Occurrence and Recovery of Depressive Episodes:
An alternating renewal process

6.1 Introduction:
Major depressive disorder is a self limiting episodic disorder where recurrent episodes of depression last for 3 to 9 months (Freedman et al. 2002). Depression cannot be cured completely but can be controlled and kept in a status of remission whereby the patient can function normally with the help of medication. Apart from taking medicines regularly, it is necessary that a patient remains in constant touch with a psychiatrist as a patient’s condition and behaviour at a particular time can be studied for recovery only by a psychiatrist. Moreover, the doses of the administered medication also need to be reviewed from time to time according to the response shown by the patient. In most treatment studies, response is defined as at least 50% improvement, whereas partial response is 25% - 50% improvement, and non response is less than 25% improvement (Hales et al. 2003). Being regular in the visits to the doctor and in taking medicine is essential not only during a depressive episode but also after recovering from it. On discontinuation of the treatment process it is expected that it will recur again. This is termed as relapse (Freedman et. al, 2002, Geldar et al. 1996).

6.2 Materials and methods:
It is assumed that a patient visits a psychiatrist in an interval of time (0, t). It is known that there is time duration between occurrence of a depressive episode and its recovery. Here the time taken from occurrence to recovery of depressive episode is a random variable.

So let $Z(t) = i$, be an indicator random variable.

where $i = 0$, if depressive feelings are not present in a person

$= 1$, if depressive feelings are present in a person
{Z(t), t ≥ 0} is stochastic point process. The point of discontinuity of the process Z(t) are epochs at which the system, that is depressive episode is either in state 0 or in state 1

i.e., {Z(t), t ≥ 0} is a stochastic process with state space $\mathbb{S} = (0, 1)$. The transition is of the type 0 → 1 → 0 → 1.

Assuming that the system’s occurrence points are uniquely determined, it is easy to see that for this system {Z(t), t ≥ 0} is an alternating renewal process. Now, various operating characteristics of depression are obtained using {Z(t), t ≥ 0}.

The following notations are introduced for farther discussion:

\[ f_x(t) \] is the p.d.f. of random variable x

\[ F(t) = \int_0^t f(u) \, du \]

\[ \overline{F(t)} = 1 - F(t) \]

© is convolution symbol.

\[ f^{(n)}(t) \] is n fold convolution with itself in (0,t].

E is the event representing the status of the system.

X is random variable representing the time interval between two successive epochs of occurrence of state 1 and state 0 respectively.

Y is random variable representing the duration for which the system is in state 0, i.e. the time interval between the epochs at which a person recovers from depression and the time epoch at which depression breaks out.
Let $X_i \sim i^{th}$ time for a person to recover from depression for all $i = 1, 2, 3, \ldots$

and $Y_i \sim i^{th}$ time for a person to break out to depression for all $i = 1, 2, 3, \ldots$

Here $X_i$ and $Y_i$ are independent

$X \sim f(x)$

$Y \sim g(y)$

$T_i = \{X_i + Y_i\}$, generates a renewal process with $w(t) = f(t) \otimes g(t)$

$E(T_i) = E(X_i) + E(Y_i)$ gives the mean time between two depressive episodes.

$F(x) = 1 - e^{-\lambda x}$ … (6.1)

and corresponding p.d.f is given by

$f(x) = \lambda e^{-\lambda x}, \ x \geq 0, \ and \ \lambda > 0$ … (6.2)

The corresponding Laplace transform of $f(x)$ denoted by

$L\{f(x)\} = \frac{\lambda}{\lambda + s}$ … (6.3)

$G(y) = 1 - e^{-\mu y}$ … (6.4)

and corresponding p.d.f is given by

$g(y) = \mu e^{-\mu y}, \ y \geq 0, \ and \ \mu > 0$ … (6.5)
The corresponding Laplace transform of $g(y)$ denoted by

$$L\{g(y)\} = \frac{\mu}{\mu + s}. \quad \ldots (6.6)$$

The personality and the behaviour of a patient quiet often determine the pattern of occurrence of depressive episodes. The density function of occurrence of two consecutive depressive episodes generates the corresponding renewal process. The following cases are considered for analysis.

6.3 Case (I).

The behaviour of the random variable $T=X+Y$ is determined by the behaviour of the patient. A patient suffering from depression comes for treatment when he or she is in state 1 (depressive state) and with medication the patient visits state 0 (depression free state) after a random interval of time $X$. If the patient discontinues medicine then after a random interval of time $Y$ will again be back to the state 1.

