Order Restricted Inference for a Multiple Step-Stress Model with Long-term Survivors for a General Family of Distributions

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Abstract

In this article, we propose a failure rate based step-stress accelerated life testing (SSALT) model assuming that the time-to-event distribution belongs to a fairly general family of distributions and the underlying population consists of long term survivors. With increase in stress levels, it is expected that the mean time to the event of interest gets shortened leading to an order restriction among the mean times-to-event. We propose here a method of obtaining order restricted maximum likelihood estimators(MLEs) based on expectation maximization (EM) algorithm coupled with the method of generalized isotonic regression technique. Additionally, we address the testing of hypothesis problem for the presence of long term survivors in the underlying population based on both asymptotic and non-asymptotic approaches. To illustrate the effectiveness of the proposed method, extensive simulation experiments are carried out and a real data set is analyzed.

Key Words: Step-stress model; cure rate; failure rate based SSALT model; EM algorithm; maximum likelihood estimator; isotonic regression; confidence interval.

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1 Introduction

In reliability and survival analysis, the general perception is that the event of interest (death of patient, recurrence of disease, failure of an item etc.) is bound to happen for units (individuals/items/devices) if followed up for a long period. However, in many contexts, there might be a substantial proportion of units not experiencing the event of interest even if followed up for long. These units are referred to as "long term survivors" or "immunes" or "cured." Cure rate models are well known in statistics to model time-to-event data in presence of long term survivors. For a detailed insight into the cure rate models, see the monograph by Maller and Zhou [10]. For some of the recent references, see for example Kannan and Kundu [7], Balakrishnan and Pal [2], Wiangnak and Pal [19], Gallardo et al. [5] and the references cited therein.

Step-stress accelerated life testing (SSALT) experiment is often used to ensure a faster rate of occurrence of the event of interest, and hence it aids in obtaining information quickly about the lifetime characteristics. In this experiment, the experimenter makes the testing conditions severe usually at pre-fixed intermediate time points of the experiment. A SSALT experiment can be briefly described as follows. Suppose, n units are subjected to a life testing experiment at an initial stress level s_1 and then the stress level is gradually increased to $s_2 < s_3 < \ldots < s_{m+1}$ at pre-fixed times $\tau_1 < \tau_2 < \ldots < \tau_m$, respectively. The experimenter can fix either (a) the total duration $\tau > \tau_m$ -Type-I censoring or (b) the observed value $r\ (0 < r < n)$ of the total number of events of interest (R) -Type-II censoring.

Two most common models, namely the cumulative exposure model (CEM), proposed by Sedyakin [17], and the tampered failure rate model (TFRM), introduced by Bhattacharyya and Soejoeti [3], are being used to analyze the data obtained from SSALT experiment. An extensive amount of work has been done in this area, see for example the recent monograph by Kundu and Ganguly [9] and the references cited therein. Recently Kateri and Kamps [8] introduced a very flexible failure rate-based SSALT model. It states that the overall hazard function $h(t)$ under the step-stress pattern for $i = 1, 2, \ldots, m + 1$, is given by

$$h(t)= \begin{cases} h_1(t) & \text{if} \quad 0 < t \leq \tau_1 \\ h_i(t) & \text{if} \quad \tau_{i-1} < t \leq \tau_i. \end{cases}$$

where $h_i(.)$ is the hazard function corresponding to the time-to-event distribution at the $i-$ th stress level. Based on this model, inferential treatment of SSALT data is considered recently by some authors, see for example Pal et al. [11, 13] and Samanta and Kundu [16].

Recently, Kannan and Kundu [7] discussed about a study on altitude decompression sickness(DCS) conducted by the Air Force Research Laboaratory(AFRL). The "gradual staged ascent" profile experiment discussed in this article turns out to be an important instance of a SSALT experiment in the presence of "long term survivors" or "cured fraction". In this paper, we assume that the time-to-event distribution of the experimental units belongs to a proportional hazard (PH) family of distributions. Notable distributions of PH family include distributions like Weibull, Burr XII, Lomax, Gompertz, Pareto and so on. Because of the various shapes of the PDFs and their convenient representation of the distribution/survival functions, different members of the PH family can be used very effectively for analyzing time-to-event data in presence of censoring (see Pal and Prajapati [12] in this respect).

In a SSALT experiment, it seems very natural to assume that the mean time-to-event for the experimental units is lower at the higher stress level giving rise to an order restriction among the model parameters. Balakrishnan et al. [1] first incorporated this information and considered the order restricted estimation of model parameters for exponentially distributed lifetimes. Recently, Samanta et al. [14], Samanta and Kundu [15] and Pal et al. [11] also considered this problem for some of the other related distributions. However, in all these cases, it has been assumed that the units in the underlying population will eventually experience the event of interest if followed up for long.

In this context, this article aims at a very relevant two-fold consideration. Firstly, it develops the failure rate based multiple SSALT model for a general PH family of distributions in presence of long term survivors. Secondly, it addresses the associated order restricted

inference and its computational ease in implementation based on a number of real life scenarios. The order restricted estimation procedure has been developed based on EM algorithm and generalized isotonic regression technique. Extensive simulations have been performed to show the effectiveness of the proposed method. We have developed a very effective testing procedure to test whether a immune fraction is present in the population or not. The test is mainly for small sample sizes, and it is based on bootstrap method.

Rest of the paper is organized as follows. In Section 2, we provide the model and state the necessary assumptions. The estimation procedure has been developed in Section 3. In Section 4, we address the testing of hypothesis problem. Extensive simulation results have been presented in Section 5. Analysis of one real life data set is carried out for illustration in Section 6 and finally, we conclude the paper in Section 7.

2 Model Assumptions in the Presence of Cured Group

Suppose the experiment starts with n units at the initial stress level s_1 at time point 0. At pre-fixed time points $\tau_1 < \tau_2 < \ldots < \tau_m$, the stress level elevates to $s_2, s_3, \ldots, s_{m+1}$, respectively. The experiment continues until a fixed censoring time τ is reached with $\tau > \tau_m$ (Type-I censoring). If all the units experience the event of interest before τ, the experiment stops at the $n-$th time-to-event. Let us assume that n_k is the number of times-to-event under stress level s_k $(k = 1, \ldots, m+1)$ and $\bar{n}_j = \sum_{i=1}^{j} n_i$ is the total number of times-to-event upto the $j-$th stress level.

Under the failure rate based SSALT model consideration, we suppose that the time-to-event distribution corresponding to the stress level s_k belongs to the PH family with parameters α and λ_k. For $\alpha > 0$, $\lambda_k > 0$, the associated CDF $F_k(t)$ and hazard function (HF) $h_k(t)$ are given by

$$F_k(t) = \begin{cases} 1 - [1 - F_0(t;\alpha)]^{\lambda_k} & \text{if } t > 0 \\ 0 & \text{otherwise,} \end{cases}$$

and

$$h_k(t) \;=\; \lambda_k h_0(t;\alpha), \qquad k = 1, \ldots, m+1,$$

respectively, where $h_0(t;\alpha)$ is the baseline HF corresponding to the baseline CDF $F_0(t;\alpha)$. Since it is assumed that $F_1(\cdot), \ldots, F_{m+1}(\cdot)$ satisfy the failure rate based SSALT model assumptions, the overall HF is given by

$$h(t)= \begin{cases} \lambda_1 h_0(t;\alpha) & \text{if} \quad 0 < t \leq \tau_1 \\ \lambda_k h_0(t;\alpha) & \text{if} \quad \tau_{k-1} < t \leq \tau_k;\ k = 2, 3, \ldots, m+1. \end{cases}$$

Note that in case of no censoring, $\tau_{m+1} = \infty$. For the sake of brevity, from now on, $h_0(t;\alpha)$ and $F_0(t;\alpha)$ are denoted by $h_0(t)$ and $F_0(t)$ respectively. Using the one-to-one correspondence between the HF and the CDF, the overall CDF and the associated probability density function (PDF) for $k = 2, \ldots, m+1$ are given by

$$F(t)= \begin{cases} 0 & \text{if } t < 0 \\ 1 - [1 - F_0(t)]^{\lambda_1} & \text{if } 0 < t \leq \tau_1 \\ 1 - \Big\{ \prod_{j=1}^{k} [1 - F_0(\tau_j)]^{\lambda_j - \lambda_{j+1}} \Big\} [1 - F_0(t)]^{\lambda_{k+1}} & \text{if } \tau_{k-1} < t \leq \tau_k, \end{cases}$$

and

$$f(t)= \begin{cases} \lambda_1 [1 - F_0(t)]^{\lambda_1 - 1} f_0(t) & \text{if } 0 < t \leq \tau_1 \\ \Big\{ \prod_{j=1}^{k} [1 - F_0(\tau_j)]^{\lambda_j - \lambda_{j+1}} \Big\} \lambda_{k+1} [1 - F_0(t)]^{\lambda_{k+1} - 1} f_0(t) & \text{if } \tau_{k-1} < t \leq \tau_k, \\ 0 & \text{otherwise ,} \end{cases}$$

respectively. In real life examples, the underlying population often comprises of two groups of units - the group subject to the risk of the event of interest or the "susceptible group" and the group consisting of units who will never experience the event of interest with

respect to changes in stress level or the "cured group." The failure rate based SSALT model can be extended to include the cured units, which represents units resistant to change in stress factor levels. Based on the cure rate model, the overall survival function $\widetilde{S}_0(t)$ of the entire population can be expressed as

$$\widetilde{S}_0(t) \quad = P(T > t) = 1 - p + pS(t),$$

where $1 - p = \widetilde{S}_0(+\infty)$ is the proportion of immunes or the "cured fraction" and $S(t) = 1 - F(t)$ is the proper survival function corresponding to the "susceptible population". Associated with each unit under study, we define an indicator random variable Δ with

$$\Delta = \begin{cases} 1, & \text{if the unit belongs to the susceptible group} \\ 0, & \text{if the unit belongs to the cured group.} \end{cases}$$

Let us assume that $P\{\Delta = 1\} = p$ is the proportion of units at the risk of experiencing the event of interest and $P\{\Delta = 0\} = 1 - p$ is the cured fraction or the proportion of units who are stress resistant. Clearly, in this context, Δ is a latent random variable. If $\widetilde{S}_0(t; p, \boldsymbol{\theta}^*)$ denotes the survival function of a particular unit,

$$\widetilde{S}_0(t; p, \boldsymbol{\theta}^*) = 1 - p + pS(t; \boldsymbol{\theta}^*),$$

where $\boldsymbol{\theta}^*$ is the set of model parameters for the susceptible population and $S(t; \boldsymbol{\theta}^*)$ is the associated survival function for the susceptibles. In the next section, we discuss about the statistical inference of the unknown model parameters.

3 Point Estimation and Interval Estimation

Under Type-I censoring, the observed time-to-event data $\mathcal{D}$ obtained from the multiple SSALT experiment are given by

Table 1: Observed Type-I censored data ($\mathcal{D}$) .

