1997

An exploration of the pseudo-binomial distribution with applications to survival curve confidence intervals.

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AN EXPLORATION OF THE PSEUDO-BINOMIAL DISTRIBUTION WITH APPLICATIONS TO SURVIVAL CURVE CONFIDENCE INTERVALS

by

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A DISSERTATION

Submitted to the graduate faculty of The University of Alabama at Birmingham,
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy

BIRMINGHAM, ALABAMA

1997

underestimate the maximum likelihood estimator. A suggestion for correcting the bias in the first two moments is presented.

The pseudo-binomial confidence intervals are compared to the Greenwood and Rothman confidence intervals using data generated from the Weibull distribution. The pseudo-binomial intervals are shown to be significantly more accurate than the Greenwood intervals. They are also shown to demonstrate less error overall than the Rothman intervals, although the difference is not statistically significant.

The pseudo-binomial and Rothman intervals are then constructed using the Berliner-Hill estimator and Peto effective sample size. These are compared to the intervals constructed using the Kaplan-Meier estimator and Cutler-Ederer effective sample size. Although the Rothman intervals improved with the use of the Peto effective sample size, the pseudo-binomial intervals still demonstrated less error overall.

ACKNOWLEDGMENTS

I first acknowledge my advisor, Dr. Bradley. Thank you for giving me the opportunity to learn from "The Master." I also acknowledge the members of my committee, Dr. Katholi, Dr. Turner, Dr. Hovinga and Dr. Hardin. I appreciate your support and guidance throughout this endeavor.

I extend thanks to the faculty and staff of the Biostatistics department and to my fellow students. You have made my time at UAB enjoyable.

Finally, I recognize the love and support of the members of my family. With your encouragement, I finally finished my "paper." Most of all, I am indebted to my husband. Thank you for the support you give me when I want to do something and for your patience while I try to figure out how to do it.

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CHAPTER 1

INTRODUCTION

The term *survival time* is used to describe the measurement of time to any given event, whether it be death, end of disease remission, failure of a machine, or change in employment. Analysis of survival time data has been performed within a variety of disciplines, including biomedical research, economy, engineering, and insurance to name a few. The purpose of survival analysis, common to all fields in which survival studies are conducted, is the development of probability statements about the survival times (Gross & Clark, 1975).

A simple mortality table was published in 1693 by Halley. His work is discussed by Todhunter (1949) and Nelson (1982). Halley's table merely lists the number of people alive at each age. Since that time, reliability and mortality studies have been concerned with determining the probability of failure of a system or death of a patient. Davis (1952) introduced the conditional density function and defined its relationship with the probability density function and the cumulative probability function of failure time data. While Davis focused on the failure of machines, he noted that the force of mortality observed in actuarial studies is merely the conditional density function, where the system being observed is the human being.

Medical researchers in the past have relied on survival analysis techniques as a way to determine the effectiveness of a treatment. The *5-year cure rate*, or the proportion

of patients alive 5 years after treatment, was the preferred indicator of cancer treatment. Berkson and Gage (1952), dissatisfied with the assumptions that a) any cancer patient who survives 5 years can be considered cured, b) all deaths in the 5-year period are due to cancer, c) any person without cancer would still be alive after 5 years, and d) all deaths after the 5-year period are not attributable to cancer, introduced a survival curve. This curve was defined by an equation with two adjustable parameters, the fraction cured and the instantaneous risk of death from cancer. From their curve, an expectation of life could be determined.

Kaplan and Meier (1958) developed a nonparametric method to estimate the probability of survival. In their work, they also discussed the problem of incomplete observations, those losses not attributable to the condition being studied. Although research has continued in the area of survival analysis, the Kaplan-Meier estimator is still most commonly used. The Kaplan-Meier product-limit estimator is the basis of the LIFETEST procedure in SAS (SAS Institute, 1990).

This chapter contains a brief explanation of the functions used in the analysis of survival data. An introduction to the proposed pseudo-binomial distribution will be presented and a description of some of the topics pertaining to survival analysis that have been discussed in literature is given. Finally, an overview of the remainder of this work is presented.

Functions Used in Survival Analysis

The measured time of survival is a random variable and, therefore, forms some distribution. The distribution of the survival times is characterized by three mathematically equivalent functions: the probability density function, the hazard

The hazard function measures the proneness to an event as a function of age (Nelson, 1982). The shape of the hazard function (increasing, decreasing, constant, J-shaped, or "bathtub") is an indicator of the type of risk to which the study population is exposed as a function of time (Gross & Clark, 1975; Lee, 1992).

The survivorship function, or cumulative survival rate, is the probability of an event occurring after time t. The survival function is given by

$$\begin{aligned} S(t) &= P(\text{event occurs after time } t) \\ &= P(T > t) \end{aligned}$$

and has the following properties:

1. $S(t)$ is nonincreasing; and

2. $S(t) = \begin{cases} 1 \text{ for } t = 0 \\ 0 \text{ for } t \to \infty \end{cases}$.

The survival function is most often used to determine various percentiles of survival time with the median, or 50th percentile, being an estimate of "typical" life (Nelson, 1982). From the survival function $S(t)$, a survival curve can be drawn to illustrate the survival rate over time.

Introduction to the Pseudo-Binomial Distribution

Working with Blackstone, Kirklin, Pluth, Turner, and Parr (1977), Bradley used the relationship between the binomial probability function and the incomplete beta function to construct confidence limits for the probability of survival. In the study, the observed outcome was poppet escape after aortic valve replacement. The random variable X, the number of patients remaining event free, was termed a *pseudo-binomial*

random variable. This dissertation extends the work of Fox (1995) in describing this distribution and further examines its applicability in survival studies.

Issues in Survival Analysis

Research into survival analysis methods has considered several problematic issues. These include estimation of survival probability, the treatment of partial survival information, and the presentation of survival data. A brief introduction to these topics will be given here, with further discussion presented in chapter 3.

One topic debated in the literature is the appropriate estimation of the survivorship function. The analysis of survival data often is concerned with estimating the unknown parameters of a distribution hypothesized to fit the data. Generally, the distributions considered are the exponential, Weibull, lognormal, and gamma distributions. However, if the survival distribution of the data is not known or does not adequately describe the data, estimation must be made without assuming a distribution.

Nonparametric techniques are employed in such instances. The most commonly used nonparametric estimator of survival probability is the Kaplan-Meier estimator. A modification to that estimator, the Berliner-Hill estimator, was developed through the use of Bayesian theory. Both the Kaplan-Meier and Berliner-Hill estimators will be considered in this study.

Another area of concern is the treatment of partial survival information. In most survival studies, the exact survival time is not known for all subjects in the study. Some subjects may still be event-free at the end of the study, while others are lost to follow-up. It is likely that some events occurring during the study cannot be attributed to the condition being observed. In all of these scenarios, the subjects are considered *censored*

distribution and more complete analysis methods. Chapter 5 focuses on the pseudo-binomial and Rothman intervals, incorporating alternative survival estimation and effective sample size calculations. Chapter 6 presents the application of the pseudo-binomial confidence limits to survival data. Chapter 7 discusses the results of this study and presents suggestions for further research into the pseudo-binomial distribution and its applications.

CHAPTER 2

AN EXPLORATION OF THE PSEUDO-BINOMIAL DISTRIBUTION

The pseudo-binomial distribution, derived from the relationship between the binomial probability distribution and the incomplete beta function, was previously explored by Fox (1995). The cumulative distribution function of the pseudo-binomial distribution was defined, and numerical analysis techniques were used to approximate the first two moments of the distribution. This chapter further examines the pseudo-binomial distribution. The probability density function is derived, the analytical derivation of the first two moments is discussed, suggestions for improving the behavior of the pseudo-binomial distribution are presented, and the maximum likelihood estimator for p is given.

Probability Density Function

The cumulative distribution function of the pseudo-binomial distribution is

$$F_X(k) = \int_p^1 \frac{\Gamma(N+1)}{\Gamma(k+1)\Gamma(N-k)} \left(\frac{t}{1-t}\right)^k (1-t)^{N-1} dt .$$

The probability density function is obtained by taking the derivative of the cumulative distribution function.

$$f_X(k) = \frac{d}{dk}\left\{\int_p^1 \frac{\Gamma(N+1)}{\Gamma(k+1)\Gamma(N-k)} \left(\frac{t}{1-t}\right)^k (1-t)^{N-1} dt\right\}$$

$$= \Gamma(N-1)\frac{d}{dk}\left\{\int_p^1 \frac{1}{\Gamma(k+1)\Gamma(N-k)} \left(\frac{t}{1-t}\right)^k (1-t)^{N-1} dt\right\} .$$

The derivative of the gamma function can be determined from the digamma function, $\psi(k)$. That is,

$$\frac{d}{dk}\ln\Gamma(k) = \psi(k) = \frac{1}{\Gamma(k)}\frac{d}{dk}\Gamma(k) = \frac{\Gamma'(k)}{\Gamma(k)}.$$

Thus, $\Gamma'(k) = \Gamma(k)\psi(k)$. Also, $\frac{d}{dk}a^k = a^k \ln a$. Using these results, the probability density function is

$$f_X(k) = \int_p^t \frac{\Gamma(N+1)}{\Gamma(k+1)\Gamma(N-k)}\left(\frac{t}{1-t}\right)^k (1-t)^{N-1}\left[\psi(N-k) - \psi(k+1) + \ln\left(\frac{t}{1-t}\right)\right]dt.$$

Moments of the Pseudo-Binomial Distribution

The expected moments of a distribution can be found by using the Equation

$$E(X^\alpha) = \int_0^\infty x^\alpha f(x)\,dx = \alpha\int_0^\infty x^{\alpha-1}[1-F(x)]\,dx \qquad (1)$$

(Feller, 1966). The first two noncentral moments of the pseudo-binomial distribution are given by

$$E(X) = \int_0^{N-1} I_p(k+1, N-k)\,dk \qquad (2)$$

and

$$E(X^2) = 2\int_0^{N-1} k\; I_p(k+1, N-k)\,dk \qquad (3)$$

where $I_p(k+1, N-k)$ is the incomplete beta function. The results of the numerical analysis techniques performed by Fox (1995) suggested that the expected value and the variance of X, the pseudo-binomial random variable, are $E(X) = Np - 1/2$ and $\text{var}(X) = Np(1-p) - 1/12$ for $N \geq 50$. These initial results are shown in Table 1.

Table 1

Mean and Variance of the Pseudo-Binomial Distribution Obtained Through Numerical Integration

N	*p*	E(*X*)	var(*X*)	*N*	*p*	E(*X*)	var(*X*)
50	.10	4.5015	4.4020	80	.10	7.5001	7.1157
	.20	9.5000	7.9166		.20	15.5000	12.7167
	.30	14.5000	10.4167		.30	23.5000	16.7167
	.40	19.5000	11.9167		.40	31.5000	19.1167
	.50	24.5000	12.4167		.50	39.5000	19.9167
	.60	29.5000	11.9167		.60	47.5000	19.1167
	.70	34.5000	10.4167		.70	55.5000	16.7167
	.80	39.5001	7.9167		.80	63.5000	12.7167
	.90	44.5001	4.4173		.90	71.5000	7.1167
60	.10	5.5005	5.3107	90	.10	8.5000	8.0163
	.20	11.5000	9.5167		.20	17.5000	14.6137
	.30	17.5000	12.5167		.30	26.5000	18.8167
	.40	23.5000	14.3167		.40	35.5000	21.5167
	.50	29.5000	14.9167		.50	44.5000	22.4167
	.60	35.5000	14.3167		.60	53.5000	21.5167
	.70	41.5000	12.5167		.70	62.5000	18.8167
	.80	47.5000	9.5167		.80	71.5000	14.3167
	.90	53.5000	5.3169		.90	80.5000	8.0167
70	.10	6.5002	6.2143	100	.10	9.5000	8.9165
	.20	13.5000	11.1167		.20	19.5000	15.9167
	.30	20.5000	14.6167		.30	29.5000	20.9167
	.40	27.5000	16.7167		.40	39.5000	23.9167
	.50	34.5000	17.4167		.50	49.5000	24.9167
	.60	41.5000	16.7167		.60	59.5000	23.9167
	.70	48.5000	14.6167		.70	69.5000	20.9167
	.80	55.5000	11.1167		.80	79.5000	15.9167
	.90	62.5000	6.2167		.90	89.5000	8.9167

Note. E(*X*) is the expected value and var(*X*) is the variance of the pseudo-binomial random variable *X*.

An attempt to analytically derive the first two moments of the pseudo-binomial distribution was made. The derivations are contained in Appendix A. The Euler-Maclaurin expansion (Abramowitz & Stegun, 1974) was used to approximate the

moments as defined in Equations 2 and 3. The expansion approximated the moments as

$$E(X) \approx Np - \frac{1}{2} + \frac{(1-p)^N - p^N}{2} \tag{4}$$

and

$$E(X^2) \approx N(N-1)p^2 + \frac{1}{6} - (N-1)p^N - \frac{p^N + (1-p)^N}{6}. \tag{5}$$

The variance of X, given by $\text{var}(X) = E(X^2) - E^2(X)$, is then

$$\begin{aligned} \text{var}(X) \approx\ & Np(1-p) - \frac{1}{12} - (N-1)p^N - \frac{p^N + (1-p)^N}{6} \\ & + \left(Np - \frac{1}{2}\right)\left(p^N - (1-p)^N\right) - \left(\frac{(1-p)^N - p^N}{2}\right)^2. \end{aligned} \tag{6}$$

The analytical approximation of the mean (Equation 4) and variance (Equation 6) support the conclusion suggested by the results of the numerical integration carried out previously. Obviously, the terms containing p^N and $(1-p)^N$ will become small as N gets large. To determine at what point those terms become negligible, the numerical integration was repeated for small N and the mean and variance calculated. The expected values computed by numerical integration, denoted by μ_1, the initial estimate of the mean ($Np - 1/2$), μ_2, and the approximation of the mean defined in Equation 4, μ_3, are shown in Table 2. Similarly, the variances as computed by numerical integration (σ^2_1), using the initial estimate $Np - 1/12$ (σ^2_2), and from the definition shown in Equation 6 (σ^2_3) are contained in Table 3.

Table 2 shows that for N equal to or greater than 30, the terms containing p^N and $(1-p)^N$ have very little effect on the approximation $Np - 1/2$ of the mean. Even for N as small as 15, the simple approximation underestimates the mean by only 7% for $p = .1$,

Table 2

Comparison of Means Obtained by Different Methods

N	p	μ_1	μ_2	μ_3	N	p	μ_1	μ_2	μ_3	N	p	μ_1	μ_2	μ_3
1	.10	0.0000	-0.4000	0.0000	3	.10	0.1239	-0.2000	0.1640	5	.10	0.2513	0.0000	0.2952
	.20	0.0000	-0.3000	0.0000		.20	0.3074	0.1000	0.3520		.20	0.6259	0.5000	0.6637
	.30	0.0000	-0.2000	0.0000		.30	0.5227	0.4000	0.5580		.30	1.0588	1.0000	1.0828
	.40	0.0000	-0.1000	0.0000		.40	0.7569	0.7000	0.7760		.40	1.5225	1.5000	1.5338
	.50	0.0000	0.0000	0.0000		.50	1.0000	1.0000	1.0000		.50	2.0000	2.0000	2.0000
	.60	0.0000	0.1000	0.0000		.60	1.2431	1.3000	1.2240		.60	2.4774	2.5000	2.4662
	.70	0.0000	0.2000	0.0000		.70	1.4773	1.6000	1.4420		.70	2.9412	3.0000	2.9172
	.80	0.0000	0.3000	0.0000		.80	1.6925	1.9000	1.6480		.80	3.3741	3.5000	3.3363
	.90	0.0000	0.4000	0.0000		.90	1.8760	2.2000	1.8360		.90	3.7487	4.0000	3.7048
2	.10	0.0678	-0.3000	0.1000	4	.10	0.1850	-0.1000	0.2280	10	.10	0.6371	0.5000	0.6743
	.20	0.1619	-0.1000	0.2000		.20	0.4617	0.3000	0.5040		.20	1.5373	1.5000	1.5537
	.30	0.2686	0.1000	0.3000		.30	0.7855	0.7000	0.8160		.30	2.5089	2.5000	2.5141
	.40	0.3826	0.3000	0.4000		.40	1.1365	1.1000	1.1520		.40	3.5017	3.5000	3.5030
	.50	0.5000	0.5000	0.5000		.50	1.5000	1.5000	1.5000		.50	4.5000	4.5000	4.5000
	.60	0.6173	0.7000	0.6000		.60	1.8635	1.9000	1.8480		.60	5.4983	5.5000	5.4970
	.70	0.7313	0.9000	0.7000		.70	2.2145	2.3000	2.1840		.70	6.4911	6.5000	6.4859
	.80	0.8381	1.1000	0.8000		.80	2.5383	2.7000	2.4960		.80	7.4627	7.5000	7.4463
	.90	0.9322	1.3000	0.9000		.90	2.8150	3.1000	2.7720		.90	8.3629	8.5000	8.3257

Table 2 (Continued)

N	p	μ_1	μ_2	μ_3	N	p	μ_1	μ_2	μ_3	N	p	μ_1	μ_2	μ_3
15	.10	1.0765	1.0000	1.1029	25	.10	2.0246	2.0000	2.0359	35	.10	3.0081	3.0000	3.0125
	.20	2.5114	2.5000	2.5176		.20	4.5011	4.5000	4.5019		.20	6.5001	6.5000	6.5002
	.30	4.0014	4.0000	4.0024		.30	7.0000	7.0000	7.0001		.30	10.0000	10.0000	10.0000
	.40	5.5001	5.5000	5.5002		.40	9.5000	9.5000	9.5000		.40	13.5000	13.5000	13.5000
	.50	7.0000	7.0000	7.0000		.50	12.0000	12.0000	12.0000		.50	17.0000	17.0000	17.0000
	.60	8.4999	8.5000	8.4998		.60	14.5000	14.5000	14.5000		.60	20.5000	20.5000	20.5000
	.70	9.9986	10.0000	9.9976		.70	17.0000	17.0000	16.9999		.70	24.0000	24.0000	24.0000
	.80	11.4886	11.5000	11.4824		.80	19.4989	19.5000	19.4981		.80	27.4999	27.5000	27.4998
	.90	12.9235	13.0000	12.8971		.90	21.9754	22.0000	21.9641		.90	30.9919	31.0000	30.9875
20	.10	1.5432	1.5000	1.5608	30	.10	2.5141	2.5000	2.5212	40	.10	3.5047	3.5000	3.5074
	.20	3.5035	3.5000	3.5058		.20	5.5004	5.5000	5.5006		.20	7.5000	7.5000	7.5001
	.30	5.5002	5.5000	5.5004		.30	8.5000	8.5000	8.5000		.30	11.5000	11.5000	11.5000
	.40	7.5000	7.5000	7.5000		.40	11.5000	11.5000	11.5000		.40	15.5000	15.5000	15.5000
	.50	9.5000	9.5000	9.5000		.50	14.5000	14.5000	14.5000		.50	19.5000	19.5000	19.5000
	.60	11.5000	11.5000	11.5000		.60	17.5000	17.5000	17.5000		.60	23.5000	23.5000	23.5000
	.70	13.4998	13.5000	13.4996		.70	20.5000	20.5000	20.5000		.70	27.5000	27.5000	27.5000
	.80	15.4965	15.5000	15.4942		.80	23.4996	23.5000	23.4994		.80	31.5000	31.5000	31.4999
	.90	17.4568	17.5000	17.4392		.90	26.4859	26.5000	26.4788		.90	35.4953	35.5000	35.4926

Note. μ_1 is the expected value obtained through numerical integration, μ_2 is given by the simple approximation $Np - 1/2$, and μ_3 is the approximate expected value defined in Equation 4.

with the bias decreasing as p approaches 0.50. For N smaller than 15, more accurate results would be obtained using the approximation defined in Equation 4. It should be noted that the simple approximation underestimates the mean for $p < .50$ and overestimates the mean for $p > .50$, while the more complete approximation behaves oppositely.

Table 3 shows similar results for the variance approximation. With an N of at least 30, very little additional information over the approximation $Np(1-p)-1/12$ is gained through the use of the terms involving p^N and $(1-p)^N$. However, the simpler approximation consistently overestimates the variance of X, while the approximation defined in Equation 6 consistently underestimates the variance.

The power of a test is inversely related to the standard deviation (Rosner, 1990). That is, as the standard devation increases, the power of a test decreases. Because the true variance would be smaller than a conservative estimate of the variance, the true power of a test would be greater than the power of a test conducted using the conservative estimate. Therefore, although the bias is large for small N, the simpler approximation for the variance of the pseudo-binomial random variable X may be more desirable than the more definite approximation which underestimates the variance.

The expected value of a binomial random variable is Np, while numerical integration suggested the expected value of a pseudo-binomial random variable to be approximately $Np-1/2$. This shift in expectation is illustrated in Figures 1 and 2. Mathcad 4.0 was used to estimate the probability density function of the pseudo-binomial distribution. The probability density function of the pseudo-binomial distribution was then superimposed over the binomial probability distribution. For both figures, N was

Table 3

Comparison of Variances Obtained by Different Methods

N	p	σ^2_1	σ^2_2	σ^2_3	N	p	σ^2_1	σ^2_2	σ^2_3	N	p	σ^2_1	σ^2_2	σ^2_3
1	.10	0.0000	0.0067	0.0000	3	.10	0.0831	0.1867	0.0761	5	.10	0.2014	0.3667	0.1810
	.20	0.0000	0.0767	0.0000		.20	0.2156	0.3967	0.1801		.20	0.5202	0.7167	0.4703
	.30	0.0000	0.1267	0.0000		.30	0.3435	0.5467	0.2796		.30	0.8144	0.9667	0.7560
	.40	0.0000	0.1567	0.0000		.40	0.4335	0.6367	0.3498		.40	1.0131	1.1167	0.9586
	.50	0.0000	0.0167	0.0000		.50	0.4657	0.6667	0.3750		.50	1.0826	1.1667	1.0313
	.60	0.0000	0.1567	0.0000		.60	0.4335	0.6367	0.3498		.60	1.0131	1.1167	0.9586
	.70	0.0000	0.1267	0.0000		.70	0.3435	0.5467	0.2796		.70	0.8144	0.9667	0.7560
	.80	0.0000	0.0767	0.0000		.80	0.2156	0.3967	0.1801		.80	0.5202	0.7167	0.4703
	.90	0.0000	0.0067	0.0000		.90	0.0831	0.1867	0.0761		.90	0.2014	0.3667	0.1810
2	.10	0.0351	0.0967	0.0300	4	.10	0.1383	0.2767	0.1250	10	.10	0.6027	0.8167	0.5538
	.20	0.0831	0.2367	0.0533		.20	0.3622	0.5567	0.3193		.20	1.3872	1.5167	1.3348
	.30	0.1259	0.3367	0.0700		.30	0.5775	0.7567	0.5151		.30	1.9682	2.0167	1.9411
	.40	0.1546	0.3967	0.0800		.40	0.7279	0.8767	0.6569		.40	2.3033	2.3167	2.2939
	.50	0.1647	0.4167	0.0833		.50	0.7814	0.9167	0.7083		.50	2.4117	2.4167	2.4076
	.60	0.1546	0.3967	0.0800		.60	0.7279	0.8767	0.6569		.60	2.3033	2.3167	2.2939
	.70	0.1259	0.3367	0.0700		.70	0.5775	0.7567	0.5151		.70	1.9682	2.0167	1.9411
	.80	0.0831	0.2367	0.0533		.80	0.3622	0.5567	0.3193		.80	1.3872	1.5167	1.3348
	.90	0.0351	0.0967	0.0300		.90	0.1383	0.2767	0.1250		.90	0.6027	0.8167	0.5538

Table 3 (Continued)

N	p	σ^2_1	σ^2_2	σ^2_3	N	p	σ^2_1	σ^2_2	σ^2_3	N	p	σ^2_1	σ^2_2	σ^2_3
15	.10	1.0748	1.2667	1.0159	25	.10	2.0570	2.1667	2.0098	35	.10	3.0146	3.0667	2.9872
	.20	2.2545	2.3167	2.2225		.20	3.9061	3.9167	3.8990		.20	5.5152	5.5167	5.5140
	.30	3.0549	3.0667	3.0469		.30	5.1661	5.1667	5.1657		.30	7.2666	7.2667	7.2666
	.40	3.5152	3.5167	3.5140		.40	5.9167	5.9167	5.9166		.40	8.3167	8.3167	8.3167
	.50	3.6664	3.6667	3.6662		.50	6.1667	6.1667	6.1667		.50	8.6667	8.6667	8.6667
	.60	3.5152	3.5167	3.5140		.60	5.9167	5.9167	5.9166		.60	8.3167	8.3167	8.3167
	.70	3.0549	3.0667	3.0469		.70	5.1661	5.1667	5.1657		.70	7.2666	7.2667	7.2666
	.80	2.2545	2.3167	2.2225		.80	3.9061	3.9167	3.8990		.80	5.5152	5.5167	5.5140
	.90	1.0748	1.2667	1.0159		.90	2.0570	2.1667	2.0098		.90	3.0146	3.0667	2.9872
20	.10	1.5664	1.7167	1.5103	30	.10	2.5400	2.6167	2.5032	40	.10	3.4820	3.5167	3.4624
	.20	3.0903	3.1167	3.0744		.20	4.7126	4.7167	4.7097		.20	6.3161	6.3167	6.3157
	.30	4.1141	4.1167	4.1121		.30	6.2165	6.2167	6.2165		.30	8.3167	8.3167	8.3167
	.40	4.7165	4.7167	4.7164		.40	7.1167	7.1167	7.1167		.40	9.5167	9.5167	9.5167
	.50	4.9167	4.9167	4.9167		.50	7.4167	7.4167	7.4167		.50	9.9167	9.9167	9.9167
	.60	4.7165	4.7167	4.7164		.60	7.1167	7.1167	7.1167		.60	9.5167	9.5167	9.5167
	.70	4.1141	4.1167	4.1121		.70	6.2165	6.2167	6.2165		.70	8.3167	8.3167	8.3167
	.80	3.0903	3.1167	3.0744		.80	4.7126	4.7167	4.7097		.80	6.3161	6.3167	6.3157
	.90	1.5664	1.7167	1.5103		.90	2.5400	2.6167	2.5032		.90	3.4820	3.5167	3.4624

Note. σ^2_1 is the expected value obtained through numerical integration, σ^2_2 is given by the simple approximation $Np - 1/12$, and σ^2_3 is the approximate expected value defined in Equation 6.

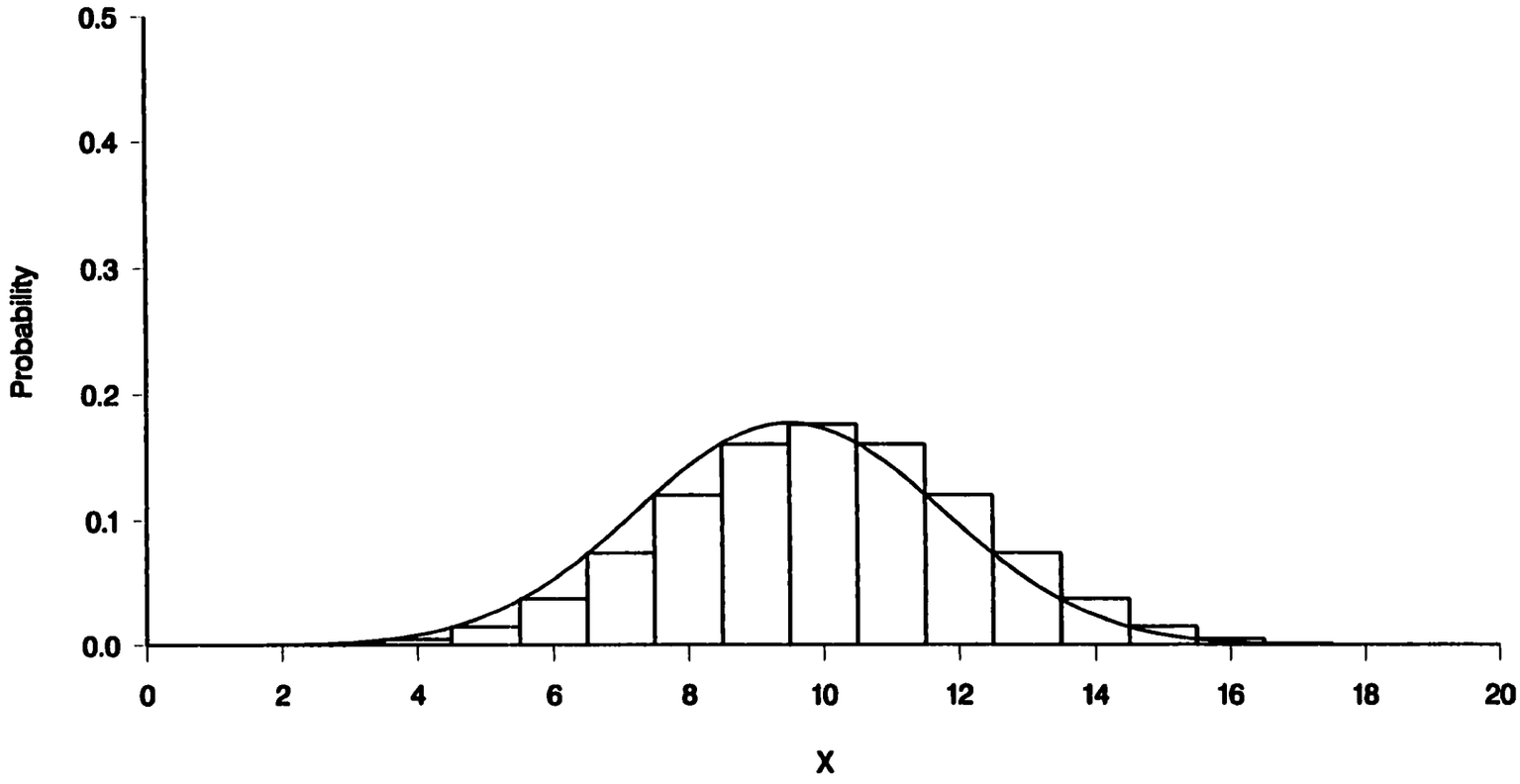


Figure 1. Probability density function of the pseudo-binomial distribution superimposed over the binomial probability distribution, $N = 20$ and $p = .50$.

