LIKELIHOOD-BASED INFERENTIAL METHODS

FOR SOME FLEXIBLE CURE RATE MODELS

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Abstract

Recently, the Conway-Maxwell Poisson (COM-Poisson) cure rate model has been proposed which includes as special cases some of the well-known cure rate models discussed in the literature. Data obtained from cancer clinical trials are often right censored and the expectation maximization (EM) algorithm can be efficiently used for the determination of the maximum likelihood estimates (MLEs) of the model parameters based on right censored data.

By assuming the lifetime distribution to be exponential, lognormal, Weibull, and gamma, the necessary steps of the EM algorithm are developed for the COM-Poisson cure rate model and some of its special cases. The inferential method is examined by means of an extensive simulation study. Model discrimination within the COM-Poisson family is carried out by likelihood ratio test as well as by information-based criteria. Finally, the proposed method is illustrated with a cutaneous melanoma data on cancer recurrence. As the lifetime distributions considered are not nested, it is not possible to carry out a formal statistical test to determine which among these provides an adequate fit to the data. For this reason, the wider class of generalized gamma distributions is considered which contains all of the above mentioned lifetime distributions as special cases. The steps of the EM algorithm are then developed for this general class of distributions and a simulation study is carried out to evaluate the performance of the proposed estimation method. Model discrimination within the generalized gamma family is carried out by likelihood ratio test and information-based criteria. Finally, for the considered cutaneous melanoma data, the two-way flexibility of the COM-Poisson family and the generalized gamma family is utilized to carry out a two-way model discrimination to select a parsimonious competing cause distribution along with a suitable choice of a lifetime distribution that provides the best fit to the data.

KEY WORDS: Cure rate models; Long-term survivors; COM-Poisson distribution; Weighted Poisson distribution; Competing cause scenario; EM algorithm; Lifetime data; Right censoring; Non-informative censoring; Profile likelihood; Asymptotic variances and covariances; MLE; Likelihood ratio test; Exponential distribution; Log-normal distribution; Weibull distribution; Gamma distribution; Generalized gamma distribution; Mixture chi-square; AIC; BIC; Model discrimination; Monte Carlo simulations; Goodness-of-fit test.

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Contents

List of Tables

List of Figures

Chapter 1

Introduction

1.1 Cure rate model

Cure rate models are models for survival or lifetime data consisting of a surviving fraction. Because of great improvements in the treatment of cancer and some other diseases, cure rate models have become increasingly popular in the analysis of data from many clinical trials. For certain types of cancers, including breast cancer, leukemia, melanoma, and prostate cancer, a substantial proportion of patients may now be cured by treatment, i.e., show no recurrence of the disease. The patients who are cured are called immunes or long-term survivors, while the remaining patients who develop a recurrence of the disease are termed susceptibles. The population of interest is thus divided into two groups and can be regarded as a mixture of these two types of patients. Traditional methods of survival analysis, including the well-known Cox regression model, assume that no patients are cured but that all remain at risk of death or relapse. These models are concerned with survival only and do not accommodate the possibility of cure. However, estimation of a treatment-specific cure rate provides valuable information that is not only of use to the investigator but is also of primary interest to the patient at the time of diagnosis.

Although the term "cure rate" sounds biomedical, we find applications of cure rate models in a wide array of other areas such as criminology, finance, demography, manufacturing, and industrial reliability. For instance, in industrial reliability, an event of interest may be the failure of circuit boards which are subjected to various levels of humidity stress. At low levels of humidity, a proportion of the boards lasts indefinitely and hence can be considered as long-term survivors. The occurrence of an event of interest can be due to a number of competing causes, which is referred to as the competing cause scenario (Cox and Oakes, 1984). For instance, in cancer clinical trials, an event of interest may be a patient's death, which can occur due to a particular type of cancer or heart attack. In industrial reliability, the failure of circuit boards can occur due to infant failure or wear-out; see Meeker and Escobar (1998). For more details in this area, one may refer to Yakovlev et al. (1993), Yakovlev and Tsodikov (1996), Ibrahim et al. (2001), and Hoggart and Griffin (2001).

Let M be a random variable denoting the number of competing causes related to the occurrence of an event of interest, with probability mass function (p.m.f.) $p_m = P[M = m]$ for $m = 0, 1, 2, \ldots$. Given $M = m$, let W_j $(j = 1, 2, \ldots, m)$ be independent random variables, independently of M, with a common distribution function $F(y) = 1 - S(y)$. The random variables W_j denote the time-to-event due to the j-th competing cause, hereafter lifetime, and $S(y)$ denotes the survival function. In the competing cause scenario, the number of competing causes M and the lifetime W_j associated with a particular cause are not observable (latent variables), but only the minimum lifetime Y among all causes is usually observed. So, in order to include those individuals who are not susceptible to the event occurrence, the lifetime is defined as

$$Y = \min\{W_0, W_1, W_2, \ldots, W_M\}, \tag{1.1.1}$$

where $P[W_0 = \infty] = 1$, which leads to a proportion p_0 of the population not susceptible to the event occurrence, also called the "cure rate".

1.2 A brief literature review

Cure rate models have been studied extensively in the literature. Boag (1949) and Berkson and Gage (1952) proposed the mixture cure rate model by introducing a component representing the proportion of cured in the population and a distribution representing the lifetime of the susceptibles. Farewell (1982) considered the mixture model and used a logistic regression for the mixture proportion and a Weibull regression for the latency. Kuk and Chen (1992) proposed a semi-parametric generalization of Farewell's model by considering a Cox proportional hazards model in the susceptible group. Yakovlev and Tsodikov (1996) and Chen et al. (1999) introduced the promotion time cure model by considering a competitive scenario. Sy and Taylor (2000) developed maximum likelihood techniques for the joint estimation of the incidence and latency regression parameters using the non-parametric form of the likelihood and an EM algorithm. Rodrigues et al. (2009) developed a flexible cure rate survival model by assuming the number of competing causes to follow the COM-Poisson distribution. This model includes some of the well-known cure rate models discussed in the literature and can be looked as a flexible alternative to the unified cure rate model discussed by Yin and Ibrahim (2005). Rodrigues et al. (2011) subsequently developed a more flexible cure rate survival model which includes a destructive process of the initial risk factors in a competitive scenario and is thus based on the biological mechanism of the occurrence of the event of interest. Recently, Rodrigues et al. (2012) proposed a new Bayesian flexible cure rate survival model which generalizes the stochastic model of Klebanov et al. (1993) and has much in common with the destructive cure rate model formulated by Rodrigues et al. (2011). Borges et al. (2012) introduced a new cure rate survival model which extends the model of Rodrigues et al. (2011) by incorporating a structure of dependence between the initiated cells. Very recently, de Freitas and Rodrigues (2013) discussed informative censoring while studying the standard exponential cure rate model.

1.3 COM-Poisson cure rate model

The COM-Poisson distribution, first introduced by Conway and Maxwell (1961), generalizes the Poisson distribution in an elegant and flexible way by adding a parameter to model over-dispersion and under-dispersion which are usually encountered in discrete data. This distribution was revived recently by Shmueli et al. (2005) and was discussed further by Kadane et al. (2006), Kokonendji et al. (2008) and Kokonendji et al. (2009). It is a member of the exponential family and can be viewed as a weighted Poisson distribution. We let the discrete competing cause random variable M to follow the COM-Poisson distribution with p.m.f. given by

$$P[M = m; \eta, \phi] = \frac{1}{Z(\eta,\phi)} \frac{\eta^m}{(m!)^\phi}, \qquad m = 0, 1, 2, \ldots, \tag{1.3.1}$$

where

$$Z(\eta,\phi) = \sum_{j=0}^{\infty} \frac{\eta^j}{(j!)^\phi}. \tag{1.3.2}$$

The cure rate then simply turns out to be

$$p_0 = P[M = 0; \eta, \phi] = \frac{1}{Z(\eta, \phi)}.$$

For $\phi = 1$, $Z(\eta, \phi) = e^{\eta}$, and this distribution is the Poisson distribution with mean η. Values of $\phi > 1$ correspond to under-dispersion while $\phi < 1$ corresponds to over-dispersion relative to the Poisson distribution. As $\phi \to \infty$, $Z(\eta, \phi) \to 1 + \eta$, and the distribution in this case approaches a Bernoulli distribution with $P[M = 1] = \frac{\eta}{1+\eta}$. When $\phi = 0$ and $\eta < 1$, $Z(\eta, \phi)$ is the geometric sum

$$Z(\eta, \phi) = \sum_{j=0}^{\infty} \eta^j = \frac{1}{1 - \eta},$$

and the distribution itself is geometric with

$$P[M = m; \eta] = \eta^m (1 - \eta) \quad \text{for} \quad m = 0, 1, 2, \ldots$$

When $\phi = 0$ and $\eta \geq 1$, $Z(\eta, \phi)$ does not converge, and hence the distribution is undefined in this case. We thus note that the COM-Poisson distribution is a very flexible family of distributions and includes some commonly used distributions as special cases.

From Rodrigues et al. (2009), the long-term survival function of the random variable Y in (1.1.1) can be expressed as

$$S_p(y) = \frac{Z(\eta S(y), \phi)}{Z(\eta, \phi)}, \tag{1.3.3}$$

where $Z(\cdot, \cdot)$ is as defined in (1.3.2). Note that the function $S_p(y)$ is not a proper survival function as $\lim_{y \to \infty} S_p(y) = p_0$. From (1.3.3), the improper density function of Y can be easily obtained as

$$f_p(y) = -S_p^{'}(y) = \frac{1}{Z(\eta,\phi)} \frac{f(y)}{S(y)} \sum_{j=1}^{\infty} \frac{j\{\eta S(y)\}^j}{(j!)^{\phi}},$$

where $f(y)$ denotes the common (proper) density function of the lifetimes in (1.1.1).

The COM-Poisson cure rate model represents a continuous bridge between under-dispersion and over-dispersion in the counts of the number of competing causes. This model encompasses the promotion time (Poisson) cure rate model when $\phi = 1$, the mixture (Bernoulli) cure rate model when $\phi \to \infty$, and the geometric cure rate model when $\phi = 0$ and $\eta < 1$.

Considering the population as a mixture of two types of patients, we can introduce an indicator variable I taking the value 0 if the subject is cured, and 1 if the subject is susceptible. Let $P[I = 0] = p_0$ and $P[I = 1] = 1 - p_0$. Further, let F_p and F_1 denote the cumulative distribution function (c.d.f.) of the overall population and of susceptibles, respectively. Then, for $0 < y < \infty$, we have

$$P[Y \le y|I = 0] = 0 \quad \text{and} \quad P[Y \le y|I = 1] = F_1(y).$$

The c.d.f. of the overall population is then given by

$$\begin{aligned} F_p(y) &= P[Y \le y] = P[Y \le y|I = 0]P[I = 0] + P[Y \le y|I = 1]P[I = 1] \\ &= (1 - p_0)F_1(y), \end{aligned}$$

and, consequently, the survival function of the overall population is given by

$$S_p(y) = 1 - F_p(y) = 1 - (1 - p_0)F_1(y) = p_0 + (1 - p_0)S_1(y), \tag{1.3.4}$$

where $S_1(y) = 1 - F_1(y)$ denotes the survival function of the susceptibles. Thus, it is possible to present an alternative expression for the long-term survival function through the concept of mixtures. An expression for $S_1(y)$ can be easily obtained as

$$S_1(y) = \frac{S_p(y) - p_0}{1 - p_0},$$

where $S_p(y)$ can be calculated using (1.3.3). We note that the function $S_1(y)$ is a proper survival function.

In Table 1.1, we present the long-term survival function, the improper density function and the cure fraction corresponding to three special cases of the COM-Poisson cure rate model.

Table 1.1: Survival function (S_p), density function (f_p), and cure fraction (p_0) for the special cases of COM-Poisson cure rate model.

Model	$S_p(y)$	$f_p(y)$	p_0
Bernoulli	$\frac{1+\eta S(y)}{1+\eta}$	$\frac{\eta}{1+\eta} f(y)$	$\frac{1}{1+\eta}$
Poisson	$\exp(-\eta(1 - S(y)))$	$\eta S_p(y) f(y)$	$\exp(-\eta)$
Geometric	$\frac{1-\eta}{1-\eta S(y)}$	$\frac{\eta}{1-\eta S(y)} S_p(y) f(y)$	$1 - \eta$

1.4 Models for lifetime data

There are numerous statistical distributions in the literature, but a few specific distributions occupy a central role because of their demonstrated usefulness in a wide range of situations and are therefore used as models for lifetime data. In this section, we present a brief summary of some of the statistical distributions that have been found to be most useful for describing lifetime data. For more details on these models, one may refer to the books by Johnson et al. (1994), Johnson et al. (1995), and

Balakrishnan and Caroni (2013).

1.4.1 Exponential distribution

The exponential distribution is the simplest and most commonly used distribution for modeling lifetime data. The probability density function (p.d.f.) of a one-parameter exponential distribution is given by

$$f(w;\gamma) = \gamma \exp(-\gamma w), \quad w > 0, \gamma > 0, \tag{1.4.1}$$

and the corresponding survival function is given by

$$S(w;\gamma) = \exp(-\gamma w), \quad w > 0.$$

The mean and variance of the above exponential distribution are

$$E(W) = \frac{1}{\gamma} \text{ and } V(W) = \frac{1}{\gamma^2},$$

respectively. The exponential distribution is characterized by a constant hazard function and this fact makes it unsuitable in many practical situations. For more details on various developments on theory, methods and applications of the exponential distribution, one may refer to the book by Balakrishnan and Basu (1995).

1.4.2 Weibull distribution

The Weibull distribution has a lot of flexibility to describe lifetime data and is one of the most widely used lifetime models. The Weibull distribution has the p.d.f.

$$f(w;\boldsymbol{\gamma}) = \frac{1}{\gamma_1 w}(\gamma_2 w)^{1/\gamma_1}\exp(-(\gamma_2 w)^{1/\gamma_1}), \quad w > 0, \gamma_1 > 0, \gamma_2 > 0, \tag{1.4.2}$$

with shape=$\frac{1}{\gamma_1}$ and scale=$\frac{1}{\gamma_2}$. The corresponding survival function is given by

$$S(w;\boldsymbol{\gamma}) = \exp(-(\gamma_2 w)^{1/\gamma_1}), \quad w > 0.$$

The mean and variance of the above Weibull distribution are

$$E(W) = \frac{1}{\gamma_2}\Gamma(1+\gamma_1) \text{ and } V(W) = \frac{1}{\gamma_2^2}[\Gamma(1+2\gamma_1) - \{\Gamma(1+\gamma_1)\}^2],$$

respectively, where

$$\Gamma(p) = \int_0^\infty e^{-x}x^{p-1}dx \tag{1.4.3}$$

is the gamma function. The hazard function can be increasing, decreasing as well as constant, a property that makes it widely applicable in both reliability and survival analyses. For more details on Weibull distribution, one may refer to Murthy et al. (2004) and Rinne (2008).

1.4.3 Gamma distribution

The gamma distribution is another statistical distribution that is quite widely used in reliability and survival analyses, and in many other areas of statistics due to its flexibility. It has the p.d.f.

$$f(w;\boldsymbol{\gamma}) = \frac{\left(\frac{\gamma_2}{\gamma_1^2}\right)^{\frac{1}{\gamma_1^2}}}{\Gamma(\frac{1}{\gamma_1^2})} \exp\left\{-\frac{\gamma_2 w}{\gamma_1^2}\right\} w^{\frac{1}{\gamma_1^2}-1}, \quad w>0, \gamma_1>0, \gamma_2>0, \tag{1.4.4}$$

with shape $= \frac{1}{\gamma_1^2}$ and scale $= \frac{\gamma_1^2}{\gamma_2}$, where $\Gamma(\cdot)$ is as defined in (1.4.3). The corresponding survival function is given by

$$S(w;\boldsymbol{\gamma}) = \frac{\Gamma\left(\frac{1}{\gamma_1^2}, \frac{\gamma_2 w}{\gamma_1^2}\right)}{\Gamma\left(\frac{1}{\gamma_1^2}\right)}, \quad w>0,$$

where

$$\Gamma(a,b) = \int_b^\infty e^{-x} x^{a-1} dx \tag{1.4.5}$$

is the upper incomplete gamma function. The mean and variance of the above gamma distribution are

$$E(W) = \frac{1}{\gamma_2} \quad \text{and} \quad V(W) = \frac{\gamma_1^2}{\gamma_2^2},$$

respectively.

1.4.4 Lognormal distribution

The lognormal distribution is another important statistical distribution and has the p.d.f.

$$f(w;\boldsymbol{\gamma}) = \frac{1}{\sqrt{2\pi}\gamma_1 w} \exp\left\{-\frac{1}{2}\left(\frac{\log(\gamma_2 w)}{\gamma_1}\right)^2\right\}, \quad w>0, \gamma_1>0, \gamma_2>0, \tag{1.4.6}$$

with $-\log(\gamma_2)$ and γ_1 as the mean and standard deviation, respectively, of the distribution of the logarithm (the normal distribution). The corresponding survival function is given by

$$S(w;\boldsymbol{\gamma}) = 1 - \Phi\left(\frac{\log(\gamma_2 w)}{\gamma_1}\right), \quad w > 0,$$

where $\Phi(\cdot)$ is the distribution function of the standard normal distribution. The mean and variance of the above lognormal distribution are

$$E(W) = \exp\left(\frac{\gamma_1^2}{2} - \log(\gamma_2)\right) \text{ and } V(W) = \exp(\gamma_1^2 - 2\log(\gamma_2))(\exp(\gamma_1^2) - 1),$$

respectively. Crow and Shimizu (1988) have presented a book-length account of various developments on theory and applications of the lognormal distribution.

1.4.5 Generalized gamma distribution

The generalized gamma distribution is a wide class of distributions introduced originally by Stacy (1962) and studied further by Prentice (1974). It has the p.d.f.

$$f(w;\boldsymbol{\gamma}) = \begin{cases} q(q^{-2})^{q^{-2}}(\lambda w)^{q^{-2}(q/\sigma)}\exp[-q^{-2}(\lambda w)^{q/\sigma}]/[\Gamma(q^{-2})\sigma w], & q > 0, \\ (\sqrt{2\pi}\sigma w)^{-1}\exp\{-[\log(\lambda w)]^2/(2\sigma^2)\}, & q = 0, \end{cases} \tag{1.4.7}$$

where $\Gamma(\cdot)$ is as defined in (1.4.3), $\boldsymbol{\gamma} = (q, \sigma, \lambda)'$, $q \geq 0$ and $\sigma > 0$ are shape parameters, and $\lambda > 0$ is a scale parameter.

The generalized gamma distribution includes all of the lifetime distributions discussed in the preceding sub-sections as special cases. For instance, it reduces to the Weibull distribution when $q = 1$, the lognormal distribution when $q = 0$ (also the limit of (1.4.7) when $q \to 0$), and the gamma distribution when $q/\sigma = 1$. The survival function of the generalized gamma distribution defined in (1.4.7) is given by

$$S(w;\boldsymbol{\gamma}) = \begin{cases} \Gamma(q^{-2}, q^{-2}(\lambda w)^{q/\sigma})/\Gamma(q^{-2}), & q > 0, \\ 1 - \Phi\left(\frac{\log(\lambda w)}{\sigma}\right), & q = 0, \end{cases} \tag{1.4.8}$$

where $\Gamma(a,b)$ is as defined in (1.4.5). The mean and variance of the above generalized gamma distribution are

$$E(W) = \frac{(q^2)^{\sigma/q}}{\lambda\Gamma(1/q^2)}\Gamma\left(\frac{\sigma}{q}+\frac{1}{q^2}\right) \text{ and } V(W) = \frac{q^{4\sigma/q}}{\lambda^2}\frac{1}{\Gamma(1/q^2)}\left[\Gamma\left(\frac{2\sigma}{q}+\frac{1}{q^2}\right)-\frac{\Gamma^2(\frac{\sigma}{q}+\frac{1}{q^2})}{\Gamma(1/q^2)}\right],$$

respectively.

1.5 Form of the data and the likelihood

We consider the situation when the lifetime in (1.1.1) is not completely observed and is subject to right censoring. Let C_i denote the censoring time. In a sample of size n, we then observe $T_i = \min\{Y_i, C_i\}$ and $\delta_i = I(Y_i \leq C_i)$, where $\delta_i = 1$ if Y_i is indeed a lifetime and $\delta_i = 0$ if it is right censored, for $i = 1, 2, \ldots, n$. Let us denote by $\boldsymbol{\gamma}$ the parameter vector of the distribution of the lifetimes in (1.1.1).

Although right censoring is the most common form of censoring encountered in many practical problems, there are some other forms of censoring as well. Occasionally, we may have left censoring which can happen, for example, in industrial reliability, when some units had failed even before we started to make proper measurements on the failure time. Another commonly encountered form of censoring is interval censoring in which the units being tested are not under continuous observation but are inspected at regular intervals. In this case, when a failed unit is observed, its exact failure time is not known, and it is only known that it failed during the time period between the present inspection and the previous inspection. Censoring can again be classified as informative or non-informative depending on whether the lifetime of units is dependent or independent of the censoring mechanism. For instance, in a medical trial, a patient may withdraw from treatment because his/her condition is deteriorating and may, therefore, need an alternative treatment. In this case, withdrawal at a time may indicate death is likely sooner than might have been expected otherwise and thus the right censoring becomes informative. Informative censoring is also encountered in industrial reliability. For instance, consider an experiment where a number of ball bearings of the same type are tested and the number of revolutions until each ball bearing fails is noted. If the experimenter decides to remove a ball bearing because it is pretty worn out and likely to fail soon, then it will be incorrect to say that the ball bearing is right censored at the time of withdrawal since we have more information on the lifetime of that ball bearing. It is thus clear that if the dependence between the censoring mechanism and the lifetime of units is ignored, the resulting inference will be biased. It is important to mention here that all the standard techniques of analyzing censored data are based on the assumption that the censoring mechanism is non-informative. For more details on different forms of censoring and inference based on such censored data, one may refer to Cohen (1991).

Now, to introduce the covariate effect in our cure rate model, we can either link the parameter η to covariates $\boldsymbol{x}_i$ by the log-linear link function η_i=exp$(\boldsymbol{x}_i'\boldsymbol{\beta}), i = 1, \ldots, n$, or link the cure rate parameter p_0 to covariates $\boldsymbol{x}_i$ by the logistic link function $p_{0i} = \frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}, i = 1, \ldots, n,$ where $\boldsymbol{\beta} = (\beta_0, \beta_1, \ldots, \beta_k)'$ denotes the vector of regression coefficients. In the latter, it is to be noted that for a fixed value of ϕ, p_0 is purely a function of η. Hence, given the link function for p_0, we can easily determine how η is linked with the covariates. Now, $p_0 = \frac{1}{Z(\eta,\phi)}$ and after linking it with the logistic link function, we have $H_\phi(\eta) = Z(\eta, \phi) = 1 + \exp(\boldsymbol{x}'\boldsymbol{\beta})$, for a fixed value of ϕ. This implies that $\eta = H_\phi^{-1}(1+\exp(\boldsymbol{x}'\boldsymbol{\beta}))$. We note that $H_\phi(\eta)$ is a monotonically increasing function of η with $H_\phi(\eta)|_{\eta=0} = 1$ and $H_\phi(\eta)|_{\eta\to\infty} = \infty$. Hence, the link function for η is a valid one for any fixed value of ϕ. We also note that although the function $H_\phi(\eta)$ is explicit, the inverse function $H_\phi^{-1}(\cdot)$ is implicit and needs to be calculated numerically. However, an explicit form of $H_\phi^{-1}(\cdot)$ can be obtained in some special cases of the COM-Poisson model and are as presented in Table 1.2.

Table 1.2: Expressions of η for some special cases of the COM-Poisson cure rate model.

Model	$H_\phi(\eta)$	$\eta = H_\phi^{-1}(1 + \exp(\boldsymbol{x}'\boldsymbol{\beta}))$
Bernoulli ($\phi \to \infty$)	$1 + \eta$	$\exp(\boldsymbol{x}'\boldsymbol{\beta})$
Poisson ($\phi = 1$)	$\exp(\eta)$	$\log\{1 + \exp(\boldsymbol{x}'\boldsymbol{\beta})\}$
geometric ($\phi = 0$)	$\frac{1}{1-\eta}$	$\frac{\exp(\boldsymbol{x}'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}'\boldsymbol{\beta})}$

From n pairs of times and censoring indicators $(t_1, \delta_1), \ldots, (t_n, \delta_n)$ as the data, the likelihood function, under the non-informative censoring assumption and using (1.3.4), can be written as

$$\begin{aligned} L(\boldsymbol{\theta}; \boldsymbol{t}, \boldsymbol{x}, \boldsymbol{\delta}) &\propto \prod_{i=1}^{n} \{f_p(t_i, \boldsymbol{x}_i; \boldsymbol{\theta})\}^{\delta_i} \{S_p(t_i, \boldsymbol{x}_i; \boldsymbol{\theta})\}^{1-\delta_i} \\ &= \prod_{I_1} f_p(t_i, \boldsymbol{x}_i; \boldsymbol{\theta}) \prod_{I_0} \{p_0(\boldsymbol{\theta}_1, \boldsymbol{x}_i) + (1 - p_0(\boldsymbol{\theta}_1, \boldsymbol{x}_i)) S_1(t_i, \boldsymbol{x}_i; \boldsymbol{\theta})\}, \end{aligned} \tag{1.5.1}$$

where $\boldsymbol{\theta} = (\phi, \boldsymbol{\beta}', \boldsymbol{\gamma}')'$, $\boldsymbol{\theta}_1 = (\phi, \boldsymbol{\beta}')'$, $\boldsymbol{t} = (t_1, \ldots, t_n)'$, $\boldsymbol{\delta} = (\delta_1, \ldots, \delta_n)'$, $I_1 = \{i : \delta_i = 1\}$, $I_0 = \{i : \delta_i = 0\}$, and $\boldsymbol{x}$ denotes the vector of $\boldsymbol{x}_i$ values.

1.6 Likelihood inference

The main objective of parametric statistical inference is to estimate the unknown parameters of the underlying statistical model based on the available data. The likelihood principle states that in the inference about the unknown parameters, after the data is observed, all relevant information about the unknown parameters is contained in the likelihood function, which is the probability of the observed data given the parameters. Maximum likelihood estimation is one of the most commonly used methods of obtaining estimators in statistical literature which adheres to the likelihood principle in a natural way. In general, for a given data and the underlying statistical model, the maximum likelihood method selects the sets of values of the model parameters that maximizes the likelihood function. This maximizes the "agreement" of the selected model with the observed data. The method of maximum likelihood thus gives a unified approach to the problem of estimation. However, it is to be noted that in some cases the MLEs may not exist or even if it exists, closed-form expressions may not be available, in which case one has to employ some numerical techniques for determining the MLEs. Maximum likelihood estimation possesses a number of attractive limiting properties, for example, consistency, asymptotic efficiency, asymptotic unbiasedness, and asymptotic normality of the MLEs, a property which can be utilized to obtain the asymptotic confidence intervals for the model parameters, thereby extending the point estimation problem to interval estimation quite naturally.

In case the available data is incomplete, for instance, if censoring is present in the data, then one needs to modify the standard approaches of parametric estimation based on complete-data. One such technique is the EM algorithm (Dempster et al. 1977), which is a broadly applicable approach to the iterative computation of the MLEs, useful in a variety of incomplete-data problems.

1.6.1 EM algorithm

In our context, we first note that if a subject's lifetime is actually observed, the indicator variable I, defined in Section 1.3, takes on the value 1. However, if the subject's lifetime is not observed, the subject might belong to the cured group and so the lifetime is censored or it might actually belong to the susceptible group but the time to event is greater than the censoring time and so the lifetime is censored. Thus, for subject's belonging to the set I_0, the value of the indicator variable I is unknown. This actually introduces the missing data and facilitates the use of EM algorithm for determining the MLE of the unknown parameter $\boldsymbol{\theta}$; see McLachlan and Krishnan (2008) for a detailed discussion on the EM algorithm.

Let us denote the complete-data by $(t_i, \delta_i, \boldsymbol{x}_i, I_i), i = 1, 2, \ldots, n$, which includes the observed data as well as the unobserved I_i's. The complete-data likelihood function is then given by

$$L_c(\boldsymbol{\theta}; \boldsymbol{t}, \boldsymbol{x}, \boldsymbol{\delta}, \boldsymbol{I}) \propto \prod_{I_1} \{f_p(t_i, \boldsymbol{x}_i; \boldsymbol{\theta})\}^{I_i} \prod_{I_0} \{p_0(\boldsymbol{\theta}_1, \boldsymbol{x}_i)\}^{1-I_i} \{(1 - p_0(\boldsymbol{\theta}_1, \boldsymbol{x}_i))S_1(t_i, \boldsymbol{x}_i; \boldsymbol{\theta})\}^{I_i},$$

where $\boldsymbol{I}$ denotes the vector of I_i values. The corresponding log-likelihood function, without the constant term, is given by

$$\begin{aligned} l_c(\boldsymbol{\theta}; \boldsymbol{t}, \boldsymbol{x}, \boldsymbol{\delta}, \boldsymbol{I}) &= \sum_{I_1} I_i \log f_p(t_i, \boldsymbol{x}_i; \boldsymbol{\theta}) + \sum_{I_0} (1 - I_i) \log p_0(\boldsymbol{\theta}_1, \boldsymbol{x}_i) \\ &\quad + \sum_{I_0} I_i \log((1 - p_0(\boldsymbol{\theta}_1, \boldsymbol{x}_i))S_1(t_i, \boldsymbol{x}_i; \boldsymbol{\theta})). \end{aligned} \tag{1.6.1}$$

E-Step: In the expectation step or the E-step, for a fixed value of ϕ, we compute the expectation of the complete-data log-likelihood function with respect to the distribution of the unobserved I_i's, given the current values of the parameter and the observed data $\boldsymbol{O}$, where $\boldsymbol{O} = \{\text{observed } I_i\text{'}s, (t_i, \delta_i, \boldsymbol{x}_i); i = 1, 2, \ldots, n\}$. It is to be noted that I_i's are Bernoulli random variables and they appear in the complete-data log-likelihood in linear form, and so we only have to compute $\pi_i^{(k)} = E(I_i|\boldsymbol{\theta}^{*(k)}, \boldsymbol{O}), i = 1, 2, \ldots, n$, where $\boldsymbol{\theta}^* = (\boldsymbol{\beta}', \boldsymbol{\gamma}')'$ and $\boldsymbol{\theta}^{*(k)}$ denotes the current parameter value at the k-th iteration step. Now, for $i \in I_0$, we have

$$\begin{aligned}
\pi_i^{(k)} &= P[I_i = 1|T_i > t_i; \boldsymbol{\theta}^{*(k)}] \\
&= \left.\frac{P[T_i > t_i|I_i = 1]P[I_i = 1]}{P[T_i > t_i]}\right|_{\boldsymbol{\theta}^* = \boldsymbol{\theta}^{*(k)}} \\
&= \left.\frac{(1 - p_0(\boldsymbol{\theta}_1, \boldsymbol{x}_i))S_1(t_i, \boldsymbol{x}_i; \boldsymbol{\theta})}{S_p(t_i, \boldsymbol{x}_i; \boldsymbol{\theta})}\right|_{\boldsymbol{\theta}^* = \boldsymbol{\theta}^{*(k)}} \\
&= w_i^{(k)},
\end{aligned}$$

and for $i \in I_1$, we simply have $\pi_i^{(k)} = I_i = 1$. Thus, the E-step replaces the I_i's in (1.6.1) by $w_i^{(k)}$ for $i \in I_0$ and by 1 for $i \in I_1$. For a fixed value of ϕ, we denote the conditional expectation of the complete-data log-likelihood function by $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$, where $\boldsymbol{\pi}^{(k)}$ is the vector of $\pi_i^{(k)}$ values.

***M-Step*:** In the maximization step or the M-step, for a fixed value of ϕ, we maximize the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\theta}^*$ over the corresponding parameter space $\boldsymbol{\Theta}^*$, given $\boldsymbol{\pi}^{(k)}$, to obtain an improved estimate of $\boldsymbol{\theta}^*$ as

$$\boldsymbol{\theta}^{*(k+1)} = \underset{\boldsymbol{\theta}^* \in \boldsymbol{\Theta}^*}{\arg\max}\, Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}).$$

For a fixed value of ϕ, the E-step and the M-step are repeated iteratively until convergence to obtain the MLE of the parameter $\boldsymbol{\theta}^*$. In our case, we do not get any explicit expressions for the MLEs of $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}$ and as such the M-step is carried out by utilizing the EM gradient algorithm (Lange, 1995). This is a one-step Newton-Raphson (NR) method and qualifies as a special case of the generalized EM algorithm. The parameter ϕ is finally estimated by using the profile likelihood approach. In this approach, we fix a set of distinct, admissible values of ϕ and for each fixed value of ϕ, we employ the EM algorithm to estimate the parameter $\boldsymbol{\theta}^*$. Finally, we take the value of ϕ for which the corresponding maximized log-likelihood function is the maximum. In what follows, we denote by n_1 the cardinality of the set I_1 and $I^* = I_0 \cup I_1$.

1.6.2 Standard errors and asymptotic confidence intervals of the MLEs

We obtain an approximation of the asymptotic variance-covariance matrix of the MLEs by inverting the observed information matrix of $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}$ under the assumption that ϕ is fixed. Although the first-order derivatives of the observed data log-likelihood function can be obtained directly from (1.5.1), an easier alternative is to use the complete-data log-likelihood function from the EM algorithm and derive the score function by using the method of Louis (1982); see Sy and Taylor (2000). Let us denote the observed data log-likelihood function by $l(\boldsymbol{\theta}; \boldsymbol{t}, \boldsymbol{x}, \boldsymbol{\delta}) = \log L(\boldsymbol{\theta}; \boldsymbol{t}, \boldsymbol{x}, \boldsymbol{\delta})$. The components of the score function, for a fixed value of ϕ, are as follows:

$$\frac{\partial}{\partial \beta_l} l(\boldsymbol{\theta}; \boldsymbol{t}, \boldsymbol{x}, \boldsymbol{\delta}) = \frac{\partial}{\partial \beta_l} l_c(\boldsymbol{\theta}; \boldsymbol{t}, \boldsymbol{x}, \boldsymbol{\delta}, \boldsymbol{I})\bigg|_{I_i = \pi_i \forall i},$$

for $l = 0, 1, \ldots, k$, and

$$\frac{\partial}{\partial \boldsymbol{\gamma}} l(\boldsymbol{\theta}; \boldsymbol{t}, \boldsymbol{x}, \boldsymbol{\delta}) = \frac{\partial}{\partial \boldsymbol{\gamma}} l_c(\boldsymbol{\theta}; \boldsymbol{t}, \boldsymbol{x}, \boldsymbol{\delta}, \boldsymbol{I})\bigg|_{I_i = \pi_i \forall i},$$

where

$$\pi_i = \frac{(1 - p_0(\boldsymbol{\theta}_1, \boldsymbol{x}_i)) S_1(t_i, \boldsymbol{x}_i; \boldsymbol{\theta})}{S_p(t_i, \boldsymbol{x}_i; \boldsymbol{\theta})} = w_i,$$

for $i \in I_0$ and $\pi_i = 1$ otherwise. We can then take the negative of the second-order derivatives of the function $l(\boldsymbol{\theta}; \boldsymbol{t}, \boldsymbol{x}, \boldsymbol{\delta})$ with respect to $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}$ to obtain the components of the observed information matrix. Once the MLEs of $(\boldsymbol{\beta}, \boldsymbol{\gamma})$ and the asymptotic variances and covariances of the MLEs are obtained, asymptotic confidence intervals for the parameters can be constructed by using the asymptotic normality of the MLEs and the estimate of the asymptotic variance-covariance matrix of the MLEs. To evaluate the accuracy of this asymptotic method, we can examine the coverage probabilities of these confidence intervals based on a Monte Carlo simulation study.

1.6.3 Estimation of the cure rate and its standard error

Let $\hat{\boldsymbol{\beta}}$ be the MLE of $\boldsymbol{\beta}$. Noting that the cure rate is a function of $\boldsymbol{\beta}$ only, the MLE of the cure rate $p_0 = g(\boldsymbol{\beta})$ is then given by $\hat{p}_0 = g(\hat{\boldsymbol{\beta}})$, which is also asymptotically normally distributed with variance $\boldsymbol{b}'\boldsymbol{\Sigma}\boldsymbol{b}$, where $\boldsymbol{b} = (\frac{\partial g(\boldsymbol{\beta})}{\partial \beta_0}, \ldots, \frac{\partial g(\boldsymbol{\beta})}{\partial \beta_k})'$ and $\boldsymbol{\Sigma}$ is the variance-covariance matrix of $\hat{\boldsymbol{\beta}}$. We can then construct confidence intervals for p_0 by using the asymptotic normality of $\hat{p}_0$ and the estimate of its asymptotic variance.

1.7 Simulation study: model fitting

An extensive Monte Carlo simulation study is carried out to evaluate the performance of the proposed estimation method. In this simulation study, we considered different sample sizes so that we can observe the behavior of the model under varying sample sizes. The total sample size is then divided into four groups. The sample size in each group can be viewed as the number of patients in the group. Stratification of patients into different groups allows us to introduce the covariate effect, wherein the patients in group j are assigned a covariate value of j, $j = 1, 2, 3, 4$. As the group category is considered to be the only covariate involved in the model, we have two regression parameters, i.e., β_0 and β_1. Again, as the cured proportion is purely a function of the regression parameters, on fixing the cured proportion for any of the two groups, the regression parameters β_0 and β_1 can be calculated easily. Once the regression parameters are obtained, the cured proportion for the remaining two groups can be automatically determined. In our study, we took the cured proportion to be decreasing with the groups and we fixed the cured proportion for the first and fourth groups. We considered two different choices of cured proportions for groups $(1, 4)$: $(0.65, 0.25)$ and $(0.40, 0.15)$. We note that lifetimes of patients who are cured are always censored. In order to introduce random censoring, we considered the distribution of the censoring times to be exponential with censoring rate α. The parameter α is to be calculated such that the proportion of censoring for a group is p (say). It is clear that α will be different for each group and it is to be noted that in most of the cases it is to be calculated numerically. We considered two different choices of censoring proportions corresponding to groups $1-4$: "High" $= (0.80, 0.65, 0.50, 0.35)$ and "Low" $= (0.50, 0.40, 0.30, 0.20)$. This allows us to observe the behavior of the model under heavy and light censoring amounts. We next discuss the method of generating data from different cure rate models.

Bernoulli cure rate model: For a group with cured proportion p_0 and censoring proportion p, we first generate a uniform random variable U and a censoring time C. If $U \leq p_0$, the observed time is taken to be the censoring time, i.e., $T = C$. Otherwise, we generate a lifetime random variable W, assuming a specific distribution for it and for a specific choice of its parameters, and then the observed time is taken to be $T = \min\{W, C\}$.

Poisson cure rate model: For a group with cured proportion p_0 and censoring proportion p, we first generate a censoring time C and a Poisson random variable M with parameter $-\log(p_0)$. If $M = 0$, the observed time is taken to be the censoring time, i.e., $T = C$. Otherwise, we generate M lifetime random variables $\{W_1, W_2, \ldots, W_M\}$ and the observed time is then taken to be $T = \min\{Y, C\}$, where $Y = \min\{W_1, W_2, \ldots, W_M\}$.

Geometric cure rate model: In this case, we follow the same procedure as in the Poisson cure rate model just described, except that the competing cause variable M is generated from a geometric distribution with parameter p_0.

COM-Poisson cure rate model: Here, we again follow the same procedure as in the Poisson cure rate model described above, except that we generate the competing cause random variable M from a COM-Poisson distribution with p.m.f. given by (1.3.1) for a specific choice of the parameter ϕ.

1.8 Simulation study: model discrimination

We have seen that the COM-Poisson family is quite flexible and includes many commonly used distributions as special cases. This feature enables us to select a simple distribution within this family that provides an adequate fit as the COM-Poisson distribution itself in many cases. Thus, we can explore the use of the COM-Poisson cure rate model in selecting a parsimonious competing cause distribution that provides an adequate fit to the data. This selection study can be further carried out in two ways, either by using the likelihood-based method or by using the information-based criterion.

1.8.1 Likelihood-based method

In this method, we investigate the performance of the likelihood ratio test in testing the null hypothesis that the competing cause distribution can be described by one of Bernoulli ($H_0 : \phi \to \infty$), Poisson ($H_0 : \phi = 1$) and geometric ($H_0 : \phi = 0$) distributions *versus* an alternative hypothesis that the competing cause distribution can be described by a member of the COM-Poisson family other than the one specified in the null hypothesis. The likelihood ratio test statistic is defined as $\Lambda = -2(\hat{l}_0 - \hat{l})$, where $\hat{l}_0$ and $\hat{l}$ denote the restricted and unrestricted maximized log-likelihood function values, respectively. We note that under standard likelihood theory, the asymptotic null distribution of Λ is a central chi-square distribution with one degree of freedom. However, if the parameter lies on the boundary of the parameter space, the asymptotic null distribution of Λ is a $50-50$ mixture of a point mass at zero and a chi-square distribution with one degree of freedom (mixture chi-square distribution), i.e., the asymptotic null distribution of Λ is such that $P[\Lambda \leq \lambda] = \frac{1}{2} + \frac{1}{2}P[\chi_1^2 \leq \lambda]$, where χ_1^2 denotes a chi-square variable with one degree of freedom (Self and Liang, 1987; Claeskens et al., 2008). Thus, for testing $H_0 : \phi = 0$ and $H_0 : \phi \to \infty$, we take into account the boundary condition and the asymptotic null distribution of the likelihood ratio test statistic, in this case, is a mixture of chi-square distributions. The likelihood ratio test statistic is used to calculate the $p-$value, which is the smallest level of significance at which the null hypothesis is rejected, to decide whether to reject the null hypothesis or not. We reject the null hypothesis in favor of the alternative hypothesis if the calculated p-value is less than the level of significance used for the test.

1.8.2 Information-based criterion

In this simulation study, we investigate the performance of Akaike information criterion (AIC) and Bayesian information criterion (BIC) in selecting one of Bernoulli, Poisson and geometric distributions (Fitted Models) for the competing cause variable, given a true competing cause distribution. We have $AIC = -2l + 2k$ and $BIC = -2l + k\log(n)$, where l is the maximized log-likelihood value of the fitted model, k is the number of parameters of the fitted model, and n is the sample size. The chosen model is the one with the minimum AIC or BIC value.

It is also of interest to study the bias and MSE involved in estimating the cured proportions corresponding to four groups under model mis-specification. For the bias, we may actually compute the ratio of the absolute bias of the cured proportion to that of the true cured proportion for each of the four groups and then add them to get the total relative bias (TRB) in estimating the cured proportions. For the MSE, one can similarly add the MSEs of the estimates of cured proportions corresponding to the four groups to get the total MSE (TMSE) in estimating the cured proportions. It is then possible to calculate the total relative efficiency (TRE) under model mis-specification, which is defined as the ratio of the TMSE of the cured proportion under true model specification to that under wrong model specification. In this simulation study, we restrict our comparisons to the three special cases of the COM-Poisson model.

When using AIC to select a working model for a given true model, we can also calculate the TRB and TMSE of the cured proportion for each of the candidate (fitted) models. Using the selection rates of the candidate models as weights, the TRB for a given true model can then be calculated as the weighted sum of TRBs of candidate models. In a similar way, the TMSE can also be calculated and the TRE for a given true model can then be calculated as the ratio of the TMSE when fitting the true model to that when using AIC as a model selection criterion.

1.9 Cutaneous melanoma data

These data are part of an assay on cutaneous melanoma (a type of malignant cancer) for the evaluation of postoperative treatment performance with a high dose of interferon alfa-2b as a drug to prevent recurrence. Patients were included in the study from 1991 to 1995, and follow-up was conducted until 1998. The data, taken from Kirkwood et al. (2000) (see also Ibrahim et al., 2001), present the survival times, representing the time in years until the patients death or the censoring time. The original sample included 427 patients, 10 of whom were removed from our analysis since their tumor thickness data (as covariate) were missing. The percentage of censored observations is 56%. The observed time has mean and standard deviation as 3.18 and 1.69, respectively.

1.10 Scope of the thesis

As already mentioned in Section 1.2, Rodrigues et al. (2009) proposed the flexible COM-Poisson cure rate model which includes some of the commonly used cure rate models as special cases. They considered the Weibull as the lifetime distribution and discussed the computation of the MLEs of the model parameters numerically by using the RS method (Rigby and Stasinopoulos, 2005) available in the GAMLSS package (Stasinopoulos and Rigby, 2007). The data obtained from cancer clinical trials are often right censored and as such the EM algorithm can be used as an alternative and efficient tool to estimate the model parameters. In this thesis, we consider the COM-Poisson cure rate model developed by Rodrigues et al. (2009) and then develop exact likelihood inference based on the EM algorithm.

The lifetime distribution is first considered to be exponential, lognormal, gamma, and Weibull. For each of these distributions, the necessary steps of the EM algorithm are developed for the determination of the MLEs of the model parameters based on right censored data and non-informative censoring mechanism. For the exponential distribution, we consider the log-linear link function and notice a problem in the case of the geometric cure rate model. To circumvent this problem, we consider the logistic link function for all other lifetime distributions. The standard errors of the MLEs are obtained by inverting the observed information matrix. Then, by using the asymptotic normality of the MLEs, the asymptotic confidence intervals of the model parameters are obtained for different nominal confidence levels. The performance of the proposed estimation method, in each case, is examined by means of an extensive Monte Carlo simulation study. The flexibility of the COM-Poisson family is utilized to select a parsimonious distribution for the competing cause variable within this family that provides an adequate fit to the data. This is carried out by using the likelihood ratio test as well as by two information-based selection criteria, namely, AIC and BIC. For each of the lifetime distributions, the proposed methodology is also illustrated with the cutaneous melanoma data described in the previous section.

It is to be noted that the lifetime distributions mentioned above are not nested and as such we cannot perform a formal statistical test of hypothesis to determine which among these distributions provides an adequate fit to the data. For this purpose, we also considered the wider class of generalized gamma distributions and developed the steps of the EM algorithm for this family of distributions. One-way model discrimination within the generalized gamma family is then carried out by using the likelihood ratio test as well as by AIC and BIC. The flexibility of the generalized gamma family as well as the flexibility of the COM-Poisson family is utilized to carry out a two-way model discrimination to select a pair of parsimonious distributions (one for the competing cause and the other for the lifetime) that jointly provide the best fit to the data. This is illustrated with the cutaneous melanoma data.

Chapter 2

Likelihood inference for exponential lifetime distribution

2.1 Introduction

In this chapter, we assume the lifetime W in (1.1.1) to follow the exponential distribution with p.d.f. as given in (1.4.1) and develop in detail the steps of the EM algorithm for the determination of the MLEs of the parameters of the COM-Poisson cure rate model and some of its special cases based on right censored data. We propose to relate the COM-Poisson parameter η in (1.3.1) to covariates $\boldsymbol{x}_i$ by the log-linear link function given by η_i=exp$(\boldsymbol{x}_i'\boldsymbol{\beta}), i = 1, \ldots, n$.

We first present the explicit expressions of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function and simplified expressions of the first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ and γ to carry out the one-step maximization in the M-step by the NR method for different cure rate models. Next, we present the simplified explicit expressions for the components of the score function and the components of the observed information matrix for different cure rate models. The results of an extensive Monte

Carlo simulation study are presented to evaluate the performance of the proposed estimation method and the results of model discrimination between different cure rate models are discussed next. Finally, we present the results of the analysis of the cutaneous melanoma data based on the considered models.

2.2 Expressions of E- and M-steps for different cure rate models

Bernoulli cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function can be expressed as

$$Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) = Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)}) + Q_2(\gamma, \boldsymbol{\pi}^{(k)}),$$

where

$$Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)}) = \sum_{I_1} \boldsymbol{x}_i'\boldsymbol{\beta} + \sum_{I_0} \pi_i^{(k)} \boldsymbol{x}_i'\boldsymbol{\beta} - \sum_{I^*} \log(1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta})),$$

and

$$Q_2(\gamma, \boldsymbol{\pi}^{(k)}) = n_1 \log\gamma - \gamma(\sum_{I_1} t_i + \sum_{I_0} \pi_i^{(k)} t_i)$$

with

$$\pi_i^{(k)} = \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}^{(k)} - \gamma^{(k)} t_i)}{1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta}^{(k)} - \gamma^{(k)} t_i)},$$

for censored cases only. We see that the function $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ can be separated into two parts, one containing the regression parameter $\boldsymbol{\beta}$ and the other containing the lifetime parameter γ. Hence, if $\boldsymbol{\beta}^{(k)}$ and $\gamma^{(k)}$ are the estimates of $\boldsymbol{\beta}$ and γ, respectively, at the k-th iteration step, then $\boldsymbol{\beta}^{(k+1)}$ can be obtained by maximizing $Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)})$ with respect to $\boldsymbol{\beta}$ and $\gamma^{(k+1)}$ can be obtained by maximizing $Q_2(\gamma, \boldsymbol{\pi}^{(k)})$ with respect to γ, separately. The first- and second-order derivatives of the function $Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)})$ with respect to $\boldsymbol{\beta}$ are as follows:

$$\begin{aligned}\frac{\partial Q_1}{\partial \beta_l} &= \sum_{I_1} x_{il} + \sum_{I_0} \pi_i^{(k)} x_{il} - \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})},\\ \frac{\partial^2 Q_1}{\partial \beta_l \partial \beta_{l'}} &= -\sum_{I^*} x_{il}x_{il'} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2},\end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$. Using the above derivatives, we can then apply the one-step NR method to find $\boldsymbol{\beta}^{(k+1)}$. To find $\gamma^{(k+1)}$, we equate the first-order derivative of the function $Q_2(\gamma)$ with respect to γ to zero, which is given by

$$\frac{n_1}{\gamma} - \sum_{I_1} t_i - \sum_{I_0} \pi_i^{(k)} t_i = 0. \tag{2.2.1}$$

We solve (2.2.1) for γ to get $\gamma^{(k+1)}$ as

$$\gamma^{(k+1)} = \frac{n_1}{\sum_{I_1} t_i + \sum_{I_0} \pi_i^{(k)} t_i}.$$

We also note that

$$\frac{\partial^2 Q_2}{\partial \gamma^2} = -\frac{n_1}{\gamma^2} < 0$$

so that the solution for γ does indeed correspond to the maxima.

Poisson cure rate model: The expression of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function in this case is given by

$$\begin{aligned}Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) &= n_1 \log\gamma + \sum_{I_1}\{\boldsymbol{x}_i'\boldsymbol{\beta} - \gamma t_i + \exp(\boldsymbol{x}_i'\boldsymbol{\beta} - \gamma t_i)\}\\ &\quad + \sum_{I_0} \pi_i^{(k)} \log(\exp(\exp(\boldsymbol{x}_i'\boldsymbol{\beta} - \gamma t_i)) - 1) - \sum_{I^*} \exp(\boldsymbol{x}_i'\boldsymbol{\beta}),\end{aligned}$$

where

$$\pi_i^{(k)} = \frac{\exp(\exp(\boldsymbol{x}_i'\boldsymbol{\beta}^{(k)} - \gamma^{(k)}t_i)) - 1}{\exp(\exp(\boldsymbol{x}_i'\boldsymbol{\beta}^{(k)} - \gamma^{(k)}t_i))},$$

for censored cases only. The required first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ and γ to carry out the maximization step are as follows:

$$\begin{aligned}
\frac{\partial Q}{\partial \beta_l} &= \sum_{I_1} x_{il}\{1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta} - \gamma t_i)\} + \sum_{I_0} \pi_i^{(k)} x_{il} A_{Pi}(\boldsymbol{\beta}, \gamma) - \sum_{I^*} x_{il} \exp(\boldsymbol{x}_i'\boldsymbol{\beta}),\\
\frac{\partial Q}{\partial \gamma} &= \frac{n_1}{\gamma} - \sum_{I_1} t_i\{1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta} - \gamma t_i)\} - \sum_{I_0} \pi_i^{(k)} t_i A_{Pi}(\boldsymbol{\beta}, \gamma),\\
\frac{\partial^2 Q}{\partial \beta_l \partial \beta_{l'}} &= \sum_{I_1} x_{il} x_{il'} \exp(\boldsymbol{x}_i'\boldsymbol{\beta} - \gamma t_i) + \sum_{I_0} \pi_i^{(k)} x_{il} x_{il'} A_{Pi}(\boldsymbol{\beta}, \gamma) D_i(\boldsymbol{\beta}, \gamma)\\
&\quad - \sum_{I^*} x_{il} x_{il'} \exp(\boldsymbol{x}_i'\boldsymbol{\beta}),\\
\frac{\partial^2 Q}{\partial \gamma^2} &= -\frac{n_1}{\gamma^2} + \sum_{I_1} t_i^2 \exp(\boldsymbol{x}_i'\boldsymbol{\beta} - \gamma t_i) + \sum_{I_0} \pi_i^{(k)} t_i^2 A_{Pi}(\boldsymbol{\beta}, \gamma) D_i(\boldsymbol{\beta}, \gamma),\\
\frac{\partial^2 Q}{\partial \beta_l \partial \gamma} &= -\sum_{I_1} x_{il} t_i \exp(\boldsymbol{x}_i'\boldsymbol{\beta} - \gamma t_i) - \sum_{I_0} \pi_i^{(k)} x_{il} t_i A_{Pi}(\boldsymbol{\beta}, \gamma) D_i(\boldsymbol{\beta}, \gamma),
\end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$A_{Pi}(\boldsymbol{\beta}, \gamma) = \frac{\exp(\exp(\boldsymbol{x}_i'\boldsymbol{\beta} - \gamma t_i) + \boldsymbol{x}_i'\boldsymbol{\beta} - \gamma t_i)}{\exp(\exp(\boldsymbol{x}_i'\boldsymbol{\beta} - \gamma t_i)) - 1},$$

and

$$D_i(\boldsymbol{\beta}, \gamma) = \frac{\exp(\exp(\boldsymbol{x}_i'\boldsymbol{\beta} - \gamma t_i)) - \exp(\boldsymbol{x}_i'\boldsymbol{\beta} - \gamma t_i) - 1}{\exp(\exp(\boldsymbol{x}_i'\boldsymbol{\beta} - \gamma t_i)) - 1},$$

for $i \in I_0$.

Geometric cure rate model: The expression of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function in this case is given by

$$\begin{aligned} Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) &= n_1 \log\gamma + \sum_{I_1}\{\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i - 2\log(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i))\} \\ &+ \sum_{I_0}\pi_i^{(k)}\{\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i - \log(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i)\} \\ &+ \sum_{I^*}\log(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})), \end{aligned}$$

where

$$\pi_i^{(k)} = \exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}^{(k)} - \gamma^{(k)} t_i),$$

for censored cases only. The required first- and second-order derivatives of the function $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ with respect to $\boldsymbol{\beta}$ and γ to carry out the maximization step are as follows:

$$\begin{aligned} \frac{\partial Q}{\partial\beta_l} &= \sum_{I_1} x_{il}\frac{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i)}{1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i)} + \sum_{I_0}\pi_i^{(k)} x_{il}\frac{1}{1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i)} \\ &\quad -\sum_{I^*} x_{il}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}, \\ \frac{\partial Q}{\partial\gamma} &= \frac{n_1}{\gamma} - \sum_{I_1} t_i\frac{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i)}{1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i)} - \sum_{I_0}\pi_i^{(k)} t_i\frac{1}{1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i)}, \\ \frac{\partial^2 Q}{\partial\beta_l\partial\beta_{l'}} &= 2\sum_{I_1} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i)}{(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i))^2} + \sum_{I_0}\pi_i^{(k)} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i)}{(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i))^2} \\ &\quad -\sum_{I^*} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))^2}, \\ \frac{\partial^2 Q}{\partial\gamma^2} &= -\frac{n_1}{\gamma^2} + 2\sum_{I_1} t_i^2\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i)}{(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i))^2} + \sum_{I_0}\pi_i^{(k)} t_i^2\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i)}{(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i))^2}, \\ \frac{\partial^2 Q}{\partial\beta_l\partial\gamma} &= -2\sum_{I_1} x_{il}t_i\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i)}{(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i))^2} - \sum_{I_0}\pi_i^{(k)} x_{il}t_i\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i)}{(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i))^2}, \end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$.

COM-Poisson cure rate model: The expression of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function, for a fixed value of ϕ, is given by

$$Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) = n_1 \log \gamma + \sum_{I_1} \log z_{2i} + \sum_{I_0} \pi_i^{(k)} \log z_{1i} - \sum_{I^*} \log z_i,$$

where

$$z = z(\boldsymbol{\theta}_1; \boldsymbol{x}) = \sum_{j=0}^{\infty} \frac{(\exp(\boldsymbol{x}'\boldsymbol{\beta}))^j}{(j!)^{\phi}},$$

$$z_1 = z_1(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{(\exp(\boldsymbol{x}'\boldsymbol{\beta} - \gamma t))^j}{(j!)^{\phi}},$$

$$z_2 = z_2(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{j(\exp(\boldsymbol{x}'\boldsymbol{\beta} - \gamma t))^j}{(j!)^{\phi}},$$

and

$$\pi_i^{(k)} = \frac{z_1(\boldsymbol{\beta}^{(k)}, \gamma^{(k)}, \phi; \boldsymbol{x}_i, t_i)}{1 + z_1(\boldsymbol{\beta}^{(k)}, \gamma^{(k)}, \phi; \boldsymbol{x}_i, t_i)},$$

for censored cases only. The required first- and second-order derivatives of the function $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ with respect to $\boldsymbol{\beta}$ and γ to carry out the maximization step are as follows:

$$\frac{\partial Q}{\partial \beta_l} = \sum_{I_1} x_{il} \frac{z_{21i}}{z_{2i}} + \sum_{I_0} \pi_i^{(k)} x_{il} \frac{z_{2i}}{z_{1i}} - \sum_{I^*} x_{il} \frac{z_{01i}}{z_i},$$

$$\frac{\partial Q}{\partial \gamma} = \frac{n_1}{\gamma} - \sum_{I_1} t_i \frac{z_{21i}}{z_{2i}} - \sum_{I_0} \pi_i^{(k)} t_i \frac{z_{2i}}{z_{1i}},$$

$$\begin{aligned}
\frac{\partial^2 Q}{\partial \beta_l \partial \beta_{l'}} &= \sum_{I_1} x_{il} x_{il'} \frac{z_{2i} z_{22i} - z_{21i}^2}{z_{2i}^2} + \sum_{I_0} \pi_i^{(k)} x_{il} x_{il'} \frac{z_{1i} z_{21i} - z_{2i}^2}{z_{1i}^2} \\
&\quad - \sum_{I^*} x_{il} x_{il'} \frac{z_i z_{02i} - z_{01i}^2}{z_i^2}, \\
\frac{\partial^2 Q}{\partial \gamma^2} &= -\frac{n_1}{\gamma^2} + \sum_{I_1} t_i^2 \frac{z_{2i} z_{22i} - z_{21i}^2}{z_{2i}^2} + \sum_{I_0} \pi_i^{(k)} t_i^2 \frac{z_{1i} z_{21i} - z_{2i}^2}{z_{1i}^2}, \\
\frac{\partial^2 Q}{\partial \beta_l \partial \gamma} &= -\sum_{I_1} x_{il} t_i \frac{z_{2i} z_{22i} - z_{21i}^2}{z_{2i}^2} - \sum_{I_0} \pi_i^{(k)} x_{il} t_i \frac{z_{1i} z_{21i} - z_{2i}^2}{z_{1i}^2},
\end{aligned}$$

for $l, l^{'} = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$z_{21} = z_{21}(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{j^2 (\exp(\boldsymbol{x}^{'} \boldsymbol{\beta} - \gamma t))^j}{(j!)^{\phi}},$$

$$z_{22} = z_{22}(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{j^3 (\exp(\boldsymbol{x}^{'} \boldsymbol{\beta} - \gamma t))^j}{(j!)^{\phi}},$$

$$z_{01} = z_{01}(\boldsymbol{\theta}_1; \boldsymbol{x}) = \sum_{j=1}^{\infty} j \frac{(\exp(\boldsymbol{x}^{'} \boldsymbol{\beta}))^j}{(j!)^{\phi}},$$

and

$$z_{02} = z_{02}(\boldsymbol{\theta}_1; \boldsymbol{x}) = \sum_{j=1}^{\infty} j^2 \frac{(\exp(\boldsymbol{x}^{'} \boldsymbol{\beta}))^j}{(j!)^{\phi}}.$$

The quantities $z_i, z_{1i}, z_{2i}, z_{21i}, z_{22i}, z_{01i}$, and z_{02i} can all be computed by truncating the numerical series for each i. Let S_n denote the n-th order partial sum of the infinite series. Then, the infinite series can be computed with n terms if $S_{n+1} - S_n \leq \epsilon$, where ϵ is a pre-fixed small positive number. In our case, we chose $\epsilon = 0.01$ for computational ease and efficiency.

2.3 Observed information matrix

In this section, we present explicit expressions of the score function and the components of the observed information matrix for different cure rate models.

Bernoulli cure rate model: The components of the score function are

$$\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il} + \sum_{I_0} w_i x_{il} - \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}, \\
\frac{\partial l}{\partial \gamma} &= \frac{n_1}{\gamma} - \sum_{I_1} t_i - \sum_{I_0} w_i t_i,
\end{aligned}$$

where

$$w_i = \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i)}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i)},$$

for censored cases only. The observed information matrix has its components as

$$\begin{aligned}
-\frac{\partial^2 l}{\partial \beta_l \partial \beta_{l'}} &= -\sum_{I_0} x_{il} x_{il'} w_i (1-w_i) + \sum_{I^*} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))^2}, \\
-\frac{\partial^2 l}{\partial \gamma^2} &= \frac{n_1}{\gamma^2} - \sum_{I_0} t_i^2 w_i (1-w_i), \\
-\frac{\partial^2 l}{\partial \beta_l \partial \gamma} &= \sum_{I_0} x_{il} t_i w_i (1-w_i),
\end{aligned}$$

for $l, l^{'} = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$.

Poisson cure rate model: The components of the score function are

$$\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il} - \sum_{I^*} x_{il} \exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})\{1-\exp(-\gamma t_i)\}, \\
\frac{\partial l}{\partial \gamma} &= \frac{n_1}{\gamma} - \sum_{I_1} t_i - \sum_{I^*} t_i \exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta} - \gamma t_i).
\end{aligned}$$

The observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial\beta_l\partial\beta_{l'}} &= \sum_{I^*} x_{il}x_{il'}\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})\{1-\exp(-\gamma t_i)\},\\
-\frac{\partial^2 l}{\partial\gamma^2} &= \frac{n_1}{\gamma^2} - \sum_{I^*} t_i^2\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i),\\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma} &= \sum_{I^*} x_{il}t_i\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i),
\end{aligned}
$$

for $l, l^{'} = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$.

Geometric cure rate model: The components of the score function are

$$
\begin{aligned}
\frac{\partial l}{\partial\beta_l} &= \sum_{I_1} x_{il}\frac{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i)}{1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i)} + \sum_{I_0} x_{il}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i)}{1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i)} - \sum_{I^*} x_{il}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})},\\
\frac{\partial l}{\partial\gamma} &= \frac{n_1}{\gamma} - \sum_{I_1} t_i\frac{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i)}{1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i)} - \sum_{I_0} t_i\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i)}{1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i)}.
\end{aligned}
$$

The observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial\beta_l\partial\beta_{l'}} &= -2\sum_{I_1} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i)}{(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i))^2} - \sum_{I_0} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i)}{(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i))^2}\\
&\quad + \sum_{I^*} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))^2},\\
-\frac{\partial^2 l}{\partial\gamma^2} &= \frac{n_1}{\gamma^2} - 2\sum_{I_1} t_i^2\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i)}{(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i))^2} - \sum_{I_0} t_i^2\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i)}{(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i))^2},\\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma} &= 2\sum_{I_1} x_{il}t_i\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i)}{(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i))^2} + \sum_{I_0} x_{il}t_i\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i)}{(1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}-\gamma t_i))^2},
\end{aligned}
$$

for $l, l^{'} = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$.

COM-Poisson cure rate model: The components of the score function, for a fixed value of ϕ, are

$$\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il} \frac{z_{21i}}{z_{2i}} + \sum_{I_0} x_{il} \frac{z_{2i}}{1+z_{1i}} - \sum_{I^*} x_{il} \frac{z_{01i}}{z_i}, \\
\frac{\partial l}{\partial \gamma} &= \frac{n_1}{\gamma} - \sum_{I_1} t_i \frac{z_{21i}}{z_{2i}} - \sum_{I_0} t_i \frac{z_{2i}}{1+z_{1i}}.
\end{aligned}$$

The observed information matrix, for a fixed value of ϕ, has its components as

$$\begin{aligned}
-\frac{\partial^2 l}{\partial \beta_l \partial \beta_{l'}} &= -\sum_{I_1} x_{il} x_{il'} \frac{z_{2i} z_{22i} - z_{21i}^2}{z_{2i}^2} - \sum_{I_0} x_{il} x_{il'} \frac{(1+z_{1i}) z_{21i} - z_{2i}^2}{(1+z_{1i})^2} \\
&\quad + \sum_{I^*} x_{il} x_{il'} \frac{z_i z_{02i} - z_{01i}^2}{z_i^2}, \\
-\frac{\partial^2 l}{\partial \gamma^2} &= \frac{n_1}{\gamma^2} - \sum_{I_1} t_i^2 \frac{z_{2i} z_{22i} - z_{21i}^2}{z_{2i}^2} - \sum_{I_0} t_i^2 \frac{(1+z_{1i}) z_{21i} - z_{2i}^2}{(1+z_{1i})^2}, \\
-\frac{\partial^2 l}{\partial \beta_l \partial \gamma} &= \sum_{I_1} x_{il} t_i \frac{z_{2i} z_{22i} - z_{21i}^2}{z_{2i}^2} + \sum_{I_0} x_{il} t_i \frac{(1+z_{1i}) z_{21i} - z_{2i}^2}{(1+z_{1i})^2},
\end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$.

2.4 Results of the simulation study

2.4.1 Model fitting

We refer to the simulation study setup described in Section 1.7. Here, we considered two sample sizes: $n = 400$ and $n = 600$ so that we can observe the behavior of the model under moderate and large sample sizes. Two different choices of the lifetime parameter γ are considered: 1 and 3, which allow us to observe the behavior of the model under low and high hazard rates. In this simulation study, we simulated data from different cure rate models under different simulation settings and the estimation method proposed in Section 1.6.1 was employed to estimate the unknown parameters of the model. To examine the performance of the estimates of the parameters, we calculated the bias and MSE of the estimates. We also calculated the coverage probabilities of the confidence intervals based on the asymptotic normality of MLEs for different nominal confidence levels. All the simulations were performed using the R software and the results were based on 1000 Monte Carlo runs.

To find an initial guess of the parameters β_0, β_1, and γ so as to start the iterative procedure, we considered the first and fourth groups and calculated the Kaplan-Meier estimates of the cured proportions for these two groups separately. Once the estimates of the cured proportions for these two groups were obtained, the estimates of β_0 and β_1 can be obtained and these were taken as their initial values. We then plugged in the estimates of β_0 and β_1 in the observed data log-likelihood function, which is then a function of γ only. Now, upon taking the first-order derivative of the observed data log-likelihood function with respect to γ, and after equating it to zero, we solved for γ to find an initial estimate of γ. We observed that the above technique provides initial values which are reasonably close to the true parameter values. Now, in our simulation study, as we have considered random censoring, it is to be noted that the largest observed time in a group may not be censored, in which case the Kaplan-Meier estimate of the cured proportion for that group becomes zero. To circumvent this problem, we ignored the largest observed time if it is not censored just for the purpose of determining the initial values.

