

BERKSON'S METHOD VS. MAXIMUM LIKELIHOOD  
IN THE LOGISTIC REGRESSION MODEL

by

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TABLE OF CONTENTS		Page
I.	Introduction.....	1
II.	Derivations	
	A. Maximum Likelihood Estimator.....	3
	B. Berkson's Estimator.....	5
III.	Review of Literature.....	7
IV.	Methodology.....	9
V.	Results and Discussion.....	11
	A. Maximum Likelihood vs. Berkson's.....	11
	1. Biases of $\hat{\beta}_0$ and $\hat{\beta}_1$ .....	11
	2. Mean Square Errors of $\hat{\beta}_0$ and $\hat{\beta}_1$ .....	11
	3. Variances of $\hat{\beta}_0$ and $\hat{\beta}_1$ .....	12
	4. Mean Square Errors of $\hat{p}$ .....	12
	B. Berkson Estimator in 9 Designs.....	13
	C. Maximum Likelihood Estimator in 9 design.....	13
	D. Comparison of Designs with Equal Sample Sizes...14	
VI.	Conclusions and Recommendations.....	72
VII.	Bibliography.....	73
VIII.	Appendices.....	74
	A. Gauss Program: Generation of Data.....	74
	B. Gauss Program: Berkson's Estimator.....	75
	C. SAS Program: Maximum Likelihood Estimator.....	76

## I. INTRODUCTION

Several experimental situations involve administering a stimulus to an experimental unit and then observing a binary response. Consider the following case : An experimenter can apply a stimulus at various levels. Subjects are assigned at random to different levels of the stimulus and for each subject, a binary response is recorded. From this set of observations, one determines a model to describe the relationship between the stimulus and the proportion responding to the stimulus. The model is called a dose-response model. These types of models can be applied to a lot of practical problems such as those presented by Chatterjee(1977), Finney(1971), and Milliken(1982). They are notably common in the field of pharmacology, in bioassay, where the levels of the stimulus may represent different doses of a drug or pesticide and the binary response is either death or survival.

Suppose a pesticide is tested at  $k$  different levels. At the level of dosage  $X_i$ , let  $m_i$  be the number of insects that die out of a total  $n_i$  exposed to the pesticide ( $i = 1, 2, \dots, k$ ). We want to estimate the relationship between dose,  $X_i$ , and the proportion dying,  $P_i$ .

The stimulus-response relationships have generally been found to be nonlinear. One nonlinear function which has been used to approximate the relationship between the dose,  $X_i$  and the response probability,  $P_i$  is

$$P_i = \frac{e^{\beta_0 + \beta_1 X_i}}{1 + e^{\beta_0 + \beta_1 X_i}} \quad (1.1)$$

where  $\beta_0$  and  $\beta_1$  are unknown parameters.

This relationship is referred to as the logistic response function and has the shape shown in Fig. 1.1. The corresponding analysis is referred to in the literature as logit analysis. The logistic function is bounded between 0 and 1, and is monotonic.

Two estimators of  $\beta_0$  and  $\beta_1$  in the model have been proposed in the literature. One estimator is the maximum likelihood estimator (MLE) and the other is the method proposed by Berkson in 1953. This study aims to further investigate and compare the behaviors of the two estimators with respect to some dose-response designs by computer simulation.

## II. DERIVATIONS

As earlier noted, the logistic response function

$$P_i = \frac{e^{\beta_0 + \beta_1 X_i}}{1 + e^{\beta_0 + \beta_1 X_i}} ,$$

is commonly used to approximate the relationship between the dose  $X_i$  and the response probability  $P_i$ . The main concern is to estimate the parameters  $\beta_0$  and  $\beta_1$ . Two estimators of the logistic regression coefficients have been proposed in the literature and are derived in this section.

A. Maximum Likelihood Estimator

Let  $X_i = i^{\text{th}}$  dose  $i = 1, 2, \dots, k$  levels,

$n_i$  = number of experimental units exposed to the stimulus,

$m_i$  = number of experimental units reacting to the stimulus,

$p_i = \frac{m_i}{n_i}$  = observed 'mortality rate'

$P_i$  = 'true mortality rate' and

$Q_i = 1 - P_i$ .

It is usually reasonable to assume that  $m_i$  is a Binomial( $n_i, P_i$ ) random variable. Thus, the probability density function of  $m_i$  is

$$f(m_i; P_i, n_i) = \binom{n_i}{m_i} P_i^{m_i} Q_i^{n_i - m_i} \quad (2.1)$$

for  $i = 1, \dots, k$ .

The log likelihood function of the model is

$$\ln L = -\sum_{i=1}^k \ln \binom{n_i}{m_i} + \sum_{i=1}^k m_i \ln P_i + \sum_{i=1}^k (n_i - m_i) \ln Q_i \quad (2.2)$$

$$\text{where } P_i = \frac{e^{\beta_0 + \beta_1 X_i}}{1 + e^{\beta_0 + \beta_1 X_i}}, \quad Q_i = 1 - P_i.$$

Differentiating  $\ln L$  with respect to  $\beta_0$  and  $\beta_1$  and setting the corresponding derivatives equal to zero, we obtain the normal equations

$$\sum_{i=1}^k n_i (p_i - \hat{P}_i) = 0 \quad (2.3)$$

and

$$\sum_{i=1}^k n_i X_i (p_i - \hat{P}_i) = 0 \quad (2.4)$$

Solving the normal equations by iteration gives the ML estimators for  $\beta_0$  and  $\beta_1$ .

## B. Berkson's Method

Let  $X_i, m_i, n_i, p_i, q_i, P_i, Q_i$  denote the same quantities as in Section II. A. In the following, we outline the derivation of Berkson's estimators of  $\beta_0$  and  $\beta_1$ .

It is well-known that

$$p_i \sim AN \left[ P_i, \frac{P_i(1-P_i)}{n_i} \right] \quad (2.5)$$

where "-AN" means "asymptotically normally distributed". Then

$$\ln \left[ \frac{P_i}{1-P_i} \right] \sim AN \left[ \beta_0 + \beta_1 X_i, \frac{1}{n_i P_i (1-P_i)} \right] \quad (2.6)$$

( See for example p.118, Theorem A, Serfling (1980) ). Let

$$l_i = \ln \left[ \frac{P_i}{1-P_i} \right] \quad \text{for } i=1, \dots, k.$$

Then one can write:

$$l_i = \beta_0 + \beta_1 X_i + \epsilon_i \quad (2.7)$$

where  $\epsilon_i \sim N(0, (n_i P_i (1-P_i))^{-1})$  for  $i=1, 2, \dots, k$ ,

and  $\epsilon_1, \dots, \epsilon_k$  are independent.

One first obtains the weighted least squares estimators of  $\beta_0$  and  $\beta_1$  by using (2.7) under the assumption that  $P_i$ 's are known. Then replacing  $P_i$  by  $p_i$  in the weighted least squares estimators of  $\beta_0$  and

$\beta_1$ , one obtains Berkson's estimators of  $\beta_0$  and  $\beta_1$  as follows:

$$\hat{\beta}_1 = \frac{\sum_{i=1}^k n_i p_i q_i 1_i X_i^2 - \frac{\sum_{i=1}^k n_i p_i q_i 1_i \sum_{i=1}^k n_i p_i q_i X_i}{\sum_{i=1}^k n_i p_i q_i}}{\sum_{i=1}^k n_i p_i q_i X_i^2 - \frac{(\sum_{i=1}^k n_i p_i q_i X_i)^2}{\sum_{i=1}^k n_i p_i q_i}} \quad (2.8)$$

and

$$\hat{\beta}_0 = \frac{\sum_{i=1}^k n_i p_i q_i 1_i - \hat{\beta}_1 \sum_{i=1}^k n_i p_i q_i X_i}{\sum_{i=1}^k n_i p_i q_i} \quad (2.9)$$



## III. REVIEW OF LITERATURE

Other than the logistic model discussed in Chapter 1, an alternative model in which the response function is represented by the cumulative normal distribution function has also been proposed. The cumulative distribution function of the normal distribution has a shape similar to that of the logistic function (see Fig 1.1). The resulting model is called the probit model and is extensively covered by Finney(1971).

