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# A SEMIPARAMETRIC MODEL FOR INTERVAL CENSORED AND TRUNCATED DATA

Abstract. In this work we consider a complex observational scheme, that is, survival data that are both interval censored and truncated. We assume a semiparametric Cox model for the survival function and consider censoring and truncation distributions as in Huber, Solev and Vonta (2006, 2007). We establish the form of the least favorable model (Slud and Vonta (2005)) for the cumulative hazard function, which plays the role of the infinite-dimensional nuisance parameter, for fixed values of the finite-dimensional parameter of interest. The least favorable model cannot be defined in closed form.

## 1. Introduction

We consider survival data that are both interval censored and truncated. Complex observational schemes occur due to the fact that observation of a process is not continuous in time and is done through a window of time which could exclude totally some individuals from the sample. For example, the time of onset of a disease in a patient, like HIV infection or toxicity of a treatment, is not exactly known, but it is usually known to have taken place between two dates $t_1$ and $t_2$; this occurs in particular when the event of interest results in an irreversible change of state of the individual: at time $t_1$, the individual is in state one, while at time $t_2$, it is in state two. Moreover, some people can escape the sample if they are observed during a period of time not including some pair of dates $t_1, t_2$ having the above property.

Turnbull (1976) proposed a nice method for nonparametric maximum likelihood estimation of the distribution function in the case of arbitrarily censored and truncated data. His method, slightly corrected by Frydman (1994), has been used extensively since by several authors, and extended to the Cox model by Alioum and Commenges (1996) and to the frailty or transformation models by Huber-Carol and Vonta, (2004). In Huber, Solev and Vonta (2006) and (2007) we give conditions on the involved distributions, namely, the censoring, truncation and survival distributions, implying the consistency of a nonparametric maximum likelihood estimator of the density of the survival process in the totally nonparametric case. We also provide the rate of convergence of the NPMLE of the density within a certain class of functions.

In sections two and three, we give a representation of the censoring and truncation mechanisms. As it is due to a non continuous observation of the survival process, the censoring mechanism is represented as a denumerable partition of the total interval of observation time $(a, b]$. Then a truncation is added to the censoring, conditioning the observations both of the survival and the censoring processes. We also consider a Cox semiparametric model for the survival function.

In section four we further assume, without loss of generality, the particular case of right truncation. In order to prove that the finite-dimensional parameter of interest can be estimated efficiently in the presence of the infinite-dimensional nuisance parameter, we will follow the methodology introduced in Slud and Vonta (2005) concerning modified profile likelihood estimators. In this section we establish the form of the least favorable model for the nuisance parameter for fixed values of the parameter of interest. The least favorable model is not given in closed form.

Assumptions and regularity conditions under which the assumptions posed in Slud and Vonta (2005) are fulfilled, and therefore the semiparametric efficiency for the parameter of interest is derived, are currently being developed.

## 2. The observation scheme

Time $X$ to an event that changes permanently the state of subject $i$ under study (state 0 before $X$, 1 afterwards) is a random variable whose distribution is to be estimated under the following observation scheme:

1. Censorship: observation of each subject $i$ does not take place continuously but is scheduled at a (random) number $K(i)$ of (random) times

$$a < Y_{i,1} < \cdots < Y_{i,K(i)} < b$$

where usually $a$ will be equal to 0 and $b$ is a finite strictly positive number. Let $\tau_i := \{Y_{i,j},\, j = 1, \cdots, K(i)\}$ the set of scheduled observation times for subject i and $t_i := \{y_{i,j},\, j = 1, \cdots, K(i)\}$ a realization of $\tau_i$.

2. Truncation: only those elements of $t_i$ that are inside a given (random) truncating window $(Z_{i,1}\ Z_{i,2}]$ give rise to an actual observation of subject $i$.

Thus, if subject $i$ is observed in state 0 at time $y_{i,j}$ and in state 1 at time $y_{i,j+1}$, inside its window $\triangle := (z_{i,1}, z_{i,2}]$, one observes subject $i$ at all times of $t_i$ included in $\triangle$. A sufficient statistic for this problem is thus the two embedded intervals "bracketing" the unobserved $X = x$ :

$$z_{i,1} \leq y_{i,k_1} \leq y_{i,j} < x \leq y_{i,j+1} \leq y_{i,k_2} \leq z_{i,2}$$

where $y_{i,k_1}$ is the smallest time in $t_i$ which is greater than or equal to $z_{i,1}$ and $y_{i,k_2}$ is the largest time in $t_i$ that is less than or equal to $z_{i,2}$.

