Estimating Treatment Effects Adjusted for Time-Varying Switching Effects Using Accelerated Failure Time Models in Randomized Controlled Trials

Kangju Son

The Graduate School
Yonsei University
Department of Biostatistics and Computing

Estimating Treatment Effects Adjusted for Time-Varying Switching Effects Using Accelerated Failure Time Models in Randomized Controlled Trials

A Dissertation Submitted to the
Department of Biostatistics and Computing
and the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy in Biostatistics and Computing

Kangju Son

December 2024

This certifies that the doctoral thesis of ***Kangju Son*** is approved.

Chung Mo Nam: Thesis Supervisor

Inkyung Jung: Thesis Committee Member #1

Sohee Park: Thesis Committee Member #2

Min Jin Ha: Thesis Committee Member #3

Se Jung Park: Thesis Committee Member #4

The Graduate School

Yonsei University

December 2024

Contents

List of Tables

List of Figures

Abstract

Estimating Treatment Effects Adjusted for Time-Varying Switching Effects Using Accelerated Failure Time Models in Randomized Controlled Trials

This study introduces methodologies for accurately estimating the true treatment effect in randomized clinical trials that permit treatment switching. Conventional approaches, such as the Accelerated Failure Time (AFT) model, may introduce bias, while the Rank Preserving Structural Failure Time Model (RPSFTM) relies on the often-unrealistic assumption of a common treatment effect.

To address these limitations, this study proposes a flexible framework for modeling time-varying switching effects (TVSE) across two groups. Specifically, it employs a full likelihood approach to account for the effect of treatment switching from the control group to the experimental group and introduces methodologies utilizing cubic B-spline and piecewise constant functions for fitting the TVSE.

Simulation studies demonstrated that the proposed methods consistently outperformed conventional approaches in estimating the true treatment effect. The results showed significantly smaller bias, stable variance, and well-calibrated confidence intervals, underscoring the robustness of the proposed methodologies.

The proposed methodologies were further applied to the National Health Insurance

Service Elderly Cohort Database to estimate survival outcomes in chronic kidney disease (CKD) patients undergoing vascular access switching from central venous catheters (CVC) to arteriovenous fistulas (AVF). Compared to the AFT model, the proposed methods yielded survival estimates indicating greater improvements for AVF patients. These findings align with simulation results and underscore the advantages of the proposed methodologies over traditional approaches.

In conclusion, the proposed method provides significant advantages in estimating the true treatment effect in clinical trials with treatment switching. However, its application to real clinical trials requires careful data examination, and results should be presented alongside existing methods to ensure comprehensive and robust conclusions.

Keywords: Treatment Switching, Time-Varying Switching Effect, Accelerated Failure Time Model, Cubic B Spline, Piecewise Constant Function

Chapter 1

Introduction

1.1 Background

A clinical trial is a prospective study that compares the effects of a treatment in humans with those of a control group (Friedman et al., 2010). The primary objective of clinical trials is to determine whether a new treatment is more effective than existing methods. Most clinical trials employ a parallel design, where participants are assigned to either an experimental group or a control group, and both groups are observed simultaneously (Friedman et al., 2010). A common example is the randomized controlled trial, which minimizes potential bias by randomly assigning participants to the experimental or control group. Randomization also tends to create comparable groups, thereby enhancing the validity of statistical significance testing (Friedman et al., 2010).

In randomized controlled trials (RCTs) comparing two groups, it is ideal for participants to remain in their initially assigned group without receiving treatment from the other group until the trial concludes. However, treatment switching is common, particularly in oncology trials, and may also occur in clinical trials for other diseases (Latimer & Abrams, 2014). Generally, switching is allowed when the new treatment is effective, as denying an effective treatment to the control group is often considered unethical (Latimer

& Abrams, 2014). However, switching can affect the evaluation of the treatment's effectiveness (Shao et al., 2005). For example, when switching occurs to provide patients with optimal care, the average survival time of patients who switch from the control group to the experimental group may be longer than their original survival time (Shao et al., 2005). Shao et al. (2005) defined this difference caused by switching as the "switching effect". If the switching effect is not properly adjusted, bias can be introduced when estimating the effectiveness of the new treatment.

Guidelines from the UK and Australia emphasize the need to adjust for treatment switching (Lee et al., 2005). These guidelines propose various methods to account for the effects of treatment switching, including intention-to-treat (ITT) analysis, per-protocol (PP) analysis, Inverse Probability of Censoring Weighting (IPCW), the Rank Preserving Structural Failure Time Model (RPSFTM), Iterative Parameter Estimation (IPE), and the Two-Stage Estimation Method (TSE) (Pharmaceutical Benefits Advisory Committee, 2013; Latimer & Abrams, 2014; Latimer et al., 2014).

The ITT method adheres the initial trial plan and does not adjust for treatment switching. The primary advantage of this method is that it maintains balance between groups due to randomization. However, when treatment switching occurs, there is a possibility that the "true" effect associated with the new treatment may be biased.

The PP method either completely excludes data from patients who switched treatments or censors the data at the point of switching. However, PP carries the risk of selection bias,

as the balance between groups achieved through randomization can be disrupted if treatment switching is influenced to patients' prognosis.

IPCW approaches treatment switching from the perspective of informative censoring. When treatment switching occurs, data are censored at the point of switching, and weights are assigned to the remaining survival time based on a model of covariate values and the probability of censoring. The key assumption of IPCW is "no unmeasured confounders" meaning that all baseline and time-dependent prognostic factor related to the risk of death must be available. However, this assumption is often difficult to meet in practice. Nonetheless, IPCW can serve as an appropriate adjustment method if all major covariates are available.

The RPSFTM is a method designed within the framework of RCTs, utilizing the counterfactual framework to estimate treatment effects. This method estimates the treatment effect under the assumption that, "in the absence of treatment, the survival times of the experimental and control groups would be the same". Here, counterfactual survival times are defined as "the survival times that would have been observed in the absence of treatment". The key assumption of RPSFTM is the "common treatment effect (CTE)" assumption. This assumption presumes that the treatment effect in the experimental group is similar to the treatment effect in patients who switch treatments. However, in practice, treatment switching usually occurs after disease progression, meaning the benefit gained by switched patients may differ from the effect experienced before progression. Therefore, the CTE assumption may not always be clinically valid. The IPE method is a parametric

approach based on RPSFTM. Consequently, IPE also relies on the CTE assumption.

TSE first estimates the initial treatment effect for patients who switched from the control group. TSE then derives the counterfactual survival times of the switched patients. These counterfactual survival times for the control group are compared with the survival times of the experimental group in order to estimate the treatment effect. During this process, the switching effect is estimated while accounting for time-dependent confounding, under the assumption of "no unmeasured confounders".

As seen above, the methods considered to adjust for the switching effect depend on strong assumptions. For instance, IPCW and TSE require the assumption of "no unmeasured confounders", meaning that data must be collected on all variables that could influence switching until the trial concludes. Furthermore, when the switching rate is high, these methods may less effective and may be unsuitable for small-scale RCTs (Watkins et al., 2013).

RPSFTM and IPE both apply the CTE assumption, which presumes that the treatment effect is consistent regardless of the timing of treatment. In practice, however, this assumption is often difficult to satisfy (Watkins et al., 2013). In particular, IPE assumes a parametric distribution, so if the data do not follow this distribution, the estimation results may be inappropriate (Latimer et al., 2014).

Several studies have evaluated RPSFTM (Morden et al., 2011; Latimer et al., 2017; Latimer et al., 2018). According to Morden et al. (2011), ITT analysis tends to introduce

bias, and this tendency becomes more pronounced as the switching rate increases. PP analysis showed relatively a smaller bias; however, this bias also increased as the switching rate rose. In contrast, the RPSFTM and IPE methods successfully provided estimates of the treatment effect even in scenarios with high switching rates (Latimer et al., 2018).

Latimer et al. (2017) reported that the RPSFTM and IPE were considered appropriate when the CTE assumption holds. However, when the treatment effect was time-varying, the bias in RPSFTM and IPE increased significantly (Latimer et al., 2017). Furthermore, Latimer et al. (2018) stated that RPSFTM and IPE exhibited less bias than ITT analysis when the acceleration factor was approximately less than 2.0 (Latimer et al. 2018), even when the CTE assumption is violated.

Since Robins and Tsiatis (1991) proposed RPSFTM, several studies have aimed to generalize and expand the application of the method. Branson and Whitehead (2002) developed the IPE method. Bowden et al. (2016) suggested using a weighted log-rank test instead of the log-rank test for data with high switching rates. However, these studies have primarily focused on extending the application of RPSFTM based on the CTE assumption. Given that the CTE assumption is often not practical, there is a need to develop RPSFTM methods that can be applied to data with time-varying switching effects (TVSE).

1.2 Objective and Outline

The primary objective of this study is to develop and evaluate methods to adjust TVSE in RCTs, with a focus on overcoming the limitations of the CTE assumption. In the previous section, RPSFTM was shown to perform well in estimating the true treatment effect in datasets that follow the CTE assumption. However, when the CTE assumption was violated, RPSFTM exhibited bias. In real clinical settings, it is difficult to expect the treatment effect to remain consistent regardless of the timing of treatment, which highlights the need to develop RPSFTM methodologies that relax the CTE assumption.

To the best of the author's knowledge, studies addressing TVSE include those by Shao et al. (2005) and Chu and Wang (2023). Shao et al. (2005) proposed a parametric form for TVSE. Chu and Wang (2023) modeled the TVSE using a cubic B-spline function and employed a full likelihood approach for estimation.

This study assumed that the TVSE varies depending on the timing of the switch. To model the TVSE, the likelihood proposed by Chu and Wang (2023) was extended for application to RCTs. For simplicity, this study assumes that treatment switching occurs only from the control group to the experimental group. Two approaches were proposed to model the TVSE. The first approach uses a cubic B-spline function, which can flexibly fit the effect over time. The second approach, the piecewise switching effect method, assumes that the acceleration factor is constant within each interval. The performance of the proposed models was evaluated by comparing the results with those from the AFT, IPE,

and Chu and Wang (2023) methods.

This study is structured as follows. Chapter 1 outlines the background and objectives. Chapter 2 reviews AFT-based methodologies for adjusting treatment switching. Chapter 3 introduces the proposed methods for modeling time-varying switching effects in RCTs. Chapter 4 presents simulation results and evaluates the proposed methods against existing ones. Chapter 5 applies the methods to real data, and Chapter 6 concludes with a discussion of the findings.

Chapter 2

Literature Review

2.1 Notation

i	Individual
T	Survival time
σ	AFT model scale parameter
ε	AFT model error term
$\overset{d}{=}$	Equality in distribution
T_D	Counterfactual survival time (without treatment)
T_S	Treatment switching time
T_R	Observed survival time
x	Treatment status covariate (1: treatment, 0: no treatment)
β	Coefficient (representing the treatment effect)
$g(T_S)$	Switching effect function evaluated at T_S

2.2 Accelerated Failure Time Model

For the i-th subject, let the treatment status covariate x_i and the survival time T_i be observed. If $x_i = 1$, the patient receives the treatment; otherwise, the patient does not receive the treatment. In the AFT model, it is assumed that the logarithm of T_i has a linear relationship with the covariates x_i (Klein et al., 2006; Kim, 2016).

$$log(T_i) = \beta_0 + \beta_1 x_i + \sigma\varepsilon_i \tag{2.1}$$

Here, β represents the regression coefficient, σ is the scale parameter, and ε is the error term, assumed to follow a probability density function $f(\varepsilon)$. It is assumed that ε follows the same distribution as the logarithm of T.

Equation 2.1 can be rewritten as follows:

$$T_i = exp(\beta_0 + \beta_1 x_i + \sigma\varepsilon) = exp(\beta_0)\, exp(\beta_1 x_i)\, exp(\sigma\varepsilon_i) \tag{2.2}$$

In Equation 2.2, when $x = 1$, i.e., for patients who received the treatment, the survival time is given by $T_{trt} = exp(\beta_1)\, exp(\beta_0)\, exp(\sigma\varepsilon_{trt})$, while for patients who did not receive the treatment, the survival time is $T_{con} = exp(\beta_0)\, exp(\sigma\varepsilon_{con})$. Here, $exp(\sigma\varepsilon_{trt})$ and $exp(\sigma\varepsilon_{con})$ are assumed to follow the same distribution. Thus, the treatment and control groups are related as follows (Branson & Whitehead, 2002).

$$T_{trt} \overset{d}{=} exp(\beta_1)\, T_{con} \tag{2.3}$$

In Equation 2.3, $\overset{d}{=}$ represents equality in distribution (Branson & Whitehead, 2002).

2.3 AFT Model for a Common Treatment Effect

Robins and Tsiatis (1991) proposed the RPSFTM to adjust for non-compliance in clinical trials. Using RPSFTM, the true treatment effect can be estimated when treatment switching occurs (Allison et al., 2017).

RPSFTM estimates the reciprocal of the treatment effect by comparing the counterfactual survival times without treatment for both groups. In this process, g-estimation is used to identify the point where the survival times of the two groups are balanced. At this point, the reciprocal of the measured value is taken to represent the treatment effect.

Branson and Whitehead (2002) demonstrated that the treatment effect could be estimated using the IPE algorithm under the RPSFTM. Regardless of the extent of switching from the control group to the experimental group, the IPE algorithm provides accurate point estimates. The IPE algorithm is implemented under the assumption of a parametric distribution for survival times.

Branson and Whitehead (2002) assumed that the following equation holds between the counterfactual survival time and the observed survival time:

$$T_D \overset{d}{=} T_S + exp(-\beta)\,(T_R - T_S) \tag{2.4}$$

In Equation 2.4, the treatment effect is denoted by $exp(\beta)$. The observed survival time and the switching time for each patient are denoted as T_R and T_S, respectively. For

patients assigned to the experimental group, $T_S = 0$. The counterfactual survival time, T_D, represents the survival time that would have been observed without treatment. If β can be estimated using the above equation, it is possible to derive the survival time that would have been observed in the absence of treatment for patients who switched.

2.4 AFT Model for Time-varying Switching Effects

Shao et al. (2005) extended the model proposed by Branson and Whitehead (2002) by modeling the treatment switching effect under a parametric setting for latent event times. Additionally, they estimated the parameters using a parametric likelihood approach.

Shao et al. (2005) formulated the following model, building upon Equation 2.4.

$$T_R \stackrel{d}{=} T_S + exp(\beta)\,(T_D - T_S) \tag{2.5}$$

As in the IPE, T_R represents the observed survival time and T_S denotes the switching time. T_D is the survival time that would have been observed in the absence of treatment. Specifically, in the experimental group, the relationship $T_R \stackrel{d}{=} exp(\beta)\,T_D$ holds. In the control group, if no treatment switching occurs, T_R is identical to T_D. When treatment switching occurs, T_R reflects a combined impact of T_S and a partially applied treatment effect.

Expanding Equation 2.5 to the case where switching is possible in both groups, the equation can be modified as follows:

$$T_R \overset{d}{=} T_S + exp\big(\beta(1-2x)\big)\,(T_D - T_S) \tag{2.6}$$

Here, x is the indicator for the initially assigned group. If the patient is in the experimental group, $x = 1$; if in the control group, $x = 0$. Shao et al. (2005) incorporated a time-varying switching effect into Equation 2.6:

$$T_R \overset{d}{=} T_S + exp\big(\beta(1-2x)\big)g(T_S)\,(T_D - T_S) \tag{2.7}$$

where $g(T_S)$ is a function of T_S. Shao et al. (2005) proposed that when T_S is close to 0, $g(T_S)$ should converge to 1. Additionally, Shao et al. (2005) proposed a conditional likelihood function for parameter estimation.

Chu and Wang (2023) developed a method for modeling the treatment switching effect when treatment switching occurs within a single group. They proposed a method using an AFT model with TVSE using a cubic B-spline function. The estimation was performed using full likelihood. Chu and Wang (2023) considered the following AFT model.

$$T_R \overset{d}{=} T_S + exp[g(T_S)]\,(T_D - T_S) \tag{2.8}$$

Here, T_R, T_D, and T_S are the same terms as in Equation 2.5. However, the function $g(T_S)$ in Equation 2.7 takes values between 1 and 0, acting multiplicatively with β, whereas $g(T_S)$ in Equation 2.8 directly represents the TVSE.

Chapter 3

Proposed Method

3.1 Notation and the Proposed Accelerated Failure Time Model

This study aimed to estimate the true treatment effect in RCTs that allow treatment switching from the control group to the experimental group by modeling the time-varying switching effect using the AFT model. To achieve this, we extend the model of Chu and Wang (2023) to the following AFT model:

$$T_R \overset{d}{=} exp(\beta x)\left[T_S + exp\big(g(T_S)(1-x)\big)\,(T_D - T_S)\right] \tag{3.1}$$

In Equation 3.1, as described above, T_R represents the observed survival time and T_S denotes the switching time. In this study, it is assumed that treatment switching occurs when progression is observed in the control group. T_D represents the survival time that would have been observed in the absence of treatment. x is an indicator for treatment status, where $x = 1$ indicates the experimental group and $x = 0$ indicates the control group. Therefore, β represents the treatment effect. In the experimental group $(x = 1)$, $T_R \overset{d}{=} exp(\beta)\,T_D$. In the control group $(x = 0)$ with switching, $T_R \overset{d}{=} T_S + exp(g(T_S))(T_D - T_S)$. In the control group $(x = 0)$ without switching, $T_R \overset{d}{=} T_D$. The function $g(T_S)$ represents the switching effect based on the time of switching. We assume

that when T_S is close to 0, $g(T_S)$ approaches β in the control group with switching, and in the control group without switching, $g(T_S)$ is assumed to be zero.

This study considered a full likelihood approach to estimate both the treatment effect and the treatment switching effect. C denotes the censoring time, which is assumed to be independent of T_D and T_S. Let δ be the indicator for censoring, where $\delta = I(T_R < C)$; when the event occurs, $\delta = 1$, otherwise, $\delta = 0$. $\gamma = I(T_S < min(T_R,\ C))$ is the indicator for switching from the control group to the experimental group. We can observe the event time $min(T_R, C)$ and the censoring indicator $\delta = I(T_R < C)$. When switching occurs $(\gamma = 1)$, $T_S = T_S$. When switching does not occur $(\gamma = 0)$, $T_S = min(T_R, C)$.

Let the probability density function of T_D be f_D, and its survival function be S_D. Similarly, let the probability density function of T_S be f_S, and its survival function be S_S. Then the likelihood function is given by:

$$L(\beta\ |x, T_R, T_S, \delta, \gamma) = \prod_i [\Big(exp(-\beta x_i)\, f_D\big(exp(-\beta x_i)\, T_{R_i}\big) S_S\big(T_{S_i}\big)\Big)^{\delta_i(1-\gamma_i)}$$

$$\times \Big(S_D\big(exp(-\beta x_i)\, T_{R_i}\big) S_S\big(T_{S_i}\big)\Big)^{(1-\delta_i)(1-\gamma_i)}$$

$$\times \left(\exp\big(g(T_S)\big)^{-1} f_D\left(\exp\big(g(T_S)\big)^{-1}\left(T_{R_i} + \big(\exp\big(g(T_S)\big) - 1\big)T_{S_i}\right)\right) f_S\big(T_{S_i}\big)\right)^{\delta_i\gamma_i}$$

$$\times \left(S_D\left(\exp\big(g(T_S)\big)^{-1}\left(T_{R_i} + \big(\exp\big(g(T_S)\big) - 1\big)T_{S_i}\right)\right) f_S\big(T_{S_i}\big)\right)^{(1-\delta_i)\gamma_i}]$$

Here, i denotes i-th subject. In the switching case, the post-switching survival time

is given by $T_R \stackrel{d}{=} T_S + exp(g(T_S))(T_D - T_S)$. Using this equation, we can derive the counterfactual survival time as $T_D \stackrel{d}{=} exp(g(T_S))^{-1}(T_R + (exp(g(T_S)) - 1)T_S)$.

The parameters were estimated by maximizing the log-likelihood function using the Broyden-Fletcher-Goldfarb-Shanno (BFGS) quasi-Newton method, which approximates the Hessian matrix (Chu & Wang, 2023). All analyses were conducted using R (version 4.1.3; R Core Team, 2022). For parameter estimation, the *optim* function from the *stats* package was used in common type scenarios, while the *ucminf* function from the *ucminf* package was employed in varying type scenarios.

3.2 Fitting Time-Varying Switching Effects

In Equation 3.1, $g(T_S)$ represents the treatment effect based on the switching time when switching from the control group to the experimental group. This study considered both a cubic B-spline function and a piecewise constant function to model the TVSE.

The cubic B-spline function formulated in this study is as follows (Chu & Wang, 2023; "BSpline", 2024; Lyche & Morken, 2008).

$$g(T_S) = \sum_{k=0}^{K-1} \zeta_k B_{k,3}(T_S)$$

Here, k represents the k-th knot, ζ_k represents the spline coefficients, and $B_{k,3}$ denotes the cubic basis function. Therefore, the total number of knots is $K + 4$, where K represents the number of internal knots. The cubic B-spline basis function is recursively

defined (“BSpline”, 2024; Lyche & Morken, 2008).

To construct the cubic basis function, it is necessary to include four additional knots beyond the internal knots. In this study, clamped knots were utilized to satisfy this requirement. Clamped knots involve adding duplicated knots at the start and end of the internal knot sequence to ensure continuity and desired boundary conditions (Piegl & Tiller, 2012).

Next, we aimed to estimate a constant switching effect for each interval within the observation period. While the switching effect may vary between intervals, it remains constant within each individual interval. The observation period was divided into K intervals, with each interval k characterized by the switching effect ξ_k. These intervals were specified by the time points $T_{S_0}, T_{S_1}, \cdots, T_{S_k}$, where $[T_{S_k}, T_{S_{k+1}})$ represents the k-th interval. The switching effect based on the switching time is given by:

$$g(T_S) = \sum_{k=0}^{K-1} \xi_k I(T_{S_k} \leq T_S < T_{S_{k+1}})$$

This study distributed the interior knots evenly across the range of observed switching times. Among various configurations of interior knots, the configuration that minimized the AIC value was selected as the final model (Chu & Wang, 2023). In this context, the number of parameters used in the AIC calculation was determined by the number of interior knots (Hastie, Tibshirani, & Friedman, 2009).

Chapter 4

Simulation Study

4.1 Simulation Setting

In Chapter 3, we proposed an AFT model to estimate the true treatment effect in the presence of treatment switching from the control group to the experimental group. Furthermore, this study incorporates a cubic B-spline function and a piecewise constant function to fit the TVSE.

To evaluate the proposed methodology, this study performed a simulation study under various scenarios. Three types of switching effects were considered: the first, where the switching effect remains constant over time (common type); the second, where the switching effect decreases over time (varying type A); and the third, where the switching effect decreases by interval but remains constant within each interval (varying type B).

We considered the following methodologies: (1) the AFT, (2) the IPE, (3) the Cubic B-spline using the control group (CBS-CG), (4) the proposed Accelerated Failure Time model (PAFT), (5) the Cubic B-spline using the overall group (CBS-OG), and (6) the Piecewise model using the overall group (PM-OG).

The AFT is a classic regression model, while the IPE method estimates the true

treatment effect using an iterative estimation algorithm under the assumption that the treatment effect does not vary over time. The CBS-CG model, proposed by Chu and Wang (2023), estimates the switching effect within a single group using a cubic B-spline model. The PAFT model, proposed in this study, separates the treatment effect and the switching effect, assuming that the switching effect remains constant over time. Extending the PAFT model, the CBS-OG assumes that the switching effect varies over time and fits the TVSE using a cubic B-spline, While the PM-OG fits the TVSE using a piecewise model.

To reflect various practical scenarios, the study varied censoring rates, switching rates, treatment effects, and group sample sizes. The censoring rate was adjusted by modifying the maximum follow-up period, while the switching rate was controlled using the switching time shape parameter. Different levels of treatment effects and sample sizes per group were also assigned (Table 4.1).

Table 4.1 Simulation Setting and Scenarios

Switching Effect Type	Method	Maximum Follow-up Period (Censoring)	Switching Time Shape Parameter (Switching)	Treatment Effect	Sample Size per Group
Common Varying(A) Varying(B)	AFT IPE CBS-CG PAFT CBS-OG PM-OG	1.4 2.0 3.0	0.2 1.0 3.5	0.0 0.2 0.4 0.5	100 200 500

Common: Type where the switching effect remains constant over time.
Varying(A): Type where the switching effect decreases over time.
Varying(B): Type where the switching effect decreases by interval.
AFT: Accelerated Failure Time model.

IPE: Iterative Parameter Estimation method.
CBS-CG: Cubic B-spline using control group.
PAFT: proposed Accelerated Failure Time model.
CBS-OG: Cubic B-spline using overall group.
PM-OG: Piecewise model using overall group.

The objective of the simulation study focused on evaluating the accuracy of the newly proposed methods in estimating the true treatment effect. The methodologies were assessed using four metrics: bias, variance, mean squared error (MSE), and coverage probability (CP). Bias quantifies the difference between the mean estimated value and the true value, indicating the accuracy of the model. Variance measures the dispersion of the estimates, serving as an indicator of model stability. MSE, as a comprehensive metric, combines bias and variance to quantify the average squared error between estimates and the true value. Finally, CP represents the proportion of simulations in which the confidence interval contains the true value, with a value near 95% suggesting well-calibrated intervals.

The simulation results and the specific aspects addressed by this study were outlined. The first aspect focused on evaluating whether the aforementioned methodologies accurately estimate the treatment effect under various scenarios. As CBS-CG is not designed to estimate the treatment effect, the simulation was conducted using five methods: AFT, IPE, PAFT, CBS-OG, and PM-OG.

The second aspect focused on comparing the estimation accuracy of the methodologies in capturing the switching effect value at time 0. For CBS-based methodologies, the time 0 value was extrapolated, while for the PM-OG model, it was replaced with the estimate

from the first interval. In the PAFT model, which assumes a constant switching effect, the estimate was directly used without additional computation. Since AFT and IPE are not designed to estimate the switching effect, the simulation was conducted using four methods: CBS-CG, PAFT, CBS-OG, and PM-OG.

The final aspect examined the effectiveness of the proposed methods in fitting the time-varying switching effect. To evaluate this, the performance of the CBS-CG, CBS-OG, and PM-OG models was assessed at various time points. A total of 100 simulations were performed, and five representative results were selected based on their performance quality. The performance quality was quantified using the Mean Squared Error between the true and estimated switching effect values. Specifically, simulation results corresponding to the 5th, 25th, 50th, 75th, and 95th percentiles of MSE across the 100 simulations were chosen for presentation.

4.2 Data Generation

To evaluate the proposed methodologies, survival times were generated based on Equation 3.1 under the Weibull distribution. For both T_S and T_D, the scale parameters (λ_S for T_S and λ_D for T_D) followed a value of 1. The shape parameter (ρ_D) for T_D was set to 3.5, while the shape parameter (ρ_S) for T_S varied according to the switching time shape parameter values specified in Table 4.1, which determine the switching rate. The switching rate was defined as the proportion of individuals who switched from the control group to the experimental group.

Censoring times were defined as $C = min(U, C_L)$, where U is a random variable following a uniform distribution over the interval [0,5]. Here, C_L represents the maximum follow-up period as specified in Table 4.1, serving as a factor influencing the censoring rate. The censoring rate was calculated as the proportion of censored individuals in the overall group.

This study defines three types of switching effects: common, varying(A), and varying(B). In the common type, the treatment effect (β) and the switching effect (g) are identical. For the varying(A) type, it is assumed that β and $g(0)$ are equal, indicating that the treatment effect and the initial switching effect are the same. As time progresses, the switching effect gradually decreases, which is modeled by the following equation:

$$g(T_S) = \beta exp(-3.0\, T_S)$$

In the equation above, when $T_S = 0$, $g(T_S)$ equals β, and the switching effect decreases over time as governed by the factor -3.0.

For the varying(B) type, the time interval from 0 to C_L is divided into three segments: in the first segment, $g(T_S) = \beta$; in the second segment, $g(T_S) = \beta/2$; and in the third segment, $g(T_S) = 0$.

The varying(B) type $g(T_S)$ is defined as:

$$g(T_S) = \begin{cases} \beta, & if\ 0 \le T_S < C_L/3 \\ \beta/2, & if\ C_L/3 \le T_S < 2C_L/3 \\ 0, & if\ 2C_L/3 \le T_S < C_L \end{cases}$$

Figure 4.1 illustrates the switching effects of three types as they change over time under the scenario where $\beta = 0.4$ and $C_L = 1.4$. The common type maintains a constant switching effect of 0.4, while the varying(A) type starts at 0.4 at time 0 and gradually decreases over time. In contrast, the Varying(B) type shows a stepwise decrease, maintaining a constant switching effect within each interval and demonstrating distinct segmental patterns.

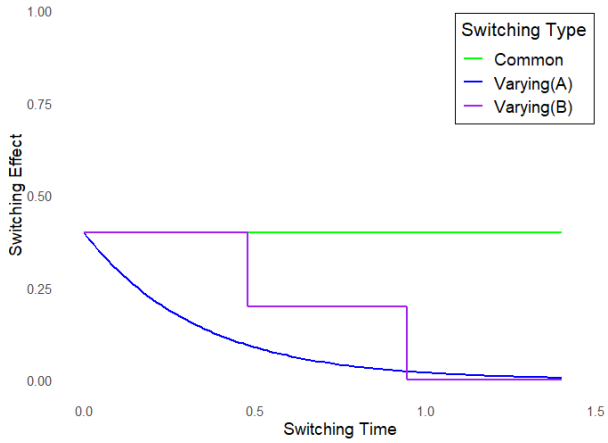


Figure 4.1 Example of Three Types of Switching Effects by Switching Time ($\boldsymbol{\beta = 0.4,\ C_L = 1.4}$)

Table 4.2 presents the censoring rate and switching rate according to the switching type, C_L, and ρ_S in a scenario where $\beta = 0.4$ and the sample size per group is 200. Overall, the censoring rate decreases as C_L increases. Additionally, the censoring rate tends to decrease at lower switching rates, likely because switching generally extends survival periods. Conversely, the switching rate is minimally influenced by C_L, as only early censoring affects the occurrence of switching. However, the switching rate decreases as ρ_S increases. Censoring rates and switching rates for other scenarios are summarized in Appendix 1.

In comparison to the types of switching effects, the censoring rate was slightly lower for the varying types. This is likely due to the gradual reduction in the switching effect over time, which leads to shorter survival periods. However, the switching rate did not show any substantial differences between the types of switching effects.