Milliken(1982) discussed dose-response analyses in the light of tolerance distributions. Tolerance of the experimental unit defined as the level of the stimulus at which a response first occurs, he described the tolerance distribution as the collection of tolerances for a population of experimental units and that the assumed form of the tolerance distribution determines the type of analysis. Aside from the most commonly used probit and logit analysis which uses the normal and logistic curves as tolerance distributions, respectively, models resulting from the use of exponential and  $e^{-x}$  to the  $e$  function as tolerance distributions were also presented.

For the logit analysis, several studies have been undertaken since the maximum likelihood estimator (MLE) and Berkson's method appeared in the literature. The MLE was first advocated for general application by R.A. Fisher. For this particular model though, the solution requires an iterative procedure as opposed to a

computationally simple estimator suggested by Berkson(1953). This is in fact one of the factors which motivated this study of comparison.

Further interest was brought about by some notable results presented in a theoretical study by Davis(1985). One of the interesting implications of her results was that Berkson's method should not be used when the number of design points is large and the average number of observations per design point is small. Furthermore, she pointed out that when the number of design points is large, Berkson's estimator is consistent if the average number of observations per design point is large. These results, which will eventually (in Chapter V) be compared with the outcome of the simulation study, further motivated this area of research.

For the logit transformation, the value of  $\ln \left[ \frac{p_i}{1-p_i} \right]$  is not defined for  $p_i = 0$  or 1. Chatterjee and Price(1977) noted that for fitting a dose-response relationship, such points are usually omitted, as there is considerable degree of uncertainty about the exact dosage at these response levels. Berkson's proposal(1955), which was used in this study, was to use the following rule:

$$p_i = \begin{cases} \frac{1}{2n_i} & , \quad m_i = 0 \\ 1 - \frac{1}{2n_i} & , \quad m_i = n_i \end{cases}$$

where  $p_i$ ,  $n_i$ , and  $m_i$  are as defined in Chapter II.

## IV. METHODOLOGY

The special case of a simple logit model with one independent variable was examined. For all experiments, the parameters of the logistic function were  $\beta_0 = -4.12$  and  $\beta_1 = 1.18$ . Nine dose-response designs were investigated: three five-dose designs, three ten-dose designs and three fifteen-dose designs. The experiments were conducted with an equal number of observations per cell,  $n_i = n$  for all  $i$ . In all three main simulations, the cell sizes were  $n = 10, 20, 30$ . Therefore, the total sample sizes for the five-dose designs were  $N = 50, 100, 150$ ;  $N = 100, 200, 300$  for the ten-dose designs and  $N = 150, 300, 450$  for the fifteen-dose designs.

For each of the 9 simulations, 500 sets of data were generated through GAUSS(1987) ( for the algorithm, see Appendix 1) and were analyzed using the two estimation methods. Here, for the aforementioned  $\beta$ 's ( $\beta_0 = -4.12$  and  $\beta_1 = 1.18$ ) and specified  $X_i$ 's (k doses

equally spaced on log doses 1-6),  $P_i = \frac{\beta_0 + \beta_1 X_i}{1 + e^{\beta_0 + \beta_1 X_i}}$  were computed

and  $n_i$ 's were generated from a Binomial( $n_i, P_i$ ) random variable where  $n_i$ 's were the specified number of observations per dose in the design. The Berkson estimates were obtained using a GAUSS algorithm while that of maximum likelihood were computed using PROC NLIN of SAS(1982).

As a basis for comparison, biases, variances and mean square

errors(MSE) of the estimated regression coefficients (  $\hat{\beta}_0, \hat{\beta}_1$  ) were calculated for each design. In addition, as a measure of how the estimated  $p$ 's(  $\hat{p}$  ) compare with the actual  $P$ 's, the quantity

$$\frac{\sum_{i=1}^k (\hat{P}_i - P_i)^2}{k}$$

was computed for each dose-response data set and averaged over 500 data sets under each design. This in essence, measures on the average, how close the predicted logistic regression curve is from the actual. Throughout the report, the quantity

$$\sum_{j=1}^s \left[ \frac{\sum_{i=1}^k (\hat{P}_i - P_i)^2}{k} \right]^2 \quad (4.1)$$

s

where s - number of data sets(in this case 500)

will be referred to as  $MSE(\hat{p})$ .

## V. RESULTS AND DISCUSSION

### A. Maximum Likelihood vs. Berkson's

Simulation estimates of the bias, variance and MSE of the sampling distributions of the estimated  $\hat{\beta}_0$  and  $\hat{\beta}_1$  are presented in Table 5.1.  $MSE(p)$  (see 4.1) are also included in the table.

#### 1. Biases of $\hat{\beta}_0$ and $\hat{\beta}_1$

Simulation results indicate that the Berkson statistic is more biased than the maximum likelihood estimator (MLE). For the small sample size within dose designs ( $k = 5, 10, 15; n=10$ ) the differences were not great. Berkson biases were only .78 to 2.5 times larger than MLE's. These are graphically demonstrated in Fig. 5.1-5.12. Differences were most pronounced in larger sample size designs ( $n=20, 30$  under all  $k$ ), as illustrated in Fig. 5.13-5.32. In these cases, MLE essentially dominated Berkson's (with Berkson bias being as much as 176 times that of MLE) except in the 5 dose,  $n=30$  design. Here, MLE bias was about 1.5 times larger than Berkson's. This was the only case where Berkson's fared better than the MLE in terms of bias. Figures 5.33-5.36 suggest though that Berkson's advantage is small.

#### 2. Mean Square Errors of $\hat{\beta}_0$ and $\hat{\beta}_1$

Mean square error results for the regression coefficients ( $\beta_0, \beta_1$ ) were consistent with the performance of the estimators with respect to biases. In this case though, the discrepancies were rather small.

Berkson MSE's were only 7% to 56% higher than MLE's, except again for the 5 dose, n=30 design where MSE of maximum likelihood estimators for  $\beta_0$  and  $\beta_1$  were 22% and 38% more than their Berkson counterparts.

### 3. Variances of $\hat{\beta}_0$ and $\hat{\beta}_1$

The variances, on the other hand, exhibited a slightly different trend. Though not extremely nor uniformly better, the Berkson estimates showed less variability as seen in Table 5.1. This was exhibited in all of the 5 dose designs (n=10, 20, 30) and in the 15 dose, n=20 design where MLE variances were 1 to 30% larger than the corresponding Berkson's. Plots in Fig. 5.29-5.32 particularly reveal this Berkson's rather slight edge over MLE in some designs. However, maximum likelihood still yielded slightly smaller variances for both  $\hat{\beta}_0$  and  $\hat{\beta}_1$  in the 15 dose, n=30 design (Fig. 5.13-5.16). In all other cases the trend was inconclusive. There was inconsistency in the behavior of the variances within a design. That is, either Berkson's gave lower variance for  $\hat{\beta}_0$  and higher variance for  $\hat{\beta}_1$  or vice-versa.

### 4. Mean Square Error of $\hat{p}$

In most cases, experimenters are not particularly interested in the specific values of  $\beta_0$  and  $\beta_1$  but are concerned with estimating  $P_i$ , which is the actual proportion of experimental units reacting to the stimulus at a certain level of dosage. A quantity which measures the 'combined ability' of  $\hat{\beta}_0$  and  $\hat{\beta}_1$ , in predicting  $p_i$  was computed. This

was the  $MSE(\hat{p})$  discussed in Chap. IV(4.1). It essentially measures how close, on the average, the predicted logistic regression curve is to the actual curve.

The maximum likelihood estimator showed complete superiority in this respect as evidenced in Fig. 5.37-5.54. Berkson's estimates produced  $MSE(\hat{p})$ 's which were 3% to 69% higher than the MLE counterparts. It was also observed that the discrepancy increased as the sample size increased within a specified number of doses ( $k$ ).

