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JACKKNIFING THE KAPLAN-MEIER SURVIVAL ESTIMATOR FOR CENSORED DA--ETC(U)
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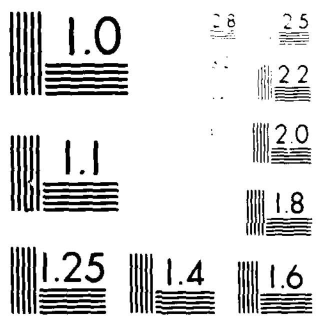
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Monterey, California

JACKKNIFING THE KAPLAN-MEIER SURVIVAL
ESTIMATOR FOR CENSORED DATA:
SIMULATION RESULTS AND ASYMPTOTIC ANALYSIS

by

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The Kaplan-Meier estimate is a non-parametric maximum likelihood estimate for the probability of equipment of human survival. This report describes a jackknife confidence limit procedure for probability of survival, based on K.-M., and describes confidence limit properties by simulation and by asymptotic analysis.

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JACKKNIFING THE KAPLAN-MEIER SURVIVAL ESTIMATOR FOR CENSORED DATA: SIMULATION RESULTS AND ASYMPTOTIC ANALYSIS

Donald P. Gaver

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1. Introduction

Censored data problems arise frequently in medical, and also in engineering system reliability, applications. For example, in medical survivorship studies some subjects may be lost to follow-up, or available data may be analyzed before all subjects have expired. In the equipment reliability context observed units may still be in operation, perhaps after several previous failures, at the time of the analysis. Considerable attention has been recently devoted to developing informative statistical methods for handling data of this type (see Kalbfleisch and Prentice (1980)).

It is straightforward, though sometimes computationally tedious, to deal with censoring in a parametric manner, i.e. by assuming a specific form for the lifetime distribution (exponential, Weibull, lognormal, or whatever) and then estimating parameters, perhaps by maximum likelihood. The approach adopted here is, instead, to begin with the Kaplan-Meier (1958) product-limit estimator of survival probability. This estimator is the non-parametric maximum likelihood estimator of a distribution function from a sample of singly-censored data. Then, since the jackknife technique has been shown to be widely useful for obtaining robust intervals, cf. Miller (1974), it is applied to the Kaplan-Meier estimate in order to obtain approximate confidence intervals for the survival probability. It is reasonable to argue that if the jackknife is to be valid under complex censoring it must perform correctly in this simplest of all situations, and if it does work here then it is likely to also work in more complex settings. Therefore, in a sense we are reporting on the results of a pilot study of an attractive procedure.

In this paper the effect of jackknifing the Kaplan-Meier estimate will be examined both by Monte Carlo simulation (sampling experiments) and by asymptotic analysis. In Section 4, we report on the results of some extensive Monte Carlo investigations, comparing confidence limits for survival probability obtained via jackknife with those from other techniques. It will be seen that the jackknife seems to perform well for moderate sample sizes, even under some rather unusual conditions. In Section 5, asymptotic results are reported that provide theoretical underpinnings for the jackknife procedure, at least for large sample sizes. Specifically, it is shown that the jackknifed estimate is approximately normal with the asymptotically correct variance, and hence produces correct confidence limits for the Kaplan-Meier estimate. Taken by itself, this result may not be terribly important, because an expression for the variance of the estimator is known, and it can be estimated by substituting estimates of any unknown functions into the expression. However, for doubly censored data (cf. Turnbull (1974)), and for data with censoring and truncation, the situation is more complex (cf. Turnbull (1978)). The fact that the jackknife works in the singly censored case makes it more likely that it works for these more complex censoring patterns and for others as well.

It should be noted that the bootstrap procedure, a re-sampling approach investigated by Efron (1979) and (1981) is also applicable to complex censoring situations, apparently giving results in good agreement with Greenwood's formula for a particular case investigated.

2. Formulation of the Problem; the Kaplan-Meier Estimate

Suppose $x_1, x_2, \ldots, x_n$ are n observed survival times, e.g. of medical patients or of equipments subject to failure. Some of these observations are of complete lifetimes (failure times) but others are not, having been censored by the time of observation. For short we refer to complete observations as deaths, and censored observations as losses. Censoring simply means that a "complete time" is not observed, although a "partial time," up to the censoring, is. Censoring complicates the problem of estimating the theoretical survival probability to time x, denoted by $\bar{F}^0(x) = 1 - F^0(x)$.

