ANALYSIS OF SEMIPARAMETRIC REGRESSION MODELS FOR THE CUMULATIVE INCIDENCE FUNCTIONS UNDER THE TWO-PHASE SAMPLING DESIGNS

by

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ABSTRACT

UNKYUNG LEE. Analysis of semiparametric regression models for the cumulative incidence functions under the two-phase sampling designs. (Under the direction of DR. YANQING SUN)

Competing risks often arise where a subject may be exposed to two or more mutually exclusive causes of failure. In the competing risks setting, the effects of covariates on the semiparmetric model for cumulative incidence function can be assessed by using direct binomial regression approach. In epidemiologic cohort studies, case-cohort study designs have been widely used to evaluate the effects of covariates on failure times when the occurrence of the failure event is rare. Under the case-cohort design, the covariate histories are investigated only for the subjects who experience the event of interest (cases) during the follow-up period and for a relatively small random sample (the subcohort) from the original cohort. In this dissertation, we study estimating procedures for the cumulative incidence function based on competing risks data under case-cohort/two-phase sampling designs.

First, we introduce missing model for the cumulative incidence function. The estimation procedure is based on the direct binomial regression model (Scheike et al., 2008), which enables us to evaluate the effects of the covariates directly when there exists competing risks. We develop an estimating equation for the missing model by using the inverse probability weighting of the complete cases. We also study the asymptotic properties of the inverse probability weighting estimators. The simulation studies show that the IPW methods have satisfactory finite-sample performance. However, this method loses the efficiency because it still use only complete data of subjects.

Second, we proposed an estimating equation by using augmented inverse probability of complete cases for the semiparametric model using identity link function. The AIPW method is doubly robust and it can improve efficiency. The asymptotic properties of the propose AIPW estimators are established. The finite-sample properties of the estimators are investigated by the simulation studies. We use the auxiliary variables that may improve efficiency through their correlation with the phase-two covariates.

The proposed estimating methods are applied to analyze data from the RV144 vaccine efficacy trial.

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CHAPTER 1: INTRODUCTION

This chapter aims to review previous work and introduce our missing data on the cumulative incidence function. In section 1.1, we review basic background for competing risks data, how to summarize the competing risks probabilities and estimate those probabilities. In section 1.2, we review literature on regression models to estimate covariate effects for the cumulative incidence function, focusing on direct regression models such as Fine and Gray model (Fine and Gray, 1999) and direct binomial model (Scheike et al., 2008). We also review case-cohort study design (Prentice, 1986), which is a form of two-phase sampling (Kulich and Lin, 2004). In section 1.3, we will allow some covariates have missing data on the flexible direct binomial model proposed by Schike and others (Scheike et al., 2008).

1.1 Competing Risks Data

The competing risks models are concerned with the situation where each individual may be exposed to two or more mutually exclusive causes of failure. These causes may compete with each other, but the eventual failure occurs due to exactly one of these causes of failure. Each of these causes is called a competing risk.

Competing risks data have arisen in many research area such as biomedical, public health, actuarial science, social science and engineering. In cancer study, death due to cancer may be of interest and deaths due to other causes such as surgical mortality and old age are competing risks (Putter et al., 2007). The study of failures of engines fitted to heavy duty vehicles (Hinds, 1996) is associated with five different competing risks. A competing risks model is also used in modeling the unemployment time (Flinn and Heckman, 1983), where failure time is the waiting time till the end of unemployment and reasons for leaving unemployment were considered as competing risks.

In the presence of competing risks data, a problem arises when the occurrence of the event of interest is precluded by that of another event.

1.1.1 Modeling Competing Risks Data

Let T_k be the kth latent failure time with $k = 1, 2, \ldots, K$ and let Z be a possibly time dependent covariate vector. Let $T = \min_{1 \le k \le K}\{T_k\}$ be the first observed failure time with the cause of failure ϵ.

In early approaches, it is well known that there are identifiable problems in modeling competing risks data in terms of latent failure time (Tsiatis, 1975). The problems arise because we only observe the earliest of those latent failures T with failure type $\epsilon = k$.

Let $S(t_1, \ldots, t_k) = P(T_1 > t_1, \ldots, T_K > t_k)$ the joint survival distribution of the time to the k different events and let $S_k(t) = P(T_k > t) = S(0, \ldots, 0, t, 0, \ldots, 0)$ be the marginal distribution. Tsiatis (1975) has proved that neither the joint survival distributions nor the marginal distributions of the latent failure times are identifiable from the observed data if the competing risks are dependent. The observed data (T, ϵ) cannot provide enough information to tell which one is the true underlying distribution among two different marginal survival functions since they reproduce the same cause specific subdistribution function. Moreover, it is not possible to test whether the assumption of independence of the marginal failure time distributions is valid.

Alternatively, the cause-specific hazard and the cumulative hazard function have been proposed to summarize the competing risks probabilities. These two functions completely specify the joint distribution of the failure time T and the failure cause ϵ (Lawless, 2003) and both are directly estimable from the competing risks data (Prentice et al., 1978). None of them makes any assumptions about the relationship between the competing risks such as independence.

Under competing risks data, the cause-specific hazard function $\lambda_k(t)$ for cause k is defined as

$$\lambda_k(t|Z) = \lim_{\Delta t \to 0} \frac{P(t \le T < t + \Delta t, \epsilon = k | T \ge t, Z)}{\Delta t}, \quad k = 1, ..., K, \tag{1.1}$$

where represents that the instantaneous failure rate from cause k at time t in the presence of all causes of K failure types, given covariates Z. The cumulative cause-specific hazard is defined by

$$\Lambda_k(t|Z) \quad = \quad \int_0^t \lambda_k(s|Z) ds. \tag{1.2}$$

Failure types are assume to be distinct, one of $\{1, \ldots, K\}$. The overall hazard function conditional on a vector of covariates Z can be defined in terms of cause-specific hazard functions as

$$\lambda(t|Z) = \lim_{\Delta t \to 0} \frac{P(t \leq T < t + \Delta t | T \geq t, Z)}{\Delta t} = \sum_{k=1}^{K} \lambda_k(t|Z).$$

An equivalent identifiable quantity is the cumulative incidence function of cause k given covariates Z is defined as

$$F_k(t|z) = P(T \leq t, \epsilon = k|Z), \tag{1.3}$$

and it represents the probability of the subject failing from cause k before given time t in the presence of all the competing risks. The total cumulative incidence function is

$$F(t|Z) = P(T \leq t|Z) = \sum_{k=1}^{K} F_k(t|Z).$$

The overall survival function $S(t|Z)$ can be expressed in terms of the cause specific hazard function

$$S(t|Z) = P(T > t|Z) = \exp(-\int_0^t \sum_{k=1}^{K} \lambda_k(s|Z) ds) = \exp(-\sum_{k=1}^{K} \Lambda_k(s|Z)), \tag{1.4}$$

which is interpreted as the probability of not having failed from any cause at time t.

From the definition of cause-specific hazard function (1.1),

$$\lambda_k(t|Z)\Delta t \approx P(t \leq T < t + \Delta t, \epsilon = k | T \geq t, Z).$$

This implies that

$$\frac{P(t \leq T < t + \Delta t, \epsilon = k|Z)}{\Delta t} \approx P(T \geq t)\lambda_k(t|Z) \tag{1.5}$$

for a infinitesimal Δt. The left-hand side of (1.5) is approximately the probability density function for cause k when Δt goes to 0. Therefore, by integrating both side of (1.5), the cumulative probability of cause k in (1.3) can be expressed in terms of the cause specific hazards and the overall survival function as

$$F_k(t|Z) = \int_0^t \lambda_k(s|Z) S(s-) ds. \tag{1.6}$$

The cumulative incidence function is also called subdistribution function (Pintilie, 2007) because it is not a proper distribution function. More precisely, the cumulative probability of failing from cause k remains less than one, as $\lim_{t\to\infty} F_k(t) = P(\epsilon = k)$. Other alternative names for this function are the cause-specific failure probability (Gaynor et al., 1993), the crude incidence curve (Korn and Dorey, 1992) and absolute cause-specific risk (Benichou and Gail, 1990).

Unfortunately, the standard survival analysis methods such as Kaplan Meire estimator and Log-rank test have been often misused to analyze competing risks in medical literature. For example, the standard Kaplan-Meier estimator for the jth failure estimates $S_j(t|Z) = \exp(-\Lambda_j(t|Z))$. However, it cannot be interpreted as marginal survival function of the jth failure time. This only makes sense when analyzing data with a single event of occurrence even in the case of independent censoring (Lawless, 2003). Furthermore, the complement of the standard Kaplan-Meier estimator, which is the probability of a subject failing from cause j before or at time t, is greater than equal to the cumulative incidence function,

$$\begin{aligned} 1 - S_j(t|Z) &= \int_0^t \lambda_j(s|Z)\exp(-\Lambda_j(s))ds \\ &\geq \int_0^t \lambda_j(s|Z)\exp(-\sum_{k=1}^{K}\Lambda_k(s))ds = F_j(t|Z) \end{aligned} \tag{1.7}$$

with equality at time t if there is no competition, $\sum_{k=1,k\neq j}^{K}\Lambda_k(s) = 0$. This shows the bias of the standard Kaplan-Meier estimator if it is used to estimate $F_j(t|Z)$ (Putter et al., 2007).

These problems come from the violation of assumption on Kaplan-Meier estimator that the distributions of times to the competing events are independent of the distribution of time to the event of interest. For example, we consider censored subjects who never failed from the event of interest. Because of independence of censoring distribution assumption, the subjects who never experience the event of interest are treated as if they could fail at a later time. In this situation, the standard Kaplan-Meier estimator overestimates the probability of failure. The bias is greater when the hazard of the competing events is larger (Putter et al., 2007).

1.1.2 Estimation for Cumulative Incidence Function

The cumulative incidence function $F_k(t)$ for cause k can be estimated using equation (1.6) in the presence of competing risk data. Let $0 < t_1 < t_2 < \cdots < t_N$ be the ordered distinct time points at which failures of any cause occur. Let d_{ki} is the number of failures from type k at time t_i, $i = 1 \ldots N$. It is allowed for a different subject to fail from the same cause k at the same time t_i. Let n_i be the risk set at time t_i, which is the number of patients who were not censored and have not failed yet from any cause up to time t_i. The discretized version of the cause-specific hazard function (1.1) is

$$\lambda_k(t_i|Z) = P(T = t_i, \epsilon = k|T > t_{i-1}), \tag{1.8}$$

and it can be estimated by

$$\hat{\lambda}_k(t|Z) = \frac{d_{ki}}{n_i}, . \tag{1.9}$$

which is the proportion of subjects at risk who fail from cause k. By using the standard Kaplan-Meier estimator, the overall survival probability at time t_i including all types of events defined in (1.4) can be estimated by

$$\begin{aligned} \hat{S}(t_i) &= \hat{S}(t_{i-1})\hat{S}(t_i|t_{i-1}) = \hat{S}(t_{i-1})(1 - \hat{\lambda}(t_i)) \\ &= \prod_{i:t_i \le t} \left(1 - \sum_{k=1}^{K} \hat{\lambda}_k(t_i)\right) \\ &= \prod_{i:t_i \le t} (1 - \frac{d_i}{n_i}), \end{aligned} \tag{1.10}$$

where $d_i = \sum_{k=1}^{K} d_{ki}$ denotes the total number of failures from any cause at t_i. Thus, by using (1.9) and (1.10), the cumulative incidence function (1.3) of cause k can be estimated by

$$\widehat{F}_k(t|Z) = \sum_{i:t_i \le t} \hat{\lambda}_k(t_i|Z)\hat{S}(t_{i-1}). \tag{1.11}$$

In the presence of competing risks, the interrelation among failure types is one of the distinct problems in the analysis of failure times. The problem of testing the equality of two cause-specific hazard rates has been studied by Bagai and Kochar (989a,b), Yip and Lam (1992), Neuhaus (1991), Sen (1979), Aras and Deshpande (1992), Aly et al. (1994), Sun and Tiwari (1995),Sun (2001) and

Gilbert et al. (2004) among others. Alternatively, Gray (1988), Benichou and Gail (1990), Fine and Gray (1999), and McKeague et al. (2001) and Scheike et al. (2008) considered the problem on the cumulative incidence functions.

1.2 Literature Review

It is important to study the covariate effects on the cumulative incidence function of a particular failure since the cumulative incidence function is a proper summary statistics for analyzing competing risks data (Zhang et al., 2008).

In the past, hazard-based regression models have been studied by many authors including Prentice et al. (1978), Cheng et al. (1988), Shen and Cheng (1999), Lin and Ying (1994), and Scheike and Zhang (2002, 2003). They used to model all cause-specific hazard functions and then estimate the cumulative incidence function based on these cause-specific hazard functions. From these approaches, it is quite easy to obtain estimation of the cumulative incidence function if the cause specific hazards are correctly modeled. However, it is difficult to summarize the effect of covariates on the cumulative incidence function in the presence of competing risks data in a simple way.

In section 1.2.1, we review Cox proportional regression model as one of the most popular hazard-based regression models in the presence of competing risk. To overcome disadvantages of hazard-based competing risks model, Fine and Gray (1999) model based on subdistribution hazard and Direct binomial regression model Scheike et al. (2008) will be discussed in section 1.2.2.

1.2.1 Hazard Based Regression Model

Prentice et al. (1978) proposed Cox regression model for the cause-specific hazard $\lambda_k(t|Z)$ with possibly time dependent covariate vector Z by

$$\lambda_k(t|Z) = \lambda_{k,0}(t)\exp(\beta_k^T Z), \tag{1.12}$$

where $\lambda_{k,0}(t)$ is an unspecified cause-specific baseline hazard rate and the vector β_k represents covariate effects on cause k. Since there is no structure on $\lambda_{k,0}(t)$, then there is no need to make any assumption on the distribution of the lifetimes of the baseline population. The covariate effects in (1.12) are proportional for the cause-specific hazards. The model (1.12) treats failures from the cause of interest k as events, and failures from causes other than k as censored observations. Under independent censoring assumption, the cumulative incidence function for cause k given covariates Z in the presence of all competing risks is

$$F_k(t|Z) = \int_0^t \lambda_k(s|Z)\exp(-\sum_{k=1}^{K}\int_0^t \lambda_k(s|Z))ds. \tag{1.13}$$

The regression coefficients on the model (1.12) can be obtained by using standard likelihood methods.

However, the effects of the covariates on the cause-specific hazard rate cannot be translated directly to an effect on the cumulative incidence function (1.13) under the model (1.12). The reason is that the failures from competing events are ignored by treating them as censored observations ($\Delta = 0$) on the analysis of competing risks data, but the cumulative incidence function (1.13) for cause k not only depends on the hazard of cause k, but also on the hazards of all other causes. For example, the important covariate effects for the cause-specific hazards will highly influence the cumulative incidence probability, but an effect on the cause specific hazard for a particular cause k may have an adverse effect on the overall survival. Therefore, the significant covariate for all cause-specific hazards may not affect the cumulative incidence probability for cause k. Also, it is possible that some covariates influence the cumulative incidence function, but it may not be significantly associated with any of the cause-specific hazards (Scheike and Zhang, 2008). Therefore, the effect of covariates through modeling the cause specific hazards can not be simply used to predict the cumulative incidence function.

1.2.2 Direct Modeling on Cumulative Incidence Function

To overcome those problems as mentioned in section 1.2.1, some new regression approaches have been considered to evaluate the covariate effects on the cumulative incidence function directly.

Fine and Gray (1999) developed a regression model that directly links the regression coefficients with the cumulative incidence function using subdistribution hazard introduced by Gray (1988). They consider a semiparametric regression model with transformation $g(u) = log\{-log(1-u)\}$ for the cumulative incidence function, which is

$$g\{F_k(t|Z)\} \quad = \quad h_{k,0}(t) + \beta_k^{\mathsf{T}} Z, \;\; k = 1, ..., K, \tag{1.14}$$

where $h_{k,0}(\cdot)$ is a completely unspecified, invertible, and monotone increasing function and β_k is a $p \times 1$ parameter vector related to cause k. The transformation $g(u) = log\{-log(1-u)\}$ leads to a reasonable assumption that there is a constant difference between cumulative incidence functions for two individuals with covariate vectors Z_1 and Z_2. That is, $g\{F_k(t|Z_1)\} - g\{F_k(t|Z_2)\} = \{Z_1 - Z_2\}^{\mathsf{T}}\beta_k$ for all t.

To directly estimate the model (1.14), they used the subdistribution hazard (Gray, 1988) for cause k

$$\begin{aligned}
\lambda_k^*(t|z) &= \lim_{\Delta t \to 0} \frac{P(t \le T < t + \Delta t, \epsilon = k | T \ge t \cup \{T < t, \epsilon \ne k\})}{\Delta t} \\
&= \frac{dF_k(t|z)/dt}{1 - F_k(t|z)} \\
&= \frac{-dlog\{1 - F_k(t|z)\}}{dt}. \qquad (1.15)
\end{aligned}$$

This subdistribution hazard function for cause k represents the probability of a subject to fail from cause k in a very small time interval Δt, given the subject experienced no event until time t or experienced an event other than k before time t. By the ordered distinct time points and definitions in subsection 1.1.2, it can be estimated at time t_i by

$$\hat{\lambda}_k^*(t_i|z) = \frac{d_{ki}}{n_i^*}, \tag{1.16}$$

where d_{ki} denotes the number of failures of cause k at time t_i and n_i^* is the modified risk set including all subjects who did not experience any event until time t_i and all subjects that failed before t_i from a cause other than k. Thus, the modified risk set has subjects having already experienced events other than cause k. Those subjects are always at future risks of event of interest cause k.

By using a semiparametric proportional hazards model with time varying covariates $Z(t)$,

$$\lambda_k^*(t|Z) \quad = \quad \lambda_{k,0}^*(t|Z) \exp(Z^{\mathsf{T}}(t)\beta_k) \tag{1.17}$$

where $\lambda_{k,0}^*(t|z)$ is a completely unspecified, nonnegative function in time t and by applying $g(u) =$

$log\{-log(1-u)\}$ transformation to (1.14) with $h_{k,0}(t) = log\{\int_0^t \lambda^*_{k,0}(t)\}$, they proposed the following cumulative incidence function for cause k

$$F_k(t|Z) \quad = \quad 1 - \exp\left[-\int_0^t \lambda^*_{k,0}(s)\exp\{\beta_k^T Z(s)\}ds\right], \tag{1.18}$$

which enables us to assess the effect of the covariates on the cumulative incidence function directly.

With complete data, the standard partial likelihood method with modified risk set can be applied (Fine and Gray, 1999). For right censored incomplete competing risks data, Fine and Gray (1999) utilized inverse probability of censoring weighted (ICPW) method (Robins and Rotnitzky, 1992) to construct an unbiased estimating function from the score function of the complete data partial likelihood (Fine and Gray, 1999). This approach can be analyzed by using the 'comprsk' package for R developed by Robert Gray.

However, the Fine and Gray model may not fit the data well even though it is easy to decide if covariates significantly affect the cumulative incidence function for a specific cause of failure (Scheike and Zhang, 2008). To remedy this problem, Scheike et al. (2008) have proposed a class of general models containing the Fine and Gray model.

Scheike et al. (2008) proposed a fully nonparametric model to evaluate covariate effects directly on the cumulative incidence function for cause k, that is

$$h\{F_k(t;\boldsymbol{\eta})\} = X_i^{\mathsf{T}}\eta(t), \;\; i = 1, ..., n \tag{1.19}$$

where $h(\cdot)$ is a known link function and $\eta(t)$ is time varying effects of the covariate X_i. The $(p+1)-$ dimensional regression coefficient $\eta(t)$ is an unspecified function and $X_i = (1, X_{i1}, \ldots, X_{ip})^{\mathsf{T}}$. The first component of X_i yields the time-dependent intercept. This model is very flexible since it allows covariates to have time varying effects. The model (1.19) contains the Aalen's generalized additive model by using log link function $h(x) = log(1-x)$. They proposed a direct binomial regression method for a regression analysis by using the inverse probability of censoring weighted response.

They also proposed a class of general semiparametric models by

$$h\{F_j(t|X,Z)\} = \{X_i^{\mathsf{T}}\eta(t)\}g(\gamma, Z_i, t), \tag{1.20}$$

$$h\{F_j(t|X,Z)\} = X_i^{\mathsf{T}}\eta(t) + g(\gamma, Z_i, t) \tag{1.21}$$

where g is a known function, $\eta(t)$ is the time varying effects of $X_i = (1, X_{i1}, \dots, X_{ip})^{\mathsf{T}}$ and γ is a time invariant coefficient of $Z_i = (Z_{i1}, \dots, Z_{iq})^{\mathsf{T}}$.

With log link function $h(x) = log(1-x)$ and $g(\gamma, Z_i, t) = \exp(\gamma^{\mathsf{T}} Z_i)$, the multiplicative model (1.20) reduces to a Cox-Aalen model which contains the Cox model and Aalen's additive model. When $x = 1$, the model (1.20) reduces to Fine and Gray (1999) model. With log link function $h(x) = log(1-x)$ and $g(\gamma, Z_i, t) = \gamma^{\mathsf{T}} Z_i t$, the model (1.21) generates a partially semiparametric additive model (McKeague and Sasieni, 1994). When $x = 1$, the model (1.21) reduces to the Lin and Ying (1994) special additive model.

Scheike and Zhang (2008) also proposed estimating equations to estimate $\eta(t)$ and γ simultaneously. They derived asymptotic results and studied the predicted cumulative incidence function for a given set of covariate values. Scheike and Zhang (2008) considered a new simple goodness-of-fit procedure for the proportional subdistribution hazards assumption.

One drawback for both direct binomial and subdistribution approaches is to estimate the censoring distribution for each individual. Usually, the Kaplan-Meier estimator is utilized for the censoring distribution. This non-augmented inverse probability weighting technique was firstly proposed by Koul et al. (1981). By using the semiparametric efficiency theory in Bickel et al. (1993), Robins and Rotnitzky (1992) showed that regression modeling of the censoring distribution improves efficiency of the inverse probability weighting technique. This is because each censored observation carries information about the relationship between event time and covariates even if the censoring is independent of the covariates.

We will allow covariates to have missing values in the general semiparametric additive model (1.21) in subsection 1.3. We develop estimating equations to analyze the missing model in chapter 2 and chapter 3.

1.2.3 Case-Cohort/Two Phase Sampling

Epidemiologic cohort studies and disease prevention trials often necessitate the follow-up of several thousand subjects for a number of years and thus can be prohibitively expensive (Prentice, 1986). The assembly of covariate histories for all cohort members result in much cost and effort in such studies. Therefore, it is an important issue to reduce cost in those studies and achieve the same goals as a cohort study.

Among several study designs proposed to reduce cost, the case-cohort design has been widely used in those studies to assess the effects of possibly time-dependent covariates on a failure time. The case-cohort design has been proposed by Prentice (1986). Under this design, the covariate histories are investigated only for the subjects who experience the event of interest during the follow-up period (the cases) and for a relatively small random sample (the subcohort) from the original cohort. This design is very useful where the occurrence of the failure event is rare in large cohort studies since it is unnecessary to investigate the covariates of event-free subjects more than it needs to be done. The case-cohort data is a biased sample and thus applying standard methods for randomly sampled data to the biased data may result in biased estimation (Sun et al., tted).

The case-cohort design is also a form of two-phase sampling. At the first phase, the study cohort is randomly sampled from a general population. The first phase covariate data are observed on all of the subjects in the cohort. There are treatment type, age and gender as examples. At the second phase, the subcohort is randomly selected from the study cohort. Complete covariate histories are assembled for the cases and the subcohort at this stage by collecting the second phase covariate including all of the expensive covariates which are not measured at the first phase. Those covariates are called the second phase covariate data.

The Cox (1972, 1975) proportional hazard model has been widely used in analysis of case cohort data. Many authors have proposed statistical methods for case-cohort studies by modifying the full data partial likelihood score function for the Cox model, giving the inverses of true or estimated sampling probabilities to the score functions as weight functions, including Prentice (1986), Self and Prentice (1988), Kalbfleisch and Lawless (1988), Lin and Ying (1993), Barlow (1994), Chen and

Lo (1999), Sørensen and P.K. (2000), Borgan et al. (2000), Chen (2001), Kulich and Lin (2004), and Samuelsen et al. (2007). The Cox model assumes that the hazard functions associated with different covariate values are proportional over time. This assumption may be too restrictive and the Cox model does not always fit data well in practice. Alternatively, the accelerated failure time model and the proportional odds model have been studied by Chen (2001) and Kong and Cai (2009), respectively.

Additive hazard model is another popular framework for the analysis of case-cohort data. This is because the risk differences between different treatment can be easily derived from the regression coefficients. It also gives a valuable public health interpretation. Kulich and Lin (2000) applied additive hazards model (Lin and Ying, 1993) to case-cohort study. Kang et al. (2013) recently proposed an estimation method for case-cohort data with the simple additive model of Lin and Ying (1994) that allows only constant covariate effects. Sun et al. (tted) proposed an estimation procedure for the semiparametric additive hazards model with case-cohort/two-phase sampling data, which allows the effects of some covriates to be time varying while specifying the effects of others to be constant. They used the inverse probability weighting of complete-case technique of Horvitz and Thompson (1952). With this approach, if a subject has a missing value for one covariate, then the observed values of other covariates together with the observed failure/censoring time of the same subject are not utilized. This leads to loss of efficiency. They also proposed an augmented estimating equation on the basis of the inverse probability weighting of complete cases by adapting the theory of Robins et al. (1994). By doing so, they showed the efficiency of the proposed estimators has been improved.

1.3 Model

Let T_i be the failure time for the ith subject, $i = 1, \ldots, n$, and $\epsilon_i \in \{1, 2, \ldots, k\}$ denote the failure type. Let $X_i = (1, X_{i1}, \ldots, X_{ip})^T$ and $Z_i = (Z_{i1}, \ldots, Z_{iq})^T$ are $(p+1)$- and q-dimensional possibly time-dependent covariate vectors, respectively. Let C_i be the right censoring time for the ith subject. Let $\Delta_i = I(T_i \leq C_i)$ be the indicator which is 1 when the observation is uncensored. The observed n independent identically distributed data can be represented by $Y_i = (X_i, Z_i, \tilde{T}_i, \tilde{\epsilon_i})$, where $\tilde{T}_i = min(T_i, C_i)$ and $\tilde{\epsilon_i} = \epsilon_i \Delta_i$. The value $\tilde{\epsilon_i} = \epsilon_i$ indicates that the system failure time is observed at $\tilde{T}_i$ and the cause of failure is of type ϵ_i, where $\epsilon_i = 1, 2, \ldots, k$. Let $[a, \tau]$ be the time period from which data are collected. We assume that (T_i, ϵ_i) are independent of C_i given covariates (X_i, Z_i). In follow-up studies, the covariates of a subject are only meaningful in the time interval when the subject is at-risk and still in the study, i.e., $t \leq \tilde{T}_i$.

Let $F_1(t|X_i, Z_i) = P(T_i \leq t, \epsilon_i = 1|X_i, Z_i)$ be the conditional cumulative incidence function given covariates (X_i, Z_i) for each ith subject. We consider the following the additive semiparametric model for $F_1(t|X_i, Z_i)$:

$$F_1(t; X_i, Z_i) = h\{X_i^{\mathsf{T}} \eta(t) + g(\gamma, Z_i, t)\} \tag{1.22}$$

where $h(\cdot)$ is a known link function, $g(\cdot)$ is a known function of (γ, Z_i, t), $\eta(t)$ is a $(p+1)$-dimensional vector of time-dependent regression coefficients and γ is a q-dimensional vector of time-invariant coefficients. The first component of X_i yields the time-dependent intercept. Under model (1.22), the effects of the covariates X_i change with time while the effects of Z_i are time-invariant.

Suppose that X_i has two parts $(X_i^{(1)}, X_i^{(2)})$. The covariates $X_i^{(1)}$ and Z_i are observed for all the cohort members, but $X_i^{(2)}$ is only observed for a subset(subcohort, phase two sample) of the study subjects. Let ξ_i be the indicator of whether the subject i is selected into the phase-two sample. The subject i with $\xi_i = 1$ has fully observed X_i and Z_i. The subject i with $\xi_i = 0$ does not have the observed values for $X_i^{(2)}$. Let $\mathcal{V}_i = \{\tilde{T}_i, \Delta_i, \tilde{\epsilon_i}, X_i^{(1)}, Z_i, A_i\}$ where A_i denotes possible auxilary variables that may be informative for selection of phase-two sample and / or phase-two covariates. We assume that the probability a subject is missing the phase-two covariates $X_i^{(2)}$ does not depend on the values of these covariates $P(\xi_i = 1|X_i^{(2)}, \mathcal{V}_i) = P(\xi_i = 1|\mathcal{V}_i)$. This assumption is the missing at random (MAR) assumption (Rubin, 1976). However, the selection probability may depend on any of the phase-one information $\mathcal{V}_i$.

Let $(\mathcal{V}_i, X_i^{(2)}, \xi_i)$, $i = 1, 2, \ldots, n$ be identically independent distributed data. The observed data are $(\mathcal{V}_i, \xi_i X_i^{(2)}, \xi_i), i = 1, 2, \ldots, n$. That is, $\{\tilde{T}_i, \Delta_i, \tilde{\epsilon_i}, X_i, Z_i, A_i\}$ are observed for a subject with $\xi_i = 1$, and $\{\tilde{T}_i, \Delta_i, \tilde{\epsilon_i}, X_i^{(1)}, Z_i, A_i\}$ are observed if $\xi_i = 0$. The selection probability, defined as the conditional probability that $X_i^{(2)}$ is observed, is $S_i = P(\xi_i = 1|\mathcal{V}_i)$. This selection probability S_i

may depend on outcomes $\tilde{\epsilon}_i$ based on the competing causes of failure and the censoring indicator. Under the competing risks model, classical case-cohort design implies that $S_i = 1$ if $\tilde{\epsilon}_i = 1$ and $S_i = P(\xi_i = 1|\mathcal{V}_i, \tilde{\epsilon}_i \neq 1) < 1$ if $\tilde{\epsilon}_i \neq 1$. A subject is referred to as the case if the failure time is observed and the failure has cause 1; and the non-case, otherwise.

CHAPTER 2: ANALYSIS OF A SEMIPARAMETRIC CUMULATIVE INCIDENCE MODEL WITH MISSING COVARIATES USING INVERSE PROBABILITY WEIGHTED METHOD

In this chapter, we analysis our missing model introduced in section 1.3 in chapter 1 by using inverse probability weighting of complete cases proposed by Horvitz and Thompson (1952). The estimation procedure is given in section 2.1. we estimate the selection probability and censoring distribution. Based on direct binomial estimation on the weighted responses (Scheike et al., 2008), we also develop estimating equation for the missing model. Asymptotic properties of the inverse probability weighting estimators will be discussed in section 2.2. We conduct simulation studies under the subdistribution models to evaluate the finite sample properties of the IPW methods in section 2.3.

2.1 Estimation

2.1.1 Estimation Procedure

The selection probability S_i is unknown in practice, but it can be estimated based on a parametric model. Assume that $\varphi(\mathcal{V}_i, \theta)$ is the parametric model for the probability of complete-case $S_i = P(\xi_i = 1|\mathcal{V}_i)$, where θ is a finite dimensional vector of parameters. For example, one can assume that the logistic model is $\text{logit}(\varphi_1(\mathcal{V}_i, \theta_1)) = \theta_1^\top \mathcal{V}_i$ for those $\tilde{\epsilon}_i = 1$ and the different logistic model is $\text{logit}(\varphi_2(\mathcal{V}_i, \theta_2)) = \theta_2^\top \mathcal{V}_i$ for those $\tilde{\epsilon}_i \neq 1$. Let $\theta = (\theta_1^\top, \theta_2^\top)^\top$. The parameter θ can be estimated by $\hat{\theta}$ as the maximizer of the observed data likelihood:

$$
\begin{aligned}
\mathrm{L}(\theta) &= \Pi_{i=1}^n \{\varphi_1(\mathcal{V}_i, \theta_1)\}^{\xi_i I(\tilde{\epsilon}_i = 1)} \{1 - \varphi_1(\mathcal{V}_i, \theta_1)\}^{(1-\xi_i) I(\tilde{\epsilon}_i = 1)} \\
&\quad \cdot \Pi_{i=1}^n \{\varphi_2(\mathcal{V}_i, \theta_2)\}^{\xi_i I(\tilde{\epsilon}_i \neq 1)} \{1 - \varphi_2(\mathcal{V}_i, \theta_2)\}^{(1-\xi_i) I(\tilde{\epsilon}_i \neq 1)} \qquad (2.1)
\end{aligned}
$$

where $I(D)$ is the indicator function of the set D.

Let $N_i(t) = I(T_i \leq t, \epsilon_i = 1)$ be the counting process associated with cause 1 and let $G(t|X_i, Z_i) =$

$P(C_i > t|X_i, Z_i)$ be the conditional survival function of the censoring time for $0 \le t \le \tau$. Assume that there exists a positive number $0 < \delta \le 1$ such that $G(\tau|x, z) \ge \delta > 0$ for (x, z) in the range of (X_i, Z_i). Under conditional independence between C_i and (T_i, ϵ_i) given the covariates (X_i, Z_i), we have $E(\Delta_i|X_i, Z_i, T_i, \epsilon_i) = G(T_i|X_i, Z_i)$. It follows that

$$\begin{aligned} E\{\frac{\Delta_i N_i(t)}{G(T_i|X_i, Z_i)}|X_i, Z_i\} &= E[E\{\frac{\Delta_i N_i(t)}{G(T_i|X_i, Z_i)}|T_i, X_i, Z_i, \epsilon_i\}|X_i, Z_i] \\ &= E[\frac{1}{G(T_i|X_i, Z_i)} E\{\Delta_i N_i(t)|T_i, X_i, Z_i, \epsilon_i\}|X_i, Z_i] \\ &= E[N_i(t)|X_i, Z_i] \\ &= P(T_i \le t, \epsilon_i = 1|X_i, Z_i) = F_1(t|X_i, Z_i). \end{aligned} \tag{2.2}$$

We consider the estimating equation based on the weighted response $\Delta_i N_i(t)/G(T_i|X_i, Z_i)$. In practice, the censoring distribution $G(t|x_i, z_i)$ is often unknown and can be estimated by the Kaplan-Meier estimator or by using a regression model for censoring times such as a Cox regression model or an additive Aalen regression model to improve efficiency. For simplicity, we use the Kaplan-Meier estimator $\widehat{G}(t)$ for $G(t)$.

Asymptotic results of the maximum likelihood estimator $\hat{\theta}$ and the censoring distribution $G(t)$ will be discussed in section 2.2.

2.1.2 Inverse Probability Weighted Complete-Case Estimation

Following Horvitz and Thompson (1952), the inverse probability weighting of the complete cases has been often used in missing data analysis.

Let $\boldsymbol{D}_{\boldsymbol{\eta},i}(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma}) = \partial F_1(t; X_i, Z_i)/\partial \boldsymbol{\eta}(t)$ and $\boldsymbol{D}_{\boldsymbol{\gamma},i}(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma}) = \partial F_1(t; X_i, Z_i)/\partial \boldsymbol{\gamma}$. Let $\psi_i(\theta) = \xi_i/\varphi(\mathcal{V}_i, \theta)$, where $\varphi(\mathcal{V}_i, \theta) = I(\tilde{\epsilon}_i = 1)\varphi_1(\mathcal{V}_i, \theta_1) + I(\tilde{\epsilon}_i \ne 1)\varphi_2(\mathcal{V}_i, \theta_2)$. By modifying the estimating equations of Scheike et al. (2008), the regression functions $\boldsymbol{\eta}(t)$ and parameters $\boldsymbol{\gamma}$ in model (1.22) can be estimated based on the following estimating functions:

$$\boldsymbol{U}_{\boldsymbol{\eta}}(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma}, \hat{\theta}) = \sum_{i=1}^{n} \psi_i(\hat{\theta}) \boldsymbol{D}_{\boldsymbol{\eta},i}(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma}) w_i(t) \left(\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)} - F_1(t; \boldsymbol{X}_i, \boldsymbol{Z}_i) \right), \tag{2.3}$$

$$\boldsymbol{U}_{\boldsymbol{\gamma}}(\tau, \boldsymbol{\eta}(\cdot), \boldsymbol{\gamma}, \hat{\theta}) = \sum_{i=1}^{n} \int_0^{\tau} \psi_i(\hat{\theta}) \boldsymbol{D}_{\boldsymbol{\gamma},i}(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma}) w_i(t) \left(\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)} - F_1(t; \boldsymbol{X}_i, \boldsymbol{Z}_i) \right) dt, \tag{2.4}$$

where $w_i(t)$ is a weight function.

Let $\boldsymbol{W}(t) = \text{diag}(w_i(t))$ and $\boldsymbol{\Psi}(\theta) = \text{diag}(\psi_i(\theta))$. Let $\boldsymbol{F}_1(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma})$ be the $n \times 1$ vector of the model $F_1(t; \boldsymbol{X}_i, \boldsymbol{Z}_i)$ in (1.22) for $i = 1, \ldots, n$, denoting the ith element of the vector $\boldsymbol{F}_1(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma})$ as $F_{1i}(t)$. $\boldsymbol{R}(t)$ be the $n \times 1$ vector of weighted responses $\Delta_i\, N_i(t)/\widehat{G}(T_i)$, $\boldsymbol{D}_{\boldsymbol{\eta}}(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma})$ and $\boldsymbol{D}_{\boldsymbol{\gamma}}(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma})$ be the $n \times (p+1)$ and $n \times q$ matrices with the ith rows equal to $\boldsymbol{D}_{\boldsymbol{\eta},i}(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma})$ and $\boldsymbol{D}_{\boldsymbol{\gamma},i}(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma})$, respectively. The estimating equations given in (2.3) and (2.4) are equivalent to

$$\boldsymbol{U}_{\boldsymbol{\eta}}(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma}, \hat{\theta}) = (\boldsymbol{D}_{\boldsymbol{\eta}}(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma}))^{\mathsf{T}} \boldsymbol{W}(t) \boldsymbol{\Psi}(\hat{\theta}) \left\{ \boldsymbol{R}(t) - \boldsymbol{F}_1(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma}) \right\}, \tag{2.5}$$

$$\boldsymbol{U}_{\boldsymbol{\gamma}}(\tau, \boldsymbol{\eta}(\cdot), \boldsymbol{\gamma}, \hat{\theta}) = \int_0^\tau (\boldsymbol{D}_{\boldsymbol{\gamma}}(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma}))^{\mathsf{T}} \boldsymbol{W}(t) \boldsymbol{\Psi}(\hat{\theta}) \left\{ \boldsymbol{R}(t) - \boldsymbol{F}_1(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma}) \right\} dt. \tag{2.6}$$

Let $l^\infty[0, \tau]$ be the set of uniformly bounded functions on $[0, \tau]$ and $\tilde{B} = (l^\infty[0, \tau])^{p+1} \times \mathbb{R}^q$. The estimating functions $\boldsymbol{U}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(\boldsymbol{\eta}, \boldsymbol{\gamma}, \hat{\theta})=\{\boldsymbol{U}_{\boldsymbol{\eta}}(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma}, \hat{\theta}), \boldsymbol{U}_{\boldsymbol{\gamma}}(\tau, \boldsymbol{\eta}(\cdot), \boldsymbol{\gamma}, \hat{\theta})\}$ are the mappings from $\tilde{B}$ to $\tilde{B}$. The inverse probability weighting of the complete-case estimators $\widehat{\boldsymbol{\eta}}(t)$ and $\widehat{\boldsymbol{\gamma}}$ of $\boldsymbol{\eta}(t)$ and $\boldsymbol{\gamma}$ solve the join estimating equation $\boldsymbol{U}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(\boldsymbol{\eta}, \boldsymbol{\gamma}, \hat{\theta})$, that is, $\boldsymbol{U}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(\widehat{\boldsymbol{\eta}}, \widehat{\boldsymbol{\gamma}}, \hat{\theta}) = 0$.

By mimicking the procedure of Scheike et al. (2008), the estimating equations (2.5) and (2.6) can be solved by using an iterative algorithm. Consider the following Taylor expansion of $\boldsymbol{F}_1(t, \widehat{\boldsymbol{\eta}}(t), \widehat{\boldsymbol{\gamma}})$ around the values $(\boldsymbol{\eta}_0(t), \boldsymbol{\gamma}_0)$:

$$\begin{aligned} \boldsymbol{F}_1(t, \widehat{\boldsymbol{\eta}}(t), \widehat{\boldsymbol{\gamma}}) &= \boldsymbol{F}_1(t, \boldsymbol{\eta}_0(t), \boldsymbol{\gamma}_0) + \boldsymbol{D}_{\boldsymbol{\eta}}(t, \boldsymbol{\eta}_0(t), \boldsymbol{\gamma}_0) \left\{ \widehat{\boldsymbol{\eta}}(t) - \boldsymbol{\eta}_0(t) \right\} \\ &+ \boldsymbol{D}_{\boldsymbol{\gamma}}(t, \boldsymbol{\eta}_0(t), \boldsymbol{\gamma}_0) \left\{ \widehat{\boldsymbol{\gamma}} - \boldsymbol{\gamma}_0 \right\} + o_p(n^{-\frac{1}{2}}). \end{aligned} \tag{2.7}$$

Replacing it into the score equations (2.5) and (2.6), and denoting $\boldsymbol{D}_{\boldsymbol{\eta}}(t) = \boldsymbol{D}_{\boldsymbol{\eta}}(t, \boldsymbol{\eta}_0(t), \boldsymbol{\gamma}_0)$, $\boldsymbol{D}_{\boldsymbol{\gamma}}(t) = \boldsymbol{D}_{\boldsymbol{\gamma}}(t, \boldsymbol{\eta}_0(t), \boldsymbol{\gamma}_0)$ and $\boldsymbol{F}_1(t) = \boldsymbol{F}_1(t, \boldsymbol{\eta}_0(t), \boldsymbol{\gamma}_0)$, we have

$$\boldsymbol{U}_{\boldsymbol{\eta}}(t, \widehat{\boldsymbol{\eta}}(t), \widehat{\boldsymbol{\gamma}}, \hat{\theta}) = \boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t) \boldsymbol{W}(t) \boldsymbol{\Psi}(\hat{\theta}) \left[\boldsymbol{R}(t) - \boldsymbol{F}_1(t) - \boldsymbol{D}_{\boldsymbol{\eta}}(t) \left\{ \widehat{\boldsymbol{\eta}}(t) - \boldsymbol{\eta}_0(t) \right\} - \boldsymbol{D}_{\boldsymbol{\gamma}}(t) \left\{ \widehat{\boldsymbol{\gamma}} - \boldsymbol{\gamma}_0 \right\} \right] + o_p(n^{\frac{1}{2}}) \tag{2.8}$$

$$\boldsymbol{U}_{\boldsymbol{\gamma}}(\tau, \widehat{\boldsymbol{\eta}}(\cdot), \widehat{\boldsymbol{\gamma}}, \hat{\theta}) = \int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t) \boldsymbol{W}(t) \boldsymbol{\Psi}(\hat{\theta}) \left[\boldsymbol{R}(t) - \boldsymbol{F}_1(t) - \boldsymbol{D}_{\boldsymbol{\eta}}(t) \left\{ \widehat{\boldsymbol{\eta}}(t) - \boldsymbol{\eta}_0(t) \right\} - \boldsymbol{D}_{\boldsymbol{\gamma}}(t) \left\{ \widehat{\boldsymbol{\gamma}} - \boldsymbol{\gamma}_0 \right\} \right] dt + o_p(n^{\frac{1}{2}}). \tag{2.9}$$

Solving equations (2.8) and (2.9) for $\widehat{\boldsymbol{\eta}}(t)$ and $\widehat{\boldsymbol{\gamma}}$, the estimators for $\boldsymbol{\gamma}$ and $\boldsymbol{\eta}(t)$ are given by

$$\widehat{\boldsymbol{\gamma}} = \boldsymbol{\gamma}_0 + \left\{\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat{\theta})\right\}^{-1} \boldsymbol{B}_{\boldsymbol{\gamma}}(\hat{\theta}) + o_p(n^{-\frac{1}{2}}) \tag{2.10}$$

$$\begin{aligned} \widehat{\boldsymbol{\eta}}(t) &= \boldsymbol{\eta}_0(t) \\ &+ \{\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\hat{\theta})\}^{-1}\{\boldsymbol{D}_{\boldsymbol{\eta}}(t)\}^{\mathsf{T}}\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\Big\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t)-\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\{\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat{\theta})\}^{-1}\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat{\theta})\Big\} + o_p(n^{-\frac{1}{2}}) \end{aligned} \tag{2.11}$$

where

$$\begin{aligned} \boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta) &= \int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta)\boldsymbol{H}(t,\theta)\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\,dt, \\ \boldsymbol{B}_{\boldsymbol{\gamma}}(\theta) &= \int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta)\boldsymbol{H}(t,\theta)\left\{\boldsymbol{R}(t) - \boldsymbol{F}_1(t)\right\}\,dt, \\ \boldsymbol{H}(t,\theta) &= I - \boldsymbol{D}_{\boldsymbol{\eta}}(t)\left[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta)\right]^{-1}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta), \\ \boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta) &= \boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta)\boldsymbol{D}_{\boldsymbol{\eta}}(t). \end{aligned} \tag{2.12}$$

The estimators $\widehat{\boldsymbol{\eta}}(t)$ and $\widehat{\boldsymbol{\gamma}}$ can be solved iteratively similar to Scheike et al. (2008) based on the equations (2.10) and (2.11). Specifically, the $(m+1)$th iterative estimators are obtained by replacing $\widehat{\boldsymbol{\gamma}}^{(m)}$ and $\widehat{\boldsymbol{\eta}}^{(m)}(t)$ for $\boldsymbol{\gamma}_0$ and $\boldsymbol{\eta}_0(t)$ on the right side of (2.10) and (2.11) as the mth step estimators, and replacing $\widehat{\boldsymbol{\gamma}}^{(m+1)}$ and $\widehat{\boldsymbol{\eta}}^{(m+1)}(t)$ for $\widehat{\boldsymbol{\gamma}}$ and $\widehat{\boldsymbol{\eta}}(t)$ on the left side (2.10) and (2.11) as the $(m+1)$th step estimators;

$$\widehat{\boldsymbol{\gamma}}^{(m+1)} = \widehat{\boldsymbol{\gamma}}^{(m)} + \left\{\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}^{(m)}(\hat{\theta})\right\}^{-1} \boldsymbol{B}_{\boldsymbol{\gamma}}^{(m)}(\hat{\theta}). \tag{2.13}$$

$$\begin{aligned} \widehat{\boldsymbol{\eta}}^{(m+1)}(t) &= \widehat{\boldsymbol{\eta}}^{(m)}(t) \\ &+ \{\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}^{(m)}(t,\hat{\theta})\}^{-1}\{\boldsymbol{D}_{\boldsymbol{\eta}}^{(m)}(t)\}^{\mathsf{T}}\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\left\{\boldsymbol{R}(t)-\boldsymbol{F}_1^{(m)}(t)-\boldsymbol{D}_{\boldsymbol{\gamma}}^{(m)}(t)\{\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}^{(m)}(\hat{\theta})\}^{-1}\boldsymbol{B}_{\boldsymbol{\gamma}}^{(i)}(\hat{\theta})\right\}, \end{aligned} \tag{2.14}$$

where $\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}^{(m)}(\hat{\theta})$, $\boldsymbol{B}_{\boldsymbol{\gamma}}^{(m)}(\hat{\theta})$, $\boldsymbol{H}^{(m)}(t,\hat{\theta})$ and $\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}^{(m)}(t,\hat{\theta})$ are mth step estimators of $\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat{\theta})$, $\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat{\theta})$, $\boldsymbol{H}(t,\hat{\theta})$ and $\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\hat{\theta})$ obtained by plugging mth step estimators $(\widehat{\boldsymbol{\eta}}^{(m)}(t),\ \widehat{\boldsymbol{\gamma}}^{(m)})$ of $(\boldsymbol{\eta}(t),\boldsymbol{\gamma})$ into $\boldsymbol{D}_{\boldsymbol{\eta}}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})$, $\boldsymbol{D}_{\boldsymbol{\gamma}}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})$ and $\boldsymbol{F}_1(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})$. This approach can be implemented by using 'timereg' package for R developed by (Scheike and Zhang, 2008).

2.2 Asymptotic Results

2.2.1 Asymptotic Results Concerning $\hat{\theta}$

The estimation method requires the following property on the maximal likelihood estimator $\hat{\theta}$ and the censoring distribution $G(t)$.

Proposition 1. *Let $\varphi_1(\mathcal{V}_i, \theta_1)$ and $\varphi_2(\mathcal{V}_i, \theta_2)$ be the parametric models for $P(\xi_i = 1|\mathcal{V}_i, \tilde{\epsilon}_i = 1)$ and $P(\xi_i = 1|\mathcal{V}_i, \tilde{\epsilon}_i \neq 1)$, respectively. Assume that the logistic model logit$(\varphi_1(\mathcal{V}_i, \theta_1)) = \theta_1^{\mathsf{T}}\mathcal{V}_i$ holds for those $\tilde{\epsilon}_i = 1$ and the different logistic model logit$(\varphi_2(\mathcal{V}_i, \theta_2)) = \theta_2^{\mathsf{T}}\mathcal{V}_i$ holds for those $\tilde{\epsilon}_i \neq 1$. Let $\theta = (\theta_1^{\mathsf{T}}, \theta_2^{\mathsf{T}})^{\mathsf{T}}$ and let $\theta_0 = (\theta_{01}^{\mathsf{T}}, \theta_{02}^{\mathsf{T}})^{\mathsf{T}}$ be the true value of θ. Then the maximum likelihood estimator $\hat{\theta}$ satisfies*

$$n^{\frac{1}{2}}(\hat{\theta} - \theta_0) = n^{-\frac{1}{2}} \left[J\left(\mathcal{V}_i, \theta_0\right)\right]^{-1} \sum_{i=1}^{n} U(\mathcal{V}_i, \theta_0) + o_p(1), \tag{2.15}$$

where the fisher information matrix

$$J(\mathcal{V}_i, \theta_0) = \begin{pmatrix} E_{\theta_0}\left[I(\tilde{\epsilon}_i = 1)\frac{\exp\{\theta_{01}^{\mathsf{T}}\mathcal{V}_i\}\mathcal{V}_i\mathcal{V}_i^{\mathsf{T}}}{(1+\exp^{\theta_{01}^{\mathsf{T}}\mathcal{V}_i})^2}\right] & 0 \\ 0 & E_{\theta_0}\left[I(\tilde{\epsilon}_i \neq 1)\frac{\exp\{\theta_{02}^{\mathsf{T}}\mathcal{V}_i\}\mathcal{V}_i\mathcal{V}_i^{\mathsf{T}}}{(1+\exp^{\theta_{02}^{\mathsf{T}}\mathcal{V}_i})^2}\right] \end{pmatrix}, \tag{2.16}$$

and

$$U(\mathcal{V}_i, \theta_0) = \begin{pmatrix} I(\tilde{\epsilon}_i = 1)[\xi_i\mathcal{V}_i - \frac{\mathcal{V}_i\exp\{\theta_{01}^{\mathsf{T}}\mathcal{V}_i\}}{1+\exp^{\theta_{01}^{\mathsf{T}}\mathcal{V}_i}}]^{\mathsf{T}} \\ \\ I(\tilde{\epsilon}_i \neq 1)[\xi_i\mathcal{V}_i - \frac{\mathcal{V}_i\exp\{\theta_{02}^{\mathsf{T}}\mathcal{V}_i\}}{1+\exp^{\theta_{02}^{\mathsf{T}}\mathcal{V}_i}}]^{\mathsf{T}} \end{pmatrix}.$$

Proof of Proposition 1 is shown in section4.1.

2.2.2 Asymptotic Results Concerning $\widehat{G}(t)$

Proposition 2. *The estimator $\widehat{G}(t)$ is asymptotically linear estimator of $G(t)$ with influence function $\mathtt{IC}_G$ such that*

(1) Assume that the censoring time is independent of the covariates. If $G(t) > 0$, then

$$n^{\frac{1}{2}}(\widehat{G}(t) - G(t)) = n^{-\frac{1}{2}}\left\{-G(t)\sum_{j=1}^{n}\int_0^{\tau} I(Y_{\bullet}(s) > 0)\frac{dM_j{}^c(s)}{y(s)}\right\} + o_p(1) \tag{2.17}$$

where $n^{-1}Y_{\bullet}(s) \xrightarrow{p} y(s)$ *as* $n \xrightarrow{p} \infty$ *with* $Y_{\bullet}(s) = \sum_{i=1}^{n} Y_i(s) = \sum_{i=1}^{n} \mathcal{I}(\widetilde{T}_i \geq s)$*, and* $M_j{}^c(s) = \mathcal{I}(\widetilde{T}_j \leq s, \Delta_j = 0) - \int_0^s Y_j(u)\, d(-\log G(u))$ *is the martingale associated with the censoring time.*

(2) If the censoring time follows the Cox model depending on the covariates (X_i, Z_i)*.*

$$n^{\frac{1}{2}}(\widehat{G}(t|X_i, Z_i) - G(t|X_i, Z_i)) = n^{-\frac{1}{2}} \left\{ -G(t|X_i, Z_i) \sum_{j=1}^{n} \int_0^{\tau} I(Y_{\bullet}(s) > 0) \frac{dM_j{}^c(s)}{y(s)} \right\} + o_p(1), \tag{2.18}$$

where $n^{-1}Y_{\bullet}(s) \xrightarrow{p} y(s)$ *as* $n \xrightarrow{p} \infty$ *with* $Y_{\bullet}(s) = \sum_{i=1}^{n} Y_i(s)\mathrm{exp}^{\beta_0^T X_i(s) + \beta_1^T Z_i(s)}$ *and* $M_j{}^c(s) = \mathcal{I}(\widetilde{T}_j \leq s, \Delta_j = 0) - \int_0^s Y_j(u)\mathrm{exp}^{\beta_0^T X_i(u) + \beta_1^T Z_i(u)}\ \Lambda_0(u)$ *with* $\Lambda_0(u) = \sum_{i=1}^{n} \int_0^u \frac{d\mathcal{I}(\widetilde{T}_j \leq s, \Delta_j = 0)}{\sum_{i=1}^{n} Y_i(s)\mathrm{exp}^{\beta_0^T X_i(s) + \beta_1^T Z_i(s)}}$ *is the martingale associated with the censoring time.*

Proof of Proposition 2 is shown in section4.1.