**2.1. Censorship: simple random covering.** Let $\tau$ be a random partition defined on $]a;b]$, where usually $a$ will be equal to 0 and $b$ is a finite strictly positive number:

$$\tau = \left\{ Y_0 = a < Y_1 < \ldots < Y_K < Y_{K+1} = b, \bigcup_{j=0}^{K} (Y_j, Y_{j+1}] = (a,b] \right\} \quad (1)$$

where $K$ is a fixed number or a random number with known law in $\{2, \ldots, K_0\}$ for some given $K_0$ such that $2 < K_0 < \infty$.

For each $x \in (a;b)$ we define

$$j(x) = \inf \{ j : \; x \leq Y_{j+1} \} . \quad (2)$$

$$\vartheta(x) = \left( Y_{j(x)}, Y_{j(x)+1} \right] := (L(x), R(x)] \;\; x \in (a,b), \quad (3)$$

where $L(x)$ and $R(x)$ may be thought of as the left and right values in partition $\tau$ that "bracket" (the survival) $X = x$.

Then it is clear that

$$\vartheta(x) = \vartheta(y), \;\text{ or }\; \vartheta(x) \cap \vartheta(y) = \emptyset \quad (4)$$

and we call $\vartheta(x)$ a simple random covering of $(a,b)$.

**2.2. Truncation.** Let $\vartheta(x) = (L(x), R(x)]$, $x \in \mathbb{R}$, be the simple random covering defined by the partition $\tau = t := \{y_j, \; j = 1, 2, \ldots, k\}$. Then, a fixed interval $\triangle = (z_1, z_2]$, and $z$ the associated vector $(z_1, z_2)$, $z_1 \leq z_2$, is a truncating interval. This means that the only available observations of the subject $i$ under investigation take place at times that are those elements of $t$ that are included in $(R(z_1); \, L(z_2)]$, which behaves like the effective "truncating window".

Our basic assumption is the following: First we assume that the random covering $\vartheta(\cdot)$, the random variable $X$ and the random interval $\Delta$ are independent. Second, we assume that the distribution of any $(Y_{m+1}, \cdots, Y_n)$ is absolutely continuous with respect to the Lebesgue measure on $\mathbb{R}^{n-m}$, and that the distribution of $(Z_1, Z_2)$ is absolutely continuous with respect to the Lebesgue measure on $\mathbb{R}^2$.

In that case a summary of the observations on the subject under investigation is the pair of embedded intervals:

$$R(z_1) \leq L(x) < R(x) \leq L(z_2)$$

where the cencoring interval $(L(X), R(X)]$ of the covering $\vartheta(\cdot)$, contains $X$, and the random interval $\Delta^* = (R(z_1), L(z_2)]$ actually truncates $X$. When $(L(X), R(X)] \not\subset \Delta$ we do not have any observation. Without loss of generality, from now on, we assume that $a = 0$.

In the special case of right truncation

$$\triangle = (0, z]$$

and a summary of the observations on the subject under investigation is the triple of random variables $(L(x), R(x), L(z))$ such that:

$$0 \leq L(x) < R(x) \leq L(z).$$

## 3. The model

Let $X$ be a random variable with density $f$ and survival function defined by

$$S(t|\Xi = \xi) = P(X > t|\Xi = \xi) = e^{-e^{\beta'\xi}\Lambda(t)} \tag{5}$$

where $\beta \in R^p$ is the parameter of interest, $\Xi$ a $p$-dimensional vector of covariates and $\Lambda$ the cumulative hazard function which plays the role of the infinite-dimensional nuisance parameter.

