SOME PROPERTIES OF SPEARMAN-TYPE ESTIMATORS
OF THE VARIANCE AND PERCENTILES IN BIOASSAY

BY

JOSEPH JOHN CHMIEL

TECHNICAL REPORT NO. 10
JULY 31, 1975

PREPARED UNDER THE AUSPICES
OF
PUBLIC HEALTH SERVICE GRANT 1 R01 GM21215-01

DIVISION OF BIOSTATISTICS
STANFORD UNIVERSITY
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CHAPTER I
INTRODUCTION

1.1 NATURE OF QUANTAL BIOASSAY

Although the procedure of performing statistical inference by means of a collection of experiments whose outcomes each consist of an all-or-none or quantal response has application in many fields of study, much of the statistical work to date has been motivated by biological problems and the terminology has reflected this. In the quantal dose-response experiment, the stimulus is applied to the subject at a specified dose and the occurrence or non-occurrence of a response is observed. For the particular subject, the occurrence of the response will depend upon whether or not the intensity of the dose exceeds that subject's threshold or tolerance. If so, the response will be observed; if not, a nonoccurrence of the response will be noted. Thus, the experiment provides information about the subject's tolerance of the stimulus. Of much greater interest, however, is the distribution of tolerances among the population, or, simply, the tolerance distribution. By performing a number of such quantal dose-response experiments, each on a different subject and each at one of a set of various dose levels, one attempts to ascertain properties of the underlying tolerance distribution in order to make inferences about the effect of the stimulus on the population.
1.2 HISTORY OF THE PROBLEM

Over the years a great deal of work has been done investigating estimators of the median of the underlying tolerance distribution, commonly called the median effective dose or ED50, i.e., the dose required to elicit a response in exactly 50% of the population. A summary of much of this work can be found in a book by Finney [10]. The most popular approach, probit analysis, a subject to which an entire book by Finney [11] has been devoted, involves assuming the tolerance distribution is normal and obtaining a maximum likelihood estimate. However, it is possible to estimate the ED50 without assuming any underlying distribution.

An estimator with many desirable statistical properties was first proposed by Spearman [17] in 1908, but it has been only recently that most of these properties have been demonstrated in papers by Brown [2], Miller [15], and Church and Cobb [4]. The estimator was also described by Kärber [14] in 1931 and hence is also often called the Spearman-Kärber estimate. In addition to being nonparametric, the Spearman estimator has the advantage of simplicity, especially compared to probit analysis.

In practice, though, it is sometimes necessary to know more about the tolerance distribution than just the median or location. Although estimators for the location parameter are quite numerous and many have been well studied, the picture is not as clear with regard to other properties of the tolerance distribution such as higher moments and, in particular, the scale parameter. Of course, probit analysis
simultaneously yields both mean and variance estimates, but most other methods of ED50 determination do not share this feature.

With regard to Spearman estimation of location, a corresponding estimator of the variance (in fact, of all higher moments) can be found in an article by Epstein and Churchman [9], and a few properties of the estimator are developed in that paper as well as in a later one by Cornfield and Mantel [5]. The major goal of this thesis is the further development of properties for the Spearman-type variance estimator comparable to those for the Spearman estimator of the mean published by Brown [2] and by Miller [15].

1.3 SCOPE OF THE WORK

In what follows there will be an investigation of certain asymptotic properties of the Spearman-type variance estimator such as convergence, mean and variance, distribution, efficiency and relationship to the Spearman estimator of the mean. In addition, a study will be made of the possibility of using a linear combination of the two estimators to find percentage points of the tolerance distribution.
CHAPTER II

MODEL AND PROBLEM

2.1 ASSUMPTIONS

To begin, we make the following assumptions:

(a) the dose levels are equally spaced,
(b) the same number of subjects are tested at each dose level,
(c) the underlying tolerance distribution is an everywhere differentiable c.d.f. with a symmetric, continuous density, and finite fourth moment,

and

(d) the observations on the subjects are mutually independent and the numbers of responses at the dose levels are mutually independently distributed binomial random variables with the mean of each being equal to the number of subjects times the value of the tolerance distribution at the corresponding dose levels.

Note that assumptions (a), (b), and (d) have been traditionally used for simplification in most prior studies of Spearman estimation. Assumption (c) is more specific to the theory which follows. However, nearly all reasonable distribution functions assumed in previous work in quantal bioassay possess these properties.
2.2 PRELIMINARY NOTATION

The following notation will be useful throughout this thesis.

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Meaning</th>
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<tbody>
<tr>
<td>$F(x)$</td>
<td>the unknown underlying tolerance distribution at dose level $x$</td>
</tr>
<tr>
<td>$f(x)$</td>
<td>$\frac{dF(x)}{dx}$</td>
</tr>
<tr>
<td>$k$</td>
<td>$2k+1$ represents the number of dose levels in the experiment</td>
</tr>
<tr>
<td>$x_i$</td>
<td>the $i^{th}$ dose level used in the experiment $(i = 0, \pm 1, \pm 2, \ldots, \pm k)$</td>
</tr>
<tr>
<td>$\delta$</td>
<td>$\equiv x_{i+1} - x_i &gt; 0$</td>
</tr>
<tr>
<td>$n$</td>
<td>the number of subjects tested at each dose level</td>
</tr>
<tr>
<td>$r_i$</td>
<td>the number of subjects responding at the $i^{th}$ dose level</td>
</tr>
<tr>
<td>$p_i$</td>
<td>$\equiv \frac{r_i}{n}$, the proportion of subjects responding at the $i^{th}$ dose level</td>
</tr>
<tr>
<td>$q_i$</td>
<td>$\equiv 1 - p_i$, the proportion of subjects not responding at the $i^{th}$ dose level</td>
</tr>
<tr>
<td>$F_i$</td>
<td>$\equiv F(x_i)$</td>
</tr>
<tr>
<td>$\mu$</td>
<td>the true mean (median) of $F$</td>
</tr>
<tr>
<td>$\sigma^2$</td>
<td>the true variance of $F$</td>
</tr>
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\[ \hat{\mu} = p_{-k}(x_{-k} - \frac{d}{2}) + \frac{k-1}{2} \sum_{i=-k}^{k} (p_{i+1} - p_i)(x_i + \frac{d}{2}) + (1-p_k)(x_k + \frac{d}{2}) \]

= \hat{x} + \frac{d}{2} - \frac{d}{2} \sum_{i=-k}^{k} p_i

= \hat{x}_0 + \frac{d}{2} + \frac{d}{2} \sum_{i=1}^{k} q_i - \frac{d}{2} \sum_{i=-k}^{0} p_i,

the Spearman estimator of the mean

\[ \varphi_Y(t) = E(e^{itY}), \text{ the characteristic function of } Y \text{ for any } \]
random variable \ Y

2.3 THE ESTIMATORS

\[ \nu_k = p_{-k}(x_{-k} - \frac{d}{2} - \mu)^2 + \frac{k-1}{2} \sum_{i=-k}^{k} (x_i + \frac{d}{2} - \mu)^2 (p_{i+1} - p_i) + (1-p_k)(x_k + \frac{d}{2} - \mu)^2, \]

the Spearman-type estimator of the variance with \ \mu \ known.

\[ \nu_U = p_{-k}(x_{-k} - \frac{d}{2} - \hat{\mu})^2 + \frac{k-1}{2} \sum_{i=-k}^{k} (x_i + \frac{d}{2} - \hat{\mu})^2 (p_{i+1} - p_i) \]

\[ + (1-p_k)(x_k + \frac{d}{2} - \hat{\mu})^2, \]

the Spearman-type estimator of the variance with \ \mu \ unknown.
2.4 THE INFINITE EXPERIMENT

In practice, quantal bioassay is often performed within the framework of Sections 2.1 and 2.2 with modest values of $n$ and $k$ and so ideally it would be desirable to work with the estimators as defined above. However, for the following development, it will be convenient to establish an infinite experiment consisting of an infinity of dose levels. This approach does present certain probabilistic difficulties that are not present with the finite experiment, but overall the effort becomes more straightforward. It is also possible to be concerned about whether the infinite experiment might yield infinite information. Fortunately, this is not the case, and, in fact, the information from the infinite experiment closely approximates that for the finite experiment in practice.

The infinite experiment will be the same as that used by Brown [2]. The number of subjects, $n$, and the distance between dose levels, $d$, initially will be fixed, just as in Section 2.2. But instead of a finite $k$, the experiment will specify an infinite number of dose levels and then asymptotic results will be obtained as $d \to 0$, with fixed $n$.

2.5 THE PROBLEM

The following two chapters will be devoted to showing that appropriate forms for the Spearman-type estimator of the variance for the infinite experiment are, indeed, random variables, and to exhibiting the asymptotic properties mentioned in Section 1.3.
CHAPTER III

THE SPEARMAN-TYPE ESTIMATOR OF THE VARIANCE FOR

THE INFINITE EXPERIMENT WITH $\mu$ KNOWN

3.1 THE RANDOM VARIABLE, $v_k$

Taking the estimator for the $\mu$ known case defined in Section 2.3, observe that:

$$
p_k(x_k - \frac{d}{2} - \mu)^2 + \sum_{i=-k}^{k-1} (x_i + \frac{d}{2} - \mu)^2 (p_{i+1} - p_i) + (1-p_k)(x_k + \frac{d}{2} - \mu)^2
$$

$$
= p_k[(x_k - \frac{d}{2} - \mu)^2 - (x_k + \frac{d}{2} - \mu)^2] + \sum_{i=-k}^{k-1} p_i[(x_{i-1} + \frac{d}{2} - \mu)^2 - (x_i + \frac{d}{2} - \mu)^2]
$$

$$
+ p_k[(x_{k-1} + \frac{d}{2} - \mu)^2 - (x_k + \frac{d}{2} - \mu)^2] + (x_k + \frac{d}{2} - \mu)^2
$$

$$
= 2p_k d(\mu - x_k) + 2 \sum_{i=-k}^{k-1} p_i d(\mu - x_i) + 2p_k d(\mu - x_k) + (x_k + \frac{d}{2} - \mu)^2
$$

$$
= 2d \sum_{i=-k}^{0} p_i (\mu - x_i) - 2d \sum_{i=1}^{k} (1-p_i)(\mu - x_i) + 2d \sum_{i=1}^{k} (\mu - x_i) + (x_k + \frac{d}{2} - \mu)^2
$$

$$
= (x_0 + \frac{d}{2} - \mu)^2 + 2d \sum_{i=-k}^{0} p_i (\mu - x_i) - 2d \sum_{i=1}^{k} (1-p_i)(\mu - x_i)
$$

So, we are motivated to use as the Spearman-type variance estimator for the infinite experiment with $\mu$ known the quantity:
\[ v_K = \lim_{k \to \infty} \left[ p_{-k}(x_{-k} - \frac{d}{2} - \mu)^2 + \sum_{i=-k}^{k-1} (x_i + \frac{d}{2} - \mu)^2 (p_{i+1} - p_i) + (1-p_k)(x_k + \frac{d}{2} - \mu)^2 \right] \]

\[ = \lim_{k \to \infty} \left[ (x_0 + \frac{d}{2} - \mu)^2 + 2d \sum_{i=-k}^{0} p_i(\mu-x_i) - 2d \sum_{i=1}^{k} (1-p_i)(\mu-x_i) \right] \]

\[ = (x_0 + \frac{d}{2} - \mu)^2 + 2d \sum_{i=-\infty}^{0} p_i(\mu-x_i) - 2d \sum_{i=1}^{\infty} (1-p_i)(\mu-x_i). \quad (1) \]

To see that \( v_K \), as defined in (1), is actually a meaningful random variable, it suffices to show that the infinite series in (1) involve only a finite number of non-zero terms with probability one, i.e., that

\[ \mathcal{P}(p_i < 1 \text{ i.o. for } i > 0) = \mathcal{P}(p_i > 0 \text{ i.o. for } i \leq 0) = 0. \quad (2) \]

For arbitrary \( \epsilon > 0 \),

\[ \sum_{i=1}^{\infty} \mathcal{P}(1 - p_i > \epsilon) \leq \sum_{i=1}^{\infty} \left[ 1 - \mathcal{P}(p_i = 1) \right] \]

\[ = \sum_{i=1}^{\infty} (1 - F_i^n) \]

\[ \leq n \sum_{i=1}^{\infty} (1 - F_i) \]

\[ < \infty \text{ by Lemma 1 of the Appendix} \]

\[ \implies \mathcal{P}(1 - p_i > \epsilon \text{ i.o. for } i > 0) = 0 \text{ by Theorem 4.2.1 of Chung} \]

[3] (i.e., Borel-Cantelli lemma).
Consequently,

\[ P(p_i < l \text{ i.o. for } i > 0) = 0. \]

A similar argument with the random variables \( p_0, p_{-1}, p_{-2}, \ldots \) completes the proof of (2).