It can be presented diagrammatically as follows:

Fig: 6.1- A patient visiting state 1 and state 0 alternately
Let $w_0(t)$ be p.d.f of $T = t$, the corresponding Laplace transform of $w_0(t)$ is

$$w_0(s) = f(s)g(s) = \frac{\lambda \mu}{(\lambda + s)(\mu + s)}$$

$$= \frac{\lambda \mu}{\mu - \lambda} \left[ \frac{1}{\lambda + s} - \frac{1}{\mu + s} \right] \quad \ldots (6.7)$$

where $\mu > \lambda, t \geq 0, |s| < 1$

The p.d.f of $t$ is

$$w_0(t) = \frac{\lambda \mu}{\mu - \lambda} [e^{-\lambda t} - e^{-\mu t}], \text{ where } \mu > \lambda, t \geq 0 \quad \ldots (6.8)$$

$$= \frac{\mu}{\mu - \lambda} (\lambda e^{-\lambda t}) - \frac{\lambda}{\mu - \lambda} (\mu e^{-\mu t}) \quad \ldots (6.9)$$

The distribution function of $t$ is

$$W_0(t) = \frac{\mu}{\mu - \lambda} (1 - e^{-\lambda t}) - \frac{\lambda}{\mu - \lambda} (1 - e^{-\mu t}) \quad \ldots (6.10)$$

$$= \frac{\mu}{\mu - \lambda} - \frac{\mu}{\mu - \lambda} (e^{-\lambda t}) - \frac{\lambda}{\mu - \lambda} + \frac{\lambda}{\mu - \lambda} (e^{-\mu t})$$

$$= 1 - \frac{1}{\mu - \lambda} (\mu e^{-\lambda t} - \lambda e^{-\mu t})$$
= 1 - \frac{\mu \lambda}{\mu - \lambda} \left[ \frac{e^{-\lambda t}}{\lambda} - \frac{e^{-\mu t}}{\mu} \right] \quad \ldots (6.11)

When t = x + y, where x and y are independent, then the mean and variance of W₀(t) are

E₀(t) = E(x) + E(y) = \frac{1}{\lambda} + \frac{1}{\mu} \quad \ldots (6.12)

V₀(t) = V(x) + V(y) = \frac{1}{\lambda^2} + \frac{1}{\mu^2} \quad \ldots (6.13)

The survival probability of t is -

1 - W₀(t) = \frac{\mu \lambda}{\mu - \lambda} \left[ \frac{e^{-\lambda t}}{\lambda} - \frac{e^{-\mu t}}{\mu} \right] \quad \ldots (6.14)

The corresponding hazard rate is

h₀(t) = \frac{W₀(t)}{1 - W₀(t)} = \frac{\lambda \mu (e^{-\lambda t} - e^{-\mu t})}{\mu e^{-\lambda t} - \lambda e^{-\mu t}} \quad \ldots (6.15)

The hazard rate corresponding to the behaviour of the random variable T=X+Y which is determined by the behaviour of the patient is depicted by the following graph. As mentioned in chapter 5, the estimated occurrence rate of depressive episodes \( \lambda = 0.25 \). The estimated recovery rate \( \mu \) is obtained from the collected data. From the data sheets it has been observed that out of 968 episodes of 518 patients, 46 episodes show improvement after the first visit to the doctor. Hence, estimated \( \mu \) is \( \frac{46}{968} = 0.048 \). Therefore \( \mu = 0.048 \) can be taken as the estimated minimum recovery rate from the observed sample.
Fig: 6.2. $h_0(t)$: Hazard rate of depressive episodes for case (1)

From the above graph, it is evident that hazard rate rises initially at a sharp rate and then stabilizes at $t = 21$ and remains constant for the rest of the period. This implies that, for the time between two consecutive depressive episodes, hazard rate becomes constant. This indicates that the time between two consecutive depressive episodes follows I.F.R distribution initially and then turns out to be exponential as time increases. This establishes the relationship between I.F.R distribution and exponential distribution (Barlow and Proschan 1965).

6.4 The Renewal Process

The closed form expression for the renewal process $\{N_0(t), t \geq 0\}$ corresponding to $W_0(t)$ cannot be obtained and hence applying the central limit theorem for large $n$ (i.e. for large $t$) the following result can be presented.

