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Buckley-James-type Estimator with Right-censored and Length-biased Data

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Summary

We present a natural generalization of the Buckley-James-type estimator for traditional survival data to right-censored length-biased data under the accelerated failure time model. Length-biased data are often encountered in prevalent cohort studies and cancer screening trials. Informative right censoring induced by length-biased sampling creates additional challenges in modeling the effects of risk factors on the unbiased failure times for the target population. In this paper, we evaluate covariate effects on the failure times of the target population under the accelerated failure time model given the observed length-biased data. We construct a Buckley-James-type estimating equation, develop an iterative computing algorithm, and establish the asymptotic properties of the estimators. We assess the finite-sample properties of the proposed estimators against the estimators obtained from the existing methods. Data from a prevalent cohort study of patients with dementia are used to illustrate the proposed methodology.

Keywords

Accelerated failure time model; Buckley-James estimator; Estimating equation; Length-biased sampling; Prevalent cohort

1. Introduction

When studying the natural history of cancer, a prevalent sampling design that draws samples from individuals with a condition or disease (e.g. diagnosed with breast cancer) at the time of enrollment is generally more efficient and practical than an incident sampling design. The individuals are then followed over time to monitor endpoints such as disease progression or death. Under this design, individuals with shorter survival times are selectively excluded, while those with longer survival times are more likely to be included in the follow-up cohort. Length-biased data arise when the probability of a subject being selected from the target population is proportional to the time from the initiation event to the failure event (Zelen and Feinleib, 1969; Vardi, 1989; Zelen, 2004). These data are often encountered in

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7. Supplementary Materials

Web Appendices referenced in Section 6 and in the Appendix are available under the Paper Information link at the Biometrics website <http://www.biometrics.tibs.org>.

epidemiologic studies, cancer screening trials, and marketing and economics studies (Nowell and Stanley, 1991; De Una-Alvarez et al., 2003).

In the Canadian Study of Health and Aging (CSHA), about ten thousand individuals age 65 and over were screened for dementia, and then were followed for their time to death. Length-biased sampling occurred here because the “observed” time intervals from the onset of dementia to death tended to be longer among those individuals in the study cohort identified to have dementia than among the general population. This occurred because individuals who had not survived to the examination time for the CSHA were excluded from the study. It is well known that statistical inference depends on the sampling scheme in which the data are obtained. An approach ignoring biased sampling could result in an overall underestimation of the deleterious effect of dementia on life expectancy and, in the presence of right censoring, lead to a biased inference of covariate effects on the failure times.

There is substantial literature on the analysis of length-biased data with diverse applications; however, a considerable methodological gap still exists. Prior work has mainly focused on nonparametric estimation for the population distribution (Wang et al., 1986; Turnbull, 1976; Lagakos et al., 1988; Tsai et al., 1987; Wang, 1991; Wang et al., 1993; Vardi, 1982, 1989; Gill et al., 1988; Asgharian et al., 2002; Asgharian and Wolfson, 2005). A limited amount of work has considered regression analysis for modeling the association between risk factors and population failure times, which is of practical interest in many applications. One prominent challenge in modeling right-censored length-biased failure times is the potential dependence between the failure times and the right censoring times, measured from the initiating event (e.g., onset of disease) to the failure event (e.g., death). Such informative censoring induced by the sampling scheme has often been avoided by prohibiting right censoring (Vardi, 1982, 1985; Wang, 1996) or by ignoring it. Another challenge is that the regression model structure assumed for the target population data is often changed for the observed length-biased data.

As an important alternative to Cox’s proportional hazards model, the accelerated failure time (AFT) model has been used for traditional survival data under independent right censoring. The AFT model has appealed to investigators because the logarithm of the failure time can be linearly related to the covariates of interest so that the interpretation of coefficients is straightforward. Large sample properties and methods of inference have been extensively investigated over the last twenty years for traditional survival data (Prentice, 1978; Buckley and James, 1979; Miller and Halpern, 1982; Ritov, 1990; Tsiatis, 1990; Lai and Ying, 1991a; Ying, 1993; Lin and Ying, 1995; Jin et al., 2003). However, little of this work has explicitly considered right-censored length-biased data. Lai and Ying (1991b) proposed a rank-based estimating equation to estimate regression coefficients for left-truncated and right-censored data under the AFT model. Lai and Ying (1994) and Gross and Lai (1996) considered M-estimators for regression analysis in the presence of left truncation and right censoring. These estimating methods, originally proposed for general left-truncated data, do not incorporate any truncation information and are consequently less efficient for length-biased data. More recently, Shen et al. (2009) proposed estimating equation approaches to estimate regression parameters under the transformation model as well as the AFT model. Although the closed form of the solution from the inverse weighted estimating equation under the AFT model is easy to calculate, there are also limitations. First, one has to either assume that the censoring distribution is independent of covariates or explicitly model and fit the covariate dependence of the censoring variable. Second, the proposed estimating equation approach may not be efficient, because the information from the covariates for censored individuals is not adequately utilized in the estimating equation. When length-biased failure times are not subject to right censoring, Chen (2010) and Mandel and Ritov (2010) proved the invariant property of the covariate effects in the AFT model under length-

biased sampling and provided the estimating methods. When length-biased failure times are subject to right censoring, the invariant property does not hold in general and the aforementioned methods cannot be easily extended to accommodate the dependent censoring.

In this paper, we propose a Buckley-James-type estimator for the regression coefficients under the AFT model in order to study the covariate effects on failure times in the target population given the observed length-biased data. The remainder of our paper is organized as follows. In Section 2, we introduce the notation and the model. In Section 3, we construct a Buckley-James-type estimating equation and develop an iterative algorithm to obtain the root of the estimating equation. We assess the empirical performance of the proposed estimators and compare them with the estimators from the inverse weighted estimating equation and from the rank-based estimating equation approach in a simulation study in Section 4, and describe an application of our methodology to a real data example in Section 5. A discussion is provided in Section 6. The Appendix details the proofs.

