CHAPTER - 4

Behaviour of symptoms during the course of treatment: A stochastic analysis
4.1 Introduction

In chapter 2 it has been mentioned that schizophrenia is characterized by various symptoms like presence of delusions and hallucinations, depression, sleepllessness, irritability, suspiciousness, irrelevant speech, sudden spells of laughing and crying, over religiousness, etc. These symptoms in isolation are however not unique to schizophrenia. A cluster of symptoms with definite weightage lead to a diagnosis of schizophrenia (Kaplan and Sadock, 1999, Gelder et al., 1996). Also, from the complete set of symptoms that can be manifested in case of schizophrenia, a particular patient will have only a few of the symptoms. The number and type of symptoms required for diagnosis of schizophrenia has already been elaborated upon. After diagnosis, a patient is given treatment according to the severity of his ailment, duration of psychotic episode and other relevant factors. That aspect regarding the type of treatment is not the concern of this research. But, the manner in which the symptoms in a patient respond to or are likely to respond to the administered treatment is being taken up for study in this chapter.

It is to be noted that schizophrenia cannot be cured completely (Gelder et al., 1996). It remains under control only if medicines are taken regularly. On subsequent visits to the doctor, it is expected that the number of symptoms i.e.,
the severity of the disease will go on decreasing till ultimately all the symptoms will be kept under control. This state is the state of complete response or complete remission. This state will continue only on regular intake of medicines and regular follow-up with the doctor, otherwise there is a possibility of relapse of the illness. This fact has been verified by studying the data sheets of 797 schizophrenics collected from the Department of Psychiatry, Gauhati Medical College Hospital (GMCH), Assam. A patient’s condition and behaviour at a particular time can be studied for recovery only by a psychiatrist. It is also necessary that doses of administered medicines be regulated from time to time. Hence regularity is a very important requirement in the treatment of schizophrenia (Tasman, 2003, Gelder et al., 1996). This aspect will be dealt with in greater detail in Chapter 5.

When a schizophrenic patient revisits a doctor in the course of treatment, his treatment process starts afresh with consideration to the number of symptoms remaining or, his response to previous medication. The data sheet that is maintained in the particular patient’s name gets renewed at every revisit the patient makes to the doctor. In this sense, every revisit that the patient makes to the doctor after initial diagnosis, i.e., after registration of the patient as a schizophrenic, can be termed as a renewal of the treatment process. There are numerous instances where the data cards are not renewed at all as quite a large number of patients do not come for follow ups after initial diagnosis. The treatment received at the first visit arrests the illness for some time and the
patients do not understand the need to follow up with the treatment process as they consider themselves cured. But these patients suffer a relapse of their symptoms due to discontinuation of medication and have to report to the doctor again in due course of time.

However, in this chapter, only the cases of patients who follow up the treatment process with a doctor on a regular basis are taken into consideration and an attempt is being made to study, by developing suitable stochastic models, the manner in which the manifested symptoms gradually respond to medication and enable the patient to function normally. In other words, an attempt is being made to study the behaviour of the symptoms of schizophrenia in relation to the successive visits to the doctor which are termed as renewals. The results of the theoretical work undertaken are then compared with the real life situation, as observed from the facts obtained by studying the data sheets of the patients undergoing treatment at GMCH and those patients considered under the previously mentioned three month follow-up study, in Chapter 7.

4.2 Model

Let N denote the total number of symptoms that can be manifested in case of schizophrenia. Of this total of N, let there be $n_1$ Type A symptoms, $n_2$ Type B symptoms and $n_3$ Type C symptoms where $n_3 = N - n_1 - n_2$. 
At the time of a psychotic episode when a patient is brought to the doctor for diagnosis of ailment, the patient will not show all the N symptoms even in the case of acute or chronic schizophrenia. As mentioned in Chapter 3, the diagnosis is possible even with one symptom of Type A. Let us suppose that a patient shows the presence of k symptoms at the time of diagnosis. Also, let n necessary and sufficient to give a diagnosis of schizophrenia. It is to be noted that these n symptoms must not all come from Type C. The presence of at least one Type A symptom or at least two Type B symptoms in absence of a Type A symptom is mandatory. Though n could take a value as small as unity, it would be necessary to take $n > n_3 + 1$ for a general study as a smaller value of n might include all of Type C symptoms and none from the other two categories.

Hence, for admissibility reasons, let us assume that $n \geq n_3 + 1$

It has been mentioned that at the initial stage any one of the N symptoms have equal chance of being present in a patient. Under these considerations, let us define

$$Y_j = 1, \text{ if the } j^{th} \text{ symptom is present}$$
$$= 0, \text{ otherwise}$$

$$j = 1, 2, 3, \ldots, N$$

(4.1)

$Y_j$'s are i.i.d with $P(Y_j = 1) = w, \quad 0 < w < 1$

and $P(Y_j = 0) = 1 - w = u$ 

(4.2)
4.2.1 General structure function

Let $\phi(y)$ be the general structure function of schizophrenia where

$$\phi(y) = 1, \text{ if } \sum_{j=1}^{N} Y_j \geq n$$

$$= 0, \text{ if } \sum_{j=1}^{N} Y_j < n \quad \text{..................(4.3)}$$

Now, $\Pr[\phi(y) = 1] = \sum_{i=n}^{N} \binom{N}{i} w^i (1-w)^{N-i}$

$$\text{..................(4.4)}$$

which is the probability that a person is in the state of schizophrenia.

4.2.2 Behaviour of the symptoms in the course of treatment

Let us keep a record as follows.

$S_0 = \text{No. of symptoms present at the time of diagnosis i.e, at the initial visit.}$

$$\therefore S_0 = \sum_{j=1}^{N} Y_j, \quad S_0 = n, n + 1, \ldots, N \quad \text{..................(4.5)}$$

$S_0$ is the sum of independent Bernoulli variates and can take values from $n$ to $N$.

Therefore the distribution of $S_0$ will be truncated Binomial.

$$P(S_0) = \frac{\binom{N}{S_0} w^{S_0} (1-w)^{N-S_0}}{\sum_{S_0}^{n-1} \binom{N}{S_0} w^{S_0} (1-w)^{N-S_0}}$$

$$= \frac{\binom{N}{S_0} w^{S_0} (1-w)^{N-S_0}}{B_0} \quad \text{..................(4.6)}$$

where $B_0$ is available from Binomial tables with known $N$, $n$ and $w$
Medical fact: On administration of medicines, the no. of symptoms gradually goes on diminishing. Normally, if a symptom is cured once, it will not recur during the course of treatment. Also, a new symptom, not seen at the time of diagnosis, will not appear at subsequent visits during treatment. Hence, as the symptoms are brought under control in the subsequent visits to the doctor, it is expected that at a certain visit, all the symptoms will disappear and the patient will then be said to show complete response to medication and be in the state of complete remission. If however, a state is reached when the patient has symptoms less than n and all symptoms are of Type C, then he would be said to be in the state of partial remission. This is a state when the patient is functionally normal but still has certain symptoms. (Freedman et al., 2002)

Note: There are some uncommon situations where a patient is considered to be in partial remission inspite of his still having Type A or Type B symptoms of much lesser intensity with which he can function more or less normally. However, due to its rarity, that aspect is not taken into consideration in this study.