**Result 1:**

For the counting variable $N_0(t)$, whose mean and variance of the corresponding density $w_0(t)$ are finite, the random variable $Z_0(t)$ defined as
Chapter 6: Occurrence and recovery of episodes

\[ Z_0(t) = \frac{N_0(t) - \frac{t}{E_0(t)}}{\sqrt{tV_0(t)/E_0(t^2)}} \]  

… (6.16)

where \( t > 0 \) converges to standard normal distribution as \( t \to \infty \)

Proof:

The proof follows from Smith (1958)

The density function corresponding to the renewal process \( \{N_0(t), t \geq 0\} \) is \( w_0(t) \).

It is required to show that \( E_0(t), V_0(t) \) and \( E_0(t^3) \) exists and are finite.

Given \( t = x + y \), where \( x \) and \( y \) are independent, then the mean and variance of \( w_0(t) \) are

\[ E_0(t) = E(x) + E(y) = \frac{1}{\lambda} + \frac{1}{\mu} \]  

… (6.17)

\[ V_0(t) = V(x) + V(y) = \frac{1}{\lambda^2} + \frac{1}{\mu^2} \]  

… (6.18)

\[ E_0(t^3) = \frac{3!}{\lambda^3} + \frac{3!}{\mu^3} \]  

… (6.19)

These are finite since \( \lambda, \mu > 0 \).

\[ Z_0(t) = \frac{\sqrt{6\lambda\mu}}{\mu + \lambda} \left\{ \frac{N_0(t)(\lambda + \mu) - t\lambda\mu}{\sqrt{t(\mu^2 + \lambda^2)}\lambda^3} \right\} \]  

… (6.20)

follows standard normal distribution as \( t \to \infty \)
6.5 Expected number of renewals of the process \( \{N_0(t), t \geq 0\} \)

Let \( M_0(t) \) be the expected number of depressive episodes corresponding to the process \( \{N_0(t), t \geq 0\} \)

Hence \( M_0(t) = E \{N_0(t)\} \), the corresponding Laplace transform is given by

\[
M_0(s) = \frac{w_0(s)}{s[1 - w_0(s)]},
\]

where \( w_0(s) = f(s)g(s) = \frac{\lambda \mu}{(\lambda + s)(\mu + s)} \)

i.e., \( M_0(s) = \frac{\lambda \mu}{s^2(s + \lambda + \mu)} \)

\[
\text{Applying partial fraction we get } M_0(t) \text{ as}
\]

\[
M_0(t) = \frac{\lambda \mu}{(\lambda + \mu)^2} e^{-(\lambda+\mu)t} - 1 + \frac{\lambda \mu}{(\lambda + \mu)} t
\]

\[
M_0(t) = \frac{1}{t} \left[ \frac{\lambda \mu}{(\lambda + \mu)^2} (e^{-(\lambda+\mu)t} - 1) \right] + \frac{\lambda \mu}{(\lambda + \mu)}
\]

\[
\lim_{t \to \infty} \frac{M_0(t)}{t} = \frac{\lambda \mu}{(\lambda + \mu)}
\]

That is, the expected number of depressive episodes per unit of time as \( t \to \infty \) is \( \frac{\lambda \mu}{\lambda + \mu} \) which is equal to depressive episodic rate [inverse of mean of \( w_0(t) \)]. This statement is a proof of renewal theorems (J.Medhi, 2009).
Fig: 6.3. $M_0(t)$: Expected number of depressive episodes for case (1)

From the above graph, it is obvious that the expected number of renewals increases from $t = 4$ onwards. This indicates renewal process increases linearly and tends to a Poisson process.

6.6 Case II.

As mentioned earlier in case (I) the behaviour of $T$ determine the pattern of depressive episodes. It has been stated earlier that a depressive patient after medication recovers, that is visits a depression free state (i.e. state 0). A patient may have relapse even though he continues treatment and is under medication, that is he may visit state 1 (i.e. depressive state) through state 0. This implies the renewal process generated by random variable $T = \{X + Y \leq t / X < Y\}$ may be viewed as an ordinary renewal process. Diagrammatically it may be presented as
Fig: 6.4. Remission time is greater than occurrence time of a depressive episode

Here \( T = \{ X + Y \leq t \mid X < Y \} \).

We have to obtain the probability distribution of \( T \) i.e.

\[
\Pr\{X + Y \leq t \mid X < Y\}
\]

Let \( T = U + Z \),

where \( U = \min (X, Y) \) and \( Z = Y - \min (X, Y) \)

Since minimum of two exponential random variables is also exponential with parameter equal to sum of the parameters of the two exponentials.