Stress level	Observations	Stress-changing time point	Termination time
1	$t_{1:n} < \ldots < t_{\bar{n}_1:n}$	τ_1	
2	$t_{\bar{n}_1+1:n} < \ldots < t_{\bar{n}_2:n}$	τ_2	
$\vdots$	$\vdots$	$\vdots$	
m	$t_{\bar{n}_{m-1}+1:n} < \ldots < t_{\bar{n}_m:n}$	τ_m	
m +1	$t_{\bar{n}_m+1:n} < \ldots < t_{\bar{n}_{m+1}:n}$		τ

Here, $\bar{n}_{m+1}$ is the total number of units experiencing the event of interest and their times-to-event are observed. The remaining $n - \bar{n}_{m+1}$ units $t_{\bar{n}_{m+1}+1:n} < \ldots < t_{n:n}$ are censored. Let $J_k = \{\bar{n}_{k-1} + 1, \bar{n}_{k-1} + 2, \ldots, \bar{n}_k\}$, $k = 1, 2, \ldots, m + 1$, denotes the set of indices for the units experiencing the event of interest at the $k-$th stress level with $\bar{n}_0 = 0$, whereas $J_{m+2} = \{\bar{n}_{m+1}+1, \bar{n}_{m+1}+2, \ldots, n\}$ denotes the set of indices for the censored units. Further assume that $J = J_1 \bigcup J_2 \bigcup \ldots \bigcup J_{m+1}$, and $\boldsymbol{\theta} = (p, \boldsymbol{\theta^*})$, the set of model parameters of interest. Note that here $\boldsymbol{\theta^*} = (\alpha, \lambda_1, \lambda_2, \ldots, \lambda_{m+1})$ is the set of parameters for the time-to-event distribution corresponding to the susceptible population.

3.1 Point Estimation

The log-likelihood function can be written as

$$\begin{aligned} l(\boldsymbol{\theta}|\mathcal{D}) &= \sum_{i \in J} \ln p + \sum_{k=1}^{m+1} n_k \ln \lambda_k + \sum_{i=1}^{\bar{n}_{m+1}} \ln f_0(t_{i:n}) + \sum_{k=1}^{m+1} \sum_{i=\bar{n}_{k-1}+1}^{\bar{n}_k} (\lambda_k - 1) \ln[1 - F_0(t_{i:n})] \\ &\quad + \sum_{k=1}^{m} (\bar{n}_{m+1} - \bar{n}_k)(\lambda_k - \lambda_{k+1}) \ln[1 - F_0(\tau_k)] + \sum_{i \in J_{m+2}} \ln \Big\{1 - p + pS(\tau, \boldsymbol{\theta^*})\Big\} \quad (1) \end{aligned}$$

Here, $\widehat{\boldsymbol{\theta}}$ (the MLE of $\boldsymbol{\theta}$), can be obtained by maximization of the log-likelihood function (1) and it requires solving a $(m+3)$ dimensional optimization problem. In particular, the MLEs of any of the model parameters cannot be obtained in closed form and the complexity of the optimization problem grows as m increases. Under Type-I censoring, it is quite likely that one may end up with too few or even no observations in one or more stress levels. $\widehat{\boldsymbol{\theta}}$ will

exist provided $n_i \geq 1 \; \forall \, i = 1, 2, \ldots, m+1$, and $\bar{n}_{m+1} \geq m+3$.

However, the maximization problem gets simplified if we treat it as a missing data problem. For $i \in J$, the associated indicator random variable Δ_i takes the value 1. Otherwise, for $i \in J_{m+2}$, there can be two possibilities. The unit might belong to the cured group or it might belong to the susceptible group but the time-to-event is greater than τ. Thus, for $i \in J_{m+2}$, Δ_i is latent and hence $\delta_i^{'}$s (observed values of Δ_i) can be treated as missing. Combining the unobserved $\delta_i^{'}$s along with the observed data, the complete data set is constructed. The likelihood function based on the complete data can be obtained as

$$\begin{aligned} L_c(\boldsymbol{\theta}|\mathcal{D}) &= \Big\{\prod_{i\in J} p\Big\}\Big\{\prod_{k=1}^{m+1} \lambda_k^{n_k}\Big\} e^{-\sum_{i=1}^{m+1}\lambda_i E_i(\alpha)} \prod_{i\in J_{m+2}} \Big[\Big(1-p\Big)^{1-\delta_i}\Big] \\ &\quad \prod_{i\in J_{m+2}} p^{\delta_i} \prod_{i=1}^{\bar{n}_{m+1}} \frac{f_0(t_{i:n})}{1-F_0(t_{i:n})}, \end{aligned} \tag{2}$$

where

$$\begin{aligned} E_i(\alpha) &= \sum_{j=i}^{m+1} n_j \ln[1-F_0(\tau_{i-1})] - \sum_{j=\bar{n}_{i-1}+1}^{\bar{n}_i} \ln[1-F_0(t_{j:n})] + \sum_{j\in J_{m+2}} \delta_j \ln[1-F_0(\tau_{i-1})] \\ &\quad - \sum_{j\in J_{m+2}} \delta_j \ln[1-F_0(\tau_i)] - \sum_{j=i+1}^{m+1} n_j \ln[1-F_0(\tau_i)], \end{aligned} \tag{3}$$

with $\tau_0 = 0$, $\tau_{m+1} = \tau$. The corresponding complete log-likelihood function is given by

$$l_c(\boldsymbol{\theta}|\mathcal{D}) = g_1(p) + g_2(\boldsymbol{\theta}^*),$$

where

$$\begin{aligned} g_1(p) &= \sum_{i\in J} \ln p + \sum_{i\in J_{m+2}} (1-\delta_i)\ln(1-p) + \sum_{i\in J_{m+2}} \delta_i \ln p, \\ g_2(\boldsymbol{\theta}^*) &= \sum_{k=1}^{m+1} n_k \ln \lambda_k - \sum_{i=1}^{m+1} \lambda_i E_i(\alpha) + \sum_{i=1}^{\bar{n}_{m+1}} \ln f_0(t_{i:n}) - \sum_{i=1}^{\bar{n}_{m+1}} \ln[1-F_0(t_{i:n})]. \end{aligned} \tag{4}$$

Now, $g_1(p)$ and $g_2(\boldsymbol{\theta}^*)$ can separately be maximized to obtain the MLEs of p and $\boldsymbol{\theta}^*$

respectively. $\widehat{p}$, the MLE of p, can be computed by maximizing $g_1(p)$ defined in (4) and is obtained explicitly as

$$\widehat{p} = \frac{\bar{n}_{m+1} + \sum_{i \in J_{m+2}} \delta_i}{n}.$$

For fixed shape parameter α, MLEs of $\lambda_i^{'}$s can explicitly be obtained on maximizing $g_2(\boldsymbol{\theta}^*)$ and are given by

$$\widehat{\lambda}_k^{(\alpha)} = \frac{n_k}{E_k(\alpha)}, \quad k = 1, 2, \ldots, m+1.$$

To obtain $\widehat{\alpha}$, (MLE of α) , we need to maximize the profile log-likelihood function of α, say $k(\alpha)$, using some numerical routines, where

$$k(\alpha) \;=\; \sum_{i=1}^{\bar{n}_{m+1}} \ln f_0(t_{i:n}) - \sum_{i=1}^{\bar{n}_{m+1}} \ln[1 - F_0(t_{i:n})] - \sum_{i=1}^{m+1} n_i \ln E_i(\alpha).$$

This gives an extra edge over simplify maximizing (1) in terms of significant dimension reduction of the maximization problem. Hence, we propose to use the EM Algorithm.

Order Restricted Maximum Likelihood Estimation

In this subsection, we consider this additional information and hence we impose the natural order restriction on the scale parameters as

$$\lambda_1 \leq \ldots \leq \lambda_{m+1}. \tag{5}$$

Now, to obtain the order restricted MLEs of the unknown model parameters, one needs to maximize (1) with respect to p, α, $\lambda_1, \ldots, \lambda_{m+1}$ based on the natural order restriction given by (5). Even in the unrestricted case, direct maximization of (1) leads to solving a $(m+3)$ dimensional optimization problem for obtaining the MLEs. Thus, it is obvious that the optimization problem turns out to be much more challenging once the natural order

restriction is imposed. Based on the missing data principle, we propose to use here the EM algorithm to obtain the order restricted MLEs of the model parameters.

For proceeding further, let $I = \{1, 2, \ldots, m+1\}$ be the set of natural numbers up to $m+1$ and $\tilde{I} = \{i \in I | n_i \geq 1\}$. The elements of $\tilde{I}$ are denoted as $i_1, i_2, \ldots, i_{|\tilde{I}|}$. In this context, it is worth mentioning that even in the unrestricted case and in absence of cured fraction ($p = 1$), MLE of λ_i (for fixed α) will only exist if $n_i \geq 1$, $i = 1, 2, \ldots, m+1$. However, the probability of non-existence of the unrestricted MLEs drastically reduces if we consider the order restricted inference. To address this, we consider two scenarios (see Pal et al. [11] in this respect) of a multiple step-stress data often encountered in practice and provide some results.

Case 1: At least one time-to-event at every stress level.

