Small-Sample Results for the Kaplan-Meier Estimator

by

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SMALL-SAMPLE RESULTS FOR THE KAPLAN-MEIER ESTIMATOR

Y. Y. CHEN, M. HOLLANDER, AND N. A. LANGBERG

Whereas much is known about the asymptotic properties of the Kaplan-Meier (1958) estimator (KME) of a survival function, exact results for small samples have been difficult to obtain. In this note, we obtain an exact expression for the $\alpha$th moment ($\alpha > 0$) of the $\hat{K}\hat{M}\hat{E}$ under a model of proportional hazards. This enables us, under proportional hazards, to (1) study the bias of the $\hat{K}\hat{M}\hat{E}$, and (2) compare the exact variance of the $\hat{K}\hat{M}\hat{E}$ to its asymptotic variance. We also characterize the proportional hazards model.

KEY WORDS: Censoring; Incomplete data; Kaplan-Meier estimator; Proportional hazards.
1. INTRODUCTION

Let \( X_1, \ldots, X_n \) be independent and identically distributed random variables denoting "lifelengths" with a common continuous "failure" distribution function \( F \), and let \( Y_1, \ldots, Y_n \) be independent and identically distributed "times-to-censorship" random variables with a common continuous distribution function \( H \). (We assume that \( (X_1, Y_1), \ldots, (X_n, Y_n) \) is an independent and identically distributed sequence of random pairs with independent nonnegative components defined on a common probability space.) Let \( I(A) \) denote the indicator function of the set \( A \), let \( Z_i = \min(X_i, Y_i) \), and \( \delta_i = I(X_i \leq Y_i) \), \( i = 1, \ldots, n \). Kaplan and Meier (1958) and Efron (1967) considered the problem of estimating \( \bar{F} = 1 - F \), the underlying survival function, from the "incomplete" sample \( (Z_1, \delta_1), \ldots, (Z_n, \delta_n) \).

This estimation problem can arise in various contexts, including:

(i) **Reliability models:** Suppose one is studying a two-component system and the system is a series system; i.e., the system functions if and only if both components are functioning. Here the \( Z \)'s are the times to failure of the system, and the \( \delta \)'s tell us whether the failure of component 1 or component 2 caused the failure of the system. On the basis of the \( Z \)'s and the \( \delta \)'s we wish to estimate \( F \), the failure distribution of component 1.

(ii) **Clinical trials:** Here \( X \) can be the time to the occurrence of an end-point event (such as relapse) and the data are analyzed before all patients have experienced the event. The lifelength is not observed if the patient has not experienced the end-point event by the time the data are analyzed.
(iii) Competing risks: A group of individuals, suffering from the same fatal disease, are under treatment for the disease and are studied from beginning of treatment to death. However, the patient is at risk to other (secondary) causes of death. The "lifelength", corresponding to the length of time from onset of treatment (for the disease under study) until death from the disease in the absence of secondary disorders, is not observed if the patient's death is due to any of the secondary causes.

The Kaplan-Meier estimator (KME), which can be applied in the preceding situations as well as in other contexts, can be defined as follows. Let \( K_n(t) \) denote the empirical distribution function of the \( Z \)'s, \( K_n(t) = n^{-1} \sum_{q=1}^{n} I(Z_q \leq t) \), and let \( \bar{F}_n(t) = 1 - K_n(t) \). Then, under our continuity assumptions, the KME \( \bar{F}_n(t) \) can be written as

\[
\bar{F}_n(t) = \prod_{i=1}^{nK(t)} \delta_i \prod_{i=1}^{c_{in}} I(Z(n) \geq t), \; t \in (-\infty, \infty),
\]

where \( c_{in} = (n - i)(n - i + 1)^{-1}, Z(n) = \max(Z_1, ..., Z_n) \) and where here, and throughout the paper, a product over an empty set of indices is defined to be 1.

Large sample properties of the KME have been studied by many authors. In particular, weak convergence of the KME (regarded as a stochastic process) has been established by Efron (1967), Breslow and Crowley (1974), and Meier (1975). Strong consistency of the KME is proved by Peterson (1977) and Langberg, Proschan, and Quinzi (1980). (Peterson (1977) also gives a good review of properties of the KME.) Small-sample exact results for the KME have received little
attention. In this note we obtain exact small-sample results for the KME under a model of proportional hazards.

Section 2 defines the proportional hazards model, characterizes the model (Theorem 2.1), and motivates the model. In Section 3 we give an exact expression for the $\alpha$th moment ($\alpha > 0$) of the KME under proportional hazards. Using this expression we can, under proportional hazards, study the bias of the KME, investigate Efron's (1967) bounds for the bias, and compare the exact variance of the KME to its asymptotic variance.

