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ESTIMATING THE CONVOLUTION OF DISTRIBUTIONS UNDER THE PARTIAL KOZIOL-GREEN MODEL OF RANDOM CENSORSHIP

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Abstract

We consider the convolution of distributions estimation problem with randomly right censored data under the partial Koziol-Green (PKG) model, which allows the lifetimes to be censored by two types of variables, one of which censors in an informative way and the other in a non-informative way. In this paper, an estimator is proposed for the convolution of distribution functions under the PKG model. Our estimator uses the partial ACL estimator for the survival function under the PKG model instead of the product limit estimator of Kaplan and Meier [7] that is used in Lagakos and Reid [9]. The asymptotic distribution of the new estimator is established.

1. Introduction

In medical follow-up studies, one is often interested in the evaluation of two or more time-dependent stochastic events and their relationships to one another when data are possibly censored. One problem of interest is to estimate the convolution of distributions. For example, in a clinical trial one studies time until disease regression, T_1, duration of disease regression, T_2, and total time to relapse,

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$T = T_1 + T_2$. If the distribution functions of T_1 and T_2 are F_1 and F_2, and T_1 and T_2 are independent, then the distribution function of T is the ordinary convolution of F_1 and F_2, that is,

$$F_1 * F_2(t) = \int_0^t F_1(t-x)\,dF_2(x). \tag{1.1}$$

We consider here estimation of the convolution of two distribution functions. Extensions to three or more distribution functions are straightforward.

In survival analysis, it is typical that the data are censored. Under the general random censoring (GRC) model, Lagakos and Reid [9] proposed an estimator for the convolution of two distribution functions which used the product limit estimators of the distribution functions, and developed the asymptotic properties of the estimator.

Although in many survival studies, the censoring is assumed non-informative, there are situations, where the censoring contains additional information about the distribution of the lifetimes we are interested and is hence called *informative*. The Koziol-Green (KG) model is a well-known model of informative censoring. Koziol and Green [8] gave an example involving a clinical trial of treatments for prostatic cancer. In the KG model, one assumes that the lifetime distribution function F and the censoring distribution function G satisfy $1 - G = (1 - F)^{\alpha}$. Under the KG model, Abdushukurov [1] and Cheng and Lin [3, 4] independently proposed the maximum likelihood estimator (MLE) of the survival distribution function, namely, Abdushukurov-Cheng-Lin (ACL) estimator, and discussed the advantage of using the MLE instead of the product limit estimator (PLE) of Kaplan and Meier [7].

The KG model does have some attractive statistical properties. However, the assumptions of the KG model are restrictive in the sense that all censored observations are assumed to be informatively censored. Gather and Pawlitschko [5] introduced an extension of the KG model, the partial Koziol-Green (PKG) model, where two types of censoring occur, one non-informative and the other informative as in the KG model. We refer to Gather and Pawlitschko [5] and Braekers and Veraverbeke [2] for examples of real data sets fitting the partial Koziol-Green model.

Under the PKG model, Gather and Pawlitschko [5] proposed a consistent nonparametric estimator of the survival function, namely, partial ACL (PACL) estimator, which is an analogue to the ACL estimator. It has been shown in Gather arid Pawlitschko [5] that the PACL estimator is asymptotically more efficient than the product limit estimator (PLE) of Kaplan and Meier [7] under the assumptions of the PKG model. Zhang [13] has shown that the PACL estimator in the PKG model is the least dispersed regular estimator.

In this paper, we propose an estimator for the convolution of two distribution functions which uses the PACL estimator of the survival function instead of the PLE that is used in Lagakos and Reid [9] under the PKG model of random censorship and establish the asymptotic distribution of the estimator of the convolution.

Section 2 proposes the estimator for the convolution under the PKG model. Section 3 gives the asymptotic distribution of the new estimator.