When at least one time-to-event occurs at every stress level, clearly $\widetilde{I} = I = \{1, 2, \ldots, m+1\}$.
E-Step : In the E-Step, the expectation of the complete log-likelihood function with respect to the distribution of the unobserved $\delta_i's$ is computed given the current values of the parameter and the observed data $\mathcal{D}$. It is clear that $\Delta_i's$ are Bernoulli random variables in the complete log-likelihood and it is only required to compute $\pi_i^{(k)} = E(\Delta_i | \boldsymbol{\theta^{(k)}}, \mathcal{D})$, $i \in J_{m+2}$, where $\boldsymbol{\theta^{(k)}}$ denotes the current parameter value at the $k-$th iteration step. Now for $i \in J_{m+2}$, we have

$$\pi_i^{(k)} = E(\Delta_i | \boldsymbol{\theta^{(k)}}, \mathcal{D}) = P(\Delta_i = 1 | T_i > \tau; \boldsymbol{\theta^{(k)}}) = \frac{p^{(k)} S(\tau | \boldsymbol{\theta^*(k)})}{1 - p^{(k)} + p^{(k)} S(\tau | \boldsymbol{\theta^*(k)})},$$

and for $i \in J$, we simply have $\pi_i^{(k)} = \delta_i = 1$. Thus, the E-Step replaces the $\delta_i's$ in the log-likelihood by $\pi_i^{(k)}$ for $i \in J_{m+2}$ and by 1 for $i \in J$. Let us denote the conditional expectation of the complete data log-likelihood function by $Q(\boldsymbol{\theta}, \boldsymbol{\pi^{(k)}})$, where $\boldsymbol{\pi^{(k)}}$ is the vector of $\pi_i^{(k)}$ values. Thus,

$$Q(\boldsymbol{\theta}, \boldsymbol{\pi^{(k)}}) = k_1(p | \boldsymbol{\theta^{(k)}}) + k_2(\boldsymbol{\theta^*} | \boldsymbol{\theta^{(k)}}),$$

where

$$
\begin{aligned}
k_1(p|\boldsymbol{\theta^{(k)}}) &= \sum_{i\in J} \ln p + \sum_{i\in J_{m+2}} (1-\pi_i^{(k)}) \ln(1-p) + \sum_{i\in J_{m+2}} \pi_i^{(k)} \ln p, \\
k_2(\boldsymbol{\theta^*}|\boldsymbol{\theta^{(k)}}) &= \sum_{k=1}^{m+1} n_k \ln \lambda_k - \sum_{i=1}^{m+1} \lambda_i E_i(\alpha) + \sum_{i=1}^{\bar{n}_{m+1}} \ln f_0(t_{i:n}) - \sum_{i=1}^{\bar{n}_{m+1}} \ln[1-F_0(t_{i:n})], \\
E_i(\alpha) &= \sum_{j=i}^{m+1} n_j \ln[1-F_0(\tau_{i-1})] - \sum_{j=\bar{n}_{i-1}+1}^{\bar{n}_i} \ln[1-F_0(t_{j:n})] + \sum_{j\in J_{m+2}} \pi_j^{(k)} \ln[1-F_0(\tau_{i-1})] \\
&\quad - \sum_{j\in J_{m+2}} \pi_j^{(k)} \ln[1-F_0(\tau_i)] - \sum_{j=i+1}^{m+1} n_j \ln[1-F_0(\tau_i)], \qquad (6)
\end{aligned}
$$

with $\tau_0 = 0$, $\tau_{m+1} = \tau$. The revised form of $E_i(\alpha)$ defined in (6) is obtained from the initial form of $E_i(\alpha)$ defined in (3) by replacing the $\delta_i' s$ by $\pi_i^{(k)}$ for $i \in J_{m+2}$.

M-Step : In the M-Step of the EM algorithm, based on the order restriction (5), we maximize $Q(\boldsymbol{\theta}, \boldsymbol{\pi^{(k)}})$ with respect to $\boldsymbol{\theta}$, given $\boldsymbol{\pi^{(k)}}$ over the parameter space, to obtain an improved estimate of $\boldsymbol{\theta}$. To compute the order restricted MLEs at the $(k+1)-$th step, let us first consider the problem of maximizing the complete data log-likelihood function $Q(\boldsymbol{\theta}, \boldsymbol{\pi^{(k)}})$ under the order restriction $\lambda_1 \leq \ldots \leq \lambda_{m+1}$. The following lemma provides the MLEs of $\lambda_1, \lambda_2, \ldots, \lambda_{m+1}$ for fixed p and α, under $\lambda_1 \leq \ldots \leq \lambda_{m+1}$.

Lemma 1. *For fixed p and α, if $Q(\boldsymbol{\theta}, \boldsymbol{\pi^{(k)}})$ (or specifically $k_2(\boldsymbol{\theta^*}|\boldsymbol{\theta^{(k)}})$) is maximized under the restriction on the scale parameters $\lambda_1 \leq \ldots \leq \lambda_{m+1}$, the MLE $\widetilde{\lambda}_{x(k+1)}^{(\alpha)}$ of λ_x, for $x = 1, 2, \ldots, m+1$, at the $(k+1)-$th step is given by*

$$
\widetilde{\lambda}_{x(k+1)}^{(\alpha)} = \Big[\min_{s\leq x} \max_{t\geq x} \frac{\sum_{r=s}^{t} E_r(\alpha)}{\sum_{r=s}^{t} n_r} \Big]^{-1}, \quad s, t \in \tilde{I} = I.
$$

Proof. See Appendix. □

Remarks

1. $\widetilde{\lambda}_{x(k+1)}^{(\alpha)}$, the MLE of λ_x, for $x = 1, 2, \ldots, m+1$ does not depend on p.

2. Plugging in the order restricted scale estimates $\widetilde{\lambda}_{x(k+1)}^{(\alpha)}$ replacing λ_x in $Q(\boldsymbol{\theta}, \boldsymbol{\pi^{(k)}})$, we

obtain the profile log-likelihood function of p and α as follows

$$\begin{aligned} m_1^{k+1}(p,\alpha) &= \bar{n}_{m+1}\ln p + \sum_{j=1}^{m+1} n_j \ln \widetilde{\lambda}_{j(k+1)}^{(\alpha)} - \sum_{j=1}^{m+1} \widetilde{\lambda}_{j(k+1)}^{(\alpha)} E_j(\alpha) + \sum_{i\in J_{m+2}} (1-\pi_i^{(k)})\ln(1-p) \\ &\quad + \sum_{i\in J_{m+2}} \pi_i^{(k)} \ln p + \sum_{i=1}^{\bar{n}_{m+1}} \ln f_0(t_{i:n}) - \sum_{i=1}^{\bar{n}_{m+1}} \ln[1-F_0(t_{i:n})]. \end{aligned} \tag{7}$$

The following result provides the existence and uniqueness of the MLE of p for fixed α.

Lemma 2. *$m_1^{k+1}(p,\alpha)$ is a unimodal function of p for fixed α.*

Proof. See Appendix. □

3. $\widehat{p}^{(k+1)}$, the MLE of p, can be obtained explicitly as $\widehat{p}^{(k+1)} = \dfrac{\bar{n}_{m+1} + \sum_{i\in J_{m+2}} \pi_i^{(k)}}{n}$.

4. To find out $\widehat{\alpha}^{(k+1)}$, the MLE of α, we need to maximize the profile log-likelihood function of α, i.e., $m_1^{k+1}(\widehat{p}^{(k+1)},\alpha)$ using some numerical routines.

5. The order restricted MLEs considered here are conditional on the event that at least one time-to-event occurs at every stress level.

6. When at least one time-to-event occurs at every stress level, both the unrestricted and the order restricted MLEs exist.

However, in practice, no time-to-event may be present in one or more stress levels (see the Fish data set in Section 6). Hence, it becomes immensely important and practical to consider the following Case 2.

Case 2: No time-to-event in at least one stress level

In a multiple step-stress experiment, it is quite natural to have no times-to-event in one or more stress levels, especially when the stress changes are frequent. We assume here that there is no time-to-event in at least one of the stress levels except the first stress level (s_1).

Thus $\tilde{I} = \{i_1 = 1, i_2, \ldots, i_{|\tilde{I}|}\}$. Note that, $i_k \geq k$, $k = 2, \ldots, |\tilde{I}|$ with $|\tilde{I}| < m+1$. For fixed p and α, we first use the similar EM algorithm as discussed in Case 1 to obtain the MLEs of λ_i, $i \in \tilde{I}$, based on the natural order, i.e., $\lambda_{i_1} \leq \ldots \leq \lambda_{i_{|\tilde{I}|}}$. Let us denote $\widetilde{\boldsymbol{\theta}} = (p, \widetilde{\boldsymbol{\theta}}^*)$, where $\widetilde{\boldsymbol{\theta}}^* = (\lambda_{i_1}, \lambda_{i_2}, \ldots \lambda_{i_{|\tilde{I}|}})$. The E-step is exactly similar to that in Case 1, while in the M-Step, we have the following lemmas.

Lemma 3. *For fixed p and α, if $Q(\boldsymbol{\theta}, \boldsymbol{\pi}^{(k)})$ is maximized under the restriction on the scale parameters in the set $\tilde{I}$, i.e., under $\lambda_{i_1} \leq \ldots \leq \lambda_{i_{|\tilde{I}|}}$, the MLE $\widetilde{\lambda}^{(\alpha)}_{x(k+1)}$ of λ_x, for $x \in \tilde{I}$ is given by*

$$\widetilde{\lambda}^{(\alpha)}_{x(k+1)} = \Big[\min_{s \leq x} \max_{t \geq x} \frac{\sum_{r=s}^{t} E_r(\alpha)}{\sum_{r=s}^{t} n_r} \Big]^{-1}, \quad s, t \in \tilde{I}.$$

Proof. See Appendix. □

Lemma 4. *Under the order restriction on the scale parameters, for fixed p and α, there exists a solution for the maximization of the complete data log-likelihood function $Q(\boldsymbol{\theta}, \boldsymbol{\pi}^{(k)})$ iff the maximization is restricted to λ_x, $x \in I$. The solution $(\lambda_1^{*(\alpha)}, \lambda_2^{*(\alpha)}, \ldots, \lambda_{m+1}^{*(\alpha)})$ is then given by*

$$\lambda^{*(\alpha)}_{x(k+1)} = \widetilde{\lambda}^{(\alpha)}_{i(x)}, \quad x \in I,$$

where $i(x)$ is defined by $i(x) = max\{i \in \tilde{I} | i \leq x\}$.

Proof. See Appendix. □

Let us denote

$$\widetilde{\lambda}^{(\alpha)}_{i(k+1)} = \begin{cases} \widetilde{\lambda}^{(\alpha)}_{i(k+1)}, & \text{if } i \in \tilde{I} \\ \lambda^{*(\alpha)}_{i(k+1)}, & \text{if } i \in I \backslash \tilde{I}. \end{cases} \tag{8}$$

Remarks

1. $\widetilde{\lambda}^{(\alpha)}_{x(k+1)}$, the MLE of of λ_x, for $i_1 \leq x \leq i_{|\tilde{I}|}$ does not depend on p.

2. Plugging in the order restricted scale estimates $\widetilde{\lambda}^{(\alpha)}_{x(k+1)}$ of λ_x, for $x \in I$ in $Q(\boldsymbol{\theta}, \boldsymbol{\pi}^{(k)})$, we

obtain the profile log-likelihood function of p and α, say $m_2^{k+1}(p,\alpha)$ where

$$\begin{aligned} m_2^{k+1}(p,\alpha) &= \bar{n}_{m+1}\ln p + \sum_{i\in\widetilde{I}} n_i \ln \widetilde{\lambda}_{i(k+1)}^{(\alpha)} - \sum_{i\in I} \widetilde{\lambda}_{i(k+1)}^{(\alpha)} E_i(\alpha) + \sum_{i\in J_{m+2}} (1-\pi_i^{(k)})\ln(1-p) \\ &\quad + \sum_{i\in J_{m+2}} \pi_i^{(k)} \ln(p) + \sum_{i=1}^{\bar{n}_{m+1}} \ln f_0(t_{i:n}) - \sum_{i=1}^{\bar{n}_{m+1}} \ln[1-F_0(t_{i:n})]. \end{aligned} \tag{9}$$

Now, $m_2^{k+1}(p,\alpha)$ needs to be maximized to obtain the MLEs of p and α. The following result provides the existence and uniqueness of the MLE of p for fixed α.

