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Estimation For the Survival Function of Quality Adjusted Lifetime

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Declaration

I, Hadeel Salah Aden Zayyat declare this work provided in this thesis, unless otherwise referenced, that this dissertation is my original work and that it has not been presented, and will not be presented, to any university for similar or any other degree award.

Signature ....

Dedication

Thanks and praise to Allah who gave me life.

To the messenger of knowledge and holy religion –prophet Mohammed. To my dear lovely country, Palestine.

To whom holds me, cares about my tiny inner feelings, let me satisfied at any time, my mother (Amal Omar).

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Abstract

Estimation for the Survival Function of Quality Adjusted Lifetime

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Recently, quality adjusted life time has received much attention because of its ability to take quality of life into consideration. The quality adjusted lifetime is a new approach to therapy evaluation in clinical trials. In this work we will present the case of censoring, assuming that a subject disappears at specific time, and reports back at any time later. We will deal with this type of censoring using two methods: The Mean Value Theorem method and the shifting method.

Also, we will find another estimator for the survival function, using the Monotonized Zhao-Tiatis estimator and Wang estimator by following Almanssra method(2005). We will study the efficiency of this estimator using simulation study to compare MSE, BIAS for the estimations and the true value of survival function by using R program.

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Chapter 1

Introduction

Survival analysis is defined as a collection of statistical procedures for data analysis for which the outcome variable of interest is the time when the event occurs. In the past, the survival analysis was obtained from initial studies where the event of interest was death only. But nowadays, the scope of the survival analysis has become wider. Today, scientists are using the survival analysis to estimate time until of set of disease, the time until stock market crash and the time until an earthquake, and so on [23].

Many clinical trials are intreasted in following patients for a long time. The event of interest in those studies is death, relapse, onset of illness, recovery from illness, adverse drug reaction or development of a new disease. The follow-up time for the study may range from a few weeks to many years.

Most clincal studies involve observations on individuals subjected to censoring. The existence of censoring in these studies causes difficulties in analyzing such data.

Two of the most popular estimators proposed to consider censored data are the Kaplan-Meier estimator and the Nelson-Aalen estimator [27].

In clinical trials of chronic diseases such as AIDS or cancer, it has been recognized that it is not enough just to consider simple time to event and points. For example, a new experimental drug may prolong the overall survival time of patients, but in the mean time, it can be toxic for a longer

period of time.
Therefore, the trade-off between the quality and quantity of life of patients needs to be considered.
Cox(1992) pointed out that we need a new measure which take in consideration both the quality and the quantity of patient's life, which is called quality-adjusted lifetime.
A lot of researchers studied quality adjusted lifetime. Gelber *et al.* (1989) noted that the use of the Kapaln-Meier estimater with censored quality adjusted lifetime data will obtianed inconsistent and biased estimation. Many different estimatiors have been proposed to solve this difficulty and estimate consistent biased estimator. One of them was studied by Korn(1993).
Zhao and Tsiatis(1997) presented a method which finds an estimation of the survival function of quality adjusted lifetime involved censored data. They proved that their estimator is consistent. Huang and Louis (1998) noted that the above Zhao-Tsiatis estimator is not a monotonic function.
Zhao-Tsiatis estimator is a member of a class of inverse probability of censoring weighted (IPCW) estimators. Huang and Louis(1998) used (IPCW) technique to propose an estimator of the distribution function of the unrestricted quality adjusted lifetime.
Zhao and Tsiatis(2000) [33] discussed the efficiency of the weighted estimators of survival functions for the quality -adjusted lifetime by proposed a modified estimator. This modified estimator is more efficient than the one proposed in Zhao-Tsiatis(1997).

Zhao-Tsiatis(2000) noted the problem of estimating the mean of the quality adjusted lifetime (QAL), which is often of interest in its own right. Because of the presence of censoring, it is impossible to obtain a consistent estimator for mean QAL over the entire health history. Therfore, they considered mean QAL restricted to a certain time, which is often determined by the follow-up time of the study. Wang(2001) [30] suggested an imporoved version of the Zhao-Tsiatis estimator, which is more efficient than the original version of Zhao- Tsiatis estimator. Since Wang estimator is an modified verision of Zhao-Tsiatis estimator it is also consistent. A survival function estimator assigned negative mass at a point if and only if the value of the survival function befor the point is smaller than its value after this point. Almanassra *et al.* (2005) studied the jump points for Zhao-Tsiatis estimator and Wang estimator and he investigated which of these estimators jump points assigned negative mass. Therefore, Zhao-Tsiatis estimator and Wang estimator are not monotonic estimators.

An estimator will be not a proper survival function, if it fails to be monotonic estimator. Since Zhao-Tsiatis estimator and Wang estimator are efficient estimators of survival function of quality adjusted lifetime but they are not monotonic, and therfore not proper survival functions, if "isotonized" to make monotoic by invistigate thier consistency and efficiency which has been done by Almanassra *et al.* (2005). Since the Simple Weighted estimator of the survival function of quality adjusted lifetime is a consistent estimator and a proper survival function, and it has been considered that it is less efficient than many estimators that are not monotonic and therefore, are not proper survival functions. They intorduced new monotonic estimators, by finding the jump points of the Simple Weighted estimator, Zhao-Tsiatis estimator, and Wang estimator and their values at these point to proposed a class of monotonic estimators for survival function of quality adjusted lifetime.

All proposed estimators derived by Almanassra *et al.*(2005) are consistant, but they are nearly as efficient as their non monotonic counter parts, when the sample size is large. So the method of modifying any consistent non-

monotonic estimator to define a class of monotonic estimators is descibed in Almanassra *et al.*(2005). This method is applied to the Zhao-Tsiats estimator and the Wang estimator using the Simple Wieghted estimator as a consistent estimator to intorduce the monotonic Zhao-Tsiatis estimator and the monotonic Wang estimator. They presented a simulation study which campares the two proposed monotonic estimators with their unmodified counterparts and the Simple Weighted estimator.
In this work, we will use the monotonic Zhao-Tsiats estimator which proposed by Almanassra *et al.* (2005) and Wang estimator to find a new estimator for the survival function of quality adjusted lifetime which we hope it will be efficient as the other estimators by following Almanassra method(2005). Also we present a case of censoring which we suppose that there is missing data in an interval in the follow-up time, then we used two methods to deal with this case of censoring, the mean value theorem to estimate the quality adjusted lifetime function for the missing data and shifing method, we will study the jump points of Simple Weighted estimator, Zhao-Tsiatis estimator and Wang estimator.

1.1 Work Plan

This thesis consists of 4 chapters. In the first chapter, we give a review of the literature and explian some of the basic ideas about survival functions. We defined Kapalan-Meier estimator and Empirical estimator when there is no censoring. we presented the mean quality adjusted lifetime and Simple Weighted estimator, Zhao-Tsiatis estimator and Wang estimator, we presented the mean value theorem and some notes for MSE and consistency.
In the second chapter, we review a case of censoring and we will present examples consider this case of censoring, and we will identify the jump points of Simple Weight estimators, Zhao-Tsiatis estimator and Wang estimator.

In the third chapter we will estimate a survival function of quality adjusted lifetime using the monotonized Zhao estimator to introduce the monotonic Wang estimator by following Almanassra *et al.* method(2005).
In the fourth chapter, we will present a simulation study compares MSE, Bias for the Simple Weighted estimator, Zhao-Tiatis estimator, Wang estimetor, monotonic Zhao-Tiatis estimator, monotoic Wang estimator an new monotonic Zhao-Wang estimator.

Chapter 2

Review

2.1 Survival Functions

One of the main concepts in survival analysis is the survival function, $S(t)$ which gives the probability that a person survives longer than some certian time t. The survival function is a monotonic noninceasing function of time. let T be a non-negative random variable representing the waiting time until the occurrance of an event.

Here, the terminology of survival analysis is limited to suppose that the death is event of intrest, and the waiting time is "survival" time, but the techniques to be studied have much widder applicability. They can be used, for example, to study duration of a marriage, the intervals between successive births to a woman, the duration of study in a city(or stay in a job) and the length of life.

It may include fields such as Fertility, mortality and migration.

The cumulative distribtion function which is the probability of the event occuring prior to or at time t is given by.

$$F(t) = P(T \leqslant t)$$

Survival function $S(t)$, also called the survivorship function, or the survival function is simply the reverse cumulative distrubution function of T.

$$S(t) = P(T > t) = (1 - P(T \leqslant t)) = 1 - F(t).$$

Where $t \in [0, \infty)$, and $S(t) \in [0, 1]$.

Which gives the probability of a life just before time t, or the probability that the event of interest has not occurred before time t [3].

The probability density function is given by $f(t)$, which is

$$f(t) = \frac{d}{dt}F(t) = \frac{-d}{dt}S(t).$$

2.2 Hazard function

The hazard function, $\lambda(t)$ also known as the conditional failure rate [3]. The hazard function is the limiting probability that the failure event occurs in a given interval, conditional upon the subject having survived to the beginning of that interval, divided by the width of that interval [3].

$$\lambda(t) = \lim_{\Delta t \longrightarrow 0} \frac{Pr(t + \Delta t > T > t | T > t)}{\Delta t}.$$

Let T in the interval $[t, t + \Delta t]$,

$$\lambda(t) = \lim_{\Delta t \longrightarrow 0} \frac{P("t < T \leq t + \Delta t" \bigcap "T > t")}{P(T > t)\Delta t}.$$

$$\lambda(t) = \lim_{\Delta \longrightarrow 0} \frac{P(t < T \leqslant t + \Delta t)}{p(T > t)\Delta t}.$$

By the defintion of $S(t) = P(T > t)$.

Since,

$$f(t) = \lim_{\Delta t \longrightarrow 0} \frac{F(t + \Delta t) - F(t)}{\Delta t}$$

Then,

$$\lambda(t) = \frac{f(t)}{S(t)} \tag{2.1}$$

since $f(t) = \frac{d(F(t))}{dt}$

$$\lambda(t) = \frac{\frac{d(1 - S(t))}{dt}}{S(t)} = \frac{\frac{-dS(t)}{dt}}{S(t)} \tag{2.2}$$

Then,

$$\lambda(t) = \frac{-d}{dt} \log(S(t)) \tag{2.3}$$

The hazard rate can vary from zero which means no risk at all, to infinity which means the certainty of failure at that instant. The greater the hazard between times t_1 and t_2 causing greater the risk of failure in this time interval which means that over time, the hazard rate may increase, decrease, stay constant, or even take on more serpentine shapes [3].

2.2.1 Cumulative hazard function

The cumulative hazard function [3]
$\Lambda(t)$ is given by:

$$\Lambda(t) = \int_0^t \lambda(u)du. \tag{2.4}$$

$$\Lambda(t) = \int_0^t \frac{f(u)}{S(u)}du = -\int_0^t \frac{1}{S(u)}\{\frac{d}{du}S(u)\}du = -\ln(S(t)). \tag{2.5}$$

The cumulative hazard function measures the total amount of risk that has been accumulated up to time t. We can see the inverse relationship between the accumulated risk and the probability of survival function.

$$S(t) = e^{-\Lambda(t)}.$$

$$S(t) = e^{\int_0^t \lambda(u)du}.$$

Example 2.2.1

Lets obtain the risk as a constant, the hazard is given by

$$\lambda(t) = \lambda, \quad \text{for all t}$$

$$S(t) = e^{-\lambda t}.$$

This ditribution is called the exponential distribution with parameter λ. The density may be obtained by multiplying the survival function by the hazard.

$$f(t) = \lambda e^{-\lambda t}.$$

the mean turns out to be $\frac{1}{\lambda}$.

2.3 Censored Data

Most survival analysis considers a problem called censoring. Censoring occurs when we have some information about individual survival time, but we do not know the survival time exactly.

In real data-analysis situations, we often do not know when failures occurred, at least not for every observation in the dataset [3].

The censoring is defined as when the failure event occurs and the subject is not under observation [3].

There are three reasons of censoring :

A person does not experience the event before the study ends, or when a person withdraws from the study because of death (if death is not the event of the interest), or a person is lost to follow-up during the study period or some other reason like adverse drug reaction.

Broadly classifying two types of censoring are encountered, *i.e,* point and interval censoring [3] .

Point censoring is said to occur when a subject leaves the study befor an event occurs. We called that type, right censoring.

Left-censored data can occur when a person's survival time becomes incomplete on the left side of the follow-up period for this subject.

For example, we may follow up a patient for any infectious disorder from the time of his being tested positive for the infection. The exact time of exposure to the infectious agent could never be known [3].

In interval censoring we know the event occurs in a time interval, but we don't know exactly when in this interval it might occur.

Here, we are intrested in right censoring which has two types:

1. Type one: Completely random drop out, where total duration of study is fixed.

2. Type two: Study ends when a fixed number of subjects were experienced the event has occured, and the duration of the study is then random.

In random censoring, which is a more general scheme, each unit is asociated with its censoring time.

Let C_i is the time to the censoring event and T_i is the time to event. lifetime T_i, and C_i are independent variables.

We observe X_i which is the minimum of censoring and lifetime.

$X_i = \min(C_i, T_i)$ The censoring indicator is defined as

$$\Delta_i = I(T_i \leq C_i).$$

which is equal to one if the observations terminated by death or the event of interest, and zero if the observations considered as censoring.

2.3.1 Censoring and Truncation

Truncation is often confused with censoring because it also gives rise to incomplete observations over time. Truncation usually refers to complete ignorance of the event of interest and of the covariates over part of the distribution [3].

The right truncation is defined as a period over which the subject was not observed but is known not to have failed to be observed [3].

2.4 Empirical Distribution Function

The empirical distribution function is the distribution function associated with the empirical measure of a sample. This cumulative distribution function is a step function that jumps up by $\frac{1}{n}$ at each of the n point [28].

Definition 2.4.1 *The Empirical Distribution Function [4]*

Let $X_1, \ldots, X_n$ be $i.i.d$ real random variables with the cumulative distribution function $F(t)$. Then the empirical distribution function is given

$$\hat{F}_n(t) = \frac{I}{n}\sum_{i=1}^{n} I(X_i \leq t). \tag{2.6}$$

The empirical estimation of survival function provides the best estimation of the survival function since it is an unbiased and consistent estimator of $F(t)$ when we don't have censored data.

Let $C_1, \ldots, C_n$ denote the censoring time for the $i-th$ subject so we measure the pair (X_i, Δ_i), where

$X_i = \min(T_i, C_i)$.

Nelson-Aalen estimator and Kapalan-Meier estimator are the most popular estimators proposed to deal with censoring data.

2.5 Kaplan-Meier Estimator

The Kaplan-Meier method is based on individual survival times and assumes that censoring is independent of survival time. That is the reason an observation is censored and unrelated to the cause of failure [24]. The Kaplan–Meier estimator, also known as the product limit estimator, is used for estimating the survival function for lifetime data .

The main idea behind the Kaplan-Meier estimator is dividing the observed timespan of the study into a series of fine intervals to get a separate interval for each time of death or censoring.

Let $t_1, t_2, t_3, \ldots\ldots$ denote the times of death of n individulas in a study.

Let $d_1, d_2, d_3 \ldots\ldots$ denote the number of deaths that occur at each of these times.

Let $r_1, r_2, \ldots\ldots, r_n$ be the number of patients remaining in the study, or the number of patients in risk. where, $r_2 = r_1 - d_1$, $r_3 = r_2 - d_2, \ldots.$, etc.

$P(T > t_1) = S(t_1)$ is the probability of surviving beyond time t_1.

