BAYESIAN ANALYSIS AND APPLICATIONS OF A MODEL FOR SURVIVAL DATA WITH A SURVIVING FRACTION

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Bayesian Analysis and Applications of a Model for Survival Data With A Surviving Fraction

by

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Abstract

Cure rate estimation is one of the most important issues in clinical trials and cure rate models are the main models. In the past decade, the standard cure rate model has been discussed and used. However, this model involves several drawbacks. Chen, Ibrahim and Sinha (1999) considered Bayesian methods for right-censored survival data for populations with a surviving (cure) fraction. In that paper, the authors proposed the cure rate model under the Weibull distribution which is quite different from the standard cure rate model. This proposed cure rate model overcomes the drawbacks of the standard cure rate model. However, it is not clear from their work whether their proposed cure rate models can be extended to other distributions. In this practicum, we shall extend those proposed cure rate models in Chen et al (1999) to the following distributions: log-logistic, Gompertz, and Gamma. Prior elicitations will also be discussed in detail, and classes of noninformative and informative prior distributions will be proposed. Furthermore, several theoretical properties of the proposed priors and resulting posteriors will be derived.

At the end of this practicum, a melanoma clinical trial is used to illustrate applications of the log-logistic, Gompertz and Gamma distributions to the proposed cure rate models for Bayesian analysis.

KEY WORDS: Cure rate model; Historical data; Current data; Posterior distribution; Gamma distribution; Log-logistic distribution; Gompertz distribution.

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Chapter 1

Introduction

1.1 Motivation of the Problem

Cure rate models, which are survival models incorporating a cure fraction, have been researched and practised for nearly 50 years. The most popular type of cure rate models introduced by Berkson and Gage (1952), is the mixture model, which is also called the standard cure rate model. Let $S_1(t)$ be the survivor function for the entire population, $S^*(t)$ be the survivor function for the non-cured group in the population, and π be the cure rate fraction. Then the standard cure rate model is given by

$$S_1(t) = \pi + (1 - \pi)S^*(t). \tag{1.1}$$

Exponential and Weibull distributions are commonly used for $S^*(t)$. This model has been extensively discussed in the statistical literature by many authors, such as Farewell (1982, 1986), Ghitany and Zhou (1995), Kuk and Chen (1992), Peng and Dear (2000), Taylor (1995), and Yamaguchi (1992). Even though this model is widely used, it still has several drawbacks. Firstly, $S_1(t)$ cannot have a proportional hazard structure, which is a desirable property for survival models. Secondly, when including covariates through the parameter π via a standard binomial regression model, the standard cure rate model yields improper posterior distributions for many types of noninformative improper priors, including the uniform prior for the regression coefficients. This is a crucial drawback of the standard cure rate model because it implies that Bayesian inference with a standard cure rate model essentially requires a proper prior.

In 1999, Chen, Ibrahim and Sinha introduced a new model to overcome the above mentioned drawbacks inherited in the standard cure rate model. Specifically, any standard cure rate model can be written as its proposed model and vice versa. This implies that the resulting model has a mathematical relationship with the standard cure rate model. An especially solid feature of their model is that it yields a proper posterior distribution under a noninformative improper prior for the regression coefficient, including an improper uniform prior. However, under the noninformative priors, the standard cure rate model in (1.1) always leads to an improper posterior distribution. This result is stated in Theorem 1.1. This proposed model also leads to a straightforward informative prior scheme based on historical data, and the model based on historical data yields a proper prior. But, this type of prior construction based on the standard cure rate model (1.1) always leads to an improper prior as well as an improper posterior distribution. This result is summarized in Theorem 1.2. For completeness, we quote these theorems here. For detailed proofs of these theorems, interested readers are referred to Chen et al (1999).

Theorem 1.1. We consider a joint noninformative prior for $\pi(\beta, \gamma^*) \propto \pi(\gamma^*)$, where $\gamma^* = (\alpha, \lambda)$ are the parameters in $f(y|\gamma^*)$ which is the density function of the random variable Z_i which is defined the random time for the ith clonogenic cell to produce a detectable cancer mass. Detailed explanation can be obtained in Chapter 3. In Theorem 1.2, we use the same definitions. For the standard cure rate model given in (1.1), suppose that we relate the cure rate fraction π to the covariates via a standard binomial regression.

$$\pi_i = G(x_i^{'}\beta),$$

where $G(\cdot)$ is a continuous cdf, $x_i^{'}$ and β denote a $k \times 1$ vector of covariates and $k \times 1$ vector of regression coefficients respectively. The detailed explanation can be obtained in Chapter 3. Assume that the survival function $S^*(\cdot)$ for the noncured group depends on the parameter γ^*. Let $L_1(\beta, \gamma^* \mid D_{obs})$ denote the resulting likelihood function based on the observed data. Then, if we take an improper uniform prior for β (*i.e.*, $\pi(\beta) \propto 1$), the posterior distribution

$$\pi_1(\beta, \gamma^* \mid D_{obs}) \propto L_1(\beta, \gamma^* \mid D_{obs})\pi(\gamma^*) \tag{1.2}$$

is always improper regardless of the propriety of $\pi(\gamma^*)$.

Theorem 1.2. For the standard cure rate model given in (1.1), suppose that we relate the cure rate fraction π to the covariates via a standard binomial regression

$$\pi_i = G(x_i^{'}\beta),$$

where $G(\cdot)$ is a continuous cdf. Assume that the survival function for the noncured group $S^*(\cdot)$ depends on the parameter γ^*. Let $L_1(\beta, \gamma^* \mid D_{0,obs})$ and $L_1(\beta, \gamma^* \mid D_{obs})$ denote the likelihood functions based on the observed historical and current data, a_0 denote the dispersion parameter for the historical data which is between 0 and 1. $D_{0,obs}$ and D_{obs} denote the observed historical and current data. Then, if we take an improper uniform initial prior for β ($i.e., \pi(\beta) \propto 1$), the posterior distribution is

$$\pi_1(\beta, \gamma^*, a_0 \mid D_{0,obs}) \propto [L_1(\beta, \gamma^* \mid D_{0,obs})]^{a_0} \pi_0(\gamma^*) a_0^{\delta_0 - 1}(1 - a_0)^{\lambda_0 - 1},$$

where δ_0 and λ_0 are specified hyperparameters. Then, $\pi_1(\beta, \gamma^*, a_0 \mid D_{0,obs})$ is always improper regardless of the propriety of $\pi(\gamma^*)$. In addition, if we use $\pi_1(\beta, \gamma^*, a_0 \mid D_{0,obs})$ as a prior, the resulting posterior, given by

$$p_1(\beta, \gamma^*, a_0 \mid D_{obs}, D_{0,obs}) \propto L_1(\beta, \gamma^* \mid D_{obs}) \pi_1(\beta, \gamma^*, a_0 \mid D_{0,obs})$$

is also improper.

Chen et al (1999) carried out Bayesian analysis for the proposed model under the Weibull distribution. However, it is not clear from their work whether their results can be extended to other distributions. In this practicum, we extend their model to the log-logistic, Gompertz and Gamma distributions.

In Chapter 2, we provide the model including its several attractive properties and its likelihood function with covariates.

In Chapter 3, when the log-logistic, Gompertz, and Gamma distributions are used in the model, we propose novel classes of noninformative prior distributions and derive some of the theoretical properties. We also derive several properties of the resulting posterior distributions with detailed proofs.

In Chapter 4, we propose novel classes of informative priors that are based on historical data. We find that the proposed model leads to an informative prior elicitation scheme based on historical data. This procedure yields a proper prior for each distribution. These proper priors are not available using the formulation in the standard cure rate model. We derive some of the new model's theoretical properties and provide detailed proofs.

In Chapter 5, we demonstrate the proposed priors with a real data from a phase III melanoma clinical trial conducted by the Eastern Cooperative Oncology Group (ECOG). The dataset is discussed in section 1.2.

In Chapter 6, we conclude this practicum and discuss possible future research in this area.

1.2 Melanoma Data

The Melanoma data are used in this practicum to illustrate Bayesian treatment of the proposed model and examine several topics, including noninformative and informative priors with covariates included.

Melanoma incidence is increasing at a rate that exceeds all solid tumors. Although education efforts have resulted in earlier detection of melanoma, patients who have deep primary melanoma (>4mm) or melanoma metastatic to regional draining lymph nodes classified as high-risk melanoma patients, continue to have high relapse and mortality rates of 60% to 75% (Kirkwood et al., 2000). No adjuvant therapy has previously shown a significant impact on relapse-free and overall survival of melanoma. Several post-operative (adjuvant) chemotherapies which are interferon (IFN) alpha of leukocyte origin and recombinant IFN alfa-2 (IFN α-2a, Rocheo, Nutley, NJ; IFN α-2b, Schering-Plough, Kenilworth, NJ; and IFN α-2c, Bochringer, Indianapolis, IN) have been proposed for this class of melanoma patients, and the one which seems to provide the most significant impact on relapse-free survival is IFN α-2b. This chemotherapy was used in two recent ECOG phase III clinical trials, E1684 and E1673. The first trial, E1684, was a two-arm clinical trial comparing high-dose IFN to observation. There were a total of n_0=286 patients enrolled in this study which covered the period from 1984 to 1990. The study was unblinded in 1993. The results of this study suggested that IFN has a significant impact on relapse-free survival and survival. These results led to U.S. Food and Drug

Administration (FDA) approval of this regimen as an adjuvant therapy for high-risk melanoma patients. These results (E1684) have been published in Kirkwood et al (1996).

Figure 1.1 displays a Kaplan-Meier plot for overall survival. We see that the right tail of the survival curve appears to 'plateau' after sufficient follow-up. Such a phenomenon has become quite common in melanoma as well as other cancers.

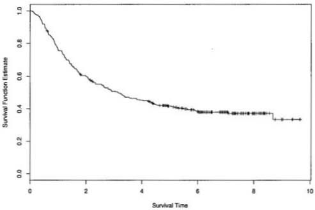

Figure 1.1: Kaplan-Meier Plot for E1684 Data

Table 1.1: Summary of E1684 Data

Survival time (year)	Median	2.91
	SD	2.83
Status (frequency)	Censored	110
	Death	174
Age (year)	Mean	47.03
	SD	13.00
Gender (frequency)	Male	171
	Female	113
PS (frequency)	Fully active	253
	Other	31

Table 1.1 provides a summary of the E1684 data. For the survival time summary in Table 1.1, the Kaplan-Meier estimate of the median survival and its standard deviation (SD) are given. PS means performance status.

The second trial, denoted by E1673, served as the historical data for our Bayesian analysis of E1684. Table 1.2 summarizes the historical data of E1673, with a total of n_0=650 patients. Three covariates which are age, gender and performance status are considered. Chen et al (1999) compared inferences between the standard cure rate model to their proposed model using a Weibull distribution, and gave a complete Bayesian analysis of the treatment of the cure rate model and examined several topics including noninformative prior elicitation and informative prior elicitation under the Weibull distribution. In this practicum, we extend their results to some other distributions, such as the log-logistic, Gompertz and Gamma distributions. PS still means performance status.

Table 1.2: Summary of E1673 Data

Survival time (year)	Median	5.72
	SD	8.20
Status (frequency)	Censored	257
	Death	393
Age (year)	Mean	48.02
	SD	13.99
Gender (frequency)	Male	375
	Female	275
PS (frequency)	Fully active	561
	Other	89

Chapter 2

The Cure Model and its Likelihood Function

2.1 The Cure Model

The cure rate model is defined in this section. For an individual in a population, let N denote the number of carcinogenic cells (often called clonogens) left active for that individual after the initial treatment. Assume that N has a Poisson distribution with mean θ, i.e.

$$P(N = n) = \frac{e^{-\theta}\theta^n}{n!}, n = 0, 1, ...$$

Let Z_i, $(i = 1, 2, ...N)$ denote the random time for the i-th clonogenic cell to produce a detectable cancer mass, where Z_i are $i.i.d$ with a common distribution function $F(t) = 1 - S(t)$. Also assume that $Z_i(i = 1, 2, ...)$ are independent of N. The time to relapse of the cancer can be defined by the random variable

$$Y = \min(Z_i, 0 \leq i \leq N),$$

where $P(Z_0 = \infty) = 1$. Hence, the survival function for the population is given by

$$\begin{aligned} S_p(y) &= P(\text{no cancer by time } y) \\ &= P(N = 0) + P(Z_1 > y, \ldots.., Z_N > y, N \geq 1) \\ &= \exp(-\theta) + \sum_{k=1}^{\infty} S(y)^k \frac{\theta^k}{k!} \exp(-\theta) \\ &= \exp(-\theta + \theta S(y)) \\ &= \exp(-\theta F(y)). \end{aligned} \tag{2.1}$$

Since $S_p(\infty) = \exp(-\theta) > 0$, (2.1) is not a proper survival function. We also know from (2.1) that the cure fraction is given by

$$S_p(\infty) = P(N = 0) = \exp(-\theta).$$

As $\theta \to \infty$, the cure fraction tends to 0, whereas as $\theta \to 0$, the cure fraction tends to 1. The density function corresponding to (2.1) is given by

$$\begin{aligned} f_p(y) &= \frac{d}{dy} F_p(y) \\ &= \frac{d}{dy}[1 - S_p(y)] \\ &= \theta f(y) \exp(-\theta F(y)). \end{aligned}$$

The hazard function is given by

$$h_p(y) = \frac{f_p(y)}{S_p(y)}$$

$$= \frac{\theta f(y)\exp(-\theta F(y))}{\exp(-\theta F(y))}$$
$$= \theta f(y).$$

Since $S_p(y)$ is not a proper survival function, $f_p(y)$ is not a proper probability density function and $h_p(y)$ is not a hazard function corresponding to a probability distribution. However, $f(y)$ is a proper probability density function and $h_p(y)$ is multiplicative in θ and $f(y)$. Thus, it has the proportional hazard structure with the covariates modelled through θ. This structure is more appealing than the one from the standard cure rate model in (1.1) and is computationally attractive. The survival function for the noncured population is given by

$$\begin{aligned} S^*(y) &= P(Y > y \mid N \geq 1) \\ &= \frac{P(N \geq 1, Y > y)}{P(N \geq 1)} \\ &= \frac{\exp(-\theta F(y)) - \exp(-\theta)}{1 - \exp(-\theta)}. \end{aligned} \tag{2.2}$$

We note that $S^*(0) = 1$ and $S^*(\infty) = 0$. So, we can say $S^*(y)$ is a proper survival function. The probability density function for the noncured population is

$$\begin{aligned} f^*(y) &= -\frac{d}{dy}S^*(y) \\ &= \frac{\exp(-\theta F(y))}{1 - \exp(-\theta)}\theta f(y), \end{aligned}$$

and the hazard function for the noncured population is given by

$$h^*(y) = \frac{f^*(y)}{S^*(y)}$$

$$
\begin{aligned}
&= \frac{\exp(-\theta F(y))}{\exp(-\theta F(y)) - \exp(-\theta)}\theta f(y) \\
&= \frac{1}{P(Y < \infty \mid Y > y)} h_p(y).
\end{aligned}
$$

The above hazard function depends on y. We can say that $h^*(y)$ does not have a proportional hazard structure. The model can be written as

$$
\begin{aligned}
S_p(y) &= \exp(-\theta F(y)) \\
&= \exp(-\theta) + [1 - \exp(-\theta)]S^*(y),
\end{aligned}
$$

where $S^*(y)$ is given by (2.2). Thus, $S_p(y)$ is a standard cure rate model with cure rate $\pi = \exp(-\theta)$ and survival function for the non-cured population given by $S^*(y)$. This shows a mathematical relationship between the model in (1.1) and (2.1).

In this model (2.1), we let the covariates depend on θ through the relationship $\theta = \exp(x'\beta)$, where x is a $p \times 1$ vector of covariates and β is a $p \times 1$ vector of regression coefficients which are the same as in (2.1).

2.2 The Likelihood Function

Following Chen, Ibrahim and Sinha (1999), we construct the likelihood function as follows. Suppose we have n subjects, and we use the following notations:

t_i : the failure time for the i-th subject, $i = 1, 2, \ldots\ldots, n$.

c_i : censoring time for the i-th subject, $i = 1, 2, \ldots\ldots, n$.

$$\delta_i = I(t_i \leq c_i) = \begin{cases} 1, & \text{failure time} \\ 0, & \text{right censoring} \end{cases} \qquad \text{i=1,2,......,n}$$

$y = (y_1, y_2, \ldots.., y_n)$: the observed time, where $y_i = \min(t_i, \delta_i)$, $i = 1, 2, \ldots.., n$.

$\delta = (\delta_1, \delta_2, \ldots.., \delta_n)$: censoring indicator.

$D_o = (n, y, \delta)$: the observed data.

$D = (n, y, \delta, N)$: the total data, where N is an unobserved vector of a latent variable.