Lastly, for future interest, observe that (2) used with the first expression for \( v_K \) in (1) yields the alternate form:

\[ v_K = \sum_{i=-\infty}^{\infty} (x_i + \frac{d}{2} - \mu)^2 (p_{i+1} - p_i). \]  \hspace{1cm} (4)

3.2 MEAN AND VARIANCE OF \( v_K \)

Moments of \( v_K \) must be computed with attention given to the placement of the doses. Noting that

\[ \sum_{i=1}^{\infty} E |(x_i + \frac{d}{2} - \mu)^2 (p_{i+1} - p_i)| \leq \sum_{i=1}^{\infty} (x_i + \frac{d}{2} - \mu)^2 [(1-F_i) + (1-F_{i+1})] < \infty \]

by Lemma 1 of the Appendix and likewise for the corresponding series with negative indices, we have from (4) that the expectation of \( v_K \) conditional on a fixed \( x_0 \) (i.e., a fixed dose mesh) is

\[ E(v_K|x_0) = \sum_{i=-\infty}^{\infty} (x_i + \frac{d}{2} - \mu)^2 (F_{i+1} - F_i) < \infty. \]  \hspace{1cm} (5)

If we then assume that the dose placement is random, in particular that \( x_0 \) is chosen randomly with respect to a uniform distribution on the interval \((0,d)\), then
\[
E(v_K) = \int_0^d \frac{1}{d} E(v_K | x_0) \, dx_0 \\
= \frac{1}{d} \int_0^d \left[ \sum_{i=-\infty}^{\infty} (x_0 + \frac{d}{2} + i d - \mu)^2 \int_{x_0 + id + d}^{x_0 + id + d} dF(x) \right] \, dx_0 \\
= \frac{1}{d} \sum_{i=-\infty}^{\infty} \int_{i d + d/2}^{(i+1)d + d/2} \left[ (y - \mu)^2 \int_{y-d/2}^{y+d/2} dF(x) \right] \, dy \\
= \frac{1}{d} \int_{-\infty}^{\infty} \left[ (y - \mu)^2 \int_{x - d/2}^{x + d/2} dF(x) \right] \, dy \\
= \int_{-\infty}^{\infty} \left[ (y - \mu)^2 + \frac{d^2}{12} \right] dF(x) \\
= \sigma^2 + \frac{d^2}{12} .
\]

(6)

The second term of (6), of course, we recognize as Sheppard's correction factor. Since the asymptotic (d → 0) theory is unaffected by this term, to avoid more cumbersome notation no adjustment of \( v_K \) will be made. However, more will be said about consideration of this factor in practice in Chapter 5.

In computing the variance of \( v_K \) it is more convenient to work with (1). If we let \( y_i = p_i (\mu - x_i) \), then

\[
\sum_{i=-\infty}^{0} E y_i = \sum_{i=-\infty}^{0} F_i (\mu - x_i) < \infty \quad \text{and} \quad \sum_{i=-\infty}^{0} \text{Var} y_i = \sum_{i=-\infty}^{0} \frac{F_i (1 - F_i)}{n} (\mu - x_i)^2 < \infty
\]

both by Lemma 1 of the Appendix. Recognition of similar properties for the other series in (1) and of the independence assumption on the \( p_i \)'s allows us to use Theorem 2.3 on p. 108 of Doob [8] to conclude
\[
\text{Var}(v_K|X_0) = \frac{4d^2}{n} \sum_{i=-\infty}^{\infty} (x_i - \mu)^2 F_i(1-F_i) < \infty.
\] (7)

(Although Doob's Theorem is powerful enough to also yield \(E(v_K|v_0)\) and the convergence of \(v_K\), the alternate approach was chosen because the form of (5) is more convenient and because (2) must be proved eventually anyway.) For random dose placement,

\[
\text{Var}(v_K) = E_{X_0} E[(v_K - \sigma^2 - \frac{d^2}{12})^2 |X_0]
\]

\[
=E_{X_0} \{ \text{Var}(v_K|X_0) + [E(v_K|X_0) - \sigma^2 - \frac{d^2}{12}]^2 \}. \tag{8}
\]

Using (7),

\[
E_{X_0} \text{Var}(v_K|X_0) = \frac{4d}{n} \sum_{i=-\infty}^{\infty} \int_{0}^{d} (x_0 - \mu + id)^2 F(x_0 + id)(1-F(x_0 + id)) \ dx_0
\]

\[
= \frac{4d}{n} \sum_{i=-\infty}^{\infty} \int_{id}^{(i+1)d} (x - \mu)^2 F(x) \ [1-F(x)] \ dx
\]

\[
= \frac{4d}{n} \int_{-\infty}^{\infty} (x - \mu)^2 F(x) \ [1-F(x)] \ dx. \tag{9}
\]

Looking now at the bias term,

\[
|E(v_K|X_0) - \sigma^2| = \bigg| \sum_{i=-\infty}^{\infty} \left( \frac{d}{2} - \mu \right)^2 \left( F_{i+1} - F_i \right) - \int_{-\infty}^{\infty} (x - \mu)^2 \ dF(x) \bigg|
\]

\[
= \left| \sum_{i=-\infty}^{\infty} \left[ \left( \frac{d}{2} - \mu \right)^2 - a_i \right] \left( F_{i+1} - F_i \right) \right|,
\]

12
where

\[ a_i = \frac{x_{i+1} \int_{x_i}^{x_{i+1}} (x-\mu)^2 \, dF(x)}{x_{i+1} \int_{x_i}^{x_{i+1}} dF(x)} . \]

But by the Mean Value Theorem,

\[ \int_{x_i}^{x_{i+1}} (x-\mu)^2 \, dF(x) = (z_i - \mu)^2 \int_{x_i}^{z_i} dF(x) \quad \text{where} \quad x_i \leq z_i \leq x_{i+1}. \]

So,

\[ |E(v_K|x_0) - \sigma^2| \leq \sum_{i=-\infty}^{\infty} \left| (x_i + \frac{d}{2} - \mu)^2 - (z_i - \mu)^2 \right| |F_{i+1} - F_i| \]

\[ \leq d \sum_{i=-\infty}^{\infty} |x_i - \mu + \Delta_i| |F_{i+1} - F_i| \quad \text{where} \quad \frac{d}{4} \leq \Delta_i \leq \frac{3d}{4} . \]

\[ \leq d \sum_{i=-\infty}^{\infty} \int_{x_i}^{x_{i+1}} (|y-\mu| + \frac{3d}{4}) dF(y) \]

\[ \leq d(\sigma + \frac{3d}{4}) . \quad (10) \]

So, using results (9) and (10), (8) becomes

\[ \text{Var}(v_K) = \frac{h_d}{n} \int_{-\infty}^{\infty} (x-\mu)^2 F(x)[1-F(x)] \, dx + O(\sigma^2) . \quad (11) \]

Results (5), (6), and (7) are in essential agreement with

Cornfield and Mantel's [5] calculations and approximation for the finite
experiment. The apparent factor of two discrepancy between (7) and their equation (23) is merely a misprint in the paper which can be verified simply by recomputing (23).

3.3 CONVERGENCE

Asymptotically (as $d \to 0$), then, we have from (6) and (11) that

$$E(v_K) \to \sigma^2,$$

$$\text{Var}(v_K) \to 0.$$ 

Consequently, $v_K \to \sigma^2$ in probability, i.e., $v_K$ is weakly consistent for $\sigma^2$.

3.4 INFORMATION

We begin by verifying that the likelihood function

$$L = \prod_{i=-\infty}^{\infty} \left( \frac{n}{r_i} \right)^{F_i(r_i)} \left( 1-F_i(r_i) \right)^{n-r_i}$$

is nonzero. Since we know from (2) that

$$\mathbb{P}(n-r_i > 0 \text{ i.o. for } i > 0) = \mathbb{P}(r_i > 0 \text{ i.o. for } i \leq 0) = 0,$$

w.p. 1, $L$ can be rewritten
\[ L = \left[ \prod_{i=-\infty}^{k_1} \binom{n_i}{r_i} F_i^0(1-F_i)^{n_i-r_i} \right] \left[ \prod_{i=k_1}^{k_2} \binom{n_i}{r_i} F_i^1(1-F_i)^{n_i-r_i} \right] \left[ \prod_{i=k_2}^{\infty} \binom{n_i}{r_i} F_i^n(1-F_i)^{n_i-r_i} \right]. \quad (12) \]

Now, from Lemma 1 of the Appendix,

\[ \sum_{i=k_2}^{\infty} (1-F_i) < \infty \]

\[ \implies \prod_{i=k_2}^{\infty} F_i > 0, \]

and so the third term of (12) is nonzero with probability one. A similar argument works for the first term and the middle term is clearly nonzero. Consequently,

\[ 0 < L < 1 \quad \text{w.p. 1}, \quad (13) \]

and we may now write

\[ \ln L = \sum_{i=-\infty}^{\infty} [\ln(n_i/r_i) + r_i \ln F_i + (n_i-r_i) \ln(1-F_i)]; \]

\[ \frac{\partial \ln L}{\partial \sigma^2} = \sum_{i=-\infty}^{\infty} \frac{\partial}{\partial \sigma^2} [\ln(n_i/r_i) + r_i \ln F_i + (n_i-r_i) \ln(1-F_i)] \]

\[ = \sum_{i=-\infty}^{\infty} \left[ \frac{F_i (r_i - nF_i)}{F_i (1-F_i)} \right], \]

where

\[ F_i^2 = \frac{\partial F_i}{\partial \sigma^2} \quad \text{and} \quad F_i^2 = F_i^2(x_i). \]
The justification for interchanging differentiation and summation is
given in the Appendix (Lemma 2) under assumptions that are weaker
than those which follow.

So, the information for $\sigma^2$ conditional on a fixed dose mesh
is given by

$$I(\sigma^2|x_0) = E \left[ \sum_{i=-\infty}^{\infty} \frac{F_i \left( \frac{r_i - nF_i}{\sigma_i} \right)^2}{\frac{F_i}{1-F_i}} \right].$$

If we now confine our attention to the class of distributions which
satisfy the conditions that $F$ is of the form $F^*[x-\mu]/\sigma$ and that
$\exists y^*, C_1 < \infty \implies$

$$\frac{d}{dx} \left[ (x-\mu)^3 f(x) \right]_{x=y} < 0 \quad \text{and} \quad \frac{f(y)}{(y-\mu)(1-F(y))} \leq C_1 \quad \forall y \geq y^*,$$

then it follows that

$$\sum_{i=0}^{\infty} \frac{F_i \left( \frac{r_i - nF_i}{\sigma_i} \right)}{\frac{F_i}{1-F_i}} = 0 \quad (14)$$

and

$$\sum_{i=0}^{\infty} \text{Var} \left[ \frac{F_i \left( \frac{r_i - nF_i}{\sigma_i} \right)}{\frac{F_i}{1-F_i}} \right] = \frac{n}{4\sigma^4} \sum_{i=0}^{\infty} \frac{(x_i - \mu)^2 f_i^2}{\frac{F_i}{1-F_i}}$$

$$\leq C_2 + C_3 \sum_{i=I+1}^{\infty} \frac{(x_i - \mu)^3 f_i}{(x_i - \mu)(1-F_i)}$$

(where $C_2, C_3$ are finite and $x_i \geq y^*$)

$$\leq C_2 + C_4 \int_{x_i}^{\infty} (x-\mu)^3 f(x) \, dx < \infty \quad (\text{where } C_4 < \infty) \quad (15)$$

since the fourth moment exists.
(Note that the class considered includes those distributions most often hypothesized in parametric work.) Thus, we may again use Doob's Theorem 2.3 with (14) and (15), and similar conditions and reasoning for the series with negative indices, to conclude that

\[ I(\sigma^2|x_0) = n \sum_{i=-\infty}^{\infty} \frac{F_i^2}{F_i(1-F_i)} . \]

Finally, integrating out \( x_0 \),

\[
I = \frac{1}{d} \int_0^1 n \sum_{i=-\infty}^{\infty} \frac{F_i^2}{F_i(1-F_i)} \, dx_0 \\
= \frac{n}{d} \int_{-\infty}^{\infty} \frac{F^2}{F(1-F)} \, dx . \tag{16}
\]

3.5 ASYMPTOTIC NORMALITY

Let \( \{\Delta_m, m \geq 1\} \) be any arbitrary sequence of positive real numbers, \( \Delta_{m+1} < \Delta_m \ \forall \ m \) and \( \lim_{m \to \infty} \Delta_m = 0 \) where \( \Delta_m \) represents the distance between dose levels in a sequence of infinite experiments with increasingly finer dose mesh, but with a fixed reference \( x_0 \). Then define the random variable

\[
Y_{mj} = \begin{cases} 
\frac{2\Delta_m (1-p_{j-1}) (x_{j} - \mu) - \omega_{mj}}{\beta_m} & \text{for } j = 1, 2, 3, \ldots \\
\frac{2\Delta_m p_{j} (\mu - x_j) - \omega_{mj}}{\beta_m} & \text{for } j = 0, -1, -2, \ldots 
\end{cases} \text{ for } m = 1, 2, 3, \ldots
\]

where
\[ \omega_{m,j} = \begin{cases} 
2\Delta_m (1-F_j)(x_j-\mu) & \text{for } j > 0 \\
2\Delta_m F_j (\mu-x_j) & \text{for } j \leq 0 
\end{cases} \]

and

\[ \beta_m = \sqrt{\frac{4\Delta_m^2}{n} \sum_{j=-\infty}^{\infty} (x_j-\mu)^2 F_j (1-F_j)} \cdot \]

(Note that \( \beta_m \) was shown to be finite in Section 3.2.) Examining the first three moments of \( Y_{m,j} \):

\[ E(Y_{m,j}) = 0 \quad \forall j, \forall m; \]

\[ \sigma_{m,j}^2 = \text{Var}(Y_{m,j}) = \frac{(4\Delta_m^2/n) (x_j-\mu)^2 F_j (1-F_j)}{\beta_m^2} \]

and

\[ \sum_{j=-\infty}^{\infty} \sigma_{m,j}^2 = 1; \]

\[ \gamma_{m,j} = E(|Y_{m,j}|^3) = \frac{8\Delta_m^3 (x_j-\mu)^3 E(|F_j-p_j|^3)}{\beta_m^3} \]

and

\[ \Gamma_m = \sum_{j=-\infty}^{\infty} \gamma_{m,j} \leq \frac{8\Delta_m^3 \sum_{j=-\infty}^{\infty} (x_j-\mu)^3 \text{Var}(F_j-p_j)}{\beta_m^3} \]

\[ = \sqrt{\frac{\Delta_m}{n_0} \sum_{j=-\infty}^{\infty} (x_j-\mu)^2 F_j (1-F_j)} \cdot \]