2.2.3 Asymptotic Properties for IPW Estimator

We denote $F_1(t; \boldsymbol{X}_i, \boldsymbol{Z}_i)$, $\boldsymbol{D}_{\boldsymbol{\eta},i}(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma})$ and $\boldsymbol{D}_{\boldsymbol{\gamma},i}(t, \boldsymbol{\eta}(t), \boldsymbol{\gamma})$ by $\boldsymbol{F}_{1i}(t)$, $\boldsymbol{D}_{\boldsymbol{\eta},i}(t)$ and $\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)$, respectively. Let

$$\begin{aligned}
\boldsymbol{A}_i(\theta) &= \partial\psi_i(\theta)/\partial\theta \\
\boldsymbol{k}(t,\theta) &= E\left\{\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t) w_i(t) \boldsymbol{\psi}_i(\theta) \boldsymbol{D}_{\boldsymbol{\eta},i}(t)\right\} \left[E\left\{\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t) w_i(t) \boldsymbol{\psi}_i(\theta) \boldsymbol{D}_{\boldsymbol{\eta},i}(t)\right\}\right]^{-1} \\
\boldsymbol{q}_{\boldsymbol{\gamma}}(s,t,\theta) &= \mathrm{E}\left[\left\{\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},j}(t) - \boldsymbol{k}(t,\theta)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},j}(t)\right\} w_j(t) \boldsymbol{\psi}_j(\theta) \frac{\Delta_j N_j(t)}{G(T_j)} \mathcal{I}(s \leq \widetilde{T}_j \leq t)\right] \\
g(\tau,\theta) &= E\left\{\int_0^{\tau} \left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t) - \boldsymbol{k}(t,\theta)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right] w_i(t) \boldsymbol{A}_i(\theta) \left\{\frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t)\right\} dt\right\} \\
\boldsymbol{\zeta}_{\boldsymbol{\gamma},i}(t,\theta) &= \left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t) - \boldsymbol{k}(t,\theta)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right] w_i(t) \boldsymbol{\psi}_i(\theta) \left\{\frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t)\right\} \\
M_i{}^c(t) &= \mathcal{I}(\widetilde{T}_i \leq t, \Delta_i = 0) - \int_0^t Y_i(s) d(-\log G(s)), \text{ where } Y_i(s) = \mathcal{I}(\widetilde{T}_i \geq s) \\
y(t) &= \lim_{n\to\infty} n^{-1} \sum_{i=1}^{n} \mathcal{I}(\widetilde{T}_i \geq t), \quad \text{uniformly} \quad t \in [0,\tau] \\
\boldsymbol{\kappa}_{\boldsymbol{\gamma},i}(t,\theta) &= \left\{\int_0^{\tau} \frac{\boldsymbol{q}_{\boldsymbol{\gamma}}(s,t,\theta)}{y(s)} dM_i^c(s)\right\}
\end{aligned} \tag{2.19}$$

Theorem 2.1. *Under Condition I in section 4.1,*

$$\sqrt{n}(\widehat{\boldsymbol{\gamma}} - \boldsymbol{\gamma}_0) \xrightarrow{d} \mathcal{N}\left(0, \boldsymbol{\Sigma}_\gamma\right) \tag{2.20}$$

where $\boldsymbol{\Sigma}_\gamma = \boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta_0)^{-1}\, E\left\{\boldsymbol{W}_{\gamma,i}(\tau,\theta_0)\right\}^{\otimes 2} \boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta_0)^{-1}$ *and where*

$$\begin{aligned}
\boldsymbol{W}_{\gamma,i}(\tau,\theta) &= \int_0^\tau \boldsymbol{\zeta}_{\boldsymbol{\gamma},i}(t,\theta)\,dt + \int_0^\tau \boldsymbol{\kappa}_{\boldsymbol{\gamma},i}(t,\theta)\,dt + g(\tau,\theta)\left[J\left(\mathcal{V}_i,\theta\right)\right]^{-1} U(\mathcal{V}_i,\theta),\\
\boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta) &= E\left\{\int_a^\tau \left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t) - \boldsymbol{k}(t,\theta)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right] w_i(t)\boldsymbol{\psi}_i(\theta)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\,dt\right\}.
\end{aligned}$$

The asymptotic covariance matrix of $\sqrt{n}(\widehat{\boldsymbol{\gamma}} - \boldsymbol{\gamma}_0)$ can be consistently estimated by

$$\widehat{\boldsymbol{\Sigma}}_\gamma = \widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}^{-1}(\hat{\theta})\, n^{-1}\sum_{i=1}^{n}\left\{\widehat{\boldsymbol{W}}_{\gamma,i}(\tau,\hat{\theta})\right\}^{\otimes 2} \widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}^{-1}(\hat{\theta}), \tag{2.21}$$

where

$$\begin{aligned}
\widehat{\boldsymbol{W}}_{\gamma,i}(\tau,\theta) &= \int_0^\tau \widehat{\boldsymbol{\zeta}}_{\boldsymbol{\gamma},i}(t,\theta)\,dt + \int_0^\tau \widehat{\boldsymbol{\kappa}}_{\boldsymbol{\gamma},i}(t,\theta)\,dt + \hat{g}(\tau,\theta)\left[\widehat{J}(\mathcal{V}_i,\theta)\right]^{-1} U(\mathcal{V}_i,\theta),\\
\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}(\theta) &= n^{-1}\sum_{i=1}^{n}\int_0^\tau \left[\widehat{\boldsymbol{D}}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t) - \widehat{\boldsymbol{K}}(t,\theta)\widehat{\boldsymbol{D}}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right] w_i(t)\boldsymbol{\psi}_i(\theta)\widehat{\boldsymbol{D}}_{\boldsymbol{\gamma},i}(t)\,dt,
\end{aligned}$$

where $\widehat{\boldsymbol{\zeta}}_{\boldsymbol{\gamma},i}(t,\theta)$, $\widehat{\boldsymbol{\kappa}}_{\boldsymbol{\gamma},i}(t,\theta)$ and $\hat{g}(\tau,\theta)$, defined in (4.29) in section 4.1, are the estimators of $\boldsymbol{\zeta}_{\boldsymbol{\gamma},i}(t,\theta)$, $\boldsymbol{\kappa}_{\boldsymbol{\gamma},i}(t,\theta)$ and $g(\tau,\theta)$. Those estimators can be obtained by replacing $\psi_i(\theta)$ with $\psi_i(\hat{\theta}) = \xi_i/\varphi(\mathcal{V}_i,\hat{\theta})$ and by replacing $\boldsymbol{F}_{1i}(t)$, $\boldsymbol{D}_{\boldsymbol{\eta},i}(t)$,$\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)$,$\boldsymbol{k}(t,\theta)$, $M_i^c(t)$, $\boldsymbol{q}_{\boldsymbol{\gamma}}(s,t,\theta)$, $y(t)$ with $\widehat{\boldsymbol{F}}_{1i}(t)$, $\widehat{\boldsymbol{D}}_{\boldsymbol{\eta},i}(t)$, $\widehat{\boldsymbol{D}}_{\boldsymbol{\gamma},i}(t)$, $\widehat{\boldsymbol{K}}(t,\theta)$, $\widehat{\boldsymbol{q}}_{\boldsymbol{\gamma}}(s,t,\theta)$, $\hat{y}(t)$, $\widehat{M_i}^c(t)$ defined in (4.29), which can be estimated by inserting the estimators $\hat{\theta}$,$\widehat{\boldsymbol{\eta}}(t)$, $\widehat{\gamma}$, $\widehat{G}(t)$. For the logistic regression models for the selection probabilities $\boldsymbol{A}_i(\theta)$ can be estimated as

$$\begin{aligned}
\boldsymbol{A}_i(\hat{\theta}) &= -\xi_i I(\tilde{\epsilon}_i = 1)\varphi_1'(\mathcal{V}_i,\hat{\theta}_1)/\varphi_1^2(\mathcal{V}_i,\hat{\theta}_1) - \xi_i I(\tilde{\epsilon}_i \neq 1)\varphi_2'(\mathcal{V}_i,\hat{\theta}_2)/\varphi_2^2(\mathcal{V}_i,\hat{\theta}_2)\\
&= -\xi_i\mathcal{V}_i\{I(\tilde{\epsilon}_i = 1)\exp(-\hat{\theta}_1\mathcal{V}_i) + I(\tilde{\epsilon}_i \neq 1)\exp(-\hat{\theta}_2\mathcal{V}_i)\},
\end{aligned}$$

where $\varphi_1'(\mathcal{V}_i,\theta_1) = d\varphi_1(\mathcal{V}_i,\theta_1)/d\theta_1$ and $\varphi_2'(\mathcal{V}_i,\theta_2) = d\varphi_2(\mathcal{V}_i,\theta_2)/d\theta_2$.

Under the logistic models for the probabilities of the complete case given in Proposition 1,

$$\widehat{J}(\mathcal{V}_i,\hat{\theta}) = \operatorname{diag}(\widehat{J}_1(\mathcal{V}_i,\hat{\theta}_1), \widehat{J}_2(\mathcal{V}_i,\hat{\theta}_2))$$

where $\widehat{J}_1(\mathcal{V}_i,\theta_1) = n^{-1}\sum_{i=1}^n I(\tilde{\epsilon}_i = 1)\frac{\exp(\theta_1^{\mathsf{T}}\mathcal{V}_i)\mathcal{V}_i\mathcal{V}_i^{\mathsf{T}}}{(1+\exp(\theta_1^{\mathsf{T}}\mathcal{V}_i))^2}$ and $\widehat{J}_2(\mathcal{V}_i,\theta_2) = n^{-1}\sum_{i=1}^n I(\tilde{\epsilon}_i \neq 1)\frac{\exp(\theta_2^{\mathsf{T}}\mathcal{V}_i)\mathcal{V}_i\mathcal{V}_i^{\mathsf{T}}}{(1+\exp(\theta_2^{\mathsf{T}}\mathcal{V}_i))^2}$, and

$$U(\mathcal{V}_i,\hat{\theta}) = \begin{pmatrix} U_1(\mathcal{V}_i,\hat{\theta}_1) \\ \\ U_2(\mathcal{V}_i,\hat{\theta}_2) \end{pmatrix} = \begin{pmatrix} I(\tilde{\epsilon}_i = 1)\left[\xi_i\mathcal{V}_i - \frac{\mathcal{V}_i\exp(\hat{\theta}_1^\intercal\mathcal{V}_i)}{1+\exp(\hat{\theta}_1^\intercal\mathcal{V}_i)}\right] \\ \\ I(\tilde{\epsilon}_i \neq 1)\left[\xi_i\mathcal{V}_i - \frac{\mathcal{V}_i\exp(\hat{\theta}_2^\intercal\mathcal{V}_i)}{1+\exp(\hat{\theta}_2^\intercal\mathcal{V}_i)}\right] \end{pmatrix}.$$

Let

$$\begin{aligned}
\boldsymbol{\zeta}_{\boldsymbol{\eta},i}(t,\theta) &= \boldsymbol{D}^\intercal_{\boldsymbol{\eta},i}(t)w_i(t)\boldsymbol{\psi}_i(\theta)\left\{\frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t)\right\}, \\
\boldsymbol{q}_{\boldsymbol{\eta}}(s,t,\theta) &= E\left\{\boldsymbol{D}^\intercal_{\boldsymbol{\eta},j}(t)w_j(t)\boldsymbol{\psi}_j(\theta)\frac{\Delta_j N_j(t)}{G(T_j)}\mathcal{I}(s\le\tilde{T}_j\le t)\right\}, \\
\boldsymbol{\kappa}_{\boldsymbol{\eta},i}(t,\theta) &= \left\{\int_0^\tau \frac{\boldsymbol{q}_{\boldsymbol{\eta}}(s,t,\theta)}{y(s)}dM_i^c(s)\right\}, \\
\boldsymbol{Q}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta) &= E\{\boldsymbol{D}^\intercal_{\boldsymbol{\eta},i}(t)w_i(t)\psi_i(\theta)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\}.
\end{aligned}$$

Theorem 2.2. *Under Condition I in section 4.1,*

$$\sqrt{n}(\widehat{\boldsymbol{\eta}}(t) - \boldsymbol{\eta}_0(t))) = \left\{\boldsymbol{Q}_{\boldsymbol{\eta}}(t,\theta_0)\right\}^{-1} n^{-\frac{1}{2}}\sum_{i=1}^n \boldsymbol{W}_{\boldsymbol{\eta},i}(t,\theta_0) + o_p(1) \quad (2.22)$$

uniformly in $t\in[0,\tau]$, where

$$\boldsymbol{W}_{\boldsymbol{\eta},i}(t,\theta) = \left\{\boldsymbol{\zeta}_{\boldsymbol{\eta},i}(t,\theta) + \boldsymbol{\kappa}_{\boldsymbol{\eta},i}(t,\theta) - \boldsymbol{Q}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta)\left\{\boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta)\right\}^{-1}\boldsymbol{W}_{\gamma,i}(\tau,\theta)\right\}, \quad (2.23)$$

$$\boldsymbol{Q}_{\boldsymbol{\eta}}(t,\theta) = E\{\boldsymbol{D}^T_{\boldsymbol{\eta},i}(t)w_i(t)\psi_i(\theta)\boldsymbol{D}_{\boldsymbol{\eta},i}(t)\}. \quad (2.24)$$

Thus, $\sqrt{n}(\widehat{\boldsymbol{\eta}}(t) - \boldsymbol{\eta}_0(t))$ converges weakly to a mean zero Gaussian process on $t\in[0,\tau]$ with the covariance matrix $\boldsymbol{\Sigma}_{\boldsymbol{\eta}} = \boldsymbol{Q}_{\boldsymbol{\eta}}^{-1}(t,\theta_0)\,E\left\{\boldsymbol{W}_{\boldsymbol{\eta},i}(t,\theta_0)\right\}^{\otimes 2}\,\boldsymbol{Q}_{\boldsymbol{\eta}}^{-1}(t,\theta_0)$.

The asymptotic covariance matrix of $\sqrt{n}(\widehat{\boldsymbol{\eta}}(t) - \boldsymbol{\eta}_0(t))$ can be consistently estimated by

$$\widehat{\boldsymbol{\Sigma}}_{\boldsymbol{\eta}} = \widehat{\boldsymbol{Q}}_{\boldsymbol{\eta}}^{-1}(t,\hat{\theta})\,n^{-1}\sum_{i=1}^n\left\{\widehat{\boldsymbol{W}}_{\boldsymbol{\eta},i}(t,\hat{\theta})\right\}^{\otimes 2}\,\widehat{\boldsymbol{Q}}_{\boldsymbol{\eta}}^{-1}(t,\hat{\theta}).$$

where

$$\begin{aligned}
\widehat{\boldsymbol{W}}_{\boldsymbol{\eta},i}(t,\theta) &= \left\{\widehat{\boldsymbol{\zeta}}_{\boldsymbol{\eta},i}(t,\theta) + \widehat{\boldsymbol{\kappa}}_{\boldsymbol{\eta},i}(t,\theta) - \widehat{\boldsymbol{Q}}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta)\left\{\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}(\theta)\right\}^{-1}\widehat{\boldsymbol{W}}_{\gamma,i}(\tau,\theta)\right\}, \\
\widehat{\boldsymbol{Q}}_{\boldsymbol{\eta}}(t,\theta) &= n^{-1}\sum_{i=1}^n \widehat{\boldsymbol{D}}^\intercal_{\boldsymbol{\eta},i}(t)w_i(t)\boldsymbol{\psi}_i(\theta)\widehat{\boldsymbol{D}}_{\boldsymbol{\eta},i}(t).
\end{aligned}$$

where $\widehat{\boldsymbol{\zeta}}_{\boldsymbol{\eta},i}(t,\theta)$, $\widehat{\boldsymbol{\kappa}}_{\boldsymbol{\eta},i}(t,\theta)$, $\widehat{\boldsymbol{Q}}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta)$, defined in (4.42) in section 4.1, are the estimators of $\boldsymbol{\zeta}_{\boldsymbol{\eta},i}(t,\theta)$, $\boldsymbol{\kappa}_{\boldsymbol{\eta},i}(t,\theta)$, $\boldsymbol{Q}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta)$. Similarly, those estimators can be obtained by replacing $\psi_i(\theta)$, $\boldsymbol{F}_{1i}(t)$, $\boldsymbol{D}_{\boldsymbol{\eta},i}(t)$,$\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)$, $\boldsymbol{q}_{\boldsymbol{\eta}}(s,t,\theta)$, $M_i^c(t)$, $y(s)$ with $\psi_i(\hat{\theta})$, $\widehat{\boldsymbol{F}}_{1i}(t)$, $\widehat{\boldsymbol{D}}_{\boldsymbol{\eta},i}(t)$, $\widehat{\boldsymbol{D}}_{\boldsymbol{\gamma},i}(t)$, $\widehat{\boldsymbol{q}}_{\boldsymbol{\eta}}(s,t,\theta)$, $\widehat{M_i}^c(t)$, $\hat{y}(s)$ defined in (4.42) in section 4.1, which can be estimated by inserting the estimators $\hat{\theta}$, $\widehat{\boldsymbol{\eta}}(t)$, $\widehat{\boldsymbol{\gamma}}$, $\widehat{G}(t)$. The estimators $\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}(\theta)$ and $\widehat{\boldsymbol{W}}_{\gamma,i}(\tau,\theta)$ are described in Theorem 2.1.

2.3 Simulations

In this section, simulation studies have been conducted to evaluate the finite sample properties of the inverse probability weighted estimators of $(\eta(t),\gamma)$. In the simulation study, the cumulative incidence function (1.22) has been considered with two different link functions. Let X_i and Z_i be Bernoulli random variables with $P(X_i = 1) = 0.5$ and $P(Z_i = 1) = 0.5X + 0.2$ for a subjec i. The covariate X_i are always observed and the covariate Z_i can be missing. Let $\epsilon_i = k,\ k \in \{1,2\}$ be the types of failure and let the event of interest among two competing risks be the $k = 1$. We consider the following semi-parametric models for the cumulative incidence function with cause 1:

$$\log\{1 - F_{1i}(t,X_i,Z_i)\} = -\eta_0(t)\exp(\gamma_1 X_i + \gamma_2 Z_i), \tag{2.25}$$

$$\text{logit}\{F_{1i}(t,X_i,Z_i)\} = \eta_0(t) + \gamma_1 X_i + \gamma_2 Z_i, \tag{2.26}$$

for $0 \le t \le \tau$ and $\tau = 3$, where $\gamma_1 = -0.3$, $\gamma_2 = 0.3$, $\eta_0(t) = 0.2 \times t$ for model (2.25) and $\eta_0(t) = \log(\frac{p(t)}{1-p(t)})$ with $p(t) = 0.01 + \beta\sqrt{t}$ and $\beta = 0.2$ for model (2.26).

Given $\eta(t),\gamma,X,Z$, the conditional probability of observed failure for cause 1 is

$$\begin{aligned} F_{1i}(\tau) &= 1 - \exp(-\eta_0(\tau)\exp({\gamma_1}^{\mathsf{T}} x_i + {\gamma_2}^{\mathsf{T}} z_i)), \\ F_{1i}(\tau) &= \frac{\exp(\eta_0(\tau) + {\gamma_1}^{\mathsf{T}} x_i + {\gamma_2}^{\mathsf{T}} z_i)}{1 + \exp(\eta_0(\tau) + {\gamma_1}^{\mathsf{T}} x_i + {\gamma_2}^{\mathsf{T}} z_i)}, \end{aligned}$$

where $0 < t \le \tau$ for each individual $i = 1,2,\ldots,n$ and $\tau = 3$ for model (2.25) and (2.26), respectively. The types of failure ϵ_i for ith individual have been determined by generating a Bernoulli random variable with the probability $F_1(\tau)$, that is, $P(\epsilon_i = 1) = F_{1i}(\tau),\ i = 1,\ldots,n$. The failure time T_i is generated by conditional probability

$$\tilde{F}_{1i}(t) = P(T_1 \le t|\epsilon_i = 1) = \frac{F_{1i}(t)}{P(\epsilon_i = 1)} = \frac{F_{1i}(t; x, z, \eta, \gamma)}{F_{1i}(\tau)} = \frac{F_{1i}(t)}{F_{1i}(\tau)}.$$

for ith individual and $\tau = 3$.

Let ${C_i}^*$ follow an uniform distribution on [0,3] for both models (2.25) and (2.26). The censoring time C_i is generated by $C_i = \min(C_i^*, \tau)$. Let $\tilde{T}_i$ be the observed failure time defined as $\tilde{T}_i = \min(T_i, C_i)$. This gives approximately 45% subjects who are censored before $\tau = 3$ for both models (2.25) and (2.26). Let $\tilde{\epsilon}_i = \epsilon_i \Delta_i$ where $\Delta_i = I(T_i \le C_i)$.

We consider three simulation scenarios in terms of whether the missing probabilities depend on the outcome variables $\tilde{\epsilon}_i$ and how the phase-two covariate Z_i is missing. The first two scenarios are called phase-two sampling design: (I) The first scenario is classical case cohort sampling design, where phase-two covariate Z_i is sampled for all cases $\tilde{\epsilon}_i = 1$ and the information of the covariate Z_i will be missing for the non-cases $\tilde{\epsilon}_i = 0$ or 2; (II)The second scenario is generalized case-cohort sampling design, which allows the phase-two covariate Z_i to be missing for both cases and non-cases. In the third scenario, (III) the missing probability does not depend on $\tilde{\epsilon}_i$ and phase-two covariate Z_i is a simple random sample from the phase-one covariates.

Let m_0 be the average of total missing probability. We consider $m_0 = 0.3$ and 0.5 for each sampling scenario. Let m_1 and m_2 be the average missing probabilities for the cases and the non-cases, respectively. First, we consider $m_0 = 0.3$ for each scenario in model (2.25). For scenario (I), missing probability $\vartheta_{1i} = P(\xi_i = 0|\mathcal{V}_i, \tilde{\epsilon}_i = 1) = 0$ for cases. For non-cases $\epsilon_i = 0$ or 2, we assume that the missing probability $\vartheta_{2i} = P(\xi_i = 0|\mathcal{V}_i, \tilde{\epsilon}_i \ne 1)$ follows the logistic regression model

$$\text{logit}(\varphi(\mathcal{V}_i, \theta_2)) \quad = \quad \theta_{20} + \theta_{21}\tilde{T}_i + \theta_{22}X_i + \theta_{23}I(\tilde{\epsilon}_i = 2) \tag{2.27}$$

We obtain the average missing probability $m_2 = 0.5$ by choosing $\theta_2 = (-2.0, 0.6, 0.8, 1.0)$ in model (2.27) based on phase-one covariates. Similarly, in the same setting with $m_0 = 0.5$, we have $\vartheta_{1i} = P(\xi_i = 0|\mathcal{V}_i, \tilde{\epsilon}_i = 1) = 0$ for cases. We have about $m_2 = 0.65$ by choosing $\theta_2 = (1.0, 0.3, 0.1, 0.3)$ in (2.27).

For (II), the missing probability $\vartheta_k i = P(\xi_i = 0|\mathcal{V}_i, \tilde{\epsilon}_i = k)$ for both cases and non-cases can be obtained by the following the logistic regression model

$$\text{logit}(\varphi(\mathcal{V}_i,\theta_k)) \quad = \quad \theta_{k0}+\theta_{k1}\tilde{T}_i+\theta_{k2}X_i+\theta_{k3}I(\tilde{\epsilon}_i=1)+\theta_{k4}I(\tilde{\epsilon}_i=2), \tag{2.28}$$

,which gives $m_1 = 0.15$ and $m_2 = 0.35$ when $\theta_k = (-1.0, 0.1, 0.3, -1.0, 0.5)$. Similarly, for getting $m_0 = 0.5$ in the same setting, we have about $m_1 = 0.45$ and $m_2 = 0.60$ by choosing $\theta_2 = (1.0, -0.6, -0.4, -0.6, 0.3)$ in (2.27).

For (III), we use the following logistic model for the missing probability $\vartheta_i = P(\xi_i = 0|\mathcal{V}_i)$:

$$\text{logit}(\varphi(\mathcal{V}_i,\theta)) \quad = \quad \theta_0+\theta_1 X_i. \tag{2.29}$$

We have $\vartheta_i = 0.3$ with $\theta = (-1.0, 0.1)$ in (2.29), yielding $m_0 = 0.3$. The average of total missing probability $m_0 = 0.5$ can be obtained by choosing $\theta_3 = (-0.1, 0.3)$ in (2.29).

Similar arguments can be applied for model (2.26). Under the average of total missing probability $m_0 = 0.3$, each sampling scenario has the average missing probabilities for case and non-case. Let I, II and III be the classical case-cohort design, the generalized case-cohort design and the simple random sampling, respectively. In the design I, we have about $m_2 = 0.40$ by choosing $\theta_2 = (-1.5, 0.4, 0.2, 0.4)$. In the design II, we have about $m_1 = 0.15$ and $m_2 = 0.30$ when $\theta_k = (-1.5, 0.2, 0.4, -0.5, 0.5)$. From III, we can get $m_0 = 0.3$ by choosing $\theta = (-1.0, 0.2)$. Similarly, we consider $m_0 = 0.5$ for model (2.26). In the design I, we have about $m_2 = 0.65$ by choosing $\theta_2 = (-0.5, 0.3, 0.5, 1.5)$. In the design II, we have about $m_1 = 0.60$ and $m_2 = 0.50$ when $\theta_k = (0.5, -0.3, -0.1, 0.1, -0.3)$. From III, we can get $m_0 = 0.5$ by choosing $\theta = (0.3, -0.5)$.

We denote the full estimators as Full when all the values of phase-two covariate Z are fully observed and complete-case estimators as CC where subjects having missing covariate Z are removed. The performances of the proposed IPW estimators for γ and $\eta(t)$ for $t \in [0, 3]$ are summarized by the bias (Bias), the empirical standard error (SSE), the average of the estimated standard error (ESE), the empirical coverage probability (CP) of 95% confidence interval. We take sample size $n = 550, 700, 900$ and obtain the average of total missing probabilities as $m_0 = 0.3$, and 0.5 by choosing different missing probabilities (m_1, m_2) for cases and non-cases. We denote a classical case cohort design as I, a generalized case cohort design as II and a simple random sampling design as

III. Each entry of the tables is estimated based on 1000 simulations runs.

Table 1 and 2 summarize the Bias, SEE, ESE, CP and REE of the proposed IPW estimator for γ_1 and γ_2 under the three sampling designs I, II, and III for models (2.25) and (2.26). Those tables show that the IPW is unbiased estimator. The empirical standard errors tend to decrease as the sample size increases and the averages of the estimated standard errors are close to the empirical standard errors. The relative efficiencies of the IPW estimator tend to increase as the sample size increases. The coverage probabilities are close to the 95% nominal level. At the higher average of total missing probability with $m_0 = 0.5$, the empirical standard errors are much larger.

Table 3 and 4 compare the Bias, SSE and ESE of IPW estimator and those of complete case (CC) estimator for γ_1 and γ_2 under model (2.25) and (2.26), respectively. The Full estimator is presented as a gold standard. Table 3 shows that the biases of the CC estimator are larger than those of the IPW estimator. It means that CC is not a consistent estimator. The CC estimator has the largest bias when the missing probabilities for the cases and the non-cases differ the most in each average of total missing probability. Table 4 shows that the empirical standard errors of each estimator tend to be smaller as the sample size increases. However, the empirical standard errors of the IPW estimator are worse than or similar to those of the complete-case (CC) estimator. It shows that the variance of the IPW estimator is not efficient. This is because we still discard the information of subjects when some of their covariates have been missing. It results in the loss of efficiencies of the IPW estimator.

Figure 1 to 3 and figure 4 to 6 show that the comparison of the Full, IPW and CC estimators for the cumulative time varying regression coefficient $\eta_0(t),\ t \in [0, 3]$ under model (2.25) and (2.26), respectively. Under model (2.25) , the classical case-cohort, the generalized case-cohort and a simple random sampling design in figure 1, 2 and 3, respectively. Under model (2.26), those sampling designs have been considered in figure 4, 5 and 6, respectively. We take the sample size $n = 550$. In each figure, (a) to (d) are the plots of the Bias, SSE, ESE and the coverage probability for $\eta_0(t)$ over $t \in [0, 3]$ with the average of total missing probability $m_0 = 30\%$ and (e) to (h) are the plots of those with $m_0 = 50\%$. The plots show that the IPW estimator is unbiased, comparable to Full estimators as if all the values of the covariate Z were observed. The biases of complete case (CC) estimator of $\eta_0(t)$ are much larger, meaning that those estimators are inconsistent. However, under the simple random sampling III, the biases of the CC estimator are small. This is because the design III is not depending on outcomes $\tilde{\epsilon}_i$, giving small biases of all those estimators. The average of the estimated standard errors (ESE) are close to the empirical standard errors (SSE). The coverage probabilities of the IPW estimators are close to 0.95 nominal with the average of total missing probabilities $m_0 = 0.3$. However, the coverage probabilities of the IPW estimators are not very close to the 0.95 nominal with $m_0 = 0.5$. This result shows that variances of the IPW are not good enough. It seams to appeal another approach to improve the efficiency of the IPW estimators.

2.4 Application

The RV144 vaccine efficacy trial randomized 16,394 HIV negative volunteers to the vaccine ($n = 8198$) and placebo ($n = 8196$) groups. We apply the proposed estimating procedures for IPW method to the vaccine group, which included 5035 men and 3163 women. Subjects enrolled in the RV144 trial were vaccinated at weeks 0,4,12 and 24. 43 of 8198 vaccine recipients acquired the primary endpoint of HIV infection after the Week 26 biomarker sampling time point through to the end of follow-up at 42 months (?). Vaccine recipients were distributed in the Low, Medium, and High baseline behavioral risk scores, defined as in (?) with 3863 Low, 2370 Medium, and 1965 High.

Three HIV gp 120 sequences were included in the vaccine construct; 92TH023 in the ALVAC canarypox vector prime component; and A244 and MN in the AIDSVAX protein boost component. The 92TH023 and A244 are subtype E HIVs whereas MN is subtype B. However, the analysis focuses on the 92TH023 and A244 insert sequences. This is because the subtype E vaccine-insert sequences are genetically much closer to the infecting (and regional circulating) sequences than MN, meaning that the subtype E HIVs are more likely to stimulate protective immune responses. The observed failure time $\tilde{T}_i$ is the time to HIV infection diagnosis, which is minimum of failure time or right-censoring time.

Because vaccine recipients with higher levels of antibodies binding to the V1V2 portion of the HIV envelope protein had a significantly lower rate of HIV infection((**?**), (**?**), (**?**)), the V1V2 sub-region of gp120 may have been involved in the partial vaccine efficacy administered by the vaccine regimen. The region contains epitopes recognized by antibodies induced by the vaccine. Therefore, we study the genetic distance of an infecting HIV V1V2 sequence to the corresponding V1V2 sequence in the vaccine construct(using a multiple sequence alignment), which is called as marks.

For the analysis, two marks V are considered, based on the 92TH023 and A244 vaccine construct sequences. The way of measuring in the genetic distances is described in **?**. The distance V were re-scaled to take values between 0 and 1. We denote these two genetic distance marks 92TH023V1V2 and A244V1V2 as V_{1i} and V_{2i}, respectively, for a subject i. We use each mark to form two causes of failure by considering each of V_{1i} and V_{2i} one at a time. Let M_1 be the median of the observed mark V_{1i} and M_2 be the median of the observed mark V_{2i} for each subject i.

The cause of failure ϵ_{1i} for the mark V_{1i} is generated by using the median mark M_1 of V_{1i}. We define $\epsilon_{1i} = 1$ for uncensored subjects i if the mark V_{1i} is less than M_1; otherwise $\epsilon_{1i} = 2$. Similarly, the cause of failure ϵ_{2i} for the mark V_{2i} is generated by using the median mark M_2 of V_{2i}. We define $\epsilon_{2i} = 1$ for uncensored subjects i if the mark V_{2i} is less than M_2; otherwise $\epsilon_{2i} = 2$. If subjects are censored, then $\epsilon_{ji} = 0$ for $j = 1, 2$.

The V1V2 seqeunce of the infecting HIVs has been investigated in (Liqi's paper). They analysis IgG and IgG3 biomarkers as correlates of 92TH023V1V2 and A244V1V2 mark-specific HIV infection for the stratified mark-specific proportional hazards model under two-phase sampling.

Following the analysis in **?**, we study IgG and IgG3 biomarkers as correlates of 92TH023V1V2 and A244V1V2 mark-specific HIV infection for the cumulative incidence model based on competing risks data. We use IPW method to analysis these subjects under two-phase sampling. In particular, paired to the 92TH023V1V2 mark variable, we study the two biomarkers Week 26 IgG and IgG3 binding antibodies to 92TH023V1V2, namely IgG-92TH023V1V2 and IgG3-92TH023V1V2; and, paired to the A244V1V2 mark variable, we study Week 26 IgG and IgG3 binding antibodies to A244V1V2, namely IgG-A244V1V2 and IgG3-A244V1V2. Therefore, we have four different immune responses IgG-92TH023V1V2, IgG3-92TH023V1V2, IgG-A244V1V2 and IgG3-A244V1V2 for the analysis.

The immune response biomarkers were measured for 34 of 43 HIV infected vaccine recipients with HIV V1V2 sequence data and 212 of 8155 uninfected vaccine recipients at the Week 26 visit post entry. These observed biomarkers were each standardized to have mean 0 and variance 1 for the analysis.

Let R_i be the immune responses R_{11_i}, R_{12_i}, R_{21_i}, and R_{22_i}, respectively, for each analysis. Let δ_i be infection status, whose value is 1 if a subject is infected HIV; and 0 if a subject is right censored over a follow-up period of 42 months. Let $\epsilon_{1i} = k$ be the causes of failure for immune responses R_{11_i} and R_{12_i}, respectively, for $k = 1, 2$. Let $\epsilon_{2i} = k$ be the causes of failure for immune responses R_{21_i} and R_{22_i}, respectively, for $k = 1, 2$. Let B_{1i} and B_{2i} be the dummy variables for baseline behavioral risk score groups B_i (High=1, Low=2, Medium=3), where $B_{1i} = 1$ if a subject is in the low risk score group; 0 otherwise, $B_{2i} = 1$ if a subject is in the medium risk score group; 0 otherwise and $B_{1i} = B_{2i} = 0$ if a subject is in the high risk group. The immune responses R_i can be missing for both case and non-case subjects, and hence are phase two covariates. The baseline behavioral risk scores B_i are measure for all subjects, and hence are phase one covariates.

We consider the following semiparametric additive model for the cumulative incidence function by using log link function for $h(x) = 1 - \exp(-x)$ in (1.22);

$$F_{ki}(t; X_i, Z_i) = 1 - \exp(-\{\eta_0(t) + \eta_1(t)R_i + \gamma_1 B_{1i}t + \gamma_2 B_{2i}t\}) \tag{2.30}$$

for $k = 1, 2$. Let $\vartheta_i = P(\xi_i = 1|\mathcal{V}_i, \delta_i)$ be the selection probabilities, where ξ_i is the indicator of the immune response data, whose values are $\xi_i = 1$ if each of four immune response data R_i is measured; otherwise $\xi_i = 0$. To predict the probability of observing the immune response R_i, the following logistic regression model

$$\text{logit}(\vartheta_i) = \theta_0 + \theta_1 \delta_i \tag{2.31}$$

The selection probabilities $\hat{\vartheta}_i = P(\xi_i = 1|\mathcal{V}_i, \delta_i)$ is given by $\hat{\theta} = (-3.6235, 4.9526)$ with standard errors (0.0696, 0.3813) of coefficients $\hat{\theta}$ in (2.31). The weights are estimated by $\psi(\hat{\theta}_i) = \xi_i/\hat{\vartheta}_i$.

We analysis the semiparametric additive model (2.30) with four different settings: (S1). The model (2.30) is analyzed with immune response $R_i = R_{11_i}$ for $\epsilon_{1i} = 1$. The IPW estimates of baseline behavioral risk score for B_{1i} and B_{2i} are $(\hat{\gamma}_1, \hat{\gamma}_2) = (-0.00115, -0.00122)$ with standard errors with (0.000739, 0.000735), yielding p-values (0.118737, 0.096528); Similarly, the model (2.30) can be analyzed with immune response $R_i = R_{11_i}$ for $\epsilon_{1i} = 2$. The IPW estimates of baseline behavioral risk score for B_{1i} and B_{2i} are $(\hat{\gamma}_1, \hat{\gamma}_2) = (-0.00015, 0.00065)$ with standard errors with (0.000360, 0.000575), yielding p-values (0.66948, 0.25593);

(S2). The model (2.30) can be analyzed with immune response $R_i = R_{12_i}$ for $\epsilon_{1i} = 1$. The IPW estimates of B_{1i} and B_{2i} are $(\hat{\gamma}_1, \hat{\gamma}_2) = (-0.00108, -0.00123)$ with standard errors (0.000751, 0.000738), yielding p-values (0.151167, 0.095754); The same model can be analyzed based on $\epsilon_{1i} = 2$. The IPW estimates of B_{1i} and B_{2i} are $(\hat{\gamma}_1, \hat{\gamma}_2) = (-0.00017, 0.00064)$ with standard errors (0.000342, 0.000571), yielding p-values (0.62405, 0.25967);

(S3). The model (2.30) can be analyzed with immune response $R_i = R_{21_i}$ for $\epsilon_{2i} = 1$. The IPW estimates of B_{1i} and B_{2i} are $(\hat{\gamma}_1, \hat{\gamma}_2) = (-0.00036, -0.00038)$ with standard errors (0.000591, 0.000581), yielding p-values (0.54059, 0.51436); The same setting with $\epsilon_{2i} = 2$ can be also analyzed. The IPW estimates of B_{1i} and B_{2i} are $(\hat{\gamma}_1, \hat{\gamma}_2) = (-0.00086, -0.00010)$ with standard errors (0.00050, 0.00067), yielding p-values (0.086647, 0.880498);

(S4). The model (2.30) for cases $\epsilon_{2i} = 1$ is analyzed with immune response $R_i = R_{22_i}$. The IPW estimates of B_{1i} and B_{2i} for this analysis are (-0.00039, -0.00042) with standard errors (0.000611, 0.000592), yielding p-values (0.52576, 0.47455); The same model can be analyzed for $\epsilon_{2i} = 2$. The IPW estimates of B_{1i} and B_{2i} for this analysis are (-0.00082, -0.00009) with standard errors (0.00050, 0.00067), yielding p-values (0.097105, 0.892526).

Figure 7 to 10 compares IPW estimates of baseline cumulative coefficients $\eta_0(t)$ and cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the four different immune responses of R_i for $\epsilon_{ji} = 1$ and $\epsilon_{ji} = 2$, respectively, $j = 1, 2$. The analysis with R_{11_i} and R_{12_i} for $\epsilon_{1i} = 1$ have larger IPW estimates of baseline cumulative coefficients $\eta_0(t)$ than the analysis with R_{11_i} and R_{12_i} for $\epsilon_{1i} = 2$. The analysis with R_{21_i} and R_{22_i} for $\epsilon_{2i} = 1$ has similar IPW estimates of baseline cumulative coefficients $\eta_0(t)$ to the analysis with R_{21_i} and R_{22_i} for $\epsilon_{2i} = 2$.

For the IPW estimates of cumulative coefficients $\eta_1(t)$, while the effects of immune responses

R_{12_i}(IgG3-92TH023V1V2) are close to zero over study time with $\epsilon_{ji} = 1$, $j = 1, 2$ in 8, the immune responses R_{11_i}(IgG-92TH023V1V2), R_{21_i}(IgG-A244V1V2) and R_{22_i}(IgG3-A244V1V2) have negative effects on the cumulative incidence function with $\epsilon_{ji} = 1$, $j = 1, 2$ in figure 7, 9 and 10. However, the negative effects of R_{11_i}(IgG-92TH023V1V2) is less obvious than those negative effects of R_{21_i}(IgG-A244V1V2) and R_{22_i}(IgG3-A244V1V2). On the other hands, none of four immune responses R_i has significant negative effects on cumulative incidence function with $\epsilon_{ji} = 2$, $j = 1, 2$ over study time. By comparing figure 7 to 9 and comparing figure 8 to 10, IgG and IgG3 binding antibodies responding to A244V1V2 than to 92TH023V1V2 have significantly negatively effects on the cumulative incidence function, i.e A244 would be more relevant for protection.

Figure 11 to figure 14 show that the cumulative incidence function has been evaluated for $\epsilon_{ji} = 1$ and $\epsilon_{ji} = 2$, $j = 1, 2$, respectively, depending on the behavioral risks scores at the first, second and third quartiles Q_1, Q_2 and $Q3$ of the observed the immune responses R_i. We expected to have larger probability of getting infected by HIVs V1V2 sequences if one has higher behavioral risk scores. We also expected to have lower probability of getting infected by HIVs with V1V2 sequences closer to 92TH023 or A244 ($\epsilon_{ji} = 1$, $j = 1, 2$) and have higher probability of getting infected by HIVs with V1V2 sequences far away from 92TH023 or A244 ($\epsilon_{ji} = 2$, $j = 1, 2$).

Furthermore, since the numbers of behavioral risks scores for $\epsilon_{1i} = 1$ and $\epsilon_{1i} = 2$ are uneven, figure 11 and 12 did not show the desirable results we have expected. For example, for mark 92TH023V1V2 with $\epsilon_{1i} = 1$, the number of observed behavioral risks scores are 9, 6, and 4 for high, row and medium, respectively. However, for mark 92TH023V1V2 with $\epsilon_{1i} = 2$, the number of observed behavioral risks scores are 3, 5, and 7 for high, row and medium, respectively. This is because the probability of getting infection by HIVs with $\epsilon_{1i} = 2$ (3 for high) lower than the probability of getting infection by HIVs with $\epsilon_{1i} = 2$ (9 for high), which can not be comparable. For the mark A244V1V2 with $\epsilon_{1i} = 1$, the number of observed behavioral risks scores are 6, 7, and 5 for high, row and medium, respectively and for the mark A244V1V2 with $\epsilon_{1i} = 2$, the number of observed behavioral risks scores are 6, 4, and 6 for high, row and medium, respectively, which are relatively comparable. Therefore it is reasonable to look at the results on figure 13 and 14. Figure 13 and 14 show that the subjects with higher behavioral risk scores have higher probability of getting infected by HIVs with V1V2 sequences than the subjects with lower behavioral risks scores. On the medium risk and high risks graphs, predicted probability of infection by HIVs with V1V2 sequence with $\epsilon_{2i} = 1$ tends to have lower probability of infection by HIVs with V1V2 sequences with $\epsilon_{2i} = 2$.

These results imply that since IgG3 antibodies to 92TH023V1V2 does not have effect on cumulative incidence function on Figure 8, other IgG subclasses besides type3 induced by 92TH023 would have negative effects on the cumulative incidence function, then would be relevant for protection. This seems that A244 was more important than 92TH023 for induction of protective IgG3 antibodies. These results also imply that mark distances smaller than the median of observed marks has more protection against the HIV infection than mark distances larger than the median marker. Therefore, it supports the hypothesis that vaccine recipients exposed to HIVs with V1V2 sequences close to A244 (smaller markers than the median marker) may be more likely to be protected by antibodies than vaccine recipients exposed to HIVs with V1V2 sequences with larger markers than the median marker.

Table 1: Bias, empirical standard error(SSE), average of the estimated standard error(ESE), the relative efficiencies (REE) compared to the Full estimators and empirical coverage probability (CP) of 95% confidence intervals for the IPW estimators of γ_1, γ_2 under model (2.25) with average of total missing probabilities $m_0 = 0.3,\ 0.5$ and about 45% censoring percentage based on 1000 simulation for each sampling scenario where m_1 and m_2 are average of missing probabilities for cases and non-cases, respectively.

				γ_1				γ_2			
sampling	m_0	(m_1, m_2)	n	Bias	SSE	ESE	CP	Bias	SSE	ESE	CP
I	0.3	(0,0.40)	550	-0.0091	0.2519	0.2473	0.948	0.0123	0.2536	0.2468	0.951
			700	-0.0108	0.2090	0.2178	0.957	0.0144	0.2142	0.2174	0.955
			900	-0.0033	0.1884	0.1904	0.956	0.0035	0.2028	0.1899	0.955
II		(0.15,0.35)	550	-0.0047	0.2592	0.2529	0.955	0.0012	0.2545	0.2527	0.956
			700	-0.0076	0.2211	0.2233	0.955	0.0072	0.2171	0.2229	0.954
			900	-0.0048	0.1962	0.1954	0.956	0.0081	0.2053	0.1950	0.945
III			550	-0.0076	0.2701	0.2620	0.948	0.0074	0.2618	0.2618	0.954
			700	-0.0077	0.2363	0.2321	0.945	0.0065	0.2276	0.2318	0.957
			900	-0.0074	0.2045	0.2027	0.962	0.0061	0.2077	0.2025	0.940
I	0.5	(0,0.65)	550	-0.0268	0.5032	0.3479	0.948	0.0190	0.3860	0.3464	0.925
			700	-0.0029	0.3161	0.3103	0.936	0.0208	0.3363	0.3083	0.926
			900	-0.0107	0.2798	0.2730	0.962	0.0171	0.3021	0.2712	0.912
II		(0.45,0.60)	550	0.0015	0.3092	0.3037	0.947	0.0013	0.3106	0.3060	0.954
			700	-0.0205	0.2812	0.2686	0.939	0.0099	0.2862	0.2708	0.947
			900	-0.0160	0.2359	0.2320	0.947	0.0152	0.2414	0.2309	0.936
III			550	-0.0121	0.3308	0.3224	0.961	0.0082	0.3173	0.3210	0.963
			700	-0.0099	0.2885	0.2883	0.956	0.0013	0.2861	0.2821	0.953
			900	0.0044	0.2616	0.2476	0.940	-0.0013	0.2617	0.2464	0.944

Table 2: Bias, empirical standard error(SSE), average of the estimated standard error(ESE), the relative efficiencies (REE) compared to the Full estimators and empirical coverage probability (CP) of 95% confidence intervals for the IPW estimators of γ_1, γ_2 under model (2.26) with average of total missing probabilities $m_0 = 0.3,\ 0.5$ and about 58% censoring percentage based on 1000 simulation for each sampling scenario where m_1 and m_2 are average of missing probabilities for cases and non-cases, respectively.

				γ_1				γ_2			
sampling	m_0	(m_1, m_2)	n	Bias	SSE	ESE	CP	Bias	SSE	ESE	CP
I	0.3	(0,0.40)	550	-0.0112	0.2846	0.2804	0.955	0.0142	0.2990	0.2812	0.935
			700	-0.0021	0.2414	0.2455	0.957	-0.0034	0.2431	0.2462	0.955
			900	-0.0105	0.2091	0.2161	0.955	-0.0010	0.2162	0.2167	0.951
II		(0.15,0.30)	550	-0.0051	0.3020	0.2880	0.941	0.0113	0.3007	0.2882	0.949
			700	-0.0023	0.2576	0.2535	0.947	-0.0090	0.2518	0.2536	0.953
			900	-0.0073	0.2282	0.2230	0.948	-0.0019	0.2225	0.2231	0.959
III			550	-0.0055	0.3141	0.3008	0.942	0.0105	0.3085	0.3010	0.948
			700	-0.0031	0.2757	0.2645	0.940	-0.0054	0.2629	0.2646	0.953
			900	-0.0068	0.2388	0.2330	0.944	-0.0023	0.2341	0.2331	0.957
I	0.5	(0,0.65)	550	-0.0171	0.3404	0.3408	0.957	0.0350	0.3607	0.3414	0.948
			700	-0.0035	0.2879	0.2987	0.962	-0.0014	0.3078	0.2993	0.955
			900	-0.0180	0.2460	0.2623	0.969	0.0074	0.2574	0.2627	0.960
II		(0.60,0.50)	550	-0.0077	0.4220	0.3868	0.941	0.0136	0.4008	0.3877	0.949
			700	-0.0130	0.3445	0.3397	0.951	0.0024	0.3455	0.3400	0.944
			900	-0.0144	0.2937	0.2976	0.949	-0.0009	0.3126	0.2987	0.946
III		(0.5,0.5)	550	-0.0196	0.4023	0.3756	0.943	0.0278	0.4015	0.3778	0.945
			700	-0.0065	0.3403	0.3263	0.937	-0.0062	0.3297	0.3283	0.952
			900	-0.0136	0.2944	0.2859	0.949	-0.0035	0.2923	0.2879	0.953

Table 3: The bias (Bias) for Full, IPW and CC estimators of γ_1 and γ_2 under model (2.25) and (2.26) with average of total missing probabilities $m_0 = 0.3,\ 0.5$ and about 45% censoring percentage based on 1000 simulation for each sampling scenario where m_1 and m_2 are average of missing probabilities for cases and non-cases, respectively.

					Bias(γ_1)			Bias(γ_2)		
Model	Sample	m_0	(m_1, m_2)	n	Full	IPW	CC	Full	IPW	CC
(2.25)	I	0.3	(0,0.40)	550	-0.0042	-0.0091	0.2548	0.0030	0.0123	-0.0025
				700	-0.0054	-0.0108	0.2523	0.0070	0.0144	-0.0024
				900	-0.0002	-0.0033	0.2627	0.0018	0.0035	-0.0108
	II		(0.15,0.35)	550		-0.0047	0.0626		0.0012	-0.0095
				700		-0.0076	0.0612		0.0072	-0.0034
				900		-0.0048	0.0628		0.0081	-0.0019
	III			550		-0.0076	-0.0187		0.0074	0.0069
				700		-0.0077	-0.0081		0.0065	0.0066
				900		-0.0074	-0.0078		0.0061	0.0063
	I	0.5	(0,0.65)	550		-0.0268	0.2674		0.0190	0.0260
				700		-0.0029	0.3341		0.0208	-0.0753
				900		-0.0107	0.2772		0.0171	0.0264
	II		(0.45,0.60)	550		0.0015	-0.0424		0.0013	-0.0082
				700		-0.0205	-0.0533		0.0099	-0.0069
				900		-0.0160	0.0532		0.0152	0.0020
	III			550		-0.0121	-0.0160		0.0082	0.0092
				700		-0.0099	-0.0117		0.0013	0.0022
				900		0.0044	0.0020		-0.0013	0.0002
(2.26)	I	0.3	(0,0.40)	550	-0.0078	-0.0112	0.0752	0.0119	0.0142	0.0180
				700	0.0005	-0.0021	0.0759	-0.0073	-0.0034	0.0044
				900	-0.0091	-0.0105	0.0708	-0.0011	-0.0010	0.0066
	II		(0.15,0.30)	550		-0.0051	0.0489		0.0113	0.0118
				700		-0.0023	0.0534		-0.0090	-0.0085
				900		-0.0073	0.0477		-0.0019	-0.0015
	III			550		-0.0055	-0.0063		0.0105	0.0109
				700		-0.0031	-0.0036		-0.0054	-0.0059
				900		-0.0068	-0.0072		-0.0023	-0.0021
	I	50%	(0,0.65)	550		-0.0171	0.3192		0.0350	0.0448
				700		-0.0035	0.3081		-0.0014	0.0114
				900		-0.0180	0.3109		0.0074	0.0215
	II		(0.60,0.50)	550		-0.0077	0.0057		0.0136	0.0102
				700		-0.0130	0.0024		0.0024	-0.0003
				900		-0.0144	-0.0004		-0.0009	-0.0021
	III		(0.5,0.5)	550		-0.0196	-0.0124		0.0278	0.0236
				700		-0.0065	-0.0028		0.0062	0.0061
				900		-0.0136	-0.0108		-0.0035	-0.0042

Table 4: The empirical standard error (SSE) and average of the estimated standard error (ESE) for Full, IPW and CC estimators of γ_1 and γ_2 under (2.25) and (2.26) with average of total missing probabilities $m_0 = 0.3,\ 0.5$ and about 45% censoring percentage based on 1000 simulation for each sampling scenario, where m_1 and m_2 are average of missing probabilities for cases and non-cases, respectively.

					SSE(γ_1)			SSE(γ_2)			ESE(γ_1)			ESE(γ_2)			CP(γ_1)			CP(γ_2)		
Model	Sample	m_0	(m_1, m_2)	n	Full	IPW	CC	Full	IPW	CC	Full	IPW	CC	Full	IPW	CC	Full	IPW	CC	Full	IPW	CC
(2.25)	I	0.3	(0,0.40)	550	0.2329	0.2519	0.2528	0.2239	0.2536	0.2475	0.2213	0.2473	0.2415	0.2213	0.2468	0.2422	0.943	0.948	0.944	0.951	0.951	0.949
				700	0.1988	0.2090	0.2193	0.1949	0.2142	0.2113	0.1957	0.2178	0.2127	0.1956	0.2174	0.2132	0.947	0.957	0.938	0.953	0.955	0.943
				900	0.1776	0.1884	0.1886	0.1835	0.2028	0.1972	0.1711	0.1904	0.1861	0.1711	0.1899	0.1866	0.949	0.956	0.949	0.929	0.932	0.933
	II		(0.15,0.35)	550		0.2592	0.2541		0.2545	0.2493		0.2529	0.2477		0.2527	0.2478		0.955	0.955		0.956	0.959
				700		0.2211	0.2204		0.2171	0.2126		0.2233	0.2188		0.2229	0.2187		0.947	0.935		0.954	0.953
				900		0.1962	0.1941		0.2053	0.2004		0.1954	0.1914		0.1950	0.1914		0.956	0.949		0.945	0.945
	III			550		0.2701	0.2699		0.2618	0.2618		0.2620	0.2618		0.2618	0.2617		0.948	0.948		0.954	0.954
				700		0.2363	0.2357		0.2276	0.2275		0.2321	0.2321		0.2318	0.2320		0.945	0.945		0.957	0.957
				900		0.2045	0.2045		0.2077	0.2077		0.2027	0.2027		0.2025	0.2026		0.962	0.961		0.940	0.939
	I	0.5	(0,0.65)	550		0.5032	0.2929		0.3860	0.4743		0.3479	0.2841		0.3464	0.2854		0.948	0.941		0.925	0.938
				700		0.3161	2.0961		0.3363	2.1256		0.3103	0.2493		0.3083	0.2502		0.936	0.930		0.926	0.953
				900		0.2798	0.2299		0.3021	1.2207		0.2730	0.2184		0.2712	0.2193		0.938	0.943		0.912	0.938
	II		(0.45,0.60)	550		0.3092	0.3018		0.3106	0.3004		0.3037	0.2963		0.3060	0.2958		0.947	0.946		0.954	0.959
				700		0.2812	0.2717		0.2862	0.2702		0.2686	0.2617		0.2708	0.2614		0.939	0.944		0.947	0.952
				900		0.2359	0.2280		0.2414	0.2302		0.2320	0.2244		0.2309	0.2238		0.947	0.942		0.936	0.941
	III			550		0.3308	0.3314		0.3173	0.3169		0.3224	0.3229		0.3210	0.3214		0.961	0.959		0.963	0.967
				700		0.2885	0.2885		0.2861	0.2865		0.2833	0.2838		0.2821	0.2828		0.956	0.953		0.953	0.954
				900		0.2616	0.2606		0.2617	0.2601		0.2476	0.2479		0.2464	0.2468		0.940	0.942		0.944	0.946
(2.26)	I	0.3	(0,0.40)	550	0.2666	0.2846	0.3023	0.2630	0.2990	0.3026	0.2523	0.2804	0.2856	0.2527	0.2812	0.2866	0.942	0.955	0.944	0.943	0.935	0.938
				700	0.2275	0.2414	0.2614	0.2188	0.2431	0.2468	0.2218	0.2455	0.2509	0.2221	0.2462	0.2517	0.943	0.957	0.936	0.949	0.955	0.952
				900	0.1995	0.2091	0.2223	0.1951	0.2162	0.2205	0.1954	0.2161	0.2209	0.1958	0.2167	0.2216	0.943	0.955	0.954	0.952	0.951	0.958
	II		(0.15,0.30)	550		0.3020	0.3050		0.3007	0.2994		0.2880	0.2879		0.2882	0.2883		0.941	0.939		0.949	0.945
				700		0.2576	0.2593		0.2518	0.2526		0.2535	0.2537		0.2536	0.2541		0.947	0.945		0.953	0.952
				900		0.2282	0.2313		0.2225	0.2226		0.2230	0.2232		0.2231	0.2235		0.948	0.943		0.959	0.958
	III			550		0.3141	0.3149		0.3085	0.3088		0.3008	0.3008		0.3010	0.3012		0.942	0.936		0.948	0.948
				700		0.2757	0.2765		0.2629	0.2639		0.2645	0.2647		0.2646	0.2650		0.940	0.937		0.953	0.948
				900		0.2388	0.2396		0.2341	0.2344		0.2330	0.2332		0.2331	0.2335		0.944	0.944		0.957	0.959
	I	0.5	(0,0.65)	550		0.3404	0.3464		0.3607	0.3498		0.3408	0.3407		0.3414	0.3423		0.957	0.958		0.948	0.950
				700		0.2879	0.3092		0.3078	0.3045		0.2987	0.3008		0.2993	0.3021		0.962	0.950		0.955	0.946
				900		0.2460	0.2701		0.2574	0.2609		0.2623	0.2641		0.2627	0.2652		0.969	0.942		0.960	0.962
	II		(0.60,0.50)	550		0.4220	0.4297		0.4008	0.4056		0.3868	0.3874		0.3877	0.3875		0.941	0.938		0.949	0.949
				700		0.3445	0.3475		0.3455	0.3463		0.3397	0.3409		0.3400	0.3404		0.951	0.948		0.944	0.952
				900		0.2937	0.2946		0.3126	0.3127		0.2976	0.2979		0.2987	0.2982		0.949	0.956		0.946	0.951
	III			550		0.4023	0.3985		0.4015	0.3939		0.3756	0.3708		0.3778	0.3690		0.943	0.941		0.945	0.950
				700		0.3403	0.3375		0.3297	0.3237		0.3263	0.3229		0.3283	0.3214		0.937	0.937		0.952	0.957
				900		0.2944	0.2930		0.2923	0.2847		0.2859	0.2831		0.2879	0.2819		0.949	0.948		0.953	0.953

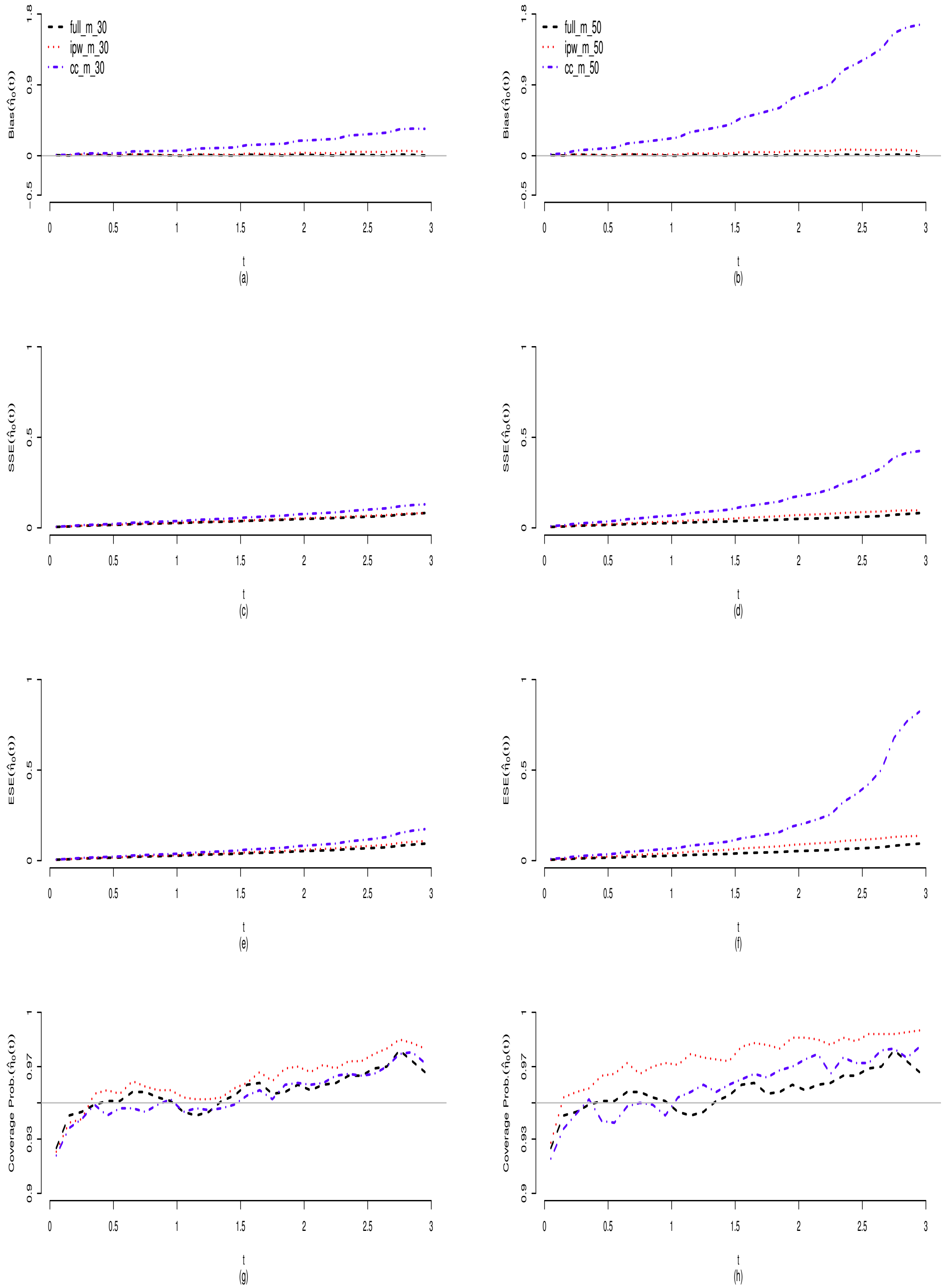


Figure 1: Comparison of Full, IPW, CC estimators for the basline cumulative coefficient $\eta(t)$ under (2.25) with $m_0 = 0.3,\ 0.5$, $n = 700$ and about 45% censoring percentage based on 1000 simulation for sampling design I. Left graphs are for $m_0 = 0.3$. Right graphs are for $m_0 = 0.5$. (a), (b): The plots of the biases of the estimates. (c), (d): The plots of the empirical standard errors of the estimates. (e), (f): The plots of the average of the estimated standard errors of the estimates. (g), (h): The plots of the coverage probabilities of the estimators.