N_i: the number of carcinogenic cells for the i-th subject, following a Poisson distribution with mean θ, $i = 1, 2, \ldots.., n$. That is,

$$P(N_i = k) = \frac{e^{-\theta}\theta^k}{k!}.$$

In our model formation, the N_i's are not observed and can be viewed as latent variables. Further, suppose that $Z_{i1}, Z_{i2}, \ldots.., Z_{iN_i}$ are the *i.i.d.* incubation times for the N_i carcinogenic cells for the i-th subject following a cdf $F(\cdot)$, $i = 1, \ldots., n$. In this practicum we specify a parametric form for $F(\cdot)$, such as log-logistic, Gompertz or Gamma distribution. We denote the indexing parameter by γ, and thus write $F(\cdot|\gamma)$ and $S(\cdot|\gamma)$. We incorporate covariates for the cure rate model through the cure rate parameter θ. When covariates are included, we have a different cure rate parameter, θ_i, for each subject, $i = 1, \ldots., n$. Let $x_i' = (x_{i1}, \ldots, x_{ik})$ denote the $k \times 1$ vector of covariates for the ith subject, and let $\beta = (\beta_1, \ldots, \beta_k)$ denote the corresponding vector of regression coefficients. We relate θ to the covariates by $\theta_i = \exp(x_i'\beta)$. Therefore, the complete-data likelihood function of the parameters (γ, β) can be written as

$$\begin{aligned} L(\gamma,\beta \mid D) &= f(D \mid \gamma,\beta) \\ &= f(n,y,\delta,N \mid \gamma,\beta) \\ &= \prod_{i=1}^{n} f(y_i,\delta_i,N_i \mid \gamma,\beta) \\ &= \prod_{i=1}^{n} f(y_i,\delta_i \mid \gamma,N_i) P(N_i \mid \beta) \\ &= \left\{\prod_{i=1}^{n} f_p(y_i \mid \gamma,N_i)^{\delta_i} S_p(y_i \mid \gamma,N_i)^{1-\delta_i}\right\} \cdot \left\{\prod_{i=1}^{n} \frac{e^{-\theta_i}\theta_i^{N_i}}{N_i!}\right\}, \end{aligned}$$

where

$$\begin{aligned} S_p(y_i \mid \gamma,N_i) &= P_r(Y > y_i \mid \gamma,N_i) \\ &= P_r(Z_{i1} > y_i, Z_{i2} > y_i, \ldots\ldots, Z_{iN_i} > y_i \mid \gamma,N_i) \\ &= P_r(Z_{i1} > y_i \mid \gamma,N_i) \cdot P_r(Z_{i2} > y_i \mid \gamma,N_i) \cdot \cdots P_r(Z_{iN_i} > y_i \mid \gamma,N_i) \\ &= S(y_i \mid \gamma,N_i)^{N_i}, \end{aligned}$$

and

$$\begin{aligned} f_p(y_i \mid \gamma,N_i) &= -\frac{dS_p(y_i \mid \gamma,N_i)}{dy_i} \\ &= \left\{\prod_{i=1}^{n}(N_i S(y_i \mid \gamma)^{N_i-1} f(y_i \mid \gamma))^{\delta_i} \cdot (S(y_i \mid \gamma)^{N_i})^{1-\delta_i}\right\} \cdot \prod_{i=1}^{n} \frac{e^{-\theta_i} \cdot \theta_i^{N_i}}{N_i!} \\ &= \left\{\prod_{i=1}^{n}(N_i \cdot f(y_i \mid \gamma))^{\delta_i} \cdot (S(y_i \mid \gamma))^{N_i-\delta_i}\right\} \cdot \prod_{i=1}^{n} \frac{e^{-\theta_i} \cdot \theta_i^{N_i}}{N_i!} \\ &= \left\{\prod_{i=1}^{n} S(y_i \mid \gamma)^{N_i-\delta_i} \cdot (N_i f(y_i \mid \gamma))^{\delta_i}\right\} \\ &\quad \times \exp\left\{\sum_{i=1}^{n}(N_i \log(\theta_i) - \log(N_i!) - \theta_i)\right\}. \end{aligned}$$

The complete-data likelihood function of (β, γ) becomes

$$\begin{aligned} L(\beta,\gamma \mid D) &= \left\{\prod_{i=1}^{n} S(y_i \mid \gamma)^{N_i-\delta_i} \cdot (N_i f(y_i \mid \gamma))^{\delta_i}\right\} \\ &\quad \times \exp\left\{\Sigma_{i=1}^{n} N_i \log(\theta_i) - \log(N_i!) - n\theta_i\right\} \\ &= \left\{\prod_{i=1}^{n} S(y_i \mid \gamma)^{N_i-\delta_i} \cdot (N_i f(y_i \mid \gamma))^{\delta_i}\right\} \\ &\quad \times \exp\left\{\sum (N_i x_i^{'}\beta - \log(N_i!) - \exp(x_i^{'}\beta))\right\}, \qquad (2.3) \end{aligned}$$

where $\theta_i = \exp(x_i^{'}\beta)$. Following results of Chen et al (1999), by summing out the observed latent vector N, the complete-data likelihood function given in (2.3) can be reduced to

$$\begin{aligned} L(\beta,\gamma \mid D_{obs}) &= \sum_N L(\beta,\gamma \mid D) \\ &= \sum_N \left\{\left[\prod_{i=1}^{n} S(y_i \mid \gamma)^{N_i-\delta_i}(N_i f(y_i \mid \gamma))^{\delta_i}\right] \cdot \prod_{i=1}^{n} \frac{e^{-\theta_i}\theta_i^{N_i}}{N_i!}\right\} \\ &= \sum_N \left\{\prod_{i=1}^{n} \left[S(y_i \mid \gamma)^{N_i-\delta_i}(N_i f(y_i \mid \gamma))^{\delta_i} \cdot \frac{e^{-\theta_i}\theta_i^{N_i}}{N_i!}\right]\right\} \\ &= \prod_{i=1}^{n} f(y_i \mid \gamma)^{\delta_i} \cdot e^{-\theta_i} \cdot \left\{\sum_N \left[\prod_{i=1}^{n} S(y_i \mid \gamma)^{N_i-\delta_i} \cdot N_i^{\delta_i} \cdot \frac{\theta_i^{N_i}}{N_i!}\right]\right\} \\ &= \left\{\prod_{i=1}^{n} f(y_i \mid \gamma)^{\delta_i} \cdot e^{-\theta_i} \cdot S(y_i \mid \gamma)^{-\delta_i}\right\} \\ &\quad \times \left\{\sum_N \left[\prod_{i=1}^{n} S(y_i \mid \gamma)^{N_i} \cdot N_i^{\delta_i} \cdot \frac{\theta_i^{N_i}}{N_i!}\right]\right\} \\ &= \prod_{i=1}^{n} (\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))). \qquad (2.4) \end{aligned}$$

Chapter 3

The Noninformative Prior Distribution

In this chapter, we discuss classes of noninformative prior distributions, and examine some of their properties under log-logistic, Gompertz and Gamma distributions for $F(\cdot)$.

We suppose a joint noninformative prior for $\pi(\beta, \gamma)$ of the form $\pi(\beta, \gamma) \propto \pi(\gamma)$, where $\gamma = (\alpha, \lambda)$ are the parameters in $f(y|\gamma)$. This noninformative prior implies that β and γ are independent priors and that $\pi(\beta) \propto 1$ is a uniform improper prior. Hence, the posterior distribution of (β, γ) based on the observed data $D_{obs} = (n, y, x, \delta)$ is given by

$$p(\beta, \gamma \mid D_{obs}) = \frac{\pi(\beta, \gamma, D_{obs})}{\pi(D_{obs})}$$

$$
\begin{aligned}
&= \frac{\pi(D_{obs} \mid \beta, \gamma)\pi(\beta, \gamma)}{\pi(D_{obs})} \\
&= \frac{L(\beta, \gamma \mid D_{obs}) \cdot \pi(\beta, \gamma)}{\pi(D_{obs})} \\
&\propto L(\beta, \gamma \mid D_{obs}) \cdot \pi(\gamma). \qquad (3.1)
\end{aligned}
$$

From (2.4),

$$p(\beta, \gamma \mid D_{obs}) \propto \prod_{i=1}^{n} (\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma)))\pi(\gamma). \qquad (3.2)$$

Chen et al (1999) proved that equation (3.2) with $f(y|\gamma)$ following a Weibull distribution is proper whether $\pi(\gamma)$ is proper or not. In this chapter, we consider three distributions for $f(y|\gamma)$: log-logistic, Gompertz and Gamma distributions. For each distribution we investigate properties of the posterior distributions.

3.1 Log-logistic Distribution

When $f(y_i \mid \gamma)$ follows a log-logistic distribution, we have $f(y_i \mid \gamma) = \frac{\alpha y_i^{\alpha-1}\lambda}{(1+\lambda y_i^{\alpha})^2}$ and $S(y_i \mid \gamma) = \frac{1}{1+\lambda y_i^{\alpha}}$, where $\alpha > 0, \lambda > 0, y_i \geq 0$, α is the shape parameter and λ is the scale parameter.

We assume throughout this subsection that

$$\pi(\gamma) = \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda),$$

where

$$\pi(\alpha \mid \nu_0, \tau_0) \propto \alpha^{\nu_0 - 1} \exp(-\tau_0 \alpha),$$

and ν_0, τ_0 are two specified hyperparameters. With these specifications, the posterior distribution of (β, γ) based on the observed data $D_{obs} = (n, y, x, \delta)$ is given by

$$p(\beta, \gamma \mid D_{obs}) \propto L(\beta, \gamma \mid D_{obs}) \cdot \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda). \tag{3.3}$$

The following theorem gives conditions concerning the propriety of the posterior distribution in (3.3), using the noninformative $\pi(\beta, \gamma) \propto \pi(\gamma)$.

Theorem 3.1 Let $d = \sum_{i=1}^{n} \delta_i$ and X^* be an $n \times k$ matrix with rows $\delta_i x_i'$. Then the posterior given in (3.3) is proper if the following conditions are satisfied:

(a) X^* is of full rank,

(b) $\pi(\lambda)$ is proper,

(c) $\tau_0 > 0$ and $\nu_0 > -d$.

Even though $\gamma = (\alpha, \lambda)$ are the log-logistic parameters in $f(y|\gamma)$, we can obtain similar results as in Chen et al (1999). To be more specific, a proper prior for α is not required to obtain a proper posterior. This can be observed from condition (c), because $\pi(\alpha \mid \nu_0, \tau_0)$ is no longer proper when $\nu_0 < 0$. Based on condition (b), $\pi(\lambda)$ is required to be proper. Although several choices can be made, we prefer to use a normal density for $\pi(\lambda)$ in the data analysis, which will be discussed in Chapter 5.

Proof of Theorem 3.1: We adapt the proof of Chen et al (1999) for this case. In order to prove Theorem 3.1, we must first show that there exists a constant $M > 1$, such that

$$(\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \leq \alpha^{\delta_i} \cdot M. \tag{3.4}$$

When $\delta_i = 0$,

$$(\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) = \exp(-\theta_i(1 - S(y_i \mid \gamma))) \leq 1.$$

When $\delta_i = 1$,

$$\begin{aligned}
& (\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&= \theta_i f(y_i \mid \gamma) \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&= \frac{f(y_i \mid \gamma)}{1 - S(y_i \mid \gamma)} \cdot (1 - S(y_i \mid \gamma)) \cdot \theta_i \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&= \frac{\frac{\alpha y_i^{\alpha-1}\lambda}{(1+\lambda y_i^{\alpha})^2}}{1 - \frac{1}{1+\lambda y_i^{\alpha}}}(1 - S(y_i \mid \gamma))\theta_i \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&= y_i^{-1} \cdot \frac{\alpha}{1 + \lambda y_i^{\alpha}} \{(1 - S(y_i \mid \gamma))\theta_i \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma)))\}. \quad (3.5)
\end{aligned}$$

Let

$$\begin{aligned}
g_1 &= \frac{1}{1 + \lambda y_i^{\alpha}}, \\
g_2 &= \{(1 - S(y_i \mid \gamma))\theta_i \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma)))\}.
\end{aligned}$$

The equation (3.5) becomes

$$y_i^{-1}\alpha \cdot g_1 \cdot g_2.$$

Since, $\alpha > 0$, $\lambda > 0$, $y_i > 0$, we know $g_1 = \frac{1}{1+\lambda y_i^{\alpha}} \leq 1$ and $g_2 \leq 1$. Therefore, it can be shown that there exists a common constant $g_0 > 0$, such that

$$g_1 \leq g_0 \quad \text{and} \quad g_2 \leq g_0. \tag{3.6}$$

Using (3.6), (3.5) is less than $y_i^{-1}\alpha g_0^2$. Thus, taking $M^* = \max_{\{i:\delta_i=1\}}\{g_0^2 y_i^{-1}\}$ and $M = \max\{1, M^*\}$, we obtain (3.4), which is

$$(\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \leq \alpha^{\delta_i} M.$$

Because X^* is of full rank, there must exist k linearly independent row vectors $x'_{i_1}, x'_{i_2}, ..., x'_{i_k}$, such that $\delta_{i_1} = \delta_{i_2} = ... = \delta_{i_k} = 1$. Using (2.4) and (3.4),

$$\begin{aligned}
&\int_0^\infty \int_0^\infty \int_{R^k} L(\beta, \gamma \mid D_{obs}) \pi(\alpha \mid \nu_0, \tau_0) \pi(\lambda) d\beta d\alpha d\lambda \\
&= \int_0^\infty \int_0^\infty \int_{R^k} \prod_{i=1}^{n} (\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&\quad \times \pi(\alpha \mid \nu_0, \tau_0) \pi(\lambda) d\beta d\alpha d\lambda \\
&= \int_0^\infty \int_0^\infty \int_{R^k} \prod_{i=1}^{n-k} (\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&\quad \times \left\{ \prod_{j=1}^{k} (\theta_i f(y_{i_j} \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_{i_j} \mid \gamma))) \right\} \\
&\quad \times \pi(\alpha \mid \nu_0, \tau_0) \pi(\lambda) d\beta d\alpha d\lambda \\
&\leq \int_0^\infty \int_0^\infty \int_{R^k} \prod_{i=1}^{n-k} (\alpha^{\delta_i} M) \\
&\quad \times \left\{ \prod_{j=1}^{k} (\theta_{i_j} f(y_{i_j} \mid \gamma))^{\delta_{i_j}} \cdot \exp(-\theta_{i_j}(1 - S(y_{i_j} \mid \gamma))) \right\} \\
&\quad \times \pi(\alpha \mid \nu_0, \tau_0) \pi(\lambda) d\beta d\alpha d\lambda \\
&\leq \int_0^\infty \int_0^\infty \int_{R^k} (\alpha M)^{d-k} \prod_{j=1}^{k} f(y_{i_j} \mid \gamma) \\
&\quad \times \exp(x'_{i_j}\beta - (1 - S(y_{i_j} \mid \gamma)) \exp(x'_{i_j}\beta)) \\
&\quad \times \pi(\alpha \mid \nu_0, \tau_0) \pi(\lambda) d\beta d\alpha d\lambda, \qquad (3.7)
\end{aligned}$$

where R^k denotes k-dimensional Euclidean space. We make the transformation

$u_j = x'_{i_j}\beta$ for $j = 1, 2, \ldots.., k$. This is a one-to-one linear transformation from β to $u = (u_1, u_2, \ldots\ldots u_k)'$. Thus, (3.7) is proportional to

$$\begin{aligned}
&\int_0^\infty \int_0^\infty \int_{R^k} \alpha^{d-k} \prod_{j=1}^{k} f(y_{i_j} \mid \gamma) \\
&\times \exp(u_j - (1 - S(y_{i_j} \mid \gamma)) \exp(u_j)) \\
&\times \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) du d\alpha d\lambda \\
&= \int_0^\infty \int_0^\infty \alpha^{d-k} \prod_{j=1}^{k} \\
&\left[f(y_{i_j} \mid \gamma) \int_0^\infty \exp(u_j - (1 - S(y_{i_j} \mid \gamma)) \exp(u_j)) du_j \right] \\
&\times \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\alpha d\lambda \\
&= \int_0^\infty \int_0^\infty \alpha^{d-k} \left[\prod_{j=1}^{k} \frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)} \right] \\
&\times \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\alpha d\lambda. \qquad (3.8)
\end{aligned}$$

In (3.8), using (3.6), we have

$$\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)} = \frac{\alpha y_i^{-1}}{1 + \lambda y_i^{\alpha}} \leq K_0 \alpha,$$

where $K_0 = g_0 \max_{\{1 \leq j \leq k\}} \{y_{i_j}^{-1}\}$. Thus, (3.8) is less than or equal to

$$\begin{aligned}
&\int_0^\infty \int_0^\infty \alpha^{d-k} \prod_{j=1}^{k} (k_0 \alpha) \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\alpha d\lambda \\
&= k_0^{\alpha} \int_0^\infty \int_0^\infty \alpha^{d} \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\alpha d\lambda \\
&= k_0^{\alpha} \int_0^\infty \int_0^\infty \alpha^{d+\nu_0-1} \exp(-\tau_0 \alpha)\pi(\lambda) d\alpha d\lambda. \qquad (3.9)
\end{aligned}$$

By noticing that $\pi(\alpha \mid \nu_0, \tau_0) \propto \alpha^{\nu_0 - 1} \exp(-\tau_0 \alpha)$, $\tau_0 > 0, \nu_0 > -d$ and $\pi(\lambda)$ is proper. Therefore, (3.9) $< \infty$. This completes the proof. □

3.2 Gompertz Distribution

When $f(y|\gamma)$ follows the Gompertz distribution, we have

$$\begin{aligned} f(y_i \mid \gamma) &= \alpha e^{\lambda y_i} \exp\left\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\right\}, \\ S(y_i \mid \gamma) &= \exp\left\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\right\}, \end{aligned}$$

where $\alpha > 0, \lambda > 0, y_i \geq 0$, α is the shape parameter, and λ is the scale parameter. From (3.2), we know the posterior distribution is

$$p(\beta, \gamma \mid D_{obs}) \propto \prod_{i=1}^{n} (\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma)))\pi(\gamma),$$

where $\gamma = (\alpha, \lambda)$ is the Gompertz parameters in $f(y|\gamma)$. We assume throughout this subsection that

$$\pi(\gamma) = \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda),$$

and

$$\pi(\gamma) = \pi(\lambda \mid \nu_0, \tau_0)\pi(\alpha),$$

where ν_0, τ_0 are two specified hyperparameters.

