

**ALTERNATIVE SUMMARY INDICES: PLC AND ASC
FOR THE SUMMARY RECEIVER OPERATING
CHARACTERISTIC (SROC) CURVE**

**ALTERNATIVE SUMMARY INDICES: PLC AND ASC
FOR THE SUMMARY RECEIVER OPERATING
CHARACTERISTIC (SROC) CURVE**

By

XUAN ZHANG, M.A.

A Project

Submitted to the School of Graduate Studies

in Partial Fulfilment of the Requirements

for the Degree

Master of Science

McMaster University

© Copyright by Xuan Zhang, December 2004

MASTER OF SCIENCE (2004)
(Statistics)

McMaster University
Hamilton, Ontario

TITLE: Alternative Summary Indices: PLC and ASC for
the Summary Receiver Operating Characteristic
(SROC) Curve

AUTHOR: Xuan Zhang, M.A.
(Heilongjiang University, P.R.China)

SUPERVISOR: Professor Stephen Walter

NUMBER OF PAGES: x, 72

Abstract

The receiver operating characteristic (*ROC*) curve has been recommended to represent the performance of a diagnostic test. For decades many new methods and theory of *ROC* curve have been developed. Among them the summary indices: the projected length of the *ROC* curve (*PLC*) and the area swept out by the *ROC* curve (*ASC*) firstly proposed by Lee provoked interests. More recently meta-analytic methods for diagnostic test accuracy have been developed and the summary receiver operating characteristic (*SROC*) curve has been recommended to represent the performance of a diagnostic test based on the meta-analysis. The basic properties of the *SROC* curve were discussed by Walter (2002). Based on his findings on the *SROC* curve, my project focuses on studying the summary indices *PLC* and *ASC* in the context of *SROC* curve. The mathematical expressions of these two indices and their variances are derived firstly in my project. Then the main characteristics of these two indices are discussed by resorting to software R codes in details. We find that *PLC* index is symmetric with respect to parameters $|a|$ and $|b|$ (a and b are the coefficients of the regression model proposed by Moses *et al.* (1993)); affected mostly by the new proposed index M , *ASC* index lacks symmetry with respect to b for fixed a or lacks symmetry with respect to a for fixed b . The homogeneous values of *PLC* provide a

good approximation in heterogeneous studies. PLC index gains its maximum $\sqrt{2}$ in the heterogeneous case. But as $a \rightarrow \infty$, ASC attains its maximum 0.5 in the homogeneous case. Our example illustrates that the heterogeneous variances of both PLC and ASC are larger than the homogeneous estimates and the big values of $\text{var}(\hat{PLC})$ and $\text{var}(\hat{ASC})$ both indicate the worst situation for estimating these two indices in the diagnostic test.

Key Words: ROC curve; $SROC$ curve; meta-analysis; the projected length of the curve (PLC); the area swept out by the curve (ASC); homogeneous; heterogeneous; mathematical expressions

Acknowledgements

I would first like to thank my supervisor, Dr. Stephen Walter, whose supervision, guidance and patience encouraged me and make this project possible and enjoyable.

I would also like to thank Dr. P. Macdonald and Dr. R. Viveros for serving on my supervisory committee and giving valuable advice.

I wish to sincerely thank Dr. A. Canty, Dr. A. Childs, Dr. I. Akhundov, Dr. E. Mead, Dr. N. Balakrishnan and Dr. P. Macdonald for their teaching and help in my M.Sc. study.

I would like to thank all my friends for their friendships, help and humour during the last 2 years.

Finally, I would like to thank my family, especially my husband Yichun and my dear son Albert, whose love and patience encouraged me to finish the project.

Contents

| | | |
|----------|---|-----------|
| 1 | Introduction | 1 |
| 1.1 | Historical Background | 1 |
| 1.2 | Scope of the Study | 2 |
| 2 | ROC and SROC Curve | 5 |
| 2.1 | Introduction | 5 |
| 2.2 | ROC Curve and its Features | 6 |
| 2.3 | SROC Curve and its Features | 11 |
| 3 | The Projected Length of the SROC Curve (PLC) | 15 |
| 3.1 | Derivation of Equations of PLC | 15 |
| 3.2 | The Behaviour of PLC | 20 |
| 3.2.1 | Introduction | 20 |
| 3.2.2 | The Behaviour of PLC | 21 |
| 3.3 | Derivation of the Variance of PLC | 25 |

| | | |
|----------|---|-----------|
| 3.4 | The Behaviour of the Variance of PLC | 28 |
| 4 | The Area Swept Out by the SROC Curve (ASC) | 34 |
| 4.1 | Derivation of Equations of ASC | 34 |
| 4.2 | The Behaviour of ASC | 40 |
| 4.3 | Derivation of the Variance of ASC | 45 |
| 4.4 | The Behaviour of the Variance of ASC | 49 |
| 5 | Conclusion | 55 |
| A | Source R codes for PLC | 57 |
| B | Source R codes for ASC | 61 |
| C | Source R codes for Graphs | 64 |

List of Tables

| | | |
|------|---|----|
| 3.1 | values of $2\hat{d}_1$ | 23 |
| 3.2 | values of $2\hat{d}_2$ | 23 |
| 3.3 | values of PLC | 24 |
| 3.4 | values of PLC when $0 \leq b \leq 0.9$ and $1 \leq a \leq 10$ | 24 |
| 3.5 | values of $\partial\hat{d}_1/\partial a$ | 30 |
| 3.6 | values of $\partial\hat{d}_2/\partial a$ | 30 |
| 3.7 | values of $\partial\hat{d}_1/\partial b$ | 31 |
| 3.8 | values of $\partial\hat{d}_2/\partial b$ | 31 |
| 3.9 | values of $\partial PLC/\partial a$ | 32 |
| 3.10 | values of $\partial PLC/\partial b$ | 32 |
| 3.11 | values of $\text{var}(\hat{PLC})$ | 33 |
| 4.1 | values of M when $-0.3 \leq b \leq 0.3$ | 42 |
| 4.2 | values of AUC when $-0.3 \leq b \leq 0.3$ | 42 |
| 4.3 | values of ASC when $-0.3 \leq b \leq 0.3$ | 43 |

| | | |
|------|---|----|
| 4.4 | values of M when $0 \leq b \leq 0.9$ and $1 \leq a \leq 10$ | 43 |
| 4.5 | values of AUC when $0 \leq b \leq 0.9$ and $1 \leq a \leq 10$ | 44 |
| 4.6 | values of ASC when $0 \leq b \leq 0.9$ and $1 \leq a \leq 10$ | 44 |
| 4.7 | values of $\partial AUC/\partial a$ | 51 |
| 4.8 | values of $\partial M/\partial a$ | 51 |
| 4.9 | values of $\partial AUC/\partial b$ | 52 |
| 4.10 | values of $\partial M/\partial b$ | 52 |
| 4.11 | values of $\partial ASC/\partial a$ | 53 |
| 4.12 | values of $\partial ASC/\partial b$ | 53 |
| 4.13 | values of $\text{var}(\hat{ASC})$ | 54 |

List of Figures

| | | |
|-----|--|----|
| 2.1 | Two hypothetical <i>ROC</i> curves that consist of three segments of straight lines: (a) to demonstrate <i>PLC</i> index and (b) to demonstrate <i>ASC</i> index | 9 |
| 2.2 | A hypothetical <i>ROC</i> curve to demonstrate Lee's example | 10 |
| 3.1 | <i>SROC</i> curve (a) and (b) with various values of b ; (c) and (d) with various values of a | 19 |
| 4.1 | <i>SROC</i> curve when $b=0$ | 35 |
| 4.2 | <i>SROC</i> curve to illustrate <i>ASC</i> | 39 |

Chapter 1

Introduction

1.1 Historical Background

Before the development of the summary receiver operating characteristic (*SROC*) curve, the receiver operating characteristic (*ROC*) curve has been recommended to represent the performance of a diagnostic test. The *ROC* curve is a plot of the diagnostic test's sensitivity (i.e., the test's ability to detect the condition of interest) versus its false-positive rate (i.e., the test's inability to recognize normal anatomy) (Zhou *et al.*, 2002). In 1971, Lusted postulated that it was worthy to measure the performance of the observers with the test. He argued that the *ROC* curve provides an ideal means of studying observer performance since the curve illustrates how different criteria for interpreting a test produce different values for the test's false-positive rate and sensitivity. In 1966, Green and Swets were first to estimate the *ROC* curve by using the Gaussian model. A decade later, Metz (1978) described the studies by using the area under the *ROC* curve (*AUC*) as the measure of test accuracy. A pivotal paper was

the article written by Hanley and McNeil (1982) which provided a simple method of estimating AUC without any assumptions about the distribution of the test results. From then on, AUC was recognized as a useful index to provide a global picture of the performance of false-positive rates from 0 to 1. In 1996, Lee and Hsiao proposed two new summary indices, the projected length of the ROC curve (PLC) and the area swept out by the ROC curve (ASC), to summarize the ROC curve. These two indices can avoid the shortcoming of the traditional AUC index and render them good alternatives for evaluating the overall performance of a diagnostic test (Lee *et al.*, 1996). More recently, meta-analytic methods for diagnostic test accuracy have been developed and are generally employed to summarize the evidence in the medical literature for the efficacy of treatment. The $SROC$ curve was proposed by Moses *et al.* (1993) as a mean of summarizing a test's sensitivity and specificity from multiple studies without the assumption that all of the studies used the same cutpoint (Zhou *et al.*, 2002). New methods based on the $SROC$ curve have since been developed. The basic properties of the $SROC$ curve were discussed by Walter (2002). He proposed the AUC and Q^* as the useful summary index of the curve. The expressions for AUC and its standard error were firstly derived.

1.2 Scope of the Study

Based on Walter's findings on the $SROC$ curve, my project focuses on studying the summary indices PLC and ASC in the context of $SROC$ curve. The mathematical expressions of these two indices and their variances are mainly discussed.

In Chapter 2, *ROC* curve is discussed firstly. The discussion focuses on the summary indices of the *ROC* curve: *AUC*, *PLC* and *ASC*. The concepts of *PLC* and *ASC* were firstly mentioned by Lee *et al.* (1996). The basic properties and simple mathematical methodology of the calculation of these two indices were studied in the context of *ROC* curve. But the approach will sometimes create problems if the choice of the various cutoff points is not straightforward and the study of a diagnostic test is based on data from a meta-analysis. We need to explore the new methodology to find reasonable expressions of index *PLC* and *ASC* in the *SROC* curve and study their basic properties. In this chapter we also introduce some basic concepts and properties of *SROC* curve which lay a foundation for our further studies of *PLC* and *ASC*.

In Chapter 3, the expressions of *PLC* and the variance of *PLC* are derived. The main characteristics of *PLC* in *SROC* curve are discussed. We find that *PLC* index is symmetric with respect to parameters $|a|$ and $|b|$. The homogeneous values of *PLC* provide a good approximation in heterogeneous studies. *PLC* index gains its maximum $\sqrt{2}$ in the heterogeneous case. Our example illustrates that the heterogeneous variances of *PLC* are larger than the homogeneous estimates and the big values of $\text{var}(\hat{PLC})$ indicate the worst situation for estimating *PLC* index in the diagnostic test.

In Chapter 4, the expressions of *ASC* and the variance of *ASC* are derived. The main characteristics of *ASC* in *SROC* curve are discussed. We find that *ASC* index is affected mostly by the new proposed index *M*. Although *AUC* index is symmetric with respect to $|a|$ and $|b|$, *ASC* index lacks symmetry with respect to b for fixed a or lacks symmetry with respect to a for fixed b since *M* index performs the same. As $a \rightarrow \infty$, *ASC* attains its maximum 0.5 in the homogeneous case. Our example illustrates that the heterogeneous variances of *ASC* are larger than the homogeneous

estimates and the big values of $\text{var}(\hat{ASC})$ indicate the worst situation for estimating ASC index in the diagnostic test.

Finally, in Chapter 5, we draw some conclusions based on the work in this project.

Chapter 2

ROC and SROC Curve

2.1 Introduction

The accuracy of a diagnostic test is measured by comparing the test results to the true condition status of the patient. The true condition status is one of binary states: the condition is present or the condition is absent. Test results indicating the condition's presence are called positive; those indicating its absence, negative. If we denote the total number patients as N ; the number of patients with and without the condition is n_1 and n_0 respectively; the number of patients with the condition who test positive and negative is s_1 and s_0 respectively; and the number of patients without the condition who test positive and negative is r_1 and r_0 respectively, then $N = n_1 + n_0 = s_1 + s_0 + r_1 + r_0$.

The true positive rate (TPR , or sensitivity) is the probability that the test result is positive given that the condition is present. Here $TPR = s_1/n_1$. The true negative rate (TNR , or specificity) is the probability that the test result is negative given that

the condition is absent. Here $TNR = r_0/n_0$. These two rates are two basic measures of diagnostic accuracy. On the other hand, the false positive and negative rate can be denoted as $FPR (= 1 - TNR)$ and $FNR (= 1 - TPR)$ respectively. The true positives and negatives indicate the correct diagnosis. But the false ones can cause harm by delaying treatment and providing false reassurance.

Many diagnostic tests yield a numeric measurement rather than a binary result. Therefore, the decision threshold is often used as a cutoff to define positive and negative test and, subsequently, to define sensitivity and specificity in the diagnostic test result. In a test the observer establishes a decision threshold firstly and then uses it to label cases as positive or negative. The conditions categorizing the thresholds can be described as: definitely not present, probably not present, possibly present, probably present or definitely present. One threshold corresponds to one pair of sensitivity and specificity. Different thresholds cause the sensitivity and specificity inherently change as one increases and the other decreases. Thus both sensitivity and specificity must be reported along with the corresponding decision threshold in a diagnostic test (Zhou *et al.*, 2002).

2.2 ROC Curve and its Features

In the diagnostic medicine the parameter of interest mostly is the distinction between diseased and nondiseased on the basis of a particular threshold. For this purpose, probabilistic attributes such as TPR and TNR are often used. In studies of diagnos-

tic tests with a quantitative test result and a dichotomous reference standard (disease present/absent), the relation between TPR and TNR is often represented by a receiver operating characteristic (ROC) curve. The usual situation for a ROC curve is that in a single study one or more pairs of TPR and FPR (which is equal to $1 - TNR$) are plotted in a unit square and then connected empirically to stand for the whole range of possible threshold values graphically. Each point on the graph is generated by a different decision threshold with FPR as x-coordinate and TPR as y-coordinate. There are two key features of ROC curve that make it ideal for studying diagnostic tests. First, the curve displays all positive cut points and thus supply estimates of the frequency of various outcomes. Second, the curve allows the use of previous probabilities of the condition to determine the best cut point for a given test in a given setting (Zhou *et al.*, 2002).

Several summary indices are associated with the ROC curve. One of the most popular measures is the area under the ROC curve (AUC). AUC is the probability that the test value of a randomly selected diseased subject exceeds that of a randomly selected nondiseased subject (Seong *et al.*, 2004). AUC is a measure of the overall performance of a diagnostic test and is interpreted as the average value of sensitivity for all possible values of specificity. It can take on any value between 0 and 1, since both the x and y axes have values ranging from 0 to 1. The closer AUC is to 1, the better the overall diagnostic performance of the test, and a test with an AUC value of 1 is one that is perfectly accurate. The practical lower limit for the AUC of a diagnostic test is 0.5. The line segment from (0,0) to (1,1) has an area of 0.5. If we were to rely on pure chance to distinguish those subjects with versus those without a particular disease, the resulting ROC curve would fall along this diagonal line, which

is referred to as the chance diagonal. A diagnostic test with an AUC value greater than 0.5 is, therefore, at least better than relying on pure chance, and has at least some ability to discriminate between subjects with and without a particular disease (Seong *et al.*, 2004).

Although the AUC index plays an important role in summarizing the entire ROC curve, this index can sometimes fall short of being a good measure of overall performance. It may erroneously rate a perfect or nearly perfect threshold as one without any diagnostic value. In their paper Lee and Hsiao (1996) firstly proposed two alternative summary indices for the ROC curve: PLC (the projected length of the ROC curve) and ASC (the area swept out by the ROC curve). These two indices, as mentioned by Lee, can avoid the main drawbacks for the AUC index and can represent well the variability of the ROC curve from the diagonal line in the unit square.

PLC is the sum of all of the projected lengths of the ROC curve onto the negative diagonal line (the line connecting (0,1) and (1,0)) (Lee *et al.*, 1996). It's interesting to notice that the length of some projected segment should be counted repeatedly if some different parts of the ROC curve all project to this same segment. For ASC , we can imagine a ray emanating from the origin (0,0) to each point in the ROC curve. As the point moving from the origin to the right-uppermost point (1,1), the ray will sweep out some areas. The total area swept out by the ROC curve is denoted as ASC (Lee *et al.*, 1996). Again we can note that some areas should be counted repeatedly if these regions are swept out more than once. The hypothetical ROC curve in Figure 2.1 can be used as an illustration. The PLC index for this example (Figure 2.1 (a)) is: $a' + b' + c'$. The ASC index for this example (Figure 2.1 (b)) is: $A + 2B + C$. For a threshold with no diagnostic value, the ratio of being diseased and of being nondiseased after

measuring will be 1. The corresponding *ROC* curve in this situation runs along the diagonal line, and both the projected length and swept out areas are zero. Once the *ROC* curve deviates from the diagonal line, no matter how small the deviation is and where it occurs, the indices of *PLC* and *ASC* will sum up the deviations. This shows that each of the index may be more sensitive than the conventional *AUC* for detecting differences between the threshold distributions of the diseased and the nondiseased (Lee *et al.*, 1996). The maximal value the *PLC* can attain is $\sqrt{2}$. And the maximal value the *ASC* can get is $1/2$.