Tables 2.1−2.3 show the results for the three special cases of COM-Poisson cure rate model. The results show that the EM algorithm converges to the true parameter values quite accurately. As expected, the standard error and the MSE of the estimates both decrease with an increase in sample size and with a decrease in censoring proportion. The lifetime parameter γ does not seem to have any effect on the estimation of the regression parameters β_0 and β_1. The coverage probabilities of the confidence intervals based on the asymptotic normality of the MLEs seem to be quite close to the nominal levels.

It should be mentioned that in the case of the geometric cure rate model, the EM algorithm sometimes shows a problem with convergence, irrespective of the sample size and level of censoring. This is because we link the parameter η in (1.3.1) to covariates $\boldsymbol{x}$ through the log-linear link function $\eta = \exp(\boldsymbol{x}'\boldsymbol{\beta})$ and there is no guarantee that in the subsequent steps of the EM algorithm η is less than one, which is a condition that must hold true for the geometric cure rate model, as mentioned earlier.

Tables 2.4 and 2.5 show the results for the COM-Poisson cure rate model when ϕ is fixed at 0.5 and 2, respectively. The findings are similar to the special cases of the COM-Poisson cure rate model, where the estimates are close to their true values and the coverage probabilities close to the nominal levels. However, for all practical purposes ϕ is to be estimated from the data, for which we can employ the profile likelihood technique. The corresponding results are shown in Tables 2.6 and 2.7, where the true value of ϕ is taken to be 0.5 and 2, respectively, but now estimated from the data along with other model parameters. We note that the profile likelihood approach of estimating ϕ results in large bias and MSE of the estimate of ϕ. However, they decrease with an increase in sample size and with a decrease in censoring proportion. The standard error and the MSE of the MLEs also show similar behavior. The standard errors of the estimates of β_0, β_1 and γ are found to be underestimated and consequently the coverage probabilities fall below the nominal level. This is mainly due to the imprecision in the estimate of ϕ by using the profile likelihood technique. The undercoverage (coverage probability below the nominal level) seems to be more pronounced for β_1 and γ. Now, to estimate ϕ by the profile

Table 2.1: Estimates, bias, mean square error (MSE), and coverage probabilities (CP) for the Bernoulli cure rate model with exponential lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	MSE	CP	
						90%	95%
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.192 (0.345)	-0.001	0.117	0.913	0.967
		$\beta_1 = 0.573$	0.577 (0.128)	0.005	0.016	0.915	0.956
		$\gamma = 1$	1.004 (0.099)	0.004	0.011	0.881	0.929
	Low	$\beta_0 =$ -0.038	-0.055 (0.299)	-0.017	0.092	0.903	0.950
		$\beta_1 = 0.443$	0.454 (0.125)	0.011	0.016	0.901	0.949
		$\gamma = 1$	1.000 (0.069)	0.000	0.005	0.900	0.950
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.204 (0.345)	-0.013	0.121	0.913	0.958
		$\beta_1 = 0.573$	0.577 (0.128)	0.005	0.016	0.903	0.945
		$\gamma = 3$	3.029 (0.300)	0.029	0.096	0.893	0.947
	Low	$\beta_0 =$ -0.038	-0.049 (0.299)	-0.012	0.100	0.888	0.943
		$\beta_1 = 0.443$	0.449 (0.124)	0.006	0.017	0.884	0.943
		$\gamma = 3$	3.003 (0.209)	0.003	0.040	0.916	0.960
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.192	-1.184 (0.352)	0.008	0.127	0.899	0.950
		$\beta_1 = 0.573$	0.571 (0.124)	-0.002	0.016	0.886	0.951
		$\gamma = 1$	1.010 (0.096)	0.010	0.010	0.884	0.946
	Low	$\beta_0 =$ -0.038	-0.049 (0.306)	-0.012	0.100	0.889	0.945
		$\beta_1 = 0.443$	0.452 (0.120)	0.008	0.015	0.894	0.949
		$\gamma = 1$	0.999 (0.068)	-0.001	0.005	0.897	0.946
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.192	-1.208 (0.353)	-0.016	0.132	0.879	0.946
		$\beta_1 = 0.573$	0.580 (0.125)	0.008	0.016	0.895	0.948
		$\gamma = 3$	3.026 (0.287)	0.026	0.084	0.909	0.946
	Low	$\beta_0 =$ -0.038	-0.048 (0.306)	-0.010	0.089	0.920	0.961
		$\beta_1 = 0.443$	0.448 (0.120)	0.005	0.014	0.911	0.961
		$\gamma = 3$	3.013 (0.206)	0.013	0.045	0.895	0.940
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.192	-1.195 (0.281)	-0.003	0.081	0.900	0.946
		$\beta_1 = 0.573$	0.577 (0.104)	0.004	0.011	0.895	0.949
		$\gamma = 1$	1.002 (0.081)	0.002	0.007	0.890	0.935
	Low	$\beta_0 =$ -0.038	-0.045 (0.244)	-0.008	0.057	0.905	0.949
		$\beta_1 = 0.443$	0.449 (0.101)	0.006	0.010	0.911	0.960
		$\gamma = 1$	1.001 (0.057)	0.001	0.003	0.895	0.953

Table 2.2: Estimates, bias, mean square error (MSE), and coverage probabilities (CP) for the Poisson cure rate model with exponential lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	MSE	CP	
						90%	95%
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.232	-1.234 (0.233)	-0.003	0.055	0.896	0.947
		$\beta_1 = 0.390$	0.393 (0.076)	0.004	0.006	0.903	0.949
		$\gamma = 1$	1.000 (0.124)	0.000	0.015	0.912	0.953
	Low	$\beta_0 =$ -0.330	-0.332 (0.163)	-0.002	0.024	0.903	0.957
		$\beta_1 = 0.243$	0.243 (0.058)	0.000	0.003	0.911	0.958
		$\gamma = 1$	1.008 (0.094)	0.008	0.008	0.906	0.965
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.232	-1.238 (0.234)	-0.006	0.052	0.911	0.955
		$\beta_1 = 0.390$	0.391 (0.076)	0.001	0.006	0.911	0.957
		$\gamma = 3$	3.029 (0.376)	0.029	0.136	0.907	0.956
	Low	$\beta_0 =$ -0.330	-0.329 (0.163)	0.001	0.029	0.881	0.935
		$\beta_1 = 0.243$	0.244 (0.058)	0.002	0.004	0.876	0.931
		$\gamma = 3$	3.009 (0.281)	0.009	0.081	0.901	0.949
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.232	-1.238 (0.240)	-0.006	0.057	0.895	0.946
		$\beta_1 = 0.390$	0.391 (0.075)	0.002	0.005	0.906	0.958
		$\gamma = 1$	1.007 (0.121)	0.007	0.014	0.902	0.955
	Low	$\beta_0 =$ -0.330	-0.330 (0.167)	0.000	0.026	0.921	0.952
		$\beta_1 = 0.243$	0.244 (0.057)	0.001	0.003	0.908	0.954
		$\gamma = 1$	1.005 (0.093)	0.005	0.009	0.906	0.960
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.232	-1.239 (0.240)	-0.007	0.056	0.904	0.951
		$\beta_1 = 0.390$	0.394 (0.075)	0.004	0.006	0.911	0.947
		$\gamma = 3$	3.006 (0.362)	0.006	0.130	0.904	0.949
	Low	$\beta_0 =$ -0.330	-0.339 (0.168)	-0.009	0.028	0.906	0.951
		$\beta_1 = 0.243$	0.245 (0.057)	0.002	0.003	0.901	0.952
		$\gamma = 3$	3.015 (0.279)	0.015	0.076	0.904	0.952
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.232	-1.225 (0.190)	0.007	0.039	0.885	0.941
		$\beta_1 = 0.390$	0.387 (0.062)	-0.002	0.004	0.894	0.940
		$\gamma = 1$	1.003 (0.102)	0.003	0.011	0.889	0.945
	Low	$\beta_0 =$ -0.330	-0.330 (0.133)	0.000	0.017	0.914	0.961
		$\beta_1 = 0.243$	0.242 (0.047)	0.000	0.002	0.913	0.955
		$\gamma = 1$	1.005 (0.076)	0.005	0.005	0.911	0.960

Table 2.3: Estimates, bias, mean square error (MSE), and coverage probabilities (CP) for the geometric cure rate model with exponential lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	MSE	CP 90%	CP 95%
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.304	-1.299 (0.160)	0.004	0.026	0.889	0.946
		$\beta_1 = 0.254$	0.253 (0.043)	-0.001	0.002	0.899	0.950
		$\gamma = 1$	1.006 (0.162)	0.006	0.027	0.899	0.945
	Low	$\beta_0 =$ -0.627	-0.625 (0.083)	0.002	0.006	0.916	0.953
		$\beta_1 = 0.116$	0.115 (0.022)	-0.001	0.000	0.910	0.953
		$\gamma = 1$	1.002 (0.137)	0.002	0.018	0.914	0.963
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.304	-1.300 (0.160)	0.004	0.026	0.889	0.946
		$\beta_1 = 0.254$	0.253 (0.043)	-0.001	0.002	0.899	0.950
		$\gamma = 3$	3.018 (0.485)	0.018	0.239	0.898	0.945
	Low	$\beta_0 =$ -0.627	-0.625 (0.083)	0.002	0.006	0.916	0.953
		$\beta_1 = 0.116$	0.115 (0.022)	-0.001	0.000	0.910	0.953
		$\gamma = 3$	3.006 (0.412)	0.006	0.161	0.914	0.963
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.304	-1.295 (0.164)	0.009	0.027	0.895	0.954
		$\beta_1 = 0.254$	0.251 (0.043)	-0.003	0.002	0.902	0.950
		$\gamma = 1$	1.005 (0.159)	0.005	0.026	0.906	0.947
	Low	$\beta_0 =$ -0.627	-0.619 (0.085)	0.008	0.007	0.889	0.950
		$\beta_1 = 0.116$	0.113 (0.022)	-0.003	0.000	0.905	0.955
		$\gamma = 1$	1.002 (0.139)	0.002	0.019	0.906	0.955
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.304	-1.295 (0.164)	0.009	0.027	0.895	0.954
		$\beta_1 = 0.254$	0.251 (0.043)	-0.003	0.002	0.902	0.950
		$\gamma = 3$	3.014 (0.478)	0.014	0.231	0.906	0.947
	Low	$\beta_0 =$ -0.627	-0.619 (0.085)	0.008	0.007	0.889	0.950
		$\beta_1 = 0.116$	0.113 (0.022)	-0.003	0.000	0.905	0.955
		$\gamma = 3$	3.007 (0.417)	0.007	0.174	0.906	0.955
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.304	-1.301 (0.131)	0.003	0.018	0.894	0.941
		$\beta_1 = 0.254$	0.253 (0.035)	-0.001	0.001	0.898	0.955
		$\gamma = 1$	1.000 (0.131)	0.000	0.016	0.917	0.953
	Low	$\beta_0 =$ -0.627	-0.625 (0.068)	0.002	0.004	0.907	0.950
		$\beta_1 = 0.116$	0.115 (0.018)	-0.001	0.000	0.909	0.949
		$\gamma = 1$	1.002 (0.112)	0.002	0.012	0.914	0.954

likelihood approach, we chose the range of ϕ to be $[0.05, 2]$, where the starting value of ϕ was taken to be 0.05 and in the interval $[0.10, 1]$ ϕ was divided in steps of 0.1, whereas in the interval $[1.05, 2]$ ϕ was divided in steps of 0.05. This accounted for 31 distinct choices of ϕ ranging from 0.05 to 2. It is clear that to get an estimate of ϕ for a given dataset, we must ensure that the EM algorithm converges for all chosen values of ϕ. However, for some datasets, it was observed that for values of ϕ close to zero, the EM algorithm failed to converge and as such that dataset had to be discarded. This is because for values of ϕ close to zero, the COM-Poisson distribution approaches the geometric distribution in which case, as mentioned earlier, there is occasionally a convergence problem.

2.4.2 Model discrimination

Here, we used the likelihood ratio test to carry out the model discrimination. This simulation study was further divided into two parts: one corresponding to the under-dispersed models ($\phi > 1$), where we investigate the performance of the likelihood ratio test in testing the null hypothesis that the number of competing causes relating to the event of interest can be described by either Bernoulli ($H_0 : \phi \to \infty$) or Poisson ($H_0 : \phi = 1$) distributions *versus* the alternative hypothesis that the number of competing causes can be described by a member of the COM-Poisson distribution other than the one specified in the null hypothesis. The other part of the simulation study corresponds to the over-dispersed models ($\phi < 1$), where we investigate the performance of the likelihood ratio test in testing the null hypothesis that the number of competing causes relating to the event of interest can be described by either Poisson ($H_0 : \phi = 1$) or geometric ($H_0 : \phi = 0$) distributions *versus* the alternative hypothesis that the number of competing causes can be described by a member of the COM-

Table 2.4: Estimates, bias, mean square error (MSE), and coverage probabilities (CP) for the COM-Poisson cure rate model with ϕ fixed at 0.5 for exponential lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	MSE	CP	
						90%	95%
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.262	-1.269 (0.203)	-0.007	0.041	0.907	0.954
		$\beta_1 =$ 0.338	0.340 (0.063)	0.003	0.004	0.904	0.955
		$\gamma = 1$	1.006 (0.135)	0.006	0.019	0.887	0.941
	Low	$\beta_0 =$ -0.449	-0.448 (0.130)	0.001	0.016	0.909	0.953
		$\beta_1 =$ 0.195	0.195 (0.044)	-0.001	0.002	0.910	0.955
		$\gamma = 1$	1.003 (0.103)	0.003	0.011	0.893	0.945
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.262	-1.269 (0.203)	-0.007	0.041	0.907	0.954
		$\beta_1 =$ 0.338	0.340 (0.063)	0.003	0.004	0.904	0.955
		$\gamma = 3$	3.019 (0.406)	0.019	0.171	0.887	0.941
	Low	$\beta_0 =$ -0.449	-0.449 (0.130)	0.001	0.016	0.909	0.953
		$\beta_1 =$ 0.195	0.195 (0.044)	-0.001	0.002	0.910	0.955
		$\gamma = 3$	3.009 (0.310)	0.009	0.097	0.893	0.945
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.262	-1.265 (0.209)	-0.002	0.042	0.906	0.947
		$\beta_1 =$ 0.338	0.339 (0.062)	0.001	0.004	0.901	0.953
		$\gamma = 1$	1.007 (0.132)	0.007	0.018	0.901	0.953
	Low	$\beta_0 =$ -0.449	-0.450 (0.134)	-0.001	0.018	0.896	0.949
		$\beta_1 =$ 0.195	0.195 (0.043)	0.000	0.002	0.895	0.950
		$\gamma = 1$	1.001 (0.103)	0.001	0.010	0.895	0.944
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.262	-1.265 (0.209)	-0.002	0.042	0.906	0.947
		$\beta_1 =$ 0.338	0.339 (0.062)	0.001	0.004	0.901	0.953
		$\gamma = 3$	3.022 (0.395)	0.022	0.163	0.901	0.953
	Low	$\beta_0 =$ -0.449	-0.450 (0.134)	-0.001	0.018	0.896	0.949
		$\beta_1 =$ 0.195	0.195 (0.043)	0.000	0.002	0.895	0.950
		$\gamma = 3$	3.003 (0.308)	0.003	0.094	0.895	0.944
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.262	-1.266 (0.166)	-0.004	0.026	0.912	0.959
		$\beta_1 =$ 0.338	0.339 (0.051)	0.002	0.002	0.908	0.958
		$\gamma = 1$	1.000 (0.110)	0.000	0.012	0.890	0.942
	Low	$\beta_0 =$ -0.449	-0.446 (0.106)	0.003	0.012	0.890	0.943
		$\beta_1 =$ 0.195	0.195 (0.036)	0.000	0.001	0.894	0.941
		$\gamma = 1$	0.995 (0.084)	-0.005	0.007	0.899	0.947

Table 2.5: Estimates, bias, mean square error (MSE), and coverage probabilities (CP) for the COM-Poisson cure rate model with ϕ fixed at 2 for exponential lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	MSE	CP	
						90%	95%
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.196	-1.194 (0.274)	0.002	0.075	0.898	0.954
		$\beta_1 = 0.459$	0.460 (0.094)	0.001	0.009	0.905	0.954
		$\gamma = 1$	1.006 (0.114)	0.006	0.013	0.892	0.950
	Low	$\beta_0 =$ -0.181	-0.181 (0.207)	0.000	0.040	0.916	0.960
		$\beta_1 = 0.307$	0.309 (0.078)	0.002	0.006	0.909	0.961
		$\gamma = 1$	1.006 (0.084)	0.006	0.007	0.901	0.957
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.196	-1.194 (0.274)	0.002	0.075	0.898	0.954
		$\beta_1 = 0.459$	0.460 (0.094)	0.001	0.009	0.905	0.954
		$\gamma = 3$	3.019 (0.342)	0.019	0.119	0.892	0.950
	Low	$\beta_0 =$ -0.181	-0.181 (0.207)	0.000	0.040	0.916	0.960
		$\beta_1 = 0.307$	0.309 (0.078)	0.002	0.006	0.909	0.961
		$\gamma = 3$	3.017 (0.251)	0.017	0.061	0.901	0.957
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.196	-1.205 (0.283)	-0.009	0.085	0.895	0.945
		$\beta_1 = 0.459$	0.461 (0.092)	0.002	0.009	0.881	0.948
		$\gamma = 1$	1.007 (0.110)	0.007	0.012	0.900	0.949
	Low	$\beta_0 =$ -0.181	-0.189 (0.213)	-0.008	0.044	0.905	0.958
		$\beta_1 = 0.307$	0.311 (0.076)	0.003	0.005	0.907	0.957
		$\gamma = 1$	1.001 (0.082)	0.001	0.007	0.900	0.959
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.196	-1.205 (0.283)	-0.009	0.085	0.895	0.945
		$\beta_1 = 0.459$	0.461 (0.092)	0.002	0.009	0.881	0.948
		$\gamma = 3$	3.021 (0.331)	0.021	0.112	0.900	0.949
	Low	$\beta_0 =$ -0.181	-0.189 (0.213)	-0.008	0.044	0.905	0.958
		$\beta_1 = 0.307$	0.311 (0.076)	0.003	0.005	0.907	0.957
		$\gamma = 3$	3.003 (0.247)	0.003	0.062	0.900	0.959
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.196	-1.191 (0.224)	0.005	0.052	0.898	0.946
		$\beta_1 = 0.459$	0.457 (0.076)	-0.001	0.006	0.908	0.957
		$\gamma = 1$	1.005 (0.093)	0.005	0.009	0.902	0.949
	Low	$\beta_0 =$ -0.181	-0.178 (0.169)	0.003	0.028	0.900	0.956
		$\beta_1 = 0.307$	0.308 (0.063)	0.000	0.004	0.893	0.953
		$\gamma = 1$	0.997 (0.068)	-0.003	0.005	0.899	0.945

Table 2.6: Estimates, bias, mean square error (MSE), and coverage probabilities (CP) for the COM-Poisson cure rate model with $\phi = 0.5$ for exponential lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	MSE	CP	
						90%	95%
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.262	-1.278 (0.207)	-0.016	0.052	0.883	0.928
		$\beta_1 = 0.338$	0.352 (0.065)	0.015	0.017	0.518	0.613
		$\gamma = 1$	1.018 (0.137)	0.018	0.054	0.632	0.729
		$\phi = 0.5$	0.717 $(-)$	0.217	0.563	–	–
	Low	$\beta_0 =$ -0.449	-0.449 (0.134)	0.000	0.025	0.860	0.913
		$\beta_1 = 0.195$	0.207 (0.046)	0.011	0.008	0.535	0.617
		$\gamma = 1$	1.021 (0.105)	0.021	0.054	0.508	0.592
		$\phi = 0.5$	0.662 $(-)$	0.162	0.360	–	–
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.262	-1.278 (0.207)	-0.016	0.052	0.883	0.928
		$\beta_1 = 0.338$	0.352 (0.065)	0.015	0.017	0.518	0.613
		$\gamma = 3$	3.055 (0.411)	0.055	0.486	0.632	0.727
		$\phi = 0.5$	0.717 $(-)$	0.217	0.563	–	–
	Low	$\beta_0 =$ -0.449	-0.449 (0.134)	0.000	0.025	0.858	0.913
		$\beta_1 = 0.195$	0.207 (0.046)	0.011	0.008	0.534	0.616
		$\gamma = 3$	3.061 (0.314)	0.061	0.489	0.507	0.591
		$\phi = 0.5$	0.661 $(-)$	0.161	0.360	–	–
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.262	-1.269 (0.212)	-0.007	0.051	0.877	0.932
		$\beta_1 = 0.338$	0.348 (0.064)	0.010	0.015	0.529	0.634
		$\gamma = 1$	1.019 (0.133)	0.019	0.056	0.605	0.714
		$\phi = 0.5$	0.706 $(-)$	0.206	0.538	–	–
	Low	$\beta_0 =$ -0.449	-0.449 (0.138)	0.000	0.027	0.859	0.917
		$\beta_1 = 0.195$	0.204 (0.045)	0.009	0.008	0.568	0.650
		$\gamma = 1$	1.018 (0.104)	0.018	0.054	0.503	0.578
		$\phi = 0.5$	0.648 $(-)$	0.148	0.342	–	–
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.262	-1.269 (0.212)	-0.007	0.051	0.877	0.932
		$\beta_1 = 0.338$	0.348 (0.064)	0.010	0.015	0.529	0.634
		$\gamma = 3$	3.056 (0.400)	0.056	0.508	0.605	0.714
		$\phi = 0.5$	0.706 $(-)$	0.206	0.538	–	–
	Low	$\beta_0 =$ -0.449	-0.449 (0.138)	0.001	0.027	0.857	0.916
		$\beta_1 = 0.195$	0.204 (0.045)	0.009	0.008	0.569	0.652
		$\gamma = 3$	3.053 (0.312)	0.053	0.489	0.503	0.578
		$\phi = 0.5$	0.648 $(-)$	0.148	0.341	–	–
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.262	-1.270 (0.166)	-0.008	0.033	0.876	0.933
		$\beta_1 = 0.338$	0.342 (0.051)	0.005	0.013	0.485	0.571
		$\gamma = 1$	0.998 (0.111)	-0.002	0.043	0.559	0.668
		$\phi = 0.5$	0.632 $(-)$	0.132	0.414	–	–
	Low	$\beta_0 =$ -0.449	-0.448 (0.107)	0.001	0.017	0.823	0.914
		$\beta_1 = 0.195$	0.200 (0.036)	0.004	0.006	0.552	0.616
		$\gamma = 1$	0.998 (0.084)	-0.002	0.037	0.519	0.602
		$\phi = 0.5$	0.591 $(-)$	0.091	0.228	–	–

Table 2.7: Estimates, bias, mean square error (MSE), and coverage probabilities (CP) for the COM-Poisson cure rate model with $\phi = 2$ for exponential lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	MSE	CP	
						90%	95%
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.196	-1.176 (0.246)	0.020	0.065	0.888	0.943
		$\beta_1 = 0.459$	0.401 (0.081)	-0.057	0.018	0.684	0.735
		$\gamma = 1$	0.913 (0.112)	-0.087	0.037	0.685	0.758
		$\phi = 2$	1.434 (−)	-0.566	0.839	–	–
	Low	$\beta_0 =$ -0.181	-0.236 (0.189)	-0.055	0.042	0.851	0.908
		$\beta_1 = 0.307$	0.280 (0.070)	-0.027	0.008	0.782	0.851
		$\gamma = 1$	0.940 (0.082)	-0.060	0.020	0.733	0.784
		$\phi = 2$	1.610 (−)	-0.390	0.430	–	–
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.196	-1.176 (0.246)	0.020	0.065	0.888	0.943
		$\beta_1 = 0.459$	0.402 (0.081)	-0.057	0.018	0.684	0.735
		$\gamma = 3$	2.738 (0.336)	-0.262	0.332	0.685	0.758
		$\phi = 2$	1.434 (−)	-0.566	0.839	–	–
	Low	$\beta_0 =$ -0.181	-0.237 (0.189)	-0.055	0.042	0.852	0.909
		$\beta_1 = 0.307$	0.281 (0.070)	-0.027	0.008	0.783	0.852
		$\gamma = 3$	2.820 (0.246)	-0.180	0.180	0.732	0.784
		$\phi = 2$	1.610 (−)	-0.390	0.430	–	–
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.196	-1.183 (0.254)	0.013	0.070	0.874	0.931
		$\beta_1 = 0.459$	0.402 (0.080)	-0.057	0.017	0.686	0.734
		$\gamma = 1$	0.910 (0.108)	-0.090	0.037	0.683	0.740
		$\phi = 2$	1.432 (−)	-0.568	0.825	–	–
	Low	$\beta_0 =$ -0.181	-0.239 (0.195)	-0.058	0.044	0.857	0.911
		$\beta_1 = 0.307$	0.283 (0.068)	-0.024	0.007	0.796	0.859
		$\gamma = 1$	0.935 (0.081)	-0.065	0.020	0.717	0.774
		$\phi = 2$	1.627 (−)	-0.373	0.406	–	–
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.196	-1.184 (0.254)	0.012	0.071	0.875	0.931
		$\beta_1 = 0.459$	0.402 (0.080)	-0.056	0.017	0.686	0.734
		$\gamma = 3$	2.730 (0.324)	-0.270	0.330	0.681	0.740
		$\phi = 2$	1.432 (−)	-0.568	0.826	–	–
	Low	$\beta_0 =$ -0.181	-0.239 (0.195)	-0.058	0.044	0.858	0.910
		$\beta_1 = 0.307$	0.283 (0.068)	-0.025	0.007	0.795	0.858
		$\gamma = 3$	2.803 (0.242)	-0.197	0.181	0.716	0.773
		$\phi = 2$	1.626 (−)	-0.374	0.407	–	–
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.196	-1.172 (0.206)	0.024	0.047	0.886	0.934
		$\beta_1 = 0.459$	0.410 (0.069)	-0.049	0.012	0.713	0.774
		$\gamma = 1$	0.933 (0.092)	-0.067	0.026	0.707	0.767
		$\phi = 2$	1.531 (−)	-0.469	0.615	–	–
	Low	$\beta_0 =$ -0.181	-0.224 (0.156)	-0.043	0.030	0.838	0.903
		$\beta_1 = 0.307$	0.282 (0.058)	-0.025	0.006	0.776	0.846
		$\gamma = 1$	0.938 (0.066)	-0.062	0.015	0.697	0.761
		$\phi = 2$	1.648 (−)	-0.352	0.349	–	–

Poisson distribution other than the one specified in the null hypothesis. Based on 1000 datasets in each situation and nominal significance level 0.05, we computed observed significance levels and powers of the likelihood ratio test corresponding to the under-dispersed and over-dispersed models and reported them in Tables 2.8 and 2.9, respectively. The numbers in bold are observed levels while the other numbers are observed powers. These numbers were determined by the rejection rates of the null hypothesis.

When the Poisson distribution ($\phi = 1$) is the true competing cause distribution, the test has good power to reject the Bernoulli distribution as the competing cause distribution (with the largest observed power being 94%) and a slightly less power to reject the geometric distribution as the competing cause distribution (with the largest observed power being 85%). From Table 2.8, when the COM-Poisson distribution ($\phi > 1$) is the true competing cause distribution, the test has reasonable power to reject the Bernoulli distribution as the competing cause distribution and the power of the test decreases as the true value of ϕ increases. However, the test does not appear to have power to reject the Poisson distribution as the competing cause distribution. From Table 2.9, when the COM-Poisson distribution ($\phi < 1$) is the true competing cause distribution, the power of the test to reject the Poisson distribution as the competing cause distribution increases as the true value of ϕ decreases. This means that when the true model approaches the geometric model (ϕ close to 0), the test has the maximum power to reject the Poisson model, and the largest observed power in this case is 91%. As one would expect, when the true model is close to the geometric ($\phi = 0.05$), the power to reject the geometric model is very close to the nominal significance level. Furthermore, the power of the likelihood ratio test increases as the sample size increases and the censoring proportion decreases.

Table 2.8: Observed levels (in bold) and powers of the likelihood ratio test for under-dispersed cure rate models with exponential lifetime.

	True COM-Poisson models				
Fitted models	$\phi = 1$	$\phi = 1.2$	$\phi = 1.5$	$\phi = 1.8$	$\phi = 2$
	$n = 400$ $(110, 120, 90, 80)$, $p =$ High, $\gamma = 1$				
Bernoulli	0.482	0.433	0.333	0.254	0.259
Poisson	**0.036**	0.015	0.016	0.013	0.013
	$n = 400$ $(110, 120, 90, 80)$, $p =$ Low, $\gamma = 1$				
Bernoulli	0.837	0.752	0.670	0.587	0.540
Poisson	**0.041**	0.024	0.026	0.029	0.046
	$n = 400$ $(110, 120, 90, 80)$, $p =$ High, $\gamma = 3$				
Bernoulli	0.482	0.433	0.333	0.254	0.259
Poisson	**0.037**	0.015	0.016	0.013	0.013
	$n = 400$ $(110, 120, 90, 80)$, $p =$ Low, $\gamma = 3$				
Bernoulli	0.837	0.752	0.670	0.587	0.540
Poisson	**0.041**	0.024	0.026	0.029	0.046
	$n = 400$ $(100, 100, 100, 100)$, $p =$ High, $\gamma = 1$				
Bernoulli	0.529	0.462	0.395	0.318	0.295
Poisson	**0.050**	0.024	0.024	0.012	0.008
	$n = 400$ $(100, 100, 100, 100)$, $p =$ Low, $\gamma = 1$				
Bernoulli	0.846	0.802	0.705	0.622	0.545
Poisson	**0.030**	0.025	0.032	0.053	0.065
	$n = 400$ $(100, 100, 100, 100)$, $p =$ High, $\gamma = 3$				
Bernoulli	0.529	0.462	0.395	0.318	0.295
Poisson	**0.050**	0.024	0.024	0.012	0.008
	$n = 400$ $(100, 100, 100, 100)$, $p =$ Low, $\gamma = 3$				
Bernoulli	0.846	0.802	0.705	0.622	0.545
Poisson	**0.030**	0.025	0.032	0.053	0.065
	$n = 600$ $(165, 180, 135, 120)$, $p =$ High, $\gamma = 1$				
Bernoulli	0.644	0.552	0.453	0.354	0.310
Poisson	**0.051**	0.039	0.023	0.018	0.013
	$n = 600$ $(165, 180, 135, 120)$, $p =$ Low, $\gamma = 1$				
Bernoulli	0.936	0.887	0.815	0.745	0.687
Poisson	**0.059**	0.031	0.054	0.084	0.103

Table 2.9: Observed levels (in bold) and powers of the likelihood ratio test for over-dispersed cure rate models with exponential lifetime.

	True COM-Poisson models				
Fitted models	$\phi = 1$	$\phi = 0.8$	$\phi = 0.5$	$\phi = 0.3$	$\phi = 0.05$
	$n = 400$ $(110, 120, 90, 80)$, $p =$ High, $\gamma = 1$				
Poisson	**0.036**	0.047	0.092	0.168	0.417
Geometric	0.436	0.392	0.264	0.193	0.083
	$n = 400$ $(110, 120, 90, 80)$, $p =$ Low, $\gamma = 1$				
Poisson	**0.041**	0.061	0.174	0.333	0.795
Geometric	0.757	0.668	0.501	0.312	0.049
	$n = 400$ $(110, 120, 90, 80)$, $p =$ High, $\gamma = 3$				
Poisson	**0.037**	0.047	0.092	0.168	0.416
Geometric	0.436	0.391	0.264	0.193	0.083
	$n = 400$ $(110, 120, 90, 80)$, $p =$ Low, $\gamma = 3$				
Poisson	**0.041**	0.061	0.175	0.333	0.795
Geometric	0.757	0.666	0.499	0.310	0.049
	$n = 400$ $(100, 100, 100, 100)$, $p =$ High, $\gamma = 1$				
Poisson	**0.050**	0.041	0.092	0.196	0.468
Geometric	0.431	0.391	0.285	0.191	0.068
	$n = 400$ $(100, 100, 100, 100)$, $p =$ Low, $\gamma = 1$				
Poisson	**0.030**	0.074	0.176	0.349	0.797
Geometric	0.783	0.724	0.505	0.329	0.060
	$n = 400$ $(100, 100, 100, 100)$, $p =$ High, $\gamma = 3$				
Poisson	**0.050**	0.041	0.092	0.196	0.468
Geometric	0.432	0.390	0.285	0.192	0.068
	$n = 400$ $(100, 100, 100, 100)$, $p =$ Low, $\gamma = 3$				
Poisson	**0.030**	0.074	0.176	0.350	0.796
Geometric	0.783	0.724	0.505	0.330	0.060
	$n = 600$ $(165, 180, 135, 120)$, $p =$ High, $\gamma = 1$				
Poisson	**0.051**	0.059	0.139	0.244	0.543
Geometric	0.517	0.442	0.293	0.197	0.062
	$n = 600$ $(165, 180, 135, 120)$, $p =$ Low, $\gamma = 1$				
Poisson	**0.059**	0.072	0.193	0.433	0.913
Geometric	0.851	0.796	0.595	0.352	0.052

2.5 Analysis of cutaneous melanoma data

In this section, we illustrate the application of the proposed methodology to the cutaneous melanoma data. In our application, we selected the nodule category (1: n=111; 2: n=137; 3: n=87; 4: n=82) as the only covariate in our model. As possible models, we considered the Bernoulli, Poisson, geometric, and COM-Poisson cure rate models.

For these data, the profile likelihood approach of estimating ϕ gave $\hat{\phi} = 0.05$. So, we test the suitability of the geometric model for the number of causes M in (1.3.1). With the test procedure described in Section 1.8.1, we obtained $\Lambda = 1.366$ (p-value=0.121), and we therefore do not reject the geometric model. In this way, the candidate models have the same number of parameters. Furthermore, since $\hat{\eta}_j = \exp(\hat{\beta}_0 + j\hat{\beta}_1) < 1$, for $j = 1, 2, 3, 4$, the distributions corresponding to the nodule categories are all legitimate.

For the Bernoulli, Poisson, and COM-Poisson (geometric) cure rate models, the maximized log-likelihood function values are -535.036, -533.333, and -533.269, respectively. Hence, the best fit is achieved with the COM-Poisson (geometric) cure rate model. We note that the maximized log-likelihood value for the Poisson and the geometric cure rate models are very close to each other. So, we also test for the suitability of the Poisson model for the number of causes M in (1.3.1). In this case, we obtained $\Lambda = 1.494$ (p-value=0.222), and so we once again cannot reject the Poisson model. To explain why both the geometric and the Poisson models become acceptable for the data, we try to find an acceptable range of ϕ for the data. For this purpose, we consider testing for different values of ϕ and plot the values of ϕ against the corresponding test statistic Λ. The corresponding plot is presented in Figure 2.1. The test is rejected at $\alpha = 10\%$ level of significance if the value of the Λ statistic exceeds $\chi^2_{1,1-\alpha} = 2.71$. Now, for $\Lambda = 2.71$, the corresponding value of ϕ turns out to be 2.9 (from the plot). Hence, an admissible range of ϕ for the data becomes $[0, 2.9)$, which clearly explains why both geometric and Poisson models become acceptable for the data. On comparing the geometric and Poisson models, we adopt the geometric model as our working model based on the maximized log-likelihood values. Maximum likelihood estimates of the COM-Poisson (geometric) cure rate model parameters are presented in Table 2.10.

We finally deal with the estimation of the cure rate p_0. Estimates of the cure rates of patient's stratified by nodule category are $\hat{p}_{0j} = 1 - \exp(\hat{\beta}_0 + j\hat{\beta}_1), j = 1, 2, 3, 4$. By using the estimates in Table 2.10, we then obtain $\hat{p}_0 = 0.240$, 0.191, 0.138, and 0.082 corresponding to the four nodule categories (1−4).

Table 2.10: Maximum likelihood estimates of the parameters of the COM-Poisson (geometric) cure rate model with exponential lifetime.

Parameter	Estimate	Standard error
β_0	-0.335	0.336
β_1	0.063	0.061
γ	0.035	0.042

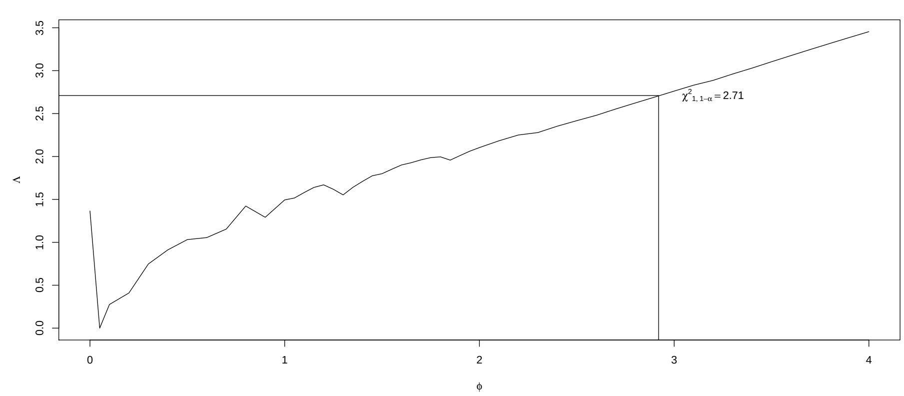

Figure 2.1: Values of ϕ against the corresponding Λ statistic for exponential lifetime.

Chapter 3

Likelihood inference for lognormal lifetime distribution

3.1 Introduction

The lognormal distribution is an important lifetime distribution and has been used extensively in reliability and survival analyses. For example, Krishnamoorthy and Mathew (2003) derived exact inferential procedures concerning the means of lognormal distributions, Gupta and Li (2006) discussed a test for the equality of the means of two independent lognormal populations, Longford (2009) proposed several estimators of the expectation, median and mode of the lognormal distribution, and Balakrishnan and Mitra (2011) developed likelihood inference for lognormal data with left truncation and right censoring based on the EM algorithm. In this chapter, by assuming the lifetime W in (1.1.1) to follow the lognormal distribution with p.d.f. as given in (1.4.6), we develop in detail the steps of the EM algorithm for the determination of the MLEs of the parameters of different cure rate models based on right censored data. To circumvent the problem with the log-linear link function in the case of the geometric cure rate model as discussed in Section 2.4.1, we relate the cure rate p_0 to covariates $\boldsymbol{x}_i$ by the logistic link function $p_{0i} = \frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}, i = 1, \ldots, n$.

We present the simplified explicit expressions of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function and expressions of the components of the score function for different cure rate models. Expressions of the first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\theta}^*$ that assist in the required maximization step and expressions of the components of the observed information matrix for different cure rate models are presented in Appendix A.1 and Appendix A.2, respectively. We then discuss the results of model fitting and model discrimination through an extensive Monte Carlo simulation study, where the model discrimination is carried out by using the likelihood-based method as well as the information-based criteria. Finally, we analyze the cutaneous melanoma data for illustrative purpose. For ease of notation, we let $u_i = \frac{\log(\gamma_2 t_i)}{\gamma_1}$ and $V(u_i) = \frac{\phi(u_i)}{1-\Phi(u_i)}$, for $i = 1, 2, \ldots, n$, where $\phi(\cdot)$ and $\Phi(\cdot)$ are the density and distribution functions, respectively, of the standard normal distribution.

3.2 Expressions of E- and M-steps for different cure rate models

Bernoulli cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function can be expressed as

$$Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) = Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)}) + Q_2(\boldsymbol{\gamma}, \boldsymbol{\pi}^{(k)}),$$

where

$$Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)}) = \sum_{I_1} \boldsymbol{x}_i'\boldsymbol{\beta} + \sum_{I_0} \pi_i^{(k)} \boldsymbol{x}_i'\boldsymbol{\beta} - \sum_{I^*} \log(1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta})),$$

and

$$Q_2(\boldsymbol{\gamma}, \boldsymbol{\pi}^{(k)}) = -n_1 \log(\sqrt{2\pi}) - n_1 \log \gamma_1 - \sum_{I_1} \log t_i - \frac{1}{2} \sum_{I_1} u_i^2 + \sum_{I_0} \pi_i^{(k)} \log(1 - \Phi(u_i))$$

with

$$\pi_i^{(k)} = \left. \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})(1 - \Phi(u_i))}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})(1 - \Phi(u_i))} \right|_{\boldsymbol{\theta}^* = \boldsymbol{\theta}^{*(k)}}, \tag{3.2.1}$$

for $i \in I_0$. As the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function can be separated into two parts, one containing the regression parameter $\boldsymbol{\beta}$ and the other containing the lifetime parameter $\boldsymbol{\gamma}$, the maximization step can be carried out by maximizing $Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)})$ with respect to $\boldsymbol{\beta}$ and $Q_2(\boldsymbol{\gamma}, \boldsymbol{\pi}^{(k)})$ with respect to $\boldsymbol{\gamma}$, separately.

Poisson cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function can be expressed as

$$\begin{aligned} Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) \quad = \quad & -n_1 \log(\sqrt{2\pi}) - n_1 \log \gamma_1 - \sum_{I_1} \log t_i - \frac{1}{2} \sum_{I_1} u_i^2 \\ & - \sum_{I_1} \log(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta}))\Phi(u_i) + \sum_{I_1} \log(\log(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta}))) \\ & - \sum_{I_0} \log(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})) + \sum_{I_0} \pi_i^{(k)} \log(\exp(A_{Li}(\boldsymbol{\beta}, \boldsymbol{\gamma})) - 1), \end{aligned}$$

where

$$A_{Li}(\boldsymbol{\beta}, \boldsymbol{\gamma}) = \log(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta}))(1 - \Phi(u_i)), \tag{3.2.2}$$

and

$$\pi_i^{(k)} = \left. \frac{\exp(A_{Li}(\boldsymbol{\beta}, \boldsymbol{\gamma})) - 1}{\exp(A_{Li}(\boldsymbol{\beta}, \boldsymbol{\gamma}))} \right|_{\boldsymbol{\theta}^* = \boldsymbol{\theta}^{*(k)}}, \tag{3.2.3}$$

for $i \in I_0$.

Geometric cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function can be expressed as

$$\begin{aligned} Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) &= -n_1 \log(\sqrt{2\pi}) - n_1 \log \gamma_1 - \sum_{I_1} \log t_i - \frac{1}{2} \sum_{I_1} u_i^2 + \sum_{I_1} \boldsymbol{x}_i' \boldsymbol{\beta} \\ &\quad -2 \sum_{I_1} \log(1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i)) - \sum_{I_0} \log(1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta})) \\ &\quad + \sum_{I_0} \pi_i^{(k)} \boldsymbol{x}_i'\boldsymbol{\beta} + \sum_{I_0} \pi_i^{(k)} \log\left(\frac{1 - \Phi(u_i)}{1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i)}\right), \end{aligned}$$

where

$$\pi_i^{(k)} = \left.\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1 - \Phi(u_i))}{1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right|_{\boldsymbol{\theta}^* = \boldsymbol{\theta}^{*(k)}}, \tag{3.2.4}$$

for $i \in I_0$.

COM-Poisson cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function, for a fixed value of ϕ, can be expressed as

$$\begin{aligned} Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) &= -n_1 \log(\sqrt{2\pi}) - n_1 \log \gamma_1 - \sum_{I_1} \log t_i - \frac{1}{2} \sum_{I_1} u_i^2 - \sum_{I_1} \log(1 - \Phi(u_i)) \\ &\quad + \sum_{I_1} \log z_{2i} + \sum_{I_0} \pi_i^{(k)} \log z_{1i} - \sum_{I^*} \log(1 + \exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})), \end{aligned}$$

where

$$z_1 = z_1(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{\{H_\phi^{-1}(1 + \exp(\boldsymbol{x}^{'}\boldsymbol{\beta}))(1 - \Phi(u))\}^j}{(j!)^\phi},$$

$$z_2 = z_2(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{j\{H_\phi^{-1}(1 + \exp(\boldsymbol{x}^{'}\boldsymbol{\beta}))(1 - \Phi(u))\}^j}{(j!)^\phi},$$

and

$$\pi_i^{(k)} = \left.\frac{z_1(\boldsymbol{\theta}; \boldsymbol{x}_i, t_i)}{1 + z_1(\boldsymbol{\theta}; \boldsymbol{x}_i, t_i)}\right|_{\boldsymbol{\theta}^* = \boldsymbol{\theta}^{*(k)}}, \tag{3.2.5}$$

for $i \in I_0$.

3.3 Components of the score function

Bernoulli cure rate model: The components of the score function are

$$
\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il} + \sum_{I_0} x_{il} w_i - \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}, \\
\frac{\partial l}{\partial \gamma_1} &= -\frac{n_1}{\gamma_1} + \frac{1}{\gamma_1}\sum_{I_1} u_i^2 + \frac{1}{\gamma_1}\sum_{I_0} w_i u_i V(u_i), \\
\frac{\partial l}{\partial \gamma_2} &= -\frac{1}{\gamma_1\gamma_2}\sum_{I_1} u_i - \frac{1}{\gamma_1\gamma_2}\sum_{I_0} w_i V(u_i),
\end{aligned}
$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$
w_i = \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})(1-\Phi(u_i))}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})(1-\Phi(u_i))}, \tag{3.3.1}
$$

for $i \in I_0$.

Poisson cure rate model: The components of the score function are

$$
\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}\left\{\frac{1}{\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))} - \Phi(u_i)\right\} - \sum_{I_0} x_{il} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})\Phi(u_i)}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}, \\
\frac{\partial l}{\partial \gamma_1} &= -\frac{n_1}{\gamma_1} + \frac{1}{\gamma_1}\sum_{I_1} u_i^2 + \frac{1}{\gamma_1}\sum_{I^*} \log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))u_i\phi(u_i), \\
\frac{\partial l}{\partial \gamma_2} &= -\frac{1}{\gamma_1\gamma_2}\sum_{I_1} u_i - \frac{1}{\gamma_1\gamma_2}\sum_{I^*} \log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\phi(u_i),
\end{aligned}
$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$.

Geometric cure rate model: The components of the score function are

$$
\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il}\left\{\frac{1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})\Phi(u_i)}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})\Phi(u_i)}\right\} + \sum_{I_0} x_{il}\frac{w_i}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})\Phi(u_i)} \\
&\quad - \sum_{I_0} x_{il}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}, \\
\frac{\partial l}{\partial \gamma_1} &= -\frac{n_1}{\gamma_1} + \frac{1}{\gamma_1}\sum_{I_1} u_i^2 + \frac{2}{\gamma_1}\sum_{I_1}\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})u_i W(u_i,\boldsymbol{\beta}) \\
&\quad + \frac{1}{\gamma_1}\sum_{I_0} w_i u_i\{V(u_i) + \exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})W(u_i,\boldsymbol{\beta})\}, \\
\frac{\partial l}{\partial \gamma_2} &= -\frac{1}{\gamma_1\gamma_2}\sum_{I_1} u_i - \frac{2}{\gamma_1\gamma_2}\sum_{I_1}\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})W(u_i,\boldsymbol{\beta}) \\
&\quad - \frac{1}{\gamma_1\gamma_2}\sum_{I_0} w_i\{V(u_i) + \exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})W(u_i,\boldsymbol{\beta})\},
\end{aligned}
$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$
w_i = \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-\Phi(u_i))}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}, \tag{3.3.2}
$$

for $i \in I_0$, and

$$
W(u_i,\boldsymbol{\beta}) = \frac{\phi(u_i)}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})\Phi(u_i)}, \tag{3.3.3}
$$

for $i = 1, 2, \ldots, n$.

COM-Poisson cure rate model: The components of the score function, for a fixed value of ϕ, are

$$
\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})z_{21i}}{z_{2i}z_{01i}} + \sum_{I_0} x_{il}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})z_{2i}}{(1+z_{1i})z_{01i}} - \sum_{I^*} x_{il}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}, \\
\frac{\partial l}{\partial \gamma_1} &= -\frac{n_1}{\gamma_1} + \frac{1}{\gamma_1}\sum_{I_1} u_i^2 + \frac{1}{\gamma_1}\sum_{I_1} u_i V(u_i)\left\{\frac{z_{21i}}{z_{2i}} - 1\right\} + \frac{1}{\gamma_1}\sum_{I_0}\frac{u_i V(u_i) z_{2i}}{1+z_{1i}}, \\
\frac{\partial l}{\partial \gamma_2} &= -\frac{1}{\gamma_1\gamma_2}\sum_{I_1} u_i - \frac{1}{\gamma_1\gamma_2}\sum_{I_1} V(u_i)\left\{\frac{z_{21i}}{z_{2i}} - 1\right\} - \frac{1}{\gamma_1\gamma_2}\sum_{I_0}\frac{V(u_i)z_{2i}}{1+z_{1i}},
\end{aligned}
$$

for $l, l' = 0, 1, \dots, k$, and $x_{i0} = 1 \forall i = 1, 2, \dots, n$, where

$$z_{21} = z_{21}(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{j^2 \{H_\phi^{-1}(1 + \exp(\boldsymbol{x}'\boldsymbol{\beta}))(1 - \Phi(u))\}^j}{(j!)^\phi},$$

and

$$z_{01} = z_{01}(\boldsymbol{\theta}_1; \boldsymbol{x}) = \sum_{j=1}^{\infty} \frac{j\{H_\phi^{-1}(1 + \exp(\boldsymbol{x}'\boldsymbol{\beta}))\}^j}{(j!)^\phi}.$$

3.4 Results of the simulation study: model fitting

We refer to the simulation setup discussed in Section 1.7. We considered two sample sizes: $n = 400$ and $n = 600$ so as to observe the behavior of the fit of the model under moderate and large sample sizes. The choice of the lifetime parameter (γ_1, γ_2) was obtained by equating the mean and variance of the underlying lognormal distribution in (1.4.6) to some fixed values. For this, we considered two different choices for the mean as 5 and 3.5, and two different choices for the variance as 3 and 1.5, which result in total to four different choices of $(\gamma_1, \gamma_2) : (0.241, 0.206), (0.337, 0.212), (0.340, 0.303),$ and $(0.468, 0.319)$. In this way, we can study the behavior of the model when the lifetime distribution has the same mean but different variance and vice-versa. In this simulation study, we simulated data from different cure rate models and then employed the estimation procedure described in Section 1.6.1 to estimate the unknown parameters of the model. We then determined the empirical bias and RMSE of the estimates so as to examine the performance of the estimates. We also calculated the coverage probabilities of the confidence intervals based on the asymptotic normality of the MLEs for different nominal confidence levels. All the simulations were performed using the R software and the results were based on 1000 Monte Carlo runs. To find an initial guess of the parameters $\beta_0, \beta_1, \gamma_1$ and γ_2 so as to start the iterative procedure for the EM algorithm, we considered a discrete grid search on (β_0, β_1). For each possible choice of (β_0, β_1), we calculated the observed data log-likelihood function. For this purpose, we sampled a value of γ_1 and γ_2 independently from a set of values of γ_1 and γ_2 obtained by taking 20% deviation off the true values of γ_1 and γ_2, respectively. Finally, we took the value of $(\beta_0, \beta_1, \gamma_1, \gamma_2)$ as the initial value for which the observed data log-likelihood function is the maximum.

The results for the three special cases of the COM-Poisson cure rate model are presented in Tables 3.1−3.3. We see that the EM algorithm converges to the true parameter values quite accurately. The standard error and the RMSE of the estimates are found to decrease with an increase in sample size and with a decrease in censoring proportion. The coverage probabilities of the confidence intervals based on the asymptotic normality of the MLEs are found to be reasonably close to the nominal levels. On comparing models having the same mean but different variance for the lifetime distribution, the model having lower variance for the lifetime distribution is found to possess lower standard errors for the estimates. Similarly, on comparing models having the same variance but different mean for the lifetime distribution, the model having lower mean for the lifetime distribution is found to have higher standard errors for the estimates. In Tables 3.4−3.6, we present the bias and RMSE of the estimates of the cured proportions corresponding to four groups for the three special cases of the COM-Poisson cure rate model. We note that the estimates are very close to the true values and the RMSE is low when the cured proportion is low and also when the sample size is high. The observations are similar to those of the special cases of the COM-Poisson model when the parameter ϕ is kept fixed at 0.5 and the corresponding results are presented in Table 3.7. However, for all practical purposes, ϕ needs to be estimated from the data itself for which we can employ the profile likelihood technique. The corresponding results are shown in Table 3.8, where the true value of ϕ is taken to be 0.5, but now estimated from the data along with other model parameters. We note that the profile likelihood approach of estimating ϕ introduces large RMSE in the estimate of ϕ. However, it is found to decrease with an increase in sample size and with a decrease in censoring proportion. The standard errors of the estimates also show similar behavior. The bias in the estimate of ϕ is particularly large when the censoring proportion is high, which is also found to decrease with an increase in sample size. The profile likelihood approach also results in underestimating the standard errors of the estimates due to which the coverage probabilities fall below the nominal levels. The undercoverage is observed to be more pronounced for γ_2. Furthermore, this undercoverage for γ_2 is more noticeable when the censoring proportion is low. It is also interesting to note that the lifetime parameters are quite robust to the cure rate model both in terms of its estimated values and the standard errors of the estimates.

To apply the profile likelihood technique, we chose the range of ϕ to be [0, 2] and in this interval ϕ was divided in steps of 0.1, which accounted for 21 distinct choices for ϕ. It is clear that to estimate ϕ by the profile likelihood approach for a given dataset, the EM algorithm must converge for all chosen values of ϕ. However, for some datasets, it was observed that the EM algorithm failed to converge for some choices of ϕ and as such that dataset had to be discarded. The convergence problem when estimating ϕ is mainly due to the fact that the likelihood function becomes very flat with respect to ϕ. The EM algorithm also showed convergence problem when estimating the parameters of the COM-Poisson model with ϕ fixed at 0.5. However, the number of samples rejected in this case was quite small. But, no convergence problem was noticed when estimating the parameters of the three special cases of the COM-Poisson cure rate model.

3.5 Model discrimination results

3.5.1 Likelihood-based method

In this simulation study, we considered the following parameter settings: Setting 1: $n = 400$ $(110, 120, 90, 80)$, $p =$ "Low", $(\gamma_1, \gamma_2) = (0.241, 0.206)$; Setting 2: $n = 600$ $(165, 180, 135, 120)$, $p =$ "Low", $(\gamma_1, \gamma_2) = (0.241, 0.206)$; Setting 3: $n = 400$ $(110, 120, 90, 80)$, $p =$ "High", $(\gamma_1, \gamma_2) = (0.241, 0.206)$. For each simulated dataset, we calculated the likelihood ratio test statistic of the fitted Bernoulli, Poisson and geometric cure rate models *versus* the fitted COM-Poisson cure rate model. Based on 1000 data sets in each situation and nominal significance level of 0.05, we computed the observed significance levels and powers of the likelihood ratio test, and these results are reported in Table 3.9.

The numbers in bold represent the observed levels while the other numbers represent the observed powers. These numbers were determined simply by the rejection rates of the null hypothesis. It can be seen that the chi-square distribution only provides a reasonable approximation to the null distribution of the likelihood ratio statistic when testing for the Poisson distribution as the observed levels are not very close to the nominal level in two of the three cases. However, the mixture chi-square distribution provides a good approximation to the null distribution of the likelihood ratio statistic when testing for the Bernoulli distribution. When testing for the geometric distribution, however, the observed levels are found to be conservative in two of the three cases, and as such the mixture chi-square distribution again does not provide a good approximation to the null distribution of the likelihood ratio test. To investigate the performance of the mixture chi-square distribution, we considered Setting 1 above and constructed histograms of the likelihood ratio statistic values when testing for the geometric model (true model being geometric) as well as when testing for the Bernoulli model (true model being Bernoulli). The corresponding plots for the geometric and Bernoulli cases are presented in Figures 3.1 and 3.2, respectively. From Figure 1, it can be seen that the likelihood ratio statistic takes the value zero 92% of times, which is significantly different from the expected 50%, and this in turn explains why the mixture chi-square distribution does not provide a good approximation in this case. However, Figure 2 represents a better mixture representation, where the likelihood ratio statistic takes the value zero 78% of times resulting in the observed level being close to the nominal level.

When the true model is geometric, the test has very high power to reject the Bernoulli model. Furthermore, as expected, the rejection rate of the Bernoulli model decreases as the true model approaches the Bernoulli. The test also appears to have good power to reject the Poisson model and the largest observed power is 89%. When the true model is Poisson, the test has reasonable power to reject the Bernoulli model (the largest observed power is 77%) and a relatively less power to reject the geometric model (the largest power is 40%). When the true model is Bernoulli, the test again has high power to reject the geometric model and the largest observed power is 96%. However, the test does not appear to have power to reject the Poisson model and the largest observed power in this case is only 23%. Also, the power to reject the geometric model increases as the true model approaches the Bernoulli. Finally, it can also be seen that the power of the test to reject the wrong model increases with an increase in sample size and with a decrease in censoring proportion, as one would expect.

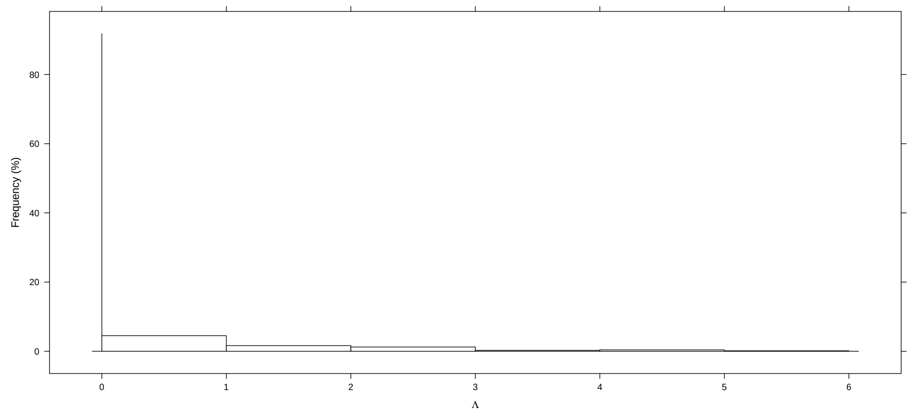

Figure 3.1: Histogram of Λ values when testing for geometric model (true model being geometric) with lognormal lifetime.

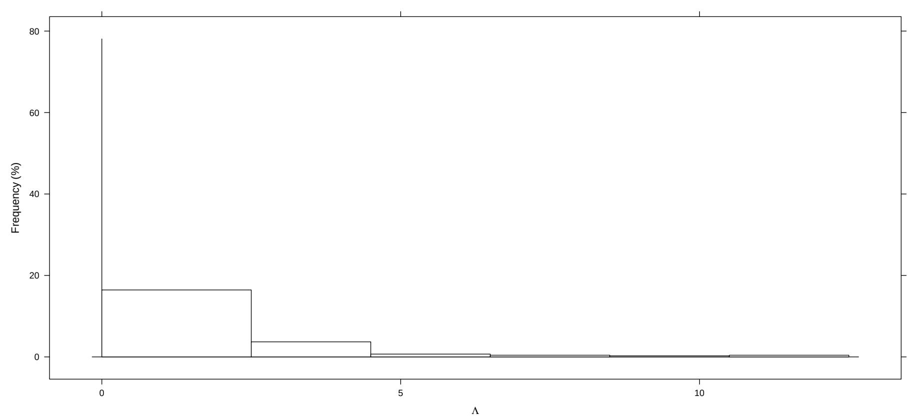

Figure 3.2: Histogram of Λ values when testing for Bernoulli model (true model being Bernoulli) with lognormal lifetime.

3.5.2 Information-based criterion

In this simulation study, considering the same parameter settings as in the previous section, we generated data from the true model, which can be one of the Bernoulli, Poisson, geometric, COM-Poisson ($\phi = 0.5$), and COM-Poisson ($\phi = 2$), and for each dataset, we calculated the AIC and BIC values of the fitted Bernoulli, Poisson and geometric models. Based on 1000 data sets in each situation, we computed the observed selection rates for each of the two criteria used, and these results are reported in Table 3.10.

It is easy to see that the information criteria used perform well as the selection rates for the correct model are high. Furthermore, as expected, this correct selection rate increases with an increase in sample size and a decrease in censoring proportion. Thus, the information criteria can distinguish between the three special cases of the COM-Poisson cure rate model very well. When the true model is COM-Poisson ($\phi = 0.5$), the selection rate for Poisson is higher than that of geometric. This implies that a COM-Poisson ($\phi = 0.5$) is closer to Poisson than geometric. When the true model is COM-Poisson ($\phi = 2$), the selection rate for Poisson is once again higher than that of Bernoulli, which implies that a COM-Poisson ($\phi = 2$) is closer to Poisson than Bernoulli. The correct selection rates are also found to increase with an increase in sample size and a decrease in censoring proportion. As the model discrimination using the information criteria does not involve estimation of the COM-Poisson parameter ϕ, unlike in the case of the likelihood-based method, we propose to use the information based criteria to carry out the model discrimination.

Based on 1000 data sets in each situation, we also present the TRB values when fitting different models for a given true model in Table 3.11. The values in parentheses represent the TRE values under model mis-specification. It can be seen that model mis-specification in general leads to higher TRB of the cured proportion as compared to the true model specification. We also note that in some cases, the TRB of the cured proportion under model mis-specification is much higher than under the correct model, which reveals that fitting a wrong model would lead to the estimation of cured proportion with large bias. Similarly, it can be seen that model mis-specification in general leads to loss of efficiency. As seen in Table 3.11, in some cases the TRE is considerably less than one, which implies significant loss of efficiency under model mis-specification. These findings strongly suggest that the flexibility of the COM-Poisson family should be utilized in selecting a parsimonious competing cause distribution, as otherwise there will be imprecision in estimating the cured proportion. To assess the effect of the estimation of the parameter ϕ on the TRB, we also calculated the TRB values when the true model is COM-Poisson with shape parameter $\phi = 0.5$, but the parameter ϕ is now estimated from the data. The results so obtained, based on 1000 Monte Carlo runs, are presented in Table 3.12. It is to be mentioned here that the value of ϕ selected by the profile likelihood method may be different from 0.5, but as seen from Table 3.12, the TRB of the cured proportion is small. On comparing the results for high and low censoring proportions, it can be seen that the TRB values are higher when the censoring proportion is low.

Table 3.13 shows the TRB and TRE values when using AIC as the model selection criterion. We note that for a given true model, the TRB values in some cases are less than that obtained when fitting the wrong model, as presented in Table 3.11. However, the TRE values for a given true model are always greater than those in Table 3.11 (except in one case). This further suggests that allowing AIC to select a working model out of a set of candidate models lead to significantly larger efficiency as compared to that obtained under wrong model specification. Also, the TRE values in Table 3.13 are all close to one, which implies that estimating the cured proportion from the working model selected by AIC leads to negligible loss of efficiency.

3.6 Analysis of cutaneous melanoma data

In this section, we analyze the cutaneous melanoma data for illustrative purpose. In our application, we selected the nodule category $(1 : n = 111; 2 : n = 137; 3 : n = 87; 4 : n = 82)$ as the only covariate. We first considered fitting the general COM-Poisson model to the data and obtained $\hat{\phi} \approx 0$. So, we considered testing for the suitability of the geometric model for the number of causes M in (1.3.1). With the test procedure as described in Section 1.8.1, we obtained $\Lambda \approx 0$ (p-value=0.5), and we therefore adopt the geometric model as our working model. We next considered, as candidate models, the Bernoulli, Poisson, COM-Poisson (geometric), COM-Poisson ($\phi = 0.5$) and COM-Poisson ($\phi = 2$) cure rate models. We note that the candidate models have the same number of parameters and we present the AIC, BIC and maximized log-likelihood function values for all these models in Table 3.14.

It is clear that the best fit is achieved with the COM-Poisson (geometric) model as both the AIC and BIC are monotonically increasing with ϕ and the maximized log-likelihood value is monotonically decreasing with ϕ. This is further ascertained by the plots in Figure 3.3. The COM-Poisson (geometric) model yields a closer concordance with the Kaplan-Meier estimate. To find an acceptable range of ϕ for the dataset, we considered testing for different values of ϕ and plot the values of ϕ against the corresponding likelihood ratio statistic. The corresponding plot is shown in Figure 3.4. We reject the likelihood ratio test at 10% level of significance if the value of the likelihood ratio statistic Λ exceeds $\chi^2_{1,1-\alpha} = 2.71$. Now, for $\Lambda = 2.71$, we have the corresponding value of ϕ to be 0.19 (from the plot) and hence an admissible range of ϕ for the data is $[0, 0.19)$. This further explains that the geometric model is the only acceptable model for the data among all those considered. The estimates of the parameters of the COM-Poisson (geometric) cure rate model are presented in Table 3.15.

Finally, we deal with the estimation of the cure rate p_0. Estimates of the cure rates of patients stratified by nodule category are $\hat{p}_{0j} = \frac{1}{1+\exp(\hat{\beta}_0 + j\hat{\beta}_1)}, j = 1, 2, 3, 4$. On following the procedure as described in Section 1.6.3, we present the estimates, standard errors and 95% confidence intervals of the cure rates of patients corresponding to the four nodule categories $(1-4)$ in Table 3.16. From the 95% confidence intervals

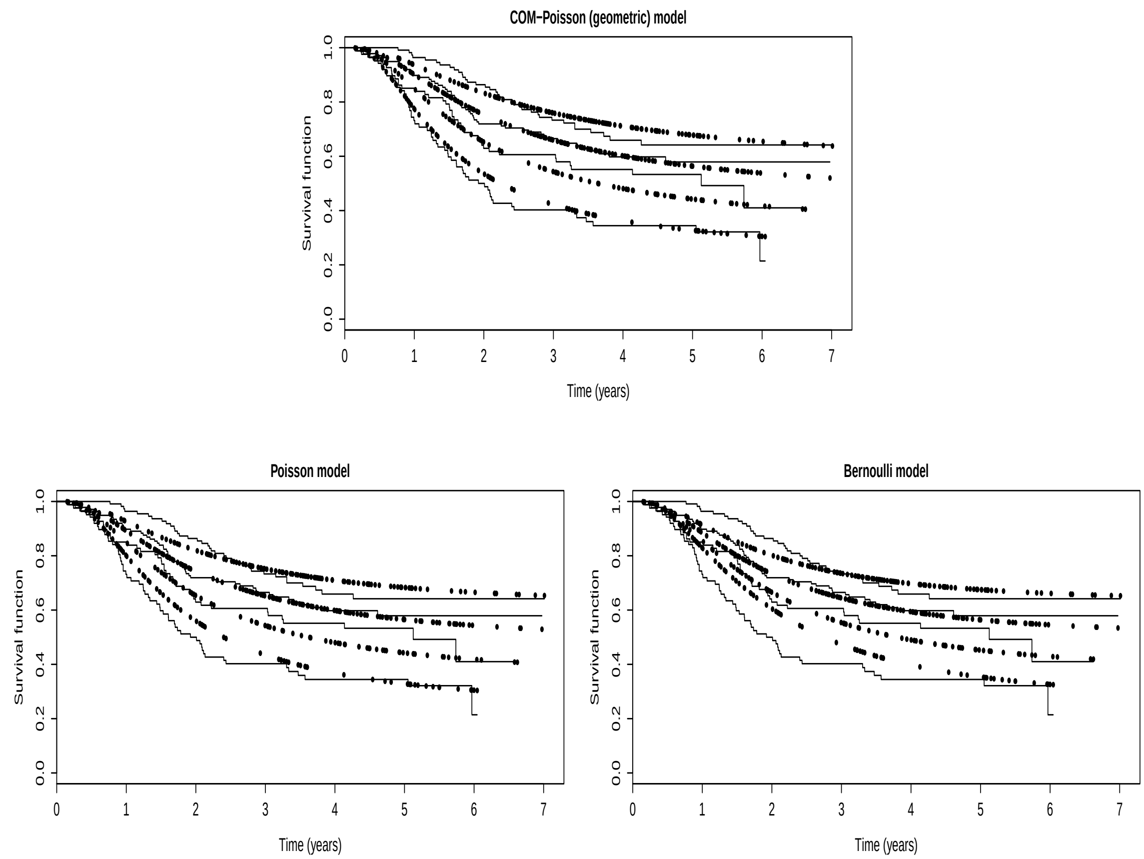

Figure 3.3: Kaplan-Meier curves stratified by nodule category (1-4), respectively, and estimates of the survival function for the COM-Poisson (geometric), Poisson and Bernoulli cure rate models with lognormal lifetime.

of cure rates for the four categories presented in Table 3.16, it is clear that the cure rate for nodule category 1 is significantly higher than those of categories 3 and 4.