When

$$\pi(\gamma) = \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda),$$

where

$$\pi(\alpha \mid \nu_0, \tau_0) \propto \alpha^{\nu_0 - 1} \exp(-\tau_0 \alpha),$$

the posterior distribution of (β, γ) based on the observed data $D_{obs} = (n, y, x, \delta)$ is given by

$$p(\beta, \gamma \mid D_{obs}) \propto L(\beta, \gamma \mid D_{obs}) \cdot \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda). \tag{3.10}$$

The following theorem gives conditions for the propriety of the posterior distribution in (3.10). Using the noninformative $\pi(\beta, \gamma) \propto \pi(\gamma)$, we get the first theorem.

Theorem 3.2 Let $d = \sum_{i=1}^{n} \delta_i$ and X^* be an $n \times k$ matrix with rows $\delta_i x_i'$. Then the posterior (3.10) is proper if the following conditions are satisfied:

(a) X^* is of full rank,

(b) $\pi(\lambda)$ is proper,

(c) $\tau_0 > 0$ and $\nu_0 > -d$.

When

$$\pi(\gamma) = \pi(\lambda \mid \nu_0, \tau_0)\pi(\alpha),$$

where

$$\pi(\lambda \mid \nu_0, \tau_0) \propto e^{\tau_0 \lambda} \exp\left\{\frac{\nu_0}{\tau_0}\left[1 - e^{\lambda(\tau_0 + \ln \alpha)}\right]\right\},$$

the posterior distribution of (β, γ) based on the observed data $D_{obs} = (n, y, x, \delta)$ is given by

$$p(\beta, \gamma \mid D_{obs}) \propto L(\beta, \gamma \mid D_{obs}) \cdot \pi(\lambda \mid \nu_0, \tau_0)\pi(\alpha). \tag{3.11}$$

Therefore, we obtain the second theorem.

Theorem 3.2$'$ Let $d = \sum_{i=1}^{n} \delta_i$ and X^* be an $n \times k$ matrix with rows $\delta_i x_i'$. Then the posterior (3.11) is proper if the following conditions are satisfied:

(a) X^* is of full rank,

(b) $\pi(\alpha)$ is proper,

(c) $\tau_0 > 0$ and $\nu_0 > -k'd$, where $k' = \max\{y_i\}$.

The conditions stated in the above two theorems are sufficient but not necessary for the propriety of the posterior distribution. In Theorem 3.2, we note that a proper prior for α is not required and proper prior for λ is required to obtain a proper posterior. However, in Theorem 3.2$'$, we note that a proper prior for λ is not required and proper prior for α is required to obtain a proper posterior.

Proof of Theorem 3.2: The proof is very similar to the proof of Theorem 3.1. In order to obtain the propriety of the posterior distribution, we still need to show that there exists a constant $M > 1$ such that

$$(\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \leq \alpha^{\delta_i} \cdot M. \tag{3.12}$$

When $\delta_i = 0$, (3.12) is obviously true. When $\delta_i = 1$, the left side of (3.12) can be written as:

$$\begin{aligned}
&(\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&= \theta_i f(y_i \mid \gamma) \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&= \frac{f(y_i \mid \gamma)}{1 - S(y_i \mid \gamma)} \cdot (1 - S(y_i \mid \gamma)) \cdot \theta_i \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&= \frac{\alpha e^{\lambda y_i} \exp\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\}}{1 - \exp\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\}} \cdot (1 - S(y_i \mid \gamma)) \cdot \theta_i \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&= \alpha \frac{e^{\lambda y_i} \exp\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\}}{1 - \exp\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\}} \cdot \{(1 - S(y_i \mid \gamma)) \cdot \theta_i \exp(-\theta_i(1 - S(y_i \mid \gamma))\}
\end{aligned}$$

$$= \alpha g_1 g_2 \tag{3.13}$$

where

$$\begin{aligned} g_1 &= \frac{e^{\lambda y_i}\exp\{\frac{\alpha}{\lambda}(1-e^{\lambda y_i})\}}{1-\exp\{\frac{\alpha}{\lambda}(1-e^{\lambda y_i})\}}, \\ g_2 &= \{(1-S(y_i \mid \gamma))\cdot \theta_i \cdot \exp(-\theta_i(1-S(y_i \mid \gamma))\}. \end{aligned}$$

If we treat g_1 as the function of λ, and let

$$\frac{\partial g_1}{\partial \lambda} = e^{\lambda y_i} e^{\frac{\alpha(1-e^{\lambda y_i})}{\lambda}} \left\{ y_i - y_i e^{\alpha(1-e^{\lambda y_i})/\lambda} - \frac{\alpha\lambda y_i e^{\lambda y_i} + \alpha(1-e^{\lambda y_i})}{\lambda^2} \right\} = 0,$$

then $\lambda = \lambda_0$. We also know that g_1 is a continuous function, and

$$\begin{aligned} \lim_{\lambda\to\infty} g_1 &= \lim_{\lambda\to\infty} \frac{e^{\lambda y_i}\exp\{\frac{\alpha}{\lambda}(1-e^{\lambda y_i})\}}{1-\exp\{\frac{\alpha}{\lambda}(1-e^{\lambda y_i})\}} \\ &= \lim_{\lambda\to\infty} \frac{e^{\lambda y_i}}{e^{\frac{\alpha}{\lambda}e^{\lambda y_i}}} \\ &= 0, \\ \lim_{\lambda\to 0} g_1 &= \lim_{\lambda\to 0} \frac{e^{\lambda y_i}\exp\{\frac{\alpha}{\lambda}(1-e^{\lambda y_i})\}}{1-\exp\{\frac{\alpha}{\lambda}(1-e^{\lambda y_i})\}}, \\ &= \lim_{\lambda\to 0} \frac{\lambda^2 y_i - \alpha - \alpha e^{\lambda y_i}\cdot y_i \cdot \lambda + \alpha e^{\lambda y_i}}{\alpha\lambda y_i e^{\lambda y_i} + \alpha(1-e^{\lambda y_i})} \cdot e^{\lambda y_i} \\ &= 1. \end{aligned}$$

Therefore, there exists a common constant $g_0 > 0$, such that

$$g_1 \leq g_0 \quad \text{and} \quad g_2 \leq g_0. \tag{3.14}$$

Using (3.14), (3.13) $\leq \alpha g_0^2$. Let $M = \max\{1, g_0^2\}$. Thus, we get the result (3.12) which is

$$(\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1-S(y_i \mid \gamma))) \leq \alpha^{\delta_i} \cdot M.$$

Because X^* is of full rank, there must exist k linearly independent row vectors $x'_{i_1}, x'_{i_2}, ..., x'_{i_k}$, such that $\delta_{i_1} = \delta_{i_2} = ... = \delta_{i_k} = 1$. Using (3.12),

$$\begin{aligned}
&\int_0^\infty \int_0^\infty \int_{R^k} \sum_N L(\beta, \gamma \mid D)\pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\beta d\alpha d\lambda \\
&= \int_0^\infty \int_0^\infty \int_{R^k} \prod_{i=1}^{n} (\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&\quad \times \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\beta d\alpha d\lambda \\
&= \int_0^\infty \int_0^\infty \int_{R^k} \prod_{i=1}^{n-k} (\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&\quad \times \left[\prod_{j=1}^{k} (\theta_{i_j} f(y_{i_j} \mid \gamma))^{\delta_{i_j}} \cdot \exp(-\theta_{i_j}(1 - S(y_{i_j} \mid \gamma))) \right] \\
&\quad \times \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\beta d\alpha d\lambda \\
&\le \int_0^\infty \int_0^\infty \int_{R^k} \prod_{i=1}^{n-k} (\alpha^{\delta_i} M) \\
&\quad \times \left[\prod_{j=1}^{k} (\theta_{i_j} f(y_{i_j} \mid \gamma)) \exp(-\theta_{i_j}(1 - S(y_{i_j} \mid \gamma))) \right] \\
&\quad \times \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\beta d\alpha d\lambda \\
&\le \int_0^\infty \int_0^\infty \int_{R^k} (\alpha M)^{d-k} \\
&\quad \times \left[\prod_{j=1}^{k} f(y_{i_j} \mid \gamma) \exp(x'_{i_j}\beta - (1 - S(y_{i_j} \mid \gamma)) \exp(x'_{i_j}\beta)) \right] \\
&\quad \times \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\beta d\alpha d\lambda. \qquad (3.15)
\end{aligned}$$

We make the transformation $u_j = x'_{i_j}\beta$ for $j = 1, 2, ..., k$. This is a one-to-one linear transformation from β to $u = (u_1, u_2, ...u_k)'$. Thus, (3.15) is proportional to

$$\int_0^\infty \int_0^\infty \int_{R^k} \alpha^{d-k} \prod_{j=1}^{k} f(y_{i_j} \mid \gamma)$$

$$
\begin{aligned}
&\times \exp(u_j - (1 - S(y_{i_j} \mid \gamma)) \exp(u_j))\pi(\alpha \mid \nu_0, \tau_0) \\
&\times \pi(\lambda) du d\alpha d\lambda \\
&= \int_0^\infty \int_0^\infty \alpha^{d-k} \prod_{j=1}^{k} \\
&\times \left[f(y_{i_j} \mid \gamma) \cdot \int_0^\infty \exp(u_j - (1 - S(y_{i_j} \mid \gamma)) \exp(u_j)) du_j \right] \\
&\times \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\alpha d\lambda. \qquad (3.16)
\end{aligned}
$$

Integrating out u, (3.16) reduces to

$$
\int_0^\infty \int_0^\infty \alpha^{d-k} \left[\prod_{j=1}^{k} \frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)} \right] \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\alpha d\lambda. \qquad (3.17)
$$

Using (3.14), we have

$$
\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)} \;=\; \alpha \frac{e^{\lambda y_i} \cdot \exp\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\}}{1 - \exp\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\}} \le k_0 \alpha,
$$

where $k_0 = \max\{1, g_0\}$. Thus, (3.17) is less than or equal to

$$
\begin{aligned}
&\int_0^\infty \int_0^\infty \alpha^{d-k} \prod_{j=1}^{k} (k_0 \alpha) \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\alpha d\lambda \\
&= k_0^k \int_0^\infty \int_0^\infty \alpha^{d} \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\alpha d\lambda \\
&= k_0^\alpha \int_0^\infty \int_0^\infty \alpha^{d+\nu_0-1} \exp(-\tau_0 \alpha)\pi(\lambda) d\alpha d\lambda. \qquad (3.18)
\end{aligned}
$$

Noticing that $\pi(\alpha \mid \nu_0, \tau_0) \propto \alpha^{\nu_0 - 1} \exp(-\tau_0 \alpha)$, $\tau_0 > 0, \nu_0 > -d$ and $\pi(\lambda)$ is proper. Therefore, (3.18) $< \infty$. This completes the proof. □

Proof of Theorem 3.2′: In order to obtain the propriety of the posterior distribution, we still need to show that there exists a constant $M > 1$, such that

$$(\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \leq \alpha^{\delta_i} \cdot M. \tag{3.19}$$

When $\delta_i = 0$, (3.19) is obviously true. When $\delta_i = 1$, the left side of (3.19) can be written as:

$$\begin{aligned}
&(\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&= e^{\lambda y_i} \frac{\alpha \exp\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\}}{1 - \exp\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\}} \\
&\quad \times (1 - S(y_i \mid \gamma)) \cdot \theta_i \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&= e^{\lambda y_i} g_1 g_2,
\end{aligned} \tag{3.20}$$

where

$$\begin{aligned}
g_1 &= \frac{\alpha \exp\left\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\right\}}{1 - \exp\left\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\right\}}, \\
g_2 &= (1 - S(y_i \mid \gamma)) \cdot \theta_i \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))).
\end{aligned}$$

We treat g_1 as the function of α. It is very easy to see that the function of g_1 is a continuous function, and at the same time,

$$\begin{aligned}
\lim_{\alpha \to \infty} g_1 &= \lim_{\alpha \to \infty} \frac{\alpha \exp\left\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\right\}}{1 - \exp\left\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\right\}} \\
&= \lim_{\alpha \to \infty} \alpha \exp\left\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\right\} \\
&= \lim_{\alpha \to \infty} \frac{\alpha}{\exp\left\{\frac{\alpha}{\lambda}(e^{\lambda y_i} - 1)\right\}} \\
&= 0, \\
\lim_{\alpha \to 0} g_1 &= \lim_{\alpha \to 0} \frac{\alpha \exp\left\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\right\}}{1 - \exp\left\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\right\}} \\
&= 0.
\end{aligned}$$

Therefore, there exists a common constant $g_0 > 0$, such that

$$g_1 \leq g_0 \quad \text{and} \quad g_2 \leq g_0. \tag{3.21}$$

Using (3.21), we establish that (3.20) $\leq e^{\lambda y_i} g_0^2$. Let $k' = \max_{\{i,\delta_i=1\}}\{y_i\}$ and $M = \max\{1, g_0^2\}$. Then, (3.20) $\leq e^{k'\lambda} M$. Thus,

$$(\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \leq (e^{k'\lambda})^{\delta_i} \cdot M. \tag{3.22}$$

Because X^* is of full rank, there must exist k linear independent row vectors $x'_{i_1}, x'_{i_2}, \ldots\ldots, x'_{i_k}$, such that $\delta_{i_1} = \delta_{i_2} = \ldots.. = \delta_{i_k} = 1$.

$$\begin{aligned}
&\int_0^\infty \int_0^\infty \int_{R^k} \sum_N L(\beta, \gamma \mid D) \pi(\lambda \mid \nu_0, \tau_0) \pi(\alpha) d\beta d\alpha d\lambda \\
&= \int_0^\infty \int_0^\infty \int_{R^k} \prod_{i=1}^n (\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&\quad \times \pi(\lambda \mid \nu_0, \tau_0) \pi(\alpha) d\beta d\alpha d\lambda \\
&= \int_0^\infty \int_0^\infty \int_{R^k} \prod_{i=1}^{n-k} (\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&\quad \times \left[\prod_{j=1}^k (\theta_{i_j} f(y_{i_j} \mid \gamma))^{\delta_{i_j}} \cdot \exp(-\theta_{i_j}(1 - S(y_{i_j} \mid \gamma))) \right] \\
&\quad \times \pi(\lambda \mid \nu_0, \tau_0) \pi(\alpha) d\beta d\alpha d\lambda \\
&\leq \int_0^\infty \int_0^\infty \int_{R^k} \prod_{i=1}^n ((e^{k'\lambda})^{\delta_i} M) \\
&\quad \times \left[\prod_{j=1}^k (\theta_{i_j} f(y_{i_j} \mid \gamma))^{\delta_{i_j}} \exp(-\theta_{i_j}(1 - S(y_{i_j} \mid \gamma))) \right] \\
&\quad \times \pi(\lambda \mid \nu_0, \tau_0) \pi(\alpha) d\beta d\alpha d\lambda \\
&\leq \int_0^\infty \int_0^\infty \int_{R^k} (e^{k'\lambda} M)^{d-k} \prod_{j=1}^k f(y_{i_j} \mid \gamma) \\
&\quad \times \exp(x'_{i_j}\beta - (1 - S(y_{i_j} \mid \gamma)) \exp(x'_{i_j}\beta)) \\
&\quad \times \pi(\lambda \mid \nu_0, \tau_0) \pi(\alpha) d\beta d\alpha d\lambda.
\end{aligned} \tag{3.23}$$