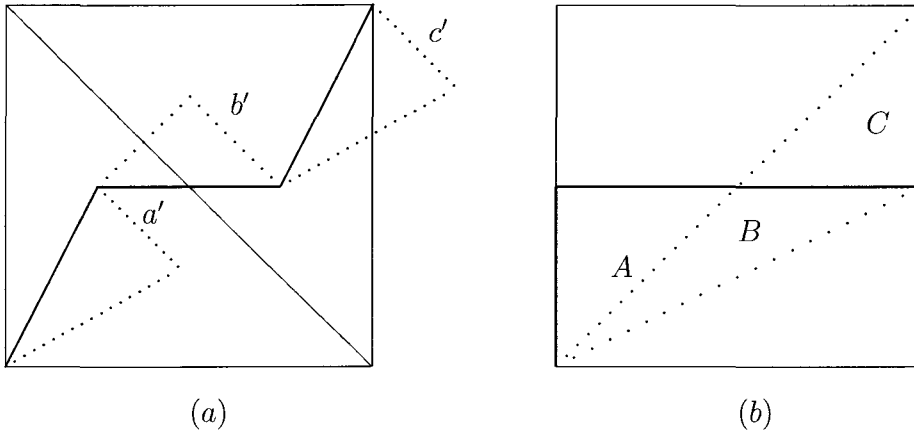


Figure 2.1: Two hypothetical *ROC* curves that consist of three segments of straight lines: (a) to demonstrate *PLC* index and (b) to demonstrate *ASC* index

In their paper Lee and Hsiao (1996) suggested ways to calculate *PLC* and *ASC* through a numerical example. The *ROC* curve in his example is an empirical curve which is formed by varying the possible cutoff points of the threshold and then connecting them with straight lines. The situations here are simplified so that the calculation

of the indices can be easily done by using the rudimentary knowledge of Calculus and Linear Algebra. Figure 2.2 presents how the *ROC* curve works in Lee's example. The hypothetical empirical *ROC* curve is composed of the line segment *AB*, *BC* and *CD*. It's clear that the index *AUC* is the sum of the areas of the two trapezoids under the curve. If $\vec{AF} : (\frac{1}{\sqrt{2}}, -\frac{1}{\sqrt{2}})$ is denoted as a unit vector parallel to the negative diagonal line, the norm of this vector $|\vec{AF}|$ is equal to 1. And the scalar projection of \vec{AB} on \vec{AF} is: $\text{comp}_{\vec{AF}} \vec{AB} = \frac{\vec{AB} \cdot \vec{AF}}{|\vec{AF}|} = \vec{AB} \cdot \vec{AF}$, the dot product of the line segment and the defined unit vector. Similarly we can get the scalar projection of \vec{BC} , \vec{CD} on \vec{AF} respectively. Thus *PLC* can be expressed as the sum of those scalar projections. Index *ASC* can also be expressed through the cross product of the vectors. Since the area of *ABC* is equal to $\frac{1}{2}|\vec{AB} \times \vec{AC}|$ and the area of *ACD* is $\frac{1}{2}|\vec{AC} \times \vec{AD}|$, *ASC* is the sum of those triangles' areas.

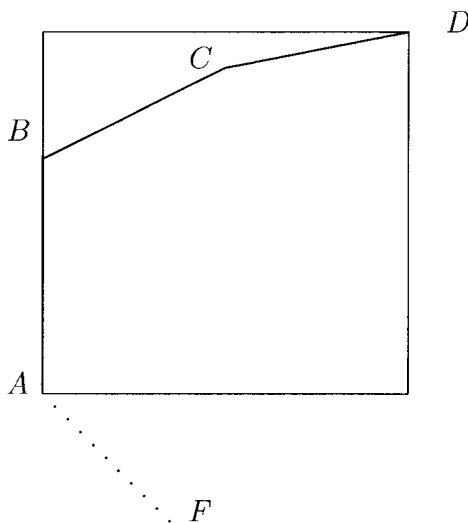


Figure 2.2: A hypothetical *ROC* curve to demonstrate Lee's example

To obtain the performance indices for a threshold measured in such simple situation, we can apply the above methodology for the calculation. But this approach will sometimes create problems if the choice of the various cutoff points is not straightforward and the study of a diagnostic test is based on data from a meta-analysis. In a meta-analysis the summary receiver-operating characteristic (*SROC*) curve instead of *ROC* curve is intended to represent the relationship between *TPR* and *FPR* across studies, recognizing they may have used different thresholds. Smoothed fitting instead of the empirically fitting of the *SROC* curve is needed by using a regression model proposed by Moses *et al.* (1993). Situations become complicated now. We need to explore the new methodology to find reasonable expressions of index *PLC* and *ASC* in the *SROC* curve and study their basic properties.

2.3 SROC Curve and its Features

More recently statistical methods for synthesizing diagnostic test accuracy studies such as meta-analysis have been developed. Meta-analysis is the systematic and quantitative review of the results of a set of individual medical studies all concerning the same or a closely related research question, intended to integrate their findings (Zhou *et al.*, 2002). Current meta-analytic methods are generally applicable to a selection of studies reporting estimates of *TPR* and *FPR* to studies whose results are reported using an equal number of ordered categories. *SROC* curve were proposed as a means of summarizing a test's *TPR* and *FPR* from multiple studies without the assumption

that all of the studies used the same thresholds. In a single study, changing the threshold necessarily results in monotonic changes in TPR and FPR . But in a meta-analysis, in contrast to the ROC analysis, the set of (FPR, TPR) points need not necessarily yield a unique, monotonic curve (Walter, 2002). At the same time, in the early days meta-analysis was always done under the assumption that the true effect measure was homogeneous across all studies. However, usually there is heterogeneity between the treatment effects in the different studies, making the homogeneity unrealistic. Those factors make the study of $SROC$ and its summary indices more complicated.

In his paper Walter (2002) firstly deduced the relationship between TPR and FPR as an expression. This expression was constructed on the smoothed fitting of the $SROC$ curve which is achieved by using a regression model proposed by Moses *et al.* (1993). In his theory, he denoted the dependent and independent variables in the regression as

$$D = \ln\left(\frac{TPR}{1 - TPR}\right) - \ln\left(\frac{FPR}{1 - FPR}\right) \quad (2.1)$$

and

$$S = \ln\left(\frac{TPR}{1 - TPR}\right) + \ln\left(\frac{FPR}{1 - FPR}\right) \quad (2.2)$$

respectively. The regression equation

$$D = a + bS \quad (2.3)$$

can be fitted by standard least squares methods, assuming that D is approximately normally distributed for a given value of S . Here, a is equal to $\ln(OR)$, the diagnostic log-odds ratio; the coefficient b represents the dependence of the test accuracy on threshold. Once the regression has been fitted, reverse the transformation in the expression of D and S and hence the relationship between TPR and FPR can be

expressed as

$$TPR = \frac{\exp(\frac{a}{1-b})(\frac{FPR}{1-FPR})^{\frac{1+b}{1-b}}}{1 + \exp(\frac{a}{1-b})(\frac{FPR}{1-FPR})^{\frac{1+b}{1-b}}} \quad (2.4)$$

This expression gives TPR at any value of FPR , and hence the entire $SROC$ curve. This expression set up the foundation of the further work on the expressions of PLC and ASC in my project.

Before we start to derive the expression for PLC and ASC , we need to introduce some basic concepts and properties of $SROC$ curve.

1. Since $SROC$ curve is defined as the plot of test TPR as the y coordinate versus its FPR as the x coordinate, the expression of TPR and FPR can be rewritten as

$$y = f(x) = \frac{\exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{1+b}{1-b}}}{1 + \exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{1+b}{1-b}}} \quad (2.5)$$

2. Since AUC is the area under the $SROC$ curve, and $0 \leq AUC \leq 1$, AUC can be calculated as

$$AUC = \int_0^1 \frac{\exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{1+b}{1-b}}}{1 + \exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{1+b}{1-b}}} dx \quad (2.6)$$

3. In the homogeneous case $b = 0$,

$$AUC_{hom} = \int_0^1 \frac{\exp(a)(\frac{x}{1-x})}{1 + \exp(a)(\frac{x}{1-x})} dx \quad (2.7)$$

where AUC_{hom} indicates the AUC for homogeneous studies. If $a = 0$, then the special value $AUC_{hom} = \frac{1}{2}$ should be used instead.

4. As suggested by Moses *et al.* (1993), at the ideal top-left corner of the $SROC$ space, we can identify a point Q^* on the curve where $TPR = 1 - FPR$. Since the family of curves defined by a fixed value of a all pass through this common

point, Q^* represents the diagnostic threshold at which the probability of a correct diagnosis is constant for all subjects. Q^* has co-ordinates

$$TPR = \frac{\exp(a/2)}{1 + \exp(a/2)}, \quad FPR = \frac{1}{1 + \exp(a/2)} \quad (2.8)$$

5. When $b \neq 0$ the *SROC* curve has a region where $TPR < FPR$ which lies below the main diagonal. In this region the test would be predicted to be performing worse than at random. Here we can identify another point Q' on the curve where the *SROC* curve crosses the diagonal and has co-ordinates

$$TPR = FPR = \frac{\exp(-a/2b)}{1 + \exp(-a/2b)} \quad (2.9)$$

whatever $b > 0$ or $b < 0$.

Chapter 3

The Projected Length of the SROC Curve (PLC)

3.1 Derivation of Equations of PLC

PLC is the sum of all of the projected lengths of the $SROC$ curve onto the negative diagonal line. Figure 3.1 shows a set of three $SROC$ curves all with $a = 2$ (Fig 3.1(a)) or $a = -2$ (Fig 3.1(b)) but different values of b and curves all with $b = 0.5$ (Fig 3.1(c)) or $b = -0.5$ (Fig 3.1(d)) but different values of a respectively. In those figures non-zero values of b make the $SROC$ curves crossing the diagonal at point Q' . Point Q' lies close to the lower-left corner when a and b have the same sign (positive or negative); and it is close to the upper-right corner when a and b have different sign. Point Q' separates the whole curve into two parts: the region lying below the main diagonal and the region lying above the main diagonal. We name these two area as Region A and Region B respectively. In each region the maximum distance between the curve

and the diagonal exists. If we denote the maximum distance in Region A as \hat{d}_1 and the maximum distance in Region B as \hat{d}_2 , PLC can be expressed as

$$PLC = 2(\hat{d}_1 + \hat{d}_2) \quad (3.1)$$

by definition.

We know that the formula for the distance d from a point $P_1(x_1, y_1)$ to the line $ax + by + c = 0$ is: $d = \frac{|ax_1 + by_1 + c|}{\sqrt{a^2 + b^2}}$. Then the distance from any point (x, y) on the $SROC$ curve to the diagonal $y = x$ (or, $-x + y = 0$) is: $d = \frac{|-x + y|}{\sqrt{2}}$. Since the curve can be expressed as

$$y = f(x) = \frac{\exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{1+b}{1-b}}}{1 + \exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{1+b}{1-b}}}$$

and the co-ordinates of point Q' are

$$TPR = FPR = \frac{\exp(-a/2b)}{1 + \exp(-a/2b)},$$

denote d_1 and d_2 as the distance from any point (x, y) on the $SROC$ curve to the diagonal $y = x$ in Region A and B respectively, then d_1 and d_2 can be expressed as

$$d_1 = \frac{x - 1 + \frac{1}{1 + \exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{1+b}{1-b}}}}{\sqrt{2}}, \quad 0 < x < \frac{\exp(-a/2b)}{1 + \exp(-a/2b)}, \quad (3.2)$$

$$d_2 = \frac{-x + 1 - \frac{1}{1 + \exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{1+b}{1-b}}}}{\sqrt{2}}, \quad \frac{\exp(-a/2b)}{1 + \exp(-a/2b)} < x < 1, \quad (3.3)$$

when $b > 0$ or

$$d_1 = \frac{x - 1 + \frac{1}{1 + \exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{1+b}{1-b}}}}{\sqrt{2}}, \quad \frac{\exp(-a/2b)}{1 + \exp(-a/2b)} < x < 1, \quad (3.4)$$

$$d_2 = \frac{-x + 1 - \frac{1}{1 + \exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{1+b}{1-b}}}}{\sqrt{2}}, \quad 0 < x < \frac{\exp(-a/2b)}{1 + \exp(-a/2b)}, \quad (3.5)$$

when $b < 0$.

Fermat's Theorem says, for a function $f(x)$, if f has a local maximum at $x = c$, and if $f'(c)$ exists, then $f'(c) = 0$ (Stewart, 2003). For the function $d_1 = g(x, a, b)$, if d_1 has the maximum \hat{d}_1 at $x = v(a, b)$, and suppose $\frac{\partial d_1}{\partial x} \Big|_{x=v(a,b)} = g'(v(a, b), a, b)$ exists, then $g'(v(a, b), a, b) = 0$ by Fermat Theorem .

If we differentiate both sides of equation (3.2) or (3.4) on x and let it equal to be 0, after some calculations, we get

$$\frac{\exp(\frac{a}{1-b})(\frac{1+b}{1-b})(\frac{x}{1-x})^{\frac{2b}{1-b}} \frac{1}{(1-x)^2}}{[1 + \exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{2b}{1-b}}]^2} = 1. \quad (3.6)$$

Similarly, if we differentiate both sides of equation (3.3) or (3.5) on x and let it equal to be 0, we also get the same equation like (3.6).

If $v_1(a, b)$ is denoted as the solution of equation (3.6) as $0 < x < \frac{\exp(-a/2b)}{1 + \exp(-a/2b)}$ for $b > 0$ or as $\frac{\exp(-a/2b)}{1 + \exp(-a/2b)} < x < 1$ for $b < 0$, d_1 has the maximum \hat{d}_1 at $x = v_1(a, b)$. Similarly, if we denote $v_2(a, b)$ as the solution of equation (3.6) as $\frac{\exp(-a/2b)}{1 + \exp(-a/2b)} < x < 1$ for $b > 0$ or as $0 < x < \frac{\exp(-a/2b)}{1 + \exp(-a/2b)}$ for $b < 0$, d_2 has the maximum \hat{d}_2 at $x = v_2(a, b)$. The maximum distance \hat{d}_1 and \hat{d}_2 can be expressed as

$$\hat{d}_1 = \frac{v_1(a, b) - 1 + \frac{1}{1 + \exp(\frac{a}{1-b})(\frac{v_1(a,b)}{1-v_1(a,b)})^{\frac{1+b}{1-b}}}}{\sqrt{2}}, \quad 0 < x < \frac{\exp(-a/2b)}{1 + \exp(-a/2b)}, \quad (3.7)$$

$$\hat{d}_2 = \frac{-v_2(a, b) + 1 - \frac{1}{1 + \exp(\frac{a}{1-b})(\frac{v_2(a,b)}{1-v_2(a,b)})^{\frac{1+b}{1-b}}}}{\sqrt{2}}, \quad \frac{\exp(-a/2b)}{1 + \exp(-a/2b)} < x < 1, \quad (3.8)$$

when $b > 0$, or

$$\hat{d}_1 = \frac{v_1(a, b) - 1 + \frac{1}{1 + \exp(\frac{a}{1-b})(\frac{v_1(a, b)}{1-v_1(a, b)})^{\frac{1+b}{1-b}}}}{\sqrt{2}}, \quad \frac{\exp(-a/2b)}{1 + \exp(-a/2b)} < x < 1, \quad (3.9)$$

$$\hat{d}_2 = \frac{-v_2(a, b) + 1 - \frac{1}{1 + \exp(\frac{a}{1-b})(\frac{v_2(a, b)}{1-v_2(a, b)})^{\frac{1+b}{1-b}}}}{\sqrt{2}}, \quad 0 < x < \frac{\exp(-a/2b)}{1 + \exp(-a/2b)}, \quad (3.10)$$

when $b < 0$. Thus, the derivation of $PLC = 2(\hat{d}_1 + \hat{d}_2)$ is obtained completely.

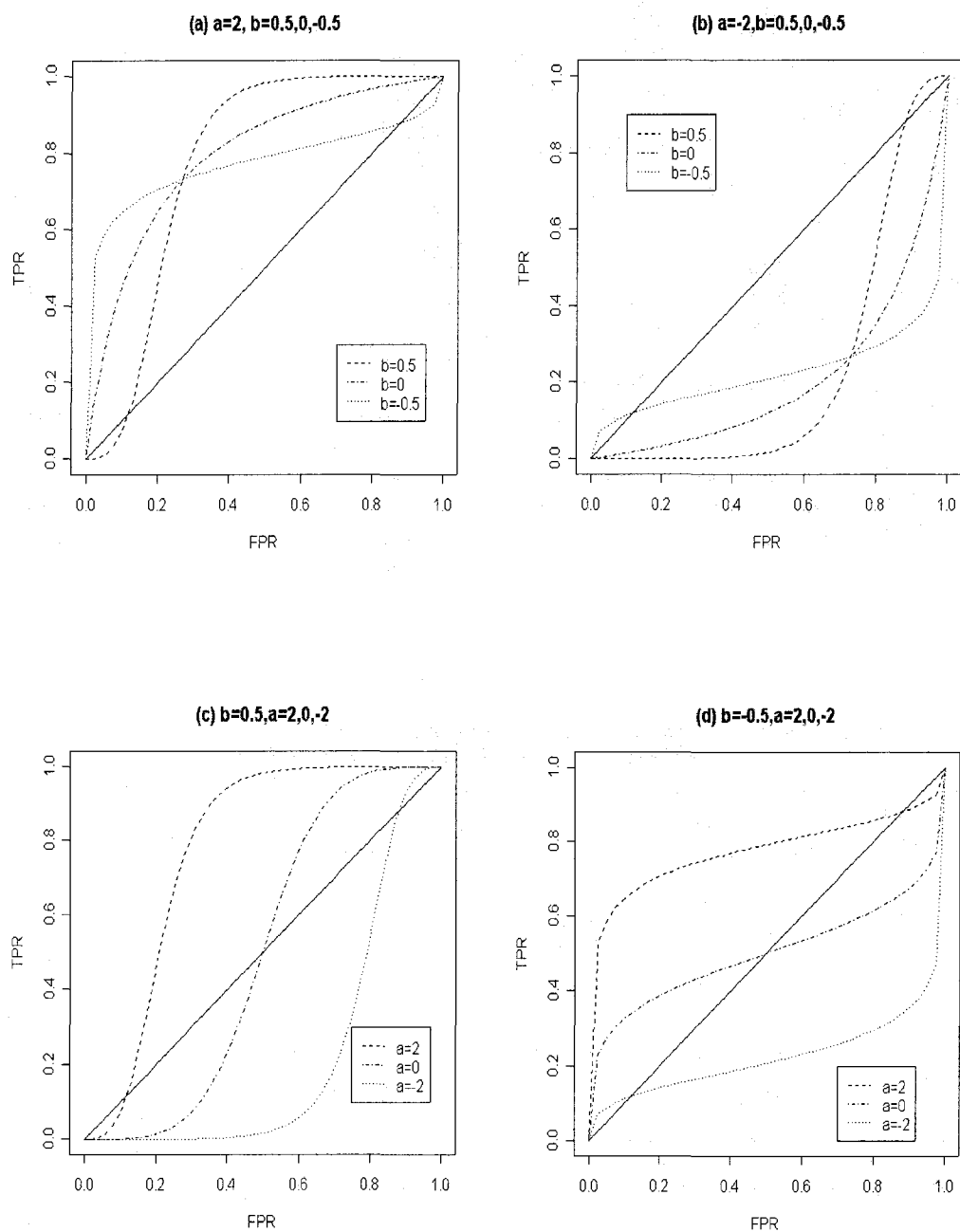


Figure 3.1: SROC curve (a) and (b) with various values of b ; (c) and (d) with various values of a .