Let \( S_1 \) = no. of symptoms remaining of the \( S_0 \) symptoms at the 1\textsuperscript{st} renewal.

\[
S_1 = \sum_{j=0}^{S_0} Y_j, \quad S_1 = 0, 1, 2, \ldots, S_0 \quad \text{..........................(4.7)}
\]

Similarly \( S_2 \) = no. of symptoms remaining at the 2\textsuperscript{nd} renewal.

\[
S_2 = \sum_{j=0}^{S_1} Y_j, \quad S_2 = 0, 1, 2, \ldots, S_1 \quad \text{..........................(4.8)}
\]
Hence \( S_i = \sum_{j=0}^{S_{i-1}} Y_j \), \( S_i = 0, 1, 2, \ldots, S_{r-1} \) ..........................(4.9)

If we consider \( r \) visits, we shall have

\( S_r = \) no. of symptoms remaining at the \( r^{th} \) renewal where

\[ N \geq S_0 \geq S_1 \geq S_2 \geq \ldots \ldots \geq S_{r-1} \geq S_r \geq 0 \]

It is desirable that \( S_r = 0 \)

Now, \( S_0 \) is a random variable. It is necessary to know \( S_0 \) as the no. of symptoms in the 1\(^{st}\) visit would come from these \( S_0 \) symptoms.

\[ \therefore \text{We find the expected no. of symptoms in the initial visit, i.e., } E(S_0). \text{ Now,} \]

\[ E(S_0) = \frac{\sum_{S_0=n}^{N} S_0 \cdot C_{S_0} \cdot w^{S_0} \cdot (1-w)^{N-S_0}}{B_0} \]

\[ = \frac{1}{B_0} \sum_{S_0=n}^{N} \frac{N(N-1)!}{S_0(S_0-1)!(N-S_0)!} w^{S_0-1}(1-w)^{N-S_0} \]

\[ = \frac{Nw}{B_0} \sum_{S_0=n}^{N-1} C_{S_0-1} w^{S_0-1}(1-w)^{N-S_0} \]

\[ = \frac{NwB_0'}{B_0} = Nwk \text{ (say) } = N_0 \text{ (say)} \] ..........................(4.10)

where \( k = \frac{B_0'(N,n,w)}{B_0(N,n,w)} \) and \( B_0' \) and \( B_0 \) are available

from Binomial tables with known \( N, n \) and \( w \)

Now, \( S_1 \) is the sum of Bernoulli variates and \( 0 < S_1 < S_0 \)

\( S_0 \) being random, it is substituted by \( E(S_0) = N_0 \). Thus, \( 0 < S_1 < N_0 \)
\[ S_i \sim B (N_0, w_1) \quad \text{where } w_1 \text{ is the probability of occurrence of a symptom in the 1st renewal} \]

Similarly, \[ S_2 \sim B (N_1, w_2) \quad \text{where } N_1 = E(S_1), \quad 0 < S_2 < N_1 \]
and \( w_2 \) is the probability of occurrence of a symptom in the 2nd renewal.

Hence, \[ S_r \sim B (N_{r-1}, w_r) \quad \text{where } N_{r-1} = E(S_{r-1}), \quad 0 < S_r < N_{r-1} \]
and \( w_r \) is the probability of occurrence of a symptom in the \( r \)th renewal.

In general,
\[ S_i \sim B (N_{i-1}, w_i), \quad i = 1, 2, 3, \ldots \quad \text{..................(4.11)} \]
where \( N_{i-1} = E(S_{i-1}), \quad 0 < S_i < N_{i-1} \)
and \( w_i \) is the probability of occurrence of a symptom in the \( i \)th renewal.

It is assumed that the probability of occurrence remains same for all symptoms at every visit though the probability of occurrence of a symptom varies, in general, in the different visits. It is expected that the probability of occurrence of a symptom gradually reduces in subsequent visits in the course of treatment i.e.,
\[ w_1 \geq w_2 \geq w_3 \geq \ldots \geq w_r \]
4.3 Result: Expected number of symptoms at the $r^{th}$ visit to the doctor

If $S_0$ be the number of symptoms present in a schizophrenic patient at the time of initial diagnosis, then the expected number of symptoms remaining at the $r^{th}$ visit to the doctor is given by

$$E(S_r) = N_0 \prod_{i=1}^{r} w_i = N_0 W$$

where $W = \prod_{i=1}^{r} w_i$, ......(4.12)

where $N_0 = E(S_0) = N k w$

where $N$ = Total number of possible symptoms

$w$ = Probability of presence of a symptom at the initial visit

$w_i$ = Probability of presence of a symptom at the $i^{th}$ visit

and $k = B'_0(N,n,w) / B_0(N,n,w)$

with $B'_0(N,n,w) = \sum_{S_0=n}^{N} C_{N}^{S_0} w^{S_0} (1-w)^{N-S_0}$

and $B_0(N,n,w) = \sum_{S_0=0}^{N} C_{N}^{S_0} w^{S_0} (1-w)^{N-S_0}$

Proof:

Given $E(S_0) = N_0 = N kw$ where k is available from binomial tables

Now, $P(S_r) = \sum_{S_0=S_r}^{N} C_{N}^{S_0} w^{S_0} (1-w)^{N-S_0}$, $S_r=0,1,2,.....,N_0$

$\therefore E(S_r) = N_0 w_r$, $r = 1,2,3,...$
Thus,

\[ E(S_1) = N_1 = N_0 w_1 = (Nkw) w_1 = Nkw w_1 = N_0 w_1 \]

\[ E(S_2) = N_2 = N_1 w_2 = (Nkw w_1) w_2 = Nkw w_1 w_2 = N_0 w_1 w_2 \]

\[ E(S_3) = N_3 = N_2 w_3 = (Nkw w_1 w_2) w_3 = Nkw w_1 w_2 w_3 = N_0 \prod_{i=1}^{3} w_i \]

....................

\[ E(S_r) = N_r = N_{r-1} w_r = (Nkw_1 w_2 \ldots w_r) = Nkw \prod_{i=1}^{r-1} w_i = N_0 \prod_{i=1}^{r} w_i \]

\[ = E(S_0) \prod_{i=1}^{r} w_i = N_0 w^r \]

Thus, if the expected number of symptoms at the initial visit is known, the doctor can estimate the expected number of symptoms likely to be present at the \(r\)th visit, \(r = 1, 2, 3, \ldots\), provided \(w_i\)'s are known. A doctor can thus ascertain the approximate number of visits that will be required to take the patient to the state of remission.

4.4 Markov model studying the number of symptoms present on subsequent visits after initial diagnosis

As mentioned earlier, it is a medically accepted fact that the number of symptoms present initially in a schizophrenic patient gradually diminishes during the subsequent visits to the doctor in the course of treatment. (This has been established in Chapter 7). Hence, the number of symptoms at a particular visit depends on the symptoms appearing at the immediately previous visit. We can
therefore suspect the presence of a Markov chain with respect to the number of symptoms present in a visit.

Let \( S_r = i, \quad i = 0,1,2,\ldots,N \) be the total number of symptoms present in a patient in the \( r^{th} \) visit to the doctor, \( r = 1, 2, 3, \ldots \).