Kaplan and Meier (1958) furnish a maximum likelihood estimate of $\bar{F}^0(x)$ from among the class of admissable distributions. This product-limit estimate may be written in several equivalent ways, assuming no ties among the observations:

$$\bar{F}_n^0(x) = \prod_{x_i < x} \left(\frac{n-r_i}{n-r_i+1}\right)^{\delta_i} \tag{2.1,a}$$

$$= \prod_{i=1}^{n} \left(\frac{n-i}{n-i+1}\right)^{\delta_i(x)} \tag{2.1,b}$$

$$= \prod_{i=1}^{k(x)} \hat{p}_i \equiv \prod_{i=1}^{k(x)} \left(\frac{n_i - \delta_i}{n_i}\right) \tag{2.1,c}$$

In (2.1,a), r_i is the rank of x_i among the ordered observations $x_{(1)} < x_{(2)} \cdots < x_{(n)}$, and δ_i is unity if x_i is an observed death, being zero otherwise. In (2.1,b),

$$\delta_i(x) = \begin{cases} 1 & \text{if} \quad x_{(i)} < x \quad \text{and is a time of death (uncensored)} \\ 0 & \text{otherwise .} \end{cases} \qquad (2.2)$$

In (2.1,c) $n_i (=n-(i-1))$ represents the number of items exposed (to either death or loss) at the ith ordered time, and $k(x)$ is the total number of deaths by time x.

A numerical example helps to explain the estimate. Suppose the data points are

$$1 < 2^* < 4 < 5^* < 7^* < 8 < 10$$

where the starred measurements are losses, and the rest deaths. Let us estimate the survival probability to or beyond $x = 6$. Then, since $n = 7$, and $k(6) = 2$

$$\bar{F}_7(6) = \left(\frac{7-1}{7}\right)^1 \left(\frac{7-2}{7-1}\right)^0 \left(\frac{7-3}{7-2}\right)^1 \left(\frac{7-4}{7-3}\right)^0 = \left(\frac{6}{7}\right)\left(\frac{4}{5}\right)$$

by (2.1,b)

$$= \left(\frac{7-1}{7}\right)^1 \left(\frac{7-2-1}{7-2}\right)^1$$

by (2.1,c).

Note that by definition (2.2) the estimate jumps down following data values that are deaths, does not jump at losses, and remains constant between down-jumps. Technically, $\bar{F}_n^0(x)$ is a left-continuous monotonically non-increasing step function; this makes $F_n^0(x)$, the estimated distribution of time of death, left-continuous as well.

3. Interval Estimates for the Kaplan-Meier Estimate

For a given set of data the K.-M. estimate provides a point estimate of the survival probability. It is, of course, desirable to assess the stability of such an estimate under reasonable assumptions about the origin of the data; specifically it is useful to furnish approximate confidence intervals for a survival distribution $F^0(x)$. The jackknife procedure, see Miller (1974) and Mosteller and Tukey (1977), is one way of producing such limits. In this section we describe the computation of jackknife limits, and compare the results to confidence limits obtained by alternative procedures. Comparisons are made by simulation.

3.1. The Jackknife Procedure

The jackknife procedure is well-described in Mosteller and Tukey (1977), where it is pointed out that a preliminary transformation to approximately symmetrize the sampling distribution of the estimator is beneficial; see also Cressie (1981). For this study we have chosen to utilize the classical "inverse sine" transformation that tends to stabilize the variance of--and also approximately symmetrize--binomial count data. This transformation is suggested since the number of samples surviving a fixed time would be binomial under ideal conditions if there were no censoring. Initial experiments with a logistic transformation proved to be less satisfactory, as was a simple log transformation; in practice, both log and logistic transformations must involve a "start," see Tukey [1977], which influences the coverage. A natural choice is $1/2n$, see Cox [1972], but systematic confidence interval undercoverage results, empirically suggesting a larger value. Here is our procedure.

(a) Select a value of x at which to estimate survival probability.

(b) Compute $\bar{F}_n^0(x)$, e.g. by (2.1).

(c) Compute $A_n(x) = \sin^{-1}\sqrt{\bar{F}_n^0(x)}$.