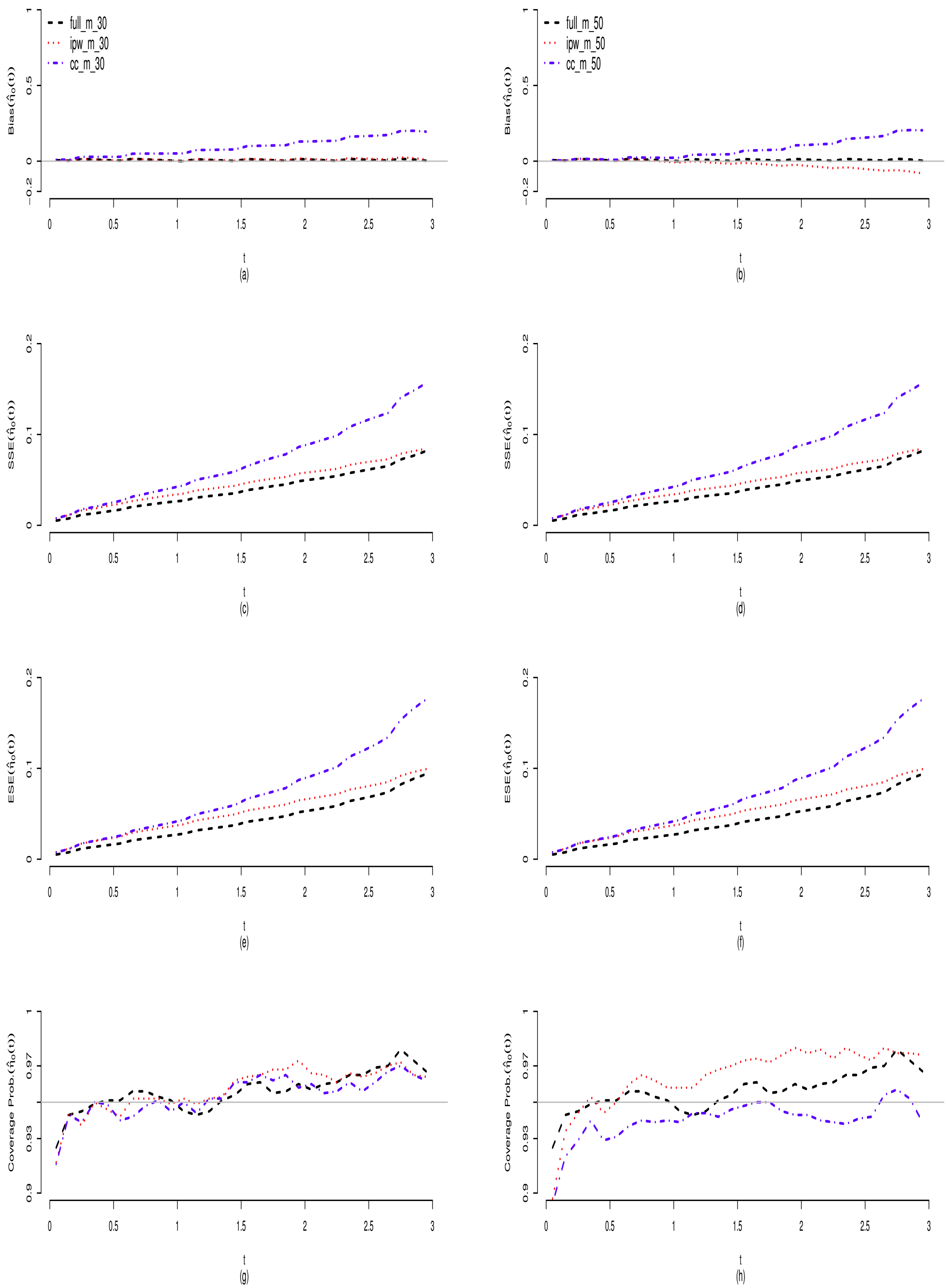


Figure 2: Comparison of Full, IPW, CC estimators for the basline cumulative coefficient $\eta(t)$ under (2.25) with $m_0 = 30\%,\ 50\%$, $n = 700$ and about 45% censoring percentage based on 1000 simulation for sampling design II. Left graphs are for $m_0 = 0.3$. Right graphs are for $m_0 = 0.5$. (a), (b): The plots of the biases of the estimates. (c), (d): The plots of the empirical standard errors of the estimates. (e), (f): The plots of the average of the estimated standard errors of the estimates. (g), (h): The plots of the coverage probabilities of the estimators.

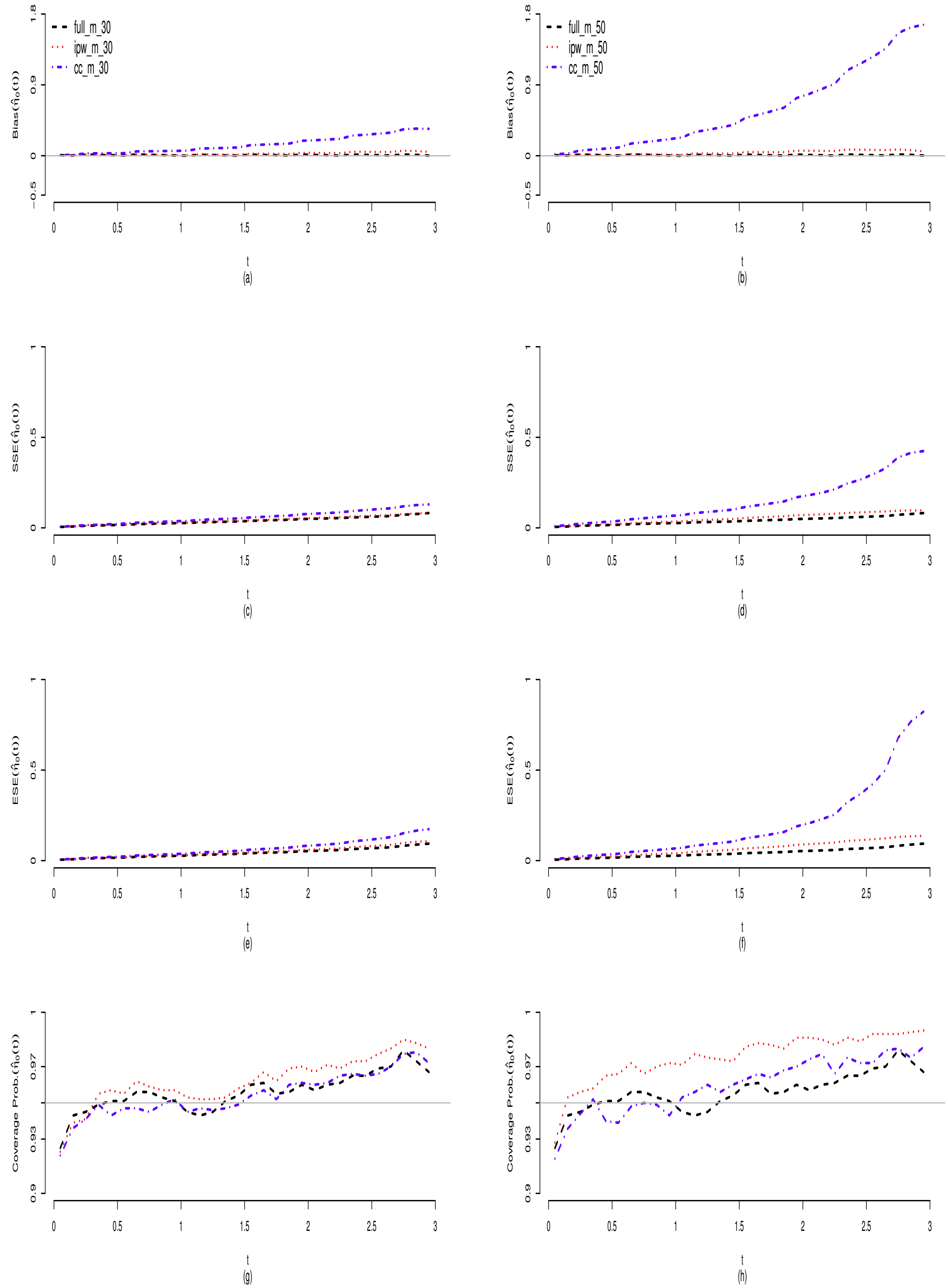


Figure 3: Comparison of Full, IPW, CC estimators for the basline cumulative coefficient $\eta(t)$ under (2.25) with $m_0 = 0.3,\ 0.5$ $n = 700$ and about 45% censoring percentage based on 1000 simulation for sampling design III. Left graphs are for $m_0 = 0.3$. Right graphs are for $m_0 = 0.5$. (a), (b): The plots of the biases of the estimates. (c), (d): The plots of the empirical standard errors of the estimates. (e), (f): The plots of the average of the estimated standard errors of the estimates. (g), (h): The plots of the coverage probabilities of the estimators.

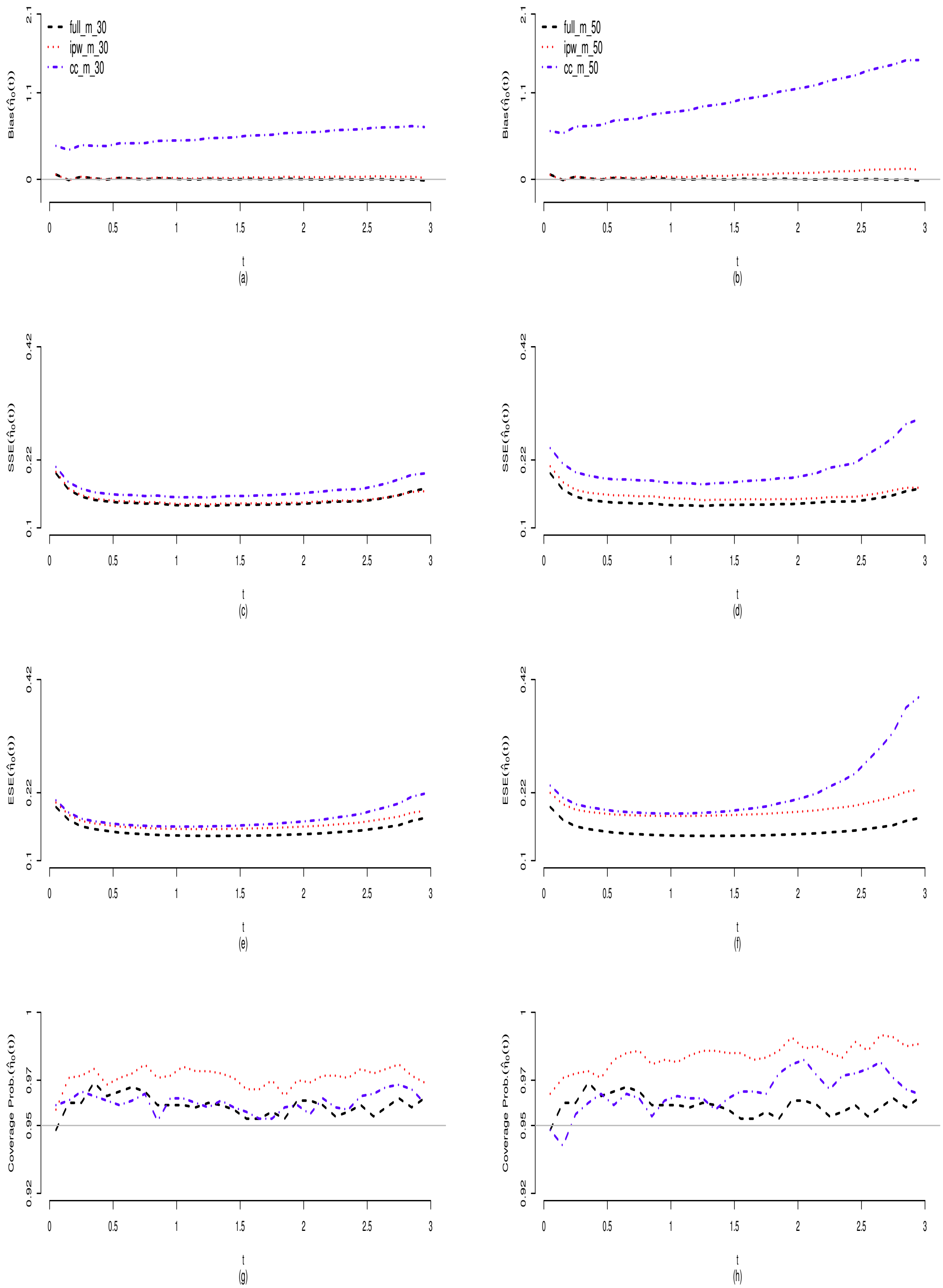


Figure 4: Comparison of Full, IPW, CC estimators for the basline cumulative coefficient $\eta(t)$ under (2.26) with $m_0 = 0.3,\ 0.5$, $n = 700$ and about 45% censoring percentage based on 1000 simulation for sampling design I. Left graphs are for $m_0 = 0.3$. Right graphs are for $m_0 = 0.5$. (a), (b): The plots of the biases of the estimates. (c), (d): The plots of the empirical standard errors of the estimates. (e), (f): The plots of the average of the estimated standard errors of the estimates. (g), (h): The plots of the coverage probabilities of the estimators.

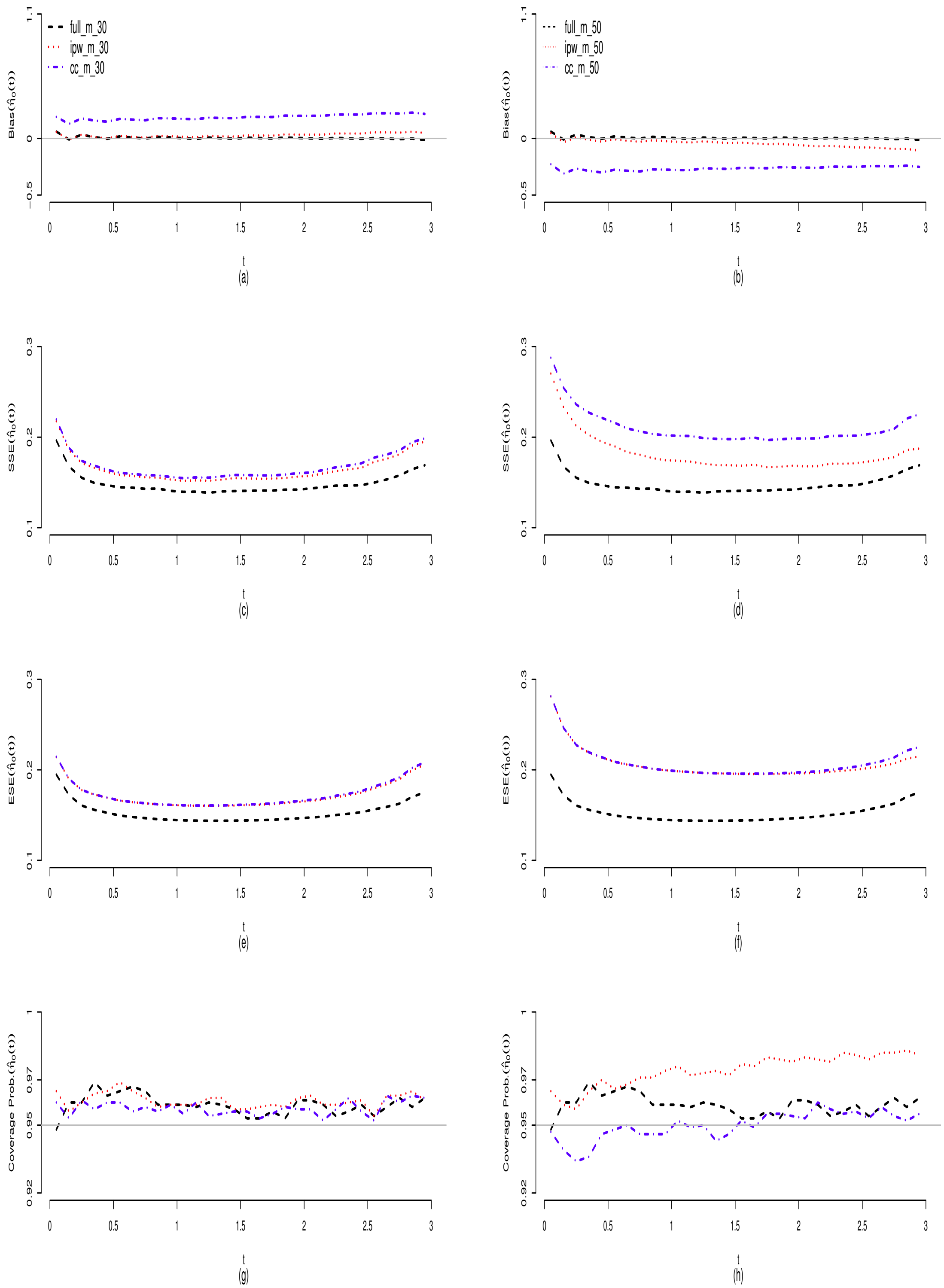


Figure 5: Comparison of Full, IPW, CC estimators for the basline cumulative coefficient $\eta(t)$ under (2.26) with $m_0 = 0.3,\ 0.5$ and about 45% censoring percentage based on 1000 simulation for sampling design II. Left graphs are for $m_0 = 0.3$. Right graphs are for $m_0 = 0.5$. (a), (b): The plots of the biases of the estimates. (c), (d): The plots of the empirical standard errors of the estimates. (e), (f): The plots of the average of the estimated standard errors of the estimates. (g), (h): The plots of the coverage probabilities of the estimators.

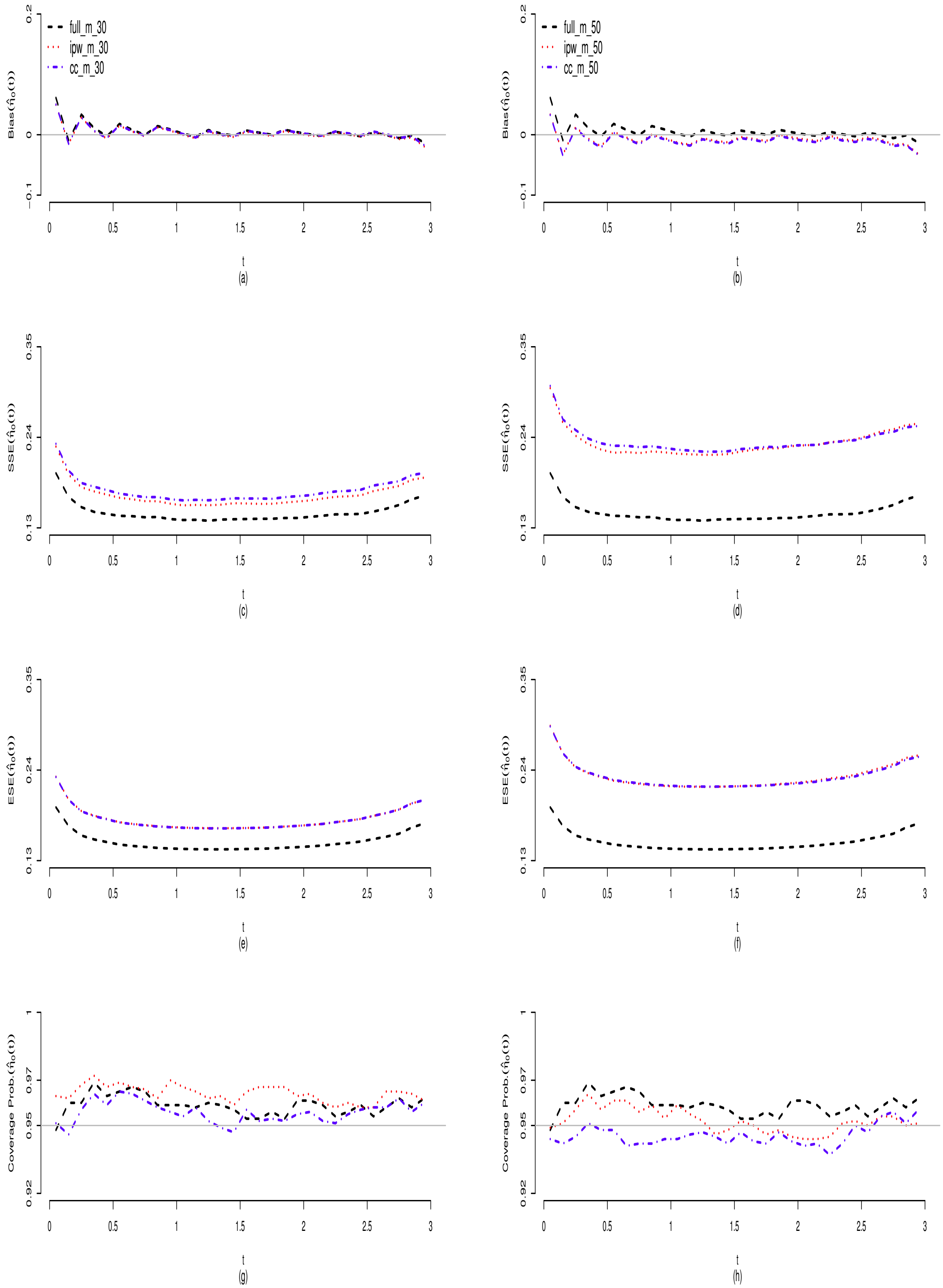


Figure 6: Comparison of Full, IPW, CC estimators for the basline cumulative coefficient $\eta(t)$ under (2.26) with $m_0 = 0.3,\ 0.5$, $n = 700$ and about 55% censoring percentage based on 1000 simulation for sampling design III. Left graphs are for $m_0 = 0.3$. Right graphs are for $m_0 = 0.5$. (a), (b): The plots of the biases of the estimates. (c), (d): The plots of the empirical standard errors of the estimates. (e), (f): The plots of the average of the estimated standard errors of the estimates. (g), (h): The plots of the coverage probabilities of the estimators.

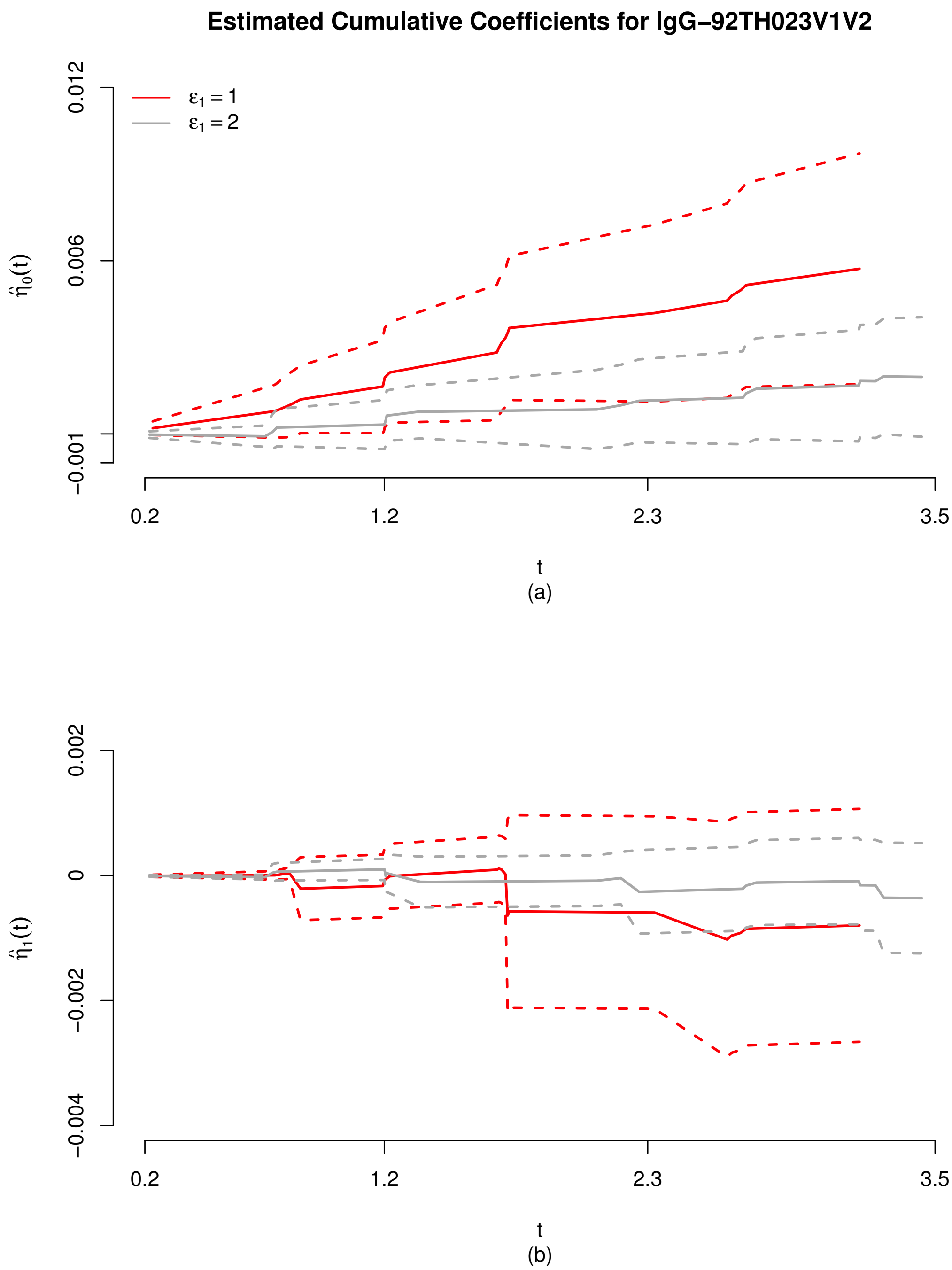
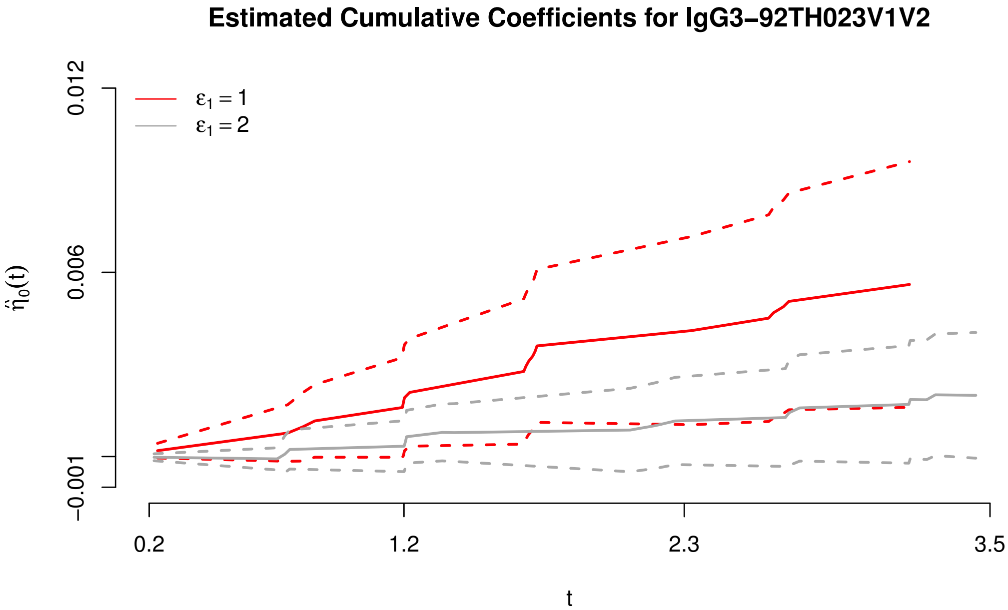
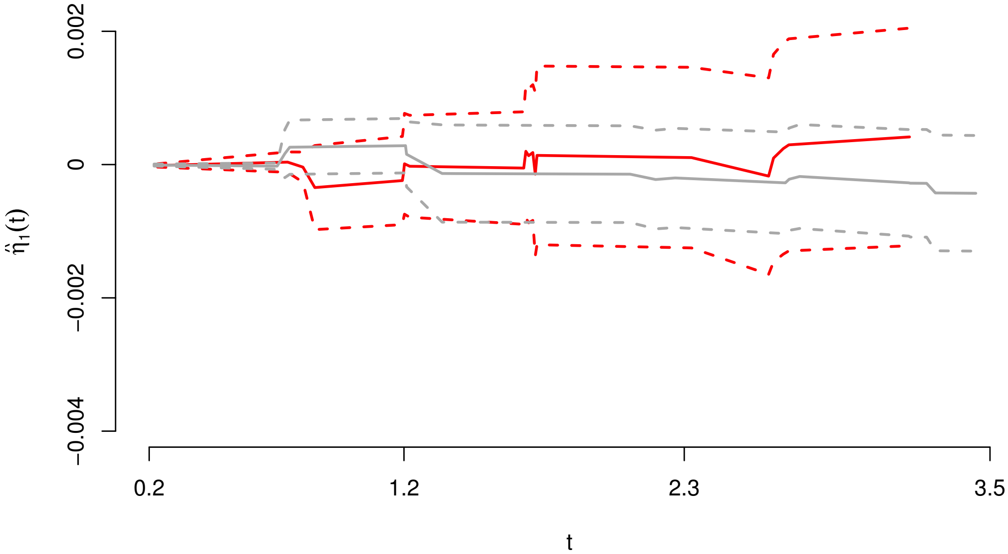


Figure 7: (a) and (b) show that comparison of the IPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the immune response R_i (IgG-92TH023V1V2) in model (2.30) for $\epsilon_1 i = 1$ (red) and $\epsilon_1 i = 2$ (grey), respectively .



(a)



(b)

Figure 8: (a) and (b) show that comparison of the IPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the immune response R_i (IgG3-92TH023V1V2) in model (2.30) for $\epsilon_1 i = 1$ (red) and $\epsilon_1 i = 2$ (grey), respectively.

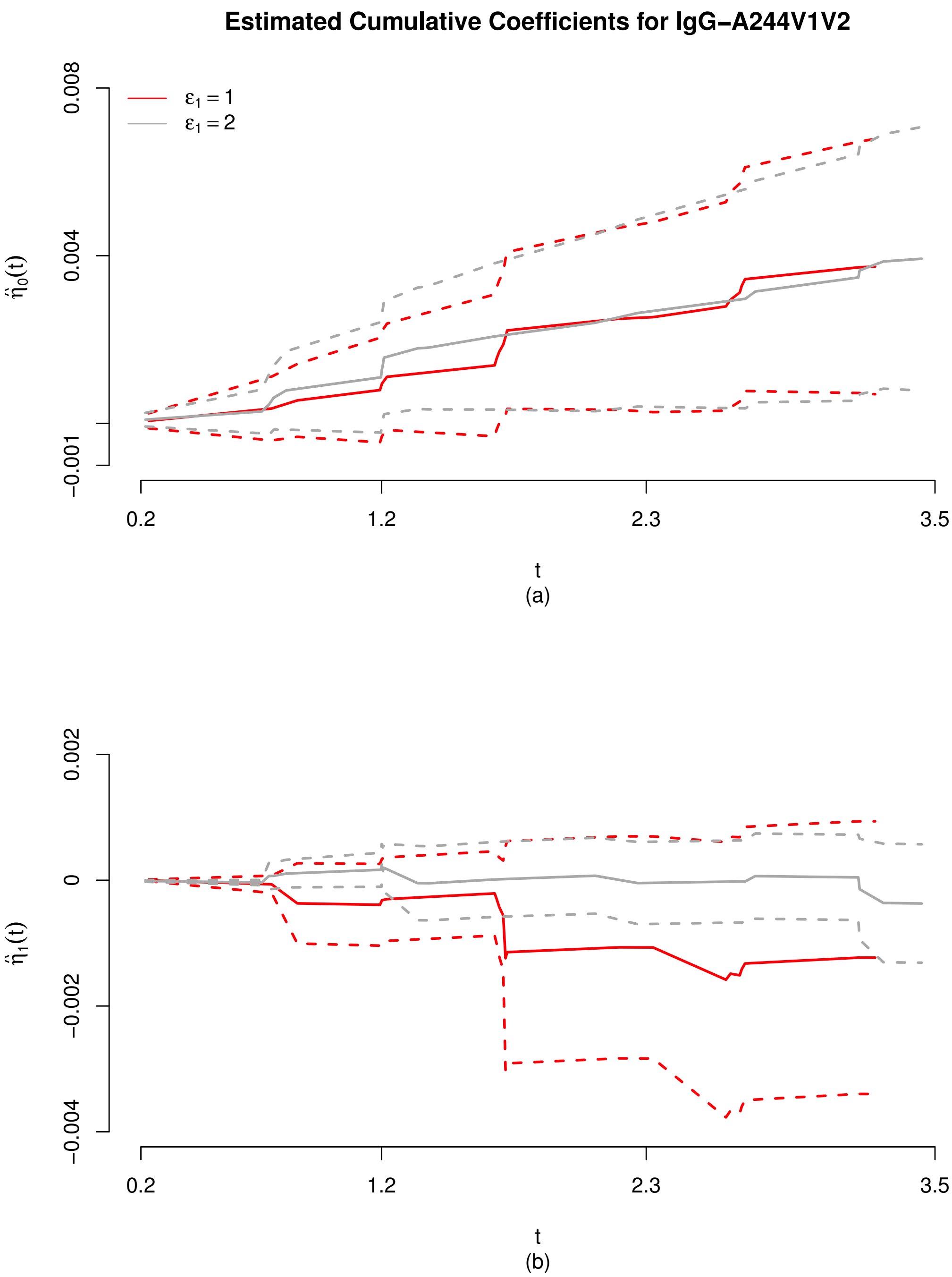
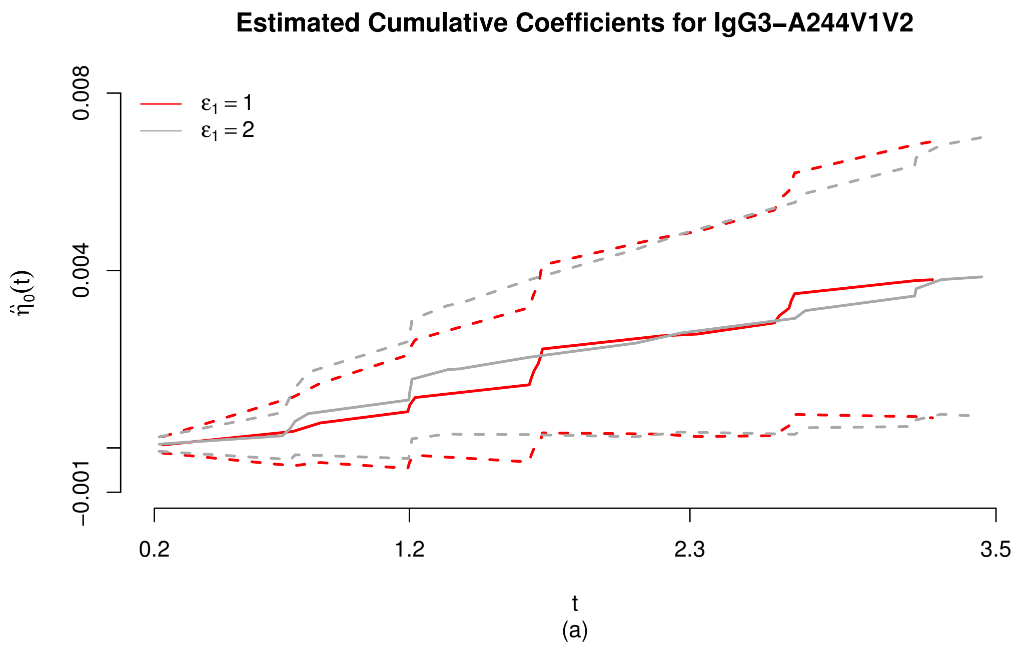


Figure 9: (a) and (b) show that comparison of the IPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the immune response R_i (IgG-A244V1V2) in model (2.30) for $\epsilon_2 i = 1$ (red) and $\epsilon_2 i = 2$ (grey), respectively.



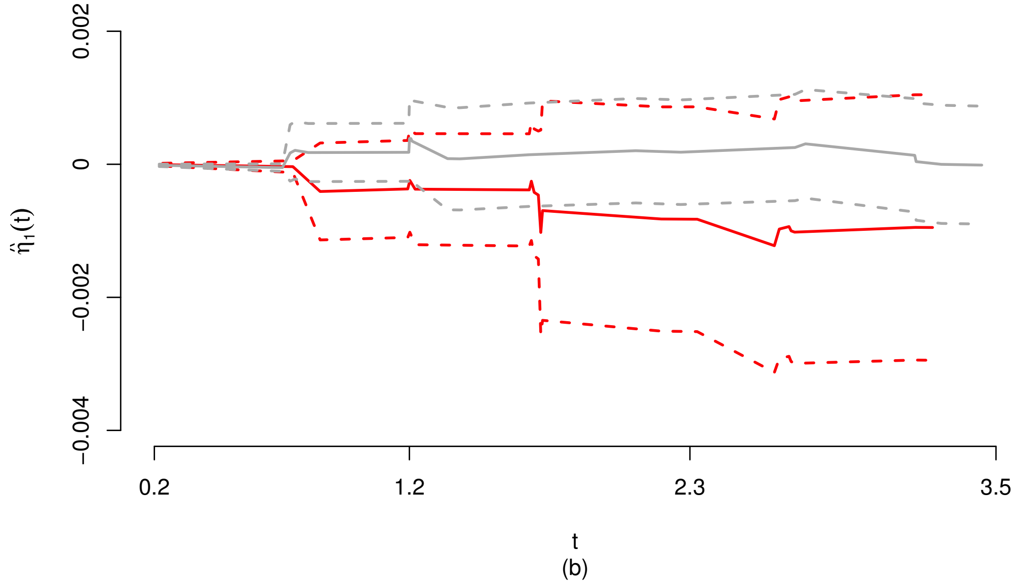


Figure 10: (a) and (b) show that comparison of the IPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the observed immune response R_i (IgG3-A244V1V2) in model (2.30) for $\epsilon_2 i = 1$ (red) and $\epsilon_2 i = 2$ (grey), respectively.

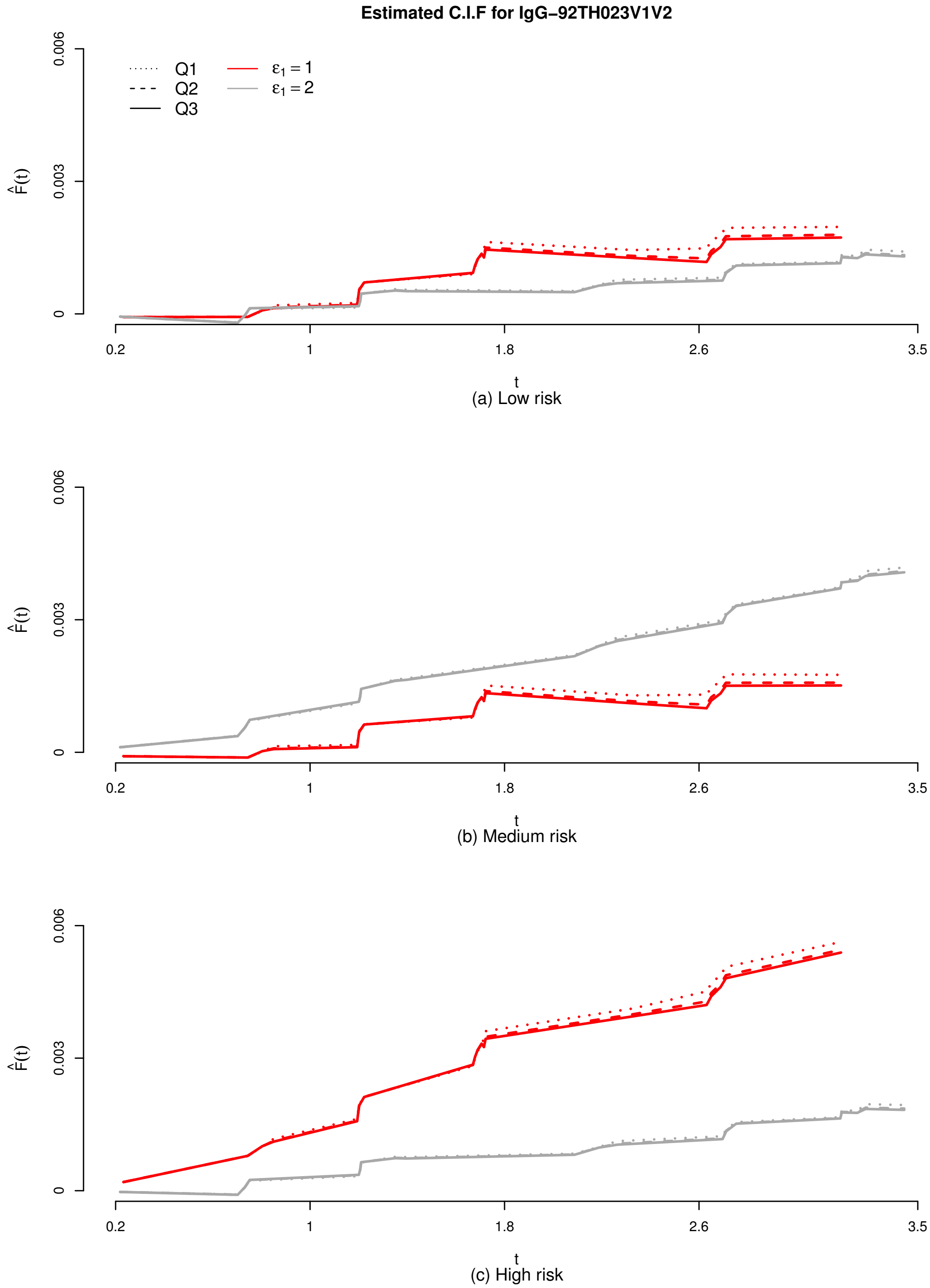


Figure 11: Q_1, Q_2, Q_3 are the first, second and third qualtie of the observed the immune response $R_i = R_{11_i}$ (IgG-92TH023V1V2), where $Q_1 = 0.09027, Q_2 = 0.31310$ and $Q_3 = 0.39230$. (a), (b) and (c) show the predicted cumulative incidence function $\hat{F}$ for $\epsilon_{1i} = 1$ (red) and $\epsilon_{1i} = 2$ (grey) at each level of behavioral risk score group(low, medium, high),respectively, based on the model (2.30).

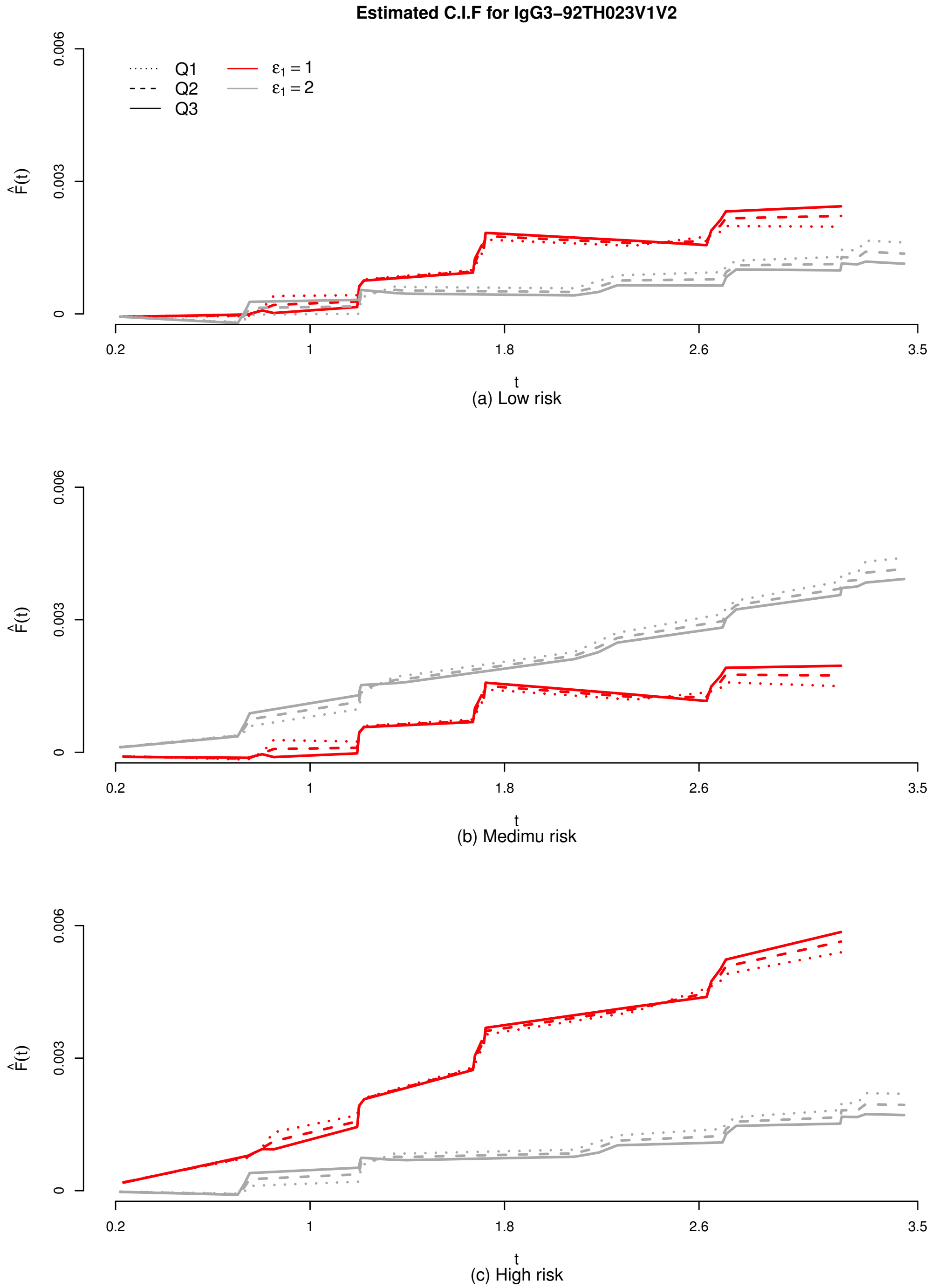


Figure 12: Q_1, Q_2, Q_3 are the first, second and third qualtie of the observed the immune response $R_i = R_{12_i}$ (IgG3-92TH023V1V2), where $Q_1 = -0.4677, Q_2 = 0.1196$ and $Q_3 = 0.6484$. (a), (b) and (c) show the predicted cumulative incidence function $\hat{F}$ for $\epsilon_{1i} = 1$ (red) and $\epsilon_{1i} = 2$ (grey) at each level of behavioral risk score group(low, medium, high),respectively, based on the model (2.30).

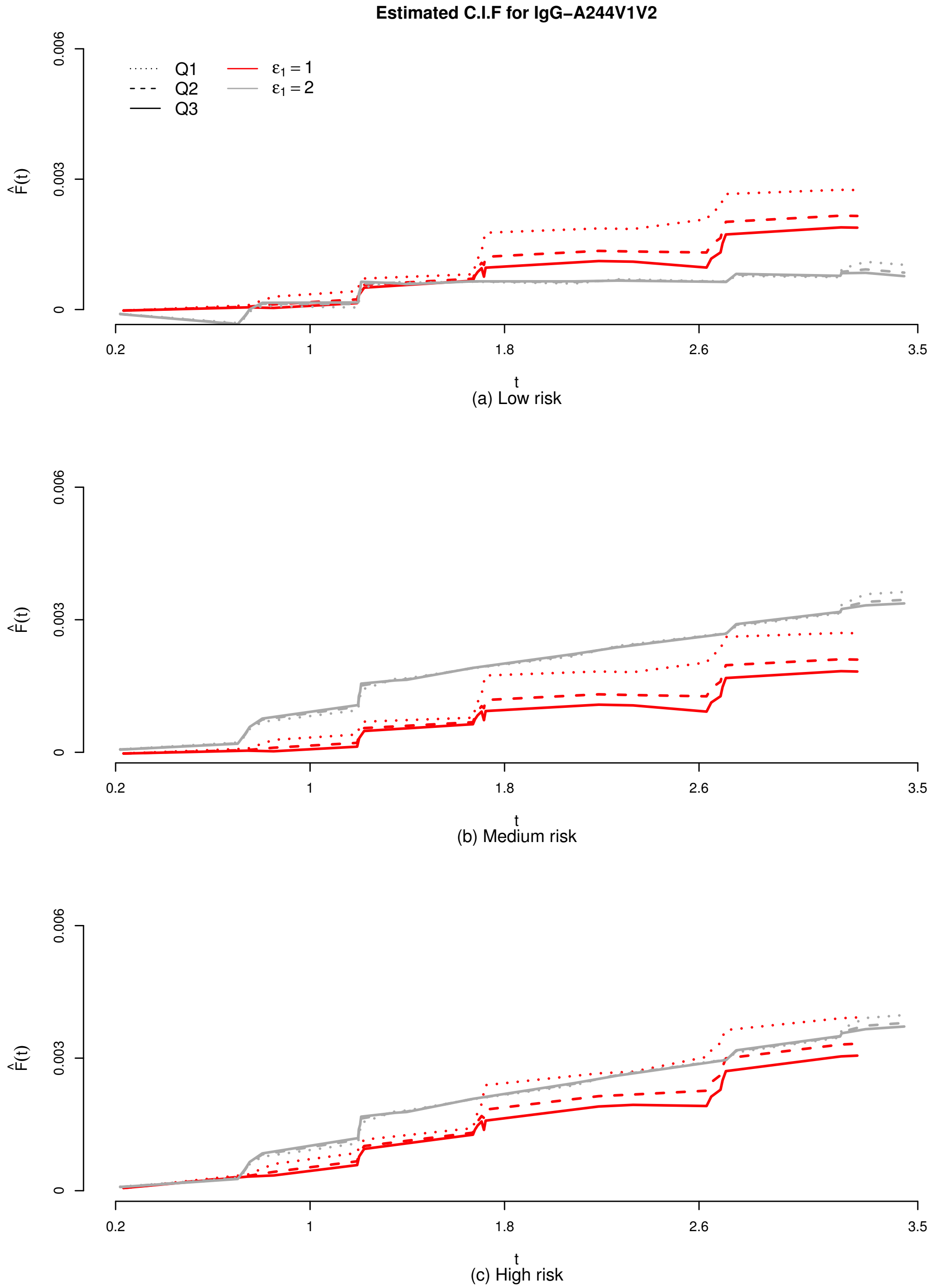


Figure 13: Q_1, Q_2, Q_3 are the first, second and third qualtie of the observed the immune response $R_i = R_{21_i}$ (IgG-A244V1V2), where$Q_1 = -0.1530, Q_2 = 0.3321$ and $Q_3 = 0.5514$. (a), (b) and (c) show the predicted cumulative incidence function $\hat{F}$ for $\epsilon_2 i = 1$ (red) and $\epsilon_2 i = 2$ (black) at each level of behavioral risk score group(low, medium, high),respectively, based on the model (2.30).

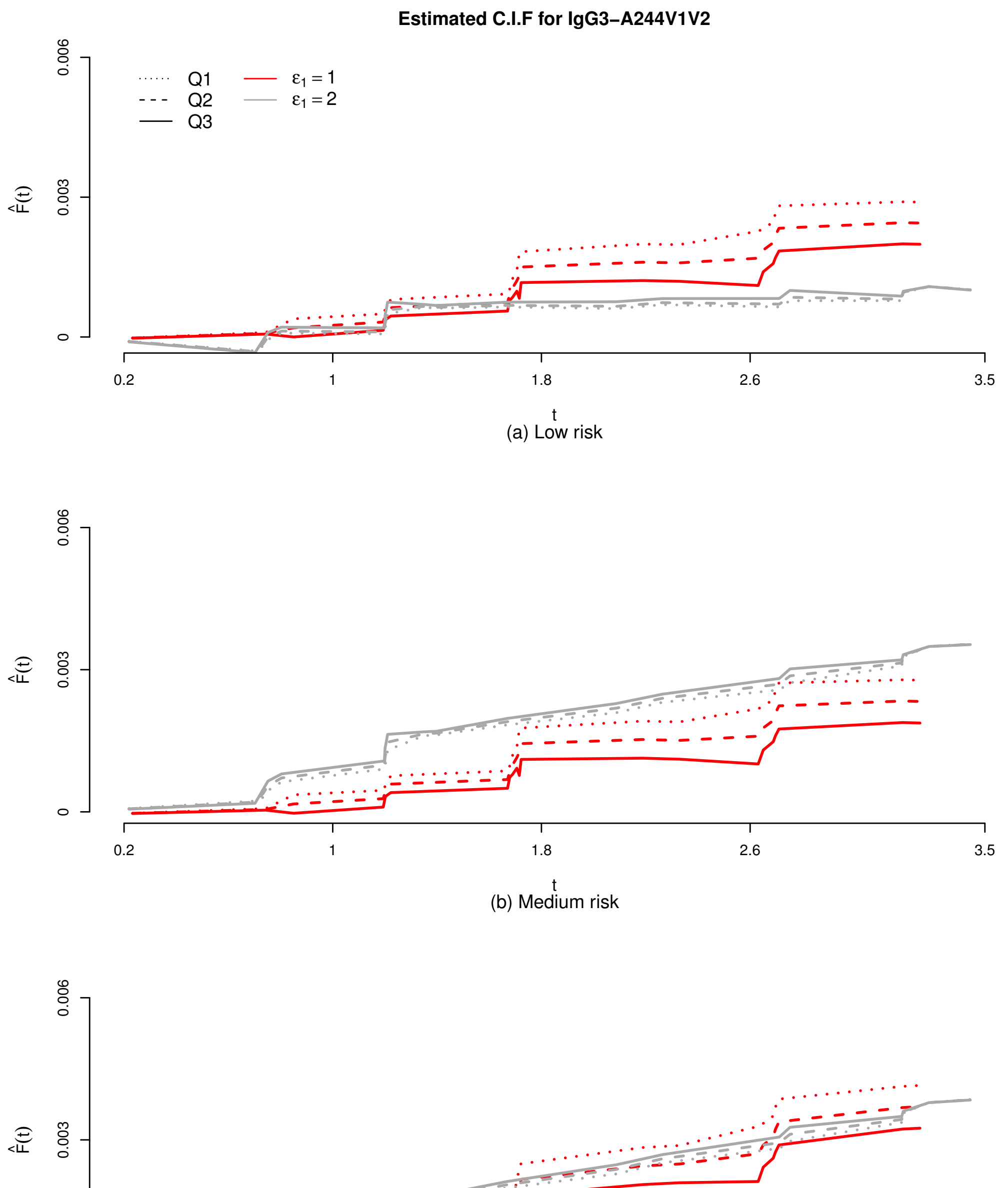


Figure 14: Q_1, Q_2, Q_3 are the first, second and third qualtie of the observed the immune response $R_i = R_{22_i}$ (IgG3-A244V1V2), where $Q_1 = -0.3851, Q_2 = 0.08807$ and $Q_3 = 0.5680$. (a), (b) and (c) show the predicted cumulative incidence function $\hat{F}$ for $\epsilon_2 i = 1$ (red) and $\epsilon_2 i = 2$ (black) at each level of behavioral risk score group(low, medium, high),respectively, based on the model (2.30).

CHAPTER 3: ANALYSIS A SEMIPARAMETRIC ADDITIVE MODEL WITH MISSING COVARIATE USING AUGMENTED INVERSE PROBABILITY WEIGHTED COMPLETE CASE METHOD

In this chapter, we propose an improved estimating equation by adapting the theory of Robins, Rotnizky and Zhao (1994). In section 3.1, augmented IPW of complete case estimating equations have been derived for a semiparametric additive model using identity link function in model (1.22). We also describe the estimation procedure to obtain the augmented IPW estimators. In section 3.2, asymptotic results have been investigated. Some simulation results for the AIPW estimator have been discussed in section 3.3, showing that those estimator improve efficiency.

3.1 Augmented IPW of Complete Case Estimating Equation for a Semiparametric Additive Model

We assume that the selection probability S_i, the conditional expectations $E\{X_i^{(2)}|\mathcal{V}_i\}$ and $E\{X_i^{(2)}(X_i^{(2)})^{\mathsf{T}}|\mathcal{V}_i\}$ are known for those with missing covariates $X_i^{(2)}$.

Let

$$\begin{aligned} e_{i,\eta(t)}(t) &= E\left[\boldsymbol{D}_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})w_i(t)\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)} - F_1(t;\boldsymbol{X}_i,\boldsymbol{Z}_i)\right\}|\mathcal{V}_i\right], \\ e_{i,\gamma}(t) &= E\left[\boldsymbol{D}_{\boldsymbol{\gamma},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})w_i(t)\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)} - F_1(t;\boldsymbol{X}_i,\boldsymbol{Z}_i)\right\}|\mathcal{V}_i\right], \end{aligned}$$

where observed phase-one $\mathcal{V}_i = \{\tilde{T}_i, \Delta_i, \tilde{\epsilon}_i, X_i^{(1)}, Z_i, A_i\}$. Following the augmentation theory of Robins, Rotnizky and Zhao (1994), we consider the following augmented IPW estimating equations for $(\boldsymbol{\eta}(\cdot), \boldsymbol{\gamma}, \hat{\theta})$:

$$\widetilde{\boldsymbol{U}}_{\boldsymbol{\eta}}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\hat{\theta}) = \sum_{i=1}^{n}\left[\psi_i(\hat{\theta})\boldsymbol{D}_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})w_i(t)\left\{\frac{\Delta_i\, N_i(t)}{\widehat{G}(T_i)} - F_1(t;\boldsymbol{X}_i,\boldsymbol{Z}_i)\right\} + (1-\psi_i(\hat{\theta}))e_{i,\eta(t)}(t)\right], \quad (3.1)$$

$$\widetilde{\boldsymbol{U}}_{\boldsymbol{\gamma}}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\hat{\theta}) = \sum_{i=1}^{n}\int_0^{\tau}\left[\psi_i(\hat{\theta})\boldsymbol{D}_{\boldsymbol{\gamma},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})w_i(t)\left\{\frac{\Delta_i\, N_i(t)}{\widehat{G}(T_i)} - F_1(t;\boldsymbol{X}_i,\boldsymbol{Z}_i)\right\} + (1-\psi_i(\hat{\theta}))e_{i,\gamma}(t)\right]dt. (3.2)$$

In equation (3.1), the first part of the contribution, $\psi_i(\hat{\theta})\boldsymbol{D}_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})w_i(t)\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)} - F_1(t;\boldsymbol{X}_i,\boldsymbol{Z}_i)\right\}$, represents the inverse probability weighting of complete case. The second part of the contribution, $(1-\psi_i(\hat{\theta}))e_{i,\eta(t)}(t)$, is the augmentation to the first part with the knowledge of the conditional expectations $E\{X_i^{(2)}|\mathcal{V}_i\}$ and $E\{X_i^{(2)}(X_i^{(2)})^\mathsf{T}|\mathcal{V}_i\}$ for the missing covariates. The contribution from subject i with $\xi_i = 0$ only involves the conditional expectation $e_{i,\eta(t)}(t)$. A similar interpretation applies to the equation (3.2).