With the nodule category being a categorical variable (with four categories), a flexible analysis can also be carried out by constructing dummy variables for the nodule category. In the present example, we define the following three dummy variables: $x_i = 1$ if nodule category = i and = 0 otherwise, for $i = 1, 2, 3$. We note that $x_1 = x_2 = x_3 = 0$ implies nodule category = 4. Considering these three dummy variables as our covariates, we now have four regression parameters. The profile like-

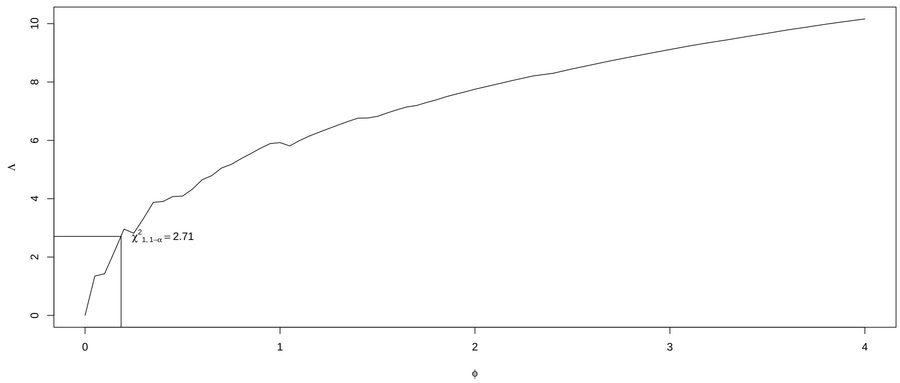

Figure 3.4: Values of ϕ against the corresponding Λ-statistic for lognormal lifetime.

lihood approach, in this case, gave $\hat{\phi} \approx 0$ and thus, we again consider the geometric model to be the working model. The estimates of the parameters of the COM-Poisson (geometric) model are presented in Table 3.17. Estimates of cure rates of patients stratified by nodule category are now given by $\hat{p}^*_{0i} = \frac{1}{1+\exp(\hat{\beta}^*_0+\hat{\beta}^*_i)}$, for $i = 1, 2, 3$ and $\hat{p}^*_{04} = \frac{1}{1+\exp(\hat{\beta}^*_0)}$. With the estimates in Table 3.17, estimates of cure rates are obtained as 0.556, 0.457, 0.365 and 0.219 corresponding to the four nodule categories (1-4). We note that these estimates of cure rates obtained after creating the dummy variables are very close to those obtained when the nodule category is taken to be the only covariate. However, it needs to be mentioned that creating the dummy variables increases the number of regression coefficients and hence the computational complexity. In our case, we have four regression coefficients and in order to provide initial values, for carrying out the EM algorithm, we had to consider a four-dimensional discrete grid search on $(\beta^*_0, \beta^*_1, \beta^*_2, \beta^*_3)$. Clearly, finding an initial value for the regression coefficients itself becomes involved and quite time-consuming. Moreover, if the number of categories of the categorical variable is more or if there are more than one categorical variable, pertinent inference would become computationally quite complex.

Table 3.1: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the Bernoulli cure rate model with lognormal lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP 90%	CP 95%
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.208 (0.325)	-0.016	0.326	0.900	0.950
		$\beta_1 = 0.573$	0.579 (0.123)	0.006	0.122	0.909	0.950
		$\gamma_1 = 0.337$	0.334 (0.019)	-0.003	0.019	0.896	0.951
		$\gamma_2 = 0.212$	0.212 (0.006)	0.000	0.006	0.898	0.950
	Low	$\beta_0 =$ -0.038	-0.039 (0.289)	-0.001	0.292	0.899	0.953
		$\beta_1 = 0.443$	0.449 (0.121)	0.006	0.123	0.907	0.951
		$\gamma_1 = 0.337$	0.336 (0.015)	-0.001	0.015	0.892	0.948
		$\gamma_2 = 0.212$	0.212 (0.004)	0.000	0.004	0.906	0.951
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.217 (0.323)	-0.026	0.328	0.896	0.948
		$\beta_1 = 0.573$	0.580 (0.122)	0.008	0.125	0.901	0.940
		$\gamma_1 = 0.241$	0.240 (0.014)	-0.001	0.014	0.898	0.945
		$\gamma_2 = 0.206$	0.206 (0.004)	0.000	0.004	0.890	0.932
	Low	$\beta_0 =$ -0.038	-0.036 (0.287)	0.002	0.294	0.901	0.955
		$\beta_1 = 0.443$	0.446 (0.120)	0.003	0.122	0.914	0.961
		$\gamma_1 = 0.241$	0.241 (0.011)	0.000	0.011	0.893	0.943
		$\gamma_2 = 0.206$	0.206 (0.003)	0.000	0.003	0.889	0.941
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.203 (0.328)	-0.011	0.336	0.906	0.952
		$\beta_1 = 0.573$	0.574 (0.124)	0.002	0.129	0.888	0.945
		$\gamma_1 = 0.468$	0.467 (0.027)	-0.001	0.027	0.891	0.946
		$\gamma_2 = 0.319$	0.320 (0.012)	0.001	0.012	0.911	0.955
	Low	$\beta_0 =$ -0.038	-0.054 (0.291)	-0.017	0.291	0.910	0.952
		$\beta_1 = 0.443$	0.453 (0.121)	0.009	0.125	0.896	0.954
		$\gamma_1 = 0.468$	0.467 (0.021)	-0.001	0.021	0.900	0.955
		$\gamma_2 = 0.319$	0.320 (0.009)	0.001	0.010	0.902	0.945
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.198 (0.325)	-0.007	0.329	0.908	0.953
		$\beta_1 = 0.573$	0.577 (0.123)	0.005	0.125	0.900	0.954
		$\gamma_1 = 0.340$	0.339 (0.019)	-0.001	0.019	0.903	0.952
		$\gamma_2 = 0.303$	0.303 (0.008)	0.000	0.008	0.893	0.941
	Low	$\beta_0 =$ -0.038	-0.047 (0.289)	-0.009	0.297	0.901	0.944
		$\beta_1 = 0.443$	0.452 (0.121)	0.008	0.123	0.900	0.949
		$\gamma_1 = 0.340$	0.339 (0.015)	-0.001	0.016	0.887	0.944
		$\gamma_2 = 0.303$	0.303 (0.006)	0.000	0.006	0.892	0.948
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.192	-1.211 (0.334)	-0.019	0.332	0.898	0.948
		$\beta_1 = 0.573$	0.579 (0.119)	0.007	0.118	0.911	0.954
		$\gamma_1 = 0.337$	0.336 (0.019)	-0.001	0.019	0.894	0.946
		$\gamma_2 = 0.212$	0.212 (0.006)	0.000	0.006	0.886	0.939
	Low	$\beta_0 =$ -0.038	-0.042 (0.295)	-0.005	0.297	0.897	0.952
		$\beta_1 = 0.443$	0.450 (0.116)	0.007	0.119	0.892	0.945
		$\gamma_1 = 0.337$	0.335 (0.015)	-0.002	0.015	0.879	0.932
		$\gamma_2 = 0.212$	0.212 (0.004)	0.000	0.004	0.910	0.953
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.192	-1.189 (0.265)	0.002	0.276	0.898	0.946
		$\beta_1 = 0.573$	0.574 (0.100)	0.001	0.103	0.895	0.943
		$\gamma_1 = 0.337$	0.336 (0.016)	-0.001	0.016	0.897	0.945
		$\gamma_2 = 0.212$	0.212 (0.005)	0.000	0.005	0.910	0.954
	Low	$\beta_0 =$ -0.038	-0.037 (0.236)	0.000	0.238	0.892	0.943
		$\beta_1 = 0.443$	0.448 (0.098)	0.004	0.101	0.899	0.957
		$\gamma_1 = 0.337$	0.337 (0.012)	0.000	0.013	0.891	0.943
		$\gamma_2 = 0.212$	0.212 (0.004)	0.000	0.004	0.888	0.950

Table 3.2: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the Poisson cure rate model with lognormal lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP	
						90%	95%
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.213 (0.310)	-0.021	0.310	0.901	0.950
		$\beta_1 = 0.573$	0.579 (0.115)	0.007	0.115	0.904	0.946
		$\gamma_1 = 0.337$	0.336 (0.020)	-0.001	0.020	0.892	0.943
		$\gamma_2 = 0.212$	0.212 (0.006)	0.000	0.006	0.895	0.948
	Low	$\beta_0 =$ -0.038	-0.039 (0.268)	-0.002	0.270	0.895	0.942
		$\beta_1 = 0.443$	0.449 (0.109)	0.006	0.109	0.907	0.951
		$\gamma_1 = 0.337$	0.337 (0.016)	0.000	0.016	0.897	0.957
		$\gamma_2 = 0.212$	0.212 (0.005)	0.000	0.005	0.891	0.938
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.192 (0.309)	0.000	0.302	0.902	0.948
		$\beta_1 = 0.573$	0.575 (0.115)	0.002	0.114	0.911	0.953
		$\gamma_1 = 0.241$	0.240 (0.014)	-0.001	0.015	0.873	0.927
		$\gamma_2 = 0.206$	0.206 (0.004)	0.000	0.004	0.882	0.946
	Low	$\beta_0 =$ -0.038	-0.032 (0.267)	0.005	0.267	0.907	0.954
		$\beta_1 = 0.443$	0.442 (0.109)	-0.001	0.108	0.913	0.960
		$\gamma_1 = 0.241$	0.240 (0.011)	-0.001	0.011	0.903	0.947
		$\gamma_2 = 0.206$	0.206 (0.004)	0.000	0.004	0.904	0.943
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.211 (0.310)	-0.019	0.305	0.902	0.954
		$\beta_1 = 0.573$	0.579 (0.115)	0.006	0.113	0.907	0.952
		$\gamma_1 = 0.468$	0.466 (0.028)	-0.002	0.028	0.901	0.948
		$\gamma_2 = 0.319$	0.319 (0.014)	0.000	0.014	0.902	0.953
	Low	$\beta_0 =$ -0.038	-0.032 (0.268)	0.005	0.271	0.893	0.955
		$\beta_1 = 0.443$	0.444 (0.109)	0.001	0.110	0.897	0.950
		$\gamma_1 = 0.468$	0.467 (0.022)	-0.001	0.023	0.888	0.936
		$\gamma_2 = 0.319$	0.319 (0.011)	0.000	0.012	0.878	0.937
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.204 (0.309)	-0.012	0.312	0.897	0.949
		$\beta_1 = 0.573$	0.579 (0.115)	0.006	0.117	0.894	0.952
		$\gamma_1 = 0.340$	0.338 (0.020)	-0.002	0.021	0.880	0.935
		$\gamma_2 = 0.303$	0.303 (0.009)	0.000	0.009	0.912	0.949
	Low	$\beta_0 =$ -0.038	-0.044 (0.268)	-0.006	0.266	0.905	0.955
		$\beta_1 = 0.443$	0.451 (0.109)	0.007	0.108	0.903	0.953
		$\gamma_1 = 0.340$	0.340 (0.016)	0.000	0.015	0.901	0.960
		$\gamma_2 = 0.303$	0.303 (0.008)	0.000	0.007	0.912	0.954
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.192	-1.201 (0.318)	-0.009	0.327	0.898	0.939
		$\beta_1 = 0.573$	0.578 (0.112)	0.005	0.115	0.894	0.946
		$\gamma_1 = 0.337$	0.335 (0.019)	-0.002	0.020	0.893	0.942
		$\gamma_2 = 0.212$	0.212 (0.006)	0.000	0.006	0.903	0.948
	Low	$\beta_0 =$ -0.038	-0.052 (0.274)	-0.014	0.266	0.914	0.963
		$\beta_1 = 0.443$	0.453 (0.106)	0.010	0.104	0.917	0.964
		$\gamma_1 = 0.337$	0.337 (0.016)	0.000	0.016	0.882	0.947
		$\gamma_2 = 0.212$	0.212 (0.005)	0.000	0.005	0.897	0.944
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.192	-1.215 (0.253)	-0.023	0.248	0.905	0.964
		$\beta_1 = 0.573$	0.581 (0.094)	0.009	0.093	0.913	0.960
		$\gamma_1 = 0.337$	0.336 (0.016)	-0.001	0.017	0.885	0.936
		$\gamma_2 = 0.212$	0.212 (0.005)	0.000	0.005	0.878	0.937
	Low	$\beta_0 =$ -0.038	-0.035 (0.218)	0.002	0.217	0.909	0.949
		$\beta_1 = 0.443$	0.443 (0.089)	0.000	0.087	0.913	0.950
		$\gamma_1 = 0.337$	0.336 (0.013)	-0.001	0.013	0.907	0.954
		$\gamma_2 = 0.212$	0.212 (0.004)	0.000	0.004	0.900	0.944

Table 3.3: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the geometric cure rate model with lognormal lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP	
						90%	95%
400 $(110,120,90,80)$	High	$\beta_0 =$ -1.192	-1.190 (0.287)	0.002	0.280	0.907	0.951
		$\beta_1 = 0.573$	0.573 (0.103)	0.001	0.101	0.902	0.947
		$\gamma_1 = 0.337$	0.336 (0.020)	-0.001	0.020	0.889	0.946
		$\gamma_2 = 0.212$	0.212 (0.008)	0.000	0.008	0.893	0.946
	Low	$\beta_0 =$ -0.038	-0.050 (0.232)	-0.012	0.241	0.876	0.939
		$\beta_1 = 0.443$	0.448 (0.087)	0.005	0.091	0.887	0.944
		$\gamma_1 = 0.337$	0.335 (0.016)	-0.002	0.016	0.897	0.948
		$\gamma_2 = 0.212$	0.212 (0.007)	0.000	0.007	0.904	0.956
400 $(110,120,90,80)$	High	$\beta_0 =$ -1.192	-1.198 (0.287)	-0.007	0.294	0.901	0.944
		$\beta_1 = 0.573$	0.577 (0.103)	0.005	0.107	0.885	0.944
		$\gamma_1 = 0.241$	0.240 (0.014)	-0.001	0.014	0.897	0.947
		$\gamma_2 = 0.206$	0.206 (0.005)	0.000	0.005	0.912	0.959
	Low	$\beta_0 =$ -0.038	-0.030 (0.232)	0.008	0.239	0.887	0.937
		$\beta_1 = 0.443$	0.440 (0.087)	-0.003	0.090	0.884	0.942
		$\gamma_1 = 0.241$	0.240 (0.011)	-0.001	0.011	0.900	0.949
		$\gamma_2 = 0.206$	0.206 (0.005)	0.000	0.005	0.908	0.955
400 $(110,120,90,80)$	High	$\beta_0 =$ -1.192	-1.210 (0.286)	-0.018	0.286	0.908	0.947
		$\beta_1 = 0.573$	0.579 (0.102)	0.006	0.101	0.911	0.952
		$\gamma_1 = 0.468$	0.465 (0.029)	-0.003	0.030	0.887	0.939
		$\gamma_2 = 0.319$	0.320 (0.017)	0.001	0.017	0.912	0.949
	Low	$\beta_0 =$ -0.038	-0.042 (0.232)	-0.004	0.227	0.913	0.964
		$\beta_1 = 0.443$	0.448 (0.087)	0.004	0.085	0.911	0.960
		$\gamma_1 = 0.468$	0.466 (0.023)	-0.002	0.023	0.899	0.951
		$\gamma_2 = 0.319$	0.319 (0.015)	0.000	0.015	0.901	0.948
400 $(110,120,90,80)$	High	$\beta_0 =$ -1.192	-1.194 (0.287)	-0.003	0.282	0.911	0.958
		$\beta_1 = 0.573$	0.577 (0.103)	0.004	0.102	0.912	0.956
		$\gamma_1 = 0.340$	0.339 (0.020)	-0.001	0.022	0.878	0.944
		$\gamma_2 = 0.303$	0.303 (0.011)	0.000	0.011	0.906	0.952
	Low	$\beta_0 =$ -0.038	-0.052 (0.232)	-0.014	0.241	0.894	0.945
		$\beta_1 = 0.443$	0.449 (0.087)	0.006	0.089	0.901	0.946
		$\gamma_1 = 0.340$	0.339 (0.016)	-0.001	0.016	0.897	0.945
		$\gamma_2 = 0.303$	0.3 03 (0.010)	0.000	0.010	0.915	0.956
400 $(100,100,100,100)$	High	$\beta_0 =$ -1.192	-1.211 (0.296)	-0.019	0.295	0.901	0.949
		$\beta_1 = 0.573$	0.580 (0.101)	0.007	0.100	0.907	0.948
		$\gamma_1 = 0.337$	0.336 (0.020)	-0.001	0.020	0.902	0.947
		$\gamma_2 = 0.212$	0.212 (0.008)	0.000	0.008	0.898	0.949
	Low	$\beta_0 =$ -0.038	-0.048 (0.239)	-0.010	0.238	0.900	0.961
		$\beta_1 = 0.443$	0.447 (0.085)	0.004	0.087	0.896	0.945
		$\gamma_1 = 0.337$	0.335 (0.016)	-0.002	0.017	0.882	0.937
		$\gamma_2 = 0.212$	0.212 (0.007)	0.000	0.007	0.892	0.945
600 $(165,180,135,120)$	High	$\beta_0 =$ -1.192	-1.197 (0.234)	-0.005	0.233	0.909	0.957
		$\beta_1 = 0.573$	0.574 (0.084)	0.001	0.084	0.905	0.946
		$\gamma_1 = 0.337$	0.337 (0.017)	0.000	0.016	0.892	0.947
		$\gamma_2 = 0.212$	0.212 (0.006)	0.000	0.006	0.900	0.948
	Low	$\beta_0 =$ -0.038	-0.044 (0.189)	-0.007	0.195	0.888	0.948
		$\beta_1 = 0.443$	0.446 (0.071)	0.003	0.074	0.892	0.938
		$\gamma_1 = 0.337$	0.337 (0.013)	0.000	0.014	0.888	0.936
		$\gamma_2 = 0.212$	0.212 (0.006)	0.000	0.006	0.897	0.951

Table 3.4: Estimates, bias, and root mean square error (RMSE) of cured proportions corresponding to four groups for the Bernoulli cure rate model with lognormal lifetime.

n	γ	p_0	Estimate	Bias	RMSE
400 $(110, 120, 90, 80)$	$(0.337, 0.212)$	p_{01} =0.650	0.651	0.001	0.049
		p_{02} =0.512	0.512	0.001	0.035
		p_{03} =0.371	0.371	0.000	0.033
		p_{04} =0.250	0.251	0.001	0.042
		p_{01} =0.400	0.400	0.000	0.045
		p_{02} =0.300	0.298	-0.002	0.028
		p_{03} =0.216	0.214	-0.001	0.028
		p_{04} =0.150	0.150	0.000	0.033
400 $(110, 120, 90, 80)$	$(0.241, 0.206)$	p_{01} =0.650	0.652	0.002	0.049
		p_{02} =0.512	0.514	0.003	0.034
		p_{03} =0.371	0.373	0.001	0.034
		p_{04} =0.250	0.252	0.002	0.044
		p_{01} =0.400	0.400	0.000	0.046
		p_{02} =0.300	0.299	-0.001	0.027
		p_{03} =0.216	0.215	0.000	0.027
		p_{04} =0.150	0.151	0.001	0.032
400 $(110, 120, 90, 80)$	$(0.468, 0.319)$	p_{01} =0.650	0.650	0.000	0.050
		p_{02} =0.512	0.513	0.002	0.035
		p_{03} =0.371	0.373	0.002	0.035
		p_{04} =0.250	0.253	0.003	0.045
		p_{01} =0.400	0.403	0.003	0.044
		p_{02} =0.300	0.300	0.000	0.026
		p_{03} =0.216	0.215	-0.001	0.028
		p_{04} =0.150	0.150	0.000	0.033
400 $(110, 120, 90, 80)$	$(0.340, 0.303)$	p_{01} =0.650	0.649	-0.001	0.049
		p_{02} =0.512	0.511	-0.001	0.034
		p_{03} =0.371	0.370	-0.001	0.034
		p_{04} =0.250	0.250	0.000	0.043
		p_{01} =0.400	0.401	0.001	0.046
		p_{02} =0.300	0.299	-0.001	0.027
		p_{03} =0.216	0.214	-0.002	0.027
		p_{04} =0.150	0.150	0.000	0.032
400 $(100, 100, 100, 100)$	$(0.337, 0.212)$	p_{01} =0.650	0.651	0.001	0.051
		p_{02} =0.512	0.513	0.001	0.036
		p_{03} =0.371	0.372	0.000	0.032
		p_{04} =0.250	0.251	0.001	0.039
		p_{01} =0.400	0.400	0.000	0.047
		p_{02} =0.300	0.298	-0.001	0.027
		p_{03} =0.216	0.214	-0.002	0.025
		p_{04} =0.150	0.150	0.000	0.030
600 $(165, 180, 135, 120)$	$(0.337, 0.212)$	p_{01} =0.650	0.648	-0.002	0.042
		p_{02} =0.512	0.511	-0.001	0.029
		p_{03} =0.371	0.371	-0.001	0.028
		p_{04} =0.250	0.251	0.001	0.036
		p_{01} =0.400	0.399	-0.001	0.036
		p_{02} =0.300	0.298	-0.001	0.022
		p_{03} =0.216	0.214	-0.001	0.023
		p_{04} =0.150	0.150	0.000	0.027

Table 3.5: Estimates, bias, and root mean square error (RMSE) of cured proportions corresponding to four groups for the Poisson cure rate model with lognormal lifetime.

n	γ	p_0	Estimate	Bias	RMSE
400 $(110, 120, 90, 80)$	$(0.337, 0.212)$	p_{01} =0.650	0.652	0.002	0.047
		p_{02} =0.512	0.514	0.002	0.035
		p_{03} =0.371	0.372	0.001	0.034
		p_{04} =0.250	0.251	0.001	0.042
		p_{01} =0.400	0.400	0.000	0.043
		p_{02} =0.300	0.298	-0.001	0.027
		p_{03} =0.216	0.214	-0.002	0.025
		p_{04} =0.150	0.150	0.000	0.029
400 $(110, 120, 90, 80)$	$(0.241, 0.206)$	p_{01} =0.650	0.648	-0.002	0.046
		p_{02} =0.512	0.511	-0.001	0.034
		p_{03} =0.371	0.371	-0.001	0.034
		p_{04} =0.250	0.251	0.001	0.041
		p_{01} =0.400	0.400	0.000	0.042
		p_{02} =0.300	0.300	0.000	0.026
		p_{03} =0.216	0.216	0.001	0.025
		p_{04} =0.150	0.152	0.002	0.029
400 $(110, 120, 90, 80)$	$(0.468, 0.319)$	p_{01} =0.650	0.652	0.002	0.047
		p_{02} =0.512	0.513	0.002	0.034
		p_{03} =0.371	0.372	0.001	0.033
		p_{04} =0.250	0.251	0.001	0.040
		p_{01} =0.400	0.399	-0.001	0.044
		p_{02} =0.300	0.299	-0.001	0.028
		p_{03} =0.216	0.215	0.000	0.027
		p_{04} =0.150	0.151	0.001	0.031
400 $(110, 120, 90, 80)$	$(0.340, 0.303)$	p_{01} =0.650	0.650	0.000	0.047
		p_{02} =0.512	0.511	0.000	0.034
		p_{03} =0.371	0.370	-0.001	0.033
		p_{04} =0.250	0.250	0.000	0.041
		p_{01} =0.400	0.400	0.000	0.042
		p_{02} =0.300	0.299	-0.001	0.027
		p_{03} =0.216	0.214	-0.002	0.026
		p_{04} =0.150	0.149	-0.001	0.029
400 $(100, 100, 100, 100)$	$(0.337, 0.212)$	p_{01} =0.650	0.649	-0.001	0.051
		p_{02} =0.512	0.511	0.000	0.036
		p_{03} =0.371	0.370	-0.001	0.031
		p_{04} =0.250	0.250	0.000	0.038
		p_{01} =0.400	0.402	0.002	0.043
		p_{02} =0.300	0.299	-0.001	0.028
		p_{03} =0.216	0.214	-0.002	0.025
		p_{04} =0.150	0.149	-0.001	0.028
600 $(165, 180, 135, 120)$	$(0.337, 0.212)$	p_{01} =0.650	0.652	0.002	0.038
		p_{02} =0.512	0.513	0.001	0.027
		p_{03} =0.371	0.371	0.000	0.027
		p_{04} =0.250	0.249	-0.001	0.033
		p_{01} =0.400	0.400	0.000	0.035
		p_{02} =0.300	0.300	0.000	0.022
		p_{03} =0.216	0.216	0.000	0.021
		p_{04} =0.150	0.151	0.001	0.024

Table 3.6: Estimates, bias, and root mean square error (RMSE) of cured proportions corresponding to four groups for the geometric cure rate model with lognormal lifetime.

n	γ	p_0	Estimate	Bias	RMSE
400 $(110, 120, 90, 80)$	$(0.337, 0.212)$	p_{01} =0.650	0.648	-0.002	0.044
		p_{02} =0.512	0.511	-0.001	0.034
		p_{03} =0.371	0.371	0.000	0.032
		p_{04} =0.250	0.251	0.001	0.037
		p_{01} =0.400	0.402	0.002	0.041
		p_{02} =0.300	0.301	0.001	0.027
		p_{03} =0.216	0.216	0.001	0.024
		p_{04} =0.150	0.151	0.001	0.026
400 $(110, 120, 90, 80)$	$(0.241, 0.206)$	p_{01} =0.650	0.649	-0.001	0.046
		p_{02} =0.512	0.511	-0.001	0.034
		p_{03} =0.371	0.370	-0.001	0.032
		p_{04} =0.250	0.250	0.000	0.038
		p_{01} =0.400	0.399	-0.001	0.040
		p_{02} =0.300	0.300	0.000	0.026
		p_{03} =0.216	0.217	0.001	0.023
		p_{04} =0.150	0.152	0.002	0.025
400 $(110, 120, 90, 80)$	$(0.468, 0.319)$	p_{01} =0.650	0.651	0.001	0.045
		p_{02} =0.512	0.513	0.002	0.034
		p_{03} =0.371	0.372	0.001	0.031
		p_{04} =0.250	0.251	0.001	0.036
		p_{01} =0.400	0.401	0.001	0.039
		p_{02} =0.300	0.299	0.000	0.026
		p_{03} =0.216	0.215	-0.001	0.023
		p_{04} =0.150	0.150	0.000	0.025
400 $(110, 120, 90, 80)$	$(0.340, 0.303)$	p_{01} =0.650	0.648	-0.002	0.044
		p_{02} =0.512	0.510	-0.001	0.034
		p_{03} =0.371	0.370	-0.002	0.032
		p_{04} =0.250	0.249	-0.001	0.037
		p_{01} =0.400	0.403	0.003	0.041
		p_{02} =0.300	0.301	0.001	0.027
		p_{03} =0.216	0.216	0.000	0.023
		p_{04} =0.150	0.150	0.000	0.025
400 $(100, 100, 100, 100)$	$(0.337, 0.212)$	p_{01} =0.650	0.651	0.001	0.047
		p_{02} =0.512	0.513	0.001	0.035
		p_{03} =0.371	0.372	0.000	0.030
		p_{04} =0.250	0.250	0.000	0.034
		p_{01} =0.400	0.402	0.002	0.041
		p_{02} =0.300	0.301	0.001	0.027
		p_{03} =0.216	0.216	0.001	0.024
		p_{04} =0.150	0.151	0.001	0.025
600 $(165, 180, 135, 120)$	$(0.337, 0.212)$	p_{01} =0.650	0.650	0.000	0.037
		p_{02} =0.512	0.512	0.001	0.028
		p_{03} =0.371	0.372	0.001	0.026
		p_{04} =0.250	0.251	0.001	0.031
		p_{01} =0.400	0.401	0.001	0.033
		p_{02} =0.300	0.300	0.000	0.021
		p_{03} =0.216	0.216	0.000	0.019
		p_{04} =0.150	0.150	0.000	0.020

Table 3.7: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the COM-Poisson cure rate model with ϕ fixed at 0.5 for lognormal lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP	
						90%	95%
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.183 (0.303)	0.009	0.314	0.895	0.947
		$\beta_1 = 0.573$	0.571 (0.112)	-0.002	0.117	0.887	0.945
		$\gamma_1 = 0.337$	0.336 (0.020)	-0.001	0.020	0.888	0.944
		$\gamma_2 = 0.212$	0.212 (0.007)	0.000	0.007	0.899	0.944
	Low	$\beta_0 =$ -0.038	-0.058 (0.258)	-0.020	0.257	0.907	0.954
		$\beta_1 = 0.443$	0.454 (0.104)	0.011	0.104	0.911	0.953
		$\gamma_1 = 0.337$	0.336 (0.016)	-0.001	0.016	0.877	0.945
		$\gamma_2 = 0.212$	0.212 (0.006)	0.000	0.006	0.905	0.949
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.192 (0.303)	-0.001	0.297	0.906	0.963
		$\beta_1 = 0.573$	0.574 (0.112)	0.001	0.112	0.901	0.954
		$\gamma_1 = 0.241$	0.240 (0.014)	-0.001	0.015	0.893	0.941
		$\gamma_2 = 0.206$	0.206 (0.005)	0.000	0.005	0.890	0.939
	Low	$\beta_0 =$ -0.038	-0.042 (0.258)	-0.005	0.254	0.898	0.953
		$\beta_1 = 0.443$	0.445 (0.104)	0.002	0.102	0.904	0.953
		$\gamma_1 = 0.241$	0.241 (0.011)	0.000	0.011	0.892	0.951
		$\gamma_2 = 0.206$	0.206 (0.004)	0.000	0.004	0.898	0.951
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.185 (0.303)	0.006	0.301	0.906	0.951
		$\beta_1 = 0.573$	0.573 (0.112)	0.001	0.110	0.899	0.953
		$\gamma_1 = 0.468$	0.467 (0.029)	-0.001	0.029	0.898	0.950
		$\gamma_2 = 0.319$	0.319 (0.015)	0.000	0.015	0.897	0.947
	Low	$\beta_0 =$ -0.038	-0.020 (0.259)	0.018	0.269	0.892	0.934
		$\beta_1 = 0.443$	0.439 (0.104)	-0.004	0.104	0.901	0.955
		$\gamma_1 = 0.468$	0.468 (0.023)	0.000	0.023	0.902	0.946
		$\gamma_2 = 0.319$	0.318 (0.012)	-0.001	0.012	0.906	0.949
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.195 (0.303)	-0.003	0.307	0.903	0.958
		$\beta_1 = 0.573$	0.578 (0.112)	0.006	0.115	0.909	0.952
		$\gamma_1 = 0.340$	0.339 (0.020)	-0.001	0.022	0.879	0.934
		$\gamma_2 = 0.303$	0.302 (0.010)	-0.001	0.010	0.887	0.946
	Low	$\beta_0 =$ -0.038	-0.030 (0.258)	0.007	0.263	0.897	0.950
		$\beta_1 = 0.443$	0.442 (0.104)	-0.001	0.105	0.895	0.952
		$\gamma_1 = 0.340$	0.339 (0.016)	-0.001	0.016	0.885	0.942
		$\gamma_2 = 0.303$	0.3 03 (0.008)	0.000	0.008	0.905	0.952
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.192	-1.187 (0.311)	0.004	0.322	0.896	0.943
		$\beta_1 = 0.573$	0.574 (0.109)	0.002	0.111	0.904	0.946
		$\gamma_1 = 0.337$	0.336 (0.019)	-0.001	0.020	0.885	0.935
		$\gamma_2 = 0.212$	0.212 (0.007)	0.000	0.006	0.912	0.953
	Low	$\beta_0 =$ -0.038	-0.043 (0.265)	-0.006	0.266	0.892	0.940
		$\beta_1 = 0.443$	0.447 (0.101)	0.004	0.101	0.896	0.949
		$\gamma_1 = 0.337$	0.337 (0.016)	0.000	0.016	0.898	0.945
		$\gamma_2 = 0.212$	0.212 (0.006)	0.000	0.006	0.888	0.943
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.192	-1.189 (0.247)	0.003	0.245	0.910	0.956
		$\beta_1 = 0.573$	0.573 (0.091)	0.000	0.092	0.890	0.949
		$\gamma_1 = 0.337$	0.337 (0.016)	0.000	0.016	0.907	0.956
		$\gamma_2 = 0.212$	0.212 (0.006)	0.000	0.006	0.896	0.962
	Low	$\beta_0 =$ -0.038	-0.037 (0.211)	0.001	0.216	0.896	0.945
		$\beta_1 = 0.443$	0.445 (0.085)	0.002	0.086	0.890	0.943
		$\gamma_1 = 0.337$	0.336 (0.013)	-0.001	0.014	0.885	0.938
		$\gamma_2 = 0.212$	0.212 (0.005)	0.000	0.005	0.888	0.941

Table 3.8: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the COM-Poisson cure rate model with $\phi = 0.5$ for lognormal lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP	
						90%	95%
400 $(110, 120, 90, 80)$	High	$\beta_0 = -1.192$	-1.197 (0.299)	-0.006	0.325	0.868	0.937
		$\beta_1 = 0.573$	0.575 (0.109)	0.002	0.120	0.873	0.931
		$\gamma_1 = 0.337$	0.332 (0.020)	-0.005	0.021	0.870	0.920
		$\gamma_2 = 0.212$	0.211 (0.007)	-0.001	0.014	0.484	0.597
		$\phi = 0.5$	0.660 (−)	0.160	0.819	−	−
	Low	$\beta_0 = -0.038$	0.000 (0.249)	0.038	0.294	0.843	0.911
		$\beta_1 = 0.443$	0.426 (0.098)	-0.017	0.122	0.802	0.880
		$\gamma_1 = 0.337$	0.333 (0.016)	-0.004	0.017	0.861	0.918
		$\gamma_2 = 0.212$	0.208 (0.006)	-0.004	0.018	0.210	0.279
		$\phi = 0.5$	0.603 (−)	0.103	0.787	−	−
400 $(110, 120, 90, 80)$	High	$\beta_0 = -1.192$	-1.189 (0.300)	0.002	0.307	0.885	0.942
		$\beta_1 = 0.573$	0.570 (0.110)	-0.002	0.119	0.868	0.926
		$\gamma_1 = 0.241$	0.238 (0.014)	-0.003	0.014	0.891	0.935
		$\gamma_2 = 0.206$	0.205 (0.005)	-0.001	0.009	0.509	0.600
		$\phi = 0.5$	0.693 (−)	0.193	0.832	−	−
	Low	$\beta_0 = -0.038$	0.013 (0.248)	0.051	0.286	0.846	0.908
		$\beta_1 = 0.443$	0.421 (0.097)	-0.022	0.121	0.806	0.879
		$\gamma_1 = 0.241$	0.240 (0.011)	-0.001	0.012	0.877	0.938
		$\gamma_2 = 0.206$	0.202 (0.004)	-0.004	0.012	0.222	0.290
		$\phi = 0.5$	0.546 (−)	0.046	0.747	−	−
400 $(110, 120, 90, 80)$	High	$\beta_0 = -1.192$	-1.182 (0.299)	0.009	0.322	0.875	0.928
		$\beta_1 = 0.573$	0.569 (0.109)	-0.003	0.116	0.888	0.937
		$\gamma_1 = 0.468$	0.464 (0.029)	-0.004	0.030	0.871	0.936
		$\gamma_2 = 0.319$	0.317 (0.015)	-0.002	0.030	0.507	0.615
		$\phi = 0.5$	0.694 (−)	0.194	0.831	−	−
	Low	$\beta_0 = -0.038$	0.007 (0.249)	0.045	0.315	0.805	0.869
		$\beta_1 = 0.443$	0.426 (0.097)	-0.017	0.127	0.775	0.854
		$\gamma_1 = 0.468$	0.465 (0.023)	-0.003	0.022	0.902	0.944
		$\gamma_2 = 0.319$	0.309 (0.013)	-0.010	0.038	0.210	0.270
		$\phi = 0.5$	0.576 (−)	0.076	0.760	−	−
400 $(110, 120, 90, 80)$	High	$\beta_0 = -1.192$	-1.185 (0.299)	0.006	0.315	0.889	0.940
		$\beta_1 = 0.573$	0.569 (0.109)	-0.004	0.115	0.884	0.941
		$\gamma_1 = 0.340$	0.337 (0.020)	-0.003	0.021	0.886	0.935
		$\gamma_2 = 0.303$	0.301 (0.010)	-0.002	0.019	0.497	0.623
		$\phi = 0.5$	0.662 (−)	0.162	0.820	−	−
	Low	$\beta_0 = -0.038$	0.025 (0.250)	0.062	0.307	0.791	0.881
		$\beta_1 = 0.443$	0.417 (0.098)	-0.026	0.127	0.775	0.853
		$\gamma_1 = 0.340$	0.337 (0.016)	-0.003	0.017	0.870	0.932
		$\gamma_2 = 0.303$	0.297 (0.009)	-0.006	0.025	0.226	0.304
		$\phi = 0.5$	0.584 (−)	0.084	0.755	−	−
400 $(100, 100, 100, 100)$	High	$\beta_0 = -1.192$	-1.190 (0.307)	0.001	0.330	0.874	0.937
		$\beta_1 = 0.573$	0.571 (0.107)	-0.002	0.118	0.856	0.915
		$\gamma_1 = 0.337$	0.333 (0.019)	-0.004	0.021	0.864	0.923
		$\gamma_2 = 0.212$	0.210 (0.007)	-0.002	0.014	0.449	0.574
		$\phi = 0.5$	0.635 (−)	0.135	0.814	−	−
	Low	$\beta_0 = -0.038$	0.026 (0.255)	0.064	0.303	0.821	0.895
		$\beta_1 = 0.443$	0.419 (0.094)	-0.024	0.121	0.788	0.856
		$\gamma_1 = 0.337$	0.334 (0.016)	-0.003	0.017	0.882	0.927
		$\gamma_2 = 0.212$	0.206 (0.006)	-0.006	0.018	0.199	0.262
		$\phi = 0.5$	0.547 (−)	0.047	0.747	−	−
600 $(165, 180, 135, 120)$	High	$\beta_0 = -1.192$	-1.178 (0.243)	0.013	0.263	0.874	0.934
		$\beta_1 = 0.573$	0.566 (0.089)	-0.007	0.100	0.858	0.924
		$\gamma_1 = 0.337$	0.334 (0.016)	-0.003	0.017	0.877	0.926
		$\gamma_2 = 0.212$	0.209 (0.006)	-0.003	0.012	0.415	0.515
		$\phi = 0.5$	0.571 (−)	0.071	0.738	−	−
	Low	$\beta_0 = -0.038$	0.013 (0.202)	0.051	0.249	0.814	0.880
		$\beta_1 = 0.443$	0.419 (0.079)	-0.024	0.105	0.762	0.849
		$\gamma_1 = 0.337$	0.335 (0.013)	-0.002	0.014	0.870	0.918
		$\gamma_2 = 0.212$	0.206 (0.005)	-0.006	0.017	0.154	0.215
		$\phi = 0.5$	0.463 (−)	-0.037	0.661	−	−

Table 3.9: Observed levels (in bold) and powers of the likelihood ratio test for lognormal lifetime.

Fitted model	True COM-Poisson model				
	$\phi = 0$	$\phi = 0.5$	$\phi = 1$	$\phi = 2$	$\phi \to \infty$
			Setting 1		
geometric	**0.014**	0.171	0.321	0.530	0.834
Poisson	0.748	0.227	**0.103**	0.037	0.067
Bernoulli	0.990	0.843	0.643	0.354	**0.063**
			Setting 2		
geometric	**0.007**	0.191	0.398	0.673	0.960
Poisson	0.889	0.318	**0.109**	0.050	0.231
Bernoulli	1.000	0.932	0.772	0.461	**0.056**
			Setting 3		
geometric	**0.047**	0.178	0.267	0.417	0.707
Poisson	0.389	0.097	**0.038**	0.013	0.001
Bernoulli	0.899	0.600	0.440	0.253	**0.053**

Table 3.10: Observed selection rates based on AIC* with lognormal lifetime.

Fitted model	True COM-Poisson model				
	$\phi = 0$	$\phi = 0.5$	$\phi = 1$	$\phi = 2$	$\phi \to \infty$
			Setting 1		
geometric	0.832	0.341	0.166	0.076	0.003
Poisson	0.164	0.599	0.668	0.559	0.188
Bernoulli	0.004	0.060	0.166	0.365	0.809
			Setting 2		
geometric	0.912	0.328	0.144	0.041	0.001
Poisson	0.088	0.645	0.723	0.629	0.122
Bernoulli	0.000	0.027	0.133	0.330	0.877
			Setting 3		
geometric	0.750	0.408	0.248	0.135	0.030
Poisson	0.232	0.468	0.515	0.440	0.205
Bernoulli	0.018	0.124	0.237	0.425	0.765

*In all cases, the results are the same for the Bayesian information criterion as well.

Table 3.11: TRB (in %) (TRE) in estimation of cured proportions when fitting different models for a given true model with lognormal lifetime.

	True model		
Fitted model	geometric	Poisson	Bernoulli
		Setting 1	
geometric	1.316 (-)	34.228 (0.752)	64.590 (0.449)
Poisson	23.880 (0.700)	1.440 (-)	22.908 (0.907)
Bernoulli	2.410 (0.773)	1.128 (0.917)	1.536 (-)
		Setting 2	
geometric	0.721 (-)	34.310 (0.681)	64.201 (0.336)
Poisson	23.101 (0.624)	0.726 (-)	22.244 (0.841)
Bernoulli	2.468 (0.759)	2.034 (0.912)	0.934 (-)
		Setting 3	
geometric	0.582 (-)	16.633 (0.908)	31.912 (0.663)
Poisson	11.560 (0.834)	2.085 (-)	9.225 (1.005)
Bernoulli	4.720 (0.840)	3.080 (0.951)	1.736 (-)

Table 3.12: TRB (in %) when the true value of $\phi = 0.5$ and the parameter ϕ is estimated from the data with lognormal lifetime.

n	(γ_1, γ_2)	TRB (in %)	
		p=High	p=Low
400 (110,120,90,80)	(0.337, 0.212)	0.948	7.095
400 (110,120,90,80)	(0.241, 0.206)	2.262	8.796
400 (110,120,90,80)	(0.468, 0.319)	1.929	6.801
400 (110,120,90,80)	(0.340, 0.303)	2.426	9.766
400 (100,100,100,100)	(0.337, 0.212)	2.002	8.806
600 (165,180,135,120)	(0.337, 0.212)	2.572	8.780

Table 3.13: TRB (in %) and TRE when using AIC as a model selection criterion between the three considered models with lognormal lifetime.

True model	TRB (%)	TRE
	Setting 1	
geometric	7.266	0.913
Poisson	9.050	0.942
Bernoulli	6.227	0.982
	Setting 2	
geometric	3.403	0.914
Poisson	7.913	0.941
Bernoulli	4.031	0.995
	Setting 3	
geometric	5.100	0.934
Poisson	8.113	0.971
Bernoulli	6.344	0.989

Table 3.14: AIC, BIC and maximized log-likelihood function (l) values for different cure rate models with lognormal lifetime.

Model	AIC	BIC	l
COM-Poisson (geometric)	**1025.020**	**1041.152**	**-508.510**
COM-Poisson ($\phi = 0.5$)	1029.110	1045.242	-510.555
Poisson	1030.944	1047.076	-511.472
COM-Poisson ($\phi = 2$)	1032.774	1048.906	-512.387
Bernoulli	1036.940	1053.072	-514.470

Table 3.15: Maximum likelihood estimates of the parameters of the COM-Poisson (geometric) cure rate model with lognormal lifetime.

Parameter	Estimate	Standard error
β_0	-0.768	0.311
β_1	0.488	0.088
γ_1	0.961	0.105
γ_2	0.274	0.071

Table 3.16: Estimates, standard errors, and 95% confidence intervals (CI) of cure rates of patients stratified by nodule category for lognormal lifetime.

Nodule category	Cure rate	Estimate	Standard error	95% CI
1	p_{01}	0.570	0.064	$(0.445, 0.695)$
2	p_{02}	0.448	0.059	$(0.332, 0.564)$
3	p_{03}	0.333	0.055	$(0.225, 0.441)$
4	p_{04}	0.234	0.051	$(0.134, 0.334)$

Table 3.17: Maximum likelihood estimates of the parameters of the COM-Poisson (geometric) cure rate model for lognormal lifetime and with dummy variables for the nodule category.

Parameter	Estimate	Standard error
β_0^*	1.270	0.301
β_1^*	-1.496	0.280
β_2^*	-1.099	0.261
β_3^*	-0.717	0.284
γ_1^*	0.956	0.103
γ_2^*	0.276	0.070

Chapter 4

Likelihood inference for gamma lifetime distribution

4.1 Introduction

In this chapter, we assume the lifetime W in (1.1.1) to follow the gamma distribution with p.d.f. as given in (1.4.4). To introduce the covariate effect, we relate the cure rate p_0 to covariates $\boldsymbol{x}_i$ by the logistic link function $p_{0i} = \frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}, i = 1, \ldots, n$. We develop in detail the steps of the EM algorithm for the determination of the MLEs of the parameters of the COM-Poisson cure rate model and some of its special cases based on right censored data. The simplified explicit expressions of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function and the components of the score function for different cure rate models are presented. The expressions of the first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\theta}^*$ that are necessary for the maximization step and the expressions of the components of the observed information matrix are presented in Appendix B.1 and Appendix B.2, respectively. It is to be noted that the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function involves the gamma function and the incomplete gamma function. Although expressions for the derivatives of the incomplete gamma function and the gamma function are available, here we calculate all of them numerically. We then discuss the results of an extensive Monte Carlo simulation study which illustrates the performance of the proposed estimation method described in Section 1.6.1. Model discrimination between different cure rate models is carried out by using the likelihood-based method as well as the information-based criteria and the corresponding results are presented. Finally, for illustrative purpose, the cutaneous melanoma data is analyzed and the validity of the gamma as the lifetime distribution is assessed for this dataset. For simplicity in notation, we denote $G(\boldsymbol{\gamma}) = \frac{\left(\frac{\gamma_2}{\gamma_1^2}\right)^{\frac{1}{\gamma_1^2}}}{\Gamma\left(\frac{1}{\gamma_1^2}\right)}$.

4.2 Expressions of E- and M-steps for different cure rate models

Bernoulli cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function can be expressed as

$$Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) = Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)}) + Q_2(\boldsymbol{\gamma}, \boldsymbol{\pi}^{(k)}),$$

where

$$Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)}) = \sum_{I_1} \boldsymbol{x}_i'\boldsymbol{\beta} + \sum_{I_0} \pi_i^{(k)} \boldsymbol{x}_i'\boldsymbol{\beta} - \sum_{I^*} \log(1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta})),$$

and

$$Q_2(\boldsymbol{\gamma}, \boldsymbol{\pi}^{(k)}) = n_1 \log(G(\boldsymbol{\gamma})) - \left(\frac{\gamma_2}{\gamma_1^2}\right) \sum_{I_1} t_i + \left(\frac{1}{\gamma_1^2} - 1\right) \sum_{I_1} \log t_i + \sum_{I_0} \pi_i^{(k)} \log(S(t_i; \boldsymbol{\gamma}))$$

with

$$\pi_i^{(k)} = \left. \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) S(t_i; \boldsymbol{\gamma})}{1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta}) S(t_i; \boldsymbol{\gamma})} \right|_{\boldsymbol{\theta}^* = \boldsymbol{\theta}^{*(k)}}, \tag{4.2.1}$$

for $i \in I_0$. Since the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function can be separated into two parts, one containing the regression parameter $\boldsymbol{\beta}$ and the other containing the lifetime parameter $\boldsymbol{\gamma}$, the maximization step can be carried out by maximizing $Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)})$ with respect to $\boldsymbol{\beta}$ and $Q_2(\boldsymbol{\gamma}, \boldsymbol{\pi}^{(k)})$ with respect to $\boldsymbol{\gamma}$, separately.

Poisson cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function can be expressed as

$$
\begin{aligned}
Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) \quad = \quad & n_1 \log(G(\boldsymbol{\gamma})) + \sum_{I_1} \log(\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))) - \left(\frac{\gamma_2}{\gamma_1^2}\right) \sum_{I_1} t_i \\
& + \left(\frac{1}{\gamma_1^2} - 1\right) \sum_{I_1} \log t_i + \sum_{I_1} A_{Gi}(\boldsymbol{\beta}, \boldsymbol{\gamma}) \\
& + \sum_{I_0} \pi_i^{(k)} \log(\exp(A_{Gi}(\boldsymbol{\beta}, \boldsymbol{\gamma})) - 1) - \sum_{I^*} \log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})),
\end{aligned}
$$

where

$$
A_{Gi}(\boldsymbol{\beta}, \boldsymbol{\gamma}) = \log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))S(t_i; \boldsymbol{\gamma}), \tag{4.2.2}
$$

for $i = 1, 2, \ldots, n$, and

$$
\pi_i^{(k)} = \left. \frac{\exp(A_{Gi}(\boldsymbol{\beta}, \boldsymbol{\gamma})) - 1}{\exp(A_{Gi}(\boldsymbol{\beta}, \boldsymbol{\gamma}))} \right|_{\boldsymbol{\theta}^* = \boldsymbol{\theta}^{*(k)}}, \tag{4.2.3}
$$

for $i \in I_0$.

Geometric cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function can be expressed as

$$
\begin{aligned}
Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) \quad = \quad & n_1 \log(G(\boldsymbol{\gamma})) + \sum_{I_1} \boldsymbol{x}_i'\boldsymbol{\beta} - \left(\frac{\gamma_2}{\gamma_1^2}\right) \sum_{I_1} t_i + \left(\frac{1}{\gamma_1^2} - 1\right) \sum_{I_1} \log t_i \\
& - 2 \sum_{I_1} \log\{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1 - S(t_i; \boldsymbol{\gamma}))\} - \sum_{I_0} \log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})) \\
& + \sum_{I_0} \pi_i^{(k)} \boldsymbol{x}_i'\boldsymbol{\beta} + \sum_{I_0} \pi_i^{(k)} \log\left\{\frac{S(t_i; \boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1 - S(t_i; \boldsymbol{\gamma}))}\right\},
\end{aligned}
$$

where

$$\pi_i^{(k)} = \left. \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})S(t_i;\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})} \right|_{\boldsymbol{\theta}^*=\boldsymbol{\theta}^{*(k)}}, \tag{4.2.4}$$

for $i \in I_0$.

COM-Poisson cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function, for a fixed value of ϕ, can be expressed as

$$\begin{aligned} Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) &= n_1 \log(G(\boldsymbol{\gamma})) - \sum_{I_1} \log(S(t_i;\boldsymbol{\gamma})) - \left(\frac{\gamma_2}{\gamma_1^2}\right) \sum_{I_1} t_i + \left(\frac{1}{\gamma_1^2} - 1\right) \sum_{I_1} \log t_i \\ &\quad + \sum_{I_1} \log z_{2i} + \sum_{I_0} \pi_i^{(k)} \log z_{1i} - \sum_{I^*} \log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})), \end{aligned}$$

where

$$z_1 = z_1(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{\{H_\phi^{-1}(1+\exp(\boldsymbol{x}'\boldsymbol{\beta}))S(t;\boldsymbol{\gamma})\}^j}{(j!)^\phi},$$

$$z_2 = z_2(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{j\{H_\phi^{-1}(1+\exp(\boldsymbol{x}'\boldsymbol{\beta}))S(t;\boldsymbol{\gamma})\}^j}{(j!)^\phi},$$

and

$$\pi_i^{(k)} = \left. \frac{z_1(\boldsymbol{\theta}; \boldsymbol{x}_i, t_i)}{1+z_1(\boldsymbol{\theta}; \boldsymbol{x}_i, t_i)} \right|_{\boldsymbol{\theta}^*=\boldsymbol{\theta}^{*(k)}}, \tag{4.2.5}$$

for $i \in I_0$.

4.3 Components of the score function

Bernoulli cure rate model: The components of the score function are

$$
\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il} + \sum_{I_0} x_{il} w_i - \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}, \\
\frac{\partial l}{\partial \gamma_1} &= n_1 \frac{\partial}{\partial \gamma_1} \log(G(\boldsymbol{\gamma})) + \frac{2}{\gamma_1^3} \sum_{I_1} \{\gamma_2 t_i - \log t_i\} + \sum_{I_0} w_i \frac{\partial}{\partial \gamma_1} \log(S(t_i;\boldsymbol{\gamma})), \\
\frac{\partial l}{\partial \gamma_2} &= \frac{n_1}{\gamma_1^2 \gamma_2} - \frac{1}{\gamma_1^2} \sum_{I_1} t_i + \sum_{I_0} w_i \frac{\partial}{\partial \gamma_2} \log(S(t_i;\boldsymbol{\gamma})),
\end{aligned}
$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$
w_i = \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta}) S(t_i;\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i' \boldsymbol{\beta}) S(t_i;\boldsymbol{\beta})}, \tag{4.3.1}
$$

for $i \in I_0$.

Poisson cure rate model: The components of the score function are

$$
\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i' \boldsymbol{\beta})) \log(1+\exp(\boldsymbol{x}_i' \boldsymbol{\beta}))} + \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta}) \{S(t_i;\boldsymbol{\gamma}) - 1\}}{1+\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}, \\
\frac{\partial l}{\partial \gamma_1} &= n_1 \frac{\partial}{\partial \gamma_1} \log(G(\boldsymbol{\gamma})) + \frac{2}{\gamma_1^3} \sum_{I_1} \{\gamma_2 t_i - \log t_i\} + \sum_{I^*} \log(1+\exp(\boldsymbol{x}_i' \boldsymbol{\beta})) \frac{\partial}{\partial \gamma_1} S(t_i;\boldsymbol{\gamma}), \\
\frac{\partial l}{\partial \gamma_2} &= \frac{n_1}{\gamma_1^2 \gamma_2} - \frac{1}{\gamma_1^2} \sum_{I_1} t_i + \sum_{I^*} \log(1+\exp(\boldsymbol{x}_i' \boldsymbol{\beta})) \frac{\partial}{\partial \gamma_2} S(t_i;\boldsymbol{\gamma}),
\end{aligned}
$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$.

Geometric cure rate model: The components of the score function are

$$\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il}\{1 - 2B_i(\boldsymbol{\beta}, \boldsymbol{\gamma})(1 - S(t_i; \boldsymbol{\gamma}))\} - \sum_{I_0} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta})} \\
&\quad + \sum_{I_0} x_{il} w_i \{1 - B_i(\boldsymbol{\beta}, \boldsymbol{\gamma})(1 - S(t_i; \boldsymbol{\gamma}))\}, \\
\frac{\partial l}{\partial \gamma_1} &= n_1 \frac{\partial}{\partial \gamma_1} \log(G(\boldsymbol{\gamma})) + \frac{2}{\gamma_1^3} \sum_{I_1} \{\gamma_2 t_i - \log t_i\} + 2 \sum_{I_1} B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) \frac{\partial}{\partial \gamma_1} S(t_i; \boldsymbol{\gamma}) \\
&\quad + \sum_{I_0} \left\{ \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta})} \right\} \frac{\partial}{\partial \gamma_1} S(t_i; \boldsymbol{\gamma}) + \sum_{I_0} w_i B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) \frac{\partial}{\partial \gamma_1} S(t_i; \boldsymbol{\gamma}), \\
\frac{\partial l}{\partial \gamma_2} &= \frac{n_1}{\gamma_1^2 \gamma_2} - \frac{1}{\gamma_1^2} \sum_{I_1} t_i + 2 \sum_{I_1} B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) \frac{\partial}{\partial \gamma_2} S(t_i; \boldsymbol{\gamma}) \\
&\quad + \sum_{I_0} \left\{ \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta})} \right\} \frac{\partial}{\partial \gamma_2} S(t_i; \boldsymbol{\gamma}) + \sum_{I_0} w_i B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) \frac{\partial}{\partial \gamma_2} S(t_i; \boldsymbol{\gamma}),
\end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$w_i = \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) S(t_i; \boldsymbol{\gamma})}{1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta})}, \tag{4.3.2}$$

for $i \in I_0$, and

$$B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) = \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta}), (1 - S(t_i; \boldsymbol{\gamma}))} \tag{4.3.3}$$

for $i = 1, 2, \ldots, n$.

COM-Poisson cure rate model: The components of the score function, for a fixed value of ϕ, are

$$\frac{\partial l}{\partial \beta_l} = \sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) z_{21i}}{z_{2i} z_{01i}} + \sum_{I_0} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) z_{2i}}{(1 + z_{1i}) z_{01i}} - \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta})},$$

$$\begin{aligned}
\frac{\partial l}{\partial \gamma_1} &= n_1 \frac{\partial}{\partial \gamma_1} \log(G(\boldsymbol{\gamma})) + \frac{2}{\gamma_1^3} \sum_{I_1} \{\gamma_2 t_i - \log t_i\} + \sum_{I_1} \left\{ \frac{z_{21i}}{z_{2i}} - 1 \right\} \frac{\partial}{\partial \gamma_1} \log(S(t_i; \boldsymbol{\gamma})) \\
&+ \sum_{I_0} \left\{ \frac{z_{2i}}{1 + z_{1i}} \right\} \frac{\partial}{\partial \gamma_1} \log(S(t_i; \boldsymbol{\gamma})), \\
\frac{\partial l}{\partial \gamma_2} &= \frac{n_1}{\gamma_1^2 \gamma_2} - \frac{1}{\gamma_1^2} \sum_{I_1} t_i + \sum_{I_1} \left\{ \frac{z_{21i}}{z_{2i}} - 1 \right\} \frac{\partial}{\partial \gamma_2} \log(S(t_i; \boldsymbol{\gamma})) \\
&+ \sum_{I_0} \left\{ \frac{z_{2i}}{1 + z_{1i}} \right\} \frac{\partial}{\partial \gamma_2} \log(S(t_i; \boldsymbol{\gamma})),
\end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$z_{21} = z_{21}(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{j^2 \{H_\phi^{-1}(1 + \exp(\boldsymbol{x}'\boldsymbol{\beta}))S(t; \boldsymbol{\gamma})\}^j}{(j!)^\phi},$$

and

$$z_{01} = z_{01}(\boldsymbol{\theta}_1; \boldsymbol{x}) = \sum_{j=1}^{\infty} \frac{j \{H_\phi^{-1}(1 + \exp(\boldsymbol{x}'\boldsymbol{\beta}))\}^j}{(j!)^\phi}.$$

4.4 Results of the simulation study: model fitting

Referring to the simulation setup described in Section 1.7, we considered two sample sizes: $n = 400$ and $n = 600$, which allow us to study the behavior of the fitting of the model under moderate and large sample sizes. The choice of the lifetime parameter (γ_1, γ_2) was obtained by equating the mean and variance of the underlying gamma distribution in (1.4.4) to some fixed values. For this, we considered two different choices for the mean as 0.5 and 0.25, and two different choices for the variance as 0.05 and 0.1, which result in four different choices of $(\gamma_1, \gamma_2) : (0.447, 2), (0.632, 2), (0.894, 4), \text{and}(1.265, 4)$. This allows us to study the behavior of the model when the lifetime distribution has the same mean but different variance and vice-versa. We simulated data from different cure rate models and the proposed estimation method was employed for the determination of the MLEs of the parameters of the model. To examine the performance of the estimates, we calculated the empirical bias and RMSE of the estimates. We also calculated the coverage probabilities of the confidence intervals based on the asymptotic normality of the MLEs for different nominal confidence levels. All the simulations were performed using the R software and the results were based on 1000 Monte Carlo runs. To find the initial values of the parameters for starting the iterative procedure, we followed the same procedure as described in Section 3.4.

We present the results of the three special cases of the COM-Poisson model in Tables 4.1−4.3. We observe that the EM algorithm converges to the true parameter values quite accurately. As expected, the standard error and RMSE of the estimates decrease with an increase in sample size and with a decrease in censoring proportion. The coverage probabilities of the confidence intervals based on the asymptotic normality of the MLEs are found to be quite close to the nominal levels. On comparing models having the same mean and different variance for the lifetime distribution, models having a lower variance are found to have a low standard error of the estimates. Similarly, on comparing models having the same variance and different mean for the lifetime distribution, models having a lower mean are found to have a high standard error of the estimates. In Tables 4.4-4.6, we present the bias and RMSE of the estimates of the cured proportions corresponding to the four groups for the three special cases of the COM-Poisson cure rate model. We note that the estimates are very close to the true values and the RMSE decrease with an increase in sample size and with a decrease in censoring proportion. In Table 4.7, we present the results of the COM-Poisson model when the value of the parameter ϕ is kept fixed at 0.5. The findings in this case are similar to the special cases of the COM-Poisson model. However, as mentioned earlier, the parameter ϕ needs to be estimated from the data along with other model parameters, for which we can employ the profile likelihood approach. The corresponding results are shown in Table 4.8, where the true value of ϕ is taken to be 0.5 but now estimated from the data along with other model parameters. We note that the profile likelihood approach results in large RMSE in the estimate of ϕ. However, it is found to decrease with an increase in sample size and with a decrease in censoring proportion. The standard errors of the estimates also show a similar behavior. The standard errors of the model parameters are underestimated and as such the coverage probabilities fall below the nominal levels. This undercoverage is more pronounced for γ_2. Furthermore, the undercoverage for γ_2 is more noticeable when the censoring proportion is low.

To apply the profile likelihood technique, we chose the range of ϕ to be [0, 2] and in this interval ϕ was divided in steps of 0.1, which accounted for 21 distinct choices for ϕ. It is clear that to estimate ϕ by the profile likelihood approach for a given dataset, the EM algorithm must converge for all chosen values of ϕ. However, for a few datasets, the EM algorithm failed to converge for some choices of ϕ and as such those datasets had to be discarded. The EM algorithm also showed occasionally convergence problem when estimating the parameters of the COM-Poisson model with ϕ fixed at 0.5. However, the number of samples rejected in this case was quite small. But, no convergence problem was noticed while estimating the parameters of the three special cases of the COM-Poisson cure rate model.

4.5 Model discrimination results

4.5.1 Likelihood-based method

In this simulation study, we restrict ourselves to the following parameter settings. Setting 1: $n = 400$ $(110, 120, 90, 80)$, $p =$ "Low", $(\gamma_1, \gamma_2) = (0.894, 4)$; Setting 2: $n = 600$ $(165, 180, 135, 120)$, $p =$ "Low", $(\gamma_1, \gamma_2) = (0.894, 4)$; Setting 3: $n = 400$ $(110, 120, 90, 80)$, $p =$ "High", $(\gamma_1, \gamma_2) = (0.894, 4)$. For each simulated dataset, we calculated the likelihood ratio test statistic of the fitted Bernoulli, Poisson and geometric models *versus* the fitted COM-Poisson model. Based on 1000 datasets, for each parameter setting considered, and nominal significance level of 5%, we calculated the observed significance levels and powers of the likelihood ratio test and these values are presented in Table 4.9.

The observed levels are represented by numbers in bold while the other numbers represent the observed powers. These numbers were determined simply by the rejection rates of the null hypothesis. When testing for the Poisson distribution, we note that the chi-square distribution only provides a reasonable approximation to the null distribution of the likelihood ratio test statistic as the observed levels are not close to the nominal level in two of the three cases. The mixture chi-square distribution, on the other hand, provides a good approximation to the null distribution of the likelihood ratio statistic when testing for the Bernoulli distribution only. When testing for the geometric distribution, however, the observed levels are found to be too conservative. To explain the behavior of the mixture chi-square distribution, we considered Setting 1 above and constructed histograms of the likelihood ratio test statistic values when testing for the geometric as well as Bernoulli models, the true model being the same as the fitted model in each case. The corresponding plots for the geometric and Bernoulli cases are presented in Figures 4.1 and 4.2, respectively. From Figure

4.1, we note that the likelihood ratio test statistic takes the value zero 91% of the times, which is significantly different from the expected 50%. This clearly explains why the mixture chi-square distribution did not provide a good approximation to the null distribution of the likelihood ratio statistic in this case. From Figure 4.2, we get a better mixture representation, in which case the likelihood ratio statistic takes the value zero 76% of the times thereby resulting in the observed level being close to the nominal level.

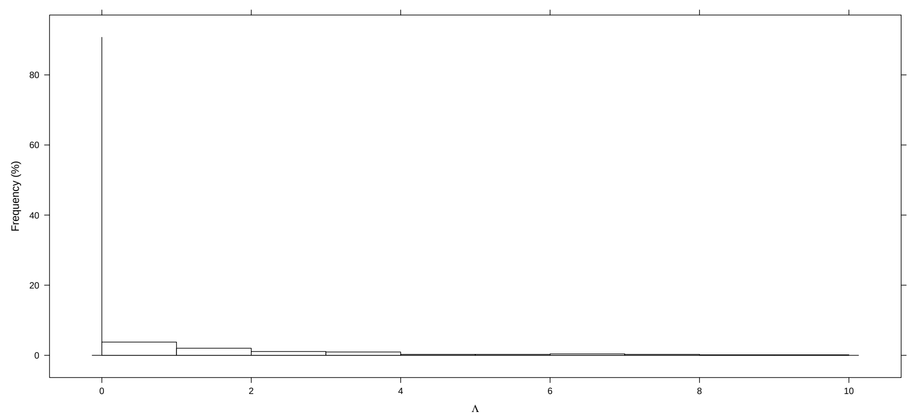

Figure 4.1: Histogram of Λ values when testing for geometric model (true model being geometric) with gamma lifetime

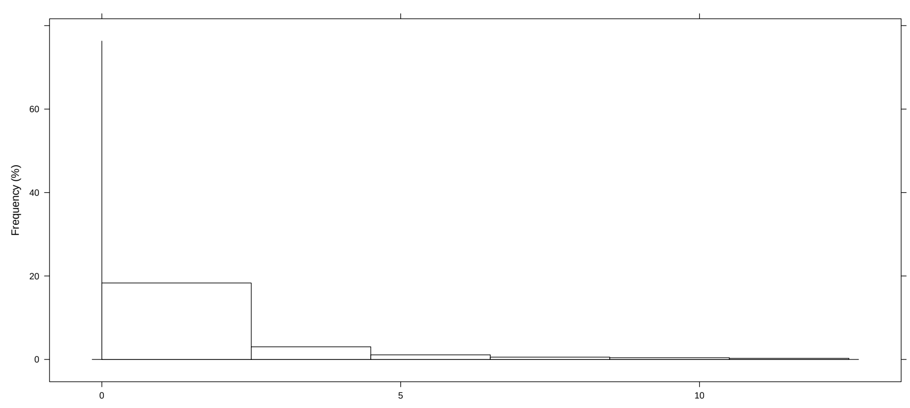

Figure 4.2: Histogram of Λ values when testing for Bernoulli model (true model being Bernoulli) with gamma lifetime

When the true model is geometric, the test has high power to reject the Bernoulli model and a good power to reject the Poisson model. When the true model is Bernoulli, the test again has high power to reject the geometric model. However, the test does not appear to have power to reject the Poisson model and the highest observed power in this case is only 25%. As expected, the rejection rates of the Bernoulli model is monotonically decreasing with the true value of ϕ whereas the rejection rates of the geometric model is monotonically increasing with the true value of ϕ. When the true model is Poisson, the test has a reasonable power to reject the Bernoulli model (the largest observed power being 79%) and a relatively less power to reject the geometric model (the largest observed power being 43%). When COM-Poisson (ϕ=0.5) is the true model, the test has good power to reject the Bernoulli model, but the power to reject the geometric and Poisson models, in this case, are very close. When the true model is COM-Poisson (ϕ=2), the test has moderate power to reject the geometric model, an even lesser power to reject the Bernoulli model, and very low power to reject the Poisson model. Hence, in this case, a COM-Poisson model with ϕ=2 can be considered to be close to Poisson than to Bernoulli. Finally, as expected, the power of the test to reject the wrong model increases with an increase in sample size and with a decrease in censoring proportion.