Lemma 5. *$m_2^{k+1}(p,\alpha)$ is a unimodal function of p for fixed α.*

Proof. The proof is exactly same as the proof of Lemma 2. So we are omitting the proof. □

3. $\widehat{p}^{(k+1)}$, the MLE of p, can be obtained explicitly as $\widehat{p}^{(k+1)} = \dfrac{\bar{n}_{m+1} + \sum_{i\in J_{m+2}} \pi_i^{(k)}}{n}$.

4. $\widehat{\alpha}^{(k+1)}$, the MLE of α, can be obtained by maximizing the profile log-likelihood function $m_2^{k+1}(\widehat{p}^{(k+1)},\alpha)$ using any numerical maximization routine.

5. The order restricted MLEs considered here are conditional on the event that there is no time-to-event in at least one of the stress levels except the first stress level.

6. The unrestricted MLEs of the model parameters will not exist in this case. More importantly, order restricted inference is a natural alternative and will always be possible to carry out. Thus, it greatly reduces the probability of the non existence of the unrestricted MLEs.

3.2 Interval Estimation

Assuming the asymptotic normality of the MLEs, one can obtain the confidence intervals (CIs) for $\boldsymbol{\theta}$ using the observed information matrix $I = \left(\left(\dfrac{\partial l(\boldsymbol{\theta}|\mathcal{D})}{\partial\theta_i\partial\theta_j}\right)\right), i,j = 1,2,\ldots,m+3$, where $l(\boldsymbol{\theta}|\mathcal{D})$ is the log-likelihood function as defined in (1). The $100(1-\gamma)\%$ asymptotic

CIs for $\boldsymbol{\theta}$ are respectively

$$(\widehat{p} \pm z_{1-\frac{\gamma}{2}}\sqrt{V_{11}},\ \widehat{\alpha} \pm z_{1-\frac{\gamma}{2}}\sqrt{V_{22}},\ \widehat{\lambda}_1 \pm z_{1-\frac{\gamma}{2}}\sqrt{V_{33}}, \ldots, \widehat{\lambda}_{m+1} \pm z_{1-\frac{\gamma}{2}}\sqrt{V_{m+3m+3}}$$

where V_{ij} is the $(i,j)-$th element of the inverse of the observed Fisher information matrix I. This method is useful for its computational flexibility and provides good coverage probabilities (close to the nominal value) for large sample sizes. For low to moderate sample sizes, interval estimates of the model parameters can be obtained using the parametric bootstrap CIs -percentile bootstrap CIs and bias adjusted percentile (BCa) bootstrap CIs. Parametric bootstrap CIs are well studied in the absence of cured fraction and similar ideas can be used in our case (see Section 3.2 of Pal et al. [13] for construction of percentile bootstrap CIs and Section 4.2 of Pal et al. [11] for bias adjusted percentile (BCa) bootstrap CIs).

4 Testing of the Presence of Cured Fraction

It is important to test whether the underlying population consists of long term survivors or not. Thus, the testing of hypothesis problem boils down to

$$H_0 : p = 1 \quad \text{vs} \quad H_1 : p < 1. \tag{10}$$

Let us denote the maximized log-likelihood (MLL) values under H_0 and H_1 by l_0 and l_1, respectively.

Asymptotic approach

Since the range of p contains the boundary point 1, applying Theorem 3 of Self and Liang [18], it follows that

$$-2(l_0 - l_1) \sim \frac{1}{2} + \frac{1}{2}\chi^2_1. \tag{11}$$

For different models, the values of the test statistic $-2(l_0 - l_1)$ and the associated p-values

are recorded. Finally, based on the p-values the experimenter can decide whether to reject or not to reject the null hypothesis.

Non-asymptotic approach

If the sample size is not very big, the above asymptotic distribution (11) may not work well. Hence, the following parametric bootstrap (simulation) approach may be adopted to approximate the distribution of the test statistic $\text{LR} = -2((l_0 - l_1))$. The distribution of the LR statistic is constructed empirically under H_0 based on the following Algorithm.

Algorithm 1:

Step 1: Obtain the order restricted ML estimates of the model parameters under the null and the alternative hypothesis and compute the LR statistic.

Step 2: Generate a parametric bootstrap sample based on the order restricted ML estimates under H_0 as true parameters. For the generated sample, compute the LR statistic.

Step 3: Repeat **Step 2** large number of times (say B) which yield an empirical estimate of the distribution of the LR statistic under the null hypothesis.

Step 4: Estimate of the p-value is obtained by comparing the distribution obtained in **Step 3** with the LR value obtained in **Step 1**. In particular, the p-value is given by the proportion of bootstrap LR values that is larger or equal to the LR value from **Step 1.** Based on the ordered bootstrap LR values the critical value, say C^{β}, of the LR test for a given significance level β, also can be obtained. It will be useful for power calculation.

Step 5: Finally, based on the estimated p-value, the experimenter can decide whether to reject or not to reject the null hypothesis.

It is important to see the power of the above test procedure under different alternatives when the parameters associated with the non-immune population remains fixed. It may be recalled that the power of a test is the probability of rejecting the null hypothesis H_0 when the alternative H_1 is true. For a specific value of $p_0 < 1$ under H_1, we can compute the

power based on the following algorithm.

Algorithm 2:

Step 1: Generate a sample using the parameters associated with the non-immune population as obtained in Step 2 of Algorithm 1, and with immune proportion as p_0. Repeat this B times.

Step 2: Compute the LR values based on the above generated samples, and let us denote them as $LR_0^1, \ldots LR_0^B$.

Step 3: For a given level of significance β, the estimated power of the test at p_0 will be the proportion of LR_0^bs which are greater than C^β, as obtained in Step 4 of Algorithm 1.

The details will be illustrated in the Data Analysis section.

5 Simulation Results

To illustrate the effectiveness of the proposed framework, a thorough simulation study has been carried out considering a multiple step-stress model with three stress levels.. In addition, we assume the Weibull distribution to model the times-to-event for the susceptible population with common shape parameter and different scale parameters across the different stress levels. For simulation purpose, values of model parameters are considered as : $\alpha = 2.5$, $\lambda_1 = 1$, $\lambda_2 = 2$, $\lambda_3 = 3$, $p = 0.85$. In addition, different sample sizes ($n = 40, 60, 80, 100$) and time points for step acceleration ;

$$\begin{aligned}(\tau_1, \tau_2, \tau) \;=\; & (0.5, 0.8, 1.2),\ (0.6, 0.8, 1.2),\ (0.6, 0.9, 1.2),\\ & (0.5, 0.8, 1.4),\ (0.6, 0.8, 1.4),\ (0.6, 0.9, 1.4)\end{aligned}$$

are considered for illustration. With these choices, samples are generated at first and the order restricted MLEs of the model parameters are obtained employing the methodology discussed in Section 3.1. The average estimates(AEs) of the order restricted MLEs and the

Table 2: AEs and MSEs of model parameters based on 5000 simulations. Actual values: $p = 0.85,\ \alpha = 2.5,\ \lambda_1 = 1,\ \lambda_2 = 2,\ \lambda_3 = 3.$

				p		α		λ_1		λ_2		λ_3	
n	τ	τ_1	τ_2	AE	MSE	AE	MSE	AE	MSE	AE	MSE	AE	MSE
40	1.2	0.5	0.8	0.8602	0.0048	2.6312	0.6159	1.2049	0.5347	2.1294	0.3567	3.2191	1.5802
	1.2	0.6	0.8	0.8549	0.0045	2.7062	0.6659	1.1711	0.3652	2.0685	0.3707	3.2738	1.5190
	1.2	0.6	0.9	0.8594	0.0048	2.6553	0.5980	1.1221	0.3109	2.0299	0.3114	3.2445	1.8776
	1.4	0.5	0.8	0.8502	0.0037	2.5936	0.5352	1.1675	0.4687	2.1086	0.3039	3.2590	1.5302
	1.4	0.6	0.8	0.8506	0.0035	2.6999	0.6287	1.1700	0.3371	2.0945	0.3571	3.1512	1.2084
	1.4	0.6	0.9	0.8517	0.0037	2.6622	0.5753	1.1274	0.2814	2.0672	0.2580	3.2152	1.7870
60	1.2	0.5	0.8	0.8557	0.0032	2.6017	0.4392	1.1506	0.3823	2.0545	0.2086	3.2023	1.1862
	1.2	0.6	0.8	0.8535	0.0031	2.6408	0.4738	1.1306	0.2562	2.0571	0.2583	3.1725	1.0593
	1.2	0.6	0.9	0.8580	0.0037	2.6331	0.4256	1.1167	0.2270	2.0386	0.2100	3.2553	1.6713
	1.4	0.5	0.8	0.8507	0.0024	2.6220	0.4030	1.1571	0.3451	2.0808	0.1947	3.1903	0.9448
	1.4	0.6	0.8	0.8507	0.0025	2.6126	0.4102	1.1144	0.2249	2.0613	0.2430	3.1637	0.8303
	1.4	0.6	0.9	0.8505	0.0026	2.6272	0.3859	1.1123	0.2032	2.0480	0.1881	3.1827	1.2866
80	1.2	0.5	0.8	0.8541	0.0025	2.5843	0.3685	1.1439	0.3230	2.0552	0.1549	3.1730	0.9625
	1.2	0.6	0.8	0.8536	0.0026	2.6181	0.3595	1.1046	0.2066	2.0482	0.1916	3.1115	0.7749
	1.2	0.6	0.9	0.8549	0.0028	2.5779	0.3097	1.0831	0.1763	2.0340	0.1559	3.1835	1.3863
	1.4	0.5	0.8	0.8512	0.0019	2.5889	0.3230	1.1490	0.2979	2.0664	0.1410	3.1670	0.7762
	1.4	0.6	0.8	0.8513	0.0019	2.6199	0.3293	1.1028	0.1720	2.0431	0.1706	3.0890	0.6163
	1.4	0.6	0.9	0.8523	0.0019	2.6009	0.2908	1.1113	0.1709	2.0311	0.1367	3.1271	0.9463
100	1.2	0.5	0.8	0.8555	0.0021	2.5753	0.3108	1.1198	0.2750	2.0594	0.1301	3.1190	0.7924
	1.2	0.6	0.8	0.8523	0.0020	2.5951	0.2777	1.0867	0.1549	2.0334	0.1591	3.0765	0.6372
	1.2	0.6	0.9	0.8517	0.0023	2.5810	0.2607	1.0835	0.1427	2.0175	0.1310	3.1791	1.2492
	1.4	0.5	0.8	0.8518	0.0017	2.5700	0.2652	1.1218	0.2446	2.0627	0.1166	3.1065	0.6304
	1.4	0.6	0.8	0.8493	0.0017	2.6068	0.2631	1.0994	0.1476	2.0327	0.1360	3.0757	0.5744
	1.4	0.6	0.9	0.8507	0.0017	2.5813	0.2364	1.0766	0.1342	2.0242	0.1172	3.1455	0.8874

associated mean squared errors (MSEs) are computed. The results are provided in Table 1. When it comes to the interval estimation problem, it is to note that the exact distribution of the order restricted MLEs is not possible to derive owing to its complex form, Hence, we resort to compute the interval estimates in terms of asymptotic confidence intervals (CIs) and parametric bootstrap CIs (percentile bootstrap CIs and BCa bootstrap CIs). The average lengths (ALs) and the associated coverage probabilities (CPs) of 95 % asymptotic and parametric bootstrap CIs are provided in Table 2-4.