The estimating functions given in (3.1) and (3.2) are equivalent to

$$\begin{aligned}
\widetilde{\boldsymbol{U}}_{\boldsymbol{\eta}}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\hat{\theta}) &= (\boldsymbol{D}_{\boldsymbol{\eta}}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma}))^\mathsf{T}\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\left\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})\right\} \\
&\quad +E\left[(\boldsymbol{D}_{\boldsymbol{\eta}}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma}))^\mathsf{T}\boldsymbol{W}(t)(I-\boldsymbol{\Psi}(\hat{\theta}))\left\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})\right\}|\boldsymbol{V}\right], \qquad (3.3) \\
\widetilde{\boldsymbol{U}}_{\boldsymbol{\gamma}}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\hat{\theta}) &= \int_0^\tau (\boldsymbol{D}_{\boldsymbol{\gamma}}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma}))^\mathsf{T}\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\left\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})\right\}dt \\
&\quad + \int_0^\tau E\left[(\boldsymbol{D}_{\boldsymbol{\gamma}}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma}))^\mathsf{T}\boldsymbol{W}(t)(I-\boldsymbol{\Psi}(\hat{\theta}))\left\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})\right\}|\boldsymbol{V}\right]dt. \qquad (3.4)
\end{aligned}$$

Consider the following semiparametric additive model by using identity link function $h(x) = x$ in (1.22):

$$F_{1i}(t;\boldsymbol{\eta},\boldsymbol{\gamma}) = X_i^\mathsf{T}\eta(t) + g(\gamma, Z_i, t). \qquad (3.5)$$

with the ith row vector $\boldsymbol{D}_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma}) = X_i^\mathsf{T}$, $\boldsymbol{D}_{\gamma,i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma}) = \partial g(\gamma,Z_i,t)/\partial\gamma$ where $X_i^\mathsf{T} = (1, X_{i1},\cdots,X_{ip})$ and $g(\gamma,Z_i,t)$ is known function.

Note that

$$\begin{aligned}
e_{i,\eta(t)}(t) &= E\left[X_i^\mathsf{T}|\mathcal{V}_i\right]w_i(t)\left\{\frac{\Delta_i\,N_i(t)}{\widehat{G}(T_i)} - g(\gamma,Z_i,t)\right\} - \{\eta(t)\}^\mathsf{T}E\left[X_iX_i^\mathsf{T}|\mathcal{V}_i\right]w_i(t), \\
e_{i,\gamma}(t) &= \{\partial g(\gamma,Z_i,t)/\partial\gamma\}^\mathsf{T}w_i(t)\left\{\frac{\Delta_i\,N_i(t)}{\widehat{G}(T_i)} - g(\gamma,Z_i,t) - E\left[X_i^\mathsf{T}|\mathcal{V}_i\right]\eta(t)\right\}.
\end{aligned}$$

Let $X = (X_1,\cdots,X_n)^\mathsf{T}$ and $\partial g(\gamma,Z,t)/\partial\gamma$ be the $n\times(p+1)$ and $n\times q$ matrices, respectively. Let $\mathcal{V} = (\mathcal{V}_1,\ldots,\mathcal{V}_n)$, $V_x = (E\{X_1|\mathcal{V}_1\},\cdots,E\{X_n|\mathcal{V}_n\})^\mathsf{T}, V_{xx}(\theta) = \sum_{i=1}^n(1-\psi_i(\theta))w_i(t)E\left[X_iX_i^\mathsf{T}|\mathcal{V}_i\right]$,

where

$$
\begin{aligned}
E\{X_i|\mathcal{V}_i\} &= \begin{pmatrix} X_i^{(1)} \\ \\ E\{X_i^{(2)}|\mathcal{V}_i\} \end{pmatrix}, \\
E\left\{X_i X_i^{\mathsf{T}}|\mathcal{V}_i\right\} &= \begin{pmatrix} X_i^{(1)}(X_i^{(1)})^{\mathsf{T}} & X_i^{(1)}E\{(X_i^{(2)})^{\mathsf{T}}|\mathcal{V}_i\} \\ \\ E\{X_i^{(2)}|\mathcal{V}_i\}(X_i^{(1)})^{\mathsf{T}} & E\{X_i^{(2)}(X_i^{(2)})^{\mathsf{T}}|\mathcal{V}_i\} \end{pmatrix} \text{ for each } i.
\end{aligned} \tag{3.6}
$$

Let

$$
a_\eta(t,\eta(t),\gamma,\theta) \;=\; V_x^{\mathsf{T}} W(t)(I-\boldsymbol{\Psi}(\theta))\left\{\boldsymbol{R}(t)-g(\gamma,Z,t)\right\} - V_{xx}(\theta)\eta(t), \tag{3.7}
$$

$$
a_\gamma(\tau,\eta(\cdot),\gamma,\theta) \;=\; \int_0^\tau \{\frac{\partial g(\gamma,Z,t)}{\partial\gamma}\}^{\mathsf{T}} \boldsymbol{W}(t)(I-\boldsymbol{\Psi}(\theta))\left\{\boldsymbol{R}(t)-V_x\eta(t)-g(\gamma,Z,t)\right\}\,dt, \tag{3.8}
$$

where $V_{xx}(\theta)=E(X^T W(t)(I-\boldsymbol{\Psi}(\theta))X|\mathcal{V})$.

The estimating equations are followed by (3.3) and (3.4) that

$$
\widetilde{\boldsymbol{U}}_{\boldsymbol{\eta}}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\hat\theta) \;=\; X^{\mathsf{T}}\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat\theta)\left\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})\right\} + a_\eta(t,\eta(t),\gamma,\hat\theta), \tag{3.9}
$$

$$
\widetilde{\boldsymbol{U}}_{\boldsymbol{\gamma}}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\hat\theta) \;=\; \int_0^\tau \{\frac{\partial g(\gamma,Z,t)}{\partial\gamma}\}^{\mathsf{T}}\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat\theta)\left\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})\right\}\,dt + a_\gamma(\tau,\eta(\cdot),\gamma,\hat\theta). \tag{3.10}
$$

3.1.1 Estimation Procedure

Let $\mu_1(\mathcal{V}_i,\alpha_1)$ and $\mu_2(\mathcal{V}_i,\alpha_2)$ be the parametric models for $E\{X_i^{(2)}|\mathcal{V}_i\}$ and $E\{X_i^{(2)}(X_i^{(2)})^{\mathsf{T}}|\mathcal{V}_i\}$, respectively, where α_1 and α_2 are r_1 and r_2 dimensional vectors of parameters belonging to some compact sets, and $\mu_1(\cdot,\alpha_1)$ and $\mu_2(\cdot,\alpha_2)$ are some smooth functions. For example, $\mu_1(\cdot,\alpha_1)$ and $\mu_2(\cdot,\alpha_2)$ can be approximated by the first order or second order linear functions of the variables in $\mathcal{V}_i$ or their transformations. In this case the parameters α_1 and α_2 can be estimated by $\hat\alpha_1$ and $\hat\alpha_2$ using the least square regressions of $X_i^{(2)}$ on $\mathcal{V}_i$ and $X_i^{(2)}(X_i^{(2)})^{\mathsf{T}}$ on $\mathcal{V}_i$, respectively, based on the observations with $\xi_i=1$.

By replacing $E\{X_i^{(2)}|\mathcal{V}_i\}$ and $E\{X_i^{(2)}(X_i^{(2)})^{\mathsf{T}}|\mathcal{V}_i\}$ with $\mu_1(\mathcal{V}_i,\hat\alpha_1)$ and $\mu_2(\mathcal{V}_i,\hat\alpha_2)$, respectively, and replacing V_x, $V_{xx}(\hat\theta)$ by $\widehat{V}_x$, $\widehat{V}_{xx}(\hat\theta)$ in $a_\gamma(\tau,\eta(\cdot),\gamma,\hat\theta)$ and $a_\gamma(\tau,\eta(\cdot),\gamma,\hat\theta)$ defined in (3.7) and

(3.8), the estimators $\hat{a}_\eta(t,\eta(t),\gamma,\hat{\theta})$ and $\hat{a}_\gamma(\tau,\eta(\cdot),\gamma,\hat{\theta})$ of $a_\eta(t,\eta(t),\gamma,\hat{\theta})$ and $a_\gamma(\tau,\eta(\cdot),\gamma,\hat{\theta})$ can be obtained, respectively,

$$\begin{aligned}\hat{a}_\eta(t,\eta(t),\gamma,\hat{\theta}) &= \widehat{V}_x^\top W(t)(I-\boldsymbol{\Psi}(\hat{\theta}))\{\boldsymbol{R}(t)-g(\gamma,Z,t)\}-\widehat{V}_{xx}(\hat{\theta})\eta(t), \quad (3.11)\\ \hat{a}_\gamma(\tau,\eta(\cdot),\gamma,\hat{\theta}) &= \int_0^\tau \{\frac{\partial g(\gamma,Z,t)}{\partial\gamma}\}^\top \boldsymbol{W}(t)(I-\boldsymbol{\Psi}(\hat{\theta}))\left\{\boldsymbol{R}(t)-\widehat{V}_x\eta(t)-g(\gamma,Z,t)\right\}dt. \quad (3.12)\end{aligned}$$

Replacing (3.11) and (3.12) into the score functions (3.9) and (3.10), we obtain the following augmented IPW estimating equation for $\boldsymbol{\eta}(t)$ and $\boldsymbol{\gamma}$:

$$\begin{aligned}\widehat{\widehat{\boldsymbol{U}}}_{\boldsymbol{\eta}}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\hat{\theta}) &= X^\top\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})\}+\hat{a}_\eta(t,\eta(t),\gamma,\hat{\theta}), \quad (3.13)\\ \widehat{\widehat{\boldsymbol{U}}}_{\boldsymbol{\gamma}}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\hat{\theta}) &= \int_0^\tau\{\frac{\partial g(\gamma,Z,t)}{\partial\gamma}\}^\top\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})\}\,dt+\hat{a}_\gamma(\tau,\eta(\cdot),\gamma,\hat{\theta}). \quad (3.14)\end{aligned}$$

The augmented inverse probability weighted of the complete-case estimators $\widehat{\boldsymbol{\eta}}(t)$ and $\widehat{\boldsymbol{\gamma}}$ of $\boldsymbol{\eta}(t)$ and $\boldsymbol{\gamma}$ solve the equation $\widehat{\widehat{\boldsymbol{U}}}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(\widehat{\boldsymbol{\eta}},\widehat{\boldsymbol{\gamma}},\hat{\theta})=0$, where $\widehat{\widehat{\boldsymbol{U}}}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(\boldsymbol{\eta},\boldsymbol{\gamma},\hat{\theta})=\{\widehat{\widehat{\boldsymbol{U}}}_{\boldsymbol{\eta}}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\hat{\theta}),\widehat{\widehat{\boldsymbol{U}}}_{\boldsymbol{\gamma}}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\hat{\theta})\}$.

Similar to numerical algorithm in section 2.1.2, the estimating equations (3.13) and (3.14) can be solved by using an iterative algorithm.

[Computational Algorithm] The estimators of $\boldsymbol{\eta}(t)$ and $\boldsymbol{\gamma}$ can be obtained though the following algorithm.

1. Given inverse probability weighting estimators $\boldsymbol{\eta}^{(0)}(t)$ and $\boldsymbol{\gamma}^{(0)}$ as initial values.

2. Estimate V_x and $V_{xx}(\hat{\theta})$ by $\widehat{V}_x$ and $\widehat{V}_{xx}(\hat{\theta})$.

3. Using Taylor expansion of $\boldsymbol{F}_1(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})$ around the values $(\widehat{\boldsymbol{\eta}}^{(i)}(t),\widehat{\boldsymbol{\gamma}}^{(i)})$ at ith iteration, we have

$$\begin{aligned}\boldsymbol{F}_1(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma}) &\approx \boldsymbol{F}_1(t,\widehat{\boldsymbol{\eta}}^{(i)}(t),\widehat{\boldsymbol{\gamma}}^{(i)})+\boldsymbol{D}_{\boldsymbol{\eta}}(t,\widehat{\boldsymbol{\eta}}^{(i)}(t),\widehat{\boldsymbol{\gamma}}^{(i)})\left\{\boldsymbol{\eta}(t)-\widehat{\boldsymbol{\eta}}^{(i)}(t)\right\}\\ &+ \boldsymbol{D}_{\boldsymbol{\gamma}}(t,\widehat{\boldsymbol{\eta}}^{(i)}(t),\widehat{\boldsymbol{\gamma}}^{(i)})\left\{\boldsymbol{\gamma}-\widehat{\boldsymbol{\gamma}}^{(i)}\right\}. \quad (3.15)\end{aligned}$$

4. Using (3.7) and (3.8), $a_\eta(t,\widehat{\boldsymbol{\eta}}^{(i)}(t),\widehat{\boldsymbol{\gamma}}^{(i)},\hat{\theta})$ and $a_\gamma(\tau,\widehat{\boldsymbol{\eta}}^{(i)}(\cdot),\widehat{\boldsymbol{\gamma}}^{(i)},\hat{\theta})$ are estimated by

$$\begin{aligned}\hat{a}_\eta(t,\widehat{\boldsymbol{\eta}}^{(i)}(t),\widehat{\boldsymbol{\gamma}}^{(i)},\hat{\theta}) &= \widehat{V}_x^\top W(t)(I-\boldsymbol{\Psi}(\hat{\theta}))\left\{\boldsymbol{R}(t)-g(\widehat{\boldsymbol{\gamma}}^{(i)},Z,t)\right\}-\widehat{V}_{xx}(\hat{\theta})\widehat{\boldsymbol{\eta}}^{(i)}(t), \quad (3.16)\\ \hat{a}_\gamma(\tau,\widehat{\boldsymbol{\eta}}^{(i)}(\cdot),\widehat{\boldsymbol{\gamma}}^{(i)},\hat{\theta}) &= \int_0^\tau\{\frac{\partial g(\widehat{\boldsymbol{\gamma}}^{(i)},Z,t)}{\partial\widehat{\boldsymbol{\gamma}}^{(i)}}\}^\top\boldsymbol{W}(t)(I-\boldsymbol{\Psi}(\hat{\theta}))\left\{\boldsymbol{R}(t)-\widehat{V}_x\widehat{\boldsymbol{\eta}}^{(i)}(t)-g(\widehat{\boldsymbol{\gamma}}^{(i)},Z,t)\right\}dt \quad (3.17)\end{aligned}$$

and we denote $\hat{a}_{\eta}^{(i)}(t,\hat{\theta}) = \hat{a}_{\eta}(t,\widehat{\boldsymbol{\eta}}^{(i)}(t),\widehat{\boldsymbol{\gamma}}^{(i)},\hat{\theta})$ and $\hat{a}_{\gamma}^{(i)}(\hat{\theta}) = \hat{a}_{\gamma}(\tau,\widehat{\boldsymbol{\eta}}^{(i)}(\cdot),\widehat{\boldsymbol{\gamma}}^{(i)},\hat{\theta})$.

5. Plugging (3.15), (3.16), and (3.17) into (3.13) and (3.14), respectively, to get the approximate estimating equations

$$
\begin{aligned}
& \widehat{\widehat{\boldsymbol{U}}}_{\boldsymbol{\eta}}(t,\widehat{\boldsymbol{\eta}}^{(i)}(t),\widehat{\boldsymbol{\gamma}}^{(i)},\hat{\theta}) \\
\approx\ & \{\boldsymbol{D}_{\boldsymbol{\eta}}^{(i)}(t)\}^{\mathsf{T}}\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\left[\boldsymbol{R}(t)-\boldsymbol{F}_1^{(i)}(t)-\boldsymbol{D}_{\boldsymbol{\eta}}^{(i)}(t)\left\{\boldsymbol{\eta}(t)-\widehat{\boldsymbol{\eta}}^{(i)}(t)\right\}-\boldsymbol{D}_{\boldsymbol{\gamma}}^{(i)}(t)\left\{\boldsymbol{\gamma}-\widehat{\boldsymbol{\gamma}}^{(i)}\right\}\right] \\
& +\hat{a}_{\eta}^{(i)}(t,\hat{\theta}) = 0, \qquad (3.18)
\end{aligned}
$$

$$
\begin{aligned}
& \widehat{\widehat{\boldsymbol{U}}}_{\boldsymbol{\gamma}}(\tau,\widehat{\boldsymbol{\eta}}^{(i)}(\cdot),\widehat{\boldsymbol{\gamma}}^{(i)},\hat{\theta}) \\
\approx\ & \int_0^{\tau}\{\boldsymbol{D}_{\boldsymbol{\gamma}}^{(i)}(t)\}^{\mathsf{T}}\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\Big[\boldsymbol{R}(t)-\boldsymbol{F}_1^{(i)}(t)-\boldsymbol{D}_{\boldsymbol{\eta}}^{(i)}(t)\Big\{\boldsymbol{\eta}(t)-\widehat{\boldsymbol{\eta}}^{(i)}(t)\Big\}-\boldsymbol{D}_{\boldsymbol{\gamma}}^{(i)}(t)\left\{\boldsymbol{\gamma}-\widehat{\boldsymbol{\gamma}}^{(i)}\right\}\Big]\,dt \\
& +\hat{a}_{\gamma}^{(i)}(\hat{\theta}) = 0, \qquad (3.19)
\end{aligned}
$$

where $\boldsymbol{D}_{\boldsymbol{\eta}}^{(i)}(t) = \boldsymbol{D}_{\boldsymbol{\eta}}^{(i)}(t,\widehat{\boldsymbol{\eta}}^{(i)}(t),\widehat{\boldsymbol{\gamma}}^{(i)})$, $\boldsymbol{D}_{\boldsymbol{\gamma}}^{(i)}(t) = \boldsymbol{D}_{\boldsymbol{\gamma}}^{(i)}(t,\widehat{\boldsymbol{\eta}}^{(i)}(t),\widehat{\boldsymbol{\gamma}}^{(i)})$, and $\boldsymbol{F}_1^{(i)}(t) = \boldsymbol{F}_1(t,\widehat{\boldsymbol{\eta}}^{(i)}(t),\widehat{\boldsymbol{\gamma}}^{(i)})$.

6. Solving equation (3.18) for $\boldsymbol{\eta}(t)$ to get

$$
\begin{aligned}
\boldsymbol{\eta}(t) \ =\ & \widehat{\boldsymbol{\eta}}^{(i)}(t) + \{\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}^{(i)}(t,\hat{\theta})\}^{-1}\{\boldsymbol{D}_{\boldsymbol{\eta}}^{(i)}(t)\}^{\mathsf{T}}\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\left\{\boldsymbol{R}(t)-\boldsymbol{F}_1^{(i)}(t)-\boldsymbol{D}_{\boldsymbol{\gamma}}^{(i)}(t)\left\{\boldsymbol{\gamma}-\widehat{\boldsymbol{\gamma}}^{(i)}\right\}\right\} \\
& +\{\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}^{(i)}(t,\hat{\theta})\}^{-1}\hat{a}_{\eta}^{(i)}(t,\hat{\theta}). \qquad (3.20)
\end{aligned}
$$

7. Plugging (3.20) into (3.19) and then solving (3.19) for $\boldsymbol{\gamma}-\widehat{\boldsymbol{\gamma}}^{(i)}$. Then the resulting estimate of $\boldsymbol{\gamma}$ is $\widehat{\boldsymbol{\gamma}}^{(i+1)}$ at $(i+1)$th step estimation. Specially, the $(i+1)$th step estimate for $\boldsymbol{\gamma}$ is

$$
\widehat{\boldsymbol{\gamma}}^{(i+1)} \ =\ \widehat{\boldsymbol{\gamma}}^{(i)} + \left\{\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}^{(i)}(\hat{\theta})\right\}^{-1}\left\{\boldsymbol{B}_{\boldsymbol{\gamma}}^{(i)}(\hat{\theta}) + \hat{a}_{\gamma}^{(i)}(\hat{\theta}) - \boldsymbol{A}_{\eta}^{(i)}(\hat{\theta})\right\}, \qquad (3.21)
$$

where

$$
\begin{aligned}
\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}^{(i)}(\hat{\theta}) &= \int_0^{\tau} \{\boldsymbol{D}_{\boldsymbol{\gamma}}^{(i)}(t)\}^{\top} \boldsymbol{W}(t) \boldsymbol{\Psi}(\hat{\theta}) \boldsymbol{H}^{(i)}(t,\hat{\theta}) \boldsymbol{D}_{\boldsymbol{\gamma}}^{(i)}(t)\, dt \\
\boldsymbol{B}_{\boldsymbol{\gamma}}^{(i)}(\hat{\theta}) &= \int_0^{\tau} \{\boldsymbol{D}_{\boldsymbol{\gamma}}^{(i)}(t)\}^{\top} \boldsymbol{W}(t) \boldsymbol{\Psi}(\hat{\theta}) \boldsymbol{H}^{(i)}(t,\hat{\theta}) \left\{ \boldsymbol{R}(t) - \boldsymbol{F}_1^{(i)}(t) \right\} dt \\
\boldsymbol{H}^{(i)}(t,\hat{\theta}) &= I - \boldsymbol{D}_{\boldsymbol{\eta}}^{(i)}(t) \left[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}^{(i)}(t,\hat{\theta}) \right]^{-1} \{\boldsymbol{D}_{\boldsymbol{\eta}}^{(i)}(t)\}^{\top} \boldsymbol{W}(t) \boldsymbol{\Psi}(\hat{\theta}) \\
\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}^{(i)}(t,\hat{\theta}) &= \{\boldsymbol{D}_{\boldsymbol{\eta}}^{(i)}(t)\}^{\top} \boldsymbol{W}(t) \boldsymbol{\Psi}(\hat{\theta}) \boldsymbol{D}_{\boldsymbol{\eta}}^{(i)}(t) \\
\boldsymbol{A}_{\eta}^{(i)}(\hat{\theta}) &= \int_0^{\tau} \boldsymbol{K}^{(i)}(t,\hat{\theta}) \hat{a}_{\eta}^{(i)}(t,\hat{\theta})\, dt \\
\boldsymbol{K}^{(i)}(t,\hat{\theta}) &= \{\boldsymbol{D}_{\boldsymbol{\gamma}}^{(i)}(t)\}^{\top} \boldsymbol{W}(t) \boldsymbol{\Psi}(\hat{\theta}) \boldsymbol{D}_{\boldsymbol{\eta}}^{(i)}(t) \left[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}^{(i)}(t,\hat{\theta}) \right]^{-1}. \qquad (3.22)
\end{aligned}
$$

8. The estimate of $\boldsymbol{\eta}(t)$ at $(i+1)$th iteration is obtained by plugging $\widehat{\boldsymbol{\gamma}}^{(i+1)}$ into (3.20). Then the $(i+1)$th step estimator for $\boldsymbol{\eta}(t)$ is

$$
\begin{aligned}
\widehat{\boldsymbol{\eta}}^{(i+1)}(t) &= \widehat{\boldsymbol{\eta}}^{(i)}(t) + \{\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}^{(i)}(t,\hat{\theta})\}^{-1} \{\boldsymbol{D}_{\boldsymbol{\eta}}^{(i)}(t)\}^{\top} \boldsymbol{W}(t) \boldsymbol{\Psi}(\hat{\theta}) \Big\{ \boldsymbol{R}(t) - \boldsymbol{F}_1^{(i)}(t) - \boldsymbol{D}_{\boldsymbol{\gamma}}^{(i)}(t) \{\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}^{(i)}(\hat{\theta})\}^{-1} \\
&\quad \left\{ \boldsymbol{B}_{\boldsymbol{\gamma}}^{(i)}(\hat{\theta}) + \hat{a}_{\gamma}^{(i)}(\hat{\theta}) - \boldsymbol{A}_{\eta}^{(i)}(\hat{\theta}) \right\} \Big\} + \{\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}^{(i)}(t,\hat{\theta})\}^{-1} \hat{a}_{\eta}^{(i)}(t,\hat{\theta}). \qquad (3.23)
\end{aligned}
$$

9. Repeat steps 7 and 8 until convergence. We use the criteria of $||\widehat{\boldsymbol{\gamma}}^{(i+1)} - \widehat{\boldsymbol{\gamma}}^{(i)}|| < 10^{-4}$.

3.2 Asymptotic Properties

We derive the expressions for the proposed AIPW estimators and study asymptotic results for those estimators.

Theorem 3.1. *Assume that the models for the selection probability $P(\xi_i = 1|\mathcal{V}_i)$ and both the conditional expectations $E\{X_i^{(2)}|\mathcal{V}_i\}$ and $E\{X_i^{(2)}(X_i^{(2)})^{\mathsf{T}}|\mathcal{V}_i\}$ of the phase-two covariates are correctly specified. The estimators of $\boldsymbol{\gamma}$ and $\boldsymbol{\eta}(t)$ obtained by solving equations (3.13) and (3.14) have the following expressions:*

$$
\widehat{\boldsymbol{\gamma}} - \boldsymbol{\gamma}_0 = \left\{ \boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta_0) \right\}^{-1} \left\{ \boldsymbol{B}_{\boldsymbol{\gamma}}(\theta_0) + \tilde{a}_{\gamma}(\theta_0) - \boldsymbol{A}_{\eta}(\theta_0) \right\} + o_p(n^{-\frac{1}{2}}), \qquad (3.24)
$$

$$
\begin{aligned}
\widehat{\boldsymbol{\eta}}(t) - \boldsymbol{\eta}_0(t) &= \{\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta_0)\}^{-1} \{\boldsymbol{D}_{\boldsymbol{\eta}}(t)\}^{T} \boldsymbol{W}(t) \boldsymbol{\Psi}(\theta_0) \big\{ \boldsymbol{R}(t) - \boldsymbol{F}_1(t) - \boldsymbol{D}_{\boldsymbol{\gamma}}(t) \{\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta_0)\}^{-1} \\
&\quad \left\{ \boldsymbol{B}_{\boldsymbol{\gamma}}(\theta_0) + \tilde{a}_{\gamma}(\theta_0) - \boldsymbol{A}_{\eta}(\theta_0) \right\} \big\} + \{\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta_0)\}^{-1} \tilde{a}_{\eta}(t,\theta_0) + o_p(n^{-\frac{1}{2}}), \qquad (3.25)
\end{aligned}
$$

where

$$\begin{aligned}
\boldsymbol{A}_\eta(\theta) &= \int_0^\tau \boldsymbol{K}(t,\theta)\tilde{a}_\eta(t,\theta)\ dt \\
\boldsymbol{K}(t,\theta) &= \boldsymbol{D}_{\boldsymbol{\gamma}}^T(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta)\boldsymbol{D}_{\boldsymbol{\eta}}(t)\left[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta)\right]^{-1} \\
\tilde{a}_\eta(t,\theta) &= V_x^T W(t)(I-\boldsymbol{\Psi}(\theta))\left\{\boldsymbol{R}(t)-g(\hat{\gamma},Z,t)\right\}-V_{xx}(\theta)\hat{\eta}(t) \\
\tilde{a}_\gamma(\theta) &= \int_0^\tau \{\frac{\partial g(\gamma_0,Z,t)}{\partial\gamma_0}\}^{\mathsf{T}}\boldsymbol{W}(t)(I-\boldsymbol{\Psi}(\hat{\theta}))\left\{\boldsymbol{R}(t)-V_x\hat{\eta}(t)-g(\hat{\gamma},Z,t)\right\}dt, \qquad (3.26)
\end{aligned}$$

and where $\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta)$, $\boldsymbol{B}_{\boldsymbol{\gamma}}(\theta)$ and $\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta)$ are defined in (2.12). Proof of Theorem 3.1 is given in section 4.1.

Let

$$\begin{aligned}
\boldsymbol{q}^*_{\boldsymbol{\gamma}}(s,t,\boldsymbol{\gamma},\theta) &= n^{-1}\sum_{i=1}^n\{\frac{\partial g(\gamma,Z_i,t)}{\partial\gamma}\}^{\mathsf{T}}w_i(t)(1-\psi_i(\theta))\frac{\Delta_i N_i(t)}{G(T_i)}I(s\le\tilde{T}_i\le t), \\
y(t) &= \lim_{n\to\infty} n^{-1}\sum_{i=1}^n \mathcal{I}(\widetilde{T}_i\ge s), \quad \text{uniformly} \quad t\in[0,\tau], \\
{M_j}^c(t) &= \mathcal{I}(\widetilde{T}_j\le t,\Delta_j=0)-\int_0^t \mathcal{I}(\widetilde{T}_i\ge s)d(-\log G(s)), \\
\boldsymbol{\kappa}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\gamma},\theta) &= \int_0^\tau \frac{\boldsymbol{q}^*_{\boldsymbol{\gamma}}(s,t,\boldsymbol{\gamma},\theta)}{y(s)}dM_i^c(s), \\
\boldsymbol{\zeta}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta) &= \sum_{i=1}^n\int_0^\tau\{\frac{\partial g(\gamma,Z_i,t)}{\partial\gamma}\}^{\mathsf{T}}w_i(t)(1-\psi_i(\theta))\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-V_{x,i}\eta(t)-g(\gamma,Z_i,t)\right\}, \\
\boldsymbol{q}^*_{\boldsymbol{\eta}}(s,t,\theta) &= n^{-1}\sum_{i=1}^n V_{x,i}^{\mathsf{T}}w_i(t)(1-\psi_i(\theta))\frac{\Delta_i N_i(t)}{G(T_i)}\mathcal{I}(s\le\widetilde{T}_i\le t), \\
\boldsymbol{\kappa}^*_{\boldsymbol{\eta},i}(t,\theta) &= \int_0^\tau\frac{\boldsymbol{q}^*_{\boldsymbol{\eta}}(s,t,\theta)}{y(s)}d{M_i}^c(s), \\
\boldsymbol{\zeta}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta) &= n^{-1}\sum_{i=1}^n\left\{V_{x,i}^{\mathsf{T}}w_i(t)(1-\psi_i(\theta))\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-g_i(\gamma,Z_i,t)\right\}-V_{xx,i}\eta(t)\right\}.
\end{aligned}$$

Theorem 3.2. *Under Condition I in Chapter 4.1, if the selection probability $P(\xi_i=1|\mathcal{V}_i)$ or both the conditional expectations $E\{X_i^{(2)}|\mathcal{V}_i\}$ and $E\{X_i^{(2)}(X_i^{(2)})^{\mathsf{T}}|\mathcal{V}_i\}$ are correctly specified, then*

$$n^{\frac{1}{2}}(\widehat{\boldsymbol{\gamma}}-\boldsymbol{\gamma}_0)\xrightarrow{d}N(0,\Sigma^*_{\boldsymbol{\gamma}}),$$

where covariance matrix $\Sigma^*_{\boldsymbol{\gamma}}=\boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta_0)^{-1}E\{\boldsymbol{W}^*_{\boldsymbol{\gamma},i}(\tau,\boldsymbol{\eta}_0(\cdot),\boldsymbol{\gamma}_0,\theta_0)\}^{\otimes 2}\boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta_0)^{-1}$, where $\boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta)$ is *defined in Theorem 2.1 and where*

$$\begin{aligned}\boldsymbol{W}^*_{\boldsymbol{\gamma},i}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\theta) &= \int_0^\tau \boldsymbol{\zeta}_{\boldsymbol{\gamma},i}(t,\theta))\,dt + \int_0^\tau \boldsymbol{\kappa}_{\boldsymbol{\gamma},i}(t,\theta)\,dt - \int_0^\tau \boldsymbol{\kappa}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\gamma},\theta)dt + \int_0^\tau \boldsymbol{\zeta}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta)\,dt \\ &- \int_0^\tau \boldsymbol{k}(t,\theta)\left\{\boldsymbol{\kappa}^*_{\boldsymbol{\eta},i}(t,\theta) - \boldsymbol{\zeta}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta)\right\}dt. \quad (3.27)\end{aligned}$$

The asymptotic covariance matrix of $n^{\frac{1}{2}}(\widehat{\boldsymbol{\gamma}} - \boldsymbol{\gamma}_0)$ *can be consistently estimated by*

$$\widehat{\boldsymbol{\Sigma}}^*_{\boldsymbol{\gamma}} = \widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}^{-1}(\hat{\theta})\ n^{-1}\sum_{i=1}^n \left\{\widehat{\boldsymbol{W}}^*_{\boldsymbol{\gamma},i}(\tau,\widehat{\boldsymbol{\eta}}(\cdot),\widehat{\boldsymbol{\gamma}},\hat{\theta})\right\}^{\otimes 2}\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}^{-1}(\hat{\theta}),$$

where

$$\begin{aligned}\widehat{\boldsymbol{W}}^*_{\boldsymbol{\gamma},i}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\theta) &= \int_0^\tau \widehat{\boldsymbol{\zeta}}_{\boldsymbol{\gamma},i}(t,\theta)\,dt + \int_0^\tau \widehat{\boldsymbol{\kappa}}_{\boldsymbol{\gamma},i}(t,\theta)\,dt - \int_0^\tau \widehat{\boldsymbol{\kappa}}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\gamma},\theta)dt + \int_0^\tau \widehat{\boldsymbol{\zeta}}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta)\,dt \\ &- \int_0^\tau \widehat{\boldsymbol{K}}(t,\theta)\left\{\widehat{\boldsymbol{\kappa}}^*_{\boldsymbol{\eta},i}(t,\theta) - \widehat{\boldsymbol{\zeta}}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta)\right\}dt,\end{aligned}$$

where $\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}(\theta)$, $\widehat{\boldsymbol{\zeta}}_{\boldsymbol{\gamma},i}(t,\theta)$, $\widehat{\boldsymbol{\kappa}}_{\boldsymbol{\gamma},i}(t,\theta)$ *are described in Theorem 2.1, and where* $\widehat{\boldsymbol{\kappa}}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\gamma},\theta)$, $\widehat{\boldsymbol{\zeta}}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta)$, $\widehat{\boldsymbol{\kappa}}^*_{\boldsymbol{\eta},i}(t,\theta)$ *and* $\widehat{\boldsymbol{\zeta}}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta)$ *are the estimators of* $\boldsymbol{\kappa}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\gamma},\theta)$, $\boldsymbol{\zeta}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta)$, $\boldsymbol{\kappa}^*_{\boldsymbol{\eta},i}(t,\theta)$ *and* $\boldsymbol{\zeta}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta)$. *Similar arguments with Theorem 2.1, those estimators can be obtained by using definition in (4.81) in section 4.2 and by replacing* V_x *and* V_{xx} *with* $\widehat{V}_x$ *and* $\widehat{V}_{xx}$, *where the unknown conditional expectations* $E(X_i^{(2)}|\mathcal{V}_i)$ *and* $E(X_i^{(2)}(X_i^{(2)})^\intercal|\mathcal{V}_i)$ *in* $E(X_i|\mathcal{V}_i)$ *and* $E(X_i(X_i)^\intercal|\mathcal{V}_i)$ *can be obtained by* $\mu_1(\mathcal{V}_i,\hat{\alpha}_1)$ *and* $\mu_2(\mathcal{V}_i,\hat{\alpha}_2)$.

Theorem 3.3. *Under Condition I in section 4.1, if the selection probability* $P(\xi_i = 1|\mathcal{V}_i)$ *or both the conditional expectations* $E\{X_i^{(2)}|\mathcal{V}_i\}$ *and* $E\{X_i^{(2)}(X_i^{(2)})^\intercal|\mathcal{V}_i\}$ *are correctly specified, then*

$$n^{\frac{1}{2}}(\widehat{\boldsymbol{\eta}}(t) - \boldsymbol{\eta}_0(t)) = \{\boldsymbol{Q}_{\boldsymbol{\eta}}(t,\theta_0)\}^{-1}\ n^{-\frac{1}{2}}\sum_{i=1}^n \boldsymbol{W}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}_0(t),\gamma_0,\theta_0) + o_p(1). \quad (3.28)$$

where $\boldsymbol{Q}_{\boldsymbol{\eta}}(t,\theta)$ *is defined in Theorem 2.2, and where*

$$\begin{aligned}\boldsymbol{W}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta) &= \boldsymbol{\zeta}_{\boldsymbol{\eta},i}(t,\theta) + \boldsymbol{\kappa}_{\boldsymbol{\eta},i}(t,\theta) - \boldsymbol{Q}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta)\left\{\boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta)\right\}^{-1} n^{-\frac{1}{2}}\ \sum_{i=1}^n \boldsymbol{W}^*_{\boldsymbol{\gamma},i}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\theta) \\ &+\boldsymbol{\kappa}^*_{\boldsymbol{\eta},i}(t,\theta) - \boldsymbol{\zeta}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta). \quad (3.29)\end{aligned}$$

By using lemma 1 of Sun and Wu (2005), $n^{\frac{1}{2}}(\widehat{\boldsymbol{\eta}}(t) - \boldsymbol{\eta}_0(t))$ *converges weakly to a mean-zero Gaussian process on* $t \in [0,\tau]$ *with the covariance matrix* $\boldsymbol{\Sigma}^*_{\boldsymbol{\eta}} = \boldsymbol{Q}_{\boldsymbol{\eta}}(t,\theta_0)^{-1}E\{\boldsymbol{W}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}_0(t),\boldsymbol{\gamma}_0,\theta_0)\}^{\otimes 2}\boldsymbol{Q}_{\boldsymbol{\eta}}(t,\theta_0)^{-1}$, *which can be consistently estimated by*

$$\widehat{\boldsymbol{\Sigma}}^*_{\boldsymbol{\eta}} \quad = \quad \widehat{\boldsymbol{Q}}_{\boldsymbol{\eta}}^{-1}(t,\hat{\theta})\, n^{-1} \sum_{i=1}^{n} \left\{ \widehat{\boldsymbol{W}}^*_{\boldsymbol{\eta},i}(t, \widehat{\boldsymbol{\eta}}(t), \widehat{\gamma}, \hat{\theta}) \right\}^{\otimes 2} \widehat{\boldsymbol{Q}}_{\boldsymbol{\eta}}^{-1}(t,\hat{\theta}),$$

where

$$\begin{aligned}\widehat{\boldsymbol{W}}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta) \quad &= \quad \widehat{\boldsymbol{\zeta}}_{\boldsymbol{\eta},i}(t,\theta) + \widehat{\boldsymbol{\kappa}}_{\boldsymbol{\eta},i}(t,\theta) - \widehat{\boldsymbol{Q}}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta) \left\{ \widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}(\theta) \right\}^{-1} n^{-\frac{1}{2}} \sum_{i=1}^{n} \widehat{\boldsymbol{W}}^*_{\boldsymbol{\gamma},i}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\theta) \\ &\quad + \widehat{\boldsymbol{\kappa}}^*_{\boldsymbol{\eta},i}(t,\theta) - \widehat{\boldsymbol{\zeta}}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta),\end{aligned}$$

where $\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}(\theta)$ *is defined in Theorem 2.1.* $\widehat{\boldsymbol{Q}}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta)$, $\widehat{\boldsymbol{Q}}_{\boldsymbol{\eta}}(t,\theta)$,$\widehat{\boldsymbol{\zeta}}_{\boldsymbol{\eta},i}(t,\theta)$, *and* $\widehat{\boldsymbol{\kappa}}_{\boldsymbol{\eta},i}(t,\theta)$ *can be obtained as described in Theorem 2.2,* $\widehat{\boldsymbol{W}}^*_{\boldsymbol{\gamma},i}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\theta)$ *is defined in Thorem 3.2, and* $\widehat{\boldsymbol{\kappa}}^*_{\boldsymbol{\eta},i}(t,\theta)$, *and* $\widehat{\boldsymbol{\zeta}}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta)$, *defined in section 4.2, are the estimators of* $\boldsymbol{\kappa}^*_{\boldsymbol{\eta},i}(t,\theta)$ *and* $\boldsymbol{\zeta}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta)$.

3.3 Simulations

In this chapter, a simulation study has been conducted to evaluate the finite sample properties of the augmented inverse probability weighted estimators of $(\boldsymbol{\eta}(t),\boldsymbol{\gamma})$. Let X be a Bernoulli random variable with $P(X=1)=0.6$ and Z be a Bernoulli random variable with $P(Z=1|X)=0.4X+0.2$. The covariate X can be missing and the covariate Z is always observed. Let $\epsilon = k$ be the types of failure and let $k=1$ be the event of interest among two competing risks $k \in \{1,2\}$. From model (3.5), we consider the following semi-parametric additive model with identity link for the cumulative incidence function with cause 1 :

$$F_1(t,x,z) = \eta_0(t) + \eta_1(t)X + \gamma Z t, \tag{3.30}$$

where $\eta_0(t) = 0.01 \times t$, $\eta_1(t) = 0.03 \times t$ and $\gamma = 0.1$ where $0 \le t \le \tau$ and $\tau = 3$.

We consider the auxiliary covariate A, which may give information on missing covariate X. The correlation coefficient ρ can be obtained from the relationship $A = \alpha_1 X + \alpha_2$ with parameters α_1 and α_2. The correlation coefficients $\rho = 0.5, 0.8$ and 0.9 are given by the choice of $(\alpha_1,\ \alpha_2) = (0.5, 0.3), (0.8, 0.12)$ and $(0.92, 0.05)$. Based on $\eta(t), \gamma, X, Z$, the conditional probability of failure for cause 1 is

$$F_{1i}(\tau) = \eta_0(\tau) + x_i^{\mathsf{T}}\eta_1(\tau) + \gamma^{\mathsf{T}} z_i \tau \quad where \quad 0 < t \leq \tau$$

for each individual, where $i = 1, 2, \ldots, n$ and $\tau = 3$. The types of failure $\epsilon_i = k$ for ith individual have been determined by generating a Bernoulli random variable with the probability $F_{1i}(\tau) = P(\epsilon_i = 1)$, $i = 1, \ldots, n$. The failure time T_i is generated by conditional probability for cause 1:

$$\tilde{F}_{1i}(t) = P(T_1 \leq t|\epsilon_i = 1) = \frac{F_{1i}(t)}{P(\epsilon_i = 1)} = \frac{F_{1i}(t; x, z, \eta, \gamma)}{F_{1i}(\tau)} = \frac{F_{1i}(t)}{F_{1i}(\tau)},$$

for ith individual and $\tau = 3$.

Let C^* follow an uniform distribution on [0,3]. The censoring time C_i is generated by $C_i = \min(C_i^*, \tau)$. Let $\tilde{T}_i = \min(T_i, C_i)$ be the observed failure time. It gives about 50% subjects who are censored before $\tau = 3$. Let $\tilde{\epsilon}_i = \epsilon_i \Delta_i$, where $\Delta_i = I(T_i \leq C_i)$.

Let $\mathcal{V}_i = \{\tilde{T}_i, \Delta_i, \tilde{\epsilon}_i, Z_i, A_i\}$ be the phase one data for each individual i. Let X_i be the phase-two covariate, which can be missing. We consider three simulation scenarios in terms of whether the missing probabilities depend on the outcome variables $\tilde{\epsilon}_i$ and how the phase-two covariate X_i is missing. The first two scenarios are called phase-two sampling design: (I) The first scenario is classical case cohort sampling design, where phase-two covariate X_i is sampled for all cases $\tilde{\epsilon}_i = 1$ and the information of the covariate X_i will be missing for the non-cases $\tilde{\epsilon}_i = 0$ or 2; (II)The second scenario is generalized case-cohort sampling design, which allows the phase-two covariate X_i to be missing for both cases and non-cases. In the third scenario, (III) the missing probability does not depend on $\tilde{\epsilon}_i$ and phase-two covariate X_i is a simple random sample from the phase-one covariates.

Let m_0 be the average of total missing probability. We consider $m_0 = 30\%$ and 60% for each sampling scenario. Let m_1 and m_2 be the average missing probabilities for the cases and the non-cases, respectively.

First, we consider $m_0 = 0.3$ and $\rho = 0.5, 0.8, 0.9$ for each scenario. For scenario (I), missing probability $\vartheta_{1i} = P(\xi_i = 0|\mathcal{V}_i, \tilde{\epsilon}_i = 1) = 0$ for cases. For non-cases $\epsilon_i = 0$ or 2, we assume that the missing probability $\vartheta_{2i} = P(\xi_i = 0|\mathcal{V}_i, \tilde{\epsilon}_i \neq 1)$ follows the logistic regression model

$$\text{logit}(\varphi_m(\mathcal{V}_i, \theta_2)) = \theta_{20} + \theta_{21} A_i + \theta_{22} \tilde{T}_i + \theta_{23} Z_i + \theta_{24} I(\tilde{\epsilon}_i = 2) \qquad (3.31)$$

based on phase-one covariates. We have about the average missing probability $m_2 = 0.36$ by choosing $\theta_2 = (-1.5, 0.3, 0.4, 0.3, 0.5)$. We have the linear model with the observed non-cases covariates A_i, Z_i and $log(\tilde{T}_i)$ to estimate $E\{X_i|V_i, \tilde{\epsilon}_i \neq 1\}$ and $E\{{X_i}^T X_i|V_i, \tilde{\epsilon}_i \neq 1\}$ for those with missing X_i:

$$E\{X_i|V_i, \tilde{\epsilon}_i \neq 1\} = \phi_{10} + \phi_{11}A_i + \phi_{12}Z_i + \phi_{13}log(\tilde{T}_i) + \phi_{14}I(\tilde{\epsilon}_i = 2), \quad (3.32)$$

$$E\{{X_i}^T X_i|V_i, \tilde{\epsilon}_i \neq 1\} = \phi_{20} + \phi_{21}A_i + \phi_{22}Z_i + \phi_{23}log(\tilde{T}_i) + \phi_{24}I(\tilde{\epsilon}_i = 2). \quad (3.33)$$

where estimators of coefficients ϕ can be obtained by fitting linear model based on the observed response variable X_i and the predictors A_i, Z_i and $log(\tilde{T}_i)$ that are observed non-cases.

For (II), the missing probability $\vartheta_i = P(\xi_i = 0|\mathcal{V}_i, \tilde{\epsilon}_i)$ for both cases and non-cases can be obtained by the following the logistic regression model

$$\text{logit}(\varphi_m(\mathcal{V}_i, \theta)) \quad = \quad \theta_1 + \theta_2 A_i + \theta_3 \tilde{T}_i + \theta_4 Z_i + \theta_5 I(\tilde{\epsilon}_i = 1) + \theta_6 I(\tilde{\epsilon}_i = 2), \quad (3.34)$$

,which gives $m_1 = 0.2$ and $m_2 = 0.3$ when $(\theta) = (-1.2, 0.1, 0.1, 0.1, -0.5, 0.5)$. We use the following linear models to estimate $E\{X_i|V_i, \tilde{\epsilon}_i\}$ and $E\{{X_i}^T X_i|V_i, \tilde{\epsilon}_i\}$:

$$E\{X_i|V_i, \tilde{\epsilon}_i\} = \phi_1 + \phi_2 A_i + \phi_3 Z_i + \phi_4 log(\tilde{T}_i) + \phi_5 I(\tilde{\epsilon}_i = 1) + \phi_6 I(\tilde{\epsilon}_i = 2), \quad (3.35)$$

for those missing X_i based on the observations that are case and non-cases and with observed value of X.

For (III), we use the following logistic model for the missing probability $\vartheta_{3i} = P(\xi_i = 0|\mathcal{V}_i)$:

$$\text{logit}(\varphi_m(\mathcal{V}_i, \theta_3)) \quad = \quad \theta_{30} + \theta_{31}A_i + \theta_{32}Z_i. \quad (3.36)$$

We have $\vartheta_{3i} = 0.3$ with $\theta_3 = (-0.5, -0.6, 0.2)$ in (3.36) and therefore, $m_0 = 0.3$. To estimate conditional expectations, we use linear models $E\{X_i|V_i\} = \phi_{10} + \phi_{11}A_i + \phi_{12}Z_i + \phi_{13}log(\tilde{T}_i)$ and $E\{{X_i}^T X_i|V_i\} = \phi_{20} + \phi_{21}A_i + \phi_{22}Z_i + \phi_{23}log(\tilde{T}_i)$ for those with missing X_i.

Similarly, we consider $m_0 = 0.6$ and $\rho = 0.5, 0.8, 0.9$ for each scenario. For (I), we have $m_1 = 0$ by $\vartheta_{1i} = 0$ and $m_2 = 0.65$ by choosing $(\theta_2) = (-1.5, 0.6, 0.6, 0.8, 2.5)$ in (3.31). Similar to (3.32) and (3.33), conditional expectations for those missing X_i can be estimated by $E\{X_i|V_i, \tilde{\epsilon}_i \neq 1\}$ and $E\{{X_i}^T X_i|V_i, \tilde{\epsilon}_i \neq 1\}$. For (II), we have about $m_1 = 0.45$ for the cases and $m_2 = 0.60$ for the non-cases by choosing $\theta = (-0.5, 0.3, 0.3, 0.4, -0.5, 1.0)$ in (3.34). Conditional expectations $E\{X_i|V_i, \tilde{\epsilon}_i\}$, $E\{{X_i}^T X_i|V_i, \tilde{\epsilon}_i\}$ can be estimated by (3.35). For (III), $\vartheta_{3i} = 0.6$ can be obtained by choosing $(\theta_3) = (-0.1, 0.5, 0.6)$ in (3.36). Similarly, $E\{X_i|V_i\}$ and $E\{{X_i}^T X_i|V_i\}$ can be estimated by using linear models with predictors A_i, Z_i and $log(\tilde{T}_i)$.

We denote the full estimators as Full when all the values of phase-two covariate X are fully observed, inverse probability weighted estimators as IPW obtained by the estimating procedure in chapter 2.1.2, and complete-case estimators as CC where subjects having missing covariate X are removed. The result of simulations for the proposed AIPW estimators for γ and $\eta(t)$, where $t \in [0, 3]$, are summarized by the bias (Bias), the empirical standard error (SSE), the average of the estimated standard error (ESE), the empirical coverage probability (CP) of 95% confidence interval and the relative efficiency (REE), which is defined by SSE of the Full estimator divided by SSE of AIPW estimator. We take sample size $n = 600, 700, 900$ and consider the total missing probability as $m_0 = 0.3$ and 0.6 by choosing different average missing probabilities (m_1, m_2) for cases and non-cases. We denote a classical case cohort design as I, a generalized case cohort design as II and a simple random sampling design as III. Each entry of the tables is estimated based on 1000 simulations runs.

Table 5 to **??** consider each sampling scenario with the average of total missing probability $m_0 = 0.3$ and the correlation coefficient $\rho = 0.5$, 0.8, 0.9. Table 5 summarizes the Bias, SSE, ESE, CP and REE for the AIPW estimator of γ. Table 5 shows the AIPW estimator for γ with correlation coefficients $\rho = 0.5, 0.8, 0.9$ performs well under three scenarios I, II and III. The biases are small for each sample size. The empirical standard errors decrease as the sample size increases and the averages of the estimated standard errors are very close to the empirical standard errors. The coverage probabilities are close to the 95% norminal level. The relative efficiency of AIPW estimator compared to the Full estimator tends to increase as the sample size increases. This tendency is more obvious in scenario I and II than III. The efficiency of the AIPW estimator is very close to 1, meaning that it can be comparable to that of the Full estimator. This is because the information on other fully observable covariates of individuals can be used in the analysis of the AIPW estimating equation, even though the individuals have missing covariates.

Table 6 compares the Bias, SSE, ESE, CP for the AIPW estimator to those for Full, IPW and CC estimators of γ. We use Full estimator as a gold standard. The biases of AIPW, IPW estimators are very small as if all the covariates of X are fully observed. The complete case (CC) estimator has much larger biases than the AIPW and IPW estimators have. However, the CC estimator has smaller biases in sampling scenario III because missingness of phase-two covariate X_i does not depend on outcome variable $\tilde{\epsilon}_i$ and phase-two covariate X_i is a simple random sample from phase-one covariates. The ESE for each estimator agrees to the SSE for the corresponding estimator, having a tendency to decrease as the sample size increases. The empirical coverage probability of each estimator is close to 95% nominal.

The similar results have been shown for each sampling scenario with the average of total missing probability $m_0 = 0.6$ and the correlation coefficient $\rho = 0.5,\ 0.8,\ 0.9$, summarized in table 7 to **??**. Table 7 shows that the Bias, SSE, ESE, CP and REE for the AIPW estimator of γ. The AIPW estimator for γ is unbiased under scenario I, II and III with $m_0 = 0.6$. At each scenario, as the sample size increases, then the SSE decreases. The ESE are getting closer to the SSE. This phenomenon is clear when the sample size increases. The coverage probabilities are close to 95% nominal level, changing between 0.94 and 0.98. When the correlation is higher between auxiliary covariate and phase-two covariate, the REE tends to be closer to 1. Table 8 compares the Bias, SSE, ESE, CP for the AIPW estimator to those for Full, IPW, and CC estimators of γ. The biases of AIPW estimator are as small as the biases of Full estimator are. The IPW and CC estimators have larger biases than AIPW estimator has. The SSE of the AIPW estimator is smaller than the SSE of the IPW estimator. The SSE of the IPW estimator is smaller than the SSE of the CC estimator. As the sample size increase, the ESE of each estimator is closer to the SSE of the estimator. The empirical coverage probability of each estimator is close to 95 % nominal.

Let AIPW-50, AIPW-80 and AIPW-90 estimators be the AIPW estimators corresponding the correlation coefficients $\rho = 0.5,\ 0.8,\ 0.9$, respectively. Figure 15 though Figure 17 compares the Full, IPW, CC estimators with $\rho = 0.5$, AIPW-50, AIPW-80 and AIPW-90 estimators for the cumulative coefficient $\eta_1(t)$ and the baseline cumulative coefficient $\eta_0(t)$. We take $n = 600$ with average of total missing probability $m_0 = 0.3$ and with 80% censoring for each scenario. The same setting with $m_0 = 0.6$ are plotted in Figure 18 though Figure 20.

Figure 15 compares those estimators under the classical case cohort design with the average missing probability $m_1 = 0$ for cases and $m_2 = 0.3$ for non-cases. Figure 1 (a) and (b) plot the biases of each of estimators for $\eta_1(t)$ and $\eta_0(t)$ for $t \in [0, 3]$, respectively. Figure 1 (c) and (d) plot the empirical standard errors and (e) and (f) plot the average of the estimated standard errors of each of estimators for $\eta_1(t)$ and $\eta_0(t)$, respectively. Figure 1 (g) and (h) plot the coverage probabilities of the those estimators.

The biases of AIPW-50, AIPW-80 and AIPW-90 estimators are very small comparable to the bias of Full estimator. The bias of the IPW estimator is relatively small, but slightly larger than the AIPW estimators. The complete case (CC) estimator for both $\eta_1(t)$ and $\eta_0(t)$ have much larger biases than the AIPW and IPW estimators have. The averages of estimated standard errors for $\eta_1(t)$ and $\eta_0(t)$ have good agreements to the empirical standard errors for those estimators by observing plots in figure 1 (c),(e) and (d), (f), respectively. The SSE of the AIPW-50 estimator is slightly smaller than the SSE of the IPW estimator when the correlation between the auxiliary variable A and the phase-two covariate X is low with $\rho = 0.5$. However, the empirical standard errors of the AIPW-80 and AIPW-90 estimators are much smaller than that of the IPW estimator. This is because the auxiliary variable A carries more information on the phase-two covariate X with the correlation coefficients $\rho = 0.8$ and 0.9. This phenomenon is more obvious where sampling design II and III. The coverage probabilities for the AIPW-50, AIPW-80 and AIPW-90 estimators are close to 95% nominal shown in Figure 1 (g) and (h).

The performances of those estimators under the sampling designs II and III in Figures 16 and 17. Those can be interpreted in a similar way to the sampling design I. However, in design III, 17 (a) and (b) show that all estimators have very small biases. There is no difference between the performances of the IPW and CC estimators. Similarly, Figure 18 and 20 plot those estimators with

$m_0 = 0.6$. The behaviors of those estimators are very similar to or even much noticeable than those with $m_0 = 0.3$. Therefore, those can be interpreted in the similar way. By comparing figure 15 to 18 and figure 16 to 19, as the total missing probability increases, the performance of the complete case (CC) gets worse under the phase two sampling designs I and II. The bias of the CC estimator with $m_0 = 0.6$ is much larger than that with $m_0 = 0.3$. The SSE of the CC estimator with $m_0 = 0.6$ is much larger than those with $m_0 = 0.3$. The performances of the AIPW estimators are robust even with larger total missing probability $m_0 = 0.6$ under all sampling designs. Figure 20 shows that SSE of the IPW estimator is even larger than that of the CC estimator. When the sampling design III does not depend on outcome variables $\tilde{\epsilon}_i$, the IPW estimator is not that useful. Even under design III, the AIPW estimators perform well by improving efficiency. The higher correlation is between the auxiliary values A and the missing values X, the better efficiency is gained.

3.4 Application

The RV144 vaccine efficacy trial randomized 16,394 HIV negative volunteers to the vaccine ($n = 8198$) and placebo ($n = 8196$) groups (ref.Liqi). We apply the proposed estimating procedures for AIPW method to the vaccine group, which included 5035 men and 3163 women. Subjects enrolled in the RV144 trial were vaccinated at weeks 0,4,12 and 24. 43 of 8198 vaccine recipients acquired the primary endpoint of HIV infection after the Week 26 biomarker sampling time point through to the end of follow-up at 42 months (ref.The New England Jounal of Medicine). Vaccine recipients were distributed in the Low, Medium, and High baseline behavioral risk scores, defined as in (**?**) with 3863 Low, 2370 Medium, and 1965 High.

Three HIV gp 120 sequences were included in the vaccine construct; 92TH023 in the ALVAC canarypox vector prime component; and A244 and MN in the AIDSVAX protein boost component. The 92TH023 and A244 are subtype E HIVs whereas MN is subtype B. However, the analysis focuses on the 92TH023 and A244 insert sequences. This is because the subtype E vaccine-insert sequences are genetically much closer to the infecting (and regional circulating) sequences than MN, meaning that the subtype E HIVs are more likely to stimulate protective immune responses. The observed failure time $\tilde{T}_i$ is the time to HIV infection diagnosis, which is minimum of failure time or right-censoring time.

Because vaccine recipients with higher levels of antibodies binding to the V1V2 portion of the HIV envelope protein had a significantly lower rate of HIV infection ((?), (?), (?)), the V1V2 sub-region of gp120 may have been involved in the partial vaccine efficacy administered by the vaccine regimen. The region contains epitopes recognized by antibodies induced by the vaccine. Therefore, we study the genetic distance of an infecting HIV V1V2 sequence to the corresponding V1V2 sequence in the vaccine construct (using a multiple sequence alignment), which is called as marks.

For the analysis, two marks V are considered, based on the 92TH023 and A244 vaccine construct sequences. The way of measuring in the genetic distances is described in ?. The distance V were re-scaled to take values between 0 and 1. We denote these two genetic distance marks 92TH023V1V2 and A244V1V2 as V_{1i} and V_{2i}, respectively, for a subject i. We use each mark to form two causes of failure by considering each of V_{1i} and V_{2i} one at a time. Let M_1 be the median of the observed mark V_{1i} and M_2 be the median of the observed mark V_{2i} for each subject i.

