Chapter 4

GENERALIZED EXPONENTIAL MODEL

\footnote{This chapter is based on T. D. Xavier and M. Manoharan (2007)}
4.1 Introduction

Censoring is a common feature in clinical trials. A Generalized Exponential Model under a more flexible and practical censoring scheme namely Type II progressive interval censoring with random removals (PICR) is appropriate in many situations like follow-up studies in organ transplant, chemotherapy and/or surgical treatment for various cancers etc. The patients are examined only at fixed regular intervals or when reporting for checkup at the hospital so that one can observe the patient only at that specified points of time. The survival time of some of these patients cannot be observed exactly since some of them withdraw from study due to the reasons only known to them.

In type II interval censoring 'n' subjects are selected in a life test, inspections are conducted at pre-determined intervals and the number of 'failures' occurring between two successive inspection times are recorded. The study will be terminated when the total number of failures is greater than or equal to a pre-assigned number 'm'. A handicap of this censoring scheme is that we could not utilize the sensitive information of drop-outs in the study. There are many real life situations, in particular clinical study, where one may come across more complicated censoring scheme combining the features of Type II censoring, interval censoring and progressive censoring with random removals. When the total time of study and the number of failed subjects are random outcomes, such a scheme is highly warranted. Xing and Tse (2005) in a clinical trial investigated a Weibull model under the censoring scheme called Type II
PICR to cope with the setting that patients are examined at fixed regular intervals and dropouts occur during the study period. In Type II PICR, the individual are examined at fixed regular intervals, at each examination the number of both dropouts and failed individuals are recorded, the study will be terminated when a pre-specified number of failed individuals are observed.

Although Weibull distribution is a popular life time distribution on account of its several advantages, the maximum likelihood estimates of the Weibull parameters may not behave properly for all parametric values even when location parameter is zero (see Bain (1978)). Also the monotonicity of Weibull hazard function reaching an infinite value when the shape parameter is greater than one, may not be appropriate in many situations. The Weibull family does not enjoy likelihood ratio ordering property like gamma family, making the problem of one sided hypothesis testing extremely difficult. Further the distribution of the mean of random sample from the Weibull distribution is not simple to compute though its distribution function has a simple form.

Gupta and Kundu (1999) introduced generalized exponential (GE) family that has some interesting features very similar to those of Weibull family and gamma family but a nice alternative to them in many situations. The generalized exponential distribution is a two-parameter distribution having distribution function

\[ F(x) = (1 - e^{-\beta x})^\alpha, \quad x > 0, \ (\alpha, \beta > 0) \]

where \( \alpha \) is the shape parameter and \( \beta \) is the scale parameter. Its density function is
given by

\[ f(x; \alpha, \beta) = \alpha \beta (1 - e^{-\beta x})^{\alpha - 1} e^{-\beta x}; x > 0 \]

It is interesting to note the similarities of the density and distribution function of GE family with corresponding gamma family and Weibull family. If the shape parameter \( \alpha = 1 \), then all the three distributions coincide with the one-parameter exponential distribution. Therefore all the three distributions are extensions or generalizations of the exponential distribution, different ways. If \( X \) has an exponential distribution with moment generating function (mgf) \( M_E(t) \) and distribution function \( F_E(x) \), and similarly, subscript symbols G, W and GE respectively represent gamma, weibull and generalized exponential distributions, then it is well known that \( M_G(t) = (M_E(t))^\alpha \) and \( F_W(x) = F_E(x^\alpha) \). The GE distribution is such that \( F_{GE}(x) = (F_E(x))^\alpha \). It can be said that GE distribution is the distribution of maximum of \( \alpha \) (an integer) number of i.i.d exponential variables. From the form of density function of the GE distribution, we see that, if \( \alpha \leq 1 \), the density function is strictly decreasing function, where as if \( \alpha > 1 \), it is a unimodel skewed density function.