Table 4.2 Rates of Censoring and Treatment Switching by Switching Type, Follow-up Period, and Switching Time Shape Parameter ($\beta = 0.4$, Sample Size per Group = 200)

	Common			Varying(A)			Varying(B)		
Censoring Rate									
	Maximum follow-up time			Maximum follow-up time			Maximum follow-up time		
Switching Time Shape parameter	1.4	2.0	3.0	1.4	2.0	3.0	1.4	2.0	3.0
0.2	0.4863	0.2811	0.2534	0.4724	0.2760	0.2502	0.4845	0.2809	0.2533
1.0	0.4555	0.2675	0.2441	0.4181	0.2556	0.2362	0.4450	0.2666	0.2440
3.5	0.4279	0.2567	0.2366	0.3935	0.2480	0.2298	0.4077	0.2538	0.2363
Switching Rate									
	Maximum follow-up time			Maximum follow-up time			Maximum follow-up time		
Switching Time Shape parameter	1.4	2.0	3.0	1.4	2.0	3.0	1.4	2.0	3.0
0.2	0.6056	0.6057	0.6057	0.6056	0.6057	0.6057	0.6056	0.6057	0.6057
1.0	0.5266	0.5272	0.5272	0.5266	0.5272	0.5272	0.5266	0.5272	0.5272
3.5	0.4216	0.4217	0.4217	0.4216	0.4217	0.4217	0.4216	0.4217	0.4217

Common: Type where the switching effect remains constant over time.
Varying(A): Type where the switching effect decreases over time.
Varying(B): Type where the switching effect decreases by interval.

Figure 4.2 presents the Kaplan-Meier curves for the experimental and control groups under the common switching type scenario. The control group is represented in two cases: one for individuals who experienced switching and one for those who did not, both originating from the same control group. As shown in Figure 4.1, the survival probability of the experimental group is higher than that of the control group. Moreover, the survival curve for the switched control group is closer to that of the experimental group than the non-switched control group. This suggests that when the treatment has a positive effect, switching reduces the observed treatment effect.

Figure 4.3 illustrates the survival curves for the experimental and control groups under three types of switching scenarios. As shown in the figure, the survival curves for the varying types are lower than those for the common type. Varying(A) demonstrates a gradual decline in survival probability over time compared to the common type. In contrast, Varying(B) exhibits a different pattern of decline compared to Varying(A). It should be noted that Figures 4.2 and 4.3 are illustrative examples derived from a single simulation among multiple conducted simulations.

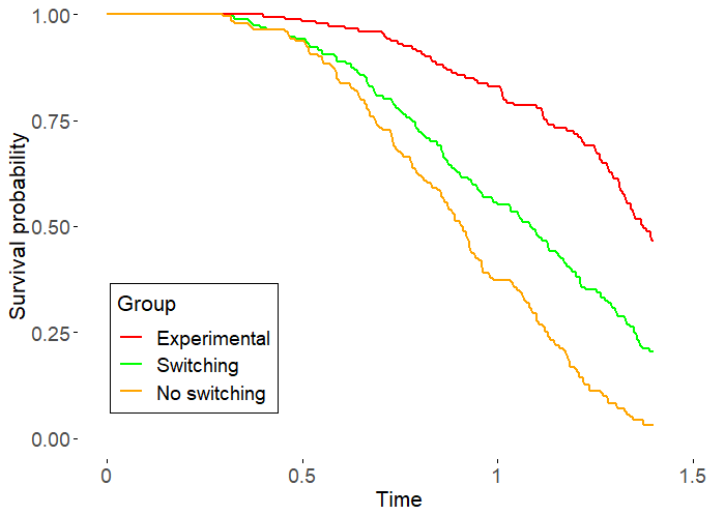


Figure 4.2 Example of Kaplan-Meier Curves by Switching Status under the Common Switching Type ($\beta = 0.4$, $\rho_S = 1.0$, $C_L = 1.4$, Sample Size per Group = 200)

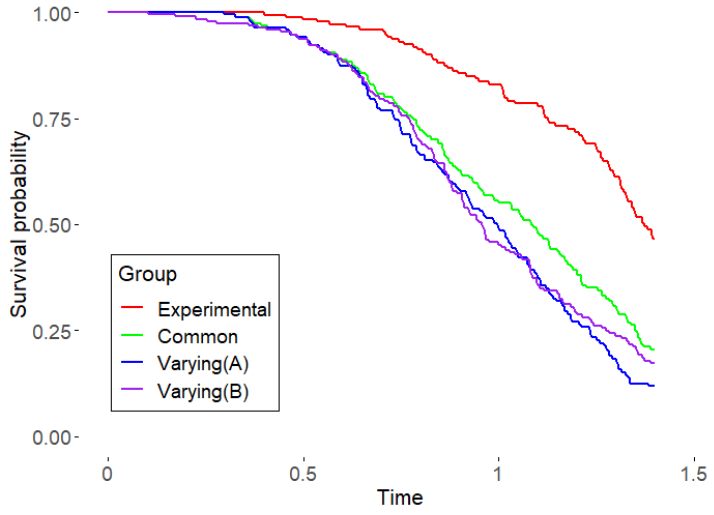


Figure 4.3 Example of Kaplan-Meier Curves by Various Switching type ($\beta = 0.4$, $\rho_S = 1.0$, $C_L = 1.4$, Sample Size per Group = 200)

4.3 Simulation Result

In this section, we evaluated the performance of the proposed methods and existing methods in estimating the true treatment effect (β) under various scenarios. Bias, variance, MSE, and CP were reported to evaluate the accuracy of the true treatment effect estimation across different scenarios and methodologies. Some of the scenarios considered in Section 4.1 are presented in the main text, while the remaining results are provided in the appendix. The scenarios included in the main text typically have a sample size per group of 200 and a maximum follow-up period of 1.4. These conditions correspond to scenarios with a medium level of sample size and the highest censoring rate among those considered.

Table 4.3 presents the bias of treatment effect estimates by methodology. Specifically, it reports the bias for β and ρ_S under the scenario where the sample size per group is 200 and C_L is 1.4. In the common type, when $\beta \leq 0.2$, all the methodologies considered exhibited similar performance. However, for $\beta > 0.2$, the performance of AFT and IPE was inferior to that of the proposed methods. Overall, PAFT, CBS-OG, and PM-OG demonstrated comparable levels of bias. In the varying type A, AFT and IPE also exhibited relatively higher levels of bias compared to the proposed methods, consistent with the common type. However, AFT provided more accurate estimates as the switching rate decreased. In the varying type A, PAFT showed higher levels of bias compared to CBS-OG and PM-OG. This pattern was similarly observed in the varying type B.

These results are presented in Figures 4.4, 4.5, and 4.6 equally. Table 4.3 and Figure

4.4, 4.5, 4.6 illustrate the bias values across various combination of β and ρ_S The parameter β represents the true treatment effect, while ρ_S is a parameter associated with the switching rate. In particular, when ρ_S is 0.2, the switching rate is notably high; however, as ρ_S increase, the switching rate gradually decreases.

Figure 4.4 illustrates the bias of each method across scenarios under the common type. PAFT, CBS-OG, and PM-OG consistently exhibited low bias across the evaluated scenarios. In contrast, AFT maintained low bias when $\beta \leq 0.2$ but experienced a notable increase in bias when β exceeded 0.2. The bias for AFT was particularly pronounced under high switching rates and decreased as the switching rate lowered. On the other hand, IPE displayed consistently biased results, tending to underestimate when $\beta \leq 0.1$ and overestimate when $\beta \geq 0.4$. Moreover, IPE's estimates of β remained unaffected by the switching rate.

Additionally, as observed in Appendix 2 Table A.3, A.4, and A.5, for the Common type, the differences across sample sizes were not substantial, but there was a slight decrease in bias as the sample size increased. PAFT, CBS-OG, and PM-OG were not significantly influenced by the censoring rate, whereas AFT and IPE exhibited a tendency to underestimate as the censoring rate decreased. PAFT, CBS-OG, PM-OG, and IPE exhibited no significant differences across varying switching rates. In contrast, AFT demonstrated a tendency toward lower bias as the switching rate decreased.

Figure 4.5 illustrates the bias in treatment effect estimation for each method under the

Varying(A) type data. Overall, the results were similar to those in Figure 4.4. CBS-OG showed the best performance, followed closely by PM-OG. However, as β increased, PAFT showed increasing bias, and this difference became more pronounced as the switching rate decreased. AFT exhibited higher bias as β increased but showed significantly reduced bias when the switching rate was lower. This pattern is likely due to the data generation process, where the varying effect diminishes over time, IPE produced results consistent with those observed in Figure 4.4.

In Appendix 2 Table A.3, A.4, and A.5, for the Varying(A) type, no significant differences were observed across sample sizes. Overall, as the censoring rate decreased, the bias of most methods tended to decrease. CBS-OG and PM-OG consistently exhibited low bias across all scenarios. PAFT showed increasing bias as β increased, with the bias becoming more pronounced as the switching rate decreased. AFT exhibited relatively low bias when $\beta \leq 0.2$. However, when $\beta \geq 0.3$, AFT's bias increased, although it decreased as the switching rate became lower in these cases. IPE consistently produced biased results, tending to underestimate as the censoring rate decreased.

Figure 4.6 illustrates the bias in treatment effect estimation for each method under the Varying(B) type data. Similarly, CBS-OG demonstrated the best performance, followed by PM-OG and PAFT, with minimal performance differences between PM-OG and PAFT. PAFT exhibited lower bias than with the Varying(A) type data. AFT showed low bias when $\beta \leq 0.2$, but its bias increased significantly when $\beta \geq 0.4$. However, as the switching rate decreased, AFT's bias tended to diminish. IPE displayed a tendency to underestimate β

when $\beta \leq 0.2$ and overestimate β when $\beta \geq 0.4$, while being largely unaffected by the switching rate.

In Appendix 2, Tables A.3, A.4, and A.5, the results for the Varying(B) type were similar to those for the Common type and Varying(A) type. While changes in bias according to sample size were not substantial, there was a general tendency for bias to decrease as the sample size increased. AFT exhibited slightly higher levels of bias compared to the results for the Varying(A) type, whereas IPE yielded results that were highly similar to those of the Varying(A) type. The proposed methodologies demonstrated superior performance compared to the existing methods. PAFT showed slightly lower levels of bias compared to the Varying(A) type, while CBS-OG and PM-OG exhibited slightly increased bias relative to the Varying(A) type. The performance of CBS-OG and PM-OG declined when the switching rate was high.

Table 4.3 Bias of Treatment Effect Estimates by Methodology (Sample Size per Group = 200, $C_L = 1.4$)

Bias				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
200	1.4	0.0	0.2	0.0004	-0.0094	0.0005	0.0006	0.0005	0.0004	-0.0094	0.0005	0.0006	0.0005	0.0004	-0.0094	0.0005	0.0006	0.0005
200	1.4	0.0	1.0	0.0004	-0.0094	0.0005	0.0006	0.0005	0.0004	-0.0094	0.0005	0.0009	0.0005	0.0004	-0.0094	0.0005	0.0009	0.0005
200	1.4	0.0	3.5	0.0004	-0.0094	0.0005	0.0006	0.0006	0.0004	-0.0094	0.0005	0.0011	0.0007	0.0004	-0.0094	0.0005	0.0011	0.0007
200	1.4	2.0	0.2	0.0016	0.0029	0.0001	0.0001	0.0001	0.0013	0.0029	0.0001	0.0001	0.0001	0.0015	0.0029	0.0001	0.0000	0.0000
200	1.4	2.0	1.0	0.0012	0.0029	0.0001	0.0001	0.0001	0.0004	0.0029	0.0000	0.0001	0.0001	0.0009	0.0029	0.0000	0.0001	0.0001
200	1.4	2.0	3.5	0.0009	0.0029	0.0001	0.0001	0.0001	0.0002	0.0029	0.0001	0.0001	0.0001	0.0004	0.0029	0.0000	0.0001	0.0002
200	1.4	4.0	0.2	0.0521	0.0252	0.0002	0.0001	0.0002	0.0435	0.0252	-0.0009	-0.0002	-0.0003	0.0508	0.0252	-0.0004	0.0008	0.0006
200	1.4	4.0	1.0	0.0387	0.0252	0.0005	0.0004	0.0005	0.0159	0.0252	-0.0024	-0.0002	-0.0001	0.0317	0.0252	-0.0024	0.0008	0.0022
200	1.4	4.0	3.5	0.0268	0.0252	0.0005	0.0004	0.0003	0.0041	0.0252	-0.0048	-0.0003	0.0020	0.0131	0.0252	-0.0026	0.0017	0.0034
200	1.4	5.0	0.2	0.1094	0.0379	-0.0005	-0.0007	-0.0006	0.0925	0.0379	-0.0029	-0.0017	-0.0018	0.1067	0.0379	-0.0021	-0.0004	-0.0009
200	1.4	5.0	1.0	0.0813	0.0379	-0.0003	-0.0003	-0.0002	0.0338	0.0379	-0.0062	-0.0019	-0.0017	0.0674	0.0379	-0.0060	-0.0005	0.0018
200	1.4	5.0	3.5	0.0559	0.0379	0.0000	-0.0001	-0.0001	0.0073	0.0379	-0.0124	-0.0022	0.0025	0.0267	0.0379	-0.0071	0.0005	0.0041

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

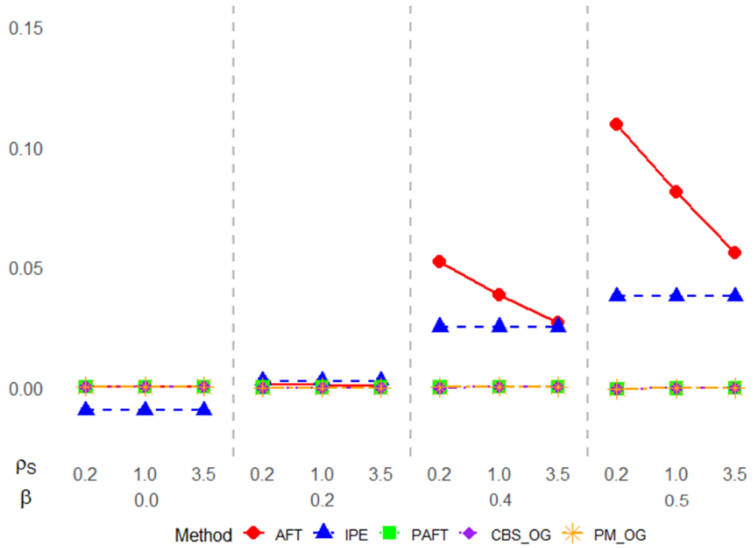


Figure 4.4 Bias of Treatment Effect Estimates by Methodology According to Treatment Effect and Switching Time Shape Parameter under Common Type (Sample Size per Group = 200, $C_L = 1.4$)

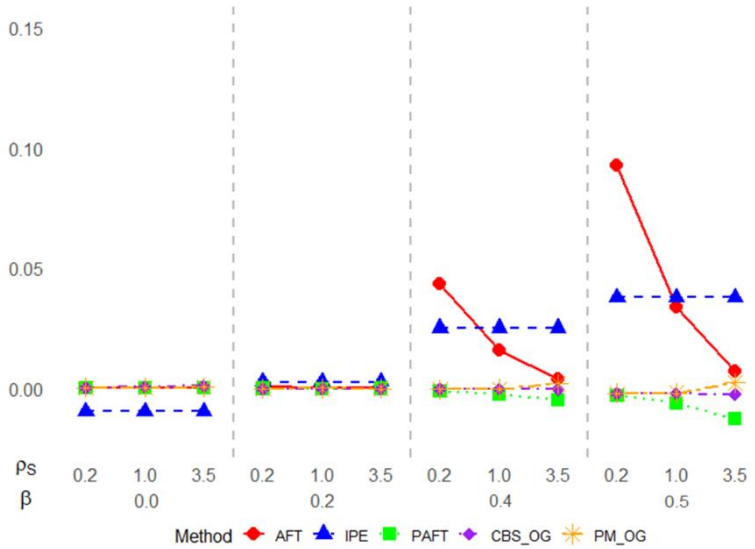


Figure 4.5 Bias of Treatment Effect Estimates by Methodology According to Treatment Effect and Switching Time Shape Parameter under Varying Type A (Sample Size per Group = 200, $C_L = 1.4$)

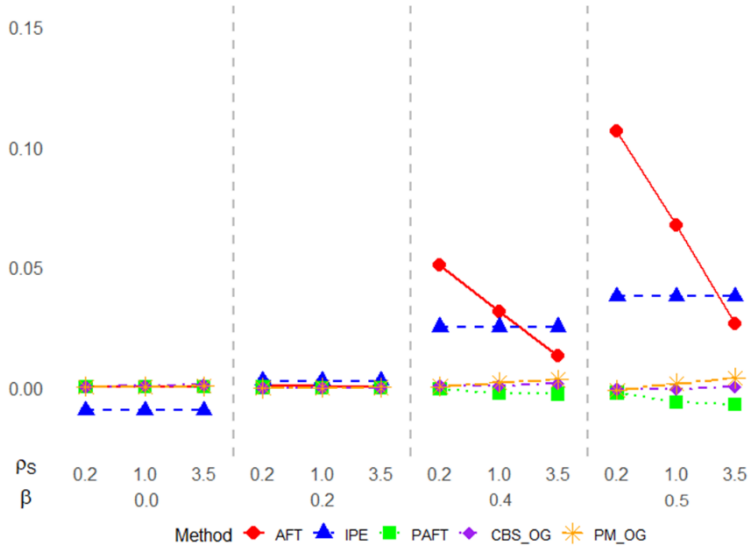


Figure 4.6 Bias of Treatment Effect Estimates by Methodology According to Treatment Effect and Switching Time Shape Parameter under Varying Type B (Sample Size per Group = 200, $C_L = 1.4$)

Table 4.4 presents the variance by methodology according to β and ρ_S under the conditions of a sample size per group of 200 and a maximum follow-up time of 1.4. The variance patterns were consistent across the Common type, Varying(A) type, and Varying(B) type. Overall, AFT showed the highest variance, followed by IPE, PM-OG, CBS-OG, and PAFT in descending order. The variance of IPE remained stable regardless of the switching rate, whereas the variance of the other methodologies tended to decrease as the switching rate decreased.

Appendix 2 Table A.6, A.7, and A.8 presents the variances of the β estimates for each method across different scenarios under the three data types. Upon examination, it was observed that in the Common type, the variance decreased as the sample size increased and as the censoring rate decreased. Overall, the variance was largest for AFT, followed by IPE, with PAFT, CBS-OG, and PM-OG exhibiting consistently lower and nearly identical variance values across all scenarios. For the Varying(A) type and Varying(B) type data, a similar pattern was observed, where PAFT, CBS-OG, and PM-OG maintain low variances across scenarios. In contrast, AFT and IPE showed relatively larger variances regardless of the data type, particularly in scenarios with smaller sample sizes for higher censoring rates.

Table 4.4 Variance of Treatment Effect Estimates by Methodology (Sample Size per Group = 200, $C_L = 1.4$)

Variance				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
200	1.4	0.0	0.2	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006
200	1.4	0.0	1.0	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006
200	1.4	0.0	3.5	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0005	0.0006	0.0006	0.0006	0.0006	0.0005	0.0006
200	1.4	0.2	0.2	0.0008	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007	0.0008	0.0008	0.0007	0.0007	0.0007
200	1.4	0.2	1.0	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007
200	1.4	0.2	3.5	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007
200	1.4	0.4	0.2	0.0021	0.0014	0.0012	0.0012	0.0012	0.0019	0.0014	0.0011	0.0012	0.0012	0.0020	0.0014	0.0012	0.0012	0.0012
200	1.4	0.4	1.0	0.0018	0.0014	0.0012	0.0012	0.0012	0.0014	0.0014	0.0011	0.0012	0.0012	0.0017	0.0014	0.0011	0.0012	0.0012
200	1.4	0.4	3.5	0.0016	0.0014	0.0012	0.0012	0.0012	0.0012	0.0014	0.0011	0.0012	0.0012	0.0013	0.0014	0.0011	0.0012	0.0012
200	1.4	0.5	0.2	0.0029	0.0019	0.0016	0.0016	0.0016	0.0029	0.0019	0.0016	0.0016	0.0016	0.0029	0.0019	0.0016	0.0016	0.0016
200	1.4	0.5	1.0	0.0028	0.0019	0.0016	0.0016	0.0016	0.0022	0.0019	0.0015	0.0016	0.0016	0.0027	0.0019	0.0015	0.0016	0.0016
200	1.4	0.5	3.5	0.0025	0.0019	0.0016	0.0016	0.0016	0.0017	0.0019	0.0014	0.0015	0.0016	0.0020	0.0019	0.0015	0.0016	0.0016

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table 4.5 presents the MSE by methodology for each data type under the conditions of a sample size per group of 200 and a maximum follow-up time of 1.4. No notable differences in the MSE patterns were observed across methodologies. In general, AFT exhibited the highest MSE, followed by IPE, while PAFT, CBS-OG, and PM-OG demonstrated similar levels of MSE. The MSE tended to increase as β increased. AFT showed a clear tendency for its MSE to decrease as the switching rate decreased. In contrast, the MSE of the other methodologies remained largely unchanged with respect to the switching rate.

Appendix 2 Table A.9, A.10, and A.11 presents the MSE for treatment effect estimates across methods and scenarios under the three data types. Across all data type, the MSE decreased with larger sample sizes and lower censoring rates. AFT and IPE showed relatively higher MSE values, whereas PAFT, CBS-OG, and PM-OG had comparable and consistently lower MSE values. When the maximum follow-up period was 2.0 or longer, the MSE for all methodologies remained consistently low.

Table 4.5 Mean Squared Error of Treatment Effect Estimates by Methodology (Sample Size per Group = 200, $C_L = 1.4$)

MSE				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
200	1.4	0.0	0.2	0.0006	0.0007	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006
200	1.4	0.0	1.0	0.0006	0.0007	0.0006	0.0005	0.0005	0.0006	0.0007	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006
200	1.4	0.0	3.5	0.0006	0.0007	0.0005	0.0005	0.0005	0.0006	0.0007	0.0005	0.0005	0.0006	0.0006	0.0007	0.0005	0.0005	0.0006
200	1.4	0.2	0.2	0.0008	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007	0.0008	0.0008	0.0007	0.0007	0.0007
200	1.4	0.2	1.0	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007
200	1.4	0.2	3.5	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0006	0.0007	0.0007
200	1.4	0.4	0.2	0.0048	0.0020	0.0012	0.0012	0.0012	0.0038	0.0020	0.0011	0.0011	0.0011	0.0046	0.0020	0.0011	0.0012	0.0012
200	1.4	0.4	1.0	0.0033	0.0020	0.0012	0.0012	0.0012	0.0017	0.0020	0.0011	0.0011	0.0011	0.0027	0.0020	0.0011	0.0012	0.0012
200	1.4	0.4	3.5	0.0023	0.0020	0.0012	0.0012	0.0012	0.0012	0.0020	0.0011	0.0011	0.0012	0.0015	0.0020	0.0011	0.0012	0.0012
200	1.4	0.5	0.2	0.0148	0.0033	0.0016	0.0016	0.0016	0.0114	0.0033	0.0016	0.0016	0.0015	0.0142	0.0033	0.0016	0.0016	0.0016
200	1.4	0.5	1.0	0.0094	0.0033	0.0016	0.0016	0.0016	0.0033	0.0033	0.0015	0.0015	0.0016	0.0072	0.0033	0.0015	0.0016	0.0016
200	1.4	0.5	3.5	0.0056	0.0033	0.0016	0.0016	0.0016	0.0017	0.0033	0.0015	0.0015	0.0016	0.0027	0.0033	0.0015	0.0016	0.0016

MSE: Mean squared error

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table 4.6 presents the CP by methodology for each data type under the conditions of a sample size per group of 200 and a maximum follow-up time of 1.4. Similar CP patterns were observed across the three data types. Overall, AFT and IPE exhibited lower CP compared to the proposed methods. While the proposed methods generally demonstrated high levels of CP, the CP of PAFT was slightly lower than that of CBS-OG and PM-OG for the varying type data. The proposed methods and IPE showed no significant changes in CP with respect to switching rate variations. In contrast, AFT exhibited a clear increase in CP levels as the switching rate decreased.

Appendix 2 Table A.12, A.13, and A.14 presents the CP values for treatment effect estimates across methods and scenarios under the three data types. CP exhibited a distinct pattern compared to variance or MSE. Across all data types, AFT demonstrated relatively good performance when the sample size was small. However, as the sample size increased, the CP values for AFT decreased in scenarios with higher censoring rates. Notable, when the censoring rate was low, AFT achieved performance comparable to the proposed methods. Overall, IPE showed relatively low CP values. While CBS-OG exhibited the best performance, its advantage over PM-OG and PAFT was not significant, indicating comparable performance among these methods.

Table 4.6 Coverage Probability of Treatment Effect Estimates by Methodology (Sample Size per Group = 200, $C_L = 1.4$)

CP				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
200	1.4	0.0	0.2	0.97	0.90	0.96	0.96	0.94	0.97	0.90	0.96	0.97	0.92	0.97	0.90	0.96	0.97	0.92
200	1.4	0.0	1.0	0.97	0.90	0.96	0.96	0.96	0.97	0.90	0.96	0.99	0.95	0.97	0.90	0.96	0.99	0.95
200	1.4	0.0	3.5	0.97	0.90	0.95	0.95	0.95	0.97	0.90	0.95	0.99	0.94	0.97	0.90	0.95	0.99	0.94
200	1.4	0.2	0.2	0.97	0.95	0.96	0.96	0.97	0.97	0.95	0.96	0.98	0.97	0.97	0.95	0.96	0.98	0.96
200	1.4	0.2	1.0	0.97	0.95	0.96	0.96	0.95	0.97	0.95	0.96	0.97	0.97	0.97	0.95	0.96	0.99	0.98
200	1.4	0.2	3.5	0.97	0.95	0.97	0.96	0.96	0.97	0.95	0.97	0.99	0.96	0.97	0.95	0.97	1.00	0.97
200	1.4	0.4	0.2	0.81	0.88	0.94	0.92	0.93	0.84	0.88	0.93	0.96	0.98	0.81	0.88	0.94	0.97	0.96
200	1.4	0.4	1.0	0.86	0.88	0.94	0.96	0.94	0.95	0.88	0.92	0.98	0.97	0.90	0.88	0.92	0.98	0.98
200	1.4	0.4	3.5	0.93	0.88	0.94	0.93	0.95	0.96	0.88	0.91	0.97	0.97	0.95	0.88	0.92	0.98	0.99
200	1.4	0.5	0.2	0.45	0.79	0.93	0.94	0.93	0.62	0.79	0.93	0.93	0.93	0.51	0.79	0.93	0.94	0.93
200	1.4	0.5	1.0	0.67	0.79	0.93	0.94	0.92	0.87	0.79	0.93	0.94	0.94	0.75	0.79	0.93	0.94	0.95
200	1.4	0.5	3.5	0.80	0.79	0.94	0.92	0.94	0.96	0.79	0.93	0.94	0.92	0.90	0.79	0.94	0.94	0.95

CP: Coverage probability

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table 4.7 and Figure 4.7, 4.8, and 4.9 present the bias of switching effect estimates at time 0 for each data type. Similar to the treatment effect bias figures, these scenarios are set with a sample size per group of 200 and C_L of 1.4, with the bias shown across various values of β and ρ_S. The comparison focused on the performance of CBS-CG, PAFT, CBS-OG, and PM-OG, which are designed to estimate the switching effect. However, the PM-OG method tended to unrealistically overestimate the switching effect at time 0 in scenarios with small β or low switching rates. To provide a clearer comparison of CBS-CG, PAFT, and CBS-OG, additional figures were included, excluding PM-OG, to focus on the results of these three methods.

Table 4.7 presents the bias of switching effect estimates by methodology as the switching time approaches 0, under the conditions of a sample size per group of 200 and a maximum follow-up time of 1.4. Across all three data types, PM-OG exhibited significantly high levels of bias in certain scenarios. Specifically, PM-OG showed higher bias with Varying(A) type data. Scenarios with high bias for PM-OG were commonly associated with small β and low switching rates. Conversely, in scenarios with large β or high switching rates, PM-OG occasionally outperformed other methodologies.

CBS-CG, PAFT, and CBS-OG generally demonstrated similar performance. However, PAFT exhibited low bias with Common type data but tended to show higher bias with Varying type data. CBS-OG showed slightly lower bias compared to CBS-CG, particularly in scenarios with low switching rates, where it demonstrated better performance.

Figure 4.7 illustrates the bias of switching effect estimates by methodology as switching time approaches 0 under the common type data. Panels (A) and (B) in Figure 4.7 present the same results, except that panel (A) includes PM-OG while panel (B) excludes it. In panel (A), the bias of PM-OG is significantly large when $\beta \leq 0.2$ but becomes smaller than that of other methods when $\beta \geq 0.3$. Notably, PM-OG showed better performance in scenarios with high switching rates. In panel (B), PAFT demonstrated the best performance, followed by CBS-OG and CBS-OG.

In Appendix 3 Table A.15, A.16, and A.17, the bias of switching effect estimates at time 0 under the common type data was examined. The results indicated a tendency for the bias to decrease as the sample size increased. No significant relationship was observed between the censoring rate and the bias. Consistent with the findings in Figure 4.7, PM-OG exhibited a very large bias when β was small, but as β increased, the bias of PM-OG became smaller compared to other methods. Overall, PAFT had the smallest bias, followed by CBS-OG and CBS-CG.