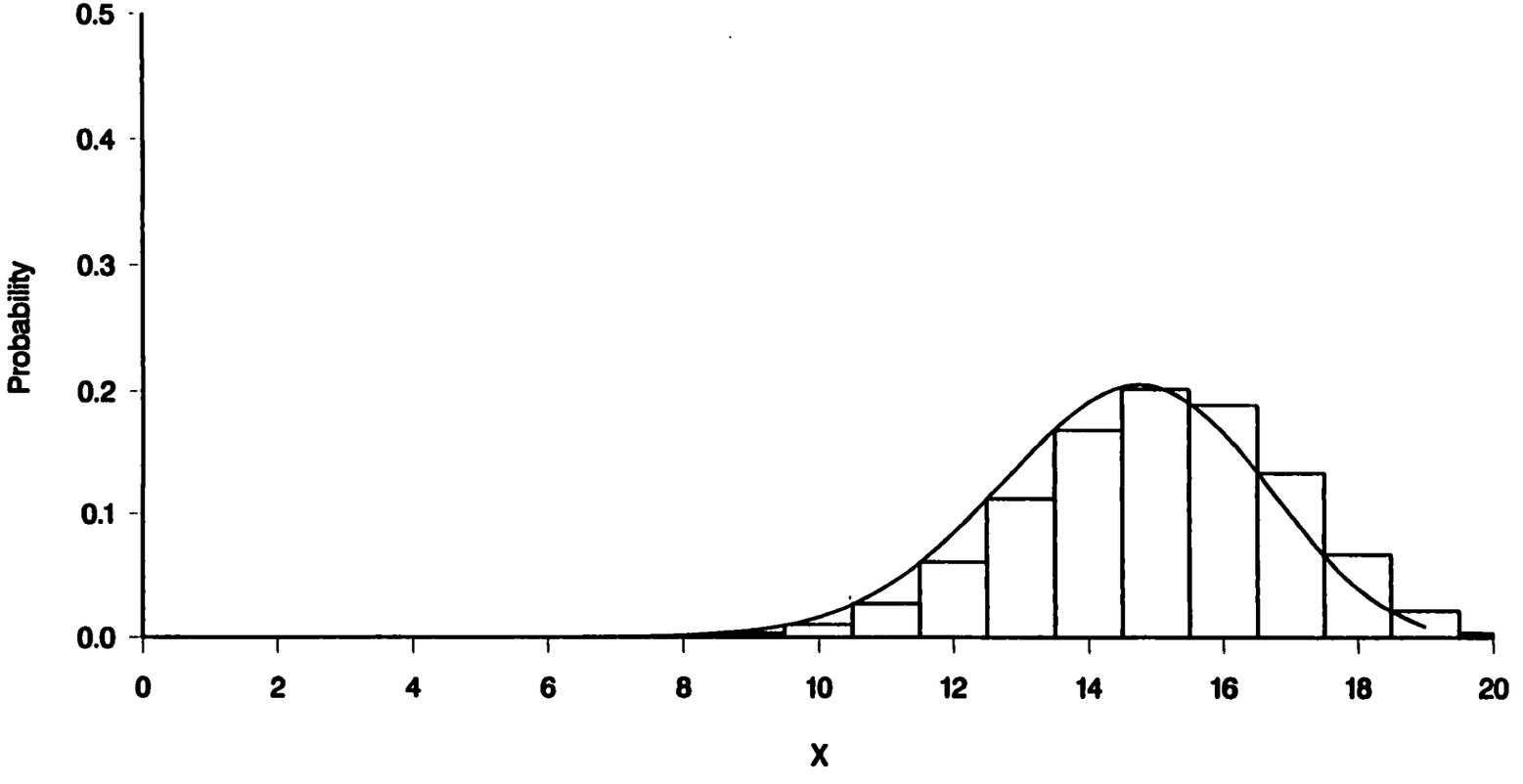


Figure 2. **Probability density function of the pseudo-binomial distribution superimposed over the binomial probability distribution, $N = 20$ and $p = .75$.**

$$E(Y) = E(X+U) = E(X) + E(U) \approx Np - 1/2 + 1/2 = Np$$

and

$$\begin{aligned} \text{var}(Y) &= \text{var}(X+U) = \text{var}(X) + \text{var}(U) + 2\,\text{cov}(X,U) \\ &\approx Np(1-p) - 1/12 + 1/12 + 0 = Np(1-p). \end{aligned}$$

The cumulative distribution function for the new random variable Y would be

$$\begin{aligned} F_Y(y) &= \Pr(Y \le y) = \Pr(X+U \le y) \\ &= \int_0^1 \Pr(X \le y-u) f_U(u)\,du \\ &= \int_0^1 F_X(y-u)\,du \end{aligned}$$

and the probability distribution function is

$$f_Y(y) = \int_0^1 f_X(y-u)\,du\,.$$

The region in which the distribution of the new random variable Y is defined is now $0 \le Y \le N$, whereas the distribution for the random variable X was defined only for $0 \le X \le N-1$. Further research into the use of the Uniform(0,1) distribution as a correction to the pseudo-binomial distribution was not conducted at this time.

Maximum Likelihood Estimation of the Pseudo-Binomial Parameter p

An unknown distributional parameter can be estimated using the likelihood function,

$$L(p) = f(X_1|p) f(X_2|p) \cdots f(X_n|p)\ .$$

The maximum likelihood estimator is that which maximizes the function $L(p)$, or equivalently, $\ln L(p)$ (Dudewicz & Mishra, 1988). In the case of the pseudo-binomial distribution, the unknown parameter p is the proportion of survivors at a given point.

Therefore, the maximum likelihood function for the pseudo-binomial distribution is merely $L(p) = f(X|p)$.

The maximum likelihood estimator of p, $\hat{p}$, is the solution of

$$\frac{\partial}{\partial p} f(X|p)\Big|_{p=\hat{p}} = \frac{\partial^2 F(X)}{\partial p \partial X}\Big|_{p=\hat{p}} = 0. \tag{7}$$

Note that

$$\frac{\partial}{\partial X} \ln \frac{-\partial F(X)}{\partial p} = \frac{\dfrac{\partial^2 F(X)}{\partial X \partial p}}{\dfrac{\partial F(X)}{\partial p}} \propto \frac{\partial^2 F(X)}{\partial X \partial p}. \tag{8}$$

Therefore, because $\frac{\partial}{\partial X} \ln \frac{-\partial F(X)}{\partial p}$ is proportional to $\frac{\partial^2 F(X)}{\partial p \partial X}$, the solution $\hat{p}$ of Equation 7 is also the estimator that will maximize Equation 8. Thus $\hat{p}$ is the solution of

$$\frac{\partial}{\partial X} \ln \frac{-\partial F(X)}{\partial p}\Big|_{p=\hat{p}} = 0.$$

The partial derivative of the cumulative distribution function of the pseudo-binomial distribution with respect to p is

$$\frac{\partial F(X)}{\partial p} = -\frac{\Gamma(N+1)}{\Gamma(X+1)\Gamma(N-X)} p^X (1-p)^{N-X-1} \tag{9}$$

so that the function to be maximized is

$$\begin{aligned} \ln \frac{-\partial F(X)}{\partial p} &= \ln\left(\frac{\Gamma(N+1)}{\Gamma(X+1)\Gamma(N-X)} p^X (1-p)^{N-X-1} \right) \\ &= \ln\Gamma(N+1) - \ln\Gamma(X+1) - \ln\Gamma(N-X) \\ &\quad + X \ln p + (N-X-1)\ln(1-p). \end{aligned} \tag{10}$$

Then the maximum likelihood estimator $\hat{p}$ is the solution to

$$\frac{\partial}{\partial X} \ln \frac{-\partial F(X)}{\partial p}\Big|_{p=\hat{p}} = -\psi(X+1) + \psi(N-X) + \ln p - \ln(1-p)\Big|_{p=\hat{p}} = 0$$

which gives

$$-\psi(X+1)+\psi(N-X)+\ln\left(\frac{\hat{p}}{1-\hat{p}}\right)=0$$

so that

$$\hat{p}=\frac{e^{\psi(X+1)}}{e^{\psi(N-X)}+e^{\psi(X+1)}}. \tag{11}$$

The usual estimate for a binomial proportion is $\hat{p}_1 = X/N$. The maximum likelihood estimator for the pseudo-binomial parameter p given by Equation 10 was compared to the usual binomial estimator $\hat{p}_1$ and the binomial estimator using the proposed new random variable $Y = X + 1/2$, $\hat{p}_2 = (X+1/2)/N$. For values of N ranging from 5 to 50, and for each X = 0, 1, ... , N-1, the values of each of the three estimators were computed. The results are contained in Table 4. The maximum likelihood estimate of the pseudo-binomial distribution is denoted by $\hat{p}$, the usual binomial estimator is denoted by $\hat{p}_1$, and the estimator using the random variable Y is denoted by $\hat{p}_2$. The results for $N = 5$ and 10 are shown to indicate the behavior for small N, and $N = 50$ for large N. Similarly, for $N = 50$, the values of X ranging from 0 to 10 and from 40 to 49 were chosen as representative of the behavior of the estimators below and above the median X value.

From Table 4, it is seen that the usual binomial estimator ($\hat{p}_1$) consistently underestimates $\hat{p}$. The estimator $\hat{p}_2$, however, underestimates $\hat{p}$ for values of X below $(N-1)/2$ and overestimates $\hat{p}$ for values of X above $(N-1)/2$. Even for small values of N, the estimator $\hat{p}_2 = (X+1/2)/N$ is a better approximation to $\hat{p}$ than the usual

CHAPTER 3

CONSIDERATIONS IN THE ANALYSIS OF SURVIVAL TIME DATA

There are several issues to be considered in the analysis of survival time data. The estimation of the survivorship function, the treatment of censored observations, and the presentation of analysis results are some of the topics that have been discussed in literature. The variety of proposed methods of analysis indicate there is no "right" way to summarize the results of a survival study. A few of the different methods that have been proposed in each of these areas will be presented and discussed in this chapter.

Estimating the Survivorship Function

Often, the analysis of survival time data is concerned with estimating the parameters of a distribution hypothesized to fit the sample data. It is usually the case, however, that there is no distribution which adequately describes the data or that the data are not recognized as following a known distribution. In such instances, an estimate of the survivorship function must be made without assuming a distribution. The Kaplan-Meier and Berliner-Hill estimators have been proposed as two different nonparametric methods of estimating the survivorship function.

The nonparametric method most commonly used in estimating the survivorship function is the Kaplan-Meier estimator. If the survival time for all subjects is exact and known, the survival estimate is calculated by first arranging the N observed survival times from smallest to largest so that $0 \leq t_{(1)} \leq t_{(2)} \leq \ldots \leq t_{(N)}$. The estimate of the

survivorship function at any given time $t_{(i)}$ is simply

$$\hat{S}(t_{(i)}) = \frac{N-i}{N} = 1 - \frac{i}{N} \ ,$$

where N-i is the number of subjects surviving longer than time $t_{(i)}$.

If the exact survival time is not known for all patients, the survivorship function can be estimated by the Kaplan-Meier product-limit method. Kaplan and Meier (1958) developed the product-limit method as a nonparametric technique to be used in the estimation of the survivorship function. The product-limit estimate for the probability of the i^{th} subject surviving for some period of time t is given by

$$\hat{S}_{KM}(t_{(i)}) = p_1 \, x \, p_2 \, x \ldots x \, p_{i-1} \, x \, p_i$$

where p_j is the proportion of subjects surviving for time $t_{(j)}$ after they have survived for time $t_{(j-1)}$. The proportion p_i is given by

$$p_i = \frac{N-i}{N-i+1}$$

which leads to the result

$$\hat{S}_{KM}(t_{(i)}) = \hat{S}_{KM}(t_{(i-1)}) \frac{N-i}{N-i+1}$$

or

$$\hat{S}_{KM}(t) = \prod_{i:t_{(i)} \le t} \frac{N-i}{N-i+1}. \qquad (12)$$

An alternative estimator based on Bayesian theory has been proposed. Berliner and Hill (1988) pointed out that the primary focus of survival studies, particularly in the medical field, is prediction rather than estimation. That is, rather than merely observing the survival time of subjects in a study, an investigator is instead trying to predict the

approximate length of time a new patient can expect to survive. Berliner and Hill argued it is often the case that a probability of 0 is assigned to a future observation for which the survival time is larger than the largest or smaller than the smallest survival time observed in the study. It is unreasonable to expect that all future patients will survive at least as long as the shortest survival time observed in a study, but no longer than the longest. Hill (1992) suggested that a substantial proportion of censored patients could be expected to survive longer than the time of the last death. Berliner and Hill believed that the inappropriate assumption that all future deaths will occur within the length of time observed in the study, particularly in the case of large survival times, led to the unsuitability of the Kaplan-Meier estimate of the probability of survival.

Based on the work of Berliner and Hill, Chang (1989) developed the Berliner-Hill estimator. His work was further discussed by Hill (1992). The Berliner-Hill estimator is calculated under the assumptions that a) a future subject is exchangeable with previous subjects, and b) the probability of the next observation falling into the open interval $I_{(i)}$ is equal for all $i = 0, \ldots, N$. While the Berliner-Hill estimator is based on Bayesian theory and the use of predictive posterior probabilities, Hill pointed out that the Berliner-Hill estimator can be easily obtained using the Kaplan-Meier product-limit method by substituting $N+1$ for N. Thus,

$$\hat{S}_{\mathrm{BH}}(t) = \prod_{i:t_{(i)} \le t} \frac{N-i+1}{N-i+2} \quad . \tag{13}$$

Chang compared the Berliner-Hill estimator to the usual Kaplan-Meier estimator and found that the Berliner-Hill estimator performed better than the Kaplan-Meier estimator in estimating the mean and quartiles in most distributions.

Variance of the Survivorship Estimators

Greenwood (1926) used the Propagation of Error, or Law of the Total Differential, to develop an approximate variance for the actuarial estimate of the survivorship function (see Appendix B). Kaplan and Meier (1958) applied Greenwood's formulation to their product-limit estimator, resulting in what they termed Greenwood's formula,

$$\hat{\text{var}}\{\hat{S}_{\text{KM}}(t)\} = \hat{S}^2_{\text{KM}}(t) \sum_{i:t_{(i)}\le t} \frac{d_i}{N_i(N_i - d_i)}, \tag{14}$$

where $\hat{S}_{\text{KM}}(t)$ is the Kaplan-Meier product-limit estimate of the survival function; d_i is 1 if the i^{th} observation is a failure and 0 if censored; and N_i is the number of observations surviving just prior to time $t_{(i)}$, $N_i = N\text{-}i\text{+}1$.

The approximate variance for the Berliner-Hill estimator is calculated the same way, recognizing that the Berliner-Hill estimator is computed by adding one observation to the number at risk at each time. Thus, the approximate variance of the Berliner-Hill estimator is

$$\hat{\text{var}}\{\hat{S}_{\text{BH}}(t)\} = \hat{S}^2_{\text{BH}}(t) \sum_{i:t_{(i)}\le t} \frac{d_i}{(N_i + 1)(N_i + 1 - d_i)} \tag{15}$$

where $\hat{S}_{\text{BH}}(t)$ is the Berliner-Hill estimator of the survival function; d_i is 1 if the observation at time t_i is a failure and 0 if censored; and N_i+1 is the number of observations, plus one, surviving just prior to time $t_{(i)}$.

Partial Survival Information and Effective Sample Size

In a study, especially one which continues for several years, one or more subjects may be *lost*. That is, a subject may withdraw from the study at some point. It is also possible that a subject may still be alive at the end of the study or a subject has died as the

result of some accident unrelated to the study. In each instance, the only survival time information available is that the subject was still alive at the time of the last contact. Such individuals are *right-censored.*

Censored observations are not the only concern when estimating the survival function. It is common to continue to enter subjects into a study after the study has begun. Thus it is possible that data from a 5-year study may include subjects who have been observed for only 1 year. The calculation of an *effective sample size* allows the partial survival information from both censored and late-entry observations to be used in the analysis. Cutler and Ederer (1958) note that "the reliability of a statistical result depends on the size of the sample" (p. 712) and so define effective sample size as the number of subjects which would have been needed, if they were all followed until death or the end of the study and had the same survival rate as calculated in the current study, to have a standard error equal to that found in the current study. An analysis using partial survival information can be said to be as reliable as an analysis based on the effective sample size where no censoring or late entry occurred.

The most commonly used effective sample size is the Cutler-Ederer definition. Cutler and Ederer (1958) defined the effective sample size as

$$N' = \frac{\hat{S}_{\mathrm{KM}}(t)\left(1-\hat{S}_{\mathrm{KM}}(t)\right)}{\hat{\mathrm{var}}\left(\hat{S}_{\mathrm{KM}}(t)\right)}, \tag{16}$$

where $\hat{S}_{KM}(t)$ is Kaplan-Meier estimate of the probability of survival and $\hat{\mathrm{var}}\left(S_{KM}(t)\right)$ is the variance obtained using Greenwood's formula (Equation 14). The Cutler-Ederer

effective sample size is the calculation usually used in the construction of confidence limits in survival analysis (Anderson, Bernstein, & Pike, 1982).

A second definition of effective sample size was also considered in this research. Peto et al. (1977) determined that the standard error as computed by Greenwood's formula tends to be underestimated in the tail of the survival curve. They proposed a more conservative estimate of the standard error, given by

$$\text{var}\{\hat{S}_{\text{KM}}(t)\} = \hat{S}^2_{\text{KM}}(t)\frac{1-\hat{S}_{\text{KM}}(t)}{N_t - d_t},$$

where $\hat{S}_{\text{KM}}(t)$ is the Kaplan-Meier estimate and N_t - d_t is the number of subjects still at risk at time t. The Peto effective sample size is then defined as

$$N'' = \frac{N_t - d_t}{\hat{S}_{\text{KM}}(t)}. \tag{17}$$

The final formulation for computing an effective sample size to be considered is the Dorey-Korn effective sample size. Dorey and Korn (1985) determined that, while the Cutler-Ederer calculation of sample size can underestimate variability when the survival curve is flat, the effective sample size as given by Peto et al. tends to be overly conservative. Therefore, they introduced a modification to the Cutler-Ederer formula. They suggested that, if a censored observation occurs at time t, one could assume that the last death before time t actually occurred at t. Let $t_{(i-1)}$ be the time at which the last failure was observed, $t_{(i-2)}$ be the time immediately preceding the last failure, and $t_{(i)}$ be the current observation. Then with N_j being the number of subjects surviving just prior to some time $t_{(j)}$, and d_j being the number of deaths occurring at time $t_{(j)}$, $S^*(t)$ and $V^*(t)$ are given by

$$S^*(t) = \left[\prod_{j=1}^{i-2} 1 - \frac{d_j}{N_j}\right]\left[1 - \frac{d_{i-1} - 1}{N_{i-1}}\right]\left[1 - \frac{d_i + 1}{N_i + 1}\right] \tag{18}$$

and

$$V^*(t) = S^{*2}(t)\left[\sum_{j=1}^{i-2} \frac{d_j}{N_j(N_j - 1)} + \frac{d_{i-1} - 1}{N_{i-1}(N_{i-1} - d_{i-1} + 1)} + \frac{d_i + 1}{N_i(N_i + 1)}\right] \tag{19}$$

where $S^*(t)$ is the estimate for the probability of survival and $V^*(t)$ is the estimate of the variance of $S^*(t)$. The formula for calculating the effective sample size N^* is

$$N^* = \frac{S^*(t)\left(1 - S^*(t)\right)}{V^*(t)} \quad . \tag{20}$$

Dorey and Korn noted that their modified effective sample size N^* reduced to the usual Cutler-Ederer estimate if no censored observations occurred between $t_{(i-1)}$ and $t_{(i)}$. It should be noted, however, that Equation 19 is incorrect. Using the Law of the Total Differential (Appendix B), Equation 19 should be

$$V^*(t) = S^{*2}(t)\left[\sum_{j=1}^{i-2} \frac{d_j}{N_j(N_j - 1)} + \frac{d_{i-1} - 1}{N_{i-1}(N_{i-1} - d_{i-1} + 1)} + \frac{d_i + 1}{(N_i + 1)(N_i - d_i)}\right]. \tag{21}$$

Dorey and Korn (1987) simplified Equations 18 and 19 in accordance with their proposal to use the estimate only for censored observations, reducing d_i to 0. Thus, the simplified equations are

$$S^*(t) = \left[\prod_{j=1}^{i-2} 1 - \frac{d_j}{N_j}\right]\left[1 - \frac{d_{i-1} - 1}{N_{i-1}}\right]\left[1 - \frac{1}{N_i + 1}\right] \tag{22}$$

and

$$V^*(t) = S^{*2}(t)\left[\sum_{j=1}^{i-2} \frac{d_j}{N_j(N_j - 1)} + \frac{d_{i-1}\ \ 1}{N_{i-1}(N_{i-1} - d_{i-1} + 1)} + \frac{1}{N_i(N_i + 1)}\right]. \tag{23}$$

The Dorey-Korn Modified Effective Sample Size and Product-Limit Estimation

When Dorey and Korn (1985, 1987) introduced their modified effective sample size, they applied their equations to data obtained from Grogan, Dorey, Rollins, and Amstutz (1986). In the Grogan et al. study, 821 patients underwent total joint arthroplasty of the knee. The outcome being observed was deep sepsis, a potentially life-threatening complication of total joint arthroplasty.

Dorey and Korn (1987) calculated their modified effective sample size only when there were no sepsis patients in an interval and compared their results to the Cutler-Ederer effective sample size (Equation 16). However, in order to better determine the usefulness of the Dorey-Korn modified effective sample size, this study calculated the Dorey-Korn effective sample size at each interval. The data, the results obtained by Dorey and Korn, and the results obtained by computing the modified effective sample size at each interval are shown in Table 5. Although Dorey and Korn presented their results with three places after the decimal, Table 5 carries the decimal four places to clarify the difference between the Dorey-Korn results when calculations are performed only at intervals with no sepsis [$S^*(t)$ and D-K] and at every interval [$S^*(t)_1$ and D-K_1]. The Kaplan-Meier estimate $\hat{S}_{KM}(t)$ and the Cutler-Ederer effective sample size (C-E) are also shown.

From the results displayed in Table 5, it was determined that the Dorey-Korn modified effective sample size changes in any interval following one in which censoring occurs, not just in the intervals in which no failures occur as suggested. Further examination of the Dorey-Korn effective sample size was made by reducing the intervals so that only one subject failed or was censored at a time. This was done by assigning a

Table 5

Comparison of the Cutler-Ederer (C-E) and Dorey-Korn (D-K) Effective Sample Sizes

Time (months)	At risk	Number sepsis	$\hat{S}_{KM}(t)$	C-E	$S^*(t)$	D-K	$S^*(t)_1$	D-K_1
2	821	4	0.9951	821.0	0.9951	821.0	0.9951	821.0
4	778	2	0.9926	807.0	0.9926	807.0	0.9925	800.4
6	772	2	0.9900	799.2	0.9900	799.2	0.9900	798.7
12	768	1	0.9887	796.4	0.9887	796.4	0.9887	796.2
14	700	0	0.9887	796.4	0.9886	786.6	0.9886	786.6
16	652	1	0.9872	777.1	0.9872	777.1	0.9870	761.4
18	640	1	0.9857	760.7	0.9857	760.7	0.9856	758.8
20	628	1	0.9841	746.2	0.9841	746.2	0.9841	744.5
24	572	0	0.9841	746.2	0.9839	736.0	0.9839	736.0
30	439	0	0.9841	746.2	0.9834	693.8	0.9834	693.8
36	399	1	0.9816	669.5	0.9816	669.5	0.9807	620.0
48	318	0	0.9816	669.5	0.9810	614.3	0.9810	614.3
60	200	0	0.9816	669.5	0.9792	456.6	0.9792	456.6
72	140	0	0.9816	669.5	0.9771	324.0	0.9771	324.0
84	90	0	0.9816	669.5	0.9733	191.0	0.9733	191.0
96	43	0	0.9816	669.5	0.9617	72.4	0.9617	72.4
108	11	0	0.9816	669.5	0.9021	14.3	0.9021	14.3

Note. $\hat{S}_{KM}(t)$ is the Kaplan-Meier probability estimator, C-E is the Cutler-Ederer effective sample size, $S^*(t)$ and D-K are the Dorey-Korn probability estimator and effective sample size calculated only for intervals with no sepsis, and $S^*(t)_1$ and D-K_1 are the Dorey-Korn probability estimator and effective sample size calculated at each interval.

new survival time to those individuals in intervals where more than one failure occurred. Again, the Dorey-Korn effective sample size was calculated only during those intervals where no sepsis occurred as well as at each interval. These results are presented in Table 6, along with Cutler-Ederer effective sample size.

The most noticeable difference seen in Table 6 is between Times 4.1 and 4.2. The Dorey-Korn effective sample size is smaller at Time 4.1 than at Time 4.2. If the estimate were calculated only for those intervals during which no sepsis occurred, that behavior

would not pose a problem. However, in most survival analysis studies, the censoring pattern is such that, at least early in the observation period, it is rare for two or more censored observations to occur in adjacent intervals. Also, because the Dorey-Korn effective sample size changes only after a censored observation occurs, unless there were two or more adjacent censored observations, no difference between the Dorey-Korn and Cutler-Ederer effective sample sizes would be seen. The problem with computing the Dorey-Korn estimator only during censored intervals and the inappropriate behavior of the Dorey-Korn effective sample size is demonstrated in Table 7.

For this example, 30 observations were generated from the negative exponential distribution, with 25% of the observations randomly censored. The Kaplan-Meier estimator and the Cutler-Ederer effective sample size were computed for each observation, and the Dorey-Korn estimator and effective sample size were computed for censored observations as well as for each observation. The results clearly show that, when the Dorey-Korn effective sample size is computed only for censored observations, no difference between it and the Cutler-Ederer effective sample size is seen unless there are two adjacent censored observations. Furthermore, when the Dorey-Korn effective sample size is computed at each observation, the effective sample size computed for an observation $t_{(i)}$ immediately following a censored observation $t_{(i-1)}$ is often smaller than the effective sample size for the next observation, $t_{(i+1)}$. Therefore, because the Dorey-Korn effective sample size is not monotonically decreasing, it will not be used as a possible alternative in computing confidence intervals. The SAS programs written to analyze the Dorey-Korn effective sample size are contained in Appendix C.

Table 6

Comparison of the Cutler-Ederer (C-E) and Dorey-Korn (D-K) Effective Sample Sizes Using One Patient per Interval

Time (months)	At risk	Number sepsis	$\hat{S}_{KM}(t)$	C-E	$S^*(t)$	D-K	$S^*(t)_I$	D-K_I
2.1	821	1	0.9988	821.0	0.9988	821.0	0.9988	821.0
2.2	820	1	0.9976	821.0	0.9976	821.0	0.9976	821.0
2.3	819	1	0.9964	821.0	0.9964	821.0	0.9964	821.0
2.4	818	1	0.9951	821.0	0.9951	821.0	0.9951	821.0
4.1	778	1	0.9939	812.5	0.9939	812.5	0.9938	804.4
4.2	777	1	0.9926	807.0	0.9926	807.0	0.9926	807.0
6.1	772	1	0.9913	802.5	0.9913	802.5	0.9913	801.9
6.2	771	1	0.9900	799.3	0.9900	799.2	0.9900	799.2
12.0	768	1	0.9887	796.4	0.9887	796.4	0.9887	796.2
14.0	700	0	0.9887	796.4	0.9886	786.6	0.9886	786.6
16.0	652	1	0.9872	777.1	0.9872	777.1	0.9870	761.4
18.0	640	1	0.9857	760.7	0.9857	760.7	0.9856	758.8
20.0	628	1	0.9841	746.2	0.9841	746.2	0.9841	744.5
24.0	572	0	0.9841	746.2	0.9839	736.0	0.9839	736.0
30.0	439	0	0.9841	746.2	0.9834	693.8	0.9834	693.8
36.0	399	1	0.9816	669.5	0.9816	669.5	0.9807	620.0
48.0	318	0	0.9816	669.5	0.9810	614.3	0.9810	614.3
60.0	200	0	0.9816	669.5	0.9792	456.6	0.9792	456.6
72.0	140	0	0.9816	669.5	0.9771	324.0	0.9771	324.0
84.0	90	0	0.9816	669.5	0.9733	191.0	0.9733	191.0
96.0	43	0	0.9816	669.5	0.9617	72.4	0.9617	72.4
108.0	11	0	0.9816	669.5	0.9021	14.3	0.9021	14.3

Note. $\hat{S}_{KM}(t)$ is the Kaplan-Meier probability estimator, C-E is the Cutler-Ederer effective sample size, $S^*(t)$ and D-K are the Dorey-Korn probability estimator and effective sample size calculated only for intervals with no sepsis, and $S^*(t)_I$ and D-K_I are the Dorey-Korn probability estimator and effective sample size calculated at each interval.

Confidence Intervals for the Survival Curve

In survival analysis, it has often been the case that the estimated median survival time or the probability of surviving longer than some period of time has been reported

Table 7

Comparison of the Cutler-Ederer (C-E) and Dorey-Korn (D-K) Effective Sample Sizes Using Data Generated From the Negative Exponential Distribution

Time	At risk	Censor	$\hat{S}_{KM}(t)$	C-E	$S^*(t)$	D-K	$S^*(t)_1$	D-K_1
0.032	30	1	1.0000	30.0	1.0000	30.0	1.0000	30.0
0.184	29	0	0.9655	29.0	0.9655	29.0	0.9644	28.2
0.185	28	0	0.9310	29.0	0.9310	29.0	0.9310	29.0
0.268	27	0	0.8966	29.0	0.8966	29.0	0.8966	29.0
0.294	26	1	0.8966	29.0	0.8966	29.0	0.8966	29.0
0.346	25	0	0.8607	28.7	0.8607	28.7	0.8594	28.4
0.445	24	0	0.8248	28.5	0.8248	28.5	0.8248	28.5
0.472	23	1	0.8248	28.5	0.8248	28.5	0.8248	28.5
0.480	22	0	0.7873	28.1	0.7873	28.1	0.7859	27.8
0.586	21	1	0.7873	28.1	0.7873	28.1	0.7873	28.1
0.718	20	1	0.7873	28.1	0.7856	27.7	0.7856	27.7
0.721	19	0	0.7459	27.2	0.7459	27.2	0.7423	26.7
0.731	18	0	0.7045	26.5	0.7045	26.5	0.7045	26.5
0.778	17	0	0.6630	26.1	0.6630	26.1	0.6630	26.1
0.870	16	1	0.6630	26.1	0.6630	26.1	0.6630	26.1
0.935	15	1	0.6630	26.1	0.6604	25.7	0.6604	25.7
1.008	14	0	0.6157	25.0	0.6157	25.0	0.6105	24.5
1.014	13	0	0.5683	24.2	0.5683	24.2	0.5683	24.2
1.030	12	1	0.5683	24.2	0.5683	24.2	0.5683	24.2
1.048	11	0	0.5166	23.1	0.5166	23.1	0.5131	22.8
1.163	10	0	0.4650	22.3	0.4650	22.3	0.4650	22.3
1.224	9	0	0.4133	21.7	0.4133	21.7	0.4133	21.7
1.272	8	0	0.3617	21.2	0.3617	21.2	0.3617	21.2
1.517	7	0	0.3100	20.8	0.3100	20.8	0.3100	20.8
1.608	6	1	0.3100	20.8	0.3100	20.8	0.3100	20.8
1.694	5	0	0.2480	19.3	0.2480	19.3	0.2411	18.9
1.819	4	1	0.2480	19.3	0.2480	19.3	0.2480	19.3
1.879	3	0	0.1653	15.6	0.1653	15.6	0.1550	15.3
2.552	2	0	0.0827	13.5	0.0827	13.5	0.0827	13.5
3.655	1	0	0.0000	13.5	0.0000	13.5	0.0000	13.5

Note. $\hat{S}_{KM}(t)$ is the Kaplan-Meier probability estimator, C-E is the Cutler-Ederer effective sample size, $S^*(t)$ and D-K are the Dorey-Korn probability estimator and effective sample size calculated only for intervals with no sepsis, and $S^*(t)_1$ and D-K_1 are the Dorey-Korn probability estimator and effective sample size calculated at each interval.

without any indication of the reliability of the estimate (Simon & Lee, 1982). Constructing a confidence interval at some predetermined level γ (usually $\gamma = .95$) around the survival curve would define the range of values in which the true value of $S(t)$ would be contained in $\gamma 100\%$ of repeated studies. The method one should use to determine the confidence limits has been a topic of interest in recent years.