\( \therefore \{ S_r, r \geq 1 \} \) is a Markov chain with state space \( \mathcal{S} = \{N, N-1, N-2, \ldots, 2,1\} \)

and transition probability matrix \( P \) given by

\[
P = (p_{ij}), \quad i, j = N, N-1, \ldots, 0; \quad p_{ij} = 0 \quad \forall \ i < j \quad \text{and} \quad p_{00} = 1 \quad \ldots\ldots\ldots(4.13)
\]

In our case, \( P = \)

\[
\begin{bmatrix}
{^NnC} \cdot \, w^n & {^NnC} \cdot \, w^{n-1}u & \cdots & {^NnC} \cdot \, w^{n-N-n}u & {^NnC} \cdot \, w^{n-N-1}u^{N-n+1} & \cdots & u^N \\
0 & {^NnC} \cdot \, w^{n-1}u & \cdots & {^NnC} \cdot \, w^{n-N-n}u & {^NnC} \cdot \, w^{n-N-1}u^{N-n+1} & \cdots & u^N \\
0 & 0 & \cdots & {^NnC} \cdot \, w^{n-2}u & {^NnC} \cdot \, w^{n-N-n}u & \cdots & u^N \\
0 & 0 & \cdots & 0 & \cdots & \cdots & \cdots \\
0 & 0 & \cdots & \cdots & \cdots & \cdots & \cdots \\
0 & 0 & \cdots & \cdots & \cdots & \cdots & \cdots \\
0 & 0 & \cdots & \cdots & \cdots & \cdots & 1
\end{bmatrix}
\]

\ldots\ldots\ldots(4.14)

Now, for a diagnosis of schizophrenia, a person has to have a minimum of \( n \) symptoms out of a total of \( N \) symptoms. It is desirable that all the symptoms disappear in the course of treatment. This state is called the state of complete remission. If however, a state is reached when the patient is cured of all Type A and Type B symptoms and is left with only the Type C symptoms, then he would be said to be in the state of partial remission. This is a state when the patient is
functionally normal but still has certain symptoms. Nevertheless, he is still a schizophrenic, as a patient once diagnosed as a schizophrenic will remain to be so, but can be in states of complete or partial remission. However, from the medical point of view, it is desirable to take a patient to the state of partial remission, if not complete remission, as he will then be able to function normally. To study this aspect we consider the following model.

4.4.1 Markov model studying the different types of schizophrenia

Let us consider the situations of a patient having symptoms of category A, B, AB, AC, BC, ABC, C and O as the different states to which a schizophrenic patient can belong. Here, C refers to the state when the patient has only Type C symptoms and thus can be said to be in partial remission whereas O refers to the state when there are no symptoms observable and hence can be considered as complete remission. The states C and O together form the state of remission. Let us name the states from 1 to 8 for convenience i.e.,

Patient with symptoms of Type A = state 1
Patient with symptoms of Type B = state 2
Patient with symptoms of Type AB = state 3
Patient with symptoms of Type AC = state 4
Patient with symptoms of Type BC = state 5
Patient with symptoms of Type ABC = state 6
Patient with symptoms of Type C = state 7
Patient with no symptoms, i.e., of Type O = state 8  ..........(4.15)
In other words, the states from 1 to 6 constitute the states of active schizophrenia whereas states 7 and 8 constitute the states of remission. The endeavour of any treatment process is to take a patient to state 8 or at least to state 7.

Let, \( X_n = i \) \( \forall i = 1, 2, \ldots, 8 \), represent the states of a schizophrenic patient at the time of the \( n^{th} \) observation, \( n = 0, 1, 2, \ldots \).

Now \( \{X_n, n = 0, 1, 2, \ldots\} \) is supposed to follow a Markov chain with state space \( S = \{1, 2, \ldots, 8\} \) and t. p. m. \( \mathbf{P}_1 = (p_{ij}), (i, j = 1, 2, \ldots, 8) \) \((4.16)\) since the medical facts assures that transition from one state to another is in accordance with Markovian property (established in Chapter 7).

Thus \( \mathbf{P}_1 \) will take the following form

\[
\mathbf{P}_1 = \begin{bmatrix}
A & B & AB & AC & BC & ABC & C & O \\
A & p_{11} & p_{12} & p_{13} & p_{14} & p_{15} & p_{16} & p_{17} & p_{18} \\
B & p_{21} & p_{22} & p_{23} & p_{24} & p_{25} & p_{26} & p_{27} & p_{28} \\
AB & p_{31} & p_{32} & p_{33} & p_{34} & p_{35} & p_{36} & p_{37} & p_{38} \\
AC & p_{41} & p_{42} & p_{43} & p_{44} & p_{45} & p_{46} & p_{47} & p_{48} \\
BC & p_{51} & p_{52} & p_{53} & p_{54} & p_{55} & p_{56} & p_{57} & p_{58} \\
ABC & p_{61} & p_{62} & p_{63} & p_{64} & p_{65} & p_{66} & p_{67} & p_{68} \\
C & p_{71} & p_{72} & p_{73} & p_{74} & p_{75} & p_{76} & p_{77} & p_{78} \\
O & p_{81} & p_{82} & p_{83} & p_{84} & p_{85} & p_{86} & p_{87} & p_{88}
\end{bmatrix}
\] \((4.17)\)
It has been mentioned that on administration of medicines, the number of symptoms gradually goes on diminishing. Normally, if a symptom is cured once, it will not recur during the course of treatment. Also, a new symptom, not seen at the time of diagnosis, will not appear at subsequent visits during treatment. Thus, if a patient does not show the presence of 'aggression' (say) at the time of diagnosis, he will not develop the symptom later during the course of treatment, provided he is regular in the treatment process. In our case therefore, a patient with Type A symptoms (state 1) can remain in state 1 or go to state 8 only whereas, a patient with symptoms of Type AB (state 3) can remain in state 3 or go to state 1 with only symptoms of Type A remaining or go to state 2 in which the Type A symptoms have been cured but Type B symptoms remain or go to state 8 in which all symptoms have been cured. Similar situations can be observed for the other states.

The various transitions that are possible from each state are separately shown in a diagrammatic representation in the following page. The different states from 1 to 8 are labeled as A, B, AB, AC, BC, ABC, C and O respectively for convenience of understanding. This diagrammatic representation is followed by a transition graph of the corresponding Markov chain.
Fig 4.1 Diagrammatic representation of possible transitions from the different states of schizophrenia.
Fig 4.2: Transition graph of the Markov Chain related to Schizophrenia
Hence, the above transition matrix $P_1$ will take the following form.

$$
P_1 = \begin{bmatrix}
A & B & AB & AC & BC & ABC & C & O \\
A & p_{11} & 0 & 0 & 0 & 0 & 0 & p_{18} \\
B & 0 & p_{22} & 0 & 0 & 0 & 0 & p_{28} \\
AB & p_{31} & p_{32} & p_{33} & 0 & 0 & 0 & p_{38} \\
AC & p_{41} & 0 & 0 & p_{44} & 0 & 0 & p_{47} & p_{48} \\
BC & 0 & p_{52} & 0 & 0 & p_{55} & 0 & p_{57} & p_{58} \\
ABC & p_{61} & p_{62} & p_{63} & p_{64} & p_{65} & p_{66} & p_{67} & p_{68} \\
C & 0 & 0 & 0 & 0 & 0 & 0 & p_{77} & p_{78} \\
O & 0 & 0 & 0 & 0 & 0 & 0 & 0 & p_{88}
\end{bmatrix}
$$

\[\text{..........(4.18)}\]

As mentioned earlier, states 1, 2, \ldots, 6 constitute the states of active schizophrenia while states 7 and 8 constitute the states of schizophrenia in partial and complete remission. Also, it is desirable to take a patient to the states of remission so that the patient can function normally even in the presence of certain symptoms.