#### B. Berkson Estimator in 9 designs

For a fixed number of doses( $k$ ), as the sample size increased the bias decreased, the variances were reduced, and MSE's decreased in all of the designs as anticipated. It is again worth noting that the Berkson estimator was at its best as far as bias was concerned in the 5 dose, 30 observations per dose design.

#### C. Maximum Likelihood Estimator in 9 designs

As the sample size  $n$  increased within a fixed number of doses( $k$ ), the improvement in bias, variance, and MSE, that is, in the performance of the estimator in general, was not as great as that in Berkson. This shows the relative stability of the MLE regardless of the design. In fact, for  $k=5$  and  $k=10$ , biases were even smaller when  $n=20$  than when  $n=30$ .

#### D. Comparison of Designs with Equal Total Sample Sizes $N$

This part of the analysis is focused on the practical aspect of experimentation. Most often, experimenters are faced with a fixed number of experimental units at hand and the immediate problem is

choosing a proper dose-response design to most closely predict  $p$  based on a fitted logistic model. Is one better off using more design points or using more observations per design point?

1.  $N=100 : k=5 \ n=20$  vs.  $k=10 \ n=10$

The 5 dose, 20 observations per dose design resulted in lower  $MSE(\hat{p})$  for both methods as shown in Table 5.1 and Fig. 5.39-5.40, 5.43-5.44. No definite trend was discerned among the  $\hat{\beta}_0$ 's and  $\hat{\beta}_1$ 's not only in this case but in the other two comparisons below as well.

2.  $N=150 : k=5 \ n=30$  vs.  $k=15 \ n=10$

Here, Table 5.1 and Fig. 5.41-5.42, 5.49-5.50 conspicuously reveal the superiority of the 5 dose, 30 observations per dose design over the 15 dose, 10 observations per dose design, in predicting the proportion( $p$ ) of experimental units responding to the stimulus.

3.  $N=300 : k=10 \ n=30$  vs.  $k=15 \ n=20$

The 15-dose, 20 observations per dose design is slightly better in predicting  $\hat{p}$  as evidenced by its low  $MSE(\hat{p})$  in both designs. Fig. 5.47-5.48, 5.51-5.52 attest to this.



Table 5.1 Simulation Estimates of the Bias, Variance and MSE of the Sampling Distributions of the Estimated  $\hat{\beta}_0$ ,  $\hat{\beta}_1$  and  $\hat{p}$  ( $\beta_0 = -4, \beta_1 = 1.18$ )

Design	$\hat{\beta}_0$			$\hat{\beta}_1$			$\hat{p}$		
	k	n	Method	Bias	Variance	MSE	Bias	Variance	MSE
5	10	Berkaon MLE	0.5338	0.5516	0.8355	-0.1509	0.0360	0.0587	0.0043
			0.3071	0.6596	0.7526	-0.0849	0.0425	0.0496	0.0041
			0.2019	0.5128	0.5526	-0.0589	0.0347	0.0381	0.0030
20	Berkaon MLE	0.0138	0.5185	0.5177	-0.0028	0.0356	0.0355	0.0025	
		0.0761	0.4076	0.4126	-0.0211	0.0261	0.0265	0.0023	
		-0.1761	0.4963	0.5270	0.0516	0.0340	0.0366	0.0019	
10	10	Berkaon MLE	0.5725	0.3441	0.6712	-0.1635	0.0230	0.0497	0.0031
			0.2650	0.3776	0.4471	-0.0763	0.0250	0.0308	0.0025
			0.3041	0.2751	0.3671	-0.0804	0.0195	0.0259	0.0017
20	Berkaon MLE	-0.0125	0.2729	0.2725	0.0016	0.0200	0.0199	0.0011	
		0.1925	0.2288	0.2655	-0.0558	0.0152	0.0183	0.0014	
		-0.0114	0.2157	0.2154	0.0036	0.0156	0.0156	0.0009	
15	10	Berkaon MLE	0.5722	0.2742	0.6011	-0.1651	0.0167	0.0440	0.0025
			-0.1637	0.5057	0.5315	0.0438	0.0355	0.0378	0.0020
			0.3065	0.1949	0.2885	-0.0889	0.0138	0.0216	0.0014
20	Berkaon MLE	0.0197	0.2157	0.2156	-0.0074	0.0154	0.0155	0.0009	
		0.2303	0.1366	0.1894	-0.0652	0.0097	0.0139	0.0009	
		0.0032	0.1221	0.1218	-0.0006	0.0089	0.0089	0.0006	