A numerical estimator $\hat{S}(t)$ of the true survival function $S(t)$ can iteratively be build by using that recursive idea.

For any time $t \in [0, t_1)$, then $\hat{S(t)} = 1$; because no deaths have yet occurred.

For any time $t \in [t_1, t_2]$,

$$\hat{S}(t) = 1 \times (\frac{r_1 - d_1}{r_1}) = \frac{r_1}{r_1} - \frac{d_1}{r_1}$$

For any time $t \in [t_2, t_3]$, we have

$$\begin{aligned}\hat{S}(t) &= P(T > t)\\ &= (1 - \frac{d_1}{r_1}) \times (\frac{r_2 - d_2}{r_2})\\ &= (1 - \frac{d_1}{r_1}) \times (1 - \frac{d_2}{r_2})\end{aligned}$$

and so on.

Now, for any $t \in [t_j, t_{j+1}], j = 1, 2, \ldots\ldots, n$ the Kaplan Meier estimater given by

$$\begin{aligned}\hat{S}(t) &= (1 - \frac{d_1}{r_1}) \times (1 - \frac{d_2}{r_2}) \times \ldots\ldots\ldots \times (1 - \frac{d_j}{r_j})\\ &= \prod_{j:t_j \leq t} (1 - \frac{d_j}{r_j}) \quad 0 < t < t_j\end{aligned}$$

Where, $t_j, j = 1, 2, \ldots, n$ is the total set of failure times recorded, d_j is the number of failures at time t_j, and r_j is the number of individuals at risk at time t_j.

If there are no censored observations, then the kaplan Meier estimator $\hat{S}(t)$ is reduce to one minus the empirical distribution funcion.

$$\hat{S}_n(t) = (1 - \hat{F}_n(t)) \tag{2.7}$$

Example 2.5.1 *Suppose that t_j = 2, 4, 5, 7, 9, 11, 16, 18, 20.*

Let n=10

Where the ordered observations in the table:

observation	*2*	*2*	*3*	*5*	*5*	*9*	*16*	*16*	*18*
Δ_i	*1*	*1*	*0*	*1*	*0*	*1*	*1*	*1*	*0*

t_j	r_{tj}	d_j	$\frac{d_j}{r_j}$	$(1-\frac{d_j}{r_j})$	$\hat{S}(t)$
2	*10-0*	*2*	$\frac{2}{10}$	*1-0.2=0.8*	*0.8*
4	*10-(1+2)=7*	*0*	$\frac{0}{7}=0$	*1-0=1*	*0.8*1*
5	*(7-0)=7*	*1*	$\frac{1}{7}$	$1-\frac{1}{7}=\frac{6}{7}$	$(0.8)(\frac{6}{7})$=*0.69*
7	*7-(1+1)=5*	*1*	$\frac{1}{5}$	$1-\frac{1}{5}=\frac{4}{5}$	$\frac{4}{5}(0.69)$ =*0.552*
9	*5-1=4*	*1*	$\frac{1}{4}$	$1-\frac{1}{4}$	$\frac{1}{4}(0.552)$=*0.41*
11	*4-1=3*	*0*	$\frac{0}{3}=0$	*1*	*0.41*1=0.41*
16	*3-0=3*	*2*	$\frac{2}{3}$	$1-\frac{2}{3}=\frac{1}{3}$	$0.41(\frac{1}{3})$
18	*3-2=1*	*0*	*0*	*1*	*0.14*
20	*1-1=0*	*0*	*not defined*	*not defind*	*not defind*

Where $K(.)$ is Kaplan-Meier estimator.

Note that as the intervals get finer and finer the approximations made in estimating the probabilities of getting through, each interval becomes more and more accurate, at the end, the estimator converges to the value of the true survival function $S(t)$ in probability.

The variance of the Kaplan-Meier estimator is estimated by [14]:

$$\hat{\sigma}(t) = \hat{S}(t)^2 \sum_{t_j \leq t} \frac{d_j}{r_j(r_j - d_j)}$$

2.6 Nelson-Aalen Estimator

The Nelson-Aalen Estimator is nonparameteric estimator, which can be used to estimate the cumulative hazard rate function from censored data [14]. The Nelson Aalen Estimator is given by

$$\hat{\Lambda}(t) = \sum_{ti \leq t} \frac{d_i}{r_j},$$

where, r_j is the number of individuals at risk alive and not censored just prior to or befor t_j.

The Nelson-Aalen is an increasing function with increasing right continuous step function with increments $\frac{d_j}{r_j}$ at the observed failure times.

The variance of the Nelson-Aalen estimator can be estimated by [14].

$$\hat{\sigma}(t) = \sum \frac{(r_j - d_j)d_j}{(r_j - 1)r_j} \tag{2.8}$$

2.6.1 The relationship between Kaplan-Meier estimator and the Nelson-Aalen estimator:

The survival distirution function $S(t)$ is absolute continuous with density function [7]

$$f(t) = -S'(t).$$

Hazard rate function

$$\lambda(t) = \frac{f(t)}{S(t)}.$$

The cumulative hazard rate function

$$\Lambda(t) = \int_0^t \lambda(u)du.$$

$$\Lambda(t) = \int_0^t \frac{dS(u)}{S(u^-)}du$$

where, $S(u^-)$ denotes the left limit of the survival distibution function at t. For an absolute contiuous distibution .

$$\Lambda(t) = -\ln S(t) = \int_0^t \lambda(u)du$$

So, the survival function takes the form

$$S(t) = e^{(-\Lambda(t))}$$

The Nelson-Aalen estimator for the cumulative hazard rate function is given by

$$\hat{\Lambda} = \sum_{tj \leq t} \frac{d_j}{r_j}$$

The Kaplan Meier estimator takes the form

$$\hat{S}(t) = \prod_{t_j \leq t} (1 - \hat{\Lambda}_j)]$$

2.7 Quality Adjusted Lifetime and its mean

Gelber *et al.*(1989) presented that the patients may experience several health states which different in their qulaity of life.

The perfect health is weighted "1" and a state of being dead is weighted "0" [12].

Then the total quality adjusted life years is the area under the quality of life over time.

U is the utility which is the measure in Quality Adjusted Life years(QALY) is given by.

$$U = \sum_{i=1}^{k} q_i s_i$$

where, $q_1, ..., q_k$ is the utility assigned to each of k-health states, and $s_1, ..., s_k$ is the time (years) spent in each state [12].

A more general form of quality adjusted life years is given by:

$$U_i(t) = q_i f(t).$$

where, $U_i(t)$ is the utility of surviving t years in health state i and $f(t)$ is a increasing monotonically function of t [23].

Gelber*et al.*(1989) defined the quality adjusted lifetime by considering three health states, which are TWiST, TX and TOX: TWiST is equal to the amount of time spent without symptoms and toxicity [10]. For the uncensored case, the TWiST is calculated for each patient by subtracting from overall time to symptomatic disease relapse any previous time that the patient experiences treatment toxicity [10].

Let TR_i the time from the start of treatment to symptomatic disease relapse for each patient [10].

TX_i is defined as the amount of toxicity which the patient would experience from the treatment, in the absence of censoring by death or relapse [10]. Note that TX_i need not be accured during censecutive time periods; e.g., a patient might have toxicity in months 1, 2 and 4, but not 3. TX_i may or may not be statistically independent of TR_i [10].

Let TOX_i is the amount of toxicity observed prior to relapse for the patient [10]. They weighted the time spent in each class according to subjective judgement as to the quality of life in each state.

By definition

$$TOX_i \leqslant TR_i$$

The definitions of TR_i and TOX_i can be adjusted to account for conditions and events, with special relevance to particular clinical situations.

Let FU_i the follow-up time for each patient [10].

Using the notation for censored survival data, let OTR_i be the observed value of TR_i and Let $OTOX_i$ be the observed value of TOX_i, with censoring indicators Δ_i [10].

$$OTR_i = min(TR_i, FU_i),$$

$$OTOX_i = min(TOX_i, FU_i),$$

Then, the observed $TWiST_i$ is given by

$$OTWiST_i = OTR_i - OTOX_i. \tag{2.9}$$

Gelber *et al.*(1989) defined also accumulated TWiST, TWiST(L), in order to reduce the amount of censoring, then TWiST(L) is the amount of TWiST observed within L time units from the start of treatment [10]

$$OTR_i = min(TR_i, FU_i, L),$$

$$OTOX_i(L) = min(TOX_i, FU_i, L),$$

The observed $TWiST_i(L)$ for patient i is given by

$$OTWiST_i(L) = OTR_i - OTOX_i(L) \tag{2.10}$$

Note that$TWiST(L)$ is never censored if $L \leqslant FU_i$ [10].

We will use these variables in our simulation study.

$Q-TWiST$ defined as a series of health states use a partitioned survival analysis to compute the average time in each state, and then weighted each state according to its quality of life to find out Quality Adjusted Lifetime [33]. Cox(1972) mentioned that we should have a new measure from evaluation of treatment for chronic diseases, expanding overall survival time that combines both the quality and the quantity of the patients life, this measure is called quality adjusted lifetime [33].
The importance of studying quality adjusted lifetime is its ability to take into conideration both quantity and the quality for the life of the patient [33]. Quality adjusted lifetime places states of health on a utility scale with reference points ranging from 0 (death) to 1(perfect life). [33]
Quality Adjusted Lifetime "QAL" is given by:

$$U = \sum Q_i T_i$$

Where, $Q_1, ..., Q_k$ are the utility coefficient assigned to each of "k" health states, and $T_1, ..., T_k$ are the time spent in each state.
Let the *i-th* patient's health history for n patients under a study be described by a discrete state continuous time $\{v_i(t), t \geq 0\}$. Where, $v_i(t)$ maps to the state space $S = \{0, 1, ..., k\}$; at any time t, the health status $v_i(t)$ may take on any of $k+1$ values corresponding to different states of health [33].

Let T_i denote the time it takes the *i-th* patient to move into the state "0", $T_i = \inf\{t : v(t) = 0\}$; T_i will be considered as the over all survival time.
Let's define v_i as the *i-th* patients health history up to time t *i.e.*

$$v_i(t) = \{v_i(u : u \leq t)\}.$$

Let $Q(.)$ be the quality of life function mapping the state space v to the interval $[0, 1]$.

The *i-th* patient's quality adjusted lifetime is [33]

$$U_i = \int_0^\infty Q\{t, v_i(t)\}dt$$

The *i-th* patient also has a potential to be censored denoted by $C_i > 0$. Then the survival distribution function for C is given by

$$K(u) = Pr(C > u),$$

To reduce the censoring, we need to consider a limit denoted by L. Then, L is an artificial endpoint.

2.8 Estimation the Survival Function of Quality Adjusted Lifetime

In this section, we will review the Simple Weighted Estimator, Zhao-Tsiatis estimator and Wang estimator.

Let $U_i = (U_1, U_2, U_3 ..., U_n)$ be a random continuous failure times variables with survival function $S(.)$ [1]. The truncated failure times given by $T_i = \min(U_i, L)$, where L is an artifical endpoint.

Zhao-Tsiatis(1997) defined restricted quality adjusted lifetime by:

$$N(T_i) = \int_0^{T_i} Q(v_i(t))dt, \tag{2.11}$$

where, $V_i(t)$ is the health status function of *i-th* individual at time t, and $Q(.)$ is a known function maps $v_i(t)$ in the interval $[0, 1]$.

The survival function of restricted quality-adjusted lifetime (RQAL) is given by

$$S_u(a) = P(N(T_i > a)), \quad 0 \leqslant a < L.$$

Let $C_i = (C_1, C_2, C_3, ..., C_n)$ be random continuous variables denoting censoring times with hazard function $\lambda_c(.)$ and survival function $K(.)$.

In the presence of censoring. Let $\{T_i, C_i, \{N(r), r \in [0, T_i], i = 1, 2, ..., n\}$ represent *iid* copies of $\{X_i = \min(T_i, C_i, \Delta_i = I(T_i \leqslant C_i), N_i(r), r \in [0, X_i], i = 1, 2, ..., n\}$ [1]. Where, n is the sample size.

The Censored Restricted Quality Adjusted Lifetime is given by [1]

$$N(X_i) = \int_0^{X_i} Q(v_i(t))dt.$$

Almanassra *et al.*(2005) mentioned that a single (censored or uncensored) observation can be classified into one of four mulually exclusive cases, depending on the answer of two questions. These questions are "Can the value of $I(N(T) > a)$ be (unambiguously) determind?" If the answer is "yes", then, what is the first time point at which the value can be determined?

He defined the values $T(a), T^{'}(a), X(a), X^{'}(a)$, to use these data to define the Simple Weighted estimator, Zhao-Tsiatis estimator and Wang estimator.

The indicator functions for a complete observation are defined by :

$$\Delta(a) = I\{T(a) \leqslant C\}$$

$$\Delta^{'}(a) = I\{T^{'}(a) \leqslant C)\}$$

A new class of estimators given by Strawderman(2000) and Almanassra *et al.* (2005) [1]:

$$\hat{\theta}_a(s,k)= \begin{cases} \frac{1}{n}\sum_{j=1}^{n}\hat{\zeta}_{s,j}(x)I(N_j(X_j)>a) & if k=1 \\ \frac{1}{n}\sum_{j=1}^{n}\frac{\hat{\zeta}_{s,j}(x)}{\hat{\zeta}_s(x)}I(N_i(X_j)>a) & if k=2 \end{cases}$$

Where the ith index s is used to explain which method of estimation is used to estimate $K(.)$, and the index k is used to indicate whether the estimator renormalized $k=1$ or not $k=2$.

Almanassra *et al.* (2005) defined the weights as follows: [1].

$$\hat{\zeta_{s,j}}(a)=\frac{\Delta_j}{\hat{K}(X_j)}, \quad if\ s=1$$

$$\hat{\zeta_{s,j}}(a)=\frac{\Delta_j(a)}{\hat{K}(X_j(a))}, \quad if\ s=2$$

$$\hat{\zeta_{s,j}}(a)=\frac{\Delta_j(a)}{\hat{K}(\hat{X}_j(a))}, \quad if s=3$$

$$\hat{\zeta_{s,j}}(x)=\frac{\Delta_j'(a)}{\hat{K}_a'(\hat{X}_j'(a))}, \quad if\ s=4$$

Let

$$\hat{\zeta}_s(a)=\frac{1}{n}\sum_{j=1}^{n}\hat{\zeta}_{s,j}(a),$$

be the mean of estimated weights.

As long as the largest observation is not censored. Then,

$\hat{\zeta}_1(a)=\hat{\zeta}_3(a)=\hat{\zeta}_4(a)=1$ for each a.

Then,

$\hat{\theta}_a(1;1)=\hat{\theta}_a(1;2), \hat{\theta}_a(3;1)=\hat{\theta}_a(3;2), \hat{\theta}_a(4;1)=\hat{\theta}_a(4;2)$ [1].

In order to estimate the weight $\hat{\zeta}_{s,j}(a)$ and their means, first, we have to estimate Kaplan-Meier estimator $K(.)$ [1].

Kaplan-Meier estimator for censoring random variable is given by

$$\hat{K}(.) = \prod_{j:t_j \leq t} \{1 - \frac{d_j}{r_j}\} \tag{2.12}$$

2.8.1 Simple Weighted Estimator

Let $\hat{\Lambda}^{(c)}(.)$ be the Nelson-Aalen estimator for the cumualtive hazard function obtained from the data $(X_i, 1 - \Delta_i)$. Therefore, the Kaplan-Meier estimator is estimated using the Nelson-Aalen estimator by the following formula

$$\hat{K}(t) = \prod_{t \leq u}(1 - \hat{\Lambda}^{(c)}(u)). \tag{2.13}$$

Then the Simple Weighted estimator using the data (X_i, Δ_i) to get the Kaplan-Meier estimator $\hat{K}(X_i)$ is given by

$$\hat{\theta}\,(1,1) = \frac{1}{n}\sum_{i=1}^{n} \frac{\Delta_i}{\hat{K}(X_i)} I(N_i(X_i > a)) \tag{2.14}$$

The Simple Weighted estimator is a consistent estimator for estimating the true survival function.