The most commonly used confidence intervals are the confidence limits based on Greenwood's formula, shown in Equation 14. These are calculated using the Equation

$$\hat{S}_{KM}(t) \pm Z\left[\frac{\hat{S}_{KM}(t)\left(1-\hat{S}_{KM}(t)\right)}{N'}\right]^{1/2} \tag{24}$$

where Z is defined as the appropriate standard normal distribution percentage point and N is the Cutler-Ederer effective sample size (Equation 16). The limits obtained using this formula are the ones most often computed and are used by SAS in the LIFETEST procedure (SAS Institute, 1990).

Rothman (1978) noted that the confidence limits based on Greenwood's formula (Equation 24) led to a symmetric interval about the point estimates. However, the sampling distribution is not symmetric except when the probability of survival is 0.5. Therefore, Rothman proposed a method for calculating confidence limits assuming that for the estimated cumulative survival probability at time t, $\hat{P} = \hat{S}_{KM}(t)$, and Cutler-Ederer effective sample size N, $X' = N'\hat{P}$ has a binomial distribution. Although binomial confidence limits could be computed exactly, Rothman instead proposed using the quadratic limits obtained by the formula

$$P^{*} = \frac{N'}{N'+Z^2}\left[\hat{P} + \frac{Z^2}{2N'} \pm Z\sqrt{\frac{\hat{P}(1-\hat{P})}{N'} + \frac{Z^2}{4N'^2}}\right], \tag{25}$$

which are accurate limits even for small, asymmetric binomials. Simon and Lee (1982) proposed constructing confidence intervals using Rothman's method (Equation 25), replacing the Cutler-Ederer effective sample size with the Peto, et al. formulation N'' (Equation 17).

Easterling (1972) used the binomial model to calculate approximate confidence limits in system reliability. He noted that a lower $\gamma 100\%$ confidence limit for reliability with x successes in n trials is given by

$$I(p_L, x, n-x+1) = 1-\gamma$$

where

$$I(s,\alpha,\beta) = \frac{\Gamma(\alpha+\beta)}{\Gamma(\alpha)\Gamma(\beta)}\int_0^s t^{\alpha-1}(1-t)^{\beta-1}dt$$

is the incomplete beta function. If $h(p)$ is the usual binomial estimate of system reliability based on N trials and N' is the effective sample size, then $X' = h(p)N'$ and the lower and upper confidence limits are given by solving for h_L and h_U in the following equations:

$$I(h_L, X', N'-X'+1) = \frac{1-\gamma}{2}$$

and

$$I(h_U, X'+1, N'-X') = \frac{1+\gamma}{2}.$$

Bradley (Blackstone et al., 1977) used the relationship between the binomial probability function and the incomplete beta function to define a distribution for X', a *pseudo-binomial* random variable. Recognizing that if X' has a beta distribution with parameters α and β, then

$$W = \frac{n_1 X'}{n_2 + n_1 X'}$$

has an F-distribution with $n_1 = 2\alpha$ numerator degrees of freedom and $n_2 = 2\beta$ denominator degrees of freedom (Mood, Graybill, & Boes, 1963). The lower $\gamma 100\%$ confidence limit for p can be given by

$$p_L = \frac{X' F_{[(1-\gamma)/2],[2X',2(N'-X'+1)]}}{(N'-X'+1) + X' F_{[(1-\gamma)/2],[2X',2(N'-X'+1)]}} \tag{26}$$

where $\alpha = X'$ and $\beta = N'-X'+1$, and the $\gamma 100\%$ upper limit is

$$p_U = \frac{(X'+1) F_{[(1+\gamma)/2],[2(X'+1),2(N'-X')]}}{(N'-X') + (X'+1) F_{[(1+\gamma)/2],[2(X'+1),2(N'-X')]}} \tag{27}$$

where $\alpha = X'+1$ and $\beta = N'-X'$ (Ostle & Malone, 1988).

Comparing the Accuracy of Confidence Intervals

Several studies have focused on determining the most accurate confidence intervals (Afifi, Elashoff, & Lee, 1986; Dorey & Korn, 1987; Rothman, 1978; Simon & Lee, 1982; Slud et al., 1984). Fox (1995), using Equations 26 and 27 to calculate pseudo-binomial confidence intervals around a survival curve, conducted Monte Carlo simulations to compare the accuracy of the Greenwood (Equation 24), Rothman (Equation 25), and pseudo-binomial confidence intervals. All confidence intervals were constructed using the Cutler-Ederer effective sample size (Equation 16). Three different

levels of confidence, $\gamma = .90, .95$, and .99, were selected to compare the three methods. Sample sizes of 30, 60, and 120 were used with 0, 5, and 10% censoring. The survival function was estimated using the Kaplan-Meier product-limit method (Equation 12).

To determine accuracy, data were generated from the negative exponential distribution. Five different survival probabilities were selected as the points of comparison. For each point, the true survival time was determined and the different confidence intervals were computed. If a confidence interval contained the true probability of survival, a success was recorded. The total number of successes for each method was calculated and a percentage was obtained by dividing the total number of successes by the total number of simulations. The *confidence level error* is defined to be the calculated percentage of successful comparison minus the true confidence level.

Table 8 shows the mean error for each of the three methods at each confidence level. At the .90 and .95 levels of confidence, the pseudo-binomial intervals were determined to be significantly different from both the Greenwood and Rothman intervals and significantly different from the Greenwood intervals at the .99 confidence level. The pseudo-binomial intervals demonstrated less absolute error than either of the other two methods; however, because tests on absolute error were not conducted, a conclusion on whether the pseudo-binomial intervals are statistically significantly more accurate than the Rothman intervals cannot be drawn. It is reasonable to conclude the pseudo-binomial confidence intervals are significantly more accurate than the Greenwood intervals.

Further analyses compared the mean error of each of the three methods for each confidence interval at each comparison point on the survival curve, at each sample size, and at each level of censoring. In all comparisons, the pseudo-binomial method

Table 8

Mean Error of the Three Methods at Each Level of Confidence

	Confidence level		
Method	.90	.95	.99
Pseudo-binomial	.018	.008	.001
Greenwood	-.0616*	-.0550*	-.0480*
Rothman	-.0202*	-.0137*	-.006

Note. Significant results shown are in relation to the pseudo-binomial method.
* $p < .05$

performed as well as or better than the Rothman method and consistently outperformed the Greenwood method. While the Rothman method tended to construct intervals with less error early in the survival curve, the pseudo-binomial confidence intervals were more accurate overall.

CHAPTER 4

COMPARISON OF CONFIDENCE INTERVALS FOR SURVIVAL ESTIMATES OF DATA FROM THE WEIBULL DISTRIBUTION

Fox (1995) compared the pseudo-binomial, Greenwood, and Rothman confidence intervals using simulated data generated from the negative exponential distribution. It was determined that the pseudo-binomial confidence intervals performed as well as or better than the Rothman intervals, with both the pseudo-binomial and Rothman methods consistently outperforming the Greenwood method. As an extension to Fox, this simulation study investigates the performance of the pseudo-binomial confidence intervals in comparison to the Greenwood and Rothman intervals using data from the more general Weibull distribution.

The survivorship function for the Weibull distribution is $F(t) = e^{-(\lambda t)^{\nu}}$, where ν determines the shape of the distribution curve and λ is the scale parameter. If $\nu = 1$, the Weibull distribution reduces to the negative exponential distribution. The negative exponential distribution has a constant hazard function; that is, the risk of an event occurring remains the same for each subject throughout the observation period. The shape parameter of the Weibull distribution allows for the possibility of changing risk. When $\nu < 1$, the risk of an event decreases with time, while for $\nu > 1$, the risk of an event increases. This simulation investigates the performance of the pseudo-binomial confidence intervals for the probability of survival when the hazard function is not

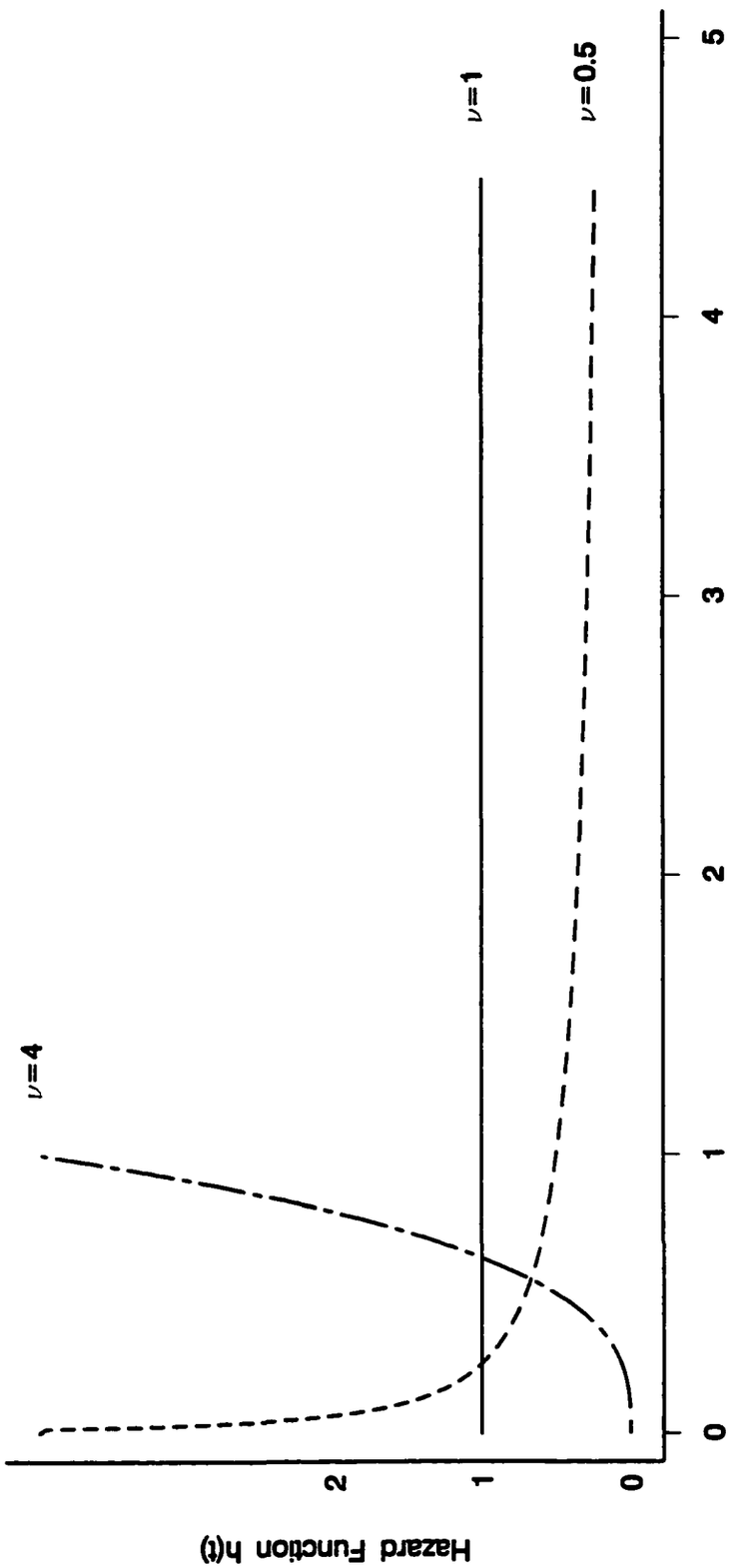


Figure 3. Hazard functions of the Weibull distribution for different shape parameter values.

Simulation Results

The analysis of variance results indicated strong significant differences overall between the three methods for all confidence levels. They also revealed that the three methods differed in behavior at different points on the survival curve and at different sample sizes. Although a strong significant effect due to the amount of censoring was found, the performance of the three intervals did not change as the amount of censoring increased. Also, the mean error of each of the three methods did not change significantly as the value of the shape parameter changed.

Table 9 lists the mean error at each confidence level. The mean error in this table was calculated over all comparison points on the survival curve, all values of the shape parameter ν, and all levels of sample size and percent censoring. For each of the three survival distributions, the pseudo-binomial intervals were conservative for all levels of confidence, while the Rothman and Greenwood intervals were anticonservative. As in the previous simulation study, the pseudo-binomial intervals were statistically significantly more accurate than the Greenwood confidence intervals. The pseudo-binomial intervals had less error than the Rothman intervals, but results were statistically significant only at the 99% confidence level.

The performance of the survival curves was also compared for each of the different values of ν, with the results shown in Table 10. The Greenwood and Rothman intervals were anticonservative for all parameter values, while the pseudo-binomial intervals remained conservative. Only the Greenwood intervals demonstrated a statistically significantly greater error than the pseudo-binomial intervals. The Rothman

Table 9

Mean Error at Each Confidence Level

	Confidence level		
Method	.90	.95	.99
Pseudo-binomial	0.0192	0.0086	0.0009
Greenwood	-0.0599**	-0.0553**	-0.0491**
Rothman	-0.0203	-0.0133	-0.0073*

* $p < 0.05$. ** $p < .01$.

Table 10

Mean Error at Each Value of ν

	ν		
Method	0.5	1.0	4.0
		γ = .90	
Pseudo-Binomial	0.0200	0.0188	0.0189
Greenwood	-0.0574**	-0.0616**	-0.0609**
Rothman	-0.0189	-0.0202	-0.0218
		γ = .95	
Pseudo-Binomial	0.0086	0.0086	0.0086
Greenwood	-0.0548**	-0.0550**	-0.0560**
Rothman	-0.0135	-0.0137	-0.0126
		γ = .99	
Pseudo-Binomial	0.0013	0.0011	0.0005
Greenwood	-0.0502**	-0.0480**	-0.0490**
Rothman	-0.0072	-0.0064	-0.0084

* $p < .05$. ** $p < .01$.

intervals consistently had more error than the pseudo-binomial intervals, although the difference was not statistically significant

The mean confidence level errors for the three methods were also compared at each specified point on the survival curve. For this analysis, the mean error was

calculated over all levels of ν, sample size, and percent censoring. The mean error for each method is illustrated in Figure 4. Statistically significant differences between the methods at each point on the survival curve are noted in Table 11. The pseudo-binomial intervals tend to be overly conservative early in the survival curve when the probability of survival is large, $S(t) = .95$ and .75. However, the Rothman and Greenwood intervals are very anticonservative at the tail of the curve, where the probability of survival is low, $S(t) = .25$ and .05.

Although not noted statistically in the table, the differences in behavior between the three methods along the survival curve can be seen. The pseudo-binomial and Rothman methods both start off with conservative intervals and tend to be anticonservative in the middle of the curve; however, the pseudo-binomial grows conservative again at the tail while the Rothman intervals continue to narrow. The Greenwood intervals behave oppositely. The are extremely anticonservative early in the survival curve, begin to widen in the middle yet remain anticonservative, and then become narrow again at the tail.

The performance of each of the three methods for different sample sizes, with the mean error calculated over the five points on the survival curve and all levels of ν and percent censoring, was evaluated. The results of this analysis, shown in Table 12, indicate statistically significant differences between the pseudo-binomial and Rothman intervals only at the 90% confidence level, while the pseudo-binomial intervals have statistically significantly less error than the Greenwood intervals in almost all instances. The pseudo-binomial intervals were conservative for the smaller samples, where $n = 30$ and 60, and anticonservative for the large sample, where $n = 120$. The Rothman

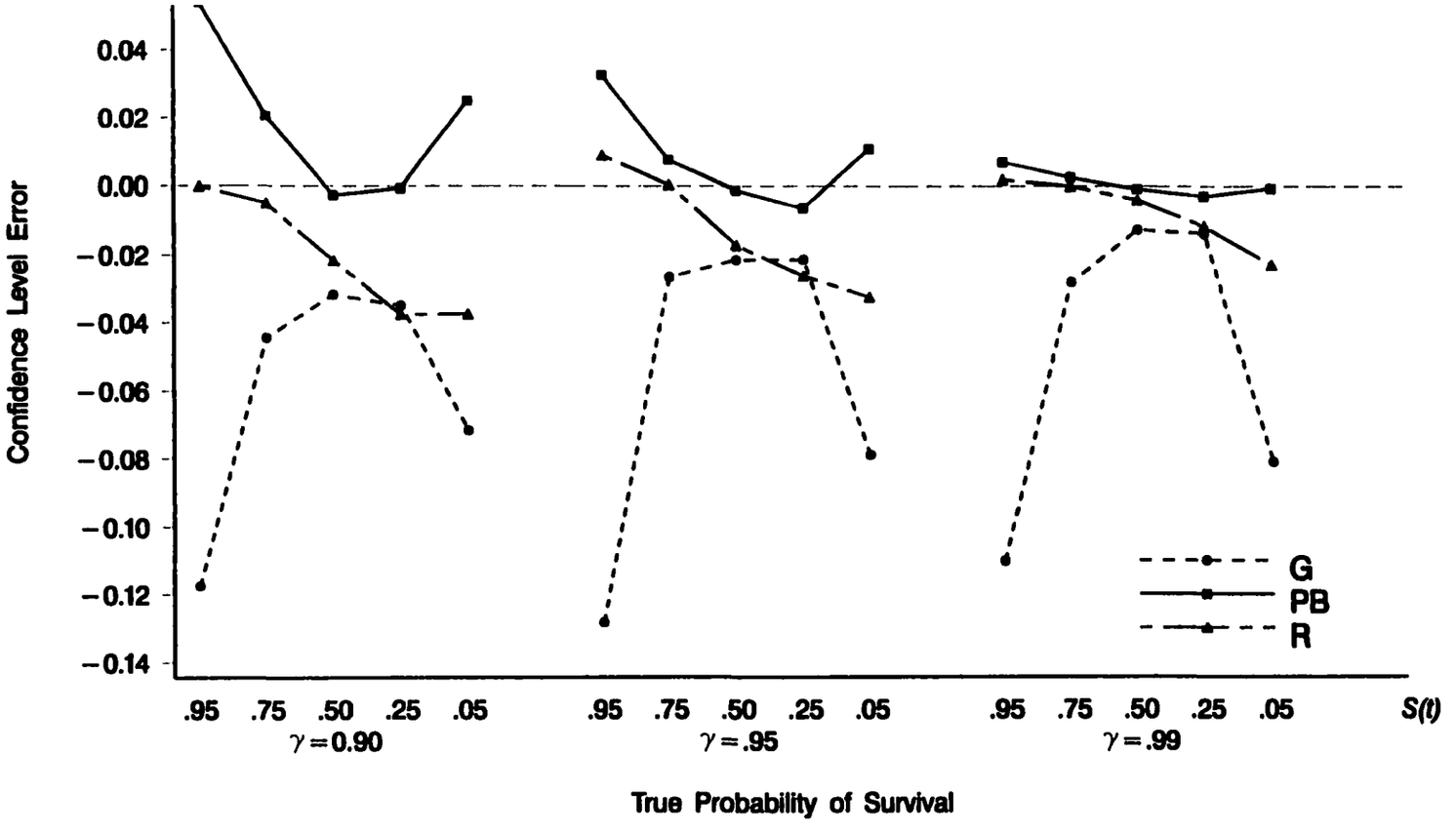


Figure 4. Mean confidence level error at each point on the survival curve for the Greenwood (G), pseudo-binomial (PB), and Rothman (R) confidence intervals.

Table 11

Mean Error at Specific Points on the Survival Curve

	S(t)				
Method	0.95	0.75	0.50	0.25	0.05
			$\gamma = .90$		
Pseudo-Binomial	0.0540	0.0206	-0.0027	-0.0007	0.0251
Greenwood	-0.1175**	-0.0444**	-0.0316**	-0.0305**	-0.0714**
Rothman	-0.0002**	-0.0051**	-0.0215**	-0.0375**	-0.0374*
			$\gamma = .95$		
Pseudo-Binomial	0.0327	0.0074	-0.0013	-0.0065	0.0108
Greenwood	-0.1283**	-0.0264**	-0.0214**	-0.0213*	-0.0789**
Rothman	0.0088**	0.0004	-0.0171*	-0.0261**	-0.0323**
			$\gamma = .99$		
Pseudo-Binomial	0.0069	0.0024	-0.0009	-0.0029	-0.0007
Greenwood	-0.1102**	-0.0280**	-0.0126*	-0.0137	-0.0810**
Rothman	0.0018	-0.0001	-0.0040	-0.0116	-0.0228**

* $p < 0.05$. ** $p < .01$.

intervals, while anticonservative, demonstrated less error than the pseudo-binomial intervals for the smaller samples, and the pseudo-binomial intervals performed better with the larger sample at all confidence levels.

Again, the significant differences in behavior between the methods as sample size increased, indicated by the analysis of variance, can also be seen. The pseudo-binomial and Rothman methods construct intervals which narrow as sample size increases, while the Greenwood intervals widen.

The last comparison focused on the behavior of the intervals as the amount of censoring increased. Table 13 lists the mean error for the different amounts of censoring in the data. The Rothman intervals were more accurate than the pseudo-binomial intervals when the amount of censoring was small, at 0 and 5%, with some significant

Table 12

Mean Error at Each Level of Sample Size

Method	Sample size		
	30	60	120
		$\gamma = .90$	
Pseudo-Binomial	0.0417	0.0131	0.0029
Greenwood	-0.0787**	-0.0540**	-0.0471**
Rothman	0.0065**	-0.0252**	-0.0424**
		$\gamma = .95$	
Pseudo-Binomial	0.0195	0.0129	-0.0065
Greenwood	-0.0773**	-0.0604**	-0.0281**
Rothman	-0.0048**	-0.0091	-0.0259**
		$\gamma = .99$	
Pseudo-Binomial	0.0048	0.0020	-0.0039
Greenwood	-0.0974**	-0.0241**	-0.0257**
Rothman	-0.0045	-0.0063	-0.0112

* $p < .05$. ** $p < .01$.

differences noted at the 90 and 95% confidence levels. The pseudo-binomial intervals were statistically significantly more accurate than the Rothman intervals at all confidence levels where there was 10% censoring of the data. All three methods constructed intervals which narrowed as censoring increased.

Conclusions and Discussion

The simulation analyses conducted in this chapter were designed to compare the accuracy of the three interval methods over different hazard functions. The value of the shape parameter, and thereby the shape of the hazard function, did not significantly affect the mean error of the confidence intervals. The pseudo-binomial intervals tended to be more conservative overall than the Rothman and Greenwood intervals, a characteristic that is desirable in the construction of confidence intervals.

are conservative at the tail of the survival curve and they demonstrate less error overall than the Greenwood and Rothman intervals.

CHAPTER 5

COMPARISON OF ESTIMATORS AND EFFECTIVE SAMPLE SIZES

The behavior of the pseudo-binomial, Rothman, and Greenwood intervals using the Kaplan-Meier estimator and Cutler-Ederer effective sample size was examined in the previous chapter. In this simulation, the accuracy of the confidence intervals constructed using the Berliner-Hill estimator will be compared to the intervals based on the Kaplan-Meier estimator. Both estimators will be used in conjunction with both the Cutler-Ederer and Peto effective sample sizes. The Kaplan-Meier estimator combined with the Cutler-Ederer effective sample size is denoted by KM, and the Berliner-Hill estimator with the Cutler-Ederer effective sample size is denoted by BH. The Kaplan-Meier and Berliner-Hill estimators used in conjunction with the Peto effective sample size are denoted by PKM and PBH, respectively. The simulation conducted in the previous chapter indicated that the pseudo-binomial and Rothman intervals were consistently superior to the Greenwood intervals. Therefore, these analyses will focus only on the pseudo-binomial and Rothman intervals.

For this simulation, the data were generated using the same seeds used previously (Appendix D). The same levels of confidence, shape parameter ν, sample size, and percent censoring were used. The points on the survival curve at which the intervals were compared were also those used in the previous simulation. The tables listing the percentage of successes for each method are contained in Appendix E. The analyses in

this chapter are presented in three parts. First, the four different pseudo-binomial intervals are compared to determine the best pseudo-binomial interval. Then, the four Rothman intervals are compared. Finally, the best pseudo-binomial interval will be compared to the best Rothman interval.

Determining the Best Pseudo-Binomial Confidence Interval

The analysis of variance results are similar to those found in the previous simulations. A significant difference in the mean confidence level error between the four methods was found. Also, although sample size had a significant effect on mean confidence level error, the behavior of each of the methods as sample size increased was not significantly different. The methods did demonstrate significantly different behaviors as censoring increased and as the true probability of survival decreased. The shape of the hazard function had no significant effect on mean confidence level error.

The mean error at each confidence level for each of the pseudo-binomial intervals is shown in Table 14. This mean was calculated over all points on the survival curve and over all levels of v, sample size, and percent censoring. The Berliner-Hill estimator constructs intervals that are less conservative than those based on the Kaplan-Meier estimator and are a statistically significant improvement over the Kaplan-Meier intervals at the lower confidence levels, where $\gamma = .90$ and .95. However, they are anticonservative at the 95 and 99% confidence levels. The intervals constructed with the Peto effective sample size are more conservative than those constructed with the Cutler-Ederer effective sample size; the conservative effect of the Peto effective sample size statistically significantly improves the anticonservative nature of the Berliner-Hill interval at the 95 and 99% confidence levels.

Table 15

Mean Error of Pseudo-Binomial Intervals at Each Level of v

Method	v 0.5	1.0	4.0
		$\gamma = .90$	
KM	0.0200_a	0.0188_a	0.0189_a
BH	0.0021_b	-0.0008_b	-0.0010_b
PKM	0.0228_a	0.0216_a	0.0220_a
PBH	0.0060_b	0.0035_b	0.0028_b
		$\gamma = .95$	
KM	$0.0086_{a,b}$	$0.0086_{a,b}$	0.0086_a
BH	$-0.0050_{a,c}$	$-0.0051_{a,c}$	-0.0033_b
PKM	0.0109_b	0.0110_b	0.0112_a
PBH	-0.0018_c	-0.0014_c	0.0001_b
		$\gamma = .99$	
KM	0.0013_a	0.0011_a	0.0005_a
BH	-0.0033_b	-0.0036_b	-0.0049_b
PKM	$0.0021_{a,b}$	0.0017_a	$0.0017_{a,c}$
PBH	$-0.0018_{a,b}$	$-0.0021_{a,b}$	-0.0032_c

Note. Means in the same column within each confidence level with different subscripts differ significantly at $p < .05$. KM denotes intervals constructed using the Kaplan-Meier estimator and the Cutler-Ederer effective sample size, BH denotes intervals constructed using the Berliner-Hill estimator and the Cutler-Ederer effective sample size, PKM denotes intervals constructed using the Kaplan-Meier estimator and the Peto effective sample size, and PBH denotes intervals constructed using the Berliner-Hill estimator with the Peto effective sample size.

17 and 18, respectively. Once again, as sample size increases, the pseudo-binomial intervals narrow. Likewise, the intervals narrow as censoring increases. The Berliner-Hill intervals are more accurate than the Kaplan-Meier intervals with smaller sample sizes and less censoring of the data.

