International Journal of Scientific Engineering and Research (IJSER)
ISSN (Online): 2347-3878
Index Copernicus Value (2015): 62.86 | Impact Factor (2015): 3.791

Estimation of Survival Time of Patients Suffering from Liver Cirrhosis Based on Preventive Maintenance Policy (PMP)

Gurprit Grover[1], Divya Seth[2]

[1, 2]Department of Statistics, University of Delhi, New Delhi, India

Abstract: ***Maintenance policy is a set of predetermine activities including preventive and corrective maintenance. Every system may be human or industrial experience deterioration. After a finite time of deterioration the system will go to breakdown status if there are no activities to maintain it. In order to illustrate this application on human system, we have developed two models for estimating survival time of the patients suffering from liver cirrhosis who are subjected to stochastic deterioration. First model based on number of transitions patient has made to reach death state and another employing preventive maintenance policy (PMP).***

Keywords: Survival time, Cirrhosis, Preventive maintenance policy

1. Introduction

Preventive maintenance is defined as the activity undertaken regularly at pre-selected intervals while the device is satisfactorily operating, to reduce or eliminate the accumulated deterioration [1]. When the cost incurred by the device failure is larger than the cost of preventive maintenance, it is worthwhile to carry out preventive maintenance. Generally, there exists two types of preventive maintenance schemes, i.e. condition based and time based preventive maintenance [2]. For condition based preventive maintenance, the action taken after each inspection is dependent on the state of the system. For time based preventive maintenance, the preventive maintenance is carried out at pre-determined time intervals to bring the system to as good as new state [3]. In this paper, we are modeling this concept on human system so we focus on both preventive maintenance schemes whichever occur earlier.

Preventive maintenance is based on monitoring the degradation at successive maintenance times. Such condition-based preventive maintenance is more efficient than the policies based on the system age and the knowledge of the statistical information on its lifetime [4-6]. Of late, the same preventive maintenance policy has been applied and found useful in the clinical follow-up studies suffering from chronic diseases such as hypertension, diabetes, cancer, liver disease, cardiovascular disease etc. We have considered patients suffering from liver cirrhosis (chronic illness) who have reached to this condition while transiting through various stages such as virus transmission, chronic hepatitis etc at random time points. Cirrhosis is a consequence of chronic liver disease, characterized by replacement of liver tissue by fibrous scar tissue as well as regenerative nodules, leading to progressive loss of liver function. The health of a cirrhotic patient deteriorates while transiting from one stage to another at random time points and each transition causing random amount of damage which accumulates over time and may result in liver cirrhosis which further leads to liver cancer or death. This process which causes deterioration in the health of liver cirrhotic patient can be controlled by regular timely clinical check-ups thus increasing the survival time of the patient. Suppose a liver cirrhotic patient visits a clinic for periodical check-up, at regular time interval of T days or whenever he faces some complication, whichever is earlier. If the patient has a variable time of check-up then the patient can take advantage of a random routine check-up policy. Policy in which T is a random variable is said to be a Random Age Replacement Policy [7]. Thus, the motivation of preventive maintenance policy is to increase system longevity or survival time of the patient.

This article is focused on the development of two models for estimating the survival time of patients suffering from liver cirrhosis under different conditions. In first part, we have estimated the survival time when N, the number of transitions, is a random variable and the intensity of transitions is constant for each interval but varying across individuals. In second part, we have estimated the survival time using preventive maintenance policy. Although much work has been done for the analysis of chronic liver disease data but to the best of our knowledge there is no such study that has systematically estimated the survival time of liver cirrhotic patients under the two possibilities mentioned above. PMP has been used widely for non living systems but its use has been very limited for human system.

2. Materials and Methods

2.1 Model Description

Liver cirrhosis is an advanced stage liver disease. Patient reaches to this stage after transiting from various stages such as fatty liver, alcoholic hepatitis, chronic viral hepatitis etc. It is an irreversible disease, i.e. once patient reach to this stage then through medication the disease can be stopped or delayed for further progression but cannot be cured completely. Patient at this stage can move to HCC, can go for liver transplant or death. Due to paucity of data, we have considered total four stages in the model viz. one disease free state (Birth), two illness states (Cirrhosis, HCC) and one death state due to liver disease (Death). We have considered those patients who have made atleast one transition to liver cirrhosis since birth.