2. Notation and Accelerated Failure Time Model

Let $\tilde{T}$ denote the unbiased time from initiation to failure in the targeted population. In the observed dataset, let T denote the length-biased failure time measured from initiation ($\tilde{T} > A$), A denote the time from initiation to recruitment (also referred to as truncation variable), V denote the time from recruitment to failure (also referred to as residual survival time), C denote the residual censoring time measured from recruitment, $\mathbf{X}$ denote the p-vector of covariates. We make the standard assumption that the residual censoring time C is independent of (A, V) conditional on $\mathbf{X}$, with covariate-specific survival function denoted by $S_c(\cdot|\mathbf{x})$. The major sampling constraint is that the value of T is observed only when $\tilde{T} > A$, which subsequently induces dependent censoring because $\text{cov}(T, A+C|\mathbf{X}) = \text{cov}(A+V, A+C|\mathbf{X}) = \text{var}(A|\mathbf{X}) + \text{cov}(V, A|\mathbf{X}) > 0$ except for in the trivial cases. For a random sample of size n , the data consist of $(y_i, a_i, \delta_i, \mathbf{x}_i)$, $i = 1, \dots, n$, where $y_i = \min\{t_i, a_i + c_i\}$ represents the observed time, δ_i indicates the type of event for which $\delta_i = 1$ if failure occurs before censoring, and $\mathbf{x}_i$ is the corresponding p-vector of covariates.

The AFT model takes the log-linear form to relate failure time and the corresponding covariates (Kalbeisch and Prentice, 2002; Cox and Oakes, 1984),

$$\log \tilde{T} = \mathbf{X}^T \boldsymbol{\beta}_0 + \varepsilon, \quad (1)$$

where $\boldsymbol{\beta}_0$ is a $P \times 1$ vector of parameters and ε has an unknown density function $q(\cdot)$ with mean zero.

Without right censoring and biased sampling, the classical least-squares principle is a natural approach to estimate $\boldsymbol{\beta}$ and yields the estimating equation

$$\sum_{i=1}^n \mathbf{x}_i (\log y_i - \mathbf{x}_i^T \boldsymbol{\beta}) = 0. \quad (2)$$

In the presence of right censoring, Buckley and James (1979) modified equation (2) by replacing the residual time of a censored observation, $\varepsilon_i(\boldsymbol{\beta}) = \log y_i - \mathbf{x}_i^T \boldsymbol{\beta}$, with its estimated conditional expectation

$$\varepsilon_i(\beta) + \int_{\varepsilon_i(\beta)}^{\infty} sd(-\widehat{S}_{\beta}(s)) / \widehat{S}_{\beta}(\varepsilon_i(\beta)),$$

where $\widehat{S}_{\beta}(\cdot)$ is the Kaplan-Meier estimator of the residual survival function based on the transformed data $(\varepsilon_i(\beta), \delta_i, i = 1, \dots, n)$. After replacing the censored data by their conditional expectations, we have following estimating equation for β :

$$\mathbf{U}(\beta) = \sum_{i=1}^n \mathbf{x}_i \left[\delta_i \varepsilon_i(\beta) + (1 - \delta_i) \left\{ \varepsilon_i(\beta) + \frac{\int_{\varepsilon_i(\beta)}^{\infty} sd(-\widehat{S}_{\beta}(s))}{\widehat{S}_{\beta}(\varepsilon_i(\beta))} \right\} \right].$$

The Buckley-James estimator is the root of $\mathbf{U}(\beta) = 0$, and its asymptotic properties have been rigorously studied (Ritov, 1990; Lai and Ying, 1994; Jin et al., 2006) for application to traditional right-censored data.

3. Buckley-James-type estimator for right-censored length-biased data

Recall that the unbiased time-to-event data are not directly observed. Instead, the biased samples and their corresponding covariates are observed. Under the stationarity assumption for disease incidence, the joint density of (A, T) given $\mathbf{X} = \mathbf{x}$ is (Wang, 1999)

$$(A, T) | \mathbf{x} \sim \frac{f(t|\mathbf{x})}{\mu(\mathbf{x})}, t > a, \quad \mu(\mathbf{x}) = \int_t f(t|\mathbf{x}) dt,$$

and the conditional distribution of A given $T = t$ and $\mathbf{X}$ is uniform $(0, t)$. Therefore, the marginal density of T given $\mathbf{X}$ is

$$T | \mathbf{x} \sim g(t|\mathbf{x}) = \frac{t f(t|\mathbf{x})}{\mu(\mathbf{x})}, \quad t > 0. \quad (3)$$

Under the AFT model (1), the covariate-specific density function of unbiased failure time $\tilde{T}$ and the corresponding length-biased density function can be expressed by

$$\begin{aligned} f(t|\mathbf{x}) &= \frac{1}{t} q(\log t - \mathbf{x}^T \beta_0), \quad t > 0 \\ g(t|\mathbf{x}) &= \frac{q(\log t - \mathbf{x}^T \beta_0)}{\mu(\mathbf{x})}, \quad t > 0, \end{aligned}$$

where $\mu(\mathbf{x}) = \int_t t f(t|\mathbf{x}) dt = \int q(\log y - \mathbf{x}^T \beta_0) dy$. Define $\tilde{T}_0 = \tilde{T} \exp(-\mathbf{x}^T \beta_0)$, $T_0 = T \exp(-\mathbf{x}^T \beta_0)$ and $\mu = \int q(\log t) dt$. Then the density functions of $\tilde{T}_0$ and T_0 are $f_0(t) = q(\log t)/t$ and $g_0(t) = q(\log t)/\mu$, respectively. Define $\tau = \inf\{t: \int_0^t g_0(s) ds = 1\}$ and assume that $\tau < \infty$. Note that τ is also the upper bound for the support of T_0 .

Without right censoring, we can prove that the expectation of $\log T_0/T_0$ is zero,

$$E\left(T_0^{-1}\log T_0\right)=\int_0^\infty \log(t)t^{-1}q(\log t)/\mu dt=\int_{-\infty}^\infty sq(s)/\mu ds=0,$$

because the mean of ε is zero. Accordingly, an unbiased estimating equation for β follows:

$$\sum_{i=1}^n \mathbf{x}_i \left\{ \frac{\log t_i - \mathbf{x}_i^T \beta}{t_i \exp(-\mathbf{x}_i^T \beta)} \right\} = 0. \quad (4)$$

In the presence of right censoring, let $A_0 = A \exp(-\mathbf{X}^T \beta_0)$, $V_0 = V \exp(-\mathbf{X}^T \beta_0)$, $C_0 = C \exp(-\mathbf{X}^T \beta_0)$, and $Y_0 = \min\{A_0 + V_0, A_0 + C_0\}$. Because of right censoring, the value of $\log T_0/T_0$ with $\delta = 0$ cannot be observed, but can be approximated naturally by its conditional expectation given the observed information. Given the joint distribution of (T_0, A_0) , $f_{T_0, A_0}(t_0, a_0) = f_0(t_0)/\mu$, $t_0 > a_0$, we have

$$E\left(\frac{\log T_0}{T_0} | C_0=c, A_0=a, V_0>C_0\right) = \frac{\int_{a+c}^\infty t^{-1} \log t dF_0(t)}{1 - F_0(a+c)},$$

where $F_0(t) = \int_0^t f_0(s) ds$.