The pseudo-binomial intervals are inherently conservative in nature. The Berliner-Hill estimator offsets the conservative behavior, yet often forces the intervals to

Table 16

Mean Error of Pseudo-Binomial Intervals at Specific Points on the Survival Curve

	S(t)				
Method	0.95	0.75	0.50	0.25	0.05
			$\gamma = .90$		
KM	0.0540_a	0.0206_a	-0.0027_a	-0.0007_a	0.0251_a
BH	0.0540_a	0.0161_a	-0.0061_a	-0.0241_b	-0.0393_b
PKM	0.0540_a	0.0224_a	-0.0003_a	0.0046_a	0.0301_a
PBH	0.0540_a	0.0173_a	-0.0023_a	-0.0187_b	-0.0299_a
			$\gamma = .95$		
KM	0.0327_a	0.0074_a	-0.0013_a	-0.0065_a	0.0108_a
BH	0.0327_a	0.0092_a	-0.0090_b	-0.0195_b	-0.0357_b
PKM	0.0327_a	0.0082_a	0.0007_a	-0.0027_a	0.0162_c
PBH	0.0327_a	0.0094_a	-0.0066_b	-0.0140_c	-0.0268_d
			$\gamma = .99$		
KM	0.0069_a	0.0024_a	$-0.0009_{a,b}$	-0.0029_a	-0.0007_a
BH	0.0069_a	0.0017_a	-0.0024_a	-0.0093_b	-0.0167_b
PKM	0.0069_a	0.0025_a	0.0000_b	-0.0015_a	0.0014_a
PBH	0.0069_a	0.0019_a	$-0.0016_{a,b}$	-0.0069_c	-0.0120_c

Note. Means in the same column within each confidence level with different subscripts differ significantly at $p<.05$. KM denotes intervals constructed using the Kaplan-Meier estimator and the Cutler-Ederer effective sample size, BH denotes intervals constructed using the Berliner-Hill estimator and the Cutler-Ederer effective sample size, PKM denotes intervals constructed using the Kaplan-Meier estimator and the Peto effective sample size, and PBH denotes intervals constructed using the Berliner-Hill estimator with the Peto effective sample size.

become anticonservative. The conservativeness of the Peto effective sample size balances the anticonservative behavior of the Berliner-Hill estimator somewhat but cannot compete with the Kaplan-Meier intervals. This undesirable characteristic of the Berliner-Hill intervals was most clearly demonstrated in Figure 5. As was discussed earlier, the emphasis of survival studies is on the tail of the survival curve. The extreme anticonservative nature of the Berliner-Hill intervals at the tail of the survival curve

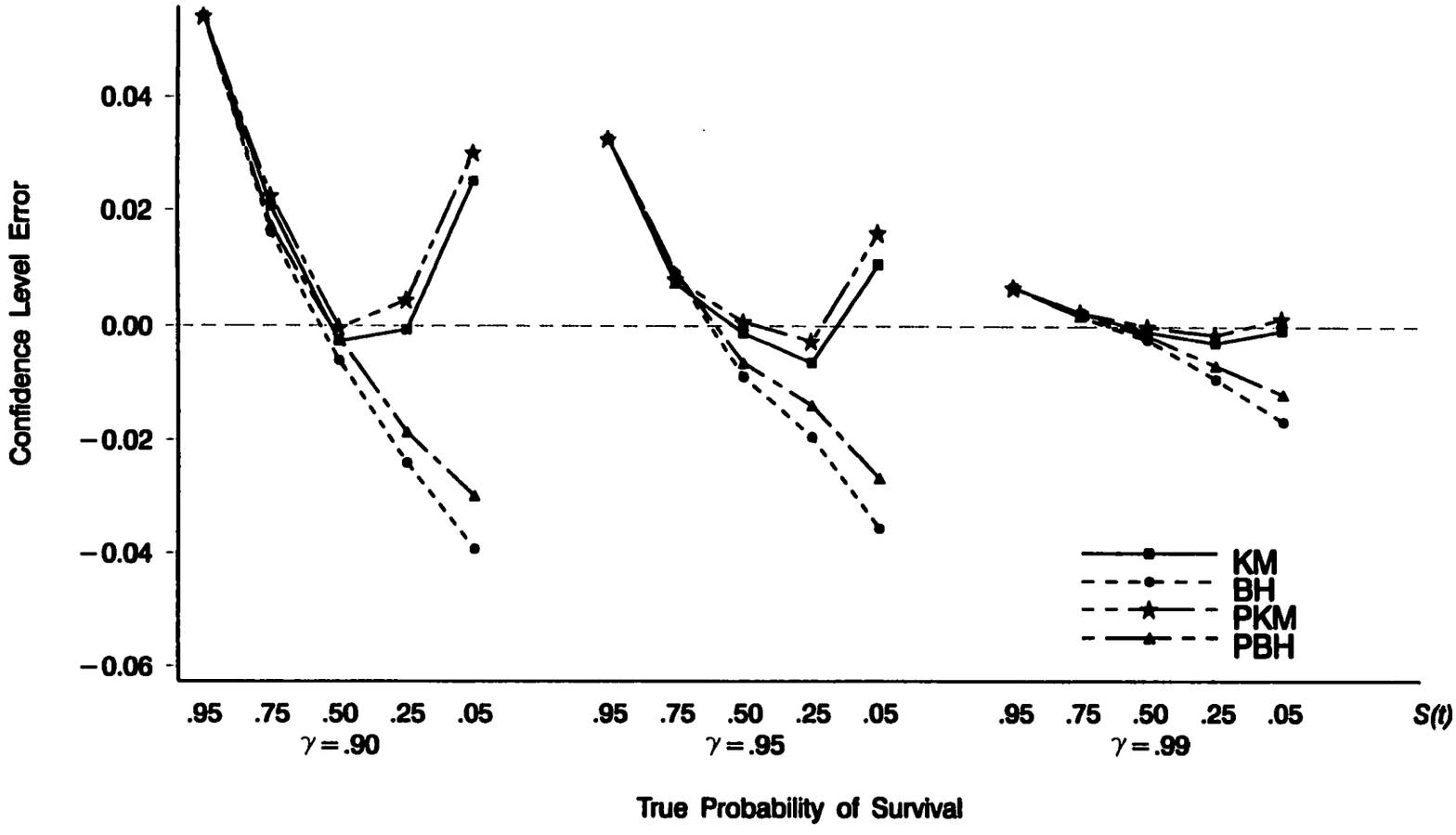


Figure 5. Mean confidence level error of the pseudo-binomial intervals at each point on the survival curve. KM denotes intervals constructed using the Kaplan-Meier estimator and the Cutler-Ederer effective sample size, BH denotes intervals constructed using the Berliner-Hill estimator and the Cutler-Ederer effective sample size, PKM denotes intervals constructed using the Kaplan-Meier estimator and Peto effective sample size, and PBH denotes intervals constructed using the Berliner-Hill estimator with the Peto effective sample size.

Table 18

Mean Error of Pseudo-Binomial Intervals at Each Level of Percent Censoring

Method	Percent censored		
	0	5	10
		$\gamma = .90$	
KM	0.0358_a	0.0258_a	-0.0039_a
BH	0.0321_a	0.0075_b	-0.0393_b
PKM	0.0358_a	0.0281_a	0.0026_a
PBH	0.0321_a	0.0109_b	-0.0308_c
		$\gamma = .95$	
KM	0.0216_a	0.0130_a	-0.0088_a
BH	0.0173_b	0.0013_b	-0.0320_b
PKM	0.0216_a	0.0146_a	-0.0032_c
PBH	0.0173_b	0.0043_b	-0.0247_d
		$\gamma = .99$	
KM	0.0056_a	0.0018_a	-0.0046_a
BH	0.0036_b	-0.0025_a	-0.0130_b
PKM	0.0056_a	0.0025_a	-0.0025_c
PBH	0.0036_b	-0.0014_a	-0.0093_d

Note. Means in the same column within each confidence level with different subscripts differ significantly at $p < .05$. KM denotes intervals constructed using the Kaplan-Meier estimator and the Cutler-Ederer effective sample size, BH denotes intervals constructed using the Berliner-Hill estimator and the Cutler-Ederer effective sample size, PKM denotes intervals constructed using the Kaplan-Meier estimator and the Peto effective sample size, and PBH denotes intervals constructed using the Berliner-Hill estimator with the Peto effective sample size.

different behavior along the survival curve and as sample size and amount of censoring increased. Once again, the shape of the hazard function did not affect the mean confidence level error.

The overall mean confidence level error for each of the Rothman intervals is shown in Table 19. The conservative nature of the Peto effective sample size combines with the anticonservative property of the Rothman method to construct a confidence

Table 19

Mean Error of Rothman Intervals at Each Confidence Level

	Confidence level		
Method	.90	.95	.99
KM	-0.0203_a	-0.0133_a	-0.0073_a
BH	-0.0484_b	-0.0403_b	-0.0204_b
PKM	-0.0172_a	-0.0107_a	-0.0060_a
PBH	-0.0444_c	-0.0370_c	-0.0179_c

Note. Means in the same column with different subscripts differ significantly at $p < .05$. KM denotes intervals constructed using the Kaplan-Meier estimator and the Cutler-Ederer effective sample size, BH denotes intervals constructed using the Berliner-Hill estimator and the Cutler-Ederer effective sample size, PKM denotes intervals constructed using the Kaplan-Meier estimator and the Peto effective sample size, and PBH denotes intervals constructed using the Berliner-Hill estimator with the Peto effective sample size.

interval with less error. However, the difference between the KM and PKM Rothman intervals is not significant. The Berliner-Hill estimator adds to the anticonservativeness of the Rothman intervals, creating confidence intervals significantly narrower than those based on the Kaplan-Meier estimator.

The mean confidence level error for each method at each point on the survival curve is shown in Table 20. Once again, the extreme anticonservative behavior of the BH and PBH intervals is seen at the tail of the curve. Figure 6 illustrates the behavior of the four methods at each point on the survival curve for each confidence level. The PKM intervals are slightly more conservative than the KM intervals, leading to less error. However, that difference is statistically significant only at $S(t) = .05$ for the 99% confidence level.

Table 21 contains the mean confidence level error for each method at each level of v. The mean confidence level error at the each sample size is shown in Table 22, and

Table 20

Mean Error of Rothman Intervals at Specific Points on the Survival Curve

	S(t)				
Method	0.95	0.75	0.50	0.25	0.05
			$\gamma = .90$		
KM	-0.0001_a	-0.0051_a	$-0.0215_{a,b}$	-0.0375_a	-0.0374_a
BH	-0.0002_a	-0.0053_a	-0.0319_c	-0.0624_b	-0.1424_b
PKM	-0.0001_a	-0.0040_a	-0.0179_a	-0.0323_a	-0.0314_a
PBH	0.0002_a	-0.0045_a	$-0.0284_{b,c}$	-0.0567_b	-0.1327_c
			$\gamma = .95$		
KM	0.0088_a	0.0004_a	-0.0171_a	-0.0261_a	-0.0323_a
BH	0.0088_a	-0.0062_a	-0.0267_b	-0.0513_b	-0.1262_b
PKM	0.0088_a	0.0009_a	-0.0152_a	-0.0209_a	0.0272_a
PBH	0.0088_a	-0.0060_a	-0.0244_b	-0.0461_b	-0.1175_c
			$\gamma = .99$		
KM	0.0018_a	-0.0001_a	$-0.0040_{a,b}$	-0.0116_a	-0.0228_a
BH	0.0018_a	0.0000_a	-0.0088_c	-0.0237_b	-0.0712_b
PKM	0.0018_a	0.0000_a	-0.0031_a	-0.0097_a	-0.0188_c
PBH	0.0018_a	0.0000_a	$-0.0075_{b,c}$	-0.0211_b	-0.0624_d

Note. Means in the same column within each confidence level with different subscripts differ significantly at $p < .05$. KM denotes intervals constructed using the Kaplan-Meier estimator and the Cutler-Ederer effective sample size, BH denotes intervals constructed using the Berliner-Hill estimator and the Cutler-Ederer effective sample size, PKM denotes intervals constructed using the Kaplan-Meier estimator and the Peto effective sample size, and PBH denotes intervals constructed using the Berliner-Hill estimator with the Peto effective sample size.

the error for each method at the different levels of censoring is listed in Table 23. In all instances, the KM and PKM intervals statistically significantly outperform the BH and PBH intervals. In general, the PKM intervals demonstrate less error than the KM intervals, although that difference is not statistically significant.

The Rothman method of constructing intervals works best with the Kaplan-Meier estimator. The anticonservative nature of the Rothman method is not improved by an

Table 21

Mean Error of Rothman Intervals at Each Level of ν

Method	ν 0.5	1.0	4.0
		$\gamma = .90$	
KM	-0.0189_a	-0.0202_a	-0.0218_a
BH	-0.0482_b	-0.0482_b	-0.0488_b
PKM	-0.0157_a	-0.0168_a	-0.0190_a
PBH	-0.0444_b	-0.0441_b	-0.0447_b
		$\gamma = .95$	
KM	-0.0135_a	-0.0137_a	-0.0126_a
BH	-0.0398_b	-0.0417_b	-0.0394_b
PKM	-0.0111_a	-0.0109_a	-0.0101_a
PBH	-0.0366_b	-0.0379_b	-0.0365_b
		$\gamma = .99$	
KM	-0.0072_a	-0.0064_a	-0.0084_a
BH	-0.0202_b	-0.0201_b	-0.0208_b
PKM	-0.0056_a	-0.0053_a	-0.0070_a
PBH	-0.0178_b	-0.0174_b	-0.0183_b

Note. Means in the same column within each confidence level with different subscripts differ significantly at $p < .05$. KM denotes intervals constructed using the Kaplan-Meier estimator and the Cutler-Ederer effective sample size, BH denotes intervals constructed using the Berliner-Hill estimator and the Cutler-Ederer effective sample size, PKM denotes intervals constructed using the Kaplan-Meier estimator and the Peto effective sample size, and PBH denotes intervals constructed using the Berliner-Hill estimator with the Peto effective sample size.

anticonservative probability estimator. The Peto effective sample size works with the Kaplan-Meier estimator to widen the Rothman intervals but is not a statistically significant improvement over the Cutler-Ederer effective sample size.

Pseudo-Binomial Versus Rothman Intervals

The simulations performed in this chapter compared confidence intervals based on different types of estimation methods. The Berliner-Hill probability estimator may have been more accurate in estimating the median and percentiles of the distribution

Table 22

Mean Error of Rothman Intervals at Each Level of Sample Size

Method	Sample size		
	30	60	120
		$\gamma = .90$	
KM	0.0065_a	-0.0252_a	-0.0424_a
BH	-0.0287_b	-0.0513_b	-0.0652_b
PKM	0.0091_a	-0.0220_a	-0.0386_a
PBH	-0.0254_b	-0.0477_b	-0.0601_b
		$\gamma = .95$	
KM	-0.0048_a	-0.0091_a	-0.0259_a
BH	-0.0459_b	-0.0314_b	-0.0436_b
PKM	-0.0029_a	-0.0064_a	-0.0228_a
PBH	-0.0437_b	-0.0281_b	-0.0393_b
		$\gamma = .99$	
KM	-0.0045_a	-0.0063_a	-0.0112_a
BH	-0.0229_b	-0.0180_b	-0.0202_b
PKM	-0.0036_a	-0.0051_a	-0.0092_a
PBH	-0.0204_b	-0.0156_b	-0.0175_b

Note. Means in the same column within each confidence level with different subscripts differ significantly at $p < .05$. KM denotes intervals constructed using the Kaplan-Meier estimator and the Cutler-Ederer effective sample size, BH denotes intervals constructed using the Berliner-Hill estimator and the Cutler-Ederer effective sample size, PKM denotes intervals constructed using the Kaplan-Meier estimator and the Peto effective sample size, and PBH denotes intervals constructed using the Berliner-Hill estimator with the Peto effective sample size.

(Chang, 1989), but using it to construct confidence intervals led to intervals that were anticonservative in nature. This characteristic, although beneficial to the pseudo-binomial intervals at the beginning of the survival curve, was too strong at the tail of the curve, forcing even the conservative pseudo-binomial method to construct extremely anticonservative intervals. Similarly, the Berliner-Hill estimator only exacerbated the anticonservative nature of the Rothman intervals. The Peto effective sample size added some conservatism to both the Berliner-Hill and Kaplan-Meier intervals, which increased

shown to be not statistically significantly different from the Rothman intervals based on the Cutler-Ederer effective sample size. Therefore, it is reasonable to conclude that any analyses comparing the PKM Rothman intervals to the KM pseudo-binomial intervals would yield similar results as the analyses in chapter 4, where the Rothman and pseudo-binomial intervals based on the Kaplan-Meier estimator and Cutler-Ederer effective sample size were compared.

At the 95% confidence level, the Rothman intervals using the Peto effective sample size had an overall mean error of -0.0107, while the psuedo-binomial intervals based on the Cutler-Ederer effective sample size had an overall mean error of 0.0086. The conservative nature of the Peto effective sample size decreased the overall error of the Rothman intervals; however, the pseudo-binomial intervals still tended to be more accurate, although not statistically significantly so. The Peto effective sample size was also not able to overcome the anticonservative nature of the Rothman intervals at the tail of the survival curve. Therefore, because the pseudo-binomial intervals demonstrated less error overall and because they had the desirable property of being conservative when the probability of survival is small, it is determined that the pseudo-binomial intervals using the Kaplan-Meier estimator and the Cutler-Ederer effective sample size are preferred over the anticonservative Rothman intervals.

CHAPTER 6

APPLICATION OF PSEUDO-BINOMIAL CONFIDENCE LIMITS TO SURVIVAL TIME DATA

Stanford Heart Transplant Program

The Stanford Heart Transplant Program was started in 1967. From the beginning of the program to February 1980, 249 patients were accepted to receive transplants. Of these, 184 received transplants and 65 died waiting for a new heart (Cox & Oakes, 1984). For each patient in the study, there is a well-defined date on which the patient was declared a heart transplant candidate. The transplant occurred usually within a few weeks after this date, although some patients waited several months (Turnbull, Brown, & Hu, 1974).

Although several factors can influence survival, such as quality of life and age of the patient, the focus of this example is only that of survival after receiving a transplant. Those patients not receiving a new heart are not included in this example. The survival time in this analysis is the length of time from transplant until death or the closing date of February 1980. Thus, the length of time a patient remained on the waiting list is also not included in this analysis.

Figure 7 shows the Kaplan-Meier survival curve with pseudo-binomial 95% confidence limits. The median survival time for these patients was approximately 20.5 months. The 95% confidence interval for the probability of surviving 20.5 months is (0.43, 0.58). The conservative nature of the pseudo-binomial confidence interval at the

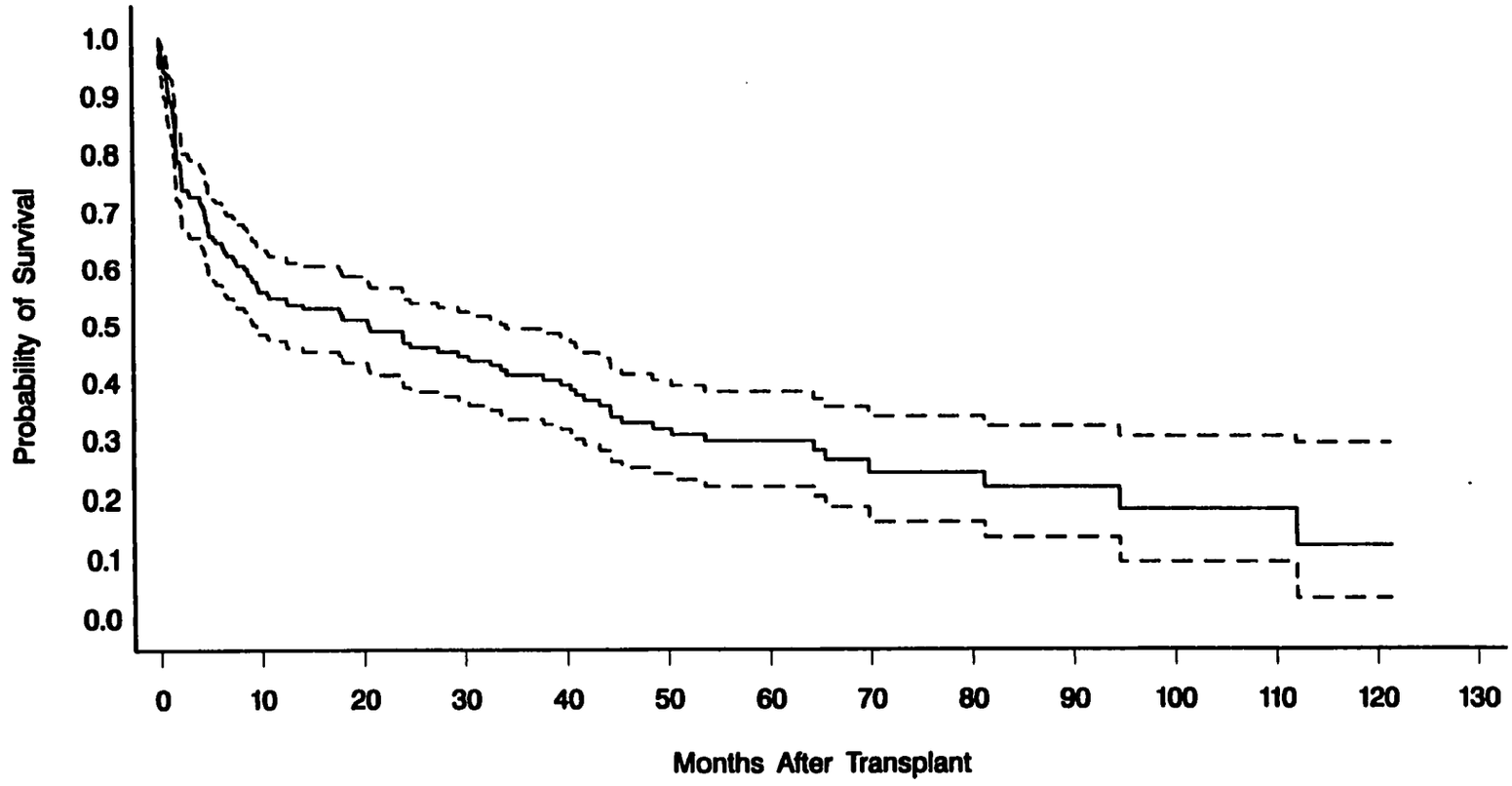


Figure 7. Kaplan-Meier survival curve with pseudo-binomial 95% confidence limits for Stanford Heart Transplant Program patients.

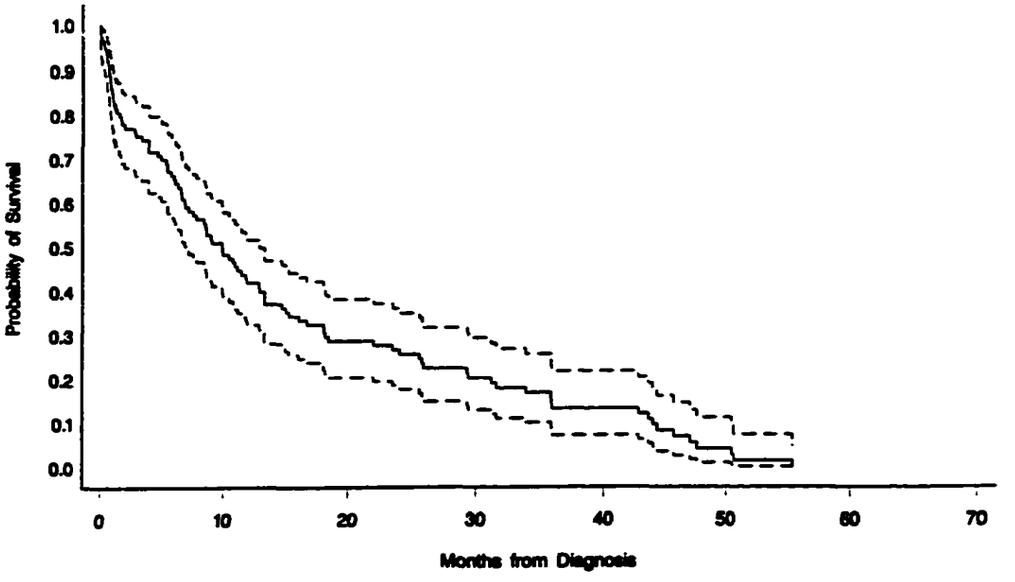
53% (n = 40) of the IDR patients entered into the consolidation phase had relapsed along with 74% (n = 48) of the DNR patients.

Vogler et al. (1992) compared the overall survival time between the two treatment groups, as well as the remission duration. They found no statitically significant difference between the overall survival rates of the two groups of all assessable patients. The IDR patients demonstrated a median survival of 11 months (n = 105), while the DNR patients had a median survival of 9 months (n = 113). Similarly, the median remission duration for patients achieving complete remission was 13 months for IDR patients and 9 months for DNR patients. No statistically significant difference was found between the duration of remission of the two treatment groups.

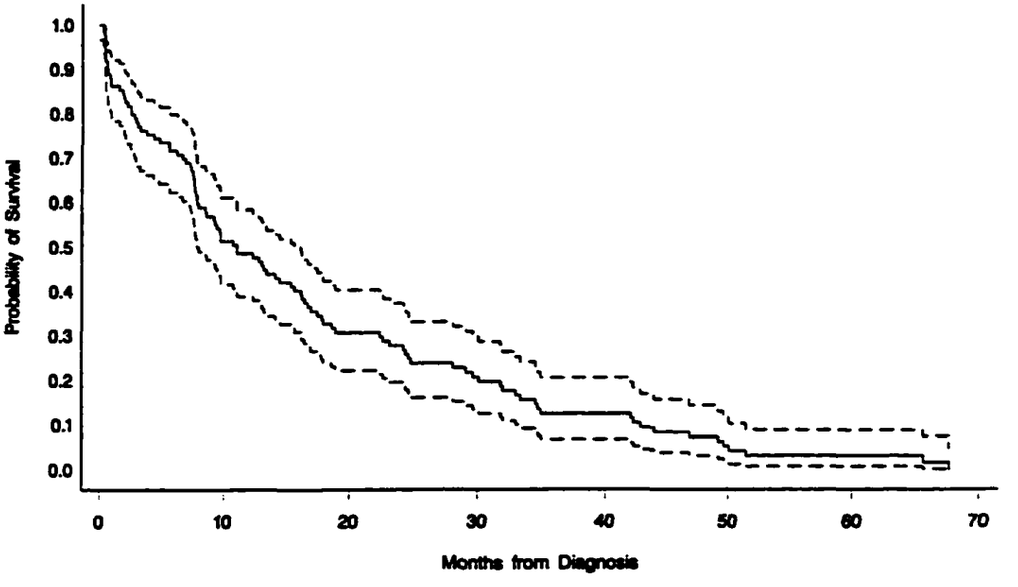
Figure 8 shows the Kaplan-Meier survival curve with pseudo-binomial 95% confidence intervals for all DNR and IDR patients entered into induction therapy. The data used to construct the survival curve was provided by Dr. A. A. Bartolucci. The survival time, shown in months, is the number of days from the date of diagnosis to death, or January 1, 1992, if still alive. The median survival time was approximately 10 months for patients receiving DNR (n = 115), while the IDR patients demonstrated a median survival of about 11 months (n = 109). Again, the conservative nature of the pseudo-binomial intervals is more clearly seen at the tail of the survival curve.

Localized Prostate Cancer

In 1978, the National Prostatic Cancer Project, later renamed the National Prostatic Cancer Treatment Group, began two randomized studies to determine the efficacy of adjuvant treatment after radical surgery (Protocol 900) or irradiation (Protocol 1000). Both protocols were closed in 1985. At that time, a total of 437 patients had been



(a)



(b)

Figure 8. Kaplan-Meier survival curve with pseudo-binomial 95% confidence limits for acute myelogenous leukemia patients treated with DNR (a) and IDR (b).

enrolled, 184 patients in protocol 900 and 235 in protocol 1000. Follow-up information, including time to the first recurrence and overall survival, was available in 170 protocol 900 and 233 protocol 1000 patients (Schmidt, Gibbons, Murphy, & Bartolucci, 1993, 1996).

After receiving protocol treatment, the patients were randomized into one of three adjuvant therapy groups: a) observation only (None), b) intravenous cyclophosphamide (Cytoxan), or c) estramustine phosphate (Emcyt). Adjuvant therapy was continued for up to 2 years. Of the 170 protocol 900 patients for which follow-up information was available, 52 received no adjuvant therapy, 57 received Cytoxan, and 61 received Emcyt. Of the 233 protocol 1000 patients, 84 received no adjuvant therapy, 77 received Cytoxan, and 72 received Emcyt. Disease progression, or recurrence, occurred in 53% of all protocol 900 patients and 66% of all protocol 1000 patients.

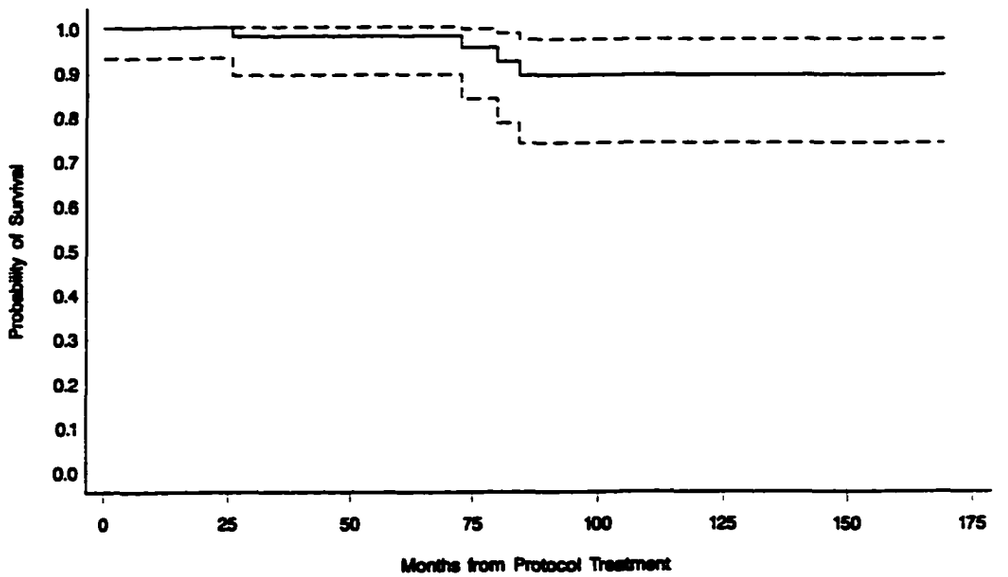
Progression-free survival and overall survival of the two protocol groups were compared within each adjuvant therapy (Schmidt et al., 1993). Also, progression-free survival and overall survival rates of the adjuvant therapy groups were compared within each protocol group (Schmidt et al., 1996). Due to the heavy censoring, or large number of survivors, of the protocol 900 patients receiving no therapy, a median survival time could not be determined. Protocol 1000 patients receiving no therapy demonstrated a median survival time of approximately 112 months. The survival rates were determined to be statistically significantly different. Similarly, progression-free survival was significantly longer for protocol 900 patients than for protocol 1000 patients.

The median progression-free survival of protocol 900 patients receiving Cytoxan was 75.7 months, while the median progression-free survival of protocol 1000 patients

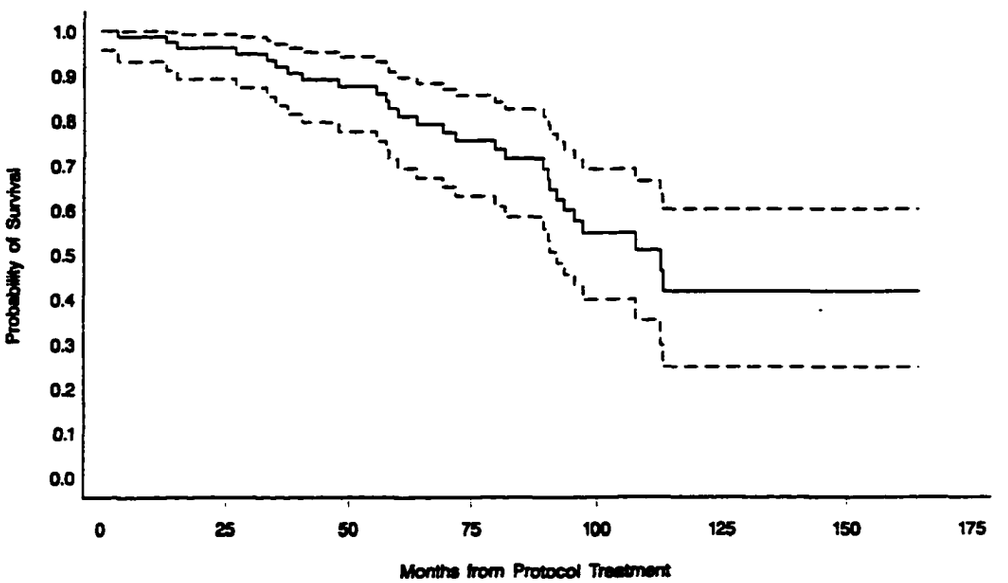
was 35.6 months. The median progression-free survival of protocol 900 patients receiving Emcyt could not be determined due to heavy censoring, but the median progression-free survival of protocol 1000 patients was 138.9 months. The progression-free survival curves for the two protocol groups were significantly different for both the Cytoxan and Emcyt therapies. The study also examined the effect of nodal involvement on survival. The authors concluded that adjuvant estramustine phosphate (Emcyt) benefitted patients with nodal involvement who received irradiation.