A schematic representation of transitions in the life of liver disease patients is provided in Fig.1. We have observed the patient from cirrhosis state from which he/she can transfer to hepatocellular carcinoma (HCC) state and then to Death state, representing death due to liver disease.

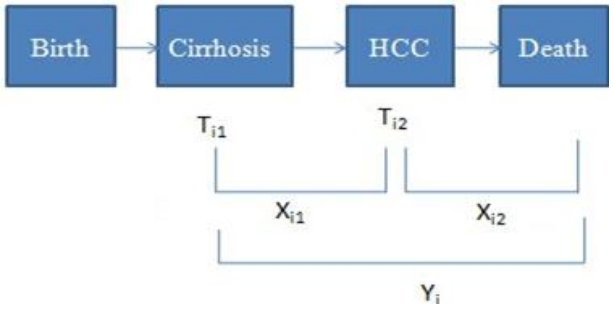

Figure 1: Graphical presentation of patients initially suffering from liver cirrhosis who experienced atleast one transition during the observed follow up.

Let T_{ij} (i= 1,2,3…n: j=1,2,3) be the time of the j^{th} transition for the i^{th} patient measured from time zero. Zero represents the time of birth of an individual and the patient is observed to undergo N transitions, N= 1,2,3. The inter-event times from T_{ij-1} to T_{ij} is denoted by X_{ij} (i= 1,2,3…n: j=1,2,3) which are independently and identically distributed random variables, each having exponential distribution with parameter, say λ.

The probability function of the time interval between transitions is given by

$$f(x_{ij}) = \lambda_i e^{-\lambda_i x_{ij}}; i = 1,2,...n;\ j = 1,2....N; \lambda > 0 \quad 1$$

Suppose that N, the number of transitions is a random variable following geometric distribution with parameter, say p. The probability function of N is given by

$$P(N) = q^{N-1}p;\ N= 1,2.....;\ 0 < p \le 1;\ N \ge 1 \quad 2$$

where p is the probability of transiting from one stage to another.

Let, Y_i be the sum of time intervals between transitions.

Then, $Y_i = X_{i1}+X_{i2}+X_{i3}+\cdots\cdots+ X_{iN} \sim \text{Gamma}(\lambda,N)$ 3

Here, we estimate the survival time of liver disease patients by assuming that the transitions occur with hazard rate λ which is constant for an individual but is varying from individual to individual according to the following probability law:

$$\phi(\lambda) = \lambda^{\alpha-1}e^{-\lambda\gamma}\frac{\gamma^{\alpha}}{\Gamma\alpha}; 0 \le \lambda < \infty; \alpha, \gamma > 0 \quad 4$$

Then the conditional distribution of survival time Y_i given N, the number of transitions and λ, the intensity with which a transition occurs, for the i^{th} patient is given by

$$g(y_i \mid N, \lambda) = y_i^{N-1}e^{-\lambda y_i}\frac{\lambda^N}{\Gamma N}; N \ge 1, y_i \ge 0, \lambda > 0 \quad 5$$

Integrating equation 5 with respect to λ over the range 0 to ∞, we get

$$h(y_i \mid N) = \int_0^{\infty} y_i^{N-1}e^{-\lambda_i y_i}\frac{\lambda_i^N}{\Gamma N}\lambda_i^{\alpha-1}e^{-\gamma\lambda_i}\frac{\gamma^{\alpha}}{\Gamma\alpha}d\lambda_i$$

$$= \frac{y_i^{N-1}}{\Gamma N}\frac{\gamma^{\alpha}}{\Gamma\alpha}\int_0^{\infty} e^{-\lambda_i(y_i+\gamma)}\lambda_i^{N+\alpha-1}d\lambda_i$$

$$h(y_i \mid N) = \frac{y_i^{N-1}}{\Gamma N}\frac{\gamma^{\alpha}}{\Gamma\alpha}\frac{\Gamma(\alpha+N)}{(y_i+\gamma)^{(\alpha+N)}}$$

which on summation over N(N = 1,2…) gives

$$f(y_i) = \sum_{N=1}^{\infty}\frac{y_i^{N-1}}{\Gamma N}\frac{\gamma^{\alpha}}{\Gamma\alpha}\frac{\Gamma(\alpha+N)}{(y_i+\gamma)^{(\alpha+N)}}q^{N-1}p$$

$$= \frac{p\gamma^{\alpha}}{\Gamma\alpha(y_i+\gamma)^{(\alpha+1)}}\sum_{N=1}^{\infty}\frac{(y_i q)^{N-1}}{(y_i+\gamma)^{(N-1)}}\frac{(\alpha+N-1)!}{\Gamma N}$$

$$f(y_i) = \frac{\alpha p\gamma^{\alpha}}{(y_i p+\gamma)^{(\alpha+1)}}$$

$$E(Y_i) = \alpha p\gamma^{\alpha}\int_0^{\infty}\frac{y_i}{(y_i p+\gamma)^{(\alpha+1)}}dy_i$$