To study this aspect, let us partition the transition matrix $P_1$ in the following way
In the context of our formulation of the structure of symptoms of schizophrenia, a patient in state 1 i.e., possessing symptoms of Type A alone can either remain in state 1 or go to state 8. The probability of remaining in state 1 is equivalent to the probability of the presence of symptoms of Type A and is given by $\psi(A)$. Consequently, the probability of going to state 8, i.e., the state of complete remission is $1 - \psi(A)$ as the row totals have to add up to unity.

Again, a patient in state 2 can either remain in state 2 with probability $\psi(B)$ or go to state 8 with probability $1 - \psi(B)$.
From state 3, i.e., the presence of both Types A and B, transition is possible to states 1, 2, and 8 or a patient can remain in state 3. When a patient goes from state 3 to state 1 (with symptoms of Type A alone), then it signifies the occurrence of Type A symptoms along with the non-occurrence of Type B symptoms. This probability is given by \( \psi(A) (\psi'(B))^c \) where \((\psi'(B))^c\) represents the complementary probability of \( \psi'(B) \). Again, transition from state 3 to state 2 signifies presence of Type B symptoms and non-occurrence of Type A symptoms, the probability of which is given by \((\psi(A))^c \psi'(B)\). The probability of remaining in state 3 is given by \( \psi(A) \psi'(B) \) and that of going to state 8 is therefore \(1 - \psi(A) (\psi'(B))^c - (\psi(A))^c \psi'(B) - \psi(A) \psi'(B)\).

It is to be noted that in states 3 and 6 where Types A and B and Types A, B and C occur together, the probability of occurrence of Type B symptoms is given by \( \psi'(B) \) as in such cases the presence of at least one Type B symptom is sufficient while in states 2 and 5, at least two Type B symptoms need to be present for the presence of schizophrenia and hence, the probability of occurrence of Type B symptoms in these two situations is given by \( \psi(B) \).

Again, transition from state 4 is possible to states 1, 7 and 8 apart from remaining in state 4. From state 5, a patient can go to states 2, 7 and 8 or remain in state 5 and from state 6 (presence of symptoms of Types A, B and C), transition is possible to all the states 1, 3, 4, 5, 7 and 8 apart from remaining in state 6. Similar explanation as that given for state 3 holds good for all the
transition probabilities from the states 4, 5, 6 and 7. State 8 is the absorbing state.

The possible transitions from state i, (i = 1, 2, 3, ..., 7) can be summarized mathematically as follows:

\[ i \rightarrow i + j \quad \text{where } j = 0, 7 \quad \text{for } i = 1 \]

\[ j = 0, 6 \quad \text{for } i = 2 \]

\[ j = 0, -2, -1, 5 \quad \text{for } i = 3 \]

\[ j = 0, -3, 3, 4 \quad \text{for } i = 4 \]

\[ j = 0, -3, 2, 3 \quad \text{for } i = 5 \]

\[ j = 0, -5, -4, -3, -2, -1, 1, 2 \quad \text{for } i = 6 \]

\[ j = 0, 1 \quad \text{for } i = 7 \]

\[ \text{..................................(4.20)} \]

Hence, \( P_1 \) takes the following form
where
\[
\begin{align*}
a &= \psi(A), & (a)^c &= (\psi(A))^c \\
b &= \psi(B), & (b)^c &= (\psi(B))^c \\
b' &= \psi'(B), & (b')^c &= (\psi'(B))^c \\
c &= \psi(C), & (c)^c &= (\psi(C))^c
\end{align*}
\]

\[
\begin{array}{|c|c|c|c|c|c|c|c|c|}
\hline
A & B & AB & AC & BC & ABC & C & O \\
\hline
a & 0 & 0 & 0 & 0 & 0 & 0 & 1-a \\
b & 0 & b & 0 & 0 & 0 & 0 & 1-b \\
a (b')^c & (a)^c & b' & a b' & 0 & 0 & 0 & 1-a (b')^c - (a)^c b' - a b' \\
(a)^c & 0 & 0 & a c & 0 & 0 & (a)^c c & 1-a (a)^c - a c - (a)^c c \\
0 & b (c)^c & 0 & 0 & 0 & 0 & (b)^c c & 1-b (c)^c - b c - (b)^c c \\
a (b)^c (c)^c & (a)^c b'(c)^c & a b'(c)^c & (a) b'^c & (a)^c b'c & 0 & (a)^c (b')^c \text{c}_1 & 1-a (b)^c (c)^c - (a)^c b'(c)^c - a b'(c)^c - (a)^c (b')^c c_1 \text{c}_1 \\
\hline
\end{array}
\]
Alternatively,

\[ \begin{bmatrix} S & R \\ O & N_s \end{bmatrix} \]

where

- \( S \) = confirmed schizophrenia
- \( R \) = schizophrenia in state of remission
- \( N_s \) = non-schizophrenic but mentally ill

### 4.4.2 Probabilities of Partial remission

Our interest lies in finding the probability of going from \( S \) to \( R \) i.e., taking a patient from the state of active schizophrenia to the state of schizophrenia in remission. From (4.17) and (4.19), we have,

- Remission probability from state 1 = \( p_{17} + p_{18} = f_1(w) \)
- Remission probability from state 2 = \( p_{27} + p_{28} = f_2(w) \)
- Remission probability from state 3 = \( p_{37} + p_{38} = f_3(w) \)
- Remission probability from state 4 = \( p_{47} + p_{48} = f_4(w) \)
- Remission probability from state 5 = \( p_{57} + p_{58} = f_5(w) \)
- Remission probability from state 6 = \( p_{67} + p_{68} = f_6(w) \)
In general, 

Remission probability from state $i = p_{i7} + p_{i8} = f_i(w), \quad i = 1, 2, 3, ..., 6$

And, $Pr[\text{going from } S \text{ to } R] = \sum_{i=1}^{6} (p_{i7} + p_{i8}) \quad \ldots \ldots \ldots \ldots (4.24)$

This is the probability of going from the state of complete schizophrenia to the state of remission.

In terms of the probabilities defined in section 3.5 of Chapter 3, we have

\[ f_1(w) = p_{17} + p_{18} = 0 + (1-a) = 0 + 1 - \psi(A) = 1 - [1 - (1-w)^4] = (1-w)^4 \]

\[ \ldots \ldots \ldots \ldots (4.25) \]

\[ f_2(w) = p_{17} + p_{28} = 0 + (1-b) = 0 + 1 - \psi(B) = 1 - [1 - (1-w^2)^6] = (1-w^2)^6 \]

\[ \ldots \ldots \ldots \ldots (4.26) \]

\[ f_3(w) = p_{37} + p_{38} = 0 + 1 - a (b')^c - (a)^c b' - a b' \]

\[ = 0 + 1 - \psi(A) (\psi'(B))^c - (\psi(A))^c \psi'(B) - \psi(A) \psi'(B) \]

\[ = 1 - 2(1 - (1-w)^4)(1-w)^4 - \{1 - (1-w)^4\}^2 \]

\[ = 1 - 2(1-w)^4 + 2(1-w)^8 - 1 + 2(1-w)^4 - (1-w)^8 \]

\[ = (1-w)^8 \quad \ldots \ldots \ldots \ldots (4.27) \]

\[ f_4(w) = p_{47} + p_{48} = (a)^c c + 1 - a (c)^c - a c - (a)^c c \]

\[ = 1 - \psi(A) (\psi(C))^c - \psi(A) \psi(C) \]