Figures 9, 10, and 11 shows the Kaplan-Meier survival curves with pseudo-binomial 95% confidence limits for protocol 900 and protocol 1000 patients. The data used to construct each survival curve was provided by Dr. A. A. Bartolucci. In each figure, the measured time of survival, shown in months, is the number of days from protocol treatment to death, or protocol closure in 1985 if still alive. The median overall survival time could not be determined for protocol 900 patients in any therapy group. Figure 9 illustrates the survival of patients receiving no adjuvant therapy. The protocol 1000 patients survived a median of approximately 90.5 months. Figure 10 demonstrates the survival curves for patients receiving Cytoxan. Protocol 1000 patients survived a median of approximately 84 months. Figure 11 shows the survival curves for patients receiving Emcyt. The median survival time for protocol 1000 patients was about 133 months. The longer survival times for surgery patients (protocol 900) could be due to a greater proportion of surgery patients having a lower stage disease (Schmidt et al., 1993).

These figures more clearly illustrate the conservative behavior of the pseudo-binomial confidence intervals at both ends of the survival curve. The lower limit is conservative at the upper end of the curve, where the probability of survival is large. The

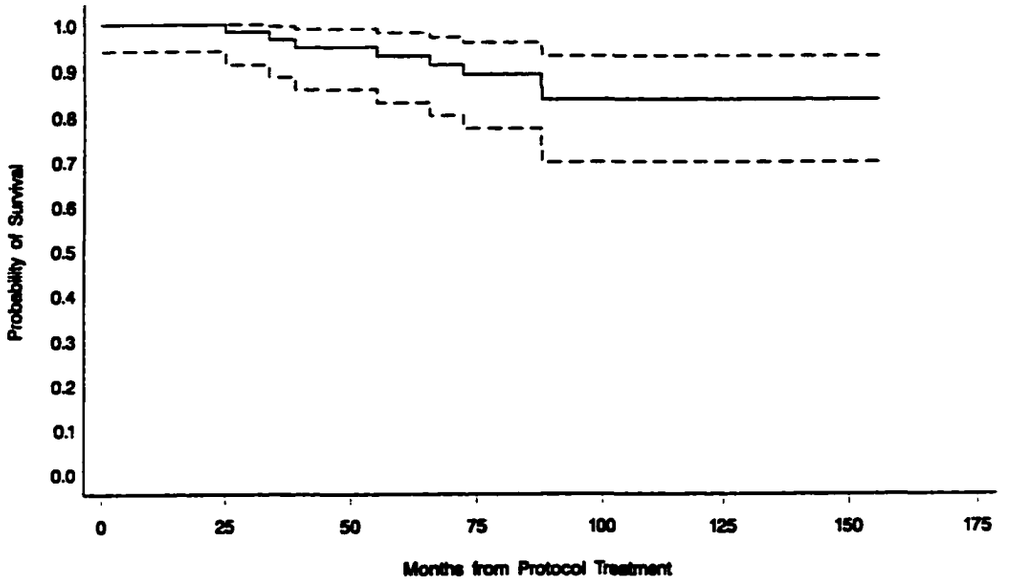


(a)

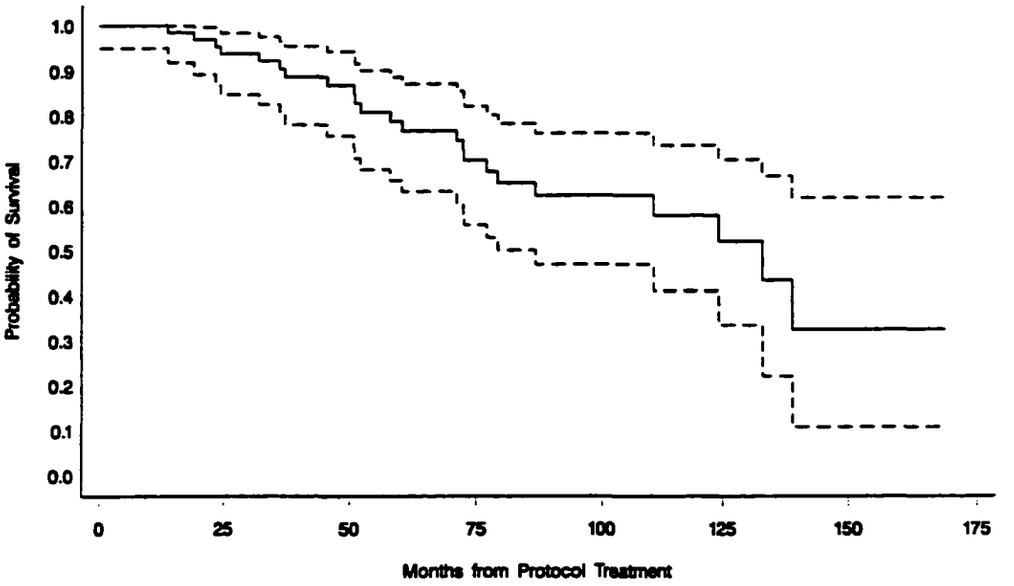


(b)

Figure 9. Kaplan-Meier survival curve with pseudo-binomial 95% confidence limits for localized prostate cancer patients not receiving therapy after protocol 900 (a) or protocol 1000 (b) treatment.



(a)



(b)

Figure 11. Kaplan-Meier survival curve with pseudo-binomial 95% confidence limits for localized prostate cancer patients receiving estramustine phosphate (Emcyt) therapy after protocol 900 (a) or protocol 1000 (b) treatment.

upper limit tends to be more conservative at the tail of the curve when there is less censoring. This can be seen in Figure 11. Protocol 900 patients survived longer, thus more censoring was present. The lower confidence limit at the tail of the curve remains conservative, while the upper limit is less so. Protocol 1000 patients , however, were less heavily censored. The upper confidence limit for those patients at the tail of the survival curve is clearly more conservative than the lower limit.

CHAPTER 7

DISCUSSION OF RESULTS AND SUGGESTIONS FOR FUTURE RESEARCH

Summary and Conclusions

Survival time studies have been and are being conducted in a variety of disciplines. The purpose of all such studies is to formulate a probability statement about the time of survival. Several different approaches to the analysis of survival time data have been proposed. Some of these are concerned with the appropriate estimator of the probability of survival. Some focus on the issue of censoring and effective sample size. Others concentrate on the construction of confidence limits around the survival curve.

The issue of constructing confidence limits led to the development of the pseudo-binomial distribution. By relating the binomial probability distribution to the incomplete beta function, the cumulative distribution of the pseudo-binomial distribution was defined. The confidence limits for the probability of survival could then be constructed using the F-distribution. The purpose of this research was two-fold: first, to further investigate the pseudo-binomial distribution, and second, to evaluate the performance of the pseudo-binomial confidence limits.

The investigation of the pseudo-binomial distribution focused on the derivation of the probability density function and the first two moments. Also, the maximum likelihood estimator for the unknown parameter p was determined. The Euler-Maclaurin expansion was utilized to approximate the first two moments. For a sample size of

$N \geq 30$, the mean can be approximated by $Np - 1/2$ while the variance can be approximated by $Np(1-p) - 1/12$. The shift in the first two moments was clearly illustrated in chapter 2. The behavior of the maximum likelihood estimate of p was also investigated. It was determined that the usual binomial proportion $\hat{p} = X / N$ consistently underestimated the value of the maximum likelihood estimate.

The performance of the pseudo-binomial confidence intervals was evaluated using data generated from the Weibull distribution. Three different shape parameters were used, along with different sample sizes and levels of censoring. The pseudo-binomial confidence intervals were found to be more accurate than the commonly used Greenwood confidence limits. They also demonstrated less error overall than the Rothman intervals, although the difference was not statistically significant.

The performance of the pseudo-binomial and Rothman confidence intervals for different survival estimators and effective sample size calculations was also evaluated. The pseudo-binomial intervals were most accurate using the usual Kaplan-Meier estimator with the Cutler-Ederer effective sample size. The Peto effective sample size combined with the Kaplan-Meier estimator improved the accuracy of the Rothman intervals. However, the pseudo-binomial intervals still demonstrated less error than the Rothman intervals overall. The Berliner-Hill estimator constructed intervals which were extremely anticonservative and, therefore, undesirable.

Finally, three examples of constructing pseudo-binomial confidence intervals around a survival curve were given. In each example, the conservative nature of the pseudo-binomial intervals was clearly illustrated.

Suggestions for Future Research

The pseudo-binomial distribution as defined demonstrated a shift in the first two moments. It is possible this shift in moments is a continuity correction factor. The shift in the first moment could be resolved by defining a new random variable $Y = X + 1/2$; however, the second moment would remain unchanged. The shifts of both the first and second moments would be corrected through the use of the Uniform(0,1) distribution. The new random variable $Y = X + U$, where X is distributed as a pseudo-binomial random variable and U as a Uniform(0,1) variable, would have an approximate expected value of Np and an approximate variance of $Np(1-p)$ for $N \geq 30$. Further research into the appropriateness and usefulness of this new definition is suggested.

The usual binomial proportion $p = X/N$ was shown to consistently underestimate the maximum likelihood estimate of p. It is possible, then, that the survival curves based on that simple proportion estimate also underestimate the probability of survival. The application of the maximum likelihood estimate to estimating the survivorship function is also an area of future research.

The confidence limits evaluated in this study were those constructed for the survival curve estimated using nonparametric techniques. However, the pseudo-binomial confidence limits could also be applied to a parametric survival curve. Further evaluation of the pseudo-binomial confidence limits in this area is warranted.

APPENDIX A

DERIVATION OF MOMENTS

The moments of a distribution can be found using the equation

$$E(X^{\alpha}) = \int_0^{\infty} x^{\alpha} f(x)dx = \alpha \int_0^{\infty} x^{\alpha-1}[1 - F(x)]dx$$

(Feller, 1966). Therefore, the moments of the pseudo-binomial distribution are given by

$$\begin{aligned} E(X) &= \int_0^{N-1} \int_0^{p} \frac{\Gamma(N+1)}{\Gamma(k+1)\Gamma(N-k)} t^k (1-t)^{N-k-1} dt\, dk \\ &= \int_0^{N-1} \frac{\Gamma(N+1)}{\Gamma(k+1)\Gamma(N-k)} \int_0^{p} t^k (1-t)^{N-k-1} dt\, dk \\ &= \int_0^{N-1} I_p(k+1, N-k)\, dk \end{aligned}$$

and

$$\begin{aligned} E(X^2) &= 2 \int_0^{N-1} \int_0^{p} k \frac{\Gamma(N+1)}{\Gamma(k+1)\Gamma(N-k)} t^k (1-t)^{N-k-1} dt\, dk \\ &= 2 \int_0^{N-1} k\ I_p(k+1, N-k)\, dk\ . \end{aligned}$$

These equations can be evaluated using the Euler-Maclaurin expansion. If a function $G(x)$ has its first $2n$ derivatives continuous on an interval (a, b), then divide the interval into m equal parts so that $h = (b-a)/m$. For some θ, $0 < \theta < 1$, the expansion is given by

$$\begin{aligned} \frac{1}{h} \int_a^b G(t)\, dt = \sum_{k=0}^{m} G(a+kh) - \frac{G(b)+G(a)}{2} - \sum_{k=1}^{n-1} \frac{h^{2k-1}}{(2k)!} B_{2k} \{G^{(2k-1)}(b) - G^{(2k-1)}(a)\} \\ - \frac{h^{2n}}{(2n)!} B_{2n} \sum_{k=0}^{m-1} G^{(2n)}(a+kh+\theta h), \end{aligned}$$

where B_j is a Bernoulli number (Abramowitz & Stegun, 1974). The expansion can be approximated using only the first three terms. That is,

$$\frac{1}{h}\int_a^b G(t)\,dt \approx \sum_{k=0}^{m} G(a+kh) - \frac{G(b)+G(a)}{2} - \sum_{k=1}^{n-1} \frac{h^{2k-1}}{(2k)!} B_{2k}\{G^{(2k-1)}(b) - G^{(2k-1)}(a)\}.$$

The limits of integration for the expansion of the pseudo-binomial distribution are $a = 0$ and $b = N-1$. In order to determine the moments of the distribution, let $m = N-1$ so that $h = 1$ and choose $n = 2$.

Derivation of the First Moment

Using the above constraints, $m = N-1$ and $n = 2$, the Euler-Maclaurin expansion of the first moment of the pseudo-binomial distribution can be written as

$$E(X) = \int_0^{N-1} I_p(k+1, N-k)\,dk \approx \sum_{k=0}^{N-1} I_p(k+1, N-k) - \frac{I_p(N,1) + I_p(1,N)}{2} - \frac{1}{2!} B_2\{I'_p(N,1) - I'_p(1,N)\}, \quad (1)$$

where $I_p(k+1, N-k)$ is the incomplete beta function and $I'_p(k)$ is the first derivative of the incomplete beta function. Equation 1 is a combination of three distinct terms. Thus, for readibility, the expansion will be evaluated in individual segments. The working equations are

$$\sum_{k=0}^{N-1} I_p(k+1, N-k), \quad (2)$$

$$\frac{I_p(N,1) + I_p(1,N)}{2}, \quad (3)$$

and

$$\frac{1}{2} B_2\{I'_p(N,1) - I'_p(1,N)\}, \quad (4)$$

so that

$$E(X) = \int_0^{N-1} I_p(k+1, N-k)\,dk \approx (2) - (3) - (4).$$

The incomplete beta function can be expressed as

$$I_p(x, n-x+1) = \sum_{j=x}^{n} \binom{n}{j} p^j (1-p)^{n-j},$$

or, in the case of the pseudo-binomial distribution,

$$I_p(k+1, N-k) = \sum_{j=k+1}^{N} \binom{N}{j} p^j (1-p)^{N-j}. \tag{5}$$

Substituting the expression in Equation 5 into the first term of the Euler-Maclaurin expansion (Equation 2) gives $\sum_{k=0}^{N-1} \sum_{j=k+1}^{N} \binom{N}{j} p^j (1-p)^{N-j}$. This leads to the result

$$\begin{aligned} \sum_{k=0}^{N-1} I_p(k+1, N-k) = {} & \binom{N}{1} p(1-p)^{N-1} + 2\binom{N}{2} p^2 (1-p)^{N-2} + 3\binom{N'}{3} p^3 (1-p)^{N-3} \\ & + \ldots + (N-1)\binom{N}{N-1} p^{N-1}(1-p) + N\binom{N}{N} p^N \end{aligned} \tag{6}$$

(see Table A1). Each of the combinatorials in Equation 6 are of the form $k\binom{N}{k}$, which can be reduced to

$$k\binom{N}{k} = \frac{k\,N!}{k!(N-k)!} = \frac{k\,N(N-1)!}{k(k-1)!(N-1-(k-1))!} = N\binom{N-1}{k-1}. \tag{7}$$

Substituting Equation 7 into Equation 6, and factoring out a p, yields

$$\sum_{k=0}^{N-1} I_p(k+1, N-k) = Np\left[\binom{N-1}{0}(1-p)^{N-1}\binom{N-1}{1}p(1-p)^{N-2} + \binom{N-1}{3}p^2(1-p)^{N-3}\right.$$
$$\left. +\ldots+\binom{N-1}{N-2}p^{N-2}(1-p)+\binom{N-1}{N-1}p^{N-1}\right]$$
$$= Np\sum_{j=0}^{N-1}\binom{N-1}{j}p^j(1-p)^{N-1-j}.$$

Since $\sum_{j=0}^{N-1}\binom{N-1}{j}p^j(1-p)^{N-1-j} = 1$, Equation 2, the first segment of the expansion, is merely

$$\sum_{k=0}^{N-1} I_p(k+1, N-k) = Np. \tag{8}$$

In order to evaluate Equation 3, the incomplete beta function must be evaluated at $k = N-1$ and $k = 0$. That is, for $k = N-1$

$$I_p(N,1) = \int_o^p \frac{\Gamma(N+1)}{\Gamma(N)\Gamma(1)} t^{N-1}(1-t)^0 dt = \frac{\Gamma(N+1)}{\Gamma(N)\Gamma(1)}\frac{t^N}{N}\Big|_o^p = p^N \tag{9}$$

and for $k = 0$

$$I_p(1,N) = \int_o^p \frac{\Gamma(N+1)}{\Gamma(1)\Gamma(N)} t^0(1-t)^{N-1} dt = -\frac{\Gamma(N+1)}{\Gamma(1)\Gamma(N)}\frac{(1-t)^N}{N}\Big|_o^p = 1-(1-p)^N. \tag{10}$$

Using these results, Equation 3, the second segment in the expansion, is

$$\frac{I_p(N,1)+I_p(1,N)}{2} = \frac{p^N+1-(1-p)^N}{2} = \frac{1}{2}+\frac{p^N-(1-p)^N}{2}. \tag{11}$$

To evaluate Equation 4, $\frac{1}{2}B_2\{I'_p(N,1) - I'_p(1,N)\}$, the first derivative of the incomplete beta function with respect to k must be evaluated at $N-1$ and 0. This gives the following results:

$$I'_p(N,1) = \int_0^p \frac{\Gamma(N+1)}{\Gamma(N)\Gamma(1)} t^{N-1}\left\{\psi(1) - \psi(N) + \ln\left(\frac{t}{1-t}\right)\right\}dt$$

$$= N\{\psi(1) - \psi(N)\}\int_0^p t^{N-1}dt + N\int_0^p t^{N-1}\ln\left(\frac{t}{1-t}\right)dt$$

$$= N\{\psi(1) - \psi(N)\}\int_0^p t^{N-1}dt + N\int_0^p t^{N-1}\ln t\,dt - N\int_0^p t^{N-1}\ln(1-t)dt$$

$$= \{\psi(1) - \psi(N)\}t^N\Big|_0^p + \left(\frac{t^N \ln t}{N} - \frac{t^N}{N^2}\right)\Big|_0^p - N\int_0^p t^{N-1}\ln(1-t)dt,$$

which yields

$$I_p(N,1) = \{\psi(1) - \psi(N)\}p^N + p^N\left(\ln p - \frac{1}{N}\right) - N\int_0^p t^{N-1}\ln(1-t)dt\,, \qquad (12)$$

and

$$I'_p(1,N) = \int_0^p \frac{\Gamma(N+1)}{\Gamma(N)\Gamma(1)}(1-t)^{N-1}\left\{\psi(N) - \psi(1) + \ln\left(\frac{t}{1-t}\right)\right\}dt$$

$$= N\{\psi(N) - \psi(1)\}\int_0^p (1-t)^{N-1}dt + N\int_0^p (1-t)^{N-1}\ln\left(\frac{t}{1-t}\right)dt$$

$$= N\{\psi(N) - \psi(1)\}\int_0^p (1-t)^{N-1}dt + N\int_0^p (1-t)^{N-1}\ln t\,dt$$

$$- N\int_0^p (1-t)^{N-1}\ln(1-t)dt$$

$$= -\{\psi(N) - \psi(1)\}t^N\Big|_0^p + \left(\frac{(1-t)^N\ln(1-t)}{N} - \frac{(1-t)^N}{N^2}\right)\Big|_0^p$$

$$+ N\int_0^p (1-t)^{N-1}\ln t\,dt$$

which is

$$I'_p(1,N) = -\{\psi(N)-\psi(1)\}\{(1-p)^N - 1\} + (1-p)^N\left(\ln(1-p) - \frac{1}{N}\right) - \frac{1}{N} - N\int_0^p (1-t)^{N-1}\ln t\ dt. \tag{13}$$

The Bernoulli number B_2 is 1/6. This identity and the results obtained in Equations 12 and 13 lead to the following solution for Equation 4:

$$\frac{1}{12}\left[\{\psi(1)-\psi(N)\}\{p^N + 1 - (1-p)^N\} + p^N \ln p - \frac{p^N}{N} - (1-p)^N \ln(1-p) + \frac{(1-p)^N}{N} + \frac{1}{N} - N\int_0^p t^{N-1}\ln(1-t) + (1-t)^{N-1}\ln t\ dt\right]. \tag{14}$$

The first moment then is approximated using Equations 8, 11, and 14, which give the result

$$\begin{aligned} E(X) &\approx Np - \frac{1}{2} - \frac{p^N - (1-p)^N}{2} \\ &\quad - \frac{1}{12}\left[\{\psi(1)-\psi(N)\}\left(p^N + 1 - (1-p)^N\right) + p^N \ln p\right. \\ &\quad - (1-p)^N \ln(1-p) - \frac{1}{N}\left(p^N - (1-p)^N - 1\right. \\ &\quad \left.\left. - N\int_0^p t^{N-1}\ln(1-t) + (1-t)^{N-1}\ln t\ dt\right]\right] \\ &\approx Np - \frac{1}{2} - \frac{p^N - (1-p)^N}{2}. \end{aligned} \tag{15}$$

Derivation of the Second Moment

The function *G(t)* to be used in the expansion of the second moment of the pseudo-binomial distribution is $G(t) = 2kI_p(k+1, N-k)$. The Euler-Maclaurin expansion for the second moment, again using $m = N-1$ and $n = 2$, is given by

$$E(X^2) = 2\int_0^{N-1} k\, I_p(k+1, N-k)\, dk \approx 2\sum_{k=0}^{N-1} k\, I_p(k+1, N-k)$$
$$-\{(N-1)\, I_p(N,1) + 0 I_p(1,N)\}$$
$$-B_2\{I_p(N,1) + (N-1) I'_p(N,1)$$
$$-I_p(1,N) - 0 I'_p(1,N)\}. \qquad (16)$$

Again, for computation and readibility purposes, the expansion will be separated into three separate terms. These are

$$2\sum_{k=0}^{N-1} k\, I_p(k+1, N-k), \qquad (17)$$

$$(N-1)\, I_p(N,1), \qquad (18)$$

and

$$B_2\{I_p(N,1) + (N-1) I'_p(N,1) - I_p(1,N) \ . \qquad (19)$$

The derivation of Equation 17 is shown in Table A2. The summation gives

$$\sum_{k=0}^{N-1} k I_p(k+1, N-k) = \binom{N}{2} p^2 (1-p)^{N-2} + \sum_{i=1}^{2} i \binom{N}{3} p^3 (1-p)^{N-3} + \ldots$$
$$+ \sum_{i=1}^{N-2} i \binom{N}{N-1} p^{N-1}(1-p) + \sum_{i=1}^{N-1} i \binom{N}{N} p^N. \qquad (20)$$

Each term has as a factor $\sum_{i=1}^{k} i$, where k increases with each term from 1 to $N-1$. Using the result $\sum_{i=1}^{n} i = \frac{n(n+1)}{2}$, Equation 20 can be written as

$$\sum_{k=0}^{N-1} k I_p(k+1, N-k) = \frac{1*2}{2}\binom{N}{2} p^2 (1-p)^{N-2} + \frac{2*3}{2}\binom{N}{3} p^3 (1-p)^{N-3} + \ldots$$
$$+ \frac{(N-2)(N-1)}{2}\binom{N}{N-1} p^{N-1}(1-p) + \frac{(N-1)N}{2}\binom{N}{N} p^N.$$

Table A2

Expansion of Summation Equation 17

$$
\begin{array}{lcccccc}
0I_p(1,N) = & 0 & & & & & \\
1I_p(2,N-1) = & & \binom{N}{2}p^2(1-p)^{N-2} + & \binom{N}{3}p^3(1-p)^{N-3} + & \cdots & \binom{N}{N-1}p^{N-1}(1-p) + & \binom{N}{N}p^N \\
2I_p(3,N-2) = & & & 2\binom{N}{3}p^3(1-p)^{N-3} + & \cdots & 2\binom{N}{N-1}p^{N-1}(1-p) + & 2\binom{N}{N}p^N \\
\vdots & & & & & & \vdots \\
(N-2)I_p(N-1,2) = & & & & & (N-2)\binom{N}{N-1}p^{N-1}(1-p) + & (N-2)\binom{N}{N}p^N \\
(N-1)I_p(N,1) = & & & & & & (N-1)\binom{N}{N}p^N
\end{array}
$$

$$
\sum_{k=0}^{N-1} kI_p(k+1,N-k) = \binom{N}{2}p^2(1-p)^{N-2} + \sum_{i=1}^{2} i\binom{N}{3}p^3(1-p)^{N-3} + \ldots + \sum_{i=1}^{N-2} i\binom{N}{N-1}p^{N-1}(1-p) + \sum_{i=1}^{N-1} i\binom{N}{N}p^N
$$

Each term is now of the form $\frac{(j-1)j}{2}\binom{N}{j}p^j(1-p)^{N-j}$. The first two factors in each term can be reduced to

$$\begin{aligned}\frac{(j-1)j}{2}\binom{N}{j} &= \frac{(j-1)j}{2}\frac{N!}{j!(N-j)!} = \frac{(j-1)j}{2}\frac{N!}{j(j-1)(j-2)!(N-j)!} \\ &= \frac{N(N-1)(N-2)!}{2(j-2)!(N-2-(j-2))!} \\ &= \frac{N(N-1)}{2}\binom{N-2}{j-2}.\end{aligned}$$

Using this result and factoring out $\frac{N(N-1)p^2}{2}$ from each term, Equation 20, the solution to Equation 17, becomes

$$\begin{aligned}2\sum_{k=0}^{N-1} kI_p(k+1,N-k) &= N(N-1)p^2\left[\binom{N-2}{0}(1-p)^{N-2}+\binom{N-2}{1}p(1-p)^{N-3}+\ldots\right. \\ &\quad \left.+\binom{N-2}{N-3}p^{N-3}(1-p)+\binom{N-2}{N-2}p^{N-2}\right] \qquad (21) \\ &= N(N-1)p^2\sum_{j=0}^{N-2}\binom{N-2}{j}p^j(1-p)^{N-2-j} \\ &= N(N-1)p^2 .\end{aligned}$$

As was shown earlier in Equation 9, $I_p(N,1)=p^N$ so that the Equation 18 becomes

$$(N-1)I_p(N,1)=(N-1)p^N . \qquad (22)$$

Equation 19 can be determined using Equations 9, 10 and 12. Equation 19 is then

$$
\begin{aligned}
& B_2\left\{I_p(N,1)+(N-1)I'_p(N,1)-I_p(1,N)\right\} \\
&= \frac{1}{6}\left\{p^N+(N-1)I'_p(N-1)-(1-(1-p)^{N'}\right\} \\
&= \frac{1}{6}\left\{p^N-1+(1-p)^{N'}+(N-1)\left[\left\{\psi(1)-\psi(N-1)\right\}p^N\right.\right. \\
&\qquad \left.\left.+p^N\left(\ln p-\frac{1}{N'}\right)-N\int_0^p t^{N-1}\ln(1-t)dt\right]\right\}.
\end{aligned}
\tag{23}
$$

Combining Equations 21, 22, and 23 approximates the second moment of the pseudo-binomial distribution. The resulting equation is

$$
\begin{aligned}
E(X^2) &\approx N(N-1)p^2-(N-1)p^N \\
&\quad -\frac{1}{6}\left\{p^N-1+(1-p)^N\right. \\
&\quad +(N-1)\left[\left\{\psi(1)-\psi(N)\right\}p^N+p^N\left(\ln p-\frac{1}{N}\right)\right. \\
&\quad \left.\left.-N\int_0^p t^{N-1}\ln(1-t)\,dt\right]\right\} \\
&\approx N(N-1)p^2+\frac{1}{6}-(N-1)p^N-\frac{p^N+(1-p)^N}{6}.
\end{aligned}
\tag{24}
$$

From Equations 15 and 24 the variance of X can be determined. The variance is given by $E(X^2)-E^2(X)$ or

$$\begin{aligned}
\operatorname{var}(X) &\approx N(N-1)p^2 + \frac{1}{6} - (N-1)p^N - \frac{p^N + (1-p)^N}{6} \\
&\quad - \left[\left(Np - \frac{1}{2}\right) - \frac{p^N - (1-p)^N}{2}\right]^2 \\
&= (Np)^2 - Np^2 + \frac{1}{6} - (Np)^2 + Np - \frac{1}{4} - (N-1)p^N - \frac{p^N + (1-p)^N}{6} \\
&\quad + \left(Np - \frac{1}{2}\right)\left(p^N - (1-p)^N\right) - \left(\frac{(1-p)^N - p^N}{2}\right)^2 \\
&= Np(1-p) - \frac{1}{12} - (N-1)p^N - \frac{p^N + (1-p)^N}{6} \\
&\quad + \left(Np - \frac{1}{2}\right)\left(p^N - (1-p)^N\right) - \left(\frac{(1-p)^N - p^N}{2}\right)^2 .
\end{aligned}$$

APPENDIX B

PROPAGATION OF ERROR

If $f(x)$ is a function of x, Taylor's series can often be used to express the effect on $f(x)$ of a small error in x (Deming, 1948). If we let Δx denote the error in x and Δf the error in $f(x)$, the propagation of error is given approximately by $\Delta f = f'(x)\Delta x$. This can be extended to functions of several variables. Thus, if F is a function of three variables, say x, y, and z, then the error in F can be expressed approximately as $\Delta F = F_x \Delta x + F_y \Delta y + F_z \Delta z$, where $F_k = \partial F / \partial K$.

Cramer (1946) developed the following theorem which was later used by Ku (1966) to derive the propagation of error formulas for various functions and determine their accuracy.