On integrating by parts, we get

$$E(Y_i) = \frac{\gamma}{(\alpha-1)p} \quad 6$$

which is the general form of estimated survival time for the i^{th} patient.

But when α < 1, we get

$$E(Y_i) = \frac{\gamma}{(1-\alpha)p}$$

Parameters α and γ have been estimated separately for each patient by the method of moments and the probability p of HCC, has been estimated by the method of maximum likelihood, which consists in maximizing the following log likelihood equation

$$\log L = \sum_{i=1}^{n}[\log\alpha` + \log p + \alpha`\log\gamma` - (\alpha`+1)\log(y_i p+\gamma`)] \quad 7$$

Where $\alpha` = \sum_{i=1}^{n}\alpha_i$ and $\gamma` = \sum_{i=1}^{n}\gamma_i$, using software R.

2.2 Model Description

a) Estimation of mean survival time of patients suffering from liver cirrhosis based on the number of follow-ups made to the health center to delay the advancement of the disease using preventive maintenance policy (PMP).

A schematic representation of clinical visits of patients to liver center is provided in Fig.2. Time (T) is a random variable representing the time between two consecutive visits. It varies from individual to individual and also, it can vary for the same individual. Z is the residual time after the last check-up has been made but before death.

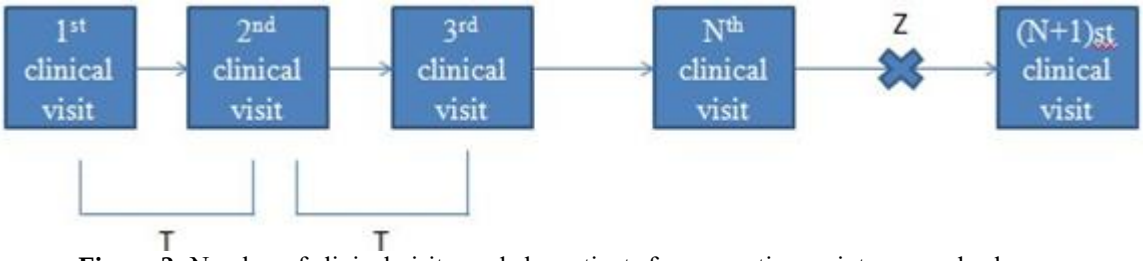

Figure 2: Number of clinical visits made by patients for preventive maintenance check-ups

T = be a random variable representing the length of time interval between successive preventive maintenance check-ups
N = be a random variable representing the number of times preventive maintenance check-ups have been made
Z = be an absolutely continuous random variable representing the residual survival time following the last check-up i.e. between N^{th} and $(N+1)^{th}$ preventive maintenance check-up.

Then, the expected survival time of liver disease patient is given by:

E(Survival Time) = E(N T) + E(Z)

E(N) E(T) + E(Z) 8

The number of preventive maintenance check-ups (N) and the time between preventive maintenance check-ups (T) are assumed to be independently distributed random variables.

Now,

$$E(N) = \sum_{n=0}^{\infty} nP(n) \quad 9$$

P(N = n) = P(N ≥ n) - P(N ≥ n+1)

P(N ≥ n) = (1 - F(T))^n 10

where F(T) represents the c.d.f. of the failure time.

P(N = n) = (1 - F(T))^n - (1 - F(T))$^{n+1}$

$$E(N) = \sum_{n=0}^{\infty} n[(1-F(T))^n - (1-F(T))^{n+1}] \quad 11$$

Therefore,

$$E(N) = \frac{1-F(T)}{F(T)} \quad 12$$

$$P(Z \le z) = \frac{F(z)}{F(T)}$$

$$P(Z > z) = 1 - \frac{F(z)}{F(T)} \quad 13$$

which implies that

$$E(Z) = \int_0^T \left(1 - \frac{F(z)}{F(T)}\right) dz \quad 14$$

Hence,

$$E(SurvivalTime) = \left[\frac{1-F(T)}{F(T)}\right] E(T) + \int_0^T \left[1 - \frac{F(z)}{F(T)}\right] dz \quad 15$$