\[ = 1 - \{1 - (1-w)^4\}(1-w)^6 - \{1 - (1-w)^4\}\{1 - (1-w)^6\} \]

\[ = 1 - (1-w)^6 + (1-w)^{10} - \{1 - (1-w)^4 \} - (1-w)^6 + (1-w)^{10} \}

\[ = (1-w)^4 = f_1(w) \quad \ldots \ldots \ldots \ldots (4.28) \]
\[ f_5(w) = p_{57} + p_{58} = (b)c + 1 - b (c)c - b c - (b)c c \]
\[ = 1 - \psi(B)(\psi(C))^3 - \psi(B) \psi(C) \]
\[ = 1 - \{1 - (1-w^2)^6\}(1-w)^6 - \{1 - (1-w)^6\}(1-w)^6 \]
\[ = 1 - (1-w)^6 + (1-w)^6(1-w^2)^6 - \{1 - (1-w^2)^6\}(1-w)^6 + (1-w^2)^6 (1-w)^6 \]
\[ = (1-w^2)^6 = f_2(w) \ ..........(4.29) \]

\[ f_6(w) = p_{67} + p_{68} \]
\[ = (a)c (b')c + 1 - a (b')c (c)c - a b'(c)c - a (b')c c - (a)c b'c - a b'c - (a)c (b')c c \]
\[ = 1 - \psi(A)(\psi'(B))c (\psi(C))^c - (\psi(A))^c \psi'(B) (\psi(C))^c - \]
\[ \psi(A) \psi'(B) (\psi(C))^c - \psi(A) (\psi'(B))^c \psi(C) - (\psi(A))^c \psi'(B) \psi(C) \]
\[ - \psi(A) \psi'(B) \psi(C) \]
\[ = 1 - \{1 - (1-w)^4\}(1-w)^4(1-w)^6 - \{1 - (1-w)^4\}(1-w)^4(1-w)^6 \]
\[ - \{1 - (1-w)^4\}^2 (1-w)^6 - \{1 - (1-w)^4\}(1-w)^6(1-w)^4 \]
\[ - \{1 - (1-w)^4\}(1-w)^6(1-w)^4 - \{1 - (1-w)^4\}^2 \{1 - (1-w)^6\} \]
\[ = 1 - 2(1-w)^{10} + 2(1-w)^{14} - \{1 - 2(1-w)^4 + (1-w)^8\}(1-w)^6 \]
\[ - 2(1-w)^4 - (1-w)^6 + (1-w)^{10}\}(1-w)^4 \]
\[ - \{1 - 2(1-w)^4 + (1-w)^8\}(1-w)^6 \}
\[ = 1 - 2(1-w)^{10} + 2(1-w)^{14} - (1-w)^6 + 2(1-w)^{10} - (1-w)^{14} - 2(1-w^4) \]
\[ + 2(1-w)^8 + 2(1-w)^{10} - 2(1-w)^{14} - \{1 - 2(1-w)^4 + (1-w)^8 - (1-w)^6 \]
\[ + 2(1-w)^{10} - (1-w)^{14} \}
\[ = (1-w)^8 = f_3(w) \ ..........(4.30) \]
The above calculations show that the remission probabilities from state A and from state AC are same. Similarly, the remission probabilities from state B and state BC are same and the remission probabilities from states AB and ABC are same. This is as it should be in reality because a patient having symptoms of Type C is considered to be in a state of partial remission and hence, presence or non presence of Type C symptoms should not make any difference in the remission probabilities.

Taking different values of $w$ from 0.05 to 1.0, the above remission probabilities have been evaluated using Microsoft excel, 2003 and the results obtained (Annexure 2A) have been presented graphically along with the interpretation.

**Fig 4.3** Graph showing probabilities of partial remission from different categories of schizophrenia
4.4.2.1 Interpretation of graph of partial remission

In the graph, \( w \), the probability of occurrence of a symptom at the time of diagnosis is taken along the x-axis and the probability of partial remission of schizophrenia is taken along the y-axis. Three line graphs representing partial remission from schizophrenia with Types A and AC, Types B and BC and Types AB and ABC symptoms have been obtained.

From the graph it is seen that as \( w \) increases, i.e., the probability of initial occurrence of a symptom increases, the probability of remission of schizophrenia gradually decreases and for \( w \geq 0.8 \), the probability of remission is approximately zero for schizophrenia with any category of symptoms.

It is observed that remission probability is greatest for patients with symptoms of Types B and BC followed by Types A and AC and then by Types AB and ABC symptoms. This implies that if only Type B symptoms are present (along with presence or non presence of Type C symptoms), it is easier to make a patient respond to medicines and reach the state of partial remission. The presence of symptoms of both Types A and B (in presence or non presence of Type C symptoms) makes it comparatively difficult for a patient to reach the state of partial remission as the remission probabilities are seen to be zero for \( w \geq 0.5 \). The central line representing partial remission from Types A and AC symptoms shows that remission probabilities for these two categories are zero for \( w \geq 0.7 \).
The rates of remission can be obtained from the graph by drawing the gradient and it has been observed that

\[ \text{gradient of Type B} > \text{gradient of Type A} > \text{gradient of Type AB} \]

for fixed occurrence probability \( w \), in presence or non presence of Type C

i.e., the rate of partial remission is highest for Type B followed by Type A and then by Type AB symptoms.

### 4.4.3 Probabilities of Complete remission

The probabilities of going to complete remission, i.e., to the state 0 can similarly be defined as follows:

- Probability of Complete Remission from state 1 = \( p_{18} = g_1(w) \)
- Probability of Complete Remission from state 2 = \( p_{28} = g_2(w) \)
- Probability of Complete Remission from state 3 = \( p_{38} = g_3(w) \)
- Probability of Complete Remission from state 4 = \( p_{48} = g_4(w) \) \( \cdots \) (4.31)
- Probability of Complete Remission from state 5 = \( p_{58} = g_5(w) \)
- Probability of Complete Remission from state 6 = \( p_{68} = g_6(w) \)
- Probability of Complete Remission from state 7 = \( p_{78} = g_7(w) \)

In terms of the probabilities defined in section 3.5 of Chapter 3, we have

\[ g_1(w) = p_{18} = (1-a) = 1- \psi(A) = 1- [1- (1-w)^4] = (1-w)^4 \] \( \cdots \) (4.32)

\[ g_2(w) = p_{28} = (1-b) = 1- \psi(B) = 1- [1- (1-w^2)^6] = (1-w^2)^6 \] \( \cdots \) (4.33)
\[ g_3(w) = p_{38} = 1 - a (b')^c - (a)^c b' - a b' \]
\[ = 1 - \psi(A) (\psi'(B))^c - (\psi(A))^c \psi'(B) - \psi(A) \psi'(B) \]
\[ = 1 - 2(1-w)^4(1-w)^4 - (1-w)^4 \]
\[ = 1 - 2(1-w)^4 + 2(1-w)^8 - (1-w)^8 \]
\[ = (1-w)^8 \] \hspace{1cm} ......(4.34) \]

\[ g_4(w) = p_{48} = 1 - a (c)^c - a c - (a)^c c \]
\[ = 1 - \psi(A)(\psi'(C))^c - \psi(A)\psi'(C) - (\psi(A))^c \psi'(C) \]
\[ = 1 - 2(1-w)^4(1-w)^6 - (1-w)^4(1-w)^6 - (1-w)^4(1-w)^6 \]
\[ = 1 - (1-w)^6 + (1-w)^10 - (1-w)^4 + (1-w)^6 + (1-w)^10 \]
\[ = (1-w)^10 \] \hspace{1cm} ......(4.35) \]