4.5.2 Information-based criterion

In this simulation study, we considered the same parameter settings as in the previous section, and for each generated dataset, we calculated the AIC and BIC values of the fitted Bernoulli, Poisson and geometric models. Based on 1000 datasets in each situation, we calculated the observed selection rates for each of the two criteria used and these results are reported in Table 4.10.

It is easy to see that the information criteria perform well in selecting the correct model as the selection rates for the correct model are high. As expected, this correct selection rates increase with an increase in sample size and with a decrease in censoring proportion. When COM-Poisson ($\phi = 0.5$) is the true model, the selection rate of Poisson is higher than that of geometric. This implies that a COM-Poisson ($\phi = 0.5$) is closer to Poisson than geometric. Again, when COM-Poisson ($\phi = 2$) is the true model, the selection rate of Poisson is higher than that of Bernoulli except when the censoring proportion is high.

Based on 1000 datasets in each situation, we also present the TRB values when fitting different models for a given true model in Table 4.11. The values in parentheses represent the TRE values. It is easy to see that fitting the wrong model leads to much higher TRB values of the cured proportion than when fitting the correct model. Thus, fitting a wrong model would lead to large bias in the estimate of cured proportion. The TRE values are always less than one and in some cases it is considerably less than one, which clearly implies significant loss of efficiency under model mis-specification. These findings clearly suggest to use the flexibility of the COM-Poisson model to select a parsimonious competing cause distribution, as otherwise the cured proportion will be estimated with less precision.

When using AIC to select a working model for a given true model, we present the results of TRB and TRE in Table 4.12. We note that, in most of the cases, for a given true model, the TRB values are less than that obtained when fitting the wrong model, as presented in Table 4.11. The TRE values are always greater than that obtained under wrong model specification. This further suggests that when we allow the AIC to select a working model out of a set of candidate models, although it selects the wrong model a certain number of times, its overall efficiency is always greater than that obtained under model mis-specification. From Table 4.12, it is also to be noted that the TRE values are all close to one, which implies that estimating the cured proportion from the models selected by AIC leads to negligible loss of efficiency.

4.6 Analysis of cutaneous melanoma data

In this section, we demonstrate an application of the proposed methodology to the cutaneous melanoma dataset. We selected the nodule category $(1 : n = 111; 2 : n = 137; 3 : n = 87; 4 : n = 82)$ as the only covariate in our model. As candidate models, we considered the commonly used Bernoulli, Poisson, and geometric cure rate models as well as the COM-Poisson model. First, we considered fitting the COM-Poisson model to the data. By employing the profile likelihood approach of estimating ϕ, we obtained $\hat{\phi} \approx 0$. So, we considered testing for the suitability of the geometric model $(H_0 : \phi = 0)$ for the number of causes M in (1.3.1). With the test procedure described in Section 1.8.1, we obtained $\Lambda \approx 0$ (p-value=0.5), and so we adopt the geometric model as our working model. When testing for the suitability of the Poisson and Bernoulli cure rate models for the competing cause variable, we obtained $\Lambda = 6.161$ (p-value=0.013) and $\Lambda = 13.540$ (p-value$\approx$0), respectively. This suggests that Poisson and Bernoulli models are not suitable for the data at 5% level of significance. In Table 4.13, we present the AIC, BIC and maximized log-likelihood values for different cure models.

We note that the candidate models have the same number of parameters and the best fit is achieved with the COM-Poisson (geometric) model as both the AIC and BIC values for the COM-Poisson (geometric) model is the least and the log-likelihood function value is the maximum. To find an acceptable range of ϕ for the data set, we considered testing for different values of ϕ and plot the values of ϕ against the corresponding likelihood ratio statistic Λ. The corresponding plot is shown in Figure

4.3. We reject the likelihood ratio test at 10% level of significance if the value of the likelihood ratio statistic Λ exceeds $\chi^2_{1,1-\alpha} = 2.71$. Now, for $\Lambda = 2.71$, we have the corresponding value of ϕ to be 0.30 (from the plot) and hence an admissible range of ϕ for the data is $[0, 0.30)$. This further explains that the geometric model is the only acceptable model for the data among all those considered. The estimates of the parameters of the COM-Poisson (geometric) cure rate model are presented in Table 4.14.

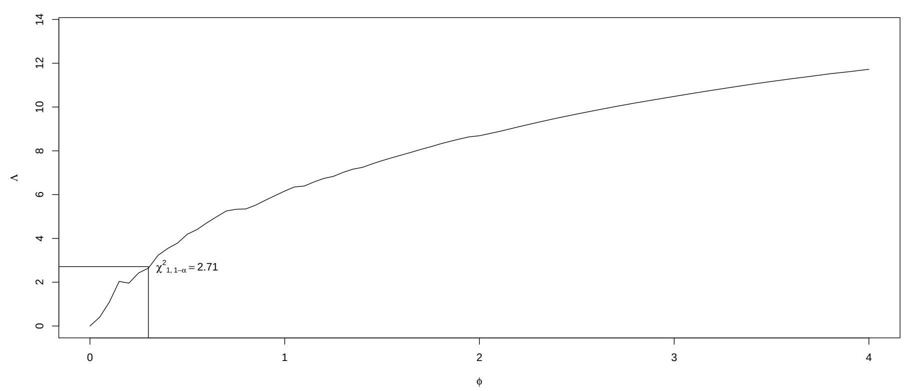

Figure 4.3: Values of ϕ against the corresponding Λ-statistic for gamma lifetime.

Finally, we deal with the estimation of the cure rate p_0. With the estimates obtained in Table 4.14, MLEs of the cure rates of patients stratified by nodule category are given by $\hat{p}_{0j} = \frac{1}{1+\exp(\hat{\beta}_0 + j\hat{\beta}_1)}, j = 1, 2, 3, 4$. With the procedure as described in Section 1.6.3, we present the estimates, standard errors and 95% confidence intervals of the estimates of cure rates of patient's corresponding to the four nodule categories $(1-4)$ in Table 4.15.

As done earlier in Section 3.6, a flexible analysis is also carried out by creating three dummy variables for the nodule category. The profile likelihood approach, in this case, again gave $\hat{\phi} \approx 0$ and so we once again consider the geometric model to be the working model. The estimates of the parameters of the COM-Poisson (geometric) model after creating the dummy variables are presented in Table 4.16. With the estimates in Table 4.16, estimates of cure rates are now obtained as 0.637, 0.541, 0.445 and 0.277 corresponding to the four nodule categories (1-4). It can be seen that these estimates of cure rates obtained after creating the dummy variables are quite close to those obtained when the nodule category is taken to be the only covariate. However, as mentioned earlier, this method is computationally more involved.

4.7 Model diagnosis

In this section, for the cutaneous melanoma data that we analyzed in the preceding section, we check the validity of the gamma assumption for the lifetime. For the gamma distribution considered in (1.4.4), we note that

$$F^{-1}(1 - S(t; \boldsymbol{\gamma})) = t,$$

where $F(\cdot)$ is the distribution function of the gamma distribution. This means that a scatter plot of the values of $F^{-1}(1 - \hat{S}(t_{(i)}))$ against $t_{(i)}$ should give a straight line if the assumption of the gamma distribution is valid, where $\hat{S}(t_{(i)})$ is the Kaplan-Meier estimate of the survival function and $t_{(i)}$ is the i-th ordered observed lifetime. For the cutaneous melanoma data, we calculated the Kaplan-Meier estimate of the survival function at the observed failure times and the plot of the values of $F^{-1}(1 - \hat{S}(t))$ against t is presented in Figure 4.4. Although the plot shows approximate linearity and as such the gamma distribution may be assumed for these data, we do notice some curvature in the plot, which suggests that the gamma distribution does not provide an accurate fit to the data. For this reason, we also considered formal goodness-of-fit tests for testing the hypothesis that the lifetime follows a gamma distribution.

A simple test can be based on the measure of correlation coefficient (r) between $F^{-1}(1-\hat{S}(t))$ and t. Noting that a perfect linearity between $F^{-1}(1-\hat{S}(t))$ and t would mean r=1, the critical region for this test will be to the left. Another test can be based on

$$SD = \frac{1}{n_1}\sum_{i=1}^{n_1}\left\{F^{-1}(1-\hat{S}(t_i)) - t_i\right\}^2$$

in which case, we will have the critical region for this test to the right.

We calculated the p-values for the above two tests by Monte Carlo simulation. For this purpose, we calculated the values of the above two test statistics for the considered dataset. We then generated 1000 such datasets and calculated the values of r and SD for each of the generated datasets, and determined the proportion of times r was less than and SD was greater than the corresponding values obtained from the observed data. The p-values for the tests based on r and SD came out to be 0.946 and 0.988, respectively, which clearly shows that the assumption of the gamma distribution for the lifetime is a valid one.

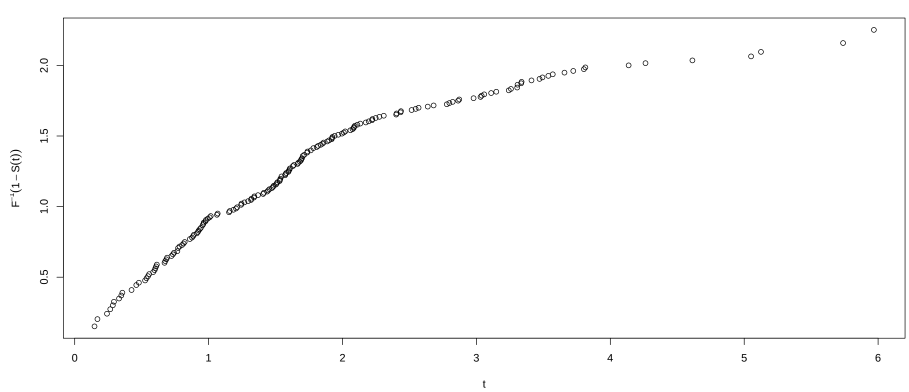

Figure 4.4: Scatter plot of the values of $F^{-1}(1-\hat{S}(t))$ against t.

Table 4.1: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the Bernoulli cure rate model with gamma lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP	
						90%	95%
400 $(110, 120, 90, 80)$	High	β_0 = -1.192	-1.209 (0.328)	-0.017	0.312	0.920	0.962
		$\beta_1 = 0.573$	0.580 (0.123)	0.007	0.119	0.915	0.958
		$\gamma_1 = 0.447$	0.445 (0.024)	-0.002	0.023	0.909	0.960
		$\gamma_2 = 2$	2.002 (0.074)	0.002	0.077	0.882	0.940
	Low	β_0 = -0.038	-0.044 (0.290)	-0.006	0.303	0.901	0.938
		$\beta_1 = 0.443$	0.450 (0.121)	0.007	0.125	0.895	0.950
		$\gamma_1 = 0.447$	0.446 (0.019)	-0.001	0.019	0.898	0.948
		$\gamma_2 = 2$	2.000 (0.057)	0.000	0.055	0.913	0.957
400 $(110, 120, 90, 80)$	High	β_0 = -1.192	-1.214 (0.333)	-0.022	0.349	0.880	0.947
		$\beta_1 = 0.573$	0.579 (0.125)	0.006	0.130	0.882	0.947
		$\gamma_1 = 0.632$	0.631 (0.033)	-0.001	0.032	0.908	0.955
		$\gamma_2 = 2$	2.007 (0.111)	0.007	0.112	0.896	0.948
	Low	β_0 = -0.038	-0.041 (0.293)	-0.004	0.294	0.903	0.950
		$\beta_1 = 0.443$	0.448 (0.122)	0.005	0.125	0.894	0.945
		$\gamma_1 = 0.632$	0.629 (0.026)	-0.003	0.027	0.896	0.946
		$\gamma_2 = 2$	2.005 (0.082)	0.005	0.084	0.892	0.946
400 $(110, 120, 90, 80)$	High	β_0 = -1.192	-1.221 (0.341)	-0.029	0.340	0.918	0.956
		$\beta_1 = 0.573$	0.584 (0.127)	0.011	0.126	0.911	0.958
		$\gamma_1 = 0.894$	0.893 (0.044)	-0.001	0.044	0.908	0.952
		$\gamma_2 = 4$	4.030 (0.351)	0.030	0.353	0.899	0.953
	Low	β_0 = -0.038	-0.039 (0.298)	-0.002	0.301	0.897	0.952
		$\beta_1 = 0.443$	0.448 (0.124)	0.005	0.125	0.899	0.948
		$\gamma_1 = 0.894$	0.892 (0.035)	-0.002	0.035	0.903	0.951
		$\gamma_2 = 4$	4.006 (0.245)	0.006	0.242	0.908	0.947
400 $(110, 120, 90, 80)$	High	β_0 = -1.192	-1.204 (0.353)	-0.013	0.348	0.912	0.959
		$\beta_1 = 0.573$	0.578 (0.130)	0.005	0.131	0.912	0.956
		$\gamma_1 = 1.265$	1.260 (0.058)	-0.005	0.060	0.891	0.936
		$\gamma_2 = 4$	4.060 (0.599)	0.060	0.619	0.899	0.948
	Low	β_0 = -0.038	-0.038 (0.304)	0.000	0.307	0.896	0.956
		$\beta_1 = 0.443$	0.447 (0.126)	0.004	0.128	0.900	0.955
		$\gamma_1 = 1.265$	1.263 (0.047)	-0.002	0.047	0.902	0.938
		$\gamma_2 = 4$	4.041 (0.383)	0.041	0.382	0.918	0.954
400 $(100, 100, 100, 100)$	High	β_0 = -1.192	-1.197 (0.350)	-0.005	0.356	0.895	0.943
		$\beta_1 = 0.573$	0.576 (0.124)	0.004	0.126	0.908	0.953
		$\gamma_1 = 0.894$	0.890 (0.043)	-0.004	0.044	0.892	0.942
		$\gamma_2 = 4$	4.020 (0.334)	0.020	0.345	0.896	0.948
	Low	β_0 = -0.038	-0.066 (0.304)	-0.029	0.305	0.896	0.950
		$\beta_1 = 0.443$	0.457 (0.119)	0.014	0.119	0.898	0.954
		$\gamma_1 = 0.894$	0.891 (0.035)	-0.003	0.037	0.883	0.942
		$\gamma_2 = 4$	4.012 (0.241)	0.012	0.243	0.894	0.945
600 $(165, 180, 135, 120)$	High	β_0 = -1.192	-1.204 (0.278)	-0.012	0.279	0.900	0.947
		$\beta_1 = 0.573$	0.579 (0.104)	0.006	0.107	0.895	0.941
		$\gamma_1 = 0.894$	0.890 (0.036)	-0.004	0.036	0.890	0.942
		$\gamma_2 = 4$	4.014 (0.284)	0.014	0.281	0.911	0.948
	Low	β_0 = -0.038	-0.037 (0.243)	0.001	0.242	0.897	0.944
		$\beta_1 = 0.443$	0.444 (0.101)	0.001	0.099	0.912	0.948
		$\gamma_1 = 0.894$	0.893 (0.029)	-0.001	0.031	0.891	0.939
		$\gamma_2 = 4$	4.005 (0.200)	0.005	0.202	0.903	0.956

Table 4.2: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the Poisson cure rate model with gamma lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP	
						90%	95%
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.200 (0.310)	-0.008	0.300	0.927	0.966
		$\beta_1 = 0.573$	0.577 (0.115)	0.005	0.111	0.910	0.960
		$\gamma_1 = 0.447$	0.445 (0.023)	-0.002	0.024	0.891	0.935
		$\gamma_2 = 2$	2.000 (0.088)	0.000	0.090	0.893	0.944
	Low	$\beta_0 =$ -0.038	-0.030 (0.268)	0.008	0.271	0.897	0.946
		$\beta_1 = 0.443$	0.444 (0.109)	0.001	0.111	0.898	0.956
		$\gamma_1 = 0.447$	0.446 (0.018)	-0.001	0.019	0.895	0.945
		$\gamma_2 = 2$	1.999 (0.071)	-0.001	0.073	0.888	0.948
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.195 (0.311)	-0.003	0.313	0.890	0.954
		$\beta_1 = 0.573$	0.573 (0.115)	0.000	0.113	0.903	0.963
		$\gamma_1 = 0.632$	0.627 (0.031)	-0.005	0.032	0.893	0.946
		$\gamma_2 = 2$	2.015 (0.137)	0.015	0.137	0.908	0.954
	Low	$\beta_0 =$ -0.038	-0.040 (0.268)	-0.002	0.266	0.906	0.957
		$\beta_1 = 0.443$	0.445 (0.109)	0.002	0.109	0.902	0.953
		$\gamma_1 = 0.632$	0.630 (0.025)	-0.002	0.025	0.889	0.938
		$\gamma_2 = 2$	2.003 (0.108)	0.003	0.108	0.902	0.953
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.207 (0.314)	-0.016	0.308	0.911	0.953
		$\beta_1 = 0.573$	0.578 (0.115)	0.005	0.113	0.891	0.946
		$\gamma_1 = 0.894$	0.890 (0.042)	-0.004	0.041	0.905	0.946
		$\gamma_2 = 4$	4.066 (0.466)	0.066	0.472	0.902	0.954
	Low	$\beta_0 =$ -0.038	-0.025 (0.270)	0.013	0.271	0.885	0.958
		$\beta_1 = 0.443$	0.443 (0.109)	0.000	0.110	0.906	0.952
		$\gamma_1 = 0.894$	0.892 (0.032)	-0.002	0.032	0.903	0.943
		$\gamma_2 = 4$	4.010 (0.343)	0.010	0.356	0.884	0.934
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.188 (0.324)	0.004	0.331	0.901	0.949
		$\beta_1 = 0.573$	0.573 (0.116)	0.000	0.120	0.884	0.947
		$\gamma_1 = 1.265$	1.261 (0.055)	-0.004	0.058	0.874	0.934
		$\gamma_2 = 4$	4.088 (0.906)	0.088	0.898	0.902	0.951
	Low	$\beta_0 =$ -0.038	-0.037 (0.272)	0.001	0.267	0.915	0.959
		$\beta_1 = 0.443$	0.446 (0.109)	0.003	0.106	0.908	0.953
		$\gamma_1 = 1.265$	1.262 (0.042)	-0.003	0.042	0.896	0.944
		$\gamma_2 = 4$	4.055 (0.604)	0.055	0.597	0.909	0.957
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.192	-1.223 (0.323)	-0.032	0.329	0.897	0.953
		$\beta_1 = 0.573$	0.586 (0.112)	0.013	0.114	0.896	0.956
		$\gamma_1 = 0.894$	0.890 (0.040)	-0.004	0.041	0.897	0.941
		$\gamma_2 = 4$	4.057 (0.451)	0.057	0.463	0.898	0.950
	Low	$\beta_0 =$ -0.038	-0.058 (0.276)	-0.020	0.272	0.911	0.952
		$\beta_1 = 0.443$	0.452 (0.105)	0.009	0.104	0.910	0.952
		$\gamma_1 = 0.894$	0.890 (0.032)	-0.004	0.032	0.899	0.949
		$\gamma_2 = 4$	4.038 (0.342)	0.038	0.347	0.898	0.952
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.192	-1.197 (0.256)	-0.005	0.257	0.910	0.957
		$\beta_1 = 0.573$	0.575 (0.094)	0.002	0.097	0.892	0.944
		$\gamma_1 = 0.894$	0.892 (0.034)	-0.002	0.034	0.909	0.951
		$\gamma_2 = 4$	4.025 (0.380)	0.025	0.387	0.903	0.944
	Low	$\beta_0 =$ -0.038	-0.040 (0.219)	-0.002	0.216	0.905	0.955
		$\beta_1 = 0.443$	0.445 (0.089)	0.001	0.089	0.898	0.945
		$\gamma_1 = 0.894$	0.893 (0.026)	-0.001	0.026	0.889	0.945
		$\gamma_2 = 4$	4.009 (0.280)	0.009	0.284	0.897	0.943

Table 4.3: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the geometric cure rate model with gamma lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP 90%	CP 95%
400 (110, 120, 90, 80)	High	$\beta_0 = $ -1.192	-1.209 (0.285)	-0.017	0.291	0.896	0.948
		$\beta_1 = 0.573$	0.577 (0.102)	0.005	0.102	0.896	0.948
		$\gamma_1 = 0.447$	0.445 (0.023)	-0.002	0.023	0.891	0.944
		$\gamma_2 = 2$	2.008 (0.110)	0.008	0.109	0.906	0.959
	Low	$\beta_0 = $ -0.038	-0.040 (0.232)	-0.003	0.235	0.900	0.947
		$\beta_1 = 0.443$	0.446 (0.087)	0.003	0.087	0.905	0.948
		$\gamma_1 = 0.447$	0.446 (0.017)	-0.001	0.018	0.877	0.940
		$\gamma_2 = 2$	2.001 (0.098)	0.001	0.096	0.912	0.959
400 (110, 120, 90, 80)	High	$\beta_0 = $ -1.192	-1.199 (0.286)	-0.007	0.287	0.901	0.956
		$\beta_1 = 0.573$	0.578 (0.100)	0.006	0.103	0.894	0.942
		$\gamma_1 = 0.632$	0.630 (0.030)	-0.002	0.030	0.884	0.943
		$\gamma_2 = 2$	2.005 (0.178)	0.005	0.183	0.880	0.945
	Low	$\beta_0 = $ -0.038	-0.034 (0.232)	0.004	0.242	0.886	0.938
		$\beta_1 = 0.443$	0.443 (0.086)	0.000	0.090	0.889	0.951
		$\gamma_1 = 0.632$	0.630 (0.023)	-0.002	0.023	0.891	0.952
		$\gamma_2 = 2$	2.006 (0.153)	0.006	0.151	0.899	0.948
400 (110, 120, 90, 80)	High	$\beta_0 = $ -1.192	-1.209 (0.291)	-0.017	0.291	0.894	0.947
		$\beta_1 = 0.573$	0.581 (0.099)	0.009	0.098	0.905	0.955
		$\gamma_1 = 0.894$	0.890 (0.039)	-0.004	0.040	0.892	0.937
		$\gamma_2 = 4$	4.056 (0.642)	0.056	0.630	0.900	0.956
	Low	$\beta_0 = $ -0.038	-0.023 (0.234)	0.015	0.230	0.911	0.955
		$\beta_1 = 0.443$	0.441 (0.086)	-0.002	0.082	0.920	0.955
		$\gamma_1 = 0.894$	0.892 (0.029)	-0.002	0.030	0.892	0.942
		$\gamma_2 = 4$	4.012 (0.513)	0.012	0.527	0.894	0.943
400 (110, 120, 90, 80)	High	$\beta_0 = $ -1.192	-1.186 (0.336)	0.006	0.332	0.926	0.962
		$\beta_1 = 0.573$	0.579 (0.098)	0.007	0.096	0.896	0.958
		$\gamma_1 = 1.265$	1.260 (0.051)	-0.005	0.052	0.902	0.940
		$\gamma_2 = 4$	4.155 (1.438)	0.155	1.446	0.911	0.954
	Low	$\beta_0 = $ -0.038	-0.039 (0.245)	-0.001	0.255	0.886	0.935
		$\beta_1 = 0.443$	0.445 (0.085)	0.001	0.089	0.886	0.935
		$\gamma_1 = 1.265$	1.258 (0.038)	-0.007	0.038	0.905	0.948
		$\gamma_2 = 4$	4.188 (1.036)	0.188	1.070	0.903	0.950
400 (100, 100, 100, 100)	High	$\beta_0 = $ -1.192	-1.193 (0.298)	-0.001	0.300	0.896	0.953
		$\beta_1 = 0.573$	0.575 (0.097)	0.003	0.097	0.897	0.944
		$\gamma_1 = 0.894$	0.888 (0.038)	-0.006	0.039	0.895	0.936
		$\gamma_2 = 4$	4.055 (0.627)	0.055	0.643	0.895	0.948
	Low	$\beta_0 = $ -0.038	-0.040 (0.240)	-0.003	0.241	0.891	0.948
		$\beta_1 = 0.443$	0.447 (0.083)	0.004	0.084	0.897	0.941
		$\gamma_1 = 0.894$	0.892 (0.029)	-0.002	0.030	0.895	0.949
		$\gamma_2 = 4$	4.043 (0.519)	0.043	0.526	0.897	0.948
600 (165, 180, 135, 120)	High	$\beta_0 = $ -1.192	-1.204 (0.237)	-0.012	0.240	0.893	0.950
		$\beta_1 = 0.573$	0.578 (0.081)	0.005	0.081	0.898	0.943
		$\gamma_1 = 0.894$	0.892 (0.032)	-0.002	0.032	0.907	0.948
		$\gamma_2 = 4$	4.046 (0.524)	0.046	0.540	0.891	0.955
	Low	$\beta_0 = $ -0.038	-0.061 (0.191)	-0.023	0.198	0.893	0.949
		$\beta_1 = 0.443$	0.453 (0.070)	0.010	0.071	0.905	0.954
		$\gamma_1 = 0.894$	0.892 (0.024)	-0.002	0.026	0.879	0.929
		$\gamma_2 = 4$	4.028 (0.419)	0.028	0.422	0.898	0.945

Table 4.4: Estimates, bias, and root mean square error (RMSE) of cured proportions corresponding to four groups for the Bernoulli cure rate model with gamma lifetime.

n	γ	p_0	Estimate	Bias	RMSE
400 $(110, 120, 90, 80)$	$(0.447, 2)$	p_{01} =0.650	0.651	0.001	0.047
		p_{02} =0.512	0.512	0.001	0.033
		p_{03} =0.371	0.371	0.000	0.033
		p_{04} =0.250	0.250	0.000	0.042
		p_{01} =0.400	0.401	0.001	0.047
		p_{02} =0.300	0.299	-0.001	0.028
		p_{03} =0.216	0.214	-0.001	0.027
		p_{04} =0.150	0.150	0.000	0.032
400 $(110, 120, 90, 80)$	$(0.632, 2)$	p_{01} =0.650	0.652	0.002	0.053
		p_{02} =0.512	0.514	0.002	0.037
		p_{03} =0.371	0.373	0.002	0.035
		p_{04} =0.250	0.252	0.002	0.044
		p_{01} =0.400	0.401	0.001	0.045
		p_{02} =0.300	0.299	-0.001	0.026
		p_{03} =0.216	0.215	-0.001	0.028
		p_{04} =0.150	0.151	0.001	0.033
400 $(110, 120, 90, 80)$	$(0.894, 4)$	p_{01} =0.650	0.652	0.002	0.051
		p_{02} =0.512	0.513	0.001	0.037
		p_{03} =0.371	0.371	-0.001	0.035
		p_{04} =0.250	0.249	-0.001	0.043
		p_{01} =0.400	0.400	0.000	0.047
		p_{02} =0.300	0.299	-0.001	0.027
		p_{03} =0.216	0.215	-0.001	0.028
		p_{04} =0.150	0.151	0.001	0.033
400 $(110, 120, 90, 80)$	$(1.265, 4)$	p_{01} =0.650	0.650	0.000	0.053
		p_{02} =0.512	0.512	0.000	0.039
		p_{03} =0.371	0.371	0.000	0.038
		p_{04} =0.250	0.251	0.001	0.047
		p_{01} =0.400	0.400	0.000	0.048
		p_{02} =0.300	0.299	-0.001	0.028
		p_{03} =0.216	0.215	-0.001	0.028
		p_{04} =0.150	0.151	0.001	0.033
400 $(100, 100, 100, 100)$	$(0.894, 4)$	p_{01} =0.650	0.648	-0.002	0.056
		p_{02} =0.512	0.511	-0.001	0.040
		p_{03} =0.371	0.371	-0.001	0.035
		p_{04} =0.250	0.251	0.001	0.042
		p_{01} =0.400	0.405	0.005	0.049
		p_{02} =0.300	0.301	0.001	0.029
		p_{03} =0.216	0.215	-0.001	0.026
		p_{04} =0.150	0.149	-0.001	0.030
600 $(165, 180, 135, 120)$	$(0.894, 4)$	p_{01} =0.650	0.650	0.000	0.042
		p_{02} =0.512	0.512	0.000	0.030
		p_{03} =0.371	0.371	-0.001	0.030
		p_{04} =0.250	0.250	0.000	0.038
		p_{01} =0.400	0.400	0.000	0.038
		p_{02} =0.300	0.300	0.000	0.023
		p_{03} =0.216	0.216	0.000	0.022
		p_{04} =0.150	0.151	0.001	0.026

Table 4.5: Estimates, bias, and root mean square error (RMSE) of cured proportions corresponding to four groups for the Poisson cure rate model with gamma lifetime.

n	γ	p_0	Estimate	Bias	RMSE
400 $(110, 120, 90, 80)$	$(0.447, 2)$	p_{01} =0.650	0.649	-0.001	0.046
		p_{02} =0.512	0.511	0.000	0.033
		p_{03} =0.371	0.371	-0.001	0.032
		p_{04} =0.250	0.250	0.000	0.039
		p_{01} =0.400	0.399	-0.001	0.043
		p_{02} =0.300	0.298	-0.001	0.027
		p_{03} =0.216	0.215	-0.001	0.026
		p_{04} =0.150	0.151	0.001	0.030
400 $(110, 120, 90, 80)$	$(0.632, 2)$	p_{01} =0.650	0.649	-0.001	0.049
		p_{02} =0.512	0.512	0.001	0.036
		p_{03} =0.371	0.373	0.001	0.034
		p_{04} =0.250	0.253	0.003	0.040
		p_{01} =0.400	0.401	0.001	0.042
		p_{02} =0.300	0.300	0.000	0.026
		p_{03} =0.216	0.216	0.000	0.026
		p_{04} =0.150	0.152	0.002	0.030
400 $(110, 120, 90, 80)$	$(0.894, 4)$	p_{01} =0.650	0.651	0.001	0.048
		p_{02} =0.512	0.513	0.001	0.037
		p_{03} =0.371	0.372	0.001	0.036
		p_{04} =0.250	0.251	0.001	0.042
		p_{01} =0.400	0.398	-0.002	0.043
		p_{02} =0.300	0.298	-0.002	0.028
		p_{03} =0.216	0.215	-0.001	0.027
		p_{04} =0.150	0.151	0.001	0.030
400 $(110, 120, 90, 80)$	$(1.265, 4)$	p_{01} =0.650	0.647	-0.003	0.054
		p_{02} =0.512	0.511	-0.001	0.043
		p_{03} =0.371	0.372	0.000	0.042
		p_{04} =0.250	0.252	0.002	0.047
		p_{01} =0.400	0.400	0.000	0.044
		p_{02} =0.300	0.299	-0.001	0.029
		p_{03} =0.216	0.215	0.000	0.027
		p_{04} =0.150	0.151	0.001	0.030
400 $(100, 100, 100, 100)$	$(0.894, 4)$	p_{01} =0.650	0.652	0.002	0.052
		p_{02} =0.512	0.513	0.001	0.040
		p_{03} =0.371	0.370	-0.001	0.035
		p_{04} =0.250	0.248	-0.002	0.040
		p_{01} =0.400	0.404	0.004	0.045
		p_{02} =0.300	0.301	0.001	0.029
		p_{03} =0.216	0.216	0.000	0.026
		p_{04} =0.150	0.150	0.000	0.028
600 $(165, 180, 135, 120)$	$(0.894, 4)$	p_{01} =0.650	0.650	0.000	0.040
		p_{02} =0.512	0.512	0.000	0.030
		p_{03} =0.371	0.372	0.000	0.031
		p_{04} =0.250	0.251	0.001	0.037
		p_{01} =0.400	0.401	0.001	0.035
		p_{02} =0.300	0.300	0.000	0.022
		p_{03} =0.216	0.216	0.000	0.022
		p_{04} =0.150	0.151	0.001	0.025

Table 4.6: Estimates, bias, and root mean square error (RMSE) of cured proportions corresponding to four groups for the geometric cure rate model with gamma lifetime.

n	γ	p_0	Estimate	Bias	RMSE
400 $(110, 120, 90, 80)$	$(0.447, 2)$	p_{01} =0.650	0.651	0.001	0.046
		p_{02} =0.512	0.514	0.002	0.036
		p_{03} =0.371	0.373	0.001	0.033
		p_{04} =0.250	0.252	0.002	0.037
		p_{01} =0.400	0.401	0.001	0.040
		p_{02} =0.300	0.300	0.000	0.027
		p_{03} =0.216	0.215	0.000	0.024
		p_{04} =0.150	0.150	0.000	0.025
400 $(110, 120, 90, 80)$	$(0.632, 2)$	p_{01} =0.650	0.649	-0.001	0.046
		p_{02} =0.512	0.510	-0.001	0.036
		p_{03} =0.371	0.370	-0.002	0.034
		p_{04} =0.250	0.249	-0.001	0.039
		p_{01} =0.400	0.400	0.000	0.041
		p_{02} =0.300	0.300	0.000	0.028
		p_{03} =0.216	0.216	0.000	0.025
		p_{04} =0.150	0.151	0.001	0.026
400 $(110, 120, 90, 80)$	$(0.894, 4)$	p_{01} =0.650	0.650	0.000	0.048
		p_{02} =0.512	0.512	0.000	0.038
		p_{03} =0.371	0.370	-0.001	0.034
		p_{04} =0.250	0.249	-0.001	0.037
		p_{01} =0.400	0.398	-0.002	0.041
		p_{02} =0.300	0.298	-0.002	0.029
		p_{03} =0.216	0.215	0.000	0.026
		p_{04} =0.150	0.151	0.001	0.026
400 $(110, 120, 90, 80)$	$(1.265, 4)$	p_{01} =0.650	0.645	-0.005	0.062
		p_{02} =0.512	0.507	-0.005	0.056
		p_{03} =0.371	0.367	-0.004	0.050
		p_{04} =0.250	0.247	-0.003	0.046
		p_{01} =0.400	0.401	0.001	0.046
		p_{02} =0.300	0.300	0.001	0.033
		p_{03} =0.216	0.216	0.001	0.028
		p_{04} =0.150	0.151	0.001	0.028
400 $(100, 100, 100, 100)$	$(0.894, 4)$	p_{01} =0.650	0.648	-0.002	0.050
		p_{02} =0.512	0.511	-0.001	0.040
		p_{03} =0.371	0.371	-0.001	0.035
		p_{04} =0.250	0.250	0.000	0.036
		p_{01} =0.400	0.401	0.001	0.043
		p_{02} =0.300	0.300	0.000	0.029
		p_{03} =0.216	0.215	0.000	0.025
		p_{04} =0.150	0.150	0.000	0.024
600 $(165, 180, 135, 120)$	$(0.894, 4)$	p_{01} =0.650	0.651	0.001	0.040
		p_{02} =0.512	0.512	0.000	0.032
		p_{03} =0.371	0.371	0.000	0.030
		p_{04} =0.250	0.250	0.000	0.031
		p_{01} =0.400	0.404	0.004	0.035
		p_{02} =0.300	0.301	0.001	0.024
		p_{03} =0.216	0.215	0.000	0.021
		p_{04} =0.150	0.149	-0.001	0.021

Table 4.7: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the COM-Poisson cure rate model with ϕ fixed at 0.5 for gamma lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP	
						90%	95%
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.197 (0.303)	-0.005	0.309	0.898	0.941
		$\beta_1 = 0.573$	0.577 (0.112)	0.004	0.113	0.902	0.937
		$\gamma_1 = 0.447$	0.445 (0.023)	-0.002	0.023	0.894	0.952
		$\gamma_2 = 2$	2.002 (0.094)	0.002	0.094	0.896	0.951
	Low	$\beta_0 =$ -0.038	-0.039 (0.258)	-0.002	0.254	0.912	0.954
		$\beta_1 = 0.443$	0.445 (0.104)	0.002	0.105	0.904	0.945
		$\gamma_1 = 0.447$	0.447 (0.018)	0.000	0.018	0.898	0.943
		$\gamma_2 = 2$	2.001 (0.079)	0.001	0.076	0.906	0.956
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.200 (0.303)	-0.008	0.303	0.903	0.952
		$\beta_1 = 0.573$	0.577 (0.111)	0.004	0.109	0.912	0.956
		$\gamma_1 = 0.632$	0.628 (0.031)	-0.004	0.031	0.893	0.942
		$\gamma_2 = 2$	2.014 (0.150)	0.014	0.155	0.888	0.948
	Low	$\beta_0 =$ -0.038	-0.031 (0.259)	0.007	0.254	0.907	0.961
		$\beta_1 = 0.443$	0.444 (0.104)	0.001	0.101	0.910	0.960
		$\gamma_1 = 0.632$	0.631 (0.024)	-0.001	0.024	0.898	0.948
		$\gamma_2 = 2$	1.996 (0.120)	-0.004	0.119	0.900	0.949
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.190 (0.306)	0.001	0.308	0.892	0.945
		$\beta_1 = 0.573$	0.575 (0.111)	0.003	0.113	0.885	0.948
		$\gamma_1 = 0.894$	0.889 (0.041)	-0.005	0.041	0.890	0.948
		$\gamma_2 = 4$	4.022 (0.513)	0.022	0.514	0.905	0.952
	Low	$\beta_0 =$ -0.038	-0.042 (0.259)	-0.005	0.261	0.900	0.952
		$\beta_1 = 0.443$	0.447 (0.103)	0.004	0.107	0.887	0.950
		$\gamma_1 = 0.894$	0.890 (0.031)	-0.004	0.031	0.896	0.944
		$\gamma_2 = 4$	4.028 (0.389)	0.028	0.390	0.897	0.949
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.195 (0.318)	-0.004	0.314	0.906	0.951
		$\beta_1 = 0.573$	0.577 (0.110)	0.004	0.112	0.894	0.940
		$\gamma_1 = 1.265$	1.262 (0.054)	-0.003	0.054	0.900	0.940
		$\gamma_2 = 4$	4.102 (1.050)	0.102	1.079	0.902	0.952
	Low	$\beta_0 =$ -0.038	-0.013 (0.263)	0.024	0.270	0.897	0.951
		$\beta_1 = 0.443$	0.440 (0.103)	-0.003	0.104	0.893	0.964
		$\gamma_1 = 1.265$	1.262 (0.041)	-0.003	0.040	0.906	0.957
		$\gamma_2 = 4$	4.038 (0.708)	0.038	0.725	0.888	0.947
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.192	-1.183 (0.314)	0.009	0.309	0.909	0.949
		$\beta_1 = 0.573$	0.572 (0.108)	-0.001	0.105	0.905	0.955
		$\gamma_1 = 0.894$	0.891 (0.040)	-0.003	0.039	0.912	0.956
		$\gamma_2 = 4$	3.987 (0.497)	-0.013	0.495	0.908	0.945
	Low	$\beta_0 =$ -0.038	-0.046 (0.265)	-0.009	0.257	0.915	0.961
		$\beta_1 = 0.443$	0.448 (0.100)	0.005	0.099	0.917	0.952
		$\gamma_1 = 0.894$	0.891 (0.031)	-0.003	0.031	0.894	0.940
		$\gamma_2 = 4$	4.033 (0.387)	0.033	0.395	0.900	0.952
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.192	-1.196 (0.249)	-0.005	0.254	0.900	0.944
		$\beta_1 = 0.573$	0.575 (0.090)	0.002	0.091	0.901	0.949
		$\gamma_1 = 0.894$	0.891 (0.033)	-0.003	0.034	0.880	0.944
		$\gamma_2 = 4$	4.036 (0.421)	0.036	0.415	0.900	0.954
	Low	$\beta_0 =$ -0.038	-0.037 (0.211)	0.000	0.213	0.898	0.949
		$\beta_1 = 0.443$	0.445 (0.084)	0.002	0.086	0.890	0.947
		$\gamma_1 = 0.894$	0.893 (0.026)	-0.001	0.025	0.907	0.963
		$\gamma_2 = 4$	4.017 (0.317)	0.017	0.325	0.886	0.944

Table 4.8: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the COM-Poisson cure rate model with $\phi = 0.5$ for gamma lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP	
						90%	95%
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.211 (0.299)	-0.020	0.325	0.885	0.942
		$\beta_1 = 0.573$	0.579 (0.109)	0.007	0.120	0.875	0.935
		$\gamma_1 = 0.447$	0.441 (0.023)	-0.006	0.024	0.871	0.922
		$\gamma_2 = 2$	1.998 (0.096)	-0.002	0.173	0.570	0.676
		$\phi = 0.5$	0.679 (−)	0.179	0.814	−	−
	Low	$\beta_0 =$ -0.038	-0.004 (0.248)	0.034	0.302	0.815	0.879
		$\beta_1 = 0.443$	0.427 (0.097)	-0.016	0.125	0.794	0.864
		$\gamma_1 = 0.447$	0.439 (0.018)	-0.008	0.022	0.813	0.880
		$\gamma_2 = 2$	1.944 (0.081)	-0.056	0.222	0.294	0.371
		$\phi = 0.5$	0.550 (−)	0.050	0.746	−	−
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.207 (0.300)	-0.015	0.336	0.862	0.922
		$\beta_1 = 0.573$	0.578 (0.109)	0.005	0.124	0.858	0.929
		$\gamma_1 = 0.632$	0.624 (0.031)	-0.008	0.034	0.848	0.921
		$\gamma_2 = 2$	1.978 (0.151)	-0.022	0.265	0.580	0.708
		$\phi = 0.5$	0.653 (−)	0.153	0.821	−	−
	Low	$\beta_0 =$ -0.038	0.003 (0.250)	0.040	0.306	0.807	0.894
		$\beta_1 = 0.443$	0.426 (0.098)	-0.017	0.126	0.770	0.867
		$\gamma_1 = 0.632$	0.620 (0.023)	-0.012	0.031	0.767	0.853
		$\gamma_2 = 2$	1.960 (0.122)	-0.040	0.320	0.304	0.385
		$\phi = 0.5$	0.597 (−)	0.097	0.753	−	−
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.191 (0.303)	0.001	0.353	0.853	0.913
		$\beta_1 = 0.573$	0.576 (0.107)	0.003	0.125	0.848	0.915
		$\gamma_1 = 0.894$	0.880 (0.040)	-0.014	0.047	0.842	0.915
		$\gamma_2 = 4$	3.940 (0.519)	-0.060	0.837	0.657	0.756
		$\phi = 0.5$	0.613 (−)	0.113	0.818	−	−
	Low	$\beta_0 =$ -0.038	0.000 (0.252)	0.038	0.310	0.811	0.895
		$\beta_1 = 0.443$	0.425 (0.097)	-0.018	0.127	0.768	0.858
		$\gamma_1 = 0.894$	0.878 (0.031)	-0.016	0.045	0.701	0.800
		$\gamma_2 = 4$	3.914 (0.390)	-0.086	0.917	0.401	0.488
		$\phi = 0.5$	0.598 (−)	0.098	0.755	−	−
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.212 (0.312)	-0.020	0.353	0.850	0.920
		$\beta_1 = 0.573$	0.561 (0.105)	-0.012	0.120	0.856	0.915
		$\gamma_1 = 1.265$	1.239 (0.053)	-0.026	0.067	0.798	0.859
		$\gamma_2 = 4$	4.460 (1.084)	0.460	1.597	0.764	0.838
		$\phi = 0.5$	0.628 (−)	0.128	0.828	−	−
	Low	$\beta_0 =$ -0.038	0.005 (0.257)	0.043	0.314	0.829	0.909
		$\beta_1 = 0.443$	0.421 (0.096)	-0.022	0.121	0.799	0.882
		$\gamma_1 = 1.265$	1.235 (0.040)	-0.030	0.073	0.565	0.656
		$\gamma_2 = 4$	3.970 (0.708)	-0.030	1.437	0.510	0.612
		$\phi = 0.5$	0.550 (−)	0.050	0.702	−	−
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.192	-1.181 (0.311)	0.011	0.353	0.839	0.908
		$\beta_1 = 0.573$	0.571 (0.105)	-0.001	0.119	0.849	0.906
		$\gamma_1 = 0.894$	0.880 (0.039)	-0.014	0.048	0.814	0.879
		$\gamma_2 = 4$	3.985 (0.502)	-0.015	0.848	0.612	0.725
		$\phi = 0.5$	0.649 (−)	0.149	0.819	−	−
	Low	$\beta_0 =$ -0.038	0.021 (0.257)	0.059	0.316	0.813	0.887
		$\beta_1 = 0.443$	0.416 (0.094)	-0.027	0.122	0.781	0.843
		$\gamma_1 = 0.894$	0.875 (0.030)	-0.019	0.049	0.644	0.730
		$\gamma_2 = 4$	3.844 (0.386)	-0.156	0.925	0.348	0.442
		$\phi = 0.5$	0.550 (−)	0.050	0.720	−	−
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.192	-1.145 (0.246)	0.046	0.277	0.861	0.920
		$\beta_1 = 0.573$	0.556 (0.087)	-0.017	0.099	0.843	0.921
		$\gamma_1 = 0.894$	0.881 (0.033)	-0.013	0.040	0.809	0.877
		$\gamma_2 = 4$	3.929 (0.422)	-0.071	0.784	0.534	0.654
		$\phi = 0.5$	0.579 (−)	0.079	0.758	−	−
	Low	$\beta_0 =$ -0.038	0.024 (0.204)	0.062	0.259	0.799	0.874
		$\beta_1 = 0.443$	0.412 (0.078)	-0.031	0.106	0.756	0.824
		$\gamma_1 = 0.894$	0.875 (0.025)	-0.019	0.044	0.600	0.705
		$\gamma_2 = 4$	3.824 (0.317)	-0.176	0.835	0.312	0.390
		$\phi = 0.5$	0.497 (−)	-0.003	0.658	−	−

Table 4.9: Observed levels (in bold) and powers of the likelihood ratio test for gamma lifetime.

Fitted model	True COM-Poisson model $\phi = 0$	$\phi = 0.5$	$\phi = 1$	$\phi = 2$	$\phi \to \infty$
			Setting 1		
geometric	**0.013**	0.202	0.361	0.586	0.920
Poisson	0.752	0.216	**0.107**	0.030	0.063
Bernoulli	0.993	0.857	0.690	0.370	**0.049**
			Setting 2		
geometric	**0.008**	0.229	0.434	0.694	0.969
Poisson	0.905	0.321	**0.123**	0.067	0.253
Bernoulli	1.000	0.947	0.795	0.485	**0.045**
			Setting 3		
geometric	**0.022**	0.144	0.240	0.370	0.615
Poisson	0.405	0.099	**0.047**	0.014	0.002
Bernoulli	0.902	0.589	0.398	0.255	**0.064**

Table 4.10: Observed selection rates based on AIC* with gamma lifetime.

Fitted model	True COM-Poisson model $\phi = 0$	$\phi = 0.5$	$\phi = 1$	$\phi = 2$	$\phi \to \infty$
			Setting 1		
geometric	0.852	0.324	0.180	0.057	0.006
Poisson	0.147	0.620	0.684	0.565	0.156
Bernoulli	0.001	0.056	0.136	0.378	0.838
			Setting 2		
geometric	0.894	0.285	0.129	0.031	0.001
Poisson	0.104	0.693	0.757	0.622	0.116
Bernoulli	0.002	0.022	0.114	0.347	0.883
			Setting 3		
geometric	0.765	0.373	0.255	0.142	0.036
Poisson	0.214	0.469	0.484	0.426	0.233
Bernoulli	0.021	0.158	0.261	0.432	0.731

*In all cases, the results are the same for the Bayesian information criterion as well.

Table 4.11: TRB (in %) (TRE) in estimation of cured proportions when fitting different models for a given true model with gamma lifetime.

Fitted model	True model: geometric	True model: Poisson	True model: Bernoulli
		Setting 1	
geometric	2.530 (-)	36.211 (0.738)	67.552 (0.453)
Poisson	24.464 (0.706)	1.501 (-)	26.766 (0.872)
Bernoulli	10.643 (0.715)	5.300 (0.891)	1.599 (-)
		Setting 2	
geometric	1.360 (-)	35.176 (0.659)	66.393 (0.336)
Poisson	26.192 (0.625)	0.710 (-)	25.078 (0.786)
Bernoulli	12.014 (0.674)	6.177 (0.859)	1.122 (-)
		Setting 3	
geometric	1.356 (-)	19.543 (0.802)	36.814 (0.502)
Poisson	13.700 (0.819)	1.641 (-)	14.548 (0.851)
Bernoulli	15.839 (0.705)	9.004 (0.883)	0.646 (-)

Table 4.12: TRB (in %) and TRE when using AIC as a model selection criterion between the three considered models with gamma lifetime.

True model	TRB (%)	TRE
	Setting 1	
geometric	6.141	0.915
Poisson	10.210	0.925
Bernoulli	4.333	0.995
	Setting 2	
geometric	4.438	0.915
Poisson	7.034	0.930
Bernoulli	3.999	0.976
	Setting 3	
geometric	4.309	0.923
Poisson	8.860	0.919
Bernoulli	4.118	0.969

Table 4.13: AIC, BIC and maximized log-likelihood function (l) values for different cure rate models with gamma lifetime.

Model	AIC	BIC	l
COM-Poisson (geometric)	**1024.088**	**1040.220**	**-508.044**
COM-Poisson ($\phi = 0.5$)	1028.280	1044.412	-510.140
Poisson	1030.248	1046.380	-511.124
COM-Poisson ($\phi = 2$)	1032.776	1048.908	-512.388
Bernoulli	1037.628	1053.760	-514.814

Table 4.14: Maximum likelihood estimates of the parameters of the COM-Poisson (geometric) cure rate model with gamma lifetime.

Parameter	Estimate	Standard error
β_0	-1.128	0.251
β_1	0.498	0.089
γ_1	0.632	0.035
γ_2	0.348	0.040

Table 4.15: Estimates, standard errors, and 95% confidence intervals (CI) of cure rates of patients stratified by nodule category for gamma lifetime.

Nodule category	Cure rate	Estimate	Standard error	95% CI
1	p_{01}	0.653	0.041	$(0.571, 0.734)$
2	p_{02}	0.533	0.035	$(0.465, 0.602)$
3	p_{03}	0.410	0.036	$(0.340, 0.480)$
4	p_{04}	0.297	0.041	$(0.216, 0.378)$

Table 4.16: Maximum likelihood estimates of the parameters of the COM-Poisson (geometric) cure rate model for gamma lifetime and with dummy variables for the nodule category.

Parameter	Estimate	Standard error
β_0^*	0.962	0.227
β_1^*	-1.524	0.281
β_2^*	-1.127	0.262
β_3^*	-0.742	0.285
γ_1^*	0.631	0.034
γ_2^*	0.348	0.039

Chapter 5

Likelihood inference for Weibull lifetime distribution

5.1 Introduction

In this chapter, we develop in detail the steps of the EM algorithm for the determination of the MLEs of the parameters of different cure rate models by assuming the lifetime in (1.1.1) to follow the Weibull distribution with p.d.f. as given in (1.4.2). We relate the cure rate p_0 to covariates $\boldsymbol{x}_i$ by the logistic link function $p_{0i} = \frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}, i = 1, \ldots, n$. We present the simplified expressions of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function and the components of the score function for the COM-Poisson cure rate model and some of its special cases. The expressions of the first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\theta}^*$ that assist us in carrying out the required maximization step and the components of the observed information matrix are presented in Appendix C.1 and Appendix C.2, respectively. The results of an extensive Monte Carlo simulation study are presented to evaluate the performance of the proposed estimation method. Model discrimination between different cure rate models is carried out by means of likelihood ratio test as well as AIC and BIC. Finally, the results of the analysis of the cutaneous melanoma data are presented and goodness-of-fit-tests for the assumption of the Weibull distribution for the lifetime are carried out for the dataset.

5.2 Expressions of E- and M-steps for different cure rate models

Bernoulli cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function can be expressed as

$$Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) = Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)}) + Q_2(\boldsymbol{\gamma}, \boldsymbol{\pi}^{(k)}),$$

where

$$Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)}) = \sum_{I_1} \boldsymbol{x}_i'\boldsymbol{\beta} + \sum_{I_0} \pi_i^{(k)} \boldsymbol{x}_i'\boldsymbol{\beta} - \sum_{I^*} \log\{1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta})\},$$

and

$$\begin{aligned} Q_2(\boldsymbol{\gamma}, \boldsymbol{\pi}^{(k)}) \quad &= \quad -n_1 \log \gamma_1 + \frac{n_1}{\gamma_1} \log \gamma_2 + \left(\frac{1}{\gamma_1} - 1\right) \sum_{I_1} \log t_i - \sum_{I_1} (\gamma_2 t_i)^{1/\gamma_1} \\ &\qquad - \sum_{I_0} \pi_i^{(k)} (\gamma_2 t_i)^{1/\gamma_1} \end{aligned}$$

with

$$\pi_i^{(k)} = \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}^{(k)} - (\gamma_2^{(k)} t_i)^{1/\gamma_1^{(k)}})}{1 + \exp(\boldsymbol{x}_i'\boldsymbol{\beta}^{(k)} - (\gamma_2^{(k)} t_i)^{1/\gamma_1^{(k)}})}, \tag{5.2.1}$$

for the i-th censored observation. Since the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function can be separated into two parts, one containing the regression parameter $\boldsymbol{\beta}$ and the other containing the lifetime parameter $\boldsymbol{\gamma}$, the maximization step can be carried out by maximizing $Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)})$ with respect to $\boldsymbol{\beta}$ and $Q_2(\boldsymbol{\gamma}, \boldsymbol{\pi}^{(k)})$ with respect to $\boldsymbol{\gamma}$, separately.

Poisson cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function can be expressed as

$$\begin{aligned} Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) &= -n_1 \log \gamma_1 + \frac{n_1}{\gamma_1} \log \gamma_2 + \left(\frac{1}{\gamma_1} - 1\right) \sum_{I_1} \log t_i - \sum_{I_1} (\gamma_2 t_i)^{1/\gamma_1} \\ &\quad + \sum_{I_1} \log[\log\{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})\}] + \sum_{I_1} A_{Wi}(\boldsymbol{\beta}, \boldsymbol{\gamma}) \\ &\quad + \sum_{I_0} \pi_i^{(k)} \log\{\exp(A_{Wi}(\boldsymbol{\beta}, \boldsymbol{\gamma})) - 1\} - \sum_{I^*} \log(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})), \end{aligned}$$

where

$$A_{Wi}(\boldsymbol{\beta}, \boldsymbol{\gamma}) = \log\{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})\} \exp\{-(\gamma_2 t_i)^{1/\gamma_1}\}, \tag{5.2.2}$$

for $i = 1, 2, \ldots, n$, and

$$\pi_i^{(k)} = \frac{\exp(A_{Wi}(\boldsymbol{\beta}^{(k)}, \boldsymbol{\gamma}^{(k)})) - 1}{\exp(A_{Wi}(\boldsymbol{\beta}^{(k)}, \boldsymbol{\gamma}^{(k)}))}, \tag{5.2.3}$$

for the i-th censored observation.

Geometric cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function can be expressed as

$$\begin{aligned} Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) &= -n_1 \log \gamma_1 + \frac{n_1}{\gamma_1} \log \gamma_2 + \left(\frac{1}{\gamma_1} - 1\right) \sum_{I_1} \log t_i + \sum_{I_1} B_{Gi}(\boldsymbol{\beta}, \boldsymbol{\gamma}) \\ &\quad -2 \sum_{I_1} \log\{1 + C_i(\boldsymbol{\beta}, \boldsymbol{\gamma})\} - \sum_{I_0} \log\{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})\} \\ &\quad + \sum_{I_0} \pi_i^{(k)} B_{Gi}(\boldsymbol{\beta}, \boldsymbol{\gamma}) - \sum_{I_0} \pi_i^{(k)} \log\{1 + C_i(\boldsymbol{\beta}, \boldsymbol{\gamma})\}, \end{aligned}$$

where

$$B_{Gi}(\boldsymbol{\beta}, \boldsymbol{\gamma}) = \boldsymbol{x}_i' \boldsymbol{\beta} - (\gamma_2 t_i)^{1/\gamma_1} \text{ and } C_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) = \{1 - \exp(-(\gamma_2 t_i)^{1/\gamma_1})\} \exp(\boldsymbol{x}_i' \boldsymbol{\beta}), \tag{5.2.4}$$

for $i = 1, 2, \ldots, n$, and

$$\pi_i^{(k)} = \frac{\exp(B_{Gi}(\boldsymbol{\beta}^{(k)}, \boldsymbol{\gamma}^{(k)}))}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta}^{(k)})}, \tag{5.2.5}$$

for the i-th censored observation.

COM-Poisson cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function, for a fixed value of ϕ, can be expressed as

$$\begin{aligned} Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) &= -n_1 \log \gamma_1 + \frac{n_1}{\gamma_1} \log \gamma_2 + \left(\frac{1}{\gamma_1} - 1 \right) \sum_{I_1} \log t_i + \sum_{I_1} \log z_{2i} \\ &\quad + \sum_{I_0} \pi_i^{(k)} \log z_{1i} - \sum_{I^*} \log\{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})\}, \end{aligned}$$

where

$$z_1 = z_1(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{\{H_\phi^{-1}(1 + \exp(\boldsymbol{x}' \boldsymbol{\beta})) \exp(-(\gamma_2 t)^{1/\gamma_1})\}^j}{(j!)^\phi},$$

$$z_2 = z_2(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{j\{H_\phi^{-1}(1 + \exp(\boldsymbol{x}' \boldsymbol{\beta})) \exp(-(\gamma_2 t)^{1/\gamma_1})\}^j}{(j!)^\phi},$$

and

$$\pi_i^{(k)} = \left. \frac{z_1(\boldsymbol{\theta}; \boldsymbol{x}_i, t_i)}{1 + z_1(\boldsymbol{\theta}; \boldsymbol{x}_i, t_i)} \right|_{\boldsymbol{\theta}^* = \boldsymbol{\theta}^{*(k)}}, \tag{5.2.6}$$

for the i-th censored observation.

5.3 Components of the score function

Bernoulli cure rate model: The components of the score function are

$$
\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il} + \sum_{I_0} x_{il} w_i - \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})}, \\
\frac{\partial l}{\partial \gamma_1} &= -\frac{n_1}{\gamma_1} - \frac{n_1}{{\gamma_1}^2} \log \gamma_2 - \frac{1}{{\gamma_1}^2} \sum_{I_1} \log t_i + \frac{1}{{\gamma_1}^2} \sum_{I_1} G_{Bi}(\boldsymbol{\gamma}) + \frac{1}{{\gamma_1}^2} \sum_{I_0} w_i G_{Bi}(\boldsymbol{\gamma}), \\
\frac{\partial l}{\partial \gamma_2} &= \frac{n_1}{\gamma_1 \gamma_2} - \frac{1}{\gamma_1 \gamma_2} \sum_{I_1} (\gamma_2 t_i)^{1/\gamma_1} - \frac{1}{\gamma_1 \gamma_2} \sum_{I_0} w_i (\gamma_2 t_i)^{1/\gamma_1}.
\end{aligned}
$$

The above is defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$
w_i = \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta} - (\gamma_2 t_i)^{1/\gamma_1})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta} - (\gamma_2 t_i)^{1/\gamma_1})}, \tag{5.3.1}
$$

for the i-th observation censored, and

$$
G_{Bi}(\boldsymbol{\gamma}) = (\gamma_2 t_i)^{1/\gamma_1} \log(\gamma_2 t_i), \tag{5.3.2}
$$

for $i = 1, 2, \ldots, n$.

Poisson cure rate model: The components of the score function are

$$
\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})) \log(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta}))} \\
&\quad - \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})} \left\{ 1 - \exp(-(\gamma_2 t_i)^{1/\gamma_1}) \right\}, \\
\frac{\partial l}{\partial \gamma_1} &= -\frac{n_1}{\gamma_1} - \frac{n_1}{{\gamma_1}^2} \log \gamma_2 - \frac{1}{{\gamma_1}^2} \sum_{I_1} \log t_i + \frac{1}{{\gamma_1}^2} \sum_{I_1} G_{Pi}(\boldsymbol{\gamma}) + \frac{1}{{\gamma_1}^2} \sum_{I^*} G_{Pi}(\boldsymbol{\gamma}) A_{Wi}(\boldsymbol{\beta}, \boldsymbol{\gamma}), \\
\frac{\partial l}{\partial \gamma_2} &= \frac{n_1}{\gamma_1 \gamma_2} - \frac{1}{\gamma_1 \gamma_2} \sum_{I_1} (\gamma_2 t_i)^{1/\gamma_1} - \frac{1}{\gamma_1 \gamma_2} \sum_{I^*} (\gamma_2 t_i)^{1/\gamma_1} A_{Wi}(\boldsymbol{\beta}, \boldsymbol{\gamma}).
\end{aligned}
$$

The above is defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$G_{Pi}(\boldsymbol{\gamma}) = (\gamma_2 t_i)^{1/\gamma_1} \log(\gamma_2 t_i), \tag{5.3.3}$$

for $i = 1, 2, \ldots, n$, and $A_{Wi}(\boldsymbol{\beta}, \boldsymbol{\gamma})$ is as defined in (5.2.2).

Geometric cure rate model: The components of the score function are

$$\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il} \frac{1 - C_i(\boldsymbol{\beta}, \boldsymbol{\gamma})}{1 + C_i(\boldsymbol{\beta}, \boldsymbol{\gamma})} - \sum_{I_0} x_{il} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})} + \sum_{I_0} x_{il} w_i \frac{1}{1 + C_i(\boldsymbol{\beta}, \boldsymbol{\gamma})}, \\
\frac{\partial l}{\partial \gamma_1} &= -\frac{n_1}{\gamma_1} - \frac{n_1}{{\gamma_1}^2} \log \gamma_2 - \frac{1}{{\gamma_1}^2} \sum_{I_1} \log t_i + \frac{1}{{\gamma_1}^2} \sum_{I_1} G_{Gi}(\boldsymbol{\gamma}) \\
&\quad + \frac{2}{{\gamma_1}^2} \sum_{I_1} \frac{G_{Gi}(\boldsymbol{\gamma}) \exp(B_{Gi}(\boldsymbol{\beta}, \boldsymbol{\gamma}))}{1 + C_i(\boldsymbol{\beta}, \boldsymbol{\gamma})} + \frac{1}{{\gamma_1}^2} \sum_{I_0} w_i G_{Gi}(\boldsymbol{\gamma}) \\
&\quad + \frac{1}{{\gamma_1}^2} \sum_{I_0} w_i \frac{G_{Gi}(\boldsymbol{\gamma}) \exp(B_{Gi}(\boldsymbol{\beta}, \boldsymbol{\gamma}))}{1 + C_i(\boldsymbol{\beta}, \boldsymbol{\gamma})}, \\
\frac{\partial l}{\partial \gamma_2} &= \frac{n_1}{\gamma_1 \gamma_2} - \frac{1}{\gamma_1 \gamma_2} \sum_{I_1} (\gamma_2 t_i)^{1/\gamma_1} - \frac{2}{\gamma_1 \gamma_2} \sum_{I_1} \frac{(\gamma_2 t_i)^{1/\gamma_1} \exp(B_{Gi}(\boldsymbol{\beta}, \boldsymbol{\gamma}))}{1 + C_i(\boldsymbol{\beta}, \boldsymbol{\gamma})} \\
&\quad - \frac{1}{\gamma_1 \gamma_2} \sum_{I_0} w_i (\gamma_2 t_i)^{1/\gamma_1} - \frac{1}{\gamma_1 \gamma_2} \sum_{I_0} w_i \frac{(\gamma_2 t_i)^{1/\gamma_1} \exp(B_{Gi}(\boldsymbol{\beta}, \boldsymbol{\gamma}))}{1 + C_i(\boldsymbol{\beta}, \boldsymbol{\gamma})}.
\end{aligned}$$

The above is defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$w_i = \frac{\exp(B_{Gi}(\boldsymbol{\beta}, \boldsymbol{\gamma}))}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})}, \tag{5.3.4}$$

for the i-th observation censored,

$$G_{Gi}(\boldsymbol{\gamma}) = (\gamma_2 t_i)^{1/\gamma_1} \log(\gamma_2 t_i), \tag{5.3.5}$$

$C_i(\boldsymbol{\beta}, \boldsymbol{\gamma})$ and $B_{Gi}(\boldsymbol{\beta}, \boldsymbol{\gamma})$ are as defined in (5.2.4).

COM-Poisson cure rate model: The components of the score function, for a fixed value of ϕ, are

$$\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) z_{21i}}{z_{2i} z_{01i}} + \sum_{I_0} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) z_{2i}}{(1+z_{1i}) z_{01i}} - \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}, \\
\frac{\partial l}{\partial \gamma_1} &= -\frac{n_1}{\gamma_1} - \frac{n_1}{{\gamma_1}^2} \log \gamma_2 - \frac{1}{{\gamma_1}^2} \sum_{I_1} \log t_i + \frac{1}{{\gamma_1}^2} \sum_{I_1} \frac{G_{Ci}(\boldsymbol{\gamma}) z_{21i}}{z_{2i}} + \frac{1}{{\gamma_1}^2} \sum_{I_0} \frac{G_{Ci}(\boldsymbol{\gamma}) z_{2i}}{1+z_{1i}}, \\
\frac{\partial l}{\partial \gamma_2} &= \frac{n_1}{\gamma_1 \gamma_2} - \frac{1}{\gamma_1 \gamma_2} \sum_{I_1} \frac{(\gamma_2 t_i)^{1/\gamma_1} z_{21i}}{z_{2i}} - \frac{1}{\gamma_1 \gamma_2} \sum_{I_0} \frac{(\gamma_2 t_i)^{1/\gamma_1} z_{2i}}{1+z_{1i}}.
\end{aligned}$$

The above is defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$z_{21} = z_{21}(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{j^2 \{H_\phi^{-1}(1+\exp(\boldsymbol{x}'\boldsymbol{\beta})) \exp(-(\gamma_2 t)^{1/\gamma_1})\}^j}{(j!)^\phi},$$

$$z_{01} = z_{01}(\boldsymbol{\theta}_1; \boldsymbol{x}) = \sum_{j=1}^{\infty} \frac{j \{H_\phi^{-1}(1+\exp(\boldsymbol{x}'\boldsymbol{\beta}))\}^j}{(j!)^\phi},$$

and

$$G_{Ci}(\boldsymbol{\gamma}) = (\gamma_2 t_i)^{1/\gamma_1} \log(\gamma_2 t_i), \tag{5.3.6}$$

for $i = 1, 2, \ldots, n$.

5.4 Results of the simulation study: model fitting

We refer to the simulation study setup described in Section 1.7. In this study, we considered three sample sizes: $n = 200, 400$ and 600 to observe the behavior of the fitting of the model under small, moderate and large sample sizes. The choice of the lifetime parameter (γ_1, γ_2) was obtained after equating the mean and variance of the underlying Weibull distribution in (1.4.2) to some fixed values. We considered two different choices for the mean as 5 and 3.5, and two different choices for the variance as 3 and 1.5. The above choices of the mean and variance lead in total to four different choices of $(\gamma_1, \gamma_2) : (0.316, 0.179), (0.215, 0.183), (0.470, 0.253)$, and $(0.320, 0.256)$. This allows us to study the behavior of the model when the lifetime distribution has the same mean but different variance and vice-versa. In this simulation study, we simulated data from different cure rate models and the estimation procedure described in Section 1.6.1 was employed to estimate the unknown parameters of the model. We then determined the empirical bias and RMSE of the estimates so as to examine the performance of the estimates. We also calculated the coverage probabilities of the confidence intervals based on the asymptotic normality of the MLEs for different nominal confidence levels. All simulations were performed using the R software and the results were based on 1000 Monte Carlo runs. To find an initial guess of the parameters $\beta_0, \beta_1, \gamma_1$ and γ_2 so as to start the iterative procedure, we again followed the same procedure as described in Section 3.4.