We make the transformation $u_j = x'_{i_j}\beta$ for $j = 1, 2, \ldots\ldots, k$. This is a one-to-one linear transformation from β to $u = (u_1, u_2, \ldots\ldots u_k)'$. Thus, (3.23) is proportional to

$$\begin{aligned}
&\int_0^\infty \int_0^\infty \int_{R^k} (e^{k'\lambda})^{d-k} \\
&\quad \times \prod_{j=1}^{k} f(y_{i_j} \mid \gamma) \exp(u_j - (1 - S(y_{i_j} \mid \gamma)) \exp(u_j)) \\
&\quad \times \pi(\lambda \mid \nu_0, \tau_0)\pi(\alpha) du d\alpha d\lambda \\
&= \int_0^\infty \int_0^\infty (e^{k'\lambda})^{d-k} \\
&\quad \times \prod_{j=1}^{k} (f(y_{i_j} \mid \gamma) \int_0^\infty \exp(u_j - (1 - S(y_{i_j} \mid \gamma)) \exp(u_j)) du_j) \\
&\quad \times \pi(\lambda \mid \nu_0, \tau_0)\pi(\alpha) d\alpha d\lambda \\
&= \int_0^\infty \int_0^\infty (e^{k'\lambda})^{d-k} \left[\prod_{j=1}^{k} \frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)} \right] \\
&\quad \times \pi(\lambda \mid \nu_0, \tau_0)\pi(\alpha) d\alpha d\lambda. \qquad (3.24)
\end{aligned}$$

Let $k' = \max_{\{i:\delta_i=1\}}\{y_i\}$. Using (3.21), we establish that

$$\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)}) = e^{\lambda y_i} \frac{\alpha \cdot \exp\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\}}{1 - \exp\{\frac{\alpha}{\lambda}(1 - e^{\lambda y_i})\}} \leq e^{k'\lambda} \cdot g_0.$$

Thus,

$$\begin{aligned}
(3.24) \quad &\leq \quad \int_0^\infty \int_0^\infty (e^{\lambda k'})^{d-k} \prod_{j=1}^{k} (e^{\lambda k'} \cdot g_0) \pi(\lambda \mid \nu_0, \tau_0)\pi(\alpha) d\alpha d\lambda \\
&= \quad g_0^k \int_0^\infty \int_0^\infty (e^{\lambda k'})^d \pi(\lambda \mid \nu_0, \tau_0)\pi(\alpha) d\alpha d\lambda \\
&= \quad g_0^k \int_0^\infty \int_0^\infty e^{\lambda(\tau_0 + k'd)} \\
&\quad\quad \times \exp\left\{\frac{\nu_0}{\tau_0}(1 - e^{\lambda(\tau_0 + \ln a)})\right\} \pi(\alpha) d\alpha d\lambda. \qquad (3.25)
\end{aligned}$$

Noticing that

$$\begin{aligned}\pi(\lambda \mid \nu_0, \tau_0) &\propto e^{\tau_0\lambda}\exp\left\{\frac{\nu_0}{\tau_0}(1 - e^{\lambda(\tau_0+\ln a)})\right\}\\ \ln a &= k^{'}d,\end{aligned}$$

$\tau_0 > 0, \nu_0 > -k^{'}d$ and $\pi(\alpha)$ is proper. Thus, (3.25) $< \infty$. This completes the proof. □

3.3 Gamma Distribution

When $f(y|\gamma)$ follows a Gamma distribution, we have

$$\begin{aligned}f(y_i \mid \gamma) &= \frac{\lambda^\alpha y_i^{\alpha-1}\exp(-\lambda y_i)}{\Gamma(\alpha)}\\ S(y_i \mid \gamma) &= 1 - I(\lambda y_i)\\ &= 1 - \int_0^{y_i} \frac{\lambda^\alpha y_i^{\alpha-1}\exp(-\lambda y_i)}{\Gamma(\alpha)}dy_i\\ &= 1 - \int_0^{\lambda y_i} \frac{(\lambda y_i)^{\alpha-1}\exp(-\lambda y_i)}{\Gamma(\alpha)}d(\lambda y_i),\end{aligned}$$

where $\alpha > 0, \lambda > 0, y_i \geq 0$, α is the shape parameter, λ is the scale parameter.

We assume throughout this subsection that

$$\pi(\gamma) = \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda),$$

where

$$\pi(\alpha \mid \nu_0, \tau_0) \propto \alpha^{\nu_0-1}\exp(-\tau_0\alpha),$$

and ν_0, τ_0 are two specified hyperparameters. With these specifications, the posterior distribution of (β, γ) based on the observed data $D_{obs} = (n, y, x, \delta)$

is given by

$$p(\beta, \gamma \mid D_{obs}) \propto L(\beta, \gamma \mid D_{obs}) \cdot \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda). \tag{3.26}$$

The following theorem gives conditions for the propriety of the posterior distribution in (3.26) using the noninformative $\pi(\beta, \gamma) \propto \pi(\gamma)$.

Theorem 3.3. Let $d = \sum_{i=1}^{n} \delta_i$ and X^* be an $n \times k$ matrix with rows $\delta_i x_i'$. Then the posterior (3.26) is proper if the following conditions are satisfied:

(a) X^* is of full rank,

(b) $\pi(\lambda)$ is proper,

(c) $\tau_0 > 0$ and $\nu_0 > -d$.

In this theorem, we obtain similar results as in Chen et al (1999). Therefore, we can extend Chen et al (1999)'s work not only to the log-logistic and Gompertz distributions, but also to the Gamma distribution.

Proof of Theorem 3.3: In order to prove Theorem 3.3, first we need to show that there exists a constant $M > 1$ such that

$$(\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \leq \alpha^{\delta_i} \cdot M. \tag{3.27}$$

When $\delta_i = 0$, (3.27) is obviously true. When $\delta_i = 1$, the left side of (3.27) is written as

$$\begin{aligned}
&(\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&= \theta_i f(y_i \mid \gamma) \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&= \frac{f(y_i \mid \gamma)}{1 - S(y_i \mid \gamma)} \cdot (1 - S(y_i \mid \gamma)) \cdot \theta_i \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))). \quad (3.28)
\end{aligned}$$

In the first part of (3.28),

$$\begin{aligned}\frac{f(y_i \mid \gamma)}{1-S(y_i \mid \gamma)} &= \frac{\frac{\lambda^\alpha y_i^{\alpha-1}\exp(-\lambda y_i)}{\Gamma(\alpha)}}{\int_0^{\lambda y_i}\frac{(\lambda y_i)^{\alpha-1}\exp(-\lambda y_i)}{\Gamma(\alpha)}d(\lambda y_i)} \\ &= \frac{\lambda^\alpha y_i^{\alpha-1}\exp(-\lambda y_i)}{\int_0^{\lambda y_i}(\lambda y_i)^{\alpha-1}\exp(-\lambda y_i)d(\lambda y_i)} \\ &= \frac{\lambda^\alpha y_i^{\alpha-1}\exp(-\lambda y_i)}{\int_0^{\lambda y_i}(t)^{\alpha-1}\exp(-t)d(t)},\end{aligned}$$

where $t = \lambda y_i$. It is very easy to see that the range of the integration is $0 < t < \lambda y_i$.

For the denominator,

$$\begin{aligned}&\int_0^{\lambda y_i} t^{\alpha-1}\exp(-t)dt > e^{-\lambda y_i}\int_0^{\lambda y_i} t^{\alpha-1}dt \\ &= \frac{1}{\alpha}(\lambda y_i)^\alpha e^{-\lambda y_i}.\end{aligned}$$

Thus,

$$\frac{f(y_i \mid \gamma)}{1-S(y_i \mid \gamma)} < \frac{\lambda^\alpha y_i^{\alpha-1}\exp(-\lambda y_i)}{\frac{1}{\alpha}(\lambda y_i)^\alpha e^{-\lambda y_i}} = \alpha y_i^{-1}.$$

If we take $M^* = \max_{\{i:\delta_i=1\}}\{y_i^{-1}\}$ and $M = \max\{1, g_0 M^*\}$, then we get

$$\frac{f(y_i \mid \gamma)}{1-S(y_i \mid \gamma)} \quad < \quad \alpha M^*$$

and

$$(\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1-S(y_i \mid \gamma))) \quad \leq \quad \alpha^{\delta_i} M.$$

Because X^* is of full rank, there must exist $k$linear independent row vectors $x'_{i_1}, x'_{i_2}, ..., x'_{i_k}$, such that $\delta_{i_1} = \delta_{i_2} = ... = \delta_{i_k} = 1$.

$$\int_0^\infty \int_0^\infty \int_{R^k} \sum_N L(\beta, \gamma \mid D)\pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda)d\beta d\alpha d\lambda$$

$$
\begin{aligned}
&= \int_0^\infty \int_0^\infty \int_{R^k} \prod_{i=1}^{n} (\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&\quad \times \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\beta d\alpha d\lambda \\
&= \int_0^\infty \int_0^\infty \int_{R^k} \prod_{i=1}^{n-k} (\theta_i f(y_i \mid \gamma))^{\delta_i} \cdot \exp(-\theta_i(1 - S(y_i \mid \gamma))) \\
&\quad \times \left[\prod_{j=1}^{k} (\theta_{i_j} f(y_{i_j} \mid \gamma))^{\delta_{i_j}} \cdot \exp(-\theta_{i_j}(1 - S(y_{i_j} \mid \gamma))) \right] \\
&\quad \times \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\beta d\alpha d\lambda \\
&\leq \int_0^\infty \int_0^\infty \int_{R^k} \prod_{i=1}^{n-k} (\alpha^{\delta_i} M) \\
&\quad \times \left[\prod_{j=1}^{k} (\theta_{i_j} f(y_{i_j} \mid \gamma))^{\delta_{i_j}} \cdot \exp(-\theta_{i_j}(1 - S(y_{i_j} \mid \gamma))) \right] \\
&\quad \times \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\beta d\alpha d\lambda \\
&\leq \int_0^\infty \int_0^\infty \int_{R^k} (\alpha M)^{d-k} \prod_{j=1}^{k} f(y_{i_j} \mid \gamma) \\
&\quad \times \exp(x_{i_j}' \beta - (1 - S(y_{i_j} \mid \gamma)) \exp(x_{i_j}' \beta)) \\
&\quad \times \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) d\beta d\alpha d\lambda, \qquad (3.29)
\end{aligned}
$$

where R^k denotes k-dimensional Euclidean space. We make the transformation $u_j = x_{i_j}' \beta$ for $j = 1, 2, \ldots\ldots, k$. This is a one-to-one linear transformation from β to $u = (u_1, u_2, \ldots\ldots u_k)'$. Thus, (3.29) is proportional to

$$
\begin{aligned}
&\int_0^\infty \int_0^\infty \int_{R^k} \alpha^{d-k} \prod_{j=1}^{k} f(y_{i_j} \mid \gamma) \\
&\quad \times \exp(u_j - (1 - S(y_{i_j} \mid \gamma)) \exp(u_j)) \\
&\quad \times \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda) du d\alpha d\lambda \\
&= \int_0^\infty \int_0^\infty \alpha^{d-k} \prod_{j=1}^{k} f(y_{i_j} \mid \gamma) \\
&\quad \times \int_0^\infty \exp(u_j - (1 - S(y_{i_j} \mid \gamma)) \exp(u_j)) du_j)
\end{aligned}
$$

$$
\begin{aligned}
&\times\pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda)d\alpha d\lambda \\
&= \int_0^\infty \int_0^\infty \alpha^{d-k} \left[\prod_{j=1}^{k} \frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)} \right] \\
&\quad \times\pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda)d\alpha d\lambda \\
&\leq \int_0^\infty \int_0^\infty \alpha^{d-k} \prod_{j=1}^{k} (M\alpha)\pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda)d\alpha d\lambda \\
&= (M^*)^k \int_0^\infty \int_0^\infty \alpha^d \pi(\alpha \mid \nu_0, \tau_0)\pi(\lambda)d\alpha d\lambda \\
&= (M^*)^k \int_0^\infty \int_0^\infty \alpha^{d+\nu_0-1} \exp(-\tau_0\alpha)\pi(\lambda)d\alpha d\lambda. \qquad (3.30)
\end{aligned}
$$

Noticing that $\frac{f(y_{i_j}|\gamma)}{1-S(y_{i_j}|\gamma)} \leq \alpha M^*$, $\pi(\alpha \mid \nu_0, \tau_0) \propto \alpha^{\nu_0-1}\exp(-\tau_0\alpha)$, $\tau_0 > 0, \nu_0 > -d$ and $\pi(\lambda)$ is proper. Thus, (3.32) $< \infty$. This completes the proof. □

From above, we obtain the same properties of the posterior distributions as those of Chen et al (1999). Therefore, by incorporating noninformative priors in the proposed models, the results of Chen et al (1999) can be extended to the log-logistic, Gompertz and Gamma distributions.

Chapter 4

Informative Prior Distribution

In this chapter, we examine classes of informative prior distributions with the use of historical data. This enables us to obtain more precise posterior estimates of the parameters in the proposed model compared to posterior estimates without the use of historical data.

Following Chen et al (1999), we now propose the informative prior construction for the proposed cure rate model. In this chapter as well as in Chapter 5, we maintain the same notations as in Chapter 3. Let n_0 denote the sample size for the historical data, y_0 be a $n_0 \times 1$ vector of right-censored failure times for the historical data with censoring indicators δ_0, N_0 be the uncensored vector of latent counts of carcinogenic cells, and X_0 be an $n_0 \times k$ matrix of covariates corresponding to y_0. Let $D_0 = (n_0, y_0, X_0, \delta_0, N_0)$ denote the complete historical data. Further, let $\pi_0(\beta, \gamma)$ denote the initial prior distribution for (β, γ). We propose a joint informative prior distribution of the form

$$\pi(\beta, \gamma \mid D_{0,obs}, a_0) \propto \left[\sum_{N_0} L(\beta, \gamma \mid D_0)\right]^{a_0} \pi_0(\beta, \gamma), \tag{4.1}$$

where $L(\beta, \gamma | D_0)$ is the complete data likelihood given in (2.3) with D being replaced by the historical data D_0, and $D_{0,obs} = (n_0, y_0, X_0, \delta_0)$. We take a noninformative prior for $\pi_0(\beta, \gamma)$, such as $\pi_0(\beta, \gamma) \propto \pi_0(\gamma)$, which implies $\pi_0(\beta) \propto 1$. A beta prior is chosen for a_0 leading to the joint prior distribution

$$\begin{aligned} \pi(\beta, \gamma, a_0 \mid D_{0,obs}) &\propto \left[\sum_{N_0} L(\beta, \gamma \mid D_0)\right]^{a_0} \pi_0(\beta, \gamma) \\ &\quad \times a_0^{\delta_0 - 1}(1 - a_0)^{\lambda_0 - 1}, \end{aligned} \tag{4.2}$$

where (δ_0, λ_0) are specified prior parameters.

Chen et al (1999) proved that equation (4.2) with $f(y|\gamma)$ following a Weibull distribution is proper whether $\pi_0(\beta, \gamma)$ is proper or not. In this chapter, we extend this property to the log-logistic, Gompertz and Gamma distributions.

4.1 Log-logistic Distribution

We use the same log-logistic distribution as in Section 3.1 in this section. The following theorem characterizes the property that equation (4.2) with $f(y|\gamma)$ following a log-logistic distribution is proper when $\pi_0(\beta, \gamma)$ is improper.

Theorem 4.1. Assume that

$$\pi_0(\beta, \gamma) \quad \propto \quad \pi_0(\gamma)$$

$$\equiv \pi_0(\alpha \mid \nu_0, \tau_0)\pi_0(\lambda)$$
$$\propto \alpha^{\nu_0 - 1}\exp(-\alpha\tau_0)\pi_0(\lambda),$$

where ν_0 and τ_0 are specified hyperparameters. Let $d_0 = \sum_{i=1}^{n_0} \delta_{0i}$ and X_0^* be an $n_0 \times k$ matrix with rows $\delta_{0i}X_{0i}'$. Then the joint prior given in (4.2) is proper if the following conditions are satisfied:

(a) X_0^* is of full rank,

(b) $\nu_0 > 0$ and $\tau_0 > 0$,

(c) $\pi_0(\lambda)$ is proper, and

(d) $\delta_0 > k$ and $\lambda_0 > 0$.