\[ g_5(w) = p_{58} = 1 - b (c)^c - b c - (b)^c c \]
\[ = f_5(w) - (\psi(B))^c \psi(C) \]
\[ = (1-w^2)^6 - (1-w^2)^6(1-w^6) \]
\[ = (1-w^2)^6 \{1 + (1-w)^6 \} \]
\[ = (1-w^2)^6(1-w)^6 \] \hspace{1cm} ......(4.36) \]

\[ g_6(w) = p_{68} = 1 - a (b')^c (c)^c - (a)^c b'(c)^c - a b'(c)^c - a (b')^c c - (a)^c b c - a b' c - (a)^c (b')^c c \]
\[ = f_6(w) - (\psi(A))^c (\psi'(B))^c \psi(C) \]
\[
= (1-w)^8 - (1- (1-w)^6) \{(1-w)^4\}^2
\]
\[
= (1-w)^8 - (1- (1-w)^6) (1-w)^8
\]
\[
= (1-w)^8 \{1- 1 + (1-w)^6\} = (1-w)^{14} \quad \ldots \ldots \ldots (4.37)
\]

\[
g_7(w) = p_{78} = (\mathbf{1-c}) = 1- \psi(C) = 1- [1- (1-w)^6] = (1-w)^6 \quad \ldots \ldots \ldots (4.38)
\]

Taking different values of \(w\) from 0.05 to 1.0, the above remission probabilities have been evaluated using Microsoft excel, 2003 and the results obtained (Annexure 2B) have been presented graphically along with the interpretation.

**Fig 4.4** Graph showing probabilities of complete remission from different categories of schizophrenia.
4.4.3.1 Interpretation of graph of complete remission

In the graph, \( w \), the probability of occurrence of a symptom at the time of diagnosis is taken along the x-axis and the probability of complete remission of schizophrenia is taken along the y-axis. Line graphs representing probabilities of complete remission from schizophrenia with different categories of symptoms have been obtained. It is seen that in general, all the line graphs show a decline as \( w \), the probability of initial occurrence of a symptom increases.

From the graph it is evident that patients with Type B symptoms alone have the greatest probability of being cured followed by those with Type A symptoms. The presence of a symptom of Type C decreases the probabilities of complete remission. When two or more types of symptoms are present together, which is usually seen in real life, the probability of remission is lower. In fact, for a patient belonging to category ABC, i.e., having all the three Types of symptoms, the probability of complete remission is very low and becomes zero for \( w \geq 0.4 \).

The rates of remission can be obtained from the graph by drawing the gradient and it has been observed that

- gradient of Type B > gradient of Type A > gradient of Type C > gradient of Type BC > gradient of Type AB > gradient of Type AC > gradient of Type ABC

for fixed occurrence probability \( w \),
4.4.4 **Transition probabilities for \( k^{th} \) transition**

\( P_i \) gives the transition probabilities for the 1st visit after initial diagnosis. The transition probabilities for the \( k^{th} \) visit can be obtained from \((P_i)^k\), where

\[
(P_i)^k = \begin{bmatrix}
S^k & R_k \\
& \vdots \\
O & (N_s)^k
\end{bmatrix}
\]

Where \( R_k = R \left[ S^{k-1} + S^{k-2}N_s + S^{k-3}(N_s)^2 + \ldots + (N_s)^{k-1} \right] \)

\[
= RS^{k-1} \left[ 1 + \frac{N_s}{S} + \left( \frac{N_s}{S} \right)^2 + \ldots + \left( \frac{N_s}{S} \right)^{k-1} \right] = RS^{k-1} \left[ \frac{(N_s/S)^k}{N_s/S - 1} - 1 \right]
\]

.........(4.39)

.........(4.40)

4.5 **Simultaneous study of renewals and symptoms**

For a simultaneous study of renewals and symptoms, let us redefine \( Y_j \) as

\[ Y_j = \text{a value corresponding to the } j^{th} \text{ symptom in the } i^{th} \text{ renewal} \]

\[ i = 0, 1, 2, \ldots, r; \quad j = 1, 2, \ldots, N \]

(0th renewal refers to initial visit)

where \( Y_j = 1 \), if the \( j^{th} \) symptom is present in the \( i^{th} \) renewal

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

with \[ P(Y_j = 1) = w_{ij} \] and \[ P(Y_j = 0) = 1 - w_{ij} \] .............(4.41)
4.5.1 Introduction of the concept of Persistence score

Consider the following table of symptoms present at various renewals.

Table 4.1 Symptom – Renewal Table

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>1</th>
<th>2</th>
<th>j</th>
<th>N</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>y₀₁</td>
<td>y₀₂</td>
<td>y₀j</td>
<td>y₀N</td>
<td>S₀</td>
</tr>
<tr>
<td>1</td>
<td>y₁₁</td>
<td>y₁₂</td>
<td>y₁j</td>
<td>y₁N</td>
<td>S₁</td>
</tr>
<tr>
<td>i</td>
<td>yᵢ₁</td>
<td>yᵢ₂</td>
<td>yᵢ</td>
<td>yᵢN</td>
<td>Sᵢ</td>
</tr>
<tr>
<td>r</td>
<td>yᵣ₁</td>
<td>yᵣ₂</td>
<td>yᵣ</td>
<td>yᵣN</td>
<td>Sᵣ</td>
</tr>
<tr>
<td>Total</td>
<td>M₁</td>
<td>M₂</td>
<td>Mᵢ</td>
<td>Mᵣ</td>
<td>T</td>
</tr>
</tbody>
</table>

This is a table consisting of 0’s and 1’s at random positions along the 1st row according to the presence or absence of a symptom. Once a symptom is marked 1, the particular column will have the value 1 as long as the symptom persists. Once the symptom is cured, the subsequent cells of the column will have the value 0. A symptom marked 0 at the 1st row will have the value 0 in all the
subsequent cells of the column as a symptom not appearing at the time of diagnosis will not appear in the subsequent visits during the course of treatment.

\[ \text{Now } M_j = \sum_{i=0}^{r} Y_{ij} \] ...........(4.42)

i.e., \( M_j \) = Number of times symptom \( j \) occurs during the \( r \) renewals, i.e., the tenacity of occurrence or persistence of a particular symptom. We define \( M_j \) as the Persistence Score of a symptom.

The Persistence Score of the \( j^{th} \) symptom follows a random walk as shown below.

Define \( M_{ij} \) = Persistence Score of the \( j^{th} \) symptom upto the \( i^{th} \) visit.