# DISTRIBUTION OF THE $\hat{B}_0$ 'S

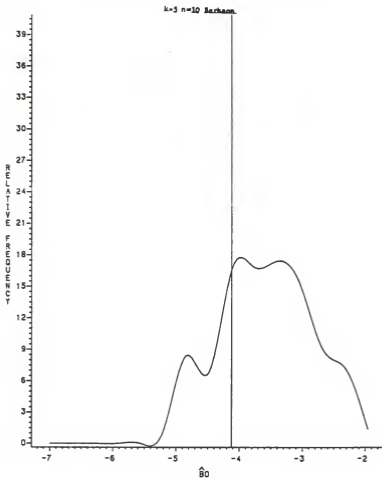


FIGURE 5.1

# DISTRIBUTION OF THE $\hat{\beta}_0$ 'S

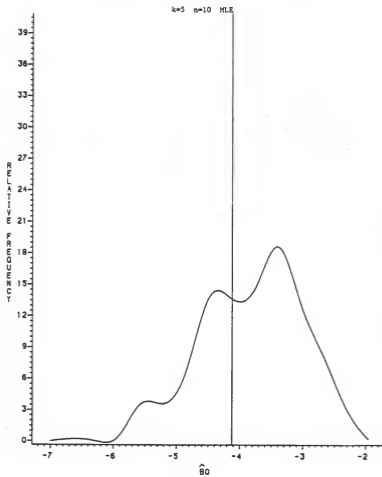


FIGURE 5.2

# DISTRIBUTION OF THE $\hat{B}_1$ 'S

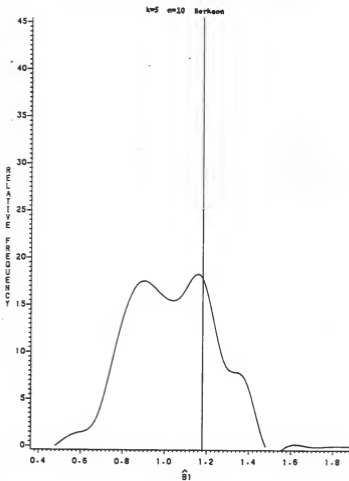


FIGURE 5.3

# DISTRIBUTION OF THE $\hat{B}_1$ 'S

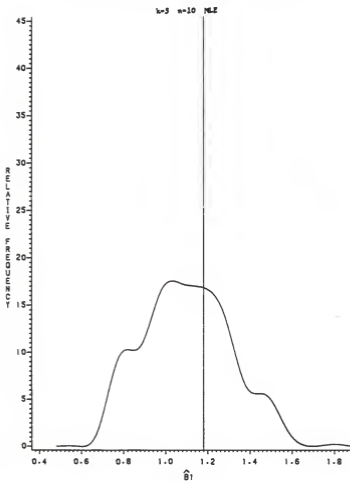


FIGURE 5.4

# DISTRIBUTION OF THE $\hat{\theta}_0$ 'S

t=10 n=10 Berkson

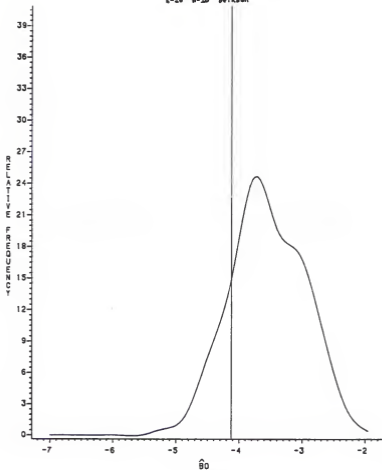


FIGURE 5.5

# DISTRIBUTION OF THE $\hat{\beta}_0$ 'S

k=10 n=10 MLE

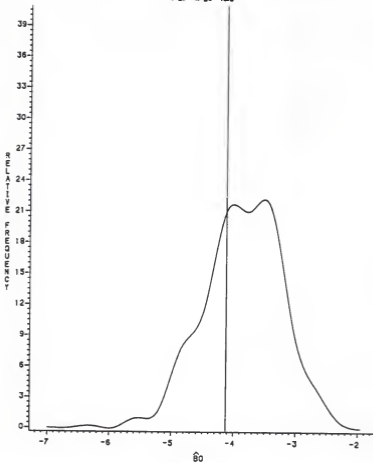


FIGURE 5.6

# DISTRIBUTION OF THE $\hat{B}_1$ 'S

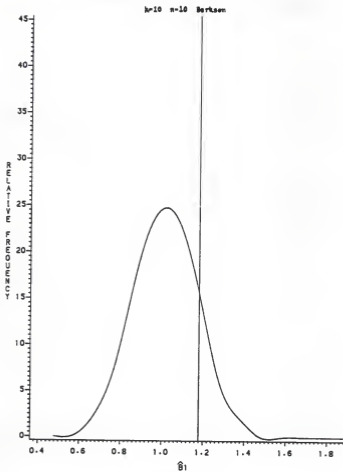


FIGURE 5.7



# DISTRIBUTION OF THE $\hat{B}_1$ 'S

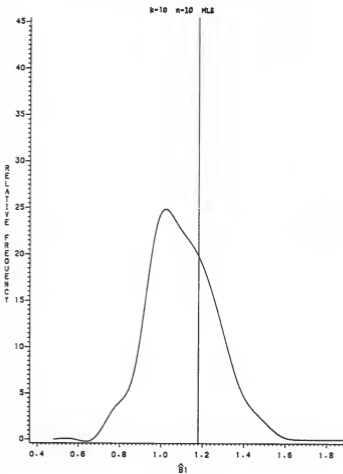


FIGURE 5.8

# DISTRIBUTION OF THE $\hat{\beta}_0$ 'S

k=15 n=10 Berkson

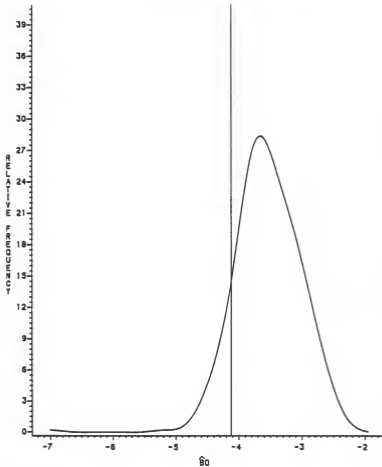


FIGURE 5.9

# DISTRIBUTION OF THE $\hat{\theta}_0$ 'S

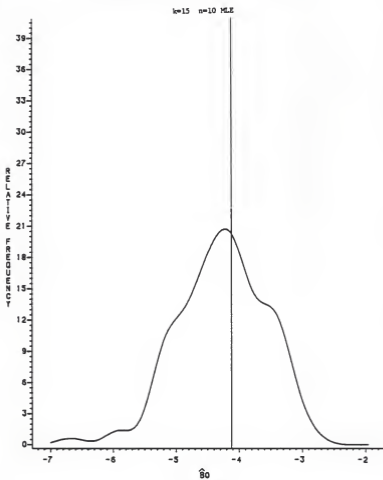


FIGURE 5.10

# DISTRIBUTION OF THE $\hat{B}_1$ 'S

k=15 n=10 Berkson

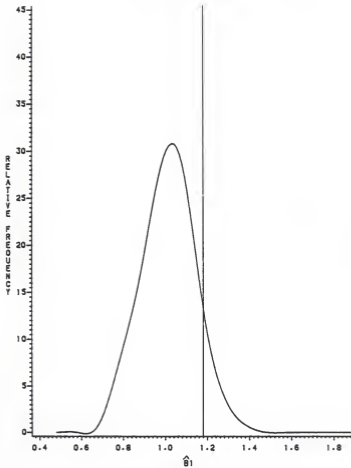


FIGURE 5.11

# DISTRIBUTION OF THE $\hat{B}_1$ 'S

$k=15$   $n=10$  MLE

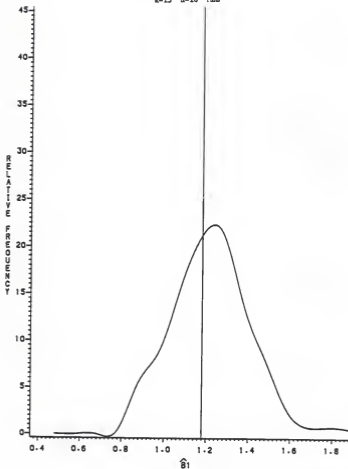


FIGURE 5.12

# DISTRIBUTION OF THE $\hat{B}_0$ 'S

k=15 n=30 Berkson

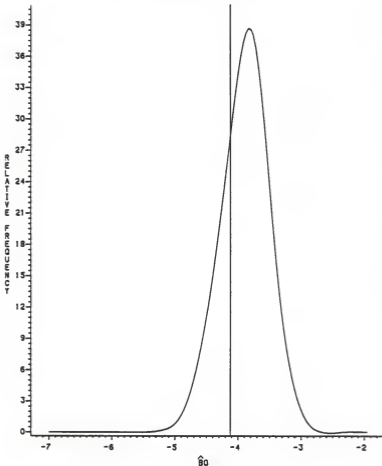


FIGURE 5.13

# DISTRIBUTION OF THE $\hat{\beta}_0$ 'S

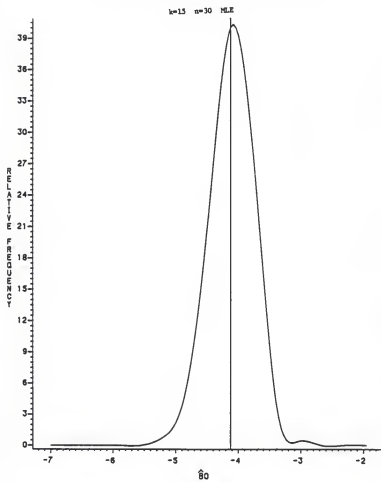


FIGURE 5.14

# DISTRIBUTION OF THE $\hat{B}_1$ 'S

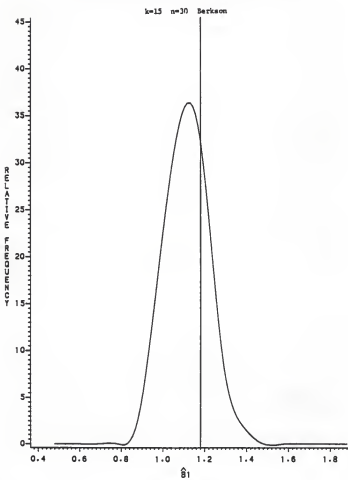


FIGURE 6.15



# DISTRIBUTION OF THE $\hat{B}_1$ 'S

$k=15$   $n=30$  MLE

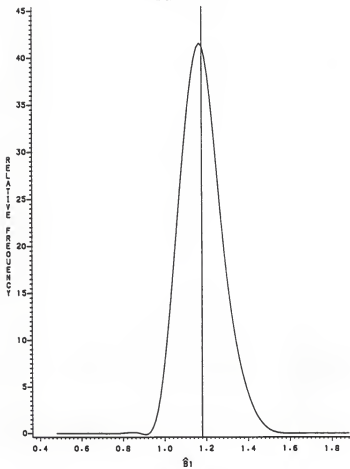


FIGURE 5.16

# DISTRIBUTION OF THE $\hat{\theta}_0$ 'S

k=15 n=20 Berkson

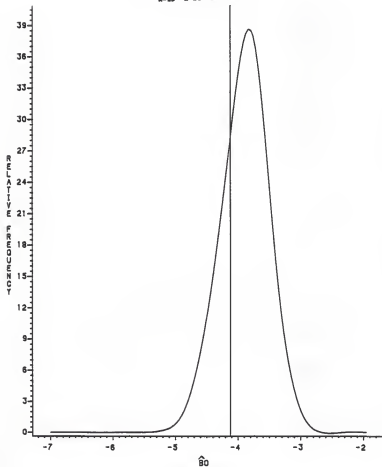


FIGURE 5.17

# DISTRIBUTION OF THE $\hat{\beta}_0$ 'S

k=15 n=20 MLE

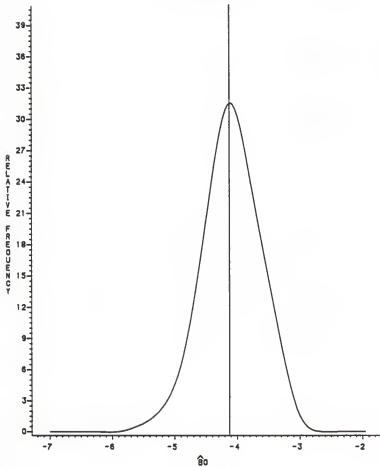


FIGURE 5.18

# DISTRIBUTION OF THE $\hat{B}_1$ 'S

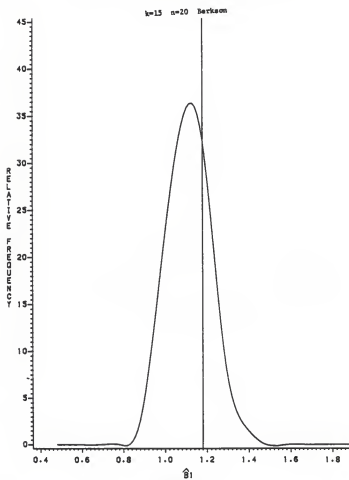


FIGURE 5.19

# DISTRIBUTION OF THE $\hat{B}_1$ 'S

$k=15$   $n=20$  MLE

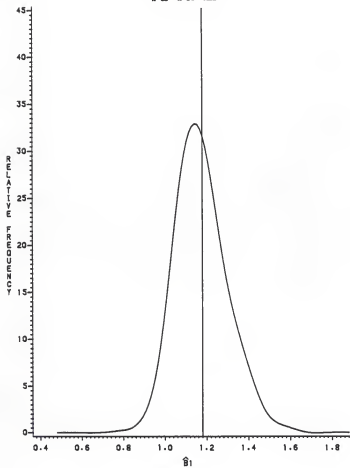


FIGURE 5.20

# DISTRIBUTION OF THE $\hat{B}_0$ 'S

$k=10$   $n=30$  Berkson