The cause of failure ϵ_{1i} for the mark V_{1i} is generated by using the median mark M_1 of V_{1i}. We define $\epsilon_{1i} = 1$ for uncensored subjects i if the mark V_{1i} is less than M_1; otherwise $\epsilon_{1i} = 2$. Similarly, the cause of failure ϵ_{2i} for the mark V_{2i} is generated by using the median mark M_2 of V_{2i}. We define $\epsilon_{2i} = 1$ for uncensored subjects i if the mark V_{2i} is less than M_2; otherwise $\epsilon_{2i} = 2$. If subjects are censored, then $\epsilon_{ji} = 0$ for $j = 1, 2$.

The V1V2 seqeunce of the infecting HIVs has been investigated in ?. They analysis IgG and IgG3 biomarkers as correlates of 92TH023V1V2 and A244V1V2 mark-specific HIV infection for the stratified mark-specific proportional hazards model under two-phase sampling.

Following ?, we study IgG and IgG3 biomarkers as correlates of 92TH023V1V2 and A244V1V2 mark-specific HIV infection for the cumulative incidence model based on competing risks data. We use AIPW method to analysis these subjects under two-phase sampling. In particular, paired to the 92TH023V1V2 mark variable, we study the two biomarkers Week 26 IgG and IgG3 binding antibodies to 92TH023V1V2, namely IgG-92TH023V1V2 and IgG3-92TH023V1V2; and, paired to the A244V1V2 mark variable, we study Week 26 IgG and IgG3 binding antibodies to A244V1V2, namely IgG-A244V1V2 and IgG3-A244V1V2. Therefore, we have four different immune responses IgG-92TH023V1V2, IgG3-92TH023V1V2, IgG-A244V1V2 and IgG3-A244V1V2 for the analysis.

The immune response biomarkers were measured for 34 of 43 HIV infected vaccine recipients with HIV V1V2 sequence data and 212 of 8155 uninfected vaccine recipients at the Week 26 visit post entry. These observed biomarkers were each standardized to have mean 0 and variance 1 for the analysis.

Let R_i be the immune responses R_{11_i}, R_{12_i}, R_{21_i}, and R_{22_i}, respectively, for each analysis. Let δ_i be infection status, whose value is 1 if a subject is infected HIV; and 0 if a subject is right censored over a follow-up period of 42 months. Let $\epsilon_{1i} = k$ be the causes of failure for immune responses R_{11_i} and R_{12_i}, respectively, for $k = 1, 2$. Let $\epsilon_{2i} = k$ be the causes of failure for immune responses R_{21_i} and R_{22_i}, respectively, for $k = 1, 2$. Let B_{1i} and B_{2i} be the dummy variables for baseline behavioral risk score groups B_i (High=1, Low=2, Medium=3), where $B_{1i} = 1$ if a subject is in the low risk score group; 0 otherwise, $B_{2i} = 1$ if a subject is in the medium risk score group; 0 otherwise and $B_{1i} = B_{2i} = 0$ if a subject is in the high risk group. The immune responses R_i can be missing for both case and non-case subjects, and hence are phase two covariates. The baseline behavioral risk scores B_i are measure for all subjects, and hence are phase one covariates.

We consider the following semiparametric additive model for the cumulative incidence function by using identity link function for $h(x) = x$:

$$F_1(t; X_i, Z_i) = \eta_0(t) + \eta(t)R_i + \gamma_2 B_{1i} t + \gamma_3 B_{2i} t \tag{3.37}$$

Let $\vartheta_i = P(\xi_i = 1|\mathcal{V}_i, \delta_i)$ be the selection probability with ξ_i be the indicator of the immune response data, whose values are $\xi_i = 1$ if each of four immune response R_i is measured at each analysis; otherwise $\xi_i = 0$. To predict the probability of observing the immune response R_i, we use a logistic regression model with

$$\text{logit}(\vartheta_i) = \theta_0 + \theta_1 \delta_i \tag{3.38}$$

The estimated selection probabilities $\hat{\vartheta}_i$ is estimated by $\theta = (-3.6235, 4.9526)$ with standard errors (0.06959, 0.38127) in the model (3.38). The weights are given by $\psi(\hat{\theta}_i) = \xi_i/\hat{\vartheta}_i$.

To implement the AIPW method, we use the following linear models:

$$
\begin{aligned}
E\{R_i|\mathcal{V}_i,\delta_i\} &= \varsigma_{10}+\varsigma_{11}B_{1i}+\varsigma_{12}B_{2i}+\varsigma_{13}\log(\tilde{T}_i)+\varsigma_{14}\delta_i+\varsigma_{15}\delta_i*\log(\tilde{T}_i),\\
E\{R_i^{\otimes 2}|\mathcal{V}_i,\delta_i\} &= \varsigma_{20}+\varsigma_{21}B_{1i}+\varsigma_{22}B_{2i}+\varsigma_{23}\log(\tilde{T}_i)+\varsigma_{24}\delta_i+\varsigma_{25}\delta_i*\log(\tilde{T}_i). \qquad (3.39)
\end{aligned}
$$

We analysis the semiparametric additive model (2.30) with four different settings: (S1). The model (3.37) is analyzed with the immune response $R_i = R_{11_i}$ for ϵ_{1i}=1. The estimated the first moment $E\{R_i|\mathcal{V}_i,\delta_i\}$ and the second moment $E\{R_i^{\otimes 2}|\mathcal{V}_i,\delta_i\}$ can be estimated by $\hat{\varsigma}_1 = (0.2538, -0.2678, 0.0118, -0.0963, -$
and $\hat{\varsigma}_2 = (-0.5754, 1.3439, -0.2953, 0.8834,$
$1.1671, -0.7601)$ in linear models (3.39). This gives AIPW estimates of B_{1i}, B_{2i} as $\hat{\gamma} = (-0.00156, -0.00157)$ with standard error of $(0.000895, 0.000978)$, yielding p-value=$(0.081469, 0.107513)$ for testing $\gamma =$ 0; Similarly, the model (3.37) is analyzed with the immune response $R_i = R_{11_i}$ for $\epsilon_{1i} = 2$. This gives AIPW estimates of B_{1i}, B_{2i} as $\hat{\gamma} = (-0.0005566, -0.0001040)$ with standard error of $(0.0004189, 0.0006799)$, yielding p-value=$(0.18394, 0.87838)$ for testing $\gamma = 0$;

(S2). The model (3.37) is analyzed with immune response $R_i = R_{12_i}$ for ϵ_{1i}. The estimated the first moment $E\{R_i|\mathcal{V}_i,\delta_i\}$ and the second moment $E\{R_i^{\otimes 2}|\mathcal{V}_i,\delta_i\}$ are estimated by $\hat{\varsigma}_1 = (0.3166, -0.3996, -0.1080, -0.$
and $\hat{\varsigma}_2 = (0.5267, 0.6413, 0.1473,$
$0.1257, 0.3857, -0.5138)$ in (3.39). This gives the AIPW estimates of B_{1i}, B_{2i} $\hat{\gamma} = (-0.001488, -0.001582)$ with standard error of $(0.000886, 0.000982)$, yielding p-value=$(0.093214, 0.107275)$ for testing $\gamma = 0$; Similarly, the model (3.37) is analyzed with immune response $R_i = R_{12_i}$ for $\epsilon_{1i} = 2$. This gives the AIPW estimates of B_{1i}, B_{2i} $\hat{\gamma} = (-0.000581, -0.000116)$ with standard error of $(0.000411, 0.000676)$, yielding p-value=$(0.15749, 0.86411)$ for testing $\gamma = 0$;

(S3). The model (3.37) with immune response $R_i = R_{21_i}$ is analyzed for $\epsilon_{2i} = 1$. The conditional expectations are obtained by $\hat{\varsigma}_1 = (0.2110, -0.2858, -0.0593, -0.0290, -0.2944, -0.0026)$ and $\hat{\varsigma}_2 = (-0.4441, 1.1693, -0.2345, 0.7951, 1.2254, -0.5539)$ in model (3.39). Our method gives the AIPW estimates of B_{2i}, B_{3i} as $\hat{\gamma} = (-0.000835, -0.000808)$ with standard error of $(0.000570, 0.000626)$, yielding p-value=$(0.14261, 0.19699)$ for testing $\gamma = 0$; Similarly, the model (3.37) with immune response $R_i = R_{21_i}$ is analyzed for $\epsilon_{2i} = 1$. Our method gives the AIPW estimates of B_{2i}, B_{3i} as $\hat{\gamma} =$

$(-0.00124, -0.000809)$ with standard error of $(0.000722, 0.000822)$, yielding p-value=$(0.08619, 0.32526)$ for testing $\gamma = 0$;

(S4). The model (3.37) with immune response $R_i = R_{22_i}$ is analyzed for cases $\epsilon_{2i} = 1$. The conditional expectations are obtained by $\hat{\varsigma}_1 = (0.3217, -0.4299, -0.1495, -0.0622, -0.2350, 0.0670)$ and $\hat{\varsigma}_2 = (0.3486, 0.5998, -0.0997, 0.3130,$
$0.9022, -0.6895)$ in model (3.39). This setting gives AIPW estimates of B_{1i}, B_{2i} as $\hat{\gamma} = (-0.000864, -0.000852)$ with standard error of $(0.000577, 0.000651)$, yielding p-value=$(0.13433, 0.19080)$ for testing $\gamma = 0$; Similarly, the model (3.37) with immune response $R_i = R_{22_i}$ is analyzed for cause $\epsilon_{2i} = 1$. This setting gives AIPW estimates of B_{1i}, B_{2i} as $\hat{\gamma} = (-0.0012116, -0.0008022)$ with standard error of $(0.000713, 0.000825)$, yielding p-value=$(0.089439, 0.330911)$ for testing $\gamma = 0$.

Figure 21 to 24 compares AIPW estimates of baseline cumulative coefficients $\eta_0(t)$ and cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the four different immune responses of R_i for $\epsilon_{ji} = 1$ and $\epsilon_{ji} = 2$, respectively, $j = 1, 2$.

The analysis with R_{11_i} and R_{12_i} for $\epsilon_{1i} = 1$ have larger AIPW estimates of baseline cumulative coefficients $\eta_0(t)$ than the analysis with R_{11_i} and R_{12_i} for $\epsilon_{1i} = 2$. The analysis with R_{21_i} and R_{22_i} for $\epsilon_{2i} = 1$ has smaller AIPW estimates of baseline cumulative coefficients $\eta_0(t)$ than the analysis with R_{21_i} and R_{22_i} for $\epsilon_{2i} = 2$.

For the AIPW estimates of cumulative coefficients $\eta_1(t)$, while the effects of immune responses R_{12_i}(IgG3-92TH023V1V2) are close to zero over study time with $\epsilon_{ji} = 1$, $j = 1, 2$, the immune responses R_{11_i}(IgG-92TH023V1V2), R_{21_i}(IgG-A244V1V2) and R_{22_i}(IgG3-A244V1V2) have negative effects on the cumulative incidence function with $\epsilon_{ji} = 1$, $j = 1, 2$. However, the negative effects of R_{11_i}(IgG-92TH023V1V2) on cumulative incidence function is less obvious than those negative effects of R_{21_i}(IgG-A244V1V2) and R_{22_i}(IgG3-A244V1V2) on cumulative incidence function. On the other hands, none of four immune responses R_i has significant negative effects on cumulative incidence function with $\epsilon_{ji} = 2$, $j = 1, 2$ over study time. By comparing figure 21 to 23 and comparing figure 22 to 24, IgG and IgG3 binding antibodies responding to A244V1V2 than to 92TH023V1V2 have significantly negative effects on the cumulative incidence function, i.e A244 would be more relevant for protection.

Figure 25 to figure 28 show that the cumulative incidence function has been evaluated for $\epsilon_{ji} = 1$ and $\epsilon_{ji} = 2$, $j = 1, 2$, respectively, depending on the behavioral risks scores at the first, second and third quartiles Q_1, Q_2 and $Q3$ of the observed the immune responses R_i. We expected to have larger probability of getting infected by HIVs V1V2 sequences if one has a higher behavioral risk score. We also expected to have lower probability of getting infected by HIVs with V1V2 sequences closer to 92TH023 or A244 ($\epsilon_{ji} = 1$, $j = 1, 2$) and have higher probability of getting infected by HIVs with V1V2 sequences far away from 92TH023 or A244 ($\epsilon_{ji} = 2$, $j = 1, 2$).

However, figure 25 and 26 did not show the desirable results we have expected since the numbers of behavioral risks scores for $\epsilon_{1i} = 1$ and $\epsilon_{1i} = 2$ are uneven. For example, for mark 92TH023V1V2 with $\epsilon_{1i} = 1$, the number of behavioral risks scores are 11, 6, and 4 for high, row and medium, respectively. However, for mark 92TH023V1V2 with $\epsilon_{1i} = 2$, the number of observed behavioral risks scores are 6, 8, and 8 for high, row and medium, respectively. Therefore, two figures can not be comparable.

However, for the mark A244V1V2 with $\epsilon_{1i} = 1$, the number of behavioral risks scores are 8, 8, and 5 for high, row and medium, respectively and for the mark A244V1V2 with $\epsilon_{1i} = 2$, the number of behavioral risks scores are 9, 6, and 7 for high, row and medium, respectively, which are relatively comparable. Therefore it is reasonable to look at the results on Figure 27 and 28. Figure 27 and 28 shows that the subjects with higher behavioral risk scores have higher probability of getting infected by HIVs with V1V2 sequences than the subjects with lower behavioral risks scores. For the low risk group, predicted probability of infection by HIVs with V1V2 sequence with $\epsilon_{2i} = 2$ is higher than predicted probability of infection by HIVs with V1V2 sequence with $\epsilon_{2i} = 1$ by the time 1.8. After that, two predicted probability of infection are similar. For the medium risk and high risks graphs, predicted probability of infection by HIVs with V1V2 sequence with $\epsilon_{2i} = 1$ tends to have lower probability of infection by HIVs with V1V2 sequences with $\epsilon_{2i} = 2$.

These results imply that since IgG3 antibodies to 92TH023V1V2 does not have effect on cumulative incidence function on figure 22, other IgG subclasses besides type3 induced by 92TH023 would have negative effects on the cumulative incidence function, then would be relevant for protection. This seems that A244 was more important than 92TH023 for induction of protective IgG3 antibodies. These results also imply that mark distances smaller than the median of observed marks has more protection against the HIV infection than mark distances larger than the median marker. Therefore, it supports the hypothesis that vaccine recipients exposed to HIVs with V1V2 sequences close to A244 (smaller markers than the median marker) may be more likely to be protected by antibodies than vaccine recipients exposed to HIVs with V1V2 sequences with larger markers than the median marker.

Table 5: Bias, empirical standard error(SSE), average of the estimated standard error(ESE), empirical coverage probability(CP) of 95% confidence intervals, and relative efficiencies(REE) for the AIPW estimator of γ under model (3.30) with $\rho = 0.5,\ 0.8,\ 0.9$ and with average of total missing probability $m_0 = 0.3$ and about 50% censoring based on 1000 simulations for each sampling scenario, I, II or III, where m_1 and m_2 are the average missing probabilities for the cases and the non-cases, respectively.

					γ			
Sampling	ρ	m_0	(m_1, m_2)	n	Bias	SSE	ESE	CP
I	0.5	0.3	(0, 0.36)	500	0.0022	0.0216	0.0220	0.952
				700	0.0025	0.0186	0.0186	0.953
				900	0.0018	0.0159	0.0163	0.956
II			(0.20, 0.30)	500	0.0019	0.0217	0.0221	0.953
				700	0.0024	0.0190	0.0187	0.953
				900	0.0018	0.0160	0.0164	0.955
III				500	0.0019	0.0220	0.0224	0.954
				700	0.0024	0.0192	0.0189	0.943
				900	0.0019	0.0163	0.0166	0.956
I	0.8	0.3	(0, 0.36)	500	0.0021	0.0215	0.0220	0.955
				700	0.0024	0.0187	0.0186	0.952
				900	0.0018	0.0159	0.0163	0.955
II			(0.20, 0.30)	500	0.0019	0.0216	0.0220	0.954
				700	0.0024	0.0187	0.0186	0.952
				900	0.0018	0.0160	0.0164	0.958
III				500	0.0019	0.0219	0.0222	0.952
				700	0.0024	0.0188	0.0187	0.945
				900	0.0018	0.0162	0.0165	0.958
I	0.9	0.3	(0, 0.30)	500	0.0021	0.0214	0.0220	0.958
				700	0.0024	0.0986	0.0186	0.953
				900	0.0018	0.0159	0.0163	0.952
II			(0.20, 0.30)	500	0.0020	0.0215	0.0220	0.959
				700	0.0024	0.0187	0.0186	0.954
				900	0.0018	0.0159	0.0163	0.953
III				500	0.0020	0.0216	0.0220	0.961
				700	0.0024	0.0187	0.0186	0.950
				900	0.0019	0.0161	0.0163	0.951

Table 6: Comparison of bias(Bias), empirical standard error (SSE), average of the estimated standard error (ESE), empirical coverage probability (CP) of 95% confidence intervals for Full, AIPW, IPW and CC estimators of γ under (3.30) with $\rho = 0.5,\ 0.8,\ 0.9$ and with average of total missing probability $m_0 = 0.3$ and about 50% censoring based on 1000 simulations for each sampling scenario, I, II or III, where m_1 and m_2 are the average missing probabilities for the cases and the non-cases, respectively.

					Bias(γ)				SSE(γ)				ESE(γ)				CP(γ)			
Sampling	ρ	m_0	(m_1, m_2)	n	Full	AIPW	IPW	CC	Full	AIPW	IPW	CC	Full	AIPW	IPW	CC	Full	AIPW	IPW	CC
I	0.5	0.3	(0,0.36)	500	0.0020	0.0022	0.0076	0.0575	0.0214	0.0216	0.0226	0.0323	0.0217	0.0220	0.0244	0.0325	0.958	0.952	0.967	0.948
				700	0.0024	0.0025	0.0080	0.0579	0.0186	0.0186	0.0196	0.0274	0.0183	0.0186	0.0206	0.0275	0.950	0.953	0.962	0.954
				900	0.0018	0.0018	0.0075	0.0570	0.0159	0.0159	0.0170	0.0238	0.0161	0.0163	0.0181	0.0242	0.959	0.956	0.958	0.948
II			(0.20,0.30)	500		0.0019	0.0057	0.0199		0.0217	0.0245	0.0278		0.0221	0.0258	0.0287		0.953	0.959	0.958
				700		0.0024	0.0068	0.0212		0.0190	0.0212	0.0244		0.0187	0.0218	0.0243		0.953	0.952	0.943
				900		0.0018	0.0058	0.0201		0.0160	0.0187	0.0215		0.0164	0.0192	0.0214		0.955	0.958	0.948
III				500		0.0019	0.0017	0.0017		0.0220	0.0255	0.0254		0.0224	0.0263	0.0263		0.954	0.951	0.953
				700		0.0024	0.0031	0.0030		0.0192	0.0224	0.0224		0.0189	0.0223	0.0223		0.943	0.935	0.935
				900		0.0019	0.0017	0.0017		0.0163	0.0194	0.0194		0.0166	0.0196	0.0196		0.956	0.957	0.957
I	0.8	0.3	(0,0.36)	500		0.0021	0.0076	0.0579		0.0215	0.0226	0.0324		0.0220	0.0244	0.0326		0.955	0.970	0.948
				700		0.0024	0.0079	0.0579		0.0187	0.0197	0.0276		0.0186	0.0206	0.0275		0.952	0.962	0.954
				900		0.0018	0.0074	0.0571		0.0159	0.0169	0.0238		0.0163	0.0181	0.0242		0.955	0.957	0.950
II			(0.20,0.30)	500		0.0019	0.0056	0.0199		0.0216	0.0245	0.0278		0.0220	0.0258	0.0287		0.954	0.960	0.957
				700		0.0024	0.0068	0.0213		0.0187	0.0211	0.0243		0.0186	0.0218	0.0243		0.952	0.951	0.945
				900		0.0018	0.0058	0.0202		0.0160	0.0188	0.0216		0.0164	0.0192	0.0214		0.958	0.960	0.949
III				500		0.0019	0.0018	0.0018		0.0219	0.0254	0.0253		0.0222	0.0262	0.0262		0.952	0.956	0.956
				700		0.0024	0.0031	0.0031		0.0188	0.0223	0.0223		0.0187	0.0222	0.0222		0.945	0.938	0.939
				900		0.0018	0.0018	0.0018		0.0162	0.0195	0.0195		0.0165	0.0195	0.0195		0.958	0.957	0.956
I	0.9	0.3	(0,0.36)	500		0.0021	0.0075	0.0578		0.0214	0.0224	0.0324		0.0220	0.0244	0.0326		0.958	0.969	0.949
				700		0.0024	0.0079	0.0580		0.0186	0.0197	0.0276		0.0186	0.0206	0.0276		0.953	0.960	0.958
				900		0.0018	0.0074	0.0572		0.0159	0.0169	0.0238		0.0163	0.0181	0.0242		0.952	0.955	0.951
II			(0.20,0.30)	500		0.0020	0.0055	0.0199		0.0215	0.0245	0.0278		0.0220	0.0258	0.0287		0.959	0.959	0.959
				700		0.0024	0.0067	0.0213		0.0187	0.0211	0.0243		0.0186	0.0219	0.0243		0.954	0.952	0.945
				900		0.0018	0.0058	0.0202		0.0159	0.0188	0.0216		0.0163	0.0192	0.0214		0.953	0.960	0.949
III				500		0.0020	0.0018	0.0018		0.0216	0.0254	0.0254		0.0220	0.0262	0.0262		0.961	0.956	0.955
				700		0.0024	0.0032	0.0031		0.0187	0.0223	0.0222		0.0186	0.0222	0.0222		0.950	0.937	0.937
				900		0.0019	0.0018	0.0017		0.0161	0.0195	0.0194		0.0163	0.0195	0.0195		0.951	0.958	0.957

Table 7: Bias, empirical standard error(SSE), average of the estimated standard error(ESE), empirical coverage probability(CP) of 95% confidence intervals, and relative efficiencies(REE) for the AIPW estimator of γ under model (3.30) with $\rho = 0.5,\ 0.8,\ 0.9$ and with average of total missing probability $m_0 = 0.6$ and about 50% censoring based on 1000 simulations for each sampling scenario, I, II or III, where m_1 and m_2 are the average missing probabilities for the cases and the non-cases, respectively.

					γ			
Sampling	ρ	m_0	(m_1, m_2)	n	Bias	SSE	ESE	CP
I	0.5	0.6	(0, 0.65)	500	0.0030	0.0226	0.0262	0.978
				700	0.0029	0.0193	0.0218	0.968
				900	0.0022	0.0167	0.0189	0.972
II			(0.45, 0.60)	500	0.0019	0.0228	0.0237	0.967
				700	0.0018	0.0195	0.0199	0.954
				900	0.0019	0.0166	0.0175	0.967
III				500	0.0023	0.0242	0.0242	0.957
				700	0.0030	0.0196	0.0204	0.960
				900	0.0017	0.0179	0.0180	0.948
I	0.8	0.6	(0, 0.65)	500	0.0025	0.0219	0.0264	0.980
				700	0.0026	0.0191	0.0219	0.969
				900	0.0020	0.0163	0.0190	0.979
II			(0.45, 0.60)	500	0.0021	0.0225	0.0232	0.959
				700	0.0026	0.0187	0.0197	0.961
				900	0.0017	0.0166	0.0173	0.949
III				500	0.0026	0.0231	0.0236	0.953
				700	0.0027	0.0188	0.0199	0.958
				900	0.0017	0.0172	0.0175	0.950
I	0.9	0.6	(0, 0.65)	500	0.0022	0.0216	0.0264	0.977
				700	0.0025	0.0187	0.0219	0.972
				900	0.0019	0.0161	0.0190	0.984
II			(0.45, 0.60)	500	0.0023	0.0222	0.0231	0.963
				700	0.0026	0.0184	0.0195	0.963
				900	0.0019	0.0164	0.0171	0.952
III				500	0.0026	0.0226	0.0232	0.952
				700	0.0027	0.0184	0.0196	0.962
				900	0.0018	0.0167	0.0172	0.947

Table 8: Comparison of bias(Bias), empirical standard error (SSE), average of the estimated standard error (ESE), empirical coverage probability (CP) of 95% confidence intervals for Full, AIPW, IPW and CC estimators of γ under (3.30) with $\rho = 0.5,\ 0.8,\ 0.9$ and with average of total missing probability $m_0 = 0.6$ and about 50% censoring based on 1000 simulations for each sampling scenario, I, II or III, where m_1 and m_2 are the average missing probabilities for the cases and the non-cases, respectively.

					Bias(γ)				SSE(γ)				ESE(γ)				CP(γ)			
Sampling	ρ	m_0	(m_1, m_2)	n	Full	AIPW	IPW	CC	Full	AIPW	IPW	CC	Full	AIPW	IPW	CC	Full	AIPW	IPW	CC
I	0.5	0.6	(0,0.65)	500	0.0020	0.0030	0.0395	0.2025	0.0214	0.0226	0.0395	0.0611	0.0217	0.0262	0.0433	0.0637	0.958	0.978	0.970	0.963
				700	0.0024	0.0029	0.0383	0.2041	0.0186	0.0193	0.0333	0.0525	0.0183	0.0218	0.0368	0.0539	0.950	0.968	0.960	0.953
				900	0.0018	0.0022	0.0370	0.2044	0.0159	0.0167	0.0292	0.0469	0.0161	0.0189	0.0327	0.0479	0.949	0.972	0.978	0.963
II			(0.45,0.65)	500		0.0019	0.0242	0.0662		0.0228	0.0395	0.0502		0.0237	0.0423	0.0505		0.967	0.964	0.957
				700		0.0018	0.0235	0.0660		0.0195	0.0340	0.0421		0.0199	0.0359	0.0430		0.954	0.968	0.949
				900		0.0019	0.0243	0.0678		0.0166	0.0291	0.0371		0.0175	0.0317	0.0382		0.967	0.968	0.949
III				500		0.0023	0.0036	0.0034		0.0242	0.0394	0.0386		0.0242	0.0377	0.0374		0.957	0.941	0.942
				700		0.0030	0.0022	0.0019		0.0196	0.0311	0.0206		0.0204	0.0319	0.0316		0.960	0.957	0.952
				900		0.0017	0.0013	0.0013		0.0179	0.0276	0.0274		0.0180	0.0281	0.0279		0.948	0.953	0.957
I	0.8	0.6%	(0,0.65)	500		0.0025	0.0387	0.2030		0.0219	0.0395	0.0617		0.0264	0.0434	0.0639		0.980	0.964	0.960
				700		0.0026	0.0379	0.2039		0.0191	0.0336	0.0528		0.0219	0.0369	0.0540		0.969	0.964	0.955
				900		0.0020	0.0368	0.2048		0.0163	0.0293	0.0469		0.0190	0.0327	0.0479		0.979	0.970	0.963
II			(0.45,0.65)	500		0.0021	0.0252	0.0685		0.0225	0.0405	0.0515		0.0232	0.0421	0.0503		0.959	0.961	0.947
				700		0.0026	0.0275	0.0714		0.0187	0.0332	0.0418		0.0197	0.0364	0.0434		0.961	0.969	0.954
				900		0.0017	0.0255	0.0685		0.0166	0.0294	0.0370		0.0173	0.0317	0.0379		0.949	0.961	0.942
III				500		0.0026	0.0033	0.0033		0.0231	0.0387	0.0381		0.0236	0.0379	0.0376		0.953	0.942	0.941
				700		0.0027	0.0020	0.0017		0.0188	0.0310	0.0305		0.0199	0.0321	0.0318		0.958	0.958	0.957
				900		0.0017	0.0005	0.0006		0.0172	0.0272	0.0271		0.0175	0.0282	0.0281		0.950	0.952	0.952
I	0.9	0.6	(0,0.65)	500		0.0022	0.0385	0.2035		0.0216	0.0396	0.0616		0.0264	0.0434	0.0640		0.977	0.964	0.957
				700		0.0025	0.0375	0.2039		0.0187	0.0334	0.0528		0.0219	0.0369	0.0541		0.972	0.963	0.953
				900		0.0019	0.0369	0.2050		0.0161	0.0294	0.0470		0.0190	0.0328	0.0479		0.984	0.965	0.965
II			(0.45,0.60)	500		0.0023	0.0252	0.0683		0.0222	0.0406	0.0513		0.0231	0.0423	0.0504		0.963	0.957	0.943
				700		0.0026	0.0273	0.0711		0.0184	0.0331	0.0417		0.0195	0.0365	0.0434		0.963	0.968	0.955
				900		0.0019	0.0257	0.0685		0.0164	0.0294	0.0368		0.0171	0.0319	0.0380		0.952	0.959	0.944
III				500		0.0026	0.0037	0.0037		0.0226	0.0387	0.0381		0.0232	0.0379	0.0377		0.952	0.947	0.944
				700		0.0027	0.0022	0.0018		0.0184	0.0312	0.0306		0.0196	0.0322	0.0320		0.962	0.956	0.958
				900		0.0018	0.0006	0.0006		0.0167	0.0272	0.0270		0.0172	0.0283	0.0281		0.947	0.954	0.956

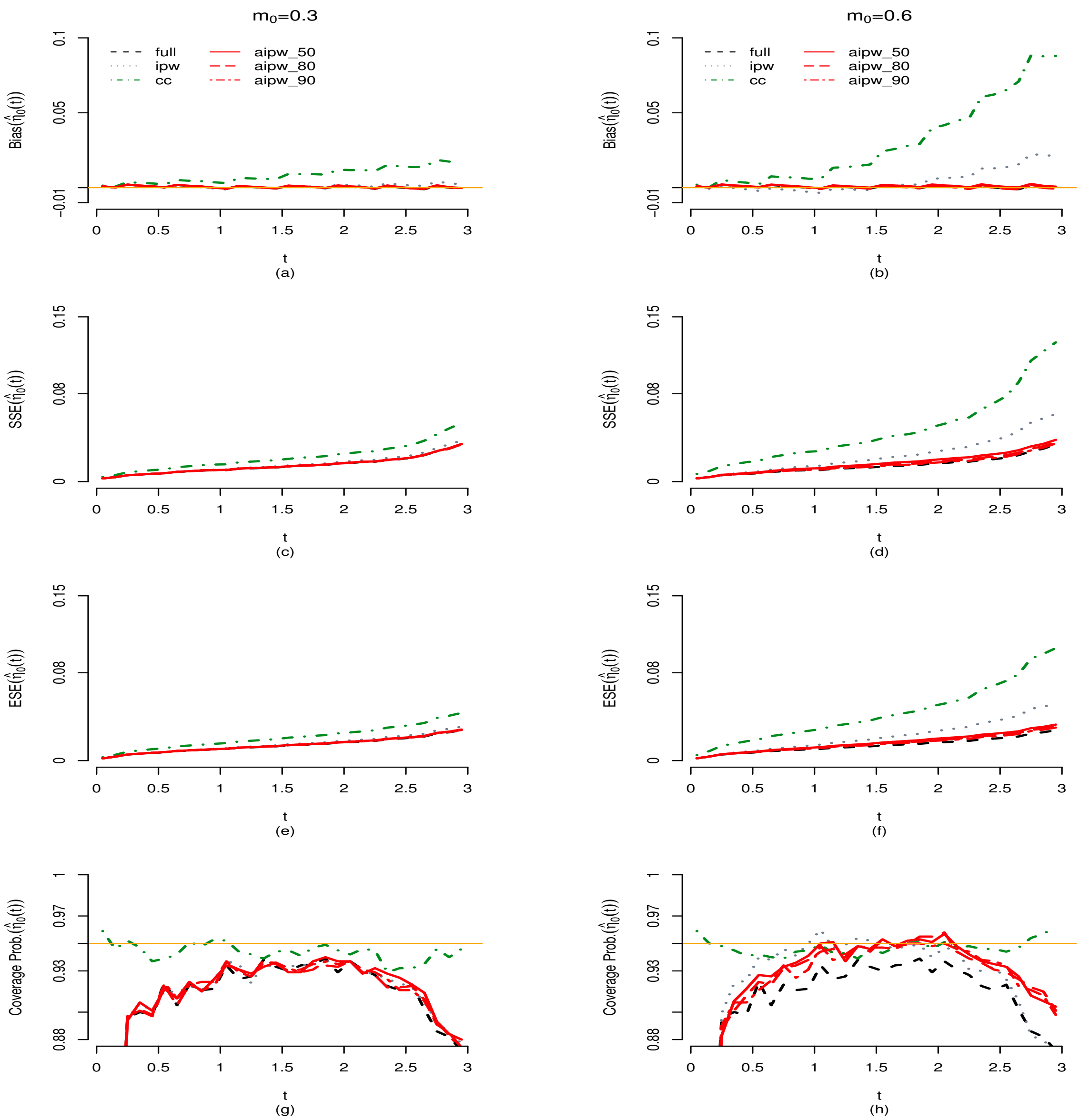


Figure 15: Comparison of Full, IPW, CC, AIPW-50, AIPW-80, AIPW-90 estimators for the baseline cumulative coefficient $\eta_0(t)$ for average of total missing probability $m_0 = 0.3$ and $m_0 = 0.6$, respectively, under (3.30) with sampling scenario I. For $m_0 = 0.3$, $m_1 = 0$ and $m_2 = 0.36$. For $m_0 = 0.6$, $m_1 = 0$ and $m_2 = 0.65$. These results are based on 1000 simulations with $n = 700$ and 50% censoring. (a) (b): The plots of the biases of the estimates of $\eta_0(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$.(c)(d):The plots of the empirical standard errors of the estimates of $\eta_0(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$. (e)(f): The plots of the average of the estimated standard errors of the estimates of $\eta_0(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$. (g)(h): The plots of the coverage probabilities of the estimators of $\eta_0(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$.

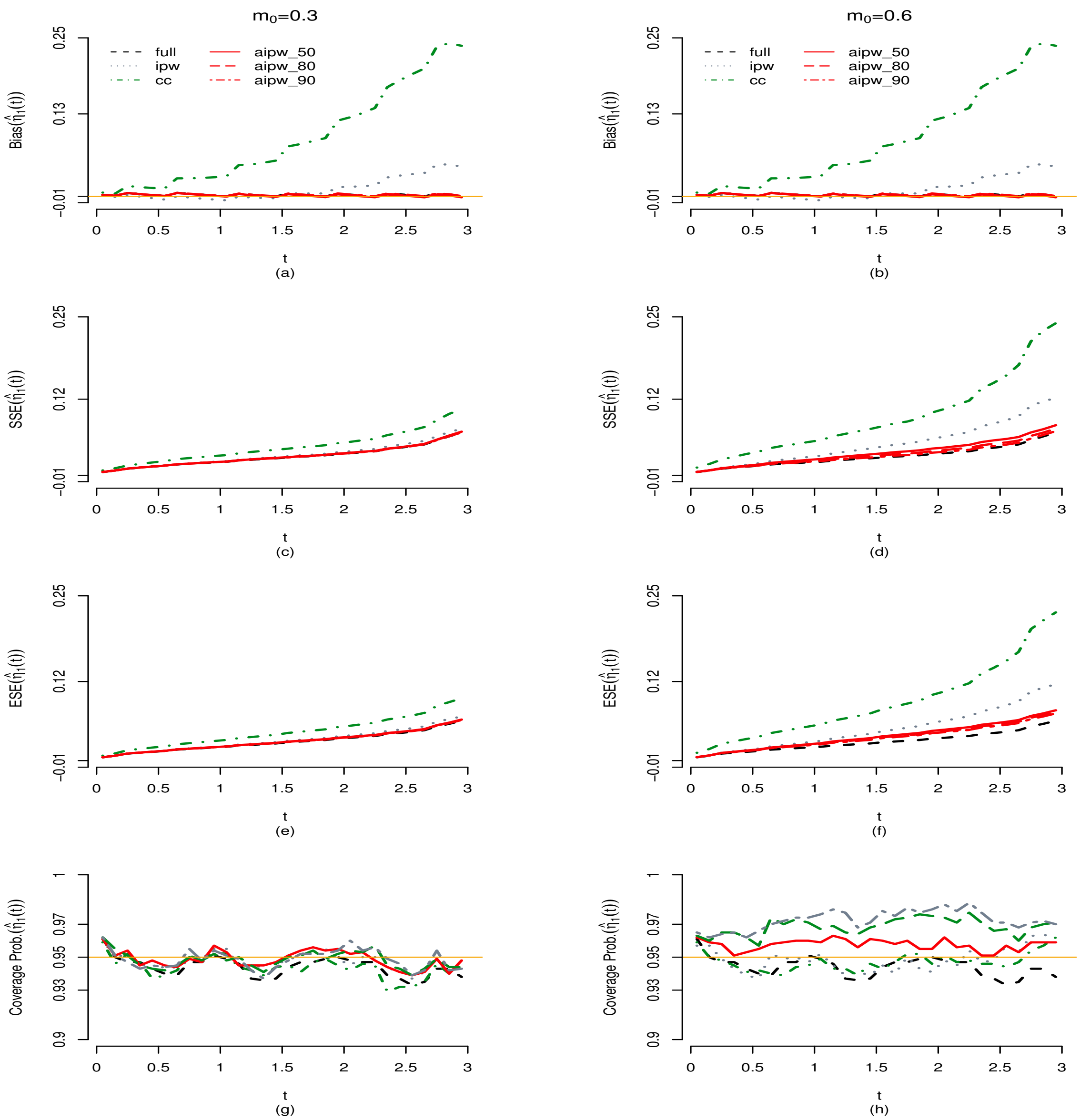


Figure 16: Comparison of Full, IPW, CC, AIPW-50, AIPW-80, AIPW-90 estimators for the cumulative coefficient $\eta_1(t)$ for average of total missing probability $m_0 = 0.3$ and $m_0 = 0.6$, respectively, under (3.30) with sampling scenario I. For $m_0 = 0.3$, $m_1 = 0$ and $m_2 = 0.36$. For $m_0 = 0.6$, $m_1 = 0$ and $m_2 = 0.65$. These results are based on 1000 simulations with $n = 700$ and 50% censoring. (a), (b): The plots of the biases of the estimates of $\eta_1(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$.(c), (d):The plots of the empirical standard errors of the estimates of $\eta_1(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$. (e), (f): The plots of the average of the estimated standard errors of the estimates of $\eta_1(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$. (g), (h): The plots of the coverage probabilities of the estimators of $\eta_1(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$.

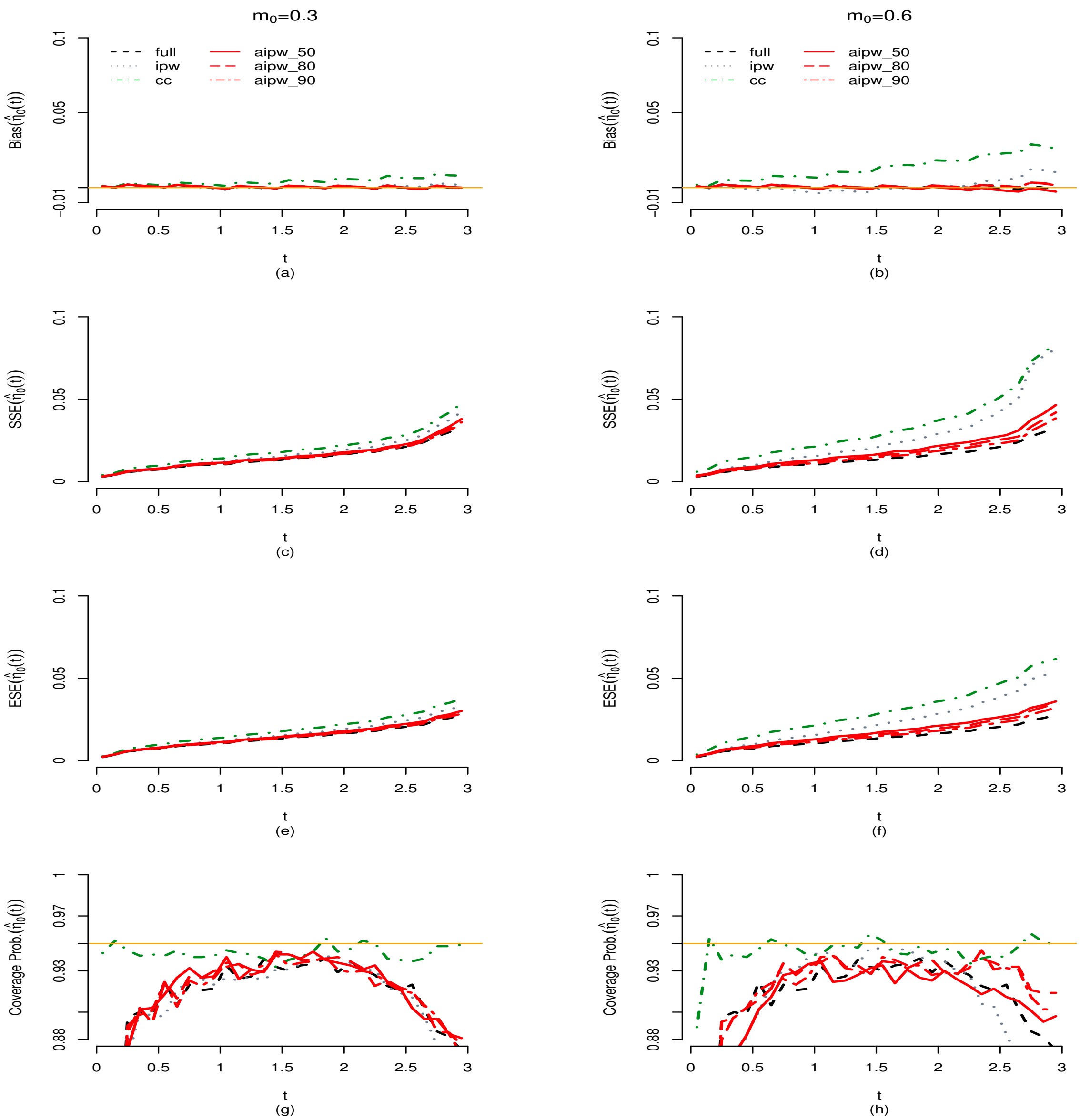


Figure 17: Comparison of Full, IPW, CC, AIPW-50, AIPW-80, AIPW-90 estimators for the baseline cumulative coefficient $\eta_0(t)$ for average of total missing probability $m_0 = 0.3$ and $m_0 = 0.6$, respectively, under (3.30) with sampling scenario II. For $m_0 = 0.3$, $m_1 = 0.2$ and $m_2 = 0.3$. For $m_0 = 0.6$, $m_1 = 0.45$ and $m_2 = 0.65$. These results are based on 1000 simulations with $n = 700$ and 50% censoring. For $m_0 = 0.3$, $m_1 = 0.2$ and $m_2 = 0.3$. (a), (b): The plots of the biases of the estimates of $\eta_0(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$.(c), (d):The plots of the empirical standard errors of the estimates of $\eta_0(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$. (e), (f): The plots of the average of the estimated standard errors of the estimates of $\eta_0(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$. (g)(h): The plots of the coverage probabilities of the estimators of $\eta_0(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$.

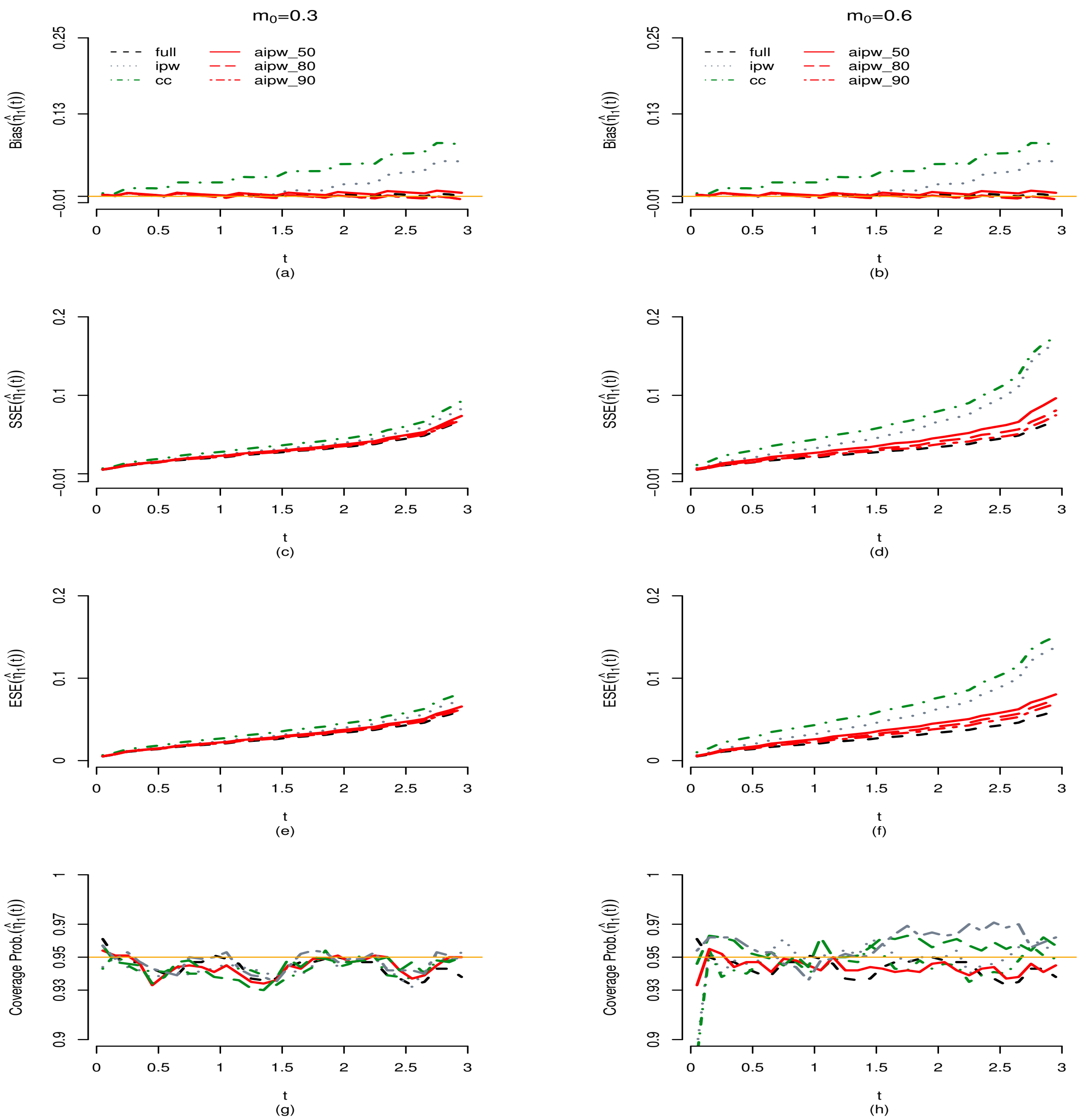


Figure 18: Comparison of Full, IPW, CC, AIPW-50, AIPW-80, AIPW-90 estimators for the cumulative coefficient $\eta_1(t)$ for average of total missing probability $m_0 = 0.3$ and $m_0 = 0.6$, respectively, under (3.30) with sampling scenario II. For $m_0 = 0.3$, $m_1 = 0.2$ and $m_2 = 0.3$. For $m_0 = 0.6$, $m_1 = 0.45$ and $m_2 = 0.65$. These results are based on 1000 simulations with $n = 700$ and 50% censoring. For $m_0 = 0.3$, $m_1 = 0.2$ and $m_2 = 0.3$. (a),(b): The plots of the biases of the estimates of $\eta_1(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$.(c),(d):The plots of the empirical standard errors of the estimates of $\eta_1(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$. (e),(f): The plots of the average of the estimated standard errors of the estimates of $\eta_1(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$. (g),(h): The plots of the coverage probabilities of the estimators of $\eta_1(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$.

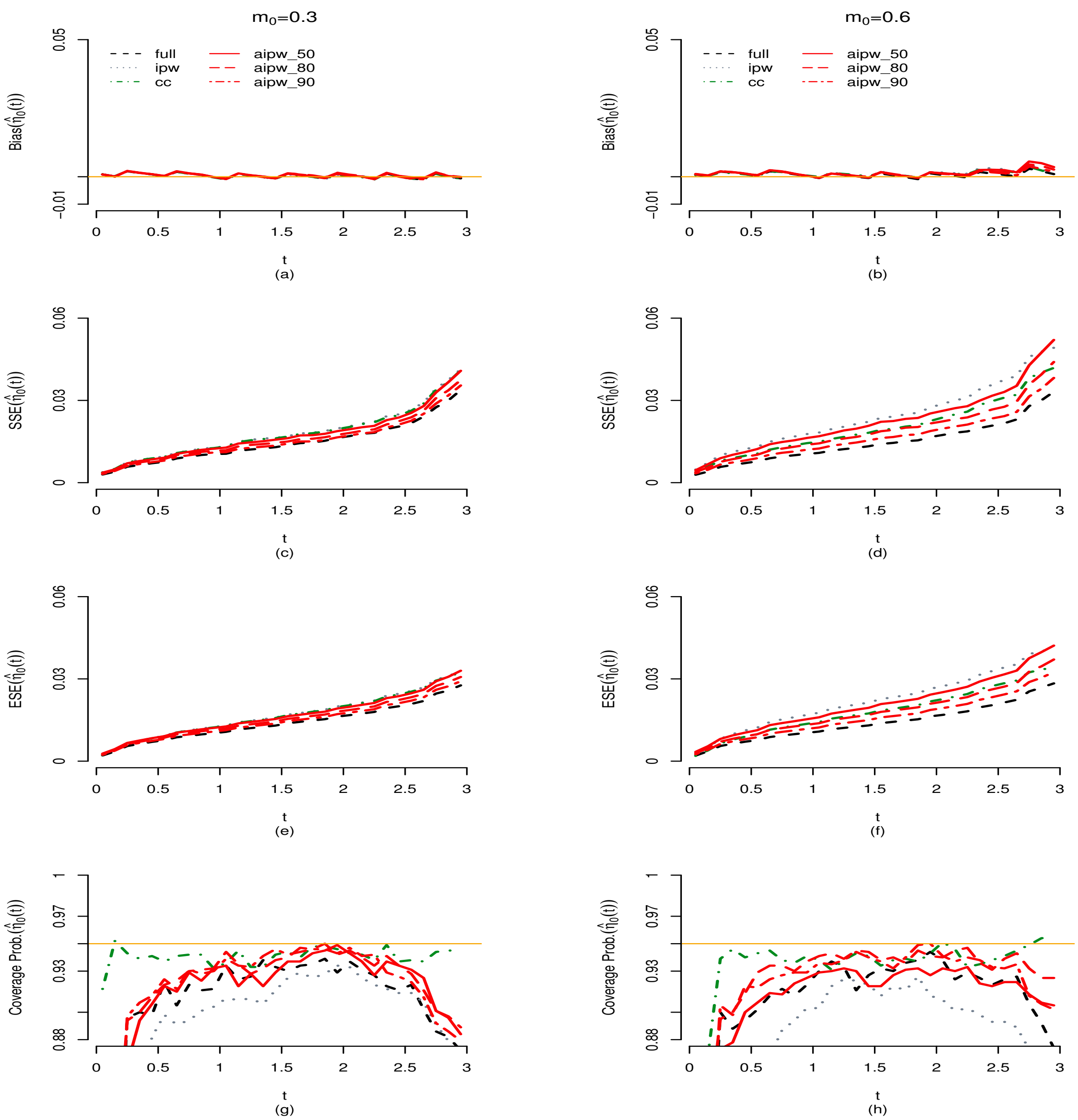


Figure 19: Comparison of Full, IPW, CC, AIPW-50, AIPW-80, AIPW-90 estimators for the baseline cumulative coefficient $\eta_0(t)$ for average of total missing probability $m_0 = 0.3$ and $m_0 = 0.6$, respectively, under (3.30) with sampling scenario III. These results are based on 1000 simulations with $n = 700$ and 50% censoring. (a), (b): The plots of the biases of the estimates of $\eta_0(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$.(c), (d):The plots of the empirical standard errors of the estimates of $\eta_0(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$. (e), (f): The plots of the average of the estimated standard errors of the estimates of $\eta_0(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$. (g), (h): The plots of the coverage probabilities of the estimators of $\eta_0(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$.

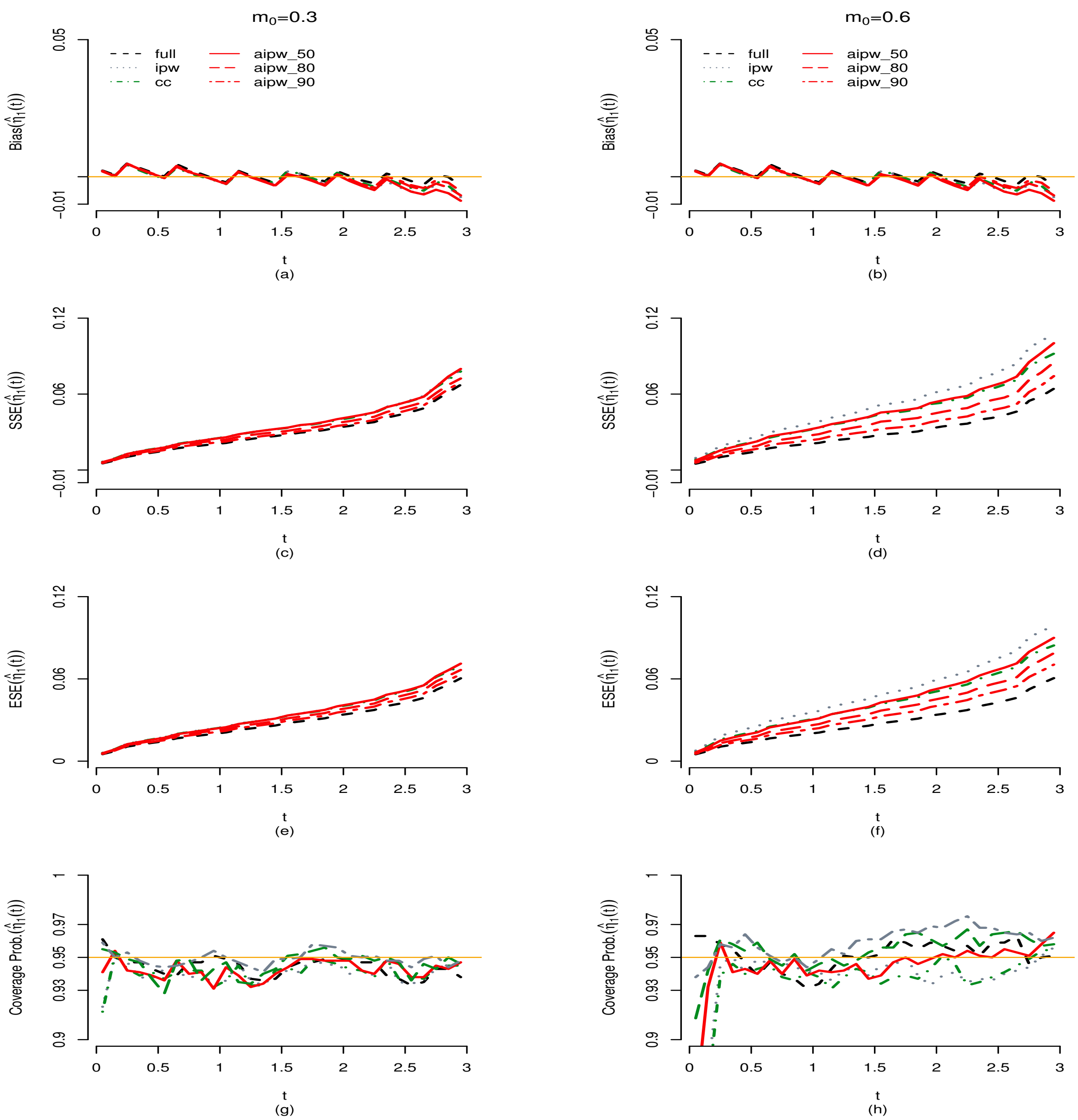
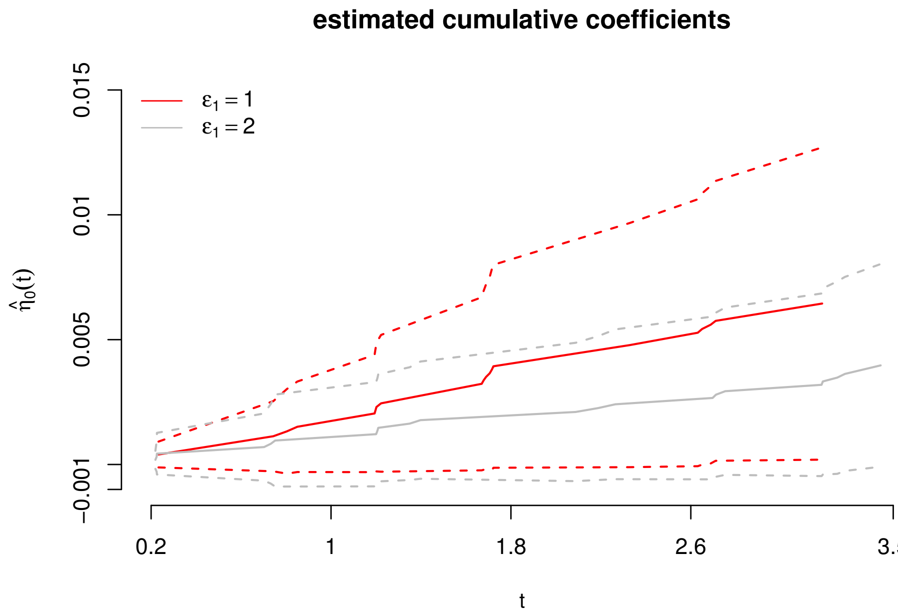
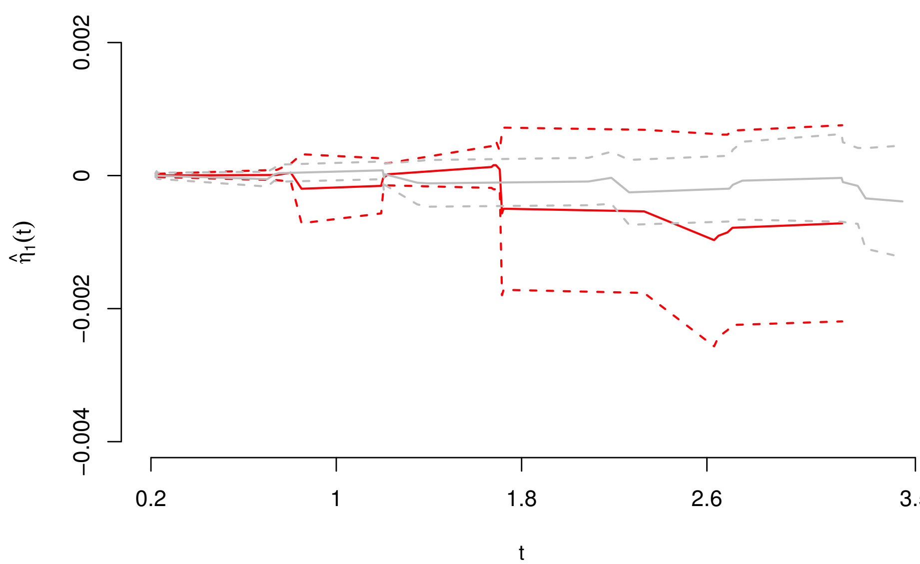


Figure 20: Comparison of Full, IPW, CC, AIPW-50, AIPW-80, AIPW-90 estimators for the cumulative coefficient $\eta_1(t)$ for average of total missing probability $m_0 = 0.3$ and $m_0 = 0.6$, respectively, under (3.30) with sampling scenario III. These results are based on 1000 simulations with $n = 700$ and 50% censoring. (a), (b): The plots of the biases of the estimates of $\eta_1(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$.(c), (d):The plots of the empirical standard errors of the estimates of $\eta_1(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$. (e), (f): The plots of the average of the estimated standard errors of the estimates of $\eta_1(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$. (g), (h): The plots of the coverage probabilities of the estimators of $\eta_1(t)$ for $m_0 = 0.3$ and $m_0 = 0.6$.



