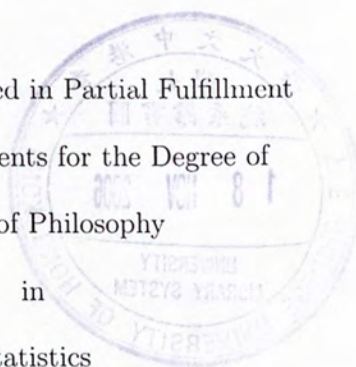


Confidence Intervals for the Risk Ratio under Inverse Sampling

IP Wing Yiu

A Thesis Submitted in Partial Fulfillment
of the Requirements for the Degree of
Master of Philosophy
in
Statistics



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Abstract of thesis entitled:

Confidence Intervals for the Risk Ratio under Inverse Sampling

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ABSTRACT

The basic principle of inverse sampling is that one continues to sample subjects until a predetermined number of index subjects with certain attribute is observed. It has been proposed as an alternative to the commonly used binomial sampling when the subjects arrive sequentially, when the studied subjects are rare, and when the maximum likelihood estimators of some epidemiologic indices are undefined. In this thesis, large sample behaviors of two statistics for the risk ratio under inverse sampling are considered. The asymptotic distributions of the two statistics are derived on the basis of Fieller's Theorem and the delta method with the logarithmic transformation respectively. Then the confidence interval of the risk ratio is constructed. Sample-based estimates and restricted maximum likelihood estimates are used for the confidence interval construction. To evaluate the performance of these methods, simulation is used to compare the actual coverage probability with the confidence level for each method and to estimate the expected length of the corresponding confidence interval in a variety of situations.

摘要

逆抽樣方法的基本原理是一直抽樣，直到有某種特徵的樣本達到預定的數目。在以下三種情況，逆抽樣方法被提議為代替普遍使用的二項抽樣方法：一、樣本是順序出現；二、有某種特徵的樣本是稀有的；三、沒有定義流行病學指數的極大概似估計量。在這篇論文中，考慮了兩個關於風險比率（Risk Ratio）的統計量。這兩個統計量的漸近分佈分別由菲勒爾定理及使用 δ 法的對數變換所推導出來。接著，我們計算了風險比率的置信區間。置信區間的計算使用了基於樣本的估計值及約束極大概似估計值。為了評價這些方法，我們使用了模擬方法，根據不同情況，比較實際範圍概率與置信區間的分別。另外，也估計置信區間的期望長度。

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1.1 Introduction

The purpose of this book is to provide a comprehensive treatment of the theory and practice of statistical inference. The book is divided into two main parts: the first part deals with the theory of statistical inference, and the second part deals with the practice of statistical inference. The first part is divided into two main sections: the first section deals with the theory of estimation, and the second section deals with the theory of testing. The second part is divided into two main sections: the first section deals with the practice of estimation, and the second section deals with the practice of testing. The book is written in a clear and concise style, and it is suitable for use as a textbook or as a reference work.

1.2 Background

The background of this book is the theory of statistical inference. The theory of statistical inference is a branch of statistics that deals with the methods of drawing conclusions from data. The theory of statistical inference is based on the theory of probability, and it is used to make decisions about the parameters of a population based on a sample of data. The theory of statistical inference is a very important part of statistics, and it is used in many different fields, such as biology, psychology, and economics. The theory of statistical inference is a very complex subject, and it is not possible to cover all of the details of the theory in this book. However, the book does provide a comprehensive overview of the theory, and it is suitable for use as a textbook or as a reference work.

Chapter 1

Introduction

1.1 Introduction

Inverse sampling is a sampling method that we continue to collect samples until a predetermined number of cases r are obtained. By using inverse sampling, we can collect appropriate number of cases in our samples. It is used when an event is rare because it is quite difficult to obtain enough samples by using binomial sampling.

1.2 Background

Chi (1980) has developed different procedures for testing homogeneity for more than two comparison groups under negative binomial distribution.

George and Elston (1993) found that using the inverse sampling instead of binomial sampling could shorten the length of the confidence interval. They derived the confidence limits which based on the geometric distribution and based on the binomial distribution respectively. Although the lower limits are the same, the upper limits are smaller for the geometric distribution.

Lui (1995) discussed three simple interval estimates for the risk ratio under inverse sampling. The estimates are derived on the basis of Fieller's Theorem, the delta method with the logarithmic transformation and an F-test statistic proposed by Bennett (1981). He found that the method with the logarithmic transformation is better than or equivalent to the other two methods in terms of coverage probability and expected length.

Lui (1997) established equivalence with respect to the risk ratio under inverse sampling. An exact and two asymptotic procedures for sample size determination are derived.

Newcombe (1998) evaluated several existing unconditional methods for setting confidence intervals for the difference between binomial proportions and found that confidence intervals constructed by sample-based test statistics perform unsatisfactorily.

Lui (1999) discussed on interval estimation of simple difference under inverse sampling. He developed three asymptotic interval estimators on the basis of the maximum likelihood estimator, the uniformly minimum variance unbiased estimator and the asymptotic likelihood ratio test. All the three methods perform well even when the predetermined number of cases r is small and when r is large, three methods are essentially equivalent.

Tang, Tang, Chan and Chan (2002) discussed sample size determination for establishing equivalence or non-inferiority of two proportions in match-pairs design. They derived sample size formulas for hypothesis testing and confidence interval estimation.

1.3 Objective

In this thesis, we follow Lui's work (1995, 1997) to perform equivalence/non-inferiority testing between a standard procedure and a new procedure. We are going to derive reliable test statistics for risk ratio R under inverse sampling. These test statistics may possess reliable asymptotic properties. By using these test statistics, confidence intervals are constructed with sample-based estimates and restricted maximum likelihood estimates respectively. By using simulation, we are going to compare the difference between using sample-based estimates and restricted maximum likelihood estimates.

1.4 Scope of the thesis

The thesis is organized as follow. In Chapter 2, we will have a more details description on inverse sampling and will introduce non-inferiority hypothesis. In Chapter 3, we will discuss two test statistics. One is dervied on the basis of Fieller's Theorem. The other one is derived on the basis of delta method with logarithm transformation. In Chapter 4, we will construct the test based confidence interval for risk ratio R by using sample-based estimates and restricted

maximum likelihood estimates respectively. In Chapter 5, we will use simulation to evaluate the performance of the test based confidence interval by using coverage probability and expected length. Chapter 6 is the conclusion of this thesis.

Chapter 2

Basic Concepts

2.1 Inverse Sampling

Suppose, when an event occurs, it is followed by a certain number of trials of a binomial sampling. In this chapter, we introduce a generalized version of binomial sampling. Inverse sampling is a sequential method for collecting samples until a predetermined number of events is obtained. By using inverse sampling, we are able to generate random numbers from the r -spare. We are going to derive the random number X from the r -spare with probability that it is a success p . The binomial distribution $B(n, p)$ among other negative binomial distribution with searching r times success.

$$P(X = x) = \binom{x-1}{r-1} p^r (1-p)^{x-r}$$

In the literature, a sample is drawn through r times until r success is observed. In this chapter, we are going to derive the random number X from the r -spare with probability that it is a success p .

Chapter 2

Basic Concepts

2.1 Inverse Sampling

Sometimes, when an event is rare, it is quite difficult to obtain enough cases by using binomial sampling. In this situation, we may employ inverse sampling instead of binomial sampling. Inverse sampling is a sampling method that we continue to collect samples until a predetermined number of cases r are obtained. By using inverse sampling, we ensure an appropriate number of cases included in the sample. We are going to observe the number of non cases, Y . Let π be the probability that it is a case in a trial. Then the random quantity Y is well known to be negative binomial distributed with probability mass function.

$$P(Y = y|\pi) = \binom{r + y - 1}{y} \pi^r (1 - \pi)^y, \quad y = 0, 1, 2, \dots$$

In this thesis, we attempt to extend the work of Lui (1995, 1997) to study the equivalence/ non-inferiority tests between a standard procedure and a new procedure.

2.2 Equivalence/ Non-inferiority Testing

Lui (1997) proposed the utility of inverse sampling in establishing equivalence/non-inferiority with respect to the risk ratio. He suggested his proposed methodology to be used in health care studies in order to establish equivalence between two study groups. The purpose was to examine whether a less toxic, easier to administer, or less expensive procedure is medically non-inferior to a standard procedure.