2.8.2 Zhao-Tsiatis Estimator

Zhao and Tsiatis presented a more efficient estimator for the survival function of quality adjusted lifetime. Zhao-Tsiatis motivatation as follows [33]: With no censoring the survival function $S_u(x)$ would be estimated simply using the empirical survival function

$$\hat{S}_u = \frac{1}{n}\sum I(N(X_i) > a).$$

With the presence of censoring, note that, for fixed a if $N(X_i)$ exceeds a, then this would be known at any time s such that $s \geq s_i^*(a)$ where [32],

$$S_i^*(a) = \inf[s : \int_0^s Q\{v_i(t)dt \geq a\}]$$

where $N(X_i)$ will be known to be less than a only if [32].

$$\int_0^{T_i^*} Q\{v_i(t)\}dt < a$$

Therefore, with censoring, it would observe the value $I(N(X_i) > a)$ if and only if $C_i > T_i(a)$

where

$$(X_i = \min\{T_i^*, S_i^*(a)\}).$$

Consequently, the indicator for a complete observation with respect to a can be defined as $\Delta_i(a) = I\{C_i > T_i(a)\}$.

That means that the typical individual whose health status would be observed until $T_i(x)$ would probability $K\{T_i(a)\}$ of not being censored where

$$K(u) = Pr(C > u). \tag{2.15}$$

Since the censoring is independent of the health status, an individual with a health history uncensored and observed up to $T_i(a)$ is on average representative of $\frac{1}{K\{T_i(a)\}}$ similar individuals some of which may be censored [32].

$$E[\frac{\Delta_i}{K(T_i)}\{I(N(X_i) > a) - S_u(a)\}]$$
$$E(E[\frac{\Delta_i}{K(T_i)}\{I(N(X_i) > a) - S_u(a)\}|T_i^*, v_i(.)])$$
$$= E\{I(N(X_i) > a) - S_u(a)\} = 0$$

Since, this estimator solved the estimation equation.

Then

$$\hat{S}_u = \frac{1}{n}\sum_{i=1}^{n}\frac{\Delta_i}{\hat{K}(T_i)}I(N(X_i) > a)$$

Since $K(t)$ is unknown, it is estimated using Kaplan-Meier estimator for the censoring random variable C, with the data $\{X_i'(a) = \min(T_i'(a), C_i), \Delta_i(a), i = 1, ..., n\}$.

Let $\hat{\Lambda}^{(c,a)}$ be the Nelson-Aalen estimator for the cumulative hazard function obtained from the data $(X_i(a), 1-\Delta_i(a))$, to estimate $K(.)$ using Kaplan-Meier estimator, using the Nelson-Aalen estimator given by

$$\hat{K}_a(t) = \prod_{u \leqslant t}(1 - d\Lambda^{\widehat{(c,a)}}(u))$$

Let a be the fixed point, the Zhao and Tsiatis estimator for the survival function of Restricted Quality Adjusted Lifetime (RQAL) using the data $(X_i(a), \Delta_i(a)$ to find $\hat{K}_a(X_i(a))$ is given by [1].

$$\hat{\theta}\,(3,1) = \frac{1}{n}\sum_{i=1}^{n}\frac{\Delta_i}{\hat{K}_a(X_i(a))}I(N_i(X_i > a)). \tag{2.16}$$

2.8.3 Wang Estimator

Wang estimator is an modified varision of Zhao-Tsiatis estimator.

If $I(N(X) > a) = 0$ and $N(X) + (L - X) < a$, to find the first time point at which this value can be determind, consider [2]

$$w(a) = \inf\{w : N(w) + L - w \leqslant a\}$$

$w(a)$ is the first time point t when $N(t) + (L - t) \leqslant a$. Since $N(t) + (L - t)$ is a decreasing function of t,$N(t) + (L - t) \leqslant a$ for all $t \geqslant w(a)$, define

$T(a) = T$, and $T'(a) = w(a)$

Let $X(a) = T(a) \wedge C$ and $X^{'}(a) = T^{'}(a) \wedge C$.

That data had been used to estimate the Wang estimator.

First, we estimate $K(.)$ using the data $(X_{a}^{'}(a), \Delta_{i}^{'}(a)$.

Let $\hat{\Lambda}^{'(c,a)}(.)$ be the Nelson-Aalen estimator for the cumulative hazard function obtianed from the data $(X_{i}^{'}(a), 1 - \Delta_{i}^{'}(a), i = 1, ..., n$, we can estimate $K(.)$ using the Kaplan-Meier estimator, based on the Nelson-Aalen estimator defined by

$$\hat{K}_{a}^{'}(t) = \prod_{u \leqslant t}(1 - d\hat{\Lambda}^{'(c,a)}(u)).$$

We get

$$\hat{\theta}\,(4,1) = \frac{1}{n}\sum_{i=1}^{n}\frac{\Delta_{i}^{'}(a)}{\hat{K}_{a}^{'}(X_{i}^{'}(a))}I(N_{i}(X_{i} > a)) \tag{2.17}$$

This is the Wang estimator for the survival function of Restricted Quality Adjusted Lifetime (RQAL) [2].

2.9 The jump points of the Simple Weighted estimator, Zhao-Tsiatis estimator, and Wang estimator

Almanassra *et al.* (2005) presented the jump points of the Simple Weighted estimator, Zhao-Tsiatis estimator and Wang estimator.

2.9.1 Jump points of the Simple weighted estimator

This estimator has a jump point at a point a if and only if there exist index i such that $a = N(X_i)$ and $\Delta_i = 1$, $i = 1, 2, ..., n$.

The estimator jumps only at points of deaths.

2.9.2 Jump Points of the Zhoa-Tsiatis estimator

The jump points of this estimator are of three kinds:

1. a is a jump point if there exists an index i such that $a = N(X_i)$, and $\Delta_i = 1$, $i = 1, 2, .., n$
2. a is a jump point if there exists an index i such that $a = N(X_i)$, and $\Delta_i = 0$, $i = 1, 2, \ldots, n$.
3. a is a jump point if there exists an index i such that $\Delta_i = 0$, $i = 1, \ldots, n$, $N(X_i) < a$.

   and there exists another index$j$ such that

   $$a = \int_0^{X_i} Q_j(t)dt,$$

   and $X_j > X_i$.

2.9.3 Jump Points of the Wang estimator

This estimator is modified version of Zhao-Tsiatis estimator, the jump points of this estimator are of four types [2]:

1. a is a jump point if there exist an index i such that
   $a = N(X_i)$, and $\Delta_i = 1$, $i = 1, 2, .., n$.
2. a may be a jump point if there exists an index i such that;
   $a = N(X_i)$ or
   $a = N(X_i) + L - X_i$,

and $\Delta_i = 0,\ i = 1, 2, .., n$.

3. a is a jump point if there exists an index i such that

   $\Delta_i = 0,\ i = 1, 2, ..., n$.

$$N(X_i) < a < N(X_i) + L - X_i,$$

and there exist another index j such that

$$a = \int_0^{X_i} Q_j(t)dt$$

and $X_j > X_i$

4. a is a jump point, if there exists an index i such that

   $\Delta_i = 0,\ i = 1, 2, ..., n$,

   $N(X_i) < a < N(X_i) + L - X_i$ and there exist another index j such that

$$a = \int_0^{X_i} Q_j(t)dt + (L - X_i),$$

and $X_j > X_i$ and $N(X_j) + L - X_j < a$.

2.10 The Mean Value Theorem

The mean value theorem is one of the most important theorem in calculas and it has been used to prove many theorems.

Theorem 2.10.1 *Mean Value Theorem*

Let $f : [a, b] \longrightarrow R$ be a continuous function on the closed interval $[a, b]$, and differentiable on the open interval (a, b), where $a < b$. Then, there exists some c in (a, b) such that [26]

$$f'(c) = \frac{f(b) - f(a)}{b - a}.$$

The Mean Value Theorem is one of the milestones in calculus. The geometric nature of the Mean Value Theorem makes it easy to believe and understand.

The defintion of average value of any continuous (or integrable) function, whether positive, negative, or both is given by [26]:

$$Average = \frac{1}{b - a} \int_a^b f(x)dx.$$

Geometrically, this means that the area under the graph of a continuous function on a closed and bounded interval is the same area of a rectangle that base is the length of the interval and the height is the value of the intergrand at some points in the interval.

The idea of the average of n numbers is their sum divided by n. A continuous function f on the interval $[a, b]$ have infintely many values, but we can sample them in an orderly way.

One divides the interval $[a, b]$ into n subintervals of equal width $\Delta x = (b - a)/n$ and calculate the value of f at the point c_k in each subinterval.

The average of the n sampled values is [26]

$$\begin{aligned}
\frac{f(c_1)+f(c_2)+\ldots+f(c_n)}{n} &= \frac{1}{n}\sum_{k=1}^{n} f(c_k) \\
&= \frac{\Delta x}{b-a}\sum_{k=1}^{n} f(c_k) \\
\Delta x &= \frac{b-a}{n} \\
\frac{1}{n} &= \frac{\Delta x}{b-a} \\
&= \frac{1}{b-a}\sum_{k=1}^{n} f(c_k)\Delta x \quad \text{(Constant Multiple Rule)}
\end{aligned}$$

So the average is obtained by dividing a Riemann sum for f on $[a,b]$ by $(b-a)$. When the size of the sample increases and let the partition of subintervals approach zero, the average of the function f approaches $(1-(a-b))\int_a^b f(x)dx$. Both points of view lead to the following definition:

Definition 2.10.1 *The average value on $[a,b]$*

Let f be integrable on $[a,b]$, then the average value of the function f on the interval $[a,b]$, also called its mean, is given by

$$average(f) = \frac{1}{b-a}\int_a^b f(x)dx.$$

2.10.1 The Mean Value theorem for Difinite Integrals

The mean value theorem for difinite integrals ensures that this average value of the function f is always taken on at least once by the function f in the interval $[a,b]$ [26].

Geometrically, the Mean Value theorem for difinite integrals says that there is a number c in the interval $[a,b]$ such that, the rectangle in which height equals to the average value $f(c)$ of the function and base width $(b-a)$ has exactly the same area as the region under the graph of the function f from the point a to the point b [26].

Theorem 2.10.2 *The Mean Value Theorem for Difinite Integrals [26]*

If the function f is continuous on the interval $[a, b]$, then at some point c in the interval $[a, b]$,

$$f(c) = \frac{1}{b-a}\int_a^b f(x)dx.$$

Note that, the continuity of the function f is important here. It is possible that a discontinuous function f never equals its average value.

2.11 MSE, Bias and Consistancy

One of the main goals of this thesis is to figure out how to chose the right stasitic (any function of data is called statistic) to estimate the true survival function θ.

Definition 2.11.1 *Unbiased estimator [29]*

Let $\hat{\theta}$ be a point estimator for a true survival function θ. Then the estimator $\hat{\theta}$ is said to be an unbiased estimator if

$$E(\hat{\theta}) = \theta.$$

If

$$E(\hat{\theta}) \neq \theta$$

$\hat{\theta}$ is said to be biased estimator [29].

Definition 2.11.2 *(Bias of a point estimator)*

The bias of a point estimator$B(\hat{\theta})$ is defined by

$$B(\hat{\theta}) = E(\hat{\theta}) - \theta.$$

Definition 2.11.3 *The Mean Squar Error [29]*

The mean square error (MSE) of a point estimator $\hat{\theta}$ is given by

$$MSE = E[(\hat{\theta} - \theta)^2]$$

The mean square error of an estimator $\hat{\theta}$ is a function of both its variance and its bias;

$$MSE(\hat{\theta}) = var(\hat{\theta}) + [B(\hat{\theta})]^2,$$

If $\hat{\theta}$ is unbiased estimator $bias(\hat{\theta}) = 0$, then

$$MSE(\hat{\theta}) = var(\hat{\theta})$$

Therefore, mean square error of an estimator $\hat{\theta}$ is small, only if this estimator has small variance and small bias and consistency [29] .

Definition 2.11.4 *Consistent Estimator [29]*

The estimator $\hat{\theta}_n$ is said to be a consistent estimator of the true value of the survival function θ, if for any positive number ϵ

$$\lim_{n \longrightarrow \infty} P(|\hat{\theta}_n - \theta| \leqslant \epsilon) = 1.$$

or, equivalently

$$\lim_{n \longrightarrow \infty} P(|\hat{\theta}_n - \theta| > \epsilon) = 0.$$

Definition 2.11.5 *Weak Consistency [29]*

Let $\hat{\theta}_1, \hat{\theta}_2, ..., \hat{\theta}_n, ...$ be a sequence of estimators of a real valued of survival function θ.

The sequence $\{\hat{\theta}_n\}$ is called a simple (or weakly) consistent estimator of θ

if for every $\epsilon > 0$

$$\lim_{n \longrightarrow \infty} P[|\hat{\theta}_n - \theta| < \epsilon] = 1.$$

For every θ in the parameter space Ω.

Chapter 3

Estimators of survival function and Jump points

In this chapter, we will present a case of censoring, assume that a subject disappears for a while but then reports back to the study, causing a gap in the follow-up. We will consider this type of censoring in estimating the survival function of restricted quality adjusted lifetime. Then we will calculate the jump pionts of the Simple Weighted estimator, Zhao-Tiatis estimator and Wang estimator.

In this chapter we will deal with the case of interval and right censoring. We suppose that the *i-th* subject will be missed at time X_{i1} and come back later at time X_{i2}. This means that the data is missed during the interval $[X_{i1}, X_{i2}]$.

To estimate the survival function of restricted quality adjusted lifetime in this case of censoring, we may ignore the area of missing data, or we may estimate the restricted quality adjusted lifetime by use the mean value theorem to estimate the average value of quality of life. In this thesis Δ_i represents right censoring only at the time X_i.

3.1 Estimating $N(X_i)$ using Shifting Method

Through the interval$[0, X_i]$ the data is missed at the partial interval $[X_{i1}, X_{i2}]$, Where $i = 1, ..., n$, n is the sample size.

we calculate the restricted quality adjusted lifetime for the first interval by:

$$N(X_{i1}) = \int_0^{X_{i1}} Q_{i1}(t)dt.$$

We calculate the restricted quality adjusted lifetime for the second interval

$$N(X_{i2}) = \int_{X_{i2}}^{X_i} Q_{i2}(t)dt.$$

Since the function of quality of life in the missing interval is an unknown function we may shift the function of quality of life of the second interval as followes:

Let $Q_i'(t)$ is the function of quality of life after shifting the function of quality of life $Q_{i2}(t)$ by $(X_{i2} - X_{i1})$ to the left.

$$Q_i'(t) = Q_{i2}(t + (X_{i2} - X_{i1})). \tag{3.1}$$

We calculate the size of the final interval by shifting the intervals where the subject exists.