2. Proposed Estimator under the PKG Model

Let Y_{ij} denote the jth independent observation drawn from the ith population, where $j = 1, \ldots, n_i$, $i = 1, 2,$ and let C_{ij} denote the censoring value corresponding to Y_{ij}. In the right censoring model, one cannot observe Y_{ij}'s but one observes

$$Z_{ij} = Y_{ij} \wedge C_{ij}, \quad \delta_{ij} = I(Y_{ij} \leq C_{ij}), \tag{2.1}$$

where $x \wedge y$ denotes the minimum of x and y, and I denotes the indicator function. We say that the observation Z_{ij} is uncensored if $\delta_{ij} = 1$ and censored if $\delta_{ij} = 0.$ Denote $S_i(t) = P(X_{ij} > t)$ the survival function for the ith population, and $F_i = 1 - S_i$ the distribution function of the survival times. Denote $G_i(t) = P(C_{ij} \leq t)$ the distribution function of censoring times. We assume that F_i and G_i are continuous and $Y_{i1}, \ldots, Y_{in_i}$ are independent of $C_{i1}, \ldots, C_{in_i}$, $i = 1, 2.$

In the general right censoring model, the most commonly used estimator of F_i is the product limit estimator of Kaplan and Meier [7] given as

$$\hat{F}_i(t) = 1 - \prod_{j:Z_{(ij)} \leq t} \{(n_i - j)/(n_i - j + 1)\}^{\delta(ij)}, \quad i = 1, 2, \tag{2.2}$$

where $Z_{(i1)} \leq Z_{(i2)} \leq \cdots \leq Z_{(in_i)}$ are the ordered observations in the ith sample with the convention that no censored observation precedes an uncensored observation of equal value, and reassigning the remaining mass to the largest observation $Z_{(in_i)}$ if it is censored and therefore $\hat{F}_i(y) = 1$ for $y > Z_{(in_i)}$, $i = 1, 2$. $\delta_{(ij)}$ is the value of δ_{ij} associated with $Z_{(ij)}$, that is, $\delta_{(ij)} = \delta_{ik}$ when $Z_{(ij)} = Z_{ik}$.

Lagakos and Reid [9] proposed an estimator for the convolution of F_1 and F_2, $F_1 * F_2(t)$, which is actually the ordinary convolution of the product limit estimates $\hat{F}_1$ and $\hat{F}_2$ given by (2.2), that is,

$$\hat{F}^*_{12}(t) = \int_0^t \hat{F}_1(t - x) d\hat{F}_2(x). \tag{2.3}$$

Lagakos and Reid [9] have shown that $\hat{F}^*_{12}(t)$ is strongly consistent for the convolution of F_1 and F_2, $F_1 * F_2(t)$ and calculated the asymptotic variance of the estimator.

An important particular case of the general right random censoring model is the so-called Koziol-Green model in which F_i and G_i are connected by the assumption that for some constant $\alpha_i > 0$,

$$1 - G_i = (1 - F_i)^{\alpha_i}, \quad i = 1, 2, \tag{2.4}$$

where α_i is referred to as the censoring parameter for the *i*th population. The case $\alpha_i = 0$ corresponds to no censoring. Indeed $\gamma_i = P(Y_{ij} \leq C_{ij}) = \int_{-\infty}^{\infty} \{1 - G_i(t)\} dF_i(t)$ $= 1/(1 + \alpha_i)$ is the expected proportion of uncensored observations in the *i*th sample. An important characterization of the KG model is that (2.4) holds if and only if Z_{ij} and δ_{ij} are independent, $j = 1, \ldots, n_i$.

Let H_i denote the distribution function of the observable Z_{ij}, $j = 1, \ldots, n_i$. By independence, we have

$$1 - F_i = (1 - H_i)^{\gamma_i}, \quad i = 1, 2. \tag{2.5}$$

Under the KG model, Abdushukurov [1] and Cheng and Lin [3, 4] independently proposed the maximum likelihood estimator, the ACL estimator, of F_i, given by

$$1 - F_{i,\,\mathrm{ACL}}(t) = (1 - H_{in_i}(t))^{\gamma_{in_i}}, \tag{2.6}$$

where H_{in_i} is the empirical distribution function of Z_{ij}, that is,

$$H_{in_i}(t) = \frac{1}{n_i} \sum_{j=1}^{n_i} I(Z_{ij} \le t), \tag{2.7}$$

and

$$\gamma_{in_i} = \frac{1}{n_i} \sum_{j=1}^{n_i} \delta_{ij} \tag{2.8}$$

is the sample proportion of uncensored observations in the *i*th sample.