Table 4.7 Bias of Switching Effect Estimates by Methodology as Switching Time Approaches 0 (Sample Size per Group = 200, $C_L = 1.4$)

Bias				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
200	1.4	0.0	0.2	-0.0094	0.0001	-0.0115	1.1137	0.0031	0.0001	0.0036	1.2354	0.0031	0.0001	0.0036	1.2354
200	1.4	0.0	1.0	-0.0004	0.0010	-0.0008	1.0645	0.0032	0.0010	0.0047	1.2250	0.0032	0.0010	0.0047	1.2250
200	1.4	0.0	3.5	0.0103	0.0041	0.0090	0.9922	0.0309	0.0041	0.0443	1.1793	0.0309	0.0041	0.0443	1.1793
200	1.4	0.2	0.2	-0.0274	-0.0017	-0.0103	-0.0013	-0.0011	-0.0216	-0.0018	-0.0230	0.0082	-0.0036	0.0066	-0.0121
200	1.4	0.2	1.0	-0.0222	0.0004	-0.0101	0.0139	-0.0191	-0.0857	-0.0180	0.1599	0.0195	-0.0154	0.0196	0.0091
200	1.4	0.2	3.5	-0.0114	0.0061	0.0030	0.1014	-0.0713	-0.1419	-0.0741	0.8782	0.0322	-0.0715	0.0361	0.5627
200	1.4	0.4	0.2	-0.0265	-0.0036	-0.0045	-0.0034	0.0106	-0.0465	-0.0096	-0.0378	0.0220	-0.0084	0.0053	-0.0196
200	1.4	0.4	1.0	-0.0288	-0.0008	-0.0164	-0.0003	-0.0421	-0.1668	-0.0450	-0.1240	0.0224	-0.0394	0.0191	-0.0306
200	1.4	0.4	3.5	-0.0100	0.0035	0.0128	-0.0009	-0.1503	-0.1979	-0.1420	0.5731	0.0600	-0.1387	0.0460	0.0392
200	1.4	0.5	0.2	-0.0395	-0.0037	-0.0193	-0.0034	0.0140	-0.0617	-0.0156	-0.0477	0.0286	-0.0116	0.0007	-0.0271
200	1.4	0.5	1.0	-0.0357	-0.0011	-0.0294	0.0020	-0.0545	-0.1913	-0.0629	-0.1701	0.0209	-0.0525	0.0132	-0.0405
200	1.4	0.5	3.5	-0.0023	0.0053	0.0270	0.0015	-0.1759	-0.2000	-0.1837	0.4211	0.0559	-0.1648	0.0407	-0.0474

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

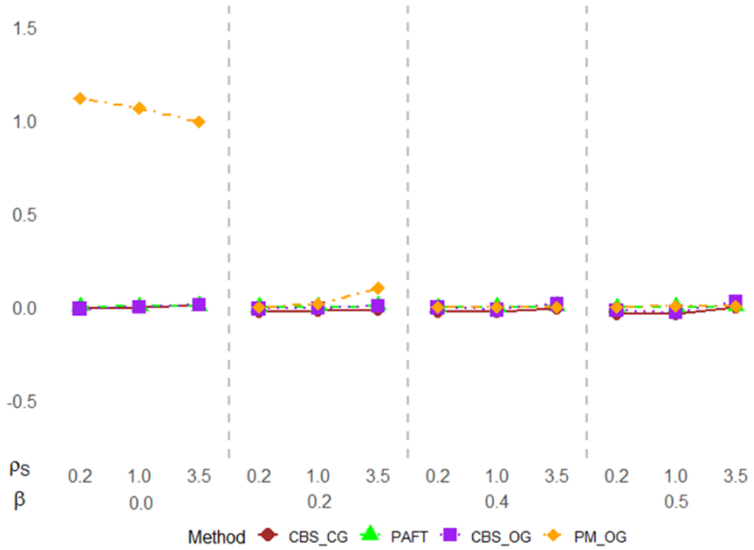
n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

CBS-CG: Cubic B-spline using control group.

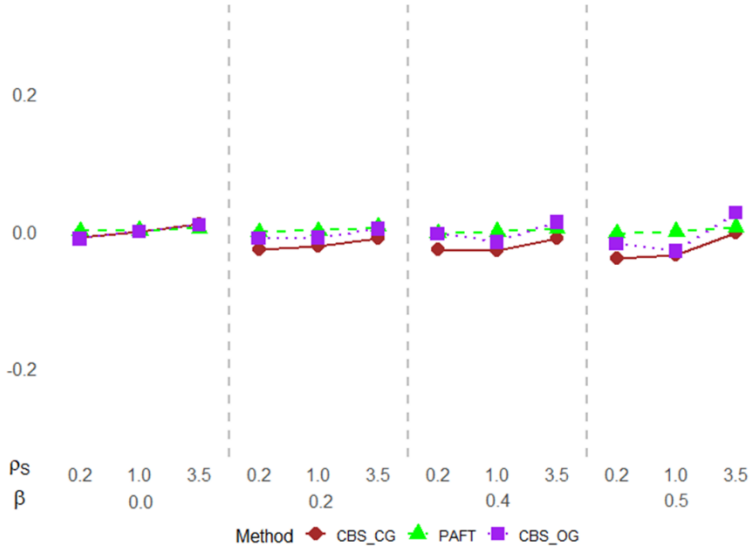
PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.



(A)



(B)

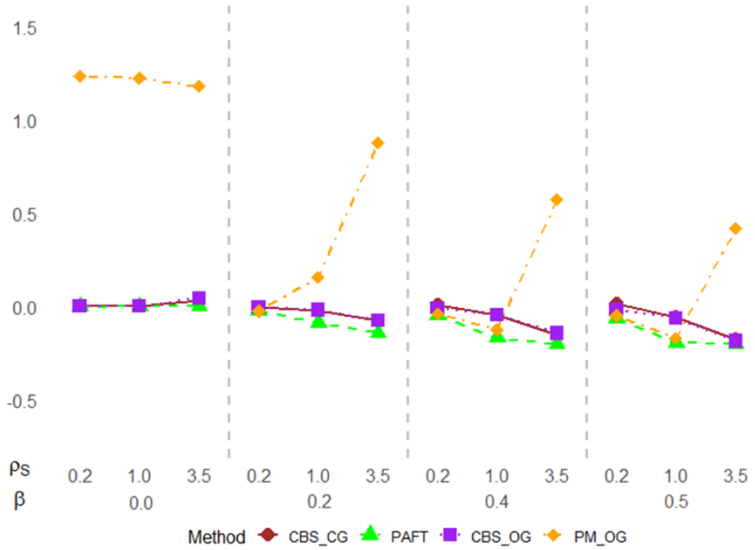
Figure 4.7 Bias of Switching Effect Estimates by Methodology as Switching Time Approaches 0 under Common Type (Sample Size per Group = 200, $C_L = 1.4$)

Figure 4.8 illustrates the bias of switching effect estimates by methodology as switching time approaches 0 under the Varying(A) type data. The bias of PM-OG was generally very large but became smaller in scenarios with larger β and higher switching rates. CBS-CG and CBS-OG displayed almost identical bias patterns. However, in scenarios with smaller β and higher switching rates, CBS-OG exhibited marginally lower bias than CBS-CG. PAFT performed worse than both CBS-CG and CBS-OG.

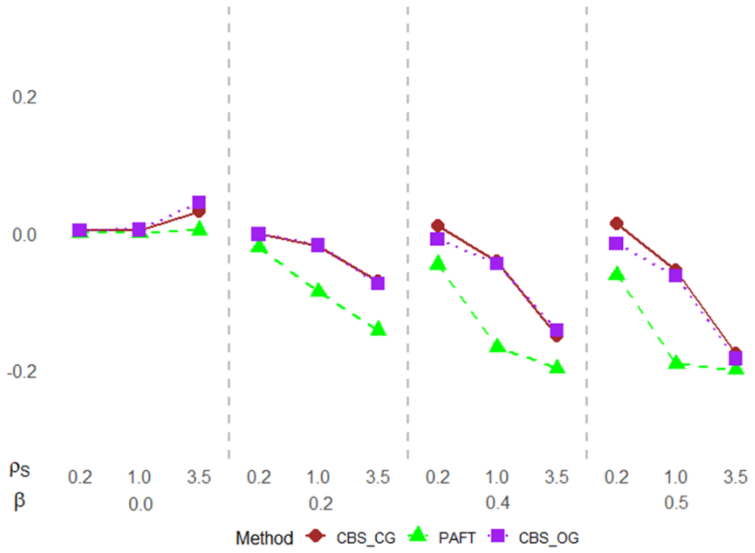
As examined in Appendix 3 Table A.15, A.16, and A.17, the bias generally decreased as the sample size increased. No evident relationship was found between the censoring rate and bias. Overall, PM-OG showed the poorest performance, followed by PAFT. CBS-CG and CBS-OG demonstrated nearly identical performance. However, in scenarios with smaller sample sizes, smaller β value, and higher switching rates, CBS-OG performed slightly better than CBS-CG.

Figure 4.9 illustrates the bias of switching effect estimates as the switching time approaches 0 under the Varying(B) type data. PM-OG demonstrated improved performance compared to Varying(A). Similar to Figures 4.7 and 4.8, PM-OG exhibited smaller bias in scenarios with larger β values or higher censoring rates. CBS-OG generally outperformed CBS-CG, while PAFT showed the poorest performance.

In Appendix 3 Table A.15, A.16, and A.17, PM-OG displayed a pattern similar to Figures 4.7 and 4.8. Overall, CBS-OG consistently performed slightly better than CBS-CG, while PAFT showed inferior performance compared to both.

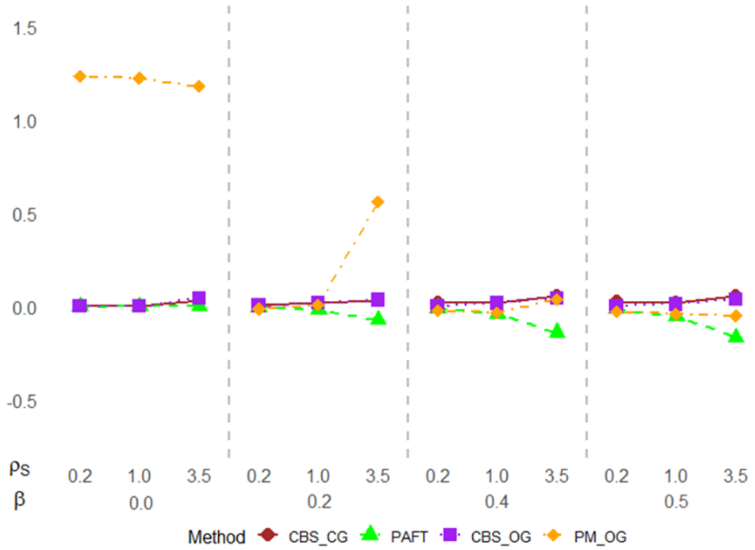


(A)

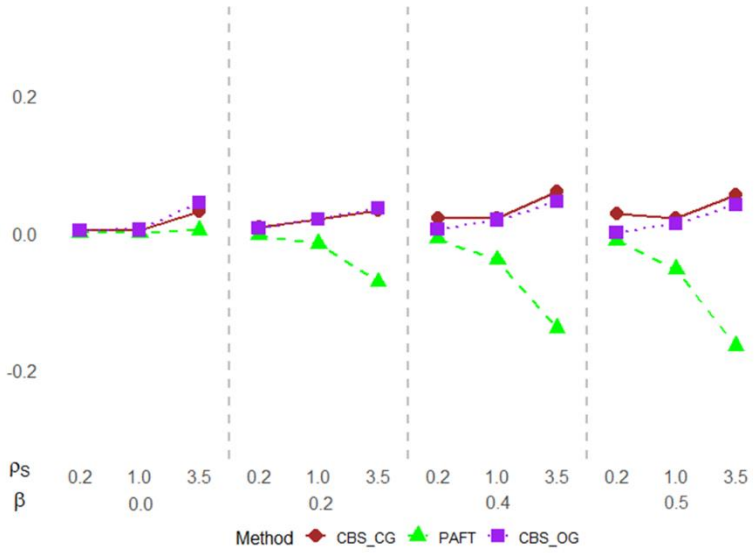


(B)

Figure 4.8 Bias of Switching Effect Estimates by Methodology as Switching Time Approaches 0 under Varying Type A (Sample Size per Group = 200, $C_L = 1.4$)



(A)



(B)

Figure 4.9 Bias of Switching Effect Estimates by Methodology as Switching Time Approaches 0 under Varying Type B (Sample Size per Group = 200, $C_L = 1.4$)

Table 4.8 presents the variance of switching effect estimates by methodology as the switching time approaches 0, under the conditions of a sample size per group of 200 and a maximum follow-up time of 1.4. Across all three data types, PM-OG exhibited high variance in scenarios with small β and low switching rates. Conversely, in scenarios with large β and high switching rates, PM-OG demonstrated the lowest variance. For the other methodologies, in the Common type, the variance was highest for CBS-CG, followed by CBS-OG and PAFT. In the Varying types, PAFT exhibited the lowest variance, while the variance of CBS-OG and CBS-CG was nearly identical.

Appendix 3 Table A.18, A.19, and A.20 presents the variances of switching effect estimates at Time 0 for each method across different scenarios under the three data types. For the common data type, the variance generally decreased as the sample size increased, with a particularly significant reduction observed for PM-OG. The relationship between the censoring rate and the variance was not distinct. However, the variance increased as the switching rate decreased. Among the methods, PAFT showed the lowest variance, followed by CBS-OG, CBS-CG, and PM-OG.

Similarly, for the Varying(A) type, the variance decreased as the sample size increased. In scenarios with high switching rates, all methods exhibited low variance, whereas the variance tended to grow as the switching rate decreased. Among the methods, PAFT exhibited the lowest variance, followed by PM-OG, CBS-OG, and CBS-CG. The variance difference between CBS-OG and CBS-CG was relatively small. Notably, a similar trend was observed for the Varying(B) type data.

Table 4.8 Variance of Switching Effect Estimates by Methodology as Switching Time Approaches 0 (Sample Size per Group = 200, $C_L = 1.4$)

Variance				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
200	1.4	0.0	0.2	0.0300	0.0009	0.0211	0.1536	0.0010	0.0009	0.0012	0.0199	0.0010	0.0009	0.0012	0.0199
200	1.4	0.0	1.0	0.0299	0.0018	0.0219	0.2019	0.0056	0.0018	0.0052	0.0315	0.0056	0.0018	0.0052	0.0315
200	1.4	0.0	3.5	0.0357	0.0053	0.0232	0.2700	0.0606	0.0053	0.0583	0.0770	0.0606	0.0053	0.0583	0.0770
200	1.4	0.2	0.2	0.0367	0.0011	0.0217	0.0012	0.0014	0.0011	0.0013	0.0016	0.0015	0.0011	0.0013	0.0017
200	1.4	0.2	1.0	0.0363	0.0022	0.0227	0.0147	0.0063	0.0020	0.0064	0.2065	0.0050	0.0022	0.0050	0.0395
200	1.4	0.2	3.5	0.0388	0.0059	0.0230	0.0963	0.0862	0.0032	0.0842	0.1618	0.0585	0.0052	0.0509	0.2978
200	1.4	0.4	0.2	0.0478	0.0017	0.0256	0.0018	0.0015	0.0015	0.0015	0.0019	0.0012	0.0017	0.0015	0.0012
200	1.4	0.4	1.0	0.0394	0.0026	0.0232	0.0036	0.0066	0.0012	0.0067	0.0146	0.0036	0.0025	0.0041	0.0028
200	1.4	0.4	3.5	0.0440	0.0070	0.0274	0.0111	0.0898	0.0001	0.0902	0.1971	0.0752	0.0040	0.0609	0.1024
200	1.4	0.5	0.2	0.0509	0.0024	0.0260	0.0025	0.0011	0.0019	0.0017	0.0019	0.0008	0.0022	0.0016	0.0016
200	1.4	0.5	1.0	0.0412	0.0035	0.0260	0.0047	0.0068	0.0004	0.0068	0.0049	0.0020	0.0033	0.0051	0.0031
200	1.4	0.5	3.5	0.0443	0.0083	0.0278	0.0114	0.0655	0.0000	0.0699	0.2047	0.0762	0.0024	0.0710	0.0606

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

CBS-CG: Cubic B-spline using control group.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table 4.9 presents the MSE of switching effect estimates by methodology as the switching time approaches 0, under the conditions of a sample size per group of 200 and a maximum follow-up time of 1.4. The MSE of PM-OG was significantly higher than that of other methodologies, but it decreased when β was large and the switching rate was high. Among the data types, the MSE of PM-OG was highest for the Varying(A) type.

For the other methodologies, in the Common type, CBS-CG exhibited the highest MSE, followed by CBS-OG and PAFT. Similarly, in the Varying types, PAFT demonstrated the lowest MSE. While the MSEs of CBS-OG and CBS-CG were similar, CBS-OG exhibited slightly lower MSE compared to CBS-CG.

Appendix 3 Table A.21, A.22, and A.23 presents the MSE of switching effect estimates at time 0 across methods and scenarios under the three data types. The MSE patterns for the common type and Varying(B) type were consistent with those observed for variance. However, in the Varying(A) type, CBS-OG performed well in scenarios with high switching rates but exhibited higher MSE in scenarios with low switching rates, indicating decreased accuracy in such cases.

Table 4.9 Mean Squared Error of Switching Effect Estimates by Methodology as Switching Time Approaches 0 (Sample Size per Group = 200, $C_L = 1.4$)

MSE				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
200	1.4	0.0	0.2	0.0298	0.0009	0.0210	1.3923	0.0010	0.0009	0.0012	1.5459	0.0010	0.0009	0.0012	1.5459
200	1.4	0.0	1.0	0.0296	0.0018	0.0217	1.3332	0.0055	0.0018	0.0052	1.5318	0.0055	0.0018	0.0052	1.5318
200	1.4	0.0	3.5	0.0354	0.0052	0.0230	1.2517	0.0609	0.0052	0.0597	1.4669	0.0609	0.0052	0.0597	1.4669
200	1.4	0.2	0.2	0.0371	0.0011	0.0216	0.0011	0.0014	0.0016	0.0013	0.0021	0.0015	0.0011	0.0014	0.0018
200	1.4	0.2	1.0	0.0364	0.0022	0.0226	0.0147	0.0066	0.0093	0.0066	0.2300	0.0053	0.0024	0.0053	0.0392
200	1.4	0.2	3.5	0.0386	0.0059	0.0228	0.1056	0.0904	0.0233	0.0889	0.9315	0.0590	0.0103	0.0517	0.6115
200	1.4	0.4	0.2	0.0481	0.0017	0.0254	0.0018	0.0016	0.0037	0.0016	0.0033	0.0016	0.0017	0.0015	0.0015
200	1.4	0.4	1.0	0.0398	0.0026	0.0233	0.0036	0.0083	0.0290	0.0087	0.0299	0.0041	0.0040	0.0044	0.0037
200	1.4	0.4	3.5	0.0436	0.0070	0.0273	0.0110	0.1115	0.0393	0.1094	0.5236	0.0780	0.0232	0.0624	0.1029
200	1.4	0.5	0.2	0.0519	0.0024	0.0261	0.0025	0.0013	0.0057	0.0019	0.0041	0.0016	0.0023	0.0016	0.0023
200	1.4	0.5	1.0	0.0421	0.0035	0.0266	0.0047	0.0097	0.0370	0.0107	0.0338	0.0024	0.0060	0.0053	0.0047
200	1.4	0.5	3.5	0.0438	0.0082	0.0283	0.0113	0.0958	0.0400	0.1029	0.3800	0.0785	0.0296	0.0720	0.0622

MSE: Mean squared error

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

CBS-CG: Cubic B-spline using control group.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Next, we evaluated the performance of CBS-CG, CBS-OG, and PM-OG in fitting the time-varying switching effects (TVSE) under Varying(A) and Varying(B) types. Consistent with previous simulation result figures, we selected scenarios with a sample size per group of 200 and the highest censoring rate. Specifically, we focused on scenarios where $\beta = 0.4$ and compared those with the highest and lowest switching rates.

In Figures 4.10 to 4.15, the true values are presented alongside the estimated values, with the MSE between the true and estimated values calculated. Simulations corresponding to the 5th, 25th, 50th, 75th, and 95th percentiles of MSE are included to represent the range of fitting accuracy across simulations. The result at the 5th percentile illustrates the best-fitting scenario, while the 95th percentile reflects the least accurate fit. This visualization provides a comprehensive assessment of the adequacy of each methodology in fitting the time-varying switching effect.

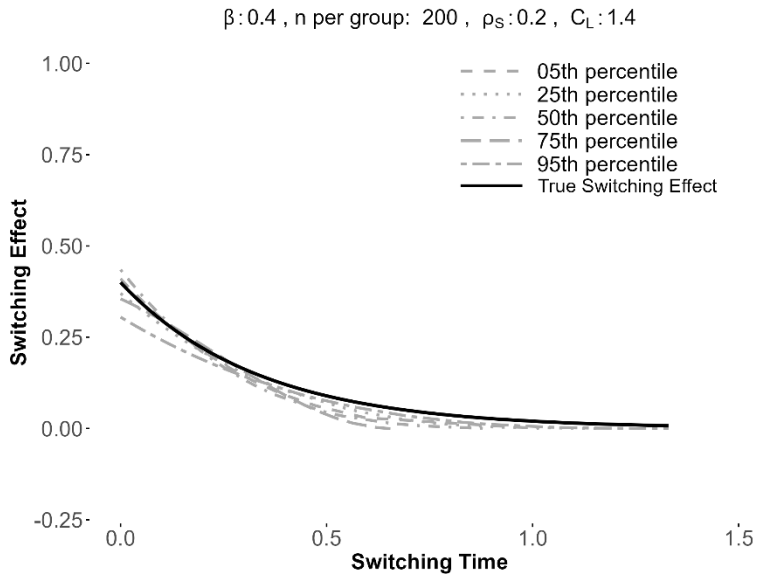
Figure 4.10, 4.11, and 4.12 illustrate the TVSE fitting for Varying(A) type data by each methodology. At $\rho = 0.2$, CBS-CG demonstrated the best fit, followed by CBS-OG and PM-OG. PM-OG provided a reasonably accurate piecewise estimation across intervals. At $\rho_S = 3.5$, CBS-OG showed slightly better fit than CBS-CG. The fit of PM-OG was lower compared to both CBS-OG and CBS-CG.

In Appendix 4, Figures A.1 to A.6 present the fitting results for the Varying(A) type data by methodology and β. Overall, the fitting of TVSE improved as the sample size increased, β became larger, and the switching rate was higher. For the Varying(A) type

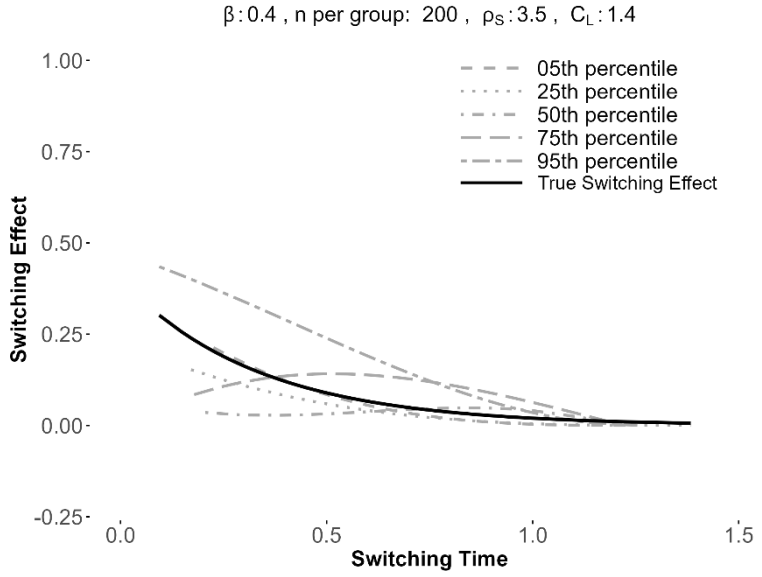
data, CBS-OG appeared to provide a slightly better fit for the TVSE compared to CBS-CG. Additionally, PM-OG was found to contribute to estimating the piecewise switching effect to some extent.

Figure 4.13, 4.14, and 4.15 present the TVSE fitting results for the Varying(B) type data. For $\rho = 0.2$, PM-OG provided the best fit, followed by CBS-OG and CBS-CG. Similarly, for $\rho_S = 3.5$, PM-OG again demonstrated the best fit, with CBS-OG slightly outperforming CBS-CG.

In Appendix 4, Figures A.7 to A.12 present the fitting results for the varying(B) type data by methodology and β. Similar to Figures A.1 to A.6, larger sample sizes, higher β values, and higher switching rates resulted in more accurate TVSE estimations. The superior performance of PM-OG can be attributed to its design, which aligns well with the characteristics of the data and the model. Meanwhile, CBS-CG and CBS-OG appeared to perform similarly.

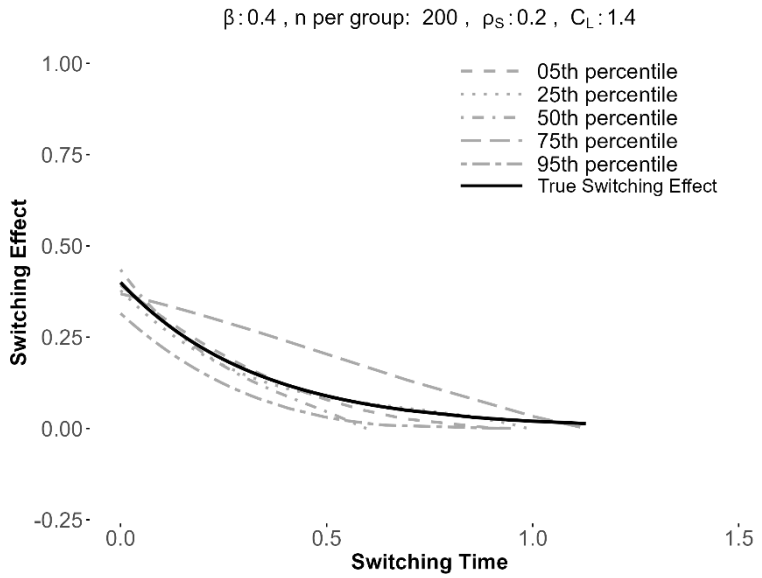


$\rho_S = 0.2$

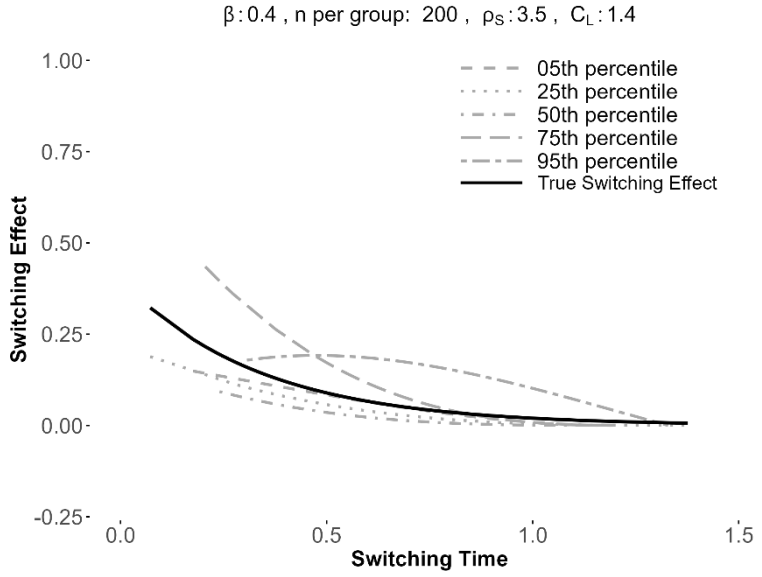


$\rho_S = 3.5$

Figure 4.10 Fit Results of the Varying Type A by CBS-CG Corresponding to the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE ($\beta = 0.4$, n per group = 200, Maximum follow-up period = 1.4)

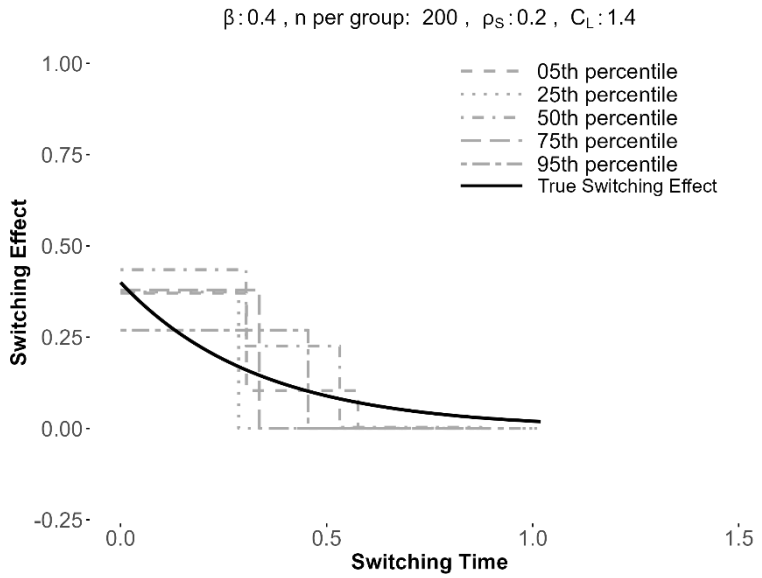


$\rho_S = 0.2$

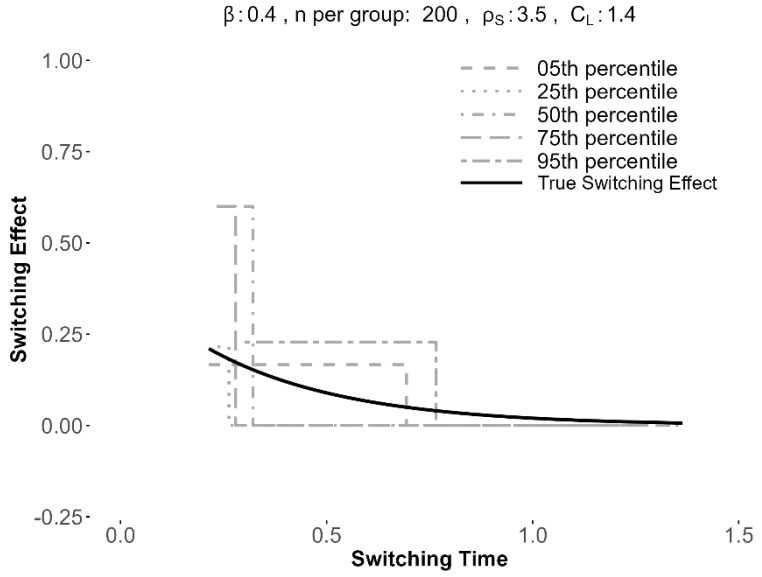


$\rho_S = 3.5$

Figure 4.11 Fit Results of the Varying Type A by CBS-OG Corresponding to the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE ($\beta = 0.4$, n per group = 200, Maximum follow-up period = 1.4)