(d) Compute $\bar{F}_{n-1,j}^0(x)$, the K.-M. estimate leaving out the j<u>th</u> observation, whether it be an observed (recorded) death, or a loss. The formula actually used was

$$\bar{F}_{n-1,i}^0(x) = \prod_{j=1}^{i-1} \left(\frac{n-1-j}{n-1}\right)^{\delta_j(x)} \prod_{j=i+1}^{n} \left(\frac{n-j}{n-j+1}\right)^{\delta_j(x)} \tag{3.1}$$

(e) Compute $A_{n-1,j}(x) = \sin^{-1}\sqrt{\bar{F}_{n-1,j}^0(x)}$

(f) Compute the j<u>th</u> pseudovalue:

$$v_j = nA_n(x) - (n-1)A_{n-1,j}(x), \qquad j = 1,2,\ldots,n$$

(g) Find the mean and variance of the pseudovalues:

$$\bar{v} = \frac{1}{n}\sum_{j=1}^{n} v_j, \quad \underline{\text{and}} \quad s_v^2 = \frac{1}{n-1}\sum_{j=1}^{n}(v_j-\bar{v})^2,$$

$$\underline{\text{and}} \quad s_v = \sqrt{s_v^2}$$

(h) Compute (approximate) two-sided $(1-\alpha)\cdot 100\%$ confidence limits as follows:

$$L \equiv \bar{v} - t_{1-\alpha/2}(n-1)\frac{s_v}{\sqrt{n}} \le \sin^{-1}\sqrt{\bar{F}^0(x)}$$

$$\le \bar{v} + t_{1-\alpha/2}(n-1)\frac{s_v}{\sqrt{n}} \equiv U, \tag{3.2}$$

where $t_{1-\alpha/2}(n-1)$ is the %-point of Student's t; then invert to obtain (approximate) two-sided $(1-\alpha)\cdot 100\%$ confidence limits for survival beyond x:

$$\sin^2(L) \le \bar{F}^0(x) \le \sin^2(U) \ . \tag{3.3}$$

Theoretical justification of such a procedure for large n is given in a final section of this paper. The quality of the product is illustrated by simulation examples to appear subsequently.

3.2. Alternatives to the Jackknife: "Greenwood's formula"

The classical estimate of the variance of the estimate $\bar{F}_n^0(x)$ is given by "Greenwood's formula," see Kaplan and Meier (1958), p. 477, or Thomas and Grunkemeier (1975), p. 867. Again when no ties are present this may be expressed as

$$\hat{V}ar\left[\bar{F}_n^0(x)\right] = \left(\bar{F}_n^0(x)\right)^2 \sum_{i=0}^{k(x)} \frac{\delta_i}{n_i(n_i-\delta_i)} \ . \tag{3.4}$$

It is interesting and reassuring that this approximate formula delivers exactly $\left(\frac{n-k}{n}\right)\left(\frac{k}{n}\right)\frac{1}{n}$ as an estimated variance when all observed events are deaths.

It follows that approximate two-sided $(1-\alpha)\cdot 100\%$ confidence limits may be obtained by this procedure:

a) Select a value of x at which to estimate survival probability.

b) Compute $\bar{F}_n^0(x)$, the point estimate of survival probability.

c) Compute $s_G^2 = \hat{V}ar\left[\bar{F}_n^0(x)\right]$ from (3.4).

d) Compute approximate two-sided $(1-\alpha) \cdot 100\%$ confidence limits:

$$L_G = \bar{F}_n^0(x) - z_{1-\alpha/2} \frac{s_G}{\sqrt{n}}, \qquad U_G = \bar{F}_n^0(x) + z_{1-\alpha/2} \frac{s_G}{\sqrt{n}}$$

where $z_{1-\alpha/2}$ is the $(1-\alpha/2) \cdot 100$ percent point of the unit Normal. Then

$$L_G \leq \bar{F}^0(x) \leq U_G \tag{3.5}$$

with approximately the quoted confidence.

For justification of the above procedure, which we will call the $\underline{Z_1}$ procedure following Thomas and Grunkemeier (1975), when n is large refer to Breslow and Crowley (1974). Simulation results appear subsequently.

3.3. An Approximate Likelihood-Ratio Interval Estimate

Thomas and Grunkemeier (1975) propose use of a likelihood-ratio based procedure for obtaining approximate $(1-\alpha) \cdot 100\%$ confidence limits. In outline, the procedure approximately maximizes the likelihood of a survival function under a constraint; this will be called the $\underline{Z_2}$ procedure. For a similar development see Madansky (1965). Specifically, one maximizes the likelihood (5d) of Kaplan and Meier, subject to the constraint that survival to time x equals $\bar{F}^0$:

$$\max_{(p_i,\lambda)} L = \sum_{i=1}^{k(x)} \{\delta_i \ln(1-p_i) + (n_i-\delta_i)\ln p_i\} + \lambda\{\sum_{i=1}^{k(x)} \ln p_i - \ln \bar{F}^0\} + \sum_{i=k(x)+1}^{n} \{\delta_i \ln(1-p_i) + (n_i-\delta_i)\ln p_i\}, \tag{3.6}$$