Suppose π_S and π_N are the probability for a randomly selected subject from the standard procedure and the new procedure respectively, for which have the disease of interest. For each procedure i ($i = S, N$), independent inverse sampling is employed. The following table summarizes the result of the samples.

Procedure	<i>New</i>	<i>Standard</i>
Non cases	y_N	y_S
Predetermined number of cases	r_N	r_S
Total	n_N	n_S

After collecting the samples, in order to compare these two procedures, we focus on the risk ratio, which is the ratio between new procedure and standard procedure, it is denoted as $R = \frac{\pi_N}{\pi_S}$. We want to test the non-inferiority hypothesis:

$$H_0 : R \leq R_0$$

versus the alternative hypothesis

$$H_1 : R > R_0$$

where $0 \leq R_0 \leq 1$, is a pre-specified quantity. In medical study, non-inferiority means that the new procedure is not worse than the standard procedure. For

example, Lui (1997) described a health care trials in which one hopes to establish no deterioration in the quality of patient care provided by nurse-practioners compared with physicians. In this case, non-inferior means that the quality provided by the nurse-practioners are not worse than that of physicians. For reducing cost, physicians can be replaced by nurse-practioners as service provided by nurse-practioners supposed to be cost and time effective.

3.1 Introduction

Suppose two independent events X and Y are observed. Let X and Y be random variables with probability distributions $F_X(x)$ and $F_Y(y)$ respectively. Let $Z = X + Y$ be the sum of X and Y . The probability density function of Z is given by the convolution of $F_X(x)$ and $F_Y(y)$. The characteristic function of Z is given by the product of the characteristic functions of X and Y .

3.2 Test Statistics for Risk Ratio

Suppose X and Y are independent random variables with probability distributions $F_X(x)$ and $F_Y(y)$ respectively. Let $Z = X + Y$ be the sum of X and Y . The probability density function of Z is given by the convolution of $F_X(x)$ and $F_Y(y)$. The characteristic function of Z is given by the product of the characteristic functions of X and Y .

Chapter 3

Inference for Risk Ratio

3.1 Introduction

Suppose two independent inverse samples are collected from the new and standard procedures respectively. Let π_N and π_S be the probabilities that there is a case from these two procedures and $R = \frac{\pi_N}{\pi_S}$ be the efficiency of the new procedure compare to the standard procedure which is our parameter of interest. In this chapter, we will introduce two test statistics which are useful for the inference of R .

3.2 Test Statistics for Risk Ratio

As mentioned before, the numbers of non-cases, $Y_i, i = N, S$ collected in sample i are

$$P(Y_i = y_i | \pi_i) = \binom{y_i + r_i - 1}{y_i} \pi_i^{r_i} (1 - \pi_i)^{y_i}.$$

The random variable Y_i can be written as the sum of r_i independent random variables $(X_{ij} - 1)$, where X_{ij} follows a geometric distribution with mean $\frac{1}{\pi_i}$ and

variance $\frac{(1-\pi_i)}{\pi_i^2}$.

$$Y_i = \sum_{j=1}^{r_i} (X_{ij} - 1) \quad (3.1)$$

where $X_{ij} \sim \text{Geometric}(\pi_i)$.

Following Fieller's Theorem (Fleiss, 1986), we consider the random variable:

$$\bar{Z} = \bar{X}_S - R\bar{X}_N \quad (3.2)$$

where $\bar{X}_i = \frac{\sum_{j=1}^{r_i} X_{ij}}{r_i} = \frac{Y_i}{r_i} + 1$, $R = \frac{E(\bar{X}_S)}{E(\bar{X}_N)} = \frac{\pi_N}{\pi_S}$, for $i = N, S$

If r_i is large, $i = N, S$, based on Central Limit Theorem, \bar{Z} would be asymptotic normal distributed with mean

$$\begin{aligned} E(\bar{Z}) &= E(\bar{X}_S) - RE(\bar{X}_N) \\ &= \frac{1}{\pi_S} - \frac{\pi_N}{\pi_S} \frac{1}{\pi_N} \\ &= 0 \end{aligned} \quad (3.3)$$

and variance

$$\begin{aligned} \text{Var}(\bar{Z}) &= \text{Var}(\bar{X}_S - R\bar{X}_N) \\ &= \text{Var}(\bar{X}_S) + R^2 \text{Var}(\bar{X}_N) \\ &= \frac{1 - \pi_S}{r_S \pi_S^2} + R^2 \left(\frac{1 - \pi_N}{r_N \pi_N^2} \right). \end{aligned} \quad (3.4)$$

We then have the test statistic T_1 :

$$T_1 = \frac{\bar{Z}}{\sqrt{\text{Var}(\bar{Z})}}. \quad (3.5)$$

However, π_S and π_N are unknown and we can replace them by any consistent estimators of π_S and π_N .

Obviously, sample proportion $p_i = \frac{r_i}{Y_i+r_i}$ is an estimator of π_i , $i = N, S$.

By delta method,

$$\begin{aligned} E(p_i) &\approx \frac{r_i}{\frac{r_i(1-\pi_i)}{\pi_i} + r_i} \\ &= \frac{r_i}{\frac{r_i - r_i\pi_i + r_i\pi_i}{\pi_i}} \\ &= \pi_i, \end{aligned} \tag{3.6}$$

$$\begin{aligned} Var(p_i) &\approx \left\{ \frac{-r_i}{\left[\frac{r_i(1-\pi_i)}{\pi_i} + r_i \right]^2} \right\}^2 Var(Y_i) \\ &= \left[\frac{-r_i}{\left(\frac{r_i - r_i\pi_i + r_i\pi_i}{\pi_i} \right)^2} \right]^2 \frac{r_i(1-\pi_i)}{\pi_i^2} \\ &= \frac{r_i^2}{\pi_i^4} \frac{r_i(1-\pi_i)}{\pi_i^2} \\ &= \frac{\pi_i^4}{r_i^2} \frac{r_i(1-\pi_i)}{\pi_i^2} \\ &= \frac{\pi_i^2(1-\pi_i)}{r_i}, \end{aligned} \tag{3.7}$$

where

$$\begin{aligned} E(Y_i) &= \frac{r_i(1-\pi_i)}{\pi_i}, \\ Var(Y_i) &= \frac{r_i(1-\pi_i)}{\pi_i^2}. \end{aligned}$$

Therefore, when r_i is large,

$$\frac{\sqrt{r_i}(p_i - \pi_i)}{\sqrt{\pi_i^2(1-\pi_i)}} \sim N(0, 1).$$

With this result, we can estimate R as

$$\hat{R} = \frac{p_N}{p_S}. \quad (3.8)$$

Note that $\hat{R} > 0$ and $\ln \hat{R}$ will possess a better asymptotic behavior than \hat{R} .

Moreover, by Delta method,

$$E(\ln \hat{R}) \approx \ln R \quad (3.9)$$

and,

$$\begin{aligned} \text{Var}(\ln \hat{R}) &\approx \text{Var}\left(\ln\left(\frac{p_N}{p_S}\right)\right) \\ &= \text{Var}(\ln p_N) + \text{Var}(\ln p_S) \\ &= \frac{1 - \pi_N}{r_N} + \frac{1 - \pi_S}{r_S}, \end{aligned} \quad (3.10)$$

where

$$\begin{aligned} E(\ln p_i) &\approx \ln \pi_i, \\ \text{Var}(\ln p_i) &\approx \left(\frac{1}{\pi_i}\right)^2 \frac{\pi_i^2(1 - \pi_i)}{r_i} \\ &= \frac{1 - \pi_i}{r_i}, \end{aligned}$$

for $i = N, S$.

Therefore, the test statistic

$$T_2 = \frac{\ln\left(\frac{p_N}{p_S}\right) - \ln(R)}{s} \quad (3.11)$$

where

$$s = \sqrt{\frac{1 - \tilde{\pi}_S}{r_S} + \frac{1 - \tilde{\pi}_N}{r_N}},$$

with any consistent estimate of π_i , $\tilde{\pi}_i$, $i = N, S$, can be used for inferring R .