Proof of Theorem 4.1: This proof is similar to that for Theorem 3.1. First, we write the complete-data likelihood function as

$$\sum_{N_0} L(\beta, \gamma, \mid D_0) = \prod_{i=1}^{n_0} (\theta_{0i} f(y_{0i} \mid \gamma))^{\delta_{0i}} \cdot e^{-\theta_{0i}(1 - S(y_{0i}|\gamma))}. \tag{4.3}$$

In order to prove Theorem 4.1, we first show that there exists a constant $M > 1$ such that

$$(\theta_{0i} f(y_{0i} \mid \gamma))^{\delta_{0i}} \cdot \exp(-\theta_{0i}(1 - S(y_{0i} \mid \gamma))) \leq \alpha^{\delta_{0i}} \cdot M. \tag{4.4}$$

When $\delta_{0i} = 0$, (4.4) is obviously true. When $\delta_{0i} = 1$, the left side of (4.4) can be written as

$$\frac{f(y_{0i}|\gamma)}{1 - S(y_{0i}|\gamma)}(1 - S(y_{0i}|\gamma)) \cdot \theta_{0i} \exp(-\theta_{0i}(1 - S(y_{0i}|\gamma)))$$
$$= \frac{\frac{\alpha y_{0i}^{\alpha-1}\lambda}{(1+\lambda y_{0i}^{\alpha})^2}}{1 - \frac{1}{1+\lambda y_{0i}^{\alpha}}}(1 - S(y_{0i} \mid \gamma)) \cdot \theta_{0i}$$

$$
\begin{aligned}
&\times \exp(-\theta_{0i}(1 - S(y_{0i} \mid \gamma))) \\
&= y_{0i}^{-1} \cdot \frac{\alpha}{1 + \lambda y_{0i}^{\alpha}} (1 - S(y_{0i} \mid \gamma)) \cdot \theta_{0i} \\
&\times \exp(-\theta_{0i}(1 - S(y_{0i} \mid \gamma))). \qquad (4.5)
\end{aligned}
$$

We let $g_1 = \frac{1}{1+\lambda y_{0i}^{\alpha}}$, and $g_2 = (1 - S(y_{0i} \mid \gamma)) \cdot \theta_{0i} \cdot \exp(-\theta_{0i}(1 - S(y_{0i} \mid \gamma)))$. Using the same idea as in the proof of Theorem 3.1, we know that there exists a common constant $g_0 > 0$ such that

$$
g_1 \leq g_0 \quad \text{and} \quad g_2 \leq g_0. \qquad (4.6)
$$

It is very easy to see that

$$
(4.5) \leq y_{0i}^{-1} \alpha g_0^2.
$$

Take $M_0^* = g_0^2 \max_{\{i:\delta_{0i}=1\}}\{y_{0i}^{-1}\}$ and $M_0 = \max(1, M_0^*)$, we then obtain

$$
(\theta_{0i} f(y_{0i} \mid \gamma))^{\delta_{0i}} \cdot \exp(-\theta_{0i}(1 - S(y_{0i} \mid \gamma))) \leq \alpha^{\delta_{0i}} M_0.
$$

Because X_0^* is of full rank, there must exist k linearly independent row vectors $x_{0i_1}^{'}, x_{0i_2}^{'}, \ldots\ldots, x_{0i_k}^{'}$, such that $\delta_{0i_1} = \delta_{0i_2} = \ldots.. = \delta_{0i_k} = 1$. Following the proof of Theorem 3.1, we have

$$
\begin{aligned}
&\int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} (\sum_{N_0} L(\beta, \gamma \mid D_0))^{a_0} \\
&\times \pi_0(\alpha \mid \nu_0, \tau_0) \pi_0(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\beta d\alpha d\lambda da_0 \\
= &\int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} \left[\prod_{i=1}^{n} (\theta_{0i} f(y_{0i} \mid \gamma))^{\delta_{0i}} \cdot \exp(-\theta_{0i}(1 - S(y_{0i} \mid \gamma))) \right]^{a_0} \\
&\times \pi_0(\alpha \mid \nu_0, \tau_0) \cdot \pi_0(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\beta d\alpha d\lambda da_0 \\
= &\int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} \left[\prod_{i=1}^{n-k} (\theta_{0i} f(y_{0i} \mid \gamma))^{\delta_{0i}} \cdot \exp(-\theta_{0i}(1 - S(y_{0i} \mid \gamma))) \right]^{a_0}
\end{aligned}
$$

$$
\begin{aligned}
&\times \left[\prod_{j=1}^{k} (\theta_{0i_j} f(y_{0i_j} \mid \gamma))^{\delta_{0i_j}} \cdot \exp(-\theta_{0i_j}(1 - S(y_{0i_j} \mid \gamma))) \right]^{a_0} \pi(\alpha \mid \nu_0, \tau_0) \\
&\times \pi(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\beta d\alpha d\lambda da_0 \\
\leq\ & \int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} (\alpha M_0)^{a_0(d_0 - k)} \\
&\times \prod_{j=1}^{k} (f(y_{0i_j} \mid \gamma))^{a_0} \exp\left[a_0 x'_{0i_j}\beta - a_0(1 - S(y_{0i_j} \mid \gamma)) \exp(x'_{0i_j}\beta) \right] \\
&\times \pi_0(\alpha \mid \nu_0, \tau_0) \pi_0(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\beta d\alpha d\lambda da_0. \qquad (4.7)
\end{aligned}
$$

We make the transformation $u_{0j} = x'_{0i_j}\beta$ for $j = 1, 2, \ldots\ldots, k$ and ignore the constant. This is a one-to-one linear transformation from β to $u = (u_{01}, u_{02}, \ldots\ldots u_{0k})'$. We also know $M_0 \geq 1$ and $0 < a_0 < 1$, so $M_0^{a_0} \leq M_0$. Thus, (4.7) is proportional to

$$
\begin{aligned}
& \int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} \alpha^{a_0(d_0 - k)} \prod_{j=1}^{k} (f(y_{0i_j} \mid \gamma))^{a_0} \\
&\times \exp(a_0 u_{0j} - a_0(1 - S(y_{0i_j} \mid \gamma)) \exp(u_{0j})) \\
&\times \pi_0(\alpha \mid \nu_0, \tau_0) \pi_0(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} du_0 d\alpha d\lambda da_0 \\
=\ & \int_0^1 \int_0^\infty \int_0^\infty \alpha^{a_0(d_0 - k)} \\
&\times \prod_{j=1}^{k} \left[f(y_{0i_j} \mid \gamma)^{a_0} \int_0^\infty \exp(a_0 u_j - a_0(1 - S(y_{0i_j} \mid \gamma)) \exp(u_{0j})) du_{0j} \right] \\
&\times \pi_0(\alpha \mid \nu_0, \tau_0) \pi_0(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0 \\
=\ & \int_0^1 \int_0^\infty \int_0^\infty \alpha^{a_0(d_0 - k)} \prod_{j=1}^{k} \left[\frac{f(y_{0i_j} \mid \gamma)}{1 - S(y_{0i_j} \mid \gamma)} \right]^{a_0} \frac{\Gamma(a_0)}{a_0^{a_0}} \\
&\times \pi_0(\alpha \mid \nu_0, \tau_0) \pi_0(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0, \qquad (4.8)
\end{aligned}
$$

where $\Gamma(\cdot)$ denotes the Gamma function.

Using (4.6), it can be shown that

$$\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)} \leq k_0\alpha \quad \text{and} \quad \left[\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)}\right]^{a_0} \leq k_0^{a_0}\alpha^{a_0}.$$

Since $K_1 = k_0^{a_0}$ is a positive constant, we have

$$\left[\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)}\right]^{a_0} \leq K_1\alpha^{a_0}.$$

Because $0 < a_0 < 1$,

$$\frac{\Gamma(a_0)}{a_0^{a_0}} = \frac{a_0^{-1}\Gamma(a_0 + 1)}{a_0^{a_0}} \leq K_2 a_0^{-1},$$

where K_2 is a positive constant. Then,

$$\left[\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)}\right]^{a_0} \cdot \frac{\Gamma(a_0)}{a_0^{a_0}} \leq (K_1K_2)\alpha^{a_0}a_0^{-1}.$$

Thus,

$$\begin{aligned}
(4.8) \quad \leq \quad & \int_0^1 \int_0^\infty \int_0^\infty \alpha^{a_0(d-k)} \prod_{j=1}^{k} (k_1\alpha^{a_0}K_2a_0^{-1}) \\
& \times \pi_0(\alpha \mid \nu_0, \tau_0)\pi_0(\lambda)a_0^{\delta_0 - 1}(1 - a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0 \\
= \quad & (k_1k_2)^k \int_0^1 \int_0^\infty \int_0^\infty \alpha^{a_0 d_0} a_0^{-k} \pi_0(\alpha \mid \nu_0, \tau_0) \\
& \times \pi_0(\lambda)a_0^{\delta_0 - 1}(1 - a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0 \\
= \quad & (k_1k_2)^k \int_0^1 \int_0^\infty \int_0^\infty \alpha^{a_0 d_0} \pi_0(\alpha \mid \nu_0, \tau_0) \\
& \times \pi_0(\lambda)a_0^{\delta_0 - k - 1}(1 - a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0 \\
\leq \quad & (k_1k_2)^k \int_0^1 \int_0^\infty \int_0^\infty (1 + \alpha^{d_0})\alpha^{\nu_0 - 1} \exp(-\tau_0\alpha) \\
& \times \pi_0(\lambda)a_0^{\delta_0 - k - 1}(1 - a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0. \qquad (4.9)
\end{aligned}$$

Noticing that $\pi(\alpha \mid \nu_0, \tau_0) \propto \alpha^{\nu_0 - 1}\exp(-\tau_0\alpha)$ and $0 \leq a_0 \leq 1$, $\nu_0 > 0$ and $\tau_0 > 0$, $\pi_0(\lambda)$ is proper and $\delta_0 > k$ and $\lambda_0 > 0$. Thus, (4.9) $< \infty$. This completes the proof. □

4.2 Gompertz Distribution

We use the same Gompertz distribution as in Section 3.2. When $f(y \mid \gamma)$ follows a Gompertz distribution, we have results for noninformative priors similar to there obtained in Section 3.2. The following two theorems characterize this property that equation (4.2) with $f(y|\gamma)$ following a Gompertz distribution is proper when $\pi_0(\beta, \gamma)$ is improper.

Theorem 4.2. Assume that

$$\begin{aligned}\pi_0(\beta,\gamma) &\propto \pi_0(\gamma)\\ &\equiv \pi_0(\alpha \mid \nu_0, \tau_0)\pi_0(\lambda)\\ &\propto \alpha^{\nu_0-1}\exp(-\alpha\tau_0)\pi_0(\lambda),\end{aligned}$$

where ν_0 and τ_0 are specified hyperparameters. Let $d_0 = \sum_{i=1}^{n_0} \delta_{0i}$ and X_0^* be an $n_0 \times k$ matrix with rows $\delta_{0i}X_{0i}'$. Then the joint prior given in (4.2) is proper if the following conditions are satisfied:

(a)X_0^* is of full rank,

(b) $\nu_0 > 0$ and $\tau_0 > 0$,

(c) $\pi_0(\lambda)$ is proper, and

(d) $\delta_0 > k$ and $\lambda_0 > 0$.

Theorem 4.2$'$. Assume that

$$\begin{aligned}\pi_0(\beta,\gamma) &\propto \pi_0(\gamma)\\ &\equiv \pi_0(\lambda \mid \nu_0,\tau_0)\pi_0(\alpha)\\ &\propto \lambda^{\nu_0-1}\exp(-\lambda\tau_0)\pi_0(\alpha),\end{aligned}$$

where ν_0 and τ_0 are specified hyperparameters. Let $d_0 = \sum_{i=1}^{n_0}\delta_{0i}$ and X_0^* be an $n_0 \times k$ matrix with rows $\delta_{0i}X_{0i}'$. Then the joint prior

$$\begin{aligned}\pi(\beta,\gamma,a_0 \mid D_{0,obs}) &= \pi(\beta,\gamma \mid D_{0,obs},a_0)\pi(a_0 \mid D_{0,obs})\\ &\propto \left[\sum_{N_0} L(\beta,\gamma \mid D_0\right]^{a_0} \pi_0(\beta,\gamma)\\ &\quad \times a_0^{\delta_0-1}(1-a_0)^{\lambda_0-1} \qquad (4.10)\end{aligned}$$

is proper if the following conditions are satisfied:

(a) X_0^* is of full rank,

(b) $\nu_0 > 0$ and $\tau_0 > k'd_0$

(c) $\pi_0(\alpha)$ is proper, and

(d) $\delta_0 > k$ and $\lambda_0 > 0$.

Proof of Theorem 4.2: We can write the complete-data likelihood function as

$$\sum_{N_0} L(\beta,\gamma,\mid D_0) = \prod_{i=1}^{n}(\theta_{0i}f(y_{0i} \mid \gamma))^{\delta_{0i}} \cdot e^{-\theta_{0i}(1-S(y_{0i}|\gamma))}. \qquad (4.11)$$

In order to prove Theorem 4.2, we first show that there exists a constant $M > 1$ such that

$$(\theta_{0i} f(y_{0i} \mid \gamma))^{\delta_{0i}} \cdot \exp(-\theta_{0i}(1 - S(y_{0i} \mid \gamma))) \leq \alpha^{\delta_{0i}} \cdot M_0. \quad (4.12)$$

Similar to the proof of Theorem (3.2), we have

$$(\theta_{0i} f(y_{0i} \mid \gamma))^{\delta_{0i}} \cdot \exp(-\theta_{0i}(1 - S(y_{0i} \mid \gamma))) \leq \alpha^{\delta_{0i}} M_0,$$

where $M_0 > 1$ is a constant.

Because X_0^* is of full rank, there must exist k linearly independent row vectors $x'_{0i_1}, x'_{0i_2}, ..., x'_{0i_k}$, such that $\delta_{0i_1} = \delta_{0i_2} = ... = \delta_{0i_k} = 1$.

$$\begin{aligned}
& \int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} \left[\sum_{N_0} L(\beta, \gamma \mid D_0) \right]^{a_0} \\
& \times \pi_0(\alpha \mid \nu_0, \tau_0) \pi_0(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\beta d\alpha d\lambda da_0 \\
= & \int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} \left[\prod_{i=1}^{n} (\theta_{0i} f(y_{0i} \mid \gamma))^{\delta_{0i}} \cdot \exp(-\theta_{0i}(1 - S(y_{0i} \mid \gamma))) \right]^{a_0} \\
& \times \pi_0(\alpha \mid \nu_0, \tau_0) \pi_0(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\beta d\alpha d\lambda da_0 \\
= & \int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} \left[\prod_{i=1}^{n-k} (\theta_{0i} f(y_{0i} \mid \gamma))^{\delta_{0i}} \cdot \exp(-\theta_{0i}(1 - S(y_{0i} \mid \gamma))) \right]^{a_0} \\
& \times \left[\prod_{j=1}^{k} (\theta_{0i_j} f(y_{0i_j} \mid \gamma))^{\delta_{0i_j}} \cdot \exp(-\theta_{0i_j}(1 - S(y_{0i_j} \mid \gamma))) \right]^{a_0} \pi(\alpha \mid \nu_0, \tau_0) \\
& \times \pi(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\beta d\alpha d\lambda da_0 \\
\leq & \int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} \prod_{i=1}^{n-k} (\alpha^{\delta_{0i}} M_0)^{a_0} \\
& \times \left[\prod_{j=1}^{k} (\theta_{0i_j} f(y_{0i_j} \mid \gamma))^{\delta_{0i_j}} \cdot \exp(-\theta_{0i_j}(1 - S(y_{0i_j} \mid \gamma))) \right]^{a_0} \\
& \times \pi(\alpha \mid \nu_0, \tau_0) \pi_0(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\beta d\alpha d\lambda da_0
\end{aligned}$$

$$\leq \int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} (\alpha M_0)^{a_0(d_0-k)}$$
$$\times \prod_{j=1}^{k} (f(y_{0i_j} \mid \gamma))^{a_0} \exp\left[a_0 x_{0i_j}' \beta - a_0(1 - S(y_{0i_j} \mid \gamma)) \exp(x_{0i_j}' \beta)\right]$$
$$\times \pi_0(\alpha \mid \nu_0, \tau_0) \pi_0(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\beta d\alpha d\lambda da_0. \tag{4.13}$$

Because $M_0 \geq 1$ and $0 < a_0 < 1$, $M_0^{a_0} \leq M_0$, we make the transformation $u_{0j} = x_{0i_j}' \beta$ for $j = 1, 2, \ldots.., k$ and ignore the constant. This is a one-to-one linear transformation from β to $u = (u_{01}, u_{02}, \ldots\ldots u_{0k})'$. Thus, (4.13) is proportional to

$$\int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} \alpha^{a_0(d_0-k)} \prod_{j=1}^{k} (f(y_{0i_j} \mid \gamma))^{a_0}$$
$$\times \exp(a_0 u_{0j} - a_0(1 - S(y_{0i_j} \mid \gamma)) \exp(u_{0j}))$$
$$\times \pi_0(\alpha \mid \nu_0, \tau_0) \pi_0(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} du_0 d\alpha d\lambda da_0$$
$$= \int_0^1 \int_0^\infty \int_0^\infty \alpha^{a_0(d_0-k)} \prod_{j=1}^{k} (f(y_{0i_j} \mid \gamma))^{a_0}$$
$$\int_0^\infty \exp(a_0 u_j - a_0(1 - S(y_{0i_j} \mid \gamma)) \exp(u_{0j})) du_{0j} \cdot$$
$$\times \pi_0(\alpha \mid \nu_0, \tau_0) \pi_0(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0$$
$$= \int_0^1 \int_0^\infty \int_0^\infty \alpha^{a_0(d_0-k)} \prod_{j=1}^{k} \left[\frac{f(y_{0i_j} \mid \gamma)}{1 - S(y_{0i_j} \mid \gamma)}\right]^{a_0} \frac{\Gamma(a_0)}{a_0^{a_0}}$$
$$\times \pi_0(\alpha \mid \nu_0, \tau_0) \pi_0(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0, \tag{4.14}$$

where $\Gamma(\cdot)$ denotes the Gamma function. Using $g_1 \leq g_0$ and $g_2 \leq g_0$, it can be shown that

$$\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)} \leq k_0 \alpha \quad \text{and} \quad \left[\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)}\right]^{a_0} \leq k_0^{a_0} \alpha^{a_0}.$$