giving estimates

$$\tilde{p}_i(\lambda) = \frac{n_i + \lambda - \delta_i}{n_i + \lambda}, \qquad i = 1,2,\ldots,k(x);$$

$$= \frac{n_i - \delta_i}{n_i}, \qquad i = k(x)+1,\ldots,n \tag{3.7}$$

and

$$\prod_{i=1}^{k(x)} \tilde{p}_i(\lambda) \equiv \bar{F}^0(x;\lambda) \tag{3.8}$$

from the constraint condition. Next (numerically) solve the equation

$$[\bar{F}_n^0(x) - \bar{F}^0(x;\lambda)]/\bar{F}^0(x;\lambda)\sqrt{\tilde{V}(\lambda)} = \pm z_{1-\alpha/2} \tag{3.9}$$

for λ_L and λ_U where $\bar{F}_n^0$ is the product-limit estimate of survival beyond x, $\bar{F}^0(x;\lambda)$ is given by (3.8), and $z_{1-\alpha/2}$ is the $(1-\alpha/2)$ 100th percent point of the unit normal distribution. Then, according to Thomas and Grunkemeier (see footnote, p. 867) $\tilde{V}(\lambda)$ may be expressed as follows:

$$\tilde{V}(\lambda) = [(n+\lambda)/n]\sum_{i=1}^{k(x)} \delta_i/(n_i+\lambda)(n_i+\lambda-\delta_i)$$

$$= [1-\bar{F}^0(x;\lambda)]/[\bar{F}^0(x;\lambda)\ n(x)] \quad \text{for} \quad \bar{F}_n^0(x;\lambda) = 1 \tag{3.10}$$

here $n(x)$ is the number of individuals exposed at x. Finally, (approximate) upper and lower confidence limits for $\bar{F}^0_{(x)}$ are obtained by substituting λ_L and λ_U into (3.8):

$$P_L = \prod_{i=1}^{k(x)}\left(\frac{n_i+\lambda_L-\delta_i}{n_i+\lambda_L}\right), \quad \underline{\text{and}} \quad P_U = \prod_{i=1}^{k(x)}\left(\frac{n_i+\lambda_U-\delta_i}{n_i+\lambda_U}\right) \tag{3.11}$$

The principle difficulty with application of this method is the numerical solution of (3.9) for the roots λ_L and λ_U. A Newton-Raphson method was utilized in the program developed for this study. It was only feasible to make extensive trials of the procedure for sample size $n = 25$.

4. Simulation Results

In order to compare the performance of the jackknife procedure to the other candidates described above, namely Z_1 and Z_2, some of the particular cases treated by Thomas and Grunkemeier (1975, p. 168ff.) were simulated, and nominal 95% and 90% confidence limits were constructed. We summarize the results in the following tables. Note that assessments are made of interval performance at three probability-of-survival levels: 0.75, 0.50, 0.25 for each combination of death and failure distributions.

Examination of the tabulations of confidence limit coverage and also the average and standard deviations of c.i. widths suggest that the jackknife confidence intervals perform in a generally conservative manner as compared to the "Greenwood's formula" results (Z_1) and the approximate likelihood ratio method (Z_2). That is, JK tends to over-cover, while Z_1 consistently under-covers; Z_2 has some tendency to under-cover with severe losses (Case 1) and for small probabilities of survival but generally performs well. Of the three estimating procedures, Z_2 is by far the most difficult and expensive to carry out. The computer time involved in computing Z_2 for $n = 50$ prohibited tabulation of those results for this study. Note that the tendency of the jackknife to over-cover is reduced as the probability of survival decreases. Actually abusrdly low values occur for survival probabilities 0.50 and 0.25 in Case 1; they are a consequence of the severe censoring assumed. In general, the results obtained indicate that the jackknife procedure is a worthy competitor of

Case 1: X_i (death times) independent unit exponential; Y_i (loss times) independent uniform (0,0.5); Sample size $n = 25$.

Nominal 95% Confidence Limits

True Survival Probabilities

Averages (of 1000)	0.75 JK	0.75 $\underline{Z}_1$	0.75 $\underline{Z}_2$
Coverage	0.977	0.891	0.942
Width	0.451	0.391	0.382
S. D. Widths	0.097	0.105	0.068

Nominal 90% Confidence Limits; Sample size $n = 25$.

True Survival Probabilities

Averages (of 1000)	0.75 JK	0.75 $\underline{Z}_1$	0.75 $\underline{Z}_2$
Coverage	0.955	0.849	0.891
Width	0.381	0.332	0.326
S. D. Widths	0.086	0.085	0.062

Case 2: X_i (death times) independent unit exponential; Y_i (loss times) independent uniform (0,0.5); Sample size $n = 50$.