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Now, $\Delta_m \sum_{j=-\infty}^{\infty} |x_j - \mu|^3 F_j(1-F_j) < \infty \quad \forall m$ by Lemma 1 of the Appendix and
\[
\lim_{m \to \infty} \Delta_m \sum_{j=-\infty}^{\infty} |x_j - \mu|^3 F_j(1-F_j) = \int_{-\infty}^{\infty} |x-\mu|^3 F(x) [1-F(x)] \, dx 
\leq \int_{-\infty}^{\mu} (\mu-x)^3 F(x) \, dx + \int_{\mu}^{\infty} (x-\mu)^3 [1-F(x)] \, dx < \infty,
\]
where the last two integrals are finite since the fourth moment of \( F \) exists. By similar reasoning
\[
\lim_{m \to \infty} [\Delta_m \sum_{j=-\infty}^{\infty} (x_j - \mu)^2 F_j(1-F_j)]^{3/2} = T < \infty
\]
and \( T \neq 0 \) because \( F \) is continuous. So, we have
\[
\lim_{m \to \infty} \Gamma_m = 0.
\]
Hence we may apply Theorem 1 [which is a generalization of an argument in Chung [3] as is the preceding lemma] of the Appendix to conclude that
\[
\sum_{j=-\infty}^{\infty} Y_{mj} \quad \text{in dist} \Rightarrow Y \sim \mathcal{N}(0,1) \quad \text{as} \quad m \to \infty.
\]
Since the sequence of \( \Delta_m \)'s was arbitrary, it follows that \( Y_K \) is asymptotically normal (as \( d \to 0 \)) with asymptotic mean \( \sigma^2 \) and asymptotic variance \( (4d/n) \int_{-\infty}^{\infty} (x-\mu)^2 F(x) [1-F(x)] \, dx \).
3.6 ASYMPTOTIC EFFICIENCY

Since, from Section 3.3, \(E(v_K) \to \sigma^2\) as \(d \to 0\) (in fact \(E(v_K - d^2/12) \equiv \sigma^2\)), we may use (16) and the final results of Sections 3.2 and 3.5 to determine the asymptotic efficiency as \(d \to 0\).

\[
\text{Eff} = \left[ \frac{n \int_{-\infty}^{\infty} \frac{F^2}{F(1-F)} \, dx}{\int_{-\infty}^{\infty} (x-\mu)^2 F(1-F) \, dx} \right]^{-1} = \left[ \frac{4 \int_{-\infty}^{\infty} \frac{F^2}{F(1-F)} \, dx \int_{-\infty}^{\infty} (x-\mu)^2 F(1-F) \, dx}{\int_{-\infty}^{\infty} \frac{4}{F(1-F)} \, dx \int_{-\infty}^{\infty} (x-\mu)^2 \frac{1}{\sigma^2} f(x) \, dx} \right]^{-1} \tag{17}
\]

It is of interest to calculate this quantity in specific cases, so four plausible tolerance distributions are examined below.

A. Logistic

\[
F(x) = \frac{1}{1 + e^{-\beta(x-\alpha)}} \quad -\infty < \alpha < \infty, \beta > 0
\]

\[
\mu = \alpha
\]

\[
f(x) = \beta F(x) [1-F(x)]
\]

\[
\sigma^2 = \frac{\pi^2}{3\beta^2}
\]

So,

\[
\text{Eff} = \left[ \frac{4 \int_{-\infty}^{\infty} \frac{F^2}{F(1-F)} \, dx \int_{-\infty}^{\infty} (x-\mu)^2 \frac{1}{\sigma^2} f(x) \, dx}{\int_{-\infty}^{\infty} \frac{4}{F(1-F)} \, dx \int_{-\infty}^{\infty} (x-\mu)^2 \frac{1}{\sigma^2} f(x) \, dx} \right]^{-1} = 1.
\]

Thus, \(v_K\) attains full asymptotic efficiency in the logistic case.
B. **Normal**

$$F(x) = \Phi(\beta(x-\alpha)) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\beta(x-\alpha)} e^{-t^2/2} dt$$

$$\alpha < \infty, \quad \beta > 0, \quad \mu = \alpha, \quad \sigma^2 = \frac{1}{\beta^2}$$

$$f(x) = \beta \Phi(\beta(x-\alpha)) = \frac{\beta}{\sqrt{2\pi}} \exp[-\beta^2(x-\alpha)^2/2]$$

$$\text{Eff} = \left[ 4 \int_{-\infty}^{\infty} \frac{1}{\Phi(\beta(x-\alpha))[1-\Phi(\beta(x-\alpha))]} dx \int (x-\alpha)^2 \Phi(\beta(x-\alpha))[1-\Phi(\beta(x-\alpha))] dx \right]^{-1}$$

$$= \left[ \frac{2}{\pi} \int_{0}^{\infty} e^{-y^2} y^2 dy \int_{0}^{\infty} y^2 \Phi(y)(1-\Phi(y)) dy \right]^{-1}.$$  

Numerical approximations yield the bound

$$0.961 < \text{Eff} < 0.965.$$  

C. **Bilateral Exponential**

$$F(x) = \begin{cases} 
\frac{1}{2} \exp[\beta(x-\alpha)] & \text{for } x < \alpha \\
1 - \frac{1}{2} \exp[-\beta(x-\alpha)] & \text{for } x \geq \alpha 
\end{cases}$$

$$\alpha < \infty, \quad \beta > 0, \quad \mu = \alpha, \quad \sigma^2 = \frac{2}{\beta^2}$$
\[ f(x) = \frac{1}{2} \beta \exp[-\beta |x-\alpha|] \]

\[
\text{Eff} = \left[ 4 \int_0^\infty \frac{y^3 \beta^3/16 e^{-2y}}{(1 - \frac{1}{2} e^{-y})e^{-y}} \, dy \right]^{-1} \int_0^\infty y^2 e^{-\beta y}(1 - \frac{1}{2} e^{-\beta y}) \, dy
\]

\[
= 4 \left( \frac{\beta^3}{4} \sum_{m=1}^\infty \frac{1}{2m^2} \right) \left( \frac{15^3}{8\beta^2} \right) = 0.9928 .
\]

D. Angular

\[ F(x) = \begin{cases} 
0 & \text{for } x \leq \alpha - \frac{\pi}{4\beta} \\
\sin^2[\beta(x-\alpha) + \frac{\pi}{4}] & \text{for } \alpha - \frac{\pi}{4\beta} < x < \alpha + \frac{\pi}{4\beta} \\
1 & \text{for } x \geq \alpha + \frac{\pi}{4\beta} 
\end{cases} \]

\[ \alpha < \alpha < \infty, \quad \beta > 0, \quad \mu = \alpha, \quad \sigma^2 = \frac{\pi^2 - 8}{16\beta^2} \]

\[
\text{Eff} = \left[ 4 \int_0^{\pi/2} \frac{256 \beta^3}{(\pi^2 - 6)^2} \frac{(y - \frac{\pi}{4})^2 \sin^2 y \cos^2 y}{\sin^2 y \cos^2 y} \, dy \right]^{-1} \int_0^{\pi/2} \frac{\pi}{2} \frac{(y - \frac{\pi}{4})^2}{\beta^3} (\sin y \cos y)^2 \, dy
\]

\[
= 4 \left( \frac{8\pi^3}{3(\pi^2 - 8)^2} \right) \left( \frac{\pi(\pi^2 - 6)}{768} \right) = 0.9928 .
\]

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The asymptotic efficiency of the Spearman estimator of the mean for the infinite experiment in cases A, B, and D are given by Brown [2] and are listed in Table 3.1 below along with the efficiencies computed above. His paper does not consider the bilateral exponential, but using his equation (7.4) we obtain

\[
\text{Eff} \hat{\mu} = \left[ \int_0^\infty e^{-\beta y} \left( 1 - \frac{1}{2} e^{-\beta y} \right) dy \int_0^\infty \frac{\beta e^{-\gamma y}}{0 e^{\gamma y} \left( 1 - \frac{1}{2} e^{-\gamma y} \right)} \right]^{-1}
\]

\[
= \frac{2}{3 \ln 2} = .9618 .
\]

Hence, comparing the values in Table 3.1, it is noteworthy that, with regard to asymptotic efficiency, \( v_K \) compares favorably with the traditional Spearman estimator of the mean.

<table>
<thead>
<tr>
<th>Distribution</th>
<th>( v_K )</th>
<th>( \hat{\mu} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logistic</td>
<td>1.0000</td>
<td>1.0000</td>
</tr>
<tr>
<td>Normal</td>
<td>.96</td>
<td>.9814</td>
</tr>
<tr>
<td>Bilateral Exponential</td>
<td>.9928</td>
<td>.9618</td>
</tr>
<tr>
<td>Angular</td>
<td>.6677</td>
<td>.8106</td>
</tr>
</tbody>
</table>
CHAPTER IV

THE SPEARMAN-TYPE ESTIMATOR OF THE VARIANCE FOR THE

INFINITE EXPERIMENT WITH $\mu$ UNKNOWN

4.1 THE RANDOM VARIABLE, $\nu_U$, AND ITS EXPECTATION

For the infinite experiment, define, following Brown [2],

$$\hat{\mu} = \lim_{k \to \infty} \left[ (x_{-k} - \frac{d}{2}) p_{-k} + \sum_{i=-k}^{k-1} \left( x_i + \frac{d}{2} \right) (p_{i+1} - p_i) + \left( x_k + \frac{d}{2} \right) (1 - p_k) \right]$$

$$= \sum_{i=-\infty}^{\infty} (p_{i+1} - p_i) (x_i + \frac{d}{2})$$

$$= x_0 + \frac{d}{2} + d \sum_{i=1}^{\infty} q_i - d \sum_{i=-\infty}^{0} p_i.$$

Then by (2), $\hat{\mu}$ is finite w.p. 1 and, as suggested in Section 2.3 we may define the random variable

$$\nu_U = \lim_{k \to \infty} \left[ (x_{-k} - \frac{d}{2} - \hat{\mu})^2 p_{-k} + \sum_{i=-k}^{k-1} \left( x_i + \frac{d}{2} - \hat{\mu} \right)^2 (p_{i+1} - p_i) + \left( x_k + \frac{d}{2} - \hat{\mu} \right)^2 (1 - p_k) \right]$$

$$= \sum_{i=-\infty}^{\infty} \left( x_i + \frac{d}{2} - \hat{\mu} \right)^2 (p_{i+1} - p_i) = \sum_{i=-\infty}^{\infty} \left( x_i + \frac{d}{2} \right)^2 (p_{i+1} - p_i) - \hat{\mu}^2$$

$$= (x_0 + \frac{d}{2})^2 - 2d \sum_{i=-\infty}^{0} p_i x_i + 2d \sum_{i=1}^{\infty} q_i x_i - (x_0 + \frac{d}{2}) + d \sum_{i=1}^{\infty} q_i - d \sum_{i=-\infty}^{0} p_i^2.$$
For the fixed dose mesh, we may appeal to the rationale used to obtain (5) to write

$$E(v_u|x_0) = \sum_{i=-\infty}^{\infty} \left( x_i + \frac{d}{2} \right)^2 \left( F_{i+1} - F_i \right) - [E(\hat{\mu}|x_0)]^2 \cdot \text{Var}(\hat{\mu}|x_0)$$

$$= \sum_{i=-\infty}^{\infty} \left( x_i + \frac{d}{2} \right)^2 \left( F_{i+1} - F_i \right) - \sum_{i=-\infty}^{\infty} \left( x_i + \frac{d}{2} \right) \left( F_{i+1} - F_i \right) - \frac{d^2}{n} \sum_{i=-\infty}^{\infty} F_i (1 - F_i)$$

directly using Brown's results 4.1 and 5.1 concerning the mean and variance of \( \hat{\mu} \) for fixed \( x_0 \).

$$E(v_u) = E_{x_0} \sum_{i=-\infty}^{\infty} \left( x_i + \frac{d}{2} \right)^2 \left( F_{i+1} - F_i \right)|x_0 - E_{x_0} \left[ E(\hat{\mu}|x_0) \right]$$

$$= \sigma^2 + \mu^2 + \frac{d^2}{12} - E_{\hat{\mu}}^2 \quad \text{[derived in the same manner as (6)]}$$

$$E(v_u) = \sigma^2 + \mu^2 + \frac{d^2}{12} - \text{Var}(\hat{\mu}) - \left( E(\hat{\mu}) \right)^2$$

$$= \sigma^2 + \frac{d^2}{12} - \frac{d}{n} \int_{-\infty}^{\infty} \frac{F(x)}{1-F(x)} dx - E_{x_0} \left[ E(\hat{\mu}|x_0) - \mu \right]^2 \quad (18)$$

from Brown's equations 6.1, 6.3 and 6.4.

The last term of the above expression has an upper bound of \( \sigma^2/4 \) by Brown's Lemma 4.1. However, by imposing any of a variety of mild conditions, the bound can be decreased substantially (e.g. under the further condition of unimodality of \( f \), \( E_{x_0} \left[ E(\hat{\mu}|x_0) - \mu \right]^2 \leq \frac{d f_m^2}{64} \), where \( f_m = \max f(x) \), so that in most reasonable circumstances this term is negligible compared to the others. A comprehensive discussion of
this quantity can be found in Brown's paper. As in Chapter III for asymptotic purposes we will be unconcerned with the second and third terms of (18). However, in practice it is desirable to alter \( v_U \) by Sheppard's correction \((-d^2/12)\) and the bias correction

\[
d^2 \sum_{i=-k}^{k} \left( \frac{p_i q_i}{n-1} \right)
\]

as suggested by Cornfield and Mantel [5], where

\[
E \frac{d^2}{n} \sum_{i=-\infty}^{\infty} \left( \frac{p_i q_i}{n-1} \right) = \frac{d}{n} \int_{-\infty}^{\infty} F(x) [1 - F(x)] \, dx .
\]

4.2 INFORMATION

For \( \mu \) unknown we will be concerned with the information matrix \( \mathcal{L} = \{ I_{ab} : a = \mu, \sigma^2 ; b = \mu, \sigma^2 \} \). Examining the off-diagonal element,

\[
I(\mu, \sigma^2 | x_0) = E \left( \frac{\partial \ln L}{\partial \mu} \frac{\partial \ln L}{\partial \sigma^2} \right)
\]

\[
= E \left[ \sum_{i=-\infty}^{\infty} \frac{F_{i} \left( r_i - n F_i \right)}{F_{i} (1 - F_i)} \sum_{j=-\infty}^{\infty} \frac{\sigma^2_j \left( r_j - n F_j \right)}{F_j (1 - F_j)} \right]
\]

where \( F_{\mu} = \frac{\partial F}{\partial \mu} \) and \( F_{\mu i} = \frac{\partial F}{\partial x_i} \).