Using the same principle as for traditional right-censored survival data, we modify the estimating equation for length-biased data without censoring in (4) by incorporating the component for right-censored data as follows:

$$\mathbf{U}_0(\beta) = \sum_{i=1}^n \mathbf{x}_i \left\{ \delta_i \frac{\log y_i - \mathbf{x}_i^T \beta}{y_i \exp(-\mathbf{x}_i^T \beta)} + (1 - \delta_i) \frac{\int_{y_{i0}}^\infty u^{-1} \log u dF_0(u; \beta)}{1 - F_0(y_{i0}; \beta)} \right\}.$$

With the unknown distribution F_0 , we need the following iterative procedure to solve for β . Note that the transformed data vectors,

$$(a_i \exp(-\mathbf{x}_i^T \beta_0), v_i \exp(-\mathbf{x}_i^T \beta_0), c_i \exp(-\mathbf{x}_i^T \beta_0), y_i \exp(-\mathbf{x}_i^T \beta_0), \mathbf{x}_i),$$

denoted by $(a_{i0}, v_{i0}, c_{i0}, y_{i0}, \mathbf{x}_i)$ are independent and identically distributed data vectors for $i = 1, \dots, n$. Using the EM algorithm proposed in Vardi (1989), one can estimate the nonparametric maximum likelihood estimator of the distribution of length-biased failure time T_0 from the likelihood

$$L_R = \prod_{i=1}^n dG_0(y_{i0})^{\delta_i} \left\{ \int_{s \geq y_{i0}} s^{-1} dG_0(s) \right\}^{1-\delta_i},$$

where $G_0(t) = \int_0^t g_0(s) ds$. With the estimated distribution $\hat{G}_0(t; \beta)$ for $G_0(t)$, we can then derive an estimator of the unbiased distribution $F_0(t)$ (Asgharian et al., 2002),

$$\widehat{F}_0(t;\beta) = \frac{\int_0^t s^{-1} d\widehat{G}_0(s;\beta)}{\int_0^\infty s^{-1} d\widehat{G}_0(s;\beta)}.$$

The Buckley-James-type estimator $\widehat{\beta}_{BJ}$ is the root of $\mathbf{U}(\beta) = 0$, where

$$\mathbf{U}(\beta) = \sum_{i=1}^n \mathbf{x}_i \left\{ \delta_i \frac{\log y_i - \mathbf{x}_i^T \beta}{y_i \exp(-\mathbf{x}_i^T \beta)} + (1 - \delta_i) \frac{\int_{y_{i0}}^\infty u^{-1} \log u d\widehat{F}_0(u;\beta)}{1 - \widehat{F}_0(y_{i0};\beta)} \right\}.$$

It is difficult to solve for β directly from $\mathbf{U}(\beta)$, especially when β is multi-dimensional, because $\mathbf{U}(\beta)$ is neither continuous nor monotone in β . Using a computational algorithm similar to that in Buckley and James (1979), we can obtain the root of the equation through an iterative procedure. We first fix an initial value $\widehat{\beta}_{(0)}$ and transform the observed data y_i to $y_i(\widehat{\beta}_{(0)}) = y_i \exp(-\mathbf{x}_i^T \widehat{\beta}_{(0)})$. We then obtain the maximum likelihood estimate of the unbiased survival function, $\widehat{F}_0(u; \widehat{\beta}_{(0)})$ given the transformed data. We can find the root of the modified equation using the estimated distribution of F_0 :

$$\mathbf{U}(\beta, \widehat{\beta}_{(0)}) = \sum_{i=1}^n \mathbf{x}_i \left\{ \delta_i \frac{\log y_i - \mathbf{x}_i^T \beta}{y_i \exp(-\mathbf{x}_i^T \beta)} + (1 - \delta_i) \frac{\int_{y_i(\widehat{\beta}_{(0)})}^\infty u^{-1} \log u d\widehat{F}_0(u; \widehat{\beta}_{(0)})}{1 - \widehat{F}_0(y_i(\widehat{\beta}_{(0)}); \widehat{\beta}_{(0)})} \right\}.$$

The iterative procedures continue until prespecified convergence criteria meet.

For traditional right-censored data, Jin et al. (2006) found that if the initial estimator $\widehat{\beta}_0$ is consistent and asymptotically normally distributed, the Buckley-James estimator at the m th step, $\widehat{\beta}_{(m)}$, should be consistent and asymptotically normally distributed for any $m \geq 1$. For length-biased right-censored data, the estimating equation in the m th step, $\mathbf{U}(\beta, \widehat{\beta}_{(m-1)})$, does not have a closed-form solution. Instead, the coefficient vector β at the m th step is obtained through one-step Newton-Raphson approximation,

$$\widehat{\beta}_{(m)} = \widehat{\beta}_{(m-1)} - \left\{ \frac{\partial \mathbf{U}(\beta, \widehat{\beta}_{(m-1)})}{\partial \beta} \right\}_{\widehat{\beta}_{(m-1)}}^{-1} \mathbf{U}(\widehat{\beta}_{(m-1)}, \widehat{\beta}_{(m-1)}). \quad (5)$$

When the residual censoring variable is independent of covariates, a consistent and asymptotically normal initial estimator, $\widehat{\beta}_{(0)}$, can be obtained from the inverse weighted estimating equation (IWEE) of Shen et al. (2009), which has a closed form expression

$$\widehat{\beta}_{(0)} = \left\{ \sum_{i=1}^n \frac{\delta_i \mathbf{x}_i \mathbf{x}_i^T}{\int_0^{y_i} \widehat{S}_c(u) du} \right\}^{-1} \sum_{i=1}^n \frac{\delta_i \mathbf{x}_i \log y_i}{\int_0^{y_i} \widehat{S}_c(u) du}, \quad (6)$$

where $\widehat{S}_c(\cdot)$ is the Kaplan-Meier estimator for the censoring survival function. We can prove that, for any fixed m , $\widehat{\beta}_{(m)}$ is consistent and asymptotically normally distributed given a

consistent and asymptotically normal initial estimator. Theorem 1 summarizes these asymptotic properties. The regularity assumptions for a rigorous justification of the results are listed in the Appendix.

Theorem 1

If the regularity assumptions 1–6 listed in the appendix are satisfied and a consistent and asymptotically normal initial estimator is chosen, then $\hat{\beta}_{(m)}$ is a consistent estimator of β_0 .