Nominal 95% Confidence Limits

True Surivial Probabilities

Averages		0.75	
(of 1000)	JK	Z_1	Z_2
Coverage	0.954	0.923	---
Width	0.298	0.291	---
S. D. Width	0.042	0.043	---

Nominal 90% Confidence Limits

True Survival Probabilities

Averages		0.75	
(of 1000)	JK	Z_1	Z_2
Coverage	0.900	0.871	---
Width	0.252	0.244	---
S. D. Width	0.036	0.036	---

Case 3: X_i (death times) independent unit exponential, Y_i (loss times) independent uniform (0,1); Sample size $n = 25$.

Nominal 95% Confidence Limits

True Survival Probabilities

Averages (of 1000)	0.75 JK	0.75 $\underline{Z}_1$	0.75 $\underline{Z}_2$	0.50 JK	0.50 $\underline{Z}_1$	0.50 $\underline{Z}_2$
Coverage	0.984	0.919	0.952	0.973	0.893	0.937
Width	0.392	0.351	0.341	0.458	0.500	0.448
S. D. Width	0.054	0.067	0.044	0.100	0.077	0.050

Nominal 90% Confidence Limits

True Survival Probabilities

Averages (of 1000)	0.75 JK	0.75 $\underline{Z}_1$	0.75 $\underline{Z}_2$	0.50 JK	0.50 $\underline{Z}_1$	0.50 $\underline{Z}_2$
Coverage	0.959	0.857	0.912	0.927	0.838	0.872
Width	0.329	0.296	0.291	0.470	0.421	0.388
S. D. Width	0.047	0.054	0.040	0.106	0.065	0.047

Case 4: X_i (death times) independent unit exponential; Y_i (loss times) independent uniform (0,1); Sample size $n = 50$.

Nominal 95% Confidence Limits

True Survival Probabilities

Averages	0.75			0.50		
(of 1000)	JK	Z_1	Z_2	JK	Z_1	Z_2
Coverage	0.954	0.933	---	0.957	0.924	---
Width	0.261	0.622	---	0.373	0.366	---
S. D. Width	0.025	0.027	---	0.043	0.038	---

Nominal 90% Confidence Limits

True Survival Probabilities

Averages	0.75			0.50		
(of 1000)	JK	Z_1	Z_2	JK	Z_1	Z_2
Coverage	0.918	0.882	---	0.915	0.878	---
Width	0.220	0.216	---	0.316	0.307	---
S. D. Width	0.021	0.023	---	0.037	0.031	---

Case 5: X_i (death times) independent unit exponential; Y_i (loss times) independent uniform (0,1.5); Sample size $n = 25$.

Nominal 95% Confidence Limits

True Survival Probabilities

Averages	0.75			0.50			0.25		
(of 1000)	JK	Z_1	Z_2	JK	Z_1	Z_2	JK	Z_1	Z_2
Coverage	0.984	0.923	0.956	0.976	0.927	0.951	0.942	0.917	0.906
Width	0.378	0.344	0.332	0.480	0.450	0.412	0.625	0.477	0.434
S. D. Width	0.044	0.058	0.038	0.048	0.040	0.030	0.155	0.094	0.054

Nominal 90% Confidence Limits

True Survival Probabilities

Averages	0.75			0.50			0.25		
(of 1000)	JK	Z_1	Z_2	JK	Z_1	Z_2	JK	Z_1	Z_2
Coverage	0.955	0.867	0.904	0.940	0.866	0.898	0.899	0.864	0.865
Width	0.317	0.290	0.282	0.404	0.378	0.354	0.566	0.409	0.377
S. D. Width	0.037	0.046	0.034	0.043	0.033	0.027	0.189	0.078	0.051

Case 6: X_i (death times) independent unit exponential; Y_i (loss times) exponential (mean X_i^{-1}), Sample size $n = 25$.