The differentiation/summation interchange justification for the first series is analogous to the proof of Lemma 2 of the Appendix. So, similar to the reasoning in Section 3.4,
\[ I(\mu, \sigma^2 | x_0) = \frac{n}{d} \sum_{i=1}^{\infty} \frac{F_{\mu, \sigma^2_i}}{F_i(1-F_i)} \cdot \]

\[ \therefore I_{\mu, \sigma^2} = \frac{n}{d} \int_{-\infty}^{\infty} \frac{F F_{\mu, \sigma^2}}{F(1-F)} dx. \]

But, if the tolerance distribution is of the form \( F^*[(x-\mu)/\sigma] \), then

\[ I_{\mu, \sigma^2} = \frac{n}{2d\sigma} \int_{-\infty}^{\infty} \frac{(x-\mu) f^2(x)}{F(x)[1-F(x)]} dx = 0 \]

since \( F \) is symmetric.

Thus, the 2, 2 element of \( \mathbf{Q}^{-1} \) is just the reciprocal of the quantity in (16).

### 4.3 ASYMPTOTIC NORMALITY

With \( A_m \) defined as in Section 3.5, let

\[ X_{mj}^{(1)} = \frac{x_j(F_{j}-p_j)}{a_{3m}} - \frac{(F_{j}-p_j)a_{2m}}{a_{1m} a_{5m}} \]

\[ X_{mj}^{(2)} = \frac{(F_{j}-p_j)}{\sqrt{a_{1m}}} \]

where
\[ a_{lm} = \frac{1}{n} \sum_{i=-\infty}^{\infty} x_i F_i (1-F_i) \]

\[ a_{2m} = \frac{1}{n} \sum_{i=-\infty}^{\infty} x_i^2 F_i (1-F_i) \]

\[ a_{3m} = \sqrt{\frac{1}{n} \sum_{i=-\infty}^{\infty} x_i^2 F_i (1-F_i) \frac{a_{2m}^2}{a_{lm}}} \]

Let any arbitrary real \( \lambda_1 \) and \( \lambda_2 \) be given and define

\[ y_{mj} = \frac{\lambda_1 x_{mj}^{(1)} + \lambda_2 x_{mj}^{(2)}}{\sqrt{\lambda_1^2 + \lambda_2^2}} \]

Clearly, \( E(y_{mj}) = 0, \forall m, j. \)

\[ \sum_{j=-\infty}^{\infty} \text{Var}(y_{mj}) \]

\[ = \frac{1}{\lambda_1^2 + \lambda_2^2} \sum_{j=-\infty}^{\infty} \left( \frac{\lambda_1 x_{mj}^{(1)} - \lambda_1 a_{2m}}{a_{jm} a_{3m}} + \frac{\lambda_2}{\sqrt{a_{lm}}} \right)^2 \text{Var}(F_j - p_j) \]

\[ = \frac{1}{n(\lambda_1^2 + \lambda_2^2)} \left[ \sum_{j=-\infty}^{\infty} \frac{x_{mj}^2 F_j (1-F_j)}{a_{jm}^2} + \frac{n \lambda_1^2 a_{2m}^2}{a_{lm} a_{3m}} + \frac{n \lambda_2^2}{a_{lm}^2} - \frac{2n \lambda_1 \lambda_2 a_{2m}^2}{a_{jm} a_{3m}} + \frac{2n \lambda_1 \lambda_2 a_{2m}}{a_{jm} \sqrt{a_{lm}}} - \frac{2n \lambda_1 \lambda_2 a_{2m}}{a_{3m} \sqrt{a_{lm}}} \right] \]

\[ = 1 \quad \forall m. \]
\[
\sum_{j=0}^{\infty} E(|Y_{nj}|^3)
\]
\[
= \frac{1}{(\lambda_1^2 + \lambda_2^2)^{3/2}} \sum_{j=0}^{\infty} \left| \frac{\lambda_1 x_{j} - \lambda_2 a_{nj} - \lambda_2 a_{nj} a_{nj}}{\sqrt{a_{nj} a_{nj}}} \right|^3 E|F_j - p_j|^3
\]
\[
\leq \frac{1}{n(\lambda_1^2 + \lambda_2^2)^{3/2}} \sum_{j=0}^{\infty} \left| \frac{\lambda_1 x_{j} - \lambda_2 a_{nj} - \lambda_2 a_{nj} a_{nj}}{\sqrt{a_{nj} a_{nj}}} \right|^3 F_j (1-F_j)
\]
\[
\leq \frac{9}{(\lambda_1^2 + \lambda_2^2)^{3/2}} \sqrt{n a_{nj}} \left[ \frac{|\lambda_1|^3 \Delta_m \sum_{j=0}^{\infty} x_j^3 F_j (1-F_j)}{(\Delta_m \sum_{i=0}^{\infty} x_i^2 F_i (1-F_i))^2} \right]^{3/2}
\]
\[
\leq \frac{|\lambda_1|^3 \Delta_m \sum_{j=0}^{\infty} x_j^3 F_j (1-F_j)}{(\Delta_m \sum_{i=0}^{\infty} x_i^2 F_i (1-F_i))^2} \right]^{3/2}
\]
\[
+ \frac{|\lambda_2|^3 \Delta_m \sum_{j=0}^{\infty} x_j^3 F_j (1-F_j)}{(\Delta_m \sum_{i=0}^{\infty} x_i^2 F_i (1-F_i))^2} \right]^{3/2}
\]
\[
\rightarrow 0 \quad \text{as} \quad m \to \infty \quad \text{by Lemma 1 of the Appendix and the existence of}
\]
the fourth moment.
Hence, by Theorem 1 of the Appendix,

\[ \sum_{j=\infty}^{\infty} Y_{mj} \xrightarrow{\text{in dist.}} Y \sim \mathcal{N}(0,1) \quad \text{as } m \to \infty. \]

And so

\[ \lambda_1 \sum_{j=\infty}^{\infty} X_{mj}^{(1)} + \lambda_2 \sum_{j=\infty}^{\infty} X_{mj}^{(2)} \xrightarrow{\text{in dist.}} \mathcal{N}(0, \lambda_1^2 + \lambda_2^2) \quad \text{as } m \to \infty. \]

But since \( \lambda_1 \) and \( \lambda_2 \) were arbitrary, it follows from a well known theorem [see, for example, (xi) in Rao [16], p. 103], that

\[
\begin{pmatrix}
\sum_{j=\infty}^{\infty} X_{mj}^{(1)} \\
\sum_{j=\infty}^{\infty} X_{mj}^{(2)}
\end{pmatrix} \xrightarrow{\text{in dist.}} \mathcal{N}_2(0, I),
\]

which is algebraically equivalent to

\[
\begin{pmatrix}
\frac{V_U + \mu^2}{\frac{2\Delta m^2}{\Delta a_{lm}^2}} - \frac{\Delta a_{2m}}{\Delta a_{lm}a_{lm}^2} \\
\frac{2\Delta a_{lm}^2}{\Delta a_{lm}^2} - \frac{\Delta a_{lm}a_{lm}^2}{\Delta a_{lm}a_{lm}^2} \\
\sum_{i=\infty}^{\infty} \left( x_i + \frac{\Delta m}{2} (F_{i+1} - F_i) \right) \\
\sum_{i=\infty}^{\infty} \left( x_i + \frac{\Delta m}{2} (F_{i+1} - F_i) \right) a_{2m} \\
\frac{\Delta}{\Delta a_{lm}} \\
\frac{\Delta a_{lm}a_{lm}^2}{\Delta a_{lm}^2}
\end{pmatrix}
\begin{pmatrix}
\frac{1}{\Delta a_{lm}^2} \\
\frac{\Delta a_{lm}a_{lm}^2}{\Delta a_{lm}^2} \\
\sum_{i=\infty}^{\infty} \left( x_i + \frac{\Delta m}{2} (F_{i+1} - F_i) \right) \\
\sum_{i=\infty}^{\infty} \left( x_i + \frac{\Delta m}{2} (F_{i+1} - F_i) \right) a_{2m} \\
\frac{\Delta}{\Delta a_{lm}} \\
\frac{\Delta a_{lm}a_{lm}^2}{\Delta a_{lm}^2}
\end{pmatrix}
\xrightarrow{\text{in dist.}} \mathcal{N}_2(0, I).
\]
Thus, by repeated applications of Lemma 1 of the Appendix and (x)(b) of Rao [16], p. 102,

\[ \sqrt{\frac{n}{\Delta_m}} \left( T_{1m} - c_1 \right) \xrightarrow{\text{in dist}} \mathcal{N}(0, \frac{1}{\Delta_m}) \]

where

\[ T_{1m} = \frac{v_U + \mu^2}{2a_2} - \frac{\mu a_2}{a_1 a_3} \]

\[ c_1 = \frac{\sigma^2 + \mu^2}{2a_3} - \frac{\mu a_2}{a_1 a_3} \]

\[ T_{2m} = \frac{\mu}{\sqrt{\Delta_m}} \]

\[ c_2 = \frac{\mu}{\sqrt{a_1}} \]

with

\[ a_1 = \int_{-\infty}^{\infty} x F(x)[1-F(x)] \, dx \]

\[ a_2 = \int_{-\infty}^{\infty} x^2 F(x)[1-F(x)] \, dx \]

and

\[ a_3 = \sqrt{\int_{-\infty}^{\infty} x^4 F(x)[1-F(x)] \, dx - a_2^2/a_1} \]

Now define

\[ g(T_{1m}, T_{2m}) = 2a_3 T_{1m} + \frac{2a_2}{\sqrt{a_1}} T_{2m} - a_1 T_{2m}^2 \]

\[ = v_U \]

Then it follows by the "s-method" (see Rao [16], p. 321) that, as \( d \to 0 \), \( v_U \) is asymptotically normal with asymptotic mean \( g(c_1, c_2) = \sigma^2 \) and asymptotic variance.
\[ \text{Var}_A(v_U) = \frac{d}{n} \left[ \left( \frac{\partial g}{\partial c_1} \right)^2 + \left( \frac{\partial g}{\partial c_2} \right)^2 \right] \]

\[ = \frac{d}{n} \left[ (2a_3)^2 + \left( \frac{2a_2}{\sqrt{a_1}} - 2a_1 c_2 \right)^2 \right] \]

\[ = \frac{h d}{n} \int_{-\infty}^{\infty} (x-\mu)^2 F(x)[1-F(x)] \, dx \]

\[ = \text{Var}_A(v_K). \]

4.4 ASYMPTOTIC EFFICIENCY

Combining the final results of Sections 4.2 and 4.3 we observe that the asymptotic efficiency for \( \mu \) unknown is identical to that in the known case given in Chapter III. Consequently, the favorable values for the asymptotic efficiency of \( v_K \) given in Table 3.1 also apply to \( v_U \).

4.5 PERCENTILE ESTIMATION

As suggested in Chapter I, an important practical use of \( v_U \) is the estimation of the 100 \( \cdot \alpha \) percentile, \( F^{-1}(\alpha) \), of the tolerance distribution by

\[ P_\alpha = \hat{\mu} + C_\alpha \sqrt{v_U} \]

where \( C_\alpha \) depends on \( \alpha \) and requires an assumption about the underlying tolerance distribution. As a result, the asymptotic properties of \( \sqrt{v_U} \) and \( P_\alpha \) are of interest.
Considering the information matrix \( \mathcal{J} = \{ I_{ab} : a = \mu, \sigma; \ b = \mu, \sigma \} \) it follows by reasoning similar to that in Sections 3.4 and 4.2 that the 2, 2 element of \( \mathcal{J}^{-1} \),

\[
I_{\sigma^2}^* = \frac{n}{d} \int_{-\infty}^{\infty} \frac{e^{-x^2}}{F(1-F)} \, dx \quad \text{where} \quad F = \frac{\partial F}{\partial \sigma}
\]

\[= 4\sigma^2 I \quad \text{where} \quad I \text{ is the quantity (16)}.\]

If we now define

\[
g_1(T_{1m}, T_{2m}) = \sqrt{g(T_{1m}, T_{2m})} = \sqrt{V_U}
\]

we may use the "\( \delta \)-method" again to conclude that \( \sqrt{V_U} \) is asymptotically normal with asymptotic mean \( g_1(c_1, c_2) = \sigma \) and

\[
\text{Var}_A(\sqrt{V_U}) = \frac{d}{n} \left[ \left( \frac{\partial g_1}{\partial c_1} \right)^2 + \left( \frac{\partial g_1}{\partial c_2} \right)^2 \right]
\]

\[= \left( \frac{1}{2 \sqrt{g(c_1, c_2)}} \right)^2 \frac{d}{n} \left[ \left( \frac{\partial g}{\partial c_1} \right)^2 + \left( \frac{\partial g}{\partial c_2} \right)^2 \right]
\]

\[= \frac{1}{4\sigma^2} \text{Var}_A(V_K).\]