(a)



(b)

Figure 21: (a) and (b) show the comparison of the AIPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the immune response R_i (IgG-92TH023V1V2) in model (3.37) for $\epsilon_{1i} = 1$ and $\epsilon_{1i} = 2$, respectively.

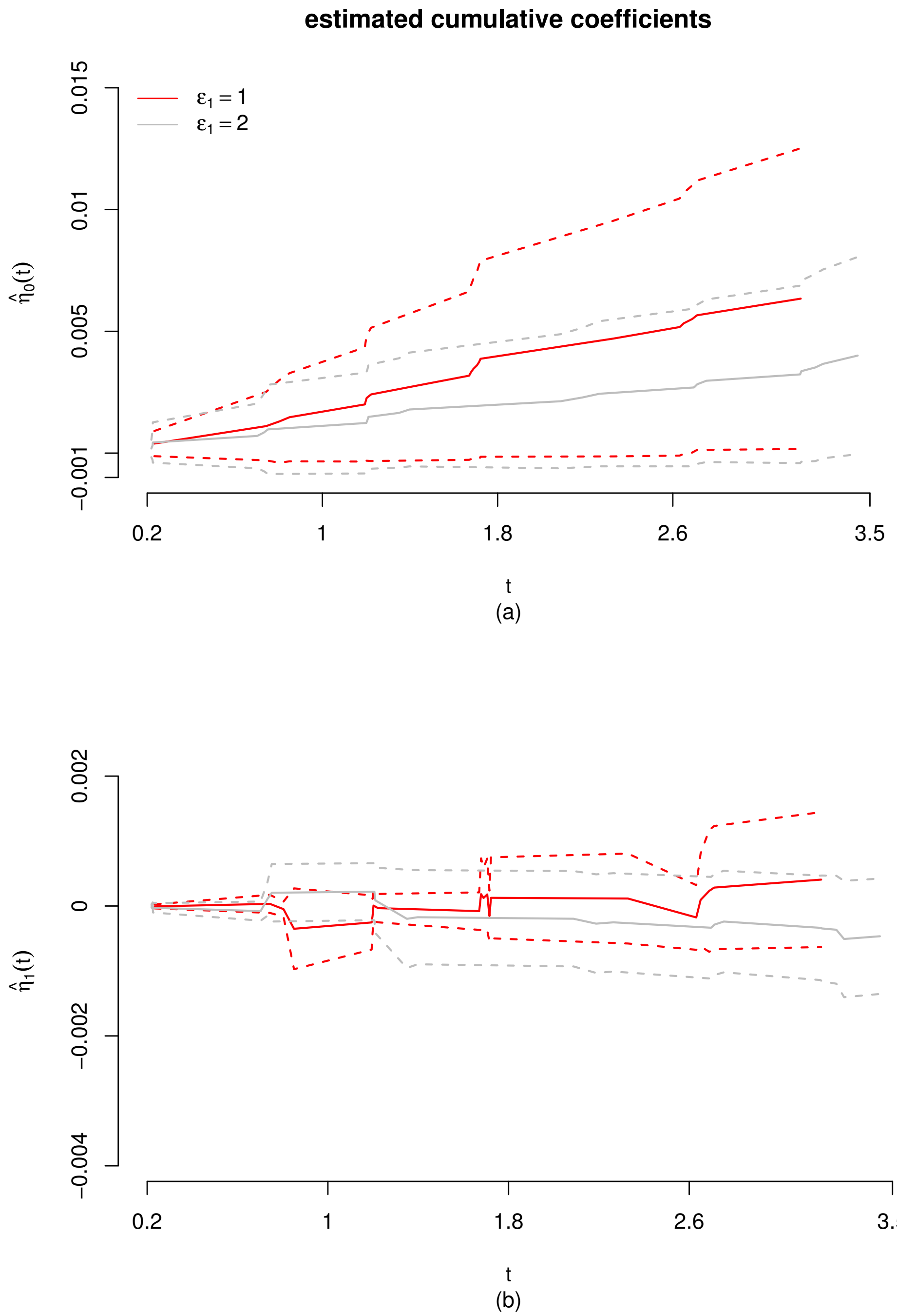
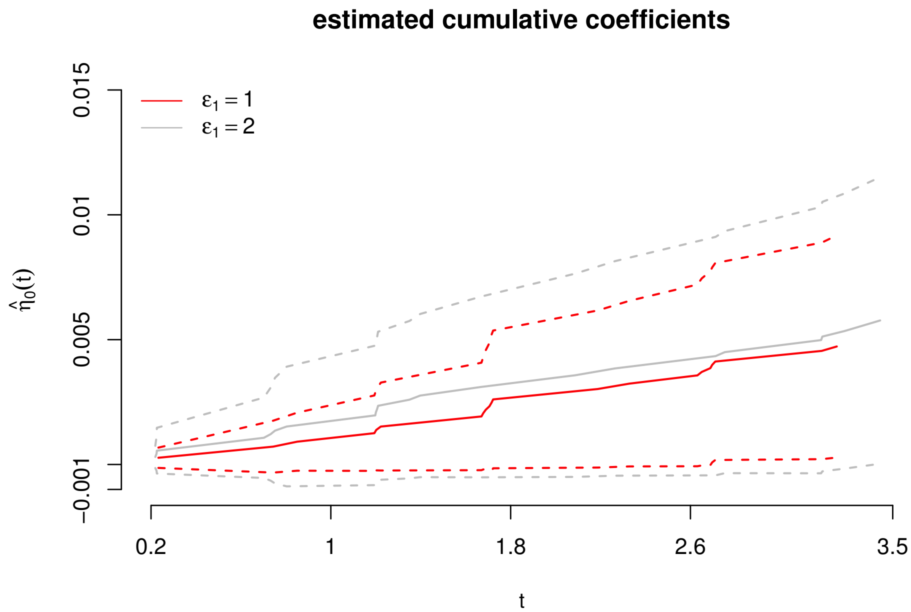
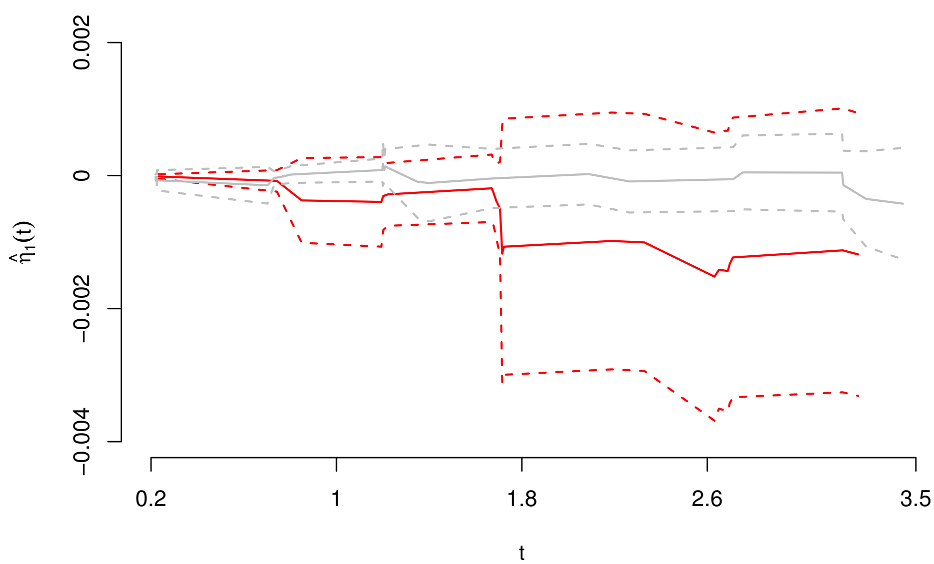


Figure 22: (a) and (b) show the comparison of the AIPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the immune response R_i (IgG3-92TH023V1V2) in model (3.37) for $\epsilon_{1i} = 1$ and $\epsilon_{1i} = 2$, respectively.



(a)



(b)

Figure 23: (a) and (b) show the comparison of the AIPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the immune response R_i (IgG-A244V1V2) in model (3.37) for $\epsilon_{2i} = 1$ and $\epsilon_{2i} = 2$, respectively.

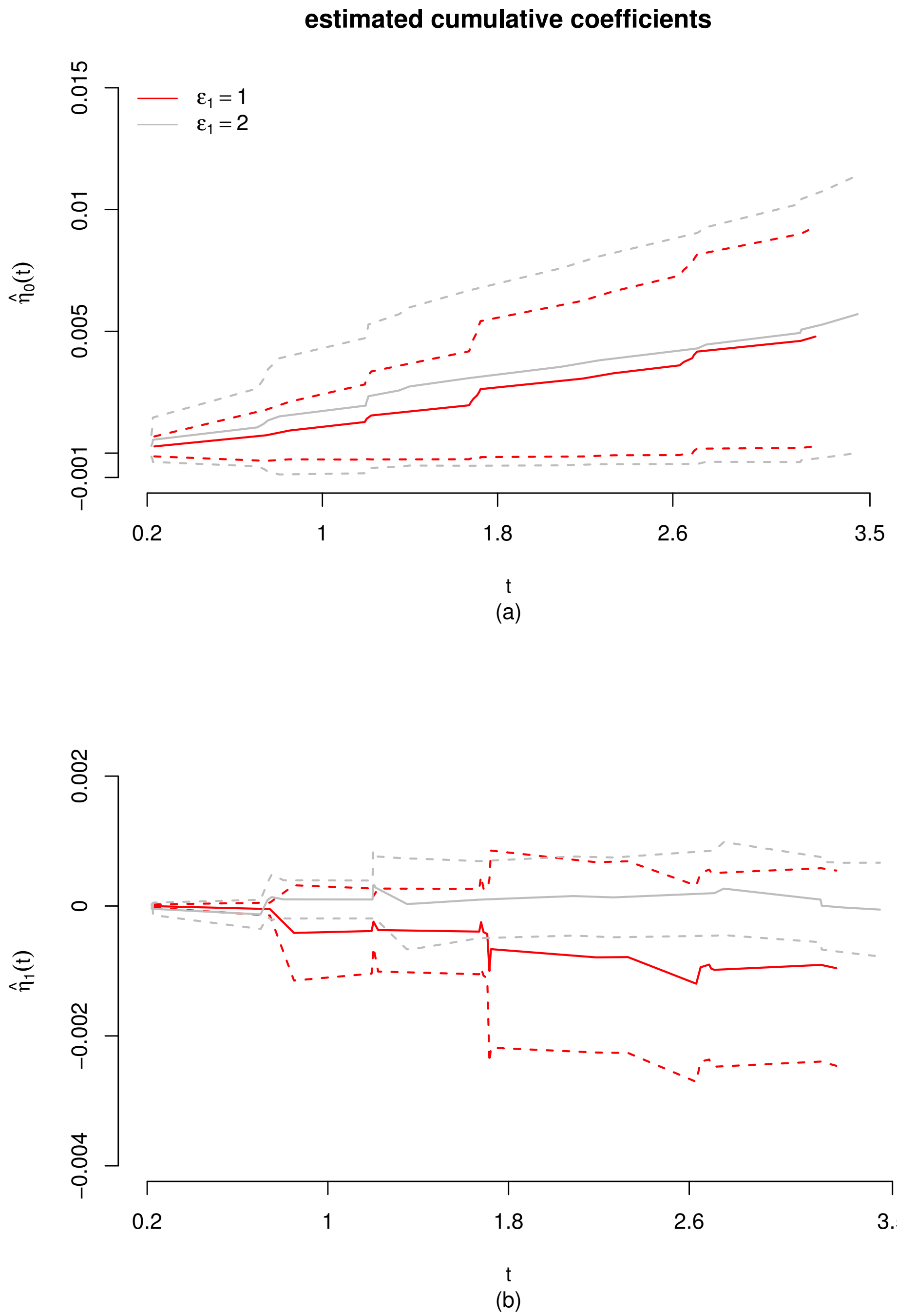


Figure 24: (a) and (b) show the comparison of the AIPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the immune response R_i (IgG3-A244V1V2) in model (3.37) for $\epsilon_{2i} = 1$ and $\epsilon_{2i} = 2$, respectively.

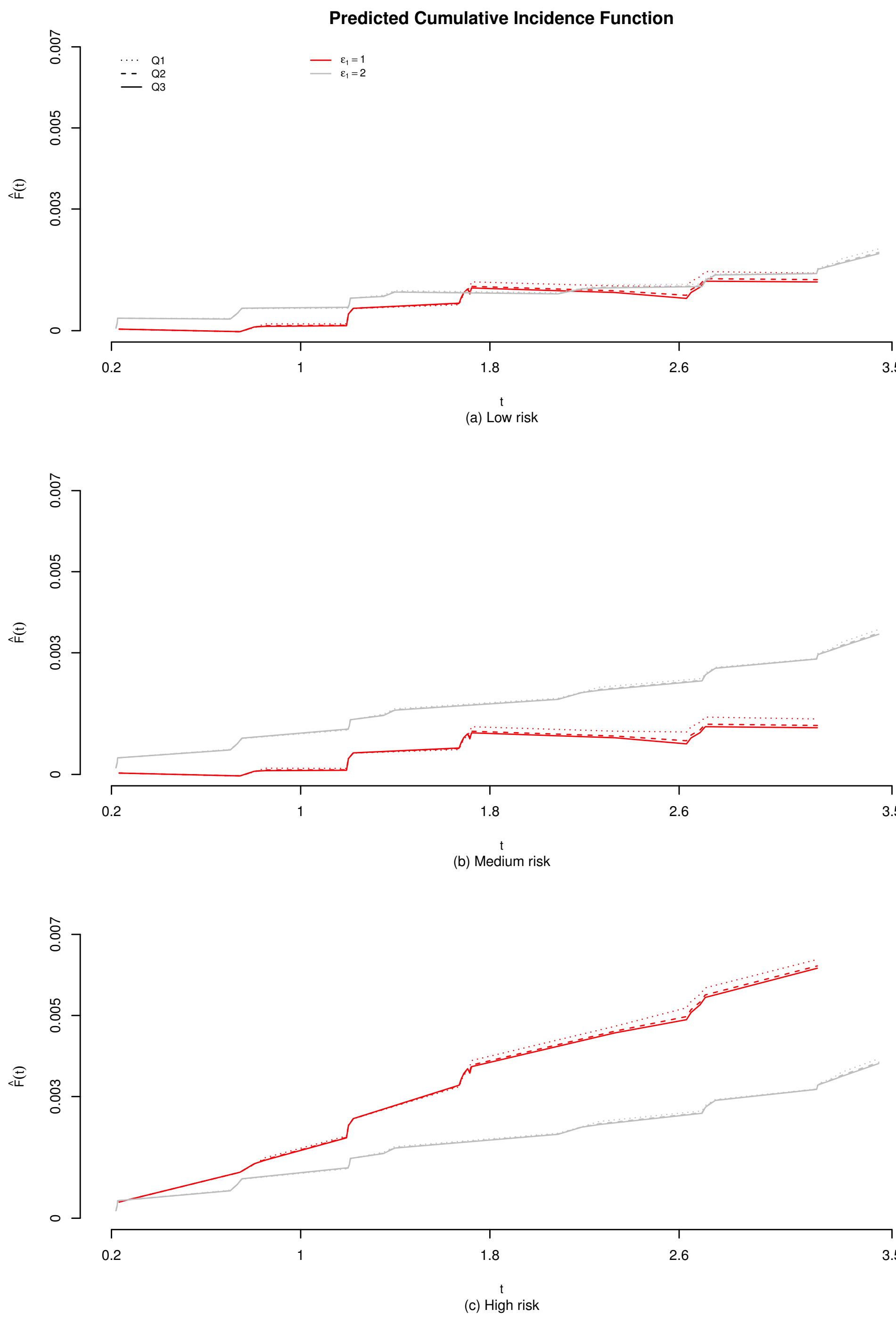


Figure 25: $Q_1 = 0.09027, Q_2 = 0.31310$ and $Q_3 = 0.39230$ are quartiles of the predicted immune response R_i (IgG-92TH023V1V2) using AIPW method. (a), (b) and (c) shows that the predicted cumulative incidence function $\hat{F}$ for $\epsilon_{1i} = 1$ (red) and $\epsilon_{1i} = 2$ (grey), respectively, at each level of behavioral risk score groups (low, medium and high) based on the model (3.37).

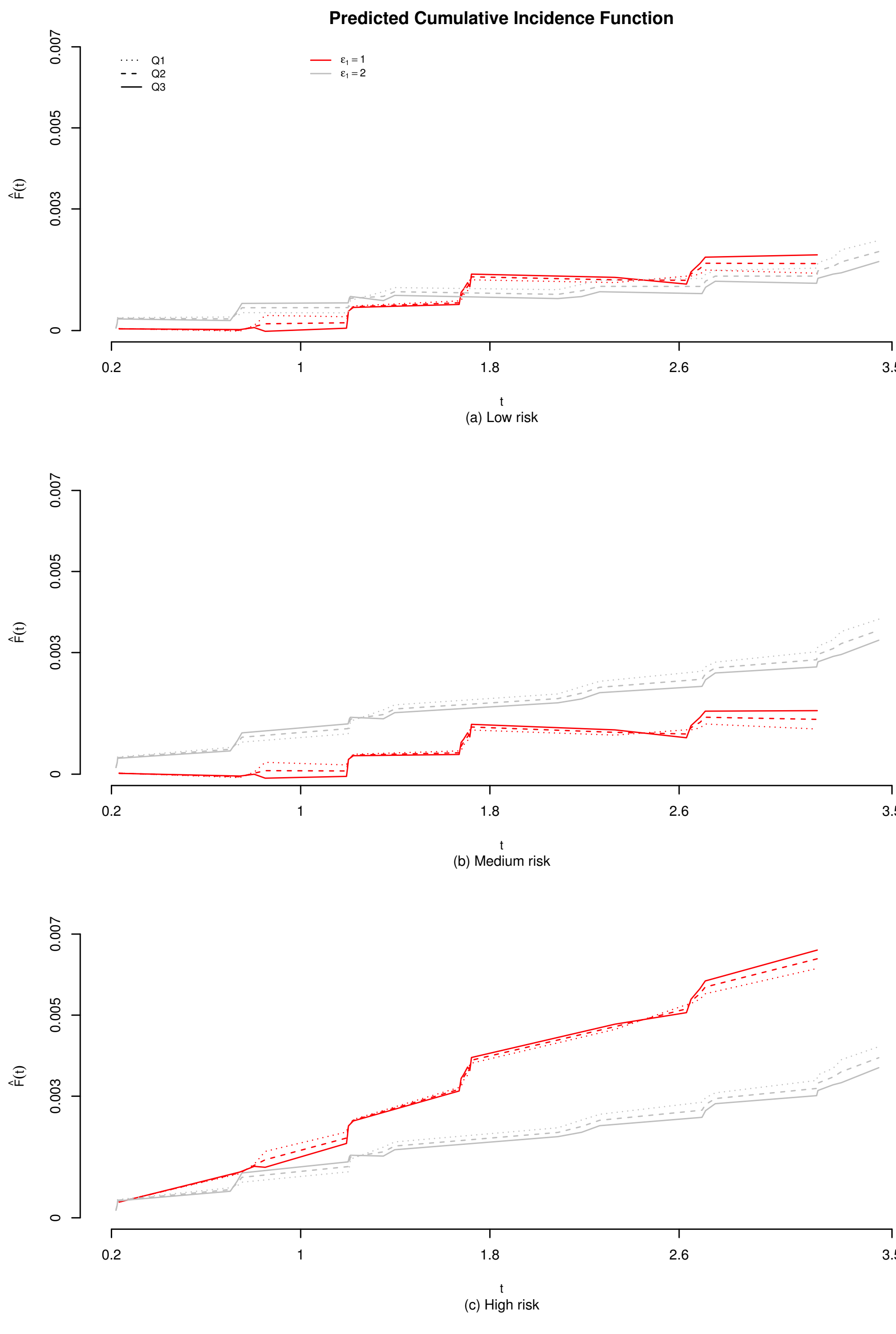


Figure 26: $Q_1 = -0.4677, Q_2 = 0.1196$ and $Q_3 = 0.6484$ are quartiles of the predicted immune response R_i (IgG3-92TH023V1V2) using AIPW method. At three quartiles of immune responses, the graphs show the predicted cumulative incidence function $\hat{F}_{1i}$ with each level of behavioral risk score groups (low, medium and high) based on the model (3.37) .

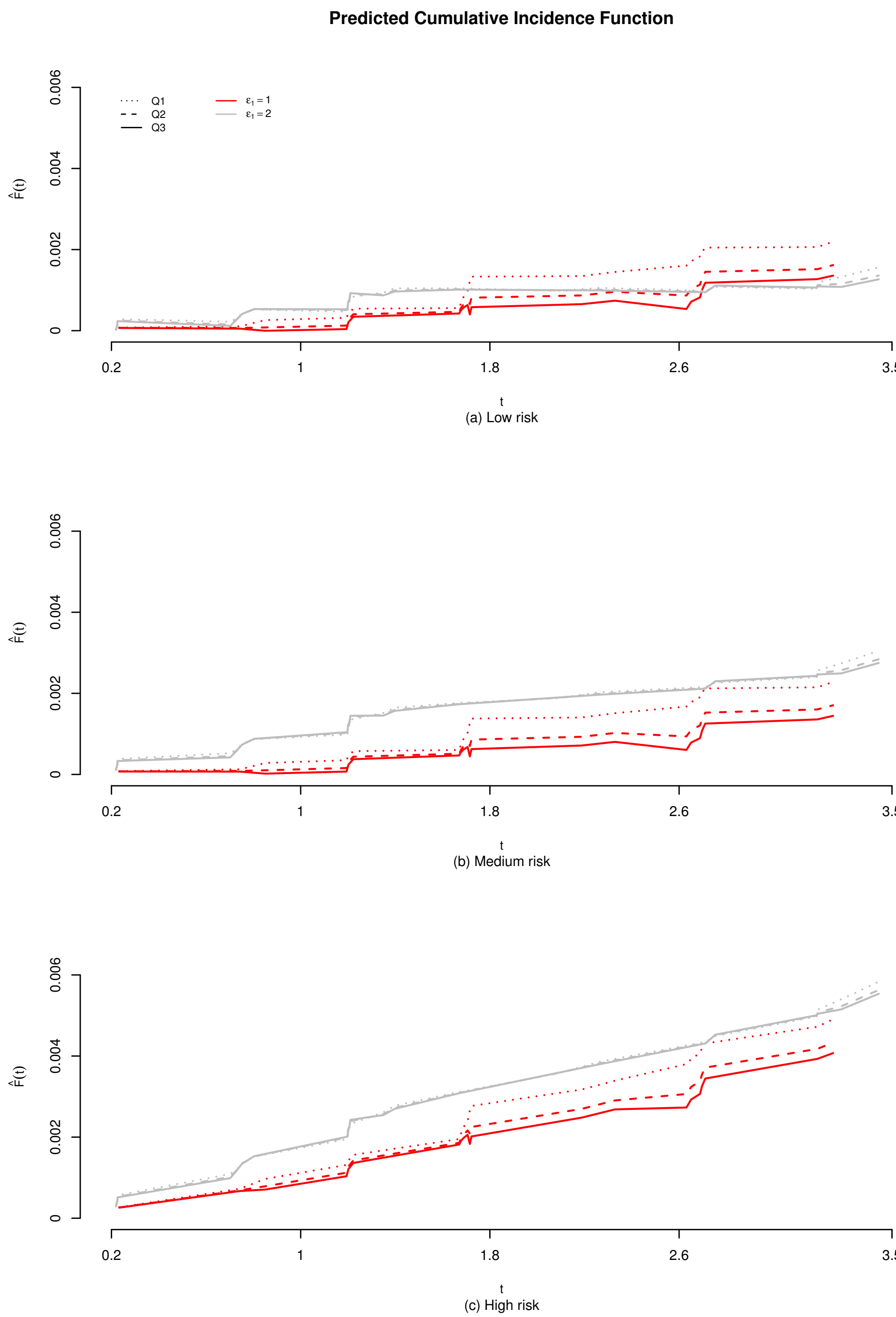


Figure 27: $Q_1 = -0.1530, Q_2 = 0.3321$ and $Q_3 = 0.5514$ are quartiles of the predicted immune response R_i (IgG-A244V1V2) using AIPW method. At three quartiles of immune responses, the graphs show the predicted cumulative incidence function $\hat{F}_{1i}$ with each level of behavioral risk score groups (low, medium and high) based on the model (3.37) .

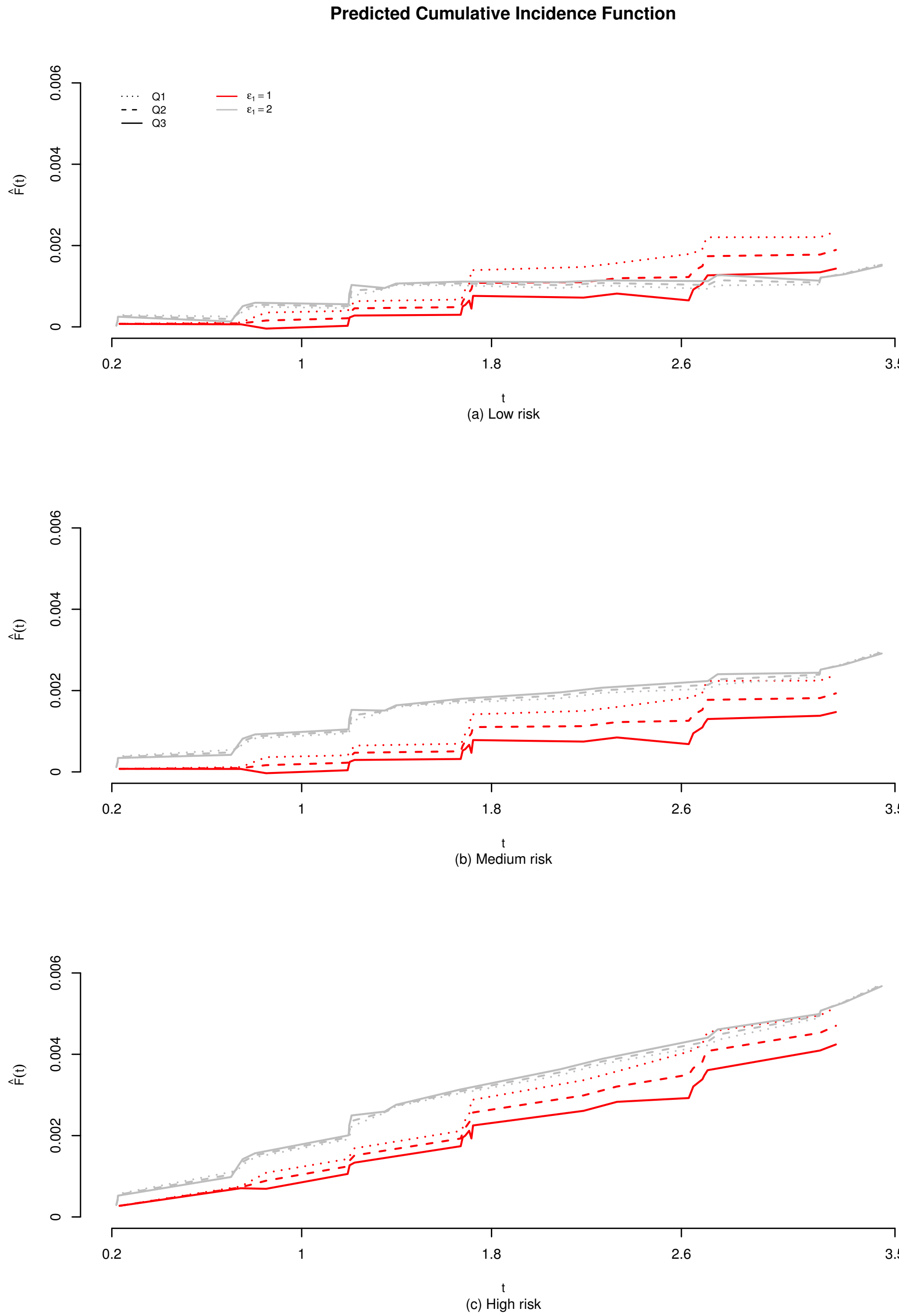


Figure 28: $Q_1 = -0.38510, Q_2 = 0.08807$ and $Q_3 = 0.56800$ are quartiles of the predicted immune response R_i (IgG3-A244V1V2) using AIPW method. At three quartiles of immune responses, the graphs show the predicted cumulative incidence function $\hat{F}_{1i}$ with each level of behavioral risk score groups (low, medium and high) based on the model (3.37).

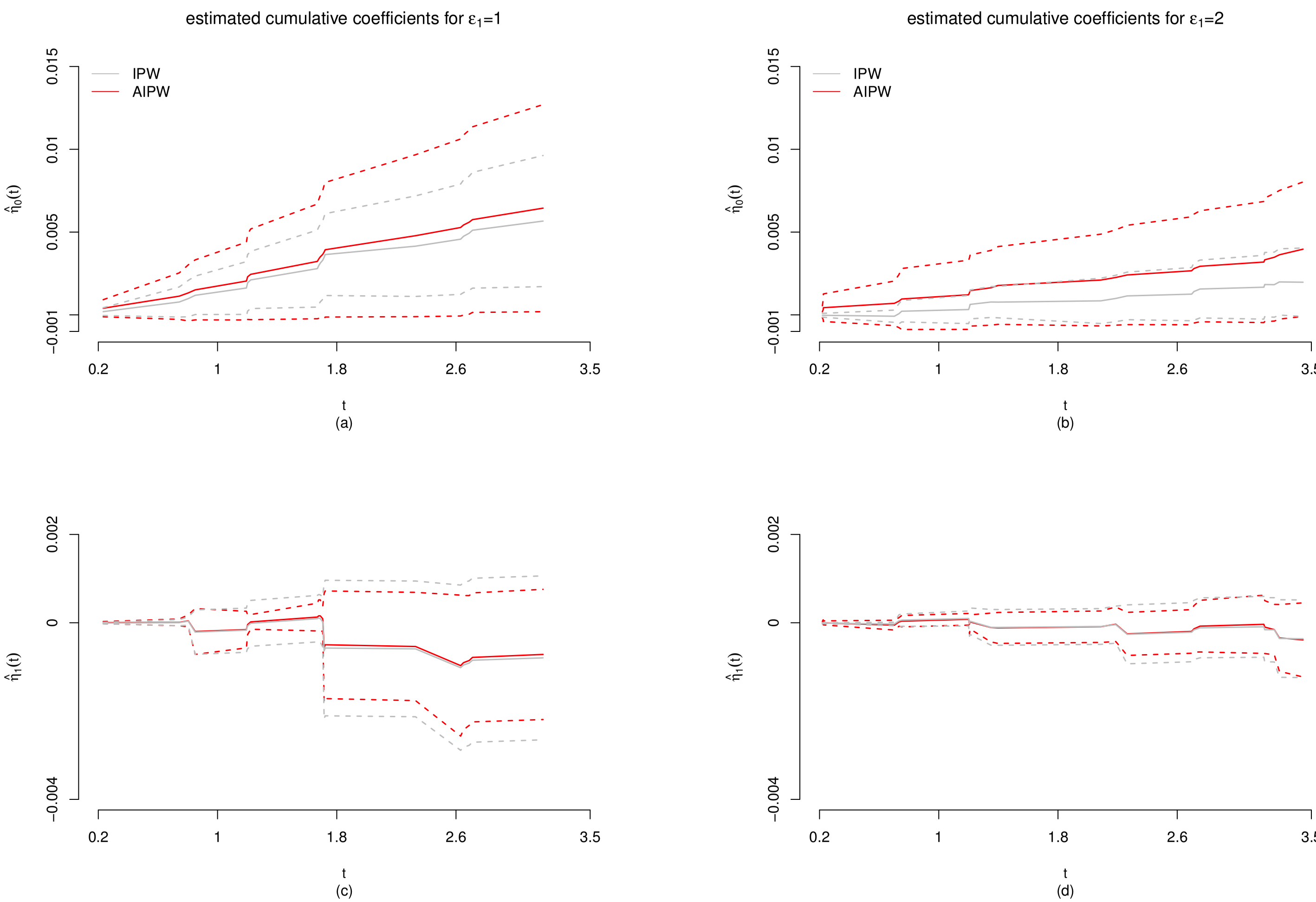


Figure 29: (a) and (b) show that the IPW and AIPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the immune response R_i (IgG-92TH023V1V2) in model (3.37) for $\epsilon_{1i} = 1$. (c) and (d) show the the IPW and AIPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the immune response R_i (IgG-92TH023V1V2) in model (3.37) for $\epsilon_{1i} = 2$.

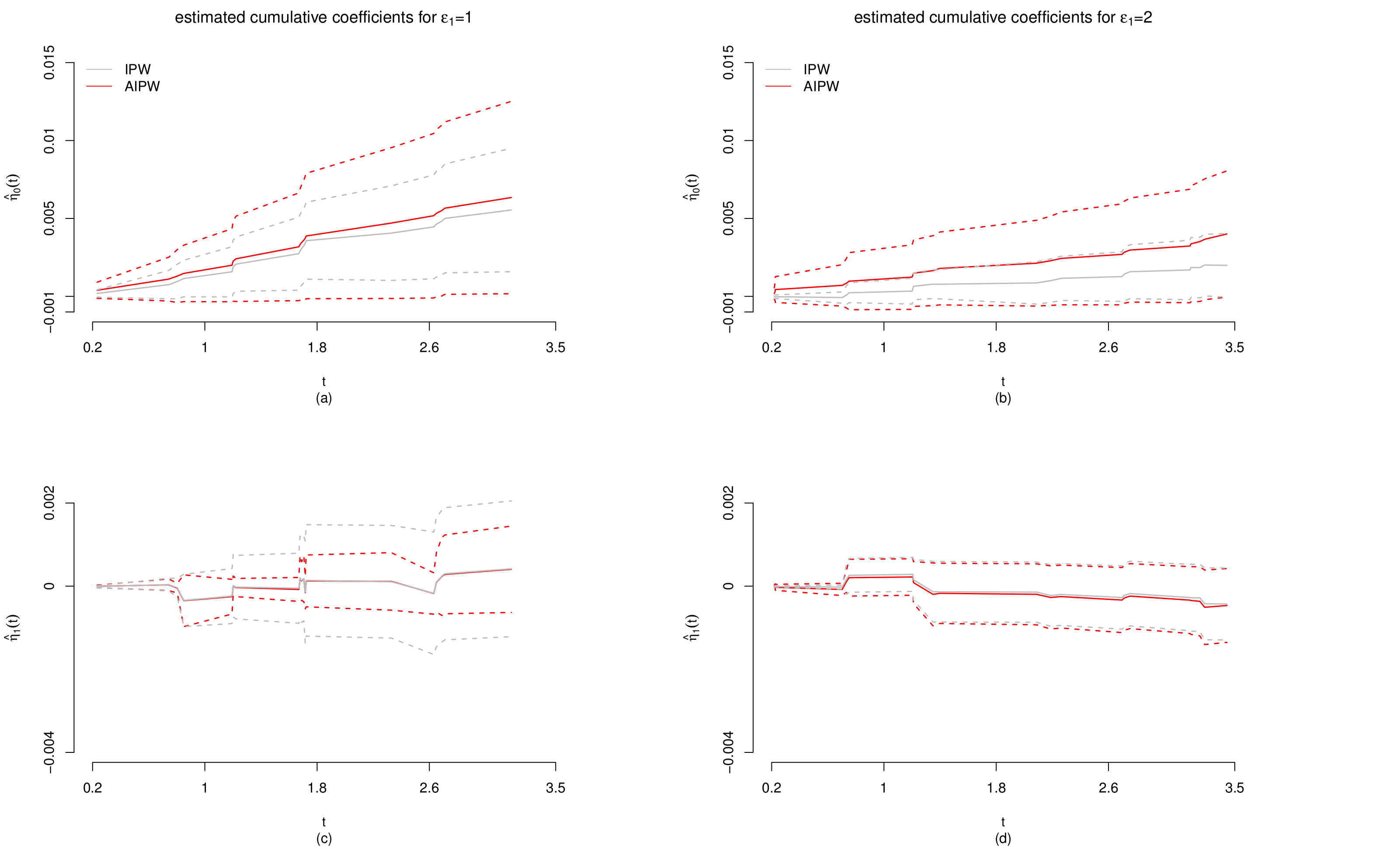


Figure 30: (a) and (b) show that the IPW and AIPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the immune response R_i (IgG3-92TH023V1V2) in model (3.37) for $\epsilon_{1i} = 1$. (c) and (d) show the the IPW and AIPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the immune response R_i (IgG3-92TH023V1V2) in model (3.37) for $\epsilon_{1i} = 2$.

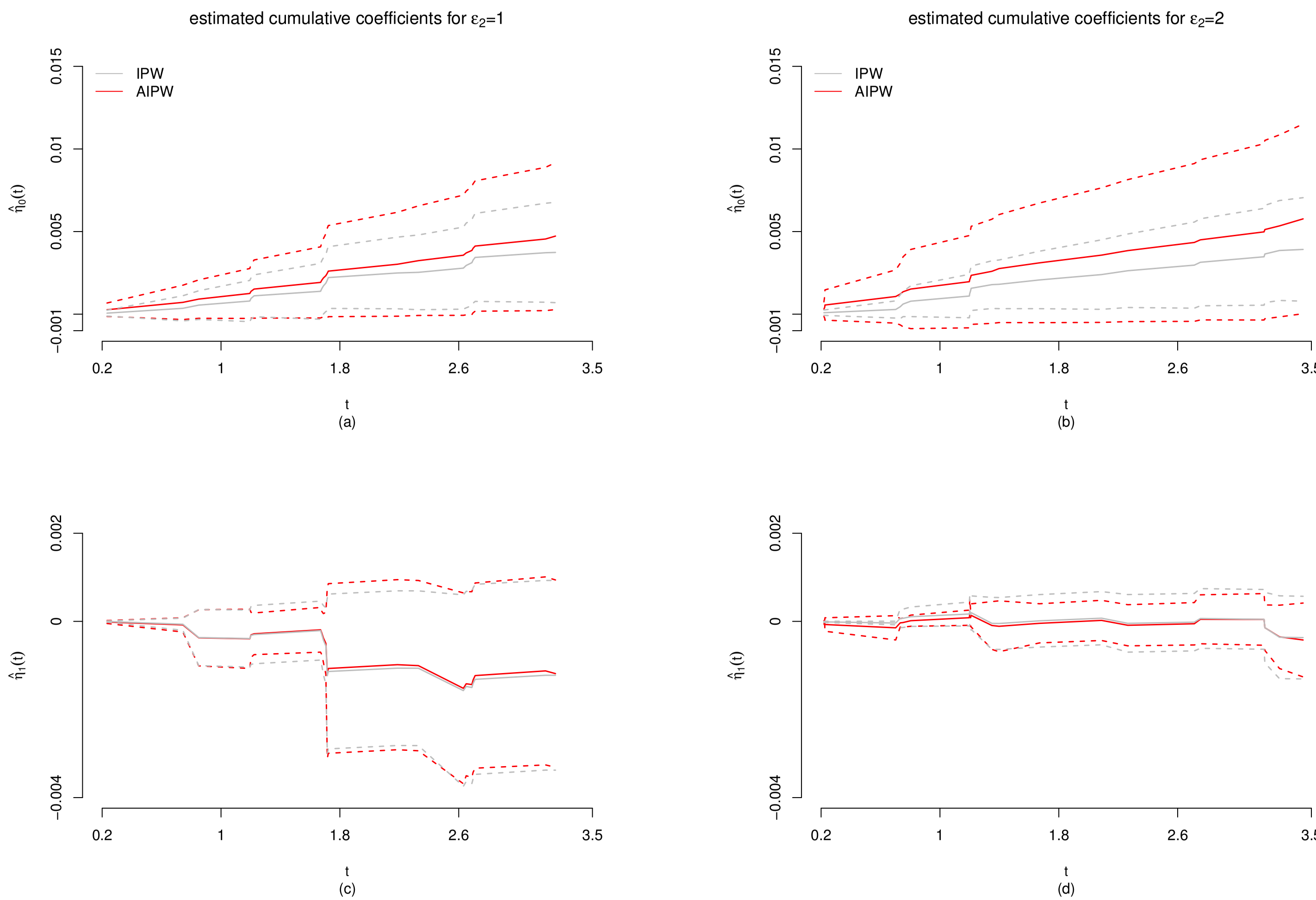


Figure 31: (a) and (b) show that the IPW and AIPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the immune response R_i (IgG-A244V1V2) in model (3.37) for $\epsilon_{2i} = 1$. (c) and (d) show the the IPW and AIPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the immune response R_i (IgG-A244V1V2) in model (3.37) for $\epsilon_{2i} = 2$.

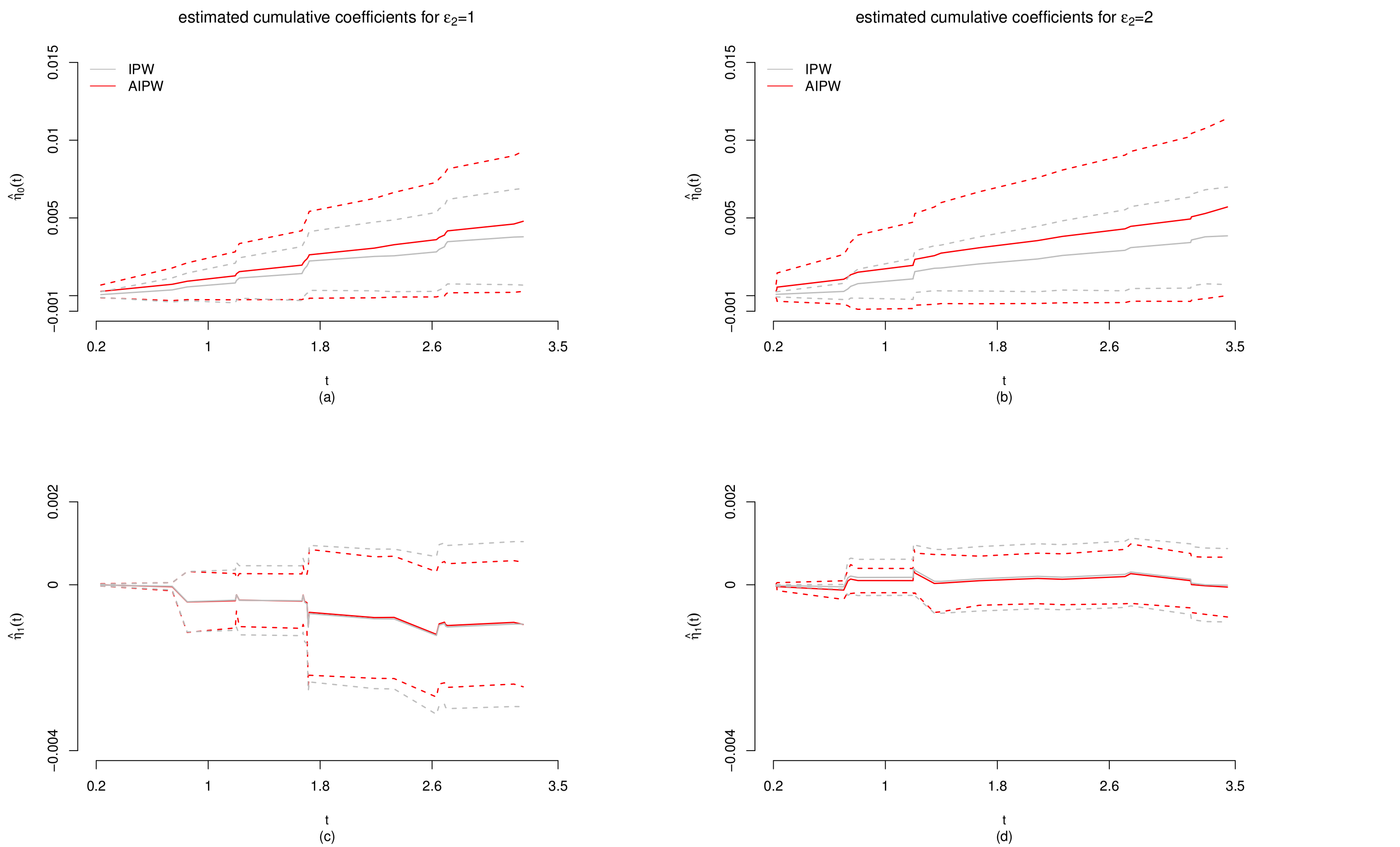


Figure 32: (a) and (b) show that the IPW and AIPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the immune response R_i (IgG3-A244V1V2) in model (3.37) for $\epsilon_{2i} = 1$. (c) and (d) show the the IPW and AIPW estimates of baseline cumulative coefficients $\eta_0(t)$ and the cumulative coefficients $\eta_1(t)$ with 95% pointwise confidence intervals for the immune response R_i (IgG3-A244V1V2) in model (3.37) for $\epsilon_{2i} = 2$.

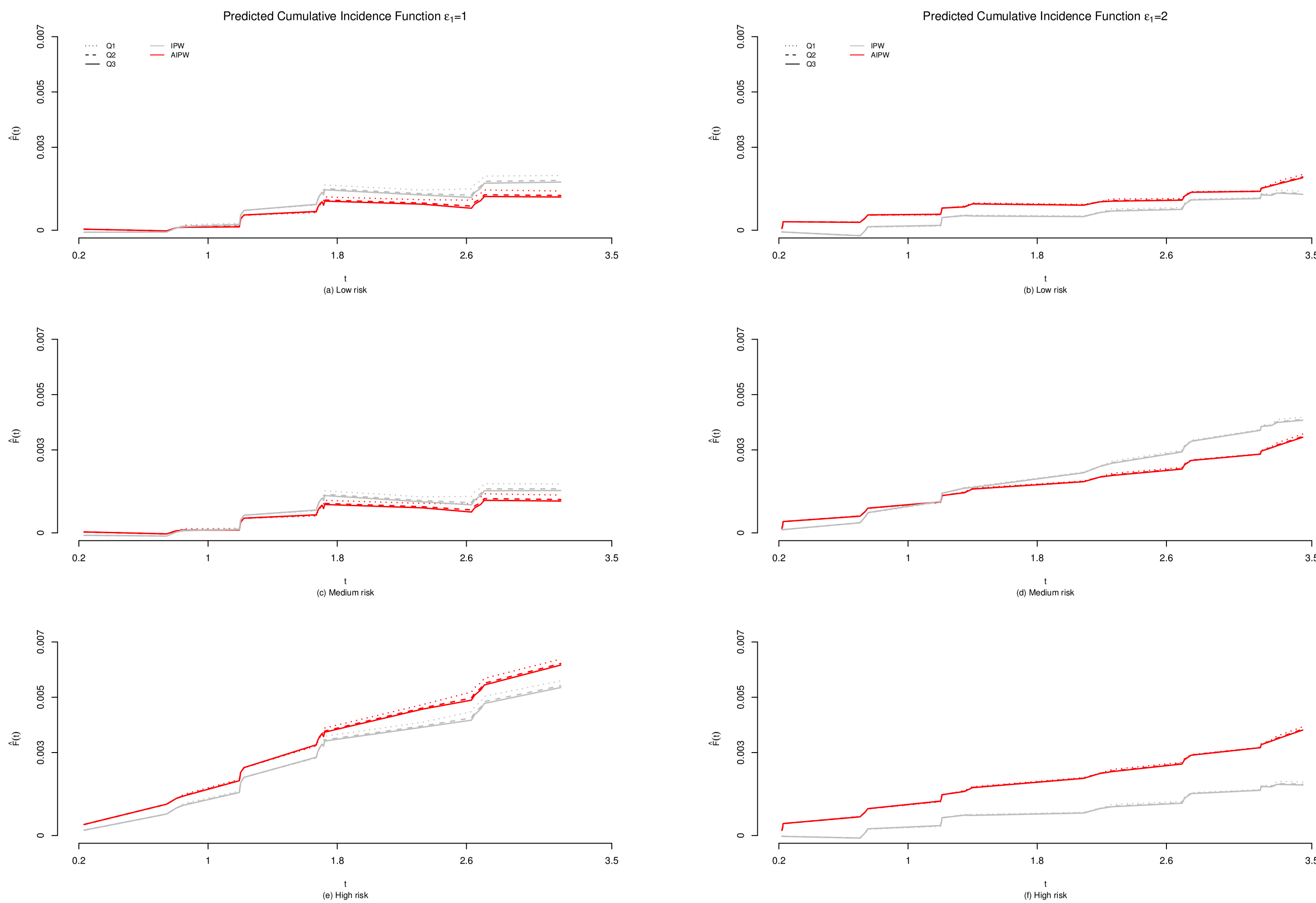


Figure 33: $Q_1 = 0.0903, Q_2 = 0.3131$ and $Q_3 = 0.3923$ are quartiles of the observed immune response R_i (IgG-92TH023V1V2). The (a), (c) and (e) show the predicted cumulative incidence function $\hat{F}_{1i}$ for $\epsilon_{1i} = 1$ at each level of behavioral risk score groups (low, medium and high) based on the model (3.37) by using IPW and AIPW method. The (b), (d) and (f) show the predicted cumulative incidence function $\hat{F}_{2i}$ for $\epsilon_{1i} = 2$ at each level of behavioral risk score groups (low, medium and high) based on the model (3.37) by using IPW and AIPW method.

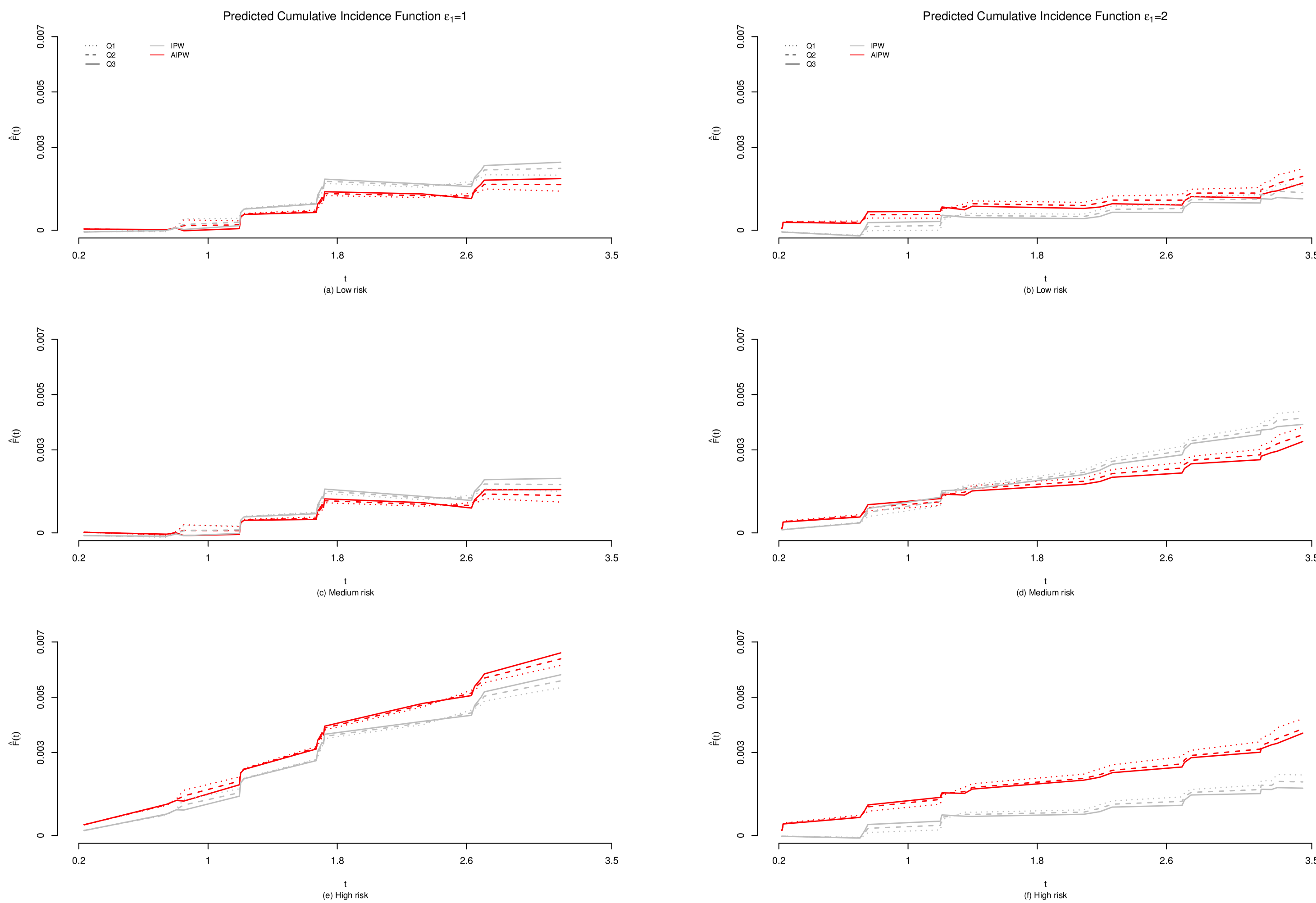


Figure 34: $Q_1 = -0.4677, Q_2 = 0.1196$ and $Q_3 = 0.6484$ are quartiles of the observed immune response R_i (IgG3-92TH023V1V2). The (a), (c) and (e) show the predicted cumulative incidence function $\hat{F}_{1i}$ for $\epsilon_{1i} = 1$ at each level of behavioral risk score groups (low, medium and high) based on the model (3.37) by using IPW and AIPW method. The (b), (d) and (f) show the predicted cumulative incidence function $\hat{F}_{2i}$ for $\epsilon_{1i} = 2$ at each level of behavioral risk score groups (low, medium and high) based on the model (3.37) by using IPW and AIPW method.

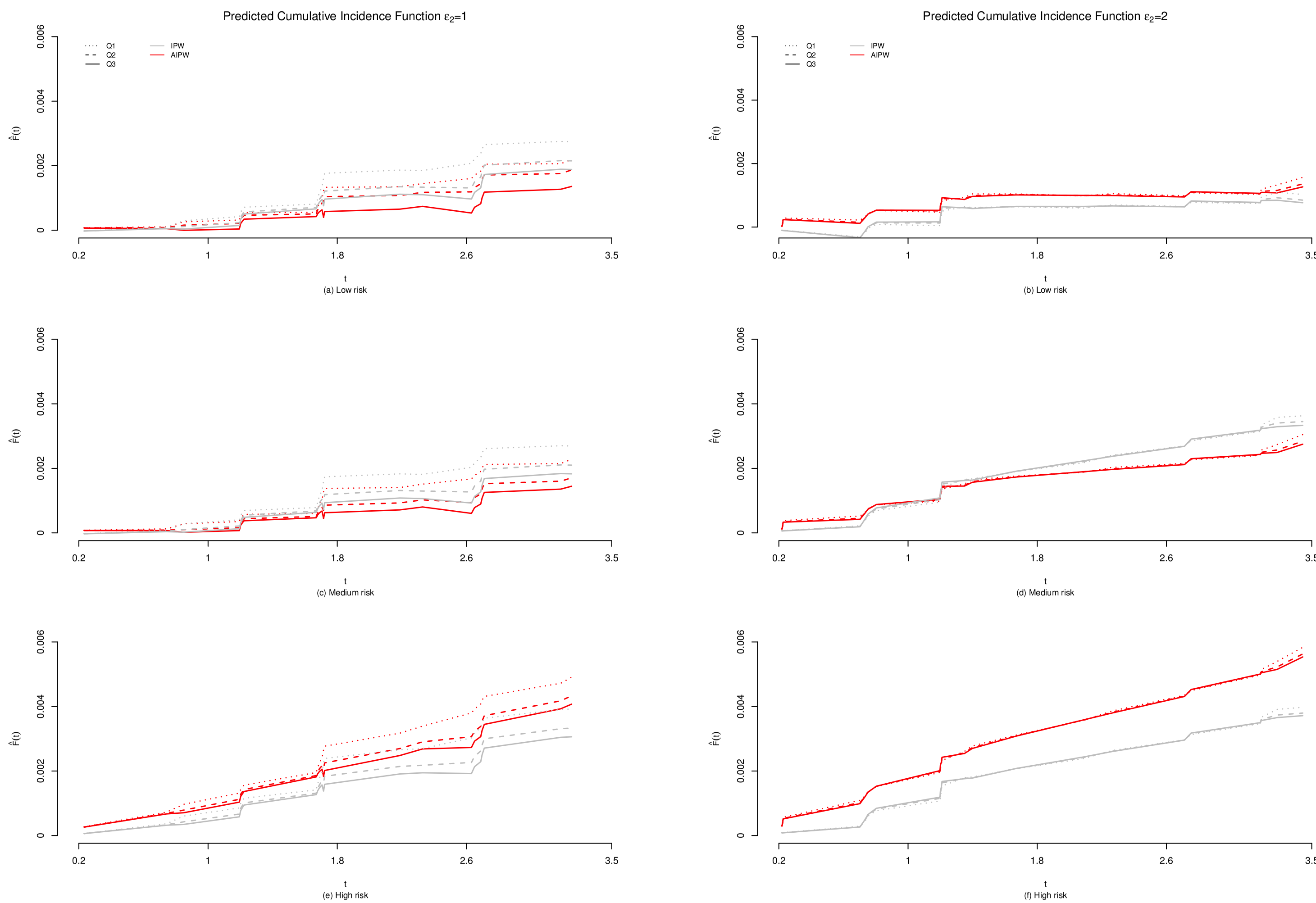


Figure 35: $Q_1 = -0.1530, Q_2 = 0.3321$ and $Q_3 = 0.5514$ are quartiles of the observed immune response R_i (IgG-A244V1V2). The (a), (c) and (e) show the predicted cumulative incidence function $\hat{F}_{1i}$ for $\epsilon_{1i} = 1$ at each level of behavioral risk score groups (low, medium and high) based on the model (3.37) by using IPW and AIPW method. The (b), (d) and (f) show the predicted cumulative incidence function $\hat{F}_{2i}$ for $\epsilon_{1i} = 2$ at each level of behavioral risk score groups (low, medium and high) based on the model (3.37) by using IPW and AIPW method.

