{ip-1}}{s[1 - p \lambda \sum (G_i)/s^{ip-1}]} \right] \]

\[ ... (5.51) \]

\[ m(s) = \frac{f(s)}{[1 - f(s)]} \]

\[ = \left[ \frac{p \lambda \sum (G_i)/s^{ip-1}}{1 - p \lambda \sum (G_i)/s^{ip-1}} \right] \]

\[ ... (5.52) \]

Alternatively, the valid root of equation \( \lambda x^p + sx - u = 0 \) is a function of \( \lambda, p, \) and \( s \) which may be denoted by \( K(\lambda, p, s) \). Therefore, one can obtain \( f(s, \lambda, p) \).

Hence Laplace transform of waiting time to \( n \)th depressive episode and expected number of depressive episode is available for analysis. A formal inversion of \( M(s) \) gives \( M(t) \) as

\[ M(t) = A_1 t^{2p} + A_2 t^{2(p+1)} + A_3 t^{2(p+2)} + \ldots, \text{ for } p > 1 \]

\[ ... (5.53) \]
Where \( A_i \)'s are functions of \( \lambda \) and \( p \)

Now putting \( p = 2 \) in the above equation we get \( M(t) \) of renewal process generated by Rayleigh distribution.

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

\[
E(x) = \left( \frac{1}{p} \right) \left( \frac{1}{\lambda^p} \right)
\]

\[\ldots (5.54)\]

5.7 The occurrence rate is

\[
h(x) = (b - x)^{-1} = \frac{1 + \frac{x}{b} + \frac{x^2}{b^2} + \ldots}{b}, \text{ for } a \leq x \leq b
\]

when the occurrence rate is \( \left[ 1 + \frac{x}{b} + \frac{x^2}{b^2} + \ldots \right] \) the sequence of random variable \( \{X_i\}, i=1,2,\ldots \) follows uniform distribution with distribution function

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

\[
1 - F(x) = \frac{(b - x)}{(b - a)}
\]

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

\[= 0, \text{ otherwise}\]

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

Assume \( S_n = X_1 + X_2 + X_3 + \ldots + X_n \) be the waiting time to \( n \)th reoccurrence of depressive episode.
Clearly \( S_j = S_{j-1} + X_j \) i.e. \( S_j \) is dependent on \( S_{1:j} \) for \( j = 2, 3, \ldots, n \)

The joint density of \( X_1, X_2, X_3, \ldots, X_n \) is

\[
\Rightarrow f(X_1, X_2, \ldots, X_n) = \frac{1}{(b-a)^n} \text{ for } a \leq x \leq b \quad \ldots (5.55)
\]

\[
\Rightarrow f(S_1, S_2, S_3, \ldots, S_n) = \frac{1}{(b-a)^n} \text{ for } a \leq S_1 < S_2 < \ldots < S_n \leq nb
\]

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

\[
\therefore f(S_1, S_2, \ldots, S_n) = \int f(S_1, S_2, \ldots, S_n) \quad \text{for } a \leq s_1 < s_2
\]

\[
\quad = \frac{(s_2 - a)}{(b-a)^n} \quad \ldots (5.56)
\]

Similarly

\[
f(S_2, S_3, \ldots, S_n) = (s_2 - a)\int f(S_2, S_3, \ldots, S_n) \quad \text{for } a < s_2 < s_3
\]

\[
\quad = \frac{(s_2 - a)(s_3 - a)}{(b-a)^n} \quad \ldots (5.57)
\]

Similarly

\[
f(S_3, S_4, \ldots, S_n) = (s_2 - a)(s_3 - a)\int f(S_3, S_4, \ldots, S_n) \quad \text{for } a < s_3 < s_4
\]
\[
\frac{(s_2 - a)(s_3 - a)(s_4 - a)}{(b - a)^n}
\]

\[\int_{s_{n-1} - a}^{1} \frac{1}{(b - a)^n} ds_{n-1} \quad \text{, } a < s_n < b
\]
\[
\frac{(s_2 - a)(s_3 - a)(s_4 - a)...(nb - a)}{(b - a)^n}
\]  
\[... (5.58)
\]

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

(i) \(\Pr \{M = x\} = n[F(x)]^{-1} f(x)\)

\[
= n \left[ \frac{(x - a)}{(b - a)} \right]^{n-1} \frac{1}{(b - a)}
\]
\[
= \frac{n}{(b - a)^n} (x - a)^{n-1}
\]
\[... (5.59)
\]

(ii) \(\Pr \{m = x\} = n[1 - F(x)]^{-1} f(x)\)

\[
= n \left[1 - \frac{(x - a)}{(b - a)} \right]^{n-1} \frac{1}{(b - a)}
\]
\[
= n \left[ \frac{b - a - x + a}{(b - a)} \right]^{n-1} \frac{1}{(b - a)}
\]
\[
= \frac{n}{(b - a)^n} (b - x)^{n-1}
\]
\[... (5.60)
\]