Hence, \( U \sim \text{Exp} (\lambda + \mu) \)

\( Z \) follows exponential with parameter \( \mu \)

(Using memoryless property of exponential distribution with parameter \( \mu \))

Hence \( T \) can be viewed as sum of two exponential random variables one with parameter \( (\lambda + \mu) \) and other with parameter \( \mu \) respectively.
That is, $T$ is convolution of two exponential random variables with parameter $(\lambda + \mu)$ and $\mu$ respectively.

In this case $f(s) = \frac{(\lambda + \mu)}{(\lambda + \mu + s)}$ \ldots \hspace{1em} (6.25)

and $g(s) = \frac{\mu}{\mu + s}$ \ldots \hspace{1em} (6.26)

\[ w_i(s) = \frac{(\lambda + \mu)\mu}{(\lambda + \mu + s)(\mu + s)} \]

\[ = \frac{(\lambda + \mu)\mu}{\lambda} \left[ \frac{1}{\mu + s} - \frac{1}{\lambda + \mu + s} \right] \] \hspace{1em} \ldots \hspace{1em} (6.27)

\[ w_i(t) = \frac{(\lambda + \mu)\mu}{\lambda} \left[ e^{-\mu t} - e^{-(\lambda + \mu) t} \right] \]

\[ = \frac{(\lambda + \mu)\mu}{\lambda} e^{-\mu t} \left[ 1 - e^{\lambda t} \right] \] \hspace{1em} \ldots \hspace{1em} (6.28)

The distribution function of $t$ is

\[ W_i(t) = \frac{(\lambda + \mu)}{\lambda} \mu e^{-\mu t} - \frac{(\lambda + \mu)\mu}{\lambda} e^{-\mu t} e^{\lambda t} \]

\[ = \frac{(\lambda + \mu)}{\lambda} \left( 1 - e^{-\mu t} \right) - \frac{\mu}{\lambda} e^{-(\lambda + \mu) t} \] \hspace{1em} \ldots \hspace{1em} (6.29)
\[
\frac{(\lambda + \mu)}{\lambda} - \frac{(\lambda + \mu)}{\lambda} e^{-\mu} - \frac{\mu}{\lambda} + \frac{\mu}{\lambda} e^{-(\lambda + \mu)t} = 1 - \frac{(\lambda + \mu)}{\lambda} e^{-\mu} + \frac{\mu}{\lambda} e^{-(\lambda + \mu)t} \quad \ldots (6.30)
\]

The survival probability of \( t \) is

\[
1 - W(t) = \frac{(\lambda + \mu)}{\lambda} e^{-\mu} - \frac{\mu}{\lambda} e^{-(\lambda + \mu)t} \quad \ldots (6.31)
\]

The corresponding hazard rate is

\[
h(t) = \frac{W(t)}{1 - W(t)} = \frac{\mu}{\lambda} e^{-\mu} (1 - e^{-\lambda t}) \quad \ldots (6.32)
\]

\[
h(t) = \frac{\mu}{\lambda} (\lambda + \mu) e^{-\mu} (1 - e^{-\lambda t})
\]

\[
= \frac{\mu}{\lambda} e^{-\mu} \left(1 - \frac{1}{\lambda + \mu} e^{-\lambda t}\right)
\]

\[
\therefore h(t) = \frac{\mu(\lambda + \mu)(1 - e^{-\lambda t})}{\lambda + \mu(1 - e^{-\lambda t})} \quad \ldots (6.33)
\]
When a patient visits state 1 through state 0 then the hazard rate of depressive episodes is depicted by the following graph.

**Fig: 6.5. \( h_1(t) \): Hazard rate of depressive episodes for case (II)**

From the above graph it is evident that hazard rate rises steeply up to \( t = 14 \) and then becomes constant for all \( t \). This indicates that if a depressive patient continues medicine but still visits state 1 through state 0. The hazard rate of \( h_1(t) \) of case (11) stabilizes at \( t=14 \) with the stabilization value 0.5 (approx). In fig. 6.2 it is observed that the hazard rate \( h_0(t) \) of case (1) stabilizes at \( t=21 \) with the stabilization value 0.05 i.e. \( h_1(t) > h_0(t) \). This happens because in case (II) there are break through relapses and the doctor needs to adjust the dose or change the medicine of the patient. If the patient does not visit the doctor and carry on with the same medicine with the same dose then the frequency of occurrence and duration of depressive episodes increases.