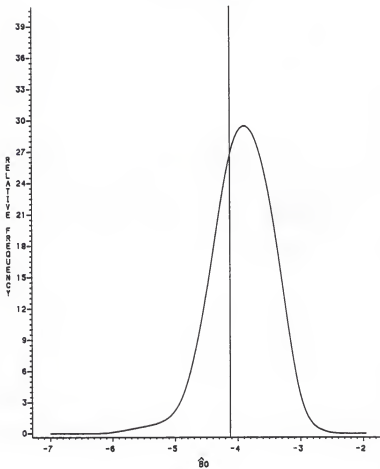


FIGURE 5.21

# DISTRIBUTION OF THE $\hat{\beta}_0$ 'S

$k=10$   $n=30$  NLE

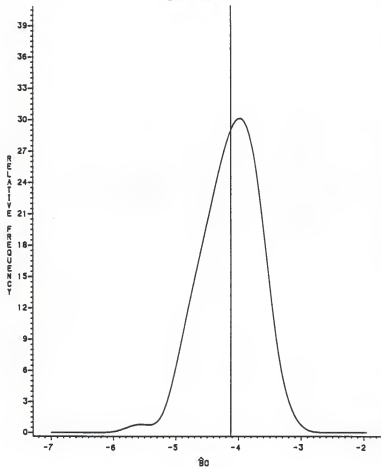


FIGURE 5.22

# DISTRIBUTION OF THE $\hat{B}_1$ 'S

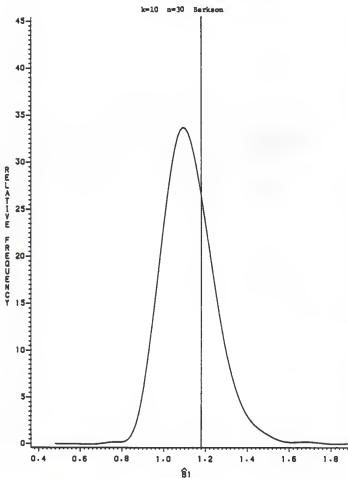


FIGURE 5.23



# DISTRIBUTION OF THE $\hat{B}_1$ 'S

$k=10$   $n=30$  MLE

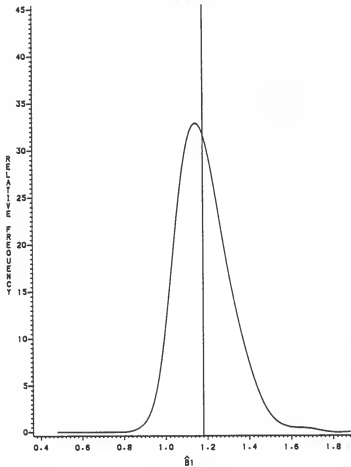


FIGURE 5.24

# DISTRIBUTION OF THE $\hat{\beta}_0$ 'S

k=10 n=20 Berkson

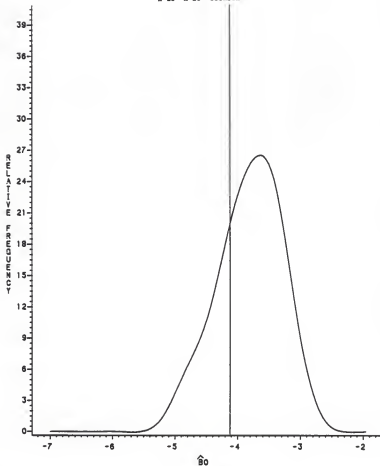


FIGURE 5.25

# DISTRIBUTION OF THE $\hat{\beta}_0$ 'S

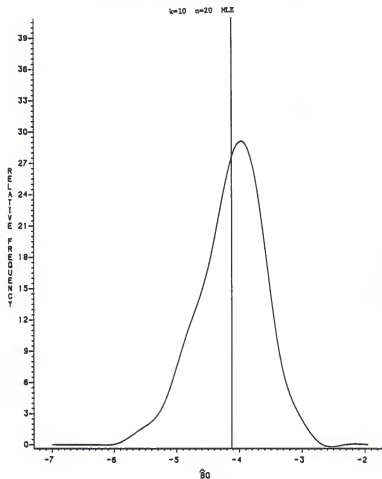


FIGURE 5.26

# DISTRIBUTION OF THE $\hat{B}_1$ 'S

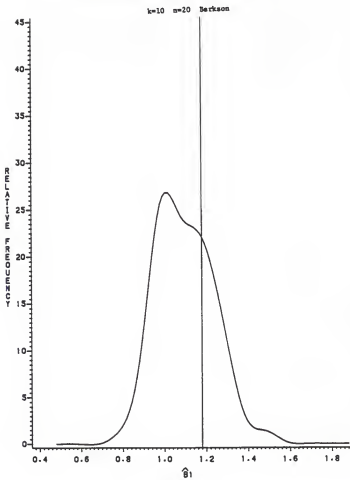


FIGURE 5.27

# DISTRIBUTION OF THE $\hat{B}_1$ 'S

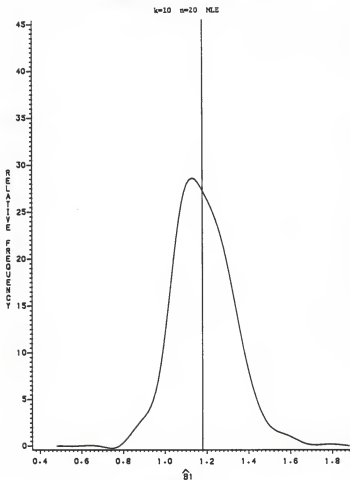


FIGURE 5.28

# DISTRIBUTION OF THE $\hat{B}_0$ 'S

$k=5$   $n=20$  Berkson

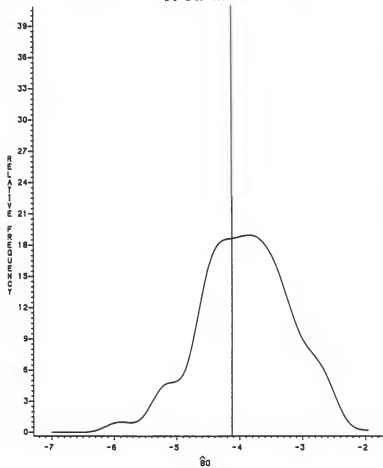


FIGURE 5.29

# DISTRIBUTION OF THE $\hat{B}_0$ 'S

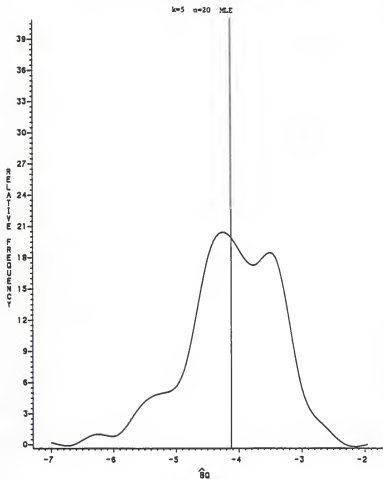


FIGURE 5.30

# DISTRIBUTION OF THE $\hat{B}_1$ 'S

$k=5$   $n=20$  Berkson

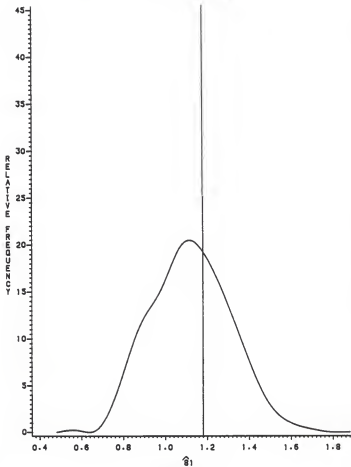


FIGURE 5.31



# DISTRIBUTION OF THE $\hat{B}_1$ 'S

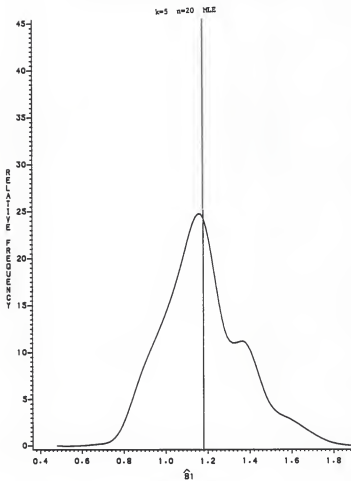


FIGURE 5.3.2

# DISTRIBUTION OF THE $\hat{B}_0$ 'S

$k=5$   $n=30$  Jackson

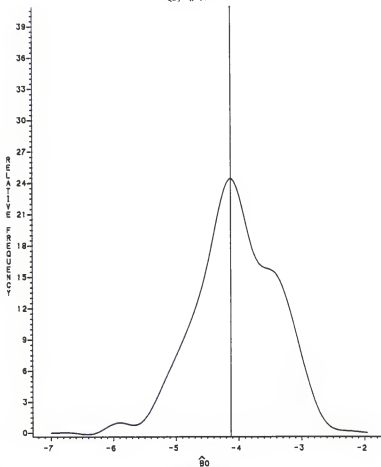


FIGURE 5.33

# DISTRIBUTION OF THE $\hat{\beta}_0$ 'S

$k=5$   $n=30$  MLE

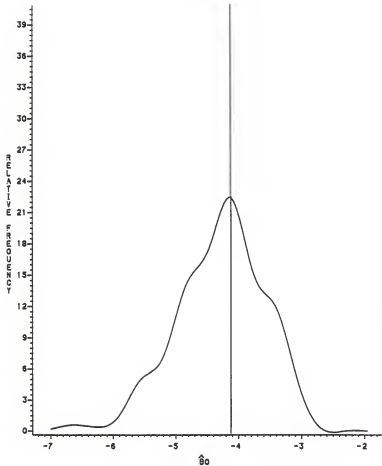


FIGURE 5.34

# DISTRIBUTION OF THE $\hat{B}_1$ 'S

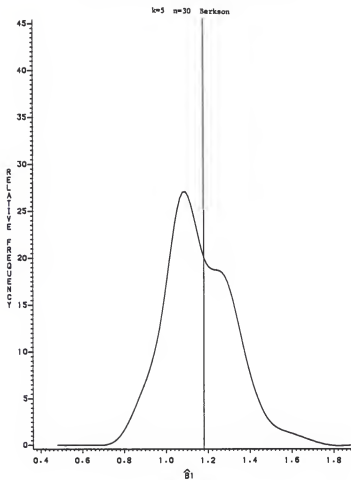


FIGURE 5.35

# DISTRIBUTION OF THE $\hat{B}_1$ 'S

$k=5$   $n=30$  NLE

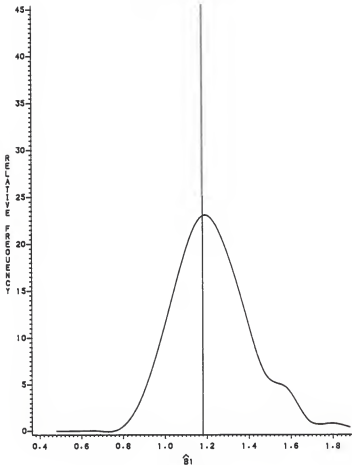


FIGURE 5.36

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

k=5 n=10 Berkson

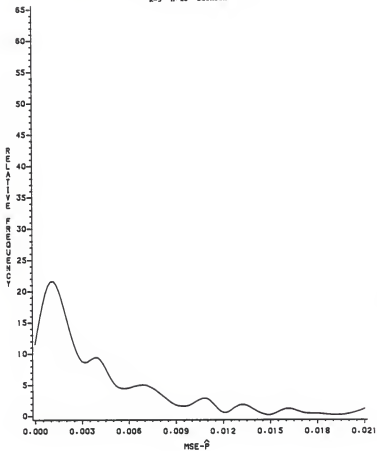


FIGURE 5.37

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

$k=5$   $n=10$  MLE

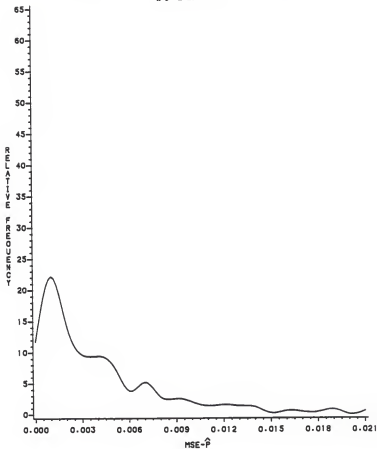


FIGURE 5.38

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

$k=5$   $n=20$  Berkson

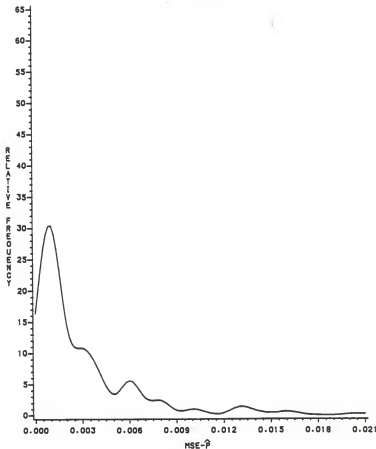


FIGURE 5.39



# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

k=5 n=20 MLE

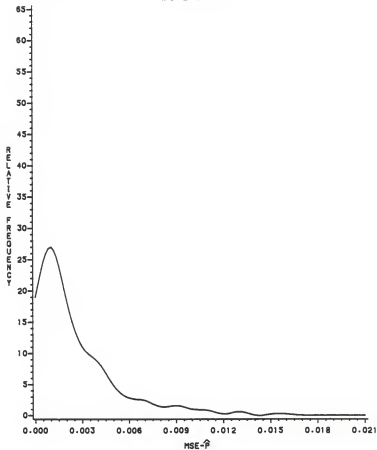