Let us define

1) Conditionally on a fixed value $t$ of $\tau$ the random interval $\Delta$ is taken from the truncating distribution

$$\mathcal{P}_t\left\{A\right\} = P\left\{\Delta \in A \,|\text{the interval } (Z_1, Z_2] \text{ contains at least two points of } t\right\}.$$

In other words, conditionally on fixed values of $\tau = t$ the random vector $Z = (Z_1, Z_2)$ is taken from the truncating distribution

$$P_t\left\{B\right\} = P\left\{Z \in B \,|R(Z_1) < L(Z_2)\right\};$$

2) Conditionally on a fixed value of $\tau = t$ and $\Delta = \triangle = (z_1, z_2]$, the random variable $X$ is taken from the truncated distribution

$$P_{t,\triangle}\{C\} = P\{X \in C \,|\, X \in (R(z_1), L(z_2)]\}.$$

In other words conditionally on fixed values of $\tau = t$ and $Z_1 = z_1, Z_2 = z_2$ the random variable $X$ is taken from the truncated distribution

$$P\{C \,|\, t, z_1, z_2\} = P\{X \in C \,|\, X \in (R(z_1|t), L(z_2|t)]\}. \tag{6}$$

We consider now the simple case of right truncation by $Z$, where for a random variable $Z$ the random interval $\Delta = (0, Z]$. We shall denote for short when there is no ambiguity about the partition $\tau = t$ simply:

$$L(Z) := L(Z|\tau = t).$$

Then, conditionally on fixed values of $\tau = t$ and $Z = z$ the random variable $X$ is taken from the truncated distribution

$$P\{C|t, z\} = P\{X \in C \,|\, X \le L(z)\}.$$

## 4. Estimation of the parameter of interest

Without loss of generality we consider the right-truncation case. The problem that we are faced with could be formulated as follows. Let $W, W_1, \ldots, W_n$ be i.i.d. random vectors, $W = (L(X), R(X), L(Z), \Xi)$, with density $p(u, v, w, \xi)$ with respect to a measure $\mu_0$ (Huber, Solev and Vonta (2007)) given as

$$p(u, v, w, \xi) = r(u, v, w) \cdot \frac{\int_u^v f(t|\xi)\, dt}{\int_0^w f(t|\xi)\, dt} \cdot \phi(\xi)$$

which is equal from the semiparametric model (5) to

$$r(u, v, w) \cdot \frac{\int_u^v e^{-e^{\beta'\xi}\Lambda(t)} e^{\beta'\xi}\lambda(t)\, dt}{\int_0^w e^{-e^{\beta'\xi}\Lambda(t)} e^{\beta'\xi}\lambda(t)\, dt} \cdot \phi(\xi) \equiv r(u, v, w) \cdot \varphi(\beta, \lambda, u, v, w) \cdot \phi(\xi) \tag{7}$$

where $0 \leq u < v \leq w \leq b$, $\xi \in \Im$, $\phi(\xi)$ is the known law of the covariate $\Xi$, $\lambda$ the hazard intensity function and $r(u,v,w)$ the known joint law of censoring and truncation. The law $r$ has two components, one denoted by $r_3$ which is absolutely continuous with respect to the Lebesgue measure on $\mathbf{R}^3$ (corresponding to the case where $u < v < w$) and a second one, denoted by $r_2$ which is absolutely continuous with respect to the Lebesgue measure on $\mathbf{R}^2$ (corresponding to the case where $u < v = w$). For details and an example of such a law $r$ see Huber, Solev and Vonta (2007).

We are interested in the efficient estimation of the parameter of interest $\beta$ in the presence of the unknown cumulative hazard function $\Lambda$ or equivalently in the presence of the hazard intensity function $\lambda$ where obviously $\lambda(t) \geq 0$. We assume for $\Lambda(t)$ that it is finite for finite times $t$ and that $\Lambda(\infty) = \infty$. We will establish in this paper the form of the least favorable model $\Lambda_\beta$ for fixed values of $\beta$ following the methodology introduced in Slud and Vonta (2005).

In the notation of Slud and Vonta (2005), let the measure $\nu$ denote the Lebesgue measure on $\mathbf{R}$. The data-space $\mathbf{D} = \mathbf{R} \times \mathbf{R} \times \mathbf{R} \times \mathbf{R}^p$ consists of vectors $x = (u,v,w,\xi)'$ . We denote the true parameters by $(\beta_0, \lambda_0)$. We define the probability law for the true model by

$$d\mu(x) \equiv p_0(x) d\mu_0(x)$$

where $p_0(x)$ denotes the density $p$ taken at the true point $(\beta_0, \lambda_0)$.