We present the results for the three special cases of the COM-Poisson cure rate model in Tables 5.1−5.3. The results show that the EM algorithm converges to the true parameter values quite accurately. As expected, the standard error and the RMSE of the estimates decrease with an increase in sample size and with a decrease in censoring proportion. On comparing models having the same mean but different variance for the lifetime distribution, the model having higher variance for the lifetime distribution is found to have a higher standard error and RMSE of the lifetime parameter $\boldsymbol{\gamma}$. Similarly, on comparing models having the same variance but different mean for the lifetime distribution, the standard error and RMSE of $\boldsymbol{\gamma}$ is found to be high in the model having a lower mean for the lifetime distribution. The coverage probabilities of the confidence intervals based on the asymptotic normality of the MLEs are found to be quite close to the nominal levels. In Tables 5.4−5.6, we present the estimate, bias and RMSE of the cured proportions corresponding to four groups for the three special cases of the COM-Poisson cure rate model. We note that the estimates are quite close to the true values and that the RMSE is low when the sample size is high and also when the cured proportion is low.

Table 5.7 shows the result for the COM-Poisson cure rate model when ϕ is fixed at 0.5. The observations are similar to the special cases of the COM-Poisson cure rate model, with the estimates being close to the true parameter values and the coverage probabilities being close to the nominal levels. However, in practice, ϕ needs to be estimated from the data along with other model parameters, for which we can employ the profile likelihood approach. The corresponding results are shown in Table 5.8, where the true value of ϕ is taken to be 0.5. We observe that the profile likelihood approach of estimating ϕ introduces large RMSE in the estimate of ϕ. However, it is found to decrease with an increase in sample size and with a decrease in censoring proportion. The standard error of the MLEs also show similar behavior. The bias in the estimate of ϕ is large especially when the censoring proportion is high. We also note that the bias and RMSE of the estimate of β_0 is high when compared to the bias and RMSE of the estimates of the other regression coefficient and lifetime parameters. The standard errors in the estimates of β_0, β_1, γ_1 and γ_2 are found to be underestimated and consequently the coverage probabilities fall below the nominal level in this case. This is mainly due to the imprecision in the estimate of ϕ by employing the profile likelihood technique. Note also that in the standard error calculation ϕ is kept fixed and as such its variation is not taken into account. However, this is a reasonable assumption as the main role of the shape parameter ϕ is to guide us to select an appropriate distribution for the competing cause and as such its variation is not of primary interest and can thus be kept fixed. The undercoverage seems to be more pronounced for the lifetime parameters. Furthermore, we note that the undercoverage is more noticeable when the censoring proportion is low. It is interesting to note that the lifetime parameters (γ_1, γ_2) are quite robust to the cure rate model both in terms of its estimated value and the standard error of the estimates.

To estimate ϕ by the profile likelihood approach, we chose the range of ϕ to be [0, 2] and in this interval ϕ was divided in steps of 0.1. This accounted for 21 distinct choices of ϕ. It is again clear that to estimate ϕ for a given dataset, the EM algorithm must converge for all chosen values of ϕ. However, for some datasets, it was observed that the EM algorithm failed to converge for some choices of ϕ and as such that dataset had to be discarded. Similar convergence problem was also occasionally noticed when estimating the parameters of the COM-Poisson cure rate model with ϕ fixed at 0.5. However, the number of samples rejected in this case was much less. No convergence problem was faced, however, when estimating the parameters of the three special cases of the COM-Poisson cure rate model.

5.5 Model discrimination results

5.5.1 Likelihood-based method

In this simulation study, we considered the following parameter settings: Setting 1: $n = 400$ $(110, 120, 90, 80)$, $p =$ "Low", $(\gamma_1, \gamma_2) = (0.215, 0.183)$; Setting 2: $n = 600$ $(165, 180, 135, 120)$, $p =$ "Low", $(\gamma_1, \gamma_2) = (0.215, 0.183)$; Setting 3: $n = 400$ $(110, 120, 90, 80)$, $p =$ "High", $(\gamma_1, \gamma_2) = (0.215, 0.183)$. For each simulated dataset, we calculated the likelihood ratio test statistic of the fitted Bernoulli, Poisson and geometric cure rate model *versus* the fitted COM-Poisson cure rate model. Based on 1000 datasets in each situation and nominal significance level of 0.05, we computed the observed significance levels and powers of the likelihood ratio test, and these results are reported in Table 5.9.

The numbers in bold represent the observed levels while the other numbers represent the observed powers. These numbers were determined simply by the rejection rates of the null hypothesis. It is easy to see that the chi-square distribution provides only a reasonable approximation to the null distribution of the likelihood ratio test when testing for the Poisson distribution as the observed levels are not so close to the nominal level in two of the three cases. However, the mixture chi-square distribution provides a good approximation to the null distribution of the likelihood ratio test when testing for the Bernoulli distribution. But, when testing for the geometric distribution, the observed levels are found to be much below the nominal level. To investigate the reason for this and to evaluate the performance of the mixture chi-square distribution, we constructed histograms of the likelihood ratio test statistic (Λ) values when testing for the geometric cure rate model (true competing cause distribution being geometric) and Bernoulli cure rate model (true competing cause distribution being Bernoulli). For this purpose, we considered Setting 1 above and the corresponding plots for the geometric and Bernoulli cases are presented in Figures 5.1 and 5.2, respectively. From Figure 5.1, we note that the likelihood ratio statistic takes the value zero 91% of times, which is significantly different from the expected 50%, and this in turn explains why the observed level falls much below the nominal level when testing for the geometric cure rate model. However, Figure 5.2 represents a better mixture representation, in which case the likelihood ratio statistic takes the value zero 73% of times resulting in the observed level being closer to the nominal level.

When the geometric distribution is the true competing cause distribution, the test has high power to reject the Bernoulli distribution as the competing cause distribution, and the largest observed power is 99%. The test also appears to have good power to reject the Poisson distribution as the competing cause distribution with the largest observed power being 88%. When the Poisson distribution is the true competing cause distribution, the test has got moderate power to reject the Bernoulli distribution as the competing cause distribution (the largest observed power is 77%) and a relatively less power to reject the geometric distribution as the competing cause distribution (the largest observed power is 40%). When the Bernoulli distribution is the true competing cause distribution, the test again has high power to reject the geometric distribution as the competing cause distribution (the largest observed power is 93%). However, the test does not appear to have power to reject the Poisson distribution as the competing cause distribution, and the largest observed power, in this case, is only 28%. As expected, the power of the test to reject the wrong model increases with an increase in sample size and with a decrease in censoring proportion. Furthermore, as the true model approaches the Bernoulli distribution, the power of the test to reject the geometric distribution increases whereas the power of the test to reject the Bernoulli distribution decreases, as we would expect.

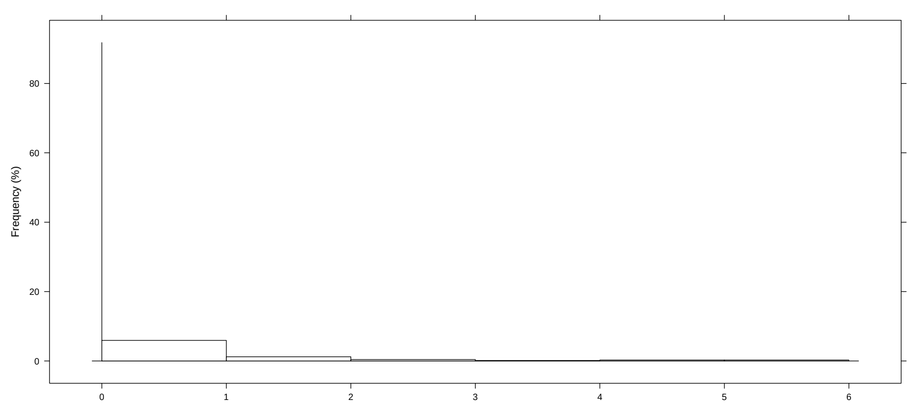

Figure 5.1: Histogram of Λ values when testing for geometric model (true model being geometric) with Weibull lifetime.

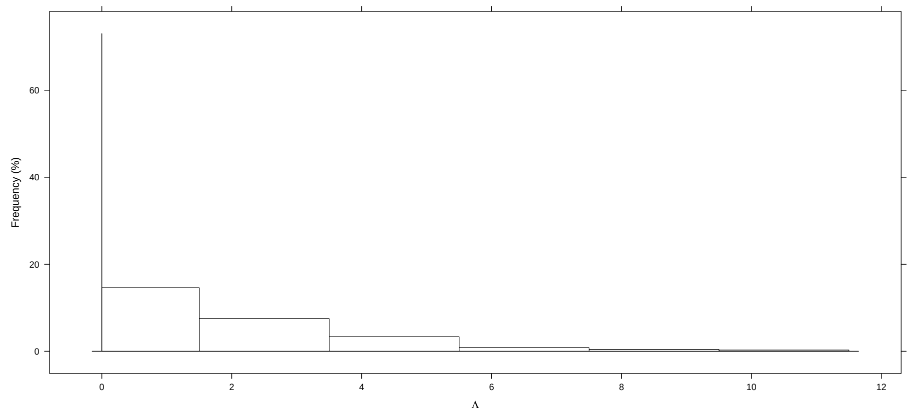

Figure 5.2: Histogram of Λ values when testing for Bernoulli model (true model being Bernoulli) with Weibull lifetime.

5.5.2 Information-based criterion

In this simulation study, we considered the same parameter settings as in the previous section. Considering the following true distributions for the competing cause random variable: Bernoulli, Poisson, geometric, COM-Poisson ($\phi = 0.5$) and COM-Poisson ($\phi = 2$), for each generated dataset, we calculated the AIC and BIC values of the fitted Bernoulli, Poisson and geometric cure rate model. Based on 1000 datasets in each situation, we computed the observed selection rates for each of the two selection criteria used, and these results are reported in Table 5.10.

When the true competing cause distribution is one of the geometric, Poisson and Bernoulli, the information criteria has high probability of selecting the correct model. Thus, the information criteria can distinguish between the Bernoulli, Poisson and geometric models with a high probability. Furthermore, as expected, this selection probability increases with an increase in sample size and a decrease in censoring proportion. When COM-Poisson ($\phi = 0.5$) is the true model, the selection rate of Poisson, as the correct model, is higher than that of geometric. This means that a COM-Poisson ($\phi = 0.5$) is closer to Poisson than geometric. When COM-Poisson ($\phi =$

2) is the true model, the selection rate of Poisson, as the correct model, is again higher than that of Bernoulli, which means that a COM-Poisson ($\phi = 2$) is closer to Poisson than Bernoulli. For model discrimination, we recommend using the information-based criterion as this method does not involve estimation of the parameter ϕ, unlike the likelihood-based method, which actually is quite time-consuming since the parameter ϕ needs to be estimated by the profile likelihood approach, in this case.

Based on 1000 datasets in each situation, we also reported the TRB values when fitting different models for a given true model in Table 5.11. The values in parentheses represents the TRE under model mis-specification. We note that model mis-specification in general leads to higher TRB of the cured proportion as compared to the true model specification. We also note that in certain situations, the TRB of the cured proportion under wrongly fitted model is much higher than that under the correct model, which reveals that fitting a wrong model would lead to the estimation of cured proportion with high bias. Similarly, it can also be seen that model mis-specification always leads to loss of efficiency. In certain situations, the TRE is considerably less than one, which implies significant loss of efficiency when fitting the wrong model. These findings strongly suggest that we should utilize the flexibility of the COM-Poisson model in selecting a parsimonious competing cause distribution, thus avoiding the risk of estimating the cured proportion inefficiently.

When allowing AIC to select a model out of a set of candidate models, we present the TRB and TRE values in Table 5.12. We note that for a given true model, the TRB values in some cases are less than that obtained when fitting the wrong model, as shown in Table 5.11. However, the TRE values for a given true model are always greater than those in Table 5.11. This in turn suggests that when we allow the AIC to select a model out of a set of candidate models, although it selects the wrong model a certain proportion of times, the overall efficiency of the method is significantly larger than that obtained under wrong model specification. Furthermore, from Table 5.12, we note that the TRE values are all close to one, which further means that the loss of efficiency is negligible when using AIC to select a working model.

5.6 Analysis of cutaneous melanoma data

In this section, we demonstrate an application of the proposed methodology to the cutaneous melanoma dataset. In our application, we selected nodule category ($1 : n = 111; 2 : n = 137; 3 : n = 87; 4 : n = 82$) as the only covariate. As possible models, we considered the Bernoulli, Poisson, geometric and general COM-Poisson cure rate models.

For these data, we obtained $\hat{\phi} \approx 0$. So, we test the suitability of the geometric model for the number of causes M in (1.3.1). With the test procedure described in Section 1.8.1, we obtained $\Lambda \approx 0$ (p-value=0.5), and we therefore adopt the geometric model as our working model. The p-values for testing the suitability of the Poisson and Bernoulli cure rate models came out to be 4.81×10^{-3} and 2.64×10^{-5}, respectively. These clearly provide evidence against the Poisson and Bernoulli models. We note that the candidate models have the same number of parameters, and so we have reported the values of the maximized log-likelihood function, AIC and BIC for different cure rate models in Table 5.13.

We observe that AIC and BIC increase with the increase in COM-Poisson parameter ϕ, whereas the maximized log-likelihood value is monotonically decreasing with respect to ϕ. Hence, the best fit is achieved with the COM-Poisson (geometric) cure rate model, thus agreeing with the decision reached by the likelihood ratio test. To find an acceptable range of ϕ for the data, we considered testing for different values of ϕ and plot the values of ϕ against the corresponding Λ-statistic. The corresponding plot is presented in Figure 5.3. We reject the test at 10% level of significance if the value of the likelihood ratio test statistic Λ exceeds $\chi^2_{1,1-\alpha} = 2.71$. Now, for $\Lambda = 2.71$, the corresponding value of ϕ is 0.18 (from the plot) and hence an admissible range of ϕ for the data is $[0, 0.18)$. This further explains that only the geometric cure rate model is acceptable for the data among all those considered. Maximum likelihood estimates of the COM-Poisson (geometric) cure rate model parameters are presented in Table 5.14. We also considered testing for the exponential distribution ($H_0 : \gamma_1 = 1$) in (1.4.2). The likelihood ratio test statistic in this case came out to be 48.428 (p-value $= 3.4 \times 10^{-12}$), which clearly gives strong evidence against the case of the exponential distribution in (1.4.2) for the lifetimes.

Finally, we deal with the estimation of the cure rate p_0. Estimates of the cure rates of patients stratified by nodule category are $\hat{p}_{0j} = \frac{1}{1+\exp(\hat{\beta}_0 + j\hat{\beta}_1)}, j = 1, 2, 3, 4$. With the procedure described in Section 1.6.3, we calculated the standard errors and the 95% confidence intervals of the cure rates of patients corresponding to the four nodule categories $(1-4)$, and these are presented in Table 5.15.

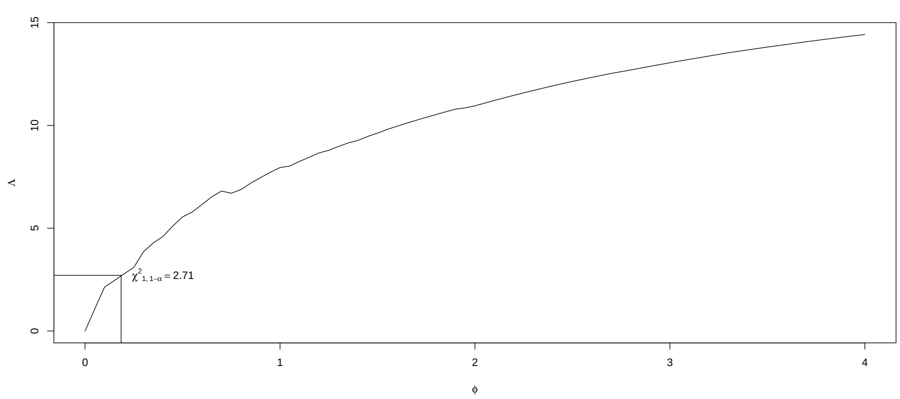

Figure 5.3: Values of ϕ against the corresponding Λ-statistic for Weibull lifetime.

5.7 Model diagnosis

In this section, we check if the Weibull assumption for the lifetime distribution is reasonable for the cutaneous melanoma data that we have analyzed in the preceding section. For the Weibull distribution in (1.4.2), we have

$$\log\{-\log S(t;\boldsymbol{\gamma})\} = \frac{1}{\gamma_1}\log\gamma_2 + \frac{1}{\gamma_1}\log t.$$

This means that a scatter plot of the values of $\log\{-\log \hat{S}(t_{(i)})\}$ against $\log t_{(i)}$ should give a straight line if the assumption of a Weibull distribution is correct, where $\hat{S}(t_{(i)})$ is the Kaplan-Meier estimate of the survival function and $t_{(i)}$ denotes the i-th ordered observed lifetime.

For the cutaneous melanoma data, we obtained the Kaplan-Meier estimate $\hat{S}(t)$ at the observed failure times and the plot of the values of $\log\{-\log \hat{S}(t)\}$ against $\log t$ is presented in Figure 5.4. Though the plot shows approximate linearity and as such the Weibull distribution may be assumed for these data, we do notice some curvature in the graph, which suggests that the Weibull distribution does not provide an accurate fit for these data, however. Hence, we also considered formal goodness-of-fit tests for testing the hypothesis that the lifetime follows a Weibull distribution. As we have stated earlier, a plot of the values of $\log\{-\log \hat{S}(t_{(i)})\}$ against $\log t_{(i)}$ should be a straight line if the assumption of a Weibull distribution is valid. Hence, a test could be based on the measure of correlation coefficient (r) between $\log\{-\log \hat{S}(t)\}$ and $\log t$. We note that a perfect linearity between $\log\{-\log \hat{S}(t)\}$ and $\log t$ would mean $r = 1$. Hence, the critical region for this test will be to the left. We can also fit a linear regression of $\log\{-\log \hat{S}(t)\}$ and $\log t$ and then base the test on $D =$ supremum of the absolute values of the residuals. In this case, we will have the critical region for this test to be on the right.

We obtained the p-values for the above two tests through Monte Carlo simulations. For this purpose, we calculated the values of the above two test statistics for the considered dataset. We then generated 1000 such datasets and for each of these datasets, we calculated the values of r and D, and determined the proportion of times r was less than and D was greater than the corresponding values determined from the observed data. We obtained the p-values for the tests based on r and D to be 0.368 and 0.432, respectively, both of which clearly show that the assumption of the Weibull distribution for the lifetime distribution is quite reasonable.

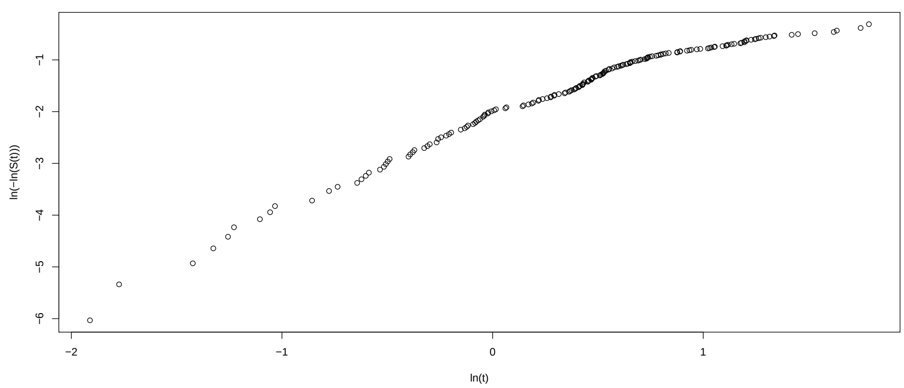

Figure 5.4: Scatter plot of the values of $\log\{-\log \hat{S}(t)\}$ against $\log t$.

Table 5.1: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the Bernoulli cure rate model with Weibull lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP 90%	CP 95%
200 $(55, 60, 45, 40)$	High	$\beta_0 =$ -1.192	-1.239 (0.464)	-0.047	0.455	0.918	0.959
		$\beta_1 = 0.573$	0.589 (0.175)	0.017	0.171	0.916	0.963
		$\gamma_1 = 0.316$	0.314 (0.027)	-0.002	0.027	0.889	0.935
		$\gamma_2 = 0.179$	0.180 (0.007)	0.001	0.007	0.908	0.959
	Low	$\beta_0 =$ -0.038	-0.058 (0.411)	-0.020	0.406	0.917	0.960
		$\beta_1 = 0.443$	0.458 (0.172)	0.015	0.173	0.918	0.966
		$\gamma_1 = 0.316$	0.314 (0.022)	-0.002	0.021	0.896	0.947
		$\gamma_2 = 0.179$	0.179 (0.005)	0.000	0.005	0.890	0.937
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.212 (0.326)	-0.021	0.336	0.891	0.941
		$\beta_1 = 0.573$	0.582 (0.123)	0.009	0.125	0.896	0.942
		$\gamma_1 = 0.316$	0.315 (0.019)	-0.001	0.019	0.892	0.942
		$\gamma_2 = 0.179$	0.179 (0.005)	0.000	0.005	0.893	0.944
	Low	$\beta_0 =$ -0.038	-0.043 (0.288)	-0.006	0.291	0.899	0.956
		$\beta_1 = 0.443$	0.447 (0.120)	0.004	0.122	0.907	0.946
		$\gamma_1 = 0.316$	0.315 (0.015)	-0.001	0.015	0.893	0.944
		$\gamma_2 = 0.179$	0.179 (0.004)	0.000	0.004	0.901	0.954
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.218 (0.323)	-0.026	0.321	0.907	0.955
		$\beta_1 = 0.573$	0.584 (0.122)	0.012	0.121	0.905	0.955
		$\gamma_1 = 0.215$	0.214 (0.013)	-0.001	0.013	0.898	0.942
		$\gamma_2 = 0.183$	0.183 (0.003)	0.000	0.003	0.912	0.961
	Low	$\beta_0 =$ -0.038	-0.031 (0.287)	0.007	0.288	0.911	0.953
		$\beta_1 = 0.443$	0.444 (0.120)	0.001	0.123	0.891	0.948
		$\gamma_1 = 0.215$	0.214 (0.010)	-0.001	0.010	0.896	0.946
		$\gamma_2 = 0.183$	0.183 (0.003)	0.000	0.003	0.881	0.940
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.203 (0.330)	-0.011	0.331	0.906	0.954
		$\beta_1 = 0.573$	0.578 (0.124)	0.005	0.127	0.902	0.950
		$\gamma_1 = 0.470$	0.467 (0.029)	-0.003	0.030	0.870	0.924
		$\gamma_2 = 0.253$	0.253 (0.010)	0.000	0.010	0.894	0.944
	Low	$\beta_0 =$ -0.038	-0.044 (0.291)	-0.007	0.293	0.889	0.949
		$\beta_1 = 0.443$	0.450 (0.121)	0.007	0.123	0.897	0.954
		$\gamma_1 = 0.470$	0.469 (0.023)	-0.001	0.023	0.884	0.945
		$\gamma_2 = 0.253$	0.253 (0.008)	0.000	0.008	0.905	0.955
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.216 (0.326)	-0.025	0.332	0.897	0.948
		$\beta_1 = 0.573$	0.583 (0.123)	0.010	0.127	0.887	0.944
		$\gamma_1 = 0.320$	0.319 (0.019)	-0.001	0.019	0.908	0.955
		$\gamma_2 = 0.256$	0.256 (0.007)	0.000	0.007	0.908	0.947
	Low	$\beta_0 =$ -0.038	-0.033 (0.289)	0.005	0.278	0.921	0.960
		$\beta_1 = 0.443$	0.445 (0.120)	0.002	0.117	0.918	0.958
		$\gamma_1 = 0.320$	0.319 (0.016)	-0.001	0.016	0.904	0.943
		$\gamma_2 = 0.256$	0.256 (0.005)	0.000	0.005	0.902	0.959
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.192	-1.201 (0.334)	-0.010	0.332	0.894	0.954
		$\beta_1 = 0.573$	0.579 (0.119)	0.006	0.118	0.894	0.965
		$\gamma_1 = 0.316$	0.315 (0.019)	-0.001	0.019	0.908	0.949
		$\gamma_2 = 0.179$	0.179 (0.005)	0.000	0.005	0.905	0.955
	Low	$\beta_0 =$ -0.038	-0.060 (0.295)	-0.022	0.297	0.897	0.958
		$\beta_1 = 0.443$	0.456 (0.116)	0.013	0.120	0.888	0.952
		$\gamma_1 = 0.316$	0.315 (0.015)	-0.001	0.015	0.893	0.951
		$\gamma_2 = 0.179$	0.179 (0.004)	0.000	0.004	0.896	0.954
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.192	-1.205 (0.265)	-0.013	0.275	0.879	0.940
		$\beta_1 = 0.573$	0.578 (0.100)	0.005	0.104	0.880	0.945
		$\gamma_1 = 0.316$	0.316 (0.016)	0.000	0.016	0.906	0.958
		$\gamma_2 = 0.179$	0.179 (0.004)	0.000	0.004	0.905	0.960
	Low	$\beta_0 =$ -0.038	-0.056 (0.235)	-0.018	0.226	0.911	0.960
		$\beta_1 = 0.443$	0.453 (0.098)	0.009	0.094	0.915	0.963
		$\gamma_1 = 0.316$	0.315 (0.013)	-0.001	0.013	0.895	0.949
		$\gamma_2 = 0.179$	0.179 (0.003)	0.000	0.003	0.917	0.952

Table 5.2: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the Poisson cure rate model with Weibull lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP	
						90%	95%
200 $(55, 60, 45, 40)$	High	$\beta_0 =$ -1.192	-1.199 (0.441)	-0.008	0.439	0.920	0.948
		$\beta_1 = 0.573$	0.579 (0.164)	0.007	0.165	0.906	0.954
		$\gamma_1 = 0.316$	0.314 (0.026)	-0.002	0.027	0.876	0.923
		$\gamma_2 = 0.179$	0.179 (0.008)	0.000	0.008	0.907	0.951
	Low	$\beta_0 =$ -0.038	-0.052 (0.380)	-0.015	0.381	0.896	0.948
		$\beta_1 = 0.443$	0.454 (0.155)	0.011	0.155	0.900	0.953
		$\gamma_1 = 0.316$	0.313 (0.020)	-0.003	0.021	0.883	0.924
		$\gamma_2 = 0.179$	0.179 (0.006)	0.000	0.006	0.903	0.951
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.209 (0.310)	-0.018	0.305	0.905	0.957
		$\beta_1 = 0.573$	0.578 (0.115)	0.006	0.114	0.913	0.949
		$\gamma_1 = 0.316$	0.314 (0.018)	-0.002	0.019	0.888	0.935
		$\gamma_2 = 0.179$	0.179 (0.006)	0.000	0.006	0.888	0.942
	Low	$\beta_0 =$ -0.038	-0.031 (0.268)	0.006	0.265	0.907	0.952
		$\beta_1 = 0.443$	0.443 (0.109)	0.000	0.107	0.905	0.950
		$\gamma_1 = 0.316$	0.314 (0.014)	-0.002	0.015	0.892	0.938
		$\gamma_2 = 0.179$	0.179 (0.005)	0.000	0.005	0.890	0.941
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.197 (0.310)	-0.005	0.321	0.896	0.944
		$\beta_1 = 0.573$	0.574 (0.115)	0.002	0.120	0.904	0.944
		$\gamma_1 = 0.215$	0.214 (0.012)	-0.001	0.013	0.901	0.949
		$\gamma_2 = 0.183$	0.183 (0.004)	0.000	0.004	0.889	0.939
	Low	$\beta_0 =$ -0.038	-0.028 (0.267)	0.009	0.267	0.901	0.956
		$\beta_1 = 0.443$	0.439 (0.109)	-0.004	0.108	0.905	0.951
		$\gamma_1 = 0.215$	0.215 (0.010)	0.000	0.010	0.865	0.934
		$\gamma_2 = 0.183$	0.183 (0.003)	0.000	0.003	0.895	0.947
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.202 (0.310)	-0.010	0.314	0.905	0.947
		$\beta_1 = 0.573$	0.576 (0.115)	0.004	0.116	0.898	0.950
		$\gamma_1 = 0.470$	0.468 (0.028)	-0.002	0.029	0.879	0.937
		$\gamma_2 = 0.253$	0.253 (0.012)	0.000	0.013	0.894	0.947
	Low	$\beta_0 =$ -0.038	-0.041 (0.268)	-0.003	0.262	0.912	0.955
		$\beta_1 = 0.443$	0.445 (0.109)	0.002	0.106	0.910	0.956
		$\gamma_1 = 0.470$	0.468 (0.022)	-0.002	0.022	0.895	0.937
		$\gamma_2 = 0.253$	0.254 (0.010)	0.001	0.010	0.881	0.940
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.190 (0.309)	0.002	0.310	0.900	0.949
		$\beta_1 = 0.573$	0.574 (0.115)	0.002	0.117	0.895	0.946
		$\gamma_1 = 0.320$	0.318 (0.019)	-0.002	0.019	0.895	0.937
		$\gamma_2 = 0.256$	0.256 (0.008)	0.000	0.008	0.890	0.945
	Low	$\beta_0 =$ -0.038	-0.054 (0.267)	-0.017	0.282	0.888	0.939
		$\beta_1 = 0.443$	0.451 (0.109)	0.008	0.115	0.887	0.944
		$\gamma_1 = 0.320$	0.319 (0.015)	-0.001	0.015	0.891	0.944
		$\gamma_2 = 0.256$	0.256 (0.007)	0.000	0.007	0.905	0.954
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.192	-1.198 (0.318)	-0.007	0.315	0.900	0.947
		$\beta_1 = 0.573$	0.576 (0.112)	0.003	0.110	0.909	0.947
		$\gamma_1 = 0.316$	0.315 (0.018)	-0.001	0.018	0.882	0.933
		$\gamma_2 = 0.179$	0.179 (0.005)	0.000	0.005	0.902	0.952
	Low	$\beta_0 =$ -0.038	-0.036 (0.274)	0.002	0.268	0.898	0.956
		$\beta_1 = 0.443$	0.444 (0.105)	0.001	0.104	0.895	0.943
		$\gamma_1 = 0.316$	0.315 (0.014)	-0.001	0.015	0.892	0.935
		$\gamma_2 = 0.179$	0.179 (0.005)	0.000	0.005	0.904	0.953
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.192	-1.194 (0.252)	-0.002	0.247	0.916	0.957
		$\beta_1 = 0.573$	0.573 (0.094)	0.000	0.094	0.904	0.949
		$\gamma_1 = 0.316$	0.315 (0.015)	-0.001	0.016	0.875	0.941
		$\gamma_2 = 0.179$	0.179 (0.005)	0.000	0.005	0.891	0.950
	Low	$\beta_0 =$ -0.038	-0.031 (0.218)	0.006	0.213	0.911	0.953
		$\beta_1 = 0.443$	0.439 (0.089)	-0.004	0.087	0.910	0.953
		$\gamma_1 = 0.316$	0.316 (0.012)	0.000	0.012	0.885	0.943
		$\gamma_2 = 0.179$	0.179 (0.004)	0.000	0.004	0.889	0.934

Table 5.3: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the geometric cure rate model with Weibull lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP	
						90%	95%
200 $(55, 60, 45, 40)$	High	$\beta_0 =$ -1.192	-1.221 (0.406)	-0.029	0.410	0.908	0.956
		$\beta_1 = 0.573$	0.585 (0.145)	0.012	0.145	0.903	0.953
		$\gamma_1 = 0.316$	0.312 (0.026)	-0.004	0.026	0.887	0.934
		$\gamma_2 = 0.179$	0.180 (0.010)	0.001	0.010	0.887	0.937
	Low	$\beta_0 =$ -0.038	-0.058 (0.328)	-0.021	0.342	0.884	0.942
		$\beta_1 = 0.443$	0.454 (0.123)	0.011	0.130	0.883	0.949
		$\gamma_1 = 0.316$	0.313 (0.021)	-0.003	0.022	0.875	0.923
		$\gamma_2 = 0.179$	0.180 (0.009)	0.001	0.009	0.900	0.939
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.207 (0.286)	-0.016	0.291	0.889	0.942
		$\beta_1 = 0.573$	0.579 (0.102)	0.007	0.105	0.903	0.945
		$\gamma_1 = 0.316$	0.314 (0.019)	-0.002	0.019	0.898	0.932
		$\gamma_2 = 0.179$	0.179 (0.007)	0.000	0.007	0.913	0.954
	Low	$\beta_0 =$ -0.038	-0.050 (0.231)	-0.013	0.229	0.911	0.953
		$\beta_1 = 0.443$	0.449 (0.087)	0.006	0.085	0.905	0.962
		$\gamma_1 = 0.316$	0.315 (0.015)	-0.001	0.015	0.908	0.957
		$\gamma_2 = 0.179$	0.179 (0.006)	0.000	0.006	0.898	0.951
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.197 (0.286)	-0.005	0.288	0.893	0.945
		$\beta_1 = 0.573$	0.575 (0.103)	0.003	0.101	0.904	0.949
		$\gamma_1 = 0.215$	0.213 (0.013)	-0.002	0.013	0.887	0.934
		$\gamma_2 = 0.183$	0.183 (0.005)	0.000	0.005	0.908	0.949
	Low	$\beta_0 =$ -0.038	-0.043 (0.231)	-0.006	0.228	0.910	0.951
		$\beta_1 = 0.443$	0.446 (0.087)	0.003	0.087	0.899	0.948
		$\gamma_1 = 0.215$	0.215 (0.010)	0.000	0.010	0.900	0.947
		$\gamma_2 = 0.183$	0.183 (0.004)	0.000	0.004	0.911	0.950
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.192 (0.284)	0.000	0.283	0.907	0.953
		$\beta_1 = 0.573$	0.574 (0.101)	0.001	0.100	0.913	0.953
		$\gamma_1 = 0.470$	0.467 (0.028)	-0.003	0.029	0.890	0.942
		$\gamma_2 = 0.253$	0.254 (0.016)	0.001	0.017	0.889	0.946
	Low	$\beta_0 =$ -0.038	-0.049 (0.231)	-0.011	0.227	0.901	0.951
		$\beta_1 = 0.443$	0.451 (0.087)	0.008	0.088	0.897	0.950
		$\gamma_1 = 0.470$	0.467 (0.022)	-0.003	0.023	0.880	0.940
		$\gamma_2 = 0.253$	0.253 (0.014)	0.000	0.014	0.895	0.946
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.196 (0.285)	-0.005	0.283	0.910	0.957
		$\beta_1 = 0.573$	0.574 (0.102)	0.001	0.102	0.906	0.951
		$\gamma_1 = 0.320$	0.317 (0.019)	-0.003	0.019	0.886	0.933
		$\gamma_2 = 0.256$	0.257 (0.010)	0.001	0.010	0.913	0.954
	Low	$\beta_0 =$ -0.038	-0.051 (0.231)	-0.013	0.223	0.913	0.956
		$\beta_1 = 0.443$	0.448 (0.087)	0.005	0.086	0.905	0.959
		$\gamma_1 = 0.320$	0.319 (0.015)	-0.001	0.015	0.902	0.956
		$\gamma_2 = 0.256$	0.256 (0.009)	0.000	0.009	0.918	0.949
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.192	-1.210 (0.295)	-0.018	0.298	0.896	0.952
		$\beta_1 = 0.573$	0.575 (0.100)	0.003	0.101	0.905	0.949
		$\gamma_1 = 0.316$	0.314 (0.018)	-0.002	0.019	0.887	0.943
		$\gamma_2 = 0.179$	0.179 (0.007)	0.000	0.007	0.894	0.947
	Low	$\beta_0 =$ -0.038	-0.046 (0.238)	-0.008	0.244	0.892	0.953
		$\beta_1 = 0.443$	0.447 (0.085)	0.004	0.087	0.894	0.948
		$\gamma_1 = 0.316$	0.315 (0.015)	-0.001	0.015	0.884	0.926
		$\gamma_2 = 0.179$	0.179 (0.006)	0.000	0.006	0.907	0.957
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.192	-1.208 (0.233)	-0.017	0.224	0.911	0.953
		$\beta_1 = 0.573$	0.581 (0.083)	0.009	0.077	0.924	0.963
		$\gamma_1 = 0.316$	0.314 (0.015)	-0.002	0.015	0.896	0.940
		$\gamma_2 = 0.179$	0.179 (0.006)	0.000	0.006	0.903	0.955
	Low	$\beta_0 =$ -0.038	-0.043 (0.189)	-0.006	0.188	0.896	0.949
		$\beta_1 = 0.443$	0.447 (0.071)	0.004	0.073	0.890	0.943
		$\gamma_1 = 0.316$	0.316 (0.012)	0.000	0.012	0.901	0.957
		$\gamma_2 = 0.179$	0.179 (0.005)	0.000	0.005	0.896	0.949

Table 5.4: Estimates, bias, and root mean square error (RMSE) of cured proportions corresponding to four groups for the Bernoulli cure rate model with Weibull lifetime.

n	γ	p_0	Estimate	Bias	RMSE
200 $(55, 60, 45, 40)$	$(0.316, 0.179)$	p_{01} =0.650	0.654	0.004	0.068
		p_{02} =0.512	0.515	0.003	0.048
		p_{03} =0.371	0.372	0.001	0.047
		p_{04} =0.250	0.251	0.001	0.058
		p_{01} =0.400	0.403	0.003	0.062
		p_{02} =0.300	0.299	-0.001	0.039
		p_{03} =0.216	0.214	-0.002	0.040
		p_{04} =0.150	0.151	0.001	0.046
400 $(110, 120, 90, 80)$	$(0.316, 0.179)$	p_{01} =0.650	0.651	0.001	0.051
		p_{02} =0.512	0.512	0.001	0.036
		p_{03} =0.371	0.371	-0.001	0.034
		p_{04} =0.250	0.250	0.000	0.043
		p_{01} =0.400	0.401	0.001	0.045
		p_{02} =0.300	0.300	0.000	0.027
		p_{03} =0.216	0.216	0.000	0.028
		p_{04} =0.150	0.151	0.001	0.032
400 $(110, 120, 90, 80)$	$(0.215, 0.183)$	p_{01} =0.650	0.652	0.002	0.048
		p_{02} =0.512	0.512	0.001	0.035
		p_{03} =0.371	0.370	-0.002	0.034
		p_{04} =0.250	0.248	-0.002	0.042
		p_{01} =0.400	0.399	-0.001	0.043
		p_{02} =0.300	0.298	-0.001	0.025
		p_{03} =0.216	0.215	-0.001	0.026
		p_{04} =0.150	0.151	0.001	0.032
400 $(110, 120, 90, 80)$	$(0.470, 0.253)$	p_{01} =0.650	0.650	0.000	0.049
		p_{02} =0.512	0.512	0.000	0.035
		p_{03} =0.371	0.371	0.000	0.035
		p_{04} =0.250	0.251	0.001	0.045
		p_{01} =0.400	0.401	0.001	0.045
		p_{02} =0.300	0.299	-0.001	0.027
		p_{03} =0.216	0.214	-0.001	0.027
		p_{04} =0.150	0.150	0.000	0.032
400 $(110, 120, 90, 80)$	$(0.320, 0.256)$	p_{01} =0.650	0.652	0.002	0.049
		p_{02} =0.512	0.513	0.001	0.035
		p_{03} =0.371	0.371	-0.001	0.035
		p_{04} =0.250	0.250	0.000	0.044
		p_{01} =0.400	0.399	-0.001	0.043
		p_{02} =0.300	0.299	-0.001	0.027
		p_{03} =0.216	0.215	-0.001	0.027
		p_{04} =0.150	0.151	0.001	0.032
400 $(100, 100, 100, 100)$	$(0.316, 0.179)$	p_{01} =0.650	0.649	-0.001	0.051
		p_{02} =0.512	0.511	-0.001	0.036
		p_{03} =0.371	0.370	-0.001	0.031
		p_{04} =0.250	0.249	-0.001	0.038
		p_{01} =0.400	0.403	0.003	0.047
		p_{02} =0.300	0.300	0.000	0.027
		p_{03} =0.216	0.214	-0.002	0.025
		p_{04} =0.150	0.149	-0.001	0.030
600 $(165, 180, 135, 120)$	$(0.316, 0.179)$	p_{01} =0.650	0.651	0.001	0.041
		p_{02} =0.512	0.512	0.001	0.029
		p_{03} =0.371	0.371	0.000	0.028
		p_{04} =0.250	0.250	0.000	0.036
		p_{01} =0.400	0.403	0.003	0.035
		p_{02} =0.300	0.300	0.000	0.021
		p_{03} =0.216	0.215	-0.001	0.021
		p_{04} =0.150	0.149	-0.001	0.025

Table 5.5: Estimates, bias, and root mean square error (RMSE) of cured proportions corresponding to four groups for the Poisson cure rate model with Weibull lifetime.

n	γ	p_0	Estimate	Bias	RMSE
200 $(55, 60, 45, 40)$	$(0.316, 0.179)$	p_{01} =0.650	0.647	-0.003	0.066
		p_{02} =0.512	0.510	-0.002	0.049
		p_{03} =0.371	0.370	-0.002	0.048
		p_{04} =0.250	0.251	0.001	0.059
		p_{01} =0.400	0.402	0.002	0.061
		p_{02} =0.300	0.300	0.000	0.038
		p_{03} =0.216	0.215	-0.001	0.037
		p_{04} =0.150	0.151	0.001	0.042
400 $(110, 120, 90, 80)$	$(0.316, 0.179)$	p_{01} =0.650	0.651	0.001	0.047
		p_{02} =0.512	0.513	0.001	0.035
		p_{03} =0.371	0.372	0.001	0.035
		p_{04} =0.250	0.251	0.001	0.042
		p_{01} =0.400	0.399	-0.001	0.042
		p_{02} =0.300	0.299	-0.001	0.026
		p_{03} =0.216	0.216	0.000	0.025
		p_{04} =0.150	0.152	0.002	0.029
400 $(110, 120, 90, 80)$	$(0.215, 0.183)$	p_{01} =0.650	0.649	-0.001	0.049
		p_{02} =0.512	0.512	0.000	0.035
		p_{03} =0.371	0.372	0.001	0.034
		p_{04} =0.250	0.252	0.002	0.042
		p_{01} =0.400	0.399	-0.001	0.043
		p_{02} =0.300	0.300	0.000	0.026
		p_{03} =0.216	0.217	0.001	0.026
		p_{04} =0.150	0.153	0.003	0.029
400 $(110, 120, 90, 80)$	$(0.470, 0.253)$	p_{01} =0.650	0.650	0.000	0.048
		p_{02} =0.512	0.512	0.001	0.035
		p_{03} =0.371	0.372	0.000	0.034
		p_{04} =0.250	0.251	0.001	0.041
		p_{01} =0.400	0.401	0.001	0.042
		p_{02} =0.300	0.300	0.001	0.028
		p_{03} =0.216	0.216	0.001	0.027
		p_{04} =0.150	0.152	0.002	0.030
400 $(110, 120, 90, 80)$	$(0.320, 0.256)$	p_{01} =0.650	0.648	-0.002	0.047
		p_{02} =0.512	0.510	-0.001	0.034
		p_{03} =0.371	0.370	-0.001	0.033
		p_{04} =0.250	0.251	0.001	0.042
		p_{01} =0.400	0.403	0.003	0.045
		p_{02} =0.300	0.301	0.001	0.027
		p_{03} =0.216	0.216	0.000	0.026
		p_{04} =0.150	0.151	0.001	0.030
400 $(100, 100, 100, 100)$	$(0.316, 0.179)$	p_{01} =0.650	0.649	-0.001	0.049
		p_{02} =0.512	0.512	0.000	0.036
		p_{03} =0.371	0.371	0.000	0.031
		p_{04} =0.250	0.251	0.001	0.037
		p_{01} =0.400	0.400	0.000	0.044
		p_{02} =0.300	0.300	0.000	0.027
		p_{03} =0.216	0.216	0.000	0.025
		p_{04} =0.150	0.151	0.001	0.028
600 $(165, 180, 135, 120)$	$(0.316, 0.179)$	p_{01} =0.650	0.650	0.000	0.038
		p_{02} =0.512	0.512	0.001	0.028
		p_{03} =0.371	0.372	0.001	0.028
		p_{04} =0.250	0.252	0.002	0.034
		p_{01} =0.400	0.400	0.000	0.034
		p_{02} =0.300	0.300	0.001	0.021
		p_{03} =0.216	0.217	0.002	0.021
		p_{04} =0.150	0.153	0.003	0.024

Table 5.6: Estimates, bias, and root mean square error (RMSE) of cured proportions corresponding to four groups for the geometric cure rate model with Weibull lifetime.

n	γ	p_0	Estimate	Bias	RMSE
$200\ (55, 60, 45, 40)$	$(0.316, 0.179)$	p_{01} =0.650	0.651	0.001	0.064
		p_{02} =0.512	0.513	0.001	0.049
		p_{03} =0.371	0.371	-0.001	0.044
		p_{04} =0.250	0.250	0.000	0.051
		p_{01} =0.400	0.404	0.004	0.057
		p_{02} =0.300	0.301	0.001	0.037
		p_{03} =0.216	0.216	0.000	0.034
		p_{04} =0.150	0.151	0.001	0.036
$400\ (110, 120, 90, 80)$	$(0.316, 0.179)$	p_{01} =0.650	0.651	0.001	0.046
		p_{02} =0.512	0.512	0.001	0.035
		p_{03} =0.371	0.371	0.000	0.033
		p_{04} =0.250	0.250	0.000	0.039
		p_{01} =0.400	0.402	0.002	0.039
		p_{02} =0.300	0.300	0.001	0.026
		p_{03} =0.216	0.215	0.000	0.023
		p_{04} =0.150	0.150	0.000	0.024
$400\ (110, 120, 90, 80)$	$(0.215, 0.183)$	p_{01} =0.650	0.649	-0.001	0.046
		p_{02} =0.512	0.511	0.000	0.035
		p_{03} =0.371	0.371	0.000	0.031
		p_{04} =0.250	0.251	0.001	0.036
		p_{01} =0.400	0.401	0.001	0.038
		p_{02} =0.300	0.300	0.001	0.025
		p_{03} =0.216	0.216	0.000	0.023
		p_{04} =0.150	0.151	0.001	0.025
$400\ (110, 120, 90, 80)$	$(0.470, 0.253)$	p_{01} =0.650	0.648	-0.002	0.045
		p_{02} =0.512	0.511	-0.001	0.035
		p_{03} =0.371	0.371	0.000	0.032
		p_{04} =0.250	0.251	0.001	0.037
		p_{01} =0.400	0.402	0.002	0.039
		p_{02} =0.300	0.300	0.000	0.026
		p_{03} =0.216	0.215	-0.001	0.024
		p_{04} =0.150	0.149	-0.001	0.026
$400\ (110, 120, 90, 80)$	$(0.320, 0.256)$	p_{01} =0.650	0.649	-0.001	0.044
		p_{02} =0.512	0.512	0.000	0.033
		p_{03} =0.371	0.372	0.001	0.031
		p_{04} =0.250	0.252	0.002	0.037
		p_{01} =0.400	0.403	0.003	0.038
		p_{02} =0.300	0.301	0.001	0.025
		p_{03} =0.216	0.216	0.001	0.023
		p_{04} =0.150	0.151	0.001	0.025
$400\ (100, 100, 100, 100)$	$(0.316, 0.179)$	p_{01} =0.650	0.652	0.002	0.047
		p_{02} =0.512	0.515	0.003	0.036
		p_{03} =0.371	0.374	0.003	0.031
		p_{04} =0.250	0.253	0.003	0.035
		p_{01} =0.400	0.402	0.002	0.042
		p_{02} =0.300	0.300	0.001	0.027
		p_{03} =0.216	0.216	0.000	0.022
		p_{04} =0.150	0.151	0.001	0.024
$600\ (165, 180, 135, 120)$	$(0.316, 0.179)$	p_{01} =0.650	0.651	0.001	0.036
		p_{02} =0.512	0.511	0.000	0.028
		p_{03} =0.371	0.369	-0.002	0.026
		p_{04} =0.250	0.248	-0.002	0.028
		p_{01} =0.400	0.401	0.001	0.032
		p_{02} =0.300	0.300	0.000	0.021
		p_{03} =0.216	0.215	0.000	0.020
		p_{04} =0.150	0.150	0.000	0.021

Table 5.7: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the COM-Poisson cure rate model with ϕ fixed at 0.5 for Weibull lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP	
						90%	95%
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.194 (0.302)	-0.003	0.295	0.912	0.958
		$\beta_1 = 0.573$	0.573 (0.112)	0.000	0.110	0.911	0.958
		$\gamma_1 = 0.316$	0.314 (0.019)	-0.002	0.018	0.900	0.948
		$\gamma_2 = 0.179$	0.180 (0.006)	0.001	0.006	0.890	0.941
	Low	$\beta_0 =$ -0.038	-0.049 (0.258)	-0.012	0.250	0.913	0.958
		$\beta_1 = 0.443$	0.450 (0.104)	0.007	0.102	0.913	0.950
		$\gamma_1 = 0.316$	0.314 (0.015)	-0.002	0.015	0.885	0.932
		$\gamma_2 = 0.179$	0.179 (0.005)	0.000	0.005	0.893	0.949
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.198 (0.303)	-0.006	0.307	0.885	0.945
		$\beta_1 = 0.573$	0.575 (0.112)	0.002	0.116	0.883	0.942
		$\gamma_1 = 0.215$	0.214 (0.013)	-0.001	0.013	0.885	0.951
		$\gamma_2 = 0.183$	0.183 (0.004)	0.000	0.004	0.888	0.935
	Low	$\beta_0 =$ -0.038	-0.032 (0.258)	0.005	0.264	0.903	0.950
		$\beta_1 = 0.443$	0.441 (0.104)	-0.002	0.106	0.904	0.946
		$\gamma_1 = 0.215$	0.214 (0.010)	-0.001	0.010	0.898	0.938
		$\gamma_2 = 0.183$	0.183 (0.003)	0.000	0.003	0.899	0.949
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.206 (0.303)	-0.014	0.299	0.913	0.956
		$\beta_1 = 0.573$	0.579 (0.111)	0.006	0.112	0.899	0.952
		$\gamma_1 = 0.470$	0.466 (0.028)	-0.004	0.028	0.904	0.944
		$\gamma_2 = 0.253$	0.254 (0.013)	0.001	0.014	0.907	0.951
	Low	$\beta_0 =$ -0.038	-0.024 (0.258)	0.013	0.256	0.902	0.946
		$\beta_1 = 0.443$	0.439 (0.103)	-0.004	0.102	0.903	0.952
		$\gamma_1 = 0.470$	0.469 (0.022)	-0.001	0.023	0.889	0.944
		$\gamma_2 = 0.253$	0.253 (0.011)	0.000	0.011	0.891	0.941
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.197 (0.303)	-0.005	0.296	0.905	0.957
		$\beta_1 = 0.573$	0.573 (0.112)	0.001	0.111	0.902	0.949
		$\gamma_1 = 0.320$	0.318 (0.019)	-0.002	0.019	0.886	0.936
		$\gamma_2 = 0.256$	0.256 (0.009)	0.000	0.009	0.901	0.951
	Low	$\beta_0 =$ -0.038	-0.033 (0.258)	0.004	0.260	0.895	0.951
		$\beta_1 = 0.443$	0.442 (0.104)	-0.001	0.106	0.889	0.949
		$\gamma_1 = 0.320$	0.319 (0.015)	-0.001	0.016	0.884	0.941
		$\gamma_2 = 0.256$	0.256 (0.007)	0.000	0.007	0.909	0.949
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.192	-1.184 (0.311)	0.008	0.308	0.906	0.957
		$\beta_1 = 0.573$	0.571 (0.109)	-0.001	0.108	0.902	0.952
		$\gamma_1 = 0.316$	0.314 (0.018)	-0.002	0.019	0.896	0.935
		$\gamma_2 = 0.179$	0.179 (0.006)	0.000	0.006	0.897	0.949
	Low	$\beta_0 =$ -0.038	-0.042 (0.265)	-0.004	0.267	0.900	0.954
		$\beta_1 = 0.443$	0.449 (0.101)	0.006	0.102	0.895	0.948
		$\gamma_1 = 0.316$	0.315 (0.015)	-0.001	0.015	0.892	0.941
		$\gamma_2 = 0.179$	0.179 (0.005)	0.000	0.005	0.884	0.934
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.192	-1.191 (0.246)	0.001	0.246	0.905	0.952
		$\beta_1 = 0.573$	0.573 (0.091)	0.000	0.090	0.907	0.947
		$\gamma_1 = 0.316$	0.315 (0.015)	-0.001	0.015	0.893	0.935
		$\gamma_2 = 0.179$	0.179 (0.005)	0.000	0.005	0.904	0.952
	Low	$\beta_0 =$ -0.038	-0.020 (0.211)	0.018	0.215	0.909	0.945
		$\beta_1 = 0.443$	0.436 (0.084)	-0.007	0.085	0.905	0.948
		$\gamma_1 = 0.316$	0.315 (0.012)	-0.001	0.012	0.900	0.954
		$\gamma_2 = 0.179$	0.179 (0.004)	0.000	0.004	0.906	0.962

Table 5.8: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the COM-Poisson cure rate model with $\phi = 0.5$ for Weibull lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP	
						90%	95%
200 $(55, 60, 45, 40)$	High	$\beta_0 =$ -1.192	-1.234 (0.426)	-0.042	0.441	0.899	0.947
		$\beta_1 = 0.573$	0.590 (0.156)	0.018	0.165	0.893	0.949
		$\gamma_1 = 0.316$	0.308 (0.026)	-0.008	0.034	0.784	0.858
		$\gamma_2 = 0.179$	0.179 (0.008)	0.000	0.012	0.706	0.806
		$\phi = 0.5$	0.710 $(-)$	0.210	0.875	$-$	$-$
	Low	$\beta_0 =$ -0.038	-0.010 (0.356)	0.028	0.405	0.856	0.926
		$\beta_1 = 0.443$	0.435 (0.140)	-0.008	0.165	0.848	0.918
		$\gamma_1 = 0.316$	0.304 (0.020)	-0.012	0.033	0.637	0.744
		$\gamma_2 = 0.179$	0.177 (0.007)	-0.002	0.016	0.422	0.538
		$\phi = 0.5$	0.654 $(-)$	0.154	0.835	$-$	$-$
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.183 (0.298)	-0.009	0.315	0.900	0.935
		$\beta_1 = 0.573$	0.571 (0.109)	-0.001	0.118	0.887	0.937
		$\gamma_1 = 0.316$	0.309 (0.018)	-0.007	0.026	0.744	0.828
		$\gamma_2 = 0.179$	0.178 (0.006)	-0.001	0.011	0.581	0.684
		$\phi = 0.5$	0.639 $(-)$	0.139	0.799	$-$	$-$
	Low	$\beta_0 =$ -0.038	0.001 (0.247)	0.039	0.299	0.821	0.897
		$\beta_1 = 0.443$	0.419 (0.096)	-0.024	0.126	0.779	0.849
		$\gamma_1 = 0.316$	0.303 (0.014)	-0.013	0.029	0.498	0.583
		$\gamma_2 = 0.179$	0.175 (0.005)	-0.004	0.014	0.273	0.363
		$\phi = 0.5$	0.495 $(-)$	-0.005	0.717	$-$	$-$
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.121 (0.297)	0.071	0.302	0.893	0.938
		$\beta_1 = 0.573$	0.550 (0.109)	-0.023	0.115	0.883	0.930
		$\gamma_1 = 0.215$	0.211 (0.012)	-0.004	0.018	0.717	0.799
		$\gamma_2 = 0.183$	0.182 (0.004)	-0.001	0.007	0.566	0.680
		$\phi = 0.5$	0.636 $(-)$	0.136	0.787	$-$	$-$
	Low	$\beta_0 =$ -0.038	0.002 (0.249)	0.040	0.293	0.837	0.911
		$\beta_1 = 0.443$	0.427 (0.098)	-0.016	0.125	0.784	0.868
		$\gamma_1 = 0.215$	0.207 (0.010)	-0.008	0.020	0.488	0.572
		$\gamma_2 = 0.183$	0.181 (0.004)	-0.002	0.010	0.259	0.347
		$\phi = 0.5$	0.587 $(-)$	0.087	0.772	$-$	$-$
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.199 (0.298)	-0.007	0.323	0.867	0.938
		$\beta_1 = 0.573$	0.573 (0.109)	0.001	0.119	0.853	0.929
		$\gamma_1 = 0.470$	0.458 (0.028)	-0.012	0.037	0.754	0.834
		$\gamma_2 = 0.253$	0.252 (0.013)	-0.001	0.025	0.555	0.668
		$\phi = 0.5$	0.644 $(-)$	0.144	0.813	$-$	$-$
	Low	$\beta_0 =$ -0.038	0.008 (0.248)	0.045	0.293	0.840	0.911
		$\beta_1 = 0.443$	0.421 (0.097)	-0.022	0.125	0.782	0.861
		$\gamma_1 = 0.470$	0.452 (0.022)	-0.018	0.042	0.514	0.621
		$\gamma_2 = 0.253$	0.247 (0.011)	-0.006	0.030	0.288	0.368
		$\phi = 0.5$	0.549 $(-)$	0.049	0.744	$-$	$-$
400 $(110, 120, 90, 80)$	High	$\beta_0 =$ -1.192	-1.180 (0.298)	0.011	0.318	0.872	0.936
		$\beta_1 = 0.573$	0.569 (0.109)	-0.004	0.117	0.873	0.939
		$\gamma_1 = 0.320$	0.313 (0.019)	-0.007	0.026	0.725	0.806
		$\gamma_2 = 0.256$	0.254 (0.009)	-0.002	0.016	0.557	0.660
		$\phi = 0.5$	0.597 $(-)$	0.097	0.774	$-$	$-$
	Low	$\beta_0 =$ -0.038	0.011 (0.248)	0.048	0.311	0.808	0.886
		$\beta_1 = 0.443$	0.422 (0.097)	-0.021	0.130	0.753	0.841
		$\gamma_1 = 0.320$	0.307 (0.015)	-0.013	0.029	0.496	0.589
		$\gamma_2 = 0.256$	0.252 (0.007)	-0.004	0.020	0.288	0.374
		$\phi = 0.5$	0.533 $(-)$	0.033	0.731	$-$	$-$
400 $(100, 100, 100, 100)$	High	$\beta_0 =$ -1.192	-1.169 (0.306)	0.022	0.328	0.867	0.928
		$\beta_1 = 0.573$	0.562 (0.106)	-0.011	0.116	0.859	0.924
		$\gamma_1 = 0.316$	0.308 (0.018)	-0.008	0.026	0.699	0.791
		$\gamma_2 = 0.179$	0.178 (0.006)	-0.001	0.012	0.496	0.613
		$\phi = 0.5$	0.622 $(-)$	0.122	0.804	$-$	$-$
	Low	$\beta_0 =$ -0.038	0.009 (0.254)	0.046	0.304	0.829	0.896
		$\beta_1 = 0.443$	0.421 (0.094)	-0.022	0.121	0.790	0.868
		$\gamma_1 = 0.316$	0.303 (0.014)	-0.013	0.029	0.490	0.560
		$\gamma_2 = 0.179$	0.176 (0.005)	-0.003	0.014	0.271	0.349
		$\phi = 0.5$	0.526 $(-)$	0.026	0.720	$-$	$-$
600 $(165, 180, 135, 120)$	High	$\beta_0 =$ -1.192	-1.145 (0.242)	0.047	0.275	0.845	0.912
		$\beta_1 = 0.573$	0.555 (0.088)	-0.017	0.100	0.832	0.910
		$\gamma_1 = 0.316$	0.310 (0.015)	-0.006	0.022	0.706	0.804
		$\gamma_2 = 0.179$	0.177 (0.005)	-0.002	0.010	0.460	0.540
		$\phi = 0.5$	0.547 $(-)$	0.047	0.723	$-$	$-$
	Low	$\beta_0 =$ -0.038	0.023 (0.202)	0.060	0.261	0.776	0.873
		$\beta_1 = 0.443$	0.414 (0.078)	-0.029	0.106	0.739	0.842
		$\gamma_1 = 0.316$	0.302 (0.012)	-0.014	0.028	0.378	0.464
		$\gamma_2 = 0.179$	0.175 (0.004)	-0.004	0.013	0.199	0.276
		$\phi = 0.5$	0.469 $(-)$	-0.031	0.664	$-$	$-$

Table 5.9: Observed levels (in bold) and powers of the likelihood ratio test with Weibull lifetime.

Fitted model	True COM-Poisson model				
	$\phi = 0$	$\phi = 0.5$	$\phi = 1$	$\phi = 2$	$\phi \to \infty$
			Setting 1		
geometric	**0.013**	0.186	0.367	0.519	0.836
Poisson	0.746	0.223	**0.092**	0.038	0.076
Bernoulli	0.992	0.819	0.600	0.405	**0.070**
			Setting 2		
geometric	**0.007**	0.214	0.402	0.682	0.934
Poisson	0.883	0.301	**0.129**	0.045	0.287
Bernoulli	0.999	0.936	0.774	0.463	**0.051**
			Setting 3		
geometric	**0.018**	0.150	0.266	0.455	0.697
Poisson	0.373	0.081	**0.049**	0.013	0.007
Bernoulli	0.901	0.610	0.428	0.221	**0.057**

Table 5.10: Observed selection rates based on AIC* with Weibull lifetime.

Fitted model	True COM-Poisson model				
	$\phi = 0$	$\phi = 0.5$	$\phi = 1$	$\phi = 2$	$\phi \to \infty$
			Setting 1		
geometric	0.860	0.356	0.194	0.082	0.003
Poisson	0.140	0.596	0.632	0.555	0.166
Bernoulli	0.000	0.048	0.174	0.363	0.831
			Setting 2		
geometric	0.887	0.330	0.148	0.045	0.001
Poisson	0.113	0.635	0.749	0.608	0.137
Bernoulli	0.000	0.035	0.103	0.347	0.862
			Setting 3		
geometric	0.766	0.401	0.265	0.117	0.034
Poisson	0.220	0.478	0.496	0.452	0.224
Bernoulli	0.014	0.121	0.239	0.431	0.742

*In all cases, the results are the same for the Bayesian information criterion (BIC) as well.

Table 5.11: TRB (in %) (TRE) in estimation of cured proportions when fitting different models for a given true model with Weibull lifetime.

	True model		
Fitted model	geometric	Poisson	Bernoulli
		Setting 1	
geometric	0.837 (-)	36.486 (0.747)	66.838 (0.438)
Poisson	23.118 (0.692)	1.511 (-)	22.437 (0.913)
Bernoulli	1.583 (0.750)	1.628 (0.923)	1.002 (-)
		Setting 2	
geometric	1.911 (-)	34.692 (0.672)	67.759 (0.333)
Poisson	23.569 (0.632)	1.330 (-)	23.727 (0.819)
Bernoulli	3.257 (0.744)	2.715 (0.880)	0.868 (-)
		Setting 3	
geometric	0.829 (-)	17.298 (0.895)	33.484 (0.634)
Poisson	11.127 (0.832)	0.499 (-)	10.637 (0.964)
Bernoulli	4.628 (0.839)	2.337 (0.945)	0.576 (-)

Table 5.12: TRB (in %) and TRE when using the as a model selection criterion between the three considered models with Weibull lifetime.

True model	TRB (%)	TRE
	Setting 1	
geometric	5.810	0.900
Poisson	8.616	0.947
Bernoulli	3.912	1.007
	Setting 2	
geometric	4.130	0.912
Poisson	8.623	0.922
Bernoulli	3.107	0.998
	Setting 3	
geometric	4.375	0.933
Poisson	8.480	0.954
Bernoulli	3.474	0.987

Table 5.13: AIC, BIC and maximized log-likelihood function (l) values for different cure rate models with Weibull lifetime.

Model	AIC	BIC	l
COM-Poisson (geometric)	**1026.838**	**1042.970**	**-509.419**
COM-Poisson ($\phi = 0.5$)	1032.388	1048.520	-512.194
Poisson	1034.788	1050.920	-513.394
COM-Poisson ($\phi = 2$)	1037.792	1053.924	-514.896
Bernoulli	1043.182	1059.314	-517.591

Table 5.14: Maximum likelihood estimates of the parameters of the COM-Poisson (geometric) cure rate model with Weibull lifetime.

Parameter	Estimate	Standard error
β_0	-1.181	0.244
β_1	0.498	0.089
γ_1	0.528	0.034
γ_2	0.340	0.029

Table 5.15: Estimates, standard errors, and 95% confidence intervals (CI) of cure rates of patients stratified by nodule category with Weibull lifetime.

Nodule category	Cure rate	Estimate	Standard error	95% CI
1	p_{01}	0.664	0.039	$(0.588, 0.740)$
2	p_{02}	0.546	0.032	$(0.483, 0.609)$
3	p_{03}	0.422	0.033	$(0.357, 0.487)$
4	p_{04}	0.308	0.040	$(0.230, 0.386)$

Chapter 6

Likelihood inference for generalized gamma distribution

6.1 Introduction

The generalized gamma distribution has been studied in the literature quite extensively. For instance, Balakrishnan and Chan (1995) investigated some computational issues relating to inference for this distribution. Its application in reliability theory was addressed by Agarwal and Kalla (1996) and its use in economics and survival analysis were addressed by Yamaguchi (1992) and Peng et al. (1998). Kalbfleisch and Prentice (2002) and Lawless (2003) described the use of this distribution in an accelerated failure time model. Balakrishnan and Peng (2006) considered this distribution in the context of frailty model. Recently, Khodabin and Ahmadabadi (2010) presented some general review of important properties of the generalized gamma family. As mentioned before, the generalized gamma distribution includes many of the commonly used lifetime distributions as special cases. Thus, it has considerable flexibility to capture the characteristics in a distribution that might have been missed when using its special cases. This motivates us to use the generalized gamma distribution as the distribution of the lifetime as it would also enable us to carry out a model discrimination within this family so as to select a parsimonious lifetime distribution that provides the best fit to the data.

In this chapter, we assume the lifetime in (1.1.1) to follow the generalized gamma distribution with p.d.f. as given in (1.4.7). We relate the cure rate p_0 to covariates $\boldsymbol{x}_i$ by the logistic link function $p_{0i} = \frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}, i = 1, \ldots, n$. For the determination of the MLEs of the model parameters, the E-step and M-step of the EM algorithm, as described in Section 1.6.1, are carried out for fixed values of q and ϕ. Finally, the parameters q and ϕ are estimated by using the two-way profile likelihood. The asymptotic variance-covariance matrix of the MLEs is also obtained under the assumption that q and ϕ are fixed. It is to be noted that for the special cases of the COM-Poisson model, we need to apply a profile likelihood on q only. We present the simplified expressions of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function, where $\boldsymbol{\theta}^* = (\boldsymbol{\beta}', \sigma, \lambda)'$, and the components of the score function for the COM-Poisson cure rate model and some of its special cases. The expressions of the first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\theta}^*$ that assist us in carrying out the required maximization step and the components of the observed information matrix are presented in Appendix D.1 and Appendix D.2, respectively. It is to be noted that to employ the EM algorithm, we need to calculate the derivatives of the gamma and incomplete gamma function. Although explicit expressions for these derivatives are available, here we calculated these numerically. For some special cases of the COM-Poisson model, the results of an extensive Monte Carlo simulation study are presented to evaluate the performance of the proposed estimation method. Next, we present the results of model discrimination within the generalized gamma family by using the likelihood-based method and the information-based criteria. Finally, the cutaneous melanoma data is analyzed to illustrate the two-way flexibility of the COM-Poisson family and the generalized gamma family so as to select a parsimonious competing cause distribution and a lifetime distribution that jointly provide an adequate fit to the data.