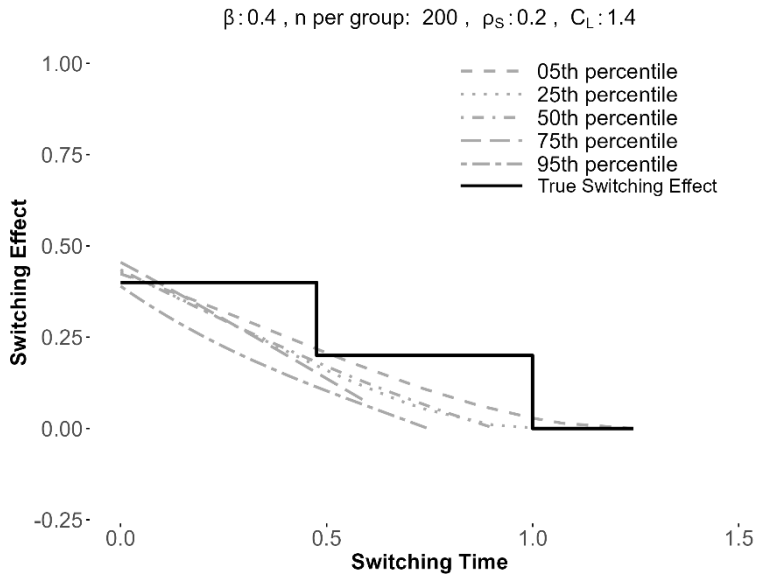


$\rho_S = 0.2$

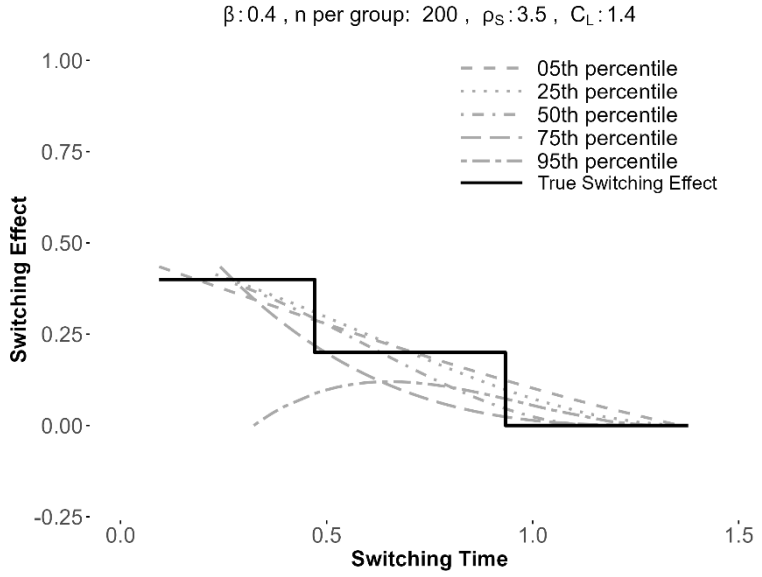


$\rho_S = 3.5$

Figure 4.12 Fit Results of the Varying Type A by PM-OG Corresponding to the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE ($\beta = 0.4$, n per group = 200, Maximum follow-up period = 1.4)

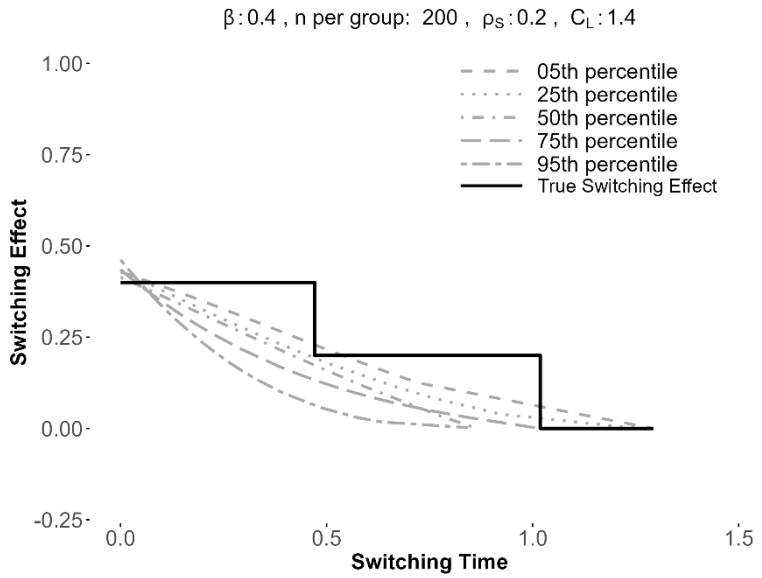


$\rho_S = 0.2$

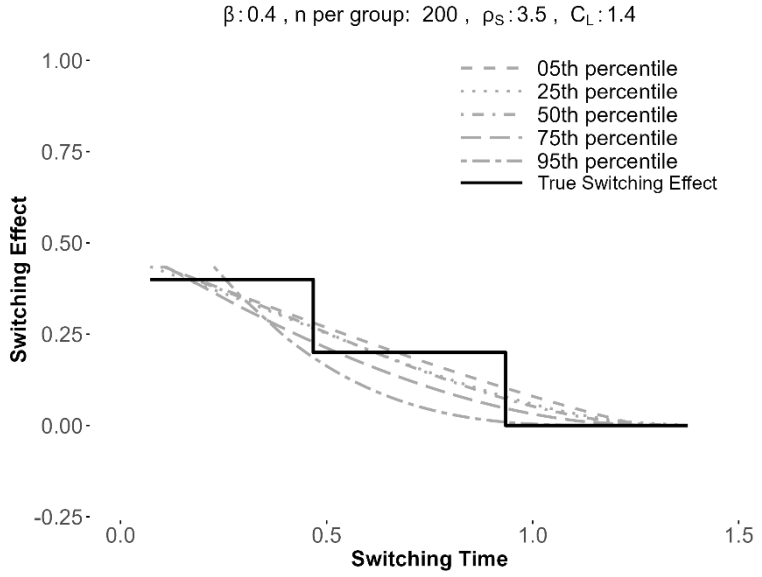


$\rho_S = 3.5$

Figure 4.13 Fit Results of the Varying Type B by CBS-CG Corresponding to the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE ($\beta = 0.4$, n per group = 200, Maximum follow-up period = 1.4)

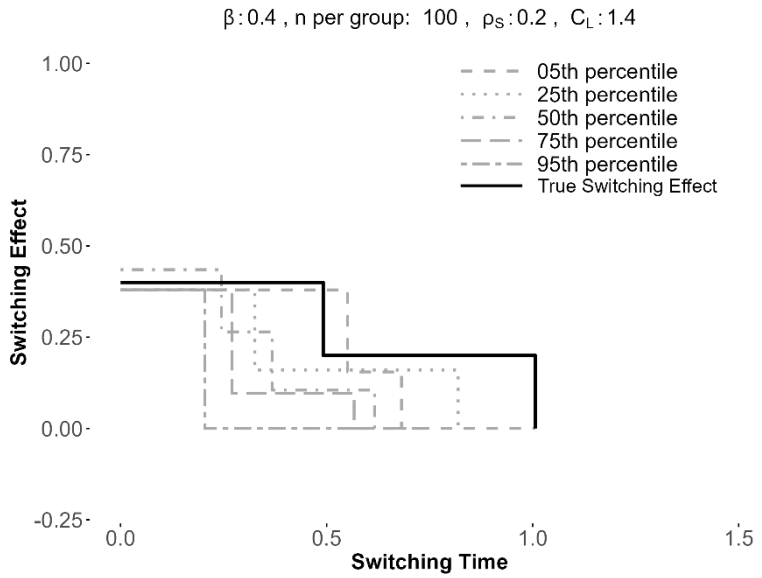


$\rho_S = 0.2$

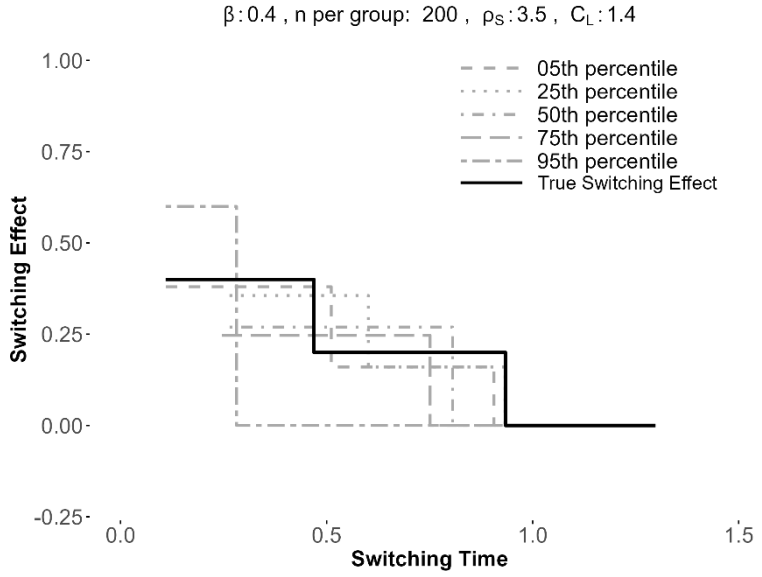


$\rho_S = 3.5$

Figure 4.14 Fit Results of the Varying Type B by CBS-OG Corresponding to the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE ($\beta = 0.4$, n per group = 200, Maximum follow-up period = 1.4)



$\rho_S = 0.2$



$\rho_S = 3.5$

Figure 4.15 Fit Results of the Varying Type B by PM-OG Corresponding to the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE ($\beta = 0.4$, n per group = 200, Maximum follow-up period = 1.4)

Chapter 5

Application to Real Data

5.1 Data Description

This study examined the impact of vascular access types on survival prognosis in chronic kidney disease (CKD) patients requiring hemodialysis. Vascular access methods include central venous catheters (CVC), arteriovenous fistulas (AVF), and arteriovenous grafts (AVG). It is well established that AVF or AVG are associated with better prognoses compared to CVC (Chu & Wang, 2023). This is because vascular access switching, particularly from CVC to AVF or AVG, is a common clinical occurrence (Bradbury et al., 2009). Using the proposed methodology, we aimed to account for switching and compare survival prognoses between CVC and AVF/AVG patients. For this study, we specifically focused on switching from CVC to AVF.

The analysis utilized data from the National Health Insurance Service Elderly Cohort Database (NHIS-2021-2-151), and the study received ethical approval from the Institutional Review Board of the National Health Insurance Service Ilsan Hospital (NHIMC 2021-04-008).

5.2 Study Population

The process for constructing the study population is outlined as follows. From the elderly cohort database, 18,319 individuals who received dialysis-related treatments between 2007 and 2019 were identified. Among these, individuals with CKD diagnoses or dialysis-related treatments between 2002 and 2006 were excluded, resulting in a remaining population of 15,326 individuals. Patients who received peritoneal dialysis (n = 639), hemofiltration, or hemodiafiltration (n = 8,369) during the observation period were also excluded. Additionally, 881 individuals with unclear initial dialysis types were removed.

To focus on patients receiving regular dialysis, those with fewer than 12 dialysis sessions within the first three months after their initial dialysis were excluded (n = 3,934). For a comparison between CVC and AVF, 69 individuals who received CVC, AVF, and AVG during the observation period were excluded, along with 314 individuals who received AVG.

The final study population consisted of 1,120 individuals. Patients who received a kidney transplant during the observation period were censored at the date of transplantation.

Of the final study population of 1,120 individuals, 767 belonged to the experimental group (AVF), and 354 to the control group (CVC). Among them, 1,075 participants did not experience an event during the observation period, resulting in a censoring rate of 95.98%. In the control group, 266 of 353 individuals switched to AVF, yielding a switching rate of 75.35%.

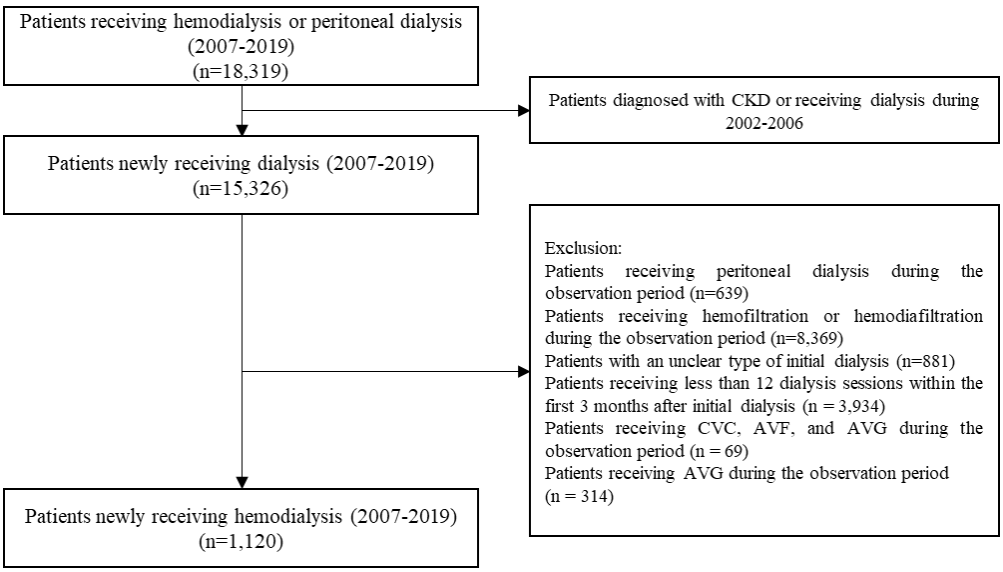


Figure 5.1 Flow Chart of the Study Population

5.3 Result

Figure 5.2 presents the survival curves comparing the CVC and AVF groups over 365 days following the initiation of hemodialysis. The results indicate that the AVF group exhibited better survival outcomes compared to the CVC group. However, the high switching rate from CVC to AVF (75.35%) may have led to an underestimation of the true effect of AVF. This suggests that, without switching, the survival difference between the groups could have been greater. To further examine this, the proposed methodology was employed to estimate the true treatment effect.

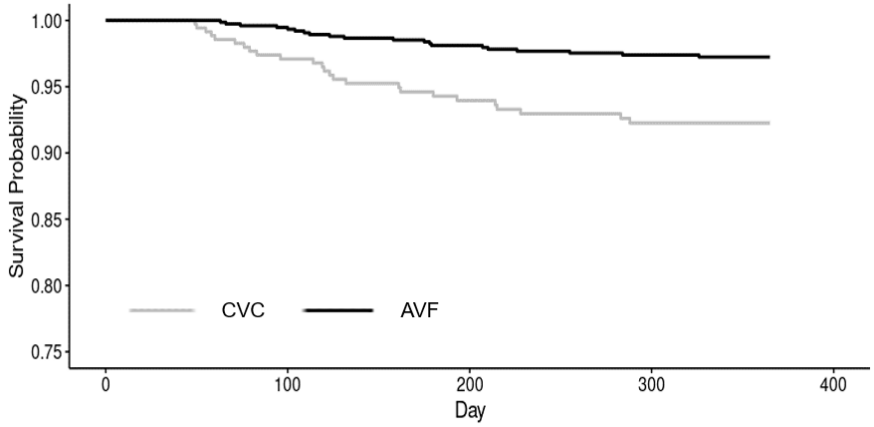


Figure 5.2 Kaplan-Meier Survival Curves by Type of Vascular Access in Chronic Kidney Disease

Table 5.1 summarizes the estimated treatment effects between CVC and AVF, including estimated values, 95% confidence intervals: AFT, IPE, PAFT, CBS-OG, and PM-OG. The $\hat{\beta}$ were as follows: 1.0681 for AFT, 1.7456 for IPE, 1.4989 for PAFT, 1.5073 for CBS-OG, and 1.4989 for PM-OG. Among the methodologies, AFT produced the smallest $\hat{\beta}$, while IPE yielded the largest. The $\hat{\beta}$ derived from the proposed methodologies clustered around 1.5.

Table 5.1 Estimated Treatment Effects by Methodology

Methods	$\hat{\beta}$	95% Confidence Interval
AFT	1.0681	(0.4258 - 1.7103)
IPE	1.7456	(1.0721 - 2.3073)
PAFT	1.4989	(0.8680 - 2.1297)
CBS-OG	1.5073	(0.8723 - 2.1422)
PM-OG	1.4989	(0.8800 - 2.1177)

CBS-OG and PM-OG were employed to estimate the TVSE. Figure 5.3 presents the TVSE estimated using CBS-OG, while Figure 5.4 illustrates the results obtained from PM-OG. The switching effect estimated by CBS-OG exhibited a decreasing trend over time. Initially, the switching effect was approximately 1.4 on the first switching day. By day 150, it had declined to around 0.5 and continued to decrease gradually throughout the remainder of the observation period.

In contrast, the estimates from PM-OG remained consistently above 1.0 over the observation period. Due to the characteristics of the PM-OG model, a piecewise decrease in the switching effect could be expected. However, as described in the methodology, we fitted models with different numbers of knots and selected the configuration that produced the lowest AIC value. In the dataset for this study, which involved the switching of vascular access methods in CKD patients, the result with zero knots had the lowest AIC. Consequently, we presented an estimate of a constant switching effect over the entire observation period without dividing it into intervals.

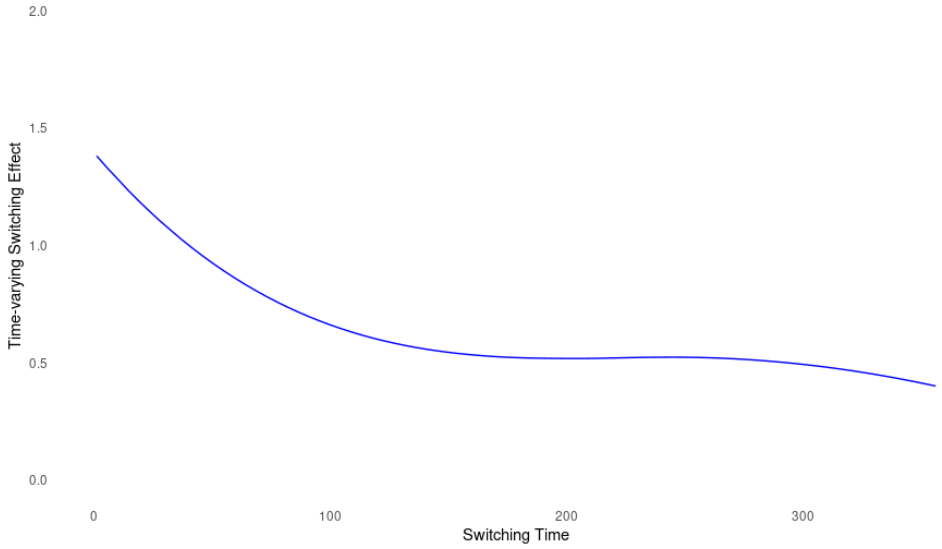


Figure 5.3 Estimated Time-varying Switching effect by CBS-OG

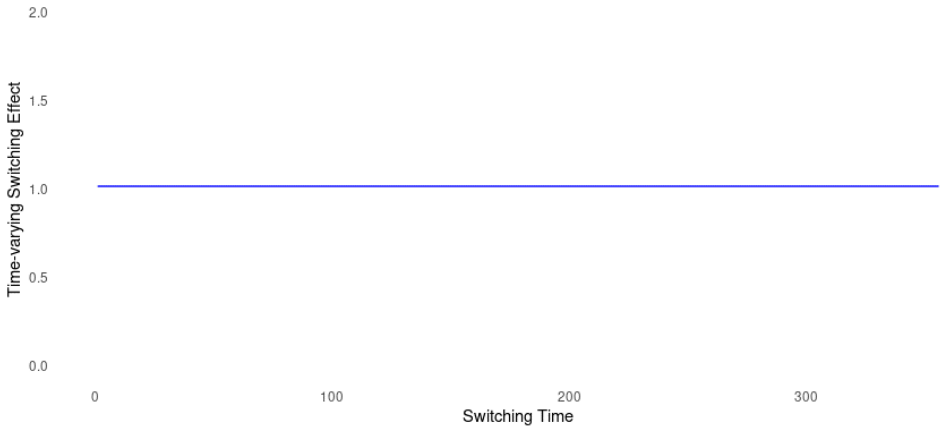


Figure 5.4 Estimated Time-varying Switching effect by PM-OG

Chapter 6

Conclusion

This study proposes a novel methodology to accurately estimate the true treatment effect in randomized clinical trials that allow treatment switching. Due to ethical considerations, treatment switching is permitted in many clinical trials. However, this can introduce bias when conventional methods are used to estimate treatment effects. To address this issue, methodologies that adjust for treatment switching have been developed.

Existing adjustment methods, such as IPCW, RPSFTM, and TSE, rely on strong assumptions. For example, RPSFTM assumes a common treatment effect, suggesting that the effect remains constant over time. however, this assumption is often unrealistic in clinical practice. The proposed methodology addresses these limitations by offering a more flexible framework for accurately estimating the true treatment effect.

Previous studies, such as those by Shao et al. (2005) and Chu and Wang (2023), have explored the TVSE modeling. Shao et al. (2005) employed a conditional likelihood approach, while Chu and Wang (2023) applied a full likelihood approach, focusing their estimation of the switching effect on a single group. Building on these studies, this research extends the full likelihood approach to model treatment switching across two groups. The proposed methodology introduces three models—PAFT, CBS-OG, and PM-OG—each

providing a flexible approach to fitting TVSE, enabling flexibility based on the specific characteristics of the TVSE.

The simulation results demonstrated that the proposed methodologies outperformed AFT and IPE in estimating the true treatment effect. The proposed methods consistently showed smaller bias, stable variance and MSE. Additionally, the confidence intervals were well-constructed, reflecting robust and reliable estimates.

In estimating the switching effect as switching time approaches 0, the proposed methodologies generally outperform CBS-CG. However, for the common type, PAFT demonstrated the best performance. In scenarios with relatively large treatment effects, the PM-OG methodology produced the most accurate results. While CBS-OG and CBS-CG produced similar outcomes, CBS-OG performed slightly better than CBS-CG in cases with smaller treatment effects or higher switching rates.

In assessing the accuracy of TVSE fitting over the observation period, CBS-CG and CBS-OG exhibited comparable performance. However, CBS-OG demonstrated slightly better performance than CBS-CG as the sample size increased, the treatment effect grew larger, and the switching rate rose. Conversely, PM-OG showed somewhat lower performance, likely due to differences in the model specification. Despite this, PM-OG demonstrated potential for effectively estimating piecewise switching effects.

The proposed methodologies were applied to real data to estimate treatment effects in cases of vascular access type switching among CKD patients. The results showed that the

survival estimates derived from the proposed methods—PAFT, CBS-OG, and PM-OG—showed greater improvements in survival prognosis for AVF patients compared to those obtained using AFT. Furthermore, the IPE method produced the most favorable survival outcomes among all methods, likely due to the high censoring rate. This finding aligns with the results observed in the simulations.

PAFT provides the advantage of estimating the overall switching effect and its confidence intervals across the entire observation period. CBS-OG demonstrated that as switching time approaches zero, the switching effect aligns closely with the treatment effect and generally follows a decreasing pattern over time. PM-OG, which does not partition the observation period into intervals, produced results comparable to those of PAFT.

This study proposes an AFT model that adjusts for TVSE to estimate the true treatment effect. From another perspective, if no treatment effect exists, no switching occurs, or the switching effect is common, the proposed methods may be unnecessarily complex. To address this, the study introduces simplified models, including the PAFT model, which fits a common switching effect, and the PM-OG model, which estimates switching effects by intervals.

The PAFT model mitigates the assumption of a common treatment effect by estimating the average switching effect after switching. The PM-OG model effectively captures interval-specific switching effects. In contrast, while cubic B-spline-based methods offer the advantage of flexibly estimating switching effects, they are limited in quantifying the

magnitude of the switching effect. PM-OG serves as a compromise, addressing the limitations of both PAFT and cubic B-spline methods.

This study develops and applies methodologies based on the assumption that switching occurs after disease progression. However, in real clinical settings, switching may be driven by factors other than disease progression. Additionally, patients may switch to treatments other than the experimental one, or those in the experimental group may switch to the control group due to adverse effects. Therefore, careful consideration is required when applying the proposed methodologies to real clinical data and interpreting the results.

Future research could focus on expanding the model to address the aforementioned cases. Additionally, this study primarily focuses on estimating treatment and switching effects. Therefore, future studies could statistically test for the presence of switching effects or evaluate whether they vary over time.

In conclusion, the proposed methodologies outperform existing approaches in reducing bias and producing stable estimates, as demonstrated through simulations and real data applications. Although the proposed methodologies enhance accuracy, careful consideration is required when applying them to real clinical data. It is advisable to analyze the data from multiple perspectives, including treatment effect levels, switching rates, and censoring rates. Following this preliminary analysis, both existing and proposed methodologies should be employed to derive comprehensive and robust conclusions.

Bibliography

Allison, A., White, I. R., & Bond, S. (2017). rpsftm: An R Package for Rank Preserving Structural Failure Time Models. *The R journal, 9*(2), 342–353.

Bowden, J., Seaman, S., Huang, X., & White, I. R. (2016). Gaining power and precision by using model-based weights in the analysis of late stage cancer trials with substantial treatment switching. *Statistics in medicine*, *35*(9), 1423–1440. https://doi.org/10.1002/sim.6801

Bradbury, B. D., Chen, F., Furniss, A., Pisoni, R. L., Keen, M., Mapes, D., & Krishnan, M. (2009). Conversion of vascular access type among incident hemodialysis patients: description and association with mortality. *American journal of kidney diseases : the official journal of the National Kidney Foundation, 53*(5), 804–814. https://doi.org/10.1053/j.ajkd.2008.11.031

Branson, M., & Whitehead, J. (2002). Estimating a treatment effect in survival studies in which patients switch treatment. *Statistics in medicine, 21*(17), 2449–2463. https://doi.org/10.1002/sim.1219

BSpline. (2024, August 26). SciPy. https://docs.scipy.org/doc/scipy/reference/generated/

scipy.interpolate.BSpline.html

Chu, F. I., & Wang, Y. (2023). Estimating Time-Varying Treatment Switching Effect Using Accelerated Failure Time Model with Application to Vascular Access for Hemodialysis. *Communications in statistics: theory and methods, 52*(15), 5145–5154. https://doi.org/10.1080/03610926.2021.2004423

Friedman, L. M., Furberg, C. D., DeMets, D. L., Reboussin, D. M., & Granger, C. B. (2015). *Fundamentals of clinical trials* (pp.1-17). Springer.

Hastie, T., Tibshirani, R., & Friedman, J. (2009). *The elements of statistical learning: Data mining, inference, and prediction* (pp.219-260). Springer.

Kim, J. (2016). *Introduction to survival analysis with R* (pp.67-93). Freeacademy.

Klein, J. P., & Moeschberger, M. L. (2006). *Survival analysis: techniques for censored and truncated data* (pp.393-423). Springer Science & Business Media.

Latimer, N. R., & Abrams, K. R. (2014). *NICE DSU Technical Support Document 16: Adjusting Survival Time Estimates in the Presence of Treatment Switching* (pp.8-11). National Institute for Health and Care Excellence (NICE).

Latimer, N. R., Abrams, K. R., Lambert, P. C., Crowther, M. J., Wailoo, A. J., Morden, J. P., Akehurst, R. L., & Campbell, M. J. (2014). Adjusting survival time estimates to account for treatment switching in randomized controlled trials--an economic evaluation context: methods, limitations, and recommendations. *Medical decision making : an international journal of the Society for Medical Decision Making, 34*(3), 387–402. https://doi.org/10.1177/0272989X13520192

Latimer, N. R., Abrams, K. R., Lambert, P. C., Crowther, M. J., Wailoo, A. J., Morden, J. P., Akehurst, R. L., & Campbell, M. J. (2017). Adjusting for treatment switching in randomised controlled trials - A simulation study and a simplified two-stage method. *Statistical methods in medical research, 26*(2), 724–751. https://doi.org/10.1177/0962280214557578

Latimer, N. R., Abrams, K. R., Lambert, P. C., Morden, J. P., & Crowther, M. J. (2018). Assessing methods for dealing with treatment switching in clinical trials: A follow-up simulation study. *Statistical methods in medical research, 27*(3), 765–784. https://doi.org/10.1177/0962280216642264

Lee, T. J., Bae, E. Y., Kang, E. J., Bae, S. J., Ahn, H. J., Cho, M. W., Han, S. K., Hong, J. H., & Lee, Y. S. (2019). *A study on the revision plan for the guidelines on economic*

evaluation of pharmaceuticals (pp.9-10). Health Insurance Review & Assessment Service.

Lyche, T., & Morken, K. (2008). *Spline methods draft* (pp.37-56). Department of Informatics, University of Oslo.

Morden, J. P., Lambert, P. C., Latimer, N., Abrams, K. R., & Wailoo, A. J. (2011). Assessing methods for dealing with treatment switching in randomised controlled trials: a simulation study. *BMC medical research methodology, 11,* 4. https://doi.org/10.1186/1471-2288-11-4

Nielsen, H. B., & Mortensen, S. B. (2022). *ucminf: General-purpose unconstrained non-linear optimization* (Version 1.1-4.1) [R package]. R Foundation for Statistical Computing. https://CRAN.R-project.org/package=ucminf

Pharmaceutical Benefits Advisory Committee. (2013). *Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee* (pp.23-59). Pharmaceutical Benefits Advisory Committee.

Piegl, L., & Tiller, W. (2012). *The NURBS book* (pp.47-79). Springer Science & Business Media.

R Core Team. (2022). *R: A language and environment for statistical computing. R Foundation for Statistical Computing*. https://www.R-project.org/

Robins, J. M., & Tsiatis, A. A. (1991). Correcting for non-compliance in randomized trials using rank preserving structural failure time models. *Communications in statistics-Theory and Methods, 20*(8), 2609-2631.