Some of the important observations are quite evident from the results in Tables 1-4. As sample size increases, the AEs approach towards the true values of the model parameters in all the cases and the corresponding MSEs decrease. For fixed n, τ_1, τ_2, as τ increases, the total number of times-to-event associated with the third stress level increases on aver-

age. Hence, the estimates of p and λ_3 improves and the corresponding MSEs decrease, as expected. Similarly for fixed n, τ_1, τ, as τ_2 increases, the estimate of λ_2 improves and the corresponding MSE decreases. Additionally, for fixed n, τ_1, τ_2, as τ increases from 1.2 to 1.4, the MSEs of the susceptible model parameters decrease as expected. When it comes to evaluating the results related to interval estimates, the performance of both types of CIs are quite satisfactory in terms of CPs. As the sample size increases, the ALs of all the model parameters decrease, which is quite expected. Further, it is observed that the ALs are smaller in percentile bootstrap CIs compared to that in asymptotic CIs, while ALs become further shorter in bias-corrected and accelerated (BCa) bootstrap CIs. All the results are based on 5000 replications and for bootstrap CIs we have taken 10000 bootstrap replications. For more illustrations of results on other parameter values, one can refer to the supplementary file.

Table 3: CP and AL of 95% asymptotic CI based on 5000 simulations.
Actual values: $p = 0.85,\ \alpha = 2.5,\ \lambda_1 = 1,\ \lambda_2 = 2,\ \lambda_3 = 3.$

				p		α		λ_1		λ_2		λ_3	
n	τ	τ_1	τ_2	CP	AL	CP	AL	CP	AL	CP	AL	CP	AL
40	1.2	0.5	0.8	0.9620	0.2896	0.9235	2.6780	0.9320	3.1635	0.9670	2.3555	0.9945	5.7974
	1.2	0.6	0.8	0.9600	0.2882	0.9270	2.5348	0.9085	2.3641	0.9635	2.5688	0.9865	5.3153
	1.2	0.6	0.9	0.9635	0.3454	0.9260	2.4807	0.9285	2.3056	0.9600	2.3919	0.9965	7.8879
	1.4	0.5	0.8	0.9440	0.2205	0.9380	2.8265	0.9245	3.2060	0.9665	2.2477	0.9815	4.9724
	1.4	0.6	0.8	0.9565	0.2208	0.9235	2.6845	0.9095	2.3455	0.9610	2.4824	0.9710	4.5270
	1.4	0.6	0.9	0.9495	0.2262	0.9260	2.5576	0.9225	2.2596	0.9555	2.1188	0.9850	5.8701
60	1.2	0.5	0.8	0.9450	0.2294	0.9360	2.1557	0.9175	2.4917	0.9605	1.8754	0.9895	4.5668
	1.2	0.6	0.8	0.9530	0.2284	0.9285	2.0025	0.9150	1.8232	0.9525	2.0554	0.9810	4.2044
	1.2	0.6	0.9	0.9660	0.2882	0.9275	1.9613	0.9040	1.8114	0.9575	1.9478	0.9905	6.3890
	1.4	0.5	0.8	0.9365	0.1809	0.9295	2.2734	0.9195	2.5312	0.9675	1.7777	0.9710	3.8716
	1.4	0.6	0.8	0.9360	0.1814	0.9240	2.1351	0.9170	1.8601	0.9605	1.9851	0.9690	3.5878
	1.4	0.6	0.9	0.9170	0.1564	0.9365	1.8392	0.9135	1.5614	0.9565	1.7004	0.9480	3.0445
80	1.2	0.5	0.8	0.9475	0.1924	0.9370	1.8224	0.9290	2.0865	0.9620	1.5774	0.9870	3.7941
	1.2	0.6	0.8	0.9520	0.1685	0.9300	1.5061	0.9285	1.3509	0.9475	1.5579	0.9685	3.1451
	1.2	0.6	0.9	0.9560	0.2328	0.9325	1.6605	0.9270	1.5170	0.9560	1.6245	0.9930	5.2022
	1.4	0.5	0.8	0.9260	0.1570	0.9295	1.9365	0.9120	2.1146	0.9600	1.5095	0.9725	3.2714
	1.4	0.6	0.8	0.9170	0.1564	0.9265	1.8392	0.9235	1.5614	0.9565	1.7004	0.9480	3.0445
	1.4	0.6	0.9	0.9175	0.1577	0.9330	1.7753	0.9325	1.5344	0.9550	1.4498	0.9625	3.8594
100	1.2	0.5	0.8	0.9475	0.1690	0.9335	1.6219	0.8730	1.8431	0.9525	1.4007	0.9765	3.3741
	1.2	0.6	0.8	0.9520	0.1685	0.9300	1.5061	0.9085	1.3509	0.9475	1.5579	0.9685	3.1451
	1.2	0.6	0.9	0.9665	0.2029	0.9355	1.4578	0.9230	1.3152	0.9490	1.4347	0.9890	4.5672
	1.4	0.5	0.8	0.9320	0.1405	0.9490	1.7302	0.9320	1.8798	0.9515	1.3389	0.9550	2.8618
	1.4	0.6	0.8	0.9335	0.1406	0.9360	1.6116	0.9240	1.3696	0.9540	1.5121	0.9425	2.6568
	1.4	0.6	0.9	0.9390	0.1410	0.9485	1.5546	0.9265	1.3341	0.9560	1.2965	0.9580	3.4176

Table 4: CP and AL of 95% percentile bootstrap CI based on 5000 simulations and $B = 10000$.
Actual values: $p = 0.85,\ \alpha = 2.5,\ \lambda_1 = 1,\ \lambda_2 = 2,\ \lambda_3 = 3$.

				p		α		λ_1		λ_2		λ_3	
n	τ	τ_1	τ_2	CP	AL	CP	AL	CP	AL	CP	AL	CP	AL
40	1.2	0.5	0.8	0.9196	0.2430	0.9788	2.5702	0.9894	2.5004	0.9716	2.3170	0.9752	5.2490
		0.6	0.8	0.9420	0.2396	0.9798	2.9501	0.9924	2.2378	0.9692	2.4630	0.9790	4.9180
		0.6	0.9	0.9232	0.2405	0.9774	2.7636	0.9774	1.9238	0.9758	2.0836	0.9866	6.1102
	1.4	0.5	0.8	0.9242	0.2089	0.9796	2.5004	0.9916	2.3512	0.9724	2.1384	0.9816	4.8108
		0.6	0.8	0.9196	0.2104	0.9784	2.8096	0.9816	2.0386	0.9586	2.3684	0.9794	4.6100
		0.6	0.9	0.9356	0.2122	0.9745	2.6346	0.9898	1.7752	0.9700	1.9818	0.9892	5.4508
60	1.2	0.5	0.8	0.9490	0.2114	0.9798	2.4074	0.9880	2.1740	0.9538	1.8598	0.9698	4.3986
		0.6	0.8	0.9492	0.2144	0.9668	2.4988	0.9796	1.8586	0.9384	2.0098	0.9684	4.0790
		0.6	0.9	0.9478	0.2094	0.9698	2.3610	0.9796	1.6898	0.9652	1.8008	0.9852	5.2376
	1.4	0.5	0.8	0.9394	0.1812	0.9724	2.2918	0.9894	2.0384	0.9584	1.7310	0.9718	3.9546
		0.6	0.8	0.9386	0.1784	0.9616	2.3890	0.9748	1.7304	0.9678	1.9018	0.9748	3.6264
		0.6	0.9	0.9482	0.1778	0.9680	2.2664	0.9780	1.6102	0.9646	1.6896	0.9868	4.5900
80	1.2	0.5	0.8	0.9466	0.1786	0.9690	2.2042	0.9780	1.9584	0.9574	1.6106	0.9722	3.8784
		0.6	0.8	0.9476	0.1864	0.9606	2.2038	0.9720	1.6458	0.9604	1.7248	0.9680	3.5294
		0.6	0.9	0.9492	0.1928	0.9684	2.0868	0.9718	1.5124	0.9508	1.5654	0.9868	4.6934
	1.4	0.5	0.8	0.9406	0.1604	0.9740	2.1214	0.9818	1.8504	0.9498	1.4902	0.9724	3.4366
		0.6	0.8	0.9386	0.1562	0.9638	2.1000	0.9681	1.5496	0.9518	1.6392	0.9686	3.1878
		0.6	0.9	0.9420	0.1558	0.9600	1.9976	0.9768	1.4198	0.9586	1.4758	0.9804	4.0690
100	1.2	0.5	0.8	0.9356	0.1704	0.9625	1.9840	0.9706	1.7540	0.9546	1.3946	0.9606	3.3524
		0.6	0.8	0.9408	0.1636	0.9528	1.9864	0.9540	1.4568	0.9440	1.5202	0.9650	3.1540
		0.6	0.9	0.9510	0.1692	0.9540	1.8852	0.9540	1.3780	0.9400	1.4003	0.9746	4.2432
	1.4	0.5	0.8	0.9354	0.1342	0.9626	1.9004	0.9626	1.6843	0.9522	1.3020	0.9646	3.0823
		0.6	0.8	0.9456	0.1340	0.9522	1.8960	0.9644	1.3908	0.9624	1.4486	0.9550	2.8126
		0.6	0.9	0.9446	0.1422	0.9616	1.8004	0.9748	1.3002	0.9546	1.3008	0.9754	3.5600

Table 5: CP and AL of 95% BCa bootstrap CI based on 5000 simulations and $B = 10000$. Actual values: $p = 0.85,\ \alpha = 2.5,\ \lambda_1 = 1,\ \lambda_2 = 2,\ \lambda_3 = 3$.