Hence, the asymptotic efficiency of \( \sqrt{V_U} \) is the same as that for \( V_U \) and \( V_K \), and as a result the values given in Table 3.1 are again applicable.
Next define

\[ g_2(T_{1m}, T_{2m}) = \sqrt{a_1} \cdot T_{2m} = \hat{\mu}. \]

Then it follows from result (iii) on p. 322 of Rao [16] that

\[
\begin{pmatrix}
\sqrt{v_U} \\
\hat{\mu}
\end{pmatrix}
\]

is asymptotically bivariate normal with asymptotic mean \( \begin{pmatrix} \sigma \\ \mu \end{pmatrix} \) and

\[
\text{Var}_A \left( \begin{pmatrix} \sqrt{v_U} \\
\hat{\mu} \end{pmatrix} \right) = \frac{d}{n} \begin{pmatrix}
\frac{\partial g_1}{\partial c_1} & \frac{\partial g_1}{\partial c_2} \\
\frac{\partial g_2}{\partial c_1} & \frac{\partial g_2}{\partial c_2}
\end{pmatrix} \begin{pmatrix}
\frac{\partial g_1}{\partial c_1} & \frac{\partial g_2}{\partial c_1} \\
\frac{\partial g_1}{\partial c_2} & \frac{\partial g_2}{\partial c_2}
\end{pmatrix}
\]

\[
= \frac{d}{n} \left( \frac{1}{\sigma^2} \int_{-\infty}^{\infty} (x-\mu)^2 \cdot F(1-F) \, dx \cdot \begin{pmatrix}
\frac{\partial g_1}{\partial c_1} & \frac{\partial g_2}{\partial c_1} \\
\frac{\partial g_1}{\partial c_2} & \frac{\partial g_2}{\partial c_2}
\end{pmatrix} \right) \left( \begin{pmatrix}
\frac{\partial g_1}{\partial c_1} & \frac{\partial g_2}{\partial c_1} \\
\frac{\partial g_1}{\partial c_2} & \frac{\partial g_2}{\partial c_2}
\end{pmatrix} \right)
\]

\[
= \frac{d}{n} \left( \frac{1}{\sigma^2} \int_{-\infty}^{\infty} (x-\mu)^2 \cdot F(1-F) \, dx \cdot \frac{1}{2 \cdot \sqrt{g(c_1, c_2)}} \cdot \left( \frac{2a_2}{\sqrt{a_1}} - 2a_1 c_2 \right) \cdot \sqrt{a_1} \right)
\]

\[
= \frac{d}{n} \left( \frac{1}{\sigma^2} \int_{-\infty}^{\infty} (x-\mu)^2 \cdot F(1-F) \, dx \cdot \frac{1}{2 \cdot \sqrt{g(c_1, c_2)}} \cdot \left( \frac{2a_2}{\sqrt{a_1}} - 2a_1 c_2 \right) \cdot \sqrt{a_1} \right)
\]

\[
= \frac{d}{n} \left( \begin{pmatrix}
\frac{1}{\sigma^2} \int_{-\infty}^{\infty} (x-\mu)^2 \cdot F(1-F) \, dx & 0 \\
0 & \int_{-\infty}^{\infty} F(1-F) \, dx
\end{pmatrix}
\right)
\]

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since \( \frac{2\sigma_2}{\sqrt{\sigma_1}} - 2\sigma_1 \sigma_2 = 2(\sigma_2 - \mu \sigma_1)/\sqrt{\sigma_1} = 0 \) when \( F \) is symmetric.

Therefore, we may conclude that \( \sqrt{V_U} \) and \( \hat{\mu} \) are asymptotically uncorrelated and that \( P_{\alpha} \) is asymptotically normal with asymptotic mean \( \mu + c_\alpha \sigma \) and

\[
\text{Var}_A(P_{\alpha}) = \frac{d}{n} \int_{-\infty}^{\infty} \left[ \frac{1}{\sqrt{2\pi}} e^{-(x-\mu)^2 / 2\sigma^2} \right] \left( 1 - F(x) \right) \, dx.
\]
CHAPTER V

A SMALL SAMPLE INVESTIGATION OF PROPERTIES
OF SPEARMAN ESTIMATORS

5.1 GOALS OF THE STUDY

Having established desirable large sample properties of the Spearman-type estimators of the variance and standard deviation, we now turn our attention to the merits of using the corresponding finite estimator of the standard deviation (with and without the bias and Sheppard corrections) together with the traditional Spearman estimator of the mean in solving the practical problem of determining percentiles of an underlying distribution. To evaluate feasibility, the biases, variances, and correlation of these two estimators will be calculated for several cases. However, of even greater interest will be a comparison for various dose placements between the Spearman estimates and the maximum likelihood estimates of the mean, standard deviation and percentiles. In order to accomplish the above, we will have to assume a particular underlying distribution. For the Spearman case, the assumption is only necessary for percentile estimation, whereas for the maximum likelihood case, it is required to estimate mean and standard deviation as well.
5.2 DESCRIPTION OF THE STUDY

Using five subjects at each of three doses \((x = -1, 0, 1)\), we specify an underlying normal tolerance distribution with mean \(\mu\) and standard deviation \(\sigma\). For each of the 216 possible outcomes of the experiment we can then compute:

- the Spearman estimate of the mean,

\[
\hat{\mu}_{\text{Spear}} = p_{-1}(x_{-1} - \frac{d}{2}) + \sum_{i=-1}^{0} (p_{i+1} - p_{i})(x_{i} + \frac{d}{2}) + (1-p_{1})(x_{1} + \frac{d}{2})
\]

\[
= \frac{3}{2} - \frac{1}{2} \sum_{i=-1}^{1} p_{1},
\]

the Spearman-type standard deviation estimate (uncorrected),

\[
s_{\text{Spear}} = \left[ p_{-1}(x_{-1} - \frac{d}{2} - \hat{\mu}_{\text{Spear}})^2 + \sum_{i=-1}^{0} (x_{i} + \frac{d}{2} - \hat{\mu}_{\text{Spear}})^2(p_{i+1} - p_{i}) + (1-p_{1})(x_{1} + \frac{d}{2} - \hat{\mu}_{\text{Spear}})^2 \right]^{1/2}
\]

\[
= \sqrt{5p_{-1} + 3p_{0} + p_{1} - (\sum_{i=-1}^{1} p_{i})^2}
\]

the Spearman-type standard deviation estimate corrected for bias,

\[
s_{\text{corbs}} = s_{\text{Spear}} \left[ \sum_{i=-1}^{1} \frac{p_{1}q_{i}}{4} \right]^{1/2}
\]
the Spearman-type standard deviation estimate with Sheppard's correction,

\[ s_{\text{Shep}} = \sqrt{s^2_{\text{Spear}} - \frac{1}{12}} , \]

and the Spearman-type standard deviation estimate with both Sheppard's and bias corrections,

\[ s_{\text{both}} = \sqrt{s^2_{\text{Spear}} + \sum_{i=-1}^{1} \frac{p_i q_i}{4} - \frac{1}{12}} . \]

Given a particular \( \mu \) and \( \sigma \), to each outcome \((r_{-1}, r_0, r_1)\) there corresponds an occurrence probability

\[ \prod_{i=-1,0,1} ^{5} \left( \begin{array}{c} 5 \\ r_i \end{array} \right) \left[ \phi \left( \frac{i-\mu}{\sigma} \right) \right]^{r_i} \left[ 1 - \phi \left( \frac{i-\mu}{\sigma} \right) \right]^{5-r_i} , \]

and so we can compute \( E_{\text{Spear}}, \text{Var} \hat{\mu}_{\text{Spear}}, E_{\text{Spear}} \text{Var} s_{\text{Spear}}, \text{Var} s_{\text{Spear}}, E_{\text{corbs}}, \text{Var} s_{\text{corbs}}, \text{Corr} \left( \hat{\mu}_{\text{Spear}}, s_{\text{Spear}} \right) \) and \( \text{Corr} \left( \hat{\mu}_{\text{Spear}}, s_{\text{corbs}} \right) \).

Because it is possible for

\[ (s^2_{\text{Spear}} - \frac{1}{12}) \quad \text{and} \quad (s^2_{\text{Spear}} + \sum_{i=-1}^{1} \frac{p_i q_i}{4} - \frac{1}{12}) \]

each to be negative, moments and correlations are omitted for \( s_{\text{Shep}} \) and \( s_{\text{both}} \).

For each outcome for which it is possible (see Section 5.3 below), maximum likelihood estimates for \( \mu \) and \( \sigma \) are also calculated.
Since a distributional form is required to do this, we will assume that the probability law governing the outcomes is normal, which it, in fact, really is. Thus, probit estimates for \(\mu\) and \(\sigma\), respectively called \(\hat{\mu}_{\text{prob}}\) and \(\hat{\sigma}_{\text{prob}}\), are obtained by means of a computer program for Stanford's IBM 360/67 by David, Lewis and Nold [7] using the method of Gill, Murray and Picken [12].

Hence, we can make probability statements concerning the ability of the probit and of the Spearman-type estimators to determine \(\mu\), \(\sigma\), and percentiles for various choices of \(\mu\) and \(\sigma\). The underlying normal assumption is again made for percentile estimation, but in this case it is applied to both the probit and Spearman-type methods. This procedure of fixing the dose levels and varying \(\mu\) and \(\sigma\) is computationally easier but equivalent to fixing \(\mu\) and \(\sigma\) and varying the dose placement. Note that a similar study by Cramer [6] was done to compare maximum likelihood and minimum normit methods using root mean square error.

5.3 PROBIT DEFICIENCIES

Unfortunately, in many cases it is impossible to maximize the likelihood function with finite parameter estimates, or, in some cases, to do so uniquely. In addition, for many other cases, the maximum likelihood estimate for \(\sigma\) is unacceptable. Let us look more closely at these cases.
a) Outcomes \((0,0,0)\) or \((5,5,5)\)

For \((0,0,0)\), any \((\hat{\mu}, \hat{\sigma}) \in \{(\hat{\mu}, \hat{\sigma}) : \hat{\sigma} = 0, \hat{\mu} > 1\} \cup \{(\hat{\mu}, \hat{\sigma}) : \hat{\sigma} \text{ finite}, \hat{\mu} = \infty\}\)

will maximize the likelihood function. For \((5,5,5)\), any

\((\hat{\mu}, \hat{\sigma}) \in \{(\hat{\mu}, \hat{\sigma}) : \hat{\sigma} = 0, \hat{\mu} < -1\} \cup \{(\hat{\mu}, \hat{\sigma}) : \hat{\sigma} \text{ finite}, \hat{\mu} = \infty\}\)

will suffice.

b) Outcomes \((0,0,5)\), \((0,5,5)\), \((5,0,0)\), \((5,5,0)\)

For these cases, maximum likelihood estimates are finite but not unique. For example, for \((0,0,5)\) the maximizing set is

\[\{(\hat{\mu}, \hat{\sigma}) : 0 < \hat{\mu} < 1, \hat{\sigma} = 0\}\]

c) Outcomes \((r,r,r)\) for \(r = 1, 2, 3, 4\) and outcomes

\((r_A, r_B, r_A)\) where \(r_A, r_B = 0, 1, 2, 3, 4, 5\) and \(r_A \neq r_B\)

The likelihood function cannot be maximized with finite \(\hat{\sigma}\)

for these outcomes.

d) Outcomes \((0,0,r)\), \((r,0,0)\), \((r,5,5)\), \((5,5,r)\), \((0,r,5)\), and

\((5,r,0)\) for \(r = 1, 2, 3, 4\)

For each of these cases the likelihood function tends to its upper limit as \((\hat{\mu}, \hat{\sigma}) \rightarrow (\mu^*, \sigma^*)\) for some \(\mu^*, \sigma^*\) (e.g. for \((0, r, 5)\), \(\mu^* = \sigma^* = 0\)). However, at \((\mu^*, \sigma^*)\) there is a discontinuity and so the supremum of the likelihood function is never achieved.

e) Outcomes which yield \(s_{\text{prob}} < 0\)

These estimates essentially indicate that, instead of the stimulus eliciting the response, it actually inhibits it. Since this
would violate a basic assumption in most practical applications, the probit estimates would likely be discarded. We could adopt the criterion of maximizing the likelihood function only for the set \( \{ \hat{\sigma} : \hat{\sigma} \geq 0 \} \), but by eliminating from consideration all cases where \( s_{\text{prob}} < 0 \) instead, we actually bias our comparisons in favor of the probit against the Spearman estimators.

Henceforth, let \( D \) refer to the set of 140 outcomes described above. Probit and Spearman estimates for outcomes not in \( D \) are given in a condensed form in Table 5.1.

For outcomes in \( D \), the investigator committed to maximum likelihood estimation would likely repeat the experiment. The Spearman method advocate might not, but in cases such as \((5,5,5)\) probably that person should too. The realization of certain elements in \( D \) is a good indication that more data should be collected. However, repeating the experiment does not favor the Spearman method in our comparisons.