> Theorem: If, in some neighborhood of the point $X = M_X$, $Y = M_Y$, the function $F(X,Y)$ is continuous and has continuous derivatives of the first and second order with respect to the arguments X and Y, the random variable $\hat{w} = F(\bar{x}, \bar{y})$ is asymptotically normal, the mean and variance of the limiting normal distribution being given by:
>
> $$mean\, \hat{w} = F(M_X, M_Y)$$
>
> and
>
> $$\text{var}\, \hat{w} = \left[\frac{\partial F}{\partial X}\right]^2 \frac{\sigma_x^2}{n} + \left[\frac{\partial F}{\partial Y}\right]^2 \frac{\sigma_y^2}{n} + 2\left[\frac{\partial F}{\partial X}\right]\left[\frac{\partial F}{\partial Y}\right]\frac{\sigma_{xy}}{n}.$$

Using these results, the approximate variance of the survivorship estimator $\hat{S}_{KM}$ can be determined.

The Kaplan-Meier estimate of the probability of survival is given by

$$\hat{S}_{KM}(t) = \prod_{i:t_{(i)} \le t} \frac{N-i}{N-i+1}$$

where the N-i is the number of subjects surviving longer than time $t_{(i)}$. Then for any given time, the proportion of survivors is

$$p_i = \frac{N-i}{N-i+1}$$

so that $\hat{S}_{KM}(t) = \prod_{i:t_{(i)} \le t} p_i$. The proportion of deaths is 1-p_i, or q_i = 1/(N-i+1). The proportion of deaths can be thought of as x_i = one success out of N - i + 1 Bernoulli trials. Thus, the variance of x_i is given by $\text{var}(x_i) = (N-i+1)q(1-q)$ and the variance of the proportion of deaths, equal to the variance of the proportion of survivors, is $\text{var}(q_i) = \text{var}(p_i) = q(1-q)/(N-i+1)$.

Taking the natural log of the survivorship estimator yields $L = \ln \hat{S}_{KM}(t) = \sum_{i:t_{(i)} \le t} \ln \hat{p}_i$, so that $dL = \sum_{i:t_{(i)} \le t} \frac{\partial L}{\partial \hat{p}_i} d\hat{p}_i = \sum_{i:t_{(i)} \le t} \frac{1}{\hat{p}_i} d\hat{p}_i$. The variance of L is approximated by

$$\hat{\sigma}_L^2 = \sum_{i:t_{(i)} \le t} \frac{1}{p_i^2} \text{var}(\hat{p}_i) = \sum_{i:t_{(i)} \le t} \frac{1}{(N-i)(N-i+1)}.$$

Now, $\hat{S}_{KM}(t) = e^L$ and $d\hat{S}_{KM}(t) = \frac{\partial \hat{S}_{KM}(t)}{\partial L} dL$. The approximate variance of the survivorship estimator is then given by

$$\hat{\sigma}_S^2 = \left(\frac{\partial \hat{S}_{KM}^2(t)}{dL} \right)^2 \hat{\sigma}_L^2$$

$$= \hat{S}_{KM}^2(t) \sum_{i:t_{(i)} \le t} \frac{1}{(N-i)(N-i+1)}.$$

The approximate variance of the Berliner-Hill estimator of the survivorship function is derived similarly by replacing N by $N+1$ in the equation.

APPENDIX C

SAS CODE USED TO ANALYZE DOREY-KORN EFFECTIVE SAMPLE SIZE

Testing Dorey-Korn Modified Effective Size Calculations for Grogan, Dorey, Rollins, and Amstutz Data

```
/* ********************************************************************** */
/* DK_TEST.SAS    SAS PROGRAM WRITTEN TO TEST COMPUTATION OF              */
/*                DOREY AND KORN EFFECTIVE SAMPLE SIZE EXAMPLE            */
/*                                                                        */
/*    LAST MODIFIED:  6/4/97                                              */
/*    LAST EXECUTED: 6/4/97                                               */
/* ********************************************************************** */
OPTIONS NODATE LS=120 PS=65 PAGENO=1 NOTES;
TITLE'DOREY AND KORN EFFECTIVE SAMPLE SIZE EXAMPLE';

DATA A;
 INPUT T COUNT CENSOR @@;
CARDS;
2 4 0 3 39 1 4 2 0 5 4 1 6 2 0 7 2 1 12 1 0 13 67 1 14 0 0
15 47 1 16 1 0 17 11 1 18 1 0 19 11 1 20 1 0 21 55 1 24 0 0 25 132 1
30 0 0 31 39 1 36 1 0 37 80 1 48 0 0 49 117 1 60 0 0 61 59 1 72 0 0
73 49 1 84 0 0 85 46 1 96 0 0 97 31 1 108 0 0 109 10 1
;;;;
PROC SORT DATA=A; BY T;

DATA B; SET A; BY T;
 KEEP TIME CENSOR NUM;
 RETAIN TIME;
 IF FIRST.T THEN TIME=T;
 IF CENSOR=0 AND COUNT=0 THEN DO;
  TIME=T; NUM=0; OUTPUT;
 END;
 ELSE IF (CENSOR=0 AND COUNT>0) THEN DO I=1 TO COUNT;
  TIME=TIME+.001; NUM=1; OUTPUT;
 END;
 ELSE IF (CENSOR=1) THEN DO I=1 TO COUNT;
  TIME=TIME+.001; NUM=0; OUTPUT;
 END;
RUN;
DATA B; SET B;
 RENAME NUM=COUNT TIME=T;
RUN;
```

```
PROC PRINT DATA=C;
TITLE2 &TITLE;
 VAR T COUNT RISK S_KM N_KM S_DKM N_DKM;
 WHERE CENSOR=0;
RUN;
%MEND;

%DK(A,IF COUNT=0 THEN DO;,END;,
   'USING COLLAPSED LIFE TABLE - CALCULATING N_DKM ONLY WHEN NO
FAILURES')
%DK(A, , ,
   'USING COLLAPSED LIFE TABLE - CALCULATING N_DKM EACH TIME')
%DK(B,IF COUNT=0 THEN DO;,END;,
   'USING EXPANDED LIFE TABLE - CALCULATING N_DKM ONLY WHEN NO
FAILURES')
%DK(B, , ,
   'USING EXPANDED LIFE TABLE - CALCULATING N_DKM EACH TIME')
```

Testing Dorey-Korn Modified Effective Sample Size Using Simulated Survival Data

```
/* ********************************************************************** */
/* DKTEST2.SAS  SAS PROGRAM WRITTEN TO FURTHER TEST THE                   */
/*              COMPUTATION OF THE DOREY AND KORN                         */
/*              EFFECTIVE SAMPLE SIZE                                     */
/*                                                                        */
/*      LAST MODIFICATION: 6/14/97                                        */
/*      LAST EXECUTION:    6/14/97                                        */
/* ********************************************************************** */
OPTIONS NODATE LS=120 PS=65 PAGENO=1 NONOTES;

DATA A;
KEEP CENSOR T;
 T=0; CENSOR=1; OUTPUT;
 DO I=1 TO 30;
  U=UNIFORM(12345);
  IF UNIFORM(12345)<.25 THEN CENSOR=1; ELSE CENSOR=0;
  T=((-LOG(U))**(1/1))/1;
  OUTPUT;
 END;
RUN;
PROC SORT DATA=A; BY T;

%MACRO DK(RESTRICT,END_R,TITLE);
DATA C; SET A; BY T;
 KEEP T CENSOR S_KM S_DKM N_KM N_DKM;
 RETAIN S_KM KM1 KM2 SURV R1 F1 N_KM N_DKM KM_SUM SUMK1
SUMK2 0;

 IF _N_=1 THEN DO;
  S_KM=1; S_DKM=1; KM1=1; KM2=1;
  N_KM=30; N_DKM=30;
  KM_SUM=0; SUMK1=0; SUMK2=0;
  SURV=30; R1=30; F1=0;
 END;

 RISK=SURV;
 NFAIL=1-CENSOR;

 KM_PROD=(RISK-NFAIL)/RISK;

 IF NFAIL NE RISK THEN KM_SUM=KM_SUM + (NFAIL/(RISK*(RISK-NFAIL)));
```

```
 S_KM=S_KM*KM_PROD;
 VAR_KM=S_KM*S_KM*KM_SUM;

 IF VAR_KM NE 0 THEN N_KM=S_KM*(1-S_KM)/VAR_KM;

 LRISK=R1; LFAIL=F1;
 OLD_KM=KM1; SUM_KOLD=SUMK1;
 IF CENSOR=0 THEN DO;
  R1=RISK; F1=NFAIL;
  KM1=KM2; SUMK1=SUMK2;
  KM2=S_KM; SUMK2=KM_SUM;
  S_DKM=S_KM; N_DKM=N_KM;
 END;

 &RESTRICT;
  S_DKM=OLD_KM * (1- (LFAIL-1)/LRISK) * (1 - (NFAIL+1)/(RISK+1));

  IF RISK NE NFAIL THEN
  VAR_DKM=S_DKM*S_DKM * (SUM_KOLD + (LFAIL-1)/(LRISK*(LRISK-
LFAIL+1))
                    + (NFAIL+1)/((RISK+1)*(RISK-NFAIL)) );

  IF S_DKM NOT IN (1,0) THEN N_DKM=S_DKM*(1-S_DKM)/VAR_DKM;
 &END_R;

 IF _N_ NE 1 THEN SURV=SURV-1;
 RUN;

PROC PRINT DATA=C;
TITLE &TITLE;
RUN;
%MEND;

%DK(IF CENSOR=1 THEN DO;,END; ,'CALCULATING N_DKM ONLY WHEN
CENSORED')
%DK( , ,'CALCULATING N_DKM EACH TIME')
```

APPENDIX D

SAS PROGRAMS USED TO GENERATE DATA AND CONSTRUCT CONFIDENCE INTERVALS

Greenwood, Psuedo-Binomial, and Rothman Intervals

```
/* ********************************************************************** */
/* NEWSIM.BLD  PROGRAM TO GENERATE DATA AND CONSTRUCT                     */
/*             CONFIDENCE INTERVALS IN WEIBULL DATA                       */
/*             SIMULATION STUDY                                           */
/*                                                                        */
/*  LAST MODIFICATION: 5/21/97                                            */
/*  LAST EXECUTION:    5/21/97                                            */
/* ********************************************************************** */

OPTIONS LS=132 PS=60 PAGENO=1 NODATE NONOTES;
LIBNAME SIM V611 'E:\LIESL\DISS\SAS_PGMS';

DATA FINAL; RUN;

%MACRO WEIBSIM(NS,MS,FC,L,NU,ALPHA,SEED);
DATA A;
KEEP J CENSOR T;
SEED=&SEED;
DO J=1 TO &MS;
 DO I=1 TO &NS;
  U=UNIFORM(SEED);
  IF UNIFORM(SEED)<&FC THEN CENSOR=1; ELSE CENSOR=0;
  T=((-LOG(U))**(1/&NU))/&L;
  OUTPUT;
 END;
END;
RUN;

DATA ZERO;
 DO J=1 TO &MS;
  T=0; CENSOR=0; OUTPUT;
 END;
RUN;
DATA A; SET A ZERO;
PROC SORT DATA=A; BY J T;

DATA C; SET A; BY J;
 KEEP J T GL GU RL RU PL PU;

 RETAIN S_KM N_KM SURV SUM 0;
 IF FIRST.J THEN DO;
  SURV=&NS+1; SUM=0; S_KM=1; N_KM=&NS; PROD=1;
 END;
```

```
CENS=1-CENSOR;
RISK=SURV;
SURV=SURV-1;

PROD=(RISK-CENS)/RISK;
IF (NOT FIRST.J) AND (NOT LAST.J) AND (CENSOR NE 1) THEN DO;
 SUM=SUM+(CENS/(RISK*(RISK-CENS)));
 S_KM=S_KM*PROD;
 VAR_KM=S_KM*S_KM*SUM;
 N_KM=S_KM*(1-S_KM)/VAR_KM;
END;
IF LAST.J THEN S_KM=S_KM*PROD;
XPRIME=N_KM*S_KM;

Z=PROBIT(1-&ALPHA/2);
ZSQ=Z*Z;

/*  CALCULATE GREENWOOD CONFIDENCE LIMITS   */
  GL=MAX(0,S_KM - Z*SQRT(S_KM*(1-S_KM)/N_KM));
  GU=MIN(1,S_KM + Z*SQRT(S_KM*(1-S_KM)/N_KM));

/*  CALCULATE  ROTHMAN CONFIDENCE LIMITS    */
  RL=MAX(0,(N_KM/(N_KM+ZSQ)) * (S_KM + ZSQ/(2*N_KM) -
       Z*SQRT((S_KM*(1-S_KM))/N_KM + ZSQ/(4*N_KM*N_KM))));
  RU=MIN(1,(N_KM/(N_KM+ZSQ)) * (S_KM + ZSQ/(2*N_KM) +
       Z*SQRT((S_KM*(1-S_KM))/N_KM + ZSQ/(4*N_KM*N_KM))));

/*  CALCULATE PSEUDO-BINOMIAL CONFIDENCE LIMITS  */
  IF XPRIME GT 0 THEN
   F1=FINV(&ALPHA/2,2*XPRIME,2*(N_KM-XPRIME+1),0);
  PL=MAX(0,XPRIME*F1/(N_KM-XPRIME+1+XPRIME*F1));
  IF XPRIME LT N_KM THEN
   F2=FINV(1-&ALPHA/2,2*(XPRIME+1),2*(N_KM-XPRIME),0);
  PU=MIN(1,(XPRIME+1)*F2/(N_KM-XPRIME+(XPRIME+1)*F2));
RUN;
```

```
 CONF_LEV=1-&ALPHA;
 SAMPLE=&NS;
 P_CENS=&FC;
 SEED=&SEED;
 LAMBDA=&L;
 NU=&NU;

 GRN_PCT=G_05/&MS; RTH_PCT=R_05/&MS; PSU_PCT=P_05/&MS; S=.05;
OUTPUT;
 GRN_PCT=G_25/&MS; RTH_PCT=R_25/&MS; PSU_PCT=P_25/&MS; S=.25;
OUTPUT;
 GRN_PCT=G_50/&MS; RTH_PCT=R_50/&MS; PSU_PCT=P_50/&MS; S=.50;
OUTPUT;
 GRN_PCT=G_75/&MS; RTH_PCT=R_75/&MS; PSU_PCT=P_75/&MS; S=.75;
OUTPUT;
 GRN_PCT=G_95/&MS; RTH_PCT=R_95/&MS; PSU_PCT=P_95/&MS; S=.95;
OUTPUT;
RUN;
DATA FINAL; SET FINAL PCT; RUN;

%MEND;

%WEIBSIM(NS,MS,FC,L,NU,ALPHA,SEED)

DATA SIM.NEWSIM; SET FINAL;
 KEEP PERCENT METHOD CONF_LEV SAMPLE P_CENS SEED LAMBDA NU S;
 IF S=. THEN DELETE;
 PERCENT=PSU_PCT; METHOD='PSEUDO-BINOMIAL'; OUTPUT;
 PERCENT=GRN_PCT; METHOD='GREENWOOD'; OUTPUT;
 PERCENT=RTH_PCT; METHOD='ROTHMAN'; OUTPUT;
RUN;
```

Pseudo-Binomial and Rothman Intervals Using Alternative Estimators and Effective Sample Sizes

```
/* ********************************************************************** */
/* NEWSIM2.BLD   PROGRAM TO GENERATE DATA AND CONSTRUCT                   */
/*               PSEUDO-BINOMIAL AND ROTHMAN CONFIDENCE                   */
/*               INTERVALS COMPARING S_BH AND S_KM ESTIMATORS             */
/*               AND DIFFERENT EFFECTIVE SAMPLE SIZES                     */
/*                                                                        */
/*          LAST MODIFICATION: 6/5/97                                     */
/*          LAST EXECUTION:    6/6/97                                     */
/* ********************************************************************** */

OPTIONS NODATE LS=132 PS=60 PAGENO=1 NONOTES;
LIBNAME SIM V611 'E:\LIESL\DISS\SAS_PGMS';

DATA FINAL; RUN;

%MACRO PBSIM(NS,MS,FC,L,NU,ALPHA,SEED);

DATA A;
KEEP J CENSOR T;
DO J=1 TO &MS;
 T=0; CENSOR=1; OUTPUT;
 DO I=1 TO &NS;
  U=UNIFORM(&SEED);
  IF UNIFORM(&SEED)<&FC THEN CENSOR=1; ELSE CENSOR=0;
  T=((-LOG(U))**(1/&NU))/&L;
  OUTPUT;
 END;
END;
RUN;
PROC SORT DATA=A; BY J T;

DATA B; SET A; BY J T;
 KEEP J T CENSOR PKML PKMU PBHL PBHU PPKML PPKMU PPBHL PPBHU
          RKML RKMU RBHL RBHU RPKML RPKMU RPBHL RPBHU;
 RETAIN S_KM S_BH SURV N_KM N_BH NPETO1 NPETO2 KM_SUM BH_SUM
0;

 IF FIRST.J THEN DO;
  S_KM=1; S_BH=1;
  N_KM=&NS; N_BH=&NS+1; NPETO1=&NS; NPETO2=&NS+1;
  KM_SUM=0; BH_SUM=0; SURV=&NS;
 END;
```

```
RISK=SURV;
NFAIL=1-CENSOR;

KM_PROD=(RISK-NFAIL)/RISK;
BH_PROD=(RISK+1-NFAIL)/(RISK+1);

IF NFAIL NE RISK THEN KM_SUM=KM_SUM + (NFAIL/(RISK*(RISK-NFAIL)));
BH_SUM=BH_SUM + (NFAIL/((RISK+1)*(RISK+1-NFAIL)));

S_KM=S_KM*KM_PROD;
S_BH=S_BH*BH_PROD;

VAR_KM=S_KM*S_KM*KM_SUM;
VAR_BH=S_BH*S_BH*BH_SUM;

IF VAR_KM NE 0 THEN DO;
 N_KM=S_KM*(1-S_KM)/VAR_KM;
 NPETO1=(RISK-NFAIL)/S_KM;
END;
IF VAR_BH NE 0 THEN DO;
 N_BH=(S_BH*(1-S_BH))/VAR_BH;
 NPETO2=(RISK+1-NFAIL)/S_BH;
END;

/* ************************************************************************ */
/* CALCULATE PSEUDO-BINOMIAL LIMITS USING KM AND N_KM                       */
  XP1=S_KM*N_KM;
  IF XP1 GT 0 THEN
   F1=FINV(&ALPHA/2,2*XP1,2*(N_KM-XP1+1),0);
  IF XP1 LT N_KM THEN
   F2=FINV(1-&ALPHA/2,2*(XP1+1),2*(N_KM-XP1),0);
  PKML=MAX(0,XP1*F1/(N_KM-XP1+1+XP1*F1));
  PKMU=MIN(1,(XP1+1)*F2/(N_KM-XP1+(XP1+1)*F2));

/* ************************************************************************ */
/* CALCULATE PSEUDO-BINOMIAL LIMITS USING BH AND S_BH                       */
  XP2=S_BH*N_BH;
  IF XP2 GT 0 THEN
   F1=FINV(&ALPHA/2,2*XP2,2*(N_BH-XP2+1),0);
  IF XP2 LT N_BH THEN
   F2=FINV(1-&ALPHA/2,2*(XP2+1),2*(N_BH-XP2),0);
  PBHL=MAX(0,XP2*F1/(N_BH-XP2+1+XP2*F1));
  PBHU=MIN(1,(XP2+1)*F2/(N_BH-XP2+(XP2+1)*F2));
```

```
/* ********************************************************************** */
/* CALCULATE ROTHMAN LIMITS USING BH AND NPETO2                           */
  RPBHL=MAX(0,(NPETO2/(NPETO2+ZSQ)) * (S_BH + ZSQ/(2*NPETO2) -
        Z*SQRT((S_BH*(1-S_BH))/NPETO2 + ZSQ/(4*NPETO2*NPETO2))));
  RPBHU=MIN(1,(NPETO2/(NPETO2+ZSQ)) * (S_BH + ZSQ/(2*NPETO2) +
        Z*SQRT((S_BH*(1-S_BH))/NPETO2 + ZSQ/(4*NPETO2*NPETO2))));
/* ********************************************************************** */

 IF NOT FIRST.J THEN SURV=SURV-1;
 RUN;

PROC SORT DATA=B; BY J DESCENDING T;
DATA TEST; SET B; BY J;
 KEEP PKM_05--PKM_95 PBH_05--PBH_95
    PPKM_05--PPKM_95 PPBH_05--PPBH_95
    RKM_05--RKM_95 RBH_05--RBH_95
    RPKM_05--RPKM_95 RPBH_05--RPBH_95;

 ARRAY S{*} S_05 S_25 S_50 S_75 S_95 (.05,.25,.50,.75,.95);

 ARRAY PKM{*} PKM_05 PKM_25 PKM_50 PKM_75 PKM_95;
 ARRAY PBH{*} PBH_05 PBH_25 PBH_50 PBH_75 PBH_95;
 ARRAY PPKM{*} PPKM_05 PPKM_25 PPKM_50 PPKM_75 PPKM_95;
 ARRAY PPBH{*} PPBH_05 PPBH_25 PPBH_50 PPBH_75 PPBH_95;

 ARRAY RKM{*} RKM_05 RKM_25 RKM_50 RKM_75 RKM_95;
 ARRAY RBH{*} RBH_05 RBH_25 RBH_50 RBH_75 RBH_95;
 ARRAY RPKM{*} RPKM_05 RPKM_25 RPKM_50 RPKM_75 RPKM_95;
 ARRAY RPBH{*} RPBH_05 RPBH_25 RPBH_50 RPBH_75 RPBH_95;

 ARRAY TRUE{*} TRUE_05 TRUE_25 TRUE_50 TRUE_75 TRUE_95;
 DO INDEX=1 TO DIM(TRUE);
  TRUE{INDEX}=((-LOG(S{INDEX}))**(1/&NU))/&L;
 END;

 RETAIN NEXT_T;
 NEXT_T=LAG(T);
 IF FIRST.J THEN NEXT_T=T;
```

```
 DO IDX=1 TO 5;
  IF T LE TRUE{IDX} LE NEXT_T THEN DO;
   IF PKML LE S{IDX} LE PKMU THEN PKM{IDX}=1; ELSE PKM{IDX}=0;
   IF PBHL LE S{IDX} LE PBHU THEN PBH{IDX}=1; ELSE PBH{IDX}=0;
   IF PPKML LE S{IDX} LE PPKMU THEN PPKM{IDX}=1; ELSE PPKM{IDX}=0;
   IF PPBHL LE S{IDX} LE PPBHU THEN PPBH{IDX}=1; ELSE PPBH{IDX}=0;

   IF RKML LE S{IDX} LE RKMU THEN RKM{IDX}=1; ELSE RKM{IDX}=0;
   IF RBHL LE S{IDX} LE RBHU THEN RBH{IDX}=1; ELSE RBH{IDX}=0;
   IF RPKML LE S{IDX} LE RPKMU THEN RPKM{IDX}=1; ELSE RPKM{IDX}=0;
   IF RPBHL LE S{IDX} LE RPBHU THEN RPBH{IDX}=1; ELSE RPBH{IDX}=0;
  END;
  IF FIRST.J AND TRUE{IDX} GT T THEN DO;
   IF PKML LE S{IDX} LE PKMU THEN PKM{IDX}=1; ELSE PKM{IDX}=0;
   IF PBHL LE S{IDX} LE PBHU THEN PBH{IDX}=1; ELSE PBH{IDX}=0;
   IF PPKML LE S{IDX} LE PPKMU THEN PPKM{IDX}=1; ELSE PPKM{IDX}=0;
   IF PPBHL LE S{IDX} LE PPBHU THEN PPBH{IDX}=1; ELSE PPBH{IDX}=0;

   IF RKML LE S{IDX} LE RKMU THEN RKM{IDX}=1; ELSE RKM{IDX}=0;
   IF RBHL LE S{IDX} LE RBHU THEN RBH{IDX}=1; ELSE RBH{IDX}=0;
   IF RPKML LE S{IDX} LE RPKMU THEN RPKM{IDX}=1; ELSE RPKM{IDX}=0;
   IF RPBHL LE S{IDX} LE RPBHU THEN RPBH{IDX}=1; ELSE RPBH{IDX}=0;
 END; END;
RUN;

PROC MEANS DATA=TEST NOPRINT;
 VAR PKM_05--PKM_95 PBH_05--PBH_95
    PPKM_05--PPKM_95 PPBH_05--PPBH_95
    RKM_05--RKM_95 RBH_05--RBH_95
    RPKM_05--RPKM_95 RPBH_05--RPBH_95;
 OUTPUT OUT=SUMS SUM= ;
RUN;

DATA PCT; SET SUMS;
 KEEP CONF_LEV SAMPLE P_CENS SEED LAMBDA NU PKM PBH PPKM PPBH
    RKM RBH RPKM RPBH S;

 CONF_LEV=1-&ALPHA;
 SAMPLE=&NS;
 P_CENS=&FC;
 SEED=&SEED;
 LAMBDA=&L;
 NU=&NU;
```

```
 PKM=PKM_05/&MS; PBH=PBH_05/&MS; PPKM=PPKM_05/&MS;
PPBH=PPBH_05/&MS;
 RKM=RKM_05/&MS; RBH=RBH_05/&MS; RPKM=RPKM_05/&MS;
RPBH=RPBH_05/&MS;
 S=.05; OUTPUT;

 PKM=PKM_25/&MS; PBH=PBH_25/&MS; PPKM=PPKM_25/&MS;
PPBH=PPBH_25/&MS;
 RKM=RKM_25/&MS; RBH=RBH_25/&MS; RPKM=RPKM_25/&MS;
RPBH=RPBH_25/&MS;
 S=.25; OUTPUT;

 PKM=PKM_50/&MS; PBH=PBH_50/&MS; PPKM=PPKM_50/&MS;
PPBH=PPBH_50/&MS;
 RKM=RKM_50/&MS; RBH=RBH_50/&MS; RPKM=RPKM_50/&MS;
RPBH=RPBH_50/&MS;
 S=.50; OUTPUT;

 PKM=PKM_75/&MS; PBH=PBH_75/&MS; PPKM=PPKM_75/&MS;
PPBH=PPBH_75/&MS;
 RKM=RKM_75/&MS; RBH=RBH_75/&MS; RPKM=RPKM_75/&MS;
RPBH=RPBH_75/&MS;
 S=.75; OUTPUT;

 PKM=PKM_95/&MS; PBH=PBH_95/&MS; PPKM=PPKM_95/&MS;
PPBH=PPBH_95/&MS;
 RKM=RKM_95/&MS; RBH=RBH_95/&MS; RPKM=RPKM_95/&MS;
RPBH=RPBH_95/&MS;
 S=.95; OUTPUT;
RUN;
DATA FINAL; SET FINAL PCT; RUN;

%MEND;

%PBSIM(NS,1000,FC,L,NU,ALPHA,SEED)
```

Seed Values Used To Generate Data For Simulations

Table D1

Random Seeds Used In Data Generation

NS = 30			NS = 60			NS = 120		
FC	ALPHA	SEED	FC	ALPHA	SEED	FC	ALPHA	SEED
				ν = .05				
0	.01	12345	0	.01	1357963	0	.01	987655
	.05	2340569		.05	357915		.05	87654
	.10	345681		.10	579137		.10	765433
.05	.01	456791	.05	.01	71359	.05	.01	6545323
	.05	56793		.05	9103581		.05	53221
	.10	6789103		.10	246803		.10	432111
.10	.01	789015	.10	.01	468027	.10	.01	321099
	.05	890125		.05	68049		.05	21989
	.10	90127		.10	8023471		.10	1098707
				ν = 1.0				
0	.01	123457	0	.01	135791	0	.01	987653
	.05	234567		.05	357913		.05	876543
	.10	345679		.10	579135		.10	765431
.05	.01	456789	.05	.01	791357	.05	.01	654321
	.05	567891		.05	913579		.05	543219
	.10	678901		.10	246801		.10	432109
.10	.01	789013	.10	.01	468025	.10	.01	321097
	.05	890123		.05	680247		.05	210987
	.10	901235		.10	802469		.10	109875
				ν = 4.0				
0	.01	223469	0	.01	285803	0	.01	11665
	.05	354579		.05	37925		.05	3165855
	.10	47561		.10	4749147		.10	405443
.05	.01	5146801	.05	.01	501369	.05	.01	594333
	.05	667903		.05	613591		.05	67231
	.10	718913		.10	76813		.10	7129121
.10	.01	82905	.10	.01	8258037	.10	.01	891109
	.05	9209135		.05	930259		.05	920999
	.10	151247		.10	192481		.10	99987

APPENDIX E

PERCENTAGE OF INTERVALS CONTAINING TRUE PROBABILITY OF SURVIVAL FOR EACH METHOD

Table E1

Percentage of Intervals Containing True Probability of Survival When $\nu = 0.5$

Confidence level	*S(t)*	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.99	0.05	30	0	0.797	0.999	0.986
			0.05	0.800	0.996	0.979
			0.10	0.796	0.990	0.951
		60	0	0.957	0.995	0.987
			0.05	0.947	0.992	0.973
			0.10	0.953	0.986	0.953
		120	0	0.926	0.992	0.992
			0.05	0.985	0.983	0.962
			0.10	0.985	0.978	0.929
	0.25	30	0	0.950	0.996	0.991
			0.05	0.978	0.997	0.987
			0.10	0.984	0.993	0.986
		60	0	0.976	0.998	0.996
			0.05	0.983	0.989	0.983
			0.10	0.981	0.983	0.970
		120	0	0.991	0.994	0.991
			0.05	0.984	0.986	0.977
			0.10	0.961	0.953	0.929
	0.5	30	0	0.977	0.995	0.995
			0.05	0.972	0.990	0.988
			0.10	0.968	0.992	0.998
		60	0	0.994	0.998	0.994
			0.05	0.981	0.989	0.987
			0.10	0.974	0.987	0.983
		120	0	0.984	0.994	0.994
			0.05	0.976	0.984	0.979
			0.10	0.962	0.970	0.965
	0.75	30	0	0.952	0.991	0.985
			0.05	0.943	0.996	0.992
			0.10	0.932	0.993	0.991