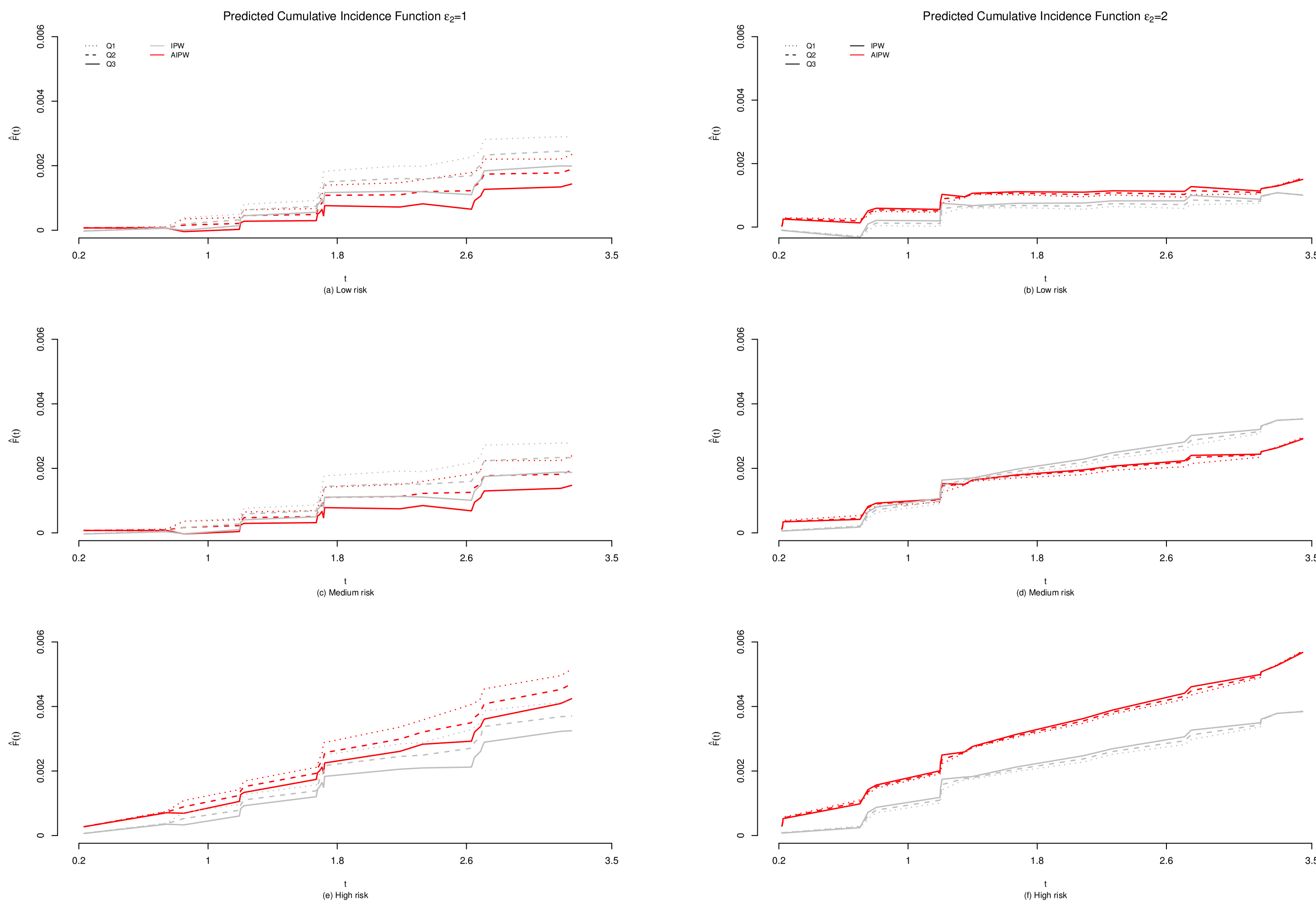


Figure 36: Graphs on the left: $Q_1 = -0.3851, Q_2 = 0.0881$ and $Q_3 = 0.5680$ are quartiles of the observed immune response R_i (IgG3-A244V1V2).The (a), (c) and (e) show the predicted cumulative incidence function $\hat{F}_{1i}$ for $\epsilon_{1i} = 1$ at each level of behavioral risk score groups (low, medium and high) based on the model (3.37) by using IPW and AIPW method. The (b), (d) and (f) show the predicted cumulative incidence function $\hat{F}_{2i}$ for $\epsilon_{1i} = 2$ at each level of behavioral risk score groups (low, medium and high) based on the model (3.37) by using IPW and AIPW method.

CHAPTER 4: PROOFS OF THE THEOREMS

4.1 Proofs of the Theorems in Chapter 2

Condition I.

I.1. The regression function $\eta(t)$ is right-continuous with left-handed limits on $[a, \tau]$.

I.2. The link function $h(\cdot)$ is three times continuously differentiable and invertible, and $\partial h(\cdot)/\partial x$ is bounded away from zero. The weight function $w(t)$ is a bounded, deterministic and continuous function.

I.3. $\varphi(\mathcal{V}_i, \theta) = I(\tilde{\epsilon_i} = 1)\varphi_1(\mathcal{V}_i, \theta) + I(\tilde{\epsilon_i} \neq 1)\varphi_1(\mathcal{V}_i, \theta)$ is twice differentiable with respect to φ and $\varphi'(\mathcal{V}_i, \theta) = d\varphi(\mathcal{V}_i, \theta)/d\theta$ is uniformly bounded and bounded away from zero, i.e., $\varphi(\mathcal{V}_i, \theta_j) \geq \epsilon > 0$.

I.4. The estimator $\hat{\theta}$ satisfies $n^{\frac{1}{2}}(\hat{\theta} - \theta_0) = n^{-\frac{1}{2}} \left[J\left(\theta_0\right)\right]^{-1} \sum_{i=1}^{n} U(\mathcal{V}_i, \theta_0) + o_p(1)$, where $J\left(\theta_0\right)$ is the positive definite fisher information matrix and $U(\mathcal{V}_i, \theta_0)$, $i = 1, \ldots, n$, are iid mean zero random variables.

I.5. The estimator $\widehat{G}(t)$ is asymptotically linear with influence function $\texttt{IC}_G$ such that

$$n^{\frac{1}{2}}(\hat{G} - G)(t, x, z) = n^{-\frac{1}{2}} \sum_{i=1}^{n} \texttt{IC}_G(t, x, z; Y_i) + o_p(1),$$

uniformly in (t, x, z).

I.6. Assume that $G(t)$ is continuous. If $\tau \in (0, \infty]$ is such that $Y(\tau) \xrightarrow{p} \infty$ as $n \to \infty$, then $\sup_{0 \leq t \leq \tau} |\widehat{G}(t) - G(t)| \xrightarrow{p} 0$ as $n \xrightarrow{p} \infty$, where $Y(t) = I\left\{T \geq t\right\}$ at risk process.

Proof of Proposition 1

Let

$$\log \mathrm{L}_1(\theta_1) = \sum_{i=1}^{n} I(\tilde{\epsilon}_i = 1) \left[\xi_i\{\theta_1^{\mathsf{T}} \mathcal{V}_i\} - \log\{1 + \exp(\theta_1^{\mathsf{T}} \mathcal{V}_i)\}\right],$$

$$\log \mathrm{L}_2(\theta_2) = \sum_{i=1}^{n} I(\tilde{\epsilon}_i \neq 1)\left[\xi_i\{\theta_2^{\intercal}\mathcal{V}_i\} - \log\{1+\exp(\theta_2^{\intercal}\mathcal{V}_i)\}\right].$$

From the likelihood defined in (2.1), we have the following log-likelihood function

$$\log \mathrm{L}(\theta) = \log \mathrm{L}_1(\theta_1) + \log \mathrm{L}_2(\theta_2).$$

By taking derivative with respect to $\theta = (\theta_1^{\intercal}, \theta_2^{\intercal})^{\intercal}$, the score functions are

$$U(\mathcal{V}_i,\theta) = \begin{pmatrix} U_1(\mathcal{V}_i,\theta_1) \\ \\ U_2(\mathcal{V}_i,\theta_2) \end{pmatrix} = \begin{pmatrix} \frac{\partial \log \mathrm{L}(\theta)}{\partial \theta_1} \\ \\ \frac{\partial \log \mathrm{L}(\theta)}{\partial \theta_2} \end{pmatrix} = \begin{pmatrix} \sum_{i=1}^{n} I(\tilde{\epsilon}_i = 1)\left[\xi_i \mathcal{V}_i - \frac{\mathcal{V}_i \exp^{\theta_1^{\intercal}\mathcal{V}_i}}{1+\exp^{\theta_1^{\intercal}\mathcal{V}_i}}\right]^{\intercal} \\ \sum_{i=1}^{n} I(\tilde{\epsilon}_i \neq 1)\left[\xi_i \mathcal{V}_i - \frac{\mathcal{V}_i \exp^{\theta_2^{\intercal}\mathcal{V}_i}}{1+\exp^{\theta_2^{\intercal}\mathcal{V}_i}}\right]^{\intercal} \end{pmatrix},$$

which has zero at $\hat{\theta}$. The second-order partial derivatives of $\log \mathrm{L}(\theta)$ is

$$H(\theta) = \begin{pmatrix} -\sum_{i=1}^{n} I(\tilde{\epsilon}_i = 1)\frac{\exp^{\theta_1^{\intercal}\mathcal{V}_i}\,\mathcal{V}_i\mathcal{V}_i^{\intercal}}{(1+\exp^{\theta_1^{\intercal}\mathcal{V}_i})^2} & 0 \\ 0 & -\sum_{i=1}^{n} I(\tilde{\epsilon}_i \neq 1)\frac{\exp^{\theta_2^{\intercal}\mathcal{V}_i}\,\mathcal{V}_i\mathcal{V}_i^{\intercal}}{(1+\exp^{\theta_2^{\intercal}\mathcal{V}_i})^2} \end{pmatrix}, \tag{4.1}$$

which is negative on $H(\theta)$. Moerover, the Jacobian of $H(\theta)$ is obviously positive. Thus, the log likelihood function $\log \mathrm{L}(\theta)$ has a local maximum at $\hat{\theta} = (\hat{\theta}_1, \hat{\theta}_2)$. Therefore, the selection probability S_i can be estimated by its parametric model $\hat{S}_i = \varphi(\mathcal{V}_i, \hat{\theta})$.

Since $\hat{\theta}$ is maximum likelihood estimator of $\log \mathrm{L}(\theta)$, the $\hat{\theta}$ is consistent estimator of the true value θ_0. Moreover, by using Taylor series expansion,

$$U(\mathcal{V}_i,\hat{\theta}) = U(\mathcal{V}_i,\theta_0) + \frac{\partial}{\partial\theta}U(\mathcal{V}_i,\theta_0)(\hat{\theta}-\theta_0) + o_p(n^{-\frac{1}{2}}), \tag{4.2}$$

where $U(\mathcal{V}_i,\hat{\theta}) = 0$. By the standard arguments of asymptotic normality for M-estimators, it can be shown that we have the following asymptotic linear expression such that

$$\sqrt{n}(\hat{\theta}-\theta_0) \quad = \quad n^{-\frac{1}{2}}\left[J(\mathcal{V}_i,\theta_0)\right]^{-1}\sum_{i=1}^{n} U(\mathcal{V}_i,\theta_0) + o_p(1), \tag{4.3}$$

and its limiting distribution

$$\sqrt{n}(\hat{\theta}-\theta_0) \quad \xrightarrow{d} \quad N\left(0, J^{-1}(\mathcal{V}_i,\theta_0)\right), \tag{4.4}$$

where the fisher information matrix

$$J(\mathcal{V}_i,\theta_0) = \begin{pmatrix} E\left[I(\tilde{\epsilon}_i = 1)\frac{\exp^{\theta_{01}^\intercal \mathcal{V}_i}\mathcal{V}_i\mathcal{V}_i^\intercal}{(1+\exp^{\theta_{01}^\intercal \mathcal{V}_i})^2}\right] & 0 \\ 0 & E\left[I(\tilde{\epsilon}_i \neq 1)\frac{\exp^{\theta_{02}^\intercal \mathcal{V}_i}\mathcal{V}_i\mathcal{V}_i^\intercal}{(1+\exp^{\theta_{02}^\intercal \mathcal{V}_i})^2}\right] \end{pmatrix}. \tag{4.5}$$

and

$$U(\mathcal{V}_i,\theta_0) \quad = \quad \begin{pmatrix} \sum_{i=1}^n I(\tilde{\epsilon}_i = 1)\left[\xi_i\mathcal{V}_i - \frac{\mathcal{V}_i\exp^{\theta_1^\intercal \mathcal{V}_i}}{1+\exp^{\theta_1^\intercal \mathcal{V}_i}}\right]^\intercal \\ \sum_{i=1}^n I(\tilde{\epsilon}_i \neq 1)\left[\xi_i\mathcal{V}_i - \frac{\mathcal{V}_i\exp^{\theta_2^\intercal \mathcal{V}_i}}{1+\exp^{\theta_2^\intercal \mathcal{V}_i}}\right]^\intercal \end{pmatrix}.$$

□

Proof of Proposition 2

(1) By the corollary 3.2.1 of (Fleming and H arrington, 2013), we have, for any $t \in [0,\tau]$ such that $G(t) > 0$,

$$\begin{aligned} n^{\frac{1}{2}}(\widehat{G}(t) - G(t)) &= n^{\frac{1}{2}}\left\{-G(t)\int_0^\tau \frac{\widehat{G}(s-)}{G(s)}I(Y(s)>0)\frac{dM(s)}{Y(s)}\right\} + o_p(1), \\ &= n^{\frac{1}{2}}\left\{-G(t)\int_0^\tau I(Y(s)>0)\frac{dM(s)}{Y(s)}\right\} \\ &+ n^{\frac{1}{2}}\left\{G(t)\int_0^\tau \left(1-\frac{\widehat{G}(s-)}{G(s)}\right)I(Y(s)>0)\frac{dM(s)}{Y(s)}\right\} + o_p(1) \end{aligned} \tag{4.6}$$

By Lenglart's inequality, the second term of (4.6) is

$$\begin{aligned} & P\left(\sup_{0\le t\le\tau}\left\{n^{\frac{1}{2}}G(t)\int_0^\tau\left(1-\frac{\widehat{G}(s-)}{G(s)}\right)I(Y(s)>0)\frac{dM(s)}{Y(s)}\right\}^2 \ge \epsilon\right) \\ \le\ & \frac{\eta}{\epsilon} + P\left\{nG^2(t)\int_0^\tau\left(1-\frac{\widehat{G}(s-)}{G(s)}\right)^2\frac{I(Y(s)>0)}{Y^2(s)}Y(s)d\Lambda(s) \ge \eta\right\} \\ \le\ & \frac{\eta}{\epsilon} + P\left\{G^2(t)\frac{nI(Y(\tau)>0)\Lambda(\tau)}{Y(\tau)} \ge \eta\right\} + P(Y(\tau)=0) \\ \le\ & \frac{\eta}{\epsilon} \end{aligned} \tag{4.7}$$

since $Y(\tau) \xrightarrow{p} \infty$ as $n \xrightarrow{p} \infty$.

Therefore, we have

$$\begin{aligned} n^{\frac{1}{2}}(\widehat{G}(t)-G(t)) &= n^{\frac{1}{2}}\left\{-G(t)\int_0^\tau I(Y(s)>0)\frac{dM(s)}{Y(s)}\right\}+o_p(1) \\ &= n^{-\frac{1}{2}}\left\{-G(t)\int_0^\tau I(Y(s)>0)\frac{dM(s)}{y(s)}\right\}+o_p(1) \qquad (4.8)\end{aligned}$$

where $n^{-1}Y(s)=n^{-1}\sum_{i=1}^n Y_i(s)\xrightarrow{p} y(s)$ with $s\in[0,\tau]$.

(2) It is easy to derive when the censoring time follows the Cox model with hazard function $\lambda(t)=\lambda_0(t)\exp(\beta_0X_i+\beta_1Z_i)$ where baseline $\lambda_0(t)$ and possibly time dependent covariates X_i and Z_i.

Proof of Theorem 2.1

Let $\boldsymbol{D}_{\boldsymbol{\eta}}(t)$, $\boldsymbol{D}_{\boldsymbol{\gamma}}(t)$, $\boldsymbol{R}(t)$, $\boldsymbol{F}_1(t)$, $\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat\theta)$, $\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat\theta)$, $\boldsymbol{H}(t,\hat\theta)$, $\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\hat\theta)$ are all evaluated at the true value $\{\boldsymbol{\eta}_0(t),\boldsymbol{\gamma}_0\}$ of $\{\boldsymbol{\eta}(t),\boldsymbol{\gamma}\}$, where $\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat\theta)$, $\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat\theta)\,\boldsymbol{H}(t,\hat\theta)$, $\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\hat\theta)$ are corresponding terms for (2.12). By (2.10), we have

$$n^{\frac{1}{2}}(\widehat{\boldsymbol{\gamma}}-\boldsymbol{\gamma}_0) \;=\; \{n^{-1}\,\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat\theta)\}^{-1}n^{-\frac{1}{2}}\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat\theta)+o_p(1). \qquad (4.9)$$

Let $\boldsymbol{A}(\theta)=\partial\boldsymbol{\Psi}(\theta)/\partial\theta$. The Taylor expansion of $\boldsymbol{\Psi}(\hat\theta)$ around the true value θ_0 is

$$\boldsymbol{\Psi}(\hat\theta)=\boldsymbol{\Psi}(\theta_0)+\boldsymbol{A}(\theta_0)(\hat\theta-\theta_0)+o_p(n^{-\frac{1}{2}}). \qquad (4.10)$$

Let $\boldsymbol{K}(t,\hat\theta)=\boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat\theta)\boldsymbol{D}_{\boldsymbol{\eta}}(t)\left[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\hat\theta)\right]^{-1}$ and evaluate at the true values $\{\boldsymbol{\eta}_0(t),\boldsymbol{\gamma}_0\}$. By plugging $\boldsymbol{H}(t,\hat\theta)$ in the formula for $\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat\theta)$ in (2.12), we have

$$\begin{aligned} n^{-\frac{1}{2}}\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat\theta) &= n^{-\frac{1}{2}}\int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat\theta)\left\{I-\boldsymbol{D}_{\boldsymbol{\eta}}(t)\left[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\hat\theta)\right]^{-1}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat\theta)\right\}\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t)\}\,dt \\ &= n^{-\frac{1}{2}}\int_0^\tau \left\{\boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)-\boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat\theta)\boldsymbol{D}_{\boldsymbol{\eta}}(t)\left[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\hat\theta)\right]^{-1}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\right\}\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat\theta)\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t)\}\,dt \\ &= n^{-\frac{1}{2}}\int_0^\tau \left\{\boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)-\boldsymbol{K}(t,\hat\theta)\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\right\}\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat\theta)\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t)\}\,dt. \qquad (4.11)\end{aligned}$$

By plugging (4.10) into (4.11) and decomposing $\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t)\}$ into $\left\{\frac{\Delta_iN_i(t)}{\widehat{G}(T_i)}-\frac{\Delta_iN_i(t)}{G(T_i)}+\frac{\Delta_iN_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}$, then (4.11) can be split into the following four terms

$$\begin{aligned}
n^{-\frac{1}{2}}\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat{\theta}) \quad = \quad & n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{K}(t,\hat{\theta})\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}dt \\
& +n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{K}(t,\hat{\theta})\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{A}_i(\theta_0)(\hat{\theta}-\theta_0)\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}dt \\
& +n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{K}(t,\hat{\theta})\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)}-\frac{\Delta_i N_i(t)}{G(T_i)}\right\}dt \\
& +n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{K}(t,\hat{\theta})\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{A}_i(\theta_0)(\hat{\theta}-\theta_0)\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)}-\frac{\Delta_i N_i(t)}{G(T_i)}\right\}dt \\
& +o_p(1). \qquad (4.12)
\end{aligned}$$

The fourth term of (4.12) is shown to be equal to $o_p(1)$ in Appendix A. That is,

$$n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{K}(t,\hat{\theta})\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{A}_i(\theta_0)(\hat{\theta}-\theta_0)\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)}-\frac{\Delta_i N_i(t)}{G(T_i)}\right\}dt=o_p(1). \qquad (4.13)$$

Denote the first term of (4.12) by

$$\widetilde{\boldsymbol{B}}_{\boldsymbol{\gamma}}(\hat{\theta}) \quad = \quad n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{K}(t,\hat{\theta})\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}dt.$$

It is shown in the Appendix A that

$$n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{K}(t,\hat{\theta})-\boldsymbol{k}(t,\theta_0)\right]\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\boldsymbol{\psi}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}dt=o_p(1). \qquad (4.14)$$

Let

$$\boldsymbol{\zeta}_{\boldsymbol{\gamma},i}(t,\theta)=\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{k}(t,\theta)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta)\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}. \qquad (4.15)$$

It follows by (4.14) that

$$\begin{aligned}
\widetilde{\boldsymbol{B}}_{\boldsymbol{\gamma}}(\hat{\theta}) \quad = \quad & n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}dt \\
& -n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{K}(t,\hat{\theta})-\boldsymbol{k}(t,\theta_0)\right]\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\boldsymbol{\psi}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}dt \\
= \quad & n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\boldsymbol{\zeta}_{\boldsymbol{\gamma},i}(t,\theta_0)\,dt+o_p(1), \qquad (4.16)
\end{aligned}$$

Denote the second term of (4.12) by

$$\boldsymbol{D}_{\boldsymbol{\gamma}}(\hat{\theta}) \quad = \quad n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_{0}^{\tau} \left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t) - \boldsymbol{K}(t,\hat{\theta})\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right] w_i(t)\boldsymbol{A}_i(\theta_0) \left\{\frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t)\right\} dt\,(\hat{\theta}-\theta_0).$$

By similar argument in (4.14), we have

$$\boldsymbol{D}_{\boldsymbol{\gamma}}(\hat{\theta}) \quad = \quad n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_{0}^{\tau} \left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t) - \boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right] w_i(t)\boldsymbol{A}_i(\theta_0) \left\{\frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t)\right\} dt\,(\hat{\theta}-\theta_0) + o_p(1).$$

By the law of large numbers,

$$n^{-1} \sum_{i=1}^{n} \int_{0}^{\tau} \left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t) - \boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right] w_i(t)\boldsymbol{A}_i(\theta_0) \left\{\frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t)\right\} dt \xrightarrow{p} g(\tau,\theta_0). \tag{4.17}$$

It follows by (2.15) in proposition 1 and (4.17) that

$$\begin{aligned}
\boldsymbol{D}_{\boldsymbol{\gamma}}(\hat{\theta}) &= n^{\frac{1}{2}}\,(\hat{\theta}-\theta_0)\,(g(\tau,\theta_0) + o_p(1)) + o_p(1). \\
&= g(\tau,\theta_0) n^{\frac{1}{2}}\,(\hat{\theta}-\theta_0) + o_p(1). \\
&= g(\tau,\theta_0) \left\{ n^{-\frac{1}{2}} J^{-1}\,(\mathcal{V}_i,\theta_0) \sum_{i=1}^{n} U(\mathcal{V}_i,\theta_0) \right\} + o_p(1).
\end{aligned} \tag{4.18}$$

Now consider the third term of (4.12). Let

$$\Delta_{\boldsymbol{\gamma}}(\hat{\theta}) \quad = \quad n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_{0}^{\tau} \left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t) - \boldsymbol{K}(t,\hat{\theta})\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right] w_i(t)\boldsymbol{\psi}_i(\theta_0)\Delta_i N_i(t) \left\{\frac{G(T_i) - \widehat{G}(T_i)}{\widehat{G}(T_i)G(T_i)}\right\} dt.$$

With similar arguments in (4.14), we have

$$\Delta_{\boldsymbol{\gamma}}(\hat{\theta}) = n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_{0}^{\tau} \left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t) - \boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right] w_i(t)\boldsymbol{\psi}_i(\theta_0)\Delta_i N_i(t) \left\{\frac{G(T_i) - \widehat{G}(T_i)}{\widehat{G}(T_i)G(T_i)}\right\} dt + o_p(1). \tag{4.19}$$

Using (2.17) in proposition 2, we have

$$n^{\frac{1}{2}}\Delta_i N_i(t)\frac{\widehat{G}(T_i) - G(T_i)}{\widehat{G}(T_i)G(T_i)} = n^{-\frac{1}{2}}\Delta_i N_i(t)\frac{-\mathcal{I}(\widetilde{T}_i \le t)}{G(T_i)} \sum_{j=1}^{n} \int_{0}^{\tau} \mathcal{I}(s \le \widetilde{T}_i)\frac{dM_j{}^c(s)}{y(s)} + o_p(1). \tag{4.20}$$

By plugging (4.20) into (4.19), we have

$$\Delta_{\boldsymbol{\gamma}}(\hat{\theta}) = n^{-\frac{1}{2}} \sum_{j=1}^{n} \int_{0}^{\tau}\int_{0}^{\tau} n^{-1} \sum_{i=1}^{n} \left\{\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t) - \boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right\} w_i(t)\boldsymbol{\psi}_i(\theta_0)\frac{\Delta_i N_i(t)}{G(T_i)}\mathcal{I}(s \le \widetilde{T}_i \le t)\,dt\frac{dM^c_j(s)}{y(s)} + o_p(1).$$

By law of large numbers,

$$n^{-1}\sum_{j=1}^{n}\left\{\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},j}(t)-\boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},j}(t)\right\}w_j(t)\boldsymbol{\psi}_j(\theta_0)\frac{\Delta_j N_j(t)}{G(T_j)}\mathcal{I}(s\le \widetilde{T}_j\le t)\xrightarrow{p}\boldsymbol{q}_{\boldsymbol{\gamma}}(s,t,\theta_0).$$

Let

$$\boldsymbol{\kappa}_{\boldsymbol{\gamma},i}(t,\theta)=\int_0^{\tau}\frac{\boldsymbol{q}_{\boldsymbol{\gamma}}(s,t,\theta)}{y(s)}dM_i^c(s). \tag{4.21}$$

Thus, we have

$$\Delta_{\boldsymbol{\gamma}}(\hat{\theta})=n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\boldsymbol{\kappa}_{\boldsymbol{\gamma},i}(t,\theta_0)dt+o_p(1). \tag{4.22}$$

Let

$$\begin{aligned}\widetilde{\boldsymbol{B}}_{\boldsymbol{\gamma}}(\theta) &= n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\boldsymbol{\zeta}_{\boldsymbol{\gamma},i}(t,\theta)\,dt,\\ \Delta_{\boldsymbol{\gamma}}(\theta) &= n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\boldsymbol{\kappa}_{\boldsymbol{\gamma},i}(t,\theta)\,dt,\\ \boldsymbol{D}_{\boldsymbol{\gamma}}(\theta) &= g(\tau,\theta)\left\{n^{-\frac{1}{2}}J^{-1}(\mathcal{V}_i,\theta)\sum_{i=1}^{n}U(\mathcal{V}_i,\theta)\right\}.\end{aligned} \tag{4.23}$$

It follows by (4.12), (4.13), (4.16), (4.18), (4.22) and (4.23) that

$$n^{-\frac{1}{2}}\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat{\theta}) = \widetilde{\boldsymbol{B}}_{\boldsymbol{\gamma}}(\theta_0)+\Delta_{\boldsymbol{\gamma}}(\theta_0)+\boldsymbol{D}_{\boldsymbol{\gamma}}(\theta_0)+o_p(1). \tag{4.24}$$

By plugging the expression of $\boldsymbol{H}(t,\hat{\theta})$ into $\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat{\theta})$ from (2.12), we have

$$n^{-1}\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat{\theta}) = \int_a^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma}}(t)-\boldsymbol{K}(t,\hat{\theta})\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta}}(t)\right]\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\,dt. \tag{4.25}$$

Let

$$\begin{aligned}n^{-1}\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta) &= n^{-1}\sum_{i=1}^{n}\int_a^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{k}(t,\theta)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\,dt\\ \boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta) &= E\left\{\int_a^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{k}(t,\theta)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\,dt\right\}.\end{aligned}$$

It is shown in the Appendix A that

$$\begin{aligned}n^{-1}\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat{\theta}) &= n^{-1}\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta_0)+o_p(1)\\ &\xrightarrow{p} \boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta_0).\end{aligned} \tag{4.26}$$

Let

$$\boldsymbol{W}_{\gamma,i}(\tau,\theta) = \int_0^\tau \boldsymbol{\zeta}_{\boldsymbol{\gamma},i}(t,\theta)\,dt + \int_0^\tau \boldsymbol{\kappa}_{\boldsymbol{\gamma},i}(t,\theta)\,dt + g(\tau,\theta)\left[J\left(\mathcal{V}_i,\theta\right)\right]^{-1} U(\mathcal{V}_i,\theta).$$

It follows by (4.9), (4.24), (4.26) that $\sqrt{n}(\widehat{\boldsymbol{\gamma}} - \boldsymbol{\gamma}_0)$ is asymptotically equivalent to the following identically independent distributed decomposition

$$n^{\frac{1}{2}}(\widehat{\boldsymbol{\gamma}} - \boldsymbol{\gamma}_0) = \left\{\boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta_0)\right\}^{-1} n^{-\frac{1}{2}} \sum_{i=1}^{n} \left\{\boldsymbol{W}_{\gamma,i}(\tau,\theta_0)\right\} + o_p(1). \tag{4.27}$$

Since $\boldsymbol{\zeta}_{\boldsymbol{\gamma},i}(t,\theta_0)$ has mean zero by (2.2), $\boldsymbol{\kappa}_{\boldsymbol{\gamma},i}(t,\theta_0)$ is mean zero local square martingale, and the score function $U(\mathcal{V}_i,\theta_0)$ has mean zero, by the law of large numbers, $n^{-1}\sum_{i=1}^{n}\left\{\boldsymbol{W}_{\gamma,i}(\tau,\theta_0)\right\}$ has mean zero. By the central limit theorem, $n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{W}_{\gamma,i}(\tau,\theta_0)$ converges in distribution to a mean zero normal random vector with covariance matrix $E\left\{\boldsymbol{W}_{\gamma,i}(\tau,\theta_0)\right\}^{\otimes 2}$.

By slutsky's theorem, we have

$$\sqrt{n}(\widehat{\boldsymbol{\gamma}} - \boldsymbol{\gamma}_0) \xrightarrow{d} \mathcal{N}\left(0, \boldsymbol{\Sigma}_{\gamma}\right), \tag{4.28}$$

where $\boldsymbol{\Sigma}_{\gamma} = \boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta_0)^{-1}\, E\left\{\boldsymbol{W}_{\gamma,i}(\tau,\theta_0)\right\}^{\otimes 2} \boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta_0)^{-1}$.

Let $\widehat{\boldsymbol{F}}_{1i}(t)$, $\widehat{\boldsymbol{D}}_{\boldsymbol{\eta},i}(t)$ and $\widehat{\boldsymbol{D}}_{\boldsymbol{\gamma},i}(t)$ be the estimator of $\boldsymbol{F}_{1i}(t)$, $\boldsymbol{D}_{\boldsymbol{\eta},i}(t)$ and $\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)$ by plugging estimators $\widehat{\boldsymbol{\eta}}(t)$ and $\widehat{\boldsymbol{\gamma}}$ into $F_{1i}(t,\boldsymbol{\eta}(t),\gamma)$, $\boldsymbol{D}_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\gamma)$, $\boldsymbol{D}_{\boldsymbol{\gamma},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})$, respectively, and let $\boldsymbol{A}_i(\hat{\theta}) = \partial\psi_i(\hat{\theta})/\partial\theta$ where $\psi_i(\hat{\theta}) = \xi_i/\varphi(\mathcal{V}_i,\hat{\theta})$.

Let

$$
\begin{aligned}
\widehat{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta) &= n^{-1}\sum_{i=1}^{n}\widehat{\boldsymbol{D}}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)\boldsymbol{\psi}_i(\theta)\widehat{\boldsymbol{D}}_{\boldsymbol{\eta},i}(t)\\
\widehat{\boldsymbol{K}}(t,\theta) &= n^{-1}\sum_{i=1}^{n}\widehat{\boldsymbol{D}}_{\boldsymbol{\gamma},i}^{\mathsf{T}}(t)w_i(t)\boldsymbol{\psi}_i(\theta)\widehat{\boldsymbol{D}}_{\boldsymbol{\eta},i}(t)\left[\widehat{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta)\right]^{-1},\\
\widehat{\boldsymbol{\zeta}}_{\boldsymbol{\gamma},i}(t,\theta) &= \left[\widehat{\boldsymbol{D}}_{\boldsymbol{\gamma},i}^{\mathsf{T}}(t)-\widehat{\boldsymbol{K}}(t,\theta)\widehat{\boldsymbol{D}}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta)\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)}-\widehat{\boldsymbol{F}}_{1i}(t)\right\},\\
\widehat{\boldsymbol{q}}_{\boldsymbol{\gamma}}(s,t,\theta) &= n^{-1}\sum_{j=1}^{n}\left\{\widehat{\boldsymbol{D}}_{\boldsymbol{\gamma},j}^{\mathsf{T}}(t)-\widehat{\boldsymbol{K}}(t,\theta)\widehat{\boldsymbol{D}}_{\boldsymbol{\eta},j}^{\mathsf{T}}(t)\right\}w_j(t)\boldsymbol{\psi}_j(\theta)\frac{\Delta_j N_j(t)}{\widehat{G}(T_j)}\mathcal{I}(s\le \widetilde{T}_j\le t),\\
\hat{y}(t) &= n^{-1}\sum_{i=1}^{n}\mathcal{I}(\widetilde{T}_i\ge t)\\
\widehat{M}_j^{\,c}(s) &= \mathcal{I}(\widetilde{T}_j\le s,\Delta_j=0)-\int_0^s \mathcal{I}(\widetilde{T}_j\ge u)\ d(-\log\widehat{G}(u))\\
\widehat{\boldsymbol{\kappa}}_{\boldsymbol{\gamma},i}(t,\theta) &= \int_0^{\tau}\frac{\widehat{\boldsymbol{q}}_{\boldsymbol{\gamma}}(s,t,\theta)}{\hat{y}(s)}d\widehat{M}_i^c(s),\\
\hat{g}(\tau,\theta) &= n^{-1}\sum_{i=1}^{n}\int_0^{\tau}\left[\widehat{\boldsymbol{D}}_{\boldsymbol{\gamma},i}^{\mathsf{T}}(t)-\widehat{\boldsymbol{K}}(t,\theta)\widehat{\boldsymbol{D}}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)\right]w_i(t)\boldsymbol{A}_i(\theta)\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)}-\widehat{\boldsymbol{F}}_{1i}(t)\right\}dt. \qquad (4.29)
\end{aligned}
$$

The asymptotic covariance matrix of $\sqrt{n}(\widehat{\boldsymbol{\gamma}}-\boldsymbol{\gamma}_0)$ can be consistently estimated by

$$
\widehat{\boldsymbol{\Sigma}}_{\gamma}=\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}^{-1}(\hat{\theta})\,n^{-1}\sum_{i=1}^{n}\left\{\widehat{\boldsymbol{W}}_{\gamma,i}(\tau,\hat{\theta})\right\}^{\otimes 2}\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}^{-1}(\hat{\theta}),
$$

where

$$
\begin{aligned}
\widehat{\boldsymbol{W}}_{\gamma,i}(\tau,\theta) &= \int_0^{\tau}\widehat{\boldsymbol{\zeta}}_{\boldsymbol{\gamma},i}(t,\theta)\,dt+\int_0^{\tau}\widehat{\boldsymbol{\kappa}}_{\boldsymbol{\gamma},i}(t,\theta)\,dt+\hat{g}(\tau,\theta)\left[\widehat{J}(\theta)\right]^{-1}U(\mathcal{V}_i,\theta),\\
\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}(\theta) &= n^{-1}\sum_{i=1}^{n}\int_0^{\tau}\left[\widehat{\boldsymbol{D}}_{\boldsymbol{\gamma},i}^{\mathsf{T}}(t)-\widehat{\boldsymbol{K}}(t,\theta)\widehat{\boldsymbol{D}}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta)\widehat{\boldsymbol{D}}_{\boldsymbol{\gamma},i}(t)\,dt. \qquad (4.30)
\end{aligned}
$$

□

Proof of Theorem 2.2.

From (2.11), we have

$$
\begin{aligned}
&\sqrt{n}(\widehat{\boldsymbol{\eta}}(t)-\boldsymbol{\eta}_0(t))\\
&=\left[n^{-1}\mathcal{I}_{\boldsymbol{\eta}}(t,\hat{\theta})\right]^{-1}n^{-\frac{1}{2}}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\left\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t)-\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\left\{\mathcal{I}_{\boldsymbol{\gamma}}(\hat{\theta})\right\}^{-1}\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat{\theta})\right\}+o_p(1). \quad (4.31)
\end{aligned}
$$

We consider the expression $n^{-\frac{1}{2}}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\left\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t)-\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\left\{\mathcal{I}_{\boldsymbol{\gamma}}(\hat{\theta})\right\}^{-1}\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat{\theta})\right\}$. It can be decomposed into two terms

$$\begin{aligned}
&n^{-\frac{1}{2}}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\left\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t)-\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\left\{\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat{\theta})\right\}^{-1}\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat{\theta})\right\}\\
&=n^{-\frac{1}{2}}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\left\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t)\right\}\\
&\quad -n^{-\frac{1}{2}}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\left\{\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat{\theta})\right\}^{-1}\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat{\theta}). \qquad (4.32)
\end{aligned}$$

The first term of (4.32) can be decomposed into four terms

$$\begin{aligned}
&n^{-\frac{1}{2}}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\left\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t)\right\}\\
&=n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)\boldsymbol{\psi}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}\\
&\quad +n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)\boldsymbol{\psi}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)}-\frac{\Delta_i N_i(t)}{G(T_i)}\right\}\\
&\quad +n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)(\boldsymbol{\psi}_i(\hat{\theta})-\boldsymbol{\psi}_i(\theta_0))\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}\\
&\quad +n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)(\boldsymbol{\psi}_i(\hat{\theta})-\boldsymbol{\psi}_i(\theta_0))\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)}-\frac{\Delta_i N_i(t)}{G(T_i)}\right\}+o_p(1). \qquad (4.33)
\end{aligned}$$

It is shown in the Appendix A that the third and the fourth term are $o_p(1)$, that is,

$$n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)(\boldsymbol{\psi}_i(\hat{\theta})-\boldsymbol{\psi}_i(\theta_0))\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}=o_p(1), \qquad (4.34)$$

$$n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)(\boldsymbol{\psi}_i(\hat{\theta})-\boldsymbol{\psi}_i(\theta_0))\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)}-\frac{\Delta_i N_i(t)}{G(T_i)}\right\}=o_p(1). \qquad (4.35)$$

It follows that

$$\begin{aligned}
&n^{-\frac{1}{2}}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\left\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t)\right\}\\
&=n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{\zeta}_{\boldsymbol{\eta},i}(t,\theta_0)+n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{\kappa}_{\boldsymbol{\eta},i}(t,\theta_0)+o_p(1), \qquad (4.36)
\end{aligned}$$

where

$$\begin{aligned}
\boldsymbol{\zeta}_{\boldsymbol{\eta},i}(t,\theta) &= \boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\boldsymbol{\psi}_i(\theta)\left\{\frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t)\right\}, \\
\boldsymbol{q}_{\boldsymbol{\eta}}(s,t,\theta) &= E\left\{\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},j}(t)w_j(t)\boldsymbol{\psi}_j(\theta)\frac{\Delta_j N_j(t)}{G(T_j)}\mathcal{I}(s \le \tilde{T}_j \le t)\right\}, \\
\boldsymbol{\kappa}_{\boldsymbol{\eta},i}(t,\theta) &= \left\{\int_0^{\tau} \frac{\boldsymbol{q}_{\boldsymbol{\eta}}(s,t,\theta)}{y(s)} dM_i^c(s)\right\} \\
y(s) &= \lim_{n\to\infty} n^{-1} \sum_{i=1}^{n} \mathcal{I}(\widetilde{T}_i \ge s), \quad \text{where } s \in [0,\tau].
\end{aligned}$$

Now we consider the second term of (4.32). Note that

$$n^{-1}\sum_{i=1}^{n} \boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\psi_i(\theta_0)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t) \xrightarrow{p} \boldsymbol{Q}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta_0).$$

where $\boldsymbol{Q}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta) = E\left\{\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\psi_i(\theta)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\right\}$. It follows by (4.9) and (4.27) that

$$\begin{aligned}
& -n^{-\frac{1}{2}}\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\left\{\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat{\theta})\right\}^{-1}\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat{\theta}) \\
= & -n^{-1}\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\left\{n^{-1}\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat{\theta})\right\}^{-1} n^{-\frac{1}{2}}\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat{\theta}) \\
= & \left\{\boldsymbol{Q}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta_0) + o_p(1)\right\}\left\{\boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta_0)\right\}^{-1}\left\{n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{W}_{\gamma,i}(\tau,\theta_0)\right\} + o_p(1). \\
= & \ \boldsymbol{Q}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta_0)\left\{\boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta_0)\right\}^{-1}\left\{n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{W}_{\gamma,i}(\tau,\theta_0)\right\} + o_p(1). \qquad (4.37)
\end{aligned}$$

It follows by (4.32), (4.36) and (4.37) that

$$\begin{aligned}
& n^{-\frac{1}{2}}\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\left\{\boldsymbol{R}(t) - \boldsymbol{F}_1(t) - \boldsymbol{D}_{\boldsymbol{\gamma}}(t)\left\{\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat{\theta})\right\}^{-1}\boldsymbol{B}_{\boldsymbol{\gamma}}(\hat{\theta})\right\} \\
= & \ n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{W}_{\boldsymbol{\eta},i}(t,\theta_0) + o_p(1), \qquad (4.38)
\end{aligned}$$

where

$$\boldsymbol{W}_{\boldsymbol{\eta},i}(t,\theta) = \left\{\boldsymbol{\zeta}_{\boldsymbol{\eta},i}(t,\theta) + \boldsymbol{\kappa}_{\boldsymbol{\eta},i}(t,\theta) - \boldsymbol{Q}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta)\left\{\boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta)\right\}^{-1}\boldsymbol{W}_{\gamma,i}(\tau,\theta)\right\}. \qquad (4.39)$$

From (2.12), we have

$$\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\hat{\theta}) = \sum_{i=1}^{n}\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\psi_i(\hat{\theta})\boldsymbol{D}_{\boldsymbol{\eta},i}(t).$$

It is shown in the Appendix A that

$$\begin{aligned} n^{-1}\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\hat{\theta}) &= n^{-1}\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta_0)+o_p(1) \\ &\xrightarrow{p} \boldsymbol{Q}_{\boldsymbol{\eta}}(t,\theta_0), \end{aligned} \tag{4.40}$$

where $\boldsymbol{Q}_{\boldsymbol{\eta}}(t,\theta)=E\{\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\psi_i(\theta)\boldsymbol{D}_{\boldsymbol{\eta},i}(t)\}$.

By plugging (4.38) and (4.40) into (4.31), $\sqrt{n}(\widehat{\boldsymbol{\eta}}(t)-\boldsymbol{\eta}_0(t))$ is asymptotically equivalent to the following identically independent distributed decomposition

$$\sqrt{n}(\widehat{\boldsymbol{\eta}}(t)-\boldsymbol{\eta}_0(t))) = \Big\{\boldsymbol{Q}_{\boldsymbol{\eta}}(t,\theta_0)\Big\}^{-1} n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{W}_{\boldsymbol{\eta},i}(t,\theta_0)+o_p(1). \tag{4.41}$$

By the functional central limit theorem for empirical process, $n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{W}_{\boldsymbol{\eta},i}(t,\theta_0)$ converges in distribution to a normal random vector with zero-mean and covariance matrix $E\left\{\boldsymbol{W}_{\boldsymbol{\eta},i}(t,\theta_0)\right\}^{\otimes 2}$. By the slutsky's theorem and an application of Theorem 19.5 of van der Vaart(1998), $\sqrt{n}(\widehat{\boldsymbol{\eta}}(t)-\boldsymbol{\eta}_0(t))$ converges weakly to a mean zero Gaussian process on $t\in[0,\tau]$ with the covariance matrix $\boldsymbol{\Sigma}_{\boldsymbol{\eta}} = \boldsymbol{Q}^{-1}_{\boldsymbol{\eta}}(t,\theta_0)\,E\left\{\boldsymbol{W}_{\boldsymbol{\eta},i}(t,\theta_0)\right\}^{\otimes 2}\,\boldsymbol{Q}^{-1}_{\boldsymbol{\eta}}(t,\theta_0)$.

Let

$$\begin{aligned} \widehat{\boldsymbol{\zeta}}_{\boldsymbol{\eta},i}(t,\theta) &= \widehat{\boldsymbol{D}}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\boldsymbol{\psi}_i(\theta)\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)}-\widehat{\boldsymbol{F}}_{1i}(t)\right\}, \\ \widehat{\boldsymbol{q}}_{\boldsymbol{\eta}}(s,t,\theta) &= n^{-1}\sum_{j=1}^{n}\widehat{\boldsymbol{D}}^{\mathsf{T}}_{\boldsymbol{\eta},j}(t)w_j(t)\boldsymbol{\psi}_j(\theta)\frac{\Delta_j N_j(t)}{\widehat{G}(T_j)}\mathcal{I}(s\le\widetilde{T}_j\le t), \\ \hat{y}(t) &= n^{-1}\sum_{i=1}^{n}\mathcal{I}(\widetilde{T}_i\ge t), \\ \widehat{M}_j^{\,c}(s) &= \mathcal{I}(\widetilde{T}_j\le s,\Delta_j=0)-\int_0^s\mathcal{I}(\widetilde{T}_j\ge u)\ d(-\log\widehat{G}(u)), \\ \widehat{\boldsymbol{\kappa}}_{\boldsymbol{\eta},i}(t,\theta) &= \int_0^\tau\frac{\widehat{\boldsymbol{q}}_{\boldsymbol{\eta}}(s,t,\theta)}{\hat{y}(s)}d\widehat{M}_i^c(s), \\ \widehat{\boldsymbol{Q}}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta) &= n^{-1}\sum_{i=1}^{n}\widehat{\boldsymbol{D}}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\boldsymbol{\psi}_i(\theta)\widehat{\boldsymbol{D}}_{\boldsymbol{\gamma},i}(t). \end{aligned} \tag{4.42}$$

The asymptotic covariance matrix of $\sqrt{n}(\widehat{\boldsymbol{\eta}}(t)-\boldsymbol{\eta}_0(t))$ can be consistently estimated by

$$\widehat{\boldsymbol{\Sigma}}_{\boldsymbol{\eta}} = \widehat{\boldsymbol{Q}}^{-1}_{\boldsymbol{\eta}}(t,\hat{\theta})\,n^{-1}\sum_{i=1}^{n}\Big\{\widehat{\boldsymbol{W}}_{\boldsymbol{\eta},i}(\tau,\hat{\theta})\Big\}^{\otimes 2}\,\widehat{\boldsymbol{Q}}^{-1}_{\boldsymbol{\eta}}(t,\hat{\theta}),$$

where

$$
\begin{aligned}
\widehat{\boldsymbol{W}}_{\boldsymbol{\eta},i}(t,\theta) &= \left\{\widehat{\boldsymbol{\zeta}}_{\boldsymbol{\eta},i}(t,\theta) + \widehat{\boldsymbol{\kappa}}_{\boldsymbol{\eta},i}(t,\theta) - \widehat{\boldsymbol{Q}}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta)\left\{\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}(\theta)\right\}^{-1}\widehat{\boldsymbol{W}}_{\gamma,i}(\tau,\theta)\right\}, \\
\widehat{\boldsymbol{Q}}_{\boldsymbol{\eta}}(t,\theta) &= n^{-1}\sum_{i=1}^{n}\widehat{\boldsymbol{D}}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)\boldsymbol{\psi}_i(\theta)\widehat{\boldsymbol{D}}_{\boldsymbol{\eta},i}(t).
\end{aligned}
$$

and where $\left\{\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}(\theta)\right\}^{-1}$ and $\widehat{\boldsymbol{W}}_{\gamma,i}(\tau,\theta)$ are defined in (4.30). □

4.2 Proofs of the Theorems in Chapter 3

Proof of Theorem 3.1

We have the following estimating equations from (3.13) and (3.14)

$$
\begin{aligned}
\widehat{\widetilde{\boldsymbol{U}}}_{\boldsymbol{\eta}}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\hat{\theta}) &= \boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\left\{\boldsymbol{R}(t) - \boldsymbol{F}_1(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})\right\} + \hat{a}_{\eta}(t,\eta(t),\gamma,\hat{\theta}), \quad (4.43)\\
\widehat{\widetilde{\boldsymbol{U}}}_{\boldsymbol{\gamma}}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\hat{\theta}) &= \int_0^{\tau}\boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\hat{\theta})\left\{\boldsymbol{R}(t) - \boldsymbol{F}_1(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})\right\}dt + \hat{a}_{\gamma}(\tau,\eta(\cdot),\gamma,\hat{\theta}). \quad (4.44)
\end{aligned}
$$

For model (3.5), $\boldsymbol{D}_{\boldsymbol{\eta}}(t)$ is the $n\times(p+1)$ matrix of $X = (X_1,\cdots,X_n)^{\mathsf{T}}$ with the ith row vector $\boldsymbol{D}_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma}) = X_i^{\mathsf{T}} = (1,X_{i1},\cdots,X_{ip})$, $\boldsymbol{D}_{\boldsymbol{\gamma}}(t)$ is the the $n\times q$ matrix of $\partial g(\gamma,Z,t)/\partial\gamma$ with the ith row vector $\boldsymbol{D}_{\gamma,i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma}) = \partial g(\gamma,Z_i,t)/\partial\gamma$, and where $\hat{a}_{\eta}(t,\eta(t),\gamma,\hat{\theta})$ and $\hat{a}_{\gamma}(\tau,\eta(\cdot),\gamma,\hat{\theta})$ are defined in (3.11) and (3.12) with $\widehat{V}_x = (\widehat{E}\{X_1|\mathcal{V}_1\},\cdots,\widehat{E}\{X_n|\mathcal{V}_n\})^{\mathsf{T}}$ and $\widehat{V}_{xx}(\hat{\theta}) = \sum_{i=1}^{n}(1-\psi_i(\hat{\theta}))w_i(t)\widehat{E}\left[X_iX_i^{\mathsf{T}}|\mathcal{V}_i\right]$.

Let

$$
\begin{aligned}
\widetilde{\boldsymbol{U}}_{\boldsymbol{\eta}}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta) &= \boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta)\left\{\boldsymbol{R}(t) - \boldsymbol{F}_1(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})\right\} + \tilde{a}_{\eta}(t,\eta(t),\gamma,\theta), \quad (4.45)\\
\widetilde{\boldsymbol{U}}_{\boldsymbol{\gamma}}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\theta) &= \int_0^{\tau}\boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta)\left\{\boldsymbol{R}(t) - \boldsymbol{F}_1(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma})\right\}dt + \tilde{a}_{\gamma}(\tau,\eta(\cdot),\gamma,\theta), \quad (4.46)
\end{aligned}
$$

where

$$
\begin{aligned}
\tilde{a}_{\eta}(t,\eta(t),\gamma,\theta) &= V_x^T W(t)(I-\boldsymbol{\Psi}(\theta))\left\{\boldsymbol{R}(t) - g(\gamma,Z,t)\right\} - V_{xx}(\theta)\eta(t),\\
\tilde{a}_{\gamma}(\tau,\eta(\cdot),\gamma,\theta) &= \int_0^{\tau}\left\{\frac{\partial g(\gamma,Z,t)}{\partial\gamma}\right\}^{\mathsf{T}}\boldsymbol{W}(t)(I-\boldsymbol{\Psi}(\theta))\left\{\boldsymbol{R}(t) - V_x\eta(t) - g(\gamma,Z,t)\right\}dt,
\end{aligned}
$$

where $V_x = (E\{X_1|\mathcal{V}_1\}, \cdots, E\{X_n|\mathcal{V}_n\})^{\mathsf{T}}$ and $V_{xx}(\theta) = \sum_{i=1}^{n}(1-\psi_i(\theta))w_i(t)E\left[X_iX_i^{\mathsf{T}}|\mathcal{V}_i\right]$.

By adapting the theory of Robins, Rotnizky and Zhao (1994), if either $P(\xi_i = 1|\mathcal{V}_i)$ or $E\{X_i^{(2)}|\mathcal{V}_i\}$ and $E\{X_i^{(2)}(X_i^{(2)})^{\mathsf{T}}|\mathcal{V}_i\}$ is correctly specified, we have $\hat{\theta} \xrightarrow{p} \theta_0$, $\hat{a}_\eta(t,\eta(t),\gamma,\hat{\theta}) \xrightarrow{p} \tilde{a}_\eta(t,\eta(t),\gamma,\theta_0)$ $\hat{a}_\gamma(\tau,\eta(\cdot),\gamma,\hat{\theta}) \xrightarrow{p} \tilde{a}_\gamma(\tau,\eta(\cdot),\gamma,\theta_0)$. It follows that the estimating equation (4.43) and (4.44) are asymptotically equivalent to (4.45) and (4.46). That is,

$$\begin{aligned}\hat{\widetilde{\boldsymbol{U}}}_{\boldsymbol{\eta}}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\hat{\theta}) &= \widetilde{\boldsymbol{U}}_{\boldsymbol{\eta}}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta_0) + o_p(n^{\frac{1}{2}}),\\ \hat{\widetilde{\boldsymbol{U}}}_{\boldsymbol{\gamma}}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\hat{\theta}) &= \widetilde{\boldsymbol{U}}_{\boldsymbol{\gamma}}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\theta_0) + o_p(n^{\frac{1}{2}}).\end{aligned}$$

By using the Taylor expansion in (2.7) and replacing it into the estimation equations (4.45) and (4.46), we have

$$\begin{aligned}\widetilde{\boldsymbol{U}}_{\boldsymbol{\eta}}(t,\widehat{\boldsymbol{\eta}}(t),\widehat{\boldsymbol{\gamma}},\theta_0) &= \boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\left[\boldsymbol{R}(t)-\boldsymbol{F}_1(t)-\boldsymbol{D}_{\boldsymbol{\eta}}(t)\left\{\widehat{\boldsymbol{\eta}}(t)-\boldsymbol{\eta}_0(t)\right\}-\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\left\{\widehat{\boldsymbol{\gamma}}-\boldsymbol{\gamma}_0\right\}\right]\\ &\quad +\tilde{a}_\eta(t,\theta_0) + o_p(n^{\frac{1}{2}}) = 0, \qquad (4.47)\\ \widetilde{\boldsymbol{U}}_{\boldsymbol{\gamma}}(\tau,\widehat{\boldsymbol{\eta}}(\cdot),\widehat{\boldsymbol{\gamma}},\hat{\theta}) &= \int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\left[\boldsymbol{R}(t)-\boldsymbol{F}_1(t)-\boldsymbol{D}_{\boldsymbol{\eta}}(t)\{\widehat{\boldsymbol{\eta}}(t)-\boldsymbol{\eta}_0(t)\}-\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\left\{\widehat{\boldsymbol{\gamma}}-\boldsymbol{\gamma}_0\right\}\right]dt\\ &\quad +\tilde{a}_\gamma(\theta_0) + o_p(n^{\frac{1}{2}}) = 0. \qquad (4.48)\end{aligned}$$

where $\boldsymbol{D}_{\boldsymbol{\eta}}(t) = \boldsymbol{D}_{\boldsymbol{\eta}}(t,\boldsymbol{\eta}_0(t),\gamma_0)$, $\boldsymbol{D}_{\boldsymbol{\gamma}}(t) = \boldsymbol{D}_{\boldsymbol{\gamma}}(t,\boldsymbol{\eta}_0(t),\gamma_0)$, $\boldsymbol{F}_1(t) = \boldsymbol{F}_1(t,\boldsymbol{\eta}_0(t),\gamma_0)$, $\tilde{a}_\eta(t,\theta_0) = \tilde{a}_\eta(t,\widehat{\boldsymbol{\eta}}(t),\widehat{\boldsymbol{\gamma}},\theta_0)$ and $\tilde{a}_\gamma(\theta_0) = \tilde{a}_\gamma(\tau,\widehat{\boldsymbol{\eta}}(\cdot),\widehat{\boldsymbol{\gamma}},\theta_0)$.

From (4.47), it can be solved for $\{\widehat{\boldsymbol{\eta}}(t)-\boldsymbol{\eta}_0(t)\}$. That is,

$$\begin{aligned}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\boldsymbol{D}_{\boldsymbol{\eta}}(t)\left\{\widehat{\boldsymbol{\eta}}(t)-\boldsymbol{\eta}_0(t)\right\} &= \boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\left[\boldsymbol{R}(t)-\boldsymbol{F}_1(t)-\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\left\{\widehat{\boldsymbol{\gamma}}-\boldsymbol{\gamma}_0\right\}\right] + \tilde{a}_\eta(t,\theta_0),\\ \widehat{\boldsymbol{\eta}}(t)-\boldsymbol{\eta}_0(t) &= \left[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta_0)\right]^{-1}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\left[\boldsymbol{R}(t)-\boldsymbol{F}_1(t)-\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\left\{\widehat{\boldsymbol{\gamma}}-\boldsymbol{\gamma}_0\right\}\right]\\ &\quad + \left[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta_0)\right]^{-1}\tilde{a}_\eta(t,\theta_0) + o_p(n^{\frac{1}{2}}), \qquad (4.49)\end{aligned}$$

where $\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta) = \boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta)\boldsymbol{D}_{\boldsymbol{\eta}}(t)$.