If \( X \sim GE(\alpha, \beta) \), the survival function and hazard function are given by

\[ S(t; \alpha, \beta) = 1 - F(t) = 1 - (1 - e^{-\beta t})^\alpha; t > 0 \quad (4.1.1) \]

\[ h(t; \alpha, \beta) = \frac{f(t; \alpha, \beta)}{S(t; \alpha, \beta)} = \frac{\alpha \beta (1 - e^{-\beta t})^{\alpha - 1} e^{-\beta t}}{1 - (1 - e^{-\beta t})^\alpha}; t > 0 \quad (4.1.2) \]

If \( \alpha = 1 \), the hazard function becomes \( \beta \), independent of \( x \)

For the Weibull distribution, if \( \alpha > 1 \), the hazard function increases from zero to
\( \infty \) and if \( \alpha < 1 \), the hazard function decreases from \( \infty \) to zero. Many authors point out that because for the gamma distribution (for \( \alpha > 1 \)), the hazard function increases from zero to a finite number, the gamma may be more appropriate as a population model when the items in the population are in a regular maintenance program. The hazard rate may increase initially, but after some time the system reaches a stable condition because of maintenance. The same comments hold for the GE distribution. Therefore, if it is known that the data are from regular environment, it may make more sense to gamma distribution or the GE distribution than the Weibull distribution.

**Type II Progressive Interval Censoring with Random Removals**

We follow the discussion on Type II PICR scheme of chapter I. Suppose that \( n \) subjects are randomly selected for the study and when specified number or percentage of total \( m \) (say) or more subjects are failed, the study will be terminated. Let \( t_1, t_2, \ldots \) be the predetermined inspection times and \( t_0=0 \). Under a Type II PICR censoring scheme, the study is terminated after the \( k^{th} \) inspection time if the total number of failed subjects is equal to or more than \( m \). At the \( i^{th} \) inspection, \( d_i \) failed subjects are observed and \( R_i \) subjects are randomly removed from the test. In other words, \( d_i \) is the number of failed subjects between any two successive inspections at \( t_{i-1} \) and \( t_i \). Thus, \( R_i \) and \( d_i \) are random variables obtained from the study. Let us denote \( Y_j = \sum_{i=1}^{j} d_i \) the total number of failed subjects observed upto the \( j^{th} \) inspection.
time \( t_j \). If \( Y_{k-1} < m \) and \( Y_k \geq m \), for the predetermined integer \( m \), \( 0 \leq m \leq n \); the test is terminated at the \( k^{th} \) inspection time \( t_k \). Denote \( D = (d_1, d_2, d_k) \) and \( R = (R_1, R_2, ..., R_{k-1}) \) where \( k \) is random and corresponds to the number of inspections before the termination of the experiment \( t_k \).

Now we discuss exponential, Weibull and generalized exponential model for the survival times under the type II PICR censoring scheme.

**Exponential Model:**

Assume that the survival time \( T \) follows an exponential distribution with parameters \( \beta \). The probability density function of \( T \) is given by

\[
f(t) = \beta e^{-\beta t}, \quad t > 0 \quad (\beta > 0).
\]  

(4.1.3)

The cumulative distribution function \( F(t) \) is given by

\[
F(t) = 1 - e^{-\beta t}, \quad t \geq 0
\]

In order to derive the joint likelihood function based on the observations under this set up, we first consider the following conditional joint probability density function. The conditional joint probability density function of number of observations \( d_i \) and
k, conditional on \( R_i \)

\[
f(d_1, ..., d_k, k|R) = \binom{n}{d_1} \binom{n - d_1 - R_1}{d_2} \cdots \binom{n - \sum_{j=1}^{k-1} d_j - \sum_{j=1}^{k-1} R_j}{d_k} \\
\times \prod_{i=1}^{k} (p_{i-1} - p_i)^{d_i} (1 - p_i)^{R_i} \tag{4.1.4}
\]

where \( R_k = n - \sum_{j=1}^{k} d_j - \sum_{j=1}^{k-1} R_j \)

\( p_0 = 0, \quad p_i = 1 - e^{-\beta t_i} \) for \( i = 1, 2, ..., k - 1 \), \( p_{k+1} = 1 \).