Moreover, $\sqrt{n}(\hat{\beta}_{(m)} - \beta_0)$ converges weakly to a normal distribution with mean zero and variance-covariance matrix V_m .

See the Appendix for the detailed proof. Since the explicit form of the asymptotic variance of $\hat{\beta}_{(m)}$ involves the complex linear operators and two unknown density functions, it is difficult to directly obtain a consistent variance estimator for $\hat{\beta}_{(m)}$. Alternatively, the bootstrap procedure can be used to estimate the asymptotic variance of $\hat{\beta}_{(m)}$. When the residual censoring time is dependent on the covariates, the estimator obtained from the IWEE may not be consistent. By contrast, the estimator obtained from the following estimating method for general left-truncated data (Lai and Ying, 1991b) remains consistent,

$$\mathbf{U}_{LT}(\beta) = \sum_{i=1}^n \delta_i \left[\tilde{x}_i - \frac{\sum_{j=1}^n \tilde{x}_j I\{a_j \exp(-\tilde{x}_j^T \tilde{\beta}) \leq y_i e^{-\tilde{x}_i^T \tilde{\beta}} \leq y_j \exp(-\tilde{x}_j^T \tilde{\beta})\}}{\sum_{j=1}^n I\{a_j \exp(-\tilde{x}_j^T \tilde{\beta}) \leq y_i e^{-\tilde{x}_i^T \tilde{\beta}} \leq y_j \exp(-\tilde{x}_j^T \tilde{\beta})\}} \right], \quad (7)$$

where $\tilde{x}_i$ is the covariate vector except for the constant one and $\tilde{\beta}$ denotes the corresponding vector of regression parameters except for the intercept. Once the estimator $\hat{\tilde{\beta}}$ is obtained by solving (7), the intercept can be estimated by the weighted average

$$\left\{ \sum_{i=1}^n \frac{\delta_i}{\int_0^{\tilde{y}_{i0}} \hat{S}_{\tilde{c}_0}(u) du} \right\}^{-1} \sum_{i=1}^n \frac{\delta_i (\log y_i - \tilde{x}_i^T \hat{\tilde{\beta}})}{\int_0^{\tilde{y}_{i0}} \hat{S}_{\tilde{c}_0}(u) du},$$

where $\tilde{y}_{i0} = y_i \exp(-\tilde{x}_i^T \hat{\tilde{\beta}})$ and $\hat{S}_{\tilde{c}_0}$ is the Kaplan-Meier estimator for the survival function of the transformed censoring $C \exp(-\tilde{X}^T \tilde{\beta})$. We refer to this estimating method as the left-truncation (LT) method. The weak convergence of the Buckley-James-type estimator with the initial consistent estimator from the LT method can be derived, similarly to that the Buckley-James-type estimator with the initial consistent estimator from the IWEE method. In the simulation study, we use the estimator from the LT method as the initial value for obtaining the Buckley-James estimator in the presence of covariate-depending censoring.

4. Simulation

4.1 Design and Data Generation

We conducted simulations to evaluate the performance of the proposed estimate and compare it with the performance of two existing methods: IWEE method given by (6) and LT method by (7) for general left-truncated data. We first generated independent pairs of (A_i, T_i) , then kept the pairs conditioning on $A_i < \tilde{T}_i$. Here, A was distributed uniformly on $(0, \omega)$ and ω was larger than the upper bound of T to ensure the stationarity assumption. We considered an AFT model with two covariates,

$$\log(\tilde{T}) = \alpha_0 + \alpha_1 X_1 + \alpha_2 X_2 + \varepsilon,$$

where X_1 is a binary covariate with $P(X_1 = 1) = 0.5$, X_2 is a continuous covariate with a uniform(0,1) distribution, and ε has a mean zero normal distribution with standard deviation of 0.3. We set $\alpha_0 = 1$, $\alpha_1 = 0.5$, and $\alpha_2 = 1$. Each study comprised 500 replications, and the bootstrap procedure used 200 re-samplings in each replication. A cohort size of 100 or 200 was used.

The censoring variables measured from the examination time, C_i , were independently generated from uniform distributions with two censoring percentages: 20% and 35%. The censoring indicator was obtained by $\delta_i = I(t_i \leq c_i + a_i)$. Aside from the scenarios in which right censoring was assumed to be independent of covariates, we also studied scenarios in which the censoring times were dependent on the covariates. Specifically, we generated censoring times either from a mixed distribution $C \sim X_1 \text{Uniform}(v_1) + (1 - X_1) \text{Uniform}(v_2)$, or from a Cox regression model $\lambda_c(t) = v_3 t \exp(X_1 + X_2)$. Here v_1 , v_2 , and v_3 are parameters to control the degree of censoring. In this setting, the estimators obtained from IWEE given by (6) may not be consistent, but the estimators obtained from LT method in equation (7) remain to be consistent. We thus use the estimator from the LT method as the initial value for obtaining the Buckley-James estimator.

4.2 Simulation Results

Table 1 lists the average of the estimators, empirical standard errors (ESE) and bootstrap standard error (BSE) of the proposed approach, the IWEE method given by (6) and the LT method by (7) under independent censoring. When the censoring percentage was low (e.g. 20%) all three types of estimators achieved good accuracy: the empirical biases were less than 1%. In the presence of moderate censoring (35%), the Buckley-James-type estimators and LT estimators were virtually unbiased, with empirical percentage biases smaller than 2%, and the biases of estimators from the IWEE method were slightly larger but still comparable. For all scenarios, the Buckley-James-type approach exhibited the best precision among three types of estimators, with empirical standard errors 1%-13% smaller than those from the IWEE approach, and 5%-26% smaller than those from the LT approach. With a sample size of 100 and 35% censoring, the empirical standard error of $\hat{\alpha}_2$ from the Buckley-James-type approach was 13% smaller than that from the IWEE, and 26% smaller than that from the LT method.

To evaluate the robustness of Buckley-James-type estimators, we simulated censoring times from a mixed distribution depending on covariates, as specified in Section 4.1. The results were presented in Table 2. Again, the Buckley-James-type estimates outperformed the other two types of estimates with smaller bias and standard error. As expected, the IWEE approach yielded biased estimates for covariate effects compared with Buckley-James-type and LT estimates, especially when the censoring percentage increased. For Buckley-James type and LT estimates, their empirical biases of estimates were smaller than 1%. When censoring was dependent on covariates, the standard errors of Buckley-James-type estimators were appreciably (1%-15%) smaller than those from the IWEE estimators, and substantially (6%-25%) smaller than the LT estimators. We also performed additional simulation to evaluate how sensitive the Buckley-James-type estimator to the consistent initial estimator, $\hat{\beta}_{(0)}$ (by using the IWEE estimator as the initial estimator when the censoring distribution depends on covariates). The results not presented here due to limited space suggest that the Buckley-James-type estimator is robust with respect to the initial estimator.