3.2 The Behaviour of PLC

3.2.1 Introduction

Odds Ratio (OR) is often used in meta-analyses of the accuracy of diagnostic tests. It is defined as the odds of a positive test result relative to a negative test result among patients with the condition divided by the odds of a positive test result relative to a negative test result among patients without the condition. It can be written as

$$OR = \frac{TPR/(1 - TPR)}{FPR/(1 - FPR)} \quad (3.11)$$

$OR > 1$ indicates the odds of a positive test result is greater for patients with the condition; $OR = 1$ indicates the positive test result is the same for patients with and without the condition; $OR < 1$ indicates the odds of a positive test result is greater for patients without the condition (Zhou *et al.*, 2002). In $SROC$ curve, $a = \ln(OR)$ and it conveys the test's accuracy in discriminating cases from non-cases. $a \rightarrow \infty$ ($OR \rightarrow \infty$), $SROC$ curve moves closer to the upper-left corner and this indicates a perfect test with no errors in distinguishing cases from non-cases; $a \approx 0$ ($OR \approx 1$), the curve is close to the diagonal and the test is no better than pure chance; $a < 0$ ($OR < 1$), the test discriminates cases and non-cases in the wrong direction and worse than at random; $a \rightarrow -\infty$ ($OR \rightarrow 0$), curve moves closer the lower-right corner and such situations are unlikely to occur in practice (Walter, 2002). Since as $a \geq 4$ ($OR \geq 55$) or $a \leq -4$ ($OR \leq 0.02$) the difference for the curve changes slowly, my project focuses on $|a| \leq 3$.

Parameter b can be interpreted as the dependence of the test accuracy on threshold. $b \approx 0$, the studies are homogeneous and there is no relationship between OR and

threshold; $|b| \rightarrow 1$, the curve degenerates to the horizontal or vertical line and there is no relationship of TPR and FPR ; $|b| > 1$, there is negative relationship between TPR and FPR and such situations are unlikely to occur in practice (Walter, 2002). In $SROC$ curve we only consider the situations under $|b| < 1$. Since $|b| > 0.4$ are the extreme values, my project focus on $|b| \leq 0.3$.

3.2.2 The Behaviour of PLC

Figure 3.1(a) shows the family of curves defined by a fixed positive value of a all pass through common point Q^* and are symmetric about it. Similar thing is seen in Figure 3.1(b) if the curves are flipped 180° around the diagonal. But this time the curves are symmetric about another common point. We call it P^* . This implies that the alternative index PLC should perform the same as $SROC$ curve, although the area under the curve (AUC) shrinks when a changes from positive to negative. The values in Table 3.1 to Table 3.4 are computed by numerical integration when $-3 \leq a \leq 3$ and $-0.3 \leq b \leq 0.3$. Table 3.3 shows the values of PLC which are symmetric for the fixed values of $|a|$ and $|b|$. This indicates PLC index in a perfect test keeps the same as the one in a worst test. But this does not suggest that the projected length \hat{d}_1 and \hat{d}_2 have the same behavior as PLC , although PLC is the sum of these two lengths. The values of \hat{d}_1 in Table 3.1 and values of \hat{d}_2 in Table 3.2 show that both \hat{d}_1 and \hat{d}_2 are only symmetric for the fixed value of a . For fixed a , all PLC , \hat{d}_1 and \hat{d}_2 decline slowly as b increases from large negative values (decreasing heterogeneity) to 0 (homogeneous studies) and increase slowly as b increases from 0 (homogeneous studies) to large positive values (increasing heterogeneity). The percentage change for PLC compared to the homogeneous values is less than 6 per cent in most cases. Accordingly, the

homogeneous values of PLC provide a good approximation in heterogeneous studies.

Interestingly, as suggested by Table 3.1 and 3.2, \hat{d}_1 and \hat{d}_2 perform on the opposite direction for the fixed value of b , but they have the same behavior for the fixed value of a . That is, they decrease first as b goes from negative to zero and then increase as b moves from zero to positive. Thus, both \hat{d}_1 and \hat{d}_2 attain the minimum value in the homogeneous case. So does the PLC .

For completeness, we must mention the situation where PLC attains its maximum. We discuss before that the maximal value the PLC index can attain in the ROC curve is $\sqrt{2}$. We can get the same conclusion for PLC index in $SROC$ curve, since the maximum value of the sum of \hat{d}_1 and \hat{d}_2 is $\sqrt{2}/2$. This can be seen from Table 3.4 which show the numerical values of PLC when $0 \leq b \leq 0.9$ and $1 \leq a \leq 10$. As $a \rightarrow \infty$, $PLC \rightarrow 1.4142$ (or $\sqrt{2}$) with a curve that is close to the upper-left corner of the $SROC$ space when $a > 0$ or a curve that is close to the lower-right corner when $a < 0$ by symmetry.

The zero value of PLC corresponds to the $SROC$ curve running along the diagonal line. This situation indicates a cut-off point with no diagnostic value. Once the $SROC$ curve deviates from the diagonal line, the PLC index will sum up the deviation. Since PLC index in a perfect test ($a \rightarrow \infty$) is symmetric to the one in a worse test ($a \rightarrow -\infty$), the greater value of PLC indicate the great probability of a correct diagonal when $a > 0$ and the great probability of a wrong diagonal when $a < 0$. We can never say the greater value of PLC implies a perfect test unless the value of AUC is bigger as well and parameter a is positive.

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| -0.3 | 0.9267306 | 0.7025319 | 0.4371681 | 0.1908746 | 0.0526614 | 0.0110170 | 0.0021253 |
| -0.2 | 0.9112282 | 0.6764624 | 0.3924688 | 0.1269060 | 0.0162252 | 0.0014047 | 0.0001158 |
| -0.1 | 0.9015382 | 0.6594725 | 0.3592875 | 0.0633532 | 0.0006988 | 0.0000047 | 0.0000000 |
| 0 | 0.8982363 | 0.6535323 | 0.3463673 | 0.0000000 | 0.0000000 | 0.0000000 | 0.0000000 |
| 0.1 | 0.9015382 | 0.6594725 | 0.3592875 | 0.0633532 | 0.0006988 | 0.0000047 | 0.0000000 |
| 0.2 | 0.9112282 | 0.6764624 | 0.3924688 | 0.1269060 | 0.0162252 | 0.0014047 | 0.0001158 |
| 0.3 | 0.9267306 | 0.7025319 | 0.4371681 | 0.1908746 | 0.0526614 | 0.0110170 | 0.0021253 |

Table 3.1: values of $2\hat{d}_1$

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| -0.3 | 0.0021253 | 0.0110170 | 0.0526614 | 0.1908746 | 0.4371681 | 0.7025319 | 0.9267306 |
| -0.2 | 0.0001158 | 0.0014047 | 0.0162252 | 0.1269060 | 0.3924688 | 0.6764624 | 0.9112282 |
| -0.1 | 0.0000000 | 0.0000047 | 0.0006988 | 0.0633532 | 0.3592875 | 0.6594725 | 0.9015382 |
| 0 | 0.0000000 | 0.0000000 | 0.0000000 | 0.0000000 | 0.3463673 | 0.6535323 | 0.8982363 |
| 0.1 | 0.0000000 | 0.0000047 | 0.0006988 | 0.0633532 | 0.3592875 | 0.6594725 | 0.9015382 |
| 0.2 | 0.0001158 | 0.0014047 | 0.0162252 | 0.1269060 | 0.3924688 | 0.6764624 | 0.9112282 |
| 0.3 | 0.0021253 | 0.0110170 | 0.0526614 | 0.1908746 | 0.4371681 | 0.7025319 | 0.9267306 |

Table 3.2: values of $2\hat{d}_2$

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| -0.3 | 0.9288559 | 0.7135490 | 0.4898295 | 0.3817493 | 0.4898295 | 0.7135490 | 0.9288559 |
| -0.2 | 0.9113441 | 0.6778671 | 0.4086940 | 0.2538119 | 0.4086940 | 0.6778671 | 0.9113441 |
| -0.1 | 0.9015383 | 0.6594772 | 0.3599863 | 0.1267064 | 0.3599863 | 0.6594772 | 0.9015383 |
| 0 | 0.8982363 | 0.6535323 | 0.3463673 | 0.0000000 | 0.3463673 | 0.6535323 | 0.8982363 |
| 0.1 | 0.9015383 | 0.6594772 | 0.3599863 | 0.1267064 | 0.3599863 | 0.6594772 | 0.9015383 |
| 0.2 | 0.9113441 | 0.6778671 | 0.4086940 | 0.2538119 | 0.4086940 | 0.6778671 | 0.9113441 |
| 0.3 | 0.9288559 | 0.7135490 | 0.4898295 | 0.3817493 | 0.4898295 | 0.7135490 | 0.9288559 |

Table 3.3: values of PLC

| $b \backslash a$ | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|------------------|-----------|-----------|-----------|----------|----------|----------|----------|----------|----------|----------|
| 0 | 0.3463673 | 0.6535323 | 0.8982363 | 1.077057 | 1.199654 | 1.280073 | 1.331306 | 1.363341 | 1.383138 | 1.395283 |
| 0.1 | 0.3599863 | 0.6594772 | 0.9015383 | 1.079000 | 1.200820 | 1.280778 | 1.331733 | 1.363600 | 1.383295 | 1.395378 |
| 0.2 | 0.4086940 | 0.6778671 | 0.9113441 | 1.084767 | 1.204291 | 1.282879 | 1.333007 | 1.364373 | 1.383764 | 1.395663 |
| 0.3 | 0.4898295 | 0.7135490 | 0.9288559 | 1.094526 | 1.210056 | 1.286354 | 1.335114 | 1.365651 | 1.384540 | 1.396134 |
| 0.4 | 0.5896391 | 0.7686353 | 0.9571719 | 1.109675 | 1.218592 | 1.291338 | 1.338083 | 1.367438 | 1.385620 | 1.396788 |
| 0.5 | 0.7005284 | 0.8405507 | 0.9982114 | 1.132305 | 1.231154 | 1.298445 | 1.342183 | 1.369841 | 1.387044 | 1.397640 |
| 0.6 | 0.8193848 | 0.9261165 | 1.0521063 | 1.164014 | 1.249291 | 1.308742 | 1.348045 | 1.373202 | 1.388989 | 1.398775 |
| 0.7 | 0.9455035 | 1.0233487 | 1.1183498 | 1.205735 | 1.274399 | 1.323485 | 1.356594 | 1.378134 | 1.391832 | 1.400417 |
| 0.8 | 1.0800848 | 1.1320446 | 1.1969599 | 1.258308 | 1.307796 | 1.344019 | 1.368964 | 1.385492 | 1.396173 | 1.402965 |
| 0.9 | 1.2276058 | 1.2551311 | 1.2900685 | 1.323737 | 1.351459 | 1.372157 | 1.386679 | 1.396471 | 1.402904 | 1.407060 |

Table 3.4: values of PLC when $0 \leq b \leq 0.9$ and $1 \leq a \leq 10$

3.3 Derivation of the Variance of PLC

From equation (3.7) to (3.10), we find that \hat{d}_1 and \hat{d}_2 are functions of the regression parameters a and b , since $v_1(a, b)$ and $v_2(a, b)$ are functions of a and b . Hence the variability in $P\hat{L}C$ is a function of the sample variation in \hat{a} and \hat{b} and can be estimated by the delta method. The delta method expands a function of a random variable about its mean, usually with a 1-step Taylor approximation, and then takes the variance. For example, if we want to approximate the variance of $G(X)$ where X is a random variable with mean μ and G is differentiable, we can try

$$G(X) \doteq G(\mu) + (X - \mu)G'(\mu)$$

by Taylor expansion so that

$$\text{var}(G(X)) \doteq \text{var}(X)[G'(\mu)]^2.$$

Thus, by using this method, an approximate variance for $P\hat{L}C$ is:

$$\text{var}(P\hat{L}C) = \left(\frac{\partial PLC}{\partial a}\right)^2 \text{var}(\hat{a}) + \left(\frac{\partial PLC}{\partial b}\right)^2 \text{var}(\hat{b}) + 2\left(\frac{\partial PLC}{\partial a}\right)\left(\frac{\partial PLC}{\partial b}\right)\text{cov}(\hat{a}, \hat{b}), \quad (3.12)$$

where,

$$\frac{\partial PLC}{\partial a} = 2\frac{\partial \hat{d}_1}{\partial a} + 2\frac{\partial \hat{d}_2}{\partial a} \quad (3.13)$$

$$\frac{\partial PLC}{\partial b} = 2\frac{\partial \hat{d}_1}{\partial b} + 2\frac{\partial \hat{d}_2}{\partial b}. \quad (3.14)$$

To solve $\partial PLC/\partial a$, we need to find the expressions of $\partial \hat{d}_1/\partial a$ and $\partial \hat{d}_2/\partial a$ separately. The expression of $\partial \hat{d}_1/\partial a$ can be expressed as

$$\begin{aligned}
\frac{\partial \hat{d}_1}{\partial a} &= \frac{\partial}{\partial a} \left[\frac{v_1(a, b) - 1 + \frac{1}{1 + \exp(\frac{a}{1-b})(\frac{v_1(a, b)}{1-v_1(a, b)})^{\frac{1+b}{1-b}}}}{\sqrt{2}} \right] \\
&= \frac{1}{\sqrt{2}} \left[\frac{\partial v_1(a, b)}{\partial a} - \frac{\frac{1}{1-b} \exp(\frac{a}{1-b})(\frac{v_1(a, b)}{1-v_1(a, b)})^{\frac{1+b}{1-b}} [1 + \frac{(1+b)}{v_1(a, b)(1-v_1(a, b))} \frac{\partial v_1(a, b)}{\partial a}]}{[1 + \exp(\frac{a}{1-b})(\frac{v_1(a, b)}{1-v_1(a, b)})^{\frac{1+b}{1-b}}]^2} \right] \quad (3.15)
\end{aligned}$$

Since $v_1(a, b)$ is denoted as the solution of equation (3.6) which can maximize the value of d_1 , the unknown factor $\partial v_1(a, b)/\partial a$ involved in the expression (3.15) can be deduced by differentiating both sides of equation (3.6) on a when $x = v_1(a, b)$ first and then reversing the transformation. Hence the result is:

$$\frac{\partial v_1(a, b)}{\partial a} = \frac{\frac{1}{1-b} - 2[1 + \exp(\frac{a}{1-b})(\frac{v_1(a, b)}{1-v_1(a, b)})^{\frac{1+b}{1-b}}] \frac{v_1(a, b)(1-v_1(a, b))}{1+b}}{2[1 + \exp(\frac{a}{1-b})(\frac{v_1(a, b)}{1-v_1(a, b)})^{\frac{1+b}{1-b}}] - \frac{2b}{(1-b)v_1(a, b)(1-v_1(a, b))} - \frac{2}{1-v_1(a, b)}}. \quad (3.16)$$

Similarly, by using the same way, $\partial \hat{d}_2/\partial a$ and the unknown factor $\partial v_2(a, b)/\partial a$ involved in the expression of $\partial \hat{d}_2/\partial a$ can be expressed respectively as

$$\frac{\partial \hat{d}_2}{\partial a} = \frac{1}{\sqrt{2}} \left[-\frac{\partial v_2(a, b)}{\partial a} + \frac{\frac{1}{1-b} \exp(\frac{a}{1-b})(\frac{v_2(a, b)}{1-v_2(a, b)})^{\frac{1+b}{1-b}} [1 + \frac{(1+b)}{v_2(a, b)(1-v_2(a, b))} \frac{\partial v_2(a, b)}{\partial a}]}{[1 + \exp(\frac{a}{1-b})(\frac{v_2(a, b)}{1-v_2(a, b)})^{\frac{1+b}{1-b}}]^2} \right], \quad (3.17)$$

$$\frac{\partial v_2(a, b)}{\partial a} = \frac{\frac{1}{1-b} - 2[1 + \exp(\frac{a}{1-b})(\frac{v_2(a, b)}{1-v_2(a, b)})^{\frac{1+b}{1-b}}] \frac{v_2(a, b)(1-v_2(a, b))}{1+b}}{2[1 + \exp(\frac{a}{1-b})(\frac{v_2(a, b)}{1-v_2(a, b)})^{\frac{1+b}{1-b}}] - \frac{2b}{(1-b)v_2(a, b)(1-v_2(a, b))} - \frac{2}{1-v_2(a, b)}}. \quad (3.18)$$

Also, to solve $\partial PLC/\partial b$ we need to find the expressions of $\partial \hat{d}_1/\partial b$ and $\partial \hat{d}_2/\partial b$

separately. By using the same method of deducing the equation of $\partial \hat{d}_1 / \partial a$ and $\partial \hat{d}_2 / \partial a$, $\partial \hat{d}_1 / \partial b$ and $\partial \hat{d}_2 / \partial b$ can be expressed as