Define X_i'

$$X_i' = |[0, X_{i1}]| + |[X_{i2}, X_i]| = X_i - (X_{i2} - X_{i1}) \tag{3.2}$$

The function of quality of life is

$$Q_i(t) = \begin{cases} Q_{1i}(t) & 0 \leq t \leq X_{i1} \\ Q_{i2}'(t) & X_{i1} < t \leq X_i' \end{cases} \tag{3.3}$$

3.1.1 Jump points of the Simple weighted estimator using shifiting method

This estimator has a jump point at a point a if and only if there exist index i such that

$$a = N(X_i') = \int_0^{X_{i1}} Q_{i1}(t)dt + \int_{X_{i1}}^{X_i'} Q_{i2}'(t)dt$$

and $\Delta_i = 1,\ i = 1, 2, ..., n$.

3.1.2 Jump Points of the Zhoa-Tsiatis Estimator using shifiting method:

The jump points of this estimator are of three kinds:

1. a is a jump point if there exists an index i such that $a = N(X_i')$, and $\Delta_i = 1, i = 1, 2, .., n$

2. a is a jump point if there exists an index i such that $a = N(X_i')$, and $\Delta_i = 0,\ i = 1, 2, \dots, n$.

3. a is a jump point if there exists an index i such that $\Delta_i = 0, i = 1, \dots, n$, $N(X_i') < a$.

   and there exists another index j such that

   Let $Q_j'(t)$ is the function of quality of life after shifted the function of quality of life $Q_{j2}(t)$ by $(X_{j2} - X_{j1})$ to the left.

$$Q_{j2}'(t) = Q_{j2}(t + (X_{j2} - X_{j1})). \tag{3.4}$$

$$Q_j(t) = \begin{cases} Q_{j1}(t) & 0 < t \leq X_{j1} \\ Q_{j2}'(t) & X_{j1} < t < X_j' \end{cases}$$

Where,

$$X_j^{'} = X_{j1} + (Xj - X_{j2})$$

And $X_j^{'} > X_i^{'}$.

3.1.3 Jump Points of the Wang Estimater using shifiting method

This estimator is a modified version of Zhao-Tsiatis estimator, the jump points of this estimator are of four types [1]:
We will adjust X_i, X_j, and Q_i, Q_j similar to what we did for the Zhao-Tsiatis jump points if it is needed.

1. a is a jump point if there exist an index i such that
   $a = N(X_i^{'})$, and $\Delta_i = 1, i = 1, 2, .., n$.

2. a may be a jump point if there exists an index i such that;
   $a = N(X_i^{'})$ or
   $a = N(X_i^{'}) + L - X_i^{'}$,
   and $\Delta_i = 0, i = 1, 2, .., n$

3. a is a jump point if there exists an index i such that
   $\Delta_i = 0, i = 1, 2, ..., n$

   $$N(X_i^{'}) < a < N(X_i^{'}) + L - X_i^{'},$$

   and there exist another index j such that

   $$a = \int_0^{X_i^{'}} Q_j(t)dt$$

   and $X_j^{'} > X_i^{'}$

4. a is a jump point, if there exists an index i such that

   $\Delta_i = 0,\ i = 1, 2, ..., n.$

   $N(X_i') < a < N(X_i') + L - X_i'$ and there exist another index j such that

$$a = \int_0^{X_i'} Q_j(t)dt + L - X_i'$$

   and $X_j' > X_i'$ and $N(X_j') + L - X_j' < a$.

3.2 Estimation $N(X_i)$ using the Mean value theorem (MVT)

To caculate the average value of a function on the interval $[a, b]$, where the function is continuous by use Mean Value Theorem for Integrals.

$$Average(Q(x)) = \frac{1}{b-a}\int_a^b Q(x)dx.$$

We will use this theorem to estimate the average value of $Q_i(t)$ for data which missed at time X_{i1} and comes back at time X_{i2}.

1. First, we find the average value of the function of quality of life of the the first interval $[0, X_{i1}]$.

$$Average(Q_1) = \frac{1}{(X_{i1} - 0)}\int_0^{X_{i1}} Q_{i1}(t)dt.$$

2. Find the average value for function of qulality of life to third interval $[X_{i2}, X_i]$.

$$Average(Q_3) = \frac{1}{(X_i - X_{i2})}\int_{X_{i2}}^{X_i} Q_{i3}(t)dt.$$

3. **Find the average for the function of quality of life for the interval that the data is missed by using the Mean Value Theorem.**

$$\begin{aligned} Q_{i2}(t) &= Average(Q_2) = \frac{(X_{i1}-0)Average(Q_{1i}) + (X_i - X_{i2})Average(Q_{i3})}{\|[0, X_{i1}]\| + \|[X_{i2}, X_i]\|} \\ &= \frac{(X_{i1}-0)Average(Q_{1i}) + (X_i - X_{i2})Average(Q_{i3})}{X_i - (X_{i2} - X_{i1})}. \end{aligned}$$

$$Q_i(t) = \begin{cases} Q_{i1}(t) & 0 \le t \le X_{i1} \\ Q_{i2}(t) & X_{i1} < t < X_{i2} \\ Q_{i3}(t) & X_{i2} \le t \le X_i \end{cases} \qquad (3.5)$$

Then $N(X_i)$ **is given by**

$$N(X_i) = \int_0^{X_{i1}} Q_{i1}(t)dt + \int_{X_i1}^{X_{i2}} Q_{i2}(t)dt + \int_{X_{i2}}^{X_i} Q_{i3}(t). \qquad (3.6)$$

The jump points will be obtained as follows:

3.2.1 Jump points of the Simple weighted estimator using MVT

This estimator has a jump point at a point a **if and only if there exists index** i **such that**

$$a = N(X_i) = \int_0^{X_i} Q_i(t)dt$$

where,

$$Q_i(t) = \begin{cases} Q_{i1}(t) & 0 \leq t \leq X_{i1} \\ Q_{i2}(t) & X_{i1} < t < X_{i2} \\ Q_{i3}(t) & X_{i2} \leq t \leq X_i \end{cases} \tag{3.7}$$

and $\Delta_i = 1,\ i = 1, 2, ..., n$.

3.2.2 Jump Points of the Zhoa-Tsiatis Estimator using MVT:

The jump points of this estimator are of three kinds:

1. a is a jump point if there exists an index i such that $a = N(X_i)$, and $\Delta_i = 1,\ i = 1, 2, .., n$.

2. a is a jump point if there exists an index i such that $a = N(X_i)$, and $\Delta_i = 0,\ i = 1, 2, \ldots, n$.

3. a is a jump point if there exists an index i such that $\Delta_i = 0, i = 1, \ldots, n$, $N(X_i) < a$.

   and there exists another index j such that

$$a = \int_0^{X_i} Q_j(t)dt,$$

   For $X_j > X_i$.

   Where, the quality of life for subject j is given by

$$Q_j(t) = \begin{cases} Q_{j1}(t) & 0 \le t \le X_{j1} \\ Q_{j2}(t) & X_{j1} < t < X_{j2} \\ Q_{j3}(t) & X_{j1} \le t < X_j \end{cases} \tag{3.8}$$

Then

$$a = \int_0^{X_i} Q_j(t)dt.$$

3.2.3 Jump Points of the Wang Estimator using MVT

The jump points of this estimator are of four types. In each type, we adjusted X_i, Q_i, $N(X_i)$, X_j, Q_j, and a as we did in finding the jump points of the Zhao-Tsiatis estimator. Therefore, the jumps of the Wang estimator will be find in a similar to section 2.9.3.

3.2.4 Example

Example 3.2.1

This example illustrates the difference between using shifting method and using MVT method

Consider $L = 80$, for observation X_i, where $X_i = 60$ and the function of quality of life is given by

$$Q_i(t) = \begin{cases} .02t & 0 \le t \le 5 \\ .01t & 20 \le t \le 60 \end{cases}$$

$$N(X_{i1}) = \int_0^5 .02tdt = .01(25) = .25.$$

$$N(X_{i2}) = \int_{20}^{60} (.01)tdt = \frac{.01}{2}(3600 - 400) = 16.$$

$$\begin{aligned} N(X_i) &= N(X_{i1}) + N(X_{i2}) \\ &= 0.25 + 16 \\ &= 16.25 \end{aligned}$$

Using the shifting method

$$\begin{aligned} Q'_{i2}(t) &= Q_{i2}(t + (X_i - X_{i2})) \\ &= .01(t + (20 - 5)) \\ &= .01t + 15(.01) \\ &= .01t + .15 \end{aligned}$$

and, $X'_i = 5 + 40 = 45$

$$\begin{aligned} N(X'_i) &= \int_0^5 0.02tdt + \int_5^{45} (0.01t + .0.15)dt \\ &= .25 + 16 \\ &= 16.25 \end{aligned}$$

Using Mean Value Theorem:

$$\begin{aligned} Average(Q_1) &= \frac{0.25}{5} = .05 \\ Average(Q_3) &= \frac{16}{60 - 20} = 0.4 \\ Average(Q_2) &= \frac{0.05(5) + 40(0.4)}{40 + 5} = 0.36 \end{aligned}$$

$$
\begin{aligned}
N(X_{i2}) &= \int_{5}^{20} 0.36dt = (0.36)(20-5) = 5.4 \\
N(X_i) &= 0.25 + 5.4 + 16 \\
&= 21.65
\end{aligned}
$$

3.2.5 Comments

Note that the value of $N(X_i)$ =16.25 using shifting method, but equals 21.65 using MVT method since we estimate the Average value of Q in the the interval of missing data.

In the following example, we will find the jump points for the Simple Wieghted estimator, Zhao-Tsiatis estimator and Wang estimator and the values of these estimators at every point by using the shifting method :

Example 3.2.2

Consider the following set of data given in table(3.1). Find the jump points of Simple Weighted estimator, Zhao-Tsiatis estimator, and Wang estimator. Then find the value of these estimator at every point by use the shifting method.

Tab. 3.1: Data for example(3.2.2)

i	X_i	Δ_i	Q(.)
1	[0,10]	0	1
2	[0,5][20,60]	0	0.3, 0.25
3	[0,60]	1	0.5
4	[0,80]	1	1

Note that for the second subject

$$Q_2(t) = \begin{cases} 0.3 & 0 \leqslant t \leqslant 5 \\ 0.25 & 5 < t \leqslant 40 \end{cases}$$

We calculate the values of $N(X_i)$.

$$\begin{aligned} N(X_1) &= \int_0^{10} dt = 10. \\ N(X_2) &= \int_0^{5} 0.3dt + \int_5^{40} 0.25dt \\ &= 1.5 + 10 \\ &= 11.5 \\ N(X_3) &= \int_0^{60} 0.5dt \\ &= 0.5 * 60 \\ &= 30. \\ N(X_4) &= \int_0^{80} 1dt \\ &= 80. \end{aligned}$$

The table of the data is become

Tab. 3.2: Data for example(3.2.2)

i	X_i	Δ_i	Q(.)	$N(X_i)$
1	10	0	1	10
2	45	0	0.3, 0.25	11.5
3	60	1	0.5	30
4	80	1	1	80

1. The jump points of the Simple Weighted estimator.

The Simple Weighted estimator has jump points at 30, 80.

2. The jump points of Zhao-Tisiatis estimator.

(a) When, $a = N(X_i)$, $\Delta_i = 1$,

the jump points are 30, 80

(b) $a = N(X_i)$, $\Delta_i = 0$, the jump points are 10, 11.5

(c) To find the jump points of third kind where,

$\Delta_i = 0$, and $N(X_i) < a$, and there exist another index j, where

$$a = \int_0^{X_i} Q_j(t)dt,$$

and $X_j > X_i$

So the first point which has $\Delta_i = 0$ is X_1, and X_2, X_3 and X_4 is greater than X_1. For X_2, we have

$$\begin{aligned} a &= \int_0^5 0.3dt + \int_5^{10} 0.25dt \\ &= 0.3 * 5 + 5 * 0.25 \\ &= 2.75 \end{aligned}$$

Since $2.75 < 10$, a is not a jump point.

ForX_3,

$$\begin{aligned} a &= \int_0^{10} 0.5dt \\ &= (0.5)(10) \\ &= 5 \end{aligned}$$

Since $5 < 10$, a is not jump point.

For X_4, $a = (10)(1) = 10$, and since 10 is not greater than 10, then a is not a jump point.

The second point which has $\Delta_i = 0$ is X_2. Now, X_3 and X_4 are greater than X_2.

For X_3,

$$
\begin{aligned}
a &= \int_0^{45} 0.5dt \\
&= 45(0.5) \\
&= 22.5
\end{aligned}
$$

Since, $22.5 > 11.5$,a is a jump point.

For X_4,

$a = 45(1) = 45$, and since $45 > 11.5$, a is a jump point

Therfore, the jump points of the Zhao-Tsiatis estimator are 10, 11.5, 22.5, 30, 45, 80.

3. The jump points for the Wang estimator

(a) $a = N(X_i)$ and $\Delta_i = 1$,

the jump poins are 30, 80.

(b) where $a = N(X_i)$, and

$\Delta_i = 0$, the jump points are 10, 11.5

When,

$$a = N(X_i) + L - X_i.$$

$\Delta_i = 0$, the jump points are 10+(80-10)=80,

and, 11.5+(80-45)=46.5

(c) $\Delta_i = 0$, and

$$N(X_i) < N(X_i) + L - X_i,$$

and there exist index j where

$$a = \int_0^{X_i} Q_j(v(t))dt.$$

Where, $X_j > X_i$.

The first point which $\Delta_i = 0$ is X_1, we do not have any jump point in this case.

The second point, which has $\Delta_i = 0$, isX_2,

both X_3 and X_4 are greater than X_2, we will check which of them lead to a jump point.

For X_3, we have $a = 45(.5) = 22.5$,

Since, $11.5 < 22.5 < 11.5 + 80 - 45$

$11.5 < 22.5 < 46.5$, then **22.5** is ajump point.

$a = 45(1) = 45$, since $11.5 < 45 < 46.5$.

Then, a is a jump point

(d) To find the jump points of the fourth kind, we have to see if there exists another index j, such that

$$a = \int_0^{X_i} Q_j((t))dt + L - X_i.$$

$X_j > X_i$, and $N(X_j) + L - X_j < a$.

The first point, which has $\Delta_i = 0$ is X_1.

Now, X_2, X_3, and X_4 are all greater than X_1, we have to check which of them lead to a jump point.

$$\begin{aligned} a &= 2.75 + 80 - 10 \\ &= 72.75 \end{aligned}$$

Since, $72.75 > 10$ **10+(80-10)=80** and since, $10 < 72.75 < 80$

$$11.5 + (80 - 45) = 46.5$$

Since, $46.5 < 72.75$, then **72.75** is a jump point.

For X_3, we have

$$\begin{aligned} a &= 10(.5) + 80 - 10 \\ &= 5 + 80 - 10 \\ &= 75 \end{aligned}$$

Since, $10 < 75 < 10 + 80 - 10$, and $10 < 75 < 80$

30+(80-60)=50, since $50 < 75$ Then, **75** is a jump point.

For X_4 we have, **a=10(1)+80-10=80**, and since **80** is not greater than **80**. Then a is not a jump point.

The second point which has $\Delta_i = 0$ is X_2,

Both X_3 and X_4 are greater than X_2, we will check which of them lead to a jump point.

$$\begin{aligned} a &= 45(0.5) + 80 - 45 \\ &= 57.5 \end{aligned}$$

Since, $11.5 < 57.5$, and $57.5 > 11.5 + 80 - 45$

$57.5 > 11.5$.

Since $57.5 > 46.5$, then a is not a jump point.

For X_4, we have

$a = 45(1) + 80 - 45 = 80$, and since 80 is not greater than 80, a is not a jump point.