6.2 Expressions of E- and M-steps for different cure rate models

Bernoulli cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function, for a fixed value of q, can be expressed as

$$Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) = Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)}) + Q_2(\boldsymbol{\gamma}^*, \boldsymbol{\pi}^{(k)}),$$

where

$$Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)}) = \sum_{I_1} \boldsymbol{x}_i' \boldsymbol{\beta} + \sum_{I_0} \pi_i^{(k)} \boldsymbol{x}_i' \boldsymbol{\beta} - \sum_{I^*} \log(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})),$$

and

$$Q_2(\boldsymbol{\gamma}^*, \boldsymbol{\pi}^{(k)}) = n_1 \log(K(\boldsymbol{\gamma})) + \left(\frac{1}{q\sigma} - 1\right) \sum_{I_1} \log t_i - \frac{1}{q^2} \sum_{I_1} (\lambda t_i)^{q/\sigma} + \sum_{I_0} \pi_i^{(k)} \log(S(t_i; \boldsymbol{\gamma}))$$

with

$$\pi_i^{(k)} = \left. \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta}) S(t_i; \boldsymbol{\gamma})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta}) S(t_i; \boldsymbol{\gamma})} \right|_{\boldsymbol{\theta}^* = \boldsymbol{\theta}^{*(k)}}, \tag{6.2.1}$$

for $i \in I_0$, and $\boldsymbol{\gamma}^* = (\sigma, \lambda)'$. We note that the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function can be separated into two parts, one containing the regression parameter and the other containing the lifetime parameter. Hence, the M-step can be carried out by maximizing $Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)})$ with respect to $\boldsymbol{\beta}$ and $Q_2(\boldsymbol{\gamma}^*, \boldsymbol{\pi}^{(k)})$ with respect to $\boldsymbol{\gamma}^*$, separately.

Poisson cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function, for a fixed value of q, can be expressed as

$$\begin{aligned} Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) &= n_1 \log(K(\boldsymbol{\gamma})) + \left(\frac{1}{q\sigma} - 1\right) \sum_{I_1} \log t_i - \frac{1}{q^2} \sum_{I_1} (\lambda t_i)^{q/\sigma} + \sum_{I_1} A_{GGi}(\boldsymbol{\beta}, \boldsymbol{\gamma}) \\ &\quad + \sum_{I_1} \log(\log(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta}))) + \sum_{I_0} \pi_i^{(k)} \log(\exp(A_{GGi}(\boldsymbol{\beta}, \boldsymbol{\gamma})) - 1) \\ &\quad - \sum_{I^*} \log(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})), \end{aligned}$$

where

$$A_{GGi}(\boldsymbol{\beta}, \boldsymbol{\gamma}) = \log(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})) S(t_i; \boldsymbol{\gamma}), \tag{6.2.2}$$

for $i = 1, 2, \ldots, n$, and

$$\pi_i^{(k)} = \left. \frac{\exp(A_{GGi}(\boldsymbol{\beta}, \boldsymbol{\gamma})) - 1}{\exp(A_{GGi}(\boldsymbol{\beta}, \boldsymbol{\gamma}))} \right|_{\boldsymbol{\theta}^* = \boldsymbol{\theta}^{*(k)}}, \tag{6.2.3}$$

for $i \in I_0$.

Geometric cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function, for a fixed value of q, can be expressed as

$$\begin{aligned} Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) &= n_1 \log(K(\boldsymbol{\gamma})) + \sum_{I_1} \boldsymbol{x}_i' \boldsymbol{\beta} + \left(\frac{1}{q\sigma} - 1\right) \sum_{I_1} \log t_i - \frac{1}{q^2} \sum_{I_1} (\lambda t_i)^{q/\sigma} \\ &\quad - 2 \sum_{I_1} \log\{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})(1 - S(t_i; \boldsymbol{\gamma}))\} - \sum_{I_0} \log(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})) \\ &\quad + \sum_{I_0} \pi_i^{(k)} \boldsymbol{x}_i' \boldsymbol{\beta} + \sum_{I_0} \pi_i^{(k)} \log\left\{ \frac{S(t_i; \boldsymbol{\gamma})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})(1 - S(t_i; \boldsymbol{\gamma}))} \right\}, \end{aligned}$$

where

$$\pi_i^{(k)} = \left. \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta}) S(t_i; \boldsymbol{\gamma})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})} \right|_{\boldsymbol{\theta}^* = \boldsymbol{\theta}^{*(k)}}, \tag{6.2.4}$$

for $i \in I_0$.

COM-Poisson cure rate model: The $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function, for a fixed value of ϕ and q, can be expressed as

$$\begin{aligned} Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)}) &= n_1 \log(K(\boldsymbol{\gamma})) + \left(\frac{1}{q\sigma} - 1\right) \sum_{I_1} \log t_i - \frac{1}{q^2} \sum_{I_1} (\lambda t_i)^{q/\sigma} - \sum_{I_1} \log(S(t_i; \boldsymbol{\gamma})) \\ &\quad + \sum_{I_1} \log z_{2i} + \sum_{I_0} \pi_i^{(k)} \log z_{1i} - \sum_{I^*} \log(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})), \end{aligned}$$

where

$$z_1 = z_1(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{\{H_\phi^{-1}(1 + \exp(\boldsymbol{x}'\boldsymbol{\beta}))S(t; \boldsymbol{\gamma})\}^j}{(j!)^\phi},$$

$$z_2 = z_2(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{j\{H_\phi^{-1}(1 + \exp(\boldsymbol{x}'\boldsymbol{\beta}))S(t; \boldsymbol{\gamma})\}^j}{(j!)^\phi},$$

and

$$\pi_i^{(k)} = \left. \frac{z_1(\boldsymbol{\theta}; \boldsymbol{x}_i, t_i)}{1 + z_1(\boldsymbol{\theta}; \boldsymbol{x}_i, t_i)} \right|_{\boldsymbol{\theta}^* = \boldsymbol{\theta}^{*(k)}}, \tag{6.2.5}$$

for $i \in I_0$.

6.3 Components of the score function

Bernoulli cure rate model: The components of the score function, for a fixed value of q, are

$$\begin{aligned} \frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il} + \sum_{I_0} x_{il} w_i - \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})}, \\ \frac{\partial l}{\partial \sigma} &= -\frac{n_1}{\sigma} \left\{1 + \frac{\log \lambda}{q\sigma}\right\} + \frac{1}{q\sigma^2} \sum_{I_1} \{(\lambda t_i)^{q/\sigma} \log(\lambda t_i) - \log t_i\} + \sum_{I_0} w_i \frac{\partial}{\partial \sigma} \log(S(t_i; \boldsymbol{\gamma})), \\ \frac{\partial l}{\partial \lambda} &= \frac{n_1}{q\sigma\lambda} - \frac{1}{q\sigma\lambda} \sum_{I_1} (\lambda t_i)^{q/\sigma} + \sum_{I_0} w_i \frac{\partial}{\partial \lambda} \log(S(t_i; \boldsymbol{\gamma})), \end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$w_i = \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})S(t_i;\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})S(t_i;\boldsymbol{\beta})}, \tag{6.3.1}$$

for $i \in I_0$.

Poisson cure rate model: The components of the score function, for a fixed value of q, are

$$\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))} + \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})\{S(t_i;\boldsymbol{\gamma})-1\}}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}, \\
\frac{\partial l}{\partial \sigma} &= -\frac{n_1}{\sigma}\left\{1+\frac{\log\lambda}{q\sigma}\right\} + \frac{1}{q\sigma^2}\sum_{I_1}\{(\lambda t_i)^{q/\sigma}\log(\lambda t_i) - \log t_i\} \\
&\quad + \sum_{I^*}\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma}), \\
\frac{\partial l}{\partial \lambda} &= \frac{n_1}{q\sigma\lambda} - \frac{1}{q\sigma\lambda}\sum_{I_1}(\lambda t_i)^{q/\sigma} + \sum_{I^*}\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma}),
\end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$.

Geometric cure rate model: The components of the score function, for a fixed value of q, are

$$\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1} x_{il}\{1-2R_i(\boldsymbol{\beta},\boldsymbol{\gamma})(1-S(t_i;\boldsymbol{\gamma}))\} - \sum_{I_0} x_{il}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})} \\
&\quad + \sum_{I_0} x_{il} w_i\{1-R_i(\boldsymbol{\beta},\boldsymbol{\gamma})(1-S(t_i;\boldsymbol{\gamma}))\},
\end{aligned}$$

$$
\begin{aligned}
\frac{\partial l}{\partial \sigma} &= -\frac{n_1}{\sigma}\left\{1+\frac{\log\lambda}{q\sigma}\right\}+\frac{1}{q\sigma^2}\sum_{I_1}\{(\lambda t_i)^{q/\sigma}\log(\lambda t_i)-\log t_i\} \\
&\quad +2\sum_{I_1}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma})+\sum_{I_0}\left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma}) \\
&\quad +\sum_{I_0}w_iR_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma}), \\
\frac{\partial l}{\partial \lambda} &= \frac{n_1}{q\sigma\lambda}-\frac{1}{q\sigma\lambda}\sum_{I_1}(\lambda t_i)^{q/\sigma}+2\sum_{I_1}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma}) \\
&\quad +\sum_{I_0}\left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma})+\sum_{I_0}w_iR_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma}),
\end{aligned}
$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$
w_i = \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})S(t_i;\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}, \tag{6.3.2}
$$

for $i \in I_0$, and

$$
R_i(\boldsymbol{\beta},\boldsymbol{\gamma}) = \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}, \tag{6.3.3}
$$

for $i = 1, 2, \ldots, n$.

COM-Poisson cure rate model: The components of the score function, for a fixed value of q and ϕ, are

$$
\begin{aligned}
\frac{\partial l}{\partial \beta_l} &= \sum_{I_1}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{21i}}{z_{2i}z_{01i}}+\sum_{I_0}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{2i}}{(1+z_{1i})z_{01i}}-\sum_{I^*}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}, \\
\frac{\partial l}{\partial \sigma} &= -\frac{n_1}{\sigma}\left\{1+\frac{\log\lambda}{q\sigma}\right\}+\frac{1}{q\sigma^2}\sum_{I_1}\{(\lambda t_i)^{q/\sigma}\log(\lambda t_i)-\log t_i\} \\
&\quad +\sum_{I_1}\left\{\frac{z_{21i}}{z_{2i}}-1\right\}\frac{\partial}{\partial\sigma}\log(S(t_i;\boldsymbol{\gamma}))+\sum_{I_0}\left\{\frac{z_{2i}}{1+z_{1i}}\right\}\frac{\partial}{\partial\sigma}\log(S(t_i;\boldsymbol{\gamma})),
\end{aligned}
$$

$$\begin{aligned}\frac{\partial l}{\partial \lambda} &= \frac{n_1}{q\sigma\lambda} - \frac{1}{q\sigma\lambda}\sum_{I_1}(\lambda t_i)^{q/\sigma} + \sum_{I_1}\left\{\frac{z_{21i}}{z_{2i}} - 1\right\}\frac{\partial}{\partial \lambda}\log(S(t_i;\boldsymbol{\gamma})) \\ &\quad + \sum_{I_0}\left\{\frac{z_{2i}}{1+z_{1i}}\right\}\frac{\partial}{\partial \lambda}\log(S(t_i;\boldsymbol{\gamma})),\end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$z_{21} = z_{21}(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{j^2\{H_\phi^{-1}(1+\exp(\boldsymbol{x}'\boldsymbol{\beta}))S(t;\boldsymbol{\gamma})\}^j}{(j!)^\phi},$$

and

$$z_{01} = z_{01}(\boldsymbol{\theta}_1; \boldsymbol{x}) = \sum_{j=1}^{\infty} \frac{j\{H_\phi^{-1}(1+\exp(\boldsymbol{x}'\boldsymbol{\beta}))\}^j}{(j!)^\phi}.$$

6.4 Results of the simulation study: model fitting

We refer to the simulation study setup described in Section 1.7. We considered two sample sizes: $n = 200$ and $n = 400$ so as to study the behavior of the model under small and moderate sample sizes. In this simulation study, we generated data from different cure rate models and then employed the proposed estimation method for the determination of the MLEs of the model parameters. To examine the performance of the estimates, we calculated the empirical bias and RMSE of the estimates. We also calculated the coverage probabilities of the confidence intervals based on the asymptotic normality of the MLEs for different nominal confidence levels. In order to obtain a choice of the parameter (σ, λ), for a given value of q, we equated the mean and the variance of the underlying generalized gamma distribution in (1.4.7) to 0.25 and 0.05, respectively. On solving the two equations, we can easily obtain the value of (σ, λ). With the parameter q being the shape parameter, we note that for different fixed values of q, we get different values of (σ, λ) for the same fixed values of the mean and variance. We considered the true value of q to be 0.5 for which we get the true value of (σ, λ) to be $(0.871, 4.632)$. For the special cases of the COM-Poisson model, we applied a profile likelihood on q for which we chose the range of q to be [0.10,1.25] and in this interval q was divided in steps of 0.05. For each chosen value of q, we employed the EM algorithm to estimate $(\beta_0, \beta_1, \sigma, \lambda)$. Finally, we took the value of q as the MLE for which the corresponding maximized log-likelihood function was the maximum. To carry out the EM algorithm, we need to provide initial values of the parameters so as to start the iterative procedure. For this purpose, we applied a discrete four-dimensional grid search on $(\beta_0, \beta_1, \sigma, \lambda)$. To generate data from the generalized gamma distribution, we made use of the fact that if W follows a generalized gamma distribution with density function in (1.4.7), then $V = W^{q/\sigma}$ follows a gamma distribution with shape parameter $\frac{1}{q^2}$ and scale parameter $\frac{q^2}{\lambda^{q/\sigma}}$. Hence, $V^{\sigma/q}$ is a generalized gamma variable with density function in (1.4.7). All the simulations were performed using the R software and the results were based on 1000 Monte Carlo runs.

We present the results for the three special cases of the COM-Poisson model in Tables 6.1−6.3. We observe that the EM algorithm converges to the true parameter values quite accurately. As expected, the standard errors and the RMSE of the estimates decrease with an increase in sample size and with a decrease in censoring proportion. The profile likelihood approach of estimating the parameter q seems to perform well with the bias in the estimate of q being small. However, it results in the underestimation of standard errors of other lifetime parameters due to which the coverage probabilities of the corresponding parameters fall below the nominal level. In case of the Bernoulli and Poisson cure rate models, the undercoverage is seen for both the lifetime parameters σ and λ. However, for the Bernoulli model, the undercoverage is more pronounced for λ, whereas for the Poisson model, the undercoverage is more pronounced for σ. In case of the geometric cure rate model, the undercoverage is only seen for the lifetime parameter σ. In Tables 6.4−6.6, we present the bias and RMSE in the estimate of the cured proportions corresponding to four groups for the three special cases of the COM-Poisson cure rate model. We note that the estimates of cured proportions are very close to the true values and that the RMSE decrease with an increase in sample size and with a decrease in censoring proportion.

Table 6.1: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the Bernoulli cure rate model with generalized gamma lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP	
						90%	95%
200 $(55, 60, 45, 40)$	High	β_0 = -1.192	-1.223 (0.487)	-0.031	0.514	0.895	0.946
		β_1 = 0.573	0.591 (0.183)	0.018	0.192	0.894	0.946
		σ = 0.871	0.859 (0.077)	-0.012	0.095	0.814	0.877
		λ = 4.632	4.715 (0.524)	0.083	0.754	0.731	0.817
		q=0.5	0.494 (-)	-0.006	0.299	-	-
200 $(55, 60, 45, 40)$	Low	β_0 = -0.038	-0.054 (0.425)	-0.016	0.428	0.913	0.952
		β_1 = 0.443	0.464 (0.178)	0.021	0.178	0.913	0.949
		σ = 0.871	0.864 (0.059)	-0.007	0.067	0.858	0.914
		λ = 4.632	4.656 (0.378)	0.024	0.589	0.678	0.776
		q=0.5	0.503 (-)	-0.003	0.232	-	-
400 $(110, 120, 90, 80)$	Low	β_0 = -0.038	-0.045 (0.298)	-0.007	0.293	0.910	0.958
		β_1 = 0.443	0.451 (0.124)	0.008	0.124	0.910	0.965
		σ = 0.871	0.871 (0.042)	0.000	0.048	0.855	0.914
		λ = 4.632	4.667 (0.270)	0.035	0.414	0.722	0.801
		q=0.5	0.482 (-)	-0.018	0.173	-	-

6.5 Simulation study: model discrimination within the generalized gamma family

The flexibility of the wider class of generalized gamma family and its inclusion of many commonly used distributions as special cases enable us to select a simple distribution within this class that provides an adequate fit as the generalized gamma distribution itself in many cases. Therefore, it is of practical interest to explore the use of this

Table 6.2: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the geometric cure rate model with generalized gamma lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP	
						90%	95%
200 $(55, 60, 45, 40)$	High	$\beta_0 =$ -1.192	-1.191 (0.417)	0.001	0.406	0.912	0.958
		$\beta_1 = 0.573$	0.580 (0.142)	0.007	0.142	0.904	0.951
		$\sigma = 0.871$	0.893 (0.091)	0.022	0.142	0.729	0.825
		$\lambda = 4.632$	4.582 (0.942)	-0.050	0.901	0.899	0.948
		q=0.5	0.480 (-)	-0.020	0.312	-	-
200 $(55, 60, 45, 40)$	Low	$\beta_0 =$ -0.038	-0.039 (0.335)	-0.002	0.345	0.899	0.956
		$\beta_1 = 0.443$	0.447 (0.122)	0.004	0.121	0.892	0.956
		$\sigma = 0.871$	0.922 (0.070)	0.051	0.120	0.691	0.772
		$\lambda = 4.632$	4.547 (0.783)	-0.085	0.785	0.882	0.934
		q=0.5	0.439 (-)	-0.061	0.247	-	-
400 $(110, 120, 90, 80)$	Low	$\beta_0 =$ -0.038	-0.036 (0.236)	0.002	0.237	0.898	0.954
		$\beta_1 = 0.443$	0.443 (0.086)	0.000	0.086	0.918	0.952
		$\sigma = 0.871$	0.917 (0.048)	0.046	0.089	0.613	0.741
		$\lambda = 4.632$	4.600 (0.551)	-0.032	0.549	0.910	0.942
		q=0.5	0.437 (-)	-0.063	0.182	-	-

Table 6.3: Estimates, bias, root mean square error (RMSE), and coverage probabilities (CP) for the Poisson cure rate model with generalized gamma lifetime.

n	p	Parameter	Estimate (s.e.)	Bias	RMSE	CP	
						90%	95%
200 $(55, 60, 45, 40)$	High	$\beta_0 =$ -1.192	-1.228 (0.448)	-0.036	0.443	0.907	0.960
		$\beta_1 = 0.573$	0.589 (0.164)	0.016	0.167	0.895	0.953
		$\sigma = 0.871$	0.851 (0.081)	-0.020	0.131	0.675	0.765
		$\lambda = 4.632$	4.713 (0.664)	0.081	0.796	0.813	0.896
		q=0.5	0.514 (-)	0.014	0.326	-	-
200 $(55, 60, 45, 40)$	Low	$\beta_0 =$ -0.038	-0.044 (0.382)	-0.007	0.390	0.898	0.946
		$\beta_1 = 0.443$	0.448 (0.155)	0.005	0.157	0.898	0.950
		$\sigma = 0.871$	0.859 (0.061)	-0.012	0.093	0.716	0.801
		$\lambda = 4.632$	4.687 (0.496)	0.055	0.587	0.828	0.900
		q=0.5	0.499 (-)	-0.001	0.236	-	-
400 $(110, 120, 90, 80)$	Low	$\beta_0 =$ -0.038	-0.033 (0.270)	0.005	0.270	0.902	0.955
		$\beta_1 = 0.443$	0.443 (0.109)	0.000	0.112	0.881	0.947
		$\sigma = 0.871$	0.868 (0.043)	-0.003	0.066	0.717	0.789
		$\lambda = 4.632$	4.667 (0.351)	0.035	0.428	0.844	0.904
		q=0.5	0.494 (-)	-0.006	0.175	-	-

generalized gamma family of distributions to select a parsimonious distribution for the lifetime that provides an adequate fit to the data. To this end, we can either consider the likelihood-based method (using the likelihood ratio test) or the information-based criteria (using the AIC and BIC).

Table 6.4: Estimates, bias, and root mean square error (RMSE) of cured proportions corresponding to four groups for the Bernoulli cure rate model with generalized gamma lifetime.

n	(σ, λ)	p_0	Estimate	Bias	RMSE
200 $(55, 60, 45, 40)$	$(0.871, 4.632)$	p_{01} =0.650	0.649	-0.001	0.076
		p_{02} =0.512	0.510	-0.001	0.053
		p_{03} =0.371	0.367	-0.004	0.050
		p_{04} =0.250	0.248	-0.002	0.062
200 $(55, 60, 45, 40)$	$(0.871, 4.632)$	p_{01} =0.400	0.401	0.001	0.062
		p_{02} =0.300	0.296	-0.003	0.037
		p_{03} =0.216	0.211	-0.005	0.037
		p_{04} =0.150	0.148	-0.002	0.044
400 $(110, 120, 90, 80)$	$(0.871, 4.632)$	p_{01} =0.400	0.401	0.001	0.043
		p_{02} =0.300	0.299	-0.001	0.026
		p_{03} =0.216	0.214	-0.001	0.027
		p_{04} =0.150	0.150	0.000	0.031

Table 6.5: Estimates, bias, and root mean square error (RMSE) of cured proportions corresponding to four groups for the geometric cure rate model with generalized gamma lifetime.

n	(σ, λ)	p_0	Estimate	Bias	RMSE
200 $(55, 60, 45, 40)$	$(0.871, 4.632)$	p_{01} =0.650	0.645	-0.004	0.058
		p_{02} =0.512	0.508	-0.003	0.049
		p_{03} =0.371	0.368	-0.003	0.046
		p_{04} =0.250	0.249	-0.001	0.050
200 $(55, 60, 45, 40)$	$(0.871, 4.632)$	p_{01} =0.400	0.401	0.001	0.044
		p_{02} =0.300	0.300	0.000	0.031
		p_{03} =0.216	0.216	0.000	0.026
		p_{04} =0.150	0.152	0.001	0.026
400 $(110, 120, 90, 80)$	$(0.871, 4.632)$	p_{01} =0.400	0.400	0.000	0.030
		p_{02} =0.300	0.300	0.000	0.021
		p_{03} =0.216	0.217	0.000	0.018
		p_{04} =0.150	0.152	0.001	0.019

6.5.1 Information-based criteria

In this simulation study, we investigate the performance of AIC and BIC in selecting one of the lognormal, gamma, Weibull and exponential distributions (Fitted models) for the lifetime variable, given a true lifetime distribution. For this purpose, we have to fix a distribution for the competing cause variable and in this study we determined

Table 6.6: Estimates, bias, and root mean square error (RMSE) of cured proportions corresponding to four groups for the Poisson cure rate model with generalized gamma lifetime.

n	(σ, λ)	p_0	Estimate	Bias	RMSE
200 $(55, 60, 45, 40)$	$(0.871, 4.632)$	p_{01} =0.650	0.651	0.001	0.068
		p_{02} =0.512	0.512	0.001	0.054
		p_{03} =0.371	0.370	-0.001	0.054
		p_{04} =0.250	0.250	0.000	0.063
200 $(55, 60, 45, 40)$	$(0.871, 4.632)$	p_{01} =0.400	0.402	0.002	0.062
		p_{02} =0.300	0.301	0.001	0.040
		p_{03} =0.216	0.217	0.001	0.039
		p_{04} =0.150	0.154	0.004	0.043
400 $(110, 120, 90, 80)$	$(0.871, 4.632)$	p_{01} =0.400	0.400	0.000	0.043
		p_{02} =0.300	0.300	0.000	0.028
		p_{03} =0.216	0.216	0.000	0.028
		p_{04} =0.150	0.152	0.002	0.032

the performance of AIC and BIC for each of the three special cases of the COM-Poisson model as well. For each generated dataset, we calculated the AIC and BIC values of the fitted models. Based on 1000 datasets in each situation, we calculated the observed selection rates for each of the two criteria used. Tables 6.7 - 6.9 show the results for Bernoulli, geometric and Poisson cure rate models, respectively.

We first note that when the true model is either lognormal or exponential, both the selection criteria perform well in selecting the correct model. Furthermore, this selection rate increases with an increase in sample size and with a decrease in censoring proportion. When the true lifetime distribution is gamma, we note that AIC selects the gamma model highest number of times provided the censoring proportion is low or the sample size is high. However, BIC performs well only when the sample size is high. When Weibull is the true lifetime distribution, we see that AIC performs better in selecting the true model as the censoring proportion decreases and the sample size increases. However, in this case, BIC always selects the exponential model the highest number of times irrespective of the sample size and level of censoring. Also, when

Table 6.7: Model discrimination based on AIC (BIC) within the generalized gamma family for Bernoulli cure rate model.

Fitted model	True generalized gamma model				
	lognormal	q=0.5	gamma	Weibull	exponential
			200 $(55, 60, 45, 40)$, High		
lognormal	0.882 (0.882)	0.404 (0.381)	0.077 (0.045)	0.062 (0.028)	0.077 (0.022)
gamma	0.109 (0.109)	0.471 (0.406)	0.275 (0.123)	0.177 (0.051)	0.086 (0.010)
Weibull	0.009 (0.009)	0.111 (0.097)	0.313 (0.118)	0.265 (0.090)	0.076 (0.012)
exponential	0.000 (0.000)	0.013 (0.115)	0.334 (0.713)	0.496 (0.830)	0.761 (0.955)
			200 $(55, 60, 45, 40)$, Low		
lognormal	0.917 (0.917)	0.363 (0.355)	0.046 (0.030)	0.026 (0.018)	0.018 (0.008)
gamma	0.083 (0.083)	0.576 (0.558)	0.395 (0.210)	0.225 (0.102)	0.094 (0.012)
Weibull	0.000 (0.000)	0.058 (0.056)	0.324 (0.181)	0.387 (0.177)	0.081 (0.017)
exponential	0.000 (0.000)	0.003 (0.031)	0.235 (0.579)	0.362 (0.703)	0.807 (0.963)
			400 $(110, 120, 90, 80)$, Low		
lognormal	0.981 (0.981)	0.318 (0.318)	0.009 (0.007)	0.000 (0.000)	0.003 (0.001)
gamma	0.019 (0.019)	0.678 (0.678)	0.578 (0.424)	0.308 (0.158)	0.086 (0.009)
Weibull	0.000 (0.000)	0.004 (0.004)	0.356 (0.248)	0.508 (0.281)	0.088 (0.006)
exponential	0.000 (0.000)	0.000 (0.000)	0.057 (0.321)	0.184 (0.561)	0.823 (0.984)

Table 6.8: Model discrimination based on AIC (BIC) within the generalized gamma family for geometric cure rate model.

Fitted model	True generalized gamma model				
	lognormal	q=0.5	gamma	Weibull	exponential
			200 $(55, 60, 45, 40)$, High		
lognormal	0.906 (0.906)	0.410 (0.408)	0.172 (0.105)	0.129 (0.057)	0.163 (0.036)
gamma	0.086 (0.086)	0.423 (0.416)	0.296 (0.160)	0.192 (0.072)	0.066 (0.013)
Weibull	0.008 (0.008)	0.167 (0.166)	0.339 (0.177)	0.340 (0.120)	0.095 (0.013)
exponential	0.000 (0.000)	0.001 (0.011)	0.193 (0.558)	0.339 (0.751)	0.675 (0.939)
			200 $(55, 60, 45, 40)$, Low		
lognormal	0.969 (0.969)	0.348 (0.348)	0.055 (0.041)	0.040 (0.026)	0.058 (0.018)
gamma	0.031 (0.031)	0.581 (0.580)	0.435 (0.296)	0.214 (0.094)	0.075 (0.009)
Weibull	0.000 (0.000)	0.071 (0.071)	0.404 (0.259)	0.390 (0.178)	0.093 (0.012)
exponential	0.000 (0.000)	0.000 (0.001)	0.106 (0.404)	0.357 (0.702)	0.774 (0.961)
			400 $(110, 120, 90, 80)$, Low		
lognormal	0.997 (0.997)	0.291 (0.291)	0.017 (0.014)	0.008 (0.007)	0.019 (0.005)
gamma	0.003 (0.003)	0.690 (0.690)	0.556 (0.477)	0.344 (0.200)	0.085 (0.006)
Weibull	0.000 (0.000)	0.019 (0.019)	0.408 (0.347)	0.475 (0.242)	0.086 (0.008)
exponential	0.000 (0.000)	0.000 (0.000)	0.019 (0.161)	0.173 (0.550)	0.810 (0.981)

$q = 0.5$, both AIC and BIC select the gamma model highest number of times. It is also of interest to note that the decision reached by AIC and BIC are exactly the same when the true model is lognormal.

Table 6.9: Model discrimination based on AIC (BIC) within the generalized gamma family for Poisson cure rate model.

	True generalized gamma model				
Fitted model	lognormal	q=0.5	gamma	Weibull	exponential
			200 $(55, 60, 45, 40)$, High		
lognormal	0.845 (0.845)	0.402 (0.395)	0.125 (0.073)	0.075 (0.028)	0.083 (0.018)
gamma	0.149 (0.149)	0.461 (0.441)	0.285 (0.125)	0.175 (0.068)	0.061 (0.014)
Weibull	0.007 (0.007)	0.135 (0.134)	0.299 (0.127)	0.268 (0.084)	0.092 (0.007)
exponential	0.000 (0.000)	0.002 (0.030)	0.291 (0.675)	0.482 (0.819)	0.765 (0.961)
			200 $(55, 60, 45, 40)$, Low		
lognormal	0.906 (0.906)	0.357 (0.356)	0.056 (0.046)	0.027 (0.017)	0.029 (0.007)
gamma	0.094 (0.094)	0.585 (0.579)	0.422 (0.267)	0.258 (0.096)	0.078 (0.009)
Weibull	0.000 (0.000)	0.058 (0.057)	0.372 (0.221)	0.353 (0.148)	0.080 (0.012)
exponential	0.000 (0.000)	0.000 (0.008)	0.150 (0.466)	0.362 (0.739)	0.813 (0.972)
			400 $(110, 120, 90, 80)$, Low		
lognormal	0.975 (0.975)	0.322 (0.322)	0.012 (0.012)	0.005 (0.004)	0.008 (0.004)
gamma	0.025 (0.025)	0.664 (0.664)	0.535 (0.441)	0.314 (0.167)	0.080 (0.010)
Weibull	0.000 (0.000)	0.014 (0.014)	0.417 (0.343)	0.504 (0.281)	0.099 (0.008)
exponential	0.000 (0.000)	0.000 (0.000)	0.036 (0.204)	0.177 (0.548)	0.813 (0.978)

6.5.2 Likelihood-based method

In this simulation study, for a given distribution of the competing cause, we examine the performance of the likelihood ratio test in testing the null hypothesis that the lifetime distribution can be described by one of lognormal ($H_0 : q = 0$), gamma ($H_0 : q = \sigma$), Weibull ($H_0 : q = 1$) and exponential ($H_0 : q = 1, \sigma = 1$) distribution *versus* the alternative hypothesis that the lifetime distribution can be described by a member of the generalized gamma family other than the one specified in the null hypothesis. Under the standard likelihood theory, we have the asymptotic null distribution of Λ to be a central chi-square distribution with degrees of freedom equal to the difference in the number of parameters between the two models. However, when testing for $H_0 : q = 0$, we take into account that the parameter q lies on the boundary of the parameter space. In this study, we only considered the Bernoulli and Poisson cure rate models. For each simulated dataset, we calculated the likelihood ratio test statistic of the fitted lognormal, gamma, Weibull and exponential models *versus* the fitted generalized gamma model. Based on 1000 datasets in each situation and nominal significance level of 5%, we calculated the observed significance levels and powers of the likelihood ratio test, determined by the rejection rates of null hypothesis, and these values are presented in Tables 6.10 and 6.11 for the Bernoulli and Poisson models, respectively. The numbers in bold represent the observed levels while the other numbers represent the observed powers.

Table 6.10: Model discrimination based on likelihood ratio test within the generalized gamma family for Bernoulli cure rate model.

	True generalized gamma model				
Fitted model	lognormal	q=0.5	gamma	Weibull	exponential
			$200\ (55, 60, 45, 40)$, High		
lognormal	**0.019**	0.409	0.786	0.869	0.837
gamma	0.719	0.173	**0.043**	0.034	0.031
Weibull	0.949	0.362	0.063	**0.028**	0.020
exponential	1.000	0.880	0.289	0.187	**0.045**
			$200\ (55, 60, 45, 40)$, Low		
lognormal	**0.021**	0.616	0.957	0.974	0.984
gamma	0.930	0.279	**0.051**	0.062	0.039
Weibull	0.999	0.560	0.070	**0.045**	0.032
exponential	1.000	0.979	0.407	0.306	**0.047**
			$400\ (110, 120, 90, 80)$, Low		
lognormal	**0.021**	0.886	0.999	1.000	1.000
gamma	1.000	0.505	**0.051**	0.091	0.052
Weibull	1.000	0.863	0.112	**0.045**	0.051
exponential	1.000	1.000	0.728	0.496	**0.048**

It can be seen that the chi-square distribution provides a good approximation to the null distribution of the likelihood ratio test as the observed levels are close to the nominal level. The mixture chi-square distribution, on the other hand, results in the observed level being too conservative. The observed powers, however, vary in different situations. When lognormal distribution is the true lifetime distribution, the test has high power to reject the gamma, Weibull and exponential as lifetime distributions. When Weibull is the true lifetime distribution, the test has high power to reject the lognormal distribution. However, in this case, the test does not appear

Table 6.11: Model discrimination based on likelihood ratio test within the generalized gamma family for Poisson cure rate model.

	True generalized gamma model				
Fitted model	lognormal	q=0.5	gamma	Weibull	exponential
			200 $(55, 60, 45, 40)$, High		
lognormal	**0.010**	0.353	0.692	0.747	0.715
gamma	0.663	0.167	**0.035**	0.027	0.031
Weibull	0.938	0.359	0.054	**0.032**	0.031
exponential	1.000	0.960	0.318	0.176	**0.048**
			200 $(55, 60, 45, 40)$, Low		
lognormal	**0.013**	0.590	0.929	0.954	0.956
gamma	0.877	0.224	**0.050**	0.046	0.037
Weibull	0.997	0.526	0.067	**0.030**	0.035
exponential	1.000	0.997	0.531	0.267	**0.030**
			400 $(110, 120, 90, 80)$, Low		
lognormal	**0.016**	0.844	0.999	0.999	0.997
gamma	0.993	0.395	**0.053**	0.079	0.050
Weibull	1.000	0.828	0.086	**0.047**	0.049
exponential	1.000	1.000	0.829	0.519	**0.045**

to have good power to reject the gamma distribution and has a low power to reject the exponential distribution. When the true lifetime distribution is gamma, the test again has high power to reject the lognormal distribution but a low power to reject the exponential distribution. However, the test does not have any power to reject the Weibull distribution. When exponential is the true lifetime distribution, the test does not have power to reject the gamma and Weibull as lifetime distributions, but has high power to reject the lognormal distribution. Based on these observations, we can conclude that both the gamma and Weibull distributions provide similar fits to the data and that they do not differ significantly. However, the difference in model fitting between the lognormal distribution and the Weibull, gamma or exponential distributions is significant enough to be detected by the likelihood ratio test under the generalized gamma setup. These findings are consistent with those of Balakrishnan and Peng (2006) in the context of frailty model.

In this section, we have utilized the flexibility of the generalized gamma family to select a parsimonious lifetime distribution within this family that provides an adequate fit to the data. It is also possible to utilize the flexibility of the COM-Poisson family together with the flexibility of the generalized gamma family to select a pair of parsimonious distributions, one for the competing cause variable and the other for the lifetime variable, that jointly provide an adequate fit to the data. This two-way model discrimination is illustrated with the data on cancer recurrence in the next section.

6.6 Two-way model discrimination using cutaneous melanoma data

In this section, we demonstrate an application of the proposed methodology to the cutaneous melanoma data. In our application, we selected the nodule category ($1 : n = 111; 2 : n = 137; 3 : n = 87; 4 : n = 82$) as the only covariate. First, we employed a two-way profile likelihood on (q, ϕ). For this, we chose the range of q to be $[0.10, 1.50]$ and in this interval q was divided in steps of 0.05. We also allowed q to take the value zero. Along with this, we chose the range of ϕ to be $[0, 2]$ and in this interval ϕ was divided in steps of 0.05. For each possible pair (q, ϕ), we employed the EM algorithm to estimate the model parameters and calculated the observed data log-likelihood function. Finally, we took the pair $(\hat{q}, \hat{\phi})$ and the corresponding estimates of the model parameters as the MLE for which the maximized log-likelihood function is the maximum.

For these data, the two-way profile likelihood gave $(\hat{q}, \hat{\phi}) \approx (0.25, 0)$. For these values of q and ϕ, the corresponding estimates of the model parameters were found to be $\hat{\beta}_0 = -0.969, \hat{\beta}_1 = 0.491, \hat{\sigma} = 0.802, \hat{\lambda} = 0.320$, and the corresponding maximized log-likelihood value as -507.766. Since the value of ϕ is close to zero, we first considered testing for the suitability of the geometric cure rate model ($H_0 : \phi = 0$) for the number of competing causes M in (1.3.1). Taking into account that ϕ lies on the boundary of the parameter space, we obtained the likelihood ratio test statistic $\Lambda \approx 0$ (p-value=0.5). We thus adopt the geometric model as our working cure rate model. With the test procedure described in Section 6.5.2, we next considered testing for the lognormal, gamma, Weibull and exponential as lifetime distributions assuming the geometric model. In Table 6.12, we present the Λ statistic values and the corresponding $p-$values for the above testing problem. We note that the likelihood ratio test gives strong evidence against the exponential distribution in (1.4.7). At 5% level of significance, any of the lognormal, gamma or Weibull distributions would provide an adequate fit to the data. However, at 10% level of significance, the assumption of the Weibull distribution in (1.4.7) gets rejected.

On assuming the geometric model, the AIC and BIC values for the generalized gamma distribution are 1025.532 and 1045.697, respectively. To find the competing cause distribution and the lifetime distribution that jointly provide the best fit to the data, we also calculated the AIC and BIC values for different lifetime and competing cause distributions and the results are presented in Table 6.13. We first note that for the exponential lifetime distribution, the AIC and BIC values are the maximum for any of the competing cause distributions considered. This suggests that the assumption of the exponential distribution is not appropriate for these data and this agrees with the decision reached by the likelihood ratio test earlier. When comparing the competing cause distributions, we note that for the geometric cure rate model, the AIC and BIC values are the minimum for all the three lognormal, gamma and Weibull lifetime distributions. This clearly explains that the geometric cure rate model provides the best fit to the data and this again agrees with the likelihood ratio test results given earlier. For the geometric model, it is interesting to note that the AIC and the BIC values for the fitted lognormal, gamma and Weibull distributions are quite close to each other, which means that all the three mentioned lifetime distributions provides similar fit to the data. However, it is clear that the best fit is achieved by the gamma lifetime distribution. For this reason, for the considered data, we adopt the COM-Poisson (geometric) cure rate model with gamma lifetime distribution as our working model. Based on this working model, the MLEs and standard errors of the model parameters as well as the estimates of the cure proportions are all as presented earlier in Tables 4.14 and 4.15.

Table 6.12: Λ values and p-values when testing for different lifetime distributions assuming the geometric model.

Lifetime distribution	Λ value	p-value
lognormal	1.488	0.111
gamma	0.556	0.456
Weibull	3.305	0.069
exponential	53.072	2.99×10^{-12}

Table 6.13: Two-way model discrimination using AIC and BIC.

Lifetime distribution		Competing cause distribution: Bernoulli	Geometric	Poisson
Lognormal	AIC	1036.940	1025.020	1030.944
	BIC	1053.072	1041.152	1047.076
Gamma	AIC	1037.628	**1024.088**	1030.248
	BIC	1053.760	**1040.220**	1046.380
Weibull	AIC	1043.182	1026.838	1034.788
	BIC	1059.315	1042.970	1050.921
Exponential	AIC	1076.072	1074.604	1073.561
	BIC	1088.171	1086.703	1085.660

Chapter 7

Concluding remarks

7.1 Summary of research

Any clinical trial would involve a heterogeneous population of patient's which, based on a treatment, may get divided into two groups, with one group consisting of all those who respond favorably to the treatment and subsequently become immune to the disease and are said to be cured, and the other group consisting of those who do not respond to the treatment and remain uncured. The main interest of the investigator is then to estimate the proportion of patients cured and to study the causes for the failure of the treatment in the non-cured group of patients. This proportion is an important and useful measure in seeing the trends in the survival of patients suffering from cancer.

Rodrigues et al. (2009) developed the flexible COM-Poisson cure rate model, which includes some of the commonly used cure rate models as special cases, and then discussed the maximum likelihood estimation of the model parameters based on right censored data using the GAMLSS package. Data obtained from cancer clinical trials are often right censored and as such the EM algorithm can be used as an alternative and efficient tool for the determination of the MLEs of the model parameters based on right censored data. In this thesis, we have considered the COM-Poisson cure rate model and the main contribution of this work is in developing an exact EM algorithm for estimating the model parameters of the COM-Poisson cure rate model and some of its special cases. The inferential procedure developed here is based on a formal theoretical ground using which an exact algorithm is developed. Furthermore, the log-linear link function used by Rodrigues et al. (2009) creates a problem in the case of geometric cure rate model as it violates the restriction on the geometric parameter. To avoid this problem, we have also considered the logistic link function to relate the cure rate parameter directly with the covariates.

We first considered the lifetime distribution to be exponential and upon using the log-linear link function, we have developed in detail the steps of the EM algorithm for the estimation of the model parameters. To evaluate the performance of the proposed estimation method, an extensive Monte Carlo simulation study has been carried out and the obtained results show that the proposed estimation method works very well. However, the profile likelihood approach of estimating the COM-Poisson shape parameter ϕ results in large bias and MSE in its estimate. It also results in undercoverage of the model parameters with coverage probabilities falling below the nominal level. Furthermore, model discrimination between the over-dispersed and under-dispersed cure rate models is carried out by means of likelihood ratio test.

We then considered the lifetime distribution to be lognormal, gamma and Weibull, and for each of these cases, upon using the logistic link function, we developed the necessary steps of the EM algorithm for the determination of the MLEs of the parameters of the COM-Poisson cure rate model and some of its special cases. Two types of simulation studies have been carried out, one dealing with the estimation of the model parameters and evaluating the performance of the proposed methodology and the other utilizing the flexibility of the COM-Poisson family to select a parsimonious competing cause distribution within this family that provides an adequate fit to the data. The results again show that the EM algorithm converges to the true parameter values quite accurately. The profile likelihood approach once again results in large bias and RMSE in the estimate of ϕ and also results in undercoverage of the model parameters, as seen in the exponential case. In this regard, one can think of a more accurate method of estimation of ϕ. Model discrimination between different cure rate models, for each of these lifetime distributions, is carried out by using the likelihood ratio test as well as by AIC and BIC. When using the likelihood ratio test, we note that when testing for the Poisson distribution, the chi-square distribution only provides a reasonable approximation to the null distribution of the likelihood ratio test statistic. The mixture chi-square distribution, on the other hand, provides a good approximation to the null distribution of the likelihood ratio statistic when testing for the Bernoulli model. When testing for the geometric model, the observed levels are found to be too conservative. Furthermore, we note that when the true model is geometric or Poisson, the likelihood ratio test has reasonable power to reject the other competing cause distributions. However, when the true model is Bernoulli, the test does not appear to have power to reject the Poisson model. When investigating the performance of AIC and BIC, we first note that both of them result in the same selection rates. Hence, in this case, inference can be based on either AIC or BIC. The results show that the information-based criteria perform well in discriminating between the three special cases of the COM-Poisson model. Also, the TRB and TRE results clearly show the importance of using the flexible COM-Poisson family in selecting a parsimonious competing cause distribution.

For all the above mentioned lifetime distributions, we have also analyzed a cutaneous melanoma data for illustrative purpose. It is interesting to note that for all the considered lifetime distributions, the geometric cure rate model provides the best fit to the data. In fact, Rodrigues et al. (2009) analyzed the same dataset assuming Weibull distribution for the lifetime and they also found the geometric model to be the working model. Moreover, the estimates of cure rates of patients that we have obtained on assuming Weibull lifetime distribution are very close to those obtained by Rodrigues et al. (2009).

To perform a formal statistical test to select a parsimonious lifetime distribution, among those considered, that provides an adequate fit to the data, we finally considered the wider class of generalized gamma distributions which contains all mentioned lifetime distributions as special cases. The necessary steps of the EM algorithm are then developed for this family of distributions and for some of the special cases of the COM-Poisson model, a simulation study has been carried out to evaluate the performance of the proposed estimation method. The results again show that the proposed methodology works well, but the profile likelihood approach of estimating the generalized gamma shape parameter q results in undercoverage of other lifetime parameters. However, for the geometric model, the undercoverage is seen only for the lifetime parameter σ. Model discrimination within the generalized gamma family is carried out by using both the likelihood-based and information-based methods. The results of the likelihood ratio test show that the gamma and Weibull distributions provide similar fits and are not significantly different from each other. However, there is a significant difference in fits between the lognormal and Weibull, gamma or exponential distributions that can be detected by the likelihood ratio test under the generalized gamma framework. The AIC and BIC results show that AIC performs better than BIC in selecting the correct model. Also, the performance of AIC is better when the sample size is large and/or the censoring proportion is low. However, BIC performs better only when the sample size is large. Finally, the cutaneous melanoma data is analyzed to illustrate the two-way flexibility of the COM-Poisson family and the generalized gamma family to carry out a two-way model discrimination within these families. In this way, we conclude that, for this dataset, the geometric distribution as a parsimonious competing cause distribution and the gamma distribution as a parsimonious lifetime distribution together provide the best fit to the data.

7.2 Future work

In this section, we discuss some of the future research directions that could be considered as natural extensions of the work carried out in this thesis.

7.2.1 Other families of distributions for the competing cause and lifetime variables

In the present work, we have considered the flexible COM-Poisson family and the wider class of generalized gamma family as the distributions of the competing cause and lifetime variables, respectively. In this regard, we can also think of other flexible families of distributions for the competing cause and the lifetime variables. For instance, we can consider the generalized power series distribution for the competing cause, as done by Borges et al. (2012), and the generalized Birnbaum-Saunders distribution for the lifetime variable. We can then develop the corresponding likelihood inference based on the EM algorithm.

7.2.2 Destructive cure rate model

As already mentioned in Section 1.2, Rodrigues et al. (2011) developed a flexible cure rate model by assuming the number of competing causes to follow a compound weighted Poisson distribution. The proposed model gives an interesting and realistic interpretation of the biological mechanism of the occurrence of an event of interest as it presumes that the original number of risk factors produced by nature undergoes a destructive process (for example, when a patient undergoes chemotherapy or radiation). Hence, what is recorded is only from the undamaged portion of the original number of risk factors. It will naturally be of interest to develop the EM algorithm for estimating the model parameters of this destructive cure rate survival model.

7.2.3 Other forms of censoring

We may also consider other modes of censoring, such as informative censoring and interval censoring, as mentioned earlier in Section 1.5, and provide the foundation for modeling and estimation for such survival data in a cure rate setup.

7.2.4 Bayesian inference

It is also possible to consider the COM-Poisson cure rate model as well as the destructive cure rate model and develop an EM algorithm to estimate the model parameters under a Bayesian framework. This would require choosing proper prior distributions for the model parameters.

7.2.5 Semi-parametric approach

Instead of looking at a particular parametric distribution that provides the basic description of the lifetimes, it will be possible to consider modeling the lifetimes through the hazard function, where we do not assume any functional form for the baseline hazard function and carry out the necessary analysis. This would lead to a semi-parametric approach, resulting in a more general form of analysis.

7.2.6 Goodness-of-fit tests

In order to check if a particular distributional assumption for the lifetime is reasonable for a given censored data, no formal statistical tests exist to examine the goodness-of-fit in such a situation. Although goodness-of-fit of a particular assumed model can be examined graphically, a formal test of the goodness-of-fit would be of interest to develop for the cure rate models discussed here.

Work on some of these problems is currently under progress.

Appendix A

Corresponding to Chapter 3

A.1 First- and second-order derivatives of the Q-function

Bernoulli cure rate model: The expressions of the first- and second-order derivatives of the $Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ are as follows:

$$\begin{aligned}
\frac{\partial Q_1}{\partial \beta_l} &= \sum_{I_1} x_{il} + \sum_{I_0} \pi_i^{(k)} x_{il} - \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})}, \\
\frac{\partial^2 Q_1}{\partial \beta_l \partial \beta_{l'}} &= -\sum_{I^*} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta}))^2},
\end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$. The required first- and second-order derivatives of the $Q_2(\boldsymbol{\gamma}, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\gamma}$ are as follows:

$$\begin{aligned}
\frac{\partial Q_2}{\partial \gamma_1} &= -\frac{n_1}{\gamma_1} + \frac{1}{\gamma_1} \sum_{I_1} u_i^2 + \frac{1}{\gamma_1} \sum_{I_0} \pi_i^{(k)} u_i V(u_i), \\
\frac{\partial Q_2}{\partial \gamma_2} &= -\frac{1}{\gamma_1 \gamma_2} \sum_{I_1} u_i - \frac{1}{\gamma_1 \gamma_2} \sum_{I_0} \pi_i^{(k)} V(u_i),
\end{aligned}$$

$$
\begin{aligned}
\frac{\partial^2 Q_2}{\partial \gamma_1^2} &= \frac{n_1}{\gamma_1^2} - \frac{3}{\gamma_1^2}\sum_{I_1} u_i^2 - \frac{1}{\gamma_1^2}\sum_{I_0} \pi_i^{(k)} u_i V(u_i)\{u_i(V(u_i)-u_i)+2\},\\
\frac{\partial^2 Q_2}{\partial \gamma_2^2} &= -\frac{1}{\gamma_1\gamma_2^2}\sum_{I_1}\left\{\frac{1}{\gamma_1}-u_i\right\} - \frac{1}{\gamma_1\gamma_2^2}\sum_{I_0}\pi_i^{(k)}V(u_i)\left\{\frac{1}{\gamma_1}\Big(V(u_i)-u_i\Big)-1\right\},\\
\frac{\partial^2 Q_2}{\partial \gamma_1\partial\gamma_2} &= \frac{2}{\gamma_2\gamma_1^2}\sum_{I_1}u_i + \frac{1}{\gamma_2\gamma_1^2}\sum_{I_0}\pi_i^{(k)}V(u_i)\{u_i(V(u_i)-u_i)+1\},
\end{aligned}
$$

where $\pi_i^{(k)}$ is as defined in (3.2.1).

Poisson cure rate model: The required first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}$ are as follows:

$$
\begin{aligned}
\frac{\partial Q}{\partial \beta_l} &= -\sum_{I_1} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i)}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})} + \sum_{I_1} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))}\\
&\quad -\sum_{I_0} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})} + \sum_{I_0}\pi_i^{(k)}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))(1-\Phi(u_i))}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))(\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1)},\\
\frac{\partial Q}{\partial \gamma_1} &= -\frac{n_1}{\gamma_1} + \frac{1}{\gamma_1}\sum_{I_1}u_i^2 + \frac{1}{\gamma_1}\sum_{I_1}\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))u_i\phi(u_i)\\
&\quad +\frac{1}{\gamma_1}\sum_{I_0}\pi_i^{(k)}\frac{\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))u_i\phi(u_i)}{\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1},\\
\frac{\partial Q}{\partial \gamma_2} &= -\frac{1}{\gamma_1\gamma_2}\sum_{I_1}u_i - \frac{1}{\gamma_1\gamma_2}\sum_{I_1}\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\phi(u_i)\\
&\quad -\frac{1}{\gamma_1\gamma_2}\sum_{I_0}\pi_i^{(k)}\frac{\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\phi(u_i)}{\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1},\\
\frac{\partial^2 Q}{\partial \beta_l\partial\beta_{l'}} &= \sum_{I_1}x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}\left\{\frac{\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))-\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})))^2}-\Phi(u_i)\right\}\\
&\quad +\sum_{I_0}\pi_i^{(k)}x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))(1-\Phi(u_i))}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2(\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1)}\\
&\quad \times\left\{1-\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-\Phi(u_i))}{\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1}\right\} - \sum_{I_0}x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2},
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial^2 Q}{\partial\beta_l\partial\gamma_1} &= \frac{1}{\gamma_1}\sum_{I_1} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})u_i\phi(u_i)}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})} + \frac{1}{\gamma_1}\sum_{I_0}\pi_i^{(k)}x_{il} \\
&\quad \times\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))u_i\phi(u_i)}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))(\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1)}\left\{1-\frac{A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma})}{\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1}\right\}, \\
\frac{\partial^2 Q}{\partial\beta_l\partial\gamma_2} &= -\frac{1}{\gamma_1\gamma_2}\sum_{I_1} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\phi(u_i)}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})} - \frac{1}{\gamma_1\gamma_2}\sum_{I_0}\pi_i^{(k)}x_{il} \\
&\quad \times\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))\phi(u_i)}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))(\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1)}\left\{1-\frac{A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma})}{\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1}\right\}, \\
\frac{\partial^2 Q}{\partial\gamma_1^2} &= \frac{n_1}{\gamma_1^2} - \frac{3}{\gamma_1^2}\sum_{I_1}u_i^2 + \frac{1}{\gamma_1^2}\sum_{I_1}\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))u_i\phi(u_i)\{u_i^2-2\} \\
&\quad +\frac{1}{\gamma_1^2}\sum_{I_0}\pi_i^{(k)}\frac{\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))u_i\phi(u_i)}{\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1} \\
&\quad \times\left\{u_i^2-2-\frac{\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))u_i\phi(u_i)}{\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1}\right\}, \\
\frac{\partial^2 Q}{\partial\gamma_2^2} &= -\frac{1}{\gamma_1\gamma_2^2}\sum_{I_1}\left\{\frac{1}{\gamma_1}-u_i\right\} + \frac{1}{\gamma_1\gamma_2^2}\sum_{I_1}\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\phi(u_i)\left\{\frac{u_i}{\gamma_1}+1\right\} \\
&\quad +\frac{1}{\gamma_1\gamma_2^2}\sum_{I_0}\pi_i^{(k)}\frac{\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))\phi(u_i)}{\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1} \\
&\quad \times\left\{\frac{u_i}{\gamma_1}+1-\frac{\frac{1}{\gamma_1}\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\phi(u_i)}{\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1}\right\}, \\
\frac{\partial^2 Q}{\partial\gamma_1\partial\gamma_2} &= \frac{2}{\gamma_2\gamma_1^2}\sum_{I_1}u_i - \frac{1}{\gamma_2\gamma_1^2}\sum_{I_1}\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\phi(u_i)\{u_i^2-1\} \\
&\quad -\frac{1}{\gamma_2\gamma_1^2}\sum_{I_0}\pi_i^{(k)}\frac{\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))\phi(u_i)}{\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1} \\
&\quad \times\left\{u_i^2-1-\frac{\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))u_i\phi(u_i)}{\exp(A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1}\right\},
\end{aligned}
$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where $A_{Li}(\boldsymbol{\beta},\boldsymbol{\gamma})$ and $\pi_i^{(k)}$ are as defined in (3.2.2) and (3.2.3), respectively.

Geometric cure rate model: The required first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}$ are as follows:

$$\begin{aligned}
\frac{\partial Q}{\partial \beta_l} &= \sum_{I_1} x_{il} \frac{1-\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i)}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i)} - \sum_{I_0} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})} \\
&\quad + \sum_{I_0} \pi_i^{(k)} x_{il} \frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i)}, \\
\frac{\partial Q}{\partial \gamma_1} &= -\frac{n_1}{\gamma_1} + \frac{1}{\gamma_1}\sum_{I_1} u_i^2 + \frac{2}{\gamma_1}\sum_{I_1} \exp(\boldsymbol{x}_i'\boldsymbol{\beta}) u_i W(u_i, \boldsymbol{\beta}) \\
&\quad + \frac{1}{\gamma_1}\sum_{I_0} \pi_i^{(k)} \{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) W(u_i, \boldsymbol{\beta}) + V(u_i)\} u_i, \\
\frac{\partial Q}{\partial \gamma_2} &= -\frac{1}{\gamma_1\gamma_2}\sum_{I_1} u_i - \frac{2}{\gamma_1\gamma_2}\sum_{I_1} \exp(\boldsymbol{x}_i'\boldsymbol{\beta}) W(u_i, \boldsymbol{\beta}) \\
&\quad - \frac{1}{\gamma_1\gamma_2}\sum_{I_0} \pi_i^{(k)} \{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) W(u_i, \boldsymbol{\beta}) + V(u_i)\}, \\
\frac{\partial^2 Q}{\partial \beta_l \partial \beta_{l'}} &= -2\sum_{I_1} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i)}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i))^2} - \sum_{I_0} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2} \\
&\quad - \sum_{I_0} \pi_i^{(k)} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i)}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i))^2}, \\
\frac{\partial^2 Q}{\partial \beta_l \partial \gamma_1} &= \frac{2}{\gamma_1}\sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) u_i W(u_i, \boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i)} + \frac{1}{\gamma_1}\sum_{I_0} \pi_i^{(k)} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) u_i W(u_i, \boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i)}, \\
\frac{\partial^2 Q}{\partial \beta_l \partial \gamma_2} &= -\frac{2}{\gamma_1\gamma_2}\sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) W(u_i, \boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i)} - \frac{1}{\gamma_1\gamma_2}\sum_{I_0} \pi_i^{(k)} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) W(u_i, \boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i)}, \\
\frac{\partial^2 Q}{\partial \gamma_1^2} &= \frac{n_1}{\gamma_1^2} - \frac{3}{\gamma_1^2}\sum_{I_1} u_i^2 + \frac{2}{\gamma_1^2}\sum_{I_1} \exp(\boldsymbol{x}_i'\boldsymbol{\beta}) u_i W(u_i, \boldsymbol{\beta}) \\
&\quad \times \{u_i(\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) W(u_i, \boldsymbol{\beta}) + u_i) - 2\} \\
&\quad - \frac{1}{\gamma_1^2}\sum_{I_0} \pi_i^{(k)} u_i V(u_i) \{u_i(V(u_i) - u_i) + 2\} \\
&\quad + \frac{1}{\gamma_1^2}\sum_{I_0} \pi_i^{(k)} \exp(\boldsymbol{x}_i'\boldsymbol{\beta}) u_i W(u_i, \boldsymbol{\beta}) \{u_i(\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) W(u_i, \boldsymbol{\beta}) + u_i) - 2\},
\end{aligned}$$

$$
\begin{aligned}
\frac{\partial^2 Q}{\partial \gamma_2^2} &= -\frac{1}{\gamma_1\gamma_2^2}\sum_{I_1}\left\{\frac{1}{\gamma_1}-u_i\right\}+\frac{2}{\gamma_1\gamma_2^2}\sum_{I_1}\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})W(u_i,\boldsymbol{\beta})\\
&\times\left\{\frac{1}{\gamma_1}\bigg(\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})W(u_i,\boldsymbol{\beta})+u_i\bigg)+1\right\}\\
&+\frac{1}{\gamma_1\gamma_2^2}\sum_{I_0}\pi_i^{(k)}\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})W(u_i,\boldsymbol{\beta})\left\{\frac{1}{\gamma_1}\bigg(\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})W(u_i,\boldsymbol{\beta})+u_i\bigg)+1\right\}\\
&-\frac{1}{\gamma_1\gamma_2^2}\sum_{I_0}\pi_i^{(k)}V(u_i)\left\{\frac{1}{\gamma_1}\bigg(V(u_i)-u_i\bigg)-1\right\},\\
\frac{\partial^2 Q}{\partial \gamma_1\partial\gamma_2} &= \frac{2}{\gamma_2\gamma_1^2}\sum_{I_1}u_i-\frac{2}{\gamma_2\gamma_1^2}\sum_{I_1}\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})W(u_i,\boldsymbol{\beta})\\
&\times\{u_i(\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})W(u_i,\boldsymbol{\beta})+u_i)-1\}\\
&+\frac{1}{\gamma_2\gamma_1^2}\sum_{I_0}\pi_i^{(k)}V(u_i)\{u_i(V(u_i)-u_i)+1\}\\
&-\frac{1}{\gamma_2\gamma_1^2}\sum_{I_0}\pi_i^{(k)}\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})W(u_i,\boldsymbol{\beta})\{u_i(\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})W(u_i,\boldsymbol{\beta})+u_i)-1\},
\end{aligned}
$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where $\pi_i^{(k)}$ and $W(u_i, \boldsymbol{\beta})$ are as defined in (3.2.4) and (3.3.3), respectively.

COM-Poisson cure rate model: The required first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}$ are as follows:

$$
\begin{aligned}
\frac{\partial Q}{\partial \beta_l} &= \sum_{I_1}x_{il}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})z_{21i}}{z_{2i}z_{01i}}+\sum_{I_0}\pi_i^{(k)}x_{il}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})z_{2i}}{z_{1i}z_{01i}}-\sum_{I^*}x_{il}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})},\\
\frac{\partial Q}{\partial \gamma_1} &= -\frac{n_1}{\gamma_1}+\frac{1}{\gamma_1}\sum_{I_1}u_i^2+\frac{1}{\gamma_1}\sum_{I_1}u_iV(u_i)\left\{\frac{z_{21i}}{z_{2i}}-1\right\}+\frac{1}{\gamma_1}\sum_{I_0}\pi_i^{(k)}\frac{u_iV(u_i)z_{2i}}{z_{1i}},\\
\frac{\partial Q}{\partial \gamma_2} &= -\frac{1}{\gamma_1\gamma_2}\sum_{I_1}u_i-\frac{1}{\gamma_1\gamma_2}\sum_{I_1}V(u_i)\left\{\frac{z_{21i}}{z_{2i}}-1\right\}-\frac{1}{\gamma_1\gamma_2}\sum_{I_0}\pi_i^{(k)}\frac{V(u_i)z_{2i}}{z_{1i}},
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial^2 Q}{\partial\beta_l\partial\beta_{l'}} &= \sum_{I_1} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(z_{2i}z_{01i})^2}\left[\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\left\{z_{2i}z_{22i}-z_{21i}^2\right\}+z_{2i}z_{21i}\right.\\
&\quad\left.\times\left\{z_{01i}-\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{02i}}{z_{01i}}\right\}\right]+\sum_{I_0}\pi_i^{(k)}x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(z_{1i}z_{01i})^2}\left[\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\right.\\
&\quad\left.\times\left\{z_{1i}z_{21i}-z_{2i}^2\right\}+z_{1i}z_{2i}\left\{z_{01i}-\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{02i}}{z_{01i}}\right\}\right]\\
&\quad-\sum_{I^*}x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2},\\
\frac{\partial^2 Q}{\partial\beta_l\partial\gamma_1} &= \frac{1}{\gamma_1}\sum_{I_1}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})u_iV(u_i)}{z_{01i}}\left\{\frac{z_{2i}z_{22i}-z_{21i}^2}{z_{2i}^2}\right\}\\
&\quad+\frac{1}{\gamma_1}\sum_{I_0}\pi_i^{(k)}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})u_iV(u_i)}{z_{01i}}\left\{\frac{z_{1i}z_{21i}-z_{2i}^2}{z_{1i}^2}\right\},\\
\frac{\partial^2 Q}{\partial\beta_l\partial\gamma_2} &= -\frac{1}{\gamma_1\gamma_2}\sum_{I_1}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})V(u_i)}{z_{01i}}\left\{\frac{z_{2i}z_{22i}-z_{21i}^2}{z_{2i}^2}\right\}\\
&\quad-\frac{1}{\gamma_1\gamma_2}\sum_{I_0}\pi_i^{(k)}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})V(u_i)}{z_{01i}}\left\{\frac{z_{1i}z_{21i}-z_{2i}^2}{z_{1i}^2}\right\},\\
\frac{\partial^2 Q}{\partial\gamma_1^2} &= \frac{n_1}{{\gamma_1}^2}-\frac{3}{\gamma_1^2}\sum_{I_1}u_i^2+\frac{1}{\gamma_1^2}\sum_{I_1}u_iV(u_i)\{u_i(V(u_i)-u_i)+2\}\\
&\quad+\frac{1}{\gamma_1^2}\sum_{I_1}\frac{u_iV(u_i)}{z_{2i}^2}\left[u_iV(u_i)\{z_{2i}z_{22i}-z_{21i}^2\}-z_{2i}z_{21i}\{u_i(V(u_i)-u_i)+2\}\right]\\
&\quad+\frac{1}{\gamma_1^2}\sum_{I_0}\pi_i^{(k)}\frac{u_iV(u_i)}{z_{1i}^2}\left[u_iV(u_i)\{z_{1i}z_{21i}-z_{2i}^2\}-z_{1i}z_{2i}\{u_i(V(u_i)-u_i)\right.\\
&\quad\left.+2\}\right],\\
\frac{\partial^2 Q}{\partial\gamma_2^2} &= -\frac{1}{\gamma_1\gamma_2^2}\sum_{I_1}\left\{\frac{1}{\gamma_1}-u_i\right\}+\frac{1}{\gamma_1\gamma_2^2}\sum_{I_1}V(u_i)\left\{\frac{1}{\gamma_1}\Big(V(u_i)-u_i\Big)-1\right\}\\
&\quad+\frac{1}{\gamma_1\gamma_2^2}\sum_{I_1}\frac{V(u_i)}{z_{2i}^2}\left[\frac{1}{\gamma_1}V(u_i)\left\{z_{2i}z_{22i}-z_{21i}^2\right\}-z_{2i}z_{21i}\left\{\frac{1}{\gamma_1}\Big(V(u_i)-u_i\Big)\right.\right.\\
&\quad\left.\left.-1\right\}\right]+\frac{1}{\gamma_1\gamma_2^2}\sum_{I_0}\pi_i^{(k)}\frac{V(u_i)}{z_{1i}^2}\left[\frac{1}{\gamma_1}V(u_i)\left\{z_{1i}z_{21i}-z_{2i}^2\right\}-z_{1i}z_{2i}\right.\\
&\quad\left.\times\left\{\frac{1}{\gamma_1}\Big(V(u_i)-u_i\Big)-1\right\}\right],
\end{aligned}
$$

$$\begin{aligned}
\frac{\partial^2 Q}{\partial\gamma_1\partial\gamma_2} &= \frac{2}{\gamma_2\gamma_1^2}\sum_{I_1} u_i - \frac{1}{\gamma_2\gamma_1^2}\sum_{I_1} V(u_i)\{u_i(V(u_i)-u_i)+1\} \\
&\quad -\frac{1}{\gamma_2\gamma_1^2}\sum_{I_1}\frac{V(u_i)}{z_{2i}^2}\Big[u_iV(u_i)\{z_{2i}z_{22i}-z_{21i}^2\} - z_{2i}z_{21i}\{u_i(V(u_i)-u_i)+1\}\Big] \\
&\quad -\frac{1}{\gamma_2\gamma_1^2}\sum_{I_0}\pi_i^{(k)}\frac{V(u_i)}{z_{1i}^2}\Big[u_iV(u_i)\{z_{1i}z_{21i}-z_{2i}^2\} - z_{1i}z_{2i}\{u_i(V(u_i)-u_i)+1\}\Big],
\end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$z_{22} = z_{22}(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty} \frac{j^3\{H_\phi^{-1}(1+\exp(\boldsymbol{x}'\boldsymbol{\beta}))(1-\Phi(u))\}^j}{(j!)^\phi},$$

$$z_{02} = z_{02}(\boldsymbol{\theta}_1; \boldsymbol{x}) = \sum_{j=1}^{\infty} \frac{j^2\{H_\phi^{-1}(1+\exp(\boldsymbol{x}'\boldsymbol{\beta}))\}^j}{(j!)^\phi},$$

and $\pi_i^{(k)}$ is as defined in (3.2.5). The quantities $z_{1i}, z_{2i}, z_{21i}, z_{22i}, z_{01i}$, and z_{02i} are all computed as described in Section 2.2.