1.

$$\begin{aligned} \frac{\partial \hat{d}_1}{\partial b} &= \frac{1}{\sqrt{2}} \left[\frac{\partial v_1(a, b)}{\partial b} \right] - \frac{1}{\sqrt{2}} \times \\ &\quad \left[\frac{\exp(\frac{a}{1-b}) (\frac{v_1(a, b)}{1-v_1(a, b)})^{\frac{1+b}{1-b}} [a + 2 \ln(\frac{v_1(a, b)}{1-v_1(a, b)}) + \frac{(1-b^2)}{v_1(a, b) - v_1(a, b)^2} \frac{\partial v_1(a, b)}{\partial b}]}{[1 + \exp(\frac{a}{1-b}) (\frac{v_1(a, b)}{1-v_1(a, b)})^{\frac{1+b}{1-b}}]^2} \right], \quad (3.19) \end{aligned}$$

2.

$$\begin{aligned} &\frac{\partial v_1(a, b)}{\partial b} \\ &= \frac{[(1 + \exp(\frac{a}{1-b}) (\frac{v_1(a, b)}{1-v_1(a, b)})^{\frac{1+b}{1-b}}) \frac{v_1(a, b)(1+v_1(a, b))}{(1+b)^2}] [a + 2 \ln(\frac{v_1(a, b)}{1-v_1(a, b)})]}{\frac{b}{1-b} \frac{1}{v_1(a, b)(1+v_1(a, b))} + \frac{1}{1-v_1(a, b)} - (1 + \exp(\frac{a}{1-b}) (\frac{v_1(a, b)}{1-v_1(a, b)})^{\frac{1+b}{1-b}})} \\ &\quad - \frac{\frac{1}{2(1-b)^2} [a + 2 \ln(\frac{v_1(a, b)}{1-v_1(a, b)})] + \frac{1}{(1+b)^2}}{\frac{b}{1-b} \frac{1}{v_1(a, b)(1+v_1(a, b))} + \frac{1}{1-v_1(a, b)} - (1 + \exp(\frac{a}{1-b}) (\frac{v_1(a, b)}{1-v_1(a, b)})^{\frac{1+b}{1-b}})}, \quad (3.20) \end{aligned}$$

3.

$$\begin{aligned} \frac{\partial \hat{d}_2}{\partial b} &= -\frac{1}{\sqrt{2}} \left[\frac{\partial v_2(a, b)}{\partial b} \right] + \frac{1}{\sqrt{2}} \times \\ &\quad \left[\frac{\exp(\frac{a}{1-b}) (\frac{v_2(a, b)}{1-v_2(a, b)})^{\frac{1+b}{1-b}} [a + 2 \ln(\frac{v_2(a, b)}{1-v_2(a, b)}) + \frac{(1-b^2)}{v_2(a, b) - v_2(a, b)^2} \frac{\partial v_2(a, b)}{\partial b}]}{[1 + \exp(\frac{a}{1-b}) (\frac{v_2(a, b)}{1-v_2(a, b)})^{\frac{1+b}{1-b}}]^2} \right], \quad (3.21) \end{aligned}$$

4.

$$\begin{aligned} &\frac{\partial v_2(a, b)}{\partial b} \\ &= \frac{[(1 + \exp(\frac{a}{1-b}) (\frac{v_2(a, b)}{1-v_2(a, b)})^{\frac{1+b}{1-b}}) \frac{v_2(a, b)(1+v_2(a, b))}{(1+b)^2}] [a + 2 \ln(\frac{v_2(a, b)}{1-v_2(a, b)})]}{\frac{b}{1-b} \frac{1}{v_1(a, b)(1+v_1(a, b))} + \frac{1}{1-v_1(a, b)} - (1 + \exp(\frac{a}{1-b}) (\frac{v_2(a, b)}{1-v_2(a, b)})^{\frac{1+b}{1-b}})} \\ &\quad - \frac{\frac{1}{2(1-b)^2} [a + 2 \ln(\frac{v_2(a, b)}{1-v_2(a, b)})] + \frac{1}{(1+b)^2}}{\frac{b}{1-b} \frac{1}{v_1(a, b)(1+v_1(a, b))} + \frac{1}{1-v_1(a, b)} - (1 + \exp(\frac{a}{1-b}) (\frac{v_2(a, b)}{1-v_2(a, b)})^{\frac{1+b}{1-b}})}. \quad (3.22) \end{aligned}$$

Thus, the derivation of $\text{var}(\hat{PLC})$ is obtained completely.

3.4 The Behaviour of the Variance of PLC

We know that, for a function $f(x)$, because $f'(x)$ represents the slope of the curve $y = f(x)$ at the point $(x, f(x))$, it tells us the direction in which the curve proceeds at each point. So it is reasonable to expect that information about $f'(x)$ will provide us with information about $f(x)$. Evaluation of $\text{var}(\hat{PLC})$ requires numerical methods to deal with the partial derivatives (3.13) and (3.14). Our next step is to study what those derivatives involved in $\text{var}(\hat{PLC})$ can tell.

The Increasing/Decreasing Test tells us that, for a function $f(x)$, if $f'(x) > 0$ on an interval, then f is increasing on that interval; if $f'(x) < 0$ on an interval, then f is decreasing on that interval (Stewart, 2003). By using this test, on the interval $-3 \leq a \leq 3$, \hat{d}_1 is a decreasing function of a for the fixed value of b ; \hat{d}_2 performs in the opposite direction under the same situation. For $-2 \leq a \leq -1$, \hat{d}_1 decreases progressively steeper. But before and after that interval, \hat{d}_1 decreases slowly. As $a \rightarrow \infty$, $\partial \hat{d}_1 / \partial a$ is close to 0 and this implies that the length of \hat{d}_1 vanishes for large a . On the opposite, for $1 \leq a \leq 2$, \hat{d}_2 increases progressively steeper. But as $a \rightarrow -\infty$, the length of \hat{d}_2 vanishes for large negative values of a . This can be verified by the numerical values in Table 3.5 and 3.6 and the Figure 3.1(c) and 3.1(d) visually.

The First Derivative Test says that, for a continuous differentiable function $f(x)$, suppose c is a critical number, if f' changes from positive to negative at c , f has

a local maximum at c ; if f' changes from negative to positive at c , f has a local minimum at c ; if f' does not change sign at c , f has no local maximum or minimum at c (Stewart, 2003). We mentioned in the last section that \hat{d}_1 and \hat{d}_2 perform on the opposite direction for the fixed value of b , but they have the same behavior for the fixed value of a . That is, both of them decrease as b goes from negative to zero and then increase as b goes from zero to positive. This conclusion can be proved again by Table 3.7 and 3.8. And since $\partial d_1/\partial b$ and $\partial d_2/\partial b$ change sign from negative to positive at $b = 0$, both \hat{d}_1 and \hat{d}_2 attain the minimum value in the homogeneous case.

Since PLC index is the sum of \hat{d}_1 and \hat{d}_2 , its performance will be affected by these two parts. In Table 3.9, $\partial PLC/\partial a$ changes sign from negative to positive at $a = 0$, PLC attains its minimum value at $a = 0$; on the other hand, in Table 3.10, $\partial PLC/\partial b$ changes sign from negative to positive at $b = 0$, PLC attains its minimum value at $b = 0$, the homogeneous case.

To explore the effects of $\text{var}(P\hat{L}C)$ we use expression (3.12) with various values of a and b and keep $\text{var}(\hat{b})$ and $\text{cov}(\hat{a}, \hat{b})$ fixed at their observed values based on data for the lymphangiography test for cervical cancer metastases (Scheidler *et al.*, 1997). In that case the values of $\text{var}(\hat{a})$, $\text{var}(\hat{b})$ and $\text{cov}(\hat{a}, \hat{b})$ are calculated by using the standard regression software and obtained as 0.14297, 0.06305 and 0.05285 respectively. If we plug in those values in (3.12), the numerical values for $\text{var}(P\hat{L}C)$ are shown in Table 3.11. This example illustrates that the heterogeneous variances are larger than the homogeneous estimates. Since PLC are symmetric for the fixed values of $|a|$ and $|b|$, $\text{var}(P\hat{L}C)$ are also symmetric under the same condition. $\text{var}(P\hat{L}C)$ decreases with respect to values of $|b|$. The big values of $\text{var}(P\hat{L}C)$ indicate the worst situation for estimating PLC index in the diagnostic test.

| b\ a | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------|-------------|------------|------------|------------|--------------|---------------|---------------|
| -0.3 | -0.09801845 | -0.1250829 | -0.1354480 | -0.1015308 | -0.038743954 | -8.945266e-03 | -1.762227e-03 |
| -0.2 | -0.10196789 | -0.1320208 | -0.1472386 | -0.1021093 | -0.019150036 | -1.747158e-03 | -1.447294e-04 |
| -0.1 | -0.10455676 | -0.1371136 | -0.1597735 | -0.1024524 | -0.001738399 | -1.182885e-05 | -7.970748e-08 |
| 0 | -0.10546247 | -0.1390256 | -0.1661727 | 0.00000000 | 0.000000000 | 0.00000000000 | 0.0000000000 |
| 0.1 | -0.10455676 | -0.1371136 | -0.1597735 | -0.1024524 | -0.001738399 | -1.182885e-05 | -7.970748e-08 |
| 0.2 | -0.10196789 | -0.1320208 | -0.1472386 | -0.1021093 | -0.019150036 | -1.747158e-03 | -1.447294e-04 |
| 0.3 | -0.09801845 | -0.1250829 | -0.1354480 | -0.1015308 | -0.038743954 | -8.945266e-03 | -1.762227e-03 |

Table 3.5: values of $\partial \hat{d}_1 / \partial a$

| b\ a | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------|--------------|--------------|-------------|-----------|-----------|-----------|------------|
| -0.3 | 1.762227e-03 | 8.945266e-03 | 0.038743954 | 0.1015308 | 0.1354480 | 0.1250829 | 0.09801845 |
| -0.2 | 1.447294e-04 | 1.747158e-03 | 0.019150036 | 0.1021093 | 0.1472386 | 0.1320208 | 0.10196789 |
| -0.1 | 7.970748e-08 | 1.182885e-05 | 0.001738399 | 0.1024524 | 0.1597735 | 0.1371136 | 0.10455676 |
| 0 | 0.0000000000 | 0.000000000 | 0.000000000 | 0.0000000 | 0.1661727 | 0.1390256 | 0.10546247 |
| 0.1 | 7.970748e-08 | 1.182885e-05 | 0.001738399 | 0.1024524 | 0.1597735 | 0.1371136 | 0.10455676 |
| 0.2 | 1.447294e-04 | 1.747158e-03 | 0.019150036 | 0.1021093 | 0.1472386 | 0.1320208 | 0.10196789 |
| 0.3 | 1.762227e-03 | 8.945266e-03 | 0.038743954 | 0.1015308 | 0.1354480 | 0.1250829 | 0.09801845 |

Table 3.6: values of $\partial \hat{d}_2 / \partial a$

| b\ a | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------|--------------|--------------|--------------|-----------|------------|--------------|--------------|
| -0.3 | -9.07990e-02 | -1.49342e-01 | -2.42068e-01 | -0.321284 | -0.2193111 | -0.078563952 | -2.12763e-02 |
| -0.2 | -6.35718e-02 | -1.09511e-01 | -2.00697e-01 | -0.318612 | -0.1368337 | -0.021031034 | -2.46447e-03 |
| -0.1 | -3.28331e-02 | -5.86550e-02 | -1.23328e-01 | -0.317095 | -0.0208897 | -0.000260315 | -2.55117e-06 |
| 0 | -1.05562e-10 | -2.84723e-10 | -3.95647e-10 | 0.0000000 | 0.0000000 | 0.0000000000 | 0.00000e+00 |
| 0.1 | 3.283310e-02 | 5.865500e-02 | 1.23328e-01 | 0.3170950 | 0.0208897 | 0.0002603150 | 2.551170e-06 |
| 0.2 | 6.357180e-02 | 1.095110e-01 | 2.00697e-01 | 0.3186120 | 0.1368337 | 0.0210310340 | 2.464470e-03 |
| 0.3 | 9.079900e-02 | 1.493420e-01 | 2.42068e-01 | 0.3212840 | 0.2193111 | 0.0785639520 | 2.127630e-02 |

Table 3.7: values of $\partial \hat{d}_1 / \partial b$

| b\ a | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------|--------------|--------------|------------|-----------|--------------|--------------|--------------|
| -0.3 | -2.12763e-02 | -0.078563952 | -0.2193111 | -0.321284 | -2.42068e-01 | -1.49342e-01 | -9.07990e-02 |
| -0.2 | -2.46447e-03 | -0.021031034 | -0.1368337 | -0.318612 | -2.00697e-01 | -1.09511e-01 | -6.35718e-02 |
| -0.1 | -2.55117e-06 | -0.000260315 | -0.0208897 | -0.317095 | -1.23328e-01 | -5.86550e-02 | -3.28331e-02 |
| 0 | 0.00000e+00 | 0.000000000 | 0.0000000 | 0.0000000 | 6.523046e-10 | 7.739514e-10 | 4.730930e-10 |
| 0.1 | 2.551170e-06 | 0.000260315 | 0.0208897 | 0.3170950 | 1.233280e-01 | 5.865500e-02 | 3.283310e-02 |
| 0.2 | 2.464470e-03 | 0.021031034 | 0.1368337 | 0.3186120 | 2.006970e-01 | 1.095110e-01 | 6.357180e-02 |
| 0.3 | 2.127630e-02 | 0.078563952 | 0.2193111 | 0.3212840 | 2.420680e-01 | 1.493420e-01 | 9.079900e-02 |

Table 3.8: values of $\partial \hat{d}_2 / \partial b$

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|------------|------------|------------|---------------|-----------|-----------|-----------|
| -0.3 | -0.1925124 | -0.2322753 | -0.1934080 | 2.4996320e-10 | 0.1934080 | 0.2322753 | 0.1925124 |
| -0.2 | -0.2036463 | -0.2605473 | -0.2561771 | 3.1519830e-10 | 0.2561771 | 0.2605473 | 0.2036463 |
| -0.1 | -0.2091134 | -0.2742035 | -0.3160703 | 1.7999340e-10 | 0.3160703 | 0.2742035 | 0.2091134 |
| 0 | -0.2109249 | -0.2780513 | -0.3323454 | 0.000000e+00 | 0.3323454 | 0.2780513 | 0.2109249 |
| 0.1 | -0.2091134 | -0.2742035 | -0.3160703 | -1.805570e-10 | 0.3160703 | 0.2742035 | 0.2091134 |
| 0.2 | -0.2036463 | -0.2605473 | -0.2561771 | -2.133612e-10 | 0.2561771 | 0.2605473 | 0.2036463 |
| 0.3 | -0.1925124 | -0.2322753 | -0.1934080 | -2.593674e-10 | 0.1934080 | 0.2322753 | 0.1925124 |

Table 3.9: values of $\partial PLC / \partial a$

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|--------------|--------------|--------------|-----------|---------------|--------------|--------------|
| -0.3 | -2.24151e-01 | -4.55812e-01 | -9.22758e-01 | -1.285136 | -9.227584e-01 | -4.55812e-01 | -2.24151e-01 |
| -0.2 | -1.32073e-01 | -2.61084e-01 | -6.75061e-01 | -1.274447 | -6.750611e-01 | -2.61084e-01 | -1.32073e-01 |
| -0.1 | -6.56714e-02 | -1.17831e-01 | -2.88435e-01 | -1.268378 | -2.884352e-01 | -1.17831e-01 | -6.56714e-02 |
| 0 | -2.11124e-10 | -5.69445e-10 | -7.91294e-10 | 0.0000000 | 1.304609e-09 | 1.547900e-09 | 9.461850e-10 |
| 0.1 | 6.567140e-02 | 1.178310e-01 | 2.884350e-01 | 1.268378 | 2.884352e-01 | 1.178310e-01 | 6.567140e-02 |
| 0.2 | 1.320730e-01 | 2.610840e-01 | 6.750610e-01 | 1.274447 | 6.750611e-01 | 2.610840e-01 | 1.320730e-01 |
| 0.3 | 2.241510e-01 | 4.558120e-01 | 9.227580e-01 | 1.285136 | 9.227584e-01 | 4.558120e-01 | 2.241510e-01 |

Table 3.10: values of $\partial PLC / \partial b$

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|-------------|------------|------------|-----------|------------|------------|-------------|
| -0.3 | 0.013027611 | 0.03200391 | 0.07789820 | 0.1041318 | 0.07789820 | 0.03200391 | 0.013027611 |
| -0.2 | 0.009871936 | 0.02119351 | 0.05639426 | 0.1024068 | 0.05639426 | 0.02119351 | 0.009871936 |
| -0.1 | 0.007975319 | 0.01504007 | 0.02916443 | 0.1014338 | 0.02916443 | 0.01504007 | 0.007975319 |
| 0 | 0.006360639 | 0.01105337 | 0.01579154 | 0.0000000 | 0.01579154 | 0.01105337 | 0.006360639 |
| 0.1 | 0.007975319 | 0.01504007 | 0.02916443 | 0.1014338 | 0.02916443 | 0.01504007 | 0.007975319 |
| 0.2 | 0.009871936 | 0.02119351 | 0.05639426 | 0.1024068 | 0.05639426 | 0.02119351 | 0.009871936 |
| 0.3 | 0.013027611 | 0.03200391 | 0.07789820 | 0.1041318 | 0.07789820 | 0.03200391 | 0.013027611 |

Table 3.11: values of $\text{var}(P\hat{L}C)$

Chapter 4

The Area Swept Out by the SROC Curve (ASC)

4.1 Derivation of Equations of ASC

AUC refers to the area under the $SROC$ curve; ASC is the area swept out by the $SROC$ curve. Since some regions of these two indices overlap, we can find a useful expression of ASC by resorting to AUC .