The closed form expression for the renewal process \( \{N_1(t), t \geq 0\} \) corresponding to \( W_1(t) \) cannot be obtained and hence applying the central limit theorem for large \( n \) (i.e., for large \( t \)) we can present the following result.
Result 2:

For the counting variable \( N_1(t) \), whose mean and variance of the corresponding density \( w_0(t) \) are finite, the random variable \( Z_1(t) \) defined as

\[
Z_1(t) = \frac{N_1(t) - \frac{t}{E_1(t)}}{\sqrt{tV_1(t)/E_1(t^3)}}
\]  

where \( t > 0 \) converges to standard normal distribution as \( t \to \infty \)

Proof:

The proof follows from Smith (1958)

The density function corresponding to the renewal process \( \{N_1(t), t \geq 0\} \) is \( w_1(t) \). It has to been shown that \( E_1(t), V_1(t) \) and \( E_1(t^3) \) exists and are finite.

Given, \( t = u + z \) where \( u \) and \( z \) are independent, then the mean and variance of \( w_1(t) \) are

\[
E_1(t) = E(u) + E(z) = \frac{1}{\lambda} + \frac{1}{\mu}
\]  

\[
V_1(t) = V(x) + V(y) = \frac{1}{(\lambda + \mu)^2} + \frac{1}{\mu^2}
\]  

\[
E_1(t^3) = \frac{3!}{(\lambda + \mu)} + \frac{3!}{\mu^3}
\]

These are finite since \( \lambda, \mu > 0 \).
Hence \[ Z_1(t) = \frac{N_1(t) - \frac{t}{\alpha}}{(\lambda + \mu)\mu} \sqrt{t \frac{\beta}{(\lambda + \mu)^2 \mu^2 / (\lambda + \mu)^2 \mu^3}} \]  

\[ \frac{6\gamma}{(\lambda + \mu)^2 \mu^2 / (\lambda + \mu)^2 \mu^3} \]  

where \( \alpha = (\lambda + 2\mu), \beta = (\lambda + \mu)^2 + \mu^2, \gamma = (\lambda + \mu)^3 + \mu^3 \)

\[ Z_1(t) = \frac{\sqrt{6\gamma} \left[ \alpha N_1(t) - t(\lambda + \mu)\mu \right]}{\alpha \sqrt{t(\lambda + \mu)\mu\beta}} \]  

\[ \frac{6\gamma}{(\lambda + \mu)^2 \mu^2 / (\lambda + \mu)^2 \mu^3} \]  

The random variable \( Z_1(t) \) follows standard normal distribution as \( t \to \infty \)

### 6.7 Expected number of renewals of the process \( \{N_1(t), t \geq 0\} \)

Let \( M_1(t) \) be the expected number of depressive episodes corresponding to the process \( \{N_1(t), t \geq 0\} \)

Hence \( M_1(t) = E\{N_1(t)\} \), the corresponding Laplace transform is given by

\[ M_1(s) = \frac{w_1(s)}{s[1 - w_1(s)]}, \]  

where \( w_1(s) = f(s)g(s) = \frac{(\lambda + \mu)\mu}{(\lambda + \mu + s)(\mu + s)} \)  

\[ \frac{(\lambda + \mu)\mu}{s^2(s + \lambda + 2\mu)} \]  

Inverting \( M_1(s) \), \( M_1(t) \) can be obtained as
\[ M_1(t) = \frac{(\lambda + \mu)\mu}{(\lambda + 2\mu)^2} \left[ e^{-(\lambda+2\mu)t} - 1 \right] + \frac{(\lambda + \mu)\mu}{\lambda + 2\mu} t \]  
\[ M_1(t) = \frac{1}{t} \left[ \frac{(\lambda + \mu)\mu}{(\lambda + 2\mu)^2} \left( e^{-(\lambda+2\mu)t} - 1 \right) \right] + \frac{(\lambda + \mu)\mu}{\lambda + 2\mu} \]  
\[ \lim_{t \to \infty} \frac{M_1(t)}{t} = \frac{(\lambda + \mu)\mu}{\lambda + 2\mu} \]  

That is, the expected number of depressive episodes per unit of time as \( t \to \infty \) is \( \frac{(\lambda + \mu)\mu}{\lambda + 2\mu} \) which is equal to depressive episodic rate [inverse of mean of \( w_1(t) \)]. This statement is a proof of renewal theorems (J. Medhi, 2009).