The partial Koziol-Green model is a generalization of the KG model. In the PKG model, the *j*th independent observation of the lifetime variable from the *i*th population Y_{ij} is subject to random right censoring by the minimum of two independent variables C_{ij} and D_{ij}, where C_{ij} is an informative censoring time in the sense that it satisfies the KG model and D_{ij} is an arbitrary non-informative censoring time, where $j = 1, \ldots, n_i$, $i = 1, 2$. Y_{ij}'s, C_{ij}'s and D_{ij}'s are assumed to be independent with distribution functions F_i, G_i, and M_i, respectively, and G_i is related to F_i by

$$1 - G_i = (1 - F_i)^{\alpha_i}, \quad i = 1, 2, \tag{2.9}$$

for some constant $\alpha_i > 0$. For $j = 1, \ldots, n_i$, $i = 1, 2$, we only observe

$$Z_{ij} = Y_{ij} \wedge C_{ij} \wedge D_{ij},$$

$$\delta_{ij} = \begin{cases} 1 & \text{if } Y_{ij} \le C_{ij} \wedge D_{ij}, \\ 0 & \text{if } C_{ij} \le Y_{ij} \wedge D_{ij}, \\ -1 & \text{if } D_{ij} \le Y_{ij} \wedge C_{ij}. \end{cases} \tag{2.10}$$

Certain conventions in the definition of δ_{ij} are adopted as follows. If $Y_{ij} \wedge C_{ij}$

$\wedge D_{ij} = Y_{ij}$ and even if C_{ij} or D_{ij} equals to Y_{ij}, then we take $\delta_{ij} = 1$. If $Y_{ij} \wedge C_{ij} \wedge D_{ij} = C_{ij}$ and even if $C_{ij} = D_{ij}$, then we take $\delta_{ij} = 0$.

Let $(Z_{i1}, \delta_{i1}), (Z_{i2}, \delta_{i2}), \dots, (Z_{in_i}, \delta_{in_i})$ be n_i independent realizations of (Z_i, δ_i) in the ith sample, $i = 1, 2$, $Z_{(i1)} \le Z_{(i2)} \le \cdots \le Z_{(in_i)}$ be the ordered values of $Z_{i1}, Z_{i2}, \dots, Z_{in_i}$, and $\delta_{[ij]}$, $j = 1, 2, \dots, n_i$ be the concomitant δ-values of the ordered Z_{ij}'s. Let $U_{ij} = Y_{ij} \wedge C_{ij}$, $j = 1, 2, \dots, n_i$, and L_i be the distribution function of the U_{ij}'s. Then

$$1 - F_i = (1 - L_i)^{\gamma_i}, \quad i = 1, 2, \tag{2.11}$$

where $\gamma_i = 1/(1 + \alpha_i)$.

Let $p_{ik} = P(\delta_{i1} = k)$, $k = -1, 0, 1$. Then $\alpha_i = p_{i0}/p_{i1}$, $i = 1, 2$. Hence

$$\gamma_i = p_{i1}/(p_{i1} + p_{i0})$$

is the probability of an uncensored observation conditional on the event that this observation is either uncensored or informatively censored for the ith population.