The bootstrap procedure can accurately capture the variability of the proposed estimators and the bootstrap confidence intervals have proper coverage probabilities close to the nominal level of 0.95, as shown in Tables 1–2. As suggested by one reviewer, we have also conducted some simulation studies to explore whether the efficiency can be improved by multiple iterations. The simulation results (for brevity the results are not presented) suggest that the estimators with a small number of iterations (such as the three-step estimator) may be sufficient to achieve adequate precision for the proposed estimators.

5. Data Application

In an epidemiologic study to evaluate the survival of patients with dementia, more than 10,000 Canadians age 65 or older were screened for dementia in the first stage of the Canadian Study of Health and Aging in 1991. The individuals identified as having dementia were classified into one of three diagnostic categories: (1) probable Alzheimer's disease, (2) possible Alzheimer's disease, and (3) vascular dementia; their dates of dementia onset were retrieved from their medical records. At the second stage of the CSHA, individuals with confirmed dementia were followed prospectively until 1996, and their dates of death or censoring were ascertained. Details of the design and analysis of the study were described by Wolfson et al. (2001). We applied the proposed method to CSHA data to assess the effect of different diagnostic categories of dementia on survival.

The data we analyzed included 818 individuals with dementia, 393 with probable Alzheimer's disease, 252 with possible Alzheimer's disease, and 173 with vascular dementia. For each individual, the date of disease onset, date of entry into the study, date of death or right censoring, and death indicator were collected.

We first examined the stationarity assumption for the cohort. The formal test of stationarity assumption given by Addona and Wolfson (2006) yields a two-sided p-value of 0.33, which suggests that the stationarity assumption is reasonable. We next assessed the applicability of the AFT model. The AFT model assumes that a covariate has a multiplicative effect on the survival time quantiles of the baseline group. For the dementia study, the survival distributions of three subgroups are compared under the AFT model. Therefore, the Q-Q plot can be used to check the AFT assumption, where the survival time quantiles of one subgroup were plotted against the survival time quantiles of another subgroup (baseline group). In the Q-Q plots shown in Figure 1, the distribution functions were estimated nonparametrically by the EM algorithm proposed by Vardi (1989). The Q-Q plots approximate well to a straight line from the original, indicating that the AFT model provides a reasonable regression structure for modeling survival times among individuals with three types of dementia. We applied the AFT model of $E(\log Y) = \alpha_0 + \alpha_1 X_1 + \alpha_2 X_2$ to the observed survival time Y 's, where X_1 and X_2 indicate whether the individual had probable Alzheimer's disease and possible Alzheimer's disease, respectively. The estimated coefficients from the Buckley-James-type equation for length-biased data, including their bootstrap standard errors, are listed in Table 3. The estimators were comparable with those obtained from the IWEE and LT approaches. Inferences from the three estimating methods adjusting for length-biased sampling agreed well. There were no significant differences in long-term survival among three subtypes of dementia.

For comparison, we also provided the estimated covariate coefficients in Table 4 under the AFT model ignoring the length-biased sampling in the data (referred to as "Naive Buckley-James estimator"). The naive estimators resulted in a median survival duration of 5.74 years (95% CI: 5.14–6.41) for vascular dementia, 6.44 years (95% CI: 6.00–6.91) for probable Alzheimer's disease, and 7.01 years (95% CI: 6.39–7.71) for possible Alzheimer's disease. Adjusting for length bias the estimators resulted in a median survival duration of 3.33 years

(95% CI: 2.87–3.86) for vascular dementia, 3.58 years (95% CI: 2.84–4.51) for probable Alzheimer's disease, and 4.01 years (95% CI: 3.35–4.80) for possible Alzheimer's disease. The substantial differences between the median survival times when using different estimation methods indicate that the use of an approach that ignores length-biased sampling will lead to a severe underestimation of the deleterious effects of dementia.

6. Concluding Remarks

The semiparametric AFT regression model has the advantage of simple interpretation for the covariate effects on time-to-event data. It is thus appealing to generalize the Buckley-James-type estimator under the AFT model for traditional survival data to length-biased right-censored data. The Buckley-James iterative algorithm is adapted to obtain the consistent root of the proposed estimating equation given a consistent estimator as the initial value. In our simulation studies, we have always found the proposed Buckley-James-type estimators to be more efficient than the two existing estimators (IWEE and LT) for analyzing length-biased data. Because the estimator from the IWEE relies only on uncensored failure times, information for the covariates of the censored times are not properly utilized in the estimating equation. In contrast, the proposed method effectively utilizes the censored observations with their conditional expectations in the estimating equations. Another advantage of the proposed method is that the estimation procedure is robust to the assumption that the censoring distribution is independent to covariates. While the rank-based method proposed for left-truncated right censoring data is also robust to the independent assumption between the censoring distribution and covariates (Lai and Ying, 1991b), the method is less efficient without utilizing the information of length-biased sampling (i.e. stationarity assumption).

The asymptotic properties of the proposed estimator hold when a consistent estimator is used as initial value in the iterations. Clearly, the two existing estimation approaches (IWEE and LT) under the AFT model can provide the initial consistent estimator for the Buckley-James-type estimators under different censoring mechanisms. Our additional empirical studies also suggest that the Buckley-James-type estimator is quite robust, even if the initial value is not a consistent estimator of β .

The implementation of the Buckley-James approach is much more challenge for length biased right-censored data than for traditional right-censored data. There is a fundamental difference in estimating the nonparametric survival distribution in the absence and presence of length bias. Unlike the approach for conventional survival data that the nonparametric maximum likelihood estimator jumps only at the observed failure time points with a closed form, the nonparametric maximum likelihood estimator based on length-bias data jumps at all the observed failure and censored time points without a closed-form expression.