Table E1 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.95	0.50	60	0	0.958	0.984	0.958
			0.05	0.927	0.953	0.933
			0.10	0.904	0.931	0.911
		120	0	0.937	0.961	0.937
			0.05	0.930	0.943	0.933
			0.10	0.866	0.884	0.872
	0.75	30	0	0.949	0.962	0.962
			0.05	0.931	0.966	0.960
			0.10	0.930	0.965	0.962
		60	0	0.942	0.961	0.954
			0.05	0.909	0.965	0.947
			0.10	0.897	0.949	0.943
		120	0	0.942	0.954	0.947
			0.05	0.927	0.958	0.950
			0.10	0.875	0.927	0.918
	0.95	30	0	0.789	0.988	0.953
			0.05	0.751	0.986	0.945
			0.10	0.764	0.994	0.962
		60	0	0.800	0.991	0.971
			0.05	0.777	0.995	0.978
			0.10	0.740	0.996	0.982
		120	0	0.921	0.963	0.947
			0.05	0.923	0.977	0.961
			0.10	0.919	0.964	0.947
0.90	0.05	30	0	0.770	0.983	0.946
			0.05	0.790	0.957	0.916
			0.10	0.779	0.929	0.841
		60	0	0.807	0.929	0.885
			0.05	0.846	0.934	0.867
			0.10	0.881	0.890	0.814
		120	0	0.869	0.957	0.889
			0.05	0.896	0.911	0.858
			0.10	0.861	0.840	0.780
	0.25	30	0	0.843	0.932	0.899
			0.05	0.872	0.922	0.888
			0.10	0.867	0.908	0.861

Table E1 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.90	0.25	60	0	0.897	0.934	0.919
			0.05	0.896	0.919	0.883
			0.10	0.870	0.886	0.839
		120	0	0.911	0.927	0.897
			0.05	0.885	0.893	0.876
			0.10	0.791	0.796	0.753
	0.5	30	0	0.899	0.899	0.899
			0.05	0.892	0.908	0.894
			0.10	0.840	0.894	0.849
		60	0	0.912	0.912	0.912
			0.05	0.878	0.912	0.888
			0.10	0.861	0.902	0.876
		120	0	0.873	0.918	0.918
			0.05	0.865	0.889	0.871
			0.10	0.784	0.823	0.790
	0.75	30	0	0.857	0.947	0.915
			0.05	0.850	0.942	0.920
			0.10	0.803	0.911	0.899
		60	0	0.884	0.932	0.900
			0.05	0.855	0.926	0.905
			0.10	0.831	0.900	0.878
		120	0	0.906	0.925	0.888
			0.05	0.889	0.919	0.897
			0.10	0.832	0.883	0.862
	0.95	30	0	0.778	0.983	0.935
			0.05	0.769	0.988	0.949
			0.10	0.743	0.989	0.954
		60	0	0.791	0.919	0.860
			0.05	0.786	0.929	0.892
			0.10	0.772	0.927	0.890
		120	0	0.854	0.955	0.873
			0.05	0.803	0.953	0.859
			0.10	0.780	0.959	0.864

Table E2 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.99	0.75	60	0	0.985	0.996	0.991
			0.05	0.965	0.993	0.992
			0.10	0.960	0.987	0.987
		120	0	0.989	0.995	0.993
			0.05	0.973	0.993	0.992
			0.10	0.956	0.988	0.988
	0.95	30	0	0.773	0.999	0.988
			0.05	0.780	0.996	0.992
			0.10	0.738	0.998	0.991
		60	0	0.963	0.998	0.990
			0.05	0.949	0.996	0.993
			0.10	0.932	0.996	0.990
		120	0	0.955	0.994	0.992
			0.05	0.925	0.993	0.996
			0.10	0.913	0.993	0.998
0.95	0.05	30	0	0.773	0.984	0.931
			0.05	0.783	0.972	0.938
			0.10	0.791	0.958	0.883
		60	0	0.808	0.986	0.963
			0.05	0.933	0.963	0.930
			0.10	0.949	0.949	0.890
		120	0	0.947	0.979	0.963
			0.05	0.921	0.955	0.922
			0.10	0.911	0.894	0.833
	0.25	30	0	0.949	0.974	0.974
			0.05	0.923	0.958	0.940
			0.10	0.935	0.954	0.910
		60	0	0.939	0.961	0.947
			0.05	0.944	0.954	0.936
			0.10	0.903	0.909	0.880
		120	0	0.946	0.960	0.947
			0.05	0.946	0.951	0.934
			0.10	0.868	0.865	0.828
	0.5	30	0	0.949	0.949	0.949
			0.05	0.942	0.957	0.946
			0.10	0.939	0.963	0.942

Table E2 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.90	0.25	60	0	0.881	0.908	0.884
			0.05	0.878	0.907	0.874
			0.10	0.845	0.867	0.823
		120	0	0.898	0.922	0.874
			0.05	0.897	0.901	0.874
			0.10	0.804	0.814	0.773
	0.5	30	0	0.908	0.908	0.908
			0.05	0.873	0.909	0.885
			0.10	0.849	0.914	0.83
		60	0	0.917	0.917	0.917
			0.05	0.871	0.912	0.876
			0.10	0.861	0.900	0.865
		120	0	0.874	0.910	0.910
			0.05	0.871	0.899	0.878
			0.10	0.810	0.844	0.820
	0.75	30	0	0.846	0.941	0.910
			0.05	0.853	0.938	0.920
			0.10	0.814	0.916	0.903
		60	0	0.862	0.917	0.899
			0.05	0.856	0.915	0.894
			0.10	0.860	0.926	0.901
		120	0	0.903	0.927	0.890
			0.05	0.877	0.910	0.882
			0.10	0.827	0.871	0.853
	0.95	30	0	0.761	0.986	0.946
			0.05	0.744	0.988	0.953
			0.10	0.735	0.988	0.962
		60	0	0.788	0.924	0.879
			0.05	0.778	0.914	0.874
			0.10	0.739	0.909	0.885
		120	0	0.843	0.943	0.868
			0.05	0.826	0.963	0.879
			0.10	0.799	0.954	0.870

Table E3

Percentage of Intervals Containing True Probability of Survival When $\nu = 4.0$

Confidence level	*S(t)*	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.99	0.05	30	0	0.806	0.997	0.983
			0.05	0.803	0.995	0.969
			0.10	0.809	0.985	0.948
		60	0	0.957	0.998	0.989
			0.05	0.953	0.990	0.961
			0.10	0.961	0.979	0.940
		120	0	0.946	0.992	0.994
			0.05	0.979	0.992	0.972
			0.10	0.987	0.966	0.923
	0.25	30	0	0.958	0.998	0.993
			0.05	0.976	0.994	0.986
			0.10	0.980	0.984	0.972
		60	0	0.972	0.992	0.988
			0.05	0.980	0.990	0.983
			0.10	0.977	0.979	0.964
		120	0	0.986	0.997	0.996
			0.05	0.982	0.980	0.970
			0.10	0.963	0.959	0.941
	0.5	30	0	0.986	0.993	0.993
			0.05	0.976	0.998	0.996
			0.10	0.978	0.992	0.991
		60	0	0.985	0.996	0.985
			0.05	0.976	0.986	0.980
			0.10	0.968	0.986	0.982
		120	0	0.986	0.993	0.993
			0.05	0.984	0.990	0.988
			0.10	0.960	0.973	0.966
	0.75	30	0	0.967	0.998	0.992
			0.05	0.955	0.997	0.993
			0.10	0.943	0.995	0.990

Table E3 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.95	0.50	60	0	0.894	0.924	0.902
			0.05	0.939	0.958	0.939
			0.10	0.950	0.959	0.952
		120	0	0.862	0.893	0.870
			0.05	0.937	0.964	0.964
			0.10	0.862	0.893	0.870
	0.75	30	0	0.937	0.964	0.964
			0.05	0.946	0.969	0.967
			0.10	0.913	0.959	0.954
		60	0	0.937	0.961	0.949
			0.05	0.916	0.952	0.939
			0.10	0.893	0.947	0.939
		120	0	0.962	0.979	0.972
			0.05	0.926	0.950	0.947
			0.10	0.885	0.930	0.924
	0.95	30	0	0.781	0.976	0.927
			0.05	0.742	0.992	0.958
			0.10	0.738	0.986	0.952
		60	0	0.807	0.992	0.966
			0.05	0.805	0.995	0.981
			0.10	0.744	0.997	0.991
		120	0	0.921	0.960	0.934
			0.05	0.912	0.962	0.943
			0.10	0.923	0.978	0.961
0.90	0.05	30	0	0.766	0.985	0.934
			0.05	0.784	0.954	0.913
			0.10	0.779	0.928	0.857
		60	0	0.812	0.921	0.856
			0.05	0.846	0.946	0.864
			0.10	0.890	0.911	0.826
		120	0	0.854	0.942	0.867
			0.05	0.882	0.913	0.871
			0.10	0.854	0.837	0.756
	0.25	30	0	0.847	0.941	0.907
			0.05	0.875	0.937	0.887
			0.10	0.858	0.901	0.840

Table E3 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.90	0.25	60	0	0.884	0.929	0.899
			0.05	0.877	0.904	0.876
			0.10	0.838	0.851	0.806
		120	0	0.903	0.921	0.882
			0.05	0.883	0.898	0.879
			0.10	0.783	0.792	0.757
	0.5	30	0	0.907	0.907	0.907
			0.05	0.893	0.926	0.909
			0.10	0.850	0.890	0.862
		60	0	0.909	0.909	0.909
			0.05	0.871	0.902	0.877
			0.10	0.839	0.888	0.847
		120	0	0.879	0.908	0.908
			0.05	0.864	0.884	0.865
			0.10	0.797	0.832	0.806
	0.75	30	0	0.851	0.946	0.914
			0.05	0.854	0.938	0.923
			0.10	0.801	0.926	0.910
		60	0	0.907	0.944	0.914
			0.05	0.855	0.912	0.889
			0.10	0.817	0.911	0.859
		120	0	0.908	0.927	0.884
			0.05	0.877	0.920	0.887
			0.10	0.827	0.885	0.867
	0.95	30	0	0.755	0.988	0.946
			0.05	0.771	0.990	0.949
			0.10	0.750	0.996	0.966
		60	0	0.809	0.935	0.879
			0.05	0.770	0.920	0.879
			0.10	0.743	0.905	0.866
		120	0	0.832	0.951	0.871
			0.05	0.820	0.940	0.863
			0.10	0.789	0.961	0.885

Table E4

Percentage of Pseudo-Binomial Intervals Containing True Probability of Survival When $\nu = 0.5$

Confidence level	*S(t)*	Sample size	Percent censored	Method		
				BH	PKM	PBH
0.99	0.05	30	0	0.986	1.999	0.986
			0.05	0.983	0.997	0.986
			0.10	0.965	0.994	0.973
		60	0	0.987	0.995	0.987
			0.05	0.979	0.993	0.928
			0.10	0.966	0.992	0.974
		120	0	0.992	0.992	0.992
			0.05	0.968	0.987	0.974
			0.10	0.950	0.978	0.959
	0.25	30	0	0.993	0.996	0.993
			0.05	0.991	0.998	0.991
			0.10	0.989	0.995	0.991
		60	0	0.996	0.998	0.996
			0.05	0.986	0.991	0.986
			0.10	0.973	0.984	0.980
		120	0	0.991	0.994	0.991
			0.05	0.980	0.986	0.981
			0.10	0.936	0.961	0.948
	0.5	30	0	0.997	0.995	0.997
			0.05	0.991	0.990	0.991
			0.10	0.992	0.994	0.993
		60	0	0.997	0.998	0.997
			0.05	0.988	0.990	0.989
			0.10	0.983	0.988	0.984
		120	0	0.994	0.994	0.994
			0.05	0.980	0.985	0.983
			0.10	0.965	0.971	0.968
	0.75	30	0	0.991	0.991	0.991
			0.05	0.996	0.996	0.996
			0.10	0.994	0.994	0.994

Table E4 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.99	0.75	60	0	0.997	0.997	0.997
			0.05	0.997	0.997	0.997
			0.10	0.992	0.993	0.993
		120	0	0.991	0.997	0.991
			0.05	0.986	0.986	0.987
			0.10	0.982	0.983	0.983
	0.95	30	0	0.991	0.991	0.991
			0.05	0.997	0.997	0.997
			0.10	1.000	1.000	1.000
		60	0	0.999	0.999	0.999
			0.05	0.999	0.999	0.999
			0.10	0.998	0.998	0.998
		120	0	0.998	0.998	0.998
			0.05	0.998	0.998	0.998
			0.10	0.996	0.996	0.996
0.95	0.05	30	0	0.934	0.985	0.934
			0.05	0.911	0.982	0.922
			0.10	0.891	0.9967	0.902
		60	0	0.966	0.996	0.966
			0.05	0.930	0.973	0.935
			0.10	0.866	0.962	0.892
		120	0	0.962	0.967	0.962
			0.05	0.909	0.952	0.919
			0.10	0.849	0.921	0.860
	0.25	30	0	0.985	0.977	0.985
			0.05	0.952	0.970	0.957
			0.10	0.932	0.955	0.935
		60	0	0.956	0.957	0.956
			0.05	0.935	0.953	0.942
			0.10	0.904	0.930	0.919
		120	0	0.964	0.970	0.964
			0.05	0.926	0.941	0.930
			0.10	0.829	0..869	0.842
	0.5	30	0	0.977	0.959	0.977
			0.05	0.959	0.968	0.960
			0.10	0.932	0.958	0.939

Table E4 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.95	0.50	60	0	0.969	0.981	0.969
			0.05	0.937	0.953	0.941
			0.10	0.914	0.934	0.918
		120	0	0.947	0.961	0.947
			0.05	0.938	0.945	0.940
			0.10	0.873	0.889	0.876
	0.75	30	0	0.976	0.962	0.976
			0.05	0.976	0.966	0.976
			0.10	0.967	0.965	0.967
		60	0	0.961	0.961	0.961
			0.05	0.959	0.965	0.961
			0.10	0.947	0.957	0.948
		120	0	0.954	0.954	0.954
			0.05	0.959	0.958	0.959
			0.10	0.926	0.929	0.926
	0.95	30	0	0.988	0.988	0.988
			0.05	0.986	0.986	0.986
			0.10	0.994	0.994	0.994
		60	0	0.991	0.991	0.991
			0.05	0.995	0.995	0.995
			0.10	0.996	0.996	0.996
		120	0	0.963	0.963	0.963
			0.05	0.977	0.977	0.977
			0.10	0.964	0.964	0.964
0.90	0.05	30	0	0.946	0.983	0.946
			0.05	0.893	0.960	0.899
			0.10	0.799	0.935	0.820
		60	0	0.930	0.929	0.930
			0.05	0.875	0.879	0.939
			0.10	0.792	0.901	0.808
		120	0	0.935	0.957	0.935
			0.05	0.846	0.918	0.857
			0.10	0.757	0.856	0.783
	0.25	30	0	0.924	0.932	0.924
			0.05	0.913	0.925	0.915
			0.10	0.868	0.914	0.876

Table E4 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.90	0.25	60	0	0.935	0.934	0.935
			0.05	0.894	0.922	0.897
			0.10	0.837	0.900	0.847
		120	0	0.913	0.927	0.913
			0.05	0.883	0.895	0.888
			0.10	0.749	0.804	0.766
	0.5	30	0	0.926	0.899	0.926
			0.05	0.918	0.919	0.919
			0.10	0.868	0.895	0.879
		60	0	0.930	0.912	0.930
			0.05	0.911	0.917	0.912
			0.10	0.886	0.907	0.896
		120	0	0.912	0.918	0.942
			0.05	0.879	0.891	0.883
			0.10	0.795	0.832	0.806
	0.75	30	0	0.947	0.947	0.947
			0.05	0.947	0.943	0.947
			0.10	0.913	0.920	0.913
		60	0	0.932	0.932	0.932
			0.05	0.925	0.927	0.926
			0.10	0.890	0.905	0.891
		120	0	0.906	0.925	0.906
			0.05	0.912	0.919	0.913
			0.10	0.877	0.884	0.880
	0.95	30	0	0.983	0.983	0.983
			0.05	0.988	0.988	0.988
			0.10	0.989	0.989	0.989
		60	0	0.919	0.919	0.919
			0.05	0.929	0.929	0.929
			0.10	0.927	0.927	0.927
		120	0	0.955	0.955	0.955
			0.05	0.953	0.953	0.953
			0.10	0.959	0.959	0.959

Table E5 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.99	0.75	60	0	0.996	0.996	0.996
			0.05	0.993	0.993	0.993
			0.10	0.987	0.987	0.987
		120	0	0.994	0.995	0.994
			0.05	0.990	0.993	0.990
			0.10	0.988	0.988	0.988
	0.95	30	0	0.999	0.999	0.999
			0.05	0.996	0.996	0.996
			0.10	0.998	0.998	0.998
		60	0	0.998	0.998	0.998
			0.05	0.996	0.996	0.996
			0.10	0.996	0.996	0.996
		120	0	0.994	0.994	0.994
			0.05	0.993	0.993	0.993
			0.10	0.993	0.993	0.993
0.95	0.05	30	0	0.931	0.984	0.931
			0.05	0.934	0.978	0.940
			0.10	0.869	0.968	0.888
		60	0	0.963	0.986	0.963
			0.05	0.922	0.966	0.930
			0.10	0.881	0.964	0.900
		120	0	0.969	0.979	0.969
			0.05	0.920	0.957	0.926
			0.10	0.828	0.903	0.856
	0.25	30	0	0.977	0.974	0.977
			0.05	0.949	0.960	0.955
			0.10	0.916	0.965	0.927
		60	0	0.961	0.961	0.961
			0.05	0.940	0.957	0.941
			0.10	0.881	0.920	0.891
		120	0	0.962	0.960	0.962
			0.05	0.937	0.953	0.944
			0.10	0.829	0.875	0.847
	0.5	30	0	0.968	0.949	0.968
			0.05	0.956	0.957	0.958
			0.10	0.950	0.966	0.954

Table E5 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.95	0.50	60	0	0.955	0.972	0.955
			0.05	0.938	0.950	0.939
			0.10	0.921	0.944	0.933
		120	0	0.965	0.973	0.965
			0.05	0.936	0.940	0.937
			0.10	0.886	0.905	0.890
	0.75	30	0	0.984	0.977	0.984
			0.05	0.976	0.968	0.976
			0.10	0.969	0.964	0.969
		60	0	0.964	0.964	0.964
			0.05	0.953	0.959	0.953
			0.10	0.937	0.948	0.937
		120	0	0.965	0.965	0.965
			0.05	0.957	0.955	0.958
			0.10	0.931	0.939	0.931
	0.95	30	0	0.980	0.980	0.980
			0.05	0.989	0.989	0.989
			0.10	0.989	0.989	0.989
		60	0	0.993	0.993	0.993
			0.05	0.995	0.995	0.995
			0.10	0.994	0.994	0.994
		120	0	0.963	0.963	0.963
			0.05	0.971	0.971	0.971
			0.10	0.967	0.967	0.967
0.90	0.05	30	0	0.940	0.985	0.940
			0.05	0.873	0.951	0.877
			0.10	0.819	0.933	0.832
		60	0	0.924	0.918	0.924
			0.05	0.868	0.934	0.878
			0.10	0.783	0.897	0.805
		120	0	0.925	0.953	0.925
			0.05	0.850	0.903	0.862
			0.10	0.768	0.875	0.793
	0.25	30	0	0.938	0.946	0.938
			0.05	0.894	0.932	0.898
			0.10	0.853	0.903	0.866

Table E5 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.90	0.25	60	0	0.925	0.908	0.925
			0.05	0.889	0.914	0.895
			0.10	0.825	0.883	0.838
		120	0	0.898	0.922	0.898
			0.05	0.875	0.907	0.880
			0.10	0.771	0.829	0.791
	0.5	30	0	0.934	0.908	0.934
			0.05	0.906	0.911	0.906
			0.10	0.889	0.916	0.894
		60	0	0.932	0.917	0.932
			0.05	0.890	0.915	0.897
			0.10	0.873	0.906	0.880
		120	0	0.920	0.910	0.920
			0.05	0.887	0.901	0.895
			0.10	0.824	0.854	0.832
	0.75	30	0	0.941	0.941	0.941
			0.05	0.940	0.941	0.940
			0.10	0.916	0.919	0.918
		60	0	0.917	0.917	0.917
			0.05	0.911	0.917	0.912
			0.10	0.918	0.930	0.920
		120	0	0.903	0.927	0.903
			0.05	0.903	0.910	0.907
			0.10	0.872	0.872	0.874
	0.95	30	0	0.986	0.986	0.986
			0.05	0.988	0.988	0.988
			0.10	0.988	0.988	0.988
		60	0	0.924	0.924	0.924
			0.05	0.914	0.914	0.914
			0.10	0.909	0.909	0.909
		120	0	0.943	0.943	0.943
			0.05	0.963	0.963	0.96
			0.10	0.954	0.954	0.954

Table E6

Percentage of Pseudo-Binomial Intervals Containing True Probability of Survival When $\nu = 4.0$

Confidence level	*S(t)*	Sample size	Percent censored	Method		
				BH	PKM	PBH
0.99	0.05	30	0	0.983	0.997	0.983
			0.05	0.973	0.996	0.978
			0.10	0.956	0.990	0.966
		60	0	0.989	0.998	0.989
			0.05	0.973	0.991	0.979
			0.10	0.953	0.986	0.962
		120	0	0.994	0.992	0.994
			0.05	0.978	0.992	0.982
			0.10	0.932	0.977	0.945
	0.25	30	0	0.993	0.998	0.993
			0.05	0.987	0.995	0.987
			0.10	0.975	0.989	0.980
		60	0	0.991	0.992	0.991
			0.05	0.985	0.990	0.986
			0.10	0.967	0.983	0.974
		120	0	0.996	0.997	0.996
			0.05	0.973	0.981	0.975
			0.10	0.945	0.967	0.954
	0.5	30	0	0.996	0.993	0.996
			0.05	0.998	0.998	0.998
			0.10	0.991	0.994	0.991
		60	0	0.991	0.996	0.991
			0.05	0.984	0.988	0.985
			0.10	0.983	0.987	0.984
		120	0	0.995	0.993	0.995
			0.05	0.988	0.992	0.989
			0.10	0.968	0.977	0.971
	0.75	30	0	0.998	0.998	0.998
			0.05	0.997	0.997	0.997
			0.10	0.995	0.995	0.995

Table E6 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.99	0.75	60	0	0.997	0.997	0.997
			0.05	0.990	0.990	0.990
			0.10	0.988	0.989	0.988
		120	0	0.985	0.991	0.985
			0.05	0.989	0.989	0.989
			0.10	0.976	0.977	0.976
	0.95	30	0	0.999	0.999	0.999
			0.05	0.997	0.997	0.997
			0.10	0.996	0.996	0.996
		60	0	0.997	0.997	0.997
			0.05	0.998	0.998	0.998
			0.10	0.999	0.999	0.999
		120	0	0.999	0.999	0.999
			0.05	0.995	0.995	0.995
			0.10	0.996	0.996	0.996
0.95	0.05	30	0	0.949	0.982	0.949
			0.05	0.918	0.979	0.925
			0.10	0.904	0.981	0.916
		60	0	0.971	0.987	0.971
			0.05	0.935	0.973	0.942
			0.10	0.857	0.950	0.882
		120	0	0.960	0.972	0.960
			0.05	0.919	0.956	0.930
			0.10	0.838	0.917	0.857
	0.25	30	0	0.981	0.975	0.981
			0.05	0.953	0.958	0.954
			0.10	0.929	0.952	0.936
		60	0	0.964	0.962	0.964
			0.05	0.930	0.945	0.937
			0.10	0.898	0.927	0.914
		120	0	0.963	0.962	0.963
			0.05	0.936	0.959	0.941
			0.10	0.834	0.890	0.848
	0.5	30	0	0.979	0.963	0.979
			0.05	0.957	0.964	0.960
			0.10	0.917	0.960	0.948

Table E6 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.95	0.50	60	0	0.968	0.979	0.968
			0.05	0.952	0.954	0.953
			0.10	0.905	0.927	0.913
		120	0	0.950	0.958	0.950
			0.05	0.956	0.961	0.957
			0.10	0.873	0.900	0.879
	0.75	30	0	0.981	0.964	0.981
			0.05	0.974	0.969	0.974
			0.10	0.962	0.959	0.962
		60	0	0.961	0.961	0.961
			0.05	0.956	0.953	0.956
			0.10	0.943	0.950	0.945
		120	0	0.979	0.979	0.979
			0.05	0.953	0.950	0.953
			0.10	0.928	0.937	0.928
	0.95	30	0	0.976	0.976	0.976
			0.05	0.992	0.992	0.992
			0.10	0.986	0.986	0.986
		60	0	0.992	0.992	0.992
			0.05	0.995	0.995	0.995
			0.10	0.997	0.997	0.997
		120	0	0.960	0.960	0.960
			0.05	0.962	0.962	0.962
			0.10	0.978	0.978	0.978
0.90	0.05	30	0	0.934	0.985	0.934
			0.05	0.877	0.956	0.889
			0.10	0.801	0.938	0.812
		60	0	0.901	0.921	0.901
			0.05	0.872	0.948	0.883
			0.10	0.799	0.923	0.820
		120	0	0.921	0.942	0.921
			0.05	0.869	0.918	0.878
			0.10	0.741	0.856	0.761
	0.25	30	0	0.939	0.941	0.939
			0.05	0.907	0.939	0.912
			0.10	0.850	1.912	0.859

Table E7

Percentage of Rothman Intervals Containing True Probability of Survival When $\nu = 0.5$

Confidence level	*S(t)*	Sample size	Percent censored	Method		
				BH	PKM	PBH
0.99	0.05	30	0	0.939	0.986	0.939
			0.05	0.915	0.981	0.922
			0.10	0.852	0.959	0.875
		60	0	0.963	0.987	0.963
			0.05	0.932	0.976	0.939
			0.10	0.888	0.961	0.904
		120	0	0.982	0.992	0.982
			0.05	0.937	0.964	0.947
			0.10	0.880	0.949	0.893
	0.25	30	0	0.975	0.991	0.975
			0.05	0.968	0.989	0.970
			0.10	0.972	0.987	0.974
		60	0	0.987	0.996	0.987
			0.05	0.962	0.985	0.965
			0.10	0.955	0.972	0.960
		120	0	0.989	0.991	0.989
			0.05	0.973	0.981	0.973
			0.10	0.914	0.938	0.920
	0.5	30	0	0.988	0.995	0.988
			0.05	0.980	0.989	0.980
			0.10	0.981	0.990	0.985
		60	0	0.997	0.994	0.997
			0.05	0.983	0.988	0.983
			0.10	0.976	0.984	0.979
		120	0	0.989	0.994	0.989
			0.05	0.974	0.983	0.976
			0.10	0.959	0.968	0.964
	0.75	30	0	0.985	0.985	0.985
			0.05	0.992	0.992	0.992
			0.10	0.991	0.991	0.991

Table E7 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.99	0.75	60	0	0.996	0.996	0.996
			0.05	0.992	0.992	0.992
			0.10	0.991	0.992	0.992
		120	0	0.997	0.997	0.997
			0.05	0.986	0.985	0.986
			0.10	0.983	0.983	0.983
	0.95	30	0	0.977	0.977	0.977
			0.05	0.981	0.981	0.981
			0.10	0.990	0.990	0.990
		60	0	0.994	0.994	0.994
			0.05	0.993	0.993	0.993
			0.10	0.994	0.994	0.994
		120	0	0.994	0.994	0.994
			0.05	0.994	0.994	0.994
			0.10	0.999	0.999	0.999
0.95	0.05	30	0	0.809	0.934	0.809
			0.05	0.773	0.922	0.778
			0.10	0.757	0.903	0.772
		60	0	0.922	0.966	0.922
			0.05	0.857	0.941	0.864
			0.10	0.748	0.896	0.767
		120	0	0.929	0.949	0.929
			0.05	0.849	0.918	0.857
			0.10	0.760	0.860	0.786
	0.25	30	0	0.944	0.977	0.944
			0.05	0.912	0.953	0.916
			0.10	0.895	0.930	0.899
		60	0	0.940	0.939	0.940
			0.05	0.914	0.933	0.919
			0.10	0.860	0.912	0.871
		120	0	0.956	0.957	0.956
			0.05	0.899	0.925	0.902
			0.10	0.784	0.840	0.804
	0.5	30	0	0.938	0.959	0.938
			0.05	0.933	0.952	0.933
			0.10	0.910	0.931	0.913

Table E7 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.95	0.50	60	0	0.969	0.958	0.969
			0.05	0.932	0.933	0.932
			0.10	0.902	0.916	0.904
		120	0	0.947	0.937	0.947
			0.05	0.927	0.935	0.928
			0.10	0.852	0.876	0.860
	0.75	30	0	0.949	0.962	0.949
			0.05	0.939	0.961	0.939
			0.10	0.948	0.962	0.948
		60	0	0.954	0.954	0.954
			0.05	0.947	0.949	0.947
			0.10	0.943	0.945	0.943
		120	0	0.947	0.947	0.947
			0.05	0.952	0.951	0.952
			0.10	0.917	0.921	0.919
	0.95	30	0	0.953	0.953	0.953
			0.05	0.945	0.945	0.945
			0.10	0.962	0.962	0.962
		60	0	0.971	0.971	0.971
			0.05	0.978	0.978	0.978
			0.10	0.982	0.982	0.982
		120	0	0.947	0.947	0.947
			0.05	0.961	0.961	0.961
			0.10	0.947	0.947	0.947
0.90	0.05	30	0	0.809	0.946	0.809
			0.05	0.767	0.922	0.776
			0.10	0.651	0.855	0.666
		60	0	0.828	0.885	0.828
			0.05	0.791	0.872	0.802
			0.10	0.685	0.826	0.700
		120	0	0.859	0.889	0.859
			0.05	0.766	0.865	0.780
			0.10	0.661	0.792	0.683
	0.25	30	0	0.881	0.899	0.881
			0.05	0.880	0.892	0.886
			0.10	0.789	0.872	0.802

Table E7 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.90	0.25	60	0	0.887	0.919	0.887
			0.05	0.859	0.886	0.863
			0.10	0.788	0.850	0.798
		120	0	0.913	0.897	0.913
			0.05	0.848	0.881	0.857
			0.10	0.714	0.767	0.724
	0.5	30	0	0.926	0.899	0.926
			0.05	0.910	0.896	0.911
			0.10	0.843	0.855	0.845
		60	0	0.883	0.912	0.883
			0.05	0.874	0.891	0.880
			0.10	0.852	0.884	0.858
		120	0	0.893	0.918	0.893
			0.05	0.861	0.877	0.862
			0.10	0.768	0.801	0.777
	0.75	30	0	0.915	0.915	0.915
			0.05	0.820	0.920	0.920
			0.10	0.902	0.899	0.902
		60	0	0.900	0.900	0.900
			0.05	0.905	0.905	0.905
			0.10	0.877	0.879	0.878
		120	0	0.906	0.888	0.906
			0.05	0.893	0.898	0.893
			0.10	0.850	0.865	0.853
	0.95	30	0	0.935	0.935	0.935
			0.05	0.949	0.949	0.949
			0.10	0.954	0.954	0.954
		60	0	0.860	0.860	0.860
			0.05	0.892	0.892	0.892
			0.10	0.890	0.890	0.890
		120	0	0.873	0.873	0.873
			0.05	0.859	0.859	0.859
			0.10	0.864	0.864	0.867