Originally, it was intended to examine the cases \( \mu = 0, \frac{1}{2}, 1; \sigma = \frac{1}{2}, 1, 2 \). (Note: No further information is gained by taking \( \mu < 0 \).) However, since the probability of probit deficiencies is so great for large \( \mu \) and for small \( \sigma \) [i.e., for \( \mu = 1, \sigma = 1 \), \( \Pr((r_1, r_0, r_1) \in D) = .43 \) and for \( \mu = 0, \sigma = \frac{1}{2} \), \( \Pr((r_1, r_0, r_1) \in D) = .80 \)], it was decided to limit the study to the six cases \( \mu = 0, \frac{1}{2}; \sigma = \frac{1}{2}, 1, 2 \).
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<th>SPEARMAN ESTIMATES</th>
<th>RELATED OUTCOME*</th>
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</tr>
<tr>
<td>2 0 4</td>
<td>0.5053 1.9135</td>
<td>0.3000 1.1662 1.2083 1.1299 1.1733</td>
<td>1 5 3</td>
</tr>
<tr>
<td>2 0 5</td>
<td>0.4753 1.4999</td>
<td>0.1000 1.0198 1.0488 0.9781 1.0083</td>
<td>0 5 3</td>
</tr>
<tr>
<td>2 1 3</td>
<td>1.0010 3.8787</td>
<td>0.3000 1.3266 1.3856 1.2969 1.3552</td>
<td>2 4 3</td>
</tr>
<tr>
<td>2 1 4</td>
<td>0.1584 1.4915</td>
<td>0.1000 1.2649 1.2649 1.1648 1.2315</td>
<td>1 4 3</td>
</tr>
<tr>
<td>2 2 2</td>
<td>0.3343 1.9406</td>
<td>0.1000 1.3598 1.4213 1.3254 1.3916</td>
<td>2 3 3</td>
</tr>
<tr>
<td>3 0 4</td>
<td>0.3270 3.9884</td>
<td>0.1000 1.3598 1.3828 1.3254 1.3626</td>
<td>1 5 2</td>
</tr>
</tbody>
</table>

*OUTCOME WITH THE SAME STANDARD DEVIATION ESTIMATES AND WITH MEAN ESTIMATES OF THE OPPOSITE SIGN
5.4 PRESENTATION OF COMPUTATIONS

For each combination of $\mu$ and $\sigma$, there corresponds a table (Tables 5.2-5.7) containing the following information:

a) the probability that the standard probit procedure will yield reasonable estimates, i.e., $\Pr[(r_{-1}, r_0, r_1) \notin D]$, 

b) the probability, given $(r_{-1}, r_0, r_1) \notin D$, that $\hat{\mu}_{\text{Spear}}$ does better, in terms of absolute deviation, than $\hat{\mu}_{\text{prob}}$ in estimating $\mu$ and conversely, e.g.,

$$\Pr[\hat{\mu}_{\text{Spear}} \text{is better than } \hat{\mu}_{\text{prob}} | (r_{-1}, r_0, r_1) \notin D] = \Pr[|\hat{\mu}_{\text{Spear}} - \mu| < |\hat{\mu}_{\text{prob}} - \mu| | (r_{-1}, r_0, r_1) \notin D],$$

c) a matrix of probabilities like those described in b) showing comparisons of all possible (ordered) pairs of the five standard deviation estimators described in Section 5.2 in their ability to estimate $\sigma$,

d) similar matrices comparing percentile estimates corresponding to the five standard deviation estimates (and subscripted accordingly) for two specific percentiles. [Note: for $\mu = .5$, the ED05 and ED95 were selected in order to examine differences in estimating percentiles above and below the estimate of the mean. Since, by symmetry, in the $\mu = 0$ cases the ED05 and ED95 comparison matrices would be identical, the ED95 and ED99 were chosen for examination.], and

e) the Spearman moments and correlations mentioned in Section 5.2.
### Table 5.2

**Underlying Normal Distribution**

\[
\mu = 0.0000, \\
\sigma = 0.8500
\]

\[
\Pr[(r_{-1}, r_0, r_1) \not\in D] = 0.6552
\]

**Probability [GIVEN \((r_{-1}, r_0, r_1) \not\in D\)]**

<table>
<thead>
<tr>
<th>(s_{\text{prob}})</th>
<th>(s_{\text{Spear}})</th>
<th>(s_{\text{corbs}})</th>
<th>(s_{\text{Shep}})</th>
<th>(s_{\text{both}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>(T_{s_{\text{prob}}})</td>
<td>0.0000</td>
<td>0.0402</td>
<td>0.2951</td>
<td>0.5936</td>
</tr>
<tr>
<td>(H_{s_{\text{Spear}}})</td>
<td>0.0593</td>
<td>0.0000</td>
<td>0.0831</td>
<td>0.5964</td>
</tr>
<tr>
<td>(A_{s_{\text{corbs}}})</td>
<td>0.7049</td>
<td>0.3169</td>
<td>0.0000</td>
<td>0.4093</td>
</tr>
<tr>
<td>(T_{s_{\text{Shep}}})</td>
<td>0.4064</td>
<td>0.4036</td>
<td>0.5907</td>
<td>0.0000</td>
</tr>
<tr>
<td>(s_{\text{both}})</td>
<td>0.9598</td>
<td>0.2222</td>
<td>0.6831</td>
<td>0.5964</td>
</tr>
</tbody>
</table>

**Expectation**

- \(\hat{\mu}_{\text{Spear}} = 0.0000\)
- \(s_{\text{Spear}} = 0.7202\)
- \(s_{\text{corbs}} = 0.7768\)
- \(s_{\text{both}} = 0.3692\)

**Variance**

- \(0.0878\)
- \(0.0661\)
- \(0.0000\)
- \(0.0000\)

**Correlation with \(\hat{\mu}_{\text{Spear}}\)**

**Probability [GIVEN \((r_{-1}, r_0, r_1) \not\in D\)]**

<table>
<thead>
<tr>
<th>(ED95_{s_{\text{prob}}})</th>
<th>(ED95_{s_{\text{Spear}}})</th>
<th>(ED95_{s_{\text{corbs}}})</th>
<th>(ED95_{s_{\text{Shep}}})</th>
<th>(ED95_{s_{\text{both}}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>(T_{s_{\text{prob}}})</td>
<td>0.0003</td>
<td>0.3646</td>
<td>0.1376</td>
<td>0.0166</td>
</tr>
<tr>
<td>(H_{s_{\text{Spear}}})</td>
<td>0.6354</td>
<td>0.0000</td>
<td>0.6695</td>
<td>0.3385</td>
</tr>
<tr>
<td>(A_{s_{\text{corbs}}})</td>
<td>0.6724</td>
<td>0.3305</td>
<td>0.0000</td>
<td>0.3331</td>
</tr>
<tr>
<td>(T_{s_{\text{Shep}}})</td>
<td>0.8332</td>
<td>0.6115</td>
<td>0.6696</td>
<td>0.0000</td>
</tr>
<tr>
<td>(s_{\text{both}})</td>
<td>0.6571</td>
<td>0.3381</td>
<td>0.6695</td>
<td>0.3385</td>
</tr>
</tbody>
</table>

**Probability [GIVEN \((r_{-1}, r_0, r_1) \not\in D\)]**

<table>
<thead>
<tr>
<th>(ED99_{s_{\text{prob}}})</th>
<th>(ED99_{s_{\text{Spear}}})</th>
<th>(ED99_{s_{\text{corbs}}})</th>
<th>(ED99_{s_{\text{Shep}}})</th>
<th>(ED99_{s_{\text{both}}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>(T_{s_{\text{prob}}})</td>
<td>0.0003</td>
<td>0.3715</td>
<td>0.3128</td>
<td>0.2358</td>
</tr>
<tr>
<td>(H_{s_{\text{Spear}}})</td>
<td>0.6285</td>
<td>0.0000</td>
<td>0.6704</td>
<td>0.3296</td>
</tr>
<tr>
<td>(A_{s_{\text{corbs}}})</td>
<td>0.6872</td>
<td>0.3296</td>
<td>0.0000</td>
<td>0.3296</td>
</tr>
<tr>
<td>(T_{s_{\text{Shep}}})</td>
<td>0.7642</td>
<td>0.5704</td>
<td>0.5704</td>
<td>0.0000</td>
</tr>
<tr>
<td>(s_{\text{both}})</td>
<td>0.6394</td>
<td>0.3346</td>
<td>0.6704</td>
<td>0.3296</td>
</tr>
</tbody>
</table>

\*i.e., \(x_{-1} = \mu - \frac{5}{6} \sigma, \ x_0 = \mu, \ x_1 = \mu + \frac{5}{6} \sigma\)
**Table 5.3**

**Underlying Normal Distribution**

\[
\hat{\mu} = 0.2000, \\
\sigma = 1.0000
\]

\[
\Pr[(r_{1-1}, r_0, r_1) \not\in \mathcal{D}] = 0.7945
\]

\[
\Pr[\hat{\mu}_{\text{Spear}} \text{ better than } \hat{\mu}_{\text{prob}} | (r_{1-1}, r_0, r_1) \not\in \mathcal{D}] = 0.9159
\]

\[
\Pr[\hat{\mu}_{\text{prob}} \text{ better than } \hat{\mu}_{\text{Spear}} | (r_{1-1}, r_0, r_1) \not\in \mathcal{D}] = 0.0841
\]

<table>
<thead>
<tr>
<th></th>
<th>S prob</th>
<th>S Spear</th>
<th>S corbs</th>
<th>S Shep</th>
<th>S both</th>
</tr>
</thead>
<tbody>
<tr>
<td>T</td>
<td>0.0000</td>
<td>0.0924</td>
<td>0.0624</td>
<td>0.5003</td>
<td>0.0924</td>
</tr>
<tr>
<td>H</td>
<td>0.0076</td>
<td>0.0000</td>
<td>0.4992</td>
<td>0.7826</td>
<td>0.5247</td>
</tr>
<tr>
<td>A</td>
<td>0.924</td>
<td>0.5038</td>
<td>0.0000</td>
<td>0.2676</td>
<td>0.5008</td>
</tr>
<tr>
<td>T</td>
<td>0.4997</td>
<td>0.2174</td>
<td>0.3733</td>
<td>0.0000</td>
<td>0.3683</td>
</tr>
<tr>
<td>T</td>
<td>0.9076</td>
<td>0.4753</td>
<td>0.4992</td>
<td>0.6317</td>
<td>0.0000</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>E95 prob</th>
<th>E95 Spear</th>
<th>E95 corbs</th>
<th>E95 Shep</th>
<th>E95 both</th>
</tr>
</thead>
<tbody>
<tr>
<td>T</td>
<td>0.0000</td>
<td>0.1483</td>
<td>0.0590</td>
<td>0.6156</td>
<td>0.1234</td>
</tr>
<tr>
<td>H</td>
<td>0.8517</td>
<td>0.0000</td>
<td>0.3793</td>
<td>0.6683</td>
<td>0.5191</td>
</tr>
<tr>
<td>A</td>
<td>0.5410</td>
<td>0.6262</td>
<td>0.0000</td>
<td>0.6482</td>
<td>0.5332</td>
</tr>
<tr>
<td>T</td>
<td>0.5844</td>
<td>0.3517</td>
<td>0.3517</td>
<td>0.0000</td>
<td>0.3517</td>
</tr>
<tr>
<td>T</td>
<td>0.8766</td>
<td>0.4809</td>
<td>0.4464</td>
<td>0.6483</td>
<td>0.0000</td>
</tr>
</tbody>
</table>

**Probability [Given \(r_{1-1}, r_0, r_1 \not\in \mathcal{D}\)]**

**Expectation**

<table>
<thead>
<tr>
<th></th>
<th>Spin</th>
<th>Variance</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\hat{\mu}_{\text{Spear}})</td>
<td>-0.0000</td>
<td>0.1034</td>
<td></td>
</tr>
<tr>
<td>(\hat{\mu}_{\text{corbs}})</td>
<td>0.8412</td>
<td>0.0736</td>
<td>0.0000</td>
</tr>
<tr>
<td>(\hat{\mu}_{\text{Shep}})</td>
<td>0.8993</td>
<td>0.0759</td>
<td>0.0000</td>
</tr>
</tbody>
</table>

\[\text{*i.e., } x_{1-1} = \mu - \sigma, \quad x_0 = \mu, \quad x_1 = \mu + \sigma\]
# Table 5.4

**Underlying Normal Distribution**

\[ \mu = 0.0000 \]
\[ \sigma = 2.0000 \]

\[ \Pr[(r_{-1}, r_0, r_1) \notin D] = 0.8014 \]

<table>
<thead>
<tr>
<th>Probability [Given ((r_{-1}, r_0, r_1) \notin D)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>IS BETTER THAN</td>
</tr>
<tr>
<td>( t_{\text{prob}} )</td>
</tr>
<tr>
<td>( t_{\text{prob}} )</td>
</tr>
<tr>
<td>( t_{\text{Spear}} )</td>
</tr>
<tr>
<td>( t_{\text{cors}} )</td>
</tr>
<tr>
<td>( t_{\text{Shep}} )</td>
</tr>
<tr>
<td>( t_{\text{both}} )</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Expectation</th>
<th>Variance</th>
<th>Correlation with ( \hat{t}_{\text{Spear}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \hat{t}_{\text{Spear}} )</td>
<td>-0.0000</td>
<td>0.1353</td>
</tr>
<tr>
<td>( t_{\text{Spear}} )</td>
<td>1.1253</td>
<td>0.0733</td>
</tr>
<tr>
<td>( t_{\text{cors}} )</td>
<td>1.1879</td>
<td>0.0730</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Probability [Given ((r_{-1}, r_0, r_1) \notin D)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>IS BETTER THAN</td>
</tr>
<tr>
<td>( t_{\text{ED95 prob}} )</td>
</tr>
<tr>
<td>( t_{\text{ED95 prob}} )</td>
</tr>
<tr>
<td>( t_{\text{ED95 Spear}} )</td>
</tr>
<tr>
<td>( t_{\text{ED95 cors}} )</td>
</tr>
<tr>
<td>( t_{\text{ED95 Shep}} )</td>
</tr>
<tr>
<td>( t_{\text{ED95 both}} )</td>
</tr>
</tbody>
</table>

\*i.e., \( x_{-1} = \mu \pm \frac{\sigma}{2} \), \( x_0 = \mu \), \( x_1 = \mu + \frac{\sigma}{2} \)
TABLE 5.5

UNDERLYING NORMAL DISTRIBUTION

\[ \mu = 0.5000 * \]
\[ \sigma = 0.8000 \]

\[ \Pr(\tau_{-1}^T, \tau_{0}^H, \tau_{1}^A) \neq 0] = 0.6696 \]