Then, 
\[
\begin{align*}
M_{1j} &= Y_{1j} \\
M_{2j} &= Y_{1j} + Y_{2j} = M_{1j} + Y_{2j} \\
M_{3j} &= Y_{1j} + Y_{2j} + Y_{3j} = M_{2j} + Y_{3j} \\
&\vdots \\
M_{ij} &= Y_{1j} + Y_{2j} + \ldots + Y_{ij} = M_{i-1,j} + Y_{ij} \\
\end{align*}
\]

\[
\begin{align*}
M_{nj} &= Y_{1j} + Y_{2j} + \ldots + Y_{nj} = M_{r-1,j} + Y_{nj} \\
\end{align*}
\]

\[ \therefore M_{ij} \text{ follows a random walk with} \]
\[ P(M_{ij} | M_{i-1,j}) = P(Y_{ij}) = w_{ij} \quad \text{and state space } S = (0, 1, \ldots, N), i = 0, 1, \ldots, r, \]
\[ 0 < w_{ij} < 1, \quad \text{where} \quad w_{ij} = \text{Probability of the } j^{th} \text{ symptom occurring in the } i^{th} \text{ renewal} \] ...............(4.43)
4.5.2 Distribution of Persistence Score

By definition, $M_j$ is the persistence score of the $j^{th}$ symptom. Then $M_j$ is the number of times the $j^{th}$ symptom occurs i.e., the number of visits in which the $j^{th}$ symptom remains non-responsive before it is finally cured. In other words, it is the number of 1's appearing in the $j^{th}$ column of the renewal-symptom table before the first 0.

Now, the number of renewals in which a symptom occurs varies from individual to individual as well as from symptom to symptom. In all possibility, we can have the following cases with respect to a particular symptom, say, the $j^{th}$ symptom, $j = 1, 2, ..., N$.

(i) The $j^{th}$ symptom might not appear in a patient at all at the time of diagnosis. In this case, there will be a '0' in the 1st row of the $j^{th}$ column and subsequently all other cells in that column will have '0'.

Hence $M_j = 0$ and $P(M_j = 0) = 1 - w_{0j}, \quad 0 < w_{0j} < 1$.

\[ \text{[ since, } P(Y_0 = 0) = 1 - w_{0j}] \quad \text{...............(4.44)} \]

(ii) Consider that the $j^{th}$ symptom is present at the initial visit but it responds to treatment immediately and gets cured before the 1st renewal.

In this case, $Y_{0j} = 1$ but $Y_{1j} = 0$ with respective probabilities $w_{0j}$ and $1 - w_{1j}$.

Thus, $M_j$ takes value 1 with
(iii) Suppose that the $j^{th}$ symptom is present till the $1^{st}$ renewal and gets cured before the $2^{nd}$ renewal. Then, in this case,

$$Y_{0j} = Y_{1j} = 1 \quad \text{and} \quad Y_{2j} = 0$$

with $P(Y_{0j} = 1) = w_{0j}$, $P(Y_{1j} = 1) = w_{1j}$ and $P(Y_{2j} = 0) = 1 - w_{2j}$

Thus, $M_j = 2$ with $P(M_j = 2) = w_{0j} w_{1j} (1 - w_{2j})$ ..........(4.46)

(iv) On similar explanations, the probabilities of $M_j$ taking values $3, 4, \ldots, r$ are given by

$$P(M_j = 3) = w_{0j} w_{1j} w_{2j} (1 - w_{3j})$$
$$P(M_j = 4) = w_{0j} w_{1j} w_{2j} w_{3j} (1 - w_{4j})$$

..........(4.47)

$$P(M_j = r) = w_{0j} w_{1j} w_{2j} \ldots w_{(r-1)j} (1 - w_{rj})$$

(v) If a symptom is present in all the $r$ renewals considered, then

$$Y_{0j} = 1, Y_{1j} = 1, Y_{2j} = 1, Y_{3j} = 1, \ldots, Y_{rj} = 1$$

with respective probabilities $w_{0j}, w_{1j}, w_{2j}, w_{3j}, \ldots, w_{rj}$.

Then,

$$M_j = \sum_{i=0}^{r} Y_{ij} = r + 1 \quad \text{with} \quad P(M_j = r + 1) = w_{0j} w_{1j} w_{2j} \ldots w_{rj}$$

..........(4.48)
In general,

\[ P(M_j = m) = \prod_{i=0}^{m-1} w_{ij} \prod_{j} w_{3j} \ldots \ldots \ldots \prod_{j=0}^{m-1} (1 - w_{mj}), \quad 0 < m \leq r + 1 \]

with \( 0 < w_{ij} < 1 \), \( i = 0,1,2,\ldots,r \) and \( w_{(r+1)j} = 0 \)

[as \( i = 0, 1, 2, \ldots, r \); i.e., the \((r+1)\)th renewal is not being considered in this scheme.]

and \( P(M_j = m) = 1 - w_0 \), \( m = 0 \) \hspace{1cm} \ldots(4.49)\)

Alternatively, we can write, in general,

For \( m = 1, 2, 3, \ldots, r + 1 \)

\[ P(M_j = m) = \left( \prod_{i=1}^{m} w_{(i-1)j} \right) (1 - w_{mj}) \]

with \( 0 < w_{ij} < 1 \), \( i = 0,1,2,\ldots,r \) and \( w_{(r+1)j} = 0 \)

[as \( i = 0, 1, 2, \ldots, r \); i.e., the \((r+1)\)th renewal is not being considered in this scheme.]

and for \( m = 0 \),

\[ P(M_j = m) = 1 - w_0 \] \hspace{1cm} \ldots(4.49a)\)

The above mentioned cases are the “all possible cases” or exhaustive cases as far as the values taken by \( M_j \) are concerned i.e., the values of “persistency score” for the \( j \)th symptom in a study of \( r \) renewals or \( r \) revisits to the doctor after initial diagnosis at epoch 0. It is observed that
\[
\sum_{m=0}^{\infty} P(M_j = m) = (1 - w_{0j}) + \sum_{m=1}^{\infty} \left\{ \prod_{i=1}^{m} w_{(r-1)j} \right\} (1-w_{mj}) \quad \cdots \cdots (4.50)
\]

Now, as \( r \to \infty \), we have,

\[
\sum_{m=0}^{\infty} P(M_j = m) = (1 - w_{0j}) + \sum_{m=1}^{\infty} \left\{ \prod_{i=1}^{m} w_{(r-1)j} \right\} (1-w_{mj}) \\
= (1 - w_{0j}) + \left\{ \prod_{i=1}^{1} w_{(r-1)j} \right\} (1-w_{1j}) + \left\{ \prod_{i=1}^{2} w_{(r-1)j} \right\} (1-w_{2j}) + \left\{ \prod_{i=1}^{3} w_{(r-1)j} \right\} (1-w_{3j}) + \\
\ldots \ldots + \left\{ \prod_{i=1}^{r} w_{(r-1)j} \right\} (1-w_{dj}) + \ldots \\
= (1 - w_{0j}) + w_{0j} (1 - w_{1j}) + w_{0j} w_{1j} (1 - w_{2j}) + w_{0j} w_{1j} w_{2j} (1 - w_{3j}) + \ldots \\
\ldots \ldots + w_{0j} w_{1j} w_{2j} w_{3j} (1 - w_{dj}) + \ldots \\
= 1 - w_{0j} - w_{0j} w_{1j} - w_{0j} w_{1j} w_{2j} - w_{0j} w_{1j} w_{2j} - w_{0j} w_{1j} w_{2j} w_{3j} \\
\ldots \ldots - w_{0j} w_{1j} w_{2j} w_{3j} - \ldots \ldots w_{0j} w_{1j} w_{2j} w_{3j} \ldots \ldots w_{dj} + w_{0j} w_{1j} w_{2j} w_{3j} \\
\ldots \ldots w_{dj} - \ldots \ldots \\
= 1 \quad \cdots \cdots (4.51)
\]

This implies that \( P(M_j = m) \) as defined in (4.49) and (4.49a) is a p.m.f. This p.m.f. is identical to that of geometric distribution with probability of occurrence varying at every trial. Thus, \( M_j \)'s may be looked upon as **non identical but independent geometric variables**.