By solving (4.48) for $\{\widehat{\boldsymbol{\gamma}}-\boldsymbol{\gamma}_0\}$,

$$\begin{aligned}\int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\left\{\widehat{\boldsymbol{\gamma}}-\boldsymbol{\gamma}_0\right\}dt &= \int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\left[\boldsymbol{R}(t)-\boldsymbol{F}_1(t)\right]dt\\ &\quad - \int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\boldsymbol{D}_{\boldsymbol{\eta}}(t)\left\{\widehat{\boldsymbol{\eta}}(t)-\boldsymbol{\eta}_0(t)\right\}dt + \tilde{a}_\gamma(\theta_0) + o_p(n^{-\frac{1}{2}}) \qquad (4.50)\end{aligned}$$

By substituting (4.49) into (4.50),

$$\begin{aligned}
&\int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\,\{\widehat{\gamma}-\boldsymbol{\gamma}_0\}\,dt \\
= \;&\int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)[\boldsymbol{R}(t)-\boldsymbol{F}_1(t)]\,dt \\
&-\int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\boldsymbol{D}_{\boldsymbol{\eta}}(t)\big[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta_0)\big]^{-1}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\,[\boldsymbol{R}(t)-\boldsymbol{F}_1(t)] \\
&+\int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\boldsymbol{D}_{\boldsymbol{\eta}}(t)\big[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta_0)\big]^{-1}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\,\{\widehat{\gamma}-\boldsymbol{\gamma}_0\} \\
&-\int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\boldsymbol{D}_{\boldsymbol{\eta}}(t)\big[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta_0)\big]^{-1}\tilde{a}_\eta(t,\theta_0)dt+\tilde{a}_\gamma(\theta_0)+o_p(n^{\frac{1}{2}}). \qquad (4.51)
\end{aligned}$$

By combining like terms of $\{\widehat{\gamma}-\boldsymbol{\gamma}_0\}$ and $\boldsymbol{R}(t)-\boldsymbol{F}_1(t)$ in (4.51), we have

$$\begin{aligned}
&\int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\Big[I-\boldsymbol{D}_{\boldsymbol{\eta}}(t)\big[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta_0)\big]^{-1}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\Big]\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\,\{\widehat{\gamma}-\boldsymbol{\gamma}_0\}\,dt \\
= \;&\int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\Big[I-\boldsymbol{D}_{\boldsymbol{\eta}}(t)\big[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta_0)\big]^{-1}\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\Big]\,[\boldsymbol{R}(t)-\boldsymbol{F}_1(t)] \\
&-\int_0^\tau \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\boldsymbol{D}_{\boldsymbol{\eta}}(t)\big[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta_0)\big]^{-1}\tilde{a}_\eta(t,\theta_0)dt+\tilde{a}_\gamma(\theta_0)+o_p(n^{\frac{1}{2}}). \qquad (4.52)
\end{aligned}$$

Let

$$\begin{aligned}
\boldsymbol{A}_\eta(\theta) &= \int_0^\tau \boldsymbol{K}(t,\theta)\tilde{a}_\eta(t,\theta)\;dt \\
\boldsymbol{K}(t,\theta) &= \boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta)\boldsymbol{D}_{\boldsymbol{\eta}}(t)\,\big[\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta)\big]^{-1}
\end{aligned}$$

Using (2.12), (4.52) can be reduced to

$$\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta_0)\,\{\widehat{\gamma}-\boldsymbol{\gamma}_0\} = \boldsymbol{B}_{\boldsymbol{\gamma}}(\theta_0)-\boldsymbol{A}_\eta(\theta_0)+\tilde{a}_\gamma(\theta_0)+o_p(n^{\frac{1}{2}}).$$

Thus, we have

$$\widehat{\gamma}-\boldsymbol{\gamma}_0 = \big[\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta_0)\big]^{-1}\big\{\boldsymbol{B}_{\boldsymbol{\gamma}}(\theta_0)-\boldsymbol{A}_\eta(\theta_0)+\tilde{a}_\gamma(\theta_0)\big\}+o_p(n^{-\frac{1}{2}}). \qquad (4.53)$$

Again by substituting (4.53) into (4.49), we have

$$\begin{aligned}
\widehat{\boldsymbol{\eta}}(t)-\boldsymbol{\eta}_0(t) = \;&\{\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta_0)\}^{-1}\{\boldsymbol{D}_{\boldsymbol{\eta}}(t)\}^{\mathsf{T}}\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\,\big\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t)-\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\{\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta_0)\}^{-1} \\
&\big\{\boldsymbol{B}_{\boldsymbol{\gamma}}(\theta_0)+\tilde{a}_\gamma(\theta_0)-\boldsymbol{A}_\eta(\theta_0)\big\}\big\}+\{\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta_0)\}^{-1}\tilde{a}_\eta(t,\theta_0)+o_p(n^{-\frac{1}{2}}).
\end{aligned}$$

□

Proof of Theorem 3.2

From (3.24), we have

$$n^{\frac{1}{2}}(\widehat{\gamma}-\boldsymbol{\gamma}_0) \;=\; \left\{\frac{1}{n}\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta_0)\right\}^{-1} n^{-\frac{1}{2}}\left\{\boldsymbol{B}_{\boldsymbol{\gamma}}(\theta_0)+\tilde{a}_{\gamma}(\theta_0)-\boldsymbol{A}_{\eta}(\theta_0)\right\}+o_p(1). \tag{4.54}$$

Consider $n^{-\frac{1}{2}}\boldsymbol{B}_{\boldsymbol{\gamma}}(\theta_0)$ in (4.54). Using (2.12), with similar arguments to (4.11), we have

$$n^{-\frac{1}{2}}\boldsymbol{B}_{\boldsymbol{\gamma}}(\theta_0) = n^{-\frac{1}{2}}\int_0^{\tau}\left\{\boldsymbol{D}_{\boldsymbol{\gamma}}^{\mathsf{T}}(t)-\boldsymbol{K}(t,\theta_0)\boldsymbol{D}_{\boldsymbol{\eta}}^{\mathsf{T}}(t)\right\}\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\left\{\boldsymbol{R}(t)-\boldsymbol{F}_1(t)\right\}dt.$$

With similar argument to (4.12), it can be decomposed by

$$\begin{aligned} n^{-\frac{1}{2}}\boldsymbol{B}_{\boldsymbol{\gamma}}(\theta_0) \;=\;& n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{D}_{\boldsymbol{\gamma},i}^{\mathsf{T}}(t)-\boldsymbol{K}(t,\theta_0)\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}dt \\ &+n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{D}_{\boldsymbol{\gamma},i}^{\mathsf{T}}(t)-\boldsymbol{K}(t,\theta_0)\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)}-\frac{\Delta_i N_i(t)}{G(T_i)}\right\}dt \end{aligned} \tag{4.55}$$

By using consistency of $\boldsymbol{K}(t,\theta_0)$ shown in (A.3) in Appendix 4.2, we have

$$n^{-\frac{1}{2}}\boldsymbol{B}_{\boldsymbol{\gamma}}(\theta_0) \;=\; n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\boldsymbol{\zeta}_{\boldsymbol{\gamma},i}(t,\theta_0)\,dt+n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\boldsymbol{\kappa}_{\boldsymbol{\gamma},i}(t,\theta_0)\,dt+o_p(1). \tag{4.56}$$

where $\boldsymbol{\zeta}_{\boldsymbol{\gamma},i}(t,\theta)$ and $\boldsymbol{\kappa}_{\boldsymbol{\gamma},i}(t,\theta_0)$ are defined in (4.15) and (4.21), respectively.

Consider $\tilde{a}_{\gamma}(\theta_0)$ is defined in Theorem 3.1. The term $n^{-\frac{1}{2}}\tilde{a}_{\gamma}(\theta_0)$ can be decomposed into four parts

$$\begin{aligned} n^{-\frac{1}{2}}\tilde{a}_{\gamma}(\theta_0) \;=\;& n^{-\frac{1}{2}}\int_0^{\tau}\sum_{i=1}^{n}\{\frac{\partial g(\gamma_0,Z_i,t)}{\partial\gamma_0}\}^{\mathsf{T}}w_i(t)(1-\psi_i(\theta_0))\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)}-\frac{\Delta_i N_i(t)}{G(T_i)}\right\}dt \\ &+\; n^{-\frac{1}{2}}\int_0^{\tau}\sum_{i=1}^{n}\{\frac{\partial g(\gamma_0,Z_i,t)}{\partial\gamma_0}\}^{\mathsf{T}}w_i(t)(1-\psi_i(\theta_0))\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-V_{x,i}\eta_0(t)-g(\gamma_0,Z_i,t)\right\}dt \\ &-\; n^{-\frac{1}{2}}\int_0^{\tau}\sum_{i=1}^{n}\{\frac{\partial g(\gamma_0,Z_i,t)}{\partial\gamma_0}\}^{\mathsf{T}}w_i(t)(1-\psi_i(\theta_0))V_{x,i}\left\{\widehat{\eta}(t)-\eta_0(t)\right\}dt \\ &-\; n^{-\frac{1}{2}}\int_0^{\tau}\sum_{i=1}^{n}\{\frac{\partial g(\gamma_0,Z_i,t)}{\partial\gamma_0}\}^{\mathsf{T}}w_i(t)(1-\psi_i(\theta_0))\left\{g(\widehat{\gamma},Z_i,t)-g(\gamma_0,Z_i,t)\right\}dt \end{aligned} \tag{4.57}$$

It is shown in the Appendix A that the third and fourth terms of the above equation are equal to $o_p(1)$, respectively. That is,

$$-\; n^{-\frac{1}{2}}\int_0^{\tau}\sum_{i=1}^{n}\{\frac{\partial g(\gamma_0,Z_i,t)}{\partial\gamma_0}\}^{\mathsf{T}}w_i(t)(1-\psi_i(\theta_0))V_{x,i}\left\{\widehat{\eta}(t)-\eta_0(t)\right\}dt=o_p(1), \tag{4.58}$$

$$-\; n^{-\frac{1}{2}}\int_0^{\tau}\sum_{i=1}^{n}\{\frac{\partial g(\gamma_0,Z_i,t)}{\partial\gamma_0}\}^{\mathsf{T}}w_i(t)(1-\psi_i(\theta_0))\left\{g(\widehat{\gamma},Z_i,t)-g(\gamma_0,Z_i,t)\right\}dt=o_p(1). \tag{4.59}$$

Consider the first term of (4.57). By using (4.20) and the law of large numbers,

$$n^{-1}\sum_{i=1}^{n}\{\frac{\partial g(\gamma_0,Z_i,t)}{\partial\gamma_0}\}^{\mathsf{T}}w_i(t)(1-\psi_i(\theta_0))\frac{\Delta_i N_i(t)}{G(T_i)}I(s\le\tilde{T}_i\le t)\xrightarrow{p}\boldsymbol{q}^*_{\boldsymbol{\gamma}}(s,t,\boldsymbol{\gamma}_0,\theta_0). \tag{4.60}$$

It follows that

$$\begin{aligned}
& n^{-\frac{1}{2}}\int_0^{\tau}\sum_{i=1}^{n}\{\frac{\partial g(\gamma_0,Z_i,t)}{\partial\gamma_0}\}^{\mathsf{T}}w_i(t)(1-\psi_i(\theta_0))\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)}-\frac{\Delta_i N_i(t)}{G(T_i)}\right\}dt \\
= & -n^{-\frac{1}{2}}\sum_{j=1}^{n}\int_0^{\tau}\int_0^{\tau}n^{-1}\sum_{i=1}^{n}\{\frac{\partial g(\gamma_0,Z_i,t)}{\partial\gamma_0}\}^{\mathsf{T}}w_i(t)(1-\psi_i(\theta_0))\frac{\Delta_i N_i(t)}{G(T_i)}\mathcal{I}(s\le\widetilde{T}_i\le t)\frac{dM_j{}^c(s)}{y(s)}\,dt+o_p(1). \\
= & -n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left\{\frac{\boldsymbol{q}^*_{\boldsymbol{\gamma}}(s,t,\boldsymbol{\gamma}_0,\theta_0)}{y(s)}+o_p(1)\right\}dM_i^c(s)+o_p(1) \\
= & -n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\boldsymbol{\kappa}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\gamma}_0,\theta_0)dt+o_p(1),
\end{aligned} \tag{4.61}$$

where $\boldsymbol{\kappa}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\gamma},\theta)=\int_0^{\tau}\{\boldsymbol{q}^*_{\boldsymbol{\gamma}}(s,t,\boldsymbol{\gamma},\theta)/y(s)\}dM_i^c(s)$.

Now consider the second term of (4.57).

$$\begin{aligned}
& n^{-\frac{1}{2}}\int_0^{\tau}\sum_{i=1}^{n}\{\frac{\partial g(\gamma_0,Z_i,t)}{\partial\gamma_0}\}^{\mathsf{T}}w_i(t)(1-\psi_i(\theta_0))\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-V_{x,i}\eta_0(t)-g(\gamma_0,Z_i,t)\right\}dt \\
= & \; n^{-\frac{1}{2}}\int_0^{\tau}\sum_{i=1}^{n}\boldsymbol{\zeta}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\eta}_0(t),\boldsymbol{\gamma}_0,\theta_0)\,dt,
\end{aligned} \tag{4.62}$$

where $\boldsymbol{\zeta}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta)=\{\frac{\partial g(\gamma,Z_i,t)}{\partial\gamma}\}^{\mathsf{T}}w_i(t)(1-\psi_i(\theta))\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-V_{x,i}\eta(t)-g(\gamma,Z_i,t)\right\}$.

Therefore, it follows by (4.57), (4.58), (4.59), (4.61) and (4.62) that

$$n^{-\frac{1}{2}}\tilde{a}_{\gamma}(\theta_0) = -n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\boldsymbol{\kappa}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\gamma}_0,\theta_0)dt+n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\boldsymbol{\zeta}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\eta}_0(t),\boldsymbol{\gamma}_0,\theta_0)dt+o_p(1). \tag{4.63}$$

Consider $-n^{-\frac{1}{2}}\boldsymbol{A}_{\eta}(\theta_0)$ in (4.54). From (3.26), we have

$$-n^{-\frac{1}{2}}\boldsymbol{A}_{\eta}(\theta_0) = \int_0^{\tau}\boldsymbol{K}(t,\theta_0)\tilde{a}_{\eta}(t,\theta_0)\,dt. \tag{4.64}$$

To finish this, first we consider i.i.d expression for $\tilde{a}_\eta(t,\theta_0)$. It can be decomposed into four terms

$$\begin{aligned}
n^{-\frac{1}{2}}\tilde{a}_\eta(t,\theta_0) &= n^{-\frac{1}{2}}\sum_{i=1}^{n} V_{x,i}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0))\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)} - \frac{\Delta_i N_i(t)}{G(T_i)}\right\} \\
&+ n^{-\frac{1}{2}}\sum_{i=1}^{n}\left[V_{x,i}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0))\left\{\frac{\Delta_i N_i(t)}{G(T_i)} - g(\gamma_0, Z_i, t)\right\} - V_{xx,i}(\theta_0)\eta_0(t)\right] \\
&- n^{-\frac{1}{2}}\sum_{i=1}^{n} V_{x,i}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0))\left\{g(\widehat{\gamma}, Z_i, t) - g(\gamma_0, Z_i, t)\right\} \\
&- n^{-\frac{1}{2}}\sum_{i=1}^{n} V_{xx,i}(\theta_0)\left\{\widehat{\eta}(t) - \eta_0(t)\right\}. \qquad (4.65)
\end{aligned}$$

It is shown in the Appendix A that the third and fourth terms of (4.65) are shown to be equal to $o_p(1)$, respectively. That is,

$$- \quad n^{-\frac{1}{2}}\sum_{i=1}^{n} V_{x,i}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0))\left\{g(\widehat{\gamma}, Z_i, t) - g(\gamma_0, Z_i, t)\right\} = o_p(1), \qquad (4.66)$$

$$- \quad n^{-\frac{1}{2}}\sum_{i=1}^{n} V_{xx,i}(\theta_0)\left\{\widehat{\eta}(t) - \eta_0(t)\right\} = o_p(1). \qquad (4.67)$$

Consider the first term of (4.65). By using (4.20) and the law of large numbers,

$$n^{-1}\sum_{j=1}^{n} V_{x,j}^{\mathsf{T}} w_j(t)(1-\psi_j(\theta_0))\frac{\Delta_j N_j(t)}{G(T_j)}\mathcal{I}(s \le \widetilde{T}_j \le t) \xrightarrow{p} \boldsymbol{q}^*_{\boldsymbol{\eta}}(s,t,\theta_0). \qquad (4.68)$$

It follows that

$$\begin{aligned}
& n^{-\frac{1}{2}}\sum_{i=1}^{n} V_{x,i}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0))\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)} - \frac{\Delta_i N_i(t)}{G(T_i)}\right\} \\
= & -n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^\tau n^{-1}\sum_{j=1}^{n} V_{x,j}^{\mathsf{T}} w_j(t)(1-\psi_j(\theta_0))\frac{\Delta_j N_j(t)}{G(T_j)}\mathcal{I}(s \le \widetilde{T}_j \le t)\frac{dM_i{}^c(s)}{y(s)} \\
= & -n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^\tau \frac{\boldsymbol{q}^*_{\boldsymbol{\eta}}(s,t,\theta_0)}{y(s)} dM_i{}^c(s) + o_p(1) \\
= & -n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{\kappa}^*_{\boldsymbol{\eta},i}(t,\theta_0) + o_p(1), \qquad (4.69)
\end{aligned}$$

where $\boldsymbol{\kappa}^*_{\boldsymbol{\eta},i}(t,\theta) = \int_0^\tau \{\boldsymbol{q}^*_{\boldsymbol{\eta}}(s,t,\theta)/y(s)\} dM_i{}^c(s)$.

Consider the second term of (4.65). We have,

$$
\begin{aligned}
& n^{-\frac{1}{2}} \sum_{i=1}^{n} \left[V_{x,i}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0)) \left\{ \frac{\Delta_i N_i(t)}{G(T_i)} - g(\gamma_0, Z_i, t) \right\} - V_{xx,i}(\theta_0)\eta_0(t) \right] \\
= \;& n^{-\frac{1}{2}} \sum_{i=1}^{n} \boldsymbol{\zeta}^*_{\boldsymbol{\eta},i}(t, \boldsymbol{\eta}_0(t), \boldsymbol{\gamma}_0, \theta_0), \qquad (4.70)
\end{aligned}
$$

where $\boldsymbol{\zeta}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta) = V_{x,i}^T w_i(t)(1-\psi_i(\theta)) \left\{ \frac{\Delta_i N_i(t)}{G(T_i)} - g(\gamma, Z_i, t) \right\} - V_{xx,i}(\theta)\eta(t)$.

It follows by (4.65), (4.66), (4.67), (4.69) and (4.70) that

$$
n^{-\frac{1}{2}} \tilde{a}_\eta(t,\theta_0) \;=\; -n^{-\frac{1}{2}} \sum_{i=1}^{n} \left\{ \boldsymbol{\kappa}^*_{\boldsymbol{\eta},i}(t,\theta_0) - \boldsymbol{\zeta}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}_0(t),\boldsymbol{\gamma}_0,\theta_0) \right\} + o_p(1) \qquad (4.71)
$$

Note that $\boldsymbol{K}(t,\theta_0) \xrightarrow{p} \boldsymbol{k}(t,\theta_0)$. From (4.64) and (4.71), we have

$$
\begin{aligned}
-n^{-\frac{1}{2}} \boldsymbol{A}_\eta(\theta_0) &= n^{-\frac{1}{2}} \int_0^\tau \boldsymbol{k}(t,\theta_0)\tilde{a}_\eta(t,\theta_0)\, dt + n^{-\frac{1}{2}} \int_0^\tau \left\{ \boldsymbol{K}(t,\theta_0) - \boldsymbol{k}(t,\theta_0) \right\} \tilde{a}_\eta(t,\theta_0)\, dt \\
&= n^{-\frac{1}{2}} \int_0^\tau \boldsymbol{k}(t,\theta_0)\tilde{a}_\eta(t,\theta_0)\, dt + o_p(1) \\
&= -n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_0^\tau \boldsymbol{k}(t,\theta_0) \left\{ \boldsymbol{\kappa}^*_{\boldsymbol{\eta},i}(t,\theta_0) - \boldsymbol{\zeta}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}_0(t),\boldsymbol{\gamma}_0,\theta_0) \right\} dt + o_p(1). \qquad (4.72)
\end{aligned}
$$

It follows by (4.26), (4.54),(4.56), (4.63), (4.72) that

$$
\begin{aligned}
n^{\frac{1}{2}}(\widehat{\boldsymbol{\gamma}} - \boldsymbol{\gamma}_0) &= \left\{ n^{-1} \boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta_0) \right\}^{-1} n^{-\frac{1}{2}} \left\{ \boldsymbol{B}_{\boldsymbol{\gamma}}(\hat{\theta}) + \tilde{a}_\gamma(\theta_0) - \boldsymbol{A}_\eta(\theta_0) \right\} \\
&= \left\{ \boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta_0) \right\}^{-1} n^{-\frac{1}{2}} \sum_{i=1}^{n} \boldsymbol{W}^*_{\boldsymbol{\gamma},i}(\tau, \boldsymbol{\eta}_0(\cdot), \boldsymbol{\gamma}_0, \theta_0) + o_p(1), \qquad (4.73)
\end{aligned}
$$

where $\boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta)$ is defined in Theorem 2.1, and where

$$
\begin{aligned}
\boldsymbol{W}^*_{\boldsymbol{\gamma},i}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\theta) &= \int_0^\tau \boldsymbol{\zeta}_{\boldsymbol{\gamma},i}(t,\theta)\, dt + \int_0^\tau \boldsymbol{\kappa}_{\boldsymbol{\gamma},i}(t,\theta)\, dt - \int_0^\tau \boldsymbol{\kappa}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\gamma},\theta) dt + \int_0^\tau \boldsymbol{\zeta}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta) dt \\
&\quad - \int_0^\tau \boldsymbol{k}(t,\theta_0) \left\{ \boldsymbol{\kappa}^*_{\boldsymbol{\eta},i}(t,\theta_0) - \boldsymbol{\zeta}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}_0(t),\boldsymbol{\gamma}_0,\theta_0) \right\} dt. \qquad (4.74)
\end{aligned}
$$

Since $\boldsymbol{\zeta}_{\boldsymbol{\gamma},i}(t,\theta_0)$ and $\boldsymbol{\kappa}_{\boldsymbol{\gamma},i}(t,\theta_0)$ has mean zero from Theorem 2.1, and since $\boldsymbol{\kappa}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\gamma},\theta_0)$ has mean zero local square martingale and, by missing at random assumption, $\boldsymbol{\zeta}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}_0(t),\boldsymbol{\gamma}_0,\theta_0)$ has mean zero, then, by the standard central limit theorem, $n^{-1} \sum_{i=1}^n \boldsymbol{W}^*_{\boldsymbol{\gamma},i}(\tau,\boldsymbol{\eta}_0(\cdot),\boldsymbol{\gamma}_0,\theta_0)$ has mean zero normal random vector with covariance matrix $E\{\boldsymbol{W}^*_{\boldsymbol{\gamma},i}(\tau,\boldsymbol{\eta}_0(\cdot),\boldsymbol{\gamma}_0,\theta_0)\}^{\otimes 2}$.

By slutsky's theorem, we have

$$
n^{\frac{1}{2}}(\widehat{\boldsymbol{\gamma}} - \boldsymbol{\gamma}_0) \xrightarrow{d} N(0, \Sigma^*_{\boldsymbol{\gamma}}), \qquad (4.75)
$$

where $\Sigma^*_{\boldsymbol{\gamma}} = \boldsymbol{Q}_{\boldsymbol{\gamma}}{}^{-1}(\theta_0) E\{\boldsymbol{W}^*_{\boldsymbol{\gamma},i}(\tau, \boldsymbol{\eta}_0(\cdot), \boldsymbol{\gamma}_0, \theta_0)\}^{\otimes 2} \boldsymbol{Q}_{\boldsymbol{\gamma}}{}^{-1}(\theta_0)$.

Let

$$\begin{aligned}
\widehat{\boldsymbol{q}}^*_{\boldsymbol{\gamma}}(s,t,\boldsymbol{\gamma},\theta) &= n^{-1}\sum_{i=1}^{n}\{\frac{\partial g(\gamma, Z_i, t)}{\partial \gamma}\}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta))\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)} I(s \le \tilde{T}_i \le t) \\
\hat{y}(t) &= n^{-1}\sum_{i=1}^{n}\mathcal{I}(\widetilde{T}_i \ge t) \\
\widehat{M_i}^c(t) &= \mathcal{I}(\widetilde{T}_j \le t, \Delta_j = 0) - \int_0^t \mathcal{I}(\widetilde{T}_j \ge s)\; d(-\log \widehat{G}(s)) \\
\widehat{\boldsymbol{\kappa}}^*_{\boldsymbol{\gamma},i}(t,\theta) &= \int_0^\tau \frac{\widehat{\boldsymbol{q}}^*_{\boldsymbol{\gamma}}(s,t,\boldsymbol{\gamma},\theta)}{\hat{y}(s)} d\widehat{M}_i^c(s) \\
\widehat{\boldsymbol{\zeta}}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta)\, dt &= n^{-1}\sum_{i=1}^{n}\int_0^\tau \{\frac{\partial g(\gamma, Z_i, t)}{\partial \gamma}\}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta))\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)} - \widehat{V}_{x,i}\eta(t) - g(\gamma, Z_i, t)\right\} dt.
\end{aligned} \tag{4.76}$$

The asymptotic covariance matrix of $n^{\frac{1}{2}}(\widehat{\boldsymbol{\gamma}} - \boldsymbol{\gamma}_0)$ can be consistently estimated by

$$\left\{\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}^{-1}(\hat{\theta})\right\}\; n^{-1}\sum_{i=1}^{n}\left\{\widehat{\boldsymbol{W}}^*_{\boldsymbol{\gamma},i}(\tau, \widehat{\boldsymbol{\eta}}(\cdot), \widehat{\gamma}, \hat{\theta})\right\}^{\otimes 2}\left\{\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}^{-1}(\hat{\theta})\right\},$$

where $\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}(\theta)$ is defined in (4.30), and where

$$\begin{aligned}
\widehat{\boldsymbol{W}}^*_{\boldsymbol{\gamma},i}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\theta) \;&=\; \int_0^\tau \widehat{\boldsymbol{\zeta}}_{\boldsymbol{\gamma},i}(t,\theta)\, dt + \int_0^\tau \widehat{\boldsymbol{\kappa}}_{\boldsymbol{\gamma},i}(t,\theta)\, dt - \int_0^\tau \widehat{\boldsymbol{\kappa}}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\gamma},\theta) dt + \int_0^\tau \widehat{\boldsymbol{\zeta}}^*_{\boldsymbol{\gamma},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta) dt \\
&- \int_0^\tau \boldsymbol{K}(t,\theta)\left\{\boldsymbol{\kappa}^*_{\boldsymbol{\eta},i}(t,\theta) - \boldsymbol{\zeta}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta)\right\} dt.
\end{aligned} \tag{4.77}$$

□

Proof of Theorem 3.3

From (3.25),

$$\begin{aligned}
n^{\frac{1}{2}}(\widehat{\boldsymbol{\eta}}(t) - \boldsymbol{\eta}_0(t)) \;&=\; \left\{n^{-1}\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\theta_0)\right\}^{-1}\; \Big[n^{-\frac{1}{2}}\{\boldsymbol{D}_{\boldsymbol{\eta}}(t)\}^{\mathsf{T}}\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\left\{\boldsymbol{R}(t) - \boldsymbol{F}_1(t)\right\} \\
&-n^{-\frac{1}{2}}\{\boldsymbol{D}_{\boldsymbol{\eta}}(t)\}^{\mathsf{T}}\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\left\{\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\{\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta_0)\}^{-1}\left\{\boldsymbol{B}_{\boldsymbol{\gamma}}(\theta_0) + \tilde{a}_\gamma(\theta_0) - \boldsymbol{A}_\eta(\theta_0)\right\}\right\} \\
&+\; n^{-\frac{1}{2}}\tilde{a}_\eta(t,\theta_0)\Big] + o_p(1).
\end{aligned} \tag{4.78}$$

Consider $-n^{-\frac{1}{2}}\{\boldsymbol{D}_{\boldsymbol{\eta}}(t)\}^{\mathsf{T}}\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\left\{\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\{\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta_0)\}^{-1}\left\{\boldsymbol{B}_{\boldsymbol{\gamma}}(\theta_0) + \tilde{a}_\gamma(\theta_0) - \boldsymbol{A}_\eta(\theta_0)\right\}\right\}$.

Note that $n^{-1}\{\boldsymbol{D}_{\boldsymbol{\eta}}(t)\}^{\mathsf{T}}\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\boldsymbol{D}_{\boldsymbol{\gamma}}(t) \xrightarrow{p} \boldsymbol{Q}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta_0)$. It follows by (4.73) that

$$\begin{aligned} & -n^{-1}\{\boldsymbol{D}_{\boldsymbol{\eta}}(t)\}^{\mathsf{T}}\boldsymbol{W}(t)\boldsymbol{\Psi}(\theta_0)\left\{\boldsymbol{D}_{\boldsymbol{\gamma}}(t)\{n^{-1}\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta_0)\}^{-1}n^{-\frac{1}{2}}\left\{\boldsymbol{B}_{\boldsymbol{\gamma}}(\theta_0)+\tilde{a}_{\gamma}(\theta_0)-\boldsymbol{A}_{\eta}(\theta_0)\right\}\right\} \\ = \quad & -\boldsymbol{Q}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta_0)\left\{\boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta_0)\right\}^{-1} n^{-\frac{1}{2}} \sum_{i=1}^{n} \boldsymbol{W}^{*}_{\boldsymbol{\gamma},i}(\tau,\boldsymbol{\eta}_0(\cdot),\boldsymbol{\gamma}_0,\theta_0)+o_p(1). \end{aligned} \tag{4.79}$$

It follows by (4.36), (4.71), (4.79) that (4.78) is

$$n^{\frac{1}{2}}(\widehat{\boldsymbol{\eta}}(t)-\boldsymbol{\eta}_0(t)) \quad = \quad \{n^{-1}\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t,\hat{\theta})\}^{-1}\; n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{W}^{*}_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}_0(t),\boldsymbol{\gamma}_0,\theta_0)+o_p(1), \tag{4.80}$$

where

$$\begin{aligned} \boldsymbol{W}^{*}_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}_0(t),\boldsymbol{\gamma}_0,\theta_0) \quad = \quad & \boldsymbol{\zeta}_{\boldsymbol{\eta},i}(t,\theta_0)+\boldsymbol{\kappa}_{\boldsymbol{\eta},i}(t,\theta_0)-\boldsymbol{Q}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta_0)\left\{\boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta_0)\right\}^{-1} n^{-\frac{1}{2}} \sum_{i=1}^{n}\boldsymbol{W}^{*}_{\boldsymbol{\gamma},i}(\tau,\boldsymbol{\eta}_0(\cdot),\boldsymbol{\gamma}_0,\theta_0) \\ & -\boldsymbol{\kappa}^{*}_{\boldsymbol{\eta},i}(t,\theta_0)+\boldsymbol{\zeta}^{*}_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}_0(t),\boldsymbol{\gamma}_0,\theta_0). \end{aligned}$$

By using (4.40), we have the following i.i.d decomposition

$$n^{\frac{1}{2}}(\widehat{\boldsymbol{\eta}}(t)-\boldsymbol{\eta}_0(t)) \quad = \quad \{\boldsymbol{Q}_{\boldsymbol{\eta}}(t,\theta_0)\}^{-1}\; n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{W}^{*}_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}_0(t),\boldsymbol{\gamma}_0,\theta_0)+o_p(1).$$

Let

$$\begin{aligned} \widehat{\boldsymbol{q}}^{*}_{\boldsymbol{\eta}}(s,t,\theta) &= n^{-1}\sum_{i=1}^{n}\widehat{V}^{T}_{x,i}w_i(t)(1-\psi_i(\theta))\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)}\mathcal{I}(s\le \widetilde{T}_i\le t) \\ \hat{y}(t) &= n^{-1}\sum_{i=1}^{n}\mathcal{I}(\widetilde{T}_i\ge t) \\ \widehat{M}_j^{\,c}(t) &= \mathcal{I}(\widetilde{T}_j\le t,\Delta_j=0)-\int_0^t \mathcal{I}(\widetilde{T}_j\ge s)\; d(-\log\widehat{G}(s)) \\ \widehat{\boldsymbol{\kappa}}^{*}_{\boldsymbol{\eta},i}(t,\theta) &= \int_0^{\tau}\frac{\widehat{\boldsymbol{q}}^{*}_{\boldsymbol{\eta}}(s,t,\theta)}{\hat{y}(s)}d\widehat{M}_j^{\,c}(s) \\ \widehat{\boldsymbol{\zeta}}^{*}_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta) &= n^{-1}\sum_{i=1}^{n}\left\{\widehat{V}^{T}_{x,i}w_i(t)(1-\psi_i(\theta))\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)}-g_i(\gamma,Z_i,t)\right\}-\widehat{V}_{xx,i}(\theta)\eta(t)\right\} \end{aligned} \tag{4.81}$$

By using lemma 1 of Sun and Wu (2005), $n^{\frac{1}{2}}(\widehat{\boldsymbol{\eta}}(t)-\boldsymbol{\eta}_0(t))$ converges weakly to a mean-zero Gaussian process on $t\in[0,\tau]$ with the covariance matrix $\boldsymbol{\Sigma}^{*}_{\boldsymbol{\eta}}=\boldsymbol{Q}_{\boldsymbol{\eta}}(t,\theta_0)^{-1}E\{\boldsymbol{W}^{*}_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}_0(t),\boldsymbol{\gamma}_0,\theta_0)\}^{\otimes 2}\boldsymbol{Q}_{\boldsymbol{\eta}}(t,\theta_0)^{-1}$, which can be consistently estimated by

$$\widehat{\boldsymbol{\Sigma}}^{*}_{\boldsymbol{\eta}} \quad = \quad \widehat{\boldsymbol{Q}}_{\boldsymbol{\eta}}^{-1}(t,\hat{\theta})\,n^{-1}\sum_{i=1}^{n}\left\{\widehat{\boldsymbol{W}}^{*}_{\boldsymbol{\eta},i}(t,\widehat{\boldsymbol{\eta}}(t),\widehat{\gamma},\hat{\theta})\right\}^{\otimes 2}\;\widehat{\boldsymbol{Q}}_{\boldsymbol{\eta}}^{-1}(t,\hat{\theta}),$$

where

$$\widehat{\boldsymbol{W}}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta) = \widehat{\boldsymbol{\zeta}}_{\boldsymbol{\eta},i}(t,\theta)+\widehat{\boldsymbol{\kappa}}_{\boldsymbol{\eta},i}(t,\theta)-\widehat{\boldsymbol{Q}}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta)\left\{\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}(\theta)\right\}^{-1} n^{-\frac{1}{2}} \sum_{i=1}^{n}\widehat{\boldsymbol{W}}^*_{\boldsymbol{\gamma},i}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\theta) -\widehat{\boldsymbol{\kappa}}^*_{\boldsymbol{\eta},i}(t,\theta)+\widehat{\boldsymbol{\zeta}}^*_{\boldsymbol{\eta},i}(t,\boldsymbol{\eta}(t),\boldsymbol{\gamma},\theta),$$

and where $\widehat{\boldsymbol{Q}}_{\boldsymbol{\gamma}}(\theta)$ is defined in (4.30), $\widehat{\boldsymbol{Q}}_{\boldsymbol{\eta},\boldsymbol{\gamma}}(t,\theta)$, $\widehat{\boldsymbol{Q}}_{\boldsymbol{\eta}}(t,\theta)$,$\widehat{\boldsymbol{\zeta}}_{\boldsymbol{\eta},i}(t,\theta)$, and $\widehat{\boldsymbol{\kappa}}_{\boldsymbol{\eta},i}(t,\theta)$ are defined in (4.42) and $\widehat{\boldsymbol{W}}^*_{\boldsymbol{\gamma},i}(\tau,\boldsymbol{\eta}(\cdot),\boldsymbol{\gamma},\hat{\theta})$ is defined in (4.77). □

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APPENDIX A: PROOFS IN CHAPTER 4

Lemmas

Lemma A.1. *Suppose* $X_n \xrightarrow{d} X$. *Then,* $X_n = Op(1)$.

Proof of Lemma A.1

Given $\epsilon > 0$, we choose sufficiently large k so that $P(|X| > k) < \epsilon$. By the assumption, $P(|X_n| > k) \to P(|X| > k)$. There exists some m such that for $n \geq m$, $P(|X_n| > k) < \epsilon$. We also choose sufficiently large k_1 so that $P(|X_i| > \epsilon) < \epsilon$, for $i = 1, ..., m-1$. Then, for $k_0 = \max(k, k_1)$, we have $P(|X_n| > k_0) < \epsilon$ for all n. □

Proof of 4.13

Let the fourth term of (4.12) be

$$\boldsymbol{C}_{\boldsymbol{\gamma}}(\hat{\theta}) \;=\; n^{-\frac{1}{n}} \sum_{i=1}^{n} \int_0^{\tau} \left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t) - \boldsymbol{K}(t,\hat{\theta})\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right] w_i(t)\boldsymbol{A}_i(\theta_0)\Delta_i N_i(t) \left\{\frac{G(T_i) - \widehat{G}(T_i)}{\widehat{G}(T_i)G(T_i)}\right\} dt(\hat{\theta} - \theta_0).$$

By using (A.3), it can be divided into two parts

$$\begin{aligned}\boldsymbol{C}_{\boldsymbol{\gamma}}(\hat{\theta}) &= n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_0^{\tau} \left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t) - \boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right] w_i(t)\boldsymbol{A}_i(\theta_0)\Delta_i N_i(t) \left\{\frac{G(T_i) - \widehat{G}(T_i)}{\widehat{G}(T_i)G(T_i)}\right\} dt(\hat{\theta} - \theta_0) \\ &\quad -n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_0^{\tau} \left[\boldsymbol{K}(t,\hat{\theta}) - \boldsymbol{k}(t,\theta_0)\right] \boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t) w_i(t)\boldsymbol{A}_i(\theta_0)\Delta_i N_i(t) \left\{\frac{G(T_i) - \widehat{G}(T_i)}{\widehat{G}(T_i)G(T_i)}\right\} dt(\hat{\theta} - \theta_0). \quad \text{(A.1)}\end{aligned}$$

In order to prove related $\boldsymbol{K}(t,\hat{\theta})$ term, we use the following properties. First, since $n^{\frac{1}{2}}(\hat{\theta} - \theta_0) = O_p(1)$, by using Delta method, we have

$$n^{\frac{1}{2}}(\boldsymbol{K}(t,\hat{\theta}) - \boldsymbol{K}(t,\theta_0)) = O_p(1). \quad \text{(A.2)}$$

Second, from definition of $\boldsymbol{K}(t,\theta_0)$, $\boldsymbol{K}(t,\theta_0) = \left[\frac{1}{n}\sum_{i=1}^{n} \boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t) w_i(t)\boldsymbol{\psi}_i(\theta_0)\boldsymbol{D}_{\boldsymbol{\eta},i}(t)\right] \left[\frac{1}{n}\sum_{i=1}^{n} \boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t) w_i(t)\boldsymbol{\psi}_i(\theta_0)\boldsymbol{D}_{\boldsymbol{\eta},}\right.$
By law of large numbers, we have

$$\boldsymbol{K}(t,\theta_0) \xrightarrow{p} \boldsymbol{k}(t,\theta_0). \quad \text{(A.3)}$$

It follows by uniform consistency of $\widehat{G}(t)$ in condition (I.6) and (A.1), the first term of (A.1) is, for $G(\tau) > 0$,

$$
\begin{aligned}
& n^{\frac{1}{2}}(\hat{\theta}-\theta_0)\ n^{-1}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{D}_{\boldsymbol{\gamma},i}^{\mathsf{T}}(t)-\boldsymbol{k}(t,\theta_0)\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)\right]w_i(t)\boldsymbol{A}_i(\theta_0)\Delta_i N_i(t)\left\{\frac{G(T_i)-\widehat{G}(T_i)}{\widehat{G}(T_i)G(T_i)}\right\}dt \\
\leq\ & O_p(1)\times n^{-1}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{D}_{\boldsymbol{\gamma},i}^{\mathsf{T}}(t)-\boldsymbol{k}(t,\theta_0)\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)\right]w_i(t)\boldsymbol{A}_i(\theta_0)\Delta_i N_i(t)\left\{\frac{1}{\widehat{G}(\tau)G(\tau)}\right\}\sup_{0\leq t\leq\tau}|G(t)-\widehat{G}(t)|\,dt \\
=\ & O_p(1)o_p(1) \\
=\ & o_p(1). \qquad \text{(A.4)}
\end{aligned}
$$

It follows by (A.2), (A.3) and (I.6) that the last term of (A.1) is equal to

$$
\begin{aligned}
& -n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{K}(t,\hat{\theta})-\boldsymbol{k}(t,\theta_0)\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)\right]w_i(t)\boldsymbol{A}_i(\theta_0)\Delta_i N_i(t)\left\{\frac{G(T_i)-\widehat{G}(T_i)}{\widehat{G}(T_i)G(T_i)}\right\}dt(\hat{\theta}-\theta_0) \\
=\ & -(\hat{\theta}-\theta_0)\times n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{K}(t,\hat{\theta})-\boldsymbol{K}(t,\theta_0)\right]\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)\boldsymbol{A}_i(\theta_0)\Delta_i N_i(t)\left\{\frac{G(T_i)-\widehat{G}(T_i)}{\widehat{G}(T_i)G(T_i)}\right\}dt \\
& -n^{\frac{1}{2}}(\hat{\theta}-\theta_0)\times n^{-1}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{K}(t,\theta_0)-\boldsymbol{k}(t,\theta_0)\right]\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)\boldsymbol{A}_i(\theta_0)\Delta_i N_i(t)\left\{\frac{G(T_i)-\widehat{G}(T_i)}{\widehat{G}(T_i)G(T_i)}\right\}dt \\
=\ & -o_p(1)\times O_p(1)\times n^{-1}\sum_{i=1}^{n}\int_0^{\tau}\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)\boldsymbol{A}_i(\theta_0)\Delta_i N_i(t)\left\{\frac{G(T_i)-\widehat{G}(T_i)}{\widehat{G}(T_i)G(T_i)}\right\}dt \\
& -O_p(1)\times o_p(1)\times n^{-1}\sum_{i=1}^{n}\int_0^{\tau}\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)\boldsymbol{A}_i(\theta_0)\Delta_i N_i(t)\left\{\frac{G(T_i)-\widehat{G}(T_i)}{\widehat{G}(T_i)G(T_i)}\right\}dt. \qquad \text{(A.5)}
\end{aligned}
$$

By the similar argument to (A.4) and Slutsky's theorem, the above equation reduce to $o_p(1)$. It follows by (A.1), (A.4) and (A.5) that the fourth term of (4.12) is $\boldsymbol{C}_{\boldsymbol{\gamma}}(\hat{\theta}) \xrightarrow{p} 0$ uniformly in $t \in [0,\tau]$.

□

Proof of 4.14 From (4.14), we have

$$
\begin{aligned}
& n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{K}(t,\hat{\theta})-\boldsymbol{k}(t,\theta_0)\right]\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)\boldsymbol{\psi}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}dt \\
=\ & n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{K}(t,\hat{\theta})-\boldsymbol{K}(t,\theta_0)\right]\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)\boldsymbol{\psi}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}dt \\
& +n^{-\frac{1}{2}}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{K}(t,\theta_0)-\boldsymbol{k}(t,\theta_0)\right]\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)\boldsymbol{\psi}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}dt \qquad \text{(A.6)}
\end{aligned}
$$

By (2.2), we note that

$$
n^{-1}\sum_{i=1}^{n}\int_0^{\tau}\frac{\partial\boldsymbol{K}(t,\theta)}{\partial\theta}\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t)w_i(t)\boldsymbol{\psi}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{G(T_i)}-\boldsymbol{F}_{1i}(t)\right\}dt
$$

has mean zero. By the central limit theorem and Lemma A.1, we have

$$n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_0^{\tau} \frac{\partial \boldsymbol{K}(t,\theta)}{\partial \theta} \boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t) w_i(t) \boldsymbol{\psi}_i(\theta_0) \left\{ \frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t) \right\} dt = O_p(1)$$

By the Taylor expansion of $\boldsymbol{K}(t,\hat{\theta})$ around the true value θ_0, the second term of A.6 is equal to

$$\begin{aligned}
& n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_0^{\tau} \left[\boldsymbol{K}(t,\hat{\theta}) - \boldsymbol{K}(t,\theta_0) \right] \boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t) w_i(t) \boldsymbol{\psi}_i(\theta_0) \left\{ \frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t) \right\} dt \\
= \;& n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_0^{\tau} \left[\frac{\partial \boldsymbol{K}(t,\theta)}{\partial \theta} (\hat{\theta} - \theta_0) + o_p(n^{-\frac{1}{2}}) \right] \boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t) w_i(t) \boldsymbol{\psi}_i(\theta_0) \left\{ \frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t) \right\} dt \\
= \;& (\hat{\theta} - \theta_0) \times n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_0^{\tau} \frac{\partial \boldsymbol{K}(t,\theta)}{\partial \theta} \boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t) w_i(t) \boldsymbol{\psi}_i(\theta_0) \left\{ \frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t) \right\} dt \\
& + o_p(1) \times n^{-1} \sum_{i=1}^{n} \int_0^{\tau} \boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t) w_i(t) \boldsymbol{\psi}_i(\theta_0) \left\{ \frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t) \right\} dt \\
= \;& o_p(1) \times O_p(1) + o_p(1) \\
= \;& o_p(1)
\end{aligned}$$

With similar arguments, by the central limit theorem, we have

$$n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_0^{\tau} \boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t) w_i(t) \boldsymbol{\psi}_i(\theta_0) \left\{ \frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t) \right\} dt = O_p(1)$$

It follows by Slutsky's theorem that the second term of (A.6) is equal to

$$\begin{aligned}
& n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_0^{\tau} \left[\boldsymbol{K}(t,\theta_0) - \boldsymbol{k}(t,\theta_0) \right] \boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t) w_i(t) \boldsymbol{\psi}_i(\theta_0) \left\{ \frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t) \right\} dt \\
& = o_p(1) \times n^{-\frac{1}{2}} \sum_{i=1}^{n} \int_0^{\tau} \boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t) w_i(t) \boldsymbol{\psi}_i(\theta_0) \left\{ \frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t) \right\} dt \\
& = o_p(1) \times O_P(1) \\
& = o_p(1)
\end{aligned}$$

where $\boldsymbol{K}(t,\theta_0) - \boldsymbol{k}(t,\theta_0) = o_p(1)$ uniformly in $t \in [0,\tau]$. □

Proof of 4.26 From (4.25), it can be decomposed into two parts.

$$
\begin{aligned}
n^{-1}\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat\theta) &= n^{-1}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{K}(t,\hat\theta)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{\psi}_i(\hat\theta)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\,dt\\
&= n^{-1}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{\psi}_i(\hat\theta)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\,dt \qquad \text{(A.7)}\\
&\quad -n^{-1}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{K}(t,\hat\theta)-\boldsymbol{k}(t,\theta_0)\right]\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\boldsymbol{\psi}_i(\hat\theta)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\,dt \qquad \text{(A.8)}\\
&= n^{-1}\sum_{i=1}^{n}\int_0^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{\psi}_i(\hat\theta)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\,dt+o_p(1). \qquad \text{(A.9)}
\end{aligned}
$$

By using (4.10), (A.9) can be decomposed as

$$
\begin{aligned}
& n^{-1}\sum_{i=1}^{n}\int_a^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta_0)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\,dt\\
& +n^{-1}\sum_{i=1}^{n}\int_a^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\left(\boldsymbol{A}_i(\theta_0)(\hat\theta-\theta_0)+o_p(n^{-\frac{1}{2}})\right)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\,dt+o_p(1).\\
= \; & n^{-1}\sum_{i=1}^{n}\int_a^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta_0)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\,dt\\
& +(\hat\theta-\theta_0)\times n^{-1}\sum_{i=1}^{n}\int_a^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{A}_i(\theta_0)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\,dt\\
& +o_p(n^{-\frac{1}{2}})\times n^{-1}\sum_{i=1}^{n}\int_a^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\,dt\\
& +o_p(1).\\
= \; & n^{-1}\sum_{i=1}^{n}\int_a^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta_0)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\,dt+o_p(1).
\end{aligned}
$$

followed by sums of the last three terms in second equality is equal to $o_p(1)$.

Let

$$
\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta_0) = n^{-1}\sum_{i=1}^{n}\int_a^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta_0)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\,dt.
$$

Therefore, we have

$$
n^{-1}\,\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\hat\theta) = n^{-1}\,\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta_0)+o_p(1).
$$

Let

$$
\boldsymbol{Q}(\theta_0) = E\left\{\int_a^{\tau}\left[\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\gamma},i}(t)-\boldsymbol{k}(t,\theta_0)\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)\right]w_i(t)\boldsymbol{\psi}_i(\theta_0)\boldsymbol{D}_{\boldsymbol{\gamma},i}(t)\,dt\right\}.
$$

By the law of large numbers,

$$n^{-1}\,\boldsymbol{\mathcal{I}}_{\boldsymbol{\gamma}}(\theta_0) \xrightarrow{p} \boldsymbol{Q}_{\boldsymbol{\gamma}}(\theta_0).$$

□

Proof of 4.34 We consider the third term of (4.33). By the law of large numbers,

$$n^{-1}\sum_{i=1}^{n}\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\boldsymbol{A}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t)\right\}$$

has mean zero.

By (4.10) and (A.1), we have

$$\begin{aligned}
& n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)(\boldsymbol{\psi}_i(\hat{\theta}) - \boldsymbol{\psi}_i(\theta_0))\left\{\frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t)\right\} \\
= \;& n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\left(\boldsymbol{A}_i(\theta_0)(\hat{\theta}-\theta_0) + o_p(n^{-\frac{1}{2}})\right)\left\{\frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t)\right\} \\
= \;& n^{\frac{1}{2}}(\hat{\theta}-\theta_0)\times n^{-1}\sum_{i=1}^{n}\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\boldsymbol{A}_i(\theta_0)\left\{\frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t)\right\} \\
+ \;& o_p(1)\times n^{-1}\sum_{i=1}^{n}\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\left\{\frac{\Delta_i N_i(t)}{G(T_i)} - \boldsymbol{F}_{1i}(t)\right\} \\
= \;& O_p(1)\times o_p(1) + o_p(1) \\
= \;& o_p(1).
\end{aligned} \tag{A.10}$$

Proof of 4.35

With similar argument, the fourth term of (4.33) is

$$\begin{aligned}
& n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)(\boldsymbol{\psi}_i(\hat{\theta}) - \boldsymbol{\psi}_i(\theta_0))\left\{\frac{\Delta_i N_i(t)}{\widehat{G}(T_i)} - \frac{\Delta_i N_i(t)}{G(T_i)}\right\} \\
= \;& n^{-\frac{1}{2}}\sum_{i=1}^{n}\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\left(\boldsymbol{A}_i(\theta_0)(\hat{\theta}-\theta_0) + o_p(n^{-\frac{1}{2}})\right)\Delta_i N_i(t)\left\{\frac{G(T_i)-\widehat{G}(T_i)}{\widehat{G}(T_i)G(T_i)}\right\} \\
= \;& n^{\frac{1}{2}}(\hat{\theta}-\theta_0)\times n^{-1}\sum_{i=1}^{n}\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\boldsymbol{A}_i(\theta_0)\Delta_i N_i(t)\left\{\frac{G(T_i)-\widehat{G}(T_i)}{\widehat{G}(T_i)G(T_i)}\right\} \\
+ \;& o_p(1)\times n^{-1}\sum_{i=1}^{n}\boldsymbol{D}^{\mathsf{T}}_{\boldsymbol{\eta},i}(t)w_i(t)\Delta_i N_i(t)\left\{\frac{G(T_i)-\widehat{G}(T_i)}{\widehat{G}(T_i)G(T_i)}\right\}
\end{aligned} \tag{A.11}$$

Similar to (4.13), by the consistency of $\widehat{G}(t)$, the fourth term of (4.33) is equal to $o_p(1)$ uniformly in $t \in [0, \tau]$ $\square$

Proof of 4.40

Let

$$\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t, \theta_0) = \sum_{i=1}^{n} \boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t) w_i(t) \psi_i(\theta_0) \boldsymbol{D}_{\boldsymbol{\eta},i}(t).$$

By using (4.10) and the consistency of $\hat{\theta}$, we have

$$\begin{aligned} n^{-1}\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t, \hat{\theta}) &= n^{-1}\sum_{i=1}^{n} \boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t) w_i(t) \psi_i(\theta_0) \boldsymbol{D}_{\boldsymbol{\eta},i}(t) \\ &\quad + (\hat{\theta} - \theta_0) \times n^{-1} \sum_{i=1}^{n} \boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t) w_i(t) \boldsymbol{A}_i(\theta_0) \boldsymbol{D}_{\boldsymbol{\eta},i}(t) + o_p(n^{-\frac{1}{2}}) \\ &= n^{-1}\sum_{i=1}^{n} \boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t) w_i(t) \psi_i(\theta_0) \boldsymbol{D}_{\boldsymbol{\eta},i}(t) + o_p(1) + o_p(n^{-\frac{1}{2}}). \end{aligned} \tag{A.12}$$

Therefore, we have

$$n^{-1}\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t, \hat{\theta}) = n^{-1}\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t, \theta_0) + o_p(1).$$

Let

$$\boldsymbol{Q}_{\boldsymbol{\eta}}(t, \theta_0) = E\{\boldsymbol{D}_{\boldsymbol{\eta},i}^{\mathsf{T}}(t) w_i(t) \psi_i(\theta_0) \boldsymbol{D}_{\boldsymbol{\eta},i}(t)\}.$$

By the law of the large numbers, we have

$$n^{-1}\boldsymbol{\mathcal{I}}_{\boldsymbol{\eta}}(t, \theta_0) \xrightarrow{p} \boldsymbol{Q}_{\boldsymbol{\eta}}(t, \theta_0).$$

$\square$

Proof of (4.58)

By the theory of Robins, Rotnizky and Zhao (1994), we have the fact that $\widehat{\eta}(t)$ is consistent estimator of $\eta_0(t)$. By the missing at random assumption, $n^{-1}\int_0^{\tau}\sum_{i=1}^{n}\{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma_0}\}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0))V_{x,i}\,dt$ has mean zero. Then, by the central limit theorem and Lemma A.1, we have

$$n^{-\frac{1}{2}}\int_0^{\tau}\sum_{i=1}^{n}\{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma_0}\}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0))V_{x,i}\,dt = O_p(1).$$

It follows by Slutsky's theorem that

$$\begin{aligned} &- \; n^{-\frac{1}{2}} \int_0^{\tau} \sum_{i=1}^{n} \{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma_0}\}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0)) V_{x,i} \left\{\widehat{\eta}(t) - \eta_0(t)\right\} \, dt \\ &= \; -\left\{\widehat{\eta}(t) - \eta_0(t)\right\} n^{-\frac{1}{2}} \int_0^{\tau} \sum_{i=1}^{n} \{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma_0}\}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0)) V_{x,i} \, dt \\ &= \; o_p(1) \times O_p(1) \\ &= \; o_p(1). \end{aligned} \tag{A.13}$$

□

Proof of (4.59)

With similar argument in the proof of (4.58), we have

$$\begin{aligned} n^{-\frac{1}{2}} \int_0^{\tau} \sum_{i=1}^{n} \{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma_0}\}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0)) \left\{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma}\right\} dt &= O_p(1) \\ n^{-1} \int_0^{\tau} \sum_{i=1}^{n} \{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma_0}\}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0)) \, dt &= o_p(1). \end{aligned}$$

and also have the fact that $\hat{\gamma}$ is consistent estimator of γ_0.

By the taylor expansion of $g(\widehat{\gamma}, Z_i, t)$ around the true value γ_0, we have

$$\begin{aligned} & -n^{-\frac{1}{2}} \int_0^{\tau} \sum_{i=1}^{n} \{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma_0}\}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0)) \left\{g(\widehat{\gamma}, Z_i, t) - g(\gamma_0, Z_i, t)\right\} \, dt \\ = \; & -n^{-\frac{1}{2}} \int_0^{\tau} \sum_{i=1}^{n} \{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma_0}\}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0)) \left\{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma} (\hat{\gamma} - \gamma_0) + o_p(n^{-\frac{1}{2}})\right\} \, dt \\ = \; & -(\hat{\gamma} - \gamma_0) \times n^{-\frac{1}{2}} \int_0^{\tau} \sum_{i=1}^{n} \{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma_0}\}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0)) \left\{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma}\right\} \, dt \\ - \; & o_p(1) \times n^{-1} \int_0^{\tau} \sum_{i=1}^{n} \{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma_0}\}^{\mathsf{T}} w_i(t)(1-\psi_i(\theta_0)) \, dt \\ = \; & o_p(1) \times O_p(1) + o_p(1) \\ = \; & o_p(1) \end{aligned}$$

□

Proof of (4.66)

With similar argument in the proof of (4.59), we have

$$-n^{-\frac{1}{2}}\sum_{i=1}^{n} V_{x,i}^{T} w_i(t)(1-\psi_i(\theta_0))\{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma_0}\} = O_p(1). \tag{A.14}$$

It follows that

$$\begin{aligned}
& -n^{-\frac{1}{2}}\sum_{i=1}^{n} V_{x,i}^{T} w_i(t)(1-\psi_i(\theta_0))\left\{g(\hat{\gamma}, Z_i, t) - g(\gamma_0, Z_i, t)\right\} \\
= & -n^{-\frac{1}{2}}\sum_{i=1}^{n} V_{x,i}^{T} w_i(t)(1-\psi_i(\theta_0))\left\{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma_0}(\hat{\gamma}-\gamma_0) + o_p(n^{-\frac{1}{2}})\right\} \\
= & -(\hat{\gamma}-\gamma_0)\times n^{-\frac{1}{2}}\sum_{i=1}^{n} V_{x,i}^{T} w_i(t)(1-\psi_i(\theta_0))\{\frac{\partial g(\gamma_0, Z_i, t)}{\partial \gamma_0}\} + o_p(1) \\
= & \ o_p(1)\times O_p(1) + o_p(1) \\
= & \ o_p(1).
\end{aligned} \tag{A.15}$$

Proof of (4.67)

With similar argument to (4.58), it can be proven to be equal to $o_p(1)$. □