Table E8

Percentage of Rothman Intervals Containing True Probability of Survival When $\nu = 1.0$

Confidence level	*S(t)*	Sample size	Percent censored	Method		
				BH	PKM	PBH
0.99	0.05	30	0	0.946	0.985	0.946
			0.05	0.903	0.981	0.918
			0.10	0.854	0.857	0.873
		60	0	0.966	0.990	0.966
			0.05	0.932	0.981	0.939
			0.10	0.884	0.957	0.901
		120	0	0.975	0.993	0.975
			0.05	0.941	0.974	0.946
			0.10	0.858	0.935	0.881
	0.25	30	0	0.978	0.992	0.978
			0.05	0.980	0.993	0.981
			0.10	0.959	0.981	0.963
		60	0	0.987	0.993	0.987
			0.05	0.969	0.984	0.970
			0.10	0.953	0.977	0.964
		120	0	0.986	0.987	0.986
			0.05	0.970	0.976	0.972
			0.10	0.927	0.947	0.934
	0.5	30	0	0.988	0.998	0.988
			0.05	0.971	0.984	0.974
			0.10	0.986	0.994	0.988
		60	0	0.997	0.993	0.997
			0.05	0.977	0.984	0.978
			0.10	0.972	0.978	0.974
		120	0	0.989	0.992	0.989
			0.05	0.980	0.983	0.981
			0.10	0.965	0.973	0.967
	0.75	30	0	0.990	0.990	0.990
			0.05	0.991	0.991	0.991
			0.10	0.996	0.996	0.996

Table E8 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.99	0.75	60	0	0.991	0.991	0.991
			0.05	0.992	0.992	0.992
			0.10	0.987	0.987	0.987
		120	0	0.993	0.993	0.993
			0.05	0.952	0.992	0.992
			0.10	0.988	0.988	0.988
	0.95	30	0	0.988	0.988	0.988
			0.05	0.992	0.992	0.992
			0.10	0.991	0.991	0.991
		60	0	0.990	0.990	0.990
			0.05	0.993	0.993	0.993
			0.10	0.990	0.990	0.990
		120	0	0.992	0.992	0.992
			0.05	0.996	0.996	0.996
			0.10	0.998	0.998	0.998
0.95	0.05	30	0	0.802	0.931	0.802
			0.05	0.818	0.940	0.822
			0.10	0.736	0.982	0.757
		60	0	0.927	0.963	0.927
			0.05	0.835	0.933	0.845
			0.10	0.762	0.898	0.787
		120	0	0.923	0.963	0.923
			0.05	0.867	0.926	0.875
			0.10	0.728	0.855	0.747
	0.25	30	0	0.947	0.974	0.947
			0.05	0.909	0.949	0.912
			0.10	0.877	0.922	0.887
		60	0	0.937	0.947	0.937
			0.05	0.901	0.938	0.906
			0.10	0.835	0.886	0.848
		120	0	0.946	0.947	0.946
			0.05	0.903	0.941	0.912
			0.10	0.790	0.845	0.802
	0.5	30	0	0.925	0.949	0.925
			0.05	0.923	0.946	0.923
			0.10	0.931	0.947	0.934

Table E8 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.95	0.50	60	0	0.955	0.949	0.955
			0.05	0.925	0.930	0.928
			0.10	0.891	0.922	0.901
		120	0	0.965	0.954	0.965
			0.05	0.919	0.930	0.923
			0.10	0.869	0.886	0.880
	0.75	30	0	0.950	0.977	0.950
			0.05	0.947	0.966	0.947
			0.10	0.939	0.958	0.939
		60	0	0.952	0.952	0.952
			0.05	0.947	0.947	0.947
			0.10	0.930	0.932	0.930
		120	0	0.954	0.954	0.954
			0.05	0.952	0.851	0.952
			0.10	0.927	0.929	0.928
	0.95	30	0	0.933	0.933	0.933
			0.05	0.952	0.952	0.952
			0.10	0.960	0.960	0.960
		60	0	0.978	0.978	0.978
			0.05	0.976	0.976	0.976
			0.10	0.978	0.978	0.978
		120	0	0.940	0.940	0.940
			0.05	0.959	0.959	0.959
			0.10	0.953	0.953	0.953
0.90	0.05	30	0	0.816	0.940	0.816
			0.05	0.764	0.909	0.775
			0.10	0.658	0.875	0.681
		60	0	0.842	0.871	0.842
			0.05	0.775	0.875	0.782
			0.10	0.682	0.817	0.700
		120	0	0.829	0.859	0.829
			0.05	0.777	0.860	0.784
			0.10	0.660	0.801	0.677
	0.25	30	0	0.905	0.916	0.905
			0.05	0.846	0.885	0.854
			0.10	0.791	0.854	0.800

Table E8 (Continued)

Confidence level	$S(t)$	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.90	0.25	60	0	0.896	0.884	0.896
			0.05	0.851	0.880	0.855
			0.10	0.777	0.836	0.788
		120	0	0.898	0.874	0.898
			0.05	0.840	0.878	0.847
			0.10	0.728	0.790	0.743
	0.5	30	0	0.934	0.908	0.934
			0.05	0.897	0.887	0.897
			0.10	0.854	0.879	0.857
		60	0	0.893	0.917	0.893
			0.05	0.871	0.880	0.875
			0.10	0.850	0.873	0.858
		120	0	0.895	0.910	0.895
			0.05	0.855	0.884	0.861
			0.10	0.785	0.825	0.799
	0.75	30	0	0.910	0.910	0.910
			0.05	0.920	0.920	0.920
			0.10	0.904	0.903	0.904
		60	0	0.899	0.899	0.899
			0.05	0.894	0.894	0.894
			0.10	0.901	0.903	0.901
		120	0	0.903	0.890	0.903
			0.05	0.878	0.885	0.880
			0.10	0.838	0.859	0.844
	0.95	30	0	0.946	0.946	0.946
			0.05	0.953	0.953	0.953
			0.10	0.962	0.962	0.962
		60	0	0.879	0.879	0.879
			0.05	0.874	0.874	0.874
			0.10	0.885	0.885	0.885
		120	0	0.868	0.868	0.868
			0.05	0.879	0.879	0.881
			0.10	0.869	0.870	0.870

Table E9

Percentage of Rothman Intervals Containing True Probability of Survival When $\nu = 4.0$

Confidence level	*S(t)*	Sample size	Percent censored	Method		
				BH	PKM	PBH
0.99	0.05	30	0	0.947	0.983	0.947
			0.05	0.907	0.973	0.914
			0.10	0.858	0.955	0.872
		60	0	0.969	0.989	0.969
			0.05	0.923	0.963	0.928
			0.10	0.871	0.948	0.886
		120	0	0.982	0.994	0.982
			0.05	0.948	0.977	0.954
			0.10	0.857	0.932	0.883
	0.25	30	0	0.982	0.993	0.982
			0.05	0.972	0.986	0.973
			0.10	0.947	0.975	0.954
		60	0	0.983	0.988	0.983
			0.05	0.979	0.983	0.980
			0.10	0.945	0.970	0.950
		120	0	0.989	0.996	0.989
			0.05	0.964	0.972	0.966
			0.10	0.926	0.945	0.935
	0.5	30	0	0.987	0.993	0.987
			0.05	0.986	0.997	0.989
			0.10	0.988	0.991	0.988
		60	0	0.991	0.985	0.991
			0.05	0.980	0.982	0.981
			0.10	0.970	0.983	0.976
		120	0	0.988	0.993	0.988
			0.05	0.984	0.989	0.984
			0.10	0.963	0.969	0.966
	0.75	30	0	0.992	0.992	0.992
			0.05	0.993	0.993	0.993
			0.10	0.990	0.990	0.990

Table E9 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.99	0.75	60	0	0.992	0.992	0.992
			0.05	0.989	0.989	0.989
			0.10	0.987	0.988	0.988
		120	0	0.988	0.988	0.988
			0.05	0.988	0.987	0.988
			0.10	0.977	0.978	0.977
	0.95	30	0	0.991	0.991	0.991
			0.05	0.992	0.992	0.992
			0.10	0.986	0.986	0.986
		60	0	0.990	0.990	0.990
			0.05	0.992	0.992	0.992
			0.10	0.995	0.995	0.995
		120	0	0.994	0.994	0.994
			0.05	0.994	0.994	0.994
			0.10	0.998	0.998	0.998
0.95	0.05	30	0	0.812	0.949	0.812
			0.05	0.775	0.925	0.776
			0.10	0.779	0.917	0.793
		60	0	0.927	0.971	0.927
			0.05	0.858	0.943	0.866
			0.10	0.762	0.887	.774
		120	0	0.921	0.950	0.921
			0.05	0.872	0.927	0.882
			0.10	0.735	0.856	0.758
	0.25	30	0	0.951	0.975	0.951
			0.05	0.918	0.947	0.922
			0.10	0.887	0.927	0.894
		60	0	0.941	0.946	0.941
			0.05	0.905	0.930	0.906
			0.10	0.848	0.912	0.857
		120	0	0.954	0.955	0.954
			0.05	0.916	0.935	0.918
			0.10	0.796	0.845	0.815
	0.5	30	0	0.936	0.963	0.936
			0.05	0.924	0.948	0.924
			0.10	0.925	0.943	0.928

Table E9 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.95	0.50	60	0	0.968	0.956	0.968
			0.05	0.936	0.942	0.937
			0.10	0.884	0.910	0.890
		120	0	0.950	0.939	0.950
			0.05	0.941	0.953	0.944
			0.10	0.852	0.876	0.857
	0.75	30	0	0.937	0.964	0.937
			0.05	0.954	0.967	0.955
			0.10	0.932	0.954	0.932
		60	0	0.949	0.949	0.949
			0.05	0.940	0.939	0.940
			0.10	0.935	0.939	0.936
		120	0	0.972	0.972	0.972
			0.05	0.947	0.947	0.947
			0.10	0.924	0.925	0.924
	0.95	30	0	0.927	0.927	0.927
			0.05	0.958	0.958	0.958
			0.10	0.952	0.952	0.952
		60	0	0.966	0.966	0.9663
			0.05	0.981	0.981	0.981
			0.10	0.991	0.991	0.991
		120	0	0.934	0.934	0.934
			0.05	0.943	0.943	0.943
			0.10	0.961	0.961	0.961
0.90	0.05	30	0	0.827	0.934	0.827
			0.05	0.768	0.914	0.780
			0.10	0.676	0.867	0.691
		60	0	0.914	0.856	0.814
			0.05	0.777	0.872	0.789
			0.10	0.688	0.834	0.706
		120	0	0.840	0.867	0.840
			0.05	0.796	0.875	0.806
			0.10	0.649	0.773	0.675
	0.25	30	0	0.888	0.907	0.888
			0.05	0.853	0.889	0.860
			0.10	0.794	0.849	0.803

Table E9 (Continued)

Confidence level	S(t)	Sample size	Percent censored	Method		
				Greenwood	Pseudo-binomial	Rothman
0.90	0.25	60	0	0.890	0.899	0.890
			0.05	0.852	0.878	0.854
			0.10	0.773	0.814	0.786
		120	0	0.900	0.882	0.900
			0.05	0.853	0.882	0.859
			0.10	0.721	0.769	0.733
	0.5	30	0	0.931	0.907	0.931
			0.05	0.917	0.911	0.917
			0.10	0.851	0.869	0.856
		60	0	0.878	0.909	0.878
			0.05	0.866	0.881	0.872
			0.10	0.827	0.857	0.832
		120	0	0.894	0.908	0.894
			0.05	0.859	0.869	0.864
			0.10	0.773	0.810	0.786
	0.75	30	0	0.914	0.914	0.914
			0.05	0.924	0.923	0.924
			0.10	0.912	0.910	0.912
		60	0	0.914	0.914	0.914
			0.05	0.890	0.889	0.890
			0.10	0.859	0.864	0.859
		120	0	0.908	0.884	0.908
			0.05	0.873	0.890	0.875
			0.10	0.849	0.871	0.856
	0.95	30	0	0.946	0.946	0.946
			0.05	0.949	0.949	0.949
			0.10	0.966	0.966	0.966
		60	0	0.879	0.879	0.879
			0.05	0.879	0.879	0.879
			0.10	0.866	0.866	0.866
		120	0	0.871	0.871	0.871
			0.05	0.863	0.863	0.864
			0.10	0.885	0.885	0.885

APPENDIX F

SAS PROGRAMS USED TO PERFORM ANALYSIS OF VARIANCE AND FISHER'S LEAST SIGNIFICANT DIFFERENCE TESTS

Program for Analysis of Variance and Fisher's LSD Test Comparing Pseudo-Binomial, Greenwood, and Rothman Confidence Intervals

```
/* ********************************************************************** */
/* FISHER.SAS  LEAST SIGNIFICANT DIFFERENCE TEST FOR MULTIPLE             */
/*             COMPARISONS OF NEWSIM.SD2 DATASET                          */
/*                                                                        */
/*             LAST MODIFIED: 7/3/97                                      */
/*             LAST EXECUTED: 7/3/97                                      */
/* ********************************************************************** */
OPTIONS NODATE LS=120 PS=65 PAGENO=1;
LIBNAME DATA V611 'E:\LIESL\DISS\SAS_PGMS';

TITLE'Least Significant Difference Test - Absolute Value Of Mean';

DATA A; SET DATA.NEWSIM;
 DIFF=PERCENT-CONF_LEV;
RUN;

PROC SORT DATA=A; BY CONF_LEV;
PROC GLM DATA=A OUTSTAT=SS_OUT;
 CLASS METHOD NU S SAMPLE P_CENS NU;
 MODEL DIFF=METHOD|NU|S|SAMPLE|P_CENS@2;
 BY CONF_LEV;
RUN;
DATA SS_OUT; SET SS_OUT; BY CONF_LEV;
 KEEP DF SS CONF_LEV;
 IF _SOURCE_='ERROR';
RUN;

%MACRO TEST(BY,NUM,OBS,TITLE);
PROC SORT DATA=A; BY CONF_LEV &BY METHOD;
PROC MEANS DATA=A NOPRINT;
 VAR DIFF;
 BY CONF_LEV &BY METHOD;
 OUTPUT OUT=MEANOUT MEAN=DIFF;
RUN;

DATA PB; SET MEANOUT; BY CONF_LEV &BY;
 KEEP CONF_LEV &BY DIFF;
 IF METHOD='PSEUDO-BINOMIAL';
 RENAME DIFF=PDIFF;
DATA MEANOUT; SET MEANOUT; BY CONF_LEV &BY;
 IF METHOD IN ('GREENWOOD','ROTHMAN');
```

```
DATA TEST; MERGE MEANOUT PB; BY CONF_LEV &BY;
 DROP _TYPE_;
RUN;

DATA SIG; MERGE TEST SS_OUT; BY CONF_LEV;
 DROP _FREQ_ DF SS MSE_CORR TEST;
 MSE_CORR=SQRT((2*SS/DF)/_FREQ_);
 TEST=ABS(ABS(PDIFF)-ABS(DIFF));
 SIG=(1-PROBT(TEST/MSE_CORR,&OBS-&NUM))*2;
RUN;

PROC SORT DATA=SIG; BY METHOD CONF_LEV &BY;
PROC PRINT DATA=SIG;
 TITLE2 &TITLE;
RUN;

%MEND;

%TEST( ,3,405,'AT EACH CONF LEVEL');
%TEST(NU,9,405,'AT EACH CONF LEVEL*NU');
%TEST(S,15,405,'AT EACH CONF LEVEL * S(T)');
%TEST(SAMPLE,9,405,'AT EACH CONF LEVEL * SAMPLE SIZE');
%TEST(P_CENS,9,405,'AT EACH CONF LEVEL * % CENSORING');
```

Program for Analysis of Variance and Fisher's LSD Test Comparing Alternative Estimators and Effective Sample Sizes

```
/* ********************************************************************** */
/* FISHER2.SAS   LEAST SIGNIFICANT DIFFERENCE TEST FOR MULTIPLE           */
/*               COMPARISONS OF NEWSIM2.SD2 DATASET                       */
/*                                                                        */
/*               LAST MODIFIED: 7/3/97                                    */
/*               LAST EXECUTED: 7/3/97                                    */
/* ********************************************************************** */
OPTIONS NODATE LS=120 PS=65 PAGENO=1;
LIBNAME DATA V611 'E:\LIESL\DISS\SAS_PGMS';

TITLE'Least Significant Difference Test - Absolute Value Of Mean';

DATA A; SET DATA.NEWSIM2;
 DIFF=PERCENT-CONF_LEV;
RUN;

PROC SORT DATA=A; BY CONF_LEV METHOD NU S SAMPLE P_CENS;

PROC GLM DATA=A OUTSTAT=P_OUT;
TITLE2'Pseudo-Binomial Confidence Limits';
 CLASS METHOD NU S SAMPLE P_CENS;
 MODEL DIFF=METHOD|NU|S|SAMPLE|P_CENS@2;
 BY CONF_LEV;
 WHERE METHOD IN ('PKM','PBH','PPKM','PPBH');
RUN;
DATA P_OUT; SET P_OUT; BY CONF_LEV;
 KEEP DF SS CONF_LEV;
 RENAME DF=DF_P SS=SS_P;
 IF _SOURCE_='ERROR';
RUN;

PROC GLM DATA=A OUTSTAT=R_OUT;
TITLE2'Rothman Confidence Limits';
 CLASS METHOD NU S SAMPLE P_CENS;
 MODEL DIFF=METHOD|NU|S|SAMPLE|P_CENS@2;
 BY CONF_LEV;
 WHERE METHOD IN ('RKM','RBH','RPKM','RPBH');
RUN;
```

```
DATA R_OUT; SET R_OUT; BY CONF_LEV;
 KEEP DF SS CONF_LEV;
 RENAME DF=DF_R SS=SS_R;
 IF _SOURCE_='ERROR';
RUN;

%MACRO TEST(BY,NUM,OBS,TITLE);
PROC SORT DATA=A; BY CONF_LEV &BY METHOD;
PROC MEANS DATA=A NOPRINT;
 VAR DIFF;
 BY CONF_LEV &BY METHOD;
 OUTPUT OUT=MEANOUT MEAN=DIFF;
RUN;

DATA PKM; SET MEANOUT; BY CONF_LEV &BY;
 KEEP CONF_LEV &BY DIFF _FREQ_;
 IF METHOD='PKM';
 RENAME DIFF=PKM _FREQ_=FREQ_P;;
DATA PBH; SET MEANOUT; BY CONF_LEV &BY;
 KEEP CONF_LEV &BY DIFF;
 IF METHOD='PBH';
 RENAME DIFF=PBH;
DATA PPKM; SET MEANOUT; BY CONF_LEV &BY;
 KEEP CONF_LEV &BY DIFF;
 IF METHOD='PPKM';
 RENAME DIFF=PPKM;
DATA PPBH; SET MEANOUT; BY CONF_LEV &BY;
 KEEP CONF_LEV &BY DIFF;
 IF METHOD='PPBH';
 RENAME DIFF=PPBH;
DATA RKM; SET MEANOUT; BY CONF_LEV &BY;
 KEEP CONF_LEV &BY DIFF _FREQ_;
 IF METHOD='RKM';
 RENAME DIFF=RKM _FREQ_=FREQ_R;;
DATA RBH; SET MEANOUT; BY CONF_LEV &BY;
 KEEP CONF_LEV &BY DIFF;
 IF METHOD='RBH';
 RENAME DIFF=RBH;
DATA RPKM; SET MEANOUT; BY CONF_LEV &BY;
 KEEP CONF_LEV &BY DIFF;
 IF METHOD='RPKM';
 RENAME DIFF=RPKM;
```

```
DATA RPBH; SET MEANOUT; BY CONF_LEV &BY;
 KEEP CONF_LEV &BY DIFF;
 IF METHOD='RPBH';
 RENAME DIFF=RPBH;

DATA TEST; MERGE PKM PBH PPKM PPBH RKM RBH RPKM RPBH; BY
CONF_LEV &BY;
RUN;

DATA SIG; MERGE TEST P_OUT R_OUT; BY CONF_LEV;
 DROP FREQ_P FREQ_R DF_P DF_R SS_P SS_R MSE_P MSE_R I J K
    PKM_PBH PKM_PPKM PKM_PPBH PBH_PPKM PBH_PPBH PPK_PPB
    RKM_RBH RKM_RPKM RKM_RPBH RBH_RPKM RBH_RPBH RPK_RPB;

 ARRAY TESTP{*} PKM_PBH PKM_PPKM PKM_PPBH PBH_PPKM PBH_PPBH
PPK_PPB;
 ARRAY TESTR{*} RKM_RBH RKM_RPKM RKM_RPBH RBH_RPKM
RBH_RPBH RPK_RPB;
 ARRAY SIGP{*}  SP_KB SP_KPK SP_KPB SP_BPK SP_BPB SP_PKPB;
 ARRAY SIGR{*}  SR_KB SR_KPK SR_KPB SR_BPK SR_BPB SR_PKPB;
 ARRAY DIFFP{*}  PKM PBH PPKM PPBH;
 ARRAY DIFFR{*}  RKM RBH RPKM RPBH;

 MSE_P=SQRT((2*SS_P/DF_P)/FREQ_P);
 MSE_R=SQRT((2*SS_R/DF_R)/FREQ_R);

  RETAIN I 1;
  I=1;
  DO J=1 TO 3;
   DO K=J+1 TO 4;
    TESTP{I}=ABS(ABS(DIFFP{J})-ABS(DIFFP{K}));
    TESTR{I}=ABS(ABS(DIFFR{J})-ABS(DIFFR{K}));
    SIGP{I}=(1-PROBT(TESTP{I}/MSE_P,&OBS-&NUM))*2;
    SIGR{I}=(1-PROBT(TESTR{I}/MSE_R,&OBS-&NUM))*2;
    I+1;
  END; END;
RUN;

PROC SORT DATA=SIG; BY CONF_LEV &BY;
PROC PRINT DATA=SIG;
 TITLE2 &TITLE;
RUN;

%MEND;
```

APPENDIX G

ANALYSIS OF VARIANCE TABLES AND RESULTS OF FISHER'S LSD TEST COMPARING GREENWOOD, ROTHMAN, AND PSEUDO-BINOMIAL INTERVALS

Table G1

Analysis of Variance Table for $\gamma = .90$

Source	*df*	*SS*	*F*
Method	2	0.42324	480.31**
Nu	2	0.00051	0.58
Method * Nu	4	0.00017	0.10
Probability of Survival	4	0.01551	8.80**
Method * Probability of Survival	8	0.21309	60.45**
Nu * Probability of Survival	8	0.00131	0.37
Sample Size	2	0.02406	27.31**
Method * Sample Size	4	0.09248	52.47**
Nu * Sample Size	4	0.00156	0.89
Probability of Survival* Sample Size	8	0.02713	7.70**
Percent Censoring	2	0.12817	145.45**
Method * Percent Censoring	4	0.00225	1.28
Nu * Percent Censoring	4	0.00131	0.74
Probability of Survival * Percent Censoring	8	0.03047	8.64**
Sample Size * Percent Censoring	4	0.02646	15.01**

* $p < .05$. ** $p < .01$.

Table G2

Analysis of Variance Table for $\gamma = .95$

Source	*df*	*SS*	*F*
Method	2	0.28476	206.98**
Nu	2	0.00000	0.00
Method * Nu	4	0.00007	0.02
Probability of Survival	4	0.04051	14.72**
Method * Probability of Survival	8	0.26060	47.36**
Nu * Probability of Survival	8	0.00043	0.08
Sample Size	2	0.00027	0.20
Method * Sample Size	4	0.08388	30.48**
Nu * Sample Size	4	0.00081	0.29
Probability of Survival* Sample Size	8	0.08195	14.89**
Percent Censoring	2	0.07590	55.16**
Method * Percent Censoring	4	0.00345	1.25
Nu * Percent Censoring	4	0.00012	0.04
Probability of Survival * Percent Censoring	8	0.02599	4.72**
Sample Size * Percent Censoring	4	0.02467	8.96**

* $p < .05$. ** $p < .01$.

Table G3

Analysis of Variance Table for $\gamma = .99$

Source	*df*	*SS*	*F*
Method	2	0.19401	231.93**
Nu	2	0.00011	0.13
Method * Nu	4	0.00011	0.07
Probability of Survival	4	0.06840	40.88**
Method * Probability of Survival	8	0.15420	46.09**
Nu * Probability of Survival	8	0.00009	0.03
Sample Size	2	0.04025	48.12**
Method * Sample Size	4	0.12033	71.92**
Nu * Sample Size	4	0.00020	0.12
Probability of Survival* Sample Size	8	0.07109	21.25**
Percent Censoring	2	0.01059	12.66**
Method * Percent Censoring	4	0.00133	0.79
Nu * Percent Censoring	4	0.00012	0.07
Probability of Survival * Percent Censoring	8	0.00141	0.42**
Sample Size * Percent Censoring	4	0.00295	1.76**

* $p < .05$. ** $p < .01$.

APPENDIX H

ANALYSIS OF VARIANCE TABLES COMPARING PSEUDO-BINOMIAL AND ROTHMAN INTERVALS CONSTRUCTED USING ALTERNATIVE ESTIMATOR AND EFFECTIVE SAMPLE SIZE EQUATIONS

Analysis of Variance Results for Pseudo-binomial Confidence Intervals

Table H1

Analysis of Variance Table for Pseudo-Binomial Intervals with $\gamma = .90$

Source	*df*	*SS*	*F*
Method	3	0.04841	95.29**
Nu	2	0.00047	1.40
Method * Nu	6	0.00012	0.12
Probability of Survival	4	0.29624	437.34**
Method * Probability of Survival	12	0.07441	36.61**
Nu * Probability of Survival	8	0.00152	1.12
Sample Size	2	0.13476	397.89**
Method * Sample Size	6	0.00019	0.19
Nu * Sample Size	4	0.00166	2.45*
Probability of Survival * Sample Size	8	0.06223	45.93**
Percent Censoring	2	0.25380	749.36**
Method * Percent Censoring	6	0.02266	22.30**
Nu * Percent Censoring	4	0.00164	2.43*
Probability of Survival * Percent Censoring	8	0.11812	87.19**
Sample Size * Percent Censoring	4	0.02829	41.76**

* $p < .05$. ** $p < .01$.

Table H2

Analysis of Variance Table for Pseudo-Binomial Intervals with $\gamma = .95$

Source	*df*	*SS*	*F*
Method	3	0.02254	82.18**
Nu	2	0.00010	0.54
Method * Nu	6	0.00008	0.15
Probability of Survival	4	0.13921	380.72**
Method * Probability of Survival	12	0.03927	35.80**
Nu * Probability of Survival	8	0.00043	0.59
Sample Size	2	0.06094	333.32**
Method * Sample Size	6	0.00023	0.42
Nu * Sample Size	4	0.00077	2.11
Probability of Survival * Sample Size	8	0.01325	18.11**
Percent Censoring	2	0.12681	693.58**
Method * Percent Censoring	6	0.00840	15.31**
Nu * Percent Censoring	4	0.00001	0.04
Probability of Survival * Percent Censoring	8	0.06542	89.46**
Sample Size * Percent Censoring	4	0.03432	93.86**

* $p < .05$. ** $p < .01$.

Table H3

Analysis of Variance Table for Pseudo-Binomial Intervals with $\gamma = .99$

Source	*df*	*SS*	*F*
Method	3	0.00304	67.99**
Nu	2	0.00011	3.59*
Method * Nu	6	0.00003	0.34
Probability of Survival	4	0.01344	225.10**
Method * Probability of Survival	12	0.00433	24.18**
Nu * Probability of Survival	8	0.00031	2.61*
Sample Size	2	0.00695	232.81**
Method * Sample Size	6	0.00004	0.41
Nu * Sample Size	4	0.00015	2.51*
Probability of Survival * Sample Size	8	0.00215	18.01**
Percent Censoring	2	0.01315	440.43**
Method * Percent Censoring	6	0.00090	10.06**
Nu * Percent Censoring	4	0.00019	3.23*
Probability of Survival * Percent Censoring	8	0.00675	56.51**
Sample Size * Percent Censoring	4	0.00448	75.05**

* $p < .05$. ** $p < .01$.

Table H4

Analysis of Variance Table for Rothman Intervals with $\gamma = .90$

Source	*df*	*SS*	*F*
Method	3	0.10516	158.23**
Nu	2	0.00030	0.68
Method * Nu	6	0.00016	0.12
Probability of Survival	4	0.53546	604.26**
Method * Probability of Survival	12	0.20437	76.88**
Nu * Probability of Survival	8	0.00170	0.96
Sample Size	2	0.16242	366.58**
Method * Sample Size	6	0.00391	2.94*
Nu * Sample Size	4	0.00305	3.45*
Probability of Survival * Sample Size	8	0.05780	32.61**
Percent Censoring	2	0.34966	789.18**
Method * Percent Censoring	6	0.02097	15.77**
Nu * Percent Censoring	4	0.00190	2.14
Probability of Survival * Percent Censoring	8	0.20767	117.18**
Sample Size * Percent Censoring	4	0.03015	34.02**

* $p < .05$. ** $p < .01$.

Table H5

Analysis of Variance Table for Rothman Intervals with $\gamma = .95$

Source	*df*	*SS*	*F*
Method	3	0.09722	177.36**
Nu	2	0.00018	0.49
Method * Nu	6	0.00007	0.06
Probability of Survival	4	0.47089	644.29**
Method * Probability of Survival	12	0.15466	70.54**
Nu * Probability of Survival	8	0.00100	0.69
Sample Size	2	0.01845	50.48**
Method * Sample Size	6	0.01438	13.11**
Nu * Sample Size	4	0.00063	0.86
Probability of Survival * Sample Size	8	0.05721	39.14**
Percent Censoring	2	0.21228	580.89**
Method * Percent Censoring	6	0.00865	7.89**
Nu * Percent Censoring	4	0.00038	0.51
Probability of Survival * Percent Censoring	8	0.16168	110.61**
Sample Size * Percent Censoring	4	0.05378	73.59**

* $p < .05$. ** $p < .01$.

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GRADUATE SCHOOL
UNIVERSITY OF ALABAMA AT BIRMINGHAM
DISSERTATION APPROVAL FORM

Name of Candidate Liesl M. Fox

Major Subject Biostatistics

Title of Dissertation An Exploration of the Pseudo-Binomial Distribution With Applications to Survival Curve Confidence Intervals

Dissertation Committee:

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Date 8/14/97

PS-14C9