The distribution of range i.e. the difference between the longest and shortest occurrence time to depressive episode is given by
\[ \Pr(R \leq r) = n \int [F(x_1 + r) - F(x_1)]^{n-1} f(x_1) dx_1, \quad a \leq x_1 \leq b \]

\[ = n \int \left[ \frac{x_1 + r - a}{b-a} - \frac{x_1 - a}{b-a} \right]^{n-1} \frac{1}{(b-a)} dx_1 \]

\[ = n \int \left[ \frac{x_1 + r - a - x_1 + a}{b-a} \right]^{n-1} \frac{1}{b-a} dx_1 \]

\[ = n \int \left[ \frac{r}{b-a} \right]^{n-1} \frac{1}{b-a} dx_1 \]

\[ = n \left( \frac{r}{b-a} \right)^n \int dx_1 \]

\[ = n \left( \frac{r}{b-a} \right)^n (r-a) \]

\[ = n \left[ \frac{r}{(b-a)} \right]^n \left[ 1 - \frac{a}{r} \right] \quad \ldots (5.61) \]

\[ M(t) \text{ which is defined in the interval } (0,t] \text{ may be obtained from the following consideration using renewal equation.} \]

\[ M(t) = \frac{(t-a)}{(b-a)} + \frac{1}{(b-a)} \int M(t-x) dx, \quad a \leq x \leq t \leq b \quad \ldots (5.62) \]

\[ = \frac{(t-a)}{(b-a)} + \frac{1}{(b-a)} \int M(y) dy \]

\[ M'(t) = -\frac{a}{(b-a)} + \frac{1}{(b-a)} M(t) \quad \ldots (5.63) \]

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

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Let \( r(t) = -ac + cM(t) \)

Hence \( r'(t) = cM'(t) \)

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

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

\[
d\{\log r(t)} = c
\]

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

\[
\Rightarrow r(t) = e^{ct} + K \quad \ldots (5.64)
\]

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

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

\[
\Rightarrow cM(t) = ac + e^{ct} + K
\]

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

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

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

\[
\Rightarrow M(t) = (b-a)e^{(b-a)^{-1}t} - 1 \quad \ldots (5.65)
\]

The expected number of depressive episodes per unit of time converges to \([E(X)]^{-1}\), where \( E(X) = \frac{b+a}{2} \) \quad \ldots (5.66)
5.8 **Discussion**: The discussion starts with following result.

**Result**: If a renewal process is generated by IHR or constant hazard rate distribution then expected number of renewals in (0, t] is also increasing in t.

**Proof**: Let \( x_1 \) and \( x_2 \) be random variable with distribution function \( F(x) \) with IHR property. Then the distribution of \( x_1+x_2 \) given by convolution of \( x_1 \) and \( x_2 \) is also a distribution with IHR property (Barlow and Proschan 1965).

Hence, if there exists random variable \( x_i \) for \( i=1,2,... \) then \( t = x_1 + x_2 + ... + x_{n-1} + x_n \) is a random variable with IHR property.

Now for \( M(t) = \sum F_n(t) \) where \( F_n(t) \) is distribution function of \( t \). Therefore \( M(t) \) is an increasing function of \( t \).

**Remark**: The consequence of the above result may be observed in the expressions for \( h(x) \) and \( M(t) \), and they may be well exhibited by their corresponding graph. The average hazard rate obtained from table 2.6 of chapter 2 is 0.25. Therefore \( \lambda = 0.25 \), is the estimated occurrence rate of depressive episodes from the collected data.

The graph of \( h(x) \) for Exponential, Rayleigh, Weibull and Uniform, distributions are presented below.

**Fig: 5.2 Hazard rate corresponding to Exponential distribution (\( \lambda = 0.25 \))**
Fig: 5.3 Hazard rate corresponding to Rayleigh distribution ($\lambda = 0.25$)

![Hazard rate corresponding to Rayleigh distribution ($\lambda = 0.25$)](image)

Fig: 5.4 Hazard rate corresponding to Weibull distribution ($\lambda = 0.25$)

![Hazard rate corresponding to Weibull distribution ($\lambda = 0.25$)](image)

Fig: 5.5 Hazard rate of uniform distribution

![Hazard rate of uniform distribution](image)
The graph shown above explains the nature of the hazard rate for different distributions. 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 the $n^{th}$ depressive episode and the range of depressive episode in a particular period of time may play a crucial role in the treatment process.

The corresponding expressions for $M(t)$ obtained above may be exhibited by the following graphs.

The range of the period is assumed to be three months to two years.

The graph showing behaviour of $M(t)$ corresponding to Exponential distribution (0.25)

**Fig: 5.6 $M(t)$ corresponding to Exponential distribution (0.25)**

The graph showing the behaviour of $M(t)$ corresponding to Rayleigh distribution (0.25).
Fig: 5.7 M (t) of Rayleigh distribution (0.25)

The graph showing the behaviour of M (t) corresponding to Weibull distribution (3, 0.25)

Fig: 5.8 M (t) of Weibull distribution (3, 0.25)

The graph showing the behaviour of M (t) corresponding to uniform distribution (24, 3)
Fig: 5.9 M (t) of Uniform distribution

The graph showing behaviour of M(t) of Uniform distribution

From the above graphs it is clear that the rate of increase in M (t) in t may be arranged in ascending order as:

M (t) of exponential distribution, M(t) of uniform distribution, M(t) of Weibull distribution and M (t) of Rayliegh distribution

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

It has already been stated above in this chapter that the waiting time to a depressive episode and the range of depressive episode in a particular period of time may play a crucial role in the treatment process. A treatment process always has a recovery time which is a random variable. The recovery time plays a pivotal role in studying the characteristics of a depressive episode. The occurrence and recovery time are always alternate. When occurrence and recovery time are taken together they construct a renewal process which can be presented as alternating renewal process. The next chapter deals with alternating renewal process generated by the distributions of X and Y.