FIGURE 5.40

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

k=5 n=30 Berkson

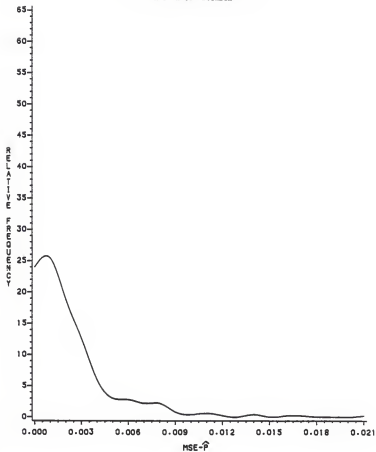


FIGURE 5.41

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

k=5 n=30 MLE

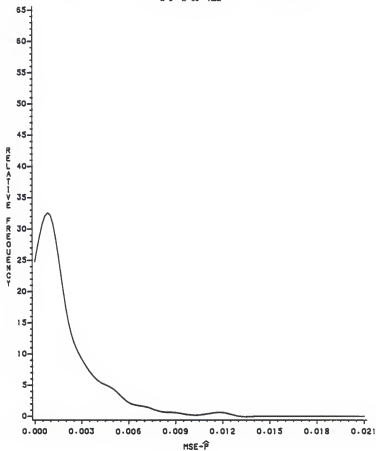


FIGURE 5.42

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

k=10 n=10 Berkeon

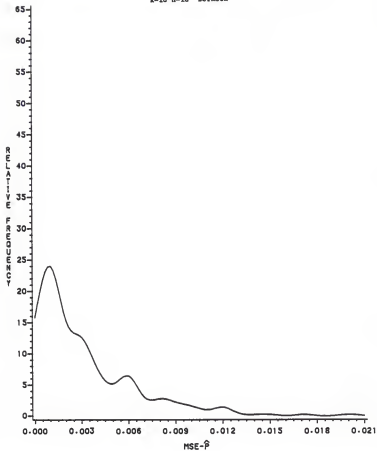


FIGURE 5.43

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

k=10 n=10 MLE

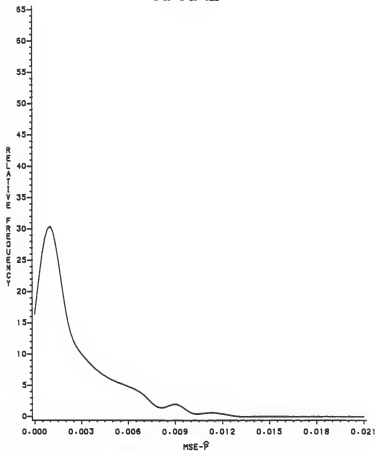


FIGURE 5.44

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

k=10 n=20 Berkson

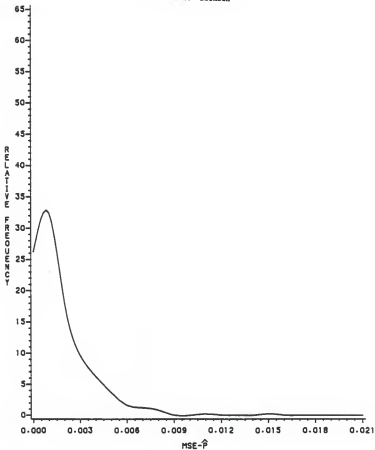


FIGURE 5.45

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

k=10 n=20 MLE

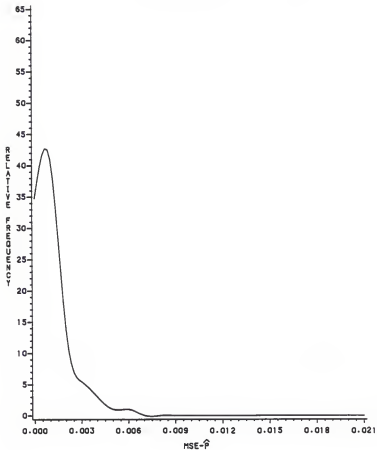


FIGURE 5.46

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

$k=10$   $n=30$  Berkson

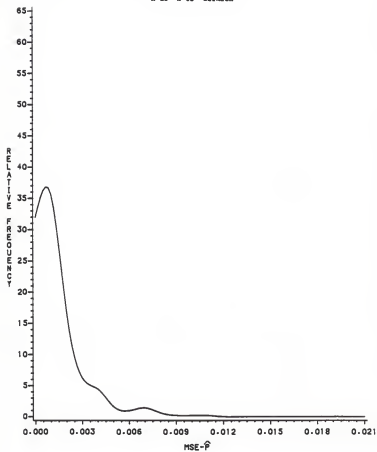


FIGURE 5.47



# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

k=10 n=30 MLE

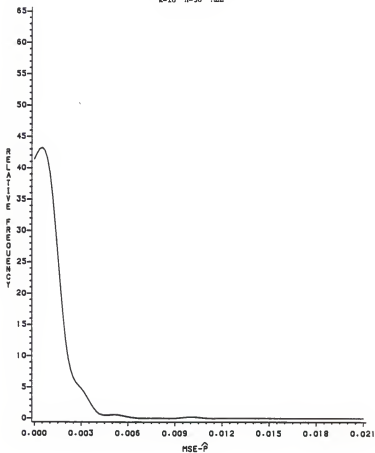


FIGURE 5.48

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

$k=15$   $n=10$  Berkson

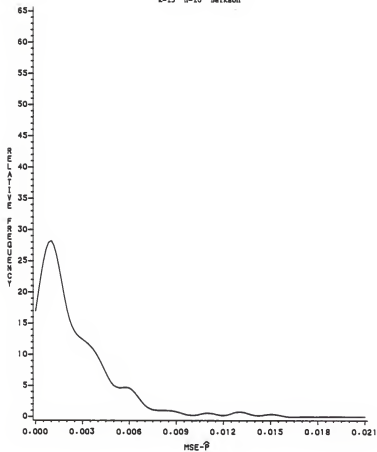


FIGURE 5.49

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

k=15 n=10 MLE

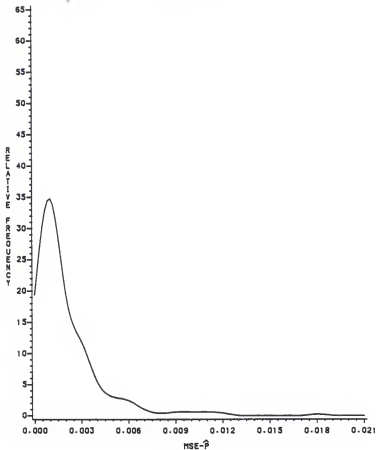


FIGURE 5.50

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

k=15 n=20 Berkson

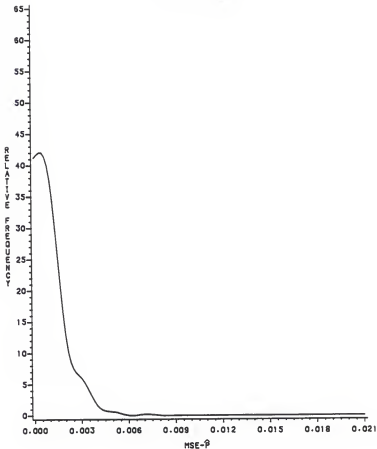


FIGURE 5.51

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

k=15 n=20 MLE

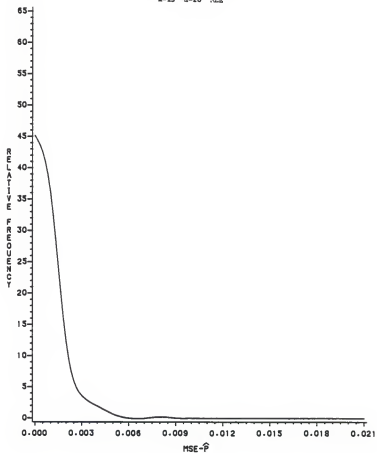


FIGURE 5.52

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

k=15 n=30 Berkson

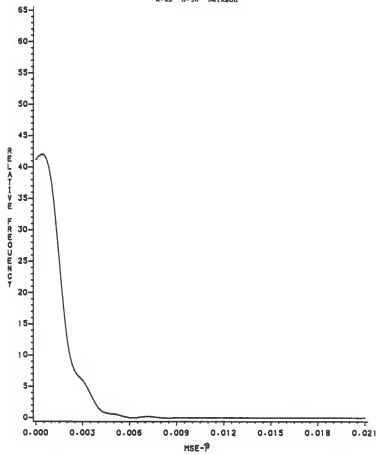


FIGURE 5.53

# DISTRIBUTION OF THE MSE $\hat{P}$ 'S

$k=15$   $n=30$  MLE

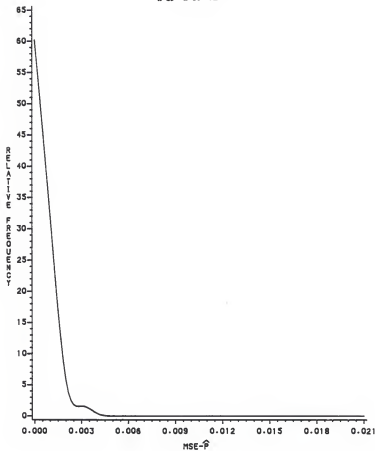


FIGURE 5.54

## VI. CONCLUSIONS AND RECOMMENDATIONS

These simulation results concur with the conclusion by Davis(1985) that Berkson's method is not advisable when the number of design points( $k$ ) is large but the average number of observations( $n$ ) per design point is small.