Shao, J., Chang, M., & Chow, S. C. (2005). Statistical inference for cancer trials with treatment switching. *Statistics in medicine, 24*(12), 1783–1790. https://doi.org/10.1002/sim.2128

Watkins, C., Huang, X., Latimer, N., Tang, Y., & Wright, E. J. (2013). Adjusting overall survival for treatment switches: commonly used methods and practical application. *Pharmaceutical statistics, 12*(6), 348–357. https://doi.org/10.1002/pst.1602

Zeng, D., Chen, Q., Chen, M. H., Ibrahim, J. G., & AMGEN RESEARCH GROUP (2012). Estimating treatment effects with treatment switching via semicompeting risks models: an application to a colorectal cancer study. *Biometrika, 99*(1), 167–184. https://doi.org/10.1093/biomet/asr062

Appendices

Appendix I

Table A.1 Rates of Censoring by Switching Type, Follow-up Period, Treatment Effect, Sample Size per Group, Switching Time Shape Parameter

Censoring Rate			Common			Varying(A)			Varying(B)		
			Maximum follow-up time			Maximum follow-up time			Maximum follow-up time		
β	n	ρ_S	1.4	2.0	3.0	1.4	2.0	3.0	1.4	2.0	3.0
0.0	100	0.2	0.2066	0.1794	0.1794	0.2066	0.1794	0.1794	0.2066	0.1794	0.1794
0.0	100	1.0	0.2066	0.1794	0.1794	0.2066	0.1794	0.1794	0.2066	0.1794	0.1794
0.0	100	3.5	0.2066	0.1794	0.1794	0.2066	0.1794	0.1794	0.2066	0.1794	0.1794
0.0	200	0.2	0.2118	0.1836	0.1836	0.2118	0.1836	0.1836	0.2118	0.1836	0.1836
0.0	200	1.0	0.2118	0.1836	0.1836	0.2118	0.1836	0.1836	0.2118	0.1836	0.1836
0.0	200	3.5	0.2118	0.1836	0.1836	0.2118	0.1836	0.1836	0.2118	0.1836	0.1836
0.0	500	0.2	0.2070	0.1791	0.1791	0.2070	0.1791	0.1791	0.2070	0.1791	0.1791
0.0	500	1.0	0.2070	0.1791	0.1791	0.2070	0.1791	0.1791	0.2070	0.1791	0.1791
0.0	500	3.5	0.2070	0.1791	0.1791	0.2070	0.1791	0.1791	0.2070	0.1791	0.1791
0.2	100	0.2	0.3244	0.2126	0.2112	0.3184	0.2112	0.2097	0.3238	0.2126	0.2112
0.2	100	1.0	0.3117	0.2083	0.2070	0.2950	0.2047	0.2035	0.3076	0.2082	0.2070
0.2	100	3.5	0.3006	0.2047	0.2036	0.2836	0.2016	0.2006	0.2902	0.2038	0.2034
0.2	200	0.2	0.3265	0.2168	0.2148	0.3206	0.2157	0.2137	0.3257	0.2167	0.2148

Censoring Rate			Common			Varying(A)			Varying(B)		
			Maximum follow-up time			Maximum follow-up time			Maximum follow-up time		
β	n	ρ_S	1.4	2.0	3.0	1.4	2.0	3.0	1.4	2.0	3.0
0.2	200	1.0	0.3143	0.2136	0.2119	0.2984	0.2096	0.2082	0.3102	0.2135	0.2118
0.2	200	3.5	0.3036	0.2098	0.2082	0.2881	0.2067	0.2052	0.2940	0.2089	0.2080
0.2	500	0.2	0.3237	0.2123	0.2108	0.3176	0.2107	0.2093	0.3228	0.2122	0.2108
0.2	500	1.0	0.3102	0.2081	0.2068	0.2944	0.2045	0.2035	0.3061	0.2078	0.2068
0.2	500	3.5	0.2993	0.2046	0.2034	0.2843	0.2013	0.2003	0.2900	0.2036	0.2033
0.4	100	0.2	0.4851	0.2752	0.2486	0.4714	0.2702	0.2458	0.4834	0.2750	0.2486
0.4	100	1.0	0.4528	0.2619	0.2398	0.4148	0.2503	0.2314	0.4424	0.2610	0.2396
0.4	100	3.5	0.4246	0.2504	0.2313	0.3880	0.2427	0.2251	0.4028	0.2481	0.2312
0.4	200	0.2	0.4863	0.2811	0.2534	0.4724	0.2760	0.2502	0.4845	0.2809	0.2533
0.4	200	1.0	0.4555	0.2675	0.2441	0.4181	0.2556	0.2362	0.4450	0.2666	0.2440
0.4	200	3.5	0.4279	0.2567	0.2366	0.3935	0.2480	0.2298	0.4077	0.2538	0.2363
0.4	500	0.2	0.4860	0.2744	0.2477	0.4709	0.2693	0.2446	0.4839	0.2742	0.2477
0.4	500	1.0	0.4532	0.2615	0.2391	0.4156	0.2499	0.2310	0.4428	0.2607	0.2390
0.4	500	3.5	0.4258	0.2510	0.2316	0.3903	0.2425	0.2248	0.4047	0.2484	0.2314
0.5	100	0.2	0.5605	0.3296	0.2700	0.5442	0.3220	0.2660	0.5588	0.3293	0.2700
0.5	100	1.0	0.5224	0.3084	0.2589	0.4732	0.2886	0.2471	0.5088	0.3072	0.2588
0.5	100	3.5	0.4858	0.2906	0.2479	0.4387	0.2780	0.2390	0.4572	0.2863	0.2477
0.5	200	0.2	0.5611	0.3338	0.2749	0.5439	0.3256	0.2708	0.5586	0.3336	0.2749
0.5	200	1.0	0.5221	0.3118	0.2626	0.4741	0.2928	0.2513	0.5091	0.3104	0.2625
0.5	200	3.5	0.4870	0.2947	0.2519	0.4418	0.2814	0.2429	0.4603	0.2904	0.2513
0.5	500	0.2	0.5611	0.3286	0.2697	0.5431	0.3202	0.2652	0.5582	0.3284	0.2696
0.5	500	1.0	0.5207	0.3078	0.2584	0.4719	0.2892	0.2474	0.5072	0.3063	0.2583
0.5	500	3.5	0.4846	0.2912	0.2483	0.4392	0.2786	0.2395	0.4574	0.2872	0.2480

Censoring Rate			Common			Varying(A)			Varying(B)		
			Maximum follow-up time			Maximum follow-up time			Maximum follow-up time		
β	n	ρ_S	1.4	2.0	3.0	1.4	2.0	3.0	1.4	2.0	3.0

Common: Type where the switching effect remains constant over time.
Varying(A): Type where the switching effect decreases over time.
Varying(B): Type where the switching effect decreases by interval.
β: Treatment effect
n: Sample size per group
ρ_S: Switching time shape parameter

Table A.2 Rates of Switching by Switching Type, Follow-up Period, Treatment Effect, Sample Size per Group, Switching Time Shape Parameter

Switching Rate			Common			Varying(A)			Varying(B)		
			Maximum follow-up time			Maximum follow-up time			Maximum follow-up time		
β	n	ρ_S	1.4	2.0	3.0	1.4	2.0	3.0	1.4	2.0	3.0
0.0	100	0.2	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097
0.0	100	1.0	0.5298	0.5302	0.5302	0.5298	0.5302	0.5302	0.5298	0.5302	0.5302
0.0	100	3.5	0.4289	0.4293	0.4293	0.4289	0.4293	0.4293	0.4289	0.4293	0.4293
0.0	200	0.2	0.6056	0.6057	0.6057	0.6056	0.6057	0.6057	0.6056	0.6057	0.6057
0.0	200	1.0	0.5266	0.5272	0.5272	0.5266	0.5272	0.5272	0.5266	0.5272	0.5272
0.0	200	3.5	0.4216	0.4217	0.4217	0.4216	0.4217	0.4217	0.4216	0.4217	0.4217
0.0	500	0.2	0.6076	0.6077	0.6077	0.6076	0.6077	0.6077	0.6076	0.6077	0.6077
0.0	500	1.0	0.5307	0.5313	0.5313	0.5307	0.5313	0.5313	0.5307	0.5313	0.5313
0.0	500	3.5	0.4271	0.4276	0.4276	0.4271	0.4276	0.4276	0.4271	0.4276	0.4276
0.2	100	0.2	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097
0.2	100	1.0	0.5298	0.5302	0.5302	0.5298	0.5302	0.5302	0.5298	0.5302	0.5302
0.2	100	3.5	0.4289	0.4293	0.4293	0.4289	0.4293	0.4293	0.4289	0.4293	0.4293
0.2	200	0.2	0.6056	0.6057	0.6057	0.6056	0.6057	0.6057	0.6056	0.6057	0.6057
0.2	200	1.0	0.5266	0.5272	0.5272	0.5266	0.5272	0.5272	0.5266	0.5272	0.5272
0.2	200	3.5	0.4216	0.4217	0.4217	0.4216	0.4217	0.4217	0.4216	0.4217	0.4217
0.2	500	0.2	0.6076	0.6077	0.6077	0.6076	0.6077	0.6077	0.6076	0.6077	0.6077
0.2	500	1.0	0.5307	0.5313	0.5313	0.5307	0.5313	0.5313	0.5307	0.5313	0.5313
0.2	500	3.5	0.4271	0.4276	0.4276	0.4271	0.4276	0.4276	0.4271	0.4276	0.4276
0.4	100	0.2	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097
0.4	100	1.0	0.5298	0.5302	0.5302	0.5298	0.5302	0.5302	0.5298	0.5302	0.5302

Switching Rate			Common			Varying(A)			Varying(B)		
			Maximum follow-up time			Maximum follow-up time			Maximum follow-up time		
β	n	ρ_S	1.4	2.0	3.0	1.4	2.0	3.0	1.4	2.0	3.0
0.4	100	3.5	0.4289	0.4293	0.4293	0.4289	0.4293	0.4293	0.4289	0.4293	0.4293
0.4	200	0.2	0.6056	0.6057	0.6057	0.6056	0.6057	0.6057	0.6056	0.6057	0.6057
0.4	200	1.0	0.5266	0.5272	0.5272	0.5266	0.5272	0.5272	0.5266	0.5272	0.5272
0.4	200	3.5	0.4216	0.4217	0.4217	0.4216	0.4217	0.4217	0.4216	0.4217	0.4217
0.4	500	0.2	0.6076	0.6077	0.6077	0.6076	0.6077	0.6077	0.6076	0.6077	0.6077
0.4	500	1.0	0.5307	0.5313	0.5313	0.5307	0.5313	0.5313	0.5307	0.5313	0.5313
0.4	500	3.5	0.4271	0.4276	0.4276	0.4271	0.4276	0.4276	0.4271	0.4276	0.4276
0.5	100	0.2	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097	0.6097
0.5	100	1.0	0.5298	0.5302	0.5302	0.5298	0.5302	0.5302	0.5298	0.5302	0.5302
0.5	100	3.5	0.4289	0.4293	0.4293	0.4289	0.4293	0.4293	0.4289	0.4293	0.4293
0.5	200	0.2	0.6056	0.6057	0.6057	0.6056	0.6057	0.6057	0.6056	0.6057	0.6057
0.5	200	1.0	0.5266	0.5272	0.5272	0.5266	0.5272	0.5272	0.5266	0.5272	0.5272
0.5	200	3.5	0.4216	0.4217	0.4217	0.4216	0.4217	0.4217	0.4216	0.4217	0.4217
0.5	500	0.2	0.6076	0.6077	0.6077	0.6076	0.6077	0.6077	0.6076	0.6077	0.6077
0.5	500	1.0	0.5307	0.5313	0.5313	0.5307	0.5313	0.5313	0.5307	0.5313	0.5313
0.5	500	3.5	0.4271	0.4276	0.4276	0.4271	0.4276	0.4276	0.4271	0.4276	0.4276

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

β: Treatment effect

n: Sample size per group

ρ_S: Switching time shape parameter

Appendix II

Table A.3 Bias of Treatment Effect Estimates by Methodology (Sample Size per Group = 100)

	Bias			Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
100	1.4	0.0	0.2	-0.0011	-0.0115	-0.0010	-0.0006	-0.0008	-0.0011	-0.0115	-0.0010	-0.0007	-0.0008	-0.0011	-0.0115	-0.0010	-0.0007	-0.0008
100	1.4	0.0	1.0	-0.0011	-0.0115	-0.0010	-0.0007	-0.0008	-0.0011	-0.0115	-0.0010	-0.0004	-0.0008	-0.0011	-0.0115	-0.0010	-0.0004	-0.0008
100	1.4	0.0	3.5	-0.0011	-0.0115	-0.0012	-0.0008	-0.0009	-0.0011	-0.0115	-0.0012	-0.0003	-0.0006	-0.0011	-0.0115	-0.0012	-0.0003	-0.0006
100	1.4	0.2	0.2	0.0012	0.0023	-0.0005	-0.0005	-0.0005	0.0009	0.0023	-0.0005	-0.0005	-0.0005	0.0012	0.0023	-0.0005	-0.0004	-0.0002
100	1.4	0.2	1.0	0.0008	0.0023	-0.0005	-0.0005	-0.0005	-0.0001	0.0023	-0.0006	-0.0005	-0.0004	0.0005	0.0023	-0.0006	-0.0004	-0.0003
100	1.4	0.2	3.5	0.0005	0.0023	-0.0004	-0.0005	-0.0003	-0.0004	0.0023	-0.0005	-0.0006	-0.0004	-0.0001	0.0023	-0.0005	-0.0005	-0.0002
100	1.4	0.4	0.2	0.0515	0.0241	-0.0014	-0.0019	-0.0015	0.0436	0.0241	-0.0021	-0.0020	-0.0018	0.0504	0.0241	-0.0020	-0.0007	-0.0008
100	1.4	0.4	1.0	0.0377	0.0241	-0.0013	-0.0019	-0.0016	0.0145	0.0240	-0.0044	-0.0023	-0.0012	0.0308	0.0240	-0.0041	-0.0003	0.0012
100	1.4	0.4	3.5	0.0251	0.0240	-0.0012	-0.0016	-0.0012	0.0015	0.0240	-0.0071	-0.0029	0.0000	0.0108	0.0240	-0.0051	-0.0003	0.0036
100	1.4	0.5	0.2	0.1101	0.0409	0.0011	0.0006	0.0009	0.0954	0.0412	-0.0006	-0.0003	-0.0005	0.1083	0.0409	0.0002	0.0015	0.0013
100	1.4	0.5	1.0	0.0844	0.0406	0.0019	0.0011	0.0014	0.0365	0.0405	-0.0047	-0.0006	0.0006	0.0708	0.0405	-0.0040	0.0023	0.0051
100	1.4	0.5	3.5	0.0578	0.0405	0.0019	0.0012	0.0015	0.0079	0.0404	-0.0112	-0.0020	0.0043	0.0273	0.0404	-0.0068	0.0021	0.0087
100	2.0	0.0	0.2	-0.0016	-0.0153	-0.0014	-0.0010	-0.0013	-0.0016	-0.0153	-0.0014	-0.0012	-0.0014	-0.0016	-0.0153	-0.0014	-0.0012	-0.0014
100	2.0	0.0	1.0	-0.0016	-0.0153	-0.0015	-0.0010	-0.0013	-0.0016	-0.0153	-0.0015	-0.0008	-0.0012	-0.0016	-0.0153	-0.0015	-0.0008	-0.0012
100	2.0	0.0	3.5	-0.0016	-0.0153	-0.0018	-0.0013	-0.0015	-0.0016	-0.0153	-0.0018	-0.0006	-0.0012	-0.0016	-0.0153	-0.0018	-0.0006	-0.0012
100	2.0	0.2	0.2	-0.0102	-0.0133	-0.0009	-0.0005	-0.0008	-0.0090	-0.0133	-0.0008	-0.0007	-0.0012	-0.0101	-0.0133	-0.0009	-0.0013	-0.0016
100	2.0	0.2	1.0	-0.0083	-0.0133	-0.0009	-0.0006	-0.0008	-0.0041	-0.0133	-0.0003	-0.0006	-0.0017	-0.0079	-0.0133	-0.0006	-0.0021	-0.0028
100	2.0	0.2	3.5	-0.0065	-0.0133	-0.0012	-0.0008	-0.0018	-0.0017	-0.0133	-0.0004	-0.0006	-0.0016	-0.0050	-0.0133	-0.0006	-0.0022	-0.0037
100	2.0	0.4	0.2	-0.0091	-0.0071	-0.0006	-0.0004	-0.0006	-0.0089	-0.0071	-0.0006	-0.0007	-0.0008	-0.0091	-0.0071	-0.0006	-0.0013	-0.0018
100	2.0	0.4	1.0	-0.0086	-0.0071	-0.0007	-0.0004	-0.0005	-0.0055	-0.0071	0.0000	-0.0004	-0.0007	-0.0085	-0.0071	-0.0003	-0.0019	-0.0026
100	2.0	0.4	3.5	-0.0072	-0.0071	-0.0008	-0.0006	-0.0007	-0.0016	-0.0071	0.0011	-0.0003	-0.0012	-0.0058	-0.0071	-0.0001	-0.0021	-0.0029
100	2.0	0.5	0.2	0.0129	-0.0007	-0.0008	-0.0008	-0.0008	0.0097	-0.0007	-0.0008	-0.0008	-0.0008	0.0128	-0.0007	-0.0008	-0.0009	-0.0010
100	2.0	0.5	1.0	0.0062	-0.0007	-0.0008	-0.0008	-0.0008	-0.0002	-0.0007	-0.0006	-0.0007	-0.0008	0.0055	-0.0007	-0.0007	-0.0011	-0.0011
100	2.0	0.5	3.5	0.0013	-0.0007	-0.0009	-0.0008	-0.0008	-0.0010	-0.0007	-0.0002	-0.0007	-0.0010	-0.0001	-0.0007	-0.0006	-0.0011	-0.0012
100	3.0	0.0	0.2	-0.0016	-0.0153	-0.0014	-0.0010	-0.0013	-0.0016	-0.0153	-0.0014	-0.0012	-0.0014	-0.0016	-0.0153	-0.0014	-0.0012	-0.0014

Bias				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
100	3.0	0.0	1.0	-0.0016	-0.0153	-0.0015	-0.0010	-0.0013	-0.0016	-0.0153	-0.0015	-0.0008	-0.0012	-0.0016	-0.0153	-0.0015	-0.0008	-0.0012
100	3.0	0.0	3.5	-0.0016	-0.0153	-0.0018	-0.0013	-0.0015	-0.0016	-0.0153	-0.0018	-0.0006	-0.0012	-0.0016	-0.0153	-0.0018	-0.0006	-0.0012
100	3.0	0.2	0.2	-0.0105	-0.0136	-0.0011	-0.0006	-0.0010	-0.0093	-0.0136	-0.0009	-0.0009	-0.0014	-0.0105	-0.0136	-0.0011	-0.0014	-0.0021
100	3.0	0.2	1.0	-0.0086	-0.0136	-0.0011	-0.0007	-0.0009	-0.0043	-0.0136	-0.0004	-0.0007	-0.0019	-0.0086	-0.0136	-0.0010	-0.0027	-0.0034
100	3.0	0.2	3.5	-0.0068	-0.0136	-0.0014	-0.0010	-0.0020	-0.0019	-0.0136	-0.0005	-0.0008	-0.0017	-0.0065	-0.0136	-0.0012	-0.0033	-0.0050
100	3.0	0.4	0.2	-0.0192	-0.0123	-0.0013	-0.0009	-0.0013	-0.0180	-0.0123	-0.0014	-0.0012	-0.0017	-0.0192	-0.0123	-0.0013	-0.0025	-0.0031
100	3.0	0.4	1.0	-0.0164	-0.0123	-0.0014	-0.0011	-0.0012	-0.0094	-0.0123	-0.0005	-0.0010	-0.0015	-0.0164	-0.0123	-0.0013	-0.0041	-0.0056
100	3.0	0.4	3.5	-0.0125	-0.0123	-0.0016	-0.0013	-0.0014	-0.0029	-0.0123	0.0011	-0.0010	-0.0022	-0.0121	-0.0123	-0.0013	-0.0052	-0.0070
100	3.0	0.5	0.2	-0.0178	-0.0114	-0.0018	-0.0014	-0.0017	-0.0177	-0.0114	-0.0018	-0.0015	-0.0019	-0.0178	-0.0114	-0.0017	-0.0030	-0.0037
100	3.0	0.5	1.0	-0.0171	-0.0114	-0.0017	-0.0013	-0.0014	-0.0115	-0.0114	-0.0006	-0.0012	-0.0016	-0.0170	-0.0114	-0.0015	-0.0044	-0.0062
100	3.0	0.5	3.5	-0.0141	-0.0114	-0.0019	-0.0016	-0.0017	-0.0035	-0.0114	0.0015	-0.0010	-0.0025	-0.0137	-0.0114	-0.0014	-0.0052	-0.0072

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.4 Bias of Treatment Effect Estimates by Methodology (Sample Size per Group = 200)

Bias				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
200	1.4	0.0	0.2	0.0004	-0.0094	0.0005	0.0006	0.0005	0.0004	-0.0094	0.0005	0.0006	0.0005	0.0004	-0.0094	0.0005	0.0006	0.0005
200	1.4	0.0	1.0	0.0004	-0.0094	0.0005	0.0006	0.0005	0.0004	-0.0094	0.0005	0.0009	0.0005	0.0004	-0.0094	0.0005	0.0009	0.0005
200	1.4	0.0	3.5	0.0004	-0.0094	0.0005	0.0006	0.0006	0.0004	-0.0094	0.0005	0.0011	0.0007	0.0004	-0.0094	0.0005	0.0011	0.0007
200	1.4	0.2	0.2	0.0016	0.0029	0.0001	0.0001	0.0001	0.0013	0.0029	0.0001	0.0001	0.0001	0.0015	0.0029	0.0001	0.0000	0.0000
200	1.4	0.2	1.0	0.0012	0.0029	0.0001	0.0001	0.0001	0.0004	0.0029	0.0000	0.0001	0.0002	0.0009	0.0029	0.0000	0.0001	0.0001
200	1.4	0.2	3.5	0.0009	0.0029	0.0001	0.0001	0.0001	0.0002	0.0029	0.0001	0.0001	0.0001	0.0004	0.0029	0.0000	0.0001	0.0002
200	1.4	0.4	0.2	0.0521	0.0252	0.0002	0.0001	0.0002	0.0435	0.0252	-0.0009	-0.0002	-0.0003	0.0508	0.0252	-0.0004	0.0008	0.0006
200	1.4	0.4	1.0	0.0387	0.0252	0.0005	0.0004	0.0005	0.0159	0.0252	-0.0024	-0.0002	-0.0001	0.0317	0.0252	-0.0024	0.0008	0.0022
200	1.4	0.4	3.5	0.0268	0.0252	0.0005	0.0004	0.0003	0.0041	0.0252	-0.0048	-0.0003	0.0020	0.0131	0.0252	-0.0026	0.0017	0.0034
200	1.4	0.5	0.2	0.1094	0.0379	-0.0005	-0.0007	-0.0006	0.0925	0.0379	-0.0029	-0.0017	-0.0018	0.1067	0.0379	-0.0021	-0.0004	-0.0009
200	1.4	0.5	1.0	0.0813	0.0379	-0.0003	-0.0003	-0.0002	0.0338	0.0379	-0.0062	-0.0019	-0.0017	0.0674	0.0379	-0.0060	-0.0005	0.0018
200	1.4	0.5	3.5	0.0559	0.0379	0.0000	-0.0001	-0.0001	0.0073	0.0379	-0.0124	-0.0022	0.0025	0.0267	0.0379	-0.0071	0.0005	0.0041
200	2.0	0.0	0.2	0.0007	-0.0122	0.0009	0.0010	0.0009	0.0007	-0.0122	0.0009	0.0011	0.0008	0.0007	-0.0122	0.0009	0.0011	0.0008
200	2.0	0.0	1.0	0.0007	-0.0122	0.0009	0.0010	0.0010	0.0007	-0.0122	0.0009	0.0013	0.0009	0.0007	-0.0122	0.0009	0.0013	0.0009
200	2.0	0.0	3.5	0.0007	-0.0122	0.0009	0.0011	0.0010	0.0007	-0.0122	0.0009	0.0018	0.0012	0.0007	-0.0122	0.0009	0.0018	0.0012
200	2.0	0.2	0.2	-0.0079	-0.0098	0.0014	0.0016	0.0015	-0.0067	-0.0098	0.0016	0.0016	0.0014	-0.0078	-0.0098	0.0015	0.0008	0.0006
200	2.0	0.2	1.0	-0.0062	-0.0098	0.0015	0.0016	0.0016	-0.0019	-0.0098	0.0021	0.0017	0.0014	-0.0057	-0.0098	0.0018	0.0004	0.0000
200	2.0	0.2	3.5	-0.0044	-0.0098	0.0015	0.0017	0.0015	0.0006	-0.0098	0.0021	0.0018	0.0011	-0.0027	-0.0098	0.0021	0.0003	-0.0003
200	2.0	0.4	0.2	-0.0079	-0.0055	0.0003	0.0004	0.0003	-0.0079	-0.0055	0.0003	0.0004	0.0003	-0.0079	-0.0055	0.0004	-0.0002	-0.0004
200	2.0	0.4	1.0	-0.0076	-0.0055	0.0003	0.0004	0.0004	-0.0046	-0.0055	0.0009	0.0005	0.0004	-0.0075	-0.0055	0.0007	-0.0006	-0.0012
200	2.0	0.4	3.5	-0.0062	-0.0055	0.0004	0.0004	0.0005	-0.0008	-0.0055	0.0021	0.0006	-0.0001	-0.0049	-0.0055	0.0011	-0.0008	-0.0015
200	2.0	0.5	0.2	0.0116	-0.0012	-0.0013	-0.0013	-0.0013	0.0084	-0.0012	-0.0013	-0.0013	-0.0013	0.0115	-0.0012	-0.0012	-0.0014	-0.0015
200	2.0	0.5	1.0	0.0052	-0.0012	-0.0013	-0.0013	-0.0013	-0.0007	-0.0012	-0.0011	-0.0012	-0.0012	0.0045	-0.0012	-0.0012	-0.0015	-0.0016
200	2.0	0.5	3.5	0.0009	-0.0012	-0.0012	-0.0013	-0.0012	-0.0015	-0.0012	-0.0005	-0.0012	-0.0014	-0.0006	-0.0012	-0.0010	-0.0015	-0.0017
200	3.0	0.0	0.2	0.0007	-0.0122	0.0009	0.0010	0.0009	0.0007	-0.0122	0.0009	0.0011	0.0008	0.0007	-0.0122	0.0009	0.0011	0.0008
200	3.0	0.0	1.0	0.0007	-0.0122	0.0009	0.0010	0.0010	0.0007	-0.0122	0.0009	0.0013	0.0009	0.0007	-0.0122	0.0009	0.0013	0.0009
200	3.0	0.0	3.5	0.0007	-0.0122	0.0009	0.0011	0.0010	0.0007	-0.0122	0.0009	0.0018	0.0012	0.0007	-0.0122	0.0009	0.0018	0.0012
200	3.0	0.2	0.2	-0.0082	-0.0102	0.0014	0.0016	0.0015	-0.0070	-0.0102	0.0015	0.0015	0.0014	-0.0082	-0.0102	0.0014	0.0009	0.0005
200	3.0	0.2	1.0	-0.0064	-0.0102	0.0014	0.0016	0.0015	-0.0020	-0.0102	0.0020	0.0017	0.0014	-0.0063	-0.0102	0.0015	0.0000	-0.0010

Bias				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
200	3.0	0.2	3.5	-0.0046	-0.0102	0.0015	0.0016	0.0014	0.0006	-0.0102	0.0021	0.0017	0.0010	-0.0042	-0.0102	0.0017	-0.0008	-0.0016
200	3.0	0.4	0.2	-0.0173	-0.0094	0.0007	0.0008	0.0007	-0.0162	-0.0094	0.0006	0.0008	0.0004	-0.0173	-0.0094	0.0007	-0.0003	-0.0006
200	3.0	0.4	1.0	-0.0146	-0.0094	0.0008	0.0009	0.0008	-0.0075	-0.0094	0.0016	0.0011	0.0009	-0.0145	-0.0094	0.0009	-0.0015	-0.0028
200	3.0	0.4	3.5	-0.0108	-0.0094	0.0008	0.0009	0.0009	-0.0009	-0.0094	0.0033	0.0012	0.0001	-0.0104	-0.0094	0.0012	-0.0026	-0.0047
200	3.0	0.5	0.2	-0.0169	-0.0094	-0.0002	-0.0001	-0.0002	-0.0168	-0.0094	-0.0004	-0.0001	-0.0004	-0.0169	-0.0094	-0.0002	-0.0012	-0.0018
200	3.0	0.5	1.0	-0.0161	-0.0094	-0.0002	-0.0001	-0.0001	-0.0103	-0.0094	0.0008	0.0003	0.0000	-0.0160	-0.0094	0.0000	-0.0024	-0.0041
200	3.0	0.5	3.5	-0.0131	-0.0094	-0.0001	0.0000	0.0000	-0.0021	-0.0094	0.0034	0.0004	-0.0007	-0.0127	-0.0094	0.0003	-0.0037	-0.0057

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.5 Bias of Treatment Effect Estimates by Methodology (Sample Size per Group = 500)