Therefore, the jump points of the Wang estimator are

10, 11.5, 22.5, 30, 45, 72.75, 75, 80.

Here, we will find the survival function using Simple Weighted estimator, the Zhao-Tsiatis estimator and Wang estimator at every jump point we calcuated.

For $a = 10$

1. To calculate the Simple Weighted estimator

$$\hat{\theta}_4(1;1) = \frac{1}{4}\sum_{i=1}^{4} \frac{\Delta_i}{K(\hat{X}_i)} I(N(X_i >) > 10)$$

Both $I(N(X_i >) > 10)$ and Δ_i are equal to the value 1 for $i = 2, 3, 4$

Therefore, we need the value of the function $\hat{K}(.)$ at the point X_3, X_4

$$\begin{aligned} \hat{K}(X_3) &= \hat{K}(X_4) \\ &= (1 - \frac{1}{4}) * (1 - \frac{1}{3}) \\ &= \frac{1}{2} \end{aligned}$$

Then,

$$\hat{\theta}_4(1;1) = \frac{1}{4}(0 + 0 + \frac{1}{\frac{1}{2}} + \frac{1}{\frac{1}{2}}) = 1$$

2. To calculate the Zhao-Tsiatis estimator

$$\hat{\theta}_{10}(3;1) = \frac{1}{4}\sum_{i=1}^{4} \frac{\Delta_i(a)}{\hat{K_{10}}(X_i(10))} I(N(X_i) > 10)$$

We have to find the values of $X_i(10)$.

Since, $N(X_i) > 10$, for X_2, X_3, X_4, we have

$X_i(10) = X_i$ for $i = 1, 2, 3, 4$

$I(N(X_2) > 10) = 1$

$$\begin{aligned} X_2(10) &= inf\{s : N(s) = s * .25 = 10\} \\ \frac{1}{4}s &= 10 \\ s &= 10 * 4 \\ X_2(10) &= 40 \\ X_3(10) &= inf\{s : N(s) = s * \frac{1}{2} = 10\} \\ X_3(10) &= 20 \\ X_4(10) &= inf\{s : N(s) = s * (1) = 10\} \\ X_4(10) &= 10 \end{aligned}$$

The values of $I(N(X_i) > 10)$ and $\Delta_i(10)$ are equal to 1 for $i = 2, 3, 4$.

Therefore, we need to calculate the value of the function $\hat{K}_{10}(.)$ at the points $X_2(10)$, $X_3(10)$, $X_4(10)$

$\hat{K}_{10}(X_2(10)) = \hat{K}_{10}(X_3(10)) = \hat{K}_{10}(X_4(10)) = 1 - \frac{1}{4}$

then,

$$\begin{aligned} \hat{\theta}_{10}(3;1) &= \frac{1}{4}(0 + \frac{3 * 4}{3}) \\ &= 1 \end{aligned}$$

3. **To calculate the Wang estimator**

$$\hat{\theta}_{10}(4;1) = \frac{1}{4}\sum_{i=1}^{4} \frac{\Delta_i'(10)}{\hat{K'}_{10}(X_i'(10))} I(N(X_i) > 10)$$

First, we have to find the values of $X_i'(10)$

We dont have $N((X_i) < 10)$ **then,**

$\hat{K}_{10}(X_i(10)) = \hat{K}_{10}'(X_i(10)) = \frac{3}{4}$

$$\begin{aligned}\hat{\theta}_{10}(4;1) &= \frac{1}{4}(0 + \frac{1}{\frac{3}{4}} + \frac{1}{\frac{3}{4}} + \frac{1}{\frac{3}{4}}) \\ &= \frac{1}{4}(0 + \frac{3*4}{3}) \\ &= 1\end{aligned}$$

We do the same calculations for each jump point, the results in the table(3,3)

Tab. 3.3: The values of the Simple Weighted estimator, the Zhao-Tsiatis estimator, and Wang estimator using shifting method.

a	SWE	Z-T	Wang
10^-	1	1	1
10^+	1	1	1
11.5^-	1	1	1
11.5^+	1	$\frac{2}{3}$	$\frac{2}{3}$
22.5^-	1	$\frac{2}{3}$	$\frac{2}{3}$
22.5^+	1	1	1
30^-	1	1	1
30^+	$\frac{1}{2}$	$\frac{1}{3}$	$\frac{1}{3}$
45^-	$\frac{1}{2}$	$\frac{1}{3}$	$\frac{1}{3}$
45^+	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{2}$
72.75^-	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{2}$
72.75^+	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{3}{8}$
75^-	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{3}{8}$
75^+	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{3}{8}$
80^-	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{3}{8}$
80^+	0	0	0

3.2.6 Comments:

As you see the simple wighted estimator is monotonic, but the Zhao-Tiatis estimator and Wang estimator are not monotonic.

Example 3.2.3

Use the data from the the example (3.2.2) to find the jump points by using the mean value theorem for the second subject, to check if the jump point are the same or not.

We have to calculate $N(X_2)$ by using mean value thorem.

$$\begin{aligned}
Q_{2,1ave} &= \frac{1}{5-0}\int_0^5 0.3dt \\
&= \frac{1.5}{5} \\
&= 0.3 \\
Q_{2,3ave} &= \frac{1}{(60-20)}\int_{20}^{60} 0.25dt \\
&= 0.25 \\
Q_{2,2ave} &= \frac{5(0.3)+40(0.25)}{40+5} = 0.26.
\end{aligned}$$

Then,

$$Q_2(t) = \begin{cases} 0.3 & 0 \leqslant t \leqslant 5 \\ 0.26 & 5 < t < 20 \\ 0.25 & 20 < t \leqslant 40 \end{cases}$$

$$\begin{aligned}
N(X_2) &= \int_0^5 0.3dt + \int_5^{20} 0.26dt + \int_{20}^{60} 0.25dt \\
&= 1.5 + 3.9 + 10 \\
&= 15.4
\end{aligned}$$

We will find the jump points for the data of the table (3.4).

Tab. 3.4: Data for example

i	X_i	Δ_i	Q(.)	$N(X_i)$
1	10	0	1	10
2	60	0	0.3, 0.26,0.25	15.4
3	60	1	0.5	30
4	80	1	1	80

1. **The Jump Points for Simple Weighted estimator:**

This estimator has jump points at 30, 80, where $\Delta_i = 1$.

2. The jump points for Zhao-Tsiatis estimator:

   (a) When $a = N(X_i)$, $\Delta_i = 1$,

   the jump points are 30, 80 .

   (b) When $a = N(X_i)$, $\Delta_i = 0$,

   the jump point is 10, 15.4 .

   (c) We may find the jump points of this kind, where $\Delta_i = 0$, and $N(X_i) < a$, and there exist another index j, where

$$a = \int_0^{X_i} Q_j(t)dt.$$

and $X_j > X_i$.

So, the first point which has $\Delta_i = 0$ is X_1,

X_2, X_3 and X_4 is greater than X_1

$$\begin{aligned} a &= \int_0^5 .3dt + + \int_5^{10} .26 \\ .3*5+.26*5 &= 1.5+1.3 \\ &= 2.8. \end{aligned}$$

Then, $a = 2.8$, since $2.8 < 10$, then a is not a jump point.

For X_3,

$a = 10(.5) = 5$, $5 < 10$, then a is not a jump point.

For X_4,

$a = 1(10) = 10$, and since 10 is not greater than 10, a is not a jump point.

The second point, which has $\Delta_i = 0$ is X_2

Only X_4 is greater than X_2.

$a = 60(1) = 60$, and $60 > 15.4$, then a is a jump point.

Therefore, the jump points of Zhao-Tsitis estimator are 10, 15.4, 30, 60 and 80.

3. The jump point for the Wang estimator

(a) $a = N(X_i)$, and $\Delta_i = 1$, the jump points are 30, 80 .

(b) When $a = N(X_i)$, and $\Delta_i = 0$, the jump point is 10, 15.4.
When $a = N(X_i) + L - X_i$, $\Delta_i = 0$, the jump points are

$$\begin{aligned} 10 + (80 - 10) &= 80 \\ 15.4 + (80 - 60) &= 35.4 \end{aligned}$$

(c) $\Delta_i = 0$, and

$$N(X_i) < a < N(X_i) + L - X_i,$$

and there exist index j such that

$$a = \int_0^{X_i} Q_j(v(t))dt.$$

Where, $X_j > X_i$
So, the first point which has $\Delta_i = 0$ is X_1,
we do not have any jump points in this case.
The second point which $\Delta_i = 0$ is X_2,

only X_4 is greater than X_2, we will check if it leads to a jump point.

For X_4, we have

$a = 60(1) = 60$,

$15.4 < 60 < 15.4 + 80 - 60$,

$15.4 < 60 < 35.4$, then 60 is a jump point.

(d) To find the jump points of the fourth kind, we have to see if there exists another index j, where

$$a = \int_0^{X_i} Q_j(t)dt + L - X_i.$$

$X_j > X_i$, and $N(X_j) + L - X_j < a$.

The first point which has $\Delta_i = 0$ is X_1,

Now, X_2, X_3 and X_4 is greater than X_1 we have to check which of them lead to a jump point.

$$\begin{aligned} a &= 2.8 + 80 - 10 \\ &= 72.8 \end{aligned}$$

Since, $72.8 > 10$, and 10+80-10=80,

and since $10 < 72.8 < 80$, and 15.4+80-60=35.4

Since, $35.4 < 72.8$, then 72.8 is a jump point.

For X_3 we have

$$\begin{aligned} a &= 10(\frac{1}{2}) + 80 - 10 \\ &= 75 \end{aligned}$$

Since, $10 < 75 < 10 + 80 - 10$, and since $10 < 75 < 80$.

30+(80-60)=50, Since $50 < 70$, then 75 is a jump point.

For X_4, we have

$a =$ 10(1)+80-10 =80 , and since 80 is not greater than 80 then a is not a jump point.

The second point which has $\Delta_i = 0$ is X_2,

X_4 is greater than X_2, we will check if it lead to a jump point or not.

a =60(1) +80 -60 =80 , and since 80 is not greate than 80, then a is not a jump point.

Therefore, the jump points of Wang Estimator are:

10, 15.4, 30, 60, 72.8, 75, and 80 .

Tab. 3.5: Jump Points from two examples

Estimator	Shift	MVT
SWE	30, 80	30, 80
Z-T	10, 11.5, 22.5, 30, 45, 80	10, 15.4, 30, 60, 80
Wang	10, 11.5, 22.5, 30, 45, 72.75, 75, 80	10, 15.4, 30, 60, 72.8, 75, 80

In this table, we present the jump points of the Simple Weighted estimator, Zhao-Tsiatis estimator and Wang estimator. In the first example, we used the shifting intervals and, in the second example, we used the Mean Value Theorem.

The jump points for the Simple Weighted estimator are the same for both methods.

We note that the number of jump points for Z-T estimator are 6 using shifting method but 5 jump points using the MVT, and the number of jump points for Wang estimator is 9 using shift method, but 8 jump points using MVT, which means that the MVT decreases the number of jump points .

The point 11.5 is a jump point of Z-T estimator use the shift method, but not a jump point using (MVT), where $N(X) = 15.4$ instead.

In the next table, we present the values of the Simple Weighted estimator, the Zhao-Tsiatis estimator and the Wang estimator for the second example using the Mean Value Thorem method.

Tab. 3.6: The values of the Simple Wieghted estimator, the Zhao-Tsiatis estimator and Wang estimator using the mean value theorem method

a	SWE	$Z-T$	**Wang**
10^-	1	1	1
10^+	1	1	1
15.4^-	1	1	1
15.4^+	1	$\frac{2}{3}$	$\frac{2}{3}$
30^-	1	$\frac{2}{3}$	$\frac{2}{3}$
30^+	$\frac{1}{2}$	$\frac{1}{3}$	$\frac{1}{3}$
60^-	$\frac{1}{2}$	$\frac{1}{3}$	$\frac{1}{3}$
60^+	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{3}$
72.8^-	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{3}$
72.8^+	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{3}{8}$
75^-	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{3}{8}$
75^+	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{3}{8}$
80^-	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{3}{8}$
80^+	0	0	0

3.2.7 Comments:

As you see the simple wighted estimator is monotonic, but the Zhao-Tiatis estimator and Wang estimator are not monotonic. Also the values of the Zhao-Tiatis estimator and Wang estimator are different at some jump points using the different methods.

Chapter 4

Monotonizing the Wang Estimator

We will preview some theorems and defintions about weak consistency. Then we will prove that the monotonized Zhao-Wang is weakly consistent.

Definition 4.0.1 *Weak Consistency [1]*

Let $\hat{\theta}_1$, $\hat{\theta}_2$, $\hat{\theta}_3$,..., $\hat{\theta}_n$, be a sequence of estimators of a parameter θ. The sequence $\{\hat{\theta}_n\}$ is defined to be a weakly (or simple) consistent sequence of estimator of θ if for every $\epsilon > 0$, then.

$$\lim_{n \longrightarrow \infty} P[|\hat{\theta_n} - \theta| < \epsilon] = 1.$$

For every θ in the parameter space(Ω).

Theorem 4.0.1 *Slutsky's Theorem [1]*

If $X_n \longrightarrow X$ in distribuation, and $Y_n \longrightarrow \alpha$, α constant, in prpbability, then:

a) $Y_n X_n \longrightarrow \alpha X$ in distribution

b)$X_n + Y_n \longrightarrow X + \alpha$ in distribution

Theorem 4.0.2 *[1]*

Let $\hat{\theta}_{1,n}$, $\hat{\theta}_{2,n}$ be two weakly consistent estimators of a parameter θ. Consider the sequence of convex linear combinations defined by

$$\hat{\theta}_n = \alpha_n \hat{\theta}_{1,n} + (1-\alpha_n)\hat{\theta}_{2,n}.$$

Where, α_n are random variables such that $0 \leqslant \alpha_n \leqslant 1$ for all integer n. Then, θ_n is a weak consistant estimator of θ.

Theorem 4.0.3

Let $\hat{\theta}_{1,n}$, $\hat{\theta}_{2,n}$, and $\hat{\theta}_{3,n}$ be three sequences of weakly consistent estimators of a parameter θ, consider the sequence of convex linear combination definded by

$$\hat{\theta}_n = \beta_n(\hat{\theta}_{4,n}) + (1-\beta_n)\hat{\theta}_{3,n}.$$

Where,

$$\hat{\theta}_{4,n} = \alpha_n(\hat{\theta}_{1,n}) + (1-\alpha_n)(\hat{\theta}_{2,n}).$$

where, α_n, β_n are random variables such that $0 \leqslant \alpha_n \leqslant 1$, $0 \leqslant \beta_n \leqslant 1$, for all integer n. Then $\hat{\theta}_n$ is weakly consistent estimator of θ.
$\hat{\theta}_{4,n}$is weakly consistent estimator by(thm4.0.2).

Proof:

$$\begin{aligned}
\hat{\theta}_n &= \beta_n(\hat{\theta}_{4,n}) + (1-\beta_n)\hat{\theta}_{3,n} \\
&= \beta_n[\alpha_n(\hat{\theta}_{1,n}) + (1-\alpha_n)\hat{\theta}_{2,n}] + (1-\beta_n)\hat{\theta}_{3,n} \\
&= \hat{\theta}_{3,n} + \alpha_n\beta_n(\hat{\theta}_{1,n} - \hat{\theta}_{2,n}) + \beta_n(\hat{\theta}_{2,n} - \hat{\theta}_{3,n}).
\end{aligned}$$

Since,
$\hat{\theta}_{1,n} \xrightarrow{P} \theta$, $\hat{\theta}_{2,n} \xrightarrow{P} \theta$ and $\hat{\theta}_{3,n} \xrightarrow{P} \theta$.