The maximum likelihood demonstrated superiority in every criterion except for the variances under all designs but one(5 dose, 30 observations per dose case). Most importantly, it fared consistently better in the  $MSE(\hat{p})$  criterion which is probably of utmost consideration in practical applications.

Although the maximum likelihood is the method recommended for use based on the results of this study, the simulation results did show some indication that Berkson's method may be better for experiments when the number of design points is small but the number of observations per design point is large. Further studies may be in order regarding that situation.



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## VIII. APPENDIX

A. Sample Gauss Program : Generation Of Data Sets

```

seed=45989;
i=451;
do while i <=500;
  dose=1;
  do while dose <= 6;
    pow=-4.12 + (1.18*dose);
    pt=1/(1+exp(-pow));
    rannum=rndus(20,1,seed);
    dead=rannum[.,1]<.pt;
    dnum=sumc(dead);if dnum=0;dnum=20*(1/40);
    endif;
    if dnum=20;dnum=20*(1-(1/40));
    endif;
    if dose = 1 ; deaths=dnum;x=dose;totl=20;
      ptrue=pt ; sampleno=i;
    else; deaths =
      deaths+dnum;x=x+dose;totl=totl+20;
      ptrue=ptrue+pt;sampleno=sampleno+i;
    endif;

    dose=dose+.555;
  endo ;

/* to form the dose response matrix x */

dataset = x-totl-deaths-ptrue-sampleno;
format /ml/rd 11,8;
output file=dat1020j on; dataset;
i=i+1;seed=seed+100;
endo;

```

B. Sample Gauss Program : Berkson Estimates

```

/* Berkson : this program computes Berkson estimates */

p=deaths./totl;
pprime=ln(p./(1-p));
weight=totl.*p.*(1-p);
wpprimex=weight.*pprime.*x;
wprim=weight.*pprime;
wx=weight.*x;
wxqr=weight.*(x.*x);
bl=((sumc(wpprimex))-(((sumc(wprim))*sumc(wx))/sumc(weight))))/
    ((sumc(wxqr))-(((sumc(wx))^2)/sumc(weight)));
bo=(meanc(pprime))-(bl*meanc(x));

/* to compute the mse */

phat=(exp(bo+(bl*x)))/(1+(exp(bo+(bl*x))));
ssep=meanc((phat-ptrue)^2);
ssebo=(bo+4.12)^2;
ssebl=(bl-1.18)^2;

/* to output into a data set */

    if i=1 ; matbl=bl;matbo=bo;matp=ssep;matsbl=ssebl;matsbo=ssebo;
        else;
matbl=matbl|bl;matbo=matbo|bo;matp=matp|ssep;matsbl=matsbl|ssebl;
        matsbo=matsbo|ssebo;
        endif;