Let $K_1 = k_0^{a_0}$. Then,

$$\left[\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)}\right]^{a_0} \leq K_1 \alpha^{a_0}.$$

Because $0 < a_0 < 1$,

$$\frac{\Gamma(a_0)}{a_0^{a_0}} = \frac{a_0^{-1}\Gamma(a_0 + 1)}{a_0^{a_0}} \leq K_2 a_0^{-1},$$

where K_2 is a positive constant. Then,

$$\left[\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)}\right]^{a_0} \cdot \frac{\Gamma(a_0)}{a_0^{a_0}} \leq (K_1 K_2) \alpha^{a_0} a_0^{-1}.$$

Thus,

$$\begin{aligned}
(4.14) \quad &\leq \int_0^1 \int_0^\infty \int_0^\infty \alpha^{a_0(d-k)} \prod_{j=1}^{k} (k_1 \alpha^{a_0} K_2 a_0^{-1}) \\
&\quad \times \pi_0(\alpha \mid \nu_0, \tau_0) \pi_0(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0 \\
&= (k_1 k_2)^k \int_0^1 \int_0^\infty \int_0^\infty \alpha^{a_0 d_0} a_0^{-k} \pi_0(\alpha \mid \nu_0, \tau_0) \\
&\quad \times \pi_0(\lambda) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0 \\
&= (k_1 k_2)^k \int_0^1 \int_0^\infty \int_0^\infty \alpha^{a_0 d_0} \pi_0(\alpha \mid \nu_0, \tau_0) \\
&\quad \times \pi_0(\lambda) a_0^{\delta_0 - k - 1} (1 - a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0 \\
&\leq (k_1 k_2)^k \int_0^1 \int_0^\infty \int_0^\infty (1 + \alpha^{d_0}) \alpha^{\nu_0 - 1} \exp(-\tau_0 \alpha) \\
&\quad \times \pi_0(\lambda) a_0^{\delta_0 - k - 1} (1 - a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0. \qquad (4.15)
\end{aligned}$$

Noticing that $\pi(\alpha \mid \nu_0, \tau_0) \propto \alpha^{\nu_0 - 1} \exp(-\tau_0 \alpha)$ and $0 \leq a_0 \leq 1$, $\nu_0 > 0$ and $\tau_0 > 0$, $\pi_0(\lambda)$ is proper and $\delta_0 > k$, and $\lambda_0 > 0$. Thus, (4.15) $< \infty$. This completes the proof. □

Proof of Theorem 4.2′: Similar to the prof of Theorem 3.2′, we have

$$(\theta_{0i} f(y_{0i} \mid \gamma))^{\delta_{0i}} \cdot \exp(-\theta_{0i}(1 - S(y_{0i} \mid \gamma))) \leq (e^{k'\lambda})^{\delta_{0i}} M_0,$$

where $M_0 > 1$ is a constant.

Because X_0^* is of full rank, there must exist k linear independent row vectors $x'_{0i_1}, x'_{0i_2}, ..., x'_{0i_k}$ such that $\delta_{0i_1} = \delta_{0i_2} = ... = \delta_{0i_k} = 1$. Following the proof of Theorem 3.2′, we have

$$\begin{aligned}
& \int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} \left[\sum_{N_0} L(\beta, \gamma \mid D_0) \right]^{a_0} \pi_0(\lambda \mid \nu_0, \tau_0) \\
& \times \pi_0(\alpha) a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\beta d\alpha d\lambda da_0 \\
= \; & \int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} \left[\prod_{i=1}^n (\theta_{0i} f(y_{0i} \mid \gamma))^{\delta_{0i}} \cdot \exp(-\theta_{0i}(1 - S(y_{0i} \mid \gamma))) \right]^{a_0} \\
& \times \pi_0(\lambda \mid \nu_0, \tau_0) \pi_0(\alpha) \cdot a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\beta d\alpha d\lambda da_0 \\
\leq \; & \int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} (e^{k'\lambda} M_0)^{a_0(d_0 - k)} \\
& \times \prod_{j=1}^k (f(y_{0i_j} \mid \gamma))^{a_0} \exp(a_0 x'_{0i_j} \beta - a_0(1 - S(y_{0i_j} \mid \gamma)) \\
& \times \exp(x'_{0i_j} \beta)) \pi_0(\lambda \mid \nu_0, \tau_0) \pi_0(\alpha) \cdot a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\beta d\alpha d\lambda da_0. \quad (4.16)
\end{aligned}$$

Because $M_0 \geq 1$ and $0 < a_0 < 1$, $M_0^{a_0} \leq M_0$, we make the transformation $u_{0j} = x'_{0i_j}\beta$ for $j = 1, 2, ..., k$ and ignore the constant. This is a one-to-one linear transformation from β to $u = (u_{01}, u_{02}, ...u_{0k})'$. Thus, (4.16) is proportional to

$$\int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} (e^{k'\lambda})^{a_0(d_0 - k)} \prod_{j=1}^k (f(y_{0i_j} \mid \gamma))^{a_0}$$

$$\times \exp(a_0 u_{0j} - a_0(1 - S(y_{0i_j} \mid \gamma)) \exp(u_{0j}))$$
$$\times \pi_0(\lambda \mid \nu_0, \tau_0) \pi_0(\alpha) a_0^{\delta_0 - 1}(1 - a_0)^{\lambda_0 - 1} du_0 d\alpha d\lambda da_0$$
$$= \int_0^1 \int_0^\infty \int_0^\infty (e^{k' \lambda})^{a_0(d_0 - k)}$$
$$\times \prod_{j=1}^k (f(y_{0i_j} \mid \gamma))^{a_0} \int_0^\infty \exp(a_0 u_{0j} - a_0(1 - S(y_{0i_j} \mid \gamma)) \exp(u_{0j})) du_{0j}) \cdot$$
$$\times \pi_0(\lambda \mid \nu_0, \tau_0) \pi_0(\alpha) a_0^{\delta_0 - 1}(1 - a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0$$
$$= \int_0^1 \int_0^\infty \int_0^\infty (e^{k' \lambda})^{a_0(d_0 - k)} \prod_{j=1}^k \left[\frac{f(y_{0i_j} \mid \gamma)}{1 - S(y_{0i_j} \mid \gamma)}) \right]^{a_0} \frac{\Gamma(a_0)}{a_0^{a_0}}$$
$$\times \pi_0(\lambda \mid \nu_0, \tau_0) \pi_0(\alpha) a_0^{\delta_0 - 1}(1 - a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0, \tag{4.17}$$

where $\Gamma(\cdot)$ denotes the Gamma function. From Theorem $3.2'$, it can be shown that

$$\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)} \leq e^{k' \lambda} \cdot g_0 \quad \text{and} \quad \left[\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)} \right]^{a_0} \leq e^{k' \lambda a_0} \cdot g_0^{a_0}.$$

Let $K_1 = g_0^{a_0}$ be a positive constant. Then,

$$\left[\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)} \right]^{a_0} \leq K_1 e^{k' \lambda a_0}.$$

Because $0 < a_0 < 1$,

$$\frac{\Gamma(a_0)}{a_0^{a_0}} = \frac{a_0^{-1} \Gamma(a_0 + 1)}{a_0^{a_0}} \leq K_2 a_0^{-1},$$

where K_2 is a positive constant. Then,

$$\left[\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \gamma)} \right]^{a_0} \cdot \frac{\Gamma(a_0)}{a_0^{a_0}} \leq (K_1 K_2) e^{k' \lambda a_0} a_0^{-1}.$$

Thus,

$$(4.17) \leq \int_0^1 \int_0^\infty \int_0^\infty (e^{k' \lambda})^{a_0(d_0 - k)} \prod_{j=1}^k (K_1 e^{k' \lambda a_0} K_2 a_0^{-1}) \pi_0(\lambda \mid \nu_0, \tau_0)$$

$$
\begin{aligned}
&\times\pi_0(\alpha)a_0^{\delta_0-1}(1-a_0)^{\lambda_0-1}d\alpha d\lambda da_0 \\
= &\ (K_1K_2)^k\int_0^1\int_0^\infty\int_0^\infty e^{k'\lambda a_0 d_0}a_0^{-k}\pi_0(\lambda \mid \nu_0,\tau_0) \\
&\times\pi_0(\alpha)a_0^{\delta_0-1}(1-a_0)^{\lambda_0-1}d\alpha d\lambda da_0 \\
\leq &\ (K_1K_2)^k\int_0^1\int_0^\infty\int_0^\infty \lambda^{\nu_0-1}\exp\left[-\lambda(\tau_0-k'd_0)\right]\pi_0(\lambda) \\
&\times a_0^{\delta_0-k-1}(1-a_0)^{\lambda_0-1}d\alpha d\lambda da_0. \qquad (4.18)
\end{aligned}
$$

Noticing that $\pi(\lambda \mid \nu_0,\tau_0) \propto \lambda^{\nu_0-1}\exp(-\tau_0\lambda)$, $\nu_0 > 0$ and $\tau_0 > k'd_0$, $\pi_0(\lambda)$ is proper and $\delta_0 > k$ and $\lambda_0 > 0$. Thus, (4.18) $< \infty$. □

4.3 Gamma Distribution

We use the same Gamma distribution as in Section 3.3 and assume that

$$
\begin{aligned}
\pi_0(\beta,\gamma) &\propto \pi_0(\gamma) \\
&\equiv \pi_0(\alpha \mid \nu_0,\tau_0)\pi_0(\lambda) \\
&\propto \alpha^{\nu_0-1}\exp(-\alpha\tau_0)\pi_0(\lambda),
\end{aligned}
$$

where ν_0 and τ_0 are specified hyperparameters. Our last theorem is.

Theorem 4.3. Let $d_0 = \sum_{i=1}^{n_0}\delta_{0i}$ and X_0^* be an $n_0 \times k$ matrix with rows $\delta_{0i}X_{0i}'$. Then the joint prior

$$
\begin{aligned}
\pi(\beta,\gamma,a_0 \mid D_{0,obs}) &= \pi(\beta,\gamma \mid D_{0,obs},a_0)\pi(a_0 \mid D_{0,obs}) \\
&\propto \left[\sum_{N_0} L(\beta,\gamma \mid D_0\right]^{a_0}\pi_0(\beta,\gamma)a_0^{\delta_0-1}(1-a_0)^{\lambda_0-1}
\end{aligned}
$$

is proper if the following conditions are satisfied:

(a) X_0^* is of full rank,

(b) $\nu_0 > 0$ and $\tau_0 > 0$

(c) $\pi_0(\lambda)$ is proper and

(d) $\delta_0 > k$ and $\lambda_0 > 0$.

Proof of Theorem 4.3: Similar to the proof of Theorem 3.3, we know that there exists a constant $M_0 > 1$ such that

$$(\theta_{0i} f(y_{0i} \mid \gamma))^{\delta_{0i}} \cdot \exp(-\theta_{0i}(1 - S(y_{0i} \mid \gamma))) \leq \alpha^{\delta_{0i}} M_0.$$

Because X_0^* is of full rank, there must exist k linear independent row vectors $x'_{0i_1}, x'_{0i_2}, \ldots\ldots, x'_{0i_k}$, such that $\delta_{0i_1} = \delta_{0i_2} = \ldots.. = \delta_{0i_k} = 1$. Following the proof of Theorem 3.3, we have

$$\begin{aligned}
& \int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} \left[\sum_{N_0} L(\beta, \gamma \mid D_0) \right]^{a_0} \pi_0(\alpha \mid \nu_0, \tau_0) \pi_0(\lambda) \\
& \times a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\beta d\alpha d\lambda da_0 \\
\leq & \int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} (\alpha M_0)^{a_0(d_0 - k)} \prod_{j=1}^{k} (f(y_{0i_j} \mid \gamma))^{a_0} \\
& \times \exp(a_0 x'_{0i_j} \beta - a_0(1 - S(y_{0i_j} \mid \gamma))) \cdot \\
& \times \exp(x'_{0i_j} \beta) \pi_0(\alpha \mid \nu_0, \tau_0) \pi_0(\lambda) \\
& \times a_0^{\delta_0 - 1} (1 - a_0)^{\lambda_0 - 1} d\beta d\alpha d\lambda da_0. \qquad (4.19)
\end{aligned}$$

Because $M_0 \geq 1$ and $0 < a_0 < 1$, $M_0^{a_0} \leq M_0$, we make the transformation $u_{0j} = x'_{0i_j}\beta$ for $j = 1, 2, \ldots.., k$ and ignore the constant. This is a one-to-one linear transformation from β to $u = (u_{01}, u_{02}, \ldots\ldots u_{0k})'$. Thus (4.19) is proportional to

$$
\begin{aligned}
& \int_0^1 \int_0^\infty \int_0^\infty \int_{R^k} \alpha^{a_0(d_0-k)} \prod_{j=1}^k (f(y_{0i_j} \mid \gamma))^{a_0} \\
& \times \exp(a_0 u_{0j} - a_0(1 - S(y_{0i_j} \mid \gamma)) \exp(u_{0j})) \\
& \times \pi_0(\alpha \mid \nu_0, \tau_0)\pi_0(\lambda) a_0^{\delta_0 - 1}(1-a_0)^{\lambda_0 - 1} du_0 d\alpha d\lambda da_0 \\
= & \int_0^1 \int_0^\infty \int_0^\infty \alpha^{a_0(d_0-k)} \prod_{j=1}^k \left[\frac{f(y_{0i_j} \mid \gamma)}{1 - S(y_{0i_j} \mid \gamma)}\right]^{a_0} \frac{\Gamma(a_0)}{a_0^{a_0}} \\
& \times \pi_0(\alpha \mid \nu_0, \tau_0)\pi_0(\lambda) a_0^{\delta_0 - 1}(1-a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0, \qquad (4.20)
\end{aligned}
$$

where $\Gamma(\cdot)$ denotes the Gamma function. From Theorem 3.3, it can be shown that

$$
\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)} \le k_0 \alpha \quad \text{and} \quad \left[\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)}\right]^{a_0} \le k_0^{a_0} \alpha^{a_0}.
$$

Let $K_1 = k_0^{a_0}$, which is a positive constant. Then,

$$
\left[\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)}\right]^{a_0} \le K_1 \alpha^{a_0}.
$$

Because $0 < a_0 < 1$,

$$
\frac{\Gamma(a_0)}{a_0^{a_0}} = \frac{a_0^{-1}\Gamma(a_0 + 1)}{a_0^{a_0}} \le K_2 a_0^{-1},
$$

where K_2 is a positive constant. Then

$$
\left[\frac{f(y_{i_j} \mid \gamma)}{1 - S(y_{i_j} \mid \gamma)}\right]^{a_0} \cdot \frac{\Gamma(a_0)}{a_0^{a_0}} \le (K_1 K_2) \alpha^{a_0} a_0^{-1}.
$$

Thus,

$$
\begin{aligned}
(4.20) \le & \int_0^1 \int_0^\infty \int_0^\infty \alpha^{a_0(d-k)} \prod_{j=1}^k (k_1 \alpha^{a_0} K_2 a_0^{-1}) \\
& \times \pi_0(\alpha \mid \nu_0, \tau_0)\pi_0(\lambda) a_0^{\delta_0 - 1}(1-a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0
\end{aligned}
$$

$$
\begin{aligned}
&= (k_1k_2)^k \int_0^1 \int_0^\infty \int_0^\infty \alpha^{a_0 d_0} a_0^{-k} \\
&\quad \times \pi_0(\alpha \mid \nu_0, \tau_0)\pi_0(\lambda) a_0^{\delta_0 - 1}(1-a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0 \\
&= (k_1k_2)^k \int_0^1 \int_0^\infty \int_0^\infty \alpha^{a_0 d_0} \\
&\quad \times \pi_0(\alpha \mid \nu_0, \tau_0)\pi_0(\lambda) a_0^{\delta_0 - k - 1}(1-a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0 \\
&\leq (k_1k_2)^k \int_0^1 \int_0^\infty \int_0^\infty (1+\alpha^{d_0})\alpha^{\nu_0 - 1} \\
&\quad \times \exp(-\tau_0\alpha)\pi_0(\lambda) a_0^{\delta_0 - k - 1}(1-a_0)^{\lambda_0 - 1} d\alpha d\lambda da_0. \qquad (4.21)
\end{aligned}
$$

Noticing that $\pi(\alpha \mid \nu_0, \tau_0) \propto \alpha^{\nu_0 - 1}\exp(-\tau_0\alpha)$, $\nu_0 > 0$ and $\tau_0 > 0$, $\pi_0(\lambda)$ is proper, $\delta_0 > k$ and $\lambda_0 > 0$. Thus, $(4.21) < \infty$. This completes the proof. □

Chapter 5

Data Analysis

In this chapter, we demonstrate the applications of our proposed model based on (2.1) in previous chapters to the phase III melanoma clinical trial data described in Chapter 1. Our first goal is to find maximum likelihood estimates (MLE's) of the parameters for the proposed model (2.1) under log-logistic, Gompertz and Gamma distributions, and to compare our results with the model under the Weibull distribution proposed in Chen et al (1999). Our second goal is to carry out a Bayesian analysis with covariates using the non-informative priors introduced in Chapter 3. Furthermore, using maximum posterior density function and second derivatives of the posterior density function. We obtain the posterior estimates of the parameters for the proposed models under log-logistic, Gompertz and Gamma distributions, and compare the inferences between each of the three proposed models and Chen et al (1999).