2.2.1 Preventive Maintenance Scheme in a Weibull Type Model

Let the time interval between preventive maintenance check-ups (T) follows Weibull distribution with parameters λ and γ where we assume that λ > 0 and γ > 1. The shape parameter γ measures the trend of the failure intensity with the operating time t between two successive preventive maintenance check-ups. If γ > 1, then this implies that the survivability of a liver patient is decreasing with time i.e. higher the value of γ, faster is the deterioration. Hence, a preventive maintenance check-up will result in the improvement of the survival time of a liver disease patient. As we know, that preventive maintenance policy (PMP) increases the survival probability if the length of the interval between preventive maintenance check-ups is characterized by a failure rate that increases with time so Weibull distribution is found to be apt for this model (Barlow and Proschan, [7]).

$$f(t) = \frac{\gamma}{\lambda}\left(\frac{t}{\lambda}\right)^{\gamma-1} \exp\left(-\frac{t}{\lambda}\right)^{\gamma} \quad 16$$

The hazard function of T is given by

$$h(t) = \lambda\gamma t^{\gamma-1} \quad 17$$

The survival function S(t) is given by

$$S(t) = \exp\left(\frac{-\lambda t^{\gamma}}{\gamma}\right) \quad 18$$

which implies that

$$F(t) = 1 - \exp\left(\frac{-\lambda t^{\gamma}}{\gamma}\right) \quad 19$$

$$E(T) = \frac{\Gamma(1+1/\gamma)}{\lambda^{1/\gamma}} \quad 20$$

Suppose the residual survival time Z, after the last check-up be a random variable which follows time dependant exponential distribution. Hence, time-dependant hazard rate is given by

h(z) = λ_1z, 0 < z < T

where λ_1 is the intensity of HCC.

The survival function S(z) is given by

$$S(z) = \exp\left(\frac{-\lambda_1 z^2}{2}\right)$$

Hence,

$$F(z) = 1 - \exp\left(\frac{-\lambda_1 z^2}{2}\right) \quad 21$$

which implies

E(survival Time) =

$$\left[\frac{e^{\left(-\lambda T^{\gamma}/\gamma\right)}}{1-e^{\left(-\lambda T^{\gamma}/\gamma\right)}}\right]\frac{\left|1+1/\gamma\right|}{\lambda^{1/\gamma}}+T-\int_0^T\left(\frac{1-e^{\left(-\lambda_1 z^2/2\right)}}{1-e^{\left(\lambda T^{\gamma}/\gamma\right)}}\right)dz \quad 22$$

$$=\left[\frac{e^{\left(-\lambda T^{\gamma}/\gamma\right)}}{1-e^{\left(-\lambda T^{\gamma}/\gamma\right)}}\right]\frac{\left|1+1/\gamma\right|}{\lambda^{1/\gamma}}+T-\frac{1}{1-e^{\left(-\lambda T^{\gamma}/\gamma\right)}}\int_0^T(1-e^{\left(-\lambda_1 z^2/2\right)})dz$$

$$=\left[\frac{e^{\left(-\lambda T^{\gamma}/\gamma\right)}}{1-e^{\left(-\lambda T^{\gamma}/\gamma\right)}}\right]\frac{\left|1+1/\gamma\right|}{\lambda^{1/\gamma}}+T-\frac{T}{1-e^{\left(-\lambda T^{\gamma}/\gamma\right)}}+\frac{1}{1-e^{\left(-\lambda T^{\gamma}/\gamma\right)}}\int_0^T e^{\left(-\lambda_1 z^2/2\right)}dz \quad 23$$

By substituting, $\lambda_1 z^2 = p$, in eq 23, we get $z=\left(\frac{2p}{\lambda_1}\right)^{1/2}$

which implies $dz=\left(\frac{1}{2\lambda_1 p}\right)^{1/2}dp$.