				p		α		λ_1		λ_2		λ_3	
n	τ	τ_1	τ_2	CP	AL	CP	AL	CP	AL	CP	AL	CP	AL
0	1.2	0.5	0.8	0.9158	0.2125	0.9705	2.5269	0.9801	2.4852	0.9709	2.2440	0.9684	5.1024
		0.6	0.8	0.9450	0.2248	0.9714	2.9367	0.9877	2.2072	0.9613	2.4215	0.9718	4.8745
		0.6	0.9	0.9250	0.2176	0.9734	2.7405	0.9708	1.8622	0.9784	2.0416	0.9782	6.0214
	1.4	0.5	0.8	0.9315	0.1746	0.9628	2.4716	0.9842	2.3262	0.9706	2.1075	0.9800	4.7846
		0.6	0.8	0.9234	0.1846	0.9742	2.7526	0.9793	1.9816	0.9596	2.3246	0.9786	4.5816
		0.6	0.9	0.9348	0.1852	0.9610	2.6046	0.9746	1.7416	0.9684	1.9518	0.9716	5.3254
60	1.2	0.5	0.8	0.9456	0.1846	0.9682	2.3746	0.9794	2.1482	0.9524	1.8312	0.9594	4.3610
		0.6	0.8	0.9458	0.1654	0.9610	2.4278	0.9728	1.7714	0.9482	1.9452	0.9473	4.0021
		0.6	0.9	0.9517	0.1610	0.9587	2.3312	0.9682	1.6543	0.9684	1.7643	0.9726	5.1108
	1.4	0.5	0.8	0.9421	0.1596	0.9708	2.2586	0.9827	1.9947	0.9601	1.7047	0.9642	3.9218
		0.6	0.8	0.9406	0.1416	0.9600	2.3542	0.9682	1.7002	0.9518	1.8746	0.9658	3.5876
		0.6	0.9	0.9502	0.1541	0.9516	2.2358	0.9724	1.5812	0.9614	1.6542	0.9800	4.5653
80	1.2	0.5	0.8	0.9454	0.1410	0.9624	2.1832	0.9700	1.9210	0.9586	1.5870	0.9704	3.8428
		0.6	0.8	0.9510	0.1542	0.9546	2.1748	0.9697	1.6204	0.9589	1.6924	0.9514	3.4906
		0.6	0.9	0.9504	0.1614	0.9540	2.0542	0.9646	1.4802	0.9556	1.5342	0.9790	4.6620
	1.4	0.5	0.8	0.9415	0.1401	0.9698	2.1000	0.9776	1.8240	0.9501	1.4620	0.9632	3.4040
		0.6	0.8	0.9401	0.1382	0.9546	2.0746	0.9540	1.5122	0.9602	1.6084	0.9572	3.1604
		0.6	0.9	0.9504	0.1248	0.9540	1.9842	0.9628	1.3828	0.9470	1.4616	0.9748	4.0304
100	1.2	0.5	0.8	0.9412	0.1416	0.9758	1.9540	0.9645	1.7210	0.9568	1.3648	0.9542	3.3278
		0.6	0.8	0.9502	0.1404	0.9604	1.9512	0.9584	1.4246	0.9458	1.4920	0.9507	3.1310
		0.6	0.9	0.9604	0.1508	0.9590	1.8540	0.9508	1.3488	0.9414	1.3964	0.9618	4.2202
	1.4	0.5	0.8	0.9406	0.1178	0.9502	1.8740	0.9546	1.6570	0.9504	1.2856	0.9584	3.0562
		0.6	0.8	0.9484	0.0842	0.9542	1.8310	0.9514	1.3410	0.9504	1.3845	0.9508	2.7416
		0.6	0.9	0.9458	0.1184	0.9658	1.8120	0.9624	1.2846	0.9500	1.2801	0.9624	3.5300

To see the effectiveness of the proposed testing procedures discussed in Section 4 for the presence of cure rate fraction, different values of p are taken ranging from 0.75 to 0.95 with an increment of 0.05. With the same choices of the model parameters, sample sizes, stress-changing time points and termination time, average power is calculated based on 5000 simulations. The corresponding results are recorded in Table 5 and Table 6 for the asymptotic and the non-asymptotic approaches respectively. Some of the observations are quite evident from the observed results. As we are shifting more towards the alternative (less value of p), power of the test increases. As expected, power of the test increases with increase in sample size keeping other quantities unaltered. In addition, as τ increases with other quantities remaining fixed, power of the test increases. Power based on the asymptotic approach is little high compared to that based on the bootstrap approach.

Table 6: Power calculation of the asymptotic test based on 5000 simulations for different choices of p generated from the parameter values: $\alpha = 2.5,\ \lambda_1 = 1,\ \lambda_2 = 2,\ \lambda_3 = 3$.

				p				
n	τ	τ_1	τ_2	0.95	0.90	0.85	0.80	0.75
40	1.2	0.5	0.8	0.5715	0.7645	0.8725	0.9255	0.9345
		0.6	0.8	0.6075	0.7885	0.8705	0.9195	0.9460
		0.6	0.9	0.5355	0.7270	0.8115	0.8755	0.9000
	1.4	0.5	0.8	0.8280	0.9725	0.9935	0.9980	0.9990
		0.6	0.8	0.8525	0.9685	0.9945	0.9985	0.9995
		0.6	0.9	0.8050	0.9565	0.9905	0.9960	0.9995
60	1.2	0.5	0.8	0.6605	0.8575	0.9300	0.9645	0.9795
		0.6	0.8	0.6600	0.8630	0.9280	0.9700	0.9800
		0.6	0.9	0.6000	0.7875	0.8890	0.9370	0.9465
	1.4	0.5	0.8	0.9100	0.9950	0.9985	0.9990	0.9995
		0.6	0.8	0.9270	0.9945	0.9990	1.0000	1.0000
		0.6	0.9	0.8990	0.9905	0.9990	0.9995	1.0000
80	1.2	0.5	0.8	0.7495	0.9095	0.9675	0.9840	0.9925
		0.6	0.8	0.7370	0.9035	0.9700	0.9800	0.9940
		0.6	0.9	0.6415	0.8495	0.9250	0.9585	0.9785
	1.4	0.5	0.8	0.9705	0.9990	1.0000	1.0000	1.0000
		0.6	0.8	0.9700	0.9985	1.0000	1.0000	1.0000
		0.6	0.9	0.9570	0.9995	1.0000	1.0000	1.0000
100	1.2	0.5	0.8	0.7835	0.9500	0.9805	0.9930	0.9985
		0.6	0.8	0.7905	0.9435	0.9850	0.9930	0.9975
		0.6	0.9	0.6980	0.8870	0.9470	0.9765	0.9880
	1.4	0.5	0.8	0.9800	1.0000	1.0000	1.0000	1.0000
		0.6	0.8	0.9850	1.0000	1.0000	1.0000	1.0000
		0.6	0.9	0.9805	0.9985	1.0000	1.0000	1.0000

Table 7: Power calculation of the non-asymptotic test based on 5000 simulations for different choices of p generated from the parameter values: $\alpha = 2.5,\ \lambda_1 = 1,\ \lambda_2 = 2,\ \lambda_3 = 3.$

				p				
n	τ	τ_1	τ_2	0.95	0.90	0.85	0.80	0.75
40	1.2	0.5	0.8	0.5160	0.7440	0.8695	0.9055	0.9433
		0.6	0.8	0.5223	0.7513	0.8470	0.8956	0.9423
		0.6	0.9	0.4256	0.7000	0.7756	0.8432	0.9014
	1.4	0.5	0.8	0.7344	0.9130	0.9470	0.9678	0.9818
		0.6	0.8	0.7644	0.9182	0.9464	0.9682	0.9820
		0.6	0.9	0.7120	0.9170	0.9385	0.9660	0.9896
60	1.2	0.5	0.8	0.6184	0.8454	0.9200	0.9436	0.9788
		0.6	0.8	0.6204	0.8510	0.9178	0.9498	0.9804
		0.6	0.9	0.5964	0.7996	0.8744	0.9326	0.9408
	1.4	0.5	0.8	0.8440	0.9356	0.9482	0.9588	0.9714
		0.6	0.8	0.8528	0.9348	0.9492	0.9680	0.9838
		0.6	0.9	0.8380	0.9396	0.9508	0.9642	0.9876
80	1.2	0.5	0.8	0.6986	0.8604	0.9144	0.9488	0.9662
		0.6	0.8	0.6850	0.8692	0.9190	0.9478	0.9694
		0.6	0.9	0.6248	0.8140	0.8752	0.9178	0.9582
	1.4	0.5	0.8	0.9000	0.9186	0.9658	0.9782	0.9896
		0.6	0.8	0.9062	0.9200	0.9788	0.9882	1.0000
		0.6	0.9	0.8968	0.9212	0.9880	1.0000	1.0000
100	1.2	0.5	0.8	0.7486	0.9144	0.9490	0.9788	0.9876
		0.6	0.8	0.7584	0.9100	0.9504	0.9790	0.9900
		0.6	0.9	0.6990	0.8700	0.9184	0.9548	0.9940
	1.4	0.5	0.8	0.9665	0.9995	1.0000	1.0000	1.0000
		0.6	0.8	0.9815	1.0000	1.0000	1.0000	1.0000
		0.6	0.9	0.9700	0.9990	1.0000	1.0000	1.0000

6 Real Data Example

In this subsection, we provide analysis of a multiple step-stress Fish data set belonging to the fluoranthene- treated group (see Greven et al. [6] in this regard). A sample of 15 fishes are swum at an initial flow rate of 15 cm/sec. The time at which a fish fails to maintain its normal position is recorded as the failure time (time-to-event). To ensure early failures, the stress level (velocity of water flow) is raised by 5 cm/sec at 110 and 130 minutes, finally the experiment stops at 150 minutes. The observed failure time data is presented in Table 8 below.

Table 8: Fish data set

Stress level	Failure times
s_1	91.00, 93.00, 94.00, 98.20
s_2	115.81, 116.00, 116.50, 117.25, 126.75, 127.50
s_3	No failures
s_4	154.33, 159.50, 164.00
s_5	184.14, 188.33

6.1 Parameter Estimation

In this case $n = 15$, $\tau_1 = 110$ minutes, $\tau_2 = 130$ minutes, $\tau = 150$ minutes, $n_1 = 4$, $n_2 = 6$, $n_3 = 0$. We have divided each data points by 150 for computational purpose and then analyze the data. It is to note that there is no failure at the last extreme stress level. Hence, order restricted inference is a obvious choice in this case and provides the MLEs of all the model parameters. We consider three members (Exponential, Weibull and Burr XII) of the PH family of distributions. The three distributions are fitted to the Fish data set and order restricted MLEs of the model parameters are obtained using the proposed EM algorithm coupled with the generalized isotonic regression technique discussed in Section 3.1. To check the goodness of fit of the two distributions, we compute the Kolmogorov-Smirnov (K-S) distances between the fitted and the empirical CDFs and the associated p-values. The order restricted MLEs, 95% bootstrap CIs, K-S distances, the associated p-values and the corresponding maximized log-likelihood (MLL) values are presented in Table 10. Since $\widehat{\lambda}_2 = \widehat{\lambda}_3$, we assume $\lambda_2 = \lambda_3$ in the model and construct the bootstrap CIs for all the model parameters. In Table 8, we have considered the complete data set (i.e. without censoring and hence without long term survivors) and carry out the order restricted inference of the associated model parameters. It is observed that K-S distances are little high in this case.