Nominal 95% Confidence Limits

Averages	0.75			0.50			0.25		
(of 1000)	JK	Z_1	Z_2	JK	Z_1	Z_2	JK	Z_1	Z_2
Coverage	0.975	0.936	0.945	0.951	0.834	0.867	0.994	0.901	0.988
Width	0.399	0.368	0.351	0.517	0.468	0.423	0.692	0.401	0.401
S. D. Width	0.041	0.054	0.036	0.075	0.057	0.038	0.169	0.111	0.063

Nominal 90% Confidence Limits

Averages	0.75			0.50			0.25		
(of 1000)	JK	Z_1	Z_2	JK	Z_1	Z_2	JK	Z_1	Z_2
Coverage	0.940	0.887	0.900	0.900	0.752	0.785	0.989	0.836	0.967
Width	0.335	0.310	0.299	0.438	0.394	0.366	0.643	0.352	0.346
S. D. Width	0.035	0.043	0.033	0.076	0.047	0.034	0.203	0.092	0.059

Case 7: X_i (death times) independent unit exponential; Y_i (loss times) exponential (mean $(0.5X_i)^{-1}$); Sample size $n = 25$.

Nominal 95% Confidence Limits

Averages		0.75			0.50			0.25	
(of 1000)	JK	Z_1	Z_2	JK	Z_1	Z_2	JK	Z_1	Z_2
Coverage	0.975	0.923	0.950	0.965	0.906	0.929	0.997	0.818	0.981
Width	0.376	0.346	0.332	0.454	0.428	0.394	0.568	0.354	0.357
S. D. Width	0.039	0.053	0.036	0.033	0.031	0.024	0.160	0.098	0.055

Nominal 90% Confidence Limits

Averages		0.75			0.50			0.25	
(of 1000)	JK	Z_1	Z_2	JK	Z_1	Z_2	JK	Z_1	Z_2
Coverage	0.941	0.859	0.890	0.911	0.848	0.868	0.991	0.748	0.914
Width	0.315	0.291	0.282	0.381	0.359	0.338	0.502	0.308	0.306
S. D. Width	0.033	0.042	0.032	0.028	0.026	0.021	0.172	0.079	0.051

Case 8: X_i (death times) independent unit exponential; Y_i (loss times) exponential (mean $(X_i(1+0.5X_i))^{-1}$); Sample size $n = 25$.

Nominal 95% Confidence Limits

Averages	0.75			0.50			0.25		
(of 1000)	JK	$\underline{Z}_1$	$\underline{Z}_2$	JK	$\underline{Z}_1$	$\underline{Z}_2$	JK	$\underline{Z}_1$	$\underline{Z}_2$
Coverage	0.981	0.926	0.944	0.980	0.892	0.915	0.980	0.943	0.972
Width	0.418	0.377	0.362	0.568	0.506	0.453	0.725	0.473	0.448
S. D. Width	0.056	0.070	0.045	0.095	0.070	0.043	0.158	0.126	0.066

Nominal 90% Confidence Limits

Averages	0.75			0.50			0.25		
(of 1000)	JK	$\underline{Z}_1$	$\underline{Z}_2$	JK	$\underline{Z}_1$	$\underline{Z}_2$	JK	$\underline{Z}_1$	$\underline{Z}_2$
Coverage	0.946	0.881	0.890	0.950	0.83	0.851	0.969	0.912	0.956
Width	0.352	0.318	0.309	0.488	0.427	0.393	0.687	0.413	0.391
S. D. Width	0.048	0.056	0.041	0.106	0.058	0.041	0.195	0.105	0.064

"Greenwood's formula" under present circumstances, and that it performs only a little less effectively than does the approximate likelihood-based procedure Z_2. The presented jackknife technique tends to be conservative.

In order to supplement the above information, a number of additional simulations were made to investigate the effect of departure from the random censoring model. Specifically, the censoring time, Y_i, was allowed to depend probabilistically upon the time of death, X_i, for a sequence of experiments. A selection of the results obtained are shown next.

In the above situations, in which X_i and Y_i are now contrived to be positively dependent, once again the jackknife tends to result in over-coverage--i.e. is conservative, and sometimes radically so. This is to be contrasted with Greenwood's formula results, Z_i, which generally under-cover. Here there is some indication that the likelihood ratio procedure, Z_2, has a tendency to under-cover when the survival probability is near 0.5. Of course, all results are for rather small sample sizes, and refer to exponentially distributed deaths.

5. Summary of Theoretical Developments

In this section a probability model for random censoring is introduced. In terms of this model it will be shown that the jackknife produces asymptotically correct confidence limits for the survival probability from the Kaplan-Meier estimator. A priori one could not be certain whether to systematically delete each observation in turn when applying the jackknife or whether to delete only the uncensored ones. Our results show that the proper method is to delete each observation, censored or uncensored.

5.1. The Model

Let $X_1^0, X_2^0, \ldots, X_n^0$ be independent random variables distributed according to cdf $F^0(x)$, which is continuous with $F^0(0) = 0$. In medical applications X_i^0 represents the survival time of the ith patient, and in engineering reliability it represents the time to failure of the ith equipment (or the ith time to failure of an equipment, when appropriate). The problem is to estimate F^0, but unfortunately the X_i^0 are not all directly observable.