Gather and Pawlitschko [5] gave the partial ACL estimator of the distribution function F_i of lifetime variable Y_{ij}, $i = 1, 2$,

$$1 - \tilde{F}_i(t) = (1 - L_{i,\mathrm{KM}}(t))^{\hat{\gamma}_i}, \tag{2.12}$$

where $L_{i,\mathrm{KM}}$ is the Kaplan-Meier estimator of L_i, $i = 1, 2$,

$$1 - L_{i,\mathrm{KM}}(t) = \prod_{j=1}^{n_i} \left(1 - \frac{\eta_{[ij]}}{n_i - j + 1}\right)^{I[Z_{(ij)} \le t]}, \tag{2.13}$$

where $\eta_{ij} = I[U_{ij} \le D_{ij}] = I[\delta_{ij} \ne -1]$, $j = 1, 2, \dots, n_i$, $\eta_{[ij]}$, $j = 1, 2, \dots, n_i$, is the concomitant η-values of the ordered Z_{ij}'s, and

$$\hat{\gamma}_i = \frac{\sum_{j=1}^{n_i} I[\delta_{ij} = 1]}{\sum_{j=1}^{n_i} I[\delta_{ij} \ne -1]}, \quad i = 1, 2, \tag{2.14}$$

which is actually the MLE of γ_i.

Now we propose the estimator for the convolution of F_1 and F_2 when the PKG model holds, which is actually the ordinary convolution of the PACL estimators $\tilde{F}_1$ and $\tilde{F}_2$, that is,

$$\tilde{F}_{12}^*(t) = \int_0^t \tilde{F}_1(t - x) d\tilde{F}_2(x), \tag{2.15}$$

where $\tilde{F}_i$ is defined by (2.12), $i = 1, 2$.

3. Asymptotic Distribution

To derive the asymptotic distribution of $\tilde{F}_{12}^*(t)$ under the PKG model, we use the influence function (or influence curve) of the estimator regarded as a bivariate functional of the PACL estimators $\tilde{F}_1$ and $\tilde{F}_2$, say $T(\tilde{F}_1, \tilde{F}_2)$. Influence function of a statistical functional is the first derivative of the functional evaluated at some point in the space of distribution functions. A von Mises functional is a functional sufficiently regular to have a series expansion in functional derivatives. For discussions of von Mises expansions and influence functions see, for example, von Mises [12], Hampel [6], Reeds [11] and Lambert [10].

If *T* is a von Mises functional and *V* is a distribution function, then the influence function $\mathrm{IF}(x;\, T, V)$ of *T* at *V* is given by

$$\mathrm{IF}(x;\, T, V) = \lim_{\varepsilon \downarrow 0} \frac{T((1 - \varepsilon)V + \varepsilon\Delta_x) - T(V)}{\varepsilon} \tag{3.1}$$

for $x \in R$, for which this limit exists, where Δ_x denotes the distribution function that puts all its probability mass at the point *x*. If some distribution function *W* is “near” *V*, then

$$T(W) = T(V) + \int \mathrm{IF}(x;\, T, V)\, d(W - V)(x) + \text{higher order terms}, \tag{3.2}$$

where

$$\int \mathrm{IF}(x;\, T, V)\, d(W - V)(x) = \frac{d}{d\varepsilon} T(V + \varepsilon(W - V))\Big|_{\varepsilon=0}. \tag{3.3}$$

For bivariate functionals $T(V_1, V_2)$, the bivariate von Mises expansion is

$$T(W_1, W_2) = T(V_1, V_2) + \int \mathrm{IF}_1(x; T, V_1, V_2)\, d(W_1 - V_1)(x)$$

$$+ \int \mathrm{IF}_2(x; T, V_1, V_2)\, d(W_2 - V_2)(x) + \text{higher order terms}, \quad (3.4)$$

where some distribution functions W_1 and W_2 are "near" distribution functions V_1 and V_2, respectively, and

$$\int \mathrm{IF}_1(x; T, V_1, V_2)\, d(W_1 - V_1)(x)$$

$$= \frac{\partial}{\partial \varepsilon} T(V_1 + \varepsilon(W_1 - V_1), V_2 + \delta(W_2 - V_2))\Big|_{\varepsilon=0,\, \delta=0}, \quad (3.5)$$

$$\int \mathrm{IF}_2(x; T, V_1, V_2)\, d(W_2 - V_2)(x)$$

$$= \frac{\partial}{\partial \delta} T(V_1 + \varepsilon(W_1 - V_1), V_2 + \delta(W_2 - V_2))\Big|_{\varepsilon=0,\, \delta=0}. \quad (3.6)$$