6.2 Testing of hypothesis

In this subsection, we have performed the testing of hypothesis for the presence of cured fraction. For this, we have used both the asymptotic approach and the non-asymptotic

Table 9: MLEs, 95% bootstrap CI,K-S distance, the corresponding p-values and the MLL values in the complete Fish data set

Model	MLEs		95% CI	K-S distance	p-value	MLL
Exponential	$\widehat{\lambda}_1$	0.3782	(0.1056, 2.8788)	0.2050	0.5047	-2.1490
	$\widehat{\lambda}_2 = \widehat{\lambda}_3$	5.6316	(2.1382, 9.9800)			
	$\widehat{\lambda}_4$	6.6342	(3.0084, 10.1642)			
	$\widehat{\lambda}_5$	9.2393	(4.6802, 15.0064)			
Weibull	$\widehat{\alpha}$	4.3132	(1.2982, 9.5682)	0.1786	0.6805	1.2309
	$\widehat{\lambda}_1$	1.1682	(0.5287, 4.2370)			
	$\widehat{\lambda}_2 = \widehat{\lambda}_3 = \widehat{\lambda}_4 = \widehat{\lambda}_5$	1.7964	(0.6806, 6.5675)			
Burr XII	$\widehat{\alpha}$	5.2450	(2.0084, 8.2428)	0.2158	0.4384	-15.3061
	$\widehat{\lambda}_1$	1.7330	(0.7054, 6.0206)			
	$\widehat{\lambda}_2 = \widehat{\lambda}_3 = \widehat{\lambda}_4 = \widehat{\lambda}_5$	3.0963	(0.9852, 9.9628)			

Table 10: MLEs, 95% bootstrap CI,K-S distance, the corresponding p-values and the MLL values in the Fish data set

Model	MLEs		95% CI	K-S distance	p-value	MLL
Exponential	$\widehat{p}$	0.6667	(0.4432,0.9860)	0.1783	0.7798	0.8685
	$\widehat{\lambda}_1$	0.5789	(0.2869,1.5254)			
	$\widehat{\lambda}_2 = \widehat{\lambda}_3$	14.9980	(5.2037,28.4091)			
Weibull	$\widehat{p}$	0.6667	(0.5333,0.8666)	0.1543	0.8356	2.5685
	$\widehat{\alpha}$	9.0557	(5.1156,12.2974)			
	$\widehat{\lambda}_1$	9.4827	(2.4069,21.5254)			
	$\widehat{\lambda}_2 = \widehat{\lambda}_3$	12.2984	(6.2932,26.3691)			
Burr XII	$\widehat{p}$	0.6667	(0.4001,0.9340)	0.1397	0.9104	0.5855
	$\widehat{\alpha}$	9.2667	(3.9623,15.3374)			
	$\widehat{\lambda}_1$	10.4230	(1.5031,38.7922)			
	$\widehat{\lambda}_2 = \widehat{\lambda}_3$	14.0902	(4.9369,39.3309)			

approach discussed in Section 4.

Table 11: MLEs, the corresponding MLL values, the values of the test statistic and the associated p-values in the Fish data set assuming cured fraction is absent

Model	MLEs		MLL (l_0)value	$-2(l_0 - l_1)$	p-value
Exponential	$\widehat{\lambda}_1$	0.3783	-7.3922	4.0896	.007375
	$\widehat{\lambda}_2$	1.8564			
	$\widehat{\lambda}_3$	1.8564			
Weibull	$\widehat{\alpha}$	3.0004	-8.4478	11.7587	< 0.00001
	$\widehat{\lambda}_1$	0.7510			
	$\widehat{\lambda}_2$	2.9953			
	$\widehat{\lambda}_3$	2.9953			
Burr XII	$\widehat{\alpha}$	4.0099	-4.3494	9.8699	0.000015
	$\widehat{\lambda}_1$	1.1900			
	$\widehat{\lambda}_2$	3.9653			
	$\widehat{\lambda}_3$	3.9653			

Under the null hypothesis H_0, the order restricted MLEs of the model parameters, the corresponding MLL (l_0) values are calculated and are reported in Table 11, while Table 10 provides with the corresponding information under the alternate hypothesis H_1.

Often, MLL values (log-likelihood value computed at the MLE) play a major part in model selection. Existing similar works on order restricted inference in multiple SSALT (see Samanta and Kundu [15],Pal et al. [11],)have not assumed the presence of long term survivors in the underlying population. From the results in Table 10 and Table 11, it can be seen that MLL values are higher if we assume the presence of long term survivors and hence the proposed model turns out to be more effective.

From the values of the test statistic $-2(l_0 - l_1)$ and the associated p-values in Table 11, we can observe that both the models lead to the rejection of the null hypothesis. It clearly indicates that cured fraction is present in the underlying population.

It will be interesting to see how is the shape of the distribution of the LR statistic under H_0 and also how the power function behaves for different p_0 values. 5000 bootstrap samples are generated using the order restricted ML estimates under H_0 as the population parameters, for the exponential, Weibull and Burr XII models (see Table 11). The histograms of the LR statistic based on 5000 bootstrap samples for exponential, Weibull and Burr XII time-to-

event distributions (see Figure 2(a) and 2(b)) give an idea about the empirical estimate of the distribution of the LR statistic under both the models. It indicates that in both the cases the PDF of the LR statistic under H_0 is a decreasing function. We have reported the $p-$values in Table 12 for all the models. It is observed that for all the models we reject the null hypothesis. It clearly indicates that cured fraction is present in the underlying population. Plots of power curve for both the models at 5% level of significance are provided in Figure 3(a) and 3(b) respectively. It shows, as expected, that the power of the test increases as p_0 decreases.

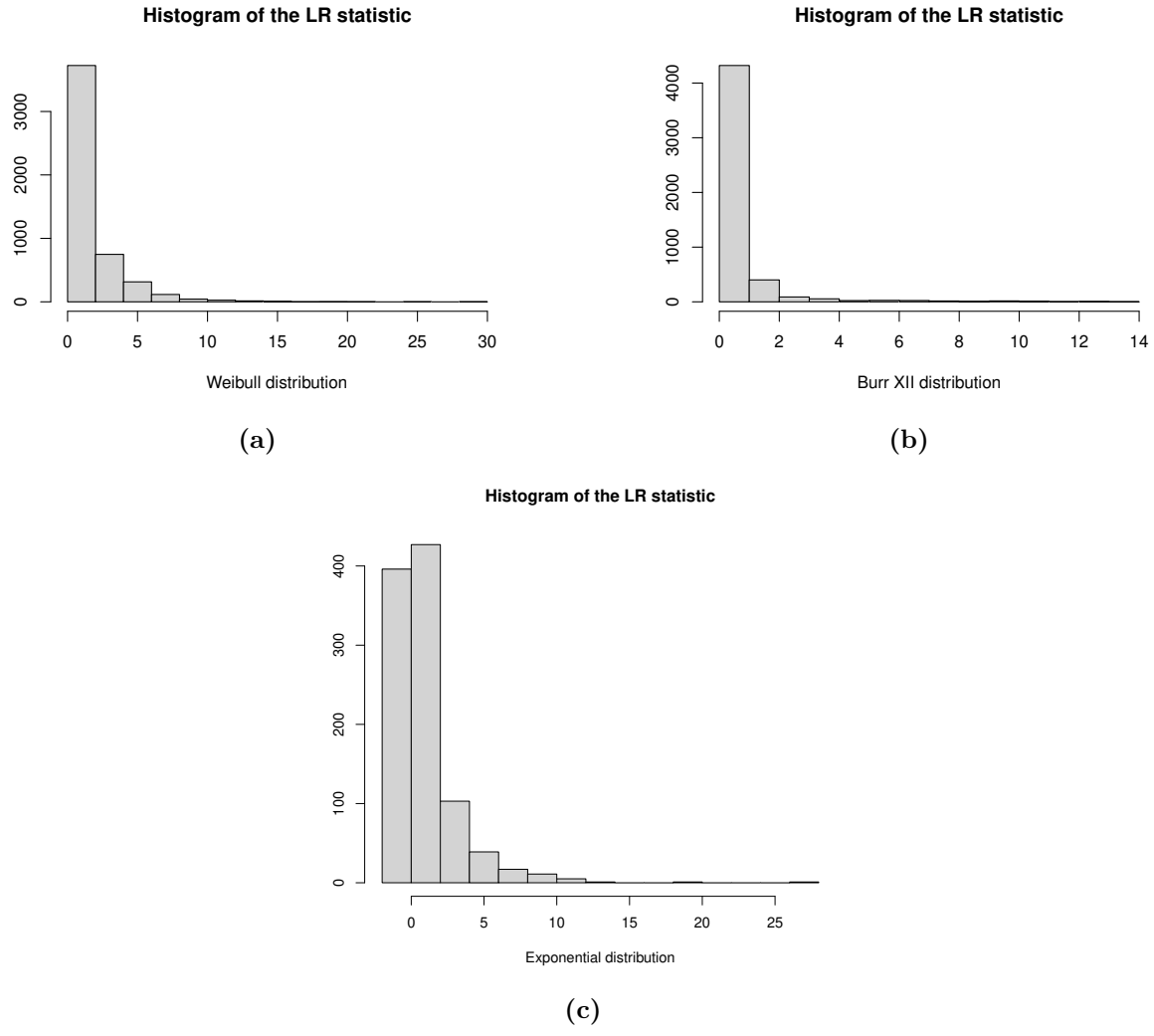

Figure 1: (a) Histogram of the LR statistic based on 5000 bootstrap samples for Weibull time-to-event distribution, (b) Histogram of the LR statistic based on 5000 bootstrap samples for Burr XII time-to-event distribution, (c) Histogram of the LR statistic based on 5000 bootstrap samples for exponential time-to-event distribution