The third goal is to carry out a Bayesian analysis with covariates using the informative priors proposed in Chapter 4. We obtain posterior estimates of the model parameters under log-logistic, Gompertz and Gamma distributions using informative priors, and compare each result with Chen et al (1999). The three covariates that are considered in the analysis are age (x_1), gender (x_2: male, female), and performance status (PS) (x_3: fully active, other).

5.1 MLE's of the Model Parameters for the E1684 Data

We now consider the analysis for the MLE's of the proposed model (2.1) with covariates to demonstrate the application of the proposed models under log-logistic, Gompertz and Gamma distributions. We also compare inferences of the proposed models under log-logistic, Gompertz and Gamma distributions with the model under the Weibull distribution, which was discussed in Chen et al (1999).

Table 5.1 reports the MLE's, their standard deviations and p-values for the proposed model under the Weibull distribution. Our estimates for the model parameters have some minor differences. However, these differences do not influence the results.

Table 5.2, Table 5.3 and Table 5.4 report the maximum likelihood estimates, standard deviations and p-values for the proposed models under log-

Table 5.1: MLE's of the Model Parameters with Weibull Distribution

Variable	MLE	SD	P-value
Age	0.006	0.004	0.12
Gender	−0.15	0.12	0.22
PS	−0.20	0.26	0.44
α	1.31	0.09	0.00
λ	−1.34	0.12	0.00

logistic, Gompertz, and Gamma distributions, respectively. Comparing the results of Table 5.1 with each of Tables 5.2, 5.3 and 5.4, we find that all results are similar. The p-values associated with the covariates are all greater than 0.05. This implies that none of age, gender and PS is statistically significant at level $\alpha = 0.05$.

Table 5.2: MLE's of the Model Parameters with log-logistic Distribution

Variable	MLE	SD	P-value
Age	0.007	0.004	0.06
Gender	−0.13	0.12	0.31
PS	−0.20	0.26	0.44
α	1.61	0.13	0.00
λ	−1.28	0.16	0.00

Table 5.3: MLE's of the Model Parameters with Gompertz Distribution

Variable	MLE	SD	P-value
Age	0.006	0.004	0.12
Gender	−0.15	0.12	0.22
PS	−0.20	0.26	0.43
α	0.27	0.03	0.00
λ	−1.97	0.19	0.00

Table 5.4: MLE's of the Model Parameters with Gamma Distribution

Variable	MLE	SD	P-value
Age	0.006	0.004	0.12
Gender	−0.15	0.12	0.22
PS	−0.20	0.26	0.44
α	1.56	0.12	0.00
λ	−0.51	0.14	0.00

5.2 The Posterior Estimates of the Model Parameters with Noninformative Priors

We carry out a Bayesian analysis with covariates using the proposed noninformative priors to demonstrate our second application of the proposed model (2.1) under the log-logistic, Gompertz and Gamma distributions. To be more specific, we compare results among the proposed models under the log-logistic, Gompertz and Gamma distributions with the proposed model (2.1) under the Weibull distribution which was discussed in Chen et al (1999).

In this section, we use the E1684 study as current data and consider an analysis with the proposed priors (3.2). For $\pi(\beta)$, we take an improper uniform prior, and for $\pi(\alpha|\nu_0, \tau_0)$, we take $\nu_0 = 1$ and $\tau_0 = 0.01$ to ensure a proper prior. The parameter λ is taken to have a normal distribution with mean 0 and variance 10,000. We use maximum posterior density function and second derivatives of the posterior density function to find the posterior estimates, posterior standard deviation and p-values.

Table 5.5 reports the posterior estimates of the model parameters with the Weibull distribution using noninformative priors. Comparing the results of Table 5.1 with Table 5.5, we find that the results are the same. Therefore, the result that incorporation of noninformative priors cannot affect the posterior estimates of the model parameters was discussed by Chen et al (1999).

Table 5.6, Table 5.7 and Table 5.8 report the posterior estimates of the model parameters with the log-logistic, Gompertz and Gamma distributions using noninformative priors. Comparing the results of Table 5.2 with Table 5.6, Table 5.3 with Table 5.7 and Table 5.4 with Table 5.8, we find similar results. Thus, incorporation of noninformative priors cannot affect the posterior estimates of the model parameters even though $F(\cdot)$ follows different distributions. This result is similar to that of Chen et al (1999).

Table 5.5: The Posterior Estimates of the Model Parameters with Weibull Distribution Using Noninformative Priors, $\alpha \sim \Gamma(1, 0.01)$ and $\lambda \sim N(0, 10000)$

Variable	Posterior estimate	Posterior SD	P-value	95% CI
Age	0.006	0.004	0.12	$(-0.002, 0.014)$
Gender	-0.15	0.12	0.22	$(-0.385, 0.085)$
PS	-0.20	0.26	0.44	$(-0.710, 0.310)$
α	1.31	0.09	0.00	$(1.134, 1.486)$
λ	-1.34	0.12	0.00	$(-1.575, -1.105)$

Table 5.6: The Posterior Estimates of the Model Parameters with log-logistic Distribution Using Noninformative Priors, $\alpha \sim \Gamma(1, 0.01)$ and $\lambda \sim N(0, 10000)$

Variable	Posterior estimate	Posterior SD	P-value	95% CI
Age	0.007	0.004	0.06	$(-0.001, 0.015)$
Gender	-0.13	0.12	0.31	$(-0.365, 0.105)$
PS	-0.20	0.26	0.44	$(-0.710, 0.310)$
α	1.61	0.13	0.00	$(1.355, 1.865)$
λ	-1.28	0.16	0.00	$(-1.594, -0.966)$

Table 5.7: The Posterior Estimates of the Model Parameters with Gompertz Distribution Using Noninformative Priors, $\alpha \sim \Gamma(1, 0.01)$ and $\lambda \sim N(0, 10000)$

Variable	Posterior estimate	Posterior SD	P-value	95% CI
Age	0.006	0.004	0.12	$(-0.002, 0.014)$
Gender	-0.15	0.12	0.22	$(-0.385, 0.085)$
PS	-0.20	0.26	0.43	$(-0.710, 0.310)$
α	0.27	0.03	0.00	$(0.211, 0.329)$
λ	-1.97	0.19	0.00	$(-2.342, -1.598)$

Table 5.8: The Posterior Estimate of the Model Parameters with Gamma Distribution Using Noninformative Priors, $\alpha \sim \Gamma(1, 0.01)$ and $\lambda \sim N(0, 10000)$

Variable	Posterior estimate	Posterior SD	P-value	95% CI
Age	0.007	0.004	0.12	$(-0.001, 0.015)$
Gender	-0.20	0.12	0.22	$(-0.435, 0.035)$
PS	-0.05	0.24	0.44	$(-0.520, 0.420)$
α	1.49	0.11	0.00	$(1.274, 1.706)$
λ	-0.60	0.15	0.00	$(-0.894, -0.306)$

5.3 The Posterior Estimates of the Model Parameters with Informative Priors

In Section 5.2, we used the noninformative priors to conduct the Bayesian analysis. In this section we use the informative priors for the Bayesian analysis. Similar to Section 5.2, we use the results of the proposed model (2.1) under the log-logistic, Gompertz and Gamma distributions to compare with those in the model (2.1) under the Weibull distribution.

In this section, E1673 serves as the historical data for our Bayesian analysis of E1684. Table 5.9 reports the posterior estimates for the Weibull distributions based on several choices of (δ_0, λ_0) using informative priors. We compare the results of Table 5.9 with each of Tables 5.10, 5.11 and 5.12 which report the posterior estimates of the parameters for the proposed models under the log-logistic, Gompertz and Gamma distributions using informative priors, respectively, it is easy to see that the results are similar to those of Chen et al (1999) which incorporating historical data can yield more precise posterior estimates of model parameters of age, gender and PS. The posterior estimates, their standard deviations and 95% confidence intervals of age, gender and PS do not change a great deal if a low or moderate weight is given to the historical data. However, if a higher than moderate weight is given to the historical data, these posterior summaries can change substantially. For example, in Table 5.9, when the posterior estimate of a_0 is less than 0.06, we can find that all 95% confidence intervals for age, gender and PS include 0. When the posterior estimate of a_0 is greater than or equal to 0.21, the posterior 95% confidence intervals for age and gender do not include 0. In Tables 5.10, 5.11 and 5.12, we obtain the similar results. Therefore, even though we use different models, we obtain the same results which suggest that age and gender are potentially important prognostic factors for predicting survival in melanoma. We also find the posterior estimate for age is positive, implying that as age goes up, the number of carcinogenic cells increases. Increased carcinogenic cells counts are associated with shorter relapse-free survival. Therefore, older patients have shorter relapse-free survival. the posterior estimate of gender is negative, implying that the number of carcinogenic cells for females are less than the number of carcinogenic cells for males. Therefore, females have longer relapse-free survival than males. This finding is very important. In addition, when the historical data and current data are equally weighted (i.e., $a_0 = 1$), the 95% confidence intervals for age and gender both do not include 0, therefore demonstrating again the importance of age and gender in predicting overall survival. These results are the same as those of Chen et al (1999).

Secondly, as the posterior estimate of a_0 increases, the posterior estimate for age becomes larger while the posterior estimates for gender and PS become smaller. The posterior standard deviations of the model parameters become smaller and the 95% confidence intervals become narrower as the posterior estimate of a_0 increases. This demonstrates that incorporation of historical data can yield precise posterior estimates of age, gender and PS parameters. For example, in Table 5.10, when $a_0 = 1$, the posterior estimates, standard deviations, and 95% confidence intervals for age and gender coefficients are $0.012/0.002/(0.008, 0.016)$ and - $0.31/0.07/(-0.447, -0.173)$, respectively, whereas when we do not incorporate any historical data (i.e., $a_0 = 0$), these values are $0.007/0.004/(-0.001, 0.015)$ and -$0.13/0.12/(-0.365, 0.105)$ respectively. We can see that there is a large difference in these estimates, especially in the standard deviations and 95% confidence intervals. We obtain similar results in Table 5.9, Table 5.11 and Table 5.12. Therefore, we can say that precise estimates of the model parameters can be obtained by incorporating historical data.

Thirdly, when a low weight is given to the historical data, the posterior estimate of PS is negative. It implies that carcinogenic cell counts for the patients whose PS is fully active are more than that when PS is not fully active after the initial treatment. When a higher weight is given to the historical data, the posterior estimate of PS becomes positive which implies that patients whose PS is fully active have longer relapse-free survival than patients whose PS is not fully active. The posterior estimates for age are all positive and their values increase when the posterior estimate of a_0 increases. This implies that as age goes up, the number of carcinogenic cells increases. Increased carcinogenic cell counts are associated with shorter relapse-free survival and when the posterior estimate of a_0 is increasing, the carcinogenic cell counts increase quickly. Therefore, the relapse-free survival decreases quickly. This tells us that incorporation historical data, we can obtain better results. We also find that the posterior estimates for gender are all negative and becomes smaller when the power (a_0) is increasing. Therefore, in the sense that there is a gender difference, where the number of carcinogenic cells for females is less than the number of carcinogenic cells for males. Thus, females have longer relapse-free survival than males. When we incorporate historical data, the difference becomes significant.

Table 5.9: The Posterior Estimates of the Model Parameters with Weibull Distribution Using Informative Priors, $\alpha \sim \Gamma(1, 0.01)$ and $\lambda \sim N(0, 10000)$

Variable	Posterior estimate	Posterior SD	95% CI	(δ_0, λ_0)
Age	0.007	0.004	$(-0.001, 0.015)$	(49,49)
Gender	-0.15	0.14	$(-0.424, 0.124)$	
PS	-0.17	0.25	$(-0.660, 0.320)$	
α	1.17	0.07	$(1.033, 1.307)$	
λ	-1.44	0.13	$(-1.695, -1.185)$	
a_0	0.03	0.0035	$(0.022, 0.037)$	
Age	0.008	0.005	$(-0.002, 0.018)$	(99,99)
Gender	-0.16	0.19	$(-0.532, 0.212)$	
PS	-0.14	0.24	$(-0.610, 0.330)$	
α	1.12	0.07	$(0.983, 1.257)$	
λ	-1.51	0.13	$(-1.765, -1.255)$	
a_0	0.06	0.006	$(0.05, 0.07)$	
Age	0.009	0.005	$(0.000, 0.019)$	(199,0)
Gender	-0.19	0.17	$(-0.523, 0.143)$	
PS	-0.08	0.21	$(-0.492, 0.332)$	
α	1.06	0.06	$(0.942, 1.178)$	
λ	-1.61	0.11	$(-1.826, -1.394)$	
a_0	0.14	0.0115	$(0.12, 0.16)$	
Age	0.01	0.003	$(0.004, 0.016)$	(399,399)
Gender	-0.21	0.10	$(-0.406, -0.014)$	
PS	-0.04	0.20	$(-0.432, 0.352)$	
α	1.04	0.05	$(0.942, 1.138)$	
λ	-1.65	0.10	$(-1.846, -1.454)$	
a_0	0.21	0.011	$(0.19, 0.23)$	
Age	0.01	0.002	$(0.006, 0.014)$	(399,0)
Gender	-0.23	0.08	$(-0.387, -0.073)$	
PS	0.00	0.18	$(-0.353, 0.353)$	
α	1.03	0.05	$(0.932, 1.128)$	
λ	-1.69	0.09	$(-1.866, -1.514)$	
a_0	0.29	0.0161	$(0.26, 0.32)$	
Age	0.01	0.001	$(0.008, 0.012)$	
Gender	-0.33	0.03	$(-0.389, -0.271)$	
PS	0.15	0.12	$(-0.085, 0.385)$	
α	1.00	0.04	$(0.922, 1.078)$	
λ	-1.82	0.06	$(-1.938, -1.703)$	
a_0	1			

Table 5.10: The Posterior Estimates of the Model Parameters with log-logistic Distribution Using Informative Priors, $\alpha \sim \Gamma(1, 0.01)$ and $\lambda \sim N(0, 10000)$

Variable	Posterior estimate	Posterior SD	95% CI	(δ_0, λ_0)
Age	0.007	0.004	$(-0.001,\ 0.015)$	
Gender	-0.14	0.12	$(-0.375,\ 0.095)$	
PS	-0.16	0.25	$(-0.650, 0.330)$	(45,45)
α	1.56	0.13	$(1.305, 1.815)$	
λ	-1.34	0.16	$(-1.654, -1.026)$	
a_0	0.03	0.004	$(0.021, 0.038)$	
Age	0.008	0.003	$(0.002, 0.014)$	
Gender	-0.16	0.12	$(-0.395, 0.075)$	
(95,95)PS	-0.13	0.23	$(-0.581, 0.321)$	(95,95)
α	1.52	0.12	$(1.285, 1.755$	
λ	-1.39	0.15	$(-1.684, -1.096)$	
a_0	0.06	0.006	$(0.050, 0.070)$	
Age	0.009	0.003	$(0.003, 0.015)$	
Gender	-0.19	0.11	$(-0.406, 0.026)$	
PS	-0.08	0.21	$(-0.492, 0.332)$	(194,0)
α	1.46	0.11	$(1.244, 1.676)$	
λ	-1.48	0.14	$(-1.754, -1.206)$	
a_0	0.14	0.010	$(0.120, 0.159)$	
Age	0.009	0.003	$(0.003, 0.015)$	
Gender	-0.21	0.10	$(-0.406, -0.014)$	
PS	-0.04	0.20	$(-0.432, 0.352)$	(395,395)
α	1.42	0.10	$(1.224, 1.616)$	
λ	-1.53	0.13	$(-1.785, -1.275)$	
a_0	0.21	0.010	$(0.190, 0.230)$	
Age	0.010	0.003	$(0.004, 0.016)$	
Gender	-0.23	0.10	$(-0.426, -0.034)$	
PS	0.00	0.18	$(-0.353, 0.353)$	(390,0)
α	1.40	0.09	$(1.224, 1.576)$	
λ	-1.59	0.12	$(-1.825, -1.355)$	
a_0	0.29	0.015	$(0.262, 0.318)$	
Age	0.012	0.002	$(0.008, 0.016)$	
Gender	-0.31	0.07	$(-0.447, -0.173)$	
PS	0.14	0.13	$(-0.115, 0.395)$	
α	1.31	0.06	$(1.192, 1.428)$	
λ	-1.78	0.09	$(-1.956, -1.604)$	
a_0	1			