For general left-truncated and right-censored data, the intercept in the AFT model or the mean of the residual is generally not estimable, especially when the censoring has support that is shorter than that of the event times. The length-biased data however, have some unique features and require different conditions compared to the setting with general left-truncated right-censored data. As established in Theorem 1 and its Corollary 2 of Asgharian et al. (2002), the mean of the target failure time ($\tilde{T}_0$), μ can be consistently estimated by $\hat{\mu} = \int_{-0}^{\tau} (1 - \hat{F}_0(x)) dx$ with $\sqrt{n}$ convergency under some mild sufficient conditions. This fact, combined with the property that τ can be consistently estimated by $\hat{\tau} = \max_{1, \dots, n} \{y_{i0}\}$ and its convergence rate is higher than $n^{-1/2}$, ensures that the intercept in the AFT model can be estimated consistently under the assumptions listed in the Appendix. Some details are provided in the Web Supplementary Materials.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

- Addona V, Wolfson DB. A formal test for the stationarity of the incidence rate using data from a prevalent cohort study with follow-up. *Lifetime Data Anal.* 2006; 12:267–274. [PubMed: 16917734]
- Asgharian M, M'Lan CE, Wolfson DB. Length-biased sampling with right censoring: An unconditional approach. *J Am Statist Assoc.* 2002; 97:201–209.
- Asgharian M, Wolfson DB. Asymptotic behavior of the unconditional NPMLE of the length-biased survivor function from right censored prevalent cohort data. *Ann Statist.* 2005; 33:2109–2131.
- Buckley J, James I. Linear regression with censored data. *Biometrika.* 1979; 66:429–436.
- Chen YQ. Semiparametric regression in size-biased sampling. *Biometrics.* 2010; 66:149–158. [PubMed: 19432792]
- Cox, DR.; Oakes, D. *Analysis of Survival Data*. Boca Raton, FL: Chapman and Hall/CRC Press; 1984.
- De Una-Alvarez J, Otero-Giraldez MS, Alvarez-Llorente G. Estimation under length-bias and right-censoring: An application to unemployment duration analysis for married women. *J Appl Statist.* 2003; 30:283–291.
- Gill RD, Vardi Y, Wellner JA. Large-sample theory of empirical distributions in biased sampling models. *Ann Statist.* 1988; 16:1069–1112.
- Gross ST, Lai TL. Nonparametric estimation and regression analysis with left-truncated and right-censored data. *J Amer Statist Assoc.* 1996; 91:1166–1180.
- Jin Z, Lin D, Wei L, Ying Z. Rank-based inference for the accelerated failure time models. *Biometrika.* 2003; 90:341–353.
- Jin Z, Lin DY, Ying Z. On least-squares regression with censored data. *Biometrika.* 2006; 93:147–161.
- Kalbeisch, JD.; Prentice, RL. *The Statistical Analysis of Failure Time Data*. John Wiley and Sons; New Jersey: 2002.
- Lagakos SW, Barraj LM, De Gruttola V. Nonparametric analysis of truncated survival data, with applications to aids. *Biometrika.* 1988; 75:515–523.
- Lai TL, Ying Z. Large sample theory of a modified Buckley-James estimator for regression analysis with censored data. *Ann Statist.* 1991a; 19:1370–1402.
- Lai TL, Ying Z. Rank regression methods for left-truncated and right-censored data. *Ann Statist.* 1991b; 19:531–556.
- Lai TL, Ying Z. A missing information principle and M-Estimators in regression analysis with censored and truncated data. *Ann Statist.* 1994; 22:1222–1255.
- Lin DY, Ying Z. Semiparametric inference for the accelerated life model with time-dependent covariates. *J Statist Plan and Inference.* 1995; 44:47–63.
- Mandel M, Ritov Y. The accelerated failure time model under biased sampling. *Bimetrics.* 2010 in press.
- Miller RG, Halpern J. Regression with censored data. *Biometrika.* 1982; 69:521–531.

- Nowell C, Stanley LR. Length-biased sampling in mall intercept surveys. *J Market Res.* 1991; 28:475–479.
- Prentice RL. Linear rank tests with right censored data. *Biometrika.* 1978; 65:167–179.
- Ritov Y. Estimation in a linear regression model with censored data. *Ann Statist.* 1990; 18:303–328.
- Shen Y, Ning J, Qin J. Analyzing length-biased data with semiparametric transformation and accelerated failure time models. *J Am Statist Assoc.* 2009; 104:1192–1202.
- Tsai WY, Jewell NP, Wang MC. A note on the product-limit estimator under right censoring and left truncation. *Biometrika.* 1987; 74:883–886.
- Tsiatis AA. Estimating regression parameters using linear rank tests for censored data. *Ann Statist.* 1990; 18:354–372.
- Turnbull BW. The empirical distribution function with arbitrarily grouped, censored and truncated data. *J R Statist Soc B.* 1976; 38:290–295.
- Vardi Y. Nonparametric estimation in the presence of length bias. *Ann Statist.* 1982; 10:616–620.
- Vardi Y. Empirical distributions in selection bias models. *Ann Statist.* 1985; 13:178–203.
- Vardi Y. Multiplicative censoring, renewal processes, deconvolution and decreasing density: Nonparametric estimation. *Biometrika.* 1989; 76:751–761.
- Wang MC. Nonparametric estimation from cross-sectional survival data. *J Am Statist Assoc.* 1991; 86:130–143.
- Wang MC. Hazards regression analysis for length-biased data. *Biometrika.* 1996; 83:343–354.
- Wang MC. Gap time bias in incident and prevalent cohorts. *Stat Sin.* 1999; 9:999–1010.
- Wang MC, Brookmeyer R, Jewell NP. Statistical models for prevalent cohort data. *Biometrics.* 1993; 49:1–11. [PubMed: 8513095]
- Wang MC, Jewell NP, Tsai WY. Asymptotic properties of the product limit estimate under random truncation. *Ann Statist.* 1986; 14:1597–1605.
- Wolfson C, Wolfson DB, Asgharian M, M'Lan CE, Ostbye T, Rockwood K, Hogan DB. the Clinical Progression of Dementia Study Group. A reevaluation of the duration of survival after the onset of dementia. *New Engl J Med.* 2001; 344:1111–1116. [PubMed: 11297701]
- Ying Z. A large sample study of rank estimation for censored regression data. *Ann Statist.* 1993; 21:76–99.
- Zelen M. Forward and backward recurrence times and length biased sampling: Age specific models. *Lifetime Data Anal.* 2004; 10:325–334. [PubMed: 15690988]
- Zelen M, Feinleib M. On the theory of screening for chronic diseases. *Biometrika.* 1969; 56:601–614.

Appendix Proof of Theorem 1

For notation simplicity, we assume covariate-independent censoring and use the estimator obtained from IWEE given by (6) as the initial value to show the weak convergence of $\hat{\beta}_{(1)}$. However, the arguments here can be readily extended to the case of covariate-dependent censoring and initial estimator from the LT method. We assume the following regularity conditions:

Assumption 1

$\mathbf{X}$ is bounded and the $n \times p$ matrix $\mathcal{X}_{n \times p} = (\mathbf{X}_1, \mathbf{X}_2, \dots, \mathbf{X}_n)^T$ is of full rank.