<table>
<thead>
<tr>
<th>IS BETTER THAN</th>
<th>( s_{\text{prob}} )</th>
<th>( s_{\text{Spear}} )</th>
<th>( s_{\text{corbs}} )</th>
<th>( s_{\text{Shep}} )</th>
<th>( s_{\text{both}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( s_{\text{prob}} )</td>
<td>0.0000</td>
<td>0.1482</td>
<td>0.0975</td>
<td>0.5703</td>
<td>0.1482</td>
</tr>
<tr>
<td>( s_{\text{Spear}} )</td>
<td>0.8516</td>
<td>0.0000</td>
<td>0.5174</td>
<td>0.6295</td>
<td>0.7006</td>
</tr>
<tr>
<td>( s_{\text{corbs}} )</td>
<td>0.9025</td>
<td>0.4826</td>
<td>0.0000</td>
<td>0.5173</td>
<td>0.4826</td>
</tr>
<tr>
<td>( s_{\text{Shep}} )</td>
<td>0.4297</td>
<td>0.3705</td>
<td>0.4827</td>
<td>0.0000</td>
<td>0.3705</td>
</tr>
<tr>
<td>( s_{\text{both}} )</td>
<td>0.8518</td>
<td>3.2994</td>
<td>0.5174</td>
<td>0.6295</td>
<td>0.0000</td>
</tr>
</tbody>
</table>

\[ \Pr(\hat{\tau}_{\text{Spear}} \text{ IS BETTER THAN } \hat{\tau}_{\text{prob}} | (\tau_{-1}^T, \tau_{0}^H, \tau_{1}^A) \neq 0] = 0.6785 \]

<table>
<thead>
<tr>
<th>EXPECTATION</th>
<th>VARIANCE</th>
<th>CORRELATION WITH ( \hat{\tau}_{\text{Spear}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \hat{\tau}_{\text{Spear}} )</td>
<td>0.4696</td>
<td>0.0840</td>
</tr>
<tr>
<td>( s_{\text{Spear}} )</td>
<td>0.6864</td>
<td>0.0716</td>
</tr>
<tr>
<td>( s_{\text{corbs}} )</td>
<td>0.7420</td>
<td>0.0716</td>
</tr>
</tbody>
</table>

*\( i.e., x = \mu - \frac{15}{8} \sigma, x = \mu - \frac{5}{8} \sigma, x = \mu + \frac{5}{8} \sigma \)
### Table 5.6

**Underlying Normal Distribution**

\[ \mu = 0.5000 \]
\[ \sigma = 1.0000 \]

\[ \Pr(r_{-1}, r_0, r_1 \neq d) = 0.7758 \]

<table>
<thead>
<tr>
<th></th>
<th>IS BETTER THAN</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \hat{\beta}_{\text{prob}} )</td>
<td>( \hat{\beta}_{\text{Spear}} )</td>
<td>( \hat{\beta}_{\text{corbs}} )</td>
</tr>
<tr>
<td>T</td>
<td>0.0000</td>
<td>0.2471</td>
<td>0.1456</td>
</tr>
<tr>
<td>( \hat{\beta}_{\text{Spear}} )</td>
<td>0.7529</td>
<td>0.0000</td>
<td>0.4110</td>
</tr>
<tr>
<td>H</td>
<td>0.8544</td>
<td>0.5890</td>
<td>0.0000</td>
</tr>
<tr>
<td>A</td>
<td>0.4211</td>
<td>0.1853</td>
<td>0.2675</td>
</tr>
<tr>
<td>T</td>
<td>0.7529</td>
<td>0.5549</td>
<td>0.4110</td>
</tr>
</tbody>
</table>

**Probability [Given \( r_{-1}, r_0, r_1 \neq d \)]

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ED5(_{\text{prob}} )</td>
<td>ED5(_{\text{Spear}} )</td>
<td>ED5(_{\text{corbs}} )</td>
<td>ED5(_{\text{Shep}} )</td>
</tr>
<tr>
<td>T</td>
<td>0.0000</td>
<td>0.2926</td>
<td>0.2435</td>
<td>0.4270</td>
</tr>
<tr>
<td>( \hat{\beta}_{\text{Spear}} )</td>
<td>0.7074</td>
<td>0.0000</td>
<td>0.4393</td>
<td>0.5607</td>
</tr>
<tr>
<td>H</td>
<td>0.7565</td>
<td>0.5607</td>
<td>0.0000</td>
<td>0.5607</td>
</tr>
<tr>
<td>A</td>
<td>0.5730</td>
<td>0.4393</td>
<td>0.4393</td>
<td>0.0000</td>
</tr>
<tr>
<td>T</td>
<td>0.7577</td>
<td>0.4453</td>
<td>0.4353</td>
<td>0.5607</td>
</tr>
</tbody>
</table>

**Probability [Given \( r_{-1}, r_0, r_1 \neq d \)]

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ED95(_{\text{prob}} )</td>
<td>ED95(_{\text{Spear}} )</td>
<td>ED95(_{\text{corbs}} )</td>
<td>ED95(_{\text{Shep}} )</td>
</tr>
<tr>
<td>T</td>
<td>0.0000</td>
<td>0.3686</td>
<td>0.3467</td>
<td>0.6485</td>
</tr>
<tr>
<td>( \hat{\beta}_{\text{Spear}} )</td>
<td>0.6314</td>
<td>0.0000</td>
<td>0.2797</td>
<td>0.7230</td>
</tr>
<tr>
<td>H</td>
<td>0.6533</td>
<td>0.7203</td>
<td>0.0000</td>
<td>0.7205</td>
</tr>
<tr>
<td>A</td>
<td>0.3515</td>
<td>0.2770</td>
<td>0.2795</td>
<td>0.0000</td>
</tr>
<tr>
<td>T</td>
<td>0.6325</td>
<td>0.5582</td>
<td>0.2941</td>
<td>0.7230</td>
</tr>
</tbody>
</table>

\[ \ast \text{ i.e., } x_{-1} = \mu - \frac{r}{2} \sigma, \quad x_{0} = \mu - \frac{r}{2} \sigma, \quad x_{1} = \mu + \frac{r}{2} \sigma \]
**TABLE 5.7**

**UNDERLYING NORMAL DISTRIBUTION**

\[
\mu = 0.5000 \quad \text{and} \quad \sigma = 2.0000
\]

\[
\Pr[(r_{-1}, r_0, r_1) \notin D] = 0.7875
\]

<table>
<thead>
<tr>
<th>Probability [GIVEN ((r_{-1}, r_0, r_1) \notin D)]</th>
<th>(\hat{\mu}_{prob})</th>
<th>(\hat{\mu}_{Spear})</th>
<th>(\hat{\mu}_{corbs})</th>
<th>(\hat{\mu}_{Shep})</th>
<th>(\hat{\mu}_{both})</th>
</tr>
</thead>
<tbody>
<tr>
<td>(T_{prob})</td>
<td>0.0000</td>
<td>0.6351</td>
<td>0.6020</td>
<td>0.7538</td>
<td>0.6351</td>
</tr>
<tr>
<td>(T_{Spear})</td>
<td>0.3649</td>
<td>0.0000</td>
<td>0.0000</td>
<td>1.0000</td>
<td>0.0735</td>
</tr>
<tr>
<td>(T_{corbs})</td>
<td>0.3980</td>
<td>1.0000</td>
<td>0.0000</td>
<td>1.0000</td>
<td>1.0000</td>
</tr>
<tr>
<td>(T_{Shep})</td>
<td>0.2462</td>
<td>0.0000</td>
<td>0.0000</td>
<td>0.0000</td>
<td>0.0000</td>
</tr>
<tr>
<td>(T_{both})</td>
<td>0.3649</td>
<td>0.9265</td>
<td>0.0000</td>
<td>1.0000</td>
<td>0.0000</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Probability [GIVEN ((r_{-1}, r_0, r_1) \notin D)]</th>
<th>(\hat{\mu}_{prob})</th>
<th>(\hat{\mu}_{Spear})</th>
<th>(\hat{\mu}_{corbs})</th>
<th>(\hat{\mu}_{Shep})</th>
<th>(\hat{\mu}_{both})</th>
</tr>
</thead>
<tbody>
<tr>
<td>(H_{prob})</td>
<td>(\hat{\mu}_{Spear})</td>
<td>0.2734</td>
<td>0.1312</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(H_{Spear})</td>
<td>1.1062</td>
<td>0.0762</td>
<td>-0.2018</td>
<td></td>
<td></td>
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<tr>
<td>(H_{corbs})</td>
<td>1.1641</td>
<td>0.0759</td>
<td>-0.2087</td>
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<td></td>
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<tr>
<td>(H_{Shep})</td>
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<td>0.6355</td>
<td>0.6160</td>
<td>0.7372</td>
<td>0.6341</td>
</tr>
<tr>
<td>(H_{both})</td>
<td>0.3605</td>
<td>0.0000</td>
<td>0.0000</td>
<td>1.0000</td>
<td>0.0735</td>
</tr>
</tbody>
</table>

\[\text{Expectation} \quad \text{Variance} \quad \text{Correlation with } \hat{\mu}_{Spear}\]

\[
\hat{\mu}_{Spear} = 0.2734, \quad \hat{\mu}_{corbs} = 1.1062, \quad \hat{\mu}_{Shep} = 1.1641, \quad \hat{\mu}_{both} = 0.0000
\]

\*i.e., \(x_{-1} = \mu - \frac{3\sigma}{4}\), \(x_0 = \mu - \frac{\sigma}{4}\), \(x_1 = \mu + \frac{\sigma}{4}\)
As an additional method of comparison, we use a slightly modified version of the worth function, which was introduced to quantal bioassay and had its merits put forth in an article by Bross [1]. Given an unknown parameter \( \omega \) (i.e., \( \mu \), \( \sigma \), or a percentage point) and an estimator \( \hat{\omega} \), we define the estimator's worth as a function of tolerance.

\[
\text{Worth}_{\hat{\omega}}(\text{Tolerance}) = \text{Worth}_{\hat{\omega}}(\delta) = \Pr[|\hat{\omega} - \omega| \leq \delta | (r_{-1}, r_0, r_1) \not\in \emptyset]
\]

(i.e., for any specified tolerance, the worth of an estimator is its probability of estimating the desired parameter within the tolerance).

Figures 5.1-5.6 show worth function plots for each of our six cases. Each figure has four graphs: one for \( \mu \) estimators, one for \( \sigma \) estimators, and one for each of the two percentiles that were evaluated for the case. In order that this process not become too cumbersome to visualize, for \( \sigma \) and percentile comparisons the maximum likelihood estimator is compared only with the applicable Spearman-type estimator using both correction factors. This selection is based on the theoretical considerations of Chapter 4.

5.5 CONCLUSIONS

Examination of the preceding tables and figures yields the following conclusions:

a) Since, for cases \((\mu = 0, \sigma = .8), (\mu = 0, \sigma = 1), \) and \((\mu = .5, \sigma = 1), \)

\[
\text{Worth}_{\text{both}}(\delta) \geq \text{Worth}_{\text{prob}}(\delta) \quad \forall \delta > 0
\]

(with strict inequality \( \forall \delta \in (0.003, 2.98) \)),
Figure 5.3
\( \mu = 0, \sigma = .8 \)

(a) \( \mu \) Estimates
Spearman and Probit

(b) \( \sigma \) Estimates
Spearman (with both corrections) and Probit

(c) HD95 Estimates
Spearman (with both corrections) and Probit

(d) HD95 Estimates
Spearman (with both corrections) and Probit
FIGURE 5.2
\(\mu = 0, \sigma = 1\)

WORTH FUNCTION GRAPHS

A. \(\hat{n}_{\text{Spear}}\) and \(\hat{n}_{\text{prob}}\)

B. \(n_{\text{both}}\) and \(n_{\text{prob}}\)

C. HD95 estimates

D. HD99 estimates
FIGURE 5.3
μ = 0, σ = 2

MULTIPLICATION GRAPHS

A. \( \mu \) ESTIMATES
SPEARMAN AND PROBIT

B. \( \sigma \) ESTIMATES
SPEARMAN (WITH BOTH CORRECTIONS) AND PROBIT

C. HD95 ESTIMATES
SPEARMAN (WITH BOTH CORRECTIONS) AND PROBIT

D. HD99 ESTIMATES
SPEARMAN (WITH BOTH CORRECTIONS) AND PROBIT

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FIGURE 5.5
\[ \mu = .5, \sigma = 1 \]

WORTH FUNCTION CHECKS

A. SPEARMAN AND PROBIT
   - \( \hat{\beta}_{\text{Spear}} \)
   - \( \hat{\beta}_{\text{prob}} \)

B. SPEARMAN (WITH BOTH CORRECTIONS) AND PROBIT
   - \( \hat{\beta}_{\text{both}} \)
   - \( \hat{\beta}_{\text{prob}} \)

C. EDDS ESTIMATES
   SPEARMAN (WITH BOTH CORRECTIONS) AND PROBIT
   - \( \hat{\beta}_{\text{both}} \)
   - \( \hat{\beta}_{\text{prob}} \)

D. EDDS ESTIMATES
   SPEARMAN (WITH BOTH CORRECTIONS) AND PROBIT
   - \( \hat{\beta}_{\text{both}} \)
   - \( \hat{\beta}_{\text{prob}} \)
and for \((\mu = 0, \sigma = 1)\),

\[
\text{Worth}_{\text{Ed}_95}^{\text{both}} (\delta) \geq \text{Worth}_{\text{ED}_95}^{\text{prob}} (\delta) \quad \forall \delta > 0,
\]

\[
\text{Worth}_{\text{Ed}_99}^{\text{both}} (\delta) \geq \text{Worth}_{\text{ED}_99}^{\text{prob}} (\delta) \quad \forall \delta > 0
\]

(with strict inequality \(\forall \delta \in (0.015, 6.22)\)),

for some dose placements, the probit estimator is inferior to
Spearman estimator in the worth function sense uniformly over all
tolerance levels.

b) The Spearman-type estimator of the standard deviation exhibits
deteriorization for \(\sigma\) large (i.e., finer dose placement) caused
by its "assumption" \(p_{k-1} = 0, p_{k+1} = 1\).

c) Based on the given study, in general, the Spearman-type estimators
are at least as good as the maximum likelihood estimators.

d) With substantial probability in reasonable circumstances, the
Spearman-type method will yield sensible estimates when the probit
method cannot.

e) Because of their theoretical merit and simplicity, the Spearman-
type estimates should be used in practice.
Lemma 1.  \[ \sum_{i=1}^{\infty} \sum_{r=0}^{\infty} a_{r} x_{i}^{r} (1-F_{i}) \] \[ \leq \infty \] \( \forall \) real \( a_{r} \), \( b_{r} \) (A1)

and \[ \sum_{i=0}^{\infty} \sum_{r=0}^{\infty} b_{r} x_{-i}^{r} F_{r} \] \[ \leq \infty \] (A2)

provided that the fourth moment of \( F \) exists.