Table 5.11: The Posterior Estimates of the Model Parameters with Gompertz Distribution Using Informative Priors, $\alpha \sim \Gamma(1, 0.01)$ and $\lambda \sim N(0, 10000)$

Variable	Posterior estimate	Posterior SD	95% CI	(δ_0, λ_0)
Age Gender PS α λ a_0	0.007 −0.13 −0.17 0.25 −9.45 0.03	0.004 0.12 0.25 0.04 8.02 0.004	(−0.001, 0.015) (−0.365, 0.105) (−0.660, 0.320) (0.172, 0.328) (−25.169, 6.269) (0.027, 0.033)	(46,46)
Age Gender PS α λ a_0	0.008 −0.15 −0.14 0.23 −10.23 0.06	0.004 0.12 0.24 0.03 11.26 0.006	(0.000, 0.016) (−0.385, 0.085) (−0.610, 0.330) (0.171, 0.289) (−32.300, 11.840) (0.048, 0.072)	(96,96)
Age Gender PS α λ a_0	0.01 −0.18 −0.08 0.21 −10.87 0.14	0.003 0.11 0.21 0.03 13.98 0.009	(0.004, 0.016) (−0.396, 0.036) (−0.492, 0.332) (0.151, 0.269) (−38.271, 16.531) (0.120, 0.159)	(239,239)
Age Gender PS α λ a_0	0.010 −0.21 −0.03 0.20 −11.13 0.21	0.003 0.10 0.20 0.02 14.77 0.010	(0.004, 0.016) (−0.406, −0.014) (−0.422, 0.362) (0.161, 0.239) (−40.079, 17.819) (0.190, 0.229)	(399,399)
Age Gender (399,0) PS α λ a_0	0.01 −0.23 0.004 0.19 −11.33 0.29	0.003 0.10 0.19 0.02 15.18 0.013	(0.004, 0.016) (−0.426, −0.034) (−0.368, 0.376) (0.151, 0.229) (−41.083, 18.423) (0.243, 0.296)	(399,0)
Age Gender PS α λ a_0	0.01 −0.33 0.15 0.16 −12.14 1	0.002 0.07 0.13 0.01 14.97	(0.006, 0.016) (−0.467, −0.193) (−0.105, 0.405) (0.140, 0.180) (−41.481, 17.201)	

Table 5.12: The Posterior Estimates of the Model Parameters with Gamma Distribution Using Informative Priors, $\alpha \sim \Gamma(1, 0.01)$ and $\lambda \sim N(0, 10000)$

Variable	Posterior estimate	Posterior SD	95% CI	(δ_0, λ_0)
Age	0.007	0.004	$(-0.001, 0.015)$	
Gender	-0.16	0.12	$(-0.385, 0.075)$	
PS	-0.17	0.25	$(-0.660, 0.320)$	(49,49)
α	1.38	0.10	$(1.184, 1.576)$	
λ	-0.80	0.15	$(-1.094, -0.506)$	
a_0	0.03	0.004	$(0.021, 0.038)$	
Age	0.008	0.0034	$(0.001, 0.015)$	
Gender	-0.17	0.12	$(-0.405, 0.065)$	
PS	-0.14	0.23	$(-0.591, 0.311)$	(99,99)
α	1.29	0.09	$(1.114, 1.466)$	
λ	-1.00	0.16	$(-1.314, -0.686)$	
a_0	0.06	0.006	$(0.05, 0.072)$	
Age	0.009	0.0032	$(0.003, 0.015)$	
Gender	-0.19	0.11	$(-0.407, 0.026)$	
(199,0) PS	-0.08	0.21	$(-0.492, 0.332)$	(199,0)
α	1.19	0.08	$(1.033, 1.347)$	
λ	-1.25	0.16	$(-1.564, -0.936)$	
a_0	0.14	0.0115	$(0.12, 0.16)$	
Age	0.01	0.003	$(0.004, 0.016)$	
Gender	-0.22	0.10	$(-0.416, -0.024)$	
(399,399) PS	-0.034	0.20	$(-0.426, 0.358)$	(399,399)
α	1.15	0.08	$(0.993, 1.307)$	
λ	-1.37	0.15	$(-1.664, -1.076)$	
a_0	0.21	0.011	$(0.19, 0.23)$	
Age	0.01	0.003	$(0.004, 0.016)$	
Gender	-0.24	0.10	$(-0.436, -0.044)$	
PS	0.004	0.18	$(-0.349, 0.357)$	(399,0)
α	1.13	0.07	$(0.993, 1.267)$	
λ	-1.46	0.14	$(-1.734, -1.186)$	
a_0	0.29	0.016	$(0.26, 0.32)$	
Age	0.012	0.002	$(0.008, 0.016)$	
Gender	-0.33	0.07	$(-0.467, -0.193)$	
PS	0.15	0.13	$(-0.105, 0.405)$	
α	1.07	0.05	$(0.972, 1.168)$	
λ	-1.70	0.10	$(-1.896, -1.504)$	
a_0	1			

5.4 Detailed Sensitivity Analysis by Varying the Hyperparameters

We now discuss a detailed sensitivity analysis for the regression coefficients by varying the hyperparameters for $\gamma = (\alpha, \lambda)$. For illustration purposes, we only show results with a fixed value for a_0. When other values of a_0 are chosen, similar results can be obtained. To be more specific, we fix the hyperparameters for $a_0 = 0.29$ and vary the hyperparameters for γ. Firstly, varying the variance of λ and α from small value to large value which implies that shape of the λ or α becomes from narrow to flat. Secondly, varying the mean of λ and α from the small to large. Based on the two conditions, we check the influence on the regression coefficients. Through these detailed sensitivity analysis, we find that the posterior estimates of age, gender and PS are also robust for a wide range of hyperparameter values.

Table 5.13 reports the posterior estimates of the model parameters with the Weibull distribution which was discussed by Chen et al (1999). Tables 5.14, 5.15 and 5.16 report the posterior estimates of the model parameters with the log-logistic, Gompertz and Gamma distributions. Comparing the results of Table 5.13 with each of Tables 5.14, 5.15 and 5.16, we see that the posterior estimates of age, gender and PS are almost the same for we choose different hyperparameter values for (α, λ). To be more specific, when $F(t)$ follows a log-logistic, Weibull or Gamma distribution, the posterior estimates of age, gender and PS are the same. However, when $F(t)$ follows the Gompertz distribution, the posterior estimates of gender and PS have change somewhat, but the posterior estimates of age remain the same. Overall, moderate to informative choices of the hyperparameters for (α, λ) led to almost the same posterior estimates of age, gender and PS.

Table 5.13: The Posterior Estimates of the Model Parameters with Weibull Distribution, $a_0 = 0.29$

Variable	Posterior estimate	Posterior SD	95% CI	α	λ
Age	0.01	0.002	$(0.006, 0.014)$		
Gender	-0.23	0.08	$(-0.387, -0.073)$		
PS	0.00	0.18	$(-0.353, 0.353)$	$\Gamma(1, 0.01)$	$N(0, 10000)$
α	1.03	0.05	$(0.932, 1.128)$		
λ	-1.69	0.09	$(-1.866, -1.514)$		
Age	0.01	0.002	$(0.006, 0.014)$		
Gender	-0.23	0.08	$(-0.387, -0.073)$		
PS	0.00	0.18	$(-0.353, 0.353)$	$\Gamma(1, 1)$	$N(0, 10)$
α	1.03	0.05	$(0.932, 1.128)$		
λ	-1.68	0.09	$(-1.856, -1.504)$		
Age	0.01	0.002	$(0.006, 0.014)$		
Gender	-0.23	0.08	$(-0.387, -0.073)$		
PS	0.00	0.18	$(-0.353, 0.353)$	$\Gamma(10, 0.01)$	$N(0, 10)$
α	1.05	0.05	$(0.952, 1.148)$		
λ	-1.71	0.09	$(-1.886, -1.534)$		
Age	0.01	0.002	$(0.006, 0.014)$		
Gender	-0.23	0.08	$(-0.387, -0.073)$		
PS	0.00	0.18	$(-0.353, 0.353)$	$\Gamma(10, 1)$	$N(10, 10)$
α	1.05	0.05	$(0.952, 1.148)$		
λ	-1.69	0.09	$(-1.866, -1.514)$		
Age	0.01	0.002	$(0.006, 0.014)$		
Gender	-0.23	0.08	$(-0.387, -0.073)$		
PS	0.00	0.18	$(-0.353, 0.353)$	$\Gamma(0.01, 1)$	$N(10, 10)$
α	1.03	0.05	$(0.932, 1.128)$		
λ	-1.67	0.09	$(-1.846, -1.494)$		

Table 5.14: The Posterior Estimates of the Model Parameters with log-logistic Distribution, $a_0 = 0.29$

Variable	Posterior estimate	Posterior SD	95% CI	α	λ
Age	0.01	0.003	$(0.004, 0.016)$		
Gender	-0.23	0.10	$(-0.426, -0.034)$		
PS	0.0004	0.18	$(-0.352, 0.353)$	$\Gamma(1, 0.01)$	$N(0, 10000)$
α	1.40	0.09	$(1.224, 1.576)$		
λ	-1.59	0.12	$(-1.825, -1.355)$		
Age	0.01	0.003	$(0.004, 0.016)$		
Gender	-0.23	0.10	$(-0.426, -0.034)$		
PS	0.00	0.18	$(-0.353, 0.353)$	$\Gamma(1, 1)$	$N(0, 10)$
α	1.39	0.09	$(1.214, 1.566)$		
λ	-1.58	0.13	$(-1.835, -1.325)$		
Age	0.01	0.003	$(0.004, 0.016)$		
Gender	-0.23	0.10	$(-0.426, -0.034)$		
PS	0.00	0.18	$(-0.353, 0.353)$	$\Gamma(10, 0.01)$	$N(0, 10)$
α	1.45	0.09	$(1.274, 1.626)$		
λ	-1.58	0.12	$(-1.815, -1.345)$		
Age	0.01	0.003	$(0.004, 0.016)$		
Gender	-0.23	0.10	$(-0.426, -0.034)$		
PS	0.00	0.18	$(-0.353, 0.353)$	$\Gamma(10, 1)$	$N(10, 10)$
α	1.44	0.09	$(1.264, 1.616)$		
λ	-1.57	0.12	$(-1.805, -1.335)$		
Age	0.01	0.003	$(0.004, 0.016)$		
Gender	-0.23	0.10	$(-0.426, -0.034)$		
PS	0.00	0.18	$(-0.353, 0.353)$	$\Gamma(0.01, 1)$	$N(10, 10)$
α	1.38	0.09	$(1.204, 1.556)$		
λ	-1.57	0.12	$(-1.805, -1.335)$		

Table 5.15: The Posterior Estimates of the Model Parameters with Gompertz Distribution, $a_0 = 0.29$

Variable	Posterior estimate	Posterior SD	95% CI	α	λ
Age	0.01	0.003	$(0.004, 0.016)$		
Gender	-0.23	0.10	$(-0.426, -0.034)$		
PS	0.004	0.19	$(-0.368, 0.376)$	$\Gamma(1, 0.01)$	$N(0, 10000)$
α	0.19	0.02	$(0.151, 0.229)$		
λ	-11.33	15.18	$(-41.083, 18.423)$		
Age	0.01	0.003	$(0.004, 0.016)$		
Gender	-0.23	0.10	$(-0.426, -0.034)$		
PS	0.004	0.19	$(-0.368, 0.376)$	$\Gamma(1, 1)$	$N(0, 10)$
α	0.19	0.02	$(0.151, 0.229)$		
λ	-5.29	0.77	$(-6.800, -3.781)$		
Age	0.01	0.003	$(0.004, 0.016)$		
Gender	-0.24	0.10	$(-0.436, -0.044)$		
PS	0.00	0.19	$(-0.372, 0.372)$	$\Gamma(10, 0.01)$	$N(0, 10)$
α	0.21	0.02	$(0.171, 0.249)$		
λ	-5.42	0.86	$(-7.106, -3.734)$		
Age	0.01	0.003	$(0.004, 0.016)$		
Gender	-0.24	0.10	$(-0.436, -0.044)$		
PS	0.00	0.19	$(-0.372, 0.372)$	$\Gamma(10, 1)$	$N(10, 10)$
α	0.20	0.02	$(0.161, 0.239)$		
λ	-4.56	0.63	$(-5.795, -3.325)$		
Age	0.01	0.003	$(0.004, 0.016)$		
Gender	-0.23	0.10	$(-0.426, -0.034)$		
PS	0.005	0.19	$(-0.367, 0.377)$	$\Gamma(0.01, 1)$	$N(10, 10)$
α	0.18	0.02	$(0.141, 0.219)$		
λ	-4.41	0.55	$(-5.488, -3.332)$		

Table 5.16: The Posterior Estimates of the Model Parameters with Gamma Distribution, $a_0 = 0.29$

Variable	Posterior estimate	Posterior SD	95% CI	α	λ
Age	0.01	0.003	(0.004, 0.016)		
Gender	−0.24	0.10	(−0.436, −0.044)		
PS	0.004	0.18	(−0.349, 0.357)	$\Gamma(1, 0.01)$	$N(0, 10000)$
α	1.13	0.07	(0.993, 1.267)		
λ	−1.46	0.14	(−1.734, −1.186)		
Age	0.01	0.003	(0.004, 0.016)		
Gender	−0.24	0.10	(−0.436, −0.044)		
PS	0.004	0.18	(−0.349, 0.357)	$\Gamma(1, 1)$	$N(0, 10)$
α	1.12	0.07	(0.983, 1.257)		
λ	−1.46	0.14	(−1.734, −1.186)		
Age	0.01	0.003	(0.004, 0.016)		
Gender	−0.24	0.10	(−0.436, −0.044)		
PS	0.004	0.18	(−0.349, 0.357)	$\Gamma(10, 0.01)$	$N(0, 10)$
α	1.18	0.07	(1.043, 1.317)		
λ	−1.38	0.13	(−1.635, −1.125)		
Age	0.01	0.003	(0.004, 0.016)		
Gender	−0.24	0.10	(−0.436, −0.044)		
PS	0.004	0.18	(−0.349, 0.357)	$\Gamma(10, 1)$	$N(10, 10)$
α	1.18	0.07	(1.043, 1.317)		
λ	−1.37	0.13	(−1.625, −1.115)		
Age	0.01	0.003	(0.004, 0.016)		
Gender	−0.24	0.10	(−0.436, −0.044)		
PS	0.004	0.18	(−0.349, 0.357)	$\Gamma(0.01, 1)$	$N(10, 10)$
α	1.13	0.07	(0.993, 1.267)		
λ	−1.45	0.14	(−1.724, −1.176)		

Chapter 6

Conclusion and Discussion

In this practicum, we extended the work of Chen, Ibrahim and Sinha (1999) to the case where $F(t)$ follows a log-logistic, Gompertz and Gamma distribution. Comparing the inferences between each of the proposed models under the log-logistic, Gompertz and Gamma distributions and the proposed model under the Weibull distribution, we have discovered that the corresponding results are similar. To be more specific, when we propose novel classes of noninformative and informative priors for (β, γ), we obtain the results that the posterior distributions of parameters are proper using an improper uniform prior with the proposed models under different distributions. This enables us to carry out noninformative or informative Bayesian inference for the regression coefficients.

We have also investigated the melanoma data using three different methods for each distribution: first, for data with MLE's; then data with noninformative priors; finally, data with an informative prior. We found that the results are the same not only for the Weibull distribution, but also for the log-logistic, Gompertz and Gamma distributions. To be more specific, using the current data E1684, if we compare the data (E1684) using the MLE's with data from noninformative priors using the results with respect to p-values, we find the p-values are almost the same. Similarly, the values for the MLE's and posterior estimates of parameters are almost the same when we compare data using the MLE's with data using noninformative priors respectively. And using different distributions do not affect the result that the incorporation of historical data can improve the posterior estimates, standard deviations and 95% confidence intervals of age, gender and PS. And age and gender are potentially important prognostic factors for predicting overall survival in melanoma. This demonstrates a desirable feature of our model. Such a conclusion is not possible based only on a frequentist or a Bayesian analysis of the current data alone. Thus, incorporating historical data can yield more precise posterior estimates of age, gender and PS.

It is possible that other distributions can be handled in a similar way. Natural candidates for this kind of extension include generated Gamma or generated F distributions. These problems require further investigations which are beyond the scope of this practicum.

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