**Weibull Model:**

Assume that the survival time \( T \) follows a Weibull distribution with parameters \( \alpha \) and \( \beta \), where \( \alpha \) is the scale parameter and \( \beta \) is the shape parameter. The probability density function of \( T \) is given by

\[
f(t) = \frac{\beta}{\alpha} \left( \frac{t}{\alpha} \right)^{\beta-1} exp \left[ - \left( \frac{t}{\alpha} \right)^{\beta} \right], \quad ; \alpha, \beta, t > 0 \tag{4.1.5}
\]

The cumulative distribution function \( F(t) \) is given by

\[
F(t) = 1 - exp \left[ - \left( \frac{t}{\alpha} \right)^{\beta} \right], \quad for \ t \geq 0
\]

Now the joint probability density function of number of observations \( d_i \) and \( k \), conditional on \( R_i \)
\[ f(d_1, ..., d_k, k|R) = \binom{n}{d_1} \binom{n-d_1-R_1}{d_2} \cdots \binom{n-\sum_{j=1}^{k-1} d_j-R_{j-1}}{d_k} \times \prod_{i=1}^{k} (p_{i-1} - p_i)^{d_i} (1 - p_i)^{R_i} \]  

where \( R_k = n - \sum_{j=1}^{k} d_j - \sum_{j=1}^{k-1} R_j \) 

\[ p_0 = 0, \quad p_i = 1 - \exp \left[ - \left( \frac{t_i}{\alpha} \right)^{\beta} \right] \quad \text{for} \quad i = 1, 2, ..., k, \quad p_{k+1} = 1. \]

Xiang and Tse(2005) discussed the maximum likelihood estimators of the parameters of this model under progressive interval censoring with random removals.

### 4.2 The Generalized Exponential Model

We assume that the survival time \( T \) follows a generalized exponential distribution with parameters \( \alpha \) and \( \beta \), where \( \alpha \) is the shape parameter and \( \beta \) is the scale parameter.

The probability density function of \( T \) is given by

\[ f(t) = \alpha \beta (1 - e^{-\beta t})^{\alpha - 1} e^{-\beta t}; \alpha, \beta, t > 0 \]  

(4.2.1)

The cumulative distribution function \( F(t) \) is given by

\[ F(t) = (1 - e^{-\beta t})^\alpha, \quad \text{for} \quad t \geq 0 \]
Now the joint probability density function of number of observations $d_i$ and $k$, conditional on $R_i$, can be derived inductively following Xiang and Tse (2005).

$$
f(d_1, ..., d_k, k|R_i) = \left(\frac{n}{d_1}\right) \left(\frac{n - d_1 - R_1}{d_2}\right) \cdots \left(\frac{n - \sum_{j=1}^{k-1} d_j - \sum_{j=1}^{k-1} R_j}{d_k}\right) \times \prod_{i=1}^{k} (p_{i-1} - p_i)^{d_i} (1 - p_i)^{R_i}$$

(4.2.2)

where $R_k = n - \sum_{j=1}^{k} d_j - \sum_{j=1}^{k-1} R_j$.

$p_0 = 0, \quad p_i = (1 - e^{-\beta_i})^\alpha \text{ for } i = 1, 2, ..., k - 1, \quad p_{k+1} = 1.$

If $R_i$ is assumed to follow a binomial distribution with parameter $\lambda$, the probability of $r_i$ subjects removed from the study at the $i^{th}$ inspection time is given by

$$Pr(R_i = r_i|R_{i-1} = r_{i-1}, ..., R_1 = r_1) = \binom{n_i - m}{r_i} \lambda^{r_i} (1 - \lambda)^{r_{i+1} - m}$$

(4.2.3)

where $n_i = n - \sum_{j=1}^{i-1} r_j, \quad 0 \leq r_i \leq n_i - m \text{ for } i = 1, 2, ..., k - 1$