A.2 Observed information matrix

Bernoulli cure rate model: The observed information matrix has its components as

$$\begin{aligned}
-\frac{\partial^2 l}{\partial\beta_l\partial\beta_{l'}} &= -\sum_{I_0} x_{il}x_{il'}w_i(1-w_i) + \sum_{I^*} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}, \\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma_1} &= -\frac{1}{\gamma_1}\sum_{I_0} x_{il}w_i(1-w_i)u_iV(u_i), \\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma_2} &= \frac{1}{\gamma_1\gamma_2}\sum_{I_0} x_{il}w_i(1-w_i)V(u_i),
\end{aligned}$$

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \gamma_1^2} &= -\frac{n_1}{{\gamma_1}^2} + \frac{3}{\gamma_1^2}\sum_{I_1} u_i^2 - \frac{1}{\gamma_1^2}\sum_{I_0} u_i V(u_i)[\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})u_i\phi(u_i)(1-w_i)^2 \\
&\quad -w_i\{u_i(V(u_i)-u_i)+2\}], \\
-\frac{\partial^2 l}{\partial \gamma_2^2} &= \frac{1}{\gamma_1\gamma_2^2}\sum_{I_1}\left\{\frac{1}{\gamma_1} - u_i\right\} + \frac{1}{\gamma_1\gamma_2^2}\sum_{I_0} V(u_i)\Bigg[w_i\Bigg\{\frac{1}{\gamma_1}\Bigg(V(u_i)-u_i\Bigg)-1\Bigg\} \\
&\quad -\frac{1}{\gamma_1}\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})\phi(u_i)(1-w_i)^2\Bigg], \\
-\frac{\partial^2 l}{\partial \gamma_1 \partial \gamma_2} &= -\frac{2}{\gamma_2\gamma_1^2}\sum_{I_1} u_i - \frac{1}{\gamma_2\gamma_1^2}\sum_{I_0} V(u_i)[w_i\{u_i(V(u_i)-u_i)+1\} \\
&\quad -\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})u_i\phi(u_i)(1-w_i)^2].
\end{aligned}
$$

The above are defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where w_i is as defined in (3.3.1).

Poisson cure rate model: The observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \beta_l \partial \beta_{l'}} &= -\sum_{I_1} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))^2}\left\{\frac{\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})))^2} - \Phi(u_i)\right\} \\
&\quad +\sum_{I_0} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})\Phi(u_i)}{(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))^2}, \\
-\frac{\partial^2 l}{\partial \beta_l \partial \gamma_1} &= -\frac{1}{\gamma_1}\sum_{I^*} x_{il}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})u_i\phi(u_i)}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}, \\
-\frac{\partial^2 l}{\partial \beta_l \partial \gamma_2} &= \frac{1}{\gamma_1\gamma_2}\sum_{I^*} x_{il}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})\phi(u_i)}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}, \\
-\frac{\partial^2 l}{\partial \gamma_1^2} &= -\frac{n_1}{{\gamma_1}^2} + \frac{3}{\gamma_1^2}\sum_{I_1} u_i^2 - \frac{1}{\gamma_1^2}\sum_{I^*}\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))u_i\phi(u_i)\{u_i^2-2\},
\end{aligned}
$$

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \gamma_2^2} &= \frac{1}{\gamma_1\gamma_2^2}\sum_{I_1}\left\{\frac{1}{\gamma_1}-u_i\right\} - \frac{1}{\gamma_1\gamma_2^2}\sum_{I^*}\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\phi(u_i)\left\{\frac{u_i}{\gamma_1}+1\right\},\\
-\frac{\partial^2 l}{\partial \gamma_1\partial\gamma_2} &= -\frac{2}{\gamma_2\gamma_1^2}\sum_{I_1}u_i + \frac{1}{\gamma_2\gamma_1^2}\sum_{I^*}\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\phi(u_i)\{u_i^2-1\}.
\end{aligned}
$$

The above are defined for $l, l' = 0, 1, \ldots, k,\ x_{i0} = 1 \forall i = 1, 2, \ldots, n$.

Geometric cure rate model: The observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \beta_l\partial\beta_{l'}} &= 2\sum_{I_1}x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i)}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i))^2}\\
&\quad -\sum_{I_0}x_{il}x_{il'}\frac{w_i(1-\exp(2\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i))}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i))^2}\\
&\quad +\sum_{I_0}x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2},\\
-\frac{\partial^2 l}{\partial \beta_l\partial\gamma_1} &= -\frac{2}{\gamma_1}\sum_{I_1}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})u_iW(u_i,\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i)} - \frac{1}{\gamma_1}\sum_{I_0}x_{il}\frac{w_iu_iV(u_i)}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\\
&\quad -\frac{1}{\gamma_1}\sum_{I_0}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})u_iw_iW(u_i,\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i))}\Bigg\{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1+\Phi(u_i))\\
&\quad +2\Bigg\},\\
-\frac{\partial^2 l}{\partial \beta_l\partial\gamma_2} &= \frac{2}{\gamma_1\gamma_2}\sum_{I_1}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})W(u_i,\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i)} + \frac{1}{\gamma_1\gamma_2}\sum_{I_0}x_{il}\frac{w_iV(u_i)}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\\
&\quad +\frac{1}{\gamma_1\gamma_2}\sum_{I_0}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})w_iW(u_i,\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Phi(u_i))}\Bigg\{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1+\Phi(u_i))\\
&\quad +2\Bigg\},
\end{aligned}
$$

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \gamma_1^2} &= -\frac{n_1}{{\gamma_1}^2} + \frac{3}{\gamma_1^2}\sum_{I_1} u_i^2 - \frac{2}{\gamma_1^2}\sum_{I_1} \exp(\boldsymbol{x}_i'\boldsymbol{\beta}) u_i W(u_i,\boldsymbol{\beta})[u_i\{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})W(u_i,\boldsymbol{\beta}) \\
&\quad +u_i\} - 2] - \frac{1}{\gamma_1^2}\sum_{I_0} \exp(\boldsymbol{x}_i'\boldsymbol{\beta}) w_i u_i W(u_i,\boldsymbol{\beta})[u_i\{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})W(u_i,\boldsymbol{\beta}) + u_i\} \\
&\quad +u_i V(u_i) - 2] - \frac{1}{\gamma_1^2}\sum_{I_0} w_i u_i V(u_i)\{u_i^2 - 2\}, \\
-\frac{\partial^2 l}{\partial \gamma_2^2} &= \frac{1}{\gamma_1\gamma_2^2}\sum_{I_1}\left\{\frac{1}{\gamma_1} - u_i\right\} - \frac{2}{\gamma_1\gamma_2^2}\sum_{I_1}\exp(\boldsymbol{x}_i'\boldsymbol{\beta})W(u_i,\boldsymbol{\beta}) \\
&\quad \times\left[\frac{1}{\gamma_1}\left\{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})W(u_i,\boldsymbol{\beta}) + u_i\right\} + 1\right] - \frac{1}{\gamma_1\gamma_2^2}\sum_{I_0}\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) w_i W(u_i,\boldsymbol{\beta}) \\
&\quad \times\left[\frac{1}{\gamma_1}\left\{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})W(u_i,\boldsymbol{\beta}) + u_i + V(u_i)\right\} + 1\right] \\
&\quad -\frac{1}{\gamma_1\gamma_2^2}\sum_{I_0} w_i V(u_i)\left\{\frac{u_i}{\gamma_1} + 1\right\}, \\
-\frac{\partial^2 l}{\partial \gamma_1 \partial \gamma_2} &= -\frac{2}{\gamma_2\gamma_1^2}\sum_{I_1} u_i + \frac{2}{\gamma_2\gamma_1^2}\sum_{I_1}\exp(\boldsymbol{x}_i'\boldsymbol{\beta})W(u_i,\boldsymbol{\beta})[u_i\{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})W(u_i,\boldsymbol{\beta}) + u_i\} \\
&\quad -1] + \frac{1}{\gamma_2\gamma_1^2}\sum_{I_0}\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) w_i W(u_i,\boldsymbol{\beta})[u_i\{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})W(u_i,\boldsymbol{\beta}) + u_i\} \\
&\quad +u_i V(u_i) - 1] + \frac{1}{\gamma_2\gamma_1^2}\sum_{I_0} w_i V(u_i)\{u_i^2 - 1\}.
\end{aligned}
$$

The above are defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where w_i and $W(u_i, \boldsymbol{\beta})$ are as defined in (3.3.2) and (3.3.3), respectively.

COM-Poisson cure rate model: For a fixed value of ϕ, the observed information matrix has its components as

$$\begin{aligned}
-\frac{\partial^2 l}{\partial\beta_l\partial\beta_{l'}} &= -\sum_{I_1} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(z_{01i}z_{2i})^2}\Bigg[\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Bigg\{z_{2i}z_{22i}-z_{21i}^2\Bigg\} \\
&+z_{2i}z_{21i}\Bigg\{z_{01i}-\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{02i}}{z_{01i}}\Bigg\}\Bigg] - \sum_{I_0} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(z_{01i}(1+z_{1i}))^2} \\
&\times\Bigg[\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Bigg\{z_{21i}(1+z_{1i})-z_{2i}^2\Bigg\}+z_{2i}(1+z_{1i})\Bigg\{z_{01i}-\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{02i}}{z_{01i}}\Bigg\}\Bigg] \\
&+\sum_{I^*} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}, \\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma_1} &= -\frac{1}{\gamma_1}\sum_{I_1} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})u_iV(u_i)}{z_{01i}}\left\{\frac{z_{2i}z_{22i}-z_{21i}^2}{z_{2i}^2}\right\} \\
&-\frac{1}{\gamma_1}\sum_{I_0} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})u_iV(u_i)}{z_{01i}}\left\{\frac{z_{21i}(1+z_{1i})-z_{2i}^2}{(1+z_{1i})^2}\right\}, \\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma_2} &= \frac{1}{\gamma_1\gamma_2}\sum_{I_1} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})V(u_i)}{z_{01i}}\left\{\frac{z_{2i}z_{22i}-z_{21i}^2}{z_{2i}^2}\right\} \\
&+\frac{1}{\gamma_1\gamma_2}\sum_{I_0} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})V(u_i)}{z_{01i}}\left\{\frac{z_{21i}(1+z_{1i})-z_{2i}^2}{(1+z_{1i})^2}\right\}, \\
-\frac{\partial^2 l}{\partial\gamma_1^2} &= -\frac{n_1}{{\gamma_1}^2}+\frac{3}{\gamma_1^2}\sum_{I_1}u_i^2-\frac{1}{\gamma_1^2}\sum_{I_1}u_iV(u_i)\{u_i(V(u_i)-u_i)+2\} \\
&-\frac{1}{\gamma_1^2}\sum_{I_1}\frac{u_iV(u_i)}{z_{2i}^2}\Bigg[u_iV(u_i)\{z_{2i}z_{22i}-z_{21i}^2\}-z_{2i}z_{21i}\{u_i(V(u_i)-u_i)+2\}\Bigg] \\
&-\frac{1}{\gamma_1^2}\sum_{I_0}\frac{u_iV(u_i)}{(1+z_{1i})^2}\Bigg[u_iV(u_i)\{z_{21i}(1+z_{1i})-z_{2i}^2\} \\
&-z_{2i}(1+z_{1i})\{u_i(V(u_i)-u_i)+2\}\Bigg],
\end{aligned}$$

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \gamma_2^2} &= \frac{1}{\gamma_1\gamma_2^2}\sum_{I_1}\left\{\frac{1}{\gamma_1}-u_i\right\}-\frac{1}{\gamma_1\gamma_2^2}\sum_{I_1}V(u_i)\left\{\frac{1}{\gamma_1}\Big(V(u_i)-u_i\Big)-1\right\} \\
&\quad -\frac{1}{\gamma_1\gamma_2^2}\sum_{I_1}\frac{V(u_i)}{z_{2i}^2}\left[\frac{1}{\gamma_1}V(u_i)\left\{z_{2i}z_{22i}-z_{21i}^2\right\}-z_{2i}z_{21i}\left\{\frac{1}{\gamma_1}\Big(V(u_i)-u_i\Big)\right.\right. \\
&\quad \left.\left.-1\right\}\right]-\frac{1}{\gamma_1\gamma_2^2}\sum_{I_0}\frac{V(u_i)}{(1+z_{1i})^2}\left[\frac{1}{\gamma_1}V(u_i)\left\{z_{21i}(1+z_{1i})-z_{2i}^2\right\}\right. \\
&\quad \left.-z_{2i}(1+z_{1i})\left\{\frac{1}{\gamma_1}\Big(V(u_i)-u_i\Big)-1\right\}\right], \\
-\frac{\partial^2 l}{\partial\gamma_1\partial\gamma_2} &= -\frac{2}{\gamma_2\gamma_1^2}\sum_{I_1}u_i+\frac{1}{\gamma_2\gamma_1^2}\sum_{I_1}V(u_i)\{u_i(V(u_i)-u_i)+1\} \\
&\quad +\frac{1}{\gamma_2\gamma_1^2}\sum_{I_1}\frac{V(u_i)}{z_{2i}^2}\Big[u_iV(u_i)\{z_{2i}z_{22i}-z_{21i}^2\}-z_{2i}z_{21i}\{u_i(V(u_i)-u_i)+1\}\Big] \\
&\quad +\frac{1}{\gamma_2\gamma_1^2}\sum_{I_0}\frac{V(u_i)}{(1+z_{1i})^2}\Big[u_iV(u_i)\{z_{21i}(1+z_{1i})-z_{2i}^2\} \\
&\quad -z_{2i}(1+z_{1i})\{u_i(V(u_i)-u_i)+1\}\Big].
\end{aligned}
$$

The above are defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$.

Appendix B

Corresponding to Chapter 4

B.1 First- and second-order derivatives of the Q-function

Bernoulli cure rate model: The expressions of the first- and second-order derivatives of the $Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ are as follows:

$$\begin{aligned}\frac{\partial Q_1}{\partial \beta_l} &= \sum_{I_1} x_{il} + \sum_{I_0} \pi_i^{(k)} x_{il} - \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}, \\ \frac{\partial^2 Q_1}{\partial \beta_l \partial \beta_{l'}} &= -\sum_{I^*} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i' \boldsymbol{\beta}))^2},\end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$. The required first- and second-order derivatives of the $Q_2(\boldsymbol{\gamma}, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\gamma}$ are as follows:

$$\frac{\partial Q_2}{\partial \gamma_1} = n_1 \frac{\partial}{\partial \gamma_1} \log(G(\boldsymbol{\gamma})) + \frac{2}{\gamma_1^3} \sum_{I_1} \{\gamma_2 t_i - \log t_i\} + \sum_{I_0} \pi_i^{(k)} \frac{\partial}{\partial \gamma_1} \log(S(t_i; \boldsymbol{\gamma})),$$

$$
\begin{aligned}
\frac{\partial Q_2}{\partial \gamma_2} &= \frac{n_1}{\gamma_1^2\gamma_2} - \frac{1}{\gamma_1^2}\sum_{I_1} t_i + \sum_{I_0} \pi_i^{(k)} \frac{\partial}{\partial \gamma_2} \log(S(t_i;\boldsymbol{\gamma})),\\
\frac{\partial^2 Q_2}{\partial \gamma_1^2} &= n_1 \frac{\partial^2}{\partial \gamma_1^2} \log(G(\boldsymbol{\gamma})) - \frac{6}{\gamma_1^4}\sum_{I_1}\{\gamma_2 t_i - \log t_i\} + \sum_{I_0} \pi_i^{(k)} \frac{\partial^2}{\partial \gamma_1^2} \log(S(t_i;\boldsymbol{\gamma})),\\
\frac{\partial^2 Q_2}{\partial \gamma_2^2} &= -\frac{n_1}{\gamma_1^2\gamma_2^2} + \sum_{I_0} \pi_i^{(k)} \frac{\partial^2}{\partial \gamma_2^2} \log(S(t_i;\boldsymbol{\gamma})),\\
\frac{\partial^2 Q_2}{\partial \gamma_2 \partial \gamma_1} &= -\frac{2n_1}{\gamma_1^3\gamma_2} + \frac{2}{\gamma_1^3}\sum_{I_1} t_i + \sum_{I_0} \pi_i^{(k)} \frac{\partial^2}{\partial \gamma_2 \partial \gamma_1} \log(S(t_i;\boldsymbol{\gamma})),
\end{aligned}
$$

where $\pi_i^{(k)}$ is as defined in (4.2.1).

Poisson cure rate model: The required first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}$ are as follows:

$$
\begin{aligned}
\frac{\partial Q}{\partial \beta_l} &= \sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) S(t_i;\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})} + \sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))}\\
&\quad + \sum_{I_0} \pi_i^{(k)} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) P_i(\boldsymbol{\beta},\boldsymbol{\gamma}) S(t_i;\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})} - \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})},\\
\frac{\partial Q}{\partial \gamma_1} &= n_1 \frac{\partial}{\partial \gamma_1} \log(G(\boldsymbol{\gamma})) + \frac{2}{\gamma_1^3}\sum_{I_1}\{\gamma_2 t_i - \log t_i\}\\
&\quad + \sum_{I_1} \log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})) \frac{\partial}{\partial \gamma_1} S(t_i;\boldsymbol{\gamma})\\
&\quad + \sum_{I_0} \pi_i^{(k)} \log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})) P_i(\boldsymbol{\beta},\boldsymbol{\gamma}) \frac{\partial}{\partial \gamma_1} S(t_i;\boldsymbol{\gamma}),\\
\frac{\partial Q}{\partial \gamma_2} &= \frac{n_1}{\gamma_2\gamma_1^2} - \frac{1}{\gamma_1^2}\sum_{I_1} t_i + \sum_{I_1} \log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})) \frac{\partial}{\partial \gamma_2} S(t_i;\boldsymbol{\gamma})\\
&\quad + \sum_{I_0} \pi_i^{(k)} \log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})) P_i(\boldsymbol{\beta},\boldsymbol{\gamma}) \frac{\partial}{\partial \gamma_2} S(t_i;\boldsymbol{\gamma}),
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial^2 Q}{\partial\beta_l\partial\beta_{l'}} &= \sum_{I_1} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}\left\{\frac{\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))-\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})))^2}+S(t_i;\boldsymbol{\gamma})\right\}\\
&\quad+\sum_{I_0}\pi_i^{(k)}x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})S(t_i;\boldsymbol{\gamma})P_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}\\
&\quad\times\left\{1-\exp(\boldsymbol{x}_i'\boldsymbol{\beta})S(t_i;\boldsymbol{\gamma})(P_i(\boldsymbol{\beta},\boldsymbol{\gamma})-1)\right\}\\
&\quad-\sum_{I^*}x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2},\\
\frac{\partial^2 Q}{\partial\beta_l\partial\gamma_1} &= \sum_{I_1}x_{il}\left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}\frac{\partial}{\partial\gamma_1}S(t_i;\boldsymbol{\gamma})\\
&\quad+\sum_{I_0}\pi_i^{(k)}x_{il}\left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})P_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}\left\{1-A_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma})(P_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right.\\
&\quad\left.-1)\right\}\frac{\partial}{\partial\gamma_1}S(t_i;\boldsymbol{\gamma}),\\
\frac{\partial^2 Q}{\partial\beta_l\partial\gamma_2} &= \sum_{I_1}x_{il}\left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}\frac{\partial}{\partial\gamma_2}S(t_i;\boldsymbol{\gamma})\\
&\quad+\sum_{I_0}\pi_i^{(k)}x_{il}\left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})P_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}\left\{1-A_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma})(P_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right.\\
&\quad\left.-1)\right\}\frac{\partial}{\partial\gamma_2}S(t_i;\boldsymbol{\gamma}),\\
\frac{\partial^2 Q}{\partial\gamma_1^2} &= n_1\frac{\partial^2}{\partial\gamma_1^2}\log(G(\boldsymbol{\gamma}))-\frac{6}{\gamma_1^4}\sum_{I_1}\{\gamma_2 t_i-\log t_i\}\\
&\quad+\sum_{I_1}\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\frac{\partial^2}{\partial\gamma_1^2}S(t_i;\boldsymbol{\gamma})+\sum_{I_0}\pi_i^{(k)}\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\\
&\quad\times\left[P_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\gamma_1^2}S(t_i;\boldsymbol{\gamma})+\frac{\partial}{\partial\gamma_1}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\gamma_1}P_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right],\\
\frac{\partial^2 Q}{\partial\gamma_2^2} &= -\frac{n_1}{\gamma_1^2\gamma_2^2}+\sum_{I_1}\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\frac{\partial^2}{\partial\gamma_2^2}S(t_i;\boldsymbol{\gamma})+\sum_{I_0}\pi_i^{(k)}\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\\
&\quad\times\left[P_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\gamma_2^2}S(t_i;\boldsymbol{\gamma})+\frac{\partial}{\partial\gamma_2}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\gamma_2}P_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right],
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial^2 Q}{\partial\gamma_2\partial\gamma_1} &= -\frac{2n_1}{\gamma_1^3\gamma_2} + \frac{2}{\gamma_1^3}\sum_{I_1} t_i + \sum_{I_1}\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\frac{\partial^2}{\partial\gamma_2\partial\gamma_1}S(t_i;\boldsymbol{\gamma}) \\
&\quad + \sum_{I_0}\pi_i^{(k)}\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\Bigg[P_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\gamma_2\partial\gamma_1}S(t_i;\boldsymbol{\gamma}) \\
&\quad + \frac{\partial}{\partial\gamma_2}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\gamma_1}P_i(\boldsymbol{\beta},\boldsymbol{\gamma})\Bigg],
\end{aligned}
$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$
P_i(\boldsymbol{\beta},\boldsymbol{\gamma}) = \frac{\exp(A_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{\exp(A_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1},
$$

for $i \in I_0$, $A_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma})$ and $\pi_i^{(k)}$ are as defined in (4.2.2) and (4.2.3), respectively.

Geometric cure rate model: The required first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}$ are as follows:

$$
\begin{aligned}
\frac{\partial Q}{\partial\beta_l} &= \sum_{I_1} x_{il}\{1 - 2B_i(\boldsymbol{\beta},\boldsymbol{\gamma})(1 - S(t_i;\boldsymbol{\gamma}))\} - \sum_{I_0} x_{il}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})} \\
&\quad + \sum_{I_0}\pi_i^{(k)} x_{il}\{1 - B_i(\boldsymbol{\beta},\boldsymbol{\gamma})(1 - S(t_i;\boldsymbol{\gamma}))\}, \\
\frac{\partial Q}{\partial\gamma_1} &= n_1\frac{\partial}{\partial\gamma_1}\log(G(\boldsymbol{\gamma})) + \frac{2}{\gamma_1^3}\sum_{I_1}\{\gamma_2 t_i - \log t_i\} + 2\sum_{I_1} B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial}{\partial\gamma_1}S(t_i;\boldsymbol{\gamma}) \\
&\quad + \sum_{I_0}\pi_i^{(k)}\left[\frac{\partial}{\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma})) + B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial}{\partial\gamma_1}S(t_i;\boldsymbol{\gamma})\right], \\
\frac{\partial Q}{\partial\gamma_2} &= \frac{n_1}{\gamma_1^2\gamma_2} - \frac{1}{\gamma_1^2}\sum_{I_1} t_i + 2\sum_{I_1} B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial}{\partial\gamma_2}S(t_i;\boldsymbol{\gamma}) \\
&\quad + \sum_{I_0}\pi_i^{(k)}\left[\frac{\partial}{\partial\gamma_2}\log(S(t_i;\boldsymbol{\gamma})) + B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial}{\partial\gamma_2}S(t_i;\boldsymbol{\gamma})\right],
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial^2 Q}{\partial \beta_l \partial \beta_{l'}} &= -2\sum_{I_1} x_{il}x_{il'}\frac{B_i(\boldsymbol{\beta},\boldsymbol{\gamma})(1-S(t_i;\boldsymbol{\gamma}))}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))} - \sum_{I_0} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2} \\
&\quad - \sum_{I_0} \pi_i^{(k)} x_{il}x_{il'}\frac{B_i(\boldsymbol{\beta},\boldsymbol{\gamma})(1-S(t_i;\boldsymbol{\gamma}))}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}, \\
\frac{\partial^2 Q}{\partial \beta_l \partial \gamma_1} &= 2\sum_{I_1} x_{il}\left\{\frac{B_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}\right\}\frac{\partial}{\partial\gamma_1}S(t_i;\boldsymbol{\gamma}) \\
&\quad + \sum_{I_0} \pi_i^{(k)} x_{il}\left\{\frac{B_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}\right\}\frac{\partial}{\partial\gamma_1}S(t_i;\boldsymbol{\gamma}), \\
\frac{\partial^2 Q}{\partial \beta_l \partial \gamma_2} &= 2\sum_{I_1} x_{il}\left\{\frac{B_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}\right\}\frac{\partial}{\partial\gamma_2}S(t_i;\boldsymbol{\gamma}) \\
&\quad + \sum_{I_0} \pi_i^{(k)} x_{il}\left\{\frac{B_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}\right\}\frac{\partial}{\partial\gamma_2}S(t_i;\boldsymbol{\gamma}), \\
\frac{\partial^2 Q}{\partial \gamma_1^2} &= n_1\frac{\partial^2}{\partial\gamma_1^2}\log(G(\boldsymbol{\gamma})) - \frac{6}{\gamma_1^4}\sum_{I_1}\{\gamma_2 t_i - \log t_i\} \\
&\quad + 2\sum_{I_1}\left[B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\gamma_1^2}S(t_i;\boldsymbol{\gamma}) + \frac{\partial}{\partial\gamma_1}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\gamma_1}B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right] \\
&\quad + \sum_{I_0}\pi_i^{(k)}\left[B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\gamma_1^2}S(t_i;\boldsymbol{\gamma}) + \frac{\partial}{\partial\gamma_1}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\gamma_1}B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right] \\
&\quad + \sum_{I_0}\pi_i^{(k)}\frac{\partial^2}{\partial\gamma_1^2}\log(S(t_i;\boldsymbol{\gamma})), \\
\frac{\partial^2 Q}{\partial \gamma_2^2} &= -\frac{n_1}{\gamma_1^2\gamma_2^2} + 2\sum_{I_1}\left[B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\gamma_2^2}S(t_i;\boldsymbol{\gamma}) + \frac{\partial}{\partial\gamma_2}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\gamma_2}B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right] \\
&\quad + \sum_{I_0}\pi_i^{(k)}\left[B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\gamma_2^2}S(t_i;\boldsymbol{\gamma}) + \frac{\partial}{\partial\gamma_2}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\gamma_2}B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right] \\
&\quad + \sum_{I_0}\pi_i^{(k)}\frac{\partial^2}{\partial\gamma_2^2}\log(S(t_i;\boldsymbol{\gamma})),
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial^2 Q}{\partial\gamma_2\partial\gamma_1} &= -\frac{2n_1}{\gamma_1^3\gamma_2} + \frac{2}{\gamma_1^3}\sum_{I_1} t_i + 2\sum_{I_1}\left[B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\gamma_2\partial\gamma_1}S(t_i;\boldsymbol{\gamma})\right. \\
&\quad \left.+\frac{\partial}{\partial\gamma_2}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\gamma_1}B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right] + \sum_{I_0}\pi_i^{(k)}\left[B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\gamma_2\partial\gamma_1}S(t_i;\boldsymbol{\gamma})\right. \\
&\quad \left.+\frac{\partial}{\partial\gamma_2}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\gamma_1}B_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right] + \sum_{I_0}\pi_i^{(k)}\frac{\partial^2}{\partial\gamma_2\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma})),
\end{aligned}
$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where $\pi_i^{(k)}$ and $B_i(\boldsymbol{\beta},\boldsymbol{\gamma})$ are as defined in (4.2.4) and (4.3.3), respectively.

COM-Poisson cure rate model: The required first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}$ are as follows:

$$
\begin{aligned}
\frac{\partial Q}{\partial\beta_l} &= \sum_{I_1} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{21i}}{z_{2i}z_{01i}} + \sum_{I_0}\pi_i^{(k)}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{2i}}{z_{1i}z_{01i}} - \sum_{I^*} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}, \\
\frac{\partial Q}{\partial\gamma_1} &= n_1\frac{\partial}{\partial\gamma_1}\log(G(\boldsymbol{\gamma})) + \frac{2}{\gamma_1^3}\sum_{I_1}\{\gamma_2 t_i - \log t_i\} \\
&\quad + \sum_{I_1}\left(\frac{z_{21i}}{z_{2i}} - 1\right)\frac{\partial}{\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma})) + \sum_{I_0}\pi_i^{(k)}\frac{z_{2i}}{z_{1i}}\frac{\partial}{\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma})), \\
\frac{\partial Q}{\partial\gamma_2} &= \frac{n_1}{\gamma_1^2\gamma_2} - \frac{1}{\gamma_1^2}\sum_{I_1} t_i + \sum_{I_1}\left(\frac{z_{21i}}{z_{2i}} - 1\right)\frac{\partial}{\partial\gamma_2}\log(S(t_i;\boldsymbol{\gamma})) \\
&\quad + \sum_{I_0}\pi_i^{(k)}\frac{z_{2i}}{z_{1i}}\frac{\partial}{\partial\gamma_2}\log(S(t_i;\boldsymbol{\gamma})),
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial^2 Q}{\partial\beta_l \partial\beta_{l'}} &= \sum_{I_1} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(z_{2i}z_{01i})^2}\Bigg[\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Big\{z_{2i}z_{22i} - z_{21i}^2\Big\} + z_{2i}z_{21i}\Big\{z_{01i} \\
&\quad -\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{02i}}{z_{01i}}\Big\}\Bigg] + \sum_{I_0} \pi_i^{(k)} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(z_{1i}z_{01i})^2}\Bigg[\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Big\{z_{1i}z_{21i} - z_{2i}^2\Big\} \\
&\quad + z_{1i}z_{2i}\Big\{z_{01i} - \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{02i}}{z_{01i}}\Big\}\Bigg] - \sum_{I^*} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}, \\
\frac{\partial^2 Q}{\partial\beta_l \partial\gamma_1} &= \sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{z_{01i}}\left\{\frac{z_{2i}z_{22i} - z_{21i}^2}{z_{2i}^2}\right\}\frac{\partial}{\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma})) \\
&\quad + \sum_{I_0} \pi_i^{(k)} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{z_{01i}}\left\{\frac{z_{1i}z_{21i} - z_{2i}^2}{z_{1i}^2}\right\}\frac{\partial}{\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma})), \\
\frac{\partial^2 Q}{\partial\beta_l \partial\gamma_2} &= \sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{z_{01i}}\left\{\frac{z_{2i}z_{22i} - z_{21i}^2}{z_{2i}^2}\right\}\frac{\partial}{\partial\gamma_2}\log(S(t_i;\boldsymbol{\gamma})) \\
&\quad + \sum_{I_0} \pi_i^{(k)} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{z_{01i}}\left\{\frac{z_{1i}z_{21i} - z_{2i}^2}{z_{1i}^2}\right\}\frac{\partial}{\partial\gamma_2}\log(S(t_i;\boldsymbol{\gamma})), \\
\frac{\partial^2 Q}{\partial\gamma_1^2} &= n_1 \frac{\partial^2}{\partial\gamma_1^2}\log(G(\boldsymbol{\gamma})) - \frac{6}{\gamma_1^4}\sum_{I_1}\{\gamma_2 t_i - \log t_i\} + \sum_{I_1}\Bigg[\left(\frac{z_{21i}}{z_{2i}} - 1\right) \\
&\quad \times \frac{\partial^2}{\partial\gamma_1^2}\log(S(t_i;\boldsymbol{\gamma})) + \left\{\frac{z_{2i}z_{22i} - z_{21i}^2}{z_{2i}^2}\right\}\left\{\frac{\partial}{\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma}))\right\}^2\Bigg] \\
&\quad + \sum_{I_0}\pi_i^{(k)}\Bigg[\frac{z_{2i}}{z_{1i}}\frac{\partial^2}{\partial\gamma_1^2}\log(S(t_i;\boldsymbol{\gamma})) + \left\{\frac{z_{1i}z_{21i} - z_{2i}^2}{z_{1i}^2}\right\}\left\{\frac{\partial}{\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma}))\right\}^2\Bigg], \\
\frac{\partial^2 Q}{\partial\gamma_2^2} &= -\frac{n_1}{\gamma_1^2\gamma_2^2} + \sum_{I_1}\Bigg[\left(\frac{z_{21i}}{z_{2i}} - 1\right)\frac{\partial^2}{\partial\gamma_2^2}\log(S(t_i;\boldsymbol{\gamma})) + \left\{\frac{z_{2i}z_{22i} - z_{21i}^2}{z_{2i}^2}\right\} \\
&\quad \times \left\{\frac{\partial}{\partial\gamma_2}\log(S(t_i;\boldsymbol{\gamma}))\right\}^2\Bigg] + \sum_{I_0}\pi_i^{(k)}\Bigg[\frac{z_{2i}}{z_{1i}}\frac{\partial^2}{\partial\gamma_2^2}\log(S(t_i;\boldsymbol{\gamma})) \\
&\quad + \left\{\frac{z_{1i}z_{21i} - z_{2i}^2}{z_{1i}^2}\right\}\left\{\frac{\partial}{\partial\gamma_2}\log(S(t_i;\boldsymbol{\gamma}))\right\}^2\Bigg],
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial^2 Q}{\partial\gamma_2\partial\gamma_1} \quad = \quad & -\frac{2n_1}{\gamma_1^3\gamma_2} + \frac{2}{\gamma_1^3}\sum_{I_1} t_i + \sum_{I_1}\left[\left(\frac{z_{21i}}{z_{2i}} - 1\right)\frac{\partial^2}{\partial\gamma_2\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma}))\right. \\
& \left. +\left\{\frac{z_{2i}z_{22i} - z_{21i}^2}{z_{2i}^2}\right\}\frac{\partial}{\partial\gamma_2}\log(S(t_i;\boldsymbol{\gamma}))\frac{\partial}{\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma}))\right] \\
& +\sum_{I_0}\pi_i^{(k)}\left[\frac{z_{2i}}{z_{1i}}\frac{\partial^2}{\partial\gamma_2\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma})) + \left\{\frac{z_{1i}z_{21i} - z_{2i}^2}{z_{1i}^2}\right\}\right. \\
& \left.\times\frac{\partial}{\partial\gamma_2}\log(S(t_i;\boldsymbol{\gamma}))\frac{\partial}{\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma}))\right],
\end{aligned}
$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$
z_{22} = z_{22}(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty}\frac{j^3\{H_\phi^{-1}(1+\exp(\boldsymbol{x}'\boldsymbol{\beta}))S(t;\boldsymbol{\gamma})\}^j}{(j!)^\phi},
$$

$$
z_{02} = z_{02}(\boldsymbol{\theta}_1; \boldsymbol{x}) = \sum_{j=1}^{\infty}\frac{j^2\{H_\phi^{-1}(1+\exp(\boldsymbol{x}'\boldsymbol{\beta}))\}^j}{(j!)^\phi},
$$

and $\pi_i^{(k)}$ is as defined in (4.2.5). The quantities $z_{1i}, z_{2i}, z_{21i}, z_{22i}, z_{01i}$, and z_{02i} are all computed as described in Section 2.2.

B.2 Observed information matrix

Bernoulli cure rate model: The observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial\beta_l\partial\beta_{l'}} \quad &= \quad -\sum_{I_0} x_{il}x_{il'}w_i(1-w_i) + \sum_{I^*} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}, \\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma_1} \quad &= \quad -\sum_{I_0} x_{il}\frac{\partial}{\partial\gamma_1}w_i,
\end{aligned}
$$

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \beta_l \partial \gamma_2} &= -\sum_{I_0} x_{il} \frac{\partial}{\partial \gamma_2} w_i, \\
-\frac{\partial^2 l}{\partial \gamma_1^2} &= -n_1 \frac{\partial^2}{\partial \gamma_1^2} \log(G(\boldsymbol{\gamma})) + \frac{6}{\gamma_1^4} \sum_{I_1} \{\gamma_2 t_i - \log t_i\} - \sum_{I_0} \Bigg\{ w_i \frac{\partial^2}{\partial \gamma_1^2} \log(S(t_i;\boldsymbol{\gamma})) \\
&\quad + \frac{\partial}{\partial \gamma_1} \log(S(t_i;\boldsymbol{\gamma})) \frac{\partial}{\partial \gamma_1} w_i \Bigg\}, \\
-\frac{\partial^2 l}{\partial \gamma_2^2} &= \frac{n_1}{\gamma_1^2 \gamma_2^2} - \sum_{I_0} \Bigg\{ w_i \frac{\partial^2}{\partial \gamma_2^2} \log(S(t_i;\boldsymbol{\gamma})) + \frac{\partial}{\partial \gamma_2} \log(S(t_i;\boldsymbol{\gamma})) \frac{\partial}{\partial \gamma_2} w_i \Bigg\}, \\
-\frac{\partial^2 l}{\partial \gamma_2 \partial \gamma_1} &= \frac{2n_1}{\gamma_1^3 \gamma_2} - \frac{2}{\gamma_1^3} \sum_{I_1} t_i - \sum_{I_0} \Bigg\{ w_i \frac{\partial^2}{\partial \gamma_2 \partial \gamma_1} \log(S(t_i;\boldsymbol{\gamma})) \\
&\quad + \frac{\partial}{\partial \gamma_2} \log(S(t_i;\boldsymbol{\gamma})) \frac{\partial}{\partial \gamma_1} w_i \Bigg\}.
\end{aligned}
$$

The above are defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where w_i is as defined in (4.3.1).

Poisson cure rate model: The observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \beta_l \partial \beta_{l'}} &= -\sum_{I_1} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2} \left\{ \frac{\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})) - \exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})))^2} \right\} \\
&\quad - \sum_{I^*} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta}) \{S(t_i;\boldsymbol{\gamma}) - 1\}}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}, \\
-\frac{\partial^2 l}{\partial \beta_l \partial \gamma_1} &= -\sum_{I^*} x_{il} \left\{ \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})} \right\} \frac{\partial}{\partial \gamma_1} S(t_i;\boldsymbol{\gamma}), \\
-\frac{\partial^2 l}{\partial \beta_l \partial \gamma_2} &= -\sum_{I^*} x_{il} \left\{ \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})} \right\} \frac{\partial}{\partial \gamma_2} S(t_i;\boldsymbol{\gamma}), \\
-\frac{\partial^2 l}{\partial \gamma_1^2} &= -n_1 \frac{\partial^2}{\partial \gamma_1^2} \log(G(\boldsymbol{\gamma})) + \frac{6}{\gamma_1^4} \sum_{I_1} \{\gamma_2 t_i - \log t_i\} \\
&\quad - \sum_{I^*} \log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})) \frac{\partial^2}{\partial \gamma_1^2} S(t_i;\boldsymbol{\gamma}),
\end{aligned}
$$

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \gamma_2^2} &= \frac{n_1}{\gamma_1^2\gamma_2^2} - \sum_{I^*} \log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\frac{\partial^2}{\partial \gamma_2^2} S(t_i;\boldsymbol{\gamma}), \\
-\frac{\partial^2 l}{\partial \gamma_2 \partial \gamma_1} &= \frac{2n_1}{\gamma_1^3\gamma_2} - \frac{2}{\gamma_1^3}\sum_{I_1} t_i - \sum_{I^*} \log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\frac{\partial^2}{\partial \gamma_2 \partial \gamma_1} S(t_i;\boldsymbol{\gamma}).
\end{aligned}
$$

The above are defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$.

Geometric cure rate model: The observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \beta_l \partial \beta_{l'}} &= 2\sum_{I_1} x_{il}x_{il'}\frac{B_i(\boldsymbol{\beta},\boldsymbol{\gamma})(1-S(t_i;\boldsymbol{\gamma}))}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))} \\
&\quad + \sum_{I_0} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2} + \sum_{I_0} x_{il}x_{il'}w_iB_i(\boldsymbol{\beta},\boldsymbol{\gamma}) \\
&\quad \times(1-S(t_i;\boldsymbol{\gamma}))\left\{\frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))} + \frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}, \\
-\frac{\partial^2 l}{\partial \beta_l \partial \gamma_1} &= -2\sum_{I_1} x_{il}\left\{\frac{B_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}\right\}\frac{\partial}{\partial \gamma_1}S(t_i;\boldsymbol{\gamma}) \\
&\quad - \sum_{I_0} x_{il}\left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}\right\}\frac{\partial}{\partial \gamma_1}S(t_i;\boldsymbol{\gamma}) - \sum_{I_0} x_{il}w_iB_i(\boldsymbol{\beta},\boldsymbol{\gamma}) \\
&\quad \times\frac{\partial}{\partial \gamma_1}S(t_i;\boldsymbol{\gamma})\left\{\frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))} + \frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}, \\
-\frac{\partial^2 l}{\partial \beta_l \partial \gamma_2} &= -2\sum_{I_1} x_{il}\left\{\frac{B_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}\right\}\frac{\partial}{\partial \gamma_2}S(t_i;\boldsymbol{\gamma}) \\
&\quad - \sum_{I_0} x_{il}\left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}\right\}\frac{\partial}{\partial \gamma_2}S(t_i;\boldsymbol{\gamma}) - \sum_{I_0} x_{il}w_iB_i(\boldsymbol{\beta},\boldsymbol{\gamma}) \\
&\quad \times\frac{\partial}{\partial \gamma_2}S(t_i;\boldsymbol{\gamma})\left\{\frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))} + \frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\},
\end{aligned}
$$

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \gamma_1^2} &= -n_1 \frac{\partial^2}{\partial \gamma_1^2} \log(G(\boldsymbol{\gamma})) + \frac{6}{\gamma_1^4} \sum_{I_1} \{\gamma_2 t_i - \log t_i\} \\
&\quad -2 \sum_{I_1} \left\{ B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) \frac{\partial^2}{\partial \gamma_1^2} S(t_i; \boldsymbol{\gamma}) + \frac{\partial}{\partial \gamma_1} S(t_i; \boldsymbol{\gamma}) \frac{\partial}{\partial \gamma_1} B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) \right\} \\
&\quad - \sum_{I_0} \left\{ \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})} \right\} \frac{\partial^2}{\partial \gamma_1^2} S(t_i; \boldsymbol{\gamma}) - \sum_{I_0} \left[w_i B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) \frac{\partial^2}{\partial \gamma_1^2} S(t_i; \boldsymbol{\gamma}) \right. \\
&\quad + \frac{\partial}{\partial \gamma_1} S(t_i; \boldsymbol{\gamma}) \left\{ w_i \frac{\partial}{\partial \gamma_1} B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) + \left\{ \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta}) B_i(\boldsymbol{\beta}, \boldsymbol{\gamma})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})} \right\} \right. \\
&\quad \left.\left. \times \frac{\partial}{\partial \gamma_1} S(t_i; \boldsymbol{\gamma}) \right\} \right], \\
-\frac{\partial^2 l}{\partial \gamma_2^2} &= \frac{n_1}{\gamma_1^2 \gamma_2^2} - 2 \sum_{I_1} \left\{ B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) \frac{\partial^2}{\partial \gamma_2^2} S(t_i; \boldsymbol{\gamma}) + \frac{\partial}{\partial \gamma_2} S(t_i; \boldsymbol{\gamma}) \frac{\partial}{\partial \gamma_2} B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) \right\} \\
&\quad - \sum_{I_0} \left\{ \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})} \right\} \frac{\partial^2}{\partial \gamma_2^2} S(t_i; \boldsymbol{\gamma}) - \sum_{I_0} \left[w_i B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) \frac{\partial^2}{\partial \gamma_2^2} S(t_i; \boldsymbol{\gamma}) \right. \\
&\quad + \frac{\partial}{\partial \gamma_2} S(t_i; \boldsymbol{\gamma}) \left\{ w_i \frac{\partial}{\partial \gamma_2} B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) + \left\{ \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta}) B_i(\boldsymbol{\beta}, \boldsymbol{\gamma})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})} \right\} \right. \\
&\quad \left.\left. \times \frac{\partial}{\partial \gamma_2} S(t_i; \boldsymbol{\gamma}) \right\} \right], \\
-\frac{\partial^2 l}{\partial \gamma_2 \partial \gamma_1} &= \frac{2n_1}{\gamma_1^3 \gamma_2} - \frac{2}{\gamma_1^3} \sum_{I_1} t_i - 2 \sum_{I_1} \left\{ B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) \frac{\partial^2}{\partial \gamma_2 \partial \gamma_1} S(t_i; \boldsymbol{\gamma}) + \frac{\partial}{\partial \gamma_2} S(t_i; \boldsymbol{\gamma}) \right. \\
&\quad \left. \times \frac{\partial}{\partial \gamma_1} B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) \right\} - \sum_{I_0} \left\{ \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})} \right\} \frac{\partial^2}{\partial \gamma_2 \partial \gamma_1} S(t_i; \boldsymbol{\gamma}) \\
&\quad - \sum_{I_0} \left[w_i B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) \frac{\partial^2}{\partial \gamma_2 \partial \gamma_1} S(t_i; \boldsymbol{\gamma}) + \frac{\partial}{\partial \gamma_2} S(t_i; \boldsymbol{\gamma}) \right. \\
&\quad \left. \times \left\{ w_i \frac{\partial}{\partial \gamma_1} B_i(\boldsymbol{\beta}, \boldsymbol{\gamma}) + \left\{ \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta}) B_i(\boldsymbol{\beta}, \boldsymbol{\gamma})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})} \right\} \frac{\partial}{\partial \gamma_1} S(t_i; \boldsymbol{\gamma}) \right\} \right].
\end{aligned}
$$

The above are defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where w_i and $B_i(\boldsymbol{\beta}, \boldsymbol{\gamma})$ are as defined in (4.3.2) and (4.3.3), respectively.

COM-Poisson cure rate model: For a fixed value of ϕ, the observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial\beta_l\partial\beta_{l'}} &= -\sum_{I_1} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(z_{01i}z_{2i})^2}\Bigg[\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Bigg\{z_{2i}z_{22i}-z_{21i}^2\Bigg\}+z_{2i}z_{21i}\Bigg\{z_{01i} \\
&\quad -\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{02i}}{z_{01i}}\Bigg\}\Bigg] - \sum_{I_0} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(z_{01i}(1+z_{1i}))^2}\Bigg[\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\Bigg\{z_{21i}(1+z_{1i}) \\
&\quad -z_{2i}^2\Bigg\}+z_{2i}(1+z_{1i})\Bigg\{z_{01i}-\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{02i}}{z_{01i}}\Bigg\}\Bigg] \\
&\quad +\sum_{I^*} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}, \\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma_1} &= -\sum_{I_1} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{z_{01i}}\left\{\frac{z_{2i}z_{22i}-z_{21i}^2}{z_{2i}^2}\right\}\frac{\partial}{\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma})) \\
&\quad -\sum_{I_0} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{z_{01i}}\left\{\frac{z_{21i}(1+z_{1i})-z_{2i}^2}{(1+z_{1i})^2}\right\}\frac{\partial}{\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma})), \\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma_2} &= -\sum_{I_1} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{z_{01i}}\left\{\frac{z_{2i}z_{22i}-z_{21i}^2}{z_{2i}^2}\right\}\frac{\partial}{\partial\gamma_2}\log(S(t_i;\boldsymbol{\gamma})) \\
&\quad -\sum_{I_0} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{z_{01i}}\left\{\frac{z_{21i}(1+z_{1i})-z_{2i}^2}{(1+z_{1i})^2}\right\}\frac{\partial}{\partial\gamma_2}\log(S(t_i;\boldsymbol{\gamma})), \\
-\frac{\partial^2 l}{\partial\gamma_1^2} &= -n_1\frac{\partial^2}{\partial\gamma_1^2}\log(G(\boldsymbol{\gamma}))+\frac{6}{\gamma_1^4}\sum_{I_1}\{\gamma_2 t_i-\log t_i\}-\sum_{I_1}\left[\left\{\frac{z_{21i}}{z_{2i}}-1\right\}\right. \\
&\quad \left.\times\frac{\partial^2}{\partial\gamma_1^2}\log(S(t_i;\boldsymbol{\gamma}))+\left\{\frac{z_{2i}z_{22i}-z_{21i}^2}{z_{2i}^2}\right\}\left\{\frac{\partial}{\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma}))\right\}^2\right] \\
&\quad -\sum_{I_0}\left[\left\{\frac{z_{2i}}{1+z_{1i}}\right\}\frac{\partial^2}{\partial\gamma_1^2}\log(S(t_i;\boldsymbol{\gamma}))+\left\{\frac{z_{21i}(1+z_{1i})-z_{2i}^2}{(1+z_{1i})^2}\right\}\right. \\
&\quad \left.\times\left\{\frac{\partial}{\partial\gamma_1}\log(S(t_i;\boldsymbol{\gamma}))\right\}^2\right],
\end{aligned}
$$

$$\begin{aligned}
-\frac{\partial^2 l}{\partial \gamma_2^2} &= \frac{n_1}{\gamma_1^2\gamma_2^2} - \sum_{I_1}\left[\left\{\frac{z_{21i}}{z_{2i}} - 1\right\}\frac{\partial^2}{\partial \gamma_2^2}\log(S(t_i;\boldsymbol{\gamma})) + \left\{\frac{z_{2i}z_{22i} - z_{21i}^2}{z_{2i}^2}\right\}\right. \\
&\quad \left. \times\left\{\frac{\partial}{\partial \gamma_2}\log(S(t_i;\boldsymbol{\gamma}))\right\}^2\right] - \sum_{I_0}\left[\left\{\frac{z_{2i}}{1+z_{1i}}\right\}\frac{\partial^2}{\partial \gamma_2^2}\log(S(t_i;\boldsymbol{\gamma}))\right. \\
&\quad \left. + \left\{\frac{z_{21i}(1+z_{1i}) - z_{2i}^2}{(1+z_{1i})^2}\right\}\left\{\frac{\partial}{\partial \gamma_2}\log(S(t_i;\boldsymbol{\gamma}))\right\}^2\right], \\
-\frac{\partial^2 l}{\partial \gamma_2 \partial \gamma_1} &= \frac{2n_1}{\gamma_1^3\gamma_2} - \frac{2}{\gamma_1^3}\sum_{I_1} t_i - \sum_{I_1}\left[\left\{\frac{z_{21i}}{z_{2i}} - 1\right\}\frac{\partial^2}{\partial \gamma_2 \partial \gamma_1}\log(S(t_i;\boldsymbol{\gamma}))\right. \\
&\quad \left. + \left\{\frac{z_{2i}z_{22i} - z_{21i}^2}{z_{2i}^2}\right\}\frac{\partial}{\partial \gamma_2}\log(S(t_i;\boldsymbol{\gamma}))\frac{\partial}{\partial \gamma_1}\log(S(t_i;\boldsymbol{\gamma}))\right] \\
&\quad - \sum_{I_0}\left[\left\{\frac{z_{2i}}{1+z_{1i}}\right\}\frac{\partial^2}{\partial \gamma_2 \partial \gamma_1}\log(S(t_i;\boldsymbol{\gamma})) + \left\{\frac{z_{21i}(1+z_{1i}) - z_{2i}^2}{(1+z_{1i})^2}\right\}\right. \\
&\quad \left. \times\frac{\partial}{\partial \gamma_2}\log(S(t_i;\boldsymbol{\gamma}))\frac{\partial}{\partial \gamma_1}\log(S(t_i;\boldsymbol{\gamma}))\right].
\end{aligned}$$

The above are defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$.

Appendix C

Corresponding to Chapter 5

C.1 First- and second-order derivatives of the Q-function

Bernoulli cure rate model: The expressions of the first- and second-order derivatives of the $Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ are as follows:

$$
\begin{aligned}
\frac{\partial Q_1}{\partial \beta_l} &= \sum_{I_1} x_{il} + \sum_{I_0} \pi_i^{(k)} x_{il} - \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})}, \\
\frac{\partial^2 Q_1}{\partial \beta_l \partial \beta_{l'}} &= -\sum_{I^*} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta}))^2},
\end{aligned}
$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$. The required first- and second-order derivatives of the $Q_2(\boldsymbol{\gamma}, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\gamma}$ are as follows:

$$
\frac{\partial Q_2}{\partial \gamma_1} = -\frac{n_1}{\gamma_1} - \frac{n_1}{{\gamma_1}^2} \log \gamma_2 - \frac{1}{{\gamma_1}^2} \sum_{I_1} \log t_i + \frac{1}{{\gamma_1}^2} \sum_{I_1} G_{Bi}(\boldsymbol{\gamma}) + \frac{1}{{\gamma_1}^2} \sum_{I_0} \pi_i^{(k)} G_{Bi}(\boldsymbol{\gamma}),
$$

$$
\begin{aligned}
\frac{\partial Q_2}{\partial \gamma_2} &= \frac{n_1}{\gamma_1\gamma_2} - \frac{1}{\gamma_1\gamma_2}\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1} - \frac{1}{\gamma_1\gamma_2}\sum_{I_0}\pi_i^{(k)}(\gamma_2 t_i)^{1/\gamma_1},\\
\frac{\partial^2 Q_2}{\partial \gamma_1^2} &= \frac{n_1}{{\gamma_1}^2} + \frac{2n_1}{{\gamma_1}^3}\log\gamma_2 + \frac{2}{{\gamma_1}^3}\sum_{I_1}\log t_i - \frac{1}{{\gamma_1}^4}\sum_{I_1} G_{Bi}(\boldsymbol{\gamma})\{\log(\gamma_2 t_i) + 2\gamma_1\}\\
&\quad - \frac{1}{{\gamma_1}^4}\sum_{I_0}\pi_i^{(k)} G_{Bi}(\boldsymbol{\gamma})\{\log(\gamma_2 t_i) + 2\gamma_1\},\\
\frac{\partial^2 Q_2}{\partial \gamma_2^2} &= -\frac{n_1}{\gamma_1{\gamma_2}^2} - \frac{1}{\gamma_1{\gamma_2}^2}\left(\frac{1}{\gamma_1} - 1\right)\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1} - \frac{1}{\gamma_1{\gamma_2}^2}\left(\frac{1}{\gamma_1} - 1\right)\sum_{I_0}\pi_i^{(k)}(\gamma_2 t_i)^{1/\gamma_1},\\
\frac{\partial^2 Q_2}{\partial \gamma_1 \partial \gamma_2} &= -\frac{n_1}{\gamma_2{\gamma_1}^2} + \frac{1}{\gamma_2{\gamma_1}^2}\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1}\left\{\frac{1}{\gamma_1}\log(\gamma_2 t_i) + 1\right\}\\
&\quad + \frac{1}{\gamma_2{\gamma_1}^2}\sum_{I_0}\pi_i^{(k)}(\gamma_2 t_i)^{1/\gamma_1}\left\{\frac{1}{\gamma_1}\log(\gamma_2 t_i) + 1\right\},
\end{aligned}
$$

where $\pi_i^{(k)}$ and $G_{Bi}(\boldsymbol{\gamma})$ are as defined in (5.2.1) and (5.3.2), respectively.

Poisson cure rate model: The required first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}$ are as follows:

$$
\begin{aligned}
\frac{\partial Q}{\partial \beta_l} &= \sum_{I_1} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1 + A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))}\\
&\quad + \sum_{I_0}\pi_i^{(k)} x_{il}\frac{\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}) + B_{Pi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))(\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})) - 1)} - \sum_{I^*} x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})},\\
\frac{\partial Q}{\partial \gamma_1} &= -\frac{n_1}{\gamma_1} - \frac{n_1}{{\gamma_1}^2}\log\gamma_2 - \frac{1}{{\gamma_1}^2}\sum_{I_1}\log t_i + \frac{1}{{\gamma_1}^2}\sum_{I_1} G_{Pi}(\boldsymbol{\gamma}) + \frac{1}{{\gamma_1}^2}\sum_{I_1} G_{Pi}(\boldsymbol{\gamma})A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\\
&\quad + \frac{1}{{\gamma_1}^2}\sum_{I_0}\pi_i^{(k)}\frac{G_{Pi}(\boldsymbol{\gamma})A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})) - 1},\\
\frac{\partial Q}{\partial \gamma_2} &= \frac{n_1}{\gamma_1\gamma_2} - \frac{1}{\gamma_1\gamma_2}\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1} - \frac{1}{\gamma_1\gamma_2}\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1} A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\\
&\quad - \frac{1}{\gamma_1\gamma_2}\sum_{I_0}\pi_i^{(k)}\frac{(\gamma_2 t_i)^{1/\gamma_1}A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})) - 1},
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial^2 Q}{\partial\beta_l\partial\beta_{l'}} &= \sum_{I_1} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\{\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))-\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\}}{\{\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\}^2} \\
&\quad +\sum_{I_1} x_{il}x_{il'}\frac{\exp(B_{Pi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}+\sum_{I_0}\pi_i^{(k)}x_{il}x_{il'} \\
&\quad \times\frac{\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})+B_{Pi}(\boldsymbol{\beta},\boldsymbol{\gamma}))\{\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))-\exp(B_{Pi}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1\}}{\{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))(\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1)\}^2} \\
&\quad -\sum_{I^*} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}, \\
\frac{\partial^2 Q}{\partial\beta_l\partial\gamma_1} &= \frac{1}{{\gamma_1}^2}\sum_{I_1} x_{il}\frac{G_{Pi}(\boldsymbol{\gamma})\exp(B_{Pi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}+\frac{1}{{\gamma_1}^2}\sum_{I_0}\pi_i^{(k)}x_{il} \\
&\quad \times\frac{G_{Pi}(\boldsymbol{\gamma})\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})+B_{Pi}(\boldsymbol{\beta},\boldsymbol{\gamma}))\{\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))-A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})-1\}}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\{\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1\}^2}, \\
\frac{\partial^2 Q}{\partial\beta_l\partial\gamma_2} &= -\frac{1}{\gamma_1\gamma_2}\sum_{I_1} x_{il}\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(B_{Pi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}-\frac{1}{\gamma_1\gamma_2}\sum_{I_0}\pi_i^{(k)}x_{il} \\
&\quad \times\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})+B_{Pi}(\boldsymbol{\beta},\boldsymbol{\gamma}))\{\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))-A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})-1\}}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\{\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1\}^2}, \\
\frac{\partial^2 Q}{\partial\gamma_1^2} &= \frac{n_1}{{\gamma_1}^2}+\frac{2n_1}{{\gamma_1}^3}\log\gamma_2+\frac{2}{{\gamma_1}^3}\sum_{I_1}\log t_i-\frac{1}{{\gamma_1}^4}\sum_{I_1}G_{Pi}(\boldsymbol{\gamma})\{\log(\gamma_2 t_i)+2\gamma_1\} \\
&\quad +\frac{1}{{\gamma_1}^4}\sum_{I_1}G_{Pi}(\boldsymbol{\gamma})A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\{G_{Pi}(\boldsymbol{\gamma})-\log(\gamma_2 t_i)-2\gamma_1\} \\
&\quad +\frac{1}{{\gamma_1}^4}\sum_{I_0}\pi_i^{(k)}\frac{G_{Pi}(\boldsymbol{\gamma})A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1)^2} \\
&\quad \times\Big[\{\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1\}\{G_{Pi}(\boldsymbol{\gamma})-\log(\gamma_2 t_i)-2\gamma_1\}-G_{Pi}(\boldsymbol{\gamma})A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\Big],
\end{aligned}
$$

$$\begin{aligned}
\frac{\partial^2 Q}{\partial \gamma_2^2} &= -\frac{n_1}{\gamma_1 {\gamma_2}^2} - \frac{1}{\gamma_1 {\gamma_2}^2}\left(\frac{1}{\gamma_1} - 1\right)\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1} \\
&\quad - \frac{1}{\gamma_1 {\gamma_2}^2}\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1} A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\left\{\frac{1}{\gamma_1} - 1 - \frac{1}{\gamma_1}(\gamma_2 t_i)^{1/\gamma_1}\right\} \\
&\quad - \frac{1}{\gamma_1 {\gamma_2}^2}\sum_{I_0}\pi_i^{(k)}\frac{(\gamma_2 t_i)^{1/\gamma_1} A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1)^2} \\
&\quad \times\left[\left\{\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1\right\}\left\{\frac{1}{\gamma_1} - 1 - \frac{1}{\gamma_1}(\gamma_2 t_i)^{1/\gamma_1}\right\} + \frac{1}{\gamma_1}(\gamma_2 t_i)^{1/\gamma_1} A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\right], \\
\frac{\partial^2 Q}{\partial \gamma_1 \partial \gamma_2} &= -\frac{n_1}{\gamma_2 {\gamma_1}^2} + \frac{1}{\gamma_2 {\gamma_1}^2}\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1}\left\{1 + \frac{1}{\gamma_1}\log(\gamma_2 t_i)\right\} \\
&\quad + \frac{1}{\gamma_2 {\gamma_1}^2}\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1} A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\left\{1 + \frac{1}{\gamma_1}\log(\gamma_2 t_i) - \frac{1}{\gamma_1}G_{Pi}(\boldsymbol{\gamma})\right\} \\
&\quad + \frac{1}{\gamma_2 {\gamma_1}^2}\sum_{I_0}\pi_i^{(k)}\frac{(\gamma_2 t_i)^{1/\gamma_1} A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1)^2} \\
&\quad \times\left[\left\{\exp(A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1\right\}\left\{1 + \frac{1}{\gamma_1}\log(\gamma_2 t_i) - \frac{1}{\gamma_1}G_{Pi}(\boldsymbol{\gamma})\right\}\right. \\
&\quad \left. + \frac{1}{\gamma_1}G_{Pi}(\boldsymbol{\gamma})A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\right],
\end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$B_{Pi}(\boldsymbol{\beta},\boldsymbol{\gamma}) = \boldsymbol{x}_i^{'}\boldsymbol{\beta} - (\gamma_2 t_i)^{1/\gamma_1}, \tag{C.1.1}$$

for $i = 1, 2, \ldots, n$, and $A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})$, $\pi_i^{(k)}$, and $G_{Pi}(\boldsymbol{\gamma})$ are as defined in (5.2.2), (5.2.3), and (5.3.3), respectively.

Geometric cure rate model: The required first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}$ are as follows:

$$\frac{\partial Q}{\partial \beta_l} = \sum_{I_1} x_{il}\frac{1 - C_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1 + C_i(\boldsymbol{\beta},\boldsymbol{\gamma})} + \sum_{I_0}\pi_i^{(k)} x_{il}\frac{1}{1 + C_i(\boldsymbol{\beta},\boldsymbol{\gamma})} - \sum_{I_0} x_{il}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})},$$

$$
\begin{aligned}
\frac{\partial Q}{\partial \gamma_1} &= -\frac{n_1}{\gamma_1} - \frac{n_1}{{\gamma_1}^2}\log\gamma_2 - \frac{1}{{\gamma_1}^2}\sum_{I_1}\log t_i + \frac{1}{{\gamma_1}^2}\sum_{I_1} G_{Gi}(\boldsymbol{\gamma}) \\
&\quad + \frac{2}{{\gamma_1}^2}\sum_{I_1}\frac{G_{Gi}(\boldsymbol{\gamma})\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})} + \frac{1}{{\gamma_1}^2}\sum_{I_0}\pi_i^{(k)} G_{Gi}(\boldsymbol{\gamma}) \\
&\quad + \frac{1}{{\gamma_1}^2}\sum_{I_0}\pi_i^{(k)}\frac{G_{Gi}(\boldsymbol{\gamma})\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})}, \\
\frac{\partial Q}{\partial \gamma_2} &= \frac{n_1}{\gamma_1\gamma_2} - \frac{1}{\gamma_1\gamma_2}\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1} - \frac{2}{\gamma_1\gamma_2}\sum_{I_1}\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})} \\
&\quad - \frac{1}{\gamma_1\gamma_2}\sum_{I_0}\pi_i^{(k)}(\gamma_2 t_i)^{1/\gamma_1} - \frac{1}{\gamma_1\gamma_2}\sum_{I_0}\pi_i^{(k)}\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})}, \\
\frac{\partial^2 Q}{\partial \beta_l \partial \beta_{l'}} &= -2\sum_{I_1} x_{il}x_{il'}\frac{C_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2} - \sum_{I_0} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2} \\
&\quad - \sum_{I_0}\pi_i^{(k)} x_{il}x_{il'}\frac{C_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2}, \\
\frac{\partial^2 Q}{\partial \beta_l \partial \gamma_1} &= \frac{2}{{\gamma_1}^2}\sum_{I_1} x_{il}\frac{G_{Gi}(\boldsymbol{\gamma})\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2} + \frac{1}{{\gamma_1}^2}\sum_{I_0}\pi_i^{(k)} x_{il}\frac{G_{Gi}(\boldsymbol{\gamma})\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2}, \\
\frac{\partial^2 Q}{\partial \beta_l \partial \gamma_2} &= -\frac{2}{\gamma_1\gamma_2}\sum_{I_1} x_{il}\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2} \\
&\quad - \frac{1}{\gamma_1\gamma_2}\sum_{I_0}\pi_i^{(k)} x_{il}\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2},
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial^2 Q}{\partial \gamma_1^2} &= \frac{n_1}{{\gamma_1}^2} + \frac{2n_1}{{\gamma_1}^3}\log\gamma_2 + \frac{2}{{\gamma_1}^3}\sum_{I_1}\log t_i - \frac{1}{{\gamma_1}^4}\sum_{I_1} G_{Gi}(\boldsymbol{\gamma})\{\log(\gamma_2 t_i) + 2\gamma_1\} \\
&+ \frac{2}{{\gamma_1}^4}\sum_{I_1}\frac{G_{Gi}(\boldsymbol{\gamma})\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2}\Bigg[G_{Gi}(\boldsymbol{\gamma})(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})) \\
&- \{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})\}\{\log(\gamma_2 t_i) + 2\gamma_1\}\Bigg] - \frac{1}{{\gamma_1}^4}\sum_{I_0}\pi_i^{(k)} G_{Gi}(\boldsymbol{\gamma})\{\log(\gamma_2 t_i) + 2\gamma_1\} \\
&+ \frac{1}{{\gamma_1}^4}\sum_{I_0}\pi_i^{(k)}\frac{G_{Gi}(\boldsymbol{\gamma})\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2}\Bigg[G_{Gi}(\boldsymbol{\gamma})(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})) \\
&- \{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})\}\{\log(\gamma_2 t_i) + 2\gamma_1\}\Bigg], \\
\frac{\partial^2 Q}{\partial \gamma_2^2} &= -\frac{n_1}{\gamma_1{\gamma_2}^2} - \frac{1}{\gamma_1{\gamma_2}^2}\left(\frac{1}{\gamma_1} - 1\right)\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1} \\
&- \frac{2}{\gamma_1{\gamma_2}^2}\sum_{I_1}\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2}\Bigg[\left(\frac{1}{\gamma_1} - 1\right)\Big\{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})\Big\} \\
&- \frac{1}{\gamma_1}(\gamma_2 t_i)^{1/\gamma_1}(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\Bigg] - \frac{1}{\gamma_1{\gamma_2}^2}\left(\frac{1}{\gamma_1} - 1\right)\sum_{I_0}\pi_i^{(k)}(\gamma_2 t_i)^{1/\gamma_1} \\
&- \frac{1}{\gamma_1{\gamma_2}^2}\sum_{I_0}\pi_i^{(k)}\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2}\Bigg[\left(\frac{1}{\gamma_1} - 1\right)\Big\{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})\Big\} \\
&- \frac{1}{\gamma_1}(\gamma_2 t_i)^{1/\gamma_1}(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\Bigg], \\
\frac{\partial^2 Q}{\partial \gamma_1 \partial \gamma_2} &= -\frac{n_1}{\gamma_2{\gamma_1}^2} + \frac{1}{\gamma_2{\gamma_1}^2}\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1}\Big\{1 + \frac{1}{\gamma_1}\log(\gamma_2 t_i)\Big\} \\
&+ \frac{2}{\gamma_2{\gamma_1}^2}\sum_{I_1}\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2} \\
&\times\Bigg[\Big\{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})\Big\}\Big\{1 + \frac{1}{\gamma_1}\log(\gamma_2 t_i)\Big\} - \frac{1}{\gamma_1}G_{Gi}(\boldsymbol{\gamma})(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\Bigg] \\
&+ \frac{1}{\gamma_2{\gamma_1}^2}\sum_{I_0}\pi_i^{(k)}(\gamma_2 t_i)^{1/\gamma_1}\Big\{1 + \frac{1}{\gamma_1}\log(\gamma_2 t_i)\Big\} \\
&+ \frac{1}{\gamma_2{\gamma_1}^2}\sum_{I_0}\pi_i^{(k)}\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2} \\
&\times\Bigg[\Big\{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})\Big\}\Big\{1 + \frac{1}{\gamma_1}\log(\gamma_2 t_i)\Big\} - \frac{1}{\gamma_1}G_{Gi}(\boldsymbol{\gamma})(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\Bigg],
\end{aligned}
$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where $\pi_i^{(k)}$ and $G_{Gi}(\boldsymbol{\gamma})$ are as defined in (5.2.5) and (5.3.5), respectively, and $B_{Gi}(\boldsymbol{\beta}, \boldsymbol{\gamma})$ and $C_i(\boldsymbol{\beta}, \boldsymbol{\gamma})$ are as defined in (5.2.4).