**Fig: 6.6.** \( M_1(t) \): Expected number of depressive episodes for case (II)

From the above graph, it is obvious that the expected number of renewals increases from \( t=7 \) onwards. This indicates renewal process increases linearly and tends to a Poisson process.
6.8 The occurrence rate and recovery rate of depression are taken as same i.e. 
\( \lambda = \mu \) for case (1) then

\[
w(t) = \lambda t e^{-\mu}, \, \lambda > 0, t \geq 0
\]

… (6.45)

follows gamma distribution with parameter 2.

And \( W_0(s) = \frac{\lambda^2}{s(\lambda + s)^2} \) [putting \( \lambda = \mu \) for \( W_0(s) \)] … (6.46)

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

\[
= \frac{\lambda}{s(\lambda + s)} - \frac{\lambda}{(\lambda + s)(\lambda + s)}
\]

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

… (6.47)

The distribution function of \( t \) is

\[
W_0(t) = 1 - e^{-\lambda t} - \lambda t e^{-\lambda t}
\]

\[
= 1 - e^{-\lambda t} (1 + \lambda t)
\]

… (6.48)

The survival probability of \( t \) is

\[
1 - W_0(t) = e^{-\lambda t} (1 + \lambda t)
\]

… (6.49)
The corresponding hazard rate is

\[ h_0(t) = \frac{W_0(t)}{1 - W_0(t)} \]

\[ = \frac{\lambda^2 t e^{-\lambda t}}{e^{-\lambda t} (1 + \lambda t)} \]

\[ \therefore h_0(t) = \frac{\lambda^2 t}{1 + \lambda t} \] \hspace{1cm} \ldots (6.50)

When occurrence and recovery rate are same the hazard rate of depressive episodes for case (I) is depicted in the following graph

**Fig: 6.7 h_0(t): Hazard rate of depressive episodes for case (I) when occurrence and recovery rate are same**

From the above graph it is evident that there is a sharp rise of hazard rate up to \( t = 14 \), and then it gradually goes on increasing at a slow rate and subsequently becomes constant.
\[ M_0(s) = \frac{w_0(s)}{s[1 - w_0(s)]} \]

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

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

\[ = \frac{\lambda^2}{s^2[2\lambda + s]} \]

where, 0 and \(-2\lambda\) are the roots of \(s^2[2\lambda + s]\)

\[ = \frac{\lambda^2}{s} \times \frac{1}{(2\lambda + s)} \times \frac{1}{s} \]

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

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

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

\[ M_0(s) = \frac{\lambda}{2s^2} - \frac{1}{4}\left[\frac{1}{s} - \frac{1}{2\lambda + s}\right] \]

\[ \therefore \quad M_0(s) = \frac{\lambda}{2s^2} - \frac{1}{4}\left[\frac{1}{s} - \frac{1}{2\lambda + s}\right] \quad \ldots (6.51) \]
Inverting $M_0(s)$, $M_0(t)$ can be obtained

\[ M_0(t) = \frac{\lambda t}{2} - \frac{1}{4} + e^{-2\lambda t} \]

\[ \lim_{t \to \infty} \frac{M_0(t)}{t} = \frac{\lambda}{2} \]

When occurrence and recovery rate are same the expected number of depressive episodes for case (I) is depicted in the following graph

**Fig: 6.8.** $M_0(t)$ : Expected number of depressive episodes for case (I) when occurrence and recovery rate are same.

From the above graph it is obvious that the expected number of depressive episodes dropped initially and started increasing from $t=7$ onwards.
6.9 If the occurrence rate and recovery rate of depression are taken as same i.e. 
\( \lambda = \mu \) for case (II) then

\[
W_1(t) = 2\lambda e^{-\lambda t} \left(1 - e^{-\lambda t}\right) \quad \lambda > 0, t \geq 0
\] 

\( \ldots (6.54) \)

The distribution function of \( t \) is

\[
W_1(t) = 1 - 2e^{-\lambda t} + e^{-2\lambda t}
\] 

\( \ldots (6.55) \)

The corresponding survival function is

\[
1 - W_1(t) = 2e^{-\lambda t} - e^{-2\lambda t}
\]

\[= e^{-\lambda t} \left(2 - e^{-\lambda t}\right) \] 

\( \ldots (6.56) \)

The hazard rate of \( W_1(t) \) is

\[
h_1(t) = \frac{2\lambda \left(1 - e^{-\lambda t}\right)}{2 - e^{-\lambda t}}
\] 