By Slutsky Theorem

$$(\hat{\theta}_{1,n} - \hat{\theta}_{2,n}) \xrightarrow{P} 0.$$

and since α_n, β_n are bounded, then

$$\alpha_n \beta_n (\hat{\theta}_{1,n} - \hat{\theta}_{2,n}) \xrightarrow{P} 0.$$

Since β_n is bounded then,

$$\beta_n (\hat{\theta}_{2,n} - \hat{\theta}_{3,n}) \xrightarrow{P} 0.$$

Also

$\hat{\theta}_{2,n} - \hat{\theta}_{3,n} \xrightarrow{P} 0.$ by Slutsky's Theorem

Now,

$$\hat{\theta}_n = \hat{\theta}_{3,n} + \alpha_n \beta_n (\hat{\theta}_{1,n} - \hat{\theta}_{2,n}) + \beta_n (\hat{\theta}_{2,n} - \hat{\theta}_{3,n})] \xrightarrow{P} \theta \text{ By Slutsky Theorem.}$$

Then, $\hat{\theta}_n$ is a weakly consistent estimator of θ. □

Definition 4.0.2 *Mean Squared-error Consistence*

Let $\theta_1, \theta_2, ..., \theta_n$ be a sequence of estimators of a real valued survival function θ. The sequence $\{\hat{\theta}_n\}$ is defined to be a mean sequared-error consistent sequence of estimator of θ, if and only if [1],

$$\lim_{n \longrightarrow \infty} E[(\hat{\theta}_n - \theta)^2] = 0.$$

We say $\hat{\theta}_n$ is a MSE consistent estimator of θ.

4.1 Monotonizing The Wang Estimator

We will give the procedure for monotonizing the Wang estimator $\hat{\theta}_a(4;1)$ by following Almanassra *et al.* (2005) method which he preasented in one of his papers to monotonize the Zhao-Tsiatis estimator and Wang estimator. The new estimator is a linear comination of the (monotonic)Zhao-Tsiatis estimator and Wang estimator, both the monotonic Zhao-Tsistis estimator and Wang estimator are consistent estimators [1].

The procedure for monotonizing the Wang estimator is given in the following steps:

1. Let $U_0 = 0$.
2. Find all possible jump points for Wang estimator.
3. Find the monotonic Zhao-Tsiatis estimator and find all possible jump points for monotonized Zhao-Tsiatis estimator.
4. Denote all possible jump points of Wang estimator and Zhao-Tsiatis estimator $U_1, U_2, ..., U_{k-1}$.
5. Let $R_1 = U_0$, and $R_2, ..., R_k$ be the possible ordered jump points.
6. Find the values of monotonic Zhao-Tsiatis and Wang estimator at these points.
7. The new Zhao-Wang estimator is a step function.

   The value of this function between successive jump points is defined by:

   $$\hat{\theta}_{MW,i}(\beta) = \beta_i \hat{\theta}_{Ri}(4;1) + (1-\beta_i)\hat{\theta}_{mzt,Ri}.$$

   Where, $i = 1, 2, ..., k$, $R_i \leq \beta < R_{i+1}$, β_i's are random numbers such that $0 \leq \beta_i \leq 1$;

$1 \geq \beta_1\hat{\theta}_{R1}(4;1) + (1-\beta_1)\hat{\theta}_{R1,mzt}$

$\beta_1\hat{\theta}_{R1}(4;1) + (1-\beta_1)\hat{\theta}_{R1,mzt} \geq \beta_2\hat{\theta}_{R2}(4;1) + (1-\beta_2)\hat{\theta}_{R2,mzt}$

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$\beta_{k-1}\hat{\theta}_{R_{k-1}}(4;1) + (1-\beta_{k-1})\hat{\theta}_{R_{k-1},mzt} \geq \beta_k\hat{\theta}_{R_k}(4;1) + (1-\beta_k)\hat{\theta}_{R_k,mzt} \geq 0$

$\beta_k\hat{\theta}_{R_k}(4;1) + (1-\beta_k)\hat{\theta}_{R_k,mzt} \geq 0$

8. **Maximizing the objective function**

$$\sum_{i=1}^{k} \mu_i\beta_i.$$

Where μ_i are known (positive) weights.

The constraints are given by

$\mu Y \geq C$

where,

$$Y = \begin{bmatrix} \beta_1 \\ \beta_2 \\ \beta_3 \\ \vdots \\ \vdots \\ \beta_k \end{bmatrix} \tag{4.1}$$

$$C = \begin{bmatrix} \hat{\theta}_{R_1,mzt} - 1 \\ \hat{\theta}_{R_2,mzt} - \hat{\theta}_{R_1,mzt} \\ \hat{\theta}_{R_3,mzt} - \hat{\theta}_{R_2,mzt} \\ \vdots \\ \vdots \\ \hat{\theta}_{R_k,mzt} - \hat{\theta}_{R_{k-1},mzt} \\ -\hat{\theta}_{R_k,mzt} \end{bmatrix}, \tag{4.2}$$

and the matrix μ is in the next page

$$\mu = \begin{bmatrix} -(\hat{\theta}_{R1}(4;1) - \hat{\theta}_{R1}(mzt)) & 0 & 0 & \cdots & 0 & 0 \\ (\hat{\theta}_{R_1}(4;1) - \hat{\theta}_{R1}(mzt)) & -(\hat{\theta}_{R2}(4;1) - \hat{\theta}_{D2}(mzt)) & 0 & \cdots & \cdots & 0 \\ 0 & (\hat{\theta}_{R2}(4;1) - \hat{\theta}_{R2}(mzt)) & -(\hat{\theta}_{R3}(4;1) - \hat{\theta}_{R3}(mzt)) & \ddots & \cdots & 0 \\ \vdots & \ddots & \ddots & \ddots & \ddots & 0 \\ 0 & \cdots & 0 & 0 & (\hat{\theta}_{D_{R-1}}(4;1) - \hat{\theta}_{D_{r-1}}(mzt) & -(\hat{\theta}_{R_k}(4;1) - \hat{\theta}_{R_k}(mzt)) \\ 0 & 0 & 0 & 0 & 0 & (\hat{\theta}_{R_k}(4;1) - \hat{\theta}_{R_k}(mzt)) \end{bmatrix}$$

9. We use linear programming to find the matrix Y.

   Note that the programming has known feasible soluation given by new the Monotonic Zhao-Wang estimator [1].

Then the Monotonic Zhao-Wang Estimator is given by:

$$\hat{\theta}_{MW}(\alpha) = \begin{cases} \beta_1\hat{\theta}_{R_1}(4;1) + (1-\beta_1)\hat{\theta}_{R_1}mzt, & R_1 \leqslant \alpha < R_2 \\ \\ \beta_2\hat{\theta}_{R_2}(4;1) + (1-\beta_2)\hat{\theta}_{R_2}mzt, & R_2 \leqslant \alpha < R_3 \\ \vdots & \\ \beta_{K-1}\hat{\theta}_{Rk-1}(4;1) + (1-\beta_{K-1})\hat{\theta}_{Rk-1}mzt, & R_{K-1} \leqslant \alpha < R_K \\ \\ 0, & R_K \leqslant \alpha \end{cases} \tag{4.3}$$

4.1.1 Examples

Example 4.1.1

First, we will use the data in the table (3.6).

We will apply the procedure given in Almanassra *et al.* (2005) to find the monotonized Zhao-Tsiatis estimator .

Let $U_0 = 0$.

The possible jump points of Zhao-Tsiatis estimator are 10, 15.4, 30, 60, 80 table (3.5).

The values of the Simple Weighted estimator and Zhao-Tisatis estimator are given in the table 3.6.

Then, we have to find the matrices W and B.

$$W = \begin{bmatrix} -(1-1) & 0 & 0 & 0 & 0 & 0 \\ (1-1) & -(1-1) & 0 & 0 & 0 & 0 \\ 0 & (1-1) & -(1-\frac{2}{3}) & 0 & 0 & 0 \\ 0 & 0 & (1-\frac{2}{3}) & -(\frac{1}{2}-\frac{1}{3}) & 0 & 0 \\ 0 & 0 & 0 & (\frac{1}{2}-\frac{1}{3}) & -(\frac{1}{2}-\frac{1}{2}) & 0 \\ 0 & 0 & 0 & 0 & (\frac{1}{2}-\frac{1}{2}) & (0-0) \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$W = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\frac{1}{3} & 0 & 0 & 0 \\ 0 & 0 & \frac{1}{3} & \frac{-1}{6} & 0 & 0 \\ 0 & 0 & 0 & \frac{1}{6} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$B = \begin{bmatrix} (1-1) \\ (1-1) \\ (1-1) \\ (\frac{1}{2}-1) \\ (\frac{1}{2}-\frac{1}{2}) \\ (0-\frac{1}{2}) \\ 0 \end{bmatrix} \tag{4.4}$$

$$B = \begin{bmatrix} 0 \\ 0 \\ 0 \\ -\frac{1}{2} \\ 0 \\ -\frac{1}{2} \\ 0 \end{bmatrix}$$

Using linear programming in R, we find the matrix

$$X = \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 0 \\ 1 \end{bmatrix} \tag{4.5}$$

Therefore, the monotonized Zhao-Tsiatis estimator is

$$\hat{\theta}_{MZ}(a) = \begin{cases} 1 & 0 \leq a < 30 \\ \frac{1}{2} & 30 \leq a < 80 \\ 0 & 50 \leq a \end{cases}$$

Now, we will use the values of the monotonized Zhao-Tsiatis estimator to calculate values of the monotonized Zhao-Wang estimator.

We will apply the procedure given above to the data to find the monotonized Zhao-Tsiatis estimator.

Let $U_0 = R_1 = 0$

The possible jump points are 10, 15.4, 30, 60, 72.8, 75, 80(as found in chapter 3).

The value of the monotonized Zhao-Tsiatis are given in part 1.

The next step is to find the matrices C and μ.

$$\mu = \begin{bmatrix} (1-1) & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -(1-1) & (1-1) & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & (1-1) & -(\frac{2}{3}-1) & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & (\frac{2}{3}-1) & -(\frac{1}{3}-\frac{1}{2}) & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & (\frac{1}{3}-\frac{1}{2}) & -(\frac{1}{3}-\frac{1}{2}) & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & (\frac{1}{3}-\frac{1}{2}) & -(\frac{3}{8}-\frac{1}{2}) & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & (\frac{3}{8}-\frac{1}{2}) & -(\frac{3}{8}-\frac{1}{2}) & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & (\frac{3}{8}-\frac{1}{2}) & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$\mu = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \frac{1}{3} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\frac{1}{3} & \frac{1}{6} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\frac{1}{6} & \frac{1}{6} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\frac{1}{6} & \frac{1}{8} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\frac{1}{8} & \frac{1}{8} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -\frac{1}{8} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

And Y is

$$Y = \begin{bmatrix} 1-1 \\ 1-1 \\ 1-1 \\ \frac{1}{2}-1 \\ \frac{1}{2}-\frac{1}{2} \\ \frac{1}{2}-\frac{1}{2} \\ \frac{1}{2}-\frac{1}{2} \\ 0-\frac{1}{2} \\ 0 \end{bmatrix}$$

$$Y = \begin{bmatrix} 0 \\ 0 \\ 0 \\ -\frac{1}{2} \\ 0 \\ 0 \\ 0 \\ -\frac{1}{2} \\ 0 \end{bmatrix}$$

Using Linear programming in R, we find the matrix

$$Y = \begin{bmatrix} 1 \\ 1 \\ 0 \\ 1 \\ 1 \\ 1 \\ 1 \\ 0 \\ 1 \end{bmatrix}$$

Therefore, the monotonized Zhao-Wang estimator is

$$\hat{\theta}_{MZW}(a) = \begin{cases} 1 & 0 \le a < 15.4 \\ .6 & 15.4 \le a < 30 \\ .5 & 30 \le a < 80 \\ 0 & 80 \le \alpha \end{cases}$$

Chapter 5

Simulation Results

5.1 Simulation Results

In this study we will use the R code to estimate and compare the mean squar erorrs of the Simple Wieght estimator, Zhao-Tiatis estimator, Wang estimator, Monotonized Zhao estimator, Monotonized Wang estimator and the new Monotonized-Zhao Wang estimator use Monotonized Zhao-Tsiatis estimator.

The parameter of interest is the survival function of time without symptoms of disease and toxicity (TWiST).

FU is the time to follow-up, that is uniformly distributed in the interval $[0, 94]$,

$$FU \sim U(0, 94)$$

TR is exponentially distributed with hazard $\lambda = \frac{1}{120}$,

$$TR \sim exp(\frac{1}{120}).$$

TOX is defined as the time of toicity which is uniformly distributed on$[0, TOX2]([0, 72])$,

$$TOX \sim U(0, 72).$$

That variables are statistically independent.

The true survival function of time without symptoms, disease and toxicity is given by Gelber *et al*(1989).

$$\Pr(TWiST > a) = \begin{cases} \frac{1}{\lambda TOX2} \exp^{-\lambda a}(1 - \exp^{-\lambda TOX2}) & 0 \leq a < L - TOX2. \\ \\ \frac{1}{\lambda TOX2}(\exp^{-\lambda a} - \exp^{-\lambda L}) & l - TOX2 \leq a \leq 0L. \end{cases}$$

To calculate all estimators, we will use

$T_i = TR \wedge L$, $\triangle_i = I(T_i \leq FU_i)$, $X_i = T_i \wedge FU_i$

We use the data $X_i, \triangle_i$ to calculate the Simple Wieghted estimator

We will use that results:

$r_i = TOX_i + a, \quad T_i(a) = r_i \wedge T_i$

$\triangle_i(a) = I(T_i \leqslant FU_i), \quad X_i(a) = T_i \wedge FU_i$

To calculate the Zhao-Tsiatis estimator and the monotonized Zhao-Tsiatis estimator.

To compute the Wang estimator and monotonized Wang estimator, we use the following results,

$if N(X_i) \leqslant a,$ and $L - TOX_i \leqslant a$ Let,

$w_i(a) = L - a, \quad T_i'(a) = w_i(a) \wedge T_i$

Otherwise,let

$r_i = TOX_i + a, \quad T_i(a) = r_i \wedge T_i$

$\triangle_i = I(T' \leqslant FU_i), \quad X_i' \wedge FU_i$

To calculate the montonic Zhao-Wang estimator, we use the data of Zhao-Tsiatis estimator and Wang estimator.

L is the artifical end point equal 80.

In this experment, we will consider different sample sizes, n= 10, 15, 20, 30, 40, 50.The number of simulations = 1000.