COM-Poisson cure rate model: The required first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}$ are as follows:

$$
\begin{aligned}
\frac{\partial Q}{\partial \beta_l} &= \sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta}) z_{21i}}{z_{2i} z_{01i}} + \sum_{I_0} \pi_i^{(k)} x_{il} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta}) z_{2i}}{z_{1i} z_{01i}} - \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta})}, \\
\frac{\partial Q}{\partial \gamma_1} &= -\frac{n_1}{\gamma_1} - \frac{n_1}{{\gamma_1}^2} \log \gamma_2 - \frac{1}{{\gamma_1}^2} \sum_{I_1} \log t_i + \frac{1}{{\gamma_1}^2} \sum_{I_1} \frac{G_{Ci}(\boldsymbol{\gamma}) z_{21i}}{z_{2i}} \\
&\quad + \frac{1}{{\gamma_1}^2} \sum_{I_0} \pi_i^{(k)} \frac{G_{Ci}(\boldsymbol{\gamma}) z_{2i}}{z_{1i}}, \\
\frac{\partial Q}{\partial \gamma_2} &= \frac{n_1}{\gamma_1 \gamma_2} - \frac{1}{\gamma_1 \gamma_2} \sum_{I_1} \frac{(\gamma_2 t_i)^{1/\gamma_1} z_{21i}}{z_{2i}} - \frac{1}{\gamma_1 \gamma_2} \sum_{I_0} \pi_i^{(k)} \frac{(\gamma_2 t_i)^{1/\gamma_1} z_{2i}}{z_{1i}}, \\
\frac{\partial^2 Q}{\partial \beta_l \partial \beta_{l'}} &= \sum_{I_1} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{(z_{2i} z_{01i})^2} \left[z_{2i} \left\{ \exp(\boldsymbol{x}_i' \boldsymbol{\beta}) z_{22i} + z_{01i} z_{21i} \right\} \right. \\
&\quad \left. - \exp(\boldsymbol{x}_i' \boldsymbol{\beta}) z_{21i} \left\{ \frac{z_{2i} z_{02i}}{z_{01i}} + z_{21i} \right\} \right] + \sum_{I_0} \pi_i^{(k)} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{(z_{1i} z_{01i})^2} \\
&\quad \times \left[z_{1i} \left\{ \exp(\boldsymbol{x}_i' \boldsymbol{\beta}) z_{21i} + z_{01i} z_{2i} \right\} - \exp(\boldsymbol{x}_i' \boldsymbol{\beta}) z_{2i} \left\{ \frac{z_{1i} z_{02i}}{z_{01i}} + z_{2i} \right\} \right] \\
&\quad - \sum_{I^*} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{(1 + \exp(\boldsymbol{x}_i' \boldsymbol{\beta}))^2}, \\
\frac{\partial^2 Q}{\partial \beta_l \partial \gamma_1} &= \frac{1}{\gamma_1^2} \sum_{I_1} x_{il} \frac{G_{Ci}(\boldsymbol{\gamma}) \exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{z_{01i} z_{2i}^2} \left\{ z_{2i} z_{22i} - z_{21i}^2 \right\} \\
&\quad + \frac{1}{\gamma_1^2} \sum_{I_0} \pi_i^{(k)} x_{il} \frac{G_{Ci}(\boldsymbol{\gamma}) \exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{z_{01i} z_{1i}^2} \left\{ z_{1i} z_{21i} - z_{2i}^2 \right\}, \\
\frac{\partial^2 Q}{\partial \beta_l \partial \gamma_2} &= -\frac{1}{\gamma_1 \gamma_2} \sum_{I_1} x_{il} \frac{(\gamma_2 t_i)^{1/\gamma_1} \exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{z_{01i} z_{2i}^2} \left\{ z_{2i} z_{22i} - z_{21i}^2 \right\} \\
&\quad - \frac{1}{\gamma_1 \gamma_2} \sum_{I_0} \pi_i^{(k)} x_{il} \frac{(\gamma_2 t_i)^{1/\gamma_1} \exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{z_{01i} z_{1i}^2} \left\{ z_{1i} z_{21i} - z_{2i}^2 \right\},
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial^2 Q}{\partial \gamma_1^2} &= \frac{n_1}{{\gamma_1}^2} + \frac{2n_1}{{\gamma_1}^3}\log\gamma_2 + \frac{2}{{\gamma_1}^3}\sum_{I_1}\log t_i + \frac{1}{\gamma_1^4}\sum_{I_1}\frac{G_{Ci}(\boldsymbol{\gamma})}{z_{2i}^2} \\
&\quad \times\left[\log(\gamma_2 t_i)z_{2i}\{(\gamma_2 t_i)^{1/\gamma_1}z_{22i} - z_{21i}\} - z_{21i}\{G_{Ci}(\boldsymbol{\gamma})z_{21i} + 2\gamma_1 z_{2i}\}\right] \\
&\quad + \frac{1}{\gamma_1^4}\sum_{I_0}\pi_i^{(k)}\frac{G_{Ci}(\boldsymbol{\gamma})}{z_{1i}^2}\left[\log(\gamma_2 t_i)z_{1i}\{(\gamma_2 t_i)^{1/\gamma_1}z_{21i} - z_{2i}\} - z_{2i}\{G_{Ci}(\boldsymbol{\gamma})z_{2i}\right. \\
&\quad \left. + 2\gamma_1 z_{1i}\}\right], \\
\frac{\partial^2 Q}{\partial \gamma_2^2} &= -\frac{n_1}{\gamma_1{\gamma_2}^2} + \frac{1}{\gamma_1{\gamma_2}^2}\sum_{I_1}\frac{(\gamma_2 t_i)^{1/\gamma_1}}{z_{2i}^2}\left[z_{2i}\left\{\frac{1}{\gamma_1}(\gamma_2 t_i)^{1/\gamma_1}z_{22i} - \left(\frac{1}{\gamma_1} - 1\right)z_{21i}\right\}\right. \\
&\quad \left. - \frac{1}{\gamma_1}(\gamma_2 t_i)^{1/\gamma_1}z_{21i}^2\right] + \frac{1}{\gamma_1{\gamma_2}^2}\sum_{I_0}\pi_i^{(k)}\frac{(\gamma_2 t_i)^{1/\gamma_1}}{z_{1i}^2}\left[z_{1i}\left\{\frac{1}{\gamma_1}(\gamma_2 t_i)^{1/\gamma_1}z_{21i}\right.\right. \\
&\quad \left.\left. - \left(\frac{1}{\gamma_1} - 1\right)z_{2i}\right\} - \frac{1}{\gamma_1}(\gamma_2 t_i)^{1/\gamma_1}z_{2i}^2\right], \\
\frac{\partial^2 Q}{\partial \gamma_1 \partial \gamma_2} &= -\frac{n_1}{\gamma_2{\gamma_1}^2} - \frac{1}{\gamma_2{\gamma_1}^2}\sum_{I_1}\frac{(\gamma_2 t_i)^{1/\gamma_1}}{z_{2i}^2}\left[z_{2i}\left\{\frac{1}{\gamma_1}G_{Ci}(\boldsymbol{\gamma})z_{22i} - z_{21i} - \frac{1}{\gamma_1}\log(\gamma_2 t_i)z_{21i}\right\}\right. \\
&\quad \left. - \frac{1}{\gamma_1}G_{Ci}(\boldsymbol{\gamma})z_{21i}^2\right] - \frac{1}{\gamma_2{\gamma_1}^2}\sum_{I_0}\pi_i^{(k)}\frac{(\gamma_2 t_i)^{1/\gamma_1}}{z_{1i}^2}\left[z_{1i}\left\{\frac{1}{\gamma_1}G_{Ci}(\boldsymbol{\gamma})z_{21i} - z_{2i}\right.\right. \\
&\quad \left.\left. - \frac{1}{\gamma_1}\log(\gamma_2 t_i)z_{2i}\right\} - \frac{1}{\gamma_1}G_{Ci}(\boldsymbol{\gamma})z_{2i}^2\right],
\end{aligned}
$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$z_{22} = z_{22}(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty}\frac{j^3\{H_\phi^{-1}(1 + \exp(\boldsymbol{x}'\boldsymbol{\beta}))\exp(-(\gamma_2 t)^{1/\gamma_1})\}^j}{(j!)^\phi},$$

$$z_{02} = z_{02}(\boldsymbol{\theta}_1; \boldsymbol{x}) = \sum_{j=1}^{\infty}\frac{j^2\{H_\phi^{-1}(1 + \exp(\boldsymbol{x}'\boldsymbol{\beta}))\}^j}{(j!)^\phi},$$

and $\pi_i^{(k)}$ and $G_{Ci}(\boldsymbol{\gamma})$ are as defined in (5.2.6) and (5.3.6), respectively. The quantities $z_{1i}, z_{2i}, z_{21i}, z_{22i}, z_{01i}$, and z_{02i} are all computed as described in Section 2.2.

C.2 Observed information matrix

Bernoulli cure rate model: The observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial\beta_l\partial\beta_{l'}} &= -\sum_{I_0} x_{il}x_{il'}w_i(1-w_i) + \sum_{I^*} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2},\\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma_1} &= -\frac{1}{{\gamma_1}^2}\sum_{I_0} x_{il}w_i(1-w_i)G_{Bi}(\boldsymbol{\gamma}),\\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma_2} &= \frac{1}{\gamma_1\gamma_2}\sum_{I_0} x_{il}w_i(1-w_i)(\gamma_2 t_i)^{1/\gamma_1},\\
-\frac{\partial^2 l}{\partial\gamma_1^2} &= -\frac{n_1}{{\gamma_1}^2} - \frac{2n_1}{{\gamma_1}^3}\log\gamma_2 - \frac{2}{{\gamma_1}^3}\sum_{I_1}\log t_i + \frac{1}{{\gamma_1}^4}\sum_{I_1} G_{Bi}(\boldsymbol{\gamma})\{\log(\gamma_2 t_i) + 2\gamma_1\}\\
&\quad -\frac{1}{{\gamma_1}^4}\sum_{I_0} w_i G_{Bi}(\boldsymbol{\gamma})\{(1-w_i)G_{Bi}(\boldsymbol{\gamma}) - \log(\gamma_2 t_i) - 2\gamma_1\},\\
-\frac{\partial^2 l}{\partial\gamma_2^2} &= \frac{n_1}{\gamma_1{\gamma_2}^2} + \frac{1}{\gamma_1{\gamma_2}^2}\left(\frac{1}{\gamma_1}-1\right)\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1}\\
&\quad +\frac{1}{\gamma_1{\gamma_2}^2}\sum_{I_0} w_i(\gamma_2 t_i)^{1/\gamma_1}\left\{\frac{1}{\gamma_1} - 1 - \frac{1}{\gamma_1}(1-w_i)(\gamma_2 t_i)^{1/\gamma_1}\right\},\\
-\frac{\partial^2 l}{\partial\gamma_1\partial\gamma_2} &= \frac{n_1}{\gamma_2{\gamma_1}^2} - \frac{1}{\gamma_2{\gamma_1}^2}\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1}\left\{\frac{1}{\gamma_1}\log(\gamma_2 t_i) + 1\right\}\\
&\quad +\frac{1}{\gamma_2{\gamma_1}^2}\sum_{I_0} w_i(\gamma_2 t_i)^{1/\gamma_1}\left\{\frac{1}{\gamma_1}(1-w_i)G_{Bi}(\boldsymbol{\gamma}) - \frac{1}{\gamma_1}\log(\gamma_2 t_i) - 1\right\}.
\end{aligned}
$$

The above are defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where w_i and $G_{Bi}(\boldsymbol{\gamma})$ are as defined in (5.3.1) and (5.3.2), respectively.

Poisson cure rate model: The observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial\beta_l\partial\beta_{l'}} &= -\sum_{I_1} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\{\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))-\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\}}{\{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\}^2} \\
&\quad+\sum_{I^*} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}\left\{1-\exp(-(\gamma_2 t_i)^{1/\gamma_1})\right\}, \\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma_1} &= -\frac{1}{{\gamma_1}^2}\sum_{I^*} x_{il}\frac{G_{Pi}(\boldsymbol{\gamma})\exp(B_{Pi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}, \\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma_2} &= \frac{1}{\gamma_1\gamma_2}\sum_{I^*} x_{il}\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(B_{Pi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}, \\
-\frac{\partial^2 l}{\partial\gamma_1^2} &= -\frac{n_1}{{\gamma_1}^2}-\frac{2n_1}{{\gamma_1}^3}\log\gamma_2-\frac{2}{{\gamma_1}^3}\sum_{I_1}\log t_i+\frac{1}{{\gamma_1}^4}\sum_{I_1}G_{Pi}(\boldsymbol{\gamma})\{\log(\gamma_2 t_i)+2\gamma_1\} \\
&\quad-\frac{1}{{\gamma_1}^4}\sum_{I^*}G_{Pi}(\boldsymbol{\gamma})A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\{G_{Pi}(\boldsymbol{\gamma})-\log(\gamma_2 t_i)-2\gamma_1\}, \\
-\frac{\partial^2 l}{\partial\gamma_2^2} &= \frac{n_1}{\gamma_1{\gamma_2}^2}+\frac{1}{\gamma_1{\gamma_2}^2}\left(\frac{1}{\gamma_1}-1\right)\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1} \\
&\quad+\frac{1}{\gamma_1{\gamma_2}^2}\sum_{I^*}(\gamma_2 t_i)^{1/\gamma_1}A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\left\{\frac{1}{\gamma_1}-1-\frac{1}{\gamma_1}(\gamma_2 t_i)^{1/\gamma_1}\right\}, \\
-\frac{\partial^2 l}{\partial\gamma_1\partial\gamma_2} &= \frac{n_1}{\gamma_2{\gamma_1}^2}-\frac{1}{\gamma_2{\gamma_1}^2}\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1}\left\{1+\frac{1}{\gamma_1}\log(\gamma_2 t_i)\right\} \\
&\quad-\frac{1}{\gamma_2{\gamma_1}^2}\sum_{I^*}(\gamma_2 t_i)^{1/\gamma_1}A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})\left\{1+\frac{1}{\gamma_1}\log(\gamma_2 t_i)-\frac{1}{\gamma_1}G_{Pi}(\boldsymbol{\gamma})\right\}.
\end{aligned}
$$

The above are defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where $A_{Wi}(\boldsymbol{\beta},\boldsymbol{\gamma})$, $G_{Pi}(\boldsymbol{\gamma})$ and $B_{Pi}(\boldsymbol{\beta},\boldsymbol{\gamma})$ are as defined in (5.2.2), (5.3.3) and (C.1.1), respectively.

Geometric cure rate model: The observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial\beta_l\partial\beta_{l'}} &= 2\sum_{I_1} x_{il}x_{il'}\frac{C_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2} + \sum_{I_0} x_{il}x_{il'}\frac{C_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}\\
&\quad + \sum_{I_0} x_{il}x_{il'}w_i\frac{C_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2}\left\{1+\frac{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\},\\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma_1} &= -\frac{2}{{\gamma_1}^2}\sum_{I_1} x_{il}\frac{G_{Gi}(\boldsymbol{\gamma})\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2} - \frac{1}{{\gamma_1}^2}\sum_{I_0} x_{il}w_iG_{Gi}(\boldsymbol{\gamma})\\
&\quad + \frac{1}{{\gamma_1}^2}\sum_{I_0} x_{il}w_i\frac{G_{Gi}(\boldsymbol{\gamma})\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2}\Bigg[\{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})\}\{1-\exp(-(\gamma_2t_i)^{1/\gamma_1})\}\\
&\quad - \exp(-(\gamma_2t_i)^{1/\gamma_1})\Bigg],\\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma_2} &= \frac{2}{\gamma_1\gamma_2}\sum_{I_1} x_{il}\frac{(\gamma_2t_i)^{1/\gamma_1}\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2}\\
&\quad + \frac{1}{\gamma_1\gamma_2}\sum_{I_0} x_{il}w_i(\gamma_2t_i)^{1/\gamma_1} + \frac{1}{\gamma_1\gamma_2}\sum_{I_0} x_{il}w_i\frac{(\gamma_2t_i)^{1/\gamma_1}\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2}\\
&\quad \times\Bigg[\exp(-(\gamma_2t_i)^{1/\gamma_1}) - \{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})\}\{1-\exp(-(\gamma_2t_i)^{1/\gamma_1})\}\Bigg],\\
-\frac{\partial^2 l}{\partial\gamma_1^2} &= -\frac{n_1}{{\gamma_1}^2} - \frac{2n_1}{{\gamma_1}^3}\log\gamma_2 - \frac{2}{{\gamma_1}^3}\sum_{I_1}\log t_i + \frac{1}{{\gamma_1}^4}\sum_{I_1} G_{Gi}(\boldsymbol{\gamma})\{\log(\gamma_2t_i)+2\gamma_1\}\\
&\quad - \frac{2}{{\gamma_1}^4}\sum_{I_1}\frac{G_{Gi}(\boldsymbol{\gamma})\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2}\Bigg[G_{Gi}(\boldsymbol{\gamma})(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\\
&\quad - \{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})\}\{\log(\gamma_2t_i)+2\gamma_1\}\Bigg] - \frac{1}{{\gamma_1}^4}\sum_{I_0} w_iG_{Gi}(\boldsymbol{\gamma})\\
&\quad \times\{G_{Gi}(\boldsymbol{\gamma}) - \log(\gamma_2t_i) - 2\gamma_1\} - \frac{1}{{\gamma_1}^4}\sum_{I_0} w_i\frac{G_{Gi}(\boldsymbol{\gamma})\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2}\\
&\quad \times\Bigg[\log(\gamma_2t_i)\{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})\}\{2(\gamma_2t_i)^{1/\gamma_1}-1\} - \{2\gamma_1(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))\\
&\quad - G_{Gi}(\boldsymbol{\gamma})\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))\}\Bigg],
\end{aligned}
$$

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \gamma_2^2} &= \frac{n_1}{\gamma_1{\gamma_2}^2} + \frac{1}{\gamma_1{\gamma_2}^2}\left(\frac{1}{\gamma_1}-1\right)\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1} \\
&\quad + \frac{2}{\gamma_1{\gamma_2}^2}\sum_{I_1}\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2}\left[\left(\frac{1}{\gamma_1}-1\right)\left\{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right\}\right. \\
&\quad \left. -\frac{1}{\gamma_1}(\gamma_2 t_i)^{1/\gamma_1}(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\right] + \frac{1}{\gamma_1{\gamma_2}^2}\sum_{I_0} w_i(\gamma_2 t_i)^{1/\gamma_1} \\
&\quad \times\left\{\frac{1}{\gamma_1}-1-\frac{1}{\gamma_1}(\gamma_2 t_i)^{1/\gamma_1}\right\} + \frac{1}{\gamma_1{\gamma_2}^2}\sum_{I_0} w_i\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2} \\
&\quad \times\left[\left\{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right\}\left\{\frac{1}{\gamma_1}-1-\frac{1}{\gamma_1}(\gamma_2 t_i)^{1/\gamma_1}\right\}\right. \\
&\quad \left. -\frac{1}{\gamma_1}(\gamma_2 t_i)^{1/\gamma_1}(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\right], \\
-\frac{\partial^2 l}{\partial \gamma_1 \partial \gamma_2} &= \frac{n_1}{\gamma_2{\gamma_1}^2} - \frac{1}{\gamma_2{\gamma_1}^2}\sum_{I_1}(\gamma_2 t_i)^{1/\gamma_1}\left\{1+\frac{1}{\gamma_1}\log(\gamma_2 t_i)\right\} \\
&\quad - \frac{2}{\gamma_2{\gamma_1}^2}\sum_{I_1}\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2}\left[\left\{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right\}\left\{1+\frac{1}{\gamma_1}\log(\gamma_2 t_i)\right\}\right. \\
&\quad \left. -\frac{1}{\gamma_1}G_{Gi}(\boldsymbol{\gamma})(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\right] - \frac{1}{\gamma_2{\gamma_1}^2}\sum_{I_0} w_i(\gamma_2 t_i)^{1/\gamma_1} \\
&\quad \times\left\{1+\frac{1}{\gamma_1}\log(\gamma_2 t_i)(1-(\gamma_2 t_i)^{1/\gamma_1})\right\} \\
&\quad - \frac{1}{\gamma_2{\gamma_1}^2}\sum_{I_0} w_i\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{(1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma}))^2}\left[\left\{1+C_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right\}\right. \\
&\quad \left. \times\left\{1+\frac{1}{\gamma_1}\log(\gamma_2 t_i)-\frac{1}{\gamma_1}G_{Gi}(\boldsymbol{\gamma})\right\} - \frac{1}{\gamma_1}G_{Gi}(\boldsymbol{\gamma})(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\right].
\end{aligned}
$$

The above are defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where $C_i(\boldsymbol{\beta},\boldsymbol{\gamma})$ and $B_{Gi}(\boldsymbol{\beta},\boldsymbol{\gamma})$ are as defined in (5.2.4), and w_i and $G_{Gi}(\boldsymbol{\gamma})$ are as defined in (5.3.4) and (5.3.5), respectively.

COM-Poisson cure rate model: For a fixed value of ϕ, the observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial\beta_l\partial\beta_{l'}} &= -\sum_{I_1} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(z_{2i}z_{01i})^2}\bigg[z_{2i}\{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})z_{22i}+z_{01i}z_{21i}\} \\
&\quad -\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})z_{21i}\bigg\{\frac{z_{2i}z_{02i}}{z_{01i}}+z_{21i}\bigg\}\bigg] - \sum_{I_0} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{((1+z_{1i})z_{01i})^2} \\
&\quad \times\bigg[(1+z_{1i})z_{01i}\bigg\{\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})z_{21i}}{z_{01i}}+z_{2i}\bigg\} - \exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})z_{2i} \\
&\quad \times\bigg\{\frac{(1+z_{1i})z_{02i}}{z_{01i}}+z_{2i}\bigg\}\bigg] + \sum_{I^*} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))^2}, \\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma_1} &= -\frac{1}{\gamma_1^2}\sum_{I_1} x_{il}\frac{G_{Ci}(\boldsymbol{\gamma})\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{z_{01i}z_{2i}^2}\bigg\{z_{2i}z_{22i}-z_{21i}^2\bigg\} \\
&\quad -\frac{1}{\gamma_1^2}\sum_{I_0} x_{il}\frac{G_{Ci}(\boldsymbol{\gamma})\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(1+z_{1i})^2 z_{01i}}\bigg\{(1+z_{1i})z_{21i}-z_{2i}^2\bigg\}, \\
-\frac{\partial^2 l}{\partial\beta_l\partial\gamma_2} &= \frac{1}{\gamma_1\gamma_2}\sum_{I_1} x_{il}\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{z_{01i}z_{2i}^2}\bigg\{z_{2i}z_{22i}-z_{21i}^2\bigg\} \\
&\quad +\frac{1}{\gamma_1\gamma_2}\sum_{I_0} x_{il}\frac{(\gamma_2 t_i)^{1/\gamma_1}\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(1+z_{1i})^2 z_{01i}}\bigg\{(1+z_{1i})z_{21i}-z_{2i}^2\bigg\}, \\
-\frac{\partial^2 l}{\partial\gamma_1^2} &= -\frac{n_1}{{\gamma_1}^2} - \frac{2n_1}{{\gamma_1}^3}\log\gamma_2 - \frac{2}{{\gamma_1}^3}\sum_{I_1}\log t_i - \frac{1}{\gamma_1^4}\sum_{I_1}\frac{G_{Ci}(\boldsymbol{\gamma})}{z_{2i}^2} \\
&\quad \times\bigg[\log(\gamma_2 t_i)z_{2i}\{(\gamma_2 t_i)^{1/\gamma_1}z_{22i}-z_{21i}\} - z_{21i}\{G_{Ci}(\boldsymbol{\gamma})z_{21i}+2\gamma_1 z_{2i}\}\bigg] \\
&\quad -\frac{1}{\gamma_1^4}\sum_{I_0}\frac{G_{Ci}(\boldsymbol{\gamma})}{(1+z_{1i})^2}\bigg[\log(\gamma_2 t_i)(1+z_{1i})\{(\gamma_2 t_i)^{1/\gamma_1}z_{21i}-z_{2i}\} \\
&\quad -z_{2i}\{G_{Ci}(\boldsymbol{\gamma})z_{2i}+2\gamma_1(1+z_{1i})\}\bigg],
\end{aligned}
$$

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \gamma_2^2} \quad &= \quad \frac{n_1}{\gamma_1 {\gamma_2}^2} - \frac{1}{\gamma_1 {\gamma_2}^2} \sum_{I_1} \frac{(\gamma_2 t_i)^{1/\gamma_1}}{z_{2i}^2} \left[z_{2i} \left\{ \frac{1}{\gamma_1} (\gamma_2 t_i)^{1/\gamma_1} z_{22i} - \left(\frac{1}{\gamma_1} - 1 \right) z_{21i} \right\} \right. \\
&\quad \left. - \frac{1}{\gamma_1} (\gamma_2 t_i)^{1/\gamma_1} z_{21i}^2 \right] + \frac{1}{\gamma_1 {\gamma_2}^2} \sum_{I_0} \frac{(\gamma_2 t_i)^{1/\gamma_1}}{(1 + z_{1i})^2} \left[\frac{1}{\gamma_1} (\gamma_2 t_i)^{1/\gamma_1} z_{2i}^2 + (1 + z_{1i}) \right. \\
&\quad \left. \times \left\{ \left(\frac{1}{\gamma_1} - 1 \right) z_{2i} - \frac{1}{\gamma_1} (\gamma_2 t_i)^{1/\gamma_1} z_{21i} \right\} \right], \\
-\frac{\partial^2 l}{\partial \gamma_1 \partial \gamma_2} \quad &= \quad \frac{n_1}{\gamma_2 {\gamma_1}^2} + \frac{1}{\gamma_2 {\gamma_1}^2} \sum_{I_1} \frac{(\gamma_2 t_i)^{1/\gamma_1}}{z_{2i}^2} \left[z_{2i} \left\{ \frac{1}{\gamma_1} G_{Ci}(\boldsymbol{\gamma}) z_{22i} - z_{21i} - \frac{1}{\gamma_1} \log(\gamma_2 t_i) z_{21i} \right\} \right. \\
&\quad \left. - \frac{1}{\gamma_1} G_{Ci}(\boldsymbol{\gamma}) z_{21i}^2 \right] - \frac{1}{\gamma_2 {\gamma_1}^2} \sum_{I_0} \frac{(\gamma_2 t_i)^{1/\gamma_1}}{(1 + z_{1i})^2} \left[(1 + z_{1i}) \left\{ z_{2i} + \frac{1}{\gamma_1} \log(\gamma_2 t_i) z_{2i} \right. \right. \\
&\quad \left. \left. - \frac{1}{\gamma_1} G_{Ci}(\boldsymbol{\gamma}) z_{21i} \right\} + \frac{1}{\gamma_1} G_{Ci}(\boldsymbol{\gamma}) z_{2i}^2 \right].
\end{aligned}
$$

The above are defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where $G_{Ci}(\boldsymbol{\gamma})$ is as defined in (5.3.6).

Appendix D

Corresponding to Chapter 6

D.1 First- and second-order derivatives of the Q-function

Bernoulli cure rate model: The expressions of the first- and second-order derivatives of the $Q_1(\boldsymbol{\beta}, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ are as follows:

$$
\begin{aligned}
\frac{\partial Q_1}{\partial \beta_l} &= \sum_{I_1} x_{il} + \sum_{I_0} \pi_i^{(k)} x_{il} - \sum_{I^*} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}, \\
\frac{\partial^2 Q_1}{\partial \beta_l \partial \beta_{l'}} &= -\sum_{I^*} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2},
\end{aligned}
$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$. The required first- and second-order derivatives of the $Q_2(\boldsymbol{\gamma}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\gamma}^*$, for a fixed value of q, are as follows:

$$\begin{aligned}
\frac{\partial Q_2}{\partial \sigma} &= -\frac{n_1}{\sigma}\left\{1+\frac{\log\lambda}{q\sigma}\right\}+\frac{1}{q\sigma^2}\sum_{I_1}\{(\lambda t_i)^{q/\sigma}\log(\lambda t_i)-\log t_i\} \\
&\quad +\sum_{I_0}\pi_i^{(k)}\frac{\partial}{\partial\sigma}\log(S(t_i;\boldsymbol{\gamma})), \\
\frac{\partial Q_2}{\partial \lambda} &= \frac{n_1}{q\sigma\lambda}-\frac{1}{q\sigma\lambda}\sum_{I_1}(\lambda t_i)^{q/\sigma}+\sum_{I_0}\pi_i^{(k)}\frac{\partial}{\partial\lambda}\log(S(t_i;\boldsymbol{\gamma})), \\
\frac{\partial^2 Q_2}{\partial \sigma^2} &= \frac{n_1}{\sigma^2}\left\{1+\frac{2\log\lambda}{q\sigma}\right\}+\frac{2}{q\sigma^3}\sum_{I_1}\log t_i-\frac{1}{\sigma^3}\sum_{I_1}(\lambda t_i)^{q/\sigma}\log(\lambda t_i)\left\{\frac{2}{q}+\frac{\log(\lambda t_i)}{\sigma}\right\} \\
&\quad +\sum_{I_0}\pi_i^{(k)}\frac{\partial^2}{\partial\sigma^2}\log(S(t_i;\boldsymbol{\gamma})), \\
\frac{\partial^2 Q_2}{\partial \lambda^2} &= -\frac{n_1}{q\sigma\lambda^2}-\left(\frac{1}{\sigma}-\frac{1}{q}\right)\frac{1}{\sigma\lambda^2}\sum_{I_1}(\lambda t_i)^{q/\sigma}+\sum_{I_0}\pi_i^{(k)}\frac{\partial^2}{\partial\lambda^2}\log(S(t_i;\boldsymbol{\gamma})), \\
\frac{\partial^2 Q_2}{\partial \sigma\partial\lambda} &= -\frac{n_1}{q\sigma^2\lambda}+\frac{1}{q\sigma^2\lambda}\sum_{I_1}(\lambda t_i)^{q/\sigma}\left\{1+\frac{q}{\sigma}\log(\lambda t_i)\right\}+\sum_{I_0}\pi_i^{(k)}\frac{\partial^2}{\partial\sigma\partial\lambda}\log(S(t_i;\boldsymbol{\gamma})),
\end{aligned}$$

where $\pi_i^{(k)}$ is as defined in (6.2.1).

Poisson cure rate model: The required first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*,\boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}^*$, for a fixed value of q, are as follows:

$$\begin{aligned}
\frac{\partial Q}{\partial \beta_l} &= \sum_{I_1}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})S(t_i;\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}+\sum_{I_1}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))} \\
&\quad +\sum_{I_0}\pi_i^{(k)}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})P_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})S(t_i;\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}-\sum_{I^*}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}, \\
\frac{\partial Q}{\partial \sigma} &= -\frac{n_1}{\sigma}\left\{1+\frac{\log\lambda}{q\sigma}\right\}+\frac{1}{q\sigma^2}\sum_{I_1}\{(\lambda t_i)^{q/\sigma}\log(\lambda t_i)-\log t_i\} \\
&\quad +\sum_{I_1}\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma})+\sum_{I_0}\pi_i^{(k)}\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})) \\
&\quad \times P_{GGi}(\boldsymbol{\beta};\boldsymbol{\gamma})\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma}),
\end{aligned}$$

$$\begin{aligned}
\frac{\partial Q}{\partial \lambda} &= \frac{n_1}{q\sigma\lambda} - \frac{1}{q\sigma\lambda}\sum_{I_1}(\lambda t_i)^{q/\sigma} + \sum_{I_1}\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma}) \\
&\quad + \sum_{I_0}\pi_i^{(k)}\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))P_{GGi}(\boldsymbol{\beta};\boldsymbol{\gamma})\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma}), \\
\frac{\partial^2 Q}{\partial\beta_l\partial\beta_{l'}} &= \sum_{I_1} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))^2}\left\{\frac{\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})))^2}+S(t_i;\boldsymbol{\gamma})\right\} \\
&\quad + \sum_{I_0}\pi_i^{(k)}x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})S(t_i;\boldsymbol{\gamma})P_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})}{(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))^2} \\
&\quad \times\left\{1-\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})S(t_i;\boldsymbol{\gamma})(P_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})-1)\right\} - \sum_{I^*}x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))^2}, \\
\frac{\partial^2 Q}{\partial\beta_l\partial\sigma} &= \sum_{I_1}x_{il}\left\{\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}\right\}\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma}) + \sum_{I_0}\pi_i^{(k)}x_{il}\left\{\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})P_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}\right\} \\
&\quad \times\left\{1-A_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})(P_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})-1)\right\}\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma}), \\
\frac{\partial^2 Q}{\partial\beta_l\partial\lambda} &= \sum_{I_1}x_{il}\left\{\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}\right\}\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma}) + \sum_{I_0}\pi_i^{(k)}x_{il}\left\{\frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})P_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}\right\} \\
&\quad \times\left\{1-A_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})(P_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})-1)\right\}\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma}), \\
\frac{\partial^2 Q}{\partial\sigma^2} &= \frac{n_1}{\sigma^2}\left\{1+\frac{2\log\lambda}{q\sigma}\right\} + \frac{2}{q\sigma^3}\sum_{I_1}\log t_i - \frac{1}{\sigma^3}\sum_{I_1}(\lambda t_i)^{q/\sigma}\log(\lambda t_i) \\
&\quad \times\left\{\frac{2}{q}+\frac{\log(\lambda t_i)}{\sigma}\right\} + \sum_{I_1}\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\frac{\partial^2}{\partial\sigma^2}S(t_i;\boldsymbol{\gamma}) \\
&\quad + \sum_{I_0}\pi_i^{(k)}\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\Bigg[P_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\sigma^2}S(t_i;\boldsymbol{\gamma}) \\
&\quad + \frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\sigma}P_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})\Bigg], \\
\frac{\partial^2 Q}{\partial\lambda^2} &= -\frac{n_1}{q\sigma\lambda^2} - \left(\frac{1}{\sigma}-\frac{1}{q}\right)\frac{1}{\sigma\lambda^2}\sum_{I_1}(\lambda t_i)^{q/\sigma} + \sum_{I_1}\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})) \\
&\quad \times\frac{\partial^2}{\partial\lambda^2}S(t_i;\boldsymbol{\gamma}) + \sum_{I_0}\pi_i^{(k)}\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))\Bigg[P_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\lambda^2}S(t_i;\boldsymbol{\gamma}) \\
&\quad + \frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\lambda}P_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})\Bigg],
\end{aligned}$$

$$\begin{aligned}\frac{\partial^2 Q}{\partial\sigma\partial\lambda} &= -\frac{n_1}{q\sigma^2\lambda}+\frac{1}{q\sigma^2\lambda}\sum_{I_1}(\lambda t_i)^{q/\sigma}\left\{1+\frac{q}{\sigma}\log(\lambda t_i)\right\}+\sum_{I_1}\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\\ &\quad\times\frac{\partial^2}{\partial\sigma\partial\lambda}S(t_i;\boldsymbol{\gamma})+\sum_{I_0}\pi_i^{(k)}\log(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))\Big[P_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\sigma\partial\lambda}S(t_i;\boldsymbol{\gamma})\\ &\quad+\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\lambda}P_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})\Big],\end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$P_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})=\frac{\exp(A_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma}))}{\exp(A_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma}))-1},$$

for $i \in I_0$, and $A_{GGi}(\boldsymbol{\beta},\boldsymbol{\gamma})$ and $\pi_i^{(k)}$ are as defined in (6.2.2) and (6.2.3), respectively.

Geometric cure rate model: The required first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}^*$, for a fixed value of q, are as follows:

$$\begin{aligned}\frac{\partial Q}{\partial\beta_l} &= \sum_{I_1}x_{il}\{1-2R_i(\boldsymbol{\beta},\boldsymbol{\gamma})(1-S(t_i;\boldsymbol{\gamma}))\}-\sum_{I_0}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\\ &\quad+\sum_{I_0}\pi_i^{(k)}x_{il}\{1-R_i(\boldsymbol{\beta},\boldsymbol{\gamma})(1-S(t_i;\boldsymbol{\gamma}))\},\\ \frac{\partial Q}{\partial\sigma} &= -\frac{n_1}{\sigma}\left\{1+\frac{\log\lambda}{q\sigma}\right\}+\frac{1}{q\sigma^2}\sum_{I_1}\{(\lambda t_i)^{q/\sigma}\log(\lambda t_i)-\log t_i\}\\ &\quad+2\sum_{I_1}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma})+\sum_{I_0}\pi_i^{(k)}\left[\frac{\partial}{\partial\sigma}\log(S(t_i;\boldsymbol{\gamma}))\right.\\ &\quad\left.+R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma})\right],\\ \frac{\partial Q}{\partial\lambda} &= \frac{n_1}{q\sigma\lambda}-\frac{1}{q\sigma\lambda}\sum_{I_1}(\lambda t_i)^{q/\sigma}+2\sum_{I_1}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma})\\ &\quad+\sum_{I_0}\pi_i^{(k)}\left[\frac{\partial}{\partial\lambda}\log(S(t_i;\boldsymbol{\gamma}))+R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma})\right],\end{aligned}$$

$$
\begin{aligned}
\frac{\partial^2 Q}{\partial \beta_l \partial \beta_{l'}} &= -2\sum_{I_1} x_{il}x_{il'}\frac{R_i(\boldsymbol{\beta},\boldsymbol{\gamma})(1-S(t_i;\boldsymbol{\gamma}))}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))} - \sum_{I_0} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2} \\
&\quad -\sum_{I_0}\pi_i^{(k)}x_{il}x_{il'}\frac{R_i(\boldsymbol{\beta},\boldsymbol{\gamma})(1-S(t_i;\boldsymbol{\gamma}))}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}, \\
\frac{\partial^2 Q}{\partial \beta_l \partial \sigma} &= 2\sum_{I_1} x_{il}\left\{\frac{R_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}\right\}\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma}) \\
&\quad +\sum_{I_0}\pi_i^{(k)}x_{il}\left\{\frac{R_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}\right\}\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma}), \\
\frac{\partial^2 Q}{\partial \beta_l \partial \lambda} &= 2\sum_{I_1} x_{il}\left\{\frac{R_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}\right\}\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma}) \\
&\quad +\sum_{I_0}\pi_i^{(k)}x_{il}\left\{\frac{R_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}\right\}\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma}), \\
\frac{\partial^2 Q}{\partial \sigma^2} &= \frac{n_1}{\sigma^2}\left\{1+\frac{2\log\lambda}{q\sigma}\right\} + \frac{2}{q\sigma^3}\sum_{I_1}\log t_i - \frac{1}{\sigma^3}\sum_{I_1}(\lambda t_i)^{q/\sigma}\log(\lambda t_i)\left\{\frac{2}{q}+\frac{\log(\lambda t_i)}{\sigma}\right\} \\
&\quad +2\sum_{I_1}\left[R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\sigma^2}S(t_i;\boldsymbol{\gamma}) + \frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\sigma}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right] \\
&\quad +\sum_{I_0}\pi_i^{(k)}\left[R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\sigma^2}S(t_i;\boldsymbol{\gamma}) + \frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\sigma}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right] \\
&\quad +\sum_{I_0}\pi_i^{(k)}\frac{\partial^2}{\partial\sigma^2}\log(S(t_i;\boldsymbol{\gamma})), \\
\frac{\partial^2 Q}{\partial \lambda^2} &= -\frac{n_1}{q\sigma\lambda^2} - \left(\frac{1}{\sigma}-\frac{1}{q}\right)\frac{1}{\sigma\lambda^2}\sum_{I_1}(\lambda t_i)^{q/\sigma} + 2\sum_{I_1}\left[R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\lambda^2}S(t_i;\boldsymbol{\gamma})\right. \\
&\quad \left.+\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\lambda}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right] + \sum_{I_0}\pi_i^{(k)}\left[R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\lambda^2}S(t_i;\boldsymbol{\gamma})\right. \\
&\quad \left.+\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\lambda}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right] + \sum_{I_0}\pi_i^{(k)}\frac{\partial^2}{\partial\lambda^2}\log(S(t_i;\boldsymbol{\gamma})),
\end{aligned}
$$

$$\begin{aligned}
\frac{\partial^2 Q}{\partial\sigma\partial\lambda} &= -\frac{n_1}{q\sigma^2\lambda}+\frac{1}{q\sigma^2\lambda}\sum_{I_1}(\lambda t_i)^{q/\sigma}\left\{1+\frac{q}{\sigma}\log(\lambda t_i)\right\}\\
&\quad +2\sum_{I_1}\left[R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\sigma\partial\lambda}S(t_i;\boldsymbol{\gamma})+\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\lambda}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right]\\
&\quad +\sum_{I_0}\pi_i^{(k)}\left[R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\sigma\partial\lambda}S(t_i;\boldsymbol{\gamma})+\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\lambda}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right]\\
&\quad +\sum_{I_0}\pi_i^{(k)}\frac{\partial^2}{\partial\sigma\partial\lambda}\log(S(t_i;\boldsymbol{\gamma})),
\end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where $\pi_i^{(k)}$ and $R_i(\boldsymbol{\beta},\boldsymbol{\gamma})$ are as defined in (6.2.4) and (6.3.3), respectively.

COM-Poisson cure rate model: The required first- and second-order derivatives of the $Q(\boldsymbol{\theta}^*, \boldsymbol{\pi}^{(k)})$ function with respect to $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}^*$, for fixed values of q and ϕ, are as follows:

$$\begin{aligned}
\frac{\partial Q}{\partial\beta_l} &= \sum_{I_1}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{21i}}{z_{2i}z_{01i}}+\sum_{I_0}\pi_i^{(k)}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{2i}}{z_{1i}z_{01i}}-\sum_{I^*}x_{il}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})},\\
\frac{\partial Q}{\partial\sigma} &= -\frac{n_1}{\sigma}\left\{1+\frac{\log\lambda}{q\sigma}\right\}+\frac{1}{q\sigma^2}\sum_{I_1}\{(\lambda t_i)^{q/\sigma}\log(\lambda t_i)-\log t_i\}\\
&\quad +\sum_{I_1}\left(\frac{z_{21i}}{z_{2i}}-1\right)\frac{\partial}{\partial\sigma}\log(S(t_i;\boldsymbol{\gamma}))+\sum_{I_0}\pi_i^{(k)}\frac{z_{2i}}{z_{1i}}\frac{\partial}{\partial\sigma}\log(S(t_i;\boldsymbol{\gamma})),\\
\frac{\partial Q}{\partial\lambda} &= \frac{n_1}{q\sigma\lambda}-\frac{1}{q\sigma\lambda}\sum_{I_1}(\lambda t_i)^{q/\sigma}+\sum_{I_1}\left(\frac{z_{21i}}{z_{2i}}-1\right)\frac{\partial}{\partial\lambda}\log(S(t_i;\boldsymbol{\gamma}))\\
&\quad +\sum_{I_0}\pi_i^{(k)}\frac{z_{2i}}{z_{1i}}\frac{\partial}{\partial\lambda}\log(S(t_i;\boldsymbol{\gamma})),
\end{aligned}$$

$$
\begin{aligned}
\frac{\partial^2 Q}{\partial\beta_l \partial\beta_{l'}} &= \sum_{I_1} x_{il}x_{il'} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(z_{2i}z_{01i})^2}\Bigg[\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})\Bigg\{z_{2i}z_{22i} - z_{21i}^2\Bigg\} + z_{2i}z_{21i}\Bigg\{z_{01i} \\
&\quad - \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})z_{02i}}{z_{01i}}\Bigg\}\Bigg] + \sum_{I_0} \pi_i^{(k)} x_{il}x_{il'} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(z_{1i}z_{01i})^2}\Bigg[\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})\Bigg\{z_{1i}z_{21i} - z_{2i}^2\Bigg\} \\
&\quad + z_{1i}z_{2i}\Bigg\{z_{01i} - \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})z_{02i}}{z_{01i}}\Bigg\}\Bigg] - \sum_{I^*} x_{il}x_{il'} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))^2}, \\
\frac{\partial^2 Q}{\partial\beta_l \partial\sigma} &= \sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{z_{01i}}\left\{\frac{z_{2i}z_{22i} - z_{21i}^2}{z_{2i}^2}\right\}\frac{\partial}{\partial\sigma}\log(S(t_i;\boldsymbol{\gamma})) \\
&\quad + \sum_{I_0} \pi_i^{(k)} x_{il} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{z_{01i}}\left\{\frac{z_{1i}z_{21i} - z_{2i}^2}{z_{1i}^2}\right\}\frac{\partial}{\partial\sigma}\log(S(t_i;\boldsymbol{\gamma})), \\
\frac{\partial^2 Q}{\partial\beta_l \partial\lambda} &= \sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{z_{01i}}\left\{\frac{z_{2i}z_{22i} - z_{21i}^2}{z_{2i}^2}\right\}\frac{\partial}{\partial\lambda}\log(S(t_i;\boldsymbol{\gamma})) \\
&\quad + \sum_{I_0} \pi_i^{(k)} x_{il} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{z_{01i}}\left\{\frac{z_{1i}z_{21i} - z_{2i}^2}{z_{1i}^2}\right\}\frac{\partial}{\partial\lambda}\log(S(t_i;\boldsymbol{\gamma})), \\
\frac{\partial^2 Q}{\partial\sigma^2} &= \frac{n_1}{\sigma^2}\left\{1 + \frac{2\log\lambda}{q\sigma}\right\} + \frac{2}{q\sigma^3}\sum_{I_1}\log t_i - \frac{1}{\sigma^3}\sum_{I_1}(\lambda t_i)^{q/\sigma}\log(\lambda t_i) \\
&\quad \times\left\{\frac{2}{q} + \frac{\log(\lambda t_i)}{\sigma}\right\} + \sum_{I_1}\Bigg[\left(\frac{z_{21i}}{z_{2i}} - 1\right)\frac{\partial^2}{\partial\sigma^2}\log(S(t_i;\boldsymbol{\gamma})) \\
&\quad + \left\{\frac{z_{2i}z_{22i} - z_{21i}^2}{z_{2i}^2}\right\}\left\{\frac{\partial}{\partial\sigma}\log(S(t_i;\boldsymbol{\gamma}))\right\}^2\Bigg] + \sum_{I_0}\pi_i^{(k)}\Bigg[\frac{z_{2i}}{z_{1i}}\frac{\partial^2}{\partial\sigma^2}\log(S(t_i;\boldsymbol{\gamma})) \\
&\quad + \left\{\frac{z_{1i}z_{21i} - z_{2i}^2}{z_{1i}^2}\right\}\left\{\frac{\partial}{\partial\sigma}\log(S(t_i;\boldsymbol{\gamma}))\right\}^2\Bigg],
\end{aligned}
$$

$$\begin{aligned}
\frac{\partial^2 Q}{\partial \lambda^2} &= -\frac{n_1}{q\sigma\lambda^2} - \left(\frac{1}{\sigma} - \frac{1}{q}\right)\frac{1}{\sigma\lambda^2}\sum_{I_1}(\lambda t_i)^{q/\sigma} + \sum_{I_1}\left[\left(\frac{z_{21i}}{z_{2i}} - 1\right)\frac{\partial^2}{\partial\lambda^2}\log(S(t_i;\boldsymbol{\gamma}))\right. \\
&\quad \left. + \left\{\frac{z_{2i}z_{22i} - z_{21i}^2}{z_{2i}^2}\right\}\left\{\frac{\partial}{\partial\lambda}\log(S(t_i;\boldsymbol{\gamma}))\right\}^2\right] + \sum_{I_0}\pi_i^{(k)}\left[\frac{z_{2i}}{z_{1i}}\frac{\partial^2}{\partial\lambda^2}\log(S(t_i;\boldsymbol{\gamma}))\right. \\
&\quad \left. + \left\{\frac{z_{1i}z_{21i} - z_{2i}^2}{z_{1i}^2}\right\}\left\{\frac{\partial}{\partial\lambda}\log(S(t_i;\boldsymbol{\gamma}))\right\}^2\right], \\
\frac{\partial^2 Q}{\partial\sigma\partial\lambda} &= -\frac{n_1}{q\sigma^2\lambda} + \frac{1}{q\sigma^2\lambda}\sum_{I_1}(\lambda t_i)^{q/\sigma}\left\{1 + \frac{q}{\sigma}\log(\lambda t_i)\right\} + \sum_{I_1}\left[\left(\frac{z_{21i}}{z_{2i}} - 1\right)\right. \\
&\quad \left. \times\frac{\partial^2}{\partial\sigma\partial\lambda}\log(S(t_i;\boldsymbol{\gamma})) + \left\{\frac{z_{2i}z_{22i} - z_{21i}^2}{z_{2i}^2}\right\}\frac{\partial}{\partial\sigma}\log(S(t_i;\boldsymbol{\gamma}))\frac{\partial}{\partial\lambda}\log(S(t_i;\boldsymbol{\gamma}))\right] \\
&\quad + \sum_{I_0}\pi_i^{(k)}\left[\frac{z_{2i}}{z_{1i}}\frac{\partial^2}{\partial\sigma\partial\lambda}\log(S(t_i;\boldsymbol{\gamma})) + \left\{\frac{z_{1i}z_{21i} - z_{2i}^2}{z_{1i}^2}\right\}\frac{\partial}{\partial\sigma}\log(S(t_i;\boldsymbol{\gamma}))\right. \\
&\quad \left. \times\frac{\partial}{\partial\lambda}\log(S(t_i;\boldsymbol{\gamma}))\right],
\end{aligned}$$

for $l, l' = 0, 1, \ldots, k$, and $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where

$$z_{22} = z_{22}(\boldsymbol{\theta}; \boldsymbol{x}, t) = \sum_{j=1}^{\infty}\frac{j^3\{H_\phi^{-1}(1 + \exp(\boldsymbol{x}'\boldsymbol{\beta}))S(t;\boldsymbol{\gamma})\}^j}{(j!)^\phi},$$

$$z_{02} = z_{02}(\boldsymbol{\theta}_1; \boldsymbol{x}) = \sum_{j=1}^{\infty}\frac{j^2\{H_\phi^{-1}(1 + \exp(\boldsymbol{x}'\boldsymbol{\beta}))\}^j}{(j!)^\phi},$$

and $\pi_i^{(k)}$ is as defined in (6.2.5). The quantities $z_{1i}, z_{2i}, z_{21i}, z_{22i}, z_{01i}$, and z_{02i} are all computed as described in Section 2.2.

D.2 Observed information matrix

Bernoulli cure rate model: The observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \beta_l \partial \beta_{l'}} &= -\sum_{I_0} x_{il} x_{il'} w_i (1-w_i) + \sum_{I^*} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i' \boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i' \boldsymbol{\beta}))^2}, \\
-\frac{\partial^2 l}{\partial \beta_l \partial \sigma} &= -\sum_{I_0} x_{il} \frac{\partial}{\partial \sigma} w_i, \\
-\frac{\partial^2 l}{\partial \beta_l \partial \lambda} &= -\sum_{I_0} x_{il} \frac{\partial}{\partial \lambda} w_i, \\
-\frac{\partial^2 l}{\partial \sigma^2} &= -\frac{n_1}{\sigma^2}\left\{1 + \frac{2\log\lambda}{q\sigma}\right\} - \frac{2}{q\sigma^3} \sum_{I_1} \log t_i + \frac{1}{\sigma^3} \sum_{I_1} (\lambda t_i)^{q/\sigma} \log(\lambda t_i) \\
&\quad \times \left\{\frac{2}{q} + \frac{\log(\lambda t_i)}{\sigma}\right\} - \sum_{I_0} \left\{ w_i \frac{\partial^2}{\partial \sigma^2} \log(S(t_i;\boldsymbol{\gamma})) + \frac{\partial}{\partial \sigma} \log(S(t_i;\boldsymbol{\gamma})) \frac{\partial}{\partial \sigma} w_i \right\}, \\
-\frac{\partial^2 l}{\partial \lambda^2} &= \frac{n_1}{q\sigma\lambda^2} + \left(\frac{1}{\sigma} - \frac{1}{q}\right) \frac{1}{\sigma\lambda^2} \sum_{I_1} (\lambda t_i)^{q/\sigma} - \sum_{I_0} \left\{ w_i \frac{\partial^2}{\partial \lambda^2} \log(S(t_i;\boldsymbol{\gamma})) \right. \\
&\quad \left. + \frac{\partial}{\partial \lambda} \log(S(t_i;\boldsymbol{\gamma})) \frac{\partial}{\partial \lambda} w_i \right\}, \\
-\frac{\partial^2 l}{\partial \sigma \partial \lambda} &= \frac{n_1}{q\sigma^2\lambda} - \frac{1}{q\sigma^2\lambda} \sum_{I_1} (\lambda t_i)^{q/\sigma} \left\{1 + \frac{q}{\sigma} \log(\lambda t_i)\right\} - \sum_{I_0} \left\{ w_i \frac{\partial^2}{\partial \sigma \partial \lambda} \log(S(t_i;\boldsymbol{\gamma})) \right. \\
&\quad \left. + \frac{\partial}{\partial \sigma} \log(S(t_i;\boldsymbol{\gamma})) \frac{\partial}{\partial \lambda} w_i \right\}.
\end{aligned}
$$

The above are defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where w_i is as defined in (6.3.1).

Poisson cure rate model: The observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \beta_l \partial \beta_{l'}} &= -\sum_{I_1} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))^2} \left\{ \frac{\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})) - \exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{(\log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})))^2} \right\} \\
&\quad - \sum_{I^*} x_{il} x_{il'} \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})\{S(t_i;\boldsymbol{\gamma}) - 1\}}{(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta}))^2}, \\
-\frac{\partial^2 l}{\partial \beta_l \partial \sigma} &= -\sum_{I^*} x_{il} \left\{ \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})} \right\} \frac{\partial}{\partial \sigma} S(t_i;\boldsymbol{\gamma}), \\
-\frac{\partial^2 l}{\partial \beta_l \partial \lambda} &= -\sum_{I^*} x_{il} \left\{ \frac{\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})} \right\} \frac{\partial}{\partial \lambda} S(t_i;\boldsymbol{\gamma}), \\
-\frac{\partial^2 l}{\partial \sigma^2} &= -\frac{n_1}{\sigma^2} \left\{ 1 + \frac{2\log\lambda}{q\sigma} \right\} - \frac{2}{q\sigma^3} \sum_{I_1} \log t_i + \frac{1}{\sigma^3} \sum_{I_1} (\lambda t_i)^{q/\sigma} \log(\lambda t_i) \\
&\quad \times \left\{ \frac{2}{q} + \frac{\log(\lambda t_i)}{\sigma} \right\} - \sum_{I^*} \log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})) \frac{\partial^2}{\partial \sigma^2} S(t_i;\boldsymbol{\gamma}), \\
-\frac{\partial^2 l}{\partial \lambda^2} &= \frac{n_1}{q\sigma\lambda^2} + \left(\frac{1}{\sigma} - \frac{1}{q} \right) \frac{1}{\sigma\lambda^2} \sum_{I_1} (\lambda t_i)^{q/\sigma} - \sum_{I^*} \log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})) \frac{\partial^2}{\partial \lambda^2} S(t_i;\boldsymbol{\gamma}), \\
-\frac{\partial^2 l}{\partial \sigma \partial \lambda} &= \frac{n_1}{q\sigma^2\lambda} - \frac{1}{q\sigma^2\lambda} \sum_{I_1} (\lambda t_i)^{q/\sigma} \left\{ 1 + \frac{q}{\sigma} \log(\lambda t_i) \right\} \\
&\quad - \sum_{I^*} \log(1+\exp(\boldsymbol{x}_i^{'}\boldsymbol{\beta})) \frac{\partial^2}{\partial \sigma \partial \lambda} S(t_i;\boldsymbol{\gamma}).
\end{aligned}
$$

The above are defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$.

Geometric cure rate model: The observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \beta_l \partial \beta_{l'}} &= 2\sum_{I_1} x_{il}x_{il'}\frac{R_i(\boldsymbol{\beta},\boldsymbol{\gamma})(1-S(t_i;\boldsymbol{\gamma}))}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))} + \sum_{I_0} x_{il}x_{il'} \\
&\quad \times \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2} + \sum_{I_0} x_{il}x_{il'}w_i R_i(\boldsymbol{\beta},\boldsymbol{\gamma})(1-S(t_i;\boldsymbol{\gamma})) \\
&\quad \times \left\{\frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))} + \frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}, \\
-\frac{\partial^2 l}{\partial \beta_l \partial \sigma} &= -2\sum_{I_1} x_{il}\left\{\frac{R_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}\right\}\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma}) - \sum_{I_0} x_{il} \\
&\quad \times \left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}\right\}\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma}) - \sum_{I_0} x_{il}w_i R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma}) \\
&\quad \times \left\{\frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))} + \frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}, \\
-\frac{\partial^2 l}{\partial \beta_l \partial \lambda} &= -2\sum_{I_1} x_{il}\left\{\frac{R_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))}\right\}\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma}) - \sum_{I_0} x_{il} \\
&\quad \times \left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2}\right\}\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma}) - \sum_{I_0} x_{il}w_i R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma}) \\
&\quad \times \left\{\frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})(1-S(t_i;\boldsymbol{\gamma}))} + \frac{1}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}, \\
-\frac{\partial^2 l}{\partial \sigma^2} &= -\frac{n_1}{\sigma^2}\left\{1+\frac{2\log\lambda}{q\sigma}\right\} - \frac{2}{q\sigma^3}\sum_{I_1}\log t_i + \frac{1}{\sigma^3}\sum_{I_1}(\lambda t_i)^{q/\sigma}\log(\lambda t_i) \\
&\quad \times \left\{\frac{2}{q}+\frac{\log(\lambda t_i)}{\sigma}\right\} - 2\sum_{I_1}\left\{R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\sigma^2}S(t_i;\boldsymbol{\gamma})\right. \\
&\quad \left. +\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\sigma}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right\} - \sum_{I_0}\left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}\frac{\partial^2}{\partial\sigma^2}S(t_i;\boldsymbol{\gamma}) \\
&\quad -\sum_{I_0}\left[w_i R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\sigma^2}S(t_i;\boldsymbol{\gamma}) + \frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma})\left\{w_i\frac{\partial}{\partial\sigma}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right.\right. \\
&\quad \left.\left. +\left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})R_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}\frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma})\right\}\right],
\end{aligned}
$$

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \lambda^2} &= \frac{n_1}{q\sigma\lambda^2} + \left(\frac{1}{\sigma} - \frac{1}{q}\right)\frac{1}{\sigma\lambda^2}\sum_{I_1}(\lambda t_i)^{q/\sigma} - 2\sum_{I_1}\left\{R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\lambda^2}S(t_i;\boldsymbol{\gamma})\right. \\
&\left. + \frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\lambda}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right\} - \sum_{I_0}\left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}\frac{\partial^2}{\partial\lambda^2}S(t_i;\boldsymbol{\gamma}) \\
&- \sum_{I_0}\left[w_i R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\lambda^2}S(t_i;\boldsymbol{\gamma}) + \frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma})\left\{w_i\frac{\partial}{\partial\lambda}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right.\right. \\
&\left.\left. + \left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})R_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma})\right\}\right], \\
-\frac{\partial^2 l}{\partial\sigma\partial\lambda} &= \frac{n_1}{q\sigma^2\lambda} - \frac{1}{q\sigma^2\lambda}\sum_{I_1}(\lambda t_i)^{q/\sigma}\left\{1 + \frac{q}{\sigma}\log(\lambda t_i)\right\} \\
&-2\sum_{I_1}\left\{R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\sigma\partial\lambda}S(t_i;\boldsymbol{\gamma}) + \frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma})\frac{\partial}{\partial\lambda}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right\} \\
&- \sum_{I_0}\left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}\frac{\partial^2}{\partial\sigma\partial\lambda}S(t_i;\boldsymbol{\gamma}) \\
&- \sum_{I_0}\left[w_i R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\frac{\partial^2}{\partial\sigma\partial\lambda}S(t_i;\boldsymbol{\gamma}) + \frac{\partial}{\partial\sigma}S(t_i;\boldsymbol{\gamma})\left\{w_i\frac{\partial}{\partial\lambda}R_i(\boldsymbol{\beta},\boldsymbol{\gamma})\right.\right. \\
&\left.\left. + \left\{\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})R_i(\boldsymbol{\beta},\boldsymbol{\gamma})}{1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}\right\}\frac{\partial}{\partial\lambda}S(t_i;\boldsymbol{\gamma})\right\}\right].
\end{aligned}
$$

The above are defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$, where w_i and $R_i(\boldsymbol{\beta},\boldsymbol{\gamma})$ are as defined in (6.3.2) and (6.3.3), respectively.

COM-Poisson cure rate model: The observed information matrix has its components as

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial\beta_l\partial\beta_{l'}} &= -\sum_{I_1} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(z_{01i}z_{2i})^2}\left[\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\left\{z_{2i}z_{22i} - z_{21i}^2\right\} + z_{2i}z_{21i}\right. \\
&\left.\times\left\{z_{01i} - \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{02i}}{z_{01i}}\right\}\right] - \sum_{I_0} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(z_{01i}(1+z_{1i}))^2}\left[\exp(\boldsymbol{x}_i'\boldsymbol{\beta})\right. \\
&\left.\times\left\{z_{21i}(1+z_{1i}) - z_{2i}^2\right\} + z_{2i}(1+z_{1i})\left\{z_{01i} - \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})z_{02i}}{z_{01i}}\right\}\right] \\
&+ \sum_{I^*} x_{il}x_{il'}\frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{(1+\exp(\boldsymbol{x}_i'\boldsymbol{\beta}))^2},
\end{aligned}
$$

$$
\begin{aligned}
-\frac{\partial^2 l}{\partial \beta_l \partial \sigma} &= -\sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{z_{01i}} \left\{ \frac{z_{2i} z_{22i} - z_{21i}^2}{z_{2i}^2} \right\} \frac{\partial}{\partial \sigma} \log(S(t_i;\boldsymbol{\gamma})) \\
&\quad - \sum_{I_0} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{z_{01i}} \left\{ \frac{z_{21i}(1+z_{1i}) - z_{2i}^2}{(1+z_{1i})^2} \right\} \frac{\partial}{\partial \sigma} \log(S(t_i;\boldsymbol{\gamma})), \\
-\frac{\partial^2 l}{\partial \beta_l \partial \lambda} &= -\sum_{I_1} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{z_{01i}} \left\{ \frac{z_{2i} z_{22i} - z_{21i}^2}{z_{2i}^2} \right\} \frac{\partial}{\partial \lambda} \log(S(t_i;\boldsymbol{\gamma})) \\
&\quad - \sum_{I_0} x_{il} \frac{\exp(\boldsymbol{x}_i'\boldsymbol{\beta})}{z_{01i}} \left\{ \frac{z_{21i}(1+z_{1i}) - z_{2i}^2}{(1+z_{1i})^2} \right\} \frac{\partial}{\partial \lambda} \log(S(t_i;\boldsymbol{\gamma})), \\
-\frac{\partial^2 l}{\partial \sigma^2} &= -\frac{n_1}{\sigma^2} \left\{ 1 + \frac{2\log\lambda}{q\sigma} \right\} - \frac{2}{q\sigma^3} \sum_{I_1} \log t_i + \frac{1}{\sigma^3} \sum_{I_1} (\lambda t_i)^{q/\sigma} \log(\lambda t_i) \\
&\quad \times \left\{ \frac{2}{q} + \frac{\log(\lambda t_i)}{\sigma} \right\} - \sum_{I_1} \left[\left\{ \frac{z_{21i}}{z_{2i}} - 1 \right\} \frac{\partial^2}{\partial \sigma^2} \log(S(t_i;\boldsymbol{\gamma})) + \left\{ \frac{z_{2i} z_{22i} - z_{21i}^2}{z_{2i}^2} \right\} \right. \\
&\quad \left. \times \left\{ \frac{\partial}{\partial \sigma} \log(S(t_i;\boldsymbol{\gamma})) \right\}^2 \right] - \sum_{I_0} \left[\left\{ \frac{z_{2i}}{1+z_{1i}} \right\} \frac{\partial^2}{\partial \sigma^2} \log(S(t_i;\boldsymbol{\gamma})) \right. \\
&\quad \left. + \left\{ \frac{z_{21i}(1+z_{1i}) - z_{2i}^2}{(1+z_{1i})^2} \right\} \left\{ \frac{\partial}{\partial \sigma} \log(S(t_i;\boldsymbol{\gamma})) \right\}^2 \right], \\
-\frac{\partial^2 l}{\partial \lambda^2} &= \frac{n_1}{q\sigma\lambda^2} + \left(\frac{1}{\sigma} - \frac{1}{q} \right) \frac{1}{\sigma\lambda^2} \sum_{I_1} (\lambda t_i)^{q/\sigma} - \sum_{I_1} \left[\left\{ \frac{z_{21i}}{z_{2i}} - 1 \right\} \frac{\partial^2}{\partial \lambda^2} \log(S(t_i;\boldsymbol{\gamma})) \right. \\
&\quad \left. + \left\{ \frac{z_{2i} z_{22i} - z_{21i}^2}{z_{2i}^2} \right\} \left\{ \frac{\partial}{\partial \lambda} \log(S(t_i;\boldsymbol{\gamma})) \right\}^2 \right] - \sum_{I_0} \left[\left\{ \frac{z_{2i}}{1+z_{1i}} \right\} \frac{\partial^2}{\partial \lambda^2} \log(S(t_i;\boldsymbol{\gamma})) \right. \\
&\quad \left. + \left\{ \frac{z_{21i}(1+z_{1i}) - z_{2i}^2}{(1+z_{1i})^2} \right\} \left\{ \frac{\partial}{\partial \lambda} \log(S(t_i;\boldsymbol{\gamma})) \right\}^2 \right], \\
-\frac{\partial^2 l}{\partial \sigma \partial \lambda} &= \frac{n_1}{q\sigma^2\lambda} - \frac{1}{q\sigma^2\lambda} \sum_{I_1} (\lambda t_i)^{q/\sigma} \left\{ 1 + \frac{q}{\sigma} \log(\lambda t_i) \right\} - \sum_{I_1} \left[\left\{ \frac{z_{21i}}{z_{2i}} - 1 \right\} \right. \\
&\quad \left. \times \frac{\partial^2}{\partial \sigma \partial \lambda} \log(S(t_i;\boldsymbol{\gamma})) + \left\{ \frac{z_{2i} z_{22i} - z_{21i}^2}{z_{2i}^2} \right\} \frac{\partial}{\partial \sigma} \log(S(t_i;\boldsymbol{\gamma})) \frac{\partial}{\partial \lambda} \log(S(t_i;\boldsymbol{\gamma})) \right] \\
&\quad - \sum_{I_0} \left[\left\{ \frac{z_{2i}}{1+z_{1i}} \right\} \frac{\partial^2}{\partial \sigma \partial \lambda} \log(S(t_i;\boldsymbol{\gamma})) + \left\{ \frac{z_{21i}(1+z_{1i}) - z_{2i}^2}{(1+z_{1i})^2} \right\} \right. \\
&\quad \left. \times \frac{\partial}{\partial \sigma} \log(S(t_i;\boldsymbol{\gamma})) \frac{\partial}{\partial \lambda} \log(S(t_i;\boldsymbol{\gamma})) \right].
\end{aligned}
$$

The above are defined for $l, l' = 0, 1, \ldots, k$, $x_{i0} = 1 \forall i = 1, 2, \ldots, n$.

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