Now calculating the integral separately, we get

$$\int_0^T \exp(-\lambda_1 z^2/2)dz=\int_0^{\lambda_1 T^2/2} e^{-p}(2\lambda_1 p)^{-1/2}dp \quad 24$$

$$=(2\lambda_1)^{\frac{1}{2}-1}\int_0^{\lambda_1 T^2/2} e^{-p}p^{\frac{1}{2}-1}dp \quad 25$$

We know that,

$$\int_0^{\lambda_1 T^2/2} e^{-p}p^{\frac{1}{2}-1}dp=\sqrt{\frac{1}{2}}-\int_{\lambda_1 T^2/2}^{\infty} e^{-p}p^{\frac{1}{2}-1}dp \text{ (Biswas, [8])} \quad 26$$

Using the approximation given by [9]

$$\frac{\int_{\lambda T^{\alpha}/\alpha}^{\infty} e^{-p}p^{1/\alpha-1}dp}{e^{\left(\frac{-\lambda T^{\alpha}}{\alpha}\right)}\left(\frac{\lambda T^{\alpha}}{\alpha}\right)^{1/\alpha-1}}=\frac{\lambda T^{\alpha}/\alpha}{\left(\frac{\lambda T^{\alpha}}{\alpha}-\frac{1}{\alpha}+1\right)}\left[1-\frac{1/\alpha-1}{\left(\frac{\lambda T^{\alpha}}{\alpha}-\frac{1}{\alpha}+1\right)^{\alpha}+\frac{2\lambda T^{\alpha}}{2}}\right] \quad 27$$

We get

$$\int_0^{\lambda_1 T^2/2} e^{-p}p^{\frac{1}{2}-1}dp=\sqrt{\frac{1}{2}}-\left\{e^{\left(\frac{-\lambda_1 T^2}{2}\right)}\left(\frac{\lambda_1 T^2}{2}\right)^{1/2-1}\frac{\left(\frac{\lambda_1 T^2}{2}\right)}{\left(\frac{\lambda_1 T^2}{2}-\frac{1}{2}+1\right)}\left[1-\frac{1/2-1}{\left(\frac{\lambda_1 T^2}{2}-\frac{1}{2}+1\right)^2+\frac{2\lambda_1 T^2}{2}}\right]\right\}$$

$$\int_0^T e(-\lambda_1 z^2/2)dz=(2\lambda_1)^{1/2}\left[\sqrt{\frac{1}{2}}-\left\{e^{\left(\frac{-\lambda_1 T^2}{2}\right)}\frac{\left(\frac{\lambda_1 T^2}{2}\right)^{1/2}}{\left(\frac{\lambda_1 T^2}{2}+\frac{1}{2}\right)}\left[1+\frac{1/2}{\left(\frac{\lambda_1 T^2}{2}+\frac{1}{2}\right)^2+\lambda_1 T^2}\right]\right\}\right] \quad 28$$

Hence, we get

$$\text{E(Survival time)}=\left[\frac{e^{\left(-\lambda T^{\gamma}/\gamma\right)}}{1-e^{\left(-\lambda T^{\gamma}/\gamma\right)}}\right]\frac{\left|1+1/\gamma\right|}{\lambda^{1/\gamma}}+T-\frac{T}{1-e^{\left(-\lambda T^{\gamma}/\gamma\right)}}+\frac{(2\lambda_1)^{-1/2}}{1-e^{\left(-\lambda T^{\gamma}/\gamma\right)}}$$

$$\left[\sqrt{\frac{1}{2}}-\left\{e^{\left(\frac{-\lambda_1 T^2}{2}\right)}\frac{\left(\frac{\lambda_1 T^2}{2}\right)^{1/2}}{\left(\frac{\lambda_1 T^2}{2}+\frac{1}{2}\right)}\left[1+\frac{1/2}{\left(\frac{\lambda_1 T^2}{2}+\frac{1}{2}\right)^2+\lambda_1 T^2}\right]\right\}\right] \quad 29$$

2.2.2 Estimation of Weibull parameters

The parameters of weibull distribution for progressively censored data can be estimated by solving these two equations: (Lee, [10])

$$r - \lambda^{\gamma}\left(\sum_{i=1}^{r} t_i^{\ \gamma} + \sum_{i=r+1}^{n} t_i^{+\ \gamma}\right) = 0$$

$$\frac{r}{\gamma} + r\log\lambda + \sum_{i=1}^{r}\log t_i - \lambda^{\gamma}\sum_{i=1}^{r} t_i^{\gamma}(\log\lambda + \log t_i) - \lambda^{\gamma}\sum_{i=r+1}^{n} t_i^{+\ \gamma}(\log\lambda + \log t_i^{+}) = 0$$

3. Application and Results

The two models developed in section 2 were applied to a retrospective data of liver disease patients. The data was obtained from Pushpawati Singhania Research Institute (PSRI), New Delhi, India for liver disease patients suffering from liver cirrhosis and HCC. A total of 824 patients who were admitted were examined during the study period and 657 patients were taken into analysis suffering from liver cirrhosis that died due to liver disease. Patients with co-morbidity like renal failure, cardiac arrest, intracerebral haemorrhage etc. were excluded because there number was not sufficient to draw valid conclusion about these identities.