3.3 Consistent Estimators of π

The likelihood function:

$$\begin{aligned} L &= P(Y_N = y_N, Y_S = y_S | \pi_N, \pi_S) \\ &= \binom{y_N + r_N - 1}{y_N} \binom{y \cdot - y_N + r_s - 1}{y \cdot - y_N} \pi_N^{r_N} \pi_S^{r_S} (1 - \pi_N)^{y_N} (1 - \pi_S)^{y_S}. \end{aligned}$$

Under the null hypothesis:

$$H_0 : R \leq R_0$$

versus the alternative hypothesis

$$H_1 : R > R_0,$$

where

Risk Ratio R

$$R = \frac{\pi_N}{\pi_S}$$

and R_0 is a pre-specified quantity

$$0 \leq R_0 \leq 1.$$

The likelihood function of π_N and R can be written as

$$L = \binom{y_N + r_N - 1}{y_N} \binom{y \cdot - y_N + r_s - 1}{y \cdot - y_N} \pi_N^{r_N} \left(\frac{\pi_N}{R}\right)^{r_S} (1 - \pi_N)^{y_N} \left(1 - \frac{\pi_N}{R}\right)^{y \cdot - y_N}, \text{ where } y \cdot = y_N + y_S.$$

The log-likelihood function is then given by,

$$\ln L = C + r_N \ln \pi_N + r_S \ln \pi_N - r_S \ln R + y_N \ln (1 - \pi_N) + (y. - y_N) \ln \left(1 - \frac{\pi_N}{R}\right),$$

where C is a constant.

The first order derivative of $\ln L$ with respect to π_N is,

$$\left. \frac{\partial \ln L}{\partial \pi_N} \right|_{R=R_0} = \frac{r_N + r_S}{\pi_N} - \frac{y_N}{1 - \pi_N} - \frac{y. - y_N}{R_0 - \pi_N}.$$

After we set $\left. \frac{\partial \ln L}{\partial \pi_N} \right|_{R=R_0}$ equal to 0 yields, (See Appendix A1)

$$(r_N + r_S + y.)\pi_N^2 - [(r_N + r_S) + (r_N + r_S + y_N)R_0 + (y. - y_N)]\pi_N + (r_N + r_S)R_0 = 0,$$

$$\hat{\pi}_N = \frac{-B \pm \sqrt{B^2 - 4AC}}{2A} \quad (3.12)$$

where

$$A = r_N + r_S + y.,$$

$$B = -[(r_N + r_S) + (r_N + r_S + y_N)R_0 + (y. - y_N)],$$

$$C = (r_N + r_S)R_0.$$

We want to show that $\hat{\pi}_N$ is the smaller root of the above quadratic equation, which is the restricted maximum likelihood estimate.

Firstly, we show that the roots of this equation are real:

$$\Delta = B^2 - 4AC$$

$$\begin{aligned}
&= [y_N R_0 + (y. - y_N) + (r_N + r_S)R_0 + (r_N + r_S)]^2 - 4(r_N + r_S + y.)(r_N + r_S)R_0 \\
&= y_N^2 R_0^2 + (y. - y_N)^2 + 2y_N R_0 (y. - y_N) + (r_N + r_S)^2 R_0^2 + (r_N + r_S)^2 \\
&\quad + 2(r_N + r_S)^2 R_0 + 2[y_N R_0 + (y. - y_N)][(r_N + r_S)R_0 + (r_N + r_S)] \\
&\quad - 4(r_N + r_S)^2 R_0 - 4y.(r_N + r_S)R_0 \\
&= y_N^2 R_0^2 + (y. - y_N)^2 + (r_N + r_S)^2 R_0^2 + (r_N + r_S)^2 + 2y_N R_0 (y. - y_N) \\
&\quad - 2(r_N + r_S)^2 R_0 + 2y_N R_0^2 (r_N + r_S) + 2y_N R_0 (r_N + r_S) \\
&\quad + 2y.(r_N + r_S)R_0 - 2y_N (r_N + r_S)R_0 + 2(y. - y_N)(r_N + r_S) - 4y.(r_N + r_S)R_0 \\
&= y_N^2 R_0^2 + (y. - y_N)^2 + (r_N + r_S)^2 R_0^2 + (r_N + r_S)^2 + 2y_N R_0 (y. - y_N) \\
&\quad - 2(r_N + r_S)^2 R_0 + 2y_N R_0^2 (r_N + r_S) - 2y.(r_N + r_S)R_0 + 2(y. - y_N)(r_N + r_S) \\
&= y_N^2 R_0^2 + (y. - y_N)^2 + (r_N + r_S)^2 R_0^2 + (r_N + r_S)^2 + 2y_N R_0 (y. - y_N) \\
&\quad - 2(r_N + r_S)^2 R_0 + 2y_N R_0^2 (r_N + r_S) - 2y_N R_0 (r_N + r_S) - 2(y. - y_N)(r_N + r_S) \\
&\quad + 2(y. - y_N)(r_N + r_S)R_0 + 4(y. - y_N)(r_N + r_S) - 4(y. - y_N)(r_N + r_S)R_0 \\
&= y_N^2 R_0^2 + (y. - y_N)^2 + 2y_N R_0 (y. - y_N) + (r_N + r_S)^2 R_0^2 + (r_N + r_S)^2 \\
&\quad - 2(r_N + r_S)^2 R_0 - 2[y_N R_0 + (y. - y_N)][(r_N + r_S) - (r_N + r_S)R_0] \\
&\quad + 4(y. - y_N)(r_N + r_S)(1 - R_0) \\
&= [y_N R_0 + (y. - y_N) - (r_N + r_S) + (r_N + r_S)R_0]^2 + 4(y. - y_N)(r_N + r_S)(1 - R_0) \\
&\geq 0 \quad (\text{since } 0 \leq R_0 \leq 1).
\end{aligned}$$

Then, we show that only the smaller root is admissible, note that π_N takes value between zero and R_0 .

Let

$$f(\pi_N) = (r_N + r_S + y.)\pi_N^2 - [(r_N + r_S) + (r_N + r_S + y_N)R_0 + (y. - y_N)]\pi_N + (r_N + r_S)R_0.$$

When $\pi_N = 0$, the equation becomes

$$f(0) = (r_N + r_S)R_0,$$

which is greater than zero.

When $\pi_N = R_0$, the equation becomes

$$f(R_0) = (y_{\cdot} - y_N)R_0(R_0 - 1),$$

which is smaller than zero.

From these two results, we can find that the quadratic equation must be a decreasing function from positive to negative value as π_N increase from 0 to R_0 , and only the smaller root of π_N is included within this interval. By Intermediate Value Theorem, there must be a value of π_N such that $f(\pi_N) = 0$. Therefore, the smaller root of the quadratic equation is the restricted maximum likelihood estimate of π_N under null hypothesis.

We then use the restricted maximum likelihood estimates, π_N and π_S ($\pi_S = \pi_N/R_0$) to replace the sample-based estimates in the test statistics T_1 and T_2 .

Chapter 4

Confidence Interval

4.1 Introduction

Assume that two independent inverse samples are drawn from the populations who received the treatment of new and standard procedures, respectively. Let π_N and π_S denote the respective probability for a randomly selected subject from these two populations who shows improvement. Let $R = \frac{\pi_N}{\pi_S}$ be the efficiency of the new procedure to the standard procedure. In this chapter, we discuss the construction of the confidence intervals of R .

Recall the test statistics T_1 and T_2 depend on the unknown parameters π_i , $i = N, S$. It is well known that these unknown quantities can be replaced by any consistent estimators of them. We will discuss this idea more detail in Section 4.3. Due to Tang, Tang, Chan and Chan (2002), a better result might be obtained by using the test-based confidence interval. In section 4.2, we will discuss the construction of confidence interval using the restricted maximum likelihood estimators of π_i , $i = N, S$ in estimating the unknown π_i , $i = N, S$.

4.2 Test-Based Confidence Interval

We are interested in constructing a confidence interval of R . Recall from Chapter 3, two statistics, T_1 and T_2 , are introduced. Both of them contain the nuisance parameter π_N . In this section, we are going to show how restricted maximum likelihood estimator of π_N is used to obtain the confidence interval.