Figure 4.1 shows the $SROC$ curve with $b = 0$. In the homogeneous case, ASC is the region between the curve and the diagonal. It can be simply expressed as

$$ASC = AUC - \frac{1}{2}, \quad \text{for all } a > 0 \quad (4.1)$$

or

$$ASC = \frac{1}{2} - AUC, \quad \text{for all } a < 0. \quad (4.2)$$

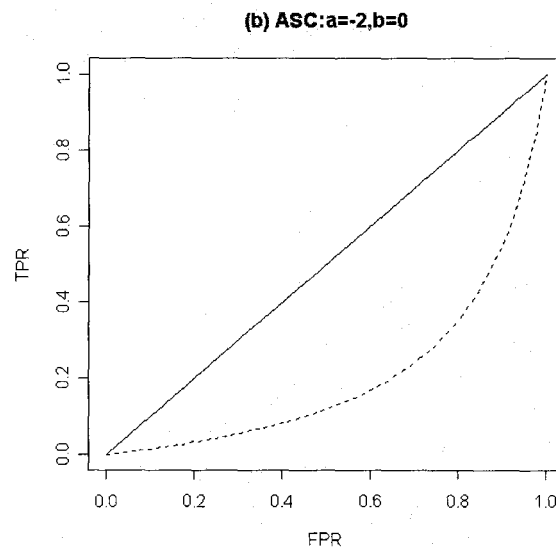
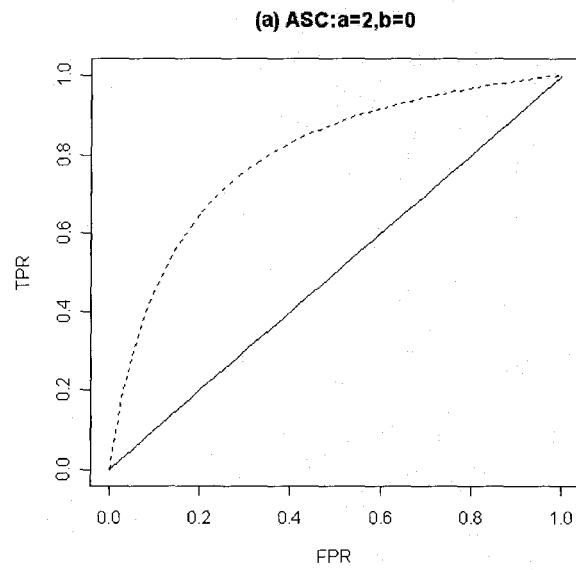


Figure 4.1: SROC curve when $b = 0$

For the heterogeneous case, when both a and b are positive (see Figure 4.2(a)), we can imagine a ray emanating from the origin $(0,0)$ to each point in the *SROC* curve. This ray is a line can be expressed as $y = kx$, here k is the slope of the line. As the point moving from the origin to the left-uppermost corner $(0,1)$, the slope of the line will reach its maximum at some point of the curve when the line still touches the curve except for the origin. This line is the tangent line of the curve. It can be expressed as $y = k^*x$, here k^* is the slope of the tangent line. We call the tangency point as $M'(h(a,b), f(h(a,b), a, b))$ and the area swept out until the tangent line as M .

Figure 4.2 (a) to (d) shows the *SROC* curve in the heterogeneous case when $a > 0$ and $b > 0$ (a), $a > 0$ and $b < 0$ (b), $a < 0$ and $b > 0$ (c) and $a < 0$ and $b < 0$ (d) respectively. The *SROC* curve crosses the diagonal at point Q' . We mentioned before that Point Q' separates the whole curve into two regions both of which are surrounded by the main diagonal and the curve; one is small and the other is big. We also notice that if we let a ray emanate from the origin to each point in the curve as described before, the area surrounded by the tangent line, main diagonal line and the curve will be swept twice. If we always define the smaller area as A , the bigger area as B , the area between the tangent line and the curve as M and the area swept out twice as C , the *ASC* index for these four situations is always $ASC = A + B + 2C$, but $C = M - A$ when a and b have the same sign and $C = M - B$ when a and b have the different sign; $B = AUC + A - \frac{1}{2}$ when a is positive and $B = A + \frac{1}{2} - AUC$ when a is negative. If we plug in the values of C and B in the expression of *ASC*, we get the final expression for *ASC* as

$$ASC = AUC + 2M - \frac{1}{2} \quad (4.3)$$

when $a > 0, b > 0$ and $a < 0, b > 0$, or

$$ASC = 2M + \frac{1}{2} - AUC \quad (4.4)$$

when $a > 0, b < 0$ and $a < 0, b < 0$.

We mentioned before that line $y = kx$ is any line that goes through the origin $O(0,0)$. k is the slope of the line. The tangent line $y = K^*x$ is a special case of $y = kx$ which goes through tangency point $M'(h(a,b), f(h(a,b), a, b))$. k^* is the slope of tangent line. It's the maximum value of k when line $y = kx$ intersects the *SROC* curve $y = f(x, a, b)$ at point M' .

To find the expression of k^* , consider equation

$$kx = f(x, a, b)$$

when the line and the curve intersect. The equation above can be rewritten as

$$k = \frac{1}{x} f(x, a, b) = \frac{1}{x} \left[1 - \frac{1}{1 + \exp\left(\frac{a}{1-b}\right)\left(\frac{x}{1-x}\right)^{\frac{1+b}{1-b}}}\right] \quad (4.5)$$

If we differentiate both sides of equation (4.5) on x and let it equal to be 0, after some calculations, we get

$$\frac{(1+b)}{(1-b)} \left(\frac{1}{1-x} \right) = 1 + \exp\left(\frac{a}{1-b}\right) \left(\frac{x}{1-x} \right)^{\frac{1+b}{1-b}} \quad (4.6)$$

Denote $h(a, b)$ as the solution of equation (4.6), by Fermat Theorem, $h(a, b)$ is the value of x that maximizes k . And the maximum value k is

$$k^* = \frac{1}{h(a, b)} f(h(a, b), a, b) \quad (4.7)$$

Since M is the area surrounded by the tangent line $y = k^*x$ and the curve $f(x, a, b)$ on the interval between the origin and tangency point $M'(h(a, b), f(h(a, b), a, b))$, M

can be expressed as

$$M = \int_0^{h(a,b)} [k^*x - f(x, a, b)]dx \quad (4.8)$$

when $a > 0, b > 0$ and $a < 0, b > 0$, or

$$M = \int_0^{h(a,b)} [f(x, a, b) - k^*x]dx \quad (4.9)$$

when $a > 0, b < 0$ and $a < 0, b < 0$. And equation (4.3) and (4.4) can be rewritten as

$$\begin{aligned} ASC &= AUC + 2M - \frac{1}{2} \\ &= \int_0^1 f(x, a, b)dx + 2 \int_0^{h(a,b)} [k^*x - f(x, a, b)]dx - \frac{1}{2} \end{aligned} \quad (4.10)$$

when $a > 0, b > 0$ and $a < 0, b > 0$, or

$$\begin{aligned} ASC &= 2M + \frac{1}{2} - AUC \\ &= 2 \int_0^{h(a,b)} [f(x, a, b) - k^*x]dx + \frac{1}{2} - \int_0^1 f(x, a, b)dx \end{aligned} \quad (4.11)$$

when $a > 0, b < 0$ and $a < 0, b < 0$.

Thus, the derivation of ASC is obtained completely.

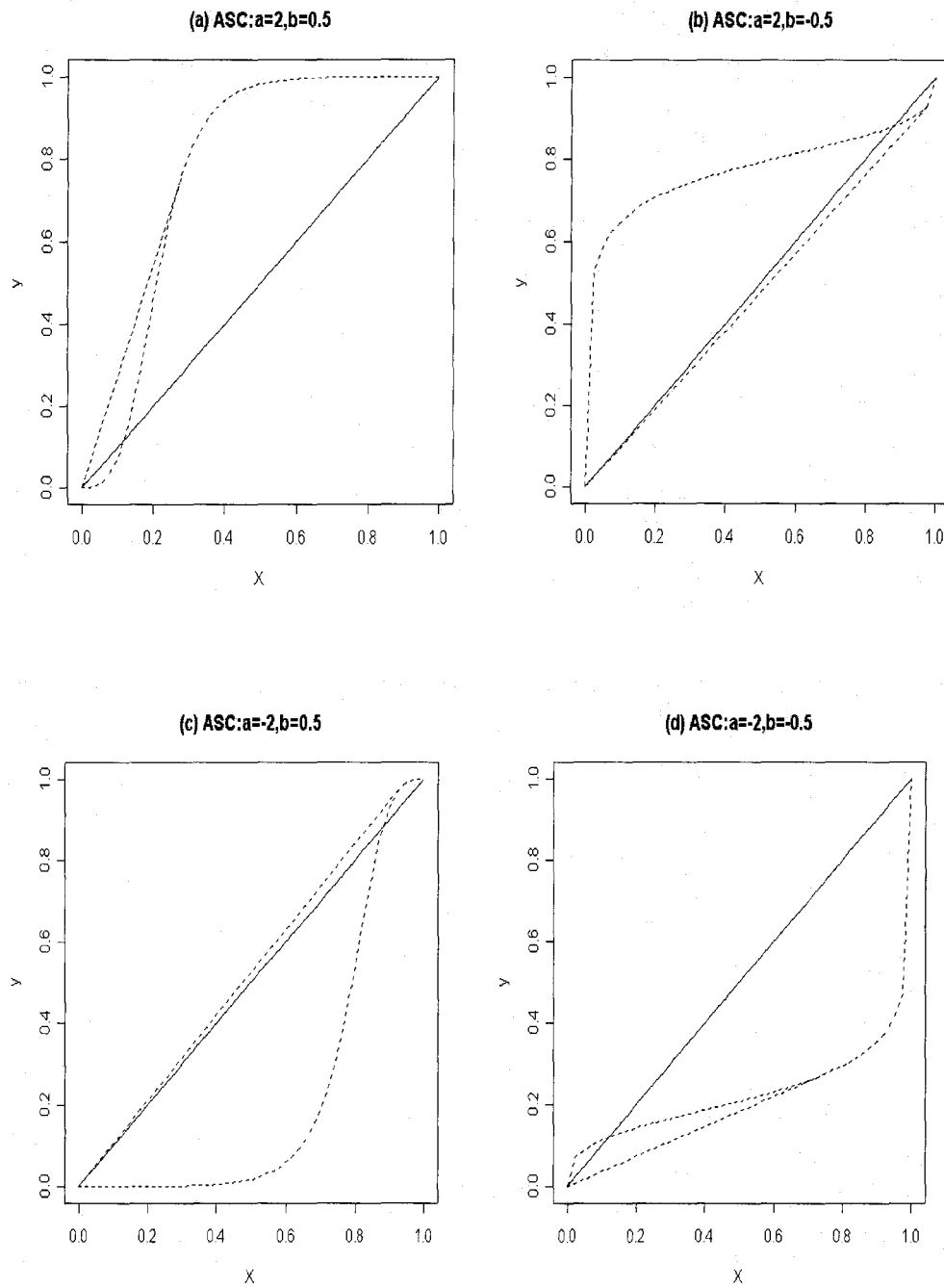


Figure 4.2: SROC curve to illustrate ASC

4.2 The Behaviour of ASC

Like *PLC* index, *ASC* index is also symmetric but in different way. Table 4.1 shows that *M* index with $a > 0$ and $b > 0$ is symmetric to *M* index with $a < 0$ and $b < 0$; *M* index with $a > 0$ and $b < 0$ is symmetric to *M* index with $a < 0$ and $b > 0$. Table 4.2 shows that *AUC* index with $a > 0$ and $b > 0$ is symmetric to *AUC* index with $a > 0$ and $b < 0$; *AUC* index with $a < 0$ and $b > 0$ is symmetric to *AUC* index with $a < 0$ and $b < 0$. Although *ASC* is affected both by *AUC* and *M*, Table 4.3 shows that *ASC* is symmetric under the same situation with *M*.

When b is positive, for a fixed number b , M decreases as a increases. Because of symmetry, M performs on the opposite direction for the fixed value of b when b is negative. When $b = 0$, as $a \rightarrow 0$, $M \rightarrow 0$. The zero value of M corresponds to the *SROC* curve running along the diagonal line. This situation indicates a cut-off point with no diagnostic value. We should notice that for a fixed value a , as b changes from negative to positive, the values do not change smoothly. The values have a big jump from small values to big ones when a is negative, and vice versa when a is positive. That's because the area defined as M are quite different when b changes the sign. Figure 4.2 can show this visually.

AUC index can be interpreted as the probability that the diagnostic test values for a random pair of diseased and non-diseased individuals would be correctly ranked. It ranges from 1 for a perfect test to 0 for a test which never diagnoses correctly. In Table 4.2, for fixed value b , as a changes from negative to positive, *AUC* increases smoothly. For fixed negative value a , *AUC* declines slowly as b increases from large negative values (decreasing heterogeneity) to 0 (homogeneous studies) and increase

slowly as b increases from 0 (homogeneous studies) to large positive values (increasing heterogeneity). For fixed positive value a , AUC behaves in the opposite direction. The percentage change in each case compared to the homogeneous values is less than 2 per cent. Accordingly, the homogeneous AUC values in each case provide a good approximation in heterogeneous studies. AUC is maximized in homogeneous case when $a > 0$.

Affected by the unsteady values of M index, for a fixed value of a , as b changes from negative to positive, the values for ASC are not smooth, too. But for the fixed b , ASC decrease as b changes from negative to zero and vice versa as b changes from zero to positive. In Table 4.6, as $a \rightarrow \infty$, $ASC \rightarrow 0.5$, the maximum values. The greater value of ASC indicate the great probability of a correct diagonal when $a > 0$ and the great probability of a wrong diagonal when $a < 0$. We can never say the greater value of ASC implies a perfect test unless the value of AUC is bigger as well and parameter a is positive.

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| -0.3 | 0.0031149 | 0.0080574 | 0.0238334 | 0.0738144 | 0.1761180 | 0.2914206 | 0.3802369 |
| -0.2 | 0.0007984 | 0.0023486 | 0.0092543 | 0.0493470 | 0.1651769 | 0.2918472 | 0.3836511 |
| -0.1 | 0.0000735 | 0.0002386 | 0.0012727 | 0.0247165 | 0.1610621 | 0.2936977 | 0.3861273 |
| 0 | 0.0000000 | 0.0000000 | 0.0000000 | 0.0000000 | 0.0000000 | 0.0000000 | 0.0000000 |
| 0.1 | 0.3861273 | 0.2936977 | 0.1610621 | 0.0247165 | 0.0012727 | 0.0002386 | 0.0000735 |
| 0.2 | 0.3836511 | 0.2918472 | 0.1651769 | 0.0493470 | 0.0092543 | 0.0023486 | 0.0007984 |
| 0.3 | 0.3802369 | 0.2914206 | 0.1761180 | 0.0738144 | 0.0238334 | 0.0080574 | 0.0031149 |

Table 4.1: values of M when $-0.3 \leq b \leq 0.3$

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|-----------|-----------|-----------|-----|-----------|-----------|-----------|
| -0.3 | 0.1205152 | 0.2124975 | 0.3430187 | 0.5 | 0.6569813 | 0.7875025 | 0.8794848 |
| -0.2 | 0.1163888 | 0.2086500 | 0.3406381 | 0.5 | 0.6593619 | 0.7913500 | 0.8836112 |
| -0.1 | 0.1138727 | 0.2063023 | 0.3391853 | 0.5 | 0.6608147 | 0.7936977 | 0.8861273 |
| 0 | 0.1130273 | 0.2055132 | 0.3386969 | 0.5 | 0.6613031 | 0.7944868 | 0.8869727 |
| 0.1 | 0.1138727 | 0.2063023 | 0.3391853 | 0.5 | 0.6608147 | 0.7936977 | 0.8861273 |
| 0.2 | 0.1163888 | 0.2086500 | 0.3406381 | 0.5 | 0.6593619 | 0.7913500 | 0.8836112 |
| 0.3 | 0.1205152 | 0.2124975 | 0.3430187 | 0.5 | 0.6569813 | 0.7875025 | 0.8794848 |

Table 4.2: values of AUC when $-0.3 \leq b \leq 0.3$

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|-----------|-----------|-----------|--------------|-----------|-----------|-----------|
| -0.3 | 0.3857146 | 0.3036173 | 0.2046481 | 1.476288e-01 | 0.1952547 | 0.2953387 | 0.3809890 |
| -0.2 | 0.3852080 | 0.2960472 | 0.1778705 | 9.869400e-02 | 0.1709919 | 0.2923444 | 0.3836910 |
| -0.1 | 0.3862743 | 0.2941749 | 0.1633601 | 4.943300e-02 | 0.1613095 | 0.2936977 | 0.3861273 |
| 0 | 0.3869727 | 0.2944868 | 0.1613031 | 1.665335e-16 | 0.1613031 | 0.2944868 | 0.3869727 |
| 0.1 | 0.3861273 | 0.2936977 | 0.1613095 | 4.943300e-02 | 0.1633601 | 0.2941749 | 0.3862743 |
| 0.2 | 0.3836910 | 0.2923444 | 0.1709919 | 9.869400e-02 | 0.1778705 | 0.2960472 | 0.3852080 |
| 0.3 | 0.3809890 | 0.2953387 | 0.1952547 | 1.476288e-01 | 0.2046481 | 0.3036173 | 0.3857146 |