The analysis for model (a) was done using R software and results are given in Table 1. When cirrhosis was the only intermediate state between birth and death i.e., only two transitions are made, the survival time is estimated using gamma distribution with parameters (3.380, 0.091). Also, the estimate of probability of death after two transitions is calculated by the method of maximum likelihood as p = 0.199. Substituting these values in equation 6, the mean survival time is estimated as 31.04 months i.e. 2 years and 7 months. On the other hand, when death state was reached after cirrhosis followed by HCC i.e. three transitions were made, survival time is estimated as gamma (3.290, 0.506). In this case, the estimate of probability of death after three transitions is found to be p = 0.146. Hence, the mean survival time when, three transitions are made to reach to death state is estimated as 45.74 months i.e., 3 years and 8 months.

Table 1: Parameter estimates and mean survival time (months) of patients with corresponding 95% confidence interval

Parameter	Number of transitions made -2			Number of transitions made – 3		
	Estimates	95% confidence interval		Estimates	95% confidence interval	
		Lower Limit	Upper Limit		Lower Limit	Upper Limit
Γ	3.380	3.33	3.43	3.290	3.060	3.520
A	0.091	0.005	1.64	0.506	0.378	0.678
P	0.199			0.146		
Mean survival time	31.04			45.74		

b) To illustrate the working of the proposed model, we generated a random sample of the length of time interval between preventive maintenance check-ups (T), using Weibull distribution of the form

$$f(t) = \frac{\gamma}{\lambda}\left(\frac{t}{\lambda}\right)^{\gamma-1}\exp\left(-\frac{t}{\lambda}\right)^{\gamma}$$

Where λ = 5.107 and γ = 0.898. Table 3 gives the expected survival time of patients suffering from liver cirrhosis under Weibull failure rates.

Table 2 depicts the expected survival time of liver cirrhosis patients using preventive maintenance policy under Weibull distribution. The parameters for weibull distribution has been estimated using R software. If the patient visits the liver clinic on monthly basis then his expected survival time is 71 months. We have shown the results varying from first month to 24th month i.e. if the patients' two consecutive visits to liver clinic are in the gap of 24 months then his expected survival time is reduced to just 19 months. The results presented in figure 3. confirms that the survival time of cirrhotic patients decreases consistently with the increase in the length of the preventive maintenance check-ups (T).

Table 2: Expected survival time by the period of preventive maintenance check-up under weibull failure rate

T (months)	E(survival time) (months)	T (months)	E(survival time) (months)
1	71.1	13	31
2	65.5	14	29.3
3	60.6	15	27.8
4	56.1	16	26.5
5	52	17	25.3
6	48.4	18	24.1
7	45.1	19	23.1
8	42.1	20	22.2
9	39.4	21	21.4
10	37	22	20.6
11	34.8	23	19.9
12	32.8	24	19.3