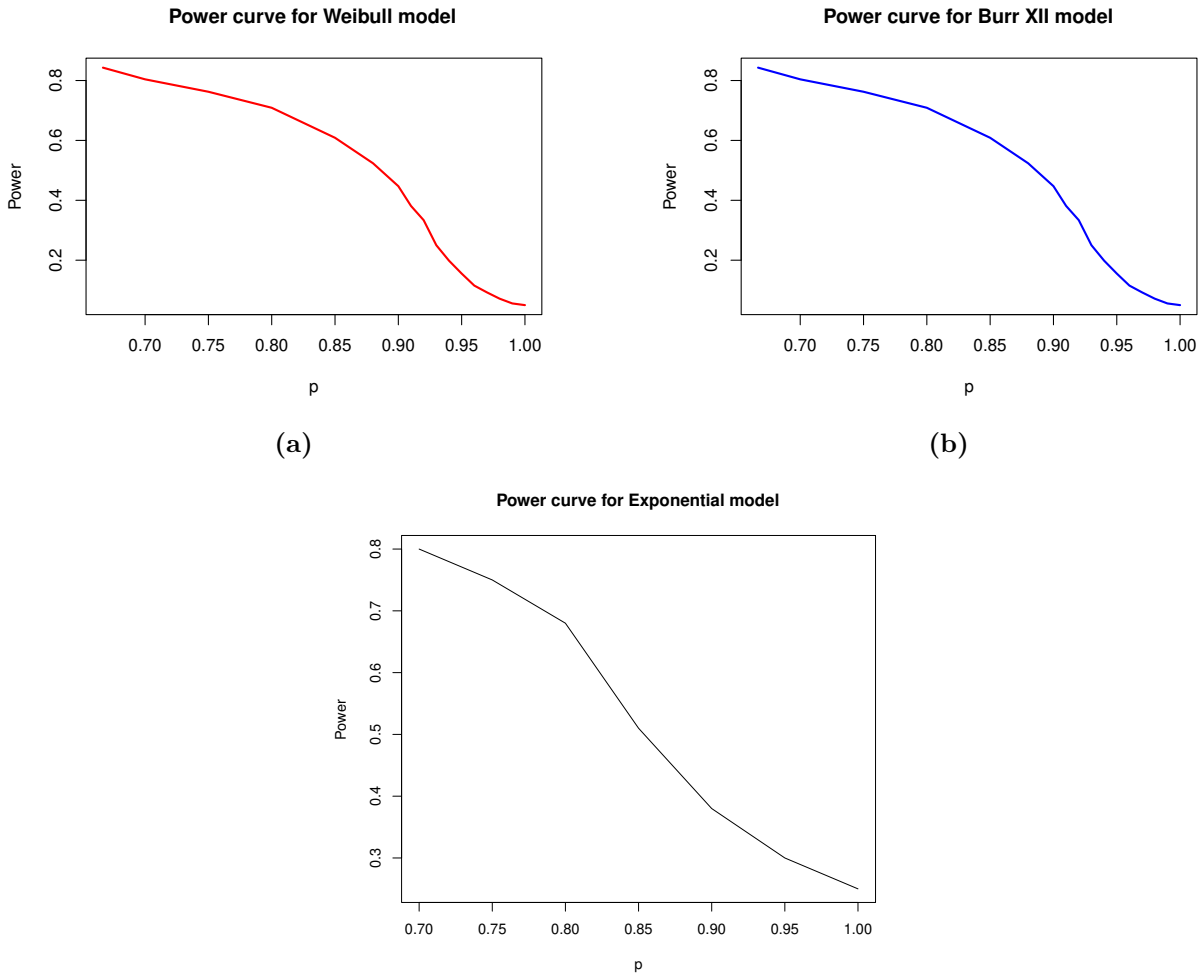

Figure 2: (a) Power curve for Weibull time-to-event distribution, (b) Power curve for Burr XII time-to-event distribution, (c) Power curve for Exponential time-to-event distribution

Table 12: Associated p-values in the Fish data set based on bootstrap method

Model	p-value
Exponential	0.0062
Weibull	0.0058
Burr XII	0.0048

7 Conclusion

In this article, we have developed a failure rate based SSALT model assuming that the underlying population consists of long term survivors. The time-to-event distribution of the susceptible units is assumed to belong to a general PH family of distributions. We propose the order restricted maximum likelihood estimation methodology for the underlying model parameters by employing the popular EM algorithm coupled with the method of generalized isotonic regression. Through simulation study, it is observed that the EM algorithm works very efficiently. For interval estimation of the model parameters, we rely mainly on the asymptotic CIs and the parametric bootstrap CIs. A real life data set is also analyzed wherein the presence of cured fraction comes out to be significant in the associated hypothesis testing problem. Possible ways to generalize our set up include considering other flexible censoring schemes and assuming the cured fraction to depend on meaningful covariates. Work is in progress along this direction and we hope to report our finding in our future works.

Conflict of Interest Statements

The authors do not have any conflict of interests in preparation of the manuscript.

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Appendix

Proof of Lemma 1

For fixed p and α, the problem here is to maximize the log-likelihood function $Q(\boldsymbol{\theta}, \boldsymbol{\pi^{(k)}})$ with respect to λ_i, $i \in I = \widetilde{I}$ based on the order restriction $\lambda_1 \leq \ldots \leq \lambda_{m+1}$. Now

$$\max_{\lambda_1 \leq \lambda_2 \leq \ldots \leq \lambda_{m+1}} Q(\boldsymbol{\theta}, \boldsymbol{\pi^{(k)}}) = \max_{\lambda_1 \leq \lambda_2 \leq \ldots \leq \lambda_{m+1}} \{ \sum_{i=1}^{m+1} [-n_i \ln \frac{1}{\lambda_i} - \frac{E_i(\alpha)}{\frac{1}{\lambda_i}}] \}.$$

We can now frame the restricted maximization of $Q(\boldsymbol{\theta}, \boldsymbol{\pi^{(k)}})$ in terms of the generalized isotonic regression problem discussed in Chapter 1 of Brunk et al. [4]. Now the proof follows exactly like the proof of Lemma 3.1 in Pal et al. [11].

Proof of Lemma 2

For fixed α, we have

$$m_1^{k+1'}(p) = \frac{\bar{n}_{m+1}}{p} + \sum_{J_{m+2}} \frac{\pi_i^{(k)}}{p} - \sum_{J_{m+2}} \frac{(1 - \pi_i^{(k)})}{1 - p}$$

and

$$m_1^{k+1''}(p) = -\frac{\bar{n}_{m+1}}{p^2} - \sum_{J_{m+2}} \frac{\pi_i^{(k)}}{p^2} - \sum_{J_{m+2}} \frac{(1 - \pi_i^{(k)})}{(1 - p)^2}.$$

Now, since $m_1^{k+1''}(p) < 0$, it immediately follows that $m_1^{k+1}(p)$ is a concave function. The result follows immediately by considering the fact that $m_1^{k+1}(p) \to -\infty$ as $p \to 0$ or $p \to 1$.

Proof of Lemma 3

For fixed p and α, the problem here is to maximize the log-likelihood function $Q(\boldsymbol{\theta}, \boldsymbol{\pi^{(k)}})$ with respect to λ_i, $i \in \widetilde{I}$ based on the order restriction $\lambda_{i_1} \leq \lambda_{i_2} \leq \ldots \leq \lambda_{i_{|\tilde{I}|}}$. Now

$$\max_{\lambda_{i_1} \leq \lambda_{i_2} \leq \ldots \leq \lambda_{i_{|\tilde{I}|}}} Q(\boldsymbol{\theta}, \boldsymbol{\pi^{(k)}}) = \max_{\lambda_{i_1} \leq \lambda_{i_2} \leq \ldots \leq \lambda_{i_{|\tilde{I}|}}} \{ \sum_{i \in \widetilde{I}} [-n_i \ln \frac{1}{\lambda_i} - \frac{E_i(\alpha)}{\frac{1}{\lambda_i}}] \}.$$

Now, the proof follows exactly along the same lines of that of Lemma 1.

Proof of Lemma 4

Proposition 1. *$E_i(\alpha)$ defined in (6) is non-negative.*

Proof.

$$\begin{aligned} E_i(\alpha) &= \sum_{j=i}^{m+1} n_j \ln[1 - F_0(\tau_{i-1})] - \sum_{j=\bar{n}_{i-1}+1}^{\bar{n}_i} \ln[1 - F_0(t_{j:n})] + \sum_{j \in J_{m+2}} \pi_j^{(k)} \ln[1 - F_0(\tau_{i-1})] \\ &\quad - \sum_{j \in J_{m+2}} \pi_j^{(k)} \ln[1 - F_0(\tau_i)] - \sum_{j=i+1}^{m+1} n_j \ln[1 - F_0(\tau_i)]. \end{aligned} \tag{12}$$

Now, since $\tau_{i-1} < \tau_i$ and ln is a monotone increasing function, $\Big[\sum_{j \in J_{m+2}} \pi_j^{(k)} \ln[1 - F_0(\tau_{i-1})] - \sum_{j \in J_{m+2}} \pi_j^{(k)} \ln[1 - F_0(\tau_i)] \Big] > 0$. Then, the remaining terms are

$$\sum_{j=i}^{m+1} n_j \ln[1 - F_0(\tau_{i-1})] - \sum_{j=\bar{n}_{i-1}+1}^{\bar{n}_i} \ln[1 - F_0(t_{j:n})] - \sum_{j=i+1}^{m+1} n_j \ln[1 - F_0(\tau_i)] \tag{13}$$

$$= \underbrace{\Big\{ \sum_{j=i+1}^{m+1} n_j \ln[1 - F_0(\tau_{i-1})] - \sum_{j=i+1}^{m+1} n_j \ln[1 - F_0(\tau_i)] \Big\}}_{M_1}$$
$$\underbrace{+\Big\{ n_i \ln[1 - F_0(\tau_{i-1})] - \sum_{j=\bar{n}_{i-1}+1}^{\bar{n}_i} \ln[1 - F_0(t_{j:n})] \Big\}}_{M_2}$$

Note that for those stress levels with no failures, $n_i = 0$. Hence, M_1 and M_2 are non-negative quantities given that $\tau_{i-1} < \tau_i$, $\tau_{i-1} < t_{j:n}$, $j = \bar{n}_{i-1}+1, \ldots \bar{n}_i$, and ln is a monotone increasing function. □

For fixed p and α, the likelihood function corresponding to $Q(\boldsymbol{\theta}, \pi^{(k)})$ can be expressed as

$$\underbrace{\Big\{ \prod_{j \in \tilde{I}} \lambda_j^{n_j} \Big\} \times \exp\Big\{ - \sum_{j \in \tilde{I}} \lambda_j E_j(\alpha) \Big\}}_{A_1} \times \underbrace{\exp\Big\{ - \sum_{i \in I \backslash \tilde{I}} \lambda_i E_i(\alpha) \Big\}}_{A_2} \tag{14}$$

Now, for fixed $\lambda_i, i \notin \tilde{I}$, A_1 in (14) is maximized at $\widehat{\lambda}_{j(k+1)}^{(\alpha)} = \widetilde{\lambda}_{j(k+1)}^{(\alpha)}, j \in \tilde{I}$. Now, for fixed p and α, $\exp\{-\lambda_j E_j(\alpha)\}$ is a decreasing function of λ_j since $E_j(\alpha) > 0 \; \forall j \in I \backslash \tilde{I}$. Hence, given the natural order restriction on the scale parameters i.e $\lambda_1 \leq \ldots \leq \lambda_{m+1}$, A_2 is maximized at $\widehat{\lambda}_{j(k+1)}^{(\alpha)} = \widetilde{\lambda}_{i(j)(k+1)}^{(\alpha)}$, $j \in I \backslash \tilde{I}$.