Let $Y_1, Y_2, \ldots Y_n$ be independent random variables, identically distributed according to cdf G, the latter being continuous with $G(0) = 0$. The observable variables are then

$$X_i = \min\{X_i^0, Y_i\} ,$$

$$\text{and} \qquad \delta_i = I\{X_i^0 \le Y_i\} , \qquad (5.1)$$

where $I\{A\}$ is the indicator function for event A. The Y_i variables represent censoring times, and are assumed to be independent of the X_i^0. The statistician actually observes the smaller of the two variables, and also knows whether the observation is uncensored (a "death") or censored (a "loss").

5.2. Cumulative Hazard Function

The Kaplan-Meier estimator $\bar{F}_n^0$ is closely related to the sample cumulative hazard function (chf). The latter is defined as

$$\Lambda_n^0(x) = \sum_{i=1}^{n} \frac{\delta_i(x)}{n-i+1} \tag{5.2}$$

where $\delta_i(x)$ is defined in (2.2). In fact Breslow and Crowley (1974) show that

$$-\ln[1-\bar{F}_n^0(x)] = \Lambda_n^0(x) + O_p(1/n) \quad , \tag{5.3}$$

and it may be shown that

$$\Lambda_n^0(x) \overset{a.s.}{\to} \int_0^x \frac{dF^0(x)}{1-F^0(x)} \quad , \tag{5.4}$$

the integral of the hazard function $\lambda^0(u) = dF^0(u)/[1-F^0(u)]$; both (5.3) and (5.4) justify the name given to Λ_n^0.

It is convenient to show that the jackknifed estimator of $\bar{F}^0$, denoted by $\bar{F}_n^0(x)$, is asymptotically normal by starting with Λ_n^0. If one shows that $\Lambda_n^0(x)$ is asymptotically normally distributed then it follows that $F_n^0(x)$ is also normal, as is true of other sufficiently smooth functions (e.g. arc sine) of $\bar{F}_n^0(x)$. If, in addition, it is shown that the jackknife variance is consistent then the jackknife confidence procedure illustrated in Section 4 is justified for large sample sizes.

5.3. Asymptotic Normality

Let $\Lambda^0_{n-1}(x;i)$ be the sample chf when the ith ordered observation $X_{(i)}$ is deleted from the sample. Then

$$\Lambda^0_{n-1}(x;i) = \sum_{j=1}^{i-1} \frac{\delta_{(j)}(x)}{n-j} + \sum_{j=i+1}^{n} \frac{\delta_{(j)}(x)}{n-j+1} . \tag{5.5}$$

The corresponding pseudo-value is

$$\begin{aligned}\Lambda^0_n(x;i) &= n\Lambda^0_n(x) - (n-1)\Lambda^0_{n-1}(x;i) \\ &= \frac{n\delta_{(i)}(x)}{n-i+1} - \sum_{j=1}^{i-1} \frac{(j-1)\delta_{(j)}(x)}{(n-j)(n-j+1)} + \sum_{j=i+1}^{n} \frac{\delta_{(j)}(x)}{n-j+1} . \end{aligned} \tag{5.6}$$

The jackknifed estimator is the average of the pseudo-values. From (5.6),

$$\begin{aligned}\tilde{\Lambda}^0_n(x) &= \frac{1}{n} \sum_{i=1}^{n} \tilde{\Lambda}^0_n(x;i) \\ &= \sum_{i=1}^{n} \frac{\delta_{(i)}(x)}{n-i+1} - \frac{1}{n} \sum_{i=2}^{n} \sum_{j=1}^{i-1} \frac{(j-1)\delta_{(j)}(x)}{(n-j)(n-j+1)} + \frac{1}{n} \sum_{i=1}^{n} \sum_{j=i+1}^{n} \frac{\delta_{(j)}(x)}{n-j+1} \\ &= \Lambda^0_n(x) - \frac{1}{n} \sum_{j=1}^{n-1} \frac{(n-j)(j-1)\delta_{(j)}(x)}{(n-j)(n-j+1)} + \frac{1}{n} \sum_{j=2}^{n} \frac{(j-1)\delta_{(j)}(x)}{n-j+1} \\ &= \Lambda^0_n(x) + \frac{n-1}{n} \delta_{(n)}(x) .\end{aligned} \tag{5.7}$$

Thus the jackknifed estimator and the original estimator differ by an asymptotically negligible term. Now it has been shown that $\Lambda^0_n(x)$ is asymptotically normal with mean $\Lambda^0(x)$ and variance

$$\frac{1}{n}\int_0^x \frac{dF^0}{(1-F)(1-F^0)} \tag{5.8}$$

(cf. Breslow and Crowley (1974), Theorem 4), and so it follows that $\Lambda_n^0(x)$ has the same asymptotic distribution.