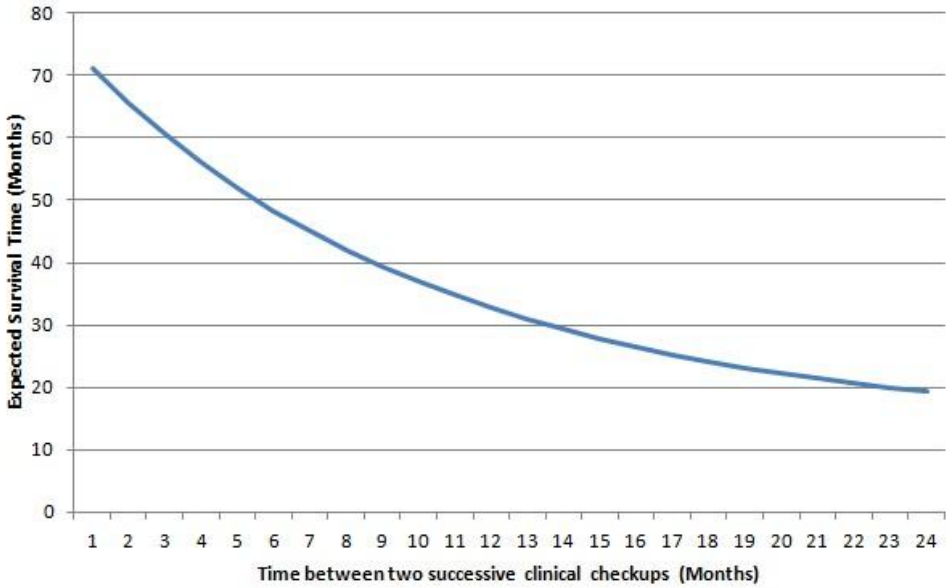

Figure 3: Expected survival time for liver cirrhosis patients under PMP under Weibull increasing failure rate

4. Discussion

Estimation of survival time is the crux of any disease, no matter whether it is chronic or acute. By estimating the survival time we can predict the future survivability of the patient suffering from the disease. It can also be used as a baseline for future studies, as it may provide greater sensitivity for detecting treatment differences than the traditional methods. In the first part, we have assumed the times between two transitions follow exponential distribution with parameter λ and the number of transitions follow geometric distribution with parameter p, which represents the probability of transiting to HCC state. Further, the hazard rate λ is taken to be constant for each individual but is varying from individual to individual. The average survival time for patients who died after cirrhosis state without entering into HCC is 2 years and 7 months (approx.). The patients who made three transitions on an average survive for 3 years and 8 months. Patients who reach death state after HCC state takes longer time as compared to patients who reaches death state after cirrhosis, a possible reason for this could be that the probability of death is higher when the patient is in HCC state ($p = 0.146$) and after contracting HCC (liver cancer) the survival is remote and death happens almost within 16 months. Patient takes time to reach to HCC state from cirrhosis state but from HCC state patient reach to death state in very short span of time. Once the patient enters into HCC state then the probability of death is very high.

The primary goal of timely clinical check-ups is not aimed merely at early detection of a disease condition but rather to improve outcome, such as reducing mortality, increasing survival time, improving quality of life or preventing complications, through effective early intervention. In the second part, we have described the method for estimating the survival time of the liver cirrhosis patients who are subjected to stochastic deterioration and failure induced by various stage of chronic liver disease. Under reasonable assumptions, we estimated the survival time of liver cirrhosis patients when the length of time interval between two preventive maintenance check-ups follows Weibul distribution. It has been show that as the time between the preventive maintenance check-ups increases the survival time of the liver cirrhosis patients decreases. Thus, the results of this study document that regular clinical check-ups can lead to a significant improvement in the health of patients suffering from liver cirrhosis and could reap substantial reductions in the total mortality.

Therefore, from authors' point of view a further improvement of the model could be that of extending the model by taking more transitions states. Also, any distribution other than Weibul can be applied under preventive maintenance policy (PMP) to evaluate the survival time.

References

[1] Sim SH, Endrenyi J. (1988). Optimal preventive maintenance with repair. IEEE Trans Reliability, 37(1), 92-96.
[2] Legat V, Zaludova AH, Cervenka V, Jurca V. (2001). Contribution to optimization of preventive maintenance. Reliability Engineering and system safety, 71, 33-44.
[3] Vaurio JK. (1997). On time-dependant availability and maintenance optimization of standby units under various maintenance policies. Reliability Engineering and system safety, 56, 79-89.
[4] Gertsbakh I. (2000). Reliability theory-With application to preventive maintenance. Springer, New York.
[5] Park K. (1988a). Optimal continuous wear-Limit replacement under periodic inspections. IEEE Trans. Reliability, 37, 97-102.
[6] Park K. (1988b). Optimal wear-Limit replacement with wear-dependent failures. IEEE Trans. Reliability, 37, 293-294.
[7] Barlow RE, Proschan F. (1965). Mathematical Theory of Reliability. New York, Wiley.
[8] Biswas S and Abid MA. (1991). Optimal time of periodic check-up preventive maintenance scheme under Bath-tub and Weibull type failure rates.

International journal of systems sciences, 22(12), 2651-2661.

[9] Gray HL, Thompson RW and McWilliams GV. (1969), Anew Approximation for Chi-square Integral, Math. Comput, 23, 85.

[10] Lee ET. (2003). Statistical Methods for Survival Data Analysis, 3rd edition, Wiley Interscience publication, John Wiley and Sons, INC.