The densities $f_W(x, \beta, \lambda)$ (Slud and Vonta (2005)) are of the form

$$\frac{\int_u^v e^{-e^{\beta'\xi}\Lambda(t)} e^{\beta'\xi} \lambda(t)\, dt}{\int_0^w e^{-e^{\beta'\xi}\Lambda(t)} e^{\beta'\xi} \lambda(t)\, dt} \times \frac{\int_0^w e^{-e^{\beta_0'\xi}\Lambda_0(t)} e^{\beta_0'\xi} \lambda_0(t)\, dt}{\int_u^v e^{-e^{\beta_0'\xi}\Lambda_0(t)} e^{\beta_0'\xi} \lambda_0(t)\, dt}. \tag{8}$$

**4.1. Least favorable model.** Following the methodology of Slud and Vonta (2005) we will find, for fixed $\beta$, the least favorable parametric submodel $(\Lambda_\beta, \beta)$ of the proposed semiparametric model.

The Kullback-Leibler functional is given by

$$\mathcal{K}(\beta, \lambda) = -\int \log\left( \frac{p(u,v,w,\xi;\beta,\lambda)}{p_0(u,v,w,\xi;\beta_0,\lambda_0)} \right) p_0(u,v,w,\xi;\beta_0,\lambda_0)\, d\mu_0(u,v,w,\xi).$$

Due to the form of the law $r(u,v,w)$ the Kullback-Leibler functional is written equivalently as

$$= -\int \log\left( \frac{p_3(u,v,w,\xi;\beta,\lambda)}{p_{0,3}(u,v,w,\xi;\beta_0,\lambda_0)} \right) p_{0,3}(u,v,w,\xi;\beta_0,\lambda_0)\, d\mu_{0,3}(u,v,w,\xi)$$

$$-\int \log\left(\frac{p_2(u,v,\xi;\beta,\lambda)}{p_{0,2}(u,v,\xi;\beta_0,\lambda_0)}\right) p_{0,2}(u,v,\xi;\beta_0,\lambda_0)\, d\mu_{0,2}(u,v,\xi)$$

which because of model (5) is equal to

$$-\int \Big\{ \log\left(\int_u^v e^{-e^{\beta'\xi}\Lambda(t)} e^{\beta'\xi}\lambda(t)dt\right) - \log\left(\int_0^w e^{-e^{\beta'\xi}\Lambda(t)} e^{\beta'\xi}\lambda(t)dt\right) \Big\}$$

$$p_{0,3}(u,v,w,\xi;\beta_0,\lambda_0)d\mu_{0,3}(u,v,w,\xi)$$

$$-\int \Big\{ \log\left(\int_u^v e^{-e^{\beta'\xi}\Lambda(t)} e^{\beta'\xi}\lambda(t)dt\right) - \log\left(\int_0^v e^{-e^{\beta'\xi}\Lambda(t)} e^{\beta'\xi}\lambda(t)dt\right) \Big\}$$

$$p_{0,2}(u,v,\xi;\beta_0,\lambda_0)d\mu_{0,2}(u,v,\xi) + C \tag{9}$$

where $C$ denotes a term that does not depend on $(\beta,\lambda)$.

Keeping $\beta$ fixed we will differentiate now with respect to the parameter $\lambda$ in the sense of Gâteaux differentiation. We consider perturbations of functions $\lambda \in \mathcal{V}$ by small multiples of functions $\gamma$ in subsets of $\mathcal{G} \subseteq \mathcal{G}_0$ for appropriately defined spaces $\mathcal{V}, \mathcal{G}$, and $\mathcal{G}_0$.

Here and in what follows, we define the differentiation operator $D_\lambda$ for all functionals $\Phi : \mathcal{V} \to \mathbf{R}$, and all $\gamma \in \mathcal{G}_0$, by:

$$(D_\lambda\, \Phi(\lambda))(\gamma) \;=\; \frac{d}{d\theta}\, \Phi(\lambda+\theta\gamma)\Big|_{\theta=0} \tag{10}$$

where $\theta$ belongs in a small neighborhood of 0. Let therefore $\lambda_\theta(t) = \lambda(t) + \theta\gamma(t)$ and subsequently $\Lambda_\theta(t) = \Lambda(t) + \theta\int_0^t \gamma(s)ds = \Lambda(t) + \theta\Gamma(t)$. The Gâteaux differentiation of $\mathcal{K}(\beta,\lambda)$ in the direction $\gamma$ is given as