Bias				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
500	1.4	0.0	0.2	0.0021	-0.0083	0.0021	0.0022	0.0021	0.0021	-0.0083	0.0021	0.0023	0.0021	0.0021	-0.0083	0.0021	0.0023	0.0021
500	1.4	0.0	1.0	0.0021	-0.0083	0.0021	0.0021	0.0021	0.0021	-0.0083	0.0021	0.0024	0.0021	0.0021	-0.0083	0.0021	0.0024	0.0021
500	1.4	0.0	3.5	0.0021	-0.0083	0.0021	0.0020	0.0021	0.0021	-0.0083	0.0021	0.0026	0.0022	0.0021	-0.0083	0.0021	0.0026	0.0022
500	1.4	0.2	0.2	0.0038	0.0050	0.0023	0.0023	0.0023	0.0035	0.0050	0.0023	0.0023	0.0023	0.0038	0.0050	0.0023	0.0023	0.0023
500	1.4	0.2	1.0	0.0034	0.0050	0.0023	0.0023	0.0023	0.0026	0.0050	0.0022	0.0023	0.0021	0.0031	0.0050	0.0023	0.0023	0.0024
500	1.4	0.2	3.5	0.0031	0.0050	0.0023	0.0023	0.0023	0.0024	0.0050	0.0023	0.0023	0.0024	0.0026	0.0050	0.0023	0.0023	0.0025
500	1.4	0.4	0.2	0.0548	0.0273	0.0020	0.0019	0.0019	0.0455	0.0273	0.0005	0.0015	0.0016	0.0533	0.0273	0.0013	0.0024	0.0024
500	1.4	0.4	1.0	0.0403	0.0273	0.0020	0.0020	0.0018	0.0175	0.0273	-0.0007	0.0015	0.0016	0.0334	0.0273	-0.0008	0.0022	0.0033
500	1.4	0.4	3.5	0.0284	0.0273	0.0020	0.0022	0.0021	0.0051	0.0273	-0.0035	0.0014	0.0029	0.0143	0.0273	-0.0009	0.0025	0.0035
500	1.4	0.5	0.2	0.1156	0.0395	0.0003	0.0001	0.0002	0.0961	0.0395	-0.0026	-0.0006	-0.0004	0.1122	0.0395	-0.0015	0.0005	0.0005
500	1.4	0.5	1.0	0.0831	0.0395	0.0003	0.0005	0.0002	0.0344	0.0395	-0.0057	-0.0011	-0.0008	0.0683	0.0395	-0.0055	-0.0004	0.0016
500	1.4	0.5	3.5	0.0560	0.0395	0.0002	0.0005	0.0005	0.0073	0.0395	-0.0121	-0.0015	0.0012	0.0266	0.0395	-0.0063	0.0002	0.0020
500	2.0	0.0	0.2	0.0015	-0.0120	0.0016	0.0017	0.0017	0.0015	-0.0120	0.0016	0.0018	0.0017	0.0015	-0.0120	0.0016	0.0018	0.0017
500	2.0	0.0	1.0	0.0015	-0.0120	0.0016	0.0017	0.0017	0.0015	-0.0120	0.0016	0.0020	0.0017	0.0015	-0.0120	0.0016	0.0020	0.0017
500	2.0	0.0	3.5	0.0015	-0.0120	0.0016	0.0016	0.0016	0.0015	-0.0120	0.0016	0.0021	0.0017	0.0015	-0.0120	0.0016	0.0021	0.0017
500	2.0	0.2	0.2	-0.0077	-0.0103	0.0018	0.0019	0.0019	-0.0064	-0.0103	0.0020	0.0019	0.0019	-0.0076	-0.0103	0.0019	0.0015	0.0014
500	2.0	0.2	1.0	-0.0058	-0.0103	0.0018	0.0019	0.0019	-0.0015	-0.0103	0.0024	0.0020	0.0019	-0.0053	-0.0103	0.0022	0.0012	0.0007
500	2.0	0.2	3.5	-0.0040	-0.0103	0.0018	0.0018	0.0017	0.0011	-0.0103	0.0022	0.0020	0.0016	-0.0024	-0.0103	0.0023	0.0010	0.0006
500	2.0	0.4	0.2	-0.0074	-0.0047	0.0017	0.0017	0.0017	-0.0072	-0.0047	0.0018	0.0018	0.0017	-0.0074	-0.0047	0.0018	0.0013	0.0011
500	2.0	0.4	1.0	-0.0068	-0.0047	0.0016	0.0017	0.0017	-0.0035	-0.0047	0.0022	0.0018	0.0017	-0.0066	-0.0047	0.0021	0.0009	0.0003
500	2.0	0.4	3.5	-0.0052	-0.0047	0.0016	0.0016	0.0016	0.0006	-0.0047	0.0035	0.0018	0.0015	-0.0038	-0.0047	0.0023	0.0008	-0.0001
500	2.0	0.5	0.2	0.0149	0.0020	0.0019	0.0019	0.0019	0.0115	0.0020	0.0019	0.0019	0.0019	0.0147	0.0020	0.0019	0.0018	0.0018
500	2.0	0.5	1.0	0.0083	0.0020	0.0019	0.0019	0.0019	0.0024	0.0020	0.0020	0.0019	0.0019	0.0076	0.0020	0.0020	0.0017	0.0016
500	2.0	0.5	3.5	0.0040	0.0020	0.0019	0.0019	0.0019	0.0016	0.0020	0.0026	0.0019	0.0018	0.0026	0.0020	0.0021	0.0017	0.0016
500	3.0	0.0	0.2	0.0015	-0.0120	0.0016	0.0017	0.0017	0.0015	-0.0120	0.0016	0.0018	0.0017	0.0015	-0.0120	0.0016	0.0018	0.0017
500	3.0	0.0	1.0	0.0015	-0.0120	0.0016	0.0017	0.0017	0.0015	-0.0120	0.0016	0.0020	0.0017	0.0015	-0.0120	0.0016	0.0020	0.0017
500	3.0	0.0	3.5	0.0015	-0.0120	0.0016	0.0016	0.0016	0.0015	-0.0120	0.0016	0.0021	0.0017	0.0015	-0.0120	0.0016	0.0021	0.0017
500	3.0	0.2	0.2	-0.0078	-0.0105	0.0019	0.0020	0.0019	-0.0065	-0.0105	0.0021	0.0019	0.0019	-0.0078	-0.0105	0.0019	0.0014	0.0013
500	3.0	0.2	1.0	-0.0059	-0.0105	0.0019	0.0019	0.0019	-0.0015	-0.0105	0.0025	0.0021	0.0020	-0.0058	-0.0105	0.0019	0.0007	0.0002

Bias				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
500	3.0	0.2	3.5	-0.0041	-0.0105	0.0018	0.0018	0.0018	0.0011	-0.0105	0.0022	0.0021	0.0016	-0.0038	-0.0105	0.0020	0.0001	-0.0005
500	3.0	0.4	0.2	-0.0170	-0.0094	0.0014	0.0014	0.0014	-0.0158	-0.0094	0.0014	0.0015	0.0013	-0.0170	-0.0094	0.0014	0.0006	0.0003
500	3.0	0.4	1.0	-0.0142	-0.0094	0.0013	0.0014	0.0014	-0.0070	-0.0094	0.0020	0.0015	0.0014	-0.0141	-0.0094	0.0015	-0.0004	-0.0017
500	3.0	0.4	3.5	-0.0103	-0.0094	0.0013	0.0013	0.0013	-0.0002	-0.0094	0.0040	0.0016	0.0011	-0.0098	-0.0094	0.0017	-0.0015	-0.0037
500	3.0	0.5	0.2	-0.0151	-0.0081	0.0015	0.0016	0.0015	-0.0150	-0.0081	0.0014	0.0016	0.0013	-0.0151	-0.0081	0.0015	0.0007	0.0002
500	3.0	0.5	1.0	-0.0144	-0.0081	0.0014	0.0015	0.0015	-0.0088	-0.0081	0.0022	0.0018	0.0014	-0.0143	-0.0081	0.0016	-0.0004	-0.0020
500	3.0	0.5	3.5	-0.0114	-0.0081	0.0014	0.0014	0.0014	-0.0005	-0.0081	0.0049	0.0019	0.0012	-0.0110	-0.0081	0.0018	-0.0013	-0.0037

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.6 Variance of Treatment Effect Estimates by Methodology (Sample Size per Group = 100)

Variance				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
100	1.4	0.0	0.2	0.0010	0.0011	0.0011	0.0011	0.0011	0.0010	0.0011	0.0011	0.0010	0.0010	0.0010	0.0011	0.0011	0.0010	0.0010
100	1.4	0.0	1.0	0.0010	0.0011	0.0011	0.0011	0.0011	0.0010	0.0011	0.0011	0.0011	0.0010	0.0010	0.0011	0.0011	0.0011	0.0010
100	1.4	0.0	3.5	0.0010	0.0011	0.0011	0.0011	0.0010	0.0010	0.0011	0.0011	0.0010	0.0010	0.0010	0.0011	0.0011	0.0010	0.0010
100	1.4	0.2	0.2	0.0014	0.0015	0.0013	0.0013	0.0013	0.0014	0.0015	0.0013	0.0013	0.0013	0.0014	0.0015	0.0013	0.0013	0.0013
100	1.4	0.2	1.0	0.0014	0.0015	0.0013	0.0012	0.0012	0.0013	0.0015	0.0012	0.0012	0.0013	0.0014	0.0015	0.0012	0.0013	0.0013
100	1.4	0.2	3.5	0.0014	0.0015	0.0013	0.0013	0.0013	0.0013	0.0015	0.0012	0.0012	0.0013	0.0013	0.0015	0.0012	0.0013	0.0013
100	1.4	0.4	0.2	0.0032	0.0023	0.0020	0.0020	0.0020	0.0032	0.0023	0.0020	0.0020	0.0020	0.0032	0.0023	0.0020	0.0020	0.0020
100	1.4	0.4	1.0	0.0029	0.0023	0.0020	0.0019	0.0019	0.0023	0.0023	0.0019	0.0019	0.0019	0.0027	0.0023	0.0019	0.0019	0.0019
100	1.4	0.4	3.5	0.0027	0.0023	0.0020	0.0020	0.0020	0.0020	0.0023	0.0018	0.0019	0.0020	0.0022	0.0023	0.0018	0.0019	0.0020
100	1.4	0.5	0.2	0.0043	0.0036	0.0031	0.0031	0.0031	0.0044	0.0037	0.0031	0.0030	0.0030	0.0043	0.0036	0.0031	0.0031	0.0030
100	1.4	0.5	1.0	0.0045	0.0035	0.0031	0.0030	0.0030	0.0037	0.0035	0.0028	0.0029	0.0030	0.0043	0.0035	0.0029	0.0031	0.0031
100	1.4	0.5	3.5	0.0043	0.0035	0.0030	0.0030	0.0030	0.0031	0.0035	0.0027	0.0029	0.0029	0.0035	0.0035	0.0028	0.0030	0.0032
100	2.0	0.0	0.2	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010
100	2.0	0.0	1.0	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010
100	2.0	0.0	3.5	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010
100	2.0	0.2	0.2	0.0010	0.0010	0.0011	0.0011	0.0011	0.0010	0.0010	0.0011	0.0010	0.0011	0.0010	0.0010	0.0011	0.0010	0.0010
100	2.0	0.2	1.0	0.0010	0.0010	0.0011	0.0011	0.0011	0.0010	0.0010	0.0011	0.0011	0.0011	0.0010	0.0010	0.0011	0.0010	0.0011
100	2.0	0.2	3.5	0.0010	0.0010	0.0011	0.0011	0.0011	0.0010	0.0010	0.0011	0.0011	0.0011	0.0010	0.0010	0.0011	0.0011	0.0011
100	2.0	0.4	0.2	0.0013	0.0012	0.0011	0.0011	0.0011	0.0013	0.0012	0.0011	0.0011	0.0011	0.0013	0.0012	0.0011	0.0011	0.0011
100	2.0	0.4	1.0	0.0012	0.0012	0.0011	0.0011	0.0011	0.0012	0.0012	0.0011	0.0011	0.0011	0.0012	0.0012	0.0011	0.0011	0.0011
100	2.0	0.4	3.5	0.0012	0.0012	0.0011	0.0011	0.0011	0.0011	0.0012	0.0011	0.0011	0.0011	0.0012	0.0012	0.0011	0.0011	0.0011
100	2.0	0.5	0.2	0.0021	0.0015	0.0013	0.0013	0.0014	0.0020	0.0015	0.0013	0.0013	0.0013	0.0021	0.0015	0.0013	0.0014	0.0014
100	2.0	0.5	1.0	0.0018	0.0015	0.0013	0.0013	0.0013	0.0016	0.0015	0.0013	0.0013	0.0013	0.0018	0.0015	0.0013	0.0014	0.0014
100	2.0	0.5	3.5	0.0017	0.0015	0.0014	0.0014	0.0014	0.0014	0.0015	0.0013	0.0013	0.0014	0.0016	0.0015	0.0013	0.0014	0.0014
100	3.0	0.0	0.2	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010
100	3.0	0.0	1.0	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010
100	3.0	0.0	3.5	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010
100	3.0	0.2	0.2	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010
100	3.0	0.2	1.0	0.0010	0.0010	0.0010	0.0011	0.0011	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010

Variance				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
100	3.0	0.2	3.5	0.0010	0.0010	0.0010	0.0010	0.0011	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010
100	3.0	0.4	0.2	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011
100	3.0	0.4	1.0	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011
100	3.0	0.4	3.5	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011	0.0011
100	3.0	0.5	0.2	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012
100	3.0	0.5	1.0	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012
100	3.0	0.5	3.5	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.7 Variance of Treatment Effect Estimates by Methodology (Sample Size per Group = 200)

Variance				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
200	1.4	0.0	0.2	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006
200	1.4	0.0	1.0	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006
200	1.4	0.0	3.5	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0005	0.0006	0.0006	0.0006	0.0006	0.0005	0.0006
200	1.4	0.2	0.2	0.0008	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007	0.0008	0.0008	0.0007	0.0007	0.0007
200	1.4	0.2	1.0	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007
200	1.4	0.2	3.5	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007
200	1.4	0.4	0.2	0.0021	0.0014	0.0012	0.0012	0.0012	0.0019	0.0014	0.0011	0.0012	0.0012	0.0020	0.0014	0.0012	0.0012	0.0012
200	1.4	0.4	1.0	0.0018	0.0014	0.0012	0.0012	0.0012	0.0014	0.0014	0.0011	0.0012	0.0012	0.0017	0.0014	0.0011	0.0012	0.0012
200	1.4	0.4	3.5	0.0016	0.0014	0.0012	0.0012	0.0012	0.0012	0.0014	0.0011	0.0012	0.0012	0.0013	0.0014	0.0011	0.0012	0.0012
200	1.4	0.5	0.2	0.0029	0.0019	0.0016	0.0016	0.0016	0.0029	0.0019	0.0016	0.0016	0.0016	0.0029	0.0019	0.0016	0.0016	0.0016
200	1.4	0.5	1.0	0.0028	0.0019	0.0016	0.0016	0.0016	0.0022	0.0019	0.0015	0.0016	0.0016	0.0027	0.0019	0.0015	0.0016	0.0016
200	1.4	0.5	3.5	0.0025	0.0019	0.0016	0.0016	0.0016	0.0017	0.0019	0.0014	0.0015	0.0016	0.0020	0.0019	0.0015	0.0016	0.0016
200	2.0	0.0	0.2	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005
200	2.0	0.0	1.0	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005
200	2.0	0.0	3.5	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005
200	2.0	0.2	0.2	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006
200	2.0	0.2	1.0	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006
200	2.0	0.2	3.5	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006
200	2.0	0.4	0.2	0.0008	0.0007	0.0006	0.0006	0.0006	0.0008	0.0007	0.0006	0.0006	0.0006	0.0008	0.0007	0.0006	0.0006	0.0006
200	2.0	0.4	1.0	0.0007	0.0007	0.0006	0.0006	0.0006	0.0007	0.0007	0.0006	0.0006	0.0006	0.0007	0.0007	0.0006	0.0006	0.0006
200	2.0	0.4	3.5	0.0007	0.0007	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006	0.0007	0.0007	0.0006	0.0006	0.0006
200	2.0	0.5	0.2	0.0011	0.0007	0.0006	0.0006	0.0006	0.0010	0.0007	0.0006	0.0006	0.0006	0.0011	0.0007	0.0006	0.0006	0.0007
200	2.0	0.5	1.0	0.0010	0.0007	0.0006	0.0006	0.0006	0.0008	0.0007	0.0006	0.0006	0.0006	0.0009	0.0007	0.0006	0.0007	0.0007
200	2.0	0.5	3.5	0.0008	0.0007	0.0006	0.0006	0.0006	0.0007	0.0007	0.0006	0.0006	0.0006	0.0008	0.0007	0.0006	0.0007	0.0007
200	3.0	0.0	0.2	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005
200	3.0	0.0	1.0	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005
200	3.0	0.0	3.5	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005	0.0005
200	3.0	0.2	0.2	0.0006	0.0005	0.0006	0.0006	0.0006	0.0006	0.0005	0.0006	0.0006	0.0006	0.0006	0.0005	0.0006	0.0006	0.0006
200	3.0	0.2	1.0	0.0006	0.0005	0.0006	0.0006	0.0006	0.0006	0.0005	0.0006	0.0006	0.0006	0.0006	0.0005	0.0006	0.0006	0.0006

Variance				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
200	3.0	0.2	3.5	0.0006	0.0005	0.0006	0.0006	0.0006	0.0006	0.0005	0.0006	0.0006	0.0006	0.0006	0.0005	0.0006	0.0006	0.0006
200	3.0	0.4	0.2	0.0007	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006	0.0006
200	3.0	0.4	1.0	0.0007	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006	0.0006
200	3.0	0.4	3.5	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006
200	3.0	0.5	0.2	0.0007	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006	0.0006
200	3.0	0.5	1.0	0.0007	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006	0.0006
200	3.0	0.5	3.5	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.8 Variance of Treatment Effect Estimates by Methodology (Sample Size per Group = 500)

Variance				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
500	1.4	0.0	0.2	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	1.4	0.0	1.0	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	1.4	0.0	3.5	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	1.4	0.2	0.2	0.0003	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0002
500	1.4	0.2	1.0	0.0003	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0002
500	1.4	0.2	3.5	0.0003	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002
500	1.4	0.4	0.2	0.0007	0.0005	0.0004	0.0004	0.0004	0.0007	0.0005	0.0004	0.0004	0.0004	0.0007	0.0005	0.0004	0.0004	0.0004
500	1.4	0.4	1.0	0.0007	0.0005	0.0004	0.0004	0.0004	0.0005	0.0005	0.0004	0.0004	0.0004	0.0006	0.0005	0.0004	0.0004	0.0005
500	1.4	0.4	3.5	0.0006	0.0005	0.0004	0.0004	0.0004	0.0004	0.0005	0.0004	0.0004	0.0004	0.0005	0.0005	0.0004	0.0004	0.0004
500	1.4	0.5	0.2	0.0011	0.0006	0.0005	0.0005	0.0005	0.0009	0.0006	0.0005	0.0005	0.0005	0.0010	0.0006	0.0005	0.0005	0.0005
500	1.4	0.5	1.0	0.0009	0.0006	0.0005	0.0005	0.0005	0.0007	0.0006	0.0005	0.0005	0.0005	0.0008	0.0006	0.0005	0.0005	0.0005
500	1.4	0.5	3.5	0.0008	0.0006	0.0005	0.0005	0.0005	0.0005	0.0006	0.0005	0.0005	0.0005	0.0006	0.0006	0.0005	0.0005	0.0005
500	2.0	0.0	0.2	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	2.0	0.0	1.0	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	2.0	0.0	3.5	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	2.0	0.2	0.2	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	2.0	0.2	1.0	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	2.0	0.2	3.5	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	2.0	0.4	0.2	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002
500	2.0	0.4	1.0	0.0003	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002
500	2.0	0.4	3.5	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	2.0	0.5	0.2	0.0004	0.0003	0.0002	0.0002	0.0002	0.0004	0.0003	0.0002	0.0002	0.0002	0.0004	0.0003	0.0002	0.0002	0.0002
500	2.0	0.5	1.0	0.0004	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0002	0.0004	0.0003	0.0002	0.0002	0.0002
500	2.0	0.5	3.5	0.0003	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0003
500	3.0	0.0	0.2	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	3.0	0.0	1.0	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	3.0	0.0	3.5	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	3.0	0.2	0.2	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	3.0	0.2	1.0	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002

Variance				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
500	3.0	0.2	3.5	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	3.0	0.4	0.2	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	3.0	0.4	1.0	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	3.0	0.4	3.5	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	3.0	0.5	0.2	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002
500	3.0	0.5	1.0	0.0003	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002
500	3.0	0.5	3.5	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.9 Mean Squared Error of Treatment Effect Estimates by Methodology (Sample Size per Group = 100)

	MSE			Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
100	1.4	0.0	0.2	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010
100	1.4	0.0	1.0	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010
100	1.4	0.0	3.5	0.0010	0.0012	0.0011	0.0010	0.0010	0.0010	0.0012	0.0011	0.0010	0.0010	0.0010	0.0012	0.0011	0.0010	0.0010
100	1.4	0.2	0.2	0.0014	0.0015	0.0012	0.0012	0.0012	0.0014	0.0015	0.0012	0.0012	0.0012	0.0014	0.0015	0.0012	0.0013	0.0013
100	1.4	0.2	1.0	0.0014	0.0015	0.0012	0.0012	0.0012	0.0013	0.0015	0.0012	0.0012	0.0013	0.0013	0.0015	0.0012	0.0012	0.0013
100	1.4	0.2	3.5	0.0013	0.0015	0.0012	0.0012	0.0013	0.0013	0.0015	0.0012	0.0012	0.0012	0.0013	0.0015	0.0012	0.0012	0.0013
100	1.4	0.4	0.2	0.0059	0.0029	0.0019	0.0020	0.0019	0.0050	0.0029	0.0020	0.0020	0.0020	0.0057	0.0029	0.0019	0.0020	0.0020
100	1.4	0.4	1.0	0.0043	0.0029	0.0019	0.0019	0.0019	0.0025	0.0029	0.0019	0.0019	0.0019	0.0036	0.0029	0.0019	0.0019	0.0019
100	1.4	0.4	3.5	0.0033	0.0029	0.0019	0.0019	0.0019	0.0020	0.0029	0.0018	0.0019	0.0019	0.0023	0.0029	0.0018	0.0019	0.0020
100	1.4	0.5	0.2	0.0164	0.0052	0.0030	0.0030	0.0030	0.0134	0.0053	0.0030	0.0030	0.0030	0.0160	0.0053	0.0030	0.0030	0.0030
100	1.4	0.5	1.0	0.0115	0.0051	0.0030	0.0030	0.0030	0.0050	0.0051	0.0028	0.0029	0.0030	0.0093	0.0051	0.0029	0.0030	0.0031
100	1.4	0.5	3.5	0.0076	0.0051	0.0030	0.0030	0.0030	0.0031	0.0051	0.0028	0.0028	0.0029	0.0042	0.0051	0.0028	0.0029	0.0033
100	2.0	0.0	0.2	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010
100	2.0	0.0	1.0	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010
100	2.0	0.0	3.5	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010
100	2.0	0.2	0.2	0.0011	0.0012	0.0010	0.0010	0.0010	0.0011	0.0012	0.0010	0.0010	0.0011	0.0011	0.0012	0.0010	0.0010	0.0010
100	2.0	0.2	1.0	0.0011	0.0012	0.0011	0.0011	0.0011	0.0010	0.0012	0.0010	0.0010	0.0010	0.0011	0.0012	0.0011	0.0010	0.0011
100	2.0	0.2	3.5	0.0011	0.0012	0.0011	0.0011	0.0011	0.0010	0.0012	0.0010	0.0010	0.0010	0.0011	0.0012	0.0011	0.0010	0.0011
100	2.0	0.4	0.2	0.0014	0.0012	0.0011	0.0011	0.0011	0.0013	0.0012	0.0011	0.0011	0.0011	0.0014	0.0012	0.0011	0.0011	0.0011
100	2.0	0.4	1.0	0.0013	0.0012	0.0011	0.0011	0.0011	0.0012	0.0012	0.0011	0.0011	0.0011	0.0013	0.0012	0.0011	0.0011	0.0011
100	2.0	0.4	3.5	0.0012	0.0012	0.0011	0.0011	0.0011	0.0011	0.0012	0.0011	0.0011	0.0011	0.0012	0.0012	0.0011	0.0011	0.0011
100	2.0	0.5	0.2	0.0022	0.0015	0.0013	0.0013	0.0013	0.0020	0.0015	0.0013	0.0013	0.0013	0.0022	0.0015	0.0013	0.0014	0.0014
100	2.0	0.5	1.0	0.0019	0.0015	0.0013	0.0013	0.0013	0.0015	0.0015	0.0013	0.0013	0.0013	0.0018	0.0015	0.0013	0.0014	0.0014
100	2.0	0.5	3.5	0.0016	0.0015	0.0013	0.0013	0.0013	0.0014	0.0015	0.0013	0.0013	0.0013	0.0016	0.0015	0.0013	0.0014	0.0014
100	3.0	0.0	0.2	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010
100	3.0	0.0	1.0	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010
100	3.0	0.0	3.5	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010
100	3.0	0.2	0.2	0.0011	0.0012	0.0010	0.0010	0.0010	0.0011	0.0012	0.0010	0.0010	0.0010	0.0011	0.0012	0.0010	0.0010	0.0010
100	3.0	0.2	1.0	0.0011	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010	0.0011	0.0012	0.0010	0.0010	0.0010

MSE				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
100	3.0	0.2	3.5	0.0011	0.0012	0.0010	0.0010	0.0011	0.0010	0.0012	0.0010	0.0010	0.0010	0.0010	0.0012	0.0010	0.0010	0.0010
100	3.0	0.4	0.2	0.0014	0.0012	0.0011	0.0011	0.0011	0.0014	0.0012	0.0011	0.0011	0.0011	0.0014	0.0012	0.0011	0.0011	0.0011
100	3.0	0.4	1.0	0.0013	0.0012	0.0011	0.0011	0.0011	0.0011	0.0012	0.0011	0.0011	0.0011	0.0013	0.0012	0.0011	0.0011	0.0011
100	3.0	0.4	3.5	0.0012	0.0012	0.0011	0.0011	0.0011	0.0011	0.0012	0.0011	0.0011	0.0011	0.0012	0.0012	0.0011	0.0011	0.0011
100	3.0	0.5	0.2	0.0015	0.0013	0.0012	0.0012	0.0012	0.0015	0.0013	0.0012	0.0012	0.0012	0.0015	0.0013	0.0012	0.0012	0.0012
100	3.0	0.5	1.0	0.0015	0.0013	0.0012	0.0012	0.0012	0.0013	0.0013	0.0012	0.0012	0.0012	0.0015	0.0013	0.0012	0.0012	0.0012
100	3.0	0.5	3.5	0.0014	0.0013	0.0012	0.0012	0.0012	0.0012	0.0013	0.0012	0.0012	0.0012	0.0014	0.0013	0.0012	0.0012	0.0012

MSE: Mean squared error

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.10 Mean Squared Error of Treatment Effect Estimates by Methodology (Sample Size per Group = 200)

	MSE			Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
200	1.4	0.0	0.2	0.0006	0.0007	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006
200	1.4	0.0	1.0	0.0006	0.0007	0.0006	0.0005	0.0005	0.0006	0.0007	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006
200	1.4	0.0	3.5	0.0006	0.0007	0.0005	0.0005	0.0005	0.0006	0.0007	0.0005	0.0005	0.0006	0.0006	0.0007	0.0005	0.0005	0.0006
200	1.4	0.2	0.2	0.0008	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007	0.0008	0.0008	0.0007	0.0007	0.0007
200	1.4	0.2	1.0	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007
200	1.4	0.2	3.5	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0007	0.0007	0.0007	0.0007	0.0008	0.0006	0.0007	0.0007
200	1.4	0.4	0.2	0.0048	0.0020	0.0012	0.0012	0.0012	0.0038	0.0020	0.0011	0.0011	0.0011	0.0046	0.0020	0.0011	0.0012	0.0012
200	1.4	0.4	1.0	0.0033	0.0020	0.0012	0.0012	0.0012	0.0017	0.0020	0.0011	0.0011	0.0011	0.0027	0.0020	0.0011	0.0012	0.0012
200	1.4	0.4	3.5	0.0023	0.0020	0.0012	0.0012	0.0012	0.0012	0.0020	0.0011	0.0011	0.0012	0.0015	0.0020	0.0011	0.0012	0.0012
200	1.4	0.5	0.2	0.0148	0.0033	0.0016	0.0016	0.0016	0.0114	0.0033	0.0016	0.0016	0.0015	0.0142	0.0033	0.0016	0.0016	0.0016
200	1.4	0.5	1.0	0.0094	0.0033	0.0016	0.0016	0.0016	0.0033	0.0033	0.0015	0.0015	0.0016	0.0072	0.0033	0.0015	0.0016	0.0016
200	1.4	0.5	3.5	0.0056	0.0033	0.0016	0.0016	0.0016	0.0017	0.0033	0.0015	0.0015	0.0016	0.0027	0.0033	0.0015	0.0016	0.0016
200	2.0	0.0	0.2	0.0005	0.0007	0.0005	0.0005	0.0005	0.0005	0.0007	0.0005	0.0005	0.0005	0.0005	0.0007	0.0005	0.0005	0.0005
200	2.0	0.0	1.0	0.0005	0.0007	0.0005	0.0005	0.0005	0.0005	0.0007	0.0005	0.0005	0.0005	0.0005	0.0007	0.0005	0.0005	0.0005
200	2.0	0.0	3.5	0.0005	0.0007	0.0005	0.0005	0.0005	0.0005	0.0007	0.0005	0.0005	0.0005	0.0005	0.0007	0.0005	0.0005	0.0005
200	2.0	0.2	0.2	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006
200	2.0	0.2	1.0	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006
200	2.0	0.2	3.5	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006
200	2.0	0.4	0.2	0.0009	0.0007	0.0006	0.0006	0.0006	0.0008	0.0007	0.0006	0.0006	0.0006	0.0009	0.0007	0.0006	0.0006	0.0006
200	2.0	0.4	1.0	0.0008	0.0007	0.0006	0.0006	0.0006	0.0007	0.0007	0.0006	0.0006	0.0006	0.0008	0.0007	0.0006	0.0006	0.0006
200	2.0	0.4	3.5	0.0007	0.0007	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006	0.0007	0.0007	0.0006	0.0006	0.0006
200	2.0	0.5	0.2	0.0012	0.0007	0.0006	0.0006	0.0006	0.0011	0.0007	0.0006	0.0006	0.0006	0.0012	0.0007	0.0006	0.0006	0.0006
200	2.0	0.5	1.0	0.0010	0.0007	0.0006	0.0006	0.0006	0.0008	0.0007	0.0006	0.0006	0.0006	0.0009	0.0007	0.0006	0.0006	0.0007
200	2.0	0.5	3.5	0.0008	0.0007	0.0006	0.0006	0.0006	0.0007	0.0007	0.0006	0.0006	0.0006	0.0008	0.0007	0.0006	0.0007	0.0007
200	3.0	0.0	0.2	0.0005	0.0007	0.0005	0.0005	0.0005	0.0005	0.0007	0.0005	0.0005	0.0005	0.0005	0.0007	0.0005	0.0005	0.0005
200	3.0	0.0	1.0	0.0005	0.0007	0.0005	0.0005	0.0005	0.0005	0.0007	0.0005	0.0005	0.0005	0.0005	0.0007	0.0005	0.0005	0.0005
200	3.0	0.0	3.5	0.0005	0.0007	0.0005	0.0005	0.0005	0.0005	0.0007	0.0005	0.0005	0.0005	0.0005	0.0007	0.0005	0.0005	0.0005
200	3.0	0.2	0.2	0.0007	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006	0.0006
200	3.0	0.2	1.0	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006

MSE				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
200	3.0	0.2	3.5	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006	0.0006
200	3.0	0.4	0.2	0.0010	0.0007	0.0006	0.0006	0.0006	0.0009	0.0007	0.0006	0.0006	0.0006	0.0010	0.0007	0.0006	0.0006	0.0006
200	3.0	0.4	1.0	0.0009	0.0007	0.0006	0.0006	0.0006	0.0007	0.0007	0.0006	0.0006	0.0006	0.0009	0.0007	0.0006	0.0006	0.0006
200	3.0	0.4	3.5	0.0007	0.0007	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006	0.0007	0.0007	0.0006	0.0006	0.0006
200	3.0	0.5	0.2	0.0010	0.0007	0.0006	0.0006	0.0006	0.0009	0.0007	0.0006	0.0006	0.0006	0.0010	0.0007	0.0006	0.0006	0.0006
200	3.0	0.5	1.0	0.0009	0.0007	0.0006	0.0006	0.0006	0.0007	0.0007	0.0006	0.0006	0.0006	0.0009	0.0007	0.0006	0.0006	0.0006
200	3.0	0.5	3.5	0.0008	0.0007	0.0006	0.0006	0.0006	0.0006	0.0007	0.0006	0.0006	0.0006	0.0008	0.0007	0.0006	0.0006	0.0006

MSE: Mean squared error

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.11 Mean Squared Error of Treatment Effect Estimates by Methodology (Sample Size per Group = 500)