\( \ldots (6.57) \)

When occurrence and recovery rate are same the hazard rate of depressive episodes for case (II) is depicted in the following graph.
Fig: 6.9 $h_1(t)$: Hazard rate of depressive episodes for case (II) when occurrence and recovery rate are same

From the above graph it is obvious that hazard rate rises steeply up to $t = 14$ and then become constant. This indicates that a depressive patient even after continuing medicine may have relapse.

$$M_1(s) = \frac{2\lambda^2}{s^2(s + 3\lambda)}$$  \hspace{1cm} \ldots (6.58)$$

$$= \frac{2\lambda}{3} \left[ \frac{1}{s} - \frac{1}{s + 3\lambda} \right] \frac{1}{s}$$

$$= \frac{2\lambda}{3} \left[ \frac{1}{s^2} - \frac{1}{s + 3\lambda} \times \frac{1}{s} \right]$$
When occurrence and recovery rate are same the expected number of depressive episodes for case (II) is depicted in the following graph

Fig: 6.10 $M_1(t)$: Expected number of depressive episodes for case (II) when occurrence and recovery rate are same.

From the above graph it is evident that the expected number of depressive episodes dropped initially and started increasing from $t = 7$ onwards.
6.10 Comparison of Hazard Rates and Expected Number of Renewals for Case (1) and case (11)

The hazard rates for case (1) and case (11) when $\lambda = 0.25, \mu = 0.048$ and $\lambda = \mu = 0.25$ are depicted in the same graph which is presented below to compare the hazard rates and have a clear idea at a glance.

**Fig: 6.11 Comparison of Hazard Rates for Case (1) and case (11)**

It is observed that there is a huge difference in hazard rates for case (1) and case (11) when $\lambda = 0.25$ and $\mu = 0.048$. Hazard rate for case (11) is much higher than hazard rate for case (1). That is the occurrence rate of depressive episodes in case (11) i.e. when a patient have break through relapses is much higher than in case (1). But when $\lambda = \mu = 0.25$ the hazard rate or rate of occurrence of depressive episodes for case (1) is less than case (11) in the initial stage and then it becomes more or less same with very minimal difference.

For demonstration purpose to compare expected number of renewals for case (1) and case (11) when $\lambda = \mu = 0.25$ are considered and plotted graphically.
Fig: 6.12 Expected number of renewals for case (I) and case (II)

![Expected number of renewals graph](image)

This shows that the expected number of visits to the doctor in case (II) is more than in case (I).

6.11 Discussion:

In almost all cases under consideration the pattern of $h(t)$ and $M(t)$ from the graph and the data reveals that

i) $h(t)$ i.e. the hazard rate initially increases as a function of time $t$ and after certain point of time becomes constant which clearly indicates that the distribution corresponding to $h(t)$ follows exponential distribution.

ii) $M(t)$ i.e. the expected number of renewals linearly increases as a function of time $t$ which is a clear indication of renewal process tending to Poisson process.

6.12 Some special cases:

1) Both occurrence and recovery time following uniform distribution.
Here $X_i$ and $Y_i$ are independent such as
Chapter 6: Occurrence and recovery of episodes

\[ X \sim f(x) = \frac{1}{\lambda}, \quad 0 < x < \lambda \quad \ldots (6.61) \]

\[ Y \sim g(y) = \frac{1}{\mu}, \quad 0 < y < \mu \quad \ldots (6.62) \]

The Laplace transform of \( f(x) \) and \( g(y) \) are

\[ f(s) = \frac{(1 - e^{-\lambda s})}{\lambda s} \text{ and} \quad \ldots (6.63) \]

\[ g(s) = \frac{(1 - e^{-\mu s})}{\mu s} \quad \ldots (6.64) \]

\( \{ T_i = X_i + Y_i \} \), generates a renewal process with \( w_0(t) = f(t) \otimes g(t) \) and finite mean \( \left( \frac{\mu + \lambda}{2} \right) \).