$$\frac{d}{d\theta}\mathcal{K}(\beta,\lambda_\theta)|_{\theta=0} = -\int \Big\{ \frac{\int_u^v e^{-e^{\beta'\xi}\Lambda(t)} e^{\beta'\xi}(-\lambda(t)e^{\beta'\xi}\Gamma(t)+\gamma(t))dt}{\int_u^v e^{-e^{\beta'\xi}\Lambda(t)} e^{\beta'\xi}\lambda(t)dt}$$

$$-\frac{\int_0^w e^{-e^{\beta'\xi}\Lambda(t)} e^{\beta'\xi}(-\lambda(t)e^{\beta'\xi}\Gamma(t)+\gamma(t))dt}{\int_0^w e^{-e^{\beta'\xi}\Lambda(t)} e^{\beta'\xi}\lambda(t)dt}\Big\} p_{0,3}d\mu_{0,3}$$

$$-\int \Big\{ \frac{\int_u^v e^{-e^{\beta'\xi}\Lambda(t)} e^{\beta'\xi}(-\lambda(t)e^{\beta'\xi}\Gamma(t)+\gamma(t))dt}{\int_u^v e^{-e^{\beta'\xi}\Lambda(t)} e^{\beta'\xi}\lambda(t)dt}$$

$$-\frac{\int_0^v e^{-e^{\beta'\xi}\Lambda(t)}e^{\beta'\xi}(-\lambda(t)e^{\beta'\xi}\Gamma(t)+\gamma(t))dt}{\int_0^v e^{-e^{\beta'\xi}\Lambda(t)}e^{\beta'\xi}\lambda(t)dt}\Big\}p_{0,2}d\mu_{0,2}. \tag{11}$$

By an integration by parts, the integral

$$-\int_u^v e^{-e^{\beta'\xi}\Lambda(t)}e^{\beta'\xi}\lambda(t)e^{\beta'\xi}\Gamma(t)dt = \Gamma(t)e^{-e^{\beta'\xi}\Lambda(t)}e^{\beta'\xi}\Big|_u^v$$
$$-\int_u^v e^{-e^{\beta'\xi}\Lambda(t)}e^{\beta'\xi}\gamma(t)dt$$

and therefore the first numerator of (11) simplifies to $\Gamma(t)e^{-e^{\beta'\xi}\Lambda(t)}e^{\beta'\xi}\Big|_u^v$. By a similar integration by parts we simplify the other three numerators of (11) to get that

$$\frac{d}{d\theta}\mathcal{K}(\beta,\lambda_\theta)|_{\theta=0} = -\int\Big\{\frac{\Gamma(v)e^{-e^{\beta'\xi}\Lambda(v)}e^{\beta'\xi}-\Gamma(u)e^{-e^{\beta'\xi}\Lambda(u)}e^{\beta'\xi}}{\int_u^v e^{-e^{\beta'\xi}\Lambda(t)}e^{\beta'\xi}\lambda(t)dt}$$
$$-\frac{\Gamma(w)e^{-e^{\beta'\xi}\Lambda(w)}e^{\beta'\xi}-\Gamma(0)e^{-e^{\beta'\xi}\Lambda(0)}e^{\beta'\xi}}{\int_0^w e^{-e^{\beta'\xi}\Lambda(t)}e^{\beta'\xi}\lambda(t)dt}\Big\}p_{0,3}d\mu_{0,3}$$
$$-\int\Big\{\frac{\Gamma(v)e^{-e^{\beta'\xi}\Lambda(v)}e^{\beta'\xi}-\Gamma(u)e^{-e^{\beta'\xi}\Lambda(u)}e^{\beta'\xi}}{\int_u^v e^{-e^{\beta'\xi}\Lambda(t)}e^{\beta'\xi}\lambda(t)dt}$$
$$-\frac{\Gamma(v)e^{-e^{\beta'\xi}\Lambda(v)}e^{\beta'\xi}-\Gamma(0)e^{-e^{\beta'\xi}\Lambda(0)}e^{\beta'\xi}}{\int_0^v e^{-e^{\beta'\xi}\Lambda(t)}e^{\beta'\xi}\lambda(t)dt}\Big\}p_{0,2}d\mu_{0,2}.$$

Finally, we have

$$\frac{d}{d\theta}\mathcal{K}(\beta,\lambda_\theta)|_{\theta=0}$$
$$=\int\Big\{\frac{(\Gamma(u)S(u)-\Gamma(v)S(v))e^{\beta'\xi}}{S(u)-S(v)}+\frac{\Gamma(w)S(w)e^{\beta'\xi}}{1-S(w)}\Big\}p_{0,3}d\mu_{0,3}$$
$$+\int\Big\{\frac{(\Gamma(u)S(u)-\Gamma(v)S(v))e^{\beta'\xi}}{S(u)-S(v)}+\frac{\Gamma(v)S(v)e^{\beta'\xi}}{1-S(v)}\Big\}p_{0,2}d\mu_{0,2}.$$

The survival function $S(.)=S(.|\xi)$ but the dependence on $\xi$ is omitted for convenience of notation.