For a statistic $T(R, \pi_N)$, a test-based $100(1 - \alpha)\%$ confidence interval is defined as the interval (R_L, R_U) , where for any value $R^* \in (R_L, R_U)$, the hypothesis $H_0 : R \leq R_0$ is accepted with α level of significance with the nuisance parameter π_N is replaced by its restricted maximum likelihood estimator. We will discuss the construction of this confidence interval more detail.

Under the following null hypotheses:

For lower bound:

$$H_0^L : R \leq R_L$$

versus the alternative hypothesis

$$H_1^L : R > R_L.$$

For upper bound:

$$H_0^U : R \geq R_U$$

versus the alternative hypothesis

$$H_1^U : R < R_U.$$

We want to test whether the risk ratio R is larger than the lower bound. The rejection rule is: we reject H_0^L if $T_i > z_{\frac{\alpha}{2}}$, for $i = 1, 2$. And, we want to test whether the risk ratio R is smaller than the upper bound. The rejection rule is: we reject H_0^U if $T_i < -z_{\frac{\alpha}{2}}$, for $i = 1, 2$. The lower limit is the minimum R_L such that H_0^L is accepted and the upper limit is the maximum R_U such that H_0^U is accepted. T_1, T_2 are the test statistics derived on the basis of Fieller's Theorem and on the basis of delta method with logarithm transformation respectively.

$$T_1 = \frac{\bar{Z}}{\sqrt{Var(\bar{Z})}}, \quad (4.1)$$

$$T_2 = \frac{\ln(\frac{\hat{p}_N}{\hat{p}_S}) - \ln(R)}{s}. \quad (4.2)$$

Afterwards, we can obtain the $(1 - \alpha)\%$ confidence interval for risk ratio:

$$(R_L^*, R_U^*) \quad (4.3)$$

where R_L^* is the minimum R_L such that H_0^L is accepted and R_U^* is the maximum R_U such that H_0^U is accepted.

4.3 Using sample-based estimates

Lui (1995) followed Fieller's Theorem, using T_1 to construct the confidence limits. Because $Var(\bar{Z})$ is a quadratic function of R , the inequality $\frac{\bar{Z}^2}{Var(\bar{Z})} \leq z_{\alpha/2}^2$ can be rewritten as $AR^2 - 2BR + C \leq 0$ (See Appendix A2),

where

$$\begin{aligned} A &= \bar{X}_N^2 - z_{\alpha/2}^2 \left(\frac{1 - \pi_N}{r_N \pi_N^2} \right), \\ B &= \bar{X}_S \bar{X}_N, \\ C &= \bar{X}_S^2 - z_{\alpha/2}^2 \left(\frac{1 - \pi_S}{r_S \pi_S^2} \right). \end{aligned}$$

If $A > 0$ and $B^2 - AC > 0$, then $P(R_l < \frac{\pi_N}{\pi_S} < R_u) \doteq 1 - \alpha$, where R_u is the larger root and R_l is the smaller root. We can see that the confidence limits R_l and R_u depend on π_i . In this method, Lui used the unbiased estimator of $\hat{\pi}_i = \frac{r_i - 1}{y_i + r_i - 1}$ for π_i (Haldane 1945).

The $(1 - \alpha)\%$ confidence interval for risk ratio:

$$(R_l, R_u). \quad (4.4)$$

Following Lui (1997), we observed the test statistic T_2 also has the asymptotic standard normal distribution. Lui (1997) simply suggested $\tilde{\pi}_i = p_i$, for $i = N, S$, which is the sample-based estimate. For confidence interval construction, $(1 - \alpha)\%$

Confidence Interval for risk ratio R :

$$\left(\exp \left\{ \ln \left(\frac{p_N}{p_S} \right) - z_{\frac{\alpha}{2}} s \right\}, \exp \left\{ \ln \left(\frac{p_N}{p_S} \right) + z_{\frac{\alpha}{2}} s \right\} \right) \quad (4.5)$$

where

$$\begin{aligned} s &= \sqrt{\frac{1 - \tilde{\pi}_N}{r_N} + \frac{1 - \tilde{\pi}_S}{r_S}}, \\ p_i &= \frac{r_i}{r_i + y_i}, \quad \text{for } i = N, S. \end{aligned}$$

In the next chapter, by using simulation, we will use our method to compare with the two methods that following Lui. To evaluate their performance, based on these test statistics, confidence intervals would be constructed and evaluated in terms of expected length and coverage probability.

Four methods are used to estimate the coverage probability and expected length, for convenience, we define:

Method I: using T_1 and $\hat{\pi}_i = \frac{r_i - 1}{y_i + r_i - 1}$, $i = N, S$

Method II: using T_1 and restricted maximum likelihood estimates

Method III: using T_2 and $\tilde{\pi} = \frac{r_i}{r_i + y_i}$, $i = N, S$

Method IV: using T_2 and restricted maximum likelihood estimates

5.2 Simulation Procedures

Chapter 5

Simulation

5.1 Introduction

To evaluate the performance of the above four methods, we apply Monte Carlo simulation. For simplicity, we assume r_S, r_N are equal to r , and setting r equals to 20, 30, 50, 100, π_S equals to 0.01, 0.1, 0.2, R_0 equals to 0.6, 0.7, 0.8, 0.9, 1, $R_0 = \frac{\pi_N}{\pi_S}$ and α value equals to 0.01, 0.05, 0.1. S-plus is used to generate 10000 random observations which follow negative binomial distribution.

After simulation, we would like to estimate the coverage probability and the expected length of the confidence interval. The coverage probability is simply the percentage of the cases of the true value of R that covered by the confidence interval and the expected length is the average of the length of the confidence interval.

5.2 Simulation Procedures

There are five steps in the simulation procedures:

Step 1

Setting the parameters:

$$r = 20, 30, 50, 100$$

$$R_0 = 0.6, 0.7, 0.8, 0.9, 1$$

$$\pi_S = 0.01, 0.1, 0.2, \pi_N = \frac{R_0}{\pi_S}$$

Step 2

Generating 10000 random observations which follow negative binomial distribution with parameter (r, π_S) and (r, π_N) for each configuration.

Step 3

For each configuration, we use the 10000 random observations, estimate the sample-based estimates and restricted maximum likelihood estimates.

Step 4

Using the estimates and the test statistics mentioned before to estimate the lower limits and upper limits.

Step 5

Computing the expected length and the coverage probability for each configuration.

5.3 Simulation Results

With the same r , R_0 , π_S and α , we found that method I has the largest coverage probabilities when comparing to other three methods. The other three methods consistently agree with the nominal confidence interval $(1 - \alpha)\%$ quite well. However, within the three methods, the coverage probabilities of method II do not agree with the nominal confidence interval of $(1 - \alpha)\%$. The difference between the coverage probability and the nominal confidence interval $(1 - \alpha)\%$ is a little bit larger than those of method III and IV. We can note this result from Table 5.1.

Table 5.1: $r = 20$, $\alpha = 0.05$, $\pi_S = 0.01$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9779	0.975	0.9724	0.9787	0.9773
	II	0.9568	0.9519	0.9479	0.9543	0.9564
	III	0.9544	0.9491	0.9457	0.9512	0.9504
	IV	0.9503	0.9454	0.9417	0.9475	0.9473

For the expected length, we observed that Method I has the longest expected lengths and method IV has the shortest expected lengths. We can note this result from Table 5.2.

Table 5.2: $r = 20$, $\alpha = 0.05$, $\pi_S = 0.01$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.983098	1.147631	1.316196	1.480007	1.633557
	II	0.851583	0.996245	1.144361	1.288542	1.423728
	III	0.829387	0.968442	1.110962	1.249527	1.379583
	IV	0.819464	0.95858	1.101033	1.239508	1.369455

With the same r , R_0 and π_S but different α , we can obtain similar results, moreover, as α is larger, the coverage probabilities of method I become much more disagree with the nominal confidence interval $(1 - \alpha)\%$. We can note this result from Table 5.3.