Table 4.3: values of ASC when $-0.3 \leq b \leq 0.3$

| $b \backslash a$ | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 0 | 0.0000000 | 0.0000000 | 0.0000000 | 0.0000000 | 0.0000000 | 0.0000000 | 0.0000000 | 0.0000000 | 0.0000000 | 0.0000000 |
| 0.1 | 0.0012727 | 0.0002386 | 0.0000735 | 0.0000267 | 0.0000103 | 0.0000041 | 0.0000016 | 0.0000007 | 0.0000001 | 0.0000000 |
| 0.2 | 0.0092543 | 0.0023486 | 0.0007984 | 0.0003118 | 0.0001294 | 0.0000551 | 0.0000237 | 0.0000103 | 0.0000043 | 0.0000015 |
| 0.3 | 0.0238334 | 0.0080574 | 0.0031149 | 0.0013183 | 0.0005849 | 0.0002656 | 0.0001219 | 0.0000561 | 0.0000260 | 0.0000120 |
| 0.4 | 0.0423160 | 0.0177131 | 0.0077593 | 0.0035632 | 0.0016865 | 0.0008117 | 0.0003940 | 0.0001920 | 0.0000938 | 0.0000458 |
| 0.5 | 0.0630129 | 0.0307949 | 0.0150383 | 0.0074594 | 0.0037527 | 0.0019052 | 0.0009723 | 0.0004976 | 0.0002551 | 0.0001309 |
| 0.6 | 0.0850644 | 0.0466232 | 0.0249310 | 0.0132587 | 0.0070574 | 0.0037637 | 0.0020102 | 0.0010747 | 0.0005748 | 0.0003074 |
| 0.7 | 0.1080855 | 0.0646656 | 0.0372780 | 0.0210838 | 0.0118151 | 0.0065916 | 0.0036693 | 0.0020401 | 0.0011335 | 0.0006295 |
| 0.8 | 0.1320571 | 0.0846568 | 0.0519554 | 0.0310134 | 0.0182066 | 0.0105848 | 0.0061193 | 0.0035262 | 0.0020282 | 0.0011648 |
| 0.9 | 0.1575374 | 0.1068256 | 0.0691217 | 0.0432612 | 0.0264845 | 0.0159882 | 0.0095685 | 0.0056969 | 0.0033811 | 0.0020028 |

Table 4.4: values of M when $0 \leq b \leq 0.9$ and $1 \leq a \leq 10$

| $b \backslash a$ | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 0 | 0.6613031 | 0.7944868 | 0.8869727 | 0.9426356 | 0.9726354 | 0.9875386 | 0.9945183 | 0.9976513 | 0.9990155 | 0.9995975 |
| 0.1 | 0.6608147 | 0.7936977 | 0.8861273 | 0.9419086 | 0.9720952 | 0.9871774 | 0.9942950 | 0.9975210 | 0.9989419 | 0.9995562 |
| 0.2 | 0.6593619 | 0.7913500 | 0.8836112 | 0.9397430 | 0.9704833 | 0.9860960 | 0.9936239 | 0.9971284 | 0.9987224 | 0.9994365 |
| 0.3 | 0.6569813 | 0.7875025 | 0.8794848 | 0.9361842 | 0.9678236 | 0.9842998 | 0.9924978 | 0.9964609 | 0.9983432 | 0.9992279 |
| 0.4 | 0.6537347 | 0.7822532 | 0.8738467 | 0.9313053 | 0.9641543 | 0.9817966 | 0.9909055 | 0.9954987 | 0.9977836 | 0.9989117 |
| 0.5 | 0.6497090 | 0.7757380 | 0.8668315 | 0.9252036 | 0.9595246 | 0.9785959 | 0.9888322 | 0.9942167 | 0.9970173 | 0.9984650 |
| 0.6 | 0.6450156 | 0.7681285 | 0.8586050 | 0.9179955 | 0.9539918 | 0.9747081 | 0.9862608 | 0.9925864 | 0.9960144 | 0.9978616 |
| 0.7 | 0.6397887 | 0.7596272 | 0.8493575 | 0.9098109 | 0.9476182 | 0.9701449 | 0.9831736 | 0.9905778 | 0.9947432 | 0.9970733 |
| 0.8 | 0.6341802 | 0.7504593 | 0.8392955 | 0.9007879 | 0.9404704 | 0.9649206 | 0.9795552 | 0.9881623 | 0.9931722 | 0.9960706 |
| 0.9 | 0.6283513 | 0.7408600 | 0.8286313 | 0.8910686 | 0.9326193 | 0.9590547 | 0.9753946 | 0.9853145 | 0.9912712 | 0.9948246 |

Table 4.5: values of AUC when $0 \leq b \leq 0.9$ and $1 \leq a \leq 10$

| $b \backslash a$ | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 0 | 0.1613031 | 0.2944868 | 0.3869727 | 0.4426356 | 0.4726354 | 0.4875386 | 0.4945183 | 0.4976513 | 0.4990155 | 0.4995973 |
| 0.1 | 0.1633601 | 0.2941749 | 0.3862743 | 0.4419620 | 0.4721158 | 0.4871856 | 0.4942982 | 0.4975224 | 0.4989421 | 0.4995562 |
| 0.2 | 0.1778705 | 0.2960472 | 0.3852080 | 0.4403666 | 0.4707421 | 0.4862062 | 0.4936713 | 0.4971490 | 0.4987310 | 0.4994395 |
| 0.3 | 0.2046481 | 0.3036173 | 0.3857146 | 0.4388208 | 0.4689934 | 0.4848310 | 0.4927416 | 0.4965731 | 0.4983952 | 0.4992519 |
| 0.4 | 0.2383667 | 0.3176794 | 0.3893653 | 0.4384317 | 0.4675273 | 0.4834200 | 0.4916935 | 0.4958827 | 0.4979712 | 0.4990033 |
| 0.5 | 0.2757348 | 0.3373278 | 0.3969081 | 0.4401224 | 0.4670300 | 0.4824063 | 0.4907768 | 0.4952119 | 0.4975275 | 0.4987268 |
| 0.6 | 0.3151444 | 0.3613749 | 0.4084670 | 0.4445129 | 0.4681066 | 0.4822355 | 0.4902812 | 0.4947358 | 0.4971640 | 0.4984764 |
| 0.7 | 0.3559597 | 0.3889584 | 0.4239135 | 0.4519785 | 0.4712484 | 0.4833281 | 0.4905122 | 0.4946580 | 0.4970102 | 0.4983323 |
| 0.8 | 0.3982944 | 0.4197729 | 0.4432063 | 0.4628147 | 0.4768836 | 0.4860902 | 0.4917938 | 0.4952147 | 0.4972286 | 0.4984002 |
| 0.9 | 0.4434261 | 0.4545112 | 0.4668747 | 0.4775910 | 0.4855883 | 0.4910311 | 0.4945316 | 0.4967083 | 0.4980334 | 0.4988302 |

Table 4.6: values of ASC when $0 \leq b \leq 0.9$ and $1 \leq a \leq 10$

4.3 Derivation of the Variance of ASC

From equation (4.8) and (4.9), we find that M is the functions of the regression parameters a and b , since $h(a, b)$ is the functions of a and b . Hence the variability in $A\hat{S}C$ is a function of the sample variation in \hat{a} and \hat{b} . Using the delta method, an approximate variance for $A\hat{S}C$ is:

$$\text{var}(A\hat{S}C) = \left(\frac{\partial ASC}{\partial a}\right)^2 \text{var}(\hat{a}) + \left(\frac{\partial ASC}{\partial b}\right)^2 \text{var}(\hat{b}) + 2\left(\frac{\partial ASC}{\partial a}\right)\left(\frac{\partial ASC}{\partial b}\right)\text{cov}(\hat{a}, \hat{b}) \quad (4.12)$$

here,

$$\frac{\partial ASC}{\partial a} = \frac{\partial AUC}{\partial a} + 2\frac{\partial M}{\partial a} \quad (4.13)$$

when $a > 0, b > 0$ and $a < 0, b > 0$ or

$$\frac{\partial ASC}{\partial a} = 2\frac{\partial M}{\partial a} - \frac{\partial AUC}{\partial a} \quad (4.14)$$

when $a > 0, b < 0$ and $a < 0, b < 0$. Similarly,

$$\frac{\partial ASC}{\partial b} = \frac{\partial AUC}{\partial b} + 2\frac{\partial M}{\partial b} \quad (4.15)$$

when $a > 0, b > 0$ and $a < 0, b > 0$ or

$$\frac{\partial ASC}{\partial b} = 2\frac{\partial M}{\partial b} - \frac{\partial AUC}{\partial b} \quad (4.16)$$

when $a > 0, b < 0$ and $a < 0, b < 0$.

For the sake of convenience we only consider the situation when $a > 0, b > 0$. The calculation under other situations are similar.

To solve $\partial ASC/\partial a$ we need to find the expressions of $\partial AUC/\partial a$ and $\partial M/\partial a$ separately. $\partial AUC/\partial a$ is easily calculated and can be expressed as

$$\begin{aligned}
\frac{\partial AUC}{\partial a} &= \frac{\partial}{\partial a} \left[\int_0^1 \frac{\exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{1+b}{1-b}}}{1 + \exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{1+b}{1-b}}} dx \right] \\
&= \left(\frac{1}{1-b} \right) \exp\left(\frac{a}{1-b}\right) \int_0^1 \frac{(\frac{x}{1-x})^{\frac{1+b}{1-b}}}{\left[1 + \exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{1+b}{1-b}}\right]^2} dx. \tag{4.17}
\end{aligned}$$

We know that the Leibniz integral rule can give a formula for differentiation of a definite integral whose limits are functions of the differential variable. That is,

$$\frac{\partial}{\partial z} \int_{a(z)}^{b(z)} f(x, z) dx = \int_{a(z)}^{b(z)} \frac{\partial f(x, z)}{\partial z} dx + f(b(z), z) \frac{\partial b(z)}{\partial z} - f(a(z), z) \frac{\partial a(z)}{\partial z} \tag{4.18}$$

Since the limits ($h(a, b)$) of the differentiation of the integral of M are functions of the differential variable, if we apply the Leibniz integral rule, $\partial M / \partial a$ can be expressed as

$$\begin{aligned}
\frac{\partial M}{\partial a} &= \frac{\partial}{\partial a} \int_0^{h(a,b)} \left[\frac{f(h(a,b), a, b)}{h(a,b)} x - f(x, a, b) \right] dx \\
&= \int_0^{h(a,b)} \frac{\partial}{\partial a} \left[\frac{f(h(a,b), a, b)}{h(a,b)} x - f(x, a, b) \right] dx \\
&\quad + \frac{\partial h(a,b)}{\partial a} \left[\frac{f(h(a,b), a, b)}{h(a,b)} h(a,b) - f(h(a,b), a, b) \right] \\
&= \int_0^{h(a,b)} \frac{\partial}{\partial a} \left[\frac{f(h(a,b), a, b)}{h(a,b)} x - f(x, a, b) \right] dx \\
&= \frac{\partial}{\partial a} \left[\frac{f(h(a,b), a, b)}{h(a,b)} \right] \int_0^{h(a,b)} x dx - \int_0^{h(a,b)} \frac{\partial}{\partial a} f(x, a, b) dx \\
&= \frac{\partial}{\partial a} \left[\frac{f(h(a,b), a, b)}{h(a,b)} \right] \frac{[h(a,b)]^2}{2} - \int_0^{h(a,b)} \frac{\partial}{\partial a} f(x, a, b) dx. \tag{4.19}
\end{aligned}$$

The next step is to solve the two parts of the differentiation (4.19) of M separately.

$$\begin{aligned}
&\int_0^{h(a,b)} \frac{\partial}{\partial a} f(x, a, b) dx \\
&= \int_0^{h(a,b)} \frac{\partial}{\partial a} \left[\frac{\exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{1+b}{1-b}}}{1 + \exp(\frac{a}{1-b})(\frac{x}{1-x})^{\frac{1+b}{1-b}}} \right] dx
\end{aligned}$$

$$= \left(\frac{1}{1-b}\right) \exp\left(\frac{a}{1-b}\right) \int_0^{h(a,b)} \frac{\left(\frac{x}{1-x}\right)^{\frac{1+b}{1-b}}}{\left[1 + \exp\left(\frac{a}{1-b}\right)\left(\frac{x}{1-x}\right)^{\frac{1+b}{1-b}}\right]^2} dx \quad (4.20)$$

and

$$\begin{aligned} \frac{\partial}{\partial a} \left[\frac{f(h(a,b), a, b)}{h(a,b)} \right] &= \left[\frac{\partial}{\partial a} f(h(a,b), a, b) \right] \frac{1}{h(a,b)} - \frac{f(h(a,b), a, b)}{[h(a,b)]^2} \frac{\partial h(a,b)}{\partial a} \\ &= \frac{\frac{R}{1-b} \left[1 + \frac{1+b}{h(a,b)(1-h(a,b))} \frac{\partial h(a,b)}{\partial a} \right]}{(1+R)^2 h(a,b)} - \frac{R \left(\frac{\partial h(a,b)}{\partial a} \right)}{(1+R)[h(a,b)]^2} \end{aligned} \quad (4.21)$$

where, $R = \exp\left(\frac{a}{1-b}\right)\left(\frac{h(a,b)}{1-h(a,b)}\right)^{\frac{1+b}{1-b}}$, and $\partial h(a,b)/\partial a$ can be expressed as

$$\frac{\partial h(a,b)}{\partial a} = \frac{\exp\left(\frac{a}{1-b}\right)\left(\frac{h(a,b)}{1-h(a,b)}\right)^{\frac{1+b}{1-b}}}{\frac{1+b}{[1-h(a,b)]^2} \left[1 - \exp\left(\frac{a}{1-b}\right)\left(\frac{h(a,b)}{1-h(a,b)}\right)^{\frac{1+b}{1-b}} \right]} \quad (4.22)$$

which is solved by differentiating both sides of equation (4.6) on a .

If we plug all the results of equation (4.20), (4.21) and (4.22) into the expression of (4.19), $\partial M/\partial a$ can be expressed finally as:

$$\begin{aligned} \frac{\partial M}{\partial a} &= \frac{\partial}{\partial a} \left[\frac{f(h(a,b), a, b)}{h(a,b)} \right] \frac{[h(a,b)]^2}{2} \\ &\quad - \left(\frac{1}{1-b}\right) \exp\left(\frac{a}{1-b}\right) \int_0^{h(a,b)} \frac{\left(\frac{x}{1-x}\right)^{\frac{1+b}{1-b}}}{\left[1 + \exp\left(\frac{a}{1-b}\right)\left(\frac{x}{1-x}\right)^{\frac{1+b}{1-b}}\right]^2} dx. \end{aligned} \quad (4.23)$$

Similarly, to solve $\partial ASC/\partial b$ we need to find the expressions of $\partial AUC/\partial b$ and $\partial M/\partial b$ separately. $\partial AUC/\partial b$ is easily calculated and can be expressed as

$$\begin{aligned} \frac{\partial AUC}{\partial b} &= \frac{\partial}{\partial b} \left[\int_0^1 \frac{\exp\left(\frac{a}{1-b}\right)\left(\frac{x}{1-x}\right)^{\frac{1+b}{1-b}}}{1 + \exp\left(\frac{a}{1-b}\right)\left(\frac{x}{1-x}\right)^{\frac{1+b}{1-b}}} dx \right] \\ &= \left(\frac{1}{1-b}\right)^2 \exp\left(\frac{a}{1-b}\right) \int_0^1 \frac{\left(\frac{x}{1-x}\right)^{\frac{1+b}{1-b}} [a + 2 \ln\left(\frac{x}{1-x}\right)]}{\left[1 + \left(\frac{x}{1-x}\right)^{\frac{1+b}{1-b}} \exp\left(\frac{a}{1-b}\right)\right]^2} dx \end{aligned} \quad (4.24)$$

and $\partial M/\partial b$ can be expressed as

$$\begin{aligned}
\frac{\partial M}{\partial b} &= \frac{\partial}{\partial b} \int_0^{h(a,b)} \left[\frac{f(h(a,b), a, b)}{h(a,b)} x - f(x, a, b) \right] dx \\
&= \int_0^{h(a,b)} \frac{\partial}{\partial b} \left[\frac{f(h(a,b), a, b)}{h(a,b)} x - f(x, a, b) \right] dx \\
&\quad + \frac{\partial h(a,b)}{\partial b} \left[\frac{f(h(a,b), a, b)}{h(a,b)} h(a,b) - f(h(a,b), a, b) \right] \\
&= \int_0^{h(a,b)} \frac{\partial}{\partial b} \left[\frac{f(h(a,b), a, b)}{h(a,b)} x - f(x, a, b) \right] dx \\
&= \frac{\partial}{\partial b} \left[\frac{f(h(a,b), a, b)}{h(a,b)} \right] \int_0^{h(a,b)} x dx - \int_0^{h(a,b)} \frac{\partial}{\partial b} f(x, a, b) dx \\
&= \frac{\partial}{\partial b} \left[\frac{f(h(a,b), a, b)}{h(a,b)} \right] \frac{[h(a,b)]^2}{2} - \int_0^{h(a,b)} \frac{\partial}{\partial b} f(x, a, b) dx. \tag{4.25}
\end{aligned}$$

where,

$$\begin{aligned}
&\int_0^{h(a,b)} \frac{\partial}{\partial b} f(x, a, b) dx \\
&= \int_0^{h(a,b)} \frac{\partial}{\partial b} \left[\frac{\exp(\frac{a}{1-b}) (\frac{x}{1-x})^{\frac{1+b}{1-b}}}{1 + \exp(\frac{a}{1-b}) (\frac{x}{1-x})^{\frac{1+b}{1-b}}} \right] dx \\
&= \left(\frac{1}{1-b} \right)^2 \exp\left(\frac{a}{1-b}\right) \int_0^{h(a,b)} \frac{(\frac{x}{1-x})^{\frac{1+b}{1-b}} [a + 2 \ln(\frac{x}{1-x})]}{[1 + (\frac{x}{1-x})^{\frac{1+b}{1-b}} \exp(\frac{a}{1-b})]^2} dx \tag{4.26}
\end{aligned}$$

and

$$\begin{aligned}
&\frac{\partial}{\partial b} \left[\frac{f(h(a,b), a, b)}{h(a,b)} \right] \\
&= \left[\frac{\partial}{\partial b} f(h(a,b), a, b) \right] \frac{1}{h(a,b)} - \frac{f(h(a,b), a, b)}{[h(a,b)]^2} \frac{\partial h(a,b)}{\partial b} \\
&= \frac{\frac{1}{(1-b)^2} S [a + 2 \ln(\frac{h(a,b)}{1-h(a,b)}) + \frac{(1-b^2)}{h(a,b)(1-h(a,b))} \frac{\partial h(a,b)}{\partial b}]}{[1 + S]^2 h(a,b)} - \frac{S \frac{\partial h(a,b)}{\partial b}}{[1 + S][h(a,b)]^2} \tag{4.27}
\end{aligned}$$

where, $S = \exp(\frac{a}{1-b}) (\frac{v(a,b)}{1-v(a,b)})^{\frac{1+b}{1-b}}$, and $\partial h(a,b)/\partial b$ can be expressed as

$$\frac{\partial h(a,b)}{\partial b} = \frac{\exp(\frac{a}{1-b}) (\frac{h(a,b)}{1-h(a,b)})^{\frac{1+b}{1-b}} [a + 2 \ln(\frac{v(a,b)}{1-h(a,b)})] - \frac{2}{(1-h(a,b))}}{\frac{(1-b^2)}{[1-h(a,b)]^2} [1 - \exp(\frac{a}{1-b}) (\frac{h(a,b)}{1-h(a,b)})^{\frac{1+b}{1-b}}]} \tag{4.28}$$

which is solved by differentiating both sides of equation (4.6) on b .