Assumption 2

$P(V < C) > 0$.

Assumption 3

$G_0(\cdot)$ is a continuous and differentiable distribution function over $(0, \tau)$ and $\tau < \infty$.

Assumption 4

$$\left\{ \frac{2\tau}{\int_0^\tau S_{C_0}(u)du} - \frac{1}{S_{C_0}(0)} \right\} \{1 - S_{C_0}(0)\} < 1, \text{ where } S_{C_0} \text{ is the survival function of } C_0$$

Assumption 5

There exists a $\tau_0 > 0$ such that $F_0(y) = 0, \forall y < \tau_0$.

Assumption 6

$$\int_0^\tau f_0^2(t)/(1 - F_0(t))dt < \infty.$$

Assumption 1 is to ensure the non-singularity of matrix $\mathbf{D} = \lim_{n \rightarrow \infty} \frac{1}{n} \frac{\partial \mathbf{U}(\beta, \hat{\beta}_{(0)})}{\partial \beta} \Big|_{\hat{\beta}_{(0)}}$. Assumptions 2 to 5 are to ensure uniform consistency and weak convergence of the estimator $\hat{F}_0$ for all $0 < t \leq \tau$ and the properties of $\hat{\mu}$ (Asgharian et al., 2002; Asgharian and Wolfson, 2005).

Assumption 6 is sufficient to ensure that various expectations are finite.

Proof of Theorem 1

Note that it suffices to show the asymptotic properties of $\hat{\beta}_{(m)}$ for $m = 1$. By equation (5), we have

$$\hat{\beta}_{(1)} - \beta_0 = \hat{\beta}_{(0)} - \beta_0 - \left\{ \frac{\partial \mathbf{U}(\beta, \hat{\beta}_{(0)})}{\partial \beta} \right\}_{\hat{\beta}_{(0)}}^{-1} \mathbf{U}(\hat{\beta}_{(0)}, \hat{\beta}_{(0)}). \quad (\text{A.1})$$

We show in the Web Supplementary Materials that the difference between the estimating equation with the true value β_0 and the estimating equation with the consistent estimate $\hat{\beta}_{(0)}$ is asymptotically linear in $\hat{\beta}_{(0)}$,

$$\begin{aligned} & \frac{1}{\sqrt{n}} \mathbf{U}(\beta_0, \beta_0) - \frac{1}{\sqrt{n}} \mathbf{U}(\hat{\beta}_{(0)}, \hat{\beta}_{(0)}) \\ &= \frac{1}{\sqrt{n}} \sum_{i=1}^n \delta_i \mathbf{x}_i \left(\frac{\log y_i - \mathbf{x}_i^T \beta_0}{y_i e^{-\mathbf{x}_i^T \beta_0}} - \frac{\log y_i - \mathbf{x}_i^T \hat{\beta}_{(0)}}{y_i e^{-\mathbf{x}_i^T \hat{\beta}_{(0)}}} \right) \\ &+ \frac{1}{\sqrt{n}} \sum_{i=1}^n (1 - \delta_i) \mathbf{x}_i \left\{ \frac{\int_{y_{i0}}^{\infty} t^{-1} \log t d\hat{F}_0(t; \beta_0)}{1 - \hat{F}_0(y_{i0}; \beta_0)} - \frac{\int_{y_i(\hat{\beta}_{(0)})}^{\infty} t^{-1} \log t d\hat{F}_0(t; \hat{\beta}_{(0)})}{1 - \hat{F}_0(y_i(\hat{\beta}_{(0)}); \hat{\beta}_{(0)})} \right\} \\ &= -\mathbf{B} \sqrt{n}(\hat{\beta}_{(0)} - \beta_0) + o_p(1), \end{aligned}$$

where $\mathbf{B}$ is a matrix defined in the Web supplementary materials. This linear approximation, together with equation (A.1), implies that

$$\hat{\beta}_{(1)} - \beta_0 = (\mathbf{I}_p + \mathbf{D}^{-1} \mathbf{B})(\hat{\beta}_{(0)} - \beta_0) + n^{-1} \mathbf{D}^{-1} \mathbf{U}(\beta_0, \beta_0) + o_p(n^{-1/2}),$$

where $\mathbf{I}_p$ is an identity matrix. It follows that $\hat{\beta}_{(1)}$ and thus $\hat{\beta}_{(m)}$ are consistent for each fixed m . Note that the estimating equation with the true parameter requires estimating the

unknown survival function, and its independent and identically distributed representations could be derived by the asymptotic properties of Vardi's estimator,

$$\mathbf{U}(\beta_0, \beta_0) = \sum_{i=1}^n \mathbf{x}_i \left\{ \delta_i \frac{\log y_i - \mathbf{x}_i^T \beta_0}{y_i e^{-\mathbf{x}_i^T \beta_0}} + (1 - \delta_i) \frac{\int_{y_{i0}}^{\infty} t^{-1} \log t dF_0(t)}{F_0(y_{i0})} \right\} + \sum_{i=1}^n \left\{ \int \mathbf{L}(t) t^{-1} \log t d\mathcal{G}(V_{\beta_0, i})(t) + \mathbf{L}_i \right\} + o_p(1),$$

$$\text{where } \mathbf{L}(t) = E \left\{ \frac{\mathbf{x}(1-\delta)I(Y_0 \leq t)}{1-F_0(Y_0)} \right\}, \mathbf{L}_i = E \left\{ \frac{\mathbf{x}(1-\delta) \int_{Y_0}^{\infty} t^{-1} \log t dF_0(t) \mathcal{G}(V_{\beta_0, i})(Y_0)}{(1-F_0(Y_0))^2} \right\},$$

$$V_{\beta_0, i}(t) = p^{1/2} \{I(y_{i0} \leq t, \delta_i = 1) - G^*(t)\} + \left(\frac{p}{1-p} \right) \{G^*(t) - G_0(t)\} \{\delta_i - p\} + (1-p)^{1/2} h(t) \int_{0 < z \leq t} \{I(y_{i0} \leq z, \delta_i = 0) - F^*(z)\} d \frac{1}{h(z)},$$