The corresponding Laplace transform is given by

\[ w(s) = f(s)g(s) \]

\[ = \frac{(1 - e^{-\lambda s})(1 - e^{-\mu s})}{\lambda \mu s^2} \]

\[ = 1 - e^{-\lambda s} - e^{-\mu s} + e^{-(\lambda + \mu)s} \]

\[ \therefore w(s) = \frac{1 - e^{-\lambda s} - e^{-\mu s} + e^{-(\lambda + \mu)s}}{\lambda \mu s^2} \quad \ldots (6.65) \]

The inversion of \( W(s) \) does not give \( W(t) \) in closed form. Hence the probabilistic structure of \( W(t) \) cannot be obtained in closed form. However the renewal rate generated
by \( w(t) \) is given by \( \left( \frac{\mu + \lambda}{2} \right)^{-1} \), which is also equal to \( \lim_{t \to \infty} \frac{M(t)}{t} \) [renewal theorem J.Medhi, 2009].

2) **Both occurrence and recovery time following Rayleigh’s distribution.**

Here \( X_i \) and \( Y_i \) are independent such as

\[
X \sim f(x) = \lambda x e^{-\lambda x^2/2}, \quad x \geq 0, \lambda > 0 \quad \ldots \ (6.66)
\]

\[
Y \sim g(y) = \mu y e^{-\mu y^2/2}, \quad y \geq 0, \mu > 0 \quad \ldots \ (6.67)
\]

The Laplace transform of \( f(x) \) and \( g(y) \) are

\[
f(s) = \left[ 1 - \left( \frac{s}{(s^2 + 2\lambda)^{1/2}} \right) \right] \quad \ldots \ (6.68)
\]

\[
g(s) = \left[ 1 - \left( \frac{s}{(s^2 + 2\mu)^{1/2}} \right) \right] \quad \ldots \ (6.69)
\]

\[
w(s) = f(s)g(s) = \left[ 1 - \left( \frac{s}{(s^2 + 2\lambda)^{1/2}} \right) \right] \left[ 1 - \left( \frac{s}{(s^2 + 2\mu)^{1/2}} \right) \right]
\]

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

Now,

\[ 1 - \frac{s^2}{(s^2 + 2\lambda)(s^2 + 2\mu)^{1/2}} \]

\[ = 1 - \left[ \frac{s^4}{(s^2 + 2\lambda)(s^2 + 2\mu)} \right]^{1/2} \]

\[ = 1 - \left[ \frac{s^4}{s^4 + 2(\lambda + \mu)s^2 + 4\lambda\mu} \right]^{1/2} \]

Putting \( \alpha = 2(\lambda + \mu) \) and \( \beta = 4\lambda\mu \) we get

\[ = 1 - \left[ \frac{s^4}{s^4 + \alpha s^2 + \beta} \right]^{1/2} \]

By actual division of \( \frac{s^4}{s^4 + \alpha s^2 + \beta} \) we get an infinite series given by

\[ 1 + A_1 s^{-2} + A_2 s^{-4} + \cdots + A_k s^{-2k} + \cdots \]

where \( A_1, A_2, \cdots A_k \) are functions of \( \lambda \) and \( \mu \).

Hence, \( w(s) = f(s) + g(s) - 1 + \left[ \frac{s^4}{s^4 + \alpha s^2 + \beta} \right]^{1/2} \]

\[ = f(s) + g(s) - 1 + (1 + A_1 s^{-2} + A_2 s^{-4} + \cdots + A_k s^{-2k} + \cdots)^{1/2} \]
\[ f(s) + g(s) - 1 + \frac{1}{2} \left( A_1 s^{-2} + A_2 s^{-4} + \cdots + A_k s^{-2k} + \cdots \right)^{1/2} \quad \ldots (6.70) \]

\[ \therefore w(t) = f(t) + g(t) + \frac{1}{2} \sum_{i=1}^{\infty} A_i L^{-1}(s^{-2i}) \]

\[ = f(t) + g(t) + \frac{1}{2} \sum_{i=1}^{\infty} A_i \frac{t^{2i-1}}{(2i-1)!} \quad \ldots (6.71) \]

Since this distribution has a complicated form, so it is not possible to find out the actual expression for \( M_0(t) \). However by applying renewal theorems we conclude that renewal rate and expected number of renewal per unit of time as \( t \to \infty \) goes to 
\[ [E(X) + E(Y)]^{-1} \]

Till now two independent random variables \( X \) and \( Y \) are considered. Here \( X \) is representing the occurrence time of a depressive episode and \( Y \) indicating the recovery time. But in real life situation \( X \) and \( Y \) may not be independent. In fact recovery time is dependent on the type of depression and the cause precipitation it. This may vary from patient to patient.

In the next chapter the assumption of independence of random variables are not taken into consideration and the characteristics of renewal process are worked up on a dependent setup. Besides this the cases of depressive episodes that occur for different causes will be considered.