We have the joint distribution of $D = (d_1, d_2, ..., d_k)$ and $R = (R_1, R_2, ..., R_{k-1})$ obtained as follows

$$P(R, \lambda) = Pr(R_{k-1} = r_{k-1}|R_{k-2} = r_{k-2}, ..., R_1 = r_1) \times Pr(R_{k-2} = r_{k-2}|R_{k-3} = r_{k-3}, ..., R_1 = r_1) \times \cdots \times Pr(R_2 = r_2|R_1 = r_1) Pr(R_1 = r_1)$$

$$= \binom{n_k - m}{r_{k-1}} \binom{n_{k-2} - m}{r_{k-2}} \cdots \binom{n_2 - m}{r_2} \binom{n_1 - m}{r_1} \lambda^{\sum_{j=1}^{k-1} r_j} \prod_{j=1}^{k-1} \frac{r_j! (n_j - m)!}{(n_j - m - r_j)!} \lambda^{\sum_{j=1}^{k-1} r_j} (1 - \lambda)^{(k-1)(n-m) - \sum_{j=1}^{k-1} (k-j)r_j}$$

(4.2.4)

Therefore, the joint likelihood function based on the observations $D = (d_1, d_2, ..., d_k)$
and \( R = (R_1, R_2, ..., R_{k-1}) \) can be written as

\[
L(\theta, \lambda, k, D, R) = f(d_1, ..., d_k, k; \theta | R) \times P(R, \lambda)
\]  \hspace{1cm} (4.2.5)

**Remark 4.2.1** Type II censoring, interval censoring and progressive censoring are particular cases of Type II PICR censoring scheme because the later combines the features of all the above three with a provision to accommodate dropouts. Thus, the probability density function under Type II progressive censoring is obtained as a special case of Eq. (4.2.2) when all \( d_i \)'s are fixed to be 1 and \( t_i = T(i) \), where \( T(i) \) is the \( i \)th ordered survival time. When \( R_i = 0 \) for all \( i \), we have the Type II censoring. On the other hand \( R_i = 0 \) for all \( i \) and \( m = n \), it will be the interval censoring.

### 4.3 Parameter Estimation

The maximum likelihood estimate of \( \lambda \) can be obtained directly by maximizing the Eqn.(4.2.4) because \( f(d_1, ..., d_k, k; \theta | R) \) does not depend on \( \lambda \). Gupta and Kundu (1999, 2000) studied the properties of maximum likelihood estimators(MLEs) of the parameters of GE distribution based on complete sample. They compared the MLEs with the other estimators like method of moments estimators, estimators based on percentages, least square estimators, weighted least square estimators etc. mainly with respect to their biases and mean square errors(MSEs)using extensive simulation technique. Further it is established that, the MLE works the best in almost all cases considered for estimating both \( \alpha \) and \( \beta \). Also the computational complexity
is minimal for MLE. For moderate or large sample sizes MLEs are well preferred to any other method. Hence we follow the maximum likelihood method estimation in the present context of Type II PICR censoring scheme.

Now normal equations are

$$\frac{\partial \ln L}{\partial \alpha} = 0 \Rightarrow \sum_{i=1}^{k} \left[ \frac{d_i}{p_i - p_{i-1}} \left( \frac{\partial p_i}{\partial \alpha} - \frac{\partial p_{i-1}}{\partial \alpha} \right) - \frac{p_i R_i \ln (1 - e^{-\beta t_i})}{1 - p_i} \right] = 0 \quad (4.3.1)$$

$$\frac{\partial \ln L}{\partial \beta} = 0 \Rightarrow \sum_{i=1}^{k} \left[ \frac{d_i}{p_i - p_{i-1}} \left( \frac{\partial p_i}{\partial \beta} - \frac{\partial p_{i-1}}{\partial \beta} \right) + \alpha R_i e^{-\beta t_i} (1 - e^{-\beta t_i})^{\alpha - 1} \right] = 0 \quad (4.3.2)$$