Table 5.3: $r = 20$, $\alpha = 0.1$, $\pi_S = 0.01$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9409	0.9354	0.9328	0.9374	0.9367
	II	0.9046	0.9006	0.8961	0.9004	0.9
	III	0.9045	0.8995	0.8985	0.9013	0.8959
	IV	0.8964	0.8922	0.8919	0.8955	0.89

When α increases, the expected lengths become shorter. Comparing Table 5.4 with Table 5.5, we can found that the expected lengths are much shorter in Table 5.5.

Table 5.4: $r = 20$, $\alpha = 0.01$, $\pi_S = 0.01$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	1.534451	1.790618	2.052845	2.307574	2.546338
	II	1.217223	1.423183	1.634541	1.839779	2.0327
	III	1.139764	1.330776	1.526603	1.716964	1.895619
	IV	1.130029	1.321097	1.516669	1.707008	1.885438

Table 5.5: $r = 20$, $\alpha = 0.1$, $\pi_S = 0.01$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.777689	0.907965	1.041371	1.171083	1.292804
	II	0.691072	0.808676	0.929204	1.046572	1.156588
	III	0.683386	0.798021	0.915355	1.029558	1.136718
	IV	0.673404	0.787962	0.905396	1.019527	1.126659

With the same r , R_0 and α but different π_S , the coverage probabilities of method I are closer to the nominal confidence interval of $(1 - \alpha)\%$ when π_S is large. We can get this result from Table 5.6.

Table 5.6: $r = 20$, $\alpha = 0.1$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9409	0.9354	0.9328	0.9374	0.9367
0.2	I	0.9394	0.937	0.9364	0.9316	0.9307

We observed from Table 5.7 that the expected length depends on π_S , when π_S is small, it is longer. When π_S is large, it is shorter.

Table 5.7: $r = 20$, $\alpha = 0.1$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.777689	0.907965	1.041371	1.171083	1.292804
	II	0.691072	0.808676	0.929204	1.046572	1.156588
	III	0.683386	0.798021	0.915355	1.029558	1.136718
	IV	0.673404	0.787962	0.905396	1.019527	1.126659
0.2	I	0.697348	0.800101	0.905935	1.012254	1.111817
	II	0.630641	0.728438	0.830165	0.93344	1.031278
	III	0.620713	0.714359	0.811372	0.909534	1.002022
	IV	0.612557	0.706268	0.80314	0.901179	0.99356

With the same π_S , R_0 and α but different r , we can see that the coverage probabilities of the four methods become smaller when r is large. The coverage probabilities of method I are being closer to the nominal confidence interval $(1 - \alpha)\%$. We can compare Table 5.8 with Table 5.9 to obtain this result.

Table 5.8: $r = 100$, $\alpha = 0.05$, $\pi_S = 0.01$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9633	0.9606	0.9545	0.9597	0.9547
	II	0.9459	0.9482	0.9433	0.9477	0.9427
	III	0.9567	0.9556	0.95	0.9535	0.9479
	IV	0.9442	0.9473	0.9418	0.9458	0.9412

Table 5.9: $r = 20$, $\alpha = 0.05$, $\pi_S = 0.01$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9779	0.975	0.9724	0.9787	0.9773
	II	0.9568	0.9519	0.9479	0.9543	0.9564
	III	0.9544	0.9491	0.9457	0.9512	0.9504
	IV	0.9503	0.9454	0.9417	0.9475	0.9473

From Table 5.2 and Table 5.10, we found that when r is small, the expected length is relatively longer, when r is large, it is shorter.

Table 5.10: $r = 100$, $\alpha = 0.05$, $\pi_S = 0.01$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.348267	0.405868	0.46418	0.522293	0.580089
	II	0.331143	0.387662	0.444746	0.501828	0.558303
	III	0.338783	0.394926	0.451773	0.508339	0.564554
	IV	0.328922	0.384986	0.441737	0.498475	0.554515

With the same π_S , r and α but different R_0 , we found that the coverage probability does not depend on R_0 , we can get similar results even though R_0 is different. We found that the expected length is longer when R_0 is larger. From the above ten tables, we can observe this result.

Chapter 6

Conclusion

From the above simulation results, we noted that using Method I tends to produce a conservative confidence interval when the pre-determined number of cases r is small. The performance of Method I depends on the size of r . Method I performs better when r is large. Its coverage probabilities are being closer to the nominal confidence level of $(1 - \alpha)\%$. And its expected lengths are shorter when r is large.

Method II uses the same test statistic as Method I with restricted maximum likelihood estimates instead of sample-based estimates. We noted that Method II performs better than Method I in all situations mentioned in the simulation. The coverage probabilities agree with the nominal confidence level of $(1 - \alpha)\%$ and the expected lengths are shorter than those by Method I.

When comparing to Method II, Method III is much better in terms of coverage probability and expected length when r is small. Method III consistently agrees with the nominal confidence level of $(1 - \alpha)\%$ well for all situations mentioned in the previous chapter. The expected lengths that we obtained by using Method III are shorter than those using Method I in all cases but only shorter than those

obtained by Method II when r is small.

Method IV uses the same test statistic as Method III. The coverage probabilities of these two methods are similar and both agree with the nominal confidence level of $(1 - \alpha)\%$ well. Using Method IV can obtain a shorter expected length in all situations.

In summary, when the pre-determined number of cases r is large, the four methods are appropriate to be used. However, Method II and Method IV perform better in terms of expected length. These two methods have a relatively shorter expected length. When r is small, Method I is conservative and should not be used. The other three methods are more appropriate to be used. But in terms of expected length, Method III and Method IV are better because these two methods have shorter expected length.

Using Method IV is appropriate for all situations because it can obtain the shortest expected length among four methods. Moreover, using restricted maximum likelihood estimates can obtain a shorter expected length and the coverage probability would agree with the nominal confidence level of $(1 - \alpha)\%$ well.

Appendix

A. Equation derivation

A1. Equation derivation 1

$$\begin{aligned} L &= P(Y_N = y_N, Y_S = y_S | \pi_N, \pi_S) \\ &= \binom{y_N + r_N - 1}{y_N} \binom{y \cdot - y_N + r_s - 1}{y \cdot - y_N} \pi_N^{r_N} \pi_S^{r_S} (1 - \pi_N)^{y_N} (1 - \pi_S)^{y_S} \end{aligned}$$

$$H_0 : R \leq R_0$$

$$H_1 : R > R_0$$

where $0 \leq R_0 \leq 1$, is a pre-specified quantity

$$L = \binom{y_N + r_N - 1}{y_N} \binom{y \cdot - y_N + r_s - 1}{y \cdot - y_N} \pi_N^{r_N} \left(\frac{\pi_N}{R_0}\right)^{r_S} (1 - \pi_N)^{y_N} \left(1 - \frac{\pi_N}{R_0}\right)^{y \cdot - y_N}$$

where $y \cdot = y_N + y_S$

$$\ln L = \text{constant} + r_N \ln \pi_N + r_S \ln \pi_N - r_S \ln R + y_N \ln (1 - \pi_N) + (y \cdot - y_N) \ln \left(1 - \frac{\pi_N}{R}\right)$$

$$\frac{\partial \ln L}{\partial \pi_N} = \frac{r_N + r_S}{\pi_N} - \frac{y_N}{1 - \pi_N} - \frac{y \cdot - y_N}{R - \pi_N}$$

Setting $\left. \frac{\partial \ln L}{\partial \pi_N} \right|_{R=R_0} = 0$

$$0 = (r_N + r_S)(1 - \pi_N)(R_0 - \pi_N) - y_N \pi_N (R_0 - \pi_N) - \pi_N (y \cdot - y_N)(1 - \pi_N)$$

$$\begin{aligned} 0 &= (r_N + r_S)[R_0 - (\pi_N + R_0 \pi_N) + \pi_N^2] - (y_N \pi_N R_0 - y_N \pi_N^2) \\ &\quad - (y \cdot - y_N)(\pi_N - \pi_N^2) \end{aligned}$$

$$0 = (r_N + r_S)(R_0) - (r_N + r_S)(1 + R_0)\pi_N + (r_N + r_S)\pi_N^2 - y_N R_0 \pi_N + y_N \pi_N^2 \\ - (y \cdot - y_N)\pi_N + (y \cdot - y_N)\pi_N^2$$

$$0 = (r_N + r_S)(R_0) - [(r_N + r_S)(1 + R_0) + y_N R_0 + (y \cdot - y_N)]\pi_N \\ + [(r_N + r_S) + y_N + (y \cdot - y_N)]\pi_N^2$$

$$0 = (r_N + r_S + y \cdot)\pi_N^2 - [(r_N + r_S) + (r_N + r_S + y_N)R_0 + (y \cdot - y_N)]\pi_N \\ + (r_N + r_S)R_0$$