2. PROPORTIONAL HAZARDS MODELS

We define a proportional hazards model. Let $(U_1, U_2)$ be a pair of independent nonnegative random variables with continuous distribution functions $G_1, G_2$ respectively. Further, let $\alpha(t) = \sup \{ t : G_q(t) < 1 \}$, and let $R_q(t) = -\ln G_q(t)$, $t \in (-\infty, \alpha(G_q))$, be the hazard function corresponding to the distribution function $G_q$, $q = 1, 2$.

Definition 2.1: We say that the pair $(U_1, U_2)$ follows a proportional hazards model if there is a positive real number $\beta$ such that

$$\bar{G}_2(t) = \{\bar{G}_1(t)\}^\beta \text{ for } t \in [0, \infty). \quad (2.1)$$

Note that from (2.1), $\alpha(G_1) = \alpha(G_2)$, and the hazard functions corresponding to $G_1, G_2$ are proportional, i.e.,

$$R_1(t) = \beta R_2(t), \quad t \in [0, \alpha(G_1)).$$
Theorem 2.1 characterizes the proportional hazards model.

**Theorem 2.1:** The pair $(U_1, U_2)$, $0 < P(U_1 \leq U_2) < 1$, follows a proportional hazards model if and only if

The random variables $U = \min(U_1, U_2)$, and $\xi = I(U_1 \leq U_2)$ are independent. \hfill(2.2)

**Proof:** Let $G$ be a continuous distribution function, let $\bar{G} = 1 - G$, and assume that $G(0) = 0$. Then for $\theta \in (-1, \infty)$, and $z \in [0, \alpha(G))$, we find

$$\int_{-\ln(\bar{G}(z))}^{\infty} \frac{(1 + \theta)^{-1}(\bar{G}(z))^{\theta+1}}{\bar{G}(z)} = \left\{\begin{array}{ll}
(1 + \theta)^{-1}(\bar{G}(z))^{\theta+1}, & \theta > -1, \\
-\ln(\bar{G}(z)), & \theta = -1.
\end{array}\right. \hfill(2.3)$$

First we prove that (2.1) implies (2.2). To verify (2.2) it suffices to show that, for $z \in [0, \infty)$,

$$P(U > z, \xi = 1) = P(U > z)P(\xi = 1). \hfill(2.4)$$

By (2.1) and (2.3),

$$P(U > z, \xi = 1) = \int_{z}^{\infty} (\bar{G}(u))^{\beta+1} dG_1(u) = \int_{z}^{\infty} (\bar{G}(u))^{\beta+1} dG_1(u) \hfill(2.5)$$

$$= (1 + \beta)^{-1}(\bar{G}(z))^{\beta+1} = (1 + \beta)^{-1}P(U > z).$$

In particular $P(\xi = 1) = P(U > 0, \xi = 1) = (1 + \beta)^{-1}$. Thus, from (2.5) we see that (2.4) holds. Consequently (2.1) implies (2.2).

Now we show that (2.2) implies (2.1). Let $\gamma = P(U_1 \leq U_2)$. By (2.2) we have

$$\gamma \bar{G}_1(z)\bar{G}_2(z) = \int_{z}^{\infty} \bar{G}_2(u) d\bar{G}_1(u), \ z \in [0, \infty).$$
Upon integration by parts we obtain
\[ \gamma \int_{0}^{\infty} g_1(u) dG_2(u) = (1 - \gamma) \int_{0}^{\infty} g_2(u) dG_1(u), \quad z \in [0, \infty). \tag{2.6} \]

Now (2.6) implies, for \( z \in [0, \min(\alpha(G_1), \alpha(G_2)) \), that
\[ \gamma \int_{0}^{z} \{g_2(u)\}^{-1} dG_2(u) = (1 - \gamma) \int_{0}^{z} \{g_1(u)\}^{-1} dG_1(u). \tag{2.7} \]

By (2.3) and (2.7), for \( t \in [0, \min(\alpha(G_1), \alpha(G_2)) \), we obtain
\[ g_2(t) = \{g_1(t)\}^{(1 - \gamma)\gamma^{-1}}. \]

Consequently (2.2) implies (2.1).

Sethuraman (1965) gives results that are related to, but different than, Theorem 2.1.