seed=seed+100;
i=i+1;

endo;

/* to print the matrix */

est=matbl-matbo-matp-matsbl-matsbo;
format /ml/rd 11,8;
exvalue=meanc(est);dev=stdc(est);summary=exvalue-dev;
lprint "ESTIMATES AND MEAN SQUARE ERRORS(CHIT1020)" est;
output file=b:chit1020 on;
lprint "SUMMARY STATS(chit1020)" summary';

```

C. SAS Program : Maximum Likelihood Estimates

```

*-----*
*           THIS PROGRAM COMPUTES THE           *
*           MAXIMUM LIKELIHOOD ESTIMATES       *
*           FOR THE LOGIT MODEL                 *
*-----*
%MACRO ANALYSIS;
  %DO I=1 %TO 500;
    DATA ANA&I;SET RJR.SIM1520;
      IF SAMPLENO=&I;
    DATA ANA2&I;SET ANA&I;
      COUNT=DEATHS;Y=1;OUTPUT;
      COUNT=TOTAL-DEATHS;Y=0;OUTPUT;
    PROC NLIN NOHALVE SIGSQ=1 /*ALGORITHM FROM SAS82 STATISTICS
P36*/;
      PARMS BO=-4.6 B1=1.3/*INITIAL ESTIMATES OF BO AND B1 FROM
PROC REG*/;
      E=EXP(BO + B1*DOSE);
      P=E/(1+E);
      MODEL Y=P;
      W=1/(P*(1-P));
      WEIGHT =W*COUNT;
      DER-E/((1+E)**2);
      DER.BO=DER;
      DER.B1=DER*DOSE;
      OUTPUT OUT=RESULTS P=PHAT PARMS=BO B1;
    DATA PREFINAL;
      KEEP BO B1 SSE;
      SET RESULTS;
      SSE=((PHAT-PTTRUE)**2);
    PROC MEANS MEAN NOPRINT;
      OUTPUT OUT=FINAL MEAN=BO B1 MSE;
    PROC APPEND BASE=FINALDAT DATA=FINAL;
  %END;
%MEND;
%ANALYSIS;
DATA RJR1.ML1520;SET FINALDAT;

```

BERKSON'S METHOD VS. MAXIMUM LIKELIHOOD  
IN THE LOGISTIC REGRESSION MODEL

by

RHONDA JENINE UMALI RAGUAL  
B.S., UNIVERSITY OF THE PHILIPPINES AT LOS BANOS, 1983

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AN ABSTRACT OF A MASTERS REPORT

submitted in partial fulfillment of the  
requirements for the degree

MASTER OF SCIENCE

Department of Statistics

KANSAS STATE UNIVERSITY  
Manhattan, Kansas  
1988

#### ABSTRACT

Two estimators (Maximum Likelihood and Berkson's (1953)) of the logistic regression model have been proposed in the literature. The two estimators were compared by simulation under 9 different dose-response designs. Maximum likelihood emerged as the better estimator in all cases considered except one. Berkson's method showed some promise in a few design point-many observations per design point set-up.