Then we set the above derivative equal to 0 to obtain the equation

$$\int \Big\{ \frac{(\Gamma(u)S(u) - \Gamma(v)S(v))e^{\beta'\xi}}{S(u) - S(v)} + \frac{\Gamma(w)S(w)e^{\beta'\xi}}{1 - S(w)} \Big\} p_{0,3} d\mu_{0,3} + \int \Big\{ \frac{(\Gamma(u)S(u) - \Gamma(v)S(v))e^{\beta'\xi}}{S(u) - S(v)} + \frac{\Gamma(v)S(v)e^{\beta'\xi}}{1 - S(v)} \Big\} p_{0,2} d\mu_{0,2} = 0 \tag{12}$$

which should hold $\forall \gamma \in \mathcal{G}_0$. Equation (12) defines implicitly the minimizer $\Lambda_\beta$ through which $\lambda_\beta$ is subsequently defined.

Now, as in Kosorok et al. (2004) we will define a recursive equation for $\Lambda_\beta(t)$ from equation (12) by considering directions $\gamma(s) = I_{s \in [0,t]} \lambda(s)$ where $t \in [0, b]$. Depending on the position of $t$ in relation to $u, v, w$ for $r = r_3$ and in relation to $u, v = w$ for $r = r_2$ respectively, we have different cases to consider. Equation (12) becomes

$$\begin{aligned}
&\int\limits_{0 \le t \le u < v < w \le b} \Lambda(t) \left(1 + \frac{S(w)}{1 - S(w)}\right) e^{\beta'\xi} p_{0,3} d\mu_{0,3} \\
&+ \int\limits_{0 \le u < t \le v < w \le b} \left( \frac{\Lambda(u)S(u) - \Lambda(t)S(v)}{S(u) - S(v)} + \frac{\Lambda(t)S(w)}{1 - S(w)} \right) e^{\beta'\xi} p_{0,3} d\mu_{0,3} \\
&+ \int\limits_{0 \le u < v < t \le w \le b} \left( \frac{\Lambda(u)S(u) - \Lambda(v)S(v)}{S(u) - S(v)} + \frac{\Lambda(t)S(w)}{1 - S(w)} \right) e^{\beta'\xi} p_{0,3} d\mu_{0,3} \\
&+ \int\limits_{0 \le u < v < w < t \le b} \left( \frac{\Lambda(u)S(u) - \Lambda(v)S(v)}{S(u) - S(v)} + \frac{\Lambda(w)S(w)}{1 - S(w)} \right) e^{\beta'\xi} p_{0,3} d\mu_{0,3} \\
&+ \int\limits_{0 \le t \le u < v \le b} \Lambda(t) \left(1 + \frac{S(v)}{1 - S(v)}\right) e^{\beta'\xi} p_{0,2} d\mu_{0,2} \\
&+ \int\limits_{0 \le u < t \le v \le b} \left( \frac{\Lambda(u)S(u) - \Lambda(t)S(v)}{S(u) - S(v)} + \frac{\Lambda(t)S(v)}{1 - S(v)} \right) e^{\beta'\xi} p_{0,2} d\mu_{0,2} \\
&+ \int\limits_{0 \le u < v < t \le b} \left( \frac{\Lambda(u)S(u) - \Lambda(v)S(v)}{S(u) - S(v)} + \frac{\Lambda(v)S(v)}{1 - S(v)} \right) e^{\beta'\xi} p_{0,2} d\mu_{0,2} = 0.
\end{aligned} \tag{13}$$