If we plug all the results of equation (4.26), (4.27) and (4.28) into the expression of (4.25), $\frac{\partial M}{\partial b}$ can be expressed finally as:

$$\begin{aligned} \frac{\partial M}{\partial b} = & \frac{\partial}{\partial b} \left[\frac{f(h(a, b), a, b)}{h(a, b)} \right] \frac{[h(a, b)]^2}{2} \\ & - \left(\frac{1}{1-b} \right)^2 \exp\left(\frac{a}{1-b}\right) \int_0^{h(a, b)} \frac{\left(\frac{x}{1-x}\right)^{\frac{1+b}{1-b}} [a + 2 \ln(\frac{x}{1-x})]}{[1 + \left(\frac{x}{1-x}\right)^{\frac{1+b}{1-b}} \exp(\frac{a}{1-b})]^2} dx. \end{aligned} \quad (4.29)$$

4.4 The Behaviour of the Variance of ASC

From Table 4.7 to 4.12 we can deduce: $\partial AUC/\partial a$ does not change sign and keeps positive everywhere; $\partial AUC/\partial b$ changes sign from negative to positive as a changes from negative to positive and b is negative and changes sign from positive to negative as a changes from negative to positive as well but b is positive; $\partial M/\partial a$ changes sign from positive to negative as b changes sign from negative to positive no matter what sign a has; $\partial M/\partial b$ changes sign from negative to positive only when $|a|$ is a small number; $\partial ASC/\partial a$ performs the similar as $\partial M/\partial a$.

By using the Increasing/Decreasing Test and the First Derivative Test, we can explain the phenomena above as: 1. $\partial AUC/\partial a$ is an increasing function of a for the overall range of a ; since $AUC \rightarrow 1$ as $a \rightarrow \infty$, it has no critical point. 2. $\partial AUC/\partial b$ is a decreasing function of b in the interval of $a < 0$, $b < 0$ or $a > 0$, $b > 0$; an increasing function in other intervals. Since it changes sign as what is described above, $\partial AUC/\partial b$ has a local minimum at $b = 0$ if a is negative and a local maximum at $b = 0$ if a is

positive. 3. $\partial M/\partial a$ is an increasing function of a as b is negative; a decreasing function of a as b is positive. Since $M \rightarrow 0$ as $a \rightarrow -\infty$ when b is negative and $M \rightarrow 0$ as $a \rightarrow \infty$ when b is positive, it has no critical value in these two intervals. 4. $\partial M/\partial b$ is an increasing function of b as a is positive; a decreasing function of b as a is negative. Since $M \rightarrow 0$ as $b \rightarrow -\infty$ when a is positive and $M \rightarrow 0$ as $b \rightarrow \infty$ when a is negative, it has no critical value in these two intervals.

For a function $f(x)$, $f'(x)$ also can be interpreted as the rate of change of $f(x)$ with respect to x (Stewart, 2003). AUC is increasing or decreasing smoothly both on a and b . It attains maximum increasing rate at $a = 0$ for $\partial AUC/\partial a$ and maximum rate of changing at $|b| = 0.3$ for $\partial AUC/\partial b$ in our study. But M is not increasing or decreasing smoothly both on a and b . It attains maximum rate of changing at $|a| = 1$ for $\partial M/\partial a$ and the one at $|b| = 0.3$ for $\partial M/\partial b$ but with a little fluctuation at $|a| = 2$. So dose the ASC , since it 's affected more by M than by AUC .

Still use the data for the lymphangiography test for cervical cancer metastases as an example. The numerical values of $\text{var}(\hat{ASC})$ are shown in Table 4.13. We find that the values are symmetric in the direction of diagonal line. Again, this example illustrates that the heterogeneous variances are larger than the homogeneous estimates. $\text{var}(\hat{ASC})$ decreases with respect to values of $|b|$. The big values of $\text{var}(\hat{ASC})$ indicate the worst situation for estimating ASC index in the diagnostic test.

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| -0.3 | 0.0729001 | 0.1117777 | 0.1472541 | 0.1620163 | 0.1472541 | 0.1117777 | 0.0729001 |
| -0.2 | 0.0726689 | 0.1126326 | 0.1492886 | 0.1645779 | 0.1492886 | 0.1126326 | 0.0726689 |
| -0.1 | 0.0725248 | 0.1131535 | 0.1505302 | 0.1661412 | 0.1505302 | 0.1131535 | 0.0725248 |
| 0 | 0.0724759 | 0.1133284 | 0.1509476 | 0.1666667 | 0.1509476 | 0.1133284 | 0.0724759 |
| 0.1 | 0.0725248 | 0.1131535 | 0.1505302 | 0.1661412 | 0.1505302 | 0.1131535 | 0.0725248 |
| 0.2 | 0.0726689 | 0.1126326 | 0.1492886 | 0.1645779 | 0.1492886 | 0.1126326 | 0.0726689 |
| 0.3 | 0.0729001 | 0.1117777 | 0.1472541 | 0.1620163 | 0.1472541 | 0.1117777 | 0.0729001 |

Table 4.7: values of $\partial AUC / \partial a$

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
| -0.3 | 2.7919530e-03 | 8.167656e-03 | 2.7296760e-02 | 7.7650190e-02 | 1.183474e-01 | 1.0537800e-01 | 7.1651820e-02 |
| -0.2 | 7.9123000e-04 | 2.802580e-03 | 1.4561570e-02 | 7.8809820e-02 | 1.353774e-01 | 1.1139440e-01 | 7.2573320e-02 |
| -0.1 | 7.8421710e-05 | 3.186230e-04 | 2.7725140e-03 | 7.9520300e-02 | 1.492981e-01 | 1.1299320e-01 | 7.2448000e-02 |
| 0 | 7.0563500e-14 | 1.032994e-14 | 1.6844760e-15 | 7.0622300e-15 | 1.684476e-15 | 1.0329940e-14 | 7.0563500e-14 |
| 0.1 | -7.244800e-02 | -1.129932e-01 | -1.492981e-01 | -7.952030e-02 | -2.772514e-03 | -3.186230e-04 | -7.842171e-05 |
| 0.2 | -7.257332e-02 | -1.113944e-01 | -1.353774e-01 | -7.880982e-02 | -1.456157e-02 | -2.802580e-03 | -7.912300e-04 |
| 0.3 | -7.165182e-02 | -1.053780e-01 | -1.183474e-01 | -7.765019e-02 | -2.729676e-02 | -8.167656e-03 | -2.791953e-03 |

Table 4.8: values of $\partial M / \partial a$

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|---------------|--------------|---------------|--------------|---------------|---------------|---------------|
| -0.3 | -4.901810e-02 | -4.56790e-02 | -2.825940e-02 | 6.759101e-17 | 2.825940e-02 | 4.567900e-02 | 4.901810e-02 |
| -0.2 | -3.334560e-02 | -3.11066e-02 | -1.924920e-02 | 2.639123e-17 | 1.924920e-02 | 3.110660e-02 | 3.334560e-02 |
| -0.1 | -1.687460e-02 | -1.57496e-02 | -9.747000e-03 | 1.274580e-17 | 9.747000e-03 | 1.574960e-02 | 1.687460e-02 |
| 0 | 1.886226e-09 | 7.11316e-10 | 2.379433e-10 | 8.406933e-18 | -2.379443e-10 | -7.113153e-10 | -1.886226e-09 |
| 0.1 | 1.687460e-02 | 1.57496e-02 | 9.747000e-03 | 2.657200e-17 | -9.747000e-03 | -1.574960e-02 | -1.687460e-02 |
| 0.2 | 3.334560e-02 | 3.11066e-02 | 1.924920e-02 | 4.293945e-17 | -1.924920e-02 | -3.110660e-02 | -3.334560e-02 |
| 0.3 | 4.901810e-02 | 4.56790e-02 | 2.825940e-02 | 4.124409e-17 | -2.825940e-02 | -4.567900e-02 | -4.901810e-02 |

Table 4.9: values of $\partial AUC / \partial b$

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|---------------|---------------|---------------|---------------|---------------|--------------|--------------|
| -0.3 | -3.393334e-02 | -7.727298e-02 | -1.690690e-01 | -2.436464e-01 | -1.333144e-01 | 1.043612e-02 | 3.394953e-02 |
| -0.2 | -1.365966e-02 | -3.733254e-02 | -1.176538e-01 | -2.456046e-01 | -7.972659e-02 | 1.620432e-02 | 3.167964e-02 |
| -0.1 | -2.515624e-03 | -8.009466e-03 | -3.974565e-02 | -2.468739e-01 | -5.056434e-03 | 1.296401e-02 | 1.541730e-02 |
| 0 | -1.008961e-07 | -3.703316e-08 | -1.361046e-08 | -1.433240e-09 | -1.361046e-08 | 3.703316e-08 | 1.008961e-07 |
| 0.1 | -1.541730e-02 | -1.296401e-02 | 5.0564340e-03 | 2.4687390e-01 | 3.9745650e-02 | 8.009466e-03 | 2.515616e-03 |
| 0.2 | -3.169902e-02 | -1.620432e-02 | 7.9726590e-02 | 2.4560460e-01 | 1.1765380e-01 | 3.733254e-02 | 1.365966e-02 |
| 0.3 | -3.394839e-02 | -1.043612e-02 | 1.3331440e-01 | 2.4364640e-01 | 1.6906900e-01 | 7.727298e-02 | 3.393334e-02 |

Table 4.10: values of $\partial M / \partial b$

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|-------------|-------------|-------------|--------------|------------|------------|------------|
| -0.3 | -0.06731619 | -0.09544239 | -0.09266058 | -0.006715919 | 0.08944073 | 0.09897828 | 0.07040353 |
| -0.2 | -0.07108644 | -0.10702744 | -0.12016545 | -0.006958249 | 0.12146625 | 0.11015619 | 0.07247775 |
| -0.1 | -0.07236796 | -0.11251625 | -0.14498517 | -0.007100600 | 0.14806625 | 0.11283281 | 0.07237119 |
| 0 | -0.07247590 | -0.11332840 | -0.15094760 | -0.166666700 | 0.15094760 | 0.11332840 | 0.07247590 |
| 0.1 | -0.07237119 | -0.11283281 | -0.14806594 | 0.007100600 | 0.14498517 | 0.11251625 | 0.07236796 |
| 0.2 | -0.07247775 | -0.11015619 | -0.12146625 | 0.006958249 | 0.12016545 | 0.10702744 | 0.07108644 |
| 0.3 | -0.07040353 | -0.09897828 | -0.08944073 | 0.006715919 | 0.09266058 | 0.09544239 | 0.06731619 |

Table 4.11: values of $\partial ASC / \partial a$

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|---------------|---------------|---------------|---------------|---------------|---------------|----------------|
| -0.3 | -1.884858e-02 | -1.088670e-01 | -3.098786e-01 | -4.872928e-01 | -2.948882e-01 | -6.655161e-02 | 1.8878680e-02 |
| -0.2 | 6.0262870e-03 | -4.355848e-02 | -2.160584e-01 | -4.912093e-01 | -1.787024e-01 | 1.3007700e-03 | 3.0052450e-02 |
| -0.1 | 1.1843350e-02 | -2.693327e-04 | -6.974429e-02 | -4.937479e-01 | -1.985987e-02 | 1.0178400e-02 | 1.3959990e-02 |
| 0 | -1.999060e-07 | -7.335500e-08 | -2.698297e-08 | 2.8664800e-09 | -2.745886e-08 | -7.477763e-08 | -2.0367840e-07 |
| 0.1 | -1.395999e-02 | -1.017840e-02 | 1.9859870e-02 | 4.9374790e-01 | 6.974429e-02 | 2.6933270e-04 | -1.184335e-02 |
| 0.2 | -3.005245e-02 | -1.300770e-03 | 1.7870240e-01 | 4.9120930e-01 | 2.160584e-01 | 4.3558480e-02 | -6.026287e-03 |
| 0.3 | -1.887868e-02 | 6.6551610e-02 | 2.9488820e-01 | 4.8729280e-01 | 3.098786e-01 | 1.0886700e-01 | 1.8848580e-02 |

Table 4.12: values of $\partial ASC / \partial b$

| $b \backslash a$ | -3 | -2 | -1 | 0 | 1 | 2 | 3 |
|------------------|--------------|-------------|-------------|-------------|-------------|-------------|--------------|
| -0.3 | 0.0008043777 | 0.003147897 | 0.010316919 | 0.014632027 | 0.009414318 | 0.002376146 | 0.0005906360 |
| -0.2 | 0.0006794769 | 0.002250099 | 0.007751964 | 0.014858760 | 0.006417216 | 0.001719800 | 0.0005777397 |
| -0.1 | 0.0006670016 | 0.001813195 | 0.004380848 | 0.015007403 | 0.003470092 | 0.001705326 | 0.0006543166 |
| 0 | 0.0006509881 | 0.001705211 | 0.003257597 | 0.003971391 | 0.003257597 | 0.001705211 | 0.0006509881 |
| 0.1 | 0.0006543166 | 0.001705326 | 0.003470092 | 0.015007403 | 0.004380848 | 0.001813195 | 0.0006670016 |
| 0.2 | 0.0005777397 | 0.001719800 | 0.006417216 | 0.014858760 | 0.007751964 | 0.002250099 | 0.0006794769 |
| 0.3 | 0.0005906360 | 0.002376146 | 0.009414318 | 0.014632027 | 0.010316919 | 0.003147897 | 0.0008043777 |

Table 4.13: values of $\text{var}(A\hat{S}C)$

Chapter 5

Conclusion

The expressions of *PLC* index and *ASC* index and their basic properties have been established in this project. All the results rely on the validity of the regression model proposed by Moses. Numerical integration are used to deal with all the deduced expressions of *PLC* and *ASC* when $-3 \leq a \leq 3$ and $-0.3 \leq b \leq 0.3$.

It was found that *PLC* index is symmetric with respect to $|a|$ and $|b|$. The homogeneous values of *PLC* provide a good approximation in heterogeneous studies. As $a \rightarrow 0$ and $b \rightarrow 0$, $PLC \rightarrow 0$, the corresponding *SROC* curve will run along the diagonal line. *PLC* attains its minimum in the homogeneous case and this indicates a cut-off point with no diagnostic value. Once the *SROC* curve deviates from the diagonal line, the *PLC* index will sum up the deviation. As $a \rightarrow \infty$, *PLC* gains its maximum $\sqrt{2}$ in the heterogeneous case. *PLC* is a decreasing function of a when a is negative and an increasing function of a vice versa. On the other hand, *PLC* is a decreasing function of b when b is negative and an increasing function of b vice versa. Our example illustrates that the heterogeneous variances of *PLC* are larger than the

homogeneous estimates and the big values of $\text{var}(\hat{PLC})$ indicate the worst situation for estimating PLC index in the diagnostic test.

The deduction of ASC 's expression related to properties of AUC . But ASC index is affected mostly by the new proposed index M . Although AUC index is symmetric with respect to $|a|$ and $|b|$, ASC index lacks symmetry with respect to b for fixed a or lacks symmetry with respect to a for fixed b since M index performs the same. Similarly, affected by the unsteady values of M , for fixed a , as b changes from negative to positive, the values for ASC are not smoothed, although AUC change smoothly. As $a \rightarrow 0$ and $b \rightarrow 0$, the emanating rays do not spread out and its ASC index is zero. Once the $SROC$ curve deviates from the diagonal line, the ASC index will sum up the deviation. When $a \rightarrow \infty$, ASC attains its maximum 0.5 in the homogeneous case. ASC is a decreasing function of a when b is positive and an increasing function of a vice versa. On the other hand ASC is a decreasing function of b when a is negative and an increasing function of b when a is positive. Our example illustrates that the heterogeneous variances of ASC are larger than the homogeneous estimates and the big values of $\text{var}(\hat{ASC})$ indicate the worst situation for estimating ASC index in the diagnostic test.