$$\frac{\partial \ln L}{\partial \lambda} = 0 \Rightarrow \frac{1}{\lambda} \sum_{j=1}^{k-1} R_j - \frac{1}{\lambda} \left[ (k - 1)(n - m) - \sum_{j=1}^{k-1} (k - j) R_j \right] = 0 \quad (4.3.3)$$

where \( \frac{\partial p_i}{\partial \alpha} = p_i \log(1 - e^{-\beta t_i}), \quad \frac{\partial p_i}{\partial \beta} = \alpha t_i e^{-\beta t_i} (1 - e^{-\beta t_i})^{\alpha - 1}. \)

The MLE of \( \lambda \) is easily obtained from Eqn.( 4.3.3), as

$$\hat{\lambda} = \frac{\sum_{j=1}^{k-1} R_j}{(k - 1)(n - m) - \sum_{j=1}^{k-1} (k - j) R_j} \quad (4.3.4)$$

On the other hand the MLE of \( \alpha \) and \( \beta \) can be solved from Eqn.( 4.3.1) and Eqn.( 4.3.2) by using iterative algorithms like Newton-Raphson method. Denote the Fisher information matrix associated with \( \alpha, \beta \) and \( \lambda \) by \( I(\alpha, \beta, \gamma) \), we write the partitioned form as follows

$$I(\alpha, \beta, \gamma) = E \begin{pmatrix}
\frac{\partial^2 \ln L}{\partial \alpha^2} & \frac{\partial^2 \ln L}{\partial \alpha \partial \beta} & 0 \\
\frac{\partial^2 \ln L}{\partial \alpha \partial \beta} & \frac{\partial^2 \ln L}{\partial \beta^2} & 0 \\
0 & 0 & \frac{\partial^2 \ln L}{\partial \lambda^2}
\end{pmatrix}$$

$$= \begin{pmatrix}
I_1(\alpha, \beta) & 0 \\
0 & I_2(\lambda)
\end{pmatrix} \quad (4.3.5)$$

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From the Eqns.(4.3.1) to (4.3.3), the second-order partial derivatives are

\[
\frac{\partial^2 \ln L}{\partial \alpha^2} = \sum_{i=1}^{k} \left[ \frac{d_i}{p_i - p_{i-1}} \left( \frac{\partial^2 p_i}{\partial \alpha^2} - \frac{\partial^2 p_{i-1}}{\partial \alpha^2} \right) - \frac{d_i}{(p_i - p_{i-1})^2} \left( \frac{\partial p_i}{\partial \alpha} - \frac{\partial p_{i-1}}{\partial \alpha} \right)^2 \right] - \sum_{i=1}^{k} \left[ \frac{p_i R_i \ln(1 - e^{-\beta t_i})^2}{(1 - p_i)^2} \right]
\]

(4.3.6)

\[
\frac{\partial^2 \ln L}{\partial \beta^2} = \sum_{i=1}^{k} \left[ \frac{d_i}{p_i - p_{i-1}} \left( \frac{\partial^2 p_i}{\partial \beta^2} - \frac{\partial^2 p_{i-1}}{\partial \beta^2} \right) - \frac{d_i}{(p_i - p_{i-1})^2} \left( \frac{\partial p_i}{\partial \beta} - \frac{\partial p_{i-1}}{\partial \beta} \right)^2 \right] - \alpha \sum_{i=1}^{k} \left[ \frac{p_i R_i t_i^2 (\alpha - e^{\beta t_i} (1 - p_i))}{(1 - e^{-\beta t_i})^2 (1 - p_i)^2} \right]
\]