Collecting the terms that involve $\Lambda(t) \equiv \Lambda_\beta(t)$ which can be pulled out of the integrals and solving for $\Lambda_\beta(t)$ we obtain the recursive equation

$$
\begin{aligned}
\Lambda_\beta(t)\Big\{ & \int\limits_{0\le t\le u<v<w\le b} \left(1+\frac{S(w)}{1-S(w)}\right) e^{\beta'\xi} p_{0,3} d\mu_{0,3} \\
+ & \int\limits_{0\le t\le u<v\le b} \left(1+\frac{S(v)}{1-S(v)}\right) e^{\beta'\xi} p_{0,2} d\mu_{0,2} \\
- & \int\limits_{0\le u<t\le v<w\le b} \left(\frac{S(v)}{S(u)-S(v)}-\frac{S(w)}{1-S(w)}\right) e^{\beta'\xi} p_{0,3} d\mu_{0,3} \\
- & \int\limits_{0\le u<t\le v\le b} \left(\frac{S(v)}{S(u)-S(v)}-\frac{S(v)}{1-S(v)}\right) e^{\beta'\xi} p_{0,2} d\mu_{0,2} \\
+ & \int\limits_{0\le u<v<t\le w\le b} \left(\frac{S(w)}{1-S(w)}\right) e^{\beta'\xi} p_{0,3} d\mu_{0,3} \Big\} \\
= - & \int\limits_{0\le u<t\le v<w\le b} \left(\frac{\Lambda_\beta(u)S(u)}{S(u)-S(v)}\right) e^{\beta'\xi} p_{0,3} d\mu_{0,3} \\
- & \int\limits_{0\le u<t\le v\le b} \left(\frac{\Lambda_\beta(u)S(u)}{S(u)-S(v)}\right) e^{\beta'\xi} p_{0,2} d\mu_{0,2} \\
- & \int\limits_{0\le u<v<t\le w\le b} \left(\frac{\Lambda_\beta(u)S(u)-\Lambda_\beta(v)S(v)}{S(u)-S(v)}\right) e^{\beta'\xi} p_{0,3} d\mu_{0,3} \\
- & \int\limits_{0\le u<v<w<t\le b} \left(\frac{\Lambda_\beta(u)S(u)-\Lambda_\beta(v)S(v)}{S(u)-S(v)}+\frac{\Lambda_\beta(w)S(w)}{1-S(w)}\right) e^{\beta'\xi} p_{0,3} d\mu_{0,3} \\
- & \int\limits_{0\le u<v<t\le b} \left(\frac{\Lambda_\beta(u)S(u)-\Lambda_\beta(v)S(v)}{S(u)-S(v)}+\frac{\Lambda_\beta(v)S(v)}{1-S(v)}\right) e^{\beta'\xi} p_{0,2} d\mu_{0,2}.
\end{aligned}
\tag{14}
$$

Equation (14) can be rewritten as

$$\Lambda_\beta(t) = \frac{I_1(t,b,\beta)}{I_2(t,b,\beta)} \tag{15}$$

where

$$I_1(t,b,\beta) = E_{p_0}\left(\frac{\Lambda_\beta(R(X))S(R(X))e^{\beta'\Xi}}{S(L(X)) - S(R(X))}\Big| R(X) > t\right)$$
$$- E_{p_0}\left(\frac{\Lambda_\beta(L(X))S(L(X))e^{\beta'\Xi}}{S(L(X)) - S(R(X))}\Big| L(X) > t\right)$$
$$- E_{p_0}\left(\frac{\Lambda_\beta(L(Z))S(L(Z))e^{\beta'\Xi}}{1 - S(L(Z))}\Big| L(Z) > t\right)$$

and

$$I_2(t,b,\beta) = E_{p_0}\left(e^{\beta'\Xi}\Big| L(X) \geq t\right)$$
$$+ E_{p_0}\left(\frac{\Lambda_\beta(L(Z))S(L(Z))e^{\beta'\Xi}}{1 - S(L(Z))}\Big| L(Z) \geq t\right)$$
$$- E_{p_0}\left(\frac{\Lambda_\beta(R(X))S(R(X))e^{\beta'\Xi}}{S(L(X)) - S(R(X))}\Big| L(X) < t \leq R(X)\right).$$

The least favorable direction $\gamma$ is defined (Slud and Vonta (2005)) implicitly through equation (15) as $\nabla_\beta \frac{d\Lambda_\beta(t)}{dt}|_{\beta=\beta_0} = \nabla_\beta \lambda_\beta(t)|_{\beta=\beta_0}$.

## References


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