In order to study the Kaplan-Meier estimator, expand the logarithm:

$$\ln \bar{F}_n^0(x) = -\Lambda_n^0(x) + \frac{1}{2}\sum_{i=1}^{n} \frac{\delta_{(i)}(x)}{(n-i+1)^2} - \ldots \tag{5.9}$$

Now jackknife, and observe that the result of jackknifing the second and higher order terms in (5.9) lead to expressions which are $o_p(1/\sqrt{n})$, and so the jackknifed version of $\ln \bar{F}_n^0(x)$ has the same asymptotic (normal) distribution as $-\Lambda_n^0(x)$. Since $\exp[\ln \bar{F}_n^0(x)] = \bar{F}_n^0(x)$, and the exponential function is smooth (possesses a power-series expansion) it may be shown that the normality of the jackknifed version of $\ln \bar{F}_n^0(x)$ implies that of the jackknifed $\bar{F}_n^0(x)$. Furthermore, the asymptotic normal distribution has mean $\bar{F}^0(x)$ and variance $\frac{(1-F^0(x))^2}{n}\int_0^x \frac{dF^0}{(1-F)(1-F^0)}$.

5.4. Consistency of the Sample Variance

It may be shown that the sample variance of pseudovalues converges (a.s.) to the correct population variance, further justifying the use of the jackknife for large samples. We merely sketch the demonstration; see Miller (1975) for details. Begin again by considering the pseudovalues obtained by jackknifing the sample cumulative hazard function. From (5.5) the jackknife variance estimate is given by

$$n\,\mathrm{Var}\,[\Lambda_n^0(x)] \equiv \frac{1}{n-1}\sum_{i=1}^{n}\{\Lambda_{n-}(x;i) - \Lambda_n^0(x)\}^2 =$$

$$= \left(\frac{1}{n-1}\right)\sum_{i=1}^{n}\left\{\frac{n\delta_{(i)}(x)}{n-i+1} - \sum_{j=1}^{i-1}\frac{(j-1)\delta_{(j)}(x)}{(n-j)(n-j+1)} + \sum_{j=i+1}^{n}\frac{\delta_{(j)}(x)}{n-j+1}\right.$$

$$\left. - \sum_{j=1}^{n}\frac{\delta_{(j)}(x)}{n-j+1} - \frac{n-1}{n}\,\delta_{(n)}(x)\right\}^2 \qquad (5.10)$$

$$= \frac{1}{n-1}\sum_{i=1}^{n}\left\{\frac{n\delta_{(i)}(x)}{n-i+1} - \sum_{j=1}^{i-1}\frac{(j-1)\delta_{(j)}(x)}{(n-j)(n-j+1)} - \sum_{n=1}^{i}\frac{\delta_{(j)}(x)}{n-j+1} - \frac{n-1}{n}\delta_{(n)}(x)\right\}^2$$

$$= (n-1)\sum_{i=1}^{n}\left\{\frac{\delta_{(i)}(x)}{n-i+1} - \sum_{j=1}^{i-1}\frac{\delta_{(j)}(x)}{(n-j)(n-j+1)} - \frac{\delta_{(n)}(x)}{n}\right\}^2 .$$

Now square and study the individual terms. In particular the first sum of squares is

$$(n-1)\sum_{i=1}^{n}\left(\frac{\delta_{(i)}(x)}{n-i+1}\right)^2 = \left(\frac{n-1}{n}\right)\sum_{i=1}^{n}\left(\frac{n}{n-i+1}\right)^2\frac{\delta_{(i)}(x)}{n}$$

$$\xrightarrow{a.s.} \int_0^x \frac{d\,F^0}{(1-F)(1-F^0)} \qquad (5.11)$$

agreeing with the correct value (5.8) multiplied by n. Consequently the remaining terms must cancel out in the a.s. limit in order that the jackknife variance function properly. The steps are omitted here; see Miller (1975) for details. Finally, the correctness of the jackknife variance for the sample chf extends to the Kaplan-Meier estimate by previous arguments. It may also be shown that the jackknife works properly on any estimator which is a smooth-enough function of $\bar{F}_n^0$; in particular the arc-sine, log, or logistic transformations may all be jackknifed, which justifies the approach taken in Sections 3 and 4.

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