$$G^*(t) = P(Y_0 \leq t | \delta = 1), F^*(t) = P(Y_0 \leq t | \delta = 0),$$

$$h(t) = \int_t^{\infty} z^{-1} dG_0(z), p = P(\delta = 1),$$

$\mathcal{G}$ and $\mathcal{F}$ are linear operators defined by

$$\mathcal{G}(v)(t) = \frac{\int_0^{\infty} s^{-1} dG_0(x) \int_0^t s^{-1} d\mathcal{F}^{-1}(v)(s) - \int_0^t s^{-1} dG_0(s) \int_0^{\infty} s^{-1} d\mathcal{F}^{-1}(v)(s)}{\left\{ \int_0^{\infty} s^{-1} dG_0(s) \right\}^2},$$

$$\mathcal{F}(u)(t) = p \int_{0 < x \leq t} \frac{g^*(\mathbf{x})}{g_0(\mathbf{x})} du(\mathbf{x}) + (1-p) \int_{0 < y \leq t} y \left(\int_{y \leq z} \frac{u(z)}{z^2} dz \right) d \left\{ \left(\frac{h(t)}{h(y)} - 1 \right) \frac{f^*(y)}{h(y)} \right\},$$

and $g^*(x)$ and $f^*(x)$ are the conditional density functions of $G^*(x)$ and $F^*(x)$, respectively. This representation, together with the asymptotic independent and identically distributed representation of the estimator $\hat{\beta}_{(0)}$, implies that $\sqrt{n}(\hat{\beta}_{(1)} - \beta_0)$ converges in distribution to a zero-mean normal distribution.

Figure 1.
QQ plots for survival time from onset of dementia to death (days)

Table 1

Simulation Study. Comparison of three estimating procedures: Buckley-James-type estimator, IWEE estimator and U_{LT} Estimator

Cohort size	C%	Buckley-James-type Estimator				IWEE Estimator				U_{LT} Estimator			
		Mean	ESE	BSE	CP of 95%CI	Mean	ESE	$(\hat{a}_0, \hat{a}_1, \hat{a}_2)$		Mean	ESE	$(\hat{a}_0, \hat{a}_1, \hat{a}_2)$	
100	0%	(1.001,.494,.997)	(.087,.068,.121)	(.085,.068,.115)	(.940,.960,.930)	(1.007,.495,.996)	(.091,.069,.128)			(.999,.500,1.005)	(.092,.081,.139)		
	20%	(1.003,.500,.999)	(.093,.066,.119)	(.090,.071,.120)	(.952,.954,.942)	(1.008,.497,.991)	(.094,.069,.127)			(1.000,.501,1.002)	(.102,.085,.151)		
	35%	(1.004,.499,.999)	(.097,.070,.126)	(.093,.076,.127)	(.954,.946,.936)	(1.019,.483,.966)	(.101,.080,.145)			(1.005,.499,.980)	(.113,.090,.171)		
200	0%	(1.003,.498,.999)	(.062,.047,.086)	(.060,.048,.083)	(.942,.948,.940)	(1.002,.498,1.000)	(.067,.049,.092)			(1.000,.501,1.002)	(.065,.055,.099)		
	20%	(1.001,.499,.999)	(.062,.049,.085)	(.073,.050,.086)	(.936,.923,.942)	(1.005,.499,.992)	(.067,.052,.090)			(.998,.503,1.003)	(.070,.058,.104)		
	35%	(1.002,.501,.998)	(.064,.051,.089)	(.065,.054,.094)	(.958,.932,.944)	(1.015,.486,.968)	(.072,.058,.101)			(.993,.502,.999)	(.076,.063,.110)		

Simulation Study. Comparison of three estimating procedures when censoring depends on covariates: Buckley-James-type estimator, IWEE estimator and U_{LT} Estimator

Table 2

Cohort	C%	Buckley-James-type Estimator				IWEE Estimator				U_{LT} Estimator			
size		$(\hat{a}_0, \hat{a}_1, \hat{a}_2)$				$(\hat{a}_0, \hat{a}_1, \hat{a}_2)$				$(\hat{a}_0, \hat{a}_1, \hat{a}_2)$			
		Mean	ESE	BSE	CP of 95%CI	Mean	ESE	Mean	ESE	Mean	ESE		
$C: X_1 Uniform(\tau_1) + (1 - X_1)Uniform(\tau_2)$													
100	20%	(1.008,.497,.994)	(.091,.070,.128)	(.095,.071,.120)	(.930,.942,.956)	(1.021,.476,.998)	(.097,.075,.136)	(1.007,.501,.993)	(.104,.084,.154)				
	35%	(1.007,.497,.995)	(.099,.074,.135)	(.103,.079,.138)	(.942,.950,.930)	(1.030,.445,.991)	(.106,.084,.158)	(1.019,.499,.968)	(.120,.090,.181)				
200	20%	(1.005,.497,.998)	(.063,.050,.091)	(.065,.049,.088)	(.944,.938,.946)	(1.015,.476,1.000)	(.068,.053,.098)	(1.005,.498,1.000)	(.071,.060,.106)				
	35%	(1.004,.497,.999)	(.073,.052,.096)	(.069,.054,.094)	(.934,.954,.954)	(1.025,.441,1.005)	(.076,.061,.116)	(1.004,.498,.999)	(.078,.063,.117)				
$C: \lambda_c(t) = v_3 f \exp(X_1 + X_2)$													
100	20%	(1.005,.501,.995)	(.095,.070,.120)	(.091,.072,.121)	(.944,.934,.944)	(.991,.513,.999)	(.098,.073,.130)	(.997,.504,.999)	(.104,.087,.149)				
	35%	(1.006,.502,.992)	(.109,.082,.133)	(.110,.087,.137)	(.946,.956,.924)	(.977,.526,1.002)	(.108,.083,.144)	(.994,.502,1.000)	(.119,.096,.168)				
200	20%	(1.002,.502,.997)	(.067,.053,.086)	(.066,.051,.088)	(.938,.942,.958)	(.987,.514,1.003)	(.072,.054,.092)	(.994,.503,1.001)	(.074,.060,.106)				
	35%	(1.003,.501,.996)	(.072,.056,.094)	(.069,.055,.091)	(.934,.940,.946)	(.970,.527,1.009)	(.080,.061,.103)	(.990,.502,1.000)	(.085,.067,.116)				

Table 3

Analysis results of dementia data

Method	Buckley-James-type estimator with length-biased		Naive Buckley-James estimator	
Parameter	Est.	SE	Est.	SE
α_0	7.102	0.075	7.648	0.056
α_1	0.073	0.132	0.115	0.064
α_2	0.187	0.123	0.200	0.075

Est., parameter estimate; SE, bootstrap standard error of the parameter estimator.