**Proof.** Let \( x_{j} \) be the smallest \( x_{i} \geq 1 \) and let \( C = \sum_{i=1}^{J} a_{3} x_{i}^{3} (1-F_{i}) \).

Then

\[ \sum_{i=1}^{\infty} a_{3} x_{i}^{3} (1-F_{i}) \leq C \leq \frac{|a_{3}|}{d} \int_{x_{j}}^{\infty} (x+d)^{3} [1-F(x)] \, dx \]

\[ = C \leq \frac{|a_{3}|}{d} \int_{x_{j}}^{\infty} f(y) \int_{x_{j}}^{\infty} (x+d)^{3} \, dx \, dy \]

\[ = C \leq \frac{|a_{3}|}{d} \left[ \frac{1}{4} \int_{x_{j}}^{\infty} f(y) \, dy + \int_{x_{j}}^{\infty} f(y) \, dy \right] \]

\[ + \frac{3d^{2}}{2} \int_{x_{j}}^{\infty} f(y) \, dy + \int_{x_{j}}^{\infty} yf(y) \, dy \]

\[ + \left( \frac{x_{j}^{4}}{4} + \frac{dx_{j}^{3} + \frac{3d^{2} x_{j}^{2}}{2} + \frac{3 dx_{j}^{3}}{2}}{x_{j}} \right) \int_{x_{j}}^{\infty} f(y) \, dy \]

\[ < \infty \] since the first 4 moments of \( F(x) \) exist. (A3)
\[ \left| \sum_{i=1}^{\infty} a_i x_i^2 (1-F_i) \right| \leq \left| \sum_{i=1}^{J-1} a_i x_i^2 (1-F_i) \right| + \left| \sum_{i=J}^{\infty} a_i x_i^2 (1-F_i) \right| < \infty \text{ by (A3).} \]

Similarly, \[ \left| \sum_{i=1}^{\infty} a_i x_i^2 (1-F_i) \right| < \infty \text{ for } \ell = 1 \text{ and } 0 \text{ and so (A1) follows.} \]

Expression (A2) can be verified in like manner.

**Lemma 2.** Assuming that \( F \) is an everywhere differentiable c.d.f. of the form \( F^* [(x-u)/c] \) with symmetric, continuous density, \( f \), and finite variance, and that \( \exists y^* < \infty \) \( \exists \)

\[ \frac{d}{dx} [(x-u) f(x)] \bigg|_{x=y} < 0 \quad \forall y > y^* , \tag{A4} \]

let \( \mu_i = \ln \left( \frac{r_i}{x_i} \right) + \ln F_i + (n-r_i) \ln (1-F_i), \quad (i = 0, \pm 1, \pm 2, \ldots). \)

Then

\[ \frac{\partial}{\partial \sigma^2} \sum_{i=0}^{\infty} \frac{\partial \mu_i}{\partial \sigma^2} = \sum_{i=0}^{\infty} \frac{\partial \mu_i}{\partial \sigma^2} \sigma^2 > 0 \text{ w.p. 1.} \]

**Proof.** Looking only at \( \sum_{i}^{\infty} \) since \( \sum_{i=-\infty}^{-1} \) works analogously and combines to give the desired result, let \( \epsilon > 0 \) be given and consider \( 0 < a < b < \infty \) with \( a \) and \( b \) otherwise arbitrary.

From the stated hypotheses, it follows that \( \mu_0, \mu_1, \mu_2, \ldots \) each have a partial derivative \( \forall \sigma^2 \in [a,b] \) and that \( \partial \mu_i / \partial \sigma^2 \)

is continuous on \([a,b]\) for \( i = 0, 1, 2, \ldots \). Also, (13)

implies that \( \sum_{i=0}^{\infty} \mu_i \) converges on \([a,b]\) w.p. 1. Then

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by (2) let $J_{1}$ be the smallest integer $\exists p_{j} = 1 \ \forall j \geq J_{1}$;

let $J_{2}$ be the smallest $j \exists x_{j} \geq \mu$;

let $J_{3}$ be the smallest $j \exists \int_{x_{j-1}}^{x_{j}} \frac{x - \mu}{\sigma} f(x) \, dx < \frac{\sigma^{2} \delta x}{n}$.

Condition (A4) implies that for the sequence $\frac{x_{0} - \mu}{\sigma}, \frac{x_{1} - \mu}{\sigma}, \frac{x_{2} - \mu}{\sigma}, \ldots$

$$\exists J_{4} \ni \forall j \geq J_{4}, \sum_{i=j}^{\infty} \frac{x_{i} - \mu}{\sigma} f(x_{i}) \leq \frac{1}{d} \int_{x_{j-1}}^{x_{j}} \frac{x - \mu}{\sigma} f(x) \, dx.$$  

Let $J = \max\{J_{1}, J_{2}, J_{3}, J_{4}\}$. Then for $j \geq J$ and $\sigma^{2} \in [a, b]$,

$$\left| \sum_{i=0}^{\infty} \frac{\partial \mu_{i}}{\partial \sigma} + \sum_{i=0}^{j-1} \frac{\partial \mu_{i}}{\partial \sigma^{2}} \right|$$

$$= \left| \sum_{i=j}^{\infty} \frac{F_{i}(r_{i} - nF_{i})}{\sigma} \right|$$

$$= \left| \frac{n}{2\sigma} \sum_{i=j}^{\infty} \frac{x_{i} - \mu}{\sigma} \frac{f(x_{i})(p_{i} - F_{i})}{F_{i}(1 - F_{i})} \right|$$

$$= \left| \frac{n}{2\sigma} \sum_{i=j}^{\infty} \frac{x_{i} - \mu}{\sigma} \frac{f(x_{i})(1 - F_{i})}{F_{i}(1 - F_{i})} \right|$$

since $j \geq J_{1}$

$$\leq \left| \frac{n}{\sigma} \sum_{i=j}^{\infty} \frac{x_{i} - \mu}{\sigma} f(x_{i}) \right|$$

since $j \geq J_{2}$

$$\leq \left| \frac{n}{\sigma d} \int_{x_{j-1}}^{x_{j}} \frac{x - \mu}{\sigma} f(x) \, dx \right|$$

since $j \geq J_{3}$

$$< \varepsilon$$

since $j \geq J_{3}$.  

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Hence, \( \sum_{i=0}^{\infty} (\partial u_i/\partial \sigma^2) \) converges uniformly on \([a, b]\) and so by Theorem 9.5B of Goldberg [13] and by the fact that \(a\) and \(b\) were arbitrary, the summation/differentiation interchange is valid \(\forall \sigma^2 > 0.\)

**Lemma 3.** Let \(\{\theta_{mj}, j = 0, \pm 1, \pm 2, \ldots; m = 1, 2, 3, \ldots\}\) be a double array of complex numbers satisfying:

(i) \(\lim_{m \to \infty} \sup_{j} |\theta_{mj}| = 0\)

(ii) \(\sum_{j=-\infty}^{\infty} |\theta_{mj}| \leq S < \infty\) where \(S\) does not depend on \(m\)

(iii) \(\lim_{m \to \infty} \left( \sum_{j=-\infty}^{\infty} \theta_{mj} \right) = \theta\) where \(\theta\) is a (finite) complex number.

Then

\[
\lim_{m \to \infty} \left[ \prod_{j=-\infty}^{\infty} (1 + \theta_{mj}) \right] = e^{\theta}. \tag{A5}
\]

**Proof.** By (i), \(\exists m_0 \geq 0\) if \(m \geq m_0\), then \(|\theta_{mj}| \leq \frac{1}{2} \forall j, \) so that \(1 + \theta_{mj} \neq 0\). Considering only such large values of \(m\), denote by \(\log(1 + \theta_{mj})\) the determination of logarithm with an angle in \((-\pi, \pi]\). Thus

\[
\log(1 + \theta_{mj}) = \theta_{mj} + \Lambda_{mj} |\theta_{mj}|^2
\]

with
\[ |\log(1 + \theta_{m_j}) - \theta_{m_j}| = \sum_{k=2}^{\infty} \frac{(-1)^{k-1}}{k} \theta_{m_j}^k \]
\[ \leq \frac{1}{2} \theta_{m_j}^2 \sum_{k=2}^{\infty} \left( \frac{1}{2} \right)^{k-2} = \theta_{m_j}^2 \]

\[ \Rightarrow |\Lambda_{m_j}| \leq 1. \]

Hence,
\[ \sum_{j=-\infty}^{\infty} \log(1 + \theta_{m_j}) = \sum_{j=-\infty}^{\infty} \theta_{m_j} + \Lambda' \sum_{j=-\infty}^{\infty} |\theta_{m_j}|^2 \]

where \(|\Lambda'| \leq 1\). \hfill (A6)

Now,
\[ \sum_{j=-\infty}^{\infty} |\theta_{m_j}|^2 \leq \sup_{j} |\theta_{m_j}| \sum_{j=-\infty}^{\infty} |\theta_{m_j}| \]
\[ \leq S \sup_{j} |\theta_{m_j}| \rightarrow 0 \quad \text{as} \quad m \rightarrow \infty \]

by (i) and (ii).

So, we may use the above and (iii) in (A6) to obtain
\[ \lim_{m \rightarrow \infty} \left[ \sum_{j=-\infty}^{\infty} \log(1 + \theta_{m_j}) \right] = \theta \]

from which (A5) follows.
Theorem 1. Let \( \{Y_{m,j}, j = 0, \pm 1, \pm 2, \ldots; m = 1, 2, 3, \ldots\} \) be a double array of random variables. Let

\[
\alpha_{m,j} = E(Y_{m,j}), \quad \sigma_{m,j}^2 = \text{Var}(Y_{m,j}) \quad \text{and} \quad \gamma_{m,j} = E(|Y_{m,j}|^3)
\]

and assume

\[
\alpha_{m,j} = 0 \quad \forall \ m, \ \forall j \quad \text{(A7)}
\]

\[
\sum_{j=-\infty}^{\infty} \sigma_{m,j}^2 = 1 \quad \forall \ m \quad \text{(A8)}
\]

\( \gamma_{m,j} \) is finite \( \forall \ m, \ \forall j \)

and

\[
\Gamma_m = \sum_{j=-\infty}^{\infty} \gamma_{m,j} \rightarrow 0 \quad \text{as} \quad m \rightarrow \infty . \quad \text{(A9)}
\]

Then \( \sum_{j=-\infty}^{\infty} Y_{m,j} \) converges in dist. to Normal(0,1).

Proof. By (A7) and (A8) and Thm. 2.3, p. 108 of Doob [8],

\[
\sum_{j=-\infty}^{\infty} Y_{m,j} \quad \text{is a random variable} \quad \forall \ m.
\]

By Liapounov's inequality and (A9)

\[
\sup_j \sigma_{m,j}^3 \leq \sup_j \gamma_{m,j} \leq \Gamma_m \rightarrow 0 \quad \text{as} \quad m \rightarrow \infty . \quad \text{(A10)}
\]
Then by Theorem 6.4.2 of Chung [3]

$$
\varphi_{m,j}(t) = 1 - \frac{1}{2} \sigma_{m,j}^2 t^2 + \Lambda_{m,j} \gamma_{m,j} |t|^3
$$

where $|\Lambda_{m,j}| \leq 1/6$.

Now we apply Lemma 3 for any fixed $t$ to

$$
\theta_{m,j} = -\frac{1}{2} \sigma_{m,j}^2 t^2 + \Lambda_{m,j} \gamma_{m,j} |t|^3.
$$

$$
\sup_j |\theta_{m,j}| \leq \frac{t^2}{2} \sup_j \sigma_{m,j}^2 + |t|^3 \sup_j \gamma_{m,j} \to 0 \text{ as } m \to \infty \text{ by (A10)}
$$

and so (i) of Lemma 3 holds.

Condition (ii) is satisfied since by (A8)

$$
\sum_{j=-\infty}^{\infty} |\theta_{m,j}| \leq \frac{t^2}{2} + |t|^3 \Gamma_m
$$

which is bounded by (A10).

Lastly, condition (iii) holds because

$$
\sum_{j=-\infty}^{\infty} \theta_{m,j} = -\frac{t^2}{2} + \Lambda |t|^3 \Gamma_m \text{ where } |\Lambda| \leq \frac{1}{6}
$$

$$
\to -\frac{t^2}{2} \text{ as } m \to \infty \text{ by (A10)}.
$$
Consequently,

\[ \lim_{m \to \infty} \Pi_{j=-\infty}^{\infty} \phi_{y_{m,j}}(t) = e^{-t^2/2} \]

from which the desired conclusion follows since

\[ \sum_{j=-\infty}^{\infty} Y_{m,j} \]

is the characteristic function of

\[ Y_{m,j} \]
REFERENCES