The corresponding distribution function is given by

\[
P(M_j \leq m) = 1 - \left\{ \prod_{i=0}^{m+1} w_i \right\} \quad \cdots \cdots (4.52)
\]
The survival function of $m$ is given by
\[ P(M_j > m) = \prod_{i=0}^{m+1} w_i \] ........(4.53)

### 4.5.3 Distribution of Persistence Score: Special case

Consider the case when every symptom has equal chance of appearing at a particular renewal, the occurrence probability varying from renewal to renewal as considered in section (3). In this case we shall have,

If $Y_{ij} = 1$, if the $j^{th}$ symptom is present in the $i^{th}$ renewal
\[ = 0, \quad \text{otherwise} \]
then
\[ P(Y_{ij} = 1) = w_j \quad \text{and} \quad P(Y_{ij} = 0) = 1 - w_j \quad \forall j = 1, 2, ..., N \]
where $0 < w_j < 1, \quad i = 0, 1, 2, ..., r$ ........(4.54)

The probability of the persistence score of the $j^{th}$ symptom $M_j$, taking a particular value $m$ as defined in (3.49) will then take the following form

For $m = 1, 2, 3, ......., r + 1$
\[ P(M_j = m) = \left\{ \prod_{i=1}^{m} w_{(i+1)} \right\} (1 - w_m) \]

with $0 < w_i < 1, \quad i = 0, 1, 2, ..., r$ and $w_{(r+1)} = 0$

[ as $i = 0, 1, 2, ..., r$; i.e., the $(r + 1)^{th}$ renewal is not being considered in this scheme.]

and for $m = 0$,
\[ P(M_j = m) = 1 - w_0 \] ........(4.55)
Therefore,
\[
\sum_{m=0}^{c} P (M_j = m) = (1 - w_0) + \sum_{m=1}^{c} \left( \prod_{i=1}^{m} w_{(i-1)} \right) (1 - w_m)
\]

Now, as \( r \to \infty \), we have,
\[
\sum_{m=0}^{\infty} P (M_j = m) = (1 - w_0) + \sum_{m=1}^{\infty} \left( \prod_{i=1}^{m} w_{(i-1)} \right) (1 - w_m) = 1 \quad \text{.........(4.56)}
\]

which under similar calculations can be shown to be equal to unity.
Thus \( P (M_j = m) \) as defined in (4.55) is also a p.m.f. of the persistence score.

4.5.4 Significance of the maximum and minimum persistence scores

The minimum persistence score relates to the symptom which is easily curable or most responsive to medicines and the maximum persistence score relates to the symptom which is most persistent i.e., difficult to cure.

These scores will differ from individual to individual. But proper monitoring and study of follow-up data might reveal that there are some particular symptoms which prove to be persistent in general. This aspect is important as doctors have to device ways to control the more persistent symptoms. A data based study is presently being carried out by the authors on this aspect.

4.5.5 Sampling scheme for estimation of \( w_{ij} \)

Let us consider a particular symptom, say the \( j^{th} \) symptom, for study. For this we consider a random sample of \( k \) schizophrenic patients for observation, under the
condition that the $j^{th}$ symptom is present in these $k$ patients. The persistence score of the $j^{th}$ symptom in $r$ renewals or visits to the doctor is recorded for each of the $k$ patients.

Let $M_{jt}$ denote the persistence score of the $j^{th}$ symptom in the $t^{th}$ patient in $r$ renewals where $j = 1, 2, ..., N$ and $t = 1, 2, ..., k$, ($r$ being fixed)

Let a score card be maintained as follows:

**For symptom no. $j$**

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Renewals / Visits to the doctor</th>
<th>Persistence Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>$1$</td>
<td></td>
<td>$M_{j1}$</td>
</tr>
<tr>
<td>$2$</td>
<td></td>
<td>$M_{j2}$</td>
</tr>
<tr>
<td>$3$</td>
<td></td>
<td>$M_{j3}$</td>
</tr>
<tr>
<td>$\cdot$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\cdot$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\cdot$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$t$</td>
<td></td>
<td>$M_{jt}$</td>
</tr>
<tr>
<td>$\cdot$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\cdot$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\cdot$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$k$</td>
<td></td>
<td>$M_{jk}$</td>
</tr>
</tbody>
</table>
This card can be filled up in the same way as in the Symptom-Renewal table (Table 4.1) by putting 1 in the cell in which the \( j \)th symptom is present and 0 in the subsequent cells in which the symptom is absent for a particular patient. The row sum gives us the number of visits in which the \( j \)th symptom remains non-responsive to medicines and persists in the corresponding patient i.e., the row sums give us the persistence score for the particular symptom under study for the corresponding patient.

The average persistence score for the \( j \)th symptom can thus be obtained as follows

\[
E( M_j ) = m_j = \frac{\sum_{k=1}^{r} M_k}{k} \tag{4.57}
\]

In this sampling scheme, one particular symptom is being studied at a time. The study can be conducted for all the \( N \) symptoms separately and ultimately it can be checked that on the average, which symptoms have greater persistence scores. Treatment strategies can then be formulated for eradication of these persistent symptoms.

For estimation of \( w_0 \), let us define

\[
X_j = \begin{cases} 
1, & \text{if the } j \text{th symptom is present in a patient} \\
0, & \text{otherwise.} 
\end{cases}
\]

\[
\therefore P( X_j = x_j ) = (w_0)^x(1-w_0)^{1-x}, \quad \text{for } i = 1, 2, \ldots, r
\]

where \( 0 < w_0 < 1 \) \hspace{1cm} \ldots \ldots \hspace{1cm} (4.58)
Since \( X_j \) is a Bernoulli random variable, the maximum likelihood estimator (M.L.E.) is given by

\[
\hat{\theta}_y = \bar{x} = \frac{\sum_{t=1}^{k} X_{jt}}{k}, \quad k > 0 \quad \ldots \ldots (4.59)
\]

**4.5.5.1 Special case**

For the special case considered in section 4.5.2.1, where the occurrence probability is considered to be equal for all the symptoms at a particular renewal or revisit, the estimators of \( \hat{w}_i \) can be obtained from the Symptom – Renewal table (Table 4.1) which gives

\[
\hat{w}_i = \frac{\text{Number of symptoms present in the } i^{th} \text{ renewal}}{\text{Number of symptoms that were present in the } (i-1)^{th} \text{ renewal}}
\]

Therefore,

\[
\hat{w}_0 = \frac{1}{N}
\]

\[
\hat{w}_1 = \frac{S_1}{S_0}
\]

\[
\hat{w}_2 = \frac{S_2}{S_1}
\]

\[
\hat{w}_r = \frac{S_r}{S_{r-1}} \quad \ldots \ldots (4.60)
\]

\[\text{..............................}\]

\[
\hat{w}_r = \frac{S_r}{S_{r-1}}
\]
4.6 Observations

The mathematical modeling of the symptoms of schizophrenia, in conjunction with the concept of regularity of a patient in his visits to the psychiatrist, is found to be rare in literature. The stochastic models developed in this chapter are expected to be of considerable help to doctors in framing their treatment strategies regarding schizophrenic patients. However, the study of the behaviour of symptoms of schizophrenia during the course of treatment cannot be considered complete without a proper study on the aspect of regularity of a patient in the treatment process. The important aspect of regularity has been studied in the next chapter to obtain the operating characteristics that actually dominate the treatment process of a patient of schizophrenia.