	MSE			Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
500	1.4	0.0	0.2	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	1.4	0.0	1.0	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	1.4	0.0	3.5	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	0.0002
500	1.4	0.2	0.2	0.0003	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0002
500	1.4	0.2	1.0	0.0003	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0002
500	1.4	0.2	3.5	0.0003	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002
500	1.4	0.4	0.2	0.0037	0.0012	0.0004	0.0004	0.0004	0.0027	0.0012	0.0004	0.0004	0.0004	0.0035	0.0012	0.0004	0.0004	0.0004
500	1.4	0.4	1.0	0.0023	0.0012	0.0004	0.0004	0.0004	0.0008	0.0012	0.0004	0.0004	0.0004	0.0017	0.0012	0.0004	0.0004	0.0005
500	1.4	0.4	3.5	0.0014	0.0012	0.0004	0.0004	0.0004	0.0005	0.0012	0.0004	0.0004	0.0004	0.0007	0.0012	0.0004	0.0004	0.0004
500	1.4	0.5	0.2	0.0144	0.0021	0.0005	0.0005	0.0005	0.0102	0.0021	0.0005	0.0005	0.0005	0.0136	0.0021	0.0005	0.0005	0.0005
500	1.4	0.5	1.0	0.0078	0.0021	0.0005	0.0005	0.0005	0.0019	0.0021	0.0005	0.0005	0.0005	0.0055	0.0021	0.0005	0.0005	0.0005
500	1.4	0.5	3.5	0.0039	0.0021	0.0005	0.0005	0.0005	0.0006	0.0021	0.0006	0.0005	0.0005	0.0013	0.0021	0.0005	0.0005	0.0005
500	2.0	0.0	0.2	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002
500	2.0	0.0	1.0	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002
500	2.0	0.0	3.5	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002
500	2.0	0.2	0.2	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002
500	2.0	0.2	1.0	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002
500	2.0	0.2	3.5	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002
500	2.0	0.4	0.2	0.0003	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0002
500	2.0	0.4	1.0	0.0003	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0002
500	2.0	0.4	3.5	0.0003	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002
500	2.0	0.5	0.2	0.0006	0.0003	0.0002	0.0002	0.0002	0.0005	0.0003	0.0002	0.0002	0.0002	0.0006	0.0003	0.0002	0.0002	0.0002
500	2.0	0.5	1.0	0.0004	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0002	0.0004	0.0003	0.0002	0.0002	0.0002
500	2.0	0.5	3.5	0.0003	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0003
500	3.0	0.0	0.2	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002
500	3.0	0.0	1.0	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002
500	3.0	0.0	3.5	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002
500	3.0	0.2	0.2	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002
500	3.0	0.2	1.0	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002

MSE				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
500	3.0	0.2	3.5	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002
500	3.0	0.4	0.2	0.0005	0.0003	0.0002	0.0002	0.0002	0.0005	0.0003	0.0002	0.0002	0.0002	0.0005	0.0003	0.0002	0.0002	0.0002
500	3.0	0.4	1.0	0.0004	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0002	0.0004	0.0003	0.0002	0.0002	0.0002
500	3.0	0.4	3.5	0.0003	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0002
500	3.0	0.5	0.2	0.0005	0.0003	0.0002	0.0002	0.0002	0.0005	0.0003	0.0002	0.0002	0.0002	0.0005	0.0003	0.0002	0.0002	0.0002
500	3.0	0.5	1.0	0.0005	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0002	0.0005	0.0003	0.0002	0.0002	0.0002
500	3.0	0.5	3.5	0.0004	0.0003	0.0002	0.0002	0.0002	0.0002	0.0003	0.0002	0.0002	0.0002	0.0003	0.0003	0.0002	0.0002	0.0002

MSE: Mean squared error

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.12 Coverage Probability of Treatment Effect Estimates by Methodology (Sample Size per Group = 100)

CP				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
100	1.4	0.0	0.2	0.95	0.91	0.95	0.93	0.93	0.95	0.91	0.95	0.94	0.94	0.95	0.91	0.95	0.94	0.94
100	1.4	0.0	1.0	0.95	0.91	0.95	0.95	0.93	0.95	0.91	0.95	0.97	0.95	0.95	0.91	0.95	0.97	0.95
100	1.4	0.0	3.5	0.95	0.91	0.95	0.96	0.95	0.95	0.91	0.95	0.94	0.96	0.95	0.91	0.95	0.94	0.96
100	1.4	0.2	0.2	0.96	0.93	0.93	0.94	0.93	0.96	0.93	0.93	0.97	0.97	0.96	0.93	0.93	0.97	0.96
100	1.4	0.2	1.0	0.96	0.93	0.93	0.93	0.93	0.94	0.93	0.93	0.97	0.96	0.96	0.93	0.93	0.98	0.97
100	1.4	0.2	3.5	0.96	0.93	0.94	0.94	0.93	0.93	0.93	0.93	0.96	0.93	0.94	0.93	0.92	0.96	0.94
100	1.4	0.4	0.2	0.92	0.93	0.98	0.98	0.98	0.93	0.93	0.98	0.99	0.99	0.92	0.93	0.98	0.99	1.00
100	1.4	0.4	1.0	0.93	0.93	0.98	0.97	0.98	0.97	0.93	0.97	0.98	0.98	0.94	0.93	0.97	0.99	0.98
100	1.4	0.4	3.5	0.95	0.93	0.98	0.97	0.98	0.99	0.93	0.96	0.97	0.99	0.98	0.93	0.97	1.00	1.00
100	1.4	0.5	0.2	0.76	0.81	0.93	0.92	0.94	0.78	0.81	0.95	0.95	0.92	0.76	0.81	0.93	0.92	0.95
100	1.4	0.5	1.0	0.84	0.81	0.95	0.95	0.95	0.96	0.81	0.92	0.94	0.93	0.87	0.81	0.92	0.94	0.94
100	1.4	0.5	3.5	0.90	0.81	0.93	0.93	0.94	0.97	0.81	0.89	0.93	0.97	0.96	0.81	0.91	0.93	0.96
100	2.0	0.0	0.2	0.96	0.90	0.96	0.94	0.93	0.96	0.90	0.96	0.96	0.95	0.96	0.90	0.96	0.96	0.95
100	2.0	0.0	1.0	0.96	0.90	0.96	0.92	0.91	0.96	0.90	0.96	0.97	0.96	0.96	0.90	0.96	0.97	0.96
100	2.0	0.0	3.5	0.96	0.90	0.96	0.95	0.93	0.96	0.90	0.96	0.95	0.96	0.96	0.90	0.96	0.95	0.96
100	2.0	0.2	0.2	0.95	0.90	0.94	0.93	0.93	0.95	0.90	0.94	0.97	0.96	0.95	0.90	0.94	0.96	0.97
100	2.0	0.2	1.0	0.95	0.90	0.94	0.93	0.94	0.95	0.90	0.94	0.98	0.96	0.95	0.90	0.94	1.00	0.98
100	2.0	0.2	3.5	0.95	0.90	0.94	0.95	0.94	0.94	0.90	0.94	0.96	0.96	0.95	0.90	0.94	0.96	0.94
100	2.0	0.4	0.2	1.00	0.95	0.94	0.92	0.97	1.00	0.95	0.95	0.96	0.98	1.00	0.95	0.94	0.98	0.99
100	2.0	0.4	1.0	1.00	0.95	0.94	0.97	0.96	0.99	0.95	0.94	1.00	0.98	1.00	0.95	0.94	1.00	1.00
100	2.0	0.4	3.5	1.00	0.95	0.94	0.95	0.95	0.96	0.95	0.93	0.97	0.95	0.99	0.95	0.94	1.00	1.00
100	2.0	0.5	0.2	0.98	0.93	0.94	0.94	0.94	0.98	0.93	0.94	0.94	0.95	0.98	0.93	0.94	0.94	0.91
100	2.0	0.5	1.0	0.98	0.93	0.94	0.94	0.94	0.96	0.93	0.94	0.95	0.98	0.98	0.93	0.94	0.96	0.95
100	2.0	0.5	3.5	0.97	0.93	0.94	0.94	0.94	0.94	0.93	0.94	0.95	0.94	0.95	0.93	0.94	0.94	0.94
100	3.0	0.0	0.2	0.96	0.90	0.96	0.94	0.93	0.96	0.90	0.96	0.96	0.95	0.96	0.90	0.96	0.96	0.95
100	3.0	0.0	1.0	0.96	0.90	0.96	0.92	0.91	0.96	0.90	0.96	0.97	0.96	0.96	0.90	0.96	0.97	0.96
100	3.0	0.0	3.5	0.96	0.90	0.96	0.95	0.93	0.96	0.90	0.96	0.95	0.96	0.96	0.90	0.96	0.95	0.96
100	3.0	0.2	0.2	0.97	0.91	0.94	0.93	0.94	0.96	0.91	0.94	0.97	0.97	0.97	0.91	0.94	0.98	0.98
100	3.0	0.2	1.0	0.96	0.91	0.94	0.93	0.94	0.95	0.91	0.94	0.99	0.96	0.96	0.91	0.94	0.99	0.98

CP				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
100	3.0	0.2	3.5	0.95	0.91	0.94	0.95	0.94	0.94	0.91	0.94	0.99	0.96	0.95	0.91	0.94	0.98	0.95
100	3.0	0.4	0.2	0.99	0.90	0.95	0.96	0.95	0.99	0.90	0.94	0.99	0.99	0.99	0.90	0.95	0.98	0.98
100	3.0	0.4	1.0	0.98	0.90	0.95	0.94	0.95	0.97	0.90	0.94	1.00	0.97	0.98	0.90	0.95	1.00	1.00
100	3.0	0.4	3.5	0.98	0.90	0.95	0.93	0.94	0.94	0.90	0.94	0.96	0.94	0.97	0.90	0.95	1.00	0.99
100	3.0	0.5	0.2	0.99	0.91	0.95	0.94	0.94	0.99	0.91	0.94	0.96	0.95	0.99	0.91	0.95	0.95	0.96
100	3.0	0.5	1.0	0.99	0.91	0.95	0.94	0.95	0.97	0.91	0.93	0.97	0.94	0.99	0.91	0.95	0.95	0.97
100	3.0	0.5	3.5	0.98	0.91	0.95	0.95	0.95	0.96	0.91	0.93	0.94	0.95	0.98	0.91	0.94	0.96	0.96

CP: Coverage probability

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.13 Coverage Probability of Treatment Effect Estimates by Methodology (Sample Size per Group = 200)

CP				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
200	1.4	0.0	0.2	0.97	0.90	0.96	0.96	0.94	0.97	0.90	0.96	0.97	0.92	0.97	0.90	0.96	0.97	0.92
200	1.4	0.0	1.0	0.97	0.90	0.96	0.96	0.96	0.97	0.90	0.96	0.99	0.95	0.97	0.90	0.96	0.99	0.95
200	1.4	0.0	3.5	0.97	0.90	0.95	0.95	0.95	0.97	0.90	0.95	0.99	0.94	0.97	0.90	0.95	0.99	0.94
200	1.4	0.2	0.2	0.97	0.95	0.96	0.96	0.97	0.97	0.95	0.96	0.98	0.97	0.97	0.95	0.96	0.98	0.96
200	1.4	0.2	1.0	0.97	0.95	0.96	0.96	0.95	0.97	0.95	0.96	0.97	0.97	0.97	0.95	0.96	0.99	0.98
200	1.4	0.2	3.5	0.97	0.95	0.97	0.96	0.96	0.97	0.95	0.97	0.99	0.96	0.97	0.95	0.97	1.00	0.97
200	1.4	0.4	0.2	0.81	0.88	0.94	0.92	0.93	0.84	0.88	0.93	0.96	0.98	0.81	0.88	0.94	0.97	0.96
200	1.4	0.4	1.0	0.86	0.88	0.94	0.96	0.94	0.95	0.88	0.92	0.98	0.97	0.90	0.88	0.92	0.98	0.98
200	1.4	0.4	3.5	0.93	0.88	0.94	0.93	0.95	0.96	0.88	0.91	0.97	0.97	0.95	0.88	0.92	0.98	0.99
200	1.4	0.5	0.2	0.45	0.79	0.93	0.94	0.93	0.62	0.79	0.93	0.93	0.93	0.51	0.79	0.93	0.94	0.93
200	1.4	0.5	1.0	0.67	0.79	0.93	0.94	0.92	0.87	0.79	0.93	0.94	0.94	0.75	0.79	0.93	0.94	0.95
200	1.4	0.5	3.5	0.80	0.79	0.94	0.92	0.94	0.96	0.79	0.93	0.94	0.92	0.90	0.79	0.94	0.94	0.95
200	2.0	0.0	0.2	0.95	0.88	0.95	0.96	0.95	0.95	0.88	0.95	0.98	0.94	0.95	0.88	0.95	0.98	0.94
200	2.0	0.0	1.0	0.95	0.88	0.95	0.92	0.94	0.95	0.88	0.95	0.98	0.95	0.95	0.88	0.95	0.98	0.95
200	2.0	0.0	3.5	0.95	0.88	0.96	0.94	0.95	0.95	0.88	0.96	0.99	0.95	0.95	0.88	0.96	0.99	0.95
200	2.0	0.2	0.2	0.96	0.89	0.95	0.95	0.95	0.97	0.89	0.95	0.99	0.97	0.96	0.89	0.95	0.99	0.97
200	2.0	0.2	1.0	0.97	0.89	0.95	0.95	0.95	0.97	0.89	0.95	0.98	0.97	0.97	0.89	0.95	0.99	0.96
200	2.0	0.2	3.5	0.97	0.89	0.95	0.93	0.95	0.95	0.89	0.95	0.99	0.96	0.97	0.89	0.95	1.00	0.98
200	2.0	0.4	0.2	0.98	0.92	0.95	0.95	0.96	0.98	0.92	0.95	0.98	0.98	0.98	0.92	0.95	0.99	0.97
200	2.0	0.4	1.0	0.98	0.92	0.95	0.96	0.95	0.97	0.92	0.95	0.99	0.97	0.98	0.92	0.95	0.99	0.98
200	2.0	0.4	3.5	0.98	0.92	0.95	0.95	0.94	0.95	0.92	0.94	0.98	0.95	0.97	0.92	0.95	0.98	0.97
200	2.0	0.5	0.2	0.99	0.93	0.95	0.95	0.95	0.99	0.93	0.95	0.95	0.95	0.99	0.93	0.95	0.95	0.94
200	2.0	0.5	1.0	0.99	0.93	0.95	0.95	0.95	0.97	0.93	0.95	0.96	0.95	0.99	0.93	0.95	0.95	0.95
200	2.0	0.5	3.5	0.98	0.93	0.95	0.95	0.95	0.95	0.93	0.95	0.95	0.95	0.98	0.93	0.95	0.95	0.96
200	3.0	0.0	0.2	0.95	0.88	0.95	0.96	0.95	0.95	0.88	0.95	0.98	0.94	0.95	0.88	0.95	0.98	0.94
200	3.0	0.0	1.0	0.95	0.88	0.95	0.92	0.94	0.95	0.88	0.95	0.98	0.95	0.95	0.88	0.95	0.98	0.95
200	3.0	0.0	3.5	0.95	0.88	0.96	0.94	0.95	0.95	0.88	0.96	0.99	0.95	0.95	0.88	0.96	0.99	0.95
200	3.0	0.2	0.2	0.96	0.89	0.94	0.95	0.93	0.97	0.89	0.94	0.98	0.97	0.96	0.89	0.94	0.98	0.99
200	3.0	0.2	1.0	0.97	0.89	0.94	0.95	0.93	0.97	0.89	0.94	0.98	0.96	0.97	0.89	0.94	1.00	0.98

CP				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
200	3.0	0.2	3.5	0.96	0.89	0.95	0.94	0.94	0.95	0.89	0.95	0.97	0.95	0.96	0.89	0.95	1.00	0.97
200	3.0	0.4	0.2	0.98	0.89	0.95	0.96	0.91	0.98	0.89	0.95	1.00	0.98	0.98	0.89	0.95	0.99	0.99
200	3.0	0.4	1.0	0.98	0.89	0.95	0.97	0.95	0.97	0.89	0.95	1.00	0.97	0.98	0.89	0.95	0.99	0.99
200	3.0	0.4	3.5	0.97	0.89	0.96	0.96	0.96	0.96	0.89	0.95	0.99	0.94	0.97	0.89	0.95	1.00	1.00
200	3.0	0.5	0.2	0.99	0.91	0.96	0.96	0.95	0.99	0.91	0.95	0.95	0.94	0.99	0.91	0.96	0.96	0.95
200	3.0	0.5	1.0	0.98	0.91	0.95	0.96	0.95	0.97	0.91	0.95	0.97	0.97	0.98	0.91	0.95	0.96	0.96
200	3.0	0.5	3.5	0.97	0.91	0.95	0.94	0.95	0.96	0.91	0.94	0.95	0.94	0.97	0.91	0.95	0.96	0.97

CP: Coverage probability

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.14 Coverage Probability of Treatment Effect Estimates by Methodology (Sample Size per Group = 500)

CP				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
500	1.4	0.0	0.2	0.98	0.91	0.98	0.97	0.95	0.98	0.91	0.98	1.00	0.95	0.98	0.91	0.98	1.00	0.95
500	1.4	0.0	1.0	0.98	0.91	0.98	0.97	0.97	0.98	0.91	0.98	0.99	0.96	0.98	0.91	0.98	0.99	0.96
500	1.4	0.0	3.5	0.98	0.91	0.97	0.97	0.95	0.98	0.91	0.97	0.99	0.97	0.98	0.91	0.97	0.99	0.97
500	1.4	0.2	0.2	0.97	0.92	0.97	0.97	0.98	0.97	0.92	0.97	0.99	0.98	0.97	0.92	0.97	0.99	0.99
500	1.4	0.2	1.0	0.97	0.92	0.97	0.96	0.97	0.97	0.92	0.97	0.99	1.00	0.97	0.92	0.97	0.99	0.99
500	1.4	0.2	3.5	0.97	0.92	0.97	0.97	0.97	0.97	0.92	0.97	0.98	0.97	0.97	0.92	0.97	0.99	0.98
500	1.4	0.4	0.2	0.46	0.73	0.96	0.95	0.96	0.59	0.73	0.95	0.98	1.00	0.49	0.73	0.96	0.98	0.98
500	1.4	0.4	1.0	0.63	0.73	0.95	0.96	0.95	0.90	0.73	0.94	1.00	0.99	0.72	0.73	0.94	0.98	0.98
500	1.4	0.4	3.5	0.78	0.73	0.95	0.94	0.96	0.97	0.73	0.92	0.98	0.98	0.92	0.73	0.94	0.99	0.99
500	1.4	0.5	0.2	0.03	0.62	0.98	0.98	0.97	0.14	0.62	0.98	0.98	0.96	0.05	0.62	0.98	0.97	0.98
500	1.4	0.5	1.0	0.24	0.62	0.98	0.97	0.98	0.77	0.62	0.98	0.98	0.98	0.39	0.62	0.98	0.97	0.97
500	1.4	0.5	3.5	0.56	0.62	0.98	0.99	0.98	0.96	0.62	0.93	0.98	0.97	0.81	0.62	0.97	0.98	0.98
500	2.0	0.0	0.2	0.99	0.83	0.99	0.99	0.95	0.99	0.83	0.99	0.99	0.97	0.99	0.83	0.99	0.99	0.97
500	2.0	0.0	1.0	0.99	0.83	0.99	0.98	0.96	0.99	0.83	0.99	1.00	0.96	0.99	0.83	0.99	1.00	0.96
500	2.0	0.0	3.5	0.99	0.83	0.99	0.98	1.00	0.99	0.83	0.99	0.98	1.00	0.99	0.83	0.99	0.98	1.00
500	2.0	0.2	0.2	0.96	0.86	0.98	0.99	0.98	0.96	0.86	0.98	0.99	0.98	0.96	0.86	0.98	0.98	0.98
500	2.0	0.2	1.0	0.97	0.86	0.98	0.98	0.98	0.98	0.86	0.98	0.99	0.98	0.97	0.86	0.98	0.99	0.98
500	2.0	0.2	3.5	0.97	0.86	0.98	0.98	0.98	0.98	0.86	0.98	0.98	0.98	0.98	0.86	0.98	0.99	0.99
500	2.0	0.4	0.2	0.98	0.94	0.98	0.99	0.98	0.98	0.94	0.98	0.99	0.98	0.98	0.94	0.98	0.99	0.99
500	2.0	0.4	1.0	0.98	0.94	0.98	0.99	0.97	0.98	0.94	0.98	0.99	0.99	0.98	0.94	0.98	1.00	0.98
500	2.0	0.4	3.5	0.98	0.94	0.98	0.98	0.98	0.98	0.94	0.96	0.98	0.98	0.98	0.94	0.98	0.99	0.98
500	2.0	0.5	0.2	0.99	0.95	0.98	0.98	0.98	0.99	0.95	0.98	0.98	0.98	0.99	0.95	0.98	0.98	0.98
500	2.0	0.5	1.0	0.99	0.95	0.98	0.98	0.97	0.98	0.95	0.97	0.98	0.98	0.99	0.95	0.97	0.98	0.98
500	2.0	0.5	3.5	0.99	0.95	0.98	0.97	0.98	0.98	0.95	0.96	0.97	0.98	0.98	0.95	0.98	0.98	0.98
500	3.0	0.0	0.2	0.99	0.83	0.99	0.99	0.95	0.99	0.83	0.99	0.99	0.97	0.99	0.83	0.99	0.99	0.97
500	3.0	0.0	1.0	0.99	0.83	0.99	0.98	0.96	0.99	0.83	0.99	1.00	0.96	0.99	0.83	0.99	1.00	0.96
500	3.0	0.0	3.5	0.99	0.83	0.99	0.98	1.00	0.99	0.83	0.99	0.98	1.00	0.99	0.83	0.99	0.98	1.00
500	3.0	0.2	0.2	0.96	0.86	0.98	0.98	0.98	0.96	0.86	0.98	0.99	0.98	0.96	0.86	0.98	0.96	0.99
500	3.0	0.2	1.0	0.97	0.86	0.98	0.98	0.98	0.98	0.86	0.98	0.99	0.98	0.97	0.86	0.98	0.99	0.99

CP				Common					Varying(A)					Varying(B)				
n	C_L	β	ρ_S	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG	AFT	IPE	PAFT	CBS-OG	PM-OG
500	3.0	0.2	3.5	0.97	0.86	0.98	0.98	0.98	0.98	0.86	0.98	0.98	0.98	0.97	0.86	0.98	0.99	1.00
500	3.0	0.4	0.2	0.91	0.88	0.98	0.98	0.98	0.91	0.88	0.98	0.98	0.98	0.91	0.88	0.98	0.99	0.98
500	3.0	0.4	1.0	0.92	0.88	0.98	0.98	0.98	0.96	0.88	0.97	0.99	0.99	0.92	0.88	0.97	1.00	1.00
500	3.0	0.4	3.5	0.95	0.88	0.98	0.98	0.98	0.98	0.88	0.96	0.99	0.98	0.95	0.88	0.97	1.00	0.99
500	3.0	0.5	0.2	0.98	0.90	0.97	0.97	0.97	0.98	0.90	0.97	0.97	0.97	0.98	0.90	0.97	0.98	0.97
500	3.0	0.5	1.0	0.98	0.90	0.97	0.97	0.97	0.98	0.90	0.97	0.97	0.98	0.98	0.90	0.97	0.97	0.99
500	3.0	0.5	3.5	0.97	0.90	0.97	0.97	0.97	0.97	0.90	0.96	0.98	0.97	0.97	0.90	0.97	0.97	0.98

CP: Coverage probability

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

AFT: Accelerated failure time model.

IPE: Iterative parameter estimation method.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Appendix III

Table A.15 Bias of Switching Effect Estimates by Methodology as Switching Time Approaches 0 (Sample Size per Group = 100)

Bias				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
100	1.4	0.0	0.2	-0.0563	-0.0058	-0.0245	1.1088	-0.0034	-0.0058	-0.0021	1.2233	-0.0034	-0.0058	-0.0021	1.2233
100	1.4	0.0	1.0	-0.0012	-0.0069	0.0043	1.0653	-0.0105	-0.0069	-0.0111	1.2193	-0.0105	-0.0069	-0.0111	1.2193
100	1.4	0.0	3.5	0.0123	-0.0146	0.0059	1.0252	-0.0505	-0.0146	-0.0739	1.1649	-0.0505	-0.0146	-0.0739	1.1649
100	1.4	0.2	0.2	-0.0565	-0.0025	-0.0215	-0.0029	-0.0018	-0.0218	-0.0030	-0.0149	0.0056	-0.0041	0.0044	-0.0156
100	1.4	0.2	1.0	-0.0249	-0.0009	-0.0061	0.0772	-0.0278	-0.0891	-0.0255	0.5148	0.0116	-0.0169	0.0136	0.1593
100	1.4	0.2	3.5	-0.0255	-0.0061	-0.0019	0.3722	-0.1421	-0.1459	-0.1491	1.0300	-0.0225	-0.0803	-0.0151	0.8915
100	1.4	0.4	0.2	-0.0436	-0.0008	-0.0040	-0.0006	0.0039	-0.0417	-0.0109	-0.0477	0.0163	-0.0048	0.0022	-0.0302
100	1.4	0.4	1.0	-0.0227	0.0017	-0.0042	0.0010	-0.0513	-0.1580	-0.0535	0.0154	0.0093	-0.0355	0.0064	-0.0585
100	1.4	0.4	3.5	-0.0494	-0.0036	0.0011	0.0132	-0.1969	-0.1944	-0.1948	0.7620	0.0284	-0.1354	0.0216	0.3565
100	1.4	0.5	0.2	-0.0746	-0.0034	-0.0386	-0.0042	0.0072	-0.0569	-0.0191	-0.0578	0.0189	-0.0089	-0.0056	-0.0390
100	1.4	0.5	1.0	-0.0010	0.0047	0.0000	0.0043	-0.0623	-0.1811	-0.0702	-0.1321	0.0122	-0.0470	0.0091	-0.0623
100	1.4	0.5	3.5	-0.0471	-0.0015	0.0078	0.0112	-0.2170	-0.1989	-0.2285	0.6352	0.0370	-0.1568	0.0225	0.1589
100	2.0	0.0	0.2	-0.0590	-0.0059	-0.0289	1.1275	-0.0045	-0.0059	-0.0035	1.2512	-0.0045	-0.0059	-0.0035	1.2512
100	2.0	0.0	1.0	0.0075	-0.0072	0.0084	1.0418	-0.0070	-0.0072	-0.0129	1.2026	-0.0070	-0.0072	-0.0129	1.2026
100	2.0	0.0	3.5	0.0188	-0.0163	0.0139	1.0500	-0.0417	-0.0163	-0.0507	1.2019	-0.0417	-0.0163	-0.0507	1.2019
100	2.0	0.2	0.2	-0.0740	-0.0048	-0.0307	-0.0056	-0.0129	-0.0230	-0.0041	-0.0266	-0.0061	-0.0053	0.0031	-0.0135
100	2.0	0.2	1.0	-0.0247	-0.0066	0.0023	0.0450	-0.0404	-0.0908	-0.0354	0.4957	0.0018	-0.0110	0.0069	0.0620
100	2.0	0.2	3.5	-0.0281	-0.0158	0.0035	0.3623	-0.1603	-0.1508	-0.1567	1.0258	-0.0228	-0.0513	0.0037	0.7303
100	2.0	0.4	0.2	-0.1090	-0.0041	-0.0244	-0.0045	-0.0223	-0.0384	-0.0101	-0.0431	-0.0089	-0.0050	0.0025	-0.0291
100	2.0	0.4	1.0	-0.0718	-0.0054	0.0006	-0.0089	-0.0623	-0.1567	-0.0549	-0.0485	-0.0029	-0.0144	0.0116	-0.0515
100	2.0	0.4	3.5	-0.0767	-0.0158	-0.0014	-0.0028	-0.2174	-0.1967	-0.2341	0.7549	0.0099	-0.0804	0.0359	0.1221
100	2.0	0.5	0.2	-0.1251	-0.0030	-0.0208	-0.0034	-0.0183	-0.0458	-0.0140	-0.0482	-0.0040	-0.0044	0.0006	-0.0274
100	2.0	0.5	1.0	-0.0939	-0.0030	-0.0022	-0.0058	-0.0800	-0.1781	-0.0683	-0.1322	-0.0045	-0.0144	0.0122	-0.0524

Bias				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
100	2.0	0.5	3.5	-0.1022	-0.0124	0.0049	-0.0036	-0.2401	-0.1998	-0.2603	0.5991	0.0354	-0.0929	0.0535	-0.0273
100	3.0	0.0	0.2	-0.0590	-0.0059	-0.0289	1.1275	-0.0045	-0.0059	-0.0035	1.2512	-0.0045	-0.0059	-0.0035	1.2512
100	3.0	0.0	1.0	0.0075	-0.0072	0.0084	1.0418	-0.0070	-0.0072	-0.0129	1.2026	-0.0070	-0.0072	-0.0129	1.2026
100	3.0	0.0	3.5	0.0188	-0.0163	0.0139	1.0500	-0.0417	-0.0163	-0.0507	1.2019	-0.0417	-0.0163	-0.0507	1.2019
100	3.0	0.2	0.2	-0.0744	-0.0047	-0.0314	-0.0054	-0.0129	-0.0229	-0.0040	-0.0265	-0.0068	-0.0048	0.0039	-0.0139
100	3.0	0.2	1.0	-0.0252	-0.0064	0.0026	0.0452	-0.0405	-0.0910	-0.0357	0.4965	0.0005	-0.0068	0.0066	0.0567
100	3.0	0.2	3.5	-0.0283	-0.0154	0.0040	0.3628	-0.1603	-0.1506	-0.1536	1.0263	-0.0379	-0.0195	-0.0212	0.6236
100	3.0	0.4	0.2	-0.1089	-0.0047	-0.0265	-0.0055	-0.0263	-0.0380	-0.0114	-0.0413	-0.0147	-0.0048	0.0027	-0.0290
100	3.0	0.4	1.0	-0.0716	-0.0056	0.0025	-0.0089	-0.0643	-0.1564	-0.0566	-0.0434	-0.0064	-0.0065	0.0081	-0.0458
100	3.0	0.4	3.5	-0.0776	-0.0152	-0.0003	-0.0036	-0.2174	-0.1964	-0.2448	0.7654	-0.0239	-0.0225	0.0161	0.0430
100	3.0	0.5	0.2	-0.1323	-0.0049	-0.0287	-0.0058	-0.0322	-0.0455	-0.0157	-0.0466	-0.0172	-0.0050	0.0007	-0.0294
100	3.0	0.5	1.0	-0.1005	-0.0048	0.0075	-0.0083	-0.0833	-0.1765	-0.0689	-0.1365	-0.0110	-0.0058	0.0108	-0.0465
100	3.0	0.5	3.5	-0.1100	-0.0126	0.0042	-0.0115	-0.2401	-0.1997	-0.2551	0.6212	-0.0308	-0.0219	0.0112	-0.0585

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

CBS-CG: Cubic B-spline using control group.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.16 Bias of Switching Effect Estimates by Methodology as Switching Time Approaches 0 (Sample Size per Group = 200)