We also need the following result to derive the asymptotic distribution of $\tilde{F}^*_{12}(t)$. Let $\tilde{F}_i$ denote the PACL estimator of F_i, as defined in (2.12), H_i denote the distribution function of Z_{ij}, $U_{ij} = Y_{ij} \wedge C_{ij}$, $j = 1, 2, \dots, n_i$, L_i denote the distribution function of the U_{ij}'s, $p_{ik} = P(\delta_{i1} = k)$, $k = -1, 0, 1$, $\gamma_i = p_{i1}/(p_{i1} + p_{i0})$ denote the probability of an uncensored observation conditional on the event that this observation is either uncensored or informatively censored for the ith population, for $i = 1, 2$, and let $\tau_M = \inf\{t : M(t) = 1\}$. Then

Lemma 3.1. *Assume that* F_i *is continuous on* $[0, \infty]$, $i = 1, 2$, *and the PKG model defined by* (2.9) *and* (2.10) *holds. Then, for* $T < \tau_{H_i}$, *the sequence of random functions* $\{n_i^{1/2}[\tilde{F}_i(t) - F_i(t)], 0 \le t \le T\}$ *converges weakly to the Gaussian process* $\xi_i(t)$ *with* $E\xi_i(t) = 0$, $i = 1, 2$. *For* $0 \le s$, $t \le T < T_{H_i}$,

$$\mathrm{cov}(\xi_i(s), \xi_i(t))$$

$$= \overline{F}_i(s)\overline{F}_i(t)\left(\gamma_i R_i(s \wedge t) + [\ln \overline{L}_i(s)][\ln \overline{L}_i(t)]\frac{\gamma_i(1 - \gamma_i)}{p_{i1} + p_{i0}}\right), \quad i = 1, 2, \quad (3.7)$$

where

$$R_i(s) = \int_0^s \frac{dF_i}{\overline{F}_i \overline{H}_i}, \quad i = 1, 2, \quad s \geq 0. \tag{3.8}$$

The proof of this lemma can be found in the proof of Theorem 4.4 of Gather and Pawlitschko [5]. We now give the asymptotic distribution of the estimator for the convolution, $\tilde{F}_{12}^*(t)$, under the PKG model.

Theorem 3.1. *Assume that* F_i *is continuous on* $[0, \infty]$, $i = 1, 2$, *the PKG model defined by* (2.9) *and* (2.10) *holds,* $n_i/n \to \lambda_i \in (0, 1)$ *as* $n = n_1 + n_2 \to \infty$, *for* $i = 1, 2$, *where* $\lambda_1 + \lambda_2 = 1$, $0 < t < \tau_{H_1} \wedge \tau_{H_2}$. *Then*

$$\sqrt{n}\left(\int_0^t \tilde{F}_1(t-x)d\tilde{F}_2(x) - \int_0^t F_1(t-x)dF_2(x)\right) \Rightarrow N(0, \sigma^2), \quad as \quad n \to \infty, \tag{3.9}$$

where

$$\sigma^2 = \frac{1}{\lambda_1}\sigma_1^2 + \frac{1}{\lambda_2}\sigma_2^2, \tag{3.10}$$

where

$$\sigma_i^2 = 2\int\int_{0<x\leq y\leq t} Q_i(x, y)dF_{3-i}(t-x)dF_{3-i}(t-y), \quad i = 1, 2, \tag{3.11}$$

and $Q_i(x, y) = \mathrm{cov}(\xi_i(x), \xi_i(y))$ *as given by* (3.7).