(4.3.7)

\[
\frac{\partial^2 \ln L}{\partial \alpha \partial \beta} = \sum_{i=1}^{k} \left[ \frac{d_i}{p_i - p_{i-1}} \left( \frac{\partial^2 p_i}{\partial \alpha \partial \beta} - \frac{\partial^2 p_{i-1}}{\partial \alpha \partial \beta} \right) - \frac{d_i}{(p_i - p_{i-1})^2} \left( \frac{\partial p_i}{\partial \alpha} - \frac{\partial p_{i-1}}{\partial \alpha} \right) \left( \frac{\partial p_i}{\partial \beta} - \frac{\partial p_{i-1}}{\partial \beta} \right) \right] + \sum_{i=1}^{k} \left[ \frac{p_i R_i t_i (1 - p_i + \alpha \ln(1 - e^{-\beta t_i}))}{(1 - e^{\beta t_i})(1 - p_i)^2} \right]
\]

(4.3.8)

\[
\frac{\partial^2 \ln L}{\partial \lambda^2} = - \left( \frac{\sum_{i=1}^{k-1} R_j}{\lambda^2} + \frac{(k-1)(n-m) - \sum_{i=1}^{k-1} (k-j) R_j}{(1 - \lambda)^2} \right)
\]

(4.3.9)

where \( \frac{\partial^2 p_i}{\partial \alpha^2} = p_i \ln(1 - e^{-\beta t_i})^2, \frac{\partial^2 p_i}{\partial \beta^2} = \frac{\alpha p_i t_i^2 (e^{-\beta t_i} - e^{-\beta t_{i-1}})}{(e^{-\beta t_i} - 1)^2} \) and \( \frac{\partial^2 p_i}{\partial \alpha \partial \beta} = \frac{p_i t_i (1 + \alpha \ln(1 - e^{-\beta t_i}))}{e^{-\beta t_{i-1}}} \).

Remark 4.3.1 The closed form of expression of the expected values of these second order partial derivatives are not readily available. These terms can be evaluated by using numerical method. The standard errors of the estimators can be evaluated by using expressions (4.3.6), (4.3.7) and (4.3.9) The joint assymptotic distribution of the MLE of \( \alpha \) and \( \beta \) is multivariate normal and in particular \( (\sqrt{n}(\hat{\alpha} - \alpha), \sqrt{n}(\hat{\beta} - \beta)) \sim N_2(0, n I_1(\alpha, \beta)) \) where \( I_1(\alpha, \beta) \) is given by (4.3.5).
4.4 An Illustrative Example

We shall illustrate the methodology using a hypothetical data on leukemia patients. Suppose that a group of 70 leukemia patients was considered, end of every month progress of the group was recorded. However during the course of study some of the patients had to be removed from the study because they developed other infections. The study was terminated after majority of them (60 %) died. The following table shows its details

<table>
<thead>
<tr>
<th>Month</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>$d_i$</td>
<td>6</td>
<td>5</td>
<td>8</td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>$r_i$</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

where $d_i$=number of patients died during the $i^{th}$ month and $r_i$=number of patients removed from the study at the $i^{th}$ month.

The data from the study can be fitted into the GE model. Here $n=70$ and $m=42$. From the normal equations 3.1 and 3.2, the maximum likelihood estimate of $\alpha$ and $\beta$ are obtained as $\hat{\alpha}=1.1563$ and $\hat{\beta}=0.2069$ with standard errors 0.618 and 0.146 respectively. The MLE of the removal probability $\hat{\lambda}=0.1234$ with standard errors 0.0403

Remark 4.4.1 The figure shows graph of Survival function $S(t)$ of both Weibull and GE model for the data given in the example. It may be noted that the two graph shows almost perfect agreement and hence it suggests that the proposed GE-model can be used as an alternative to the Weibull model.
4.5 Discussion

The type II progressive interval censoring with random removals is a more flexible and practical censoring scheme since it integrates the features of Type II censoring, interval censoring and progressive censoring with random removals. The GE distributions are more flexible than gamma and as flexible as Weibull distributions (the distribution function of GE is in a closed form, the inference based on the censored data can be handled more easily than with gamma). Therefore the GE model can be used as a better alternative for analyzing lifetime data.