Tab. 5.1: This table to compare MSE for the folowing estimators: the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, the monotonized Wang estimator and monotonized Zhao-Wang estimator, n=10

m	tru-surv	MSE.S	MSE.Z	MSE.W	MSE.MZ	MSE.MW	MSE.MZW
0	0.751981	0.089389	0.047462	0.047462	0.061633	0.062000	0.015002
4	0.727328	0.091624	0.062713	0.062713	0.069968	0.069932	0.015058
8	0.703483	0.094323	0.073214	0.073214	0.062742	0.063044	0.011472
12	0.652367	0.100102	0.087144	0.085975	0.058752	0.058911	0.019119
16	0.602927	0.105785	0.090315	0.088322	0.047042	0.047510	0.020103
20	0.555108	0.104136	0.091409	0.086540	0.037999	0.038058	0.036821
24	0.508856	0.113283	0.093788	0.085046	0.029024	0.029088	0.031193
28	0.464121	0.109453	0.088483	0.080400	0.025421	0.025210	0.039611
32	0.420852	0.101088	0.080558	0.072207	0.023189	0.022933	0.038684
36	0.379002	0.098996	0.077712	0.068021	0.025814	0.025582	0.025880
40	0.338524	0.094817	0.066738	0.056570	0.031297	0.031434	0.023046
44	0.299373	0.086577	0.059666	0.049883	0.039561	0.039713	0.022794
48	0.261505	0.083049	0.053084	0.043502	0.043387	0.043180	0.021804
52	0.224879	0.067790	0.040929	0.033696	0.042268	0.042737	0.013463
58	0.172178	0.053015	0.028250	0.022961	0.027689	0.028100	0.014702
60	0.155189	0.049627	0.026034	0.020381	0.024618	0.024559	0.013617
64	0.122049	0.044245	0.018992	0.012413	0.014811	0.014913	0.014693
68	0.089994	0.029689	0.011454	0.008612	0.009096	0.008997	0.009088
72	0.058991	0.014251	0.005503	0.003623	0.003485	0.003006	0.003487
76	0.029004	0.010840	0.002847	0.002170	0.001841	0.002000	0.001856

This table columns are MSE.S, MSE.Z, MSE.W, MSE.MZ,MSE.MW,MSE.MZW are the MSE of the simple weighted estimator ,the Zhao-Tsiatis estimator ,the Wang estimator , the monotonized Zhao-Tsiatis estimator ,monotonized Wang estimator and the monotonized Zhao-Wang estimator respectively. Each entry comes from 1000 simulation

Tab. 5.2: This table to compare the Biases for the following estimators: the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, the monotonized Wang estimator and monotonized Zhao-Wang estimator, n=10.

m	tru-surv	BIAS.S	BIAS.Z	BIAS.W	BIAS.MZ	BIAS.MW	BIAS.MZW
0	0.751981	0.055097	-0.056602	-0.056602	0.048019	0.248019	0.048019
4	0.727328	0.006636	-0.101675	-0.101675	0.260182	0.260611	0.272580
8	0.703483	-0.016559	-0.152130	-0.152130	0.236046	0.236542	0.281233
12	0.652367	-0.020370	-0.179461	-0.176321	0.212721	0.212754	0.286413
16	0.602927	-0.038605	-0.197667	-0.190613	0.172601	0.173625	0.259427
20	0.555108	-0.040316	-0.197451	-0.183876	0.132751	0.133185	0.220193
24	0.508856	-0.067786	-0.216660	-0.201811	0.085211	0.085368	0.176159
28	0.464121	-0.063862	-0.202702	-0.188805	0.040557	0.041381	0.128967
32	0.420852	-0.071276	-0.203112	-0.189703	-0.001313	-0.000621	0.080616
36	0.379002	-0.073831	-0.196536	-0.185065	-0.042005	-0.041243	0.039637
40	0.338524	-0.068030	-0.192677	-0.176395	-0.087973	-0.088207	-0.003997
44	0.299373	-0.059564	-0.174170	-0.165723	-0.132647	-0.132674	-0.048599
48	0.261505	-0.061717	-0.169703	-0.160097	-0.168032	-0.168028	-0.096116
52	0.224879	-0.060022	-0.153404	-0.139961	-0.182004	-0.182426	-0.130812
58	0.172178	-0.059700	-0.127705	-0.122712	-0.157763	-0.158151	-0.130241
60	0.155189	-0.053603	-0.109872	-0.108476	-0.150220	-0.150331	-0.139773
64	0.122049	-0.029063	-0.089879	-0.090788	-0.120896	-0.120896	-0.118079
68	0.089994	-0.033142	-0.073758	-0.070404	-0.088834	-0.088834	-0.087842
72	0.058991	-0.030490	-0.049951	-0.049901	-0.058838	-0.058838	-0.058831
76	0.029004	-0.009146	-0.023731	-0.022887	-0.028004	-0.028004	-0.027852

¿

This columns are $BIAS.S, BIAS.Z, BIAS.W, BIAS.MZ, BIAS.MW, BIAS.MZW$ **are the Biased of the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, monotonized Wang estimator and the monotonized Zhao-Wang estimator respectively. Each entry comes from 1000 simulation**

Tab. 5.3: This table to compare the MSE for the following estimators: the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, the monotonized Wang estimator and monotonized Zhao-Wang estimator, n=15.

m	tru-surv	MSE.S	MSE.Z	MSE.W	MSE.MZ	MSE.MW	MSE.MZW
0	0.751981	0.069599	0.032565	0.032565	0.062517	0.052120	0.007266
4	0.727328	0.069845	0.041842	0.041842	0.071198	0.071089	0.015241
8	0.703483	0.067036	0.053636	0.053636	0.053423	0.063729	0.013136
12	0.652367	0.071867	0.067667	0.065921	0.059516	0.059735	0.011671
16	0.602927	0.077283	0.072256	0.068716	0.051880	0.051930	0.014817
20	0.555108	0.080282	0.074559	0.068842	0.044793	0.044990	0.014786
24	0.508856	0.084424	0.074197	0.066377	0.035528	0.035577	0.032182
28	0.464121	0.087493	0.076144	0.066927	0.029033	0.029081	0.031102
32	0.420852	0.081299	0.068708	0.062167	0.022098	0.022033	0.020178
36	0.379002	0.078950	0.068356	0.056940	0.019777	0.019615	0.020799
40	0.338524	0.073500	0.060442	0.052177	0.016158	0.015905	0.020197
44	0.299373	0.075932	0.053987	0.044858	0.018891	0.018551	0.015409
48	0.261505	0.066624	0.043871	0.036690	0.020683	0.020364	0.014735
52	0.224879	0.063396	0.036521	0.030156	0.025638	0.025569	0.014770
58	0.172178	0.052681	0.026014	0.020293	0.021298	0.021530	0.014250
60	0.155189	0.049020	0.022264	0.017798	0.022189	0.022069	0.013773
64	0.122049	0.037381	0.014348	0.011323	0.01490	0.014590	0.013512
68	0.089994	0.025568	0.009456	0.007930	0.009059	0.008961	0.008660
72	0.058991	0.017219	0.005495	0.003276	0.003478	0.002999	0.002507
76	0.029004	0.009751	0.002545	0.001990	0.001841	0.001230	0.001112

This table columns are MSE.S, MSE.Z, MSE.W, MSE.MZ,MSE.MW,MSE.MZW are the MSE of the simple weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator,monotonized Wang estimator and the monotonized Zhao-Wang estimator respectively.Each entry comes from 1000 simulation

Tab. 5.4: This table to Compare the Biases for the following estimators: the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, the monotonized Wang estimator and monotonized Zhao-Wang estimator, n=15.

m	tru-surv	BIAS.S	BIAS.Z	BIAS.W	BIAS.MZ	BIAS.MW	BIAS.MZW
0	0.751981	-0.048891	-0.029446	-0.029446	0.045218	0.056762	0.056762
4	0.727328	-0.068758	-0.063801	-0.063801	-0.020915	-0.000745	-0.000745
8	0.703483	-0.097722	-0.098189	-0.098189	-0.069056	-0.040399	-0.040399
12	0.652367	-0.188390	-0.102530	-0.103198	-0.076537	-0.037545	-0.037538
16	0.602927	-0.179362	-0.102895	-0.099534	-0.080643	-0.030767	-0.030584
20	0.555108	-0.163340	-0.100864	-0.089783	-0.084091	-0.019577	-0.019112
24	0.508856	-0.252957	-0.103893	-0.079998	-0.089730	-0.010084	-0.009396
28	0.464121	-0.134614	-0.099315	-0.062438	-0.089665	0.002703	0.003437
32	0.420852	-0.123514	-0.097842	-0.030053	-0.091467	0.013017	0.014662
36	0.379002	-0.108429	-0.095470	-0.009291	-0.093395	0.025930	0.028124
40	0.338524	-0.194265	-0.098686	0.005905	-0.094301	0.036108	0.039461
44	0.299373	-0.179558	-0.092343	0.045252	-0.093614	0.046851	0.050978
48	0.261505	-0.154921	-0.084318	0.075873	-0.098344	0.054144	0.060494
52	0.224879	-0.134468	-0.075072	0.103703	-0.102418	0.062525	0.070797
58	0.172178	-0.107940	-0.071847	0.144204	-0.095014	0.083011	0.093655
60	0.155189	-0.094496	-0.060806	0.150342	-0.117431	0.064868	0.080224
64	0.122049	-0.075101	-0.053203	0.175407	-0.109872	0.055308	0.078297
68	0.089994	-0.057436	-0.046659	0.179964	-0.086773	0.039888	0.074665
72	0.058991	-0.034860	-0.029683	0.191211	-0.058813	0.004131	0.058179
76	0.029004	-0.017553	-0.016283	0.193562	-0.028004	-0.028004	0.027729

This table columns $BIAS.S, BIAS.Z, BIAS.W, BIAS.MZ, BIAS.MW, BIAS.MZW$ are the Biased of the simple weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator , the monotonized Zhao-Tsiatis estimator, monotonized Wang estimator and the monotonized Zhao-Wang estimator respectively. Each entry comes from 1000 simulation

Tab. 5.5: This table to compare the MSE for the follwing estimators: the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, the monotonized Wang estimator and monotonized Zhao-Wang estimator, n=20.

m	tru-surv	MSE.S	MSE.Z	MSE.W	MSE.MZ	MSE.MW	MSE.MZW
0	0.751981	0.065312	0.021601	0.021601	0.041823	0.021950	0.013005
4	0.727328	0.062646	0.033380	0.033380	0.031444	0.031250	0.010282
8	0.703483	0.053167	0.044844	0.044844	0.042857	0.041042	0.013512
12	0.652367	0.058835	0.056120	0.054374	0.056844	0.056819	0.011297
16	0.602927	0.059584	0.054536	0.050226	0.052912	0.053047	0.012219
20	0.555108	0.054935	0.061346	0.057246	0.047137	0.045163	0.030498
24	0.508856	0.067272	0.064506	0.057682	0.038711	0.038587	0.025925
28	0.464121	0.065938	0.066534	0.058920	0.033507	0.033167	0.026337
32	0.420852	0.064848	0.061709	0.055217	0.025754	0.025377	0.025281
36	0.379002	0.067548	0.057417	0.049281	0.020951	0.020743	0.015516
40	0.338524	0.064639	0.051140	0.043470	0.015131	0.015035	0.017733
44	0.299373	0.060233	0.048882	0.040574	0.013048	0.012923	0.012378
48	0.261505	0.057039	0.041481	0.034497	0.012066	0.011994	0.032098
52	0.224879	0.053284	0.035561	0.028914	0.015207	0.015227	0.012036
58	0.172178	0.045723	0.022726	0.018305	0.015030	0.015122	0.014331
60	0.155189	0.040358	0.020437	0.016408	0.018373	0.018350	0.024251
64	0.122049	0.029201	0.013856	0.010901	0.013500	0.013601	0.011677
68	0.089994	0.026479	0.009226	0.007251	0.008984	0.008891	0.008709
72	0.058991	0.015312	0.004966	0.002937	0.003485	0.003008	0.003616
76	0.029004	0.013045	0.003417	0.001870	0.001770	0.002012	0.001619

This table columns are MSE.S, MSE.Z, MSE.W, MSE.MZ, MSE.MW, MSE.MZW are the MSE of the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, monotonized Wang estimator and the monotonized Zhao-Wang estimator respectively. Each entry comes from 1000 simulation.

Tab. 5.6: This table to compare the Biases for the following estimators: the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, the monotonized Wang estimator and monotonized Zhao-Wang estimator, n=20.

m	tru-surv	BIAS.S	BIAS.Z	BIAS.W	BIAS.MZ	BIAS.MW	BIAS.MZW
0	0.751981	-0.053883	-0.026670	-0.026670	0.032142	0.041683	0.041683
4	0.727328	-0.168701	-0.059743	-0.059743	-0.030909	-0.013117	-0.013117
8	0.703483	-0.185160	-0.090007	-0.090007	-0.073679	-0.045959	-0.045934
12	0.652367	-0.178731	-0.093904	-0.094176	-0.077186	-0.039462	-0.039461
16	0.602927	-0.172083	-0.099003	-0.095240	-0.081640	-0.031232	-0.031192
20	0.555108	-0.163314	-0.097928	-0.082285	-0.084462	-0.020462	-0.020393
24	0.508856	-0.150053	-0.097531	-0.075456	-0.089076	-0.007897	-0.007718
28	0.464121	-0.132318	-0.100608	-0.060067	-0.089116	0.006278	0.006792
32	0.420852	-0.118162	-0.098743	-0.034785	-0.089560	0.018496	0.019076
36	0.379002	-0.107445	-0.095784	-0.011590	-0.089465	0.033626	0.035061
40	0.338524	-0.095345	-0.094235	0.030935	-0.093456	0.045702	0.047450
44	0.299373	-0.174917	-0.086562	0.064876	-0.091803	0.058549	0.061761
48	0.261505	-0.156381	-0.082956	0.097534	-0.091572	0.068165	0.072344
52	0.224879	-0.033056	-0.073145	0.020482	-0.091758	0.079137	0.084468
58	0.172178	-0.100462	-0.067636	0.057817	-0.077950	0.002647	0.010434
60	0.155189	-0.097398	-0.064474	0.067155	-0.099266	0.089960	0.003422
64	0.122049	-0.078057	-0.054870	0.081228	-0.100027	0.088077	0.005164
68	0.089994	-0.057429	-0.046738	0.097718	-0.083137	0.074745	0.074698
72	0.058991	-0.037858	-0.029961	0.100236	-0.058578	0.039024	0.092691
76	0.029004	-0.016843	-0.016220	0.201701	-0.028004	-0.03304	0.062431

This table columns $BIAS.S, BIAS.Z, BIAS.W, BIAS.MZ, BIAS.MW, BIAS.MZW$ are the Biased of the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, monotonized Wang estimator and the monotonized Zhao-Wang estimator respectively. Each entry comes from 1000 simulation

Tab. 5.7: This table to compare the MSE of the following estimators: Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, the monotonized Wang estimator and monotonized Zhao-Wang estimator, n=30

m	tru-surv	MSE.S	MSE.Z	MSE.W	MSE.MZ	MSE.MW	MSE.MZW
0	0.751981	0.061824	0.014368	0.014368	0.011514	0.012390	0.011514
4	0.727328	0.052410	0.022812	0.022812	0.021061	0.010099	0.012811
8	0.703483	0.044561	0.035314	0.035314	0.030661	0.029918	0.019059
12	0.652367	0.043971	0.043676	0.043412	0.028824	0.028424	0.015186
16	0.602927	0.045203	0.045029	0.044136	0.013784	0.013074	0.013765
20	0.555108	0.052435	0.051172	0.051078	0.039132	0.028262	0.023400
24	0.508856	0.053224	0.053843	0.049161	0.031898	0.031483	0.013171
28	0.464121	0.062434	0.05348	0.053238	0.035317	0.034981	0.023095
32	0.420852	0.046627	0.051066	0.045743	0.028484	0.028317	0.013041
36	0.379002	0.054517	0.048291	0.048418	0.023132	0.022927	0.010580
40	0.338524	0.049162	0.049049	0.042425	0.017534	0.017619	0.011107
44	0.299373	0.047250	0.043113	0.036300	0.014782	0.014926	0.015233
48	0.261505	0.040619	0.035895	0.030714	0.010968	0.011225	0.011814
52	0.224879	0.038992	0.031389	0.026246	0.010799	0.010864	0.011174
58	0.172178	0.032909	0.021043	0.017347	0.009208	0.009394	0.010574
60	0.155189	0.030676	0.018904	0.015427	0.011440	0.011263	0.010559
64	0.122049	0.025576	0.012132	0.009952	0.010018	0.009958	0.008596
68	0.089994	0.019739	0.009307	0.007105	0.008220	0.008167	0.007871
72	0.058991	0.015143	0.003555	0.002734	0.003474	0.003020	0.003029
76	0.029004	0.007793	0.002469	0.001750	0.001893	0.002051	0.002033

This table columns MSE.S, MSE.Z, MSE.W, MSE.MZ, MSE.MW, MSE.MZW are the MSE of the simple weighted estimator ,the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, monotonized Wang estimator and the monotonized Zhao-Wang estimator respectively.Each entry comes from 1000 simulation.