Proof. $\tilde{F}_{12}^*(t)$ can be viewed as a bivariate statistical functional of $\tilde{F}_1$ and $\tilde{F}_2$, $T(\tilde{F}_1, \tilde{F}_2)$, that is,

$$T(\tilde{F}_1, \tilde{F}_2) = \int_0^t \tilde{F}_1(t-x)d\tilde{F}_2(x). \tag{3.12}$$

Since $\tilde{F}_i - F_i = O_p(n_i^{-1/2})$ (Gather and Pawlitschko [5]), $i = 1, 2$, by using (3.4)-(3.6), we obtain the bivariate von Mises expansion

$$T(\tilde{F}_1, \tilde{F}_2) = T(F_1, F_2) + \int_0^t \mathrm{IF}_1(x; T, F_1, F_2)d(\tilde{F}_1 - F_1)(x)$$

$$+ \int_0^t \mathrm{IF}_2(x; T, F_1, F_2)d(\tilde{F}_2 - F_2)(x) + \text{higher order terms},$$

$$= T(F_1, F_2) + \int_0^t (\tilde{F}_1 - F_1)(t-x)\,dF_2(x)$$

$$+ \int_0^t F_1(t-x)\,d(\tilde{F}_2 - F_2)(x) + \text{higher order terms}, \tag{3.13}$$

where the higher order terms are $o_p(n^{-1/2})$. Therefore, we can write

$$\sqrt{n}(T(\tilde{F}_1, \tilde{F}_2) - T(F_1, F_2)) = \sqrt{\frac{n}{n_1}}\,\phi_{n_1}(t) + \sqrt{\frac{n}{n_2}}\,\psi_{n_2}(t) + o_p(1), \tag{3.14}$$

where

$$\phi_{n_1}(t) = \sqrt{n_1}\left(\int_0^t \tilde{F}_1(t-x)\,dF_2(x) - \int_0^t F_1(t-x)\,dF_2(x)\right), \tag{3.15}$$

$$\psi_{n_2}(t) = \sqrt{n_2}\left(\int_0^t F_1(t-x)\,d\tilde{F}_2(x) - \int_0^t F_1(t-x)\,dF_2(x)\right). \tag{3.16}$$

Without loss of generality, we assume that $F_i(0) = 0$ and $\tilde{F}_i(0) = 0$, $i = 1, 2$. Then we have $\int_0^t F_1(t-x)\,d\tilde{F}_2(x) = \int_0^t \tilde{F}_2(t-x)\,dF_1(x)$ and $\int_0^t F_1(t-x)\,dF_2(x) = \int_0^t F_2(t-x)\,dF_1(x)$. Hence, by Lemma 3.1,

$$\phi_{n_1}(t) = -\sqrt{n_1}\left(\int_0^t \tilde{F}_1(x)\,dF_2(t-x) - \int_0^t F_1(x)\,dF_2(t-x)\right)$$

$$= -\int_0^t \varphi_1(x)\,dF_2(t-x)$$

$$\Rightarrow N(0, \sigma_1^2), \quad \text{as} \quad n \to \infty, \tag{3.17}$$

where $\varphi_i(x) = \sqrt{n_i}(\tilde{F}_i(x) - F_i(x))$, $i = 1, 2$, and σ_1^2 is given by (3.11) with $i = 1$.

By Lemma 3.1, we also have

$$\psi_{n_2}(t) = \sqrt{n_1}\left(\int_0^t \tilde{F}_2(t-x)\,dF_1(x) - \int_0^t F_2(t-x)\,dF_1(x)\right)$$

$$= -\sqrt{n_1}\left(\int_0^t \tilde{F}_2(x)\,dF_1(t-x) - \int_0^t F_2(x)\,dF_1(t-x)\right)$$

$$= -\int_0^t \varphi_2(x)\,dF_2(t-x)$$

$$\Rightarrow N(0, \sigma_2^2), \quad \text{as} \quad n \to \infty, \tag{3.18}$$

where σ_2^2 is given by (3.11) with $i = 2$.

Note that $\phi_{n_1}(t)$ and $\psi_{n_2}(t)$ are independent, $n/n_i \to 1/\lambda_i$ as $n \to \infty$, for $i = 1, 2$. Consequently, from (3.14), (3.17) and (3.18), we conclude Theorem 3.1. □

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