Proportional hazards models have been used in censored data problems both to derive procedures for censored data and to study the properties of such procedures. Efron (1967) used proportional hazards models to compare, on the basis of asymptotic relative efficiency, his two-sample test for censored data with various competitors. (Efron uses the result that when \( H = F^\delta \) and \( F \) is exponential, then \( Z \) and \( \delta \) are independent, and he cites Sethuraman for calling the result to his attention.) Cox (1972), in deriving censored-data procedures for regression models, considers a general model that includes the case of proportional hazards. Koziol and Green (1976) assume that the failure distribution of interest \( F \) and the censoring distribution \( H \) are related via \( H = F^\delta \) in order to derive a Cramer-von Mises statistic for testing the goodness-of-fit hypothesis that \( F = F_0 \),
where \( F_0 \) is a completely specified distribution.
Proportional hazards models can also arise as a consequence of the structure of the system under study. Consider the reliability model (situation (i) of Section 1) where component 1 itself is a series system of \( k_1 \) (say) independent and identically distributed subcomponents, with corresponding lifetimes \( S_1, \ldots, S_{k_1} \), each having distribution \( I \) (say) and component 2 is also a series system of \( k_2 \) (say) independent and identically distributed subcomponents, with corresponding lifetimes \( T_1, \ldots, T_{k_2} \), each with life distribution \( I \). Then \( X = \min(S_1, \ldots, S_{k_1}) \), \( Y = \min(T_1, \ldots, T_{k_2}) \), and the pair \((X, Y)\) follows a proportional hazards model.

Apart from individual cases which lead to the proportional hazards model, a key advantage of the model is its tractability. Models satisfying (2.1) were successfully used by Lehmann (1953) (in the context of the two-sample problem with uncensored data) to both derive new rank tests with optimal properties and to compute exact small-sample power of rank tests under specific alternatives.

Using Theorem 2.1, under the assumption that \((X_1, Y_1)\) follows a proportional hazards model, we can conclude that

The sequences \( \delta_1, \ldots, \delta_n \) and \( Z_1, \ldots, Z_n \)

are independent.

(2.8)

This independence property greatly simplifies the computations of the mean and variance of \( \bar{F}_n(t) \), as will be seen in Section 3.
3. Moment Calculations Under Proportional Hazards

In this section we derive a general expression for the $a$th moment of the KM estimator $\bar{F}_n(t)$, under the assumption that $(X_1, Y_1)$ follows a proportional hazards model. This enables us to study, under proportional hazards, the bias of $\bar{F}_n(t)$. (Whereas it is well known that $\bar{F}_n(t)$ is asymptotically unbiased, $\bar{F}_n(t)$ is biased for finite $n$.) We also use our exact result to investigate bounds for the bias given by Efron (1967) and to compare the exact variance of $\bar{F}_n(t)$ with its asymptotic variance.

Recall from Section 1 that $K_n(t)$ is the empirical distribution function of the $Z$'s and let $K(t) = \bar{F}(t)\bar{N}(t)$, and $K(t) = 1 - K(t)$, $t \in [0, \infty)$. Then $nK_n(t)$ is a binomial random variable with parameters $n$ and $K(t)$, $\delta_1, \ldots, \delta_n$ are independent and identically distributed Bernoulli random variables with parameter $\gamma = P(X_1 \leq Y_1)$ and, by (2.8), $K_n(t)$ is independent of $\delta_1, \ldots, \delta_n$. Thus, by (1.1) and (2.8), for $t, \alpha \in (0, \infty)$, we find

$$E[\bar{F}_n(t)]^a = E\left[ \prod_{i=1}^{n} \left( \gamma c_{in}^a + (1 - \gamma) \right) I(Z(n) \geq t) \right]^a$$

$$= \sum_{q=0}^{n-1} \binom{n}{q}(K(t))^q(\bar{K}(t))^{n-q} \prod_{i=1}^{q} \left( \gamma c_{in}^a + (1 - \gamma) \right).$$

Consequently,

$$E(\bar{F}_n(t)) = \sum_{q=0}^{n-1} \binom{n}{q}(K(t))^q(\bar{K}(t))^{n-q} \prod_{i=1}^{q} \left( 1 - \gamma(n - i + 1)^{-1} \right),$$

and
\[
\text{Var}(\hat{F}_n(t)) = \sum_{q=0}^{n-1} \binom{n}{q} (K(t))^q (\hat{K}(t))^{n-q} \prod_{i=1}^{q} \left(1 - \gamma(2n - 2i + 1)(n - i + 1)^{-2}\right)
\]

\[
- \sum_{q=0}^{n-1} \binom{n}{q} (K(t))^q (\hat{K}(t))^{n-q} \prod_{i=1}^{q} \left(1 - \gamma(n - i + 1)^{-1}\right)^2.
\]