A2. Equation derivation 2

Lui (1995)

$$\begin{aligned}
 1 - \alpha &\doteq P\left(\frac{\bar{Z}^2}{\text{Var}(\bar{Z})} \leq z_{\alpha/2}^2\right) \\
 &\doteq P(\bar{Z}^2 \leq z_{\alpha/2}^2 \text{Var}(\bar{Z})) \\
 &\doteq P(\bar{Z}^2 \leq z_{\alpha/2}^2 [\text{Var}(\bar{X}_S) + R^2 \text{Var}(\bar{X}_N)]) \\
 &\doteq P(-z_{\alpha/2}^2 R^2 \text{Var}(\bar{X}_N) - z_{\alpha/2}^2 \text{Var}(\bar{X}_S) + \bar{Z}^2 \leq 0) \\
 &\doteq P(-z_{\alpha/2}^2 R^2 \text{Var}(\bar{X}_N) - z_{\alpha/2}^2 \text{Var}(\bar{X}_S) + (\bar{X}_S - R\bar{X}_N)^2 \leq 0) \\
 &\doteq P(-z_{\alpha/2}^2 R^2 \text{Var}(\bar{X}_N) - z_{\alpha/2}^2 \text{Var}(\bar{X}_S) + \bar{X}_S^2 - 2\bar{X}_S\bar{X}_NR + R^2\bar{X}_N^2 \leq 0) \\
 &\doteq P([\bar{X}_N^2 - z_{\alpha/2}^2 \text{Var}(\bar{X}_N)]R^2 - 2\bar{X}_S\bar{X}_NR + [\bar{X}_S^2 - z_{\alpha/2}^2 \text{Var}(\bar{X}_S)] \leq 0) \\
 &\doteq P(AR^2 - 2BR + C \leq 0)
 \end{aligned}$$

where $A = \bar{X}_N^2 - z_{\alpha/2}^2 \left(\frac{1-\pi_N}{r_N\pi_N^2}\right)$, $B = \bar{X}_S\bar{X}_N$, $C = \bar{X}_S^2 - z_{\alpha/2}^2 \left(\frac{1-\pi_S}{r_S\pi_S^2}\right)$

If $A > 0$ and $B^2 - AC > 0$, the $P(R_l < \frac{\pi_N}{\pi_S} < R_u) = 1 - \alpha$

where R_u is the larger root and R_l is the smaller root.

B. Table

The following tables are the results of simulation.

Table 6.1: $r = 20$, $\alpha = 0.01$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9985	0.9977	0.999	0.9983	0.9989
	II	0.9922	0.9908	0.9931	0.9924	0.9927
	III	0.9893	0.9882	0.9902	0.9903	0.989
	IV	0.988	0.9874	0.9888	0.9896	0.9882
0.1	I	0.998	0.9984	0.9986	0.9981	0.9985
	II	0.9907	0.9916	0.9926	0.9908	0.9928
	III	0.9875	0.9885	0.9897	0.9866	0.9893
	IV	0.9861	0.9881	0.9894	0.9863	0.989
0.2	I	0.9983	0.9996	0.9985	0.9989	0.9988
	II	0.9911	0.9936	0.993	0.9917	0.9921
	III	0.9876	0.9914	0.9904	0.9883	0.988
	IV	0.988	0.9917	0.9907	0.9885	0.9888

Table 6.2: $r = 20$, $\alpha = 0.01$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	1.534451	1.790618	2.052845	2.307574	2.546338
	II	1.217223	1.423183	1.634541	1.839779	2.0327
	III	1.139764	1.330776	1.526603	1.716964	1.895619
	IV	1.130029	1.321097	1.516669	1.707008	1.885438
0.1	I	1.433371	1.657071	1.873484	2.095275	2.303077
	II	1.169301	1.363218	1.553654	1.752108	1.940295
	III	1.086777	1.262928	1.43517	1.61378	1.782593
	IV	1.080152	1.255875	1.427653	1.605486	1.77329
0.2	I	1.324553	1.509273	1.696343	1.881811	2.053069
	II	1.112918	1.287001	1.468983	1.654763	1.831504
	III	1.025254	1.179298	1.338539	1.499391	1.650799
	IV	1.022702	1.176604	1.335596	1.495943	1.646884

Table 6.3: $r = 30$, $\alpha = 0.01$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.998	0.9966	0.9959	0.9964	0.9973
	II	0.9921	0.99	0.9895	0.9903	0.9924
	III	0.9913	0.9887	0.9887	0.9885	0.991
	IV	0.9899	0.9877	0.988	0.9874	0.9903
0.1	I	0.9969	0.9973	0.9968	0.9973	0.9966
	II	0.9913	0.9917	0.9914	0.9905	0.9921
	III	0.9901	0.9907	0.9901	0.9893	0.9891
	IV	0.9892	0.9899	0.989	0.9888	0.9887
0.2	I	0.9971	0.997	0.9966	0.9961	0.9963
	II	0.9919	0.9914	0.9899	0.9912	0.9909
	III	0.9898	0.9889	0.9887	0.9902	0.9885
	IV	0.9887	0.988	0.9884	0.9901	0.9886

Table 6.4: $r = 30$, $\alpha = 0.01$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	1.0469	1.218128	1.39761	1.571662	1.739
	II	0.91633	1.068319	1.227667	1.382391	1.531188
	III	0.8856	1.030703	1.182926	1.330635	1.472771
	IV	0.8757	1.020905	1.172961	1.320757	1.462659
0.1	I	0.990448	1.144028	1.303738	1.460238	1.608819
	II	0.878371	1.020069	1.16855	1.315162	1.455464
	III	0.845506	0.979136	1.118811	1.256451	1.387871
	IV	0.837236	0.970807	1.110278	1.247434	1.378419
0.2	I	0.926054	1.065358	1.202242	1.335378	1.469238
	II	0.832976	0.967288	1.10149	1.234124	1.369889
	III	0.797917	0.922602	1.046395	1.168065	1.291666
	IV	0.791967	0.916624	1.040342	1.161831	1.285004

Table 6.5: $r = 50$, $\alpha = 0.01$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9966	0.9946	0.9956	0.9949	0.9941
	II	0.9927	0.99	0.9913	0.9892	0.991
	III	0.9928	0.9898	0.9919	0.9891	0.9904
	IV	0.9913	0.9886	0.9898	0.9877	0.9896
0.1	I	0.9956	0.9959	0.9945	0.9946	0.9944
	II	0.9902	0.9907	0.9895	0.9903	0.9901
	III	0.9901	0.9906	0.9901	0.9893	0.9895
	IV	0.9882	0.9891	0.9888	0.9886	0.9886
0.2	I	0.9946	0.9953	0.9955	0.9958	0.996
	II	0.9897	0.9914	0.9886	0.9918	0.9924
	III	0.9897	0.9912	0.9899	0.9915	0.9915
	IV	0.9883	0.9897	0.9885	0.9908	0.9906

Table 6.6: $r = 50$, $\alpha = 0.01$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.717574	0.837061	0.956315	1.078963	1.195791
	II	0.663258	0.775545	0.887637	1.003004	1.112805
	III	0.656596	0.766082	0.875311	0.987697	1.094771
	IV	0.646639	0.756131	0.865447	0.977661	1.084724
0.1	I	0.683893	0.794167	0.905435	1.013324	1.121599
	II	0.635731	0.741295	0.848319	0.952492	1.057507
	III	0.628126	0.730429	0.833867	0.934476	1.035681
	IV	0.619022	0.72121	0.824506	0.924908	1.025888
0.2	I	0.647477	0.747753	0.844688	0.942068	1.038396
	II	0.605652	0.704008	0.799791	0.896727	0.993575
	III	0.597207	0.69148	0.783085	0.875591	0.967512
	IV	0.58905	0.683379	0.774902	0.86723	0.959137