Appendix A

Source R codes for PLC

```
# Function: PLC.1
function (n) {
  my.b <- matrix(NA, nrow = 7, ncol = 7)
  s <- 0
  for (b in seq(-0.3, -0.1, 0.1)) {
    my.a <- matrix(NA, nrow = 1, ncol = 7)
    t <- 0
    for (a in seq(-3, 3, 1)) {
      SROC <- function(x, a, b) {
        u = a/(1 - b)
        v = (1 + b)/(1 - b)
        d = 1 + exp(u) * (x/(1 - x))^v
        y = 1 - 1/d
      }
      Q.star <- function(a, b) {
        x = exp(-a/(2 * b))/(1 + exp(-a/(2 * b)))
        y = x
        c(x, y)
      }
      q.star <- Q.star(a, b)
      dist <- function(x, y) {
        d = abs(-x + y)/sqrt(2)
        d
      }
    }
  }
}
```

```

    }
    xx2 <- seq(q.star[1], 1, (1 - q.star[1])/n)
    d2 <- dist(xx2, SROC(xx2, a, b))
    t <- t + 1
    my.a[t] <- max(d2)
  }
  s <- s + 1
  my.b[s, ] <- my.a
}
b = 0
my.a <- matrix(NA, nrow = 1, ncol = 7)
t <- 0
for (a in seq(-3, -1, 1)) {
  SROC <- function(x, a, b) {
    u = a/(1 - b)
    v = (1 + b)/(1 - b)
    d = 1 + exp(u) * (x/(1 - x))^v
    y = 1 - 1/d
    y
  }
  Q.star <- function(a, b) {
    x = exp(-a/(2 * b))/(1 + exp(-a/(2 * b)))
    y = x
    c(x, y)
  }
  q.star <- Q.star(abs(a), b)
  dist <- function(x, y) {
    d = abs(-x + y)/sqrt(2)
    d
  }
  xx2 <- seq(q.star[1], 1, (1 - q.star[1])/n)
  d2 <- dist(xx2, SROC(xx2, a, b))
  t <- t + 1
  my.a[t] <- max(d2)
}
t <- t + 1
my.a[t] <- 0
for (a in seq(1, 3, 1)) {
  SROC <- function(x, a, b) {
    u = a/(1 - b)
    v = (1 + b)/(1 - b)

```

```

        d = 1 + exp(u) * (x/(1 - x))^v
        y = 1 - 1/d
        y
    }
    Q.star <- function(a, b) {
        x = exp(-a/(2 * b))/(1 + exp(-a/(2 * b)))
        y = x
        c(x, y)
    }
    q.star <- Q.star(a, b)
    dist <- function(x, y) {
        d = abs(-x + y)/sqrt(2)
        d
    }
    xx1 <- seq(0, q.star[1], q.star[1]/n)
    d1 <- dist(xx1, SROC(xx1, a, b))
    t <- t + 1
    my.a[t] <- max(d1)
}
s <- s + 1
my.b[s, ] <- my.a
for (b in seq(0.1, 0.3, 0.1)) {
    my.a <- matrix(NA, nrow = 1, ncol = 7)
    t <- 0
    for (a in seq(-3, 3, 1)) {
        SROC <- function(x, a, b) {
            u = a/(1 - b)
            v = (1 + b)/(1 - b)
            d = 1 + exp(u) * (x/(1 - x))^v
            y = 1 - 1/d
            y
        }
        Q.star <- function(a, b) {
            x = exp(-a/(2 * b))/(1 + exp(-a/(2 * b)))
            y = x
            c(x, y)
        }
        q.star <- Q.star(a, b)
        dist <- function(x, y) {
            d = abs(-x + y)/sqrt(2)
            d
        }

```

```

    }
    xx1 <- seq(0, q.star[1], q.star[1]/n)
    d1 <- dist(xx1, SROC(xx1, a, b))
    t <- t + 1
    my.a[t] <- max(d1)
  }
  s <- s + 1
  my.b[s, ] <- my.a
}
my.b
}

```

Appendix B

Source R codes for ASC

```
# Function: M.1
function (n) {
  my.b <- matrix(NA, nrow = 4, ncol = 7)
  s <- 0
  for (b in seq(0, 0.3, 0.1)) {
    my.area <- matrix(NA, nrow = 1, ncol = 7)
    t <- 0
    for (a in seq(-3, 3, 1)) {
      my.x <- matrix(NA, nrow = 1, ncol = n)
      my.x.star <- matrix(NA, nrow = 1, ncol = n)
      height.sroc <- matrix(NA, nrow = 1, ncol = n)
      sroc <- function(x, a, b) {
        u = a/(1 - b)
        v = (1 + b)/(1 - b)
        d = 1 + exp(u) * (x/(1 - x))^v
        y = 1 - 1/d
      }
      slope <- function(x, a, b) {
        u = a/(1 - b)
        v = (1 + b)/(1 - b)
        d = 1 + exp(u) * (x/(1 - x))^v
        k = (1 - 1/d)/x
        k
      }
      xx <- seq(1e-05, 1, len = 10000)
      k <- slope(xx, a, b)
      k.order <- order(k)
```



```

r <- k.order[10000]
the.x <- xx[r]
kx <- function(k, x) {
  y = k * x
}
base.x <- the.x/n
for (i in 1:n) {
  my.x[i] = i * base.x
  my.x.star[i] = my.x[i] - base.x/2
  height.sroc[i] = kx(max(k), my.x.star[i]) - sroc(my.x.star[i],
    a, b)
}
t <- t + 1
my.area[t] <- sum(height.sroc * base.x)
}
s <- s + 1
my.b[s, ] <- my.area
}
my.b
}

```

```

# Function: AUC.1
function (n) {
  sroc.area <- matrix(NA, nrow = 4, ncol = 7)
  r <- 0
  for (b in seq(0, 0.3, 0.1)) {
    my.area <- matrix(NA, nrow = 1, ncol = 7)
    t <- 0
    for (a in seq(-3, 3, 1)) {
      my.x <- matrix(NA, nrow = 1, ncol = n)
      my.x.star <- matrix(NA, nrow = 1, ncol = n)
      height.sroc <- matrix(NA, nrow = 1, ncol = n)
      sroc <- function(x, a, b) {
        u = a/(1 - b)
        v = (1 + b)/(1 - b)
        d = 1 + exp(u) * (x/(1 - x))^v
        y = 1 - 1/d
      }
      base.x <- 1/n
      for (i in 1:n) {

```

```

        my.x[i] = i * base.x
        my.x.star[i] = my.x[i] - base.x/2
        height.sroc[i] = sroc(my.x.star[i], a, b)
    }
    t <- t + 1
    my.area[t] <- sum(height.sroc * base.x)
}
r <- r + 1
sroc.area[r, ] <- my.area
}
sroc.area
}

```

Appendix C

Source R codes for Graphs

```
# figure 1:
function () {
  SROC <- function(x, a, b) {
    u = a/(1 - b)
    v = (1 + b)/(1 - b)
    d = 1 + exp(u) * (x/(1 - x))^v
    y = 1 - 1/d
  }
  diagonal <- function(x) {
    y = x
  }
  xgr <- seq(0, 1, len = 40)
  ygr <- seq(0, 1, len = 40)
  plot(xgr, ygr, xlab = "FPR", ylab = "TPR", main = "(a) a=2, b=0.5,0,-0.5",
       type = "n")
  lines(xgr, SROC(xgr, 2, 0.5), lty = 2)
  lines(xgr, diagonal(xgr), lty = 1)
  lines(xgr, SROC(xgr, 2, -0.5), lty = 3)
  lines(xgr, SROC(xgr, 2, 0), lty = 4)
  legend(x = 0.7, y = 0.3, legend = c("b=0.5", "b=0", "b=-0.5"),
        lty = c(2, 4, 3))
}

# figure 2:
function () {
  SROC <- function(x, a, b) {
```

```

        u = a/(1 - b)
        v = (1 + b)/(1 - b)
        d = 1 + exp(u) * (x/(1 - x))^v
        y = 1 - 1/d
    }
    diagonal <- function(x) {
        y = x
    }
    xgr <- seq(0, 1, len = 40)
    ygr <- seq(0, 1, len = 40)
    plot(xgr, ygr, xlab = "FPR", ylab = "TPR", main = "(b) a=-2,b=0.5,0,-0.5",
        type = "n")
    lines(xgr, SROC(xgr, -2, 0.5), lty = 2)
    lines(xgr, diagonal(xgr), lty = 1)
    lines(xgr, SROC(xgr, -2, -0.5), lty = 3)
    lines(xgr, SROC(xgr, -2, 0), lty = 4)
    legend(x = 0.1, y = 0.9, legend = c("b=0.5", "b=0", "b=-0.5"),
        lty = c(2, 4, 3))
}

```

#figure 3:

```

function () {
    SROC <- function(x, a, b) {
        u = a/(1 - b)
        v = (1 + b)/(1 - b)
        d = 1 + exp(u) * (x/(1 - x))^v
        y = 1 - 1/d
    }
    diagonal <- function(x) {
        y = x
    }
    xgr <- seq(0, 1, len = 40)
    ygr <- seq(0, 1, len = 40)
    plot(xgr, ygr, xlab = "FPR", ylab = "TPR", main = "(c) b=0.5,a=2,0,-2",
        type = "n")
    lines(xgr, SROC(xgr, 2, 0.5), lty = 2)
    lines(xgr, diagonal(xgr), lty = 1)
    lines(xgr, SROC(xgr, -2, 0.5), lty = 3)
    lines(xgr, SROC(xgr, 0, 0.5), lty = 4)
    legend(x = 0.75, y = 0.3, legend = c("a=2", "a=0", "a=-2"),

```

```

        lty = c(2, 4, 3))
}

```

#figure 4:

```

function () {
  SROC <- function(x, a, b) {
    u = a/(1 - b)
    v = (1 + b)/(1 - b)
    d = 1 + exp(u) * (x/(1 - x))^v
    y = 1 - 1/d
  }
  diagonal <- function(x) {
    y = x
  }
  xgr <- seq(0, 1, len = 40)
  ygr <- seq(0, 1, len = 40)
  plot(xgr, ygr, xlab = "FPR", ylab = "TPR", main = "(d) b=-0.5,a=2,0,-2",
        type = "n")
  lines(xgr, SROC(xgr, 2, -0.5), lty = 2)
  lines(xgr, diagonal(xgr), lty = 1)
  lines(xgr, SROC(xgr, -2, -0.5), lty = 3)
  lines(xgr, SROC(xgr, 0, -0.5), lty = 4)
  legend(x = 0.7, y = 0.2, legend = c("a=2", "a=0", "a=-2"),
        lty = c(2, 4, 3))
}

```

#figure 5:

```

function () {
  slope <- function(x, a, b) {
    u = a/(1 - b)
    v = (1 + b)/(1 - b)
    d = 1 + exp(u) * (x/(1 - x))^v
    k = (1 - 1/d)/x
  }
  xx1 <- seq(1e-04, 1, len = 10000)
  k <- slope(xx1, 2, 0.5)
  k.order <- order(k)
  my.xx1 <- xx1[k.order[10000]]
}

```

```

SROC <- function(x, a, b) {
  u = a/(1 - b)
  v = (1 + b)/(1 - b)
  d = 1 + exp(u) * (x/(1 - x))^v
  y = 1 - 1/d
}
diagonal <- function(x) {
  y = x
}
xgr <- seq(0, 1, len = 40)
ygr <- seq(0, 1, len = 40)
xgr.1 <- seq(0, my.xx1, len = 40)
plot(xgr, ygr, xlab = "X", ylab = "y", main = "(a) ASC:a=2,b=0.5",
     type = "n")
lines(xgr, diagonal(xgr), lty = 1)
lines(xgr, SROC(xgr, 2, 0.5), lty = 2)
lines(xgr.1, max(k) * xgr.1, lty = 2)
}

```

#figure 6:

```

function () {
  slope <- function(x, a, b) {
    u = a/(1 - b)
    v = (1 + b)/(1 - b)
    d = 1 + exp(u) * (x/(1 - x))^v
    k = (1 - 1/d)/x
    k
  }
  xx1 <- seq(1e-04, 1, len = 10000)
  k <- slope(xx1, 2, -0.5)
  k.order <- order(k)
  my.xx1 <- xx1[k.order[1]]
  SROC <- function(x, a, b) {
    u = a/(1 - b)
    v = (1 + b)/(1 - b)
    d = 1 + exp(u) * (x/(1 - x))^v
    y = 1 - 1/d
  }
  diagonal <- function(x) {
    y = x
  }
}

```

```

}
xgr <- seq(0, 1, len = 40)
ygr <- seq(0, 1, len = 40)
xgr.1 <- seq(0, my.xx1, len = 40)
plot(xgr, ygr, xlab = "X", ylab = "y", main = "(b) ASC:a=2,b=-0.5",
     type = "n")
lines(xgr, diagonal(xgr), lty = 1)
lines(xgr, SROC(xgr, 2, -0.5), lty = 2)
lines(xgr.1, min(k) * xgr.1, lty = 2)
}

```

#figure 7:

```

function () {
  slope <- function(x, a, b) {
    u = a/(1 - b)
    v = (1 + b)/(1 - b)
    d = 1 + exp(u) * (x/(1 - x))^v
    k = (1 - 1/d)/x
    k
  }
  xx1 <- seq(1e-04, 1, len = 10000)
  k <- slope(xx1, -2, 0.5)
  k.order <- order(k)
  my.xx1 <- xx1[k.order[10000]]
  SROC <- function(x, a, b) {
    u = a/(1 - b)
    v = (1 + b)/(1 - b)
    d = 1 + exp(u) * (x/(1 - x))^v
    y = 1 - 1/d
  }
  diagonal <- function(x) {
    y = x
  }
  xgr <- seq(0, 1, len = 40)
  ygr <- seq(0, 1, len = 40)
  xgr.1 <- seq(0, my.xx1, len = 40)
  plot(xgr, ygr, xlab = "X", ylab = "y", main = "(c) ASC:a=-2,b=0.5",
       type = "n")
  lines(xgr, diagonal(xgr), lty = 1)
  lines(xgr, SROC(xgr, -2, 0.5), lty = 2)
}

```

```

    lines(xgr.1, max(k) * xgr.1, lty = 2)
}

```

#figure 8:

```

function () {
  slope <- function(x, a, b) {
    u = a/(1 - b)
    v = (1 + b)/(1 - b)
    d = 1 + exp(u) * (x/(1 - x))^v
    k = (1 - 1/d)/x
    k
  }
  xx1 <- seq(1e-04, 1, len = 10000)
  k <- slope(xx1, -2, -0.5)
  k.order <- order(k)
  my.xx1 <- xx1[k.order[1]]
  SROC <- function(x, a, b) {
    u = a/(1 - b)
    v = (1 + b)/(1 - b)
    d = 1 + exp(u) * (x/(1 - x))^v
    y = 1 - 1/d
  }
  diagonal <- function(x) {
    y = x
  }
  xgr <- seq(0, 1, len = 40)
  ygr <- seq(0, 1, len = 40)
  xgr.1 <- seq(0, my.xx1, len = 40)
  plot(xgr, ygr, xlab = "X", ylab = "y", main = "(d) ASC:a=-2,b=-0.5",
       type = "n")
  lines(xgr, diagonal(xgr), lty = 1)
  lines(xgr, SROC(xgr, -2, -0.5), lty = 2)
  lines(xgr.1, min(k) * xgr.1, lty = 2)
}

```

#figure 9:

```

function () {
  SROC <- function(x, a, b) {
    u = a/(1 - b)

```



```

        v = (1 + b)/(1 - b)
        d = 1 + exp(u) * (x/(1 - x))^v
        y = 1 - 1/d
    }
    diagonal <- function(x) {
        y = x
    }
    xgr <- seq(0, 1, len = 40)
    ygr <- seq(0, 1, len = 40)
    plot(xgr, ygr, xlab = "FPR", ylab = "TPR", main = "(a) ASC:a=2,b=0",
        type = "n")
    lines(xgr, SROC(xgr, 2, 0), lty = 2)
    lines(xgr, diagonal(xgr), lty = 1)
}

#figure 10:
function () {
    SROC <- function(x, a, b) {
        u = a/(1 - b)
        v = (1 + b)/(1 - b)
        d = 1 + exp(u) * (x/(1 - x))^v
        y = 1 - 1/d
    }
    diagonal <- function(x) {
        y = x
    }
    xgr <- seq(0, 1, len = 40)
    ygr <- seq(0, 1, len = 40)
    plot(xgr, ygr, xlab = "FPR", ylab = "TPR", main = "(b) ASC:a=-2,b=0",
        type = "n")
    lines(xgr, SROC(xgr, -2, 0), lty = 2)
    lines(xgr, diagonal(xgr), lty = 1)
}

```

Bibliography

- [1] Green, D. M. and Swets, J. A. (1966). *Signal Detection Theory and Psychophysics*, John Wiley & Sons, New York.
- [2] Hanley, J. A. and McNeil, B. J. (1982). The Meaning and Use of the Area under A Receiver Operating Characteristic (ROC) curve. *Radiology*, 143, 29-36.
- [3] Lee, Wen-Chung and Hsiao, C. K. (1996). Alternative Summary Indices for the Receiver Operating Characteristic Curve. *Epidemiology*, Vol. 7, No. 6, 605-611.
- [4] Littenberg, B., Moses, L. E. and Rabinowitz, D. (1990). Estimating Diagnostic Accuracy from Multiple Conflicting Reports: A New Meta-analytic Methods. *Clin. Res.*, 138, 415a.
- [5] Lusted, L. B. (1971). Signal Detectability and Medical Decision Making. *Science*, 171, 1217-1219.
- [6] Metz, C. E. (1978). Basic Principles of ROC Analysis. *Semin. Nucl. Med.*, 8, 283-298.

- [7] Moses, L. E., Shapiro, D. E. and Littenberg, B. (1993). Combining Independent Studies of A Diagnostic Tests into A Summary ROC curve: Data-analytic Approaches and Some Additional Considerations. *Statist. Med.*, 12, 1293-1316.
- [8] Nicholson, W. K. (2003). *Linear Algebra with Applications*, 4th Edition. McGraw-Hill Ryerson, Toronto.
- [9] Scheidler, J., Hricak, H., Yu, K. K., Subak, L., Segal, M. R. (1997). Radiological Evaluation of Lymph Node Metastases in Patients with Cervical Cancer: A Meta-analysis. *Journal of the American Medical Association*, 96-1101.
- [10] Seong, H. P., Jin, M. G. and Chan, H. J. (2004). Receiver Operating Characteristic (ROC) Curve: Practical Review for Radiologists. *Korean Journal of Radiology*, Vol. 5, No. 1, 11-18.
- [11] Stewart, James (2003). *Calculus Early Transcendentals*, 5th edition. Thomson: Brooks/Cole, Belmont.
- [12] Swets, J. A. and Pickett, R. M. (1982). *Evaluation of Diagnostic System: Methods from Signal Detection Theory*, Academic Press, New York.
- [13] Walter, S. D. (2002). Properties of the Summary Receiver Operating Characteristic (SROC) curve for Diagnostic Test Data. *Statist. Med.*, 21, 1237-1256.
- [14] Zhou, X. H., Obuchowski, N. A. and McClish, D. K. (2002). *Statistical Methods in Diagnostic Medicine*, John Wiley & Sons, New York.