Tab. 5.8: This table to compare the Biases of the following estimators: the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, the monotonized Wang estimator and monotonized Zhao-Wang estimator, n=30.

m	tru-surv	BIAS.S	BIAS.Z	BIAS.W	BIAS.MZ	BIAS.MW	BIAS.MZW
0	0.751981	-0.047404	-0.031360	-0.031360	0.010278	0.018640	0.018640
4	0.727328	-0.069877	-0.063882	-0.063882	-0.044743	-0.027962	-0.027962
8	0.703483	-0.089659	-0.094211	-0.094211	-0.082195	-0.057892	-0.057892
12	0.652367	-0.079449	-0.090373	-0.090437	-0.085997	-0.048304	-0.048304
16	0.602927	-0.074934	-0.103572	-0.097771	-0.090581	-0.036164	-0.036148
20	0.555108	-0.057298	-0.097582	-0.081354	-0.092100	-0.021855	-0.021844
24	0.508856	-0.055826	-0.106111	-0.076831	-0.095623	-0.009945	-0.009877
28	0.464121	-0.038667	-0.100604	-0.047307	-0.095872	0.007176	0.007286
32	0.420852	-0.023121	-0.095012	-0.010945	-0.096149	0.021711	0.022027
36	0.379002	-0.007675	-0.097306	0.004454	-0.093568	0.038337	0.039083
40	0.338524	-0.088919	-0.091049	0.050898	-0.093814	0.053041	0.053742
44	0.299373	-0.077617	-0.096105	0.068936	-0.090219	0.069442	0.070752
48	0.261505	-0.049866	-0.079604	0.006789	-0.087811	0.083030	0.085008
52	0.224879	-0.030616	-0.074144	0.037228	-0.083707	0.097419	0.010468
58	0.172178	-0.004489	-0.067553	0.081439	-0.065808	0.021507	0.026895
60	0.155189	-0.094683	-0.060001	0.080244	-0.080651	0.013892	0.021063
64	0.122049	-0.079285	-0.058916	0.088452	-0.080009	0.014868	0.026494
68	0.089994	-0.053059	-0.040765	0.002698	-0.074828	0.009756	0.029936
72	0.058991	-0.038261	-0.032217	0.003897	-0.056971	0.084241	0.025150
76	0.029004	-0.015312	-0.013945	0.097858	-0.028004	-0.028004	0.004279

This table columns $BIAS.S, BIAS.Z, BIAS.W, BIAS.MZ, BIAS.MW, BIAS.MZW$ are the Biased of the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, monotonized Wang estimator and the monotonized Zhao-Wang estimator respectively. Each entry comes from 1000 simulation.

Tab. 5.9: This table to campare the MSE for the following estimators: the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, the monotonized Wang estimator and monotonized Zhao-Wang estimator, n=40.

m	tru-surv	MSE.S	MSE.Z	MSE.W	MSE.MZ	MSE.MW	MSE.MZW
0	0.751981	0.061528	0.010748	0.010748	0.011514	0.012258	0.010514
4	0.727328	0.050119	0.017466	0.017466	0.010409	0.011364	0.011198
8	0.703483	0.041707	0.028396	0.028396	0.029057	0.020100	0.010899
12	0.652367	0.039547	0.026833	0.025695	0.030868	0.013228	0.011725
16	0.602927	0.036468	0.025579	0.025282	0.021844	0.023703	0.013031
20	0.555108	0.039003	0.029943	0.016073	0.016707	0.018649	0.014758
24	0.508856	0.038621	0.035950	0.033264	0.038778	0.020327	0.015090
28	0.464121	0.040024	0.047648	0.046217	0.033378	0.014541	0.012186
32	0.420852	0.034382	0.040991	0.035224	0.028558	0.028955	0.021056
36	0.379002	0.038687	0.038705	0.032627	0.024534	0.025196	0.020246
40	0.338524	0.039216	0.033176	0.031703	0.018827	0.018785	0.020041
44	0.299373	0.036923	0.030661	0.029778	0.016397	0.016493	0.019036
48	0.261505	0.032966	0.034348	0.028070	0.012122	0.011985	0.015513
52	0.224879	0.032286	0.029239	0.024721	0.010930	0.010593	0.013202
58	0.172178	0.018055	0.019527	0.016739	0.008487	0.008328	0.013007
60	0.155189	0.025991	0.017532	0.014851	0.008543	0.008244	0.012686
64	0.122049	0.020786	0.011938	0.009577	0.007512	0.007255	0.007565
68	0.089994	0.016379	0.008293	0.006601	0.007144	0.007018	0.007179
72	0.058991	0.011380	0.003599	0.002676	0.003447	0.003056	0.003915
76	0.029004	0.007554	0.002169	0.001707	0.001913	0.002054	0.001405

This table columns MSE.S, MSE.Z, MSE.W, MSE.MZ,MSE.MW,MSE.MZW are the MSE of the simple weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, monotonized Wang estimator and the monotonized Zhao-Wang estimator respectively. Each entry comes from 1000 simulation.

Tab. 5.10: This table to Compare the Biases for the follwing estimators: the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, the monotonized Wang estimator and monotonized Zhao-Wang estimator, n=40.

m	tru-surv	BIAS.S	BIAS.Z	BIAS.W	BIAS.MZ	BIAS.MW	BIAS.MZW
0	0.751981	-0.045875	-0.028913	-0.028913	-0.008276	-0.000670	-0.000670
4	0.727328	-0.075411	-0.066116	-0.066116	-0.054657	-0.042283	-0.042283
8	0.703483	-0.086313	-0.093463	-0.093463	-0.089291	-0.066109	-0.066109
12	0.652367	-0.081039	-0.096355	-0.096759	-0.091848	-0.056164	-0.056164
16	0.602927	-0.076623	-0.101562	-0.095217	-0.095211	-0.045229	-0.045229
20	0.555108	-0.064641	-0.100052	-0.080535	-0.095295	-0.028615	-0.028615
24	0.508856	-0.052166	-0.101862	-0.068311	-0.099042	-0.011756	-0.011712
28	0.464121	-0.036082	-0.100513	-0.040043	-0.100100	0.006726	0.006740
32	0.420852	-0.027472	-0.102466	-0.015789	-0.099774	0.024563	0.024629
36	0.379002	-0.108848	-0.099180	0.023081	-0.097621	0.043789	0.043877
40	0.338524	-0.193709	-0.096674	0.066825	-0.094760	0.060788	0.060989
44	0.299373	-0.171508	-0.088475	0.099506	-0.089606	0.079492	0.079824
48	0.261505	-0.159382	-0.088548	0.126614	-0.089057	0.094942	0.095484
52	0.224879	-0.135580	-0.082484	0.156442	-0.084597	0.113068	0.114005
58	0.172178	-0.105768	-0.068961	0.183162	-0.062983	0.143227	0.145328
60	0.155189	-0.092870	-0.061269	0.193578	-0.072624	0.137050	0.141151
64	0.122049	-0.076001	-0.056062	0.202769	-0.068296	0.144081	0.150920
68	0.089994	-0.054767	-0.041548	0.204686	-0.061513	0.146556	0.158822
72	0.058991	-0.037066	-0.031785	0.202914	-0.051739	0.130974	0.159016
76	0.029004	-0.018578	-0.017330	0.002357	-0.028004	-0.028004	0.046784

This table columns are $BIAS.S, BIAS.Z, BIAS.W, BIAS.MZ, BIAS.MW, BIAS.MZW$ which are the Biased of the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, monotonized Wang estimator and the monotonized Zhao-Wang estimator respectively. Each entry comes from 1000 simulation.

Tab. 5.11: This table to campare the MSE for the following estimators: the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, the monotonized Wang estimator and monotonized Zhao-Wang estimator, n=50.

m	tru-surv	MSE.S	MSE.Z	MSE.W	MSE.MZ	MSE.MW	MSE.MZW
0	0.751981	0.061477	0.008359	0.008359	0.005140	0.006012	0.007148
4	0.727328	0.049223	0.005983	0.005983	0.030570	0.008099	0.001642
8	0.703483	0.049472	0.016681	0.014681	0.013196	0.016004	0.015086
12	0.652367	0.036058	0.017122	0.014807	0.018074	0.012419	0.014895
16	0.602927	0.033070	0.020379	0.020132	0.031984	0.030823	0.013368
20	0.555108	0.031356	0.020950	0.020379	0.025809	0.023779	0.014609
24	0.508856	0.031208	0.021557	0.021310	0.020969	0.021813	0.014524
28	0.464121	0.031087	0.028629	0.024566	0.020725	0.021098	0.014123
32	0.420852	0.030795	0.029610	0.021080	0.015963	0.015224	0.014004
36	0.379002	0.030535	0.027519	0.020927	0.012219	0.014765	0.013235
40	0.338524	0.028138	0.024843	0.015081	0.011965	0.011848	0.013137
44	0.299373	0.027687	0.023960	0.014757	0.011024	0.010319	0.011143
48	0.261505	0.024984	0.022295	0.013392	0.010447	0.010291	0.011088
52	0.224879	0.025614	0.021000	0.012725	0.009124	0.009868	0.010944
56	0.172178	0.020075	0.018398	0.010213	0.007559	0.007864	0.010704
60	0.155189	0.019907	0.017008	0.010149	0.007116	0.007557	0.010224
64	0.122049	0.015578	0.010990	0.009159	0.005688	0.005905	0.007251
68	0.089994	0.014014	0.007784	0.006454	0.006143	0.006165	0.006724
72	0.058991	0.008084	0.003320	0.002602	0.003250	0.002821	0.003978
76	0.029004	0.006077	0.002065	0.001684	0.001934	0.002109	0.002749

This table columns MSE.S, MSE.Z, MSE.W, MSE.MZ,MSE.MW,MSE.MZW are the MSE of the simple weighted estimator ,the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, monotonized Wang estimator and the monotonized Zhao-Wang estimator respectively. Each entry comes from 1000 simulation.

Tab. 5.12: This table to Compare the Biases for the follwing estimators: the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, the monotonized Wang estimator and monotonized Zhao-Wang estimator, n=50.

m	tru-surv	BIAS.S	BIAS.Z	BIAS.W	BIAS.MZ	BIAS.MW	BIAS.MZW
0	0.751981	-0.046007	-0.029667	-0.029667	0.048019	0.048019	0.019807
4	0.727328	-0.074083	-0.066575	-0.066575	-0.061187	-0.063421	-0.040709
8	0.703483	-0.091477	-0.097370	-0.097370	-0.013449	-0.015781	-0.075279
12	0.652367	-0.078859	-0.092218	-0.092179	-0.016403	-0.017756	-0.067375
16	0.602927	-0.075376	-0.001072	-0.001674	-0.013383	-0.012638	-0.010409
20	0.555108	-0.062305	-0.012613	-0.000317	-0.005806	-0.004342	-0.002840
24	0.508856	-0.051977	-0.012478	-0.093342	-0.096631	-0.094876	-0.029425
28	0.464121	-0.041054	-0.011019	-0.086007	-0.087956	-0.083610	-0.011673
32	0.420852	-0.024066	-0.097660	-0.069117	-0.078763	-0.073310	0.004002
36	0.379002	-0.04018	-0.095126	-0.043158	-0.066107	-0.058117	0.020922
40	0.338524	-0.091970	-0.093839	-0.021971	-0.054210	-0.044899	0.036605
44	0.299373	-0.070344	-0.086932	0.016556	-0.039768	-0.029470	0.053466
48	0.261505	-0.055631	-0.087363	0.046970	-0.028198	-0.016302	0.067389
52	0.024879	-0.134451	-0.077679	0.034923	-0.113820	-0.010765	0.081055
58	0.172178	-0.108182	-0.069447	0.150881	-0.084423	-0.069546	0.009718
60	0.155189	-0.094154	-0.065692	0.171189	-0.086213	-0.070622	0.002502
64	0.122049	-0.078373	-0.057523	0.002103	-0.073325	-0.057555	0.105762
68	0.089994	-0.057379	-0.044399	0.035701	-0.059663	-0.043400	0.103973
72	0.058991	-0.038570	-0.032364	0.068965	-0.047577	-0.032452	0.002204
76	0.029004	-0.017788	-0.016485	0.090327	-0.026277	-0.013821	-0.015584

This table columns are $BIAS.S, BIAS.Z, BIAS.W, BIAS.MZ, BIAS.MW, BIAS.MZW$ which are the Biased of the Simple Weighted estimator, the Zhao-Tsiatis estimator, the Wang estimator, the monotonized Zhao-Tsiatis estimator, monotonized Wang estimator and the monotonized Zhao-Wang estimator respectively. Each entry comes from 1000 simulation.

5.2 Conclusion

In this section, we will review some notation from our results.

The monotonized Zhao-Tsiatis Estimator, the monotonized Wang Estimator and monotonized Zhao-Wang Estimator, performed better than the Simple Weighted Estimator.

The monotonized Zhao-Wang estimator is closed to monotonized Zhao estimator and monotonized Wang estimator.

The monotonized Zhao-Wang estimator is monotonic as monotonized Zhao estimator and monotonized Wang Estimator.

The MSE for the monotonized Zhao-Wang estimator is smaller than Simple Weighted estimator, Zhao-Tsiatis estimator and Wang estimator.

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ملخص

تقدير اقتران البقاء لجودة الحياة المعدل
هديل صلاح الدين حسن زيات

في الاونة الاخيرة،تلقى جودة الحياة المعدلة اهتماما كبيرا بسبب قدرتها على اخذ نوعية الحياة بعين الاعتبار، وهو نهج جديد لتقييم العلاج في العيادات الصحية.في هذه الاطروحة سوف نقدم حالة الرقابة التي نفترض فيها ان شخصا ما يخضع لدراسة وبعد فترة من الوقت يختفي في زمن معين ثم يرجع للدراسة في زمن لاحق .وسوف تستخدم طريقتين لحساب اقتران جودة الحياة المعدلة بناء على هذه البيانات الطريقة الاولى استخدام نظرية القيمة المتوسطة لتقدير متوسط قيمة الاقتران في الفترة التي فقدت فيها بيانات الشخص او يمكن تجاهل هذه الفترة وحساب الاقتران بناء على البيانات الموجودة باستخدام طريقة ازاحة الاقترانات.

وسنقدم ايضاتقديرا للاقتران جودة لحياة المعدلة باستخدام طريقة مناصرة (٢٠٠٥) ، وسندرس كفاءة هذا المقدربعمل دراسة محاكاة للمقارنة بينه وبين مقدرات جودة الحياة المعدلة وبين القيمة الحقيقية لهذا الاقتران .