Table 6.7: $r = 100$, $\alpha = 0.01$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9941	0.9929	0.994	0.9936	0.9904
	II	0.9904	0.989	0.9894	0.9901	0.9867
	III	0.9914	0.9908	0.9914	0.9909	0.9877
	IV	0.9891	0.9887	0.9889	0.9891	0.9855
0.1	I	0.9933	0.9916	0.9913	0.9941	0.9923
	II	0.9892	0.9868	0.9861	0.9902	0.9886
	III	0.9905	0.9887	0.9886	0.9913	0.9893
	IV	0.9886	0.986	0.986	0.9895	0.9881
0.2	I	0.9926	0.9919	0.9924	0.9937	0.9928
	II	0.988	0.9887	0.9884	0.9905	0.9893
	III	0.9902	0.9899	0.9902	0.9913	0.9899
	IV	0.9871	0.9879	0.9882	0.9897	0.9883

Table 6.8: $r = 100$, $\alpha = 0.01$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.468121	0.54562	0.624063	0.702185	0.77963
	II	0.44479	0.520112	0.596382	0.672328	0.747706
	III	0.449475	0.523891	0.599192	0.674279	0.74874
	IV	0.439388	0.513873	0.589172	0.664317	0.738724
0.1	I	0.449386	0.5216	0.595272	0.666642	0.738649
	II	0.427781	0.498531	0.570824	0.641019	0.711946
	III	0.432068	0.501821	0.572988	0.642063	0.711795
	IV	0.422418	0.492173	0.563269	0.632219	0.701932
0.2	I	0.427122	0.494165	0.56074	0.625946	0.690135
	II	0.407318	0.47368	0.539917	0.60487	0.669247
	III	0.411337	0.476455	0.541285	0.604844	0.667662
	IV	0.401911	0.467114	0.531949	0.595455	0.658251

Table 6.9: $r = 20$, $\alpha = 0.05$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9779	0.975	0.9724	0.9787	0.9773
	II	0.9568	0.9519	0.9479	0.9543	0.9564
	III	0.9544	0.9491	0.9457	0.9512	0.9504
	IV	0.9503	0.9454	0.9417	0.9475	0.9473
0.1	I	0.9736	0.9741	0.9774	0.9709	0.974
	II	0.949	0.9501	0.9497	0.9427	0.9509
	III	0.9468	0.9451	0.948	0.9398	0.9452
	IV	0.9413	0.9424	0.9458	0.9377	0.9425
0.2	I	0.9761	0.9775	0.9774	0.974	0.9747
	II	0.9565	0.9581	0.9534	0.9489	0.9522
	III	0.9542	0.9537	0.9501	0.9458	0.947
	IV	0.9497	0.9506	0.9485	0.9449	0.9467

Table 6.10: $r = 20$, $\alpha = 0.05$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.983098	1.147631	1.316196	1.480007	1.633557
	II	0.851583	0.996245	1.144361	1.288542	1.423728
	III	0.829387	0.968442	1.110962	1.249527	1.379583
	IV	0.819464	0.95858	1.101033	1.239508	1.369455
0.1	I	0.931961	1.080519	1.225229	1.374544	1.515045
	II	0.81762	0.953016	1.085822	1.223946	1.35486
	III	0.793447	0.922266	1.048244	1.17904	1.302588
	IV	0.784966	0.91355	1.039309	1.169766	1.292961
0.2	I	0.873897	1.00109	1.131357	1.261879	1.383823
	II	0.777326	0.898068	1.023811	1.151557	1.272638
	III	0.75119	0.864378	0.981579	1.100084	1.211763
	IV	0.744435	0.857465	0.974529	1.09275	1.204289

Table 6.11: $r = 30$, $\alpha = 0.05$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9738	0.9682	0.968	0.9668	0.9708
	II	0.9532	0.9506	0.9478	0.9467	0.9534
	III	0.9538	0.9509	0.9494	0.9482	0.9516
	IV	0.9481	0.9456	0.9459	0.9434	0.9489
0.1	I	0.9665	0.9718	0.968	0.9698	0.9702
	II	0.9467	0.9541	0.9462	0.9481	0.9527
	III	0.9471	0.9539	0.9486	0.9491	0.9506
	IV	0.9413	0.9485	0.9451	0.9463	0.9473
0.2	I	0.9686	0.9675	0.9669	0.97	0.97
	II	0.9502	0.9515	0.9479	0.9508	0.9532
	III	0.9508	0.9513	0.9505	0.9522	0.951
	IV	0.9464	0.9462	0.9467	0.9478	0.9481

Table 6.12: $r = 30$, $\alpha = 0.05$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.724761	0.843441	0.967837	1.088583	1.204702
	II	0.659724	0.769601	0.88483	0.996617	1.104314
	III	0.653879	0.76102	0.87346	0.982485	1.087467
	IV	0.644043	0.751161	0.863367	0.972575	1.077432
0.1	I	0.690207	0.798317	0.911117	1.021956	1.1275
	II	0.632533	0.73461	0.841598	0.947153	1.048106
	III	0.625643	0.724582	0.828169	0.930205	1.027623
	IV	0.616447	0.715439	0.818795	0.920607	1.017856
0.2	I	0.649735	0.749473	0.848024	0.944429	1.041943
	II	0.599601	0.696075	0.792316	0.887317	0.984187
	III	0.591776	0.684602	0.776719	0.867243	0.959414
	IV	0.583623	0.676306	0.768238	0.858788	0.950777

Table 6.13: $r = 50$, $\alpha = 0.05$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9659	0.9626	0.9649	0.9604	0.9644
	II	0.9503	0.9473	0.9477	0.9458	0.9517
	III	0.955	0.9521	0.9534	0.9485	0.9532
	IV	0.9475	0.9458	0.9482	0.9432	0.9484
0.1	I	0.9654	0.9617	0.9615	0.9629	0.9609
	II	0.9491	0.9477	0.944	0.9503	0.9464
	III	0.9559	0.9512	0.9498	0.9523	0.9485
	IV	0.9464	0.9453	0.9442	0.9471	0.944
0.2	I	0.9614	0.9614	0.9617	0.9606	0.9624
	II	0.9474	0.9466	0.9449	0.9451	0.9501
	III	0.9519	0.9513	0.951	0.9483	0.9521
	IV	0.9447	0.9441	0.9459	0.9435	0.948

Table 6.14: $r = 50$, $\alpha = 0.05$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.519562	0.606137	0.692557	0.781456	0.866109
	II	0.487407	0.570431	0.653246	0.73835	0.819515
	III	0.490571	0.572402	0.654014	0.737981	0.818049
	IV	0.480647	0.562339	0.644028	0.728104	0.807962
0.1	I	0.496613	0.577061	0.65846	0.737349	0.816672
	II	0.467198	0.545085	0.624011	0.700879	0.778153
	III	0.469958	0.546499	0.62396	0.699315	0.775109
	IV	0.460392	0.536881	0.614274	0.689482	0.765279
0.2	I	0.471725	0.54546	0.616984	0.689018	0.760425
	II	0.445093	0.517447	0.587946	0.659249	0.730374
	III	0.447483	0.518189	0.587021	0.656349	0.725465
	IV	0.438274	0.508939	0.577665	0.647104	0.716121

Table 6.15: $r = 100$, $\alpha = 0.05$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9633	0.9606	0.9545	0.9597	0.9547
	II	0.9459	0.9482	0.9433	0.9477	0.9427
	III	0.9567	0.9556	0.95	0.9535	0.9479
	IV	0.9442	0.9473	0.9418	0.9458	0.9412
0.1	I	0.9594	0.9594	0.9539	0.9579	0.957
	II	0.9441	0.9446	0.9415	0.9464	0.9453
	III	0.9538	0.9522	0.9486	0.9521	0.9507
	IV	0.9429	0.9425	0.9391	0.945	0.944
0.2	I	0.9596	0.9579	0.9576	0.9614	0.9565
	II	0.9444	0.9443	0.9452	0.95	0.9463
	III	0.9557	0.9524	0.952	0.9568	0.9507
	IV	0.9433	0.9424	0.9445	0.9485	0.9453