We now take the lifelength distribution function \(F\) to be exponential with scale parameter 1 and the censoring distribution function \(H\) to be exponential with scale parameter \(\beta (\beta > 0)\). Table 1 displays numerical values (obtained by using (3.2) and (3.3)) of the mean and variance of the \(\hat{F}\). The table also gives values of \(-b_n(t)\) where \(b_n(t)\) is the bias, namely,

\[
b_n(t) = \mathbb{E}(\hat{F}_n(t)) - F(t).
\]

Efron (1967) gives the bounds

\[
0 \leq F(t) - \mathbb{E}(\hat{F}_n(t)) \leq F(t) \exp(-nK(t)), \quad t \in [0, \infty),
\]

and thus, in the special case of proportional hazards, (3.2) and Table 1 allow us to study how close the Efron bounds are to the true bias. (Due to round-off, the values in Table 1 will not always satisfy (3.4).) We also compare the exact variance of the \(\hat{F}\) to its asymptotic variance. The asymptotic variance of \(\frac{1}{n} \hat{F}_n(t)\) is (cf. Efron (1967))

\[
\text{Var}(\hat{F}_n(t)) \approx n^{-1} \int_0^t \left[ \frac{K(u)F(u)}{K(u)F(u) - 1} \right]^{-1} dF(u), \quad t \in [0, \infty).
\]

(3.6)
Table 1 shows that, under proportional hazards, the bias is not large, and, as we would expect, the true mean gets closer to (the asymptotically correct value) \( \bar{F}(t) \) as \( n \) gets large. Also, from Table 1, we see that for fixed \( \beta \) and \( n \) the bias increases as \( t \) increases from .5 to 1 to 2. The bias also increases, for fixed \( t \) and \( n \), as \( \beta \) increases from .5 to 1 to 2 (recall that increases in \( \beta \) correspond to increases in the amount of censoring). Furthermore, Efron's bounds are seen to be reasonably close to the true value of \( \bar{F}(t) - E(\bar{F}_n(t)) \). Table 1 also compares the exact variance of \( \bar{F}_n(t) \), obtained via (3.3), with the approximation given by the right-hand-side of (3.6).

Our calculations are performed under a particular proportional hazards model, when \( X \) and \( Y \) are exponential. However, these calculations apply to general proportional hazards models, provided the appropriate adjustments are made. More specifically assume \( \bar{H} = \bar{F}^\beta \) for some \( \beta > 0 \), and let \( R^{-1}(t) = \inf\{z: z \in [0, a(F)], -\ln F(z) > t\} \), \( t \in [0, \infty) \). Since \( F \) is continuous \( R(R^{-1}(t)) = t \) for \( t \in [0, \infty) \).

Thus, the random variables \( R(X) \) and \( R(Y) \) are exponentially distributed with scale parameters \( 1 \) and \( \beta \) respectively. Let \( Z_{i,R} = \min\{R(X_i), R(Y_i)\} \) and \( \delta_{i,R} = I\{R(X_i) \leq R(Y_i)\}, i = 1, \ldots, n \). Let \( Z_1 < \ldots < Z_n \) denote the ordered \( Z \)'s, \( \delta_1 \) is the \( \delta \) corresponding to \( Z_1 \), and let \( Z_i, \delta i, R_i, R_i \), \( i = 1, \ldots, n \) be analogously defined. Then, the random vectors \( \{(Z_1, R, \delta_1, R), \ldots, (Z_n, R, \delta_n, R)\} \) and \( \{(R(Z_1), \delta_1), \ldots, (R(Z_n), \delta_n)\} \) are stochastically equal.

Now let \( \bar{F}_{n,R} \) denote the Kaplan-Meier estimator computed from \( (Z_1, R, \delta_1, R), \ldots, (Z_n, R, \delta_n, R) \). Then for \( n = 1, 2, \ldots \), the processes \( \{\bar{F}_{n,R}(R(t)), t \in [0, \infty)\} \) and \( \{\bar{F}_n(t), t \in [0, \infty)\} \) are stochastically equal.
### Exact and Approximate Values of the Mean and Variance of the KME

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REFERENCES


 Whereas much is known about the asymptotic properties of the Kaplan-Meier (1958) estimator \( \hat{F}(t) \) of a survival function, exact results for small samples have been difficult to obtain. In this note, we obtain an exact expression for the \( \alpha \)th moment (\( \alpha > 0 \)) of the \( \hat{F}(t) \) under a model of proportional hazards. This enables us, under proportional hazards, to (1) study the bias of the \( \hat{F}(t) \), and (2) compare the exact variance of the \( \hat{F}(t) \) to its asymptotic variance. We also characterize the proportional hazards model.