Table 6.16: $r = 100$, $\alpha = 0.05$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.348267	0.405868	0.46418	0.522293	0.580089
	II	0.331143	0.387662	0.444746	0.501828	0.558303
	III	0.338783	0.394926	0.451773	0.508339	0.564554
	IV	0.328922	0.384986	0.441737	0.498475	0.554515
0.1	I	0.334624	0.388584	0.44352	0.496885	0.550703
	II	0.318335	0.371517	0.425699	0.478321	0.531428
	III	0.326017	0.378627	0.432379	0.484458	0.537115
	IV	0.316044	0.368769	0.4225	0.474601	0.52716
0.2	I	0.318484	0.368737	0.418583	0.467529	0.515863
	II	0.303039	0.35282	0.40239	0.451074	0.499309
	III	0.310578	0.359779	0.408766	0.456828	0.504311
	IV	0.300812	0.349991	0.399032	0.447012	0.494562

Table 6.17: $r = 20, \alpha = 0.1$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9409	0.9354	0.9328	0.9374	0.9367
	II	0.9046	0.9006	0.8961	0.9004	0.9
	III	0.9045	0.8995	0.8985	0.9013	0.8959
	IV	0.8964	0.8922	0.8919	0.8955	0.89
0.1	I	0.9296	0.9318	0.9352	0.9272	0.9303
	II	0.8947	0.896	0.8986	0.889	0.8971
	III	0.8948	0.8949	0.9002	0.8903	0.8941
	IV	0.8867	0.8883	0.8948	0.8863	0.8903
0.2	I	0.9394	0.937	0.9364	0.9316	0.9307
	II	0.9055	0.9031	0.8988	0.8933	0.9011
	III	0.9057	0.9023	0.9007	0.895	0.8983
	IV	0.8972	0.8974	0.8954	0.8911	0.895

Table 6.18: $r = 20, \alpha = 0.1$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.777689	0.907965	1.041371	1.171083	1.292804
	II	0.691072	0.808676	0.929204	1.046572	1.156588
	III	0.683386	0.798021	0.915355	1.029558	1.136718
	IV	0.673404	0.787962	0.905396	1.019527	1.126659
0.1	I	0.740333	0.859189	0.975075	1.094915	1.207957
	II	0.663442	0.773488	0.881237	0.993334	1.099393
	III	0.654598	0.761015	0.865022	0.973045	1.075154
	IV	0.645503	0.751752	0.855655	0.963397	1.065245
0.2	I	0.697348	0.800101	0.905935	1.012254	1.111817
	II	0.630641	0.728438	0.830165	0.93344	1.031278
	III	0.620713	0.714359	0.811372	0.909534	1.002022
	IV	0.612557	0.706268	0.80314	0.901179	0.99356

Table 6.19: $r = 30, \alpha = 0.1$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9259	0.9265	0.9245	0.9206	0.9269
	II	0.8993	0.9024	0.8925	0.8969	0.9041
	III	0.9051	0.9057	0.8992	0.8984	0.9052
	IV	0.8939	0.8965	0.8924	0.891	0.8988
0.1	I	0.9226	0.9255	0.924	0.9223	0.9252
	II	0.8946	0.8965	0.8918	0.8986	0.9024
	III	0.8992	0.8994	0.8999	0.9006	0.9034
	IV	0.8897	0.8906	0.8911	0.8936	0.8966
0.2	I	0.9283	0.9232	0.924	0.9275	0.9227
	II	0.9032	0.8951	0.8929	0.9035	0.8993
	III	0.9085	0.8987	0.9008	0.9052	0.9011
	IV	0.8983	0.8915	0.8929	0.8989	0.8953

Table 6.20: $r = 30, \alpha = 0.1$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.587366	0.683636	0.784461	0.882363	0.976566
	II	0.540954	0.631344	0.72612	0.818006	0.906522
	III	0.542014	0.630878	0.724014	0.814494	0.901447
	IV	0.532102	0.620881	0.714025	0.804385	0.891416
0.1	I	0.560617	0.648806	0.740802	0.831304	0.917574
	II	0.518586	0.602564	0.690385	0.777089	0.860008
	III	0.519065	0.601263	0.687217	0.771987	0.852848
	IV	0.509558	0.591651	0.677497	0.762073	0.842954
0.2	I	0.528966	0.610764	0.691789	0.771076	0.851526
	II	0.491495	0.570722	0.649586	0.727426	0.806814
	III	0.491456	0.568597	0.645122	0.720468	0.797072
	IV	0.482653	0.559597	0.636266	0.711588	0.788138

Table 6.21: $r = 50$, $\alpha = 0.1$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9191	0.9206	0.9176	0.9146	0.9176
	II	0.8958	0.8972	0.8958	0.8933	0.8985
	III	0.9056	0.9057	0.9035	0.8986	0.9027
	IV	0.8917	0.8941	0.8954	0.8879	0.8955
0.1	I	0.9203	0.9165	0.9163	0.9173	0.9146
	II	0.896	0.894	0.8917	0.8974	0.894
	III	0.9079	0.9036	0.902	0.9033	0.8992
	IV	0.8932	0.8907	0.892	0.8945	0.8905
0.2	I	0.9179	0.9158	0.9173	0.9159	0.9176
	II	0.8937	0.8932	0.8939	0.8965	0.8996
	III	0.9048	0.9033	0.9049	0.9023	0.9044
	IV	0.8901	0.8901	0.8947	0.8942	0.8964

Table 6.22: $r = 50$, $\alpha = 0.1$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.427775	0.499072	0.570243	0.643418	0.713163
	II	0.402619	0.471411	0.540092	0.610712	0.678004
	III	0.408609	0.476762	0.544809	0.614751	0.681462
	IV	0.398736	0.466808	0.534836	0.604691	0.671332
0.1	I	0.409309	0.475765	0.54291	0.608218	0.673736
	II	0.385765	0.450449	0.515801	0.579539	0.643633
	III	0.391712	0.455512	0.520122	0.582947	0.646146
	IV	0.381851	0.445728	0.51027	0.572986	0.636236
0.2	I	0.389293	0.450277	0.50964	0.569382	0.628727
	II	0.367487	0.42749	0.485836	0.544935	0.603834
	III	0.373128	0.432169	0.489599	0.547588	0.605235
	IV	0.36366	0.422672	0.480112	0.537969	0.595588

Table 6.23: $r = 100$, $\alpha = 0.1$, coverage probabilities

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.9132	0.9182	0.9115	0.9108	0.9063
	II	0.888	0.8966	0.8933	0.8894	0.89
	III	0.9052	0.9119	0.905	0.9016	0.8987
	IV	0.8865	0.895	0.8916	0.8881	0.8873
0.1	I	0.9122	0.9134	0.906	0.9087	0.9095
	II	0.8868	0.892	0.8852	0.891	0.8935
	III	0.9043	0.9077	0.8986	0.9017	0.9029
	IV	0.8855	0.8894	0.8837	0.8903	0.8919
0.2	I	0.9176	0.9139	0.9149	0.9155	0.9127
	II	0.8923	0.8918	0.894	0.896	0.8943
	III	0.9103	0.9075	0.9078	0.9084	0.9058
	IV	0.8907	0.8902	0.8938	0.8944	0.8929

Table 6.24: $r = 100$, $\alpha = 0.1$, expected lengths

π_S	Method	R_0				
		0.6	0.7	0.8	0.9	1
0.01	I	0.289612	0.337527	0.386072	0.434468	0.482455
	II	0.274585	0.321767	0.36947	0.417021	0.464241
	III	0.283341	0.330212	0.377701	0.425067	0.471948
	IV	0.273254	0.320229	0.367668	0.415071	0.461994
0.1	I	0.278458	0.323396	0.369203	0.41363	0.458492
	II	0.264021	0.308337	0.353538	0.397431	0.44186
	III	0.272638	0.316629	0.361545	0.405183	0.449227
	IV	0.262757	0.306735	0.351651	0.395209	0.439263
0.2	I	0.265161	0.307033	0.348706	0.389443	0.429827
	II	0.251243	0.292761	0.334144	0.374658	0.414842
	III	0.259781	0.301	0.341924	0.382213	0.421902
	IV	0.249967	0.291155	0.332154	0.372265	0.412134

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