Bias				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
200	1.4	0.0	0.2	-0.0094	0.0001	-0.0115	1.1137	0.0031	0.0001	0.0036	1.2354	0.0031	0.0001	0.0036	1.2354
200	1.4	0.0	1.0	-0.0004	0.0010	-0.0008	1.0645	0.0032	0.0010	0.0047	1.2250	0.0032	0.0010	0.0047	1.2250
200	1.4	0.0	3.5	0.0103	0.0041	0.0090	0.9922	0.0309	0.0041	0.0443	1.1793	0.0309	0.0041	0.0443	1.1793
200	1.4	0.2	0.2	-0.0274	-0.0017	-0.0103	-0.0013	-0.0011	-0.0216	-0.0018	-0.0230	0.0082	-0.0036	0.0066	-0.0121
200	1.4	0.2	1.0	-0.0222	0.0004	-0.0101	0.0139	-0.0191	-0.0857	-0.0180	0.1599	0.0195	-0.0154	0.0196	0.0091
200	1.4	0.2	3.5	-0.0114	0.0061	0.0030	0.1014	-0.0713	-0.1419	-0.0741	0.8782	0.0322	-0.0715	0.0361	0.5627
200	1.4	0.4	0.2	-0.0265	-0.0036	-0.0045	-0.0034	0.0106	-0.0465	-0.0096	-0.0378	0.0220	-0.0084	0.0053	-0.0196
200	1.4	0.4	1.0	-0.0288	-0.0008	-0.0164	-0.0003	-0.0421	-0.1668	-0.0450	-0.1240	0.0224	-0.0394	0.0191	-0.0306
200	1.4	0.4	3.5	-0.0100	0.0035	0.0128	-0.0009	-0.1503	-0.1979	-0.1420	0.5731	0.0600	-0.1387	0.0460	0.0392
200	1.4	0.5	0.2	-0.0395	-0.0037	-0.0193	-0.0034	0.0140	-0.0617	-0.0156	-0.0477	0.0286	-0.0116	0.0007	-0.0271
200	1.4	0.5	1.0	-0.0357	-0.0011	-0.0294	0.0020	-0.0545	-0.1913	-0.0629	-0.1701	0.0209	-0.0525	0.0132	-0.0405
200	1.4	0.5	3.5	-0.0023	0.0053	0.0270	0.0015	-0.1759	-0.2000	-0.1837	0.4211	0.0559	-0.1648	0.0407	-0.0474
200	2.0	0.0	0.2	-0.0133	-0.0001	-0.0145	1.1003	0.0035	-0.0001	0.0041	1.2342	0.0035	-0.0001	0.0041	1.2342
200	2.0	0.0	1.0	0.0035	0.0003	0.0018	1.0260	0.0057	0.0003	0.0091	1.2228	0.0057	0.0003	0.0091	1.2228
200	2.0	0.0	3.5	0.0090	0.0026	0.0091	0.9764	0.0491	0.0026	0.0346	1.1539	0.0491	0.0026	0.0346	1.1539
200	2.0	0.2	0.2	-0.0393	-0.0010	-0.0161	-0.0010	-0.0085	-0.0189	0.0009	-0.0212	-0.0032	-0.0015	0.0075	-0.0128
200	2.0	0.2	1.0	-0.0171	0.0009	0.0070	0.0015	-0.0224	-0.0850	-0.0198	0.1390	0.0129	-0.0039	0.0238	0.0058
200	2.0	0.2	3.5	-0.0154	0.0027	0.0101	0.1136	-0.0794	-0.1452	-0.0727	0.8924	0.0412	-0.0347	0.0449	0.2593
200	2.0	0.4	0.2	-0.0869	0.0001	-0.0126	0.0004	-0.0140	-0.0353	-0.0031	-0.0264	-0.0016	-0.0010	0.0082	-0.0117
200	2.0	0.4	1.0	-0.0624	0.0015	-0.0006	0.0027	-0.0511	-0.1584	-0.0429	-0.0973	0.0119	-0.0082	0.0285	-0.0255
200	2.0	0.4	3.5	-0.0537	0.0057	0.0103	-0.0064	-0.1451	-0.1987	-0.1596	0.5851	0.0664	-0.0659	0.0478	-0.0458
200	2.0	0.5	0.2	-0.1020	-0.0004	-0.0059	0.0000	-0.0081	-0.0446	-0.0072	-0.0339	0.0063	-0.0018	0.0081	-0.0181
200	2.0	0.5	1.0	-0.0954	0.0004	-0.0053	0.0007	-0.0700	-0.1837	-0.0518	-0.1574	0.0110	-0.0121	0.0270	-0.0225
200	2.0	0.5	3.5	-0.0751	0.0068	0.0091	-0.0031	-0.1756	-0.2000	-0.1915	0.3854	0.0693	-0.0804	0.0497	-0.0621
200	3.0	0.0	0.2	-0.0133	-0.0001	-0.0145	1.1003	0.0035	-0.0001	0.0041	1.2342	0.0035	-0.0001	0.0041	1.2342
200	3.0	0.0	1.0	0.0035	0.0003	0.0018	1.0260	0.0057	0.0003	0.0091	1.2228	0.0057	0.0003	0.0091	1.2228
200	3.0	0.0	3.5	0.0090	0.0026	0.0091	0.9764	0.0491	0.0026	0.0346	1.1539	0.0491	0.0026	0.0346	1.1539
200	3.0	0.2	0.2	-0.0384	-0.0010	-0.0155	-0.0011	-0.0091	-0.0190	0.0007	-0.0193	-0.0036	-0.0011	0.0065	-0.0135

Bias				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
200	3.0	0.2	1.0	-0.0180	0.0007	0.0067	0.0013	-0.0224	-0.0850	-0.0202	0.1274	0.0114	0.0002	0.0212	0.0002
200	3.0	0.2	3.5	-0.0157	0.0026	0.0102	0.1136	-0.0794	-0.1449	-0.0730	0.8798	0.0265	-0.0021	0.0163	0.1082
200	3.0	0.4	0.2	-0.0918	0.0004	-0.0164	0.0004	-0.0210	-0.0341	-0.0024	-0.0284	-0.0092	0.0002	0.0087	-0.0125
200	3.0	0.4	1.0	-0.0635	0.0006	0.0049	0.0017	-0.0529	-0.1587	-0.0422	-0.0974	0.0056	-0.0004	0.0268	-0.0226
200	3.0	0.4	3.5	-0.0540	0.0039	0.0099	-0.0083	-0.1451	-0.1989	-0.1584	0.6010	0.0291	-0.0048	0.0355	-0.0458
200	3.0	0.5	0.2	-0.1234	0.0006	-0.0174	0.0008	-0.0235	-0.0411	-0.0051	-0.0323	-0.0090	0.0005	0.0078	-0.0161
200	3.0	0.5	1.0	-0.1008	0.0010	0.0021	0.0024	-0.0760	-0.1831	-0.0510	-0.1559	-0.0004	-0.0003	0.0279	-0.0237
200	3.0	0.5	3.5	-0.0822	0.0033	0.0084	-0.0083	-0.1756	-0.2000	-0.1964	0.3934	0.0295	-0.0077	0.0442	-0.0696

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

CBS-CG: Cubic B-spline using control group.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.17 Bias of Switching Effect Estimates by Methodology as Switching Time Approaches 0 (Sample Size per Group = 500)

Bias				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
500	1.4	0.0	0.2	0.0016	0.0005	-0.0015	1.1035	0.0018	0.0005	0.0016	1.1792	0.0018	0.0005	0.0016	1.1792
500	1.4	0.0	1.0	-0.0149	0.0001	-0.0173	1.0154	0.0151	0.0001	0.0133	1.1909	0.0151	0.0001	0.0133	1.1909
500	1.4	0.0	3.5	0.0172	-0.0015	0.0138	1.0307	0.0341	-0.0015	0.0311	1.2193	0.0341	-0.0015	0.0311	1.2193
500	1.4	0.2	0.2	-0.0109	0.0008	-0.0044	0.0005	0.0000	-0.0195	-0.0009	-0.0161	0.0078	-0.0012	0.0065	-0.0024
500	1.4	0.2	1.0	-0.0334	-0.0006	-0.0212	-0.0021	-0.0050	-0.0866	-0.0068	-0.0690	0.0284	-0.0163	0.0264	-0.0117
500	1.4	0.2	3.5	0.0063	-0.0020	0.0131	-0.0058	-0.0498	-0.1554	-0.0576	0.7244	0.0736	-0.0795	0.0644	0.1779
500	1.4	0.4	0.2	0.0116	0.0015	0.0142	0.0008	0.0186	-0.0441	-0.0052	-0.0302	0.0364	-0.0039	0.0088	-0.0054
500	1.4	0.4	1.0	-0.0253	-0.0008	-0.0171	-0.0044	-0.0203	-0.1728	-0.0216	-0.1268	0.0373	-0.0389	0.0282	-0.0197
500	1.4	0.4	3.5	-0.0093	0.0014	0.0025	0.0085	-0.1163	-0.1997	-0.1276	0.3631	0.0911	-0.1500	0.0745	-0.0522
500	1.4	0.5	0.2	0.0083	0.0012	0.0151	0.0008	0.0346	-0.0585	-0.0090	-0.0377	0.0500	-0.0075	0.0090	-0.0100
500	1.4	0.5	1.0	0.0009	0.0001	-0.0121	-0.0006	-0.0309	-0.1961	-0.0405	-0.1616	0.0390	-0.0531	0.0303	-0.0243
500	1.4	0.5	3.5	0.0061	0.0003	0.0073	0.0067	-0.1678	-0.2000	-0.1662	0.0865	0.0881	-0.1792	0.0739	-0.0646
500	2.0	0.0	0.2	-0.0057	0.0005	-0.0079	1.0674	0.0019	0.0005	0.0018	1.1676	0.0019	0.0005	0.0018	1.1676
500	2.0	0.0	1.0	-0.0140	0.0003	-0.0183	0.9663	0.0122	0.0003	0.0139	1.2066	0.0122	0.0003	0.0139	1.2066
500	2.0	0.0	3.5	0.0104	-0.0006	0.0140	0.9814	0.0373	-0.0006	0.0409	1.2300	0.0373	-0.0006	0.0409	1.2300
500	2.0	0.2	0.2	-0.0240	0.0002	-0.0039	0.0000	-0.0094	-0.0188	-0.0007	-0.0154	-0.0047	-0.0003	0.0054	-0.0037
500	2.0	0.2	1.0	-0.0274	-0.0001	-0.0150	-0.0014	-0.0086	-0.0845	-0.0083	-0.0469	0.0174	-0.0053	0.0239	-0.0143
500	2.0	0.2	3.5	-0.0018	-0.0004	0.0197	0.0019	-0.0544	-0.1559	-0.0558	0.7315	0.0600	-0.0377	0.0624	-0.0069
500	2.0	0.4	0.2	-0.0563	-0.0005	0.0038	-0.0009	-0.0166	-0.0369	-0.0037	-0.0272	-0.0041	-0.0016	0.0072	-0.0046
500	2.0	0.4	1.0	-0.0499	-0.0007	-0.0083	-0.0021	-0.0348	-0.1643	-0.0246	-0.1241	0.0145	-0.0110	0.0309	-0.0092
500	2.0	0.4	3.5	-0.0214	-0.0014	0.0226	-0.0030	-0.1285	-0.2000	-0.1348	0.2834	0.0744	-0.0718	0.0711	-0.0453
500	2.0	0.5	0.2	-0.0850	-0.0011	0.0083	-0.0015	-0.0086	-0.0467	-0.0071	-0.0347	0.0100	-0.0025	0.0070	-0.0058
500	2.0	0.5	1.0	-0.0915	-0.0018	-0.0129	-0.0024	-0.0384	-0.1904	-0.0320	-0.1529	0.0159	-0.0152	0.0327	-0.0117
500	2.0	0.5	3.5	-0.0467	-0.0019	0.0239	-0.0043	-0.1807	-0.2000	-0.1778	0.0836	0.0756	-0.0890	0.0762	-0.0442
500	3.0	0.0	0.2	-0.0057	0.0005	-0.0079	1.0674	0.0019	0.0005	0.0018	1.1676	0.0019	0.0005	0.0018	1.1676
500	3.0	0.0	1.0	-0.0140	0.0003	-0.0183	0.9663	0.0122	0.0003	0.0139	1.2066	0.0122	0.0003	0.0139	1.2066
500	3.0	0.0	3.5	0.0104	-0.0006	0.0140	0.9814	0.0373	-0.0006	0.0409	1.2300	0.0373	-0.0006	0.0409	1.2300
500	3.0	0.2	0.2	-0.0236	0.0003	-0.0037	0.0001	-0.0094	-0.0187	-0.0005	-0.0157	-0.0051	0.0003	0.0049	-0.0026

Bias				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
500	3.0	0.2	1.0	-0.0272	-0.0001	-0.0146	-0.0015	-0.0088	-0.0845	-0.0082	-0.0478	0.0124	-0.0006	0.0188	-0.0156
500	3.0	0.2	3.5	-0.0020	-0.0007	0.0198	0.0014	-0.0544	-0.1560	-0.0531	0.7313	0.0442	-0.0053	0.0481	-0.0591
500	3.0	0.4	0.2	-0.0643	-0.0002	-0.0026	-0.0005	-0.0237	-0.0355	-0.0018	-0.0259	-0.0124	-0.0003	0.0060	-0.0052
500	3.0	0.4	1.0	-0.0571	-0.0007	-0.0126	-0.0024	-0.0364	-0.1633	-0.0240	-0.1231	0.0068	-0.0018	0.0291	-0.0120
500	3.0	0.4	3.5	-0.0291	-0.0006	0.0202	-0.0019	-0.1292	-0.2000	-0.1307	0.2754	0.0426	-0.0091	0.0565	-0.0375
500	3.0	0.5	0.2	-0.1009	-0.0005	-0.0012	-0.0007	-0.0284	-0.0436	-0.0058	-0.0323	-0.0121	-0.0006	0.0065	-0.0069
500	3.0	0.5	1.0	-0.0982	-0.0009	-0.0108	-0.0021	-0.0453	-0.1888	-0.0310	-0.1507	0.0028	-0.0022	0.0316	-0.0142
500	3.0	0.5	3.5	-0.0577	-0.0010	0.0214	-0.0029	-0.1828	-0.2000	-0.1807	0.0849	0.0353	-0.0114	0.0646	-0.0413

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

CBS-CG: Cubic B-spline using control group.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.18 Variance of Switching Effect Estimates by Methodology as Switching Time Approaches 0 (Sample Size per Group = 100)

Variance				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
100	1.4	0.0	0.2	0.0514	0.0019	0.0292	0.1735	0.0025	0.0019	0.0027	0.0490	0.0025	0.0019	0.0027	0.0490
100	1.4	0.0	1.0	0.0402	0.0036	0.0259	0.2223	0.0100	0.0036	0.0098	0.0579	0.0100	0.0036	0.0098	0.0579
100	1.4	0.0	3.5	0.0456	0.0086	0.0250	0.2585	0.1026	0.0086	0.0976	0.1052	0.1026	0.0086	0.0976	0.1052
100	1.4	0.2	0.2	0.0513	0.0027	0.0288	0.0028	0.0030	0.0027	0.0028	0.0249	0.0028	0.0027	0.0025	0.0132
100	1.4	0.2	1.0	0.0467	0.0049	0.0270	0.0740	0.0094	0.0042	0.0093	0.3114	0.0076	0.0049	0.0072	0.1754
100	1.4	0.2	3.5	0.0546	0.0117	0.0282	0.2176	0.1172	0.0047	0.1350	0.0311	0.1198	0.0083	0.0985	0.1393
100	1.4	0.4	0.2	0.0586	0.0034	0.0288	0.0036	0.0023	0.0033	0.0025	0.0028	0.0016	0.0033	0.0021	0.0026
100	1.4	0.4	1.0	0.0469	0.0064	0.0283	0.0076	0.0091	0.0027	0.0095	0.1152	0.0041	0.0060	0.0058	0.0046
100	1.4	0.4	3.5	0.0617	0.0131	0.0301	0.0205	0.1492	0.0003	0.1689	0.0792	0.1188	0.0061	0.0930	0.2029
100	1.4	0.5	0.2	0.0608	0.0048	0.0292	0.0050	0.0017	0.0040	0.0028	0.0034	0.0013	0.0047	0.0022	0.0027
100	1.4	0.5	1.0	0.0491	0.0067	0.0301	0.0082	0.0101	0.0012	0.0103	0.0356	0.0029	0.0060	0.0051	0.0045
100	1.4	0.5	3.5	0.0619	0.0147	0.0327	0.0173	0.1214	0.0000	0.1277	0.0880	0.1466	0.0042	0.1145	0.1473
100	2.0	0.0	0.2	0.0502	0.0018	0.0294	0.1638	0.0024	0.0018	0.0026	0.0211	0.0024	0.0018	0.0026	0.0211
100	2.0	0.0	1.0	0.0391	0.0034	0.0248	0.2567	0.0090	0.0034	0.0099	0.0838	0.0090	0.0034	0.0099	0.0838
100	2.0	0.0	3.5	0.0427	0.0080	0.0281	0.2506	0.0961	0.0080	0.0848	0.0788	0.0961	0.0080	0.0848	0.0788
100	2.0	0.2	0.2	0.0508	0.0019	0.0300	0.0020	0.0022	0.0020	0.0023	0.0145	0.0021	0.0019	0.0022	0.0130
100	2.0	0.2	1.0	0.0428	0.0037	0.0262	0.0514	0.0088	0.0037	0.0082	0.3112	0.0061	0.0038	0.0067	0.1110
100	2.0	0.2	3.5	0.0506	0.0084	0.0294	0.2248	0.1195	0.0039	0.1342	0.0380	0.0879	0.0080	0.0734	0.2388
100	2.0	0.4	0.2	0.0549	0.0022	0.0301	0.0023	0.0023	0.0024	0.0021	0.0024	0.0019	0.0022	0.0018	0.0023
100	2.0	0.4	1.0	0.0458	0.0039	0.0250	0.0051	0.0086	0.0024	0.0080	0.0808	0.0044	0.0040	0.0062	0.0044
100	2.0	0.4	3.5	0.0576	0.0088	0.0301	0.0186	0.1511	0.0002	0.1345	0.0867	0.0661	0.0079	0.0532	0.1426
100	2.0	0.5	0.2	0.0606	0.0027	0.0306	0.0028	0.0023	0.0027	0.0021	0.0025	0.0017	0.0027	0.0018	0.0019
100	2.0	0.5	1.0	0.0479	0.0043	0.0256	0.0056	0.0094	0.0011	0.0089	0.0351	0.0045	0.0044	0.0057	0.0044
100	2.0	0.5	3.5	0.0556	0.0091	0.0286	0.0167	0.1054	0.0000	0.1054	0.1198	0.0818	0.0073	0.0563	0.0522
100	3.0	0.0	0.2	0.0502	0.0018	0.0294	0.1638	0.0024	0.0018	0.0026	0.0211	0.0024	0.0018	0.0026	0.0211
100	3.0	0.0	1.0	0.0391	0.0034	0.0248	0.2567	0.0090	0.0034	0.0099	0.0838	0.0090	0.0034	0.0099	0.0838
100	3.0	0.0	3.5	0.0427	0.0080	0.0281	0.2506	0.0961	0.0080	0.0848	0.0788	0.0961	0.0080	0.0848	0.0788
100	3.0	0.2	0.2	0.0507	0.0019	0.0298	0.0020	0.0022	0.0020	0.0023	0.0145	0.0021	0.0019	0.0022	0.0131

Variance				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
100	3.0	0.2	1.0	0.0426	0.0037	0.0263	0.0513	0.0088	0.0037	0.0081	0.3106	0.0063	0.0037	0.0068	0.1098
100	3.0	0.2	3.5	0.0506	0.0084	0.0295	0.2245	0.1195	0.0039	0.1329	0.0380	0.0800	0.0084	0.0741	0.2777
100	3.0	0.4	0.2	0.0525	0.0020	0.0293	0.0021	0.0022	0.0023	0.0019	0.0024	0.0018	0.0020	0.0018	0.0024
100	3.0	0.4	1.0	0.0448	0.0038	0.0257	0.0048	0.0085	0.0024	0.0084	0.0802	0.0048	0.0038	0.0069	0.0040
100	3.0	0.4	3.5	0.0576	0.0086	0.0302	0.0188	0.1511	0.0002	0.1311	0.0788	0.0733	0.0086	0.1108	0.0958
100	3.0	0.5	0.2	0.0536	0.0022	0.0302	0.0023	0.0023	0.0026	0.0019	0.0026	0.0018	0.0022	0.0017	0.0022
100	3.0	0.5	1.0	0.0473	0.0039	0.0265	0.0052	0.0089	0.0014	0.0087	0.0320	0.0047	0.0040	0.0066	0.0039
100	3.0	0.5	3.5	0.0534	0.0084	0.0298	0.0124	0.1054	0.0000	0.1068	0.1056	0.0735	0.0085	0.1456	0.0266

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

CBS-CG: Cubic B-spline using control group.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.19 Variance of Switching Effect Estimates by Methodology as Switching Time Approaches 0 (Sample Size per Group = 200)

Variance				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
200	1.4	0.0	0.2	0.0300	0.0009	0.0211	0.1536	0.0010	0.0009	0.0012	0.0199	0.0010	0.0009	0.0012	0.0199
200	1.4	0.0	1.0	0.0299	0.0018	0.0219	0.2019	0.0056	0.0018	0.0052	0.0315	0.0056	0.0018	0.0052	0.0315
200	1.4	0.0	3.5	0.0357	0.0053	0.0232	0.2700	0.0606	0.0053	0.0583	0.0770	0.0606	0.0053	0.0583	0.0770
200	1.4	0.2	0.2	0.0367	0.0011	0.0217	0.0012	0.0014	0.0011	0.0013	0.0016	0.0015	0.0011	0.0013	0.0017
200	1.4	0.2	1.0	0.0363	0.0022	0.0227	0.0147	0.0063	0.0020	0.0064	0.2065	0.0050	0.0022	0.0050	0.0395
200	1.4	0.2	3.5	0.0388	0.0059	0.0230	0.0963	0.0862	0.0032	0.0842	0.1618	0.0585	0.0052	0.0509	0.2978
200	1.4	0.4	0.2	0.0478	0.0017	0.0256	0.0018	0.0015	0.0015	0.0015	0.0019	0.0012	0.0017	0.0015	0.0012
200	1.4	0.4	1.0	0.0394	0.0026	0.0232	0.0036	0.0066	0.0012	0.0067	0.0146	0.0036	0.0025	0.0041	0.0028
200	1.4	0.4	3.5	0.0440	0.0070	0.0274	0.0111	0.0898	0.0001	0.0902	0.1971	0.0752	0.0040	0.0609	0.1024
200	1.4	0.5	0.2	0.0509	0.0024	0.0260	0.0025	0.0011	0.0019	0.0017	0.0019	0.0008	0.0022	0.0016	0.0016
200	1.4	0.5	1.0	0.0412	0.0035	0.0260	0.0047	0.0068	0.0004	0.0068	0.0049	0.0020	0.0033	0.0051	0.0031
200	1.4	0.5	3.5	0.0443	0.0083	0.0278	0.0114	0.0655	0.0000	0.0699	0.2047	0.0762	0.0024	0.0710	0.0606
200	2.0	0.0	0.2	0.0306	0.0009	0.0204	0.1639	0.0011	0.0009	0.0013	0.0201	0.0011	0.0009	0.0013	0.0201
200	2.0	0.0	1.0	0.0302	0.0018	0.0223	0.2280	0.0056	0.0018	0.0057	0.0313	0.0056	0.0018	0.0057	0.0313
200	2.0	0.0	3.5	0.0365	0.0051	0.0227	0.2825	0.0538	0.0051	0.0583	0.1040	0.0538	0.0051	0.0583	0.1040
200	2.0	0.2	0.2	0.0327	0.0009	0.0196	0.0010	0.0010	0.0010	0.0011	0.0015	0.0010	0.0009	0.0011	0.0017
200	2.0	0.2	1.0	0.0363	0.0019	0.0229	0.0022	0.0054	0.0019	0.0049	0.1885	0.0044	0.0019	0.0045	0.0372
200	2.0	0.2	3.5	0.0404	0.0052	0.0235	0.1065	0.0743	0.0028	0.0727	0.1491	0.0535	0.0050	0.0599	0.2449
200	2.0	0.4	0.2	0.0390	0.0010	0.0217	0.0010	0.0012	0.0010	0.0010	0.0011	0.0011	0.0010	0.0010	0.0009
200	2.0	0.4	1.0	0.0401	0.0019	0.0233	0.0020	0.0049	0.0013	0.0050	0.0320	0.0028	0.0020	0.0040	0.0023
200	2.0	0.4	3.5	0.0470	0.0058	0.0248	0.0096	0.0782	0.0001	0.0783	0.1947	0.0398	0.0052	0.0563	0.0313
200	2.0	0.5	0.2	0.0458	0.0011	0.0235	0.0012	0.0013	0.0011	0.0011	0.0012	0.0009	0.0011	0.0011	0.0010
200	2.0	0.5	1.0	0.0382	0.0020	0.0223	0.0024	0.0056	0.0005	0.0055	0.0036	0.0025	0.0020	0.0041	0.0019
200	2.0	0.5	3.5	0.0454	0.0055	0.0255	0.0096	0.0518	0.0000	0.0589	0.2294	0.0376	0.0050	0.0577	0.0207
200	3.0	0.0	0.2	0.0306	0.0009	0.0204	0.1639	0.0011	0.0009	0.0013	0.0201	0.0011	0.0009	0.0013	0.0201
200	3.0	0.0	1.0	0.0302	0.0018	0.0223	0.2280	0.0056	0.0018	0.0057	0.0313	0.0056	0.0018	0.0057	0.0313
200	3.0	0.0	3.5	0.0365	0.0051	0.0227	0.2825	0.0538	0.0051	0.0583	0.1040	0.0538	0.0051	0.0583	0.1040
200	3.0	0.2	0.2	0.0326	0.0009	0.0194	0.0010	0.0010	0.0010	0.0011	0.0014	0.0010	0.0009	0.0011	0.0017

Variance				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
200	3.0	0.2	1.0	0.0364	0.0019	0.0230	0.0021	0.0054	0.0019	0.0049	0.1817	0.0044	0.0019	0.0043	0.0371
200	3.0	0.2	3.5	0.0405	0.0052	0.0235	0.1066	0.0743	0.0028	0.0727	0.1597	0.0537	0.0052	0.0742	0.1672
200	3.0	0.4	0.2	0.0371	0.0010	0.0209	0.0010	0.0011	0.0010	0.0010	0.0009	0.0011	0.0010	0.0010	0.0009
200	3.0	0.4	1.0	0.0394	0.0019	0.0230	0.0020	0.0048	0.0013	0.0050	0.0318	0.0032	0.0019	0.0044	0.0018
200	3.0	0.4	3.5	0.0449	0.0055	0.0246	0.0090	0.0783	0.0000	0.0775	0.1869	0.0460	0.0054	0.0652	0.0238
200	3.0	0.5	0.2	0.0392	0.0010	0.0224	0.0010	0.0012	0.0011	0.0010	0.0011	0.0011	0.0010	0.0010	0.0010
200	3.0	0.5	1.0	0.0359	0.0019	0.0229	0.0022	0.0051	0.0006	0.0055	0.0035	0.0029	0.0019	0.0040	0.0016
200	3.0	0.5	3.5	0.0429	0.0053	0.0245	0.0092	0.0518	0.0000	0.0556	0.2269	0.0431	0.0053	0.0580	0.0107

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

CBS-CG: Cubic B-spline using control group.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.20 Variance of Switching Effect Estimates by Methodology as Switching Time Approaches 0 (Sample Size per Group = 500)

Variance				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
500	1.4	0.0	0.2	0.0266	0.0004	0.0193	0.1690	0.0005	0.0004	0.0005	0.0909	0.0005	0.0004	0.0005	0.0909
500	1.4	0.0	1.0	0.0241	0.0008	0.0189	0.2467	0.0027	0.0008	0.0027	0.0760	0.0027	0.0008	0.0027	0.0760
500	1.4	0.0	3.5	0.0313	0.0022	0.0207	0.2357	0.0407	0.0022	0.0392	0.0406	0.0407	0.0022	0.0392	0.0406
500	1.4	0.2	0.2	0.0284	0.0005	0.0196	0.0006	0.0007	0.0005	0.0006	0.0008	0.0006	0.0005	0.0006	0.0007
500	1.4	0.2	1.0	0.0294	0.0009	0.0182	0.0012	0.0030	0.0009	0.0030	0.0019	0.0023	0.0010	0.0024	0.0016
500	1.4	0.2	3.5	0.0342	0.0025	0.0194	0.0048	0.0488	0.0017	0.0468	0.2700	0.0210	0.0025	0.0181	0.1961
500	1.4	0.4	0.2	0.0326	0.0007	0.0214	0.0007	0.0008	0.0006	0.0008	0.0008	0.0006	0.0007	0.0007	0.0007
500	1.4	0.4	1.0	0.0356	0.0013	0.0212	0.0017	0.0032	0.0007	0.0036	0.0021	0.0011	0.0011	0.0018	0.0009
500	1.4	0.4	3.5	0.0410	0.0032	0.0241	0.0052	0.0483	0.0000	0.0505	0.2709	0.0154	0.0021	0.0158	0.0061
500	1.4	0.5	0.2	0.0414	0.0008	0.0233	0.0009	0.0007	0.0006	0.0007	0.0008	0.0004	0.0008	0.0008	0.0008
500	1.4	0.5	1.0	0.0348	0.0016	0.0215	0.0020	0.0040	0.0001	0.0039	0.0022	0.0005	0.0012	0.0011	0.0009
500	1.4	0.5	3.5	0.0390	0.0037	0.0243	0.0070	0.0429	0.0000	0.0473	0.2388	0.0152	0.0011	0.0185	0.0075
500	2.0	0.0	0.2	0.0258	0.0004	0.0190	0.2030	0.0005	0.0004	0.0005	0.1042	0.0005	0.0004	0.0005	0.1042
500	2.0	0.0	1.0	0.0226	0.0007	0.0188	0.2814	0.0023	0.0007	0.0025	0.0593	0.0023	0.0007	0.0025	0.0593
500	2.0	0.0	3.5	0.0311	0.0021	0.0197	0.2736	0.0340	0.0021	0.0371	0.0331	0.0340	0.0021	0.0371	0.0331
500	2.0	0.2	0.2	0.0271	0.0004	0.0186	0.0004	0.0005	0.0004	0.0005	0.0006	0.0005	0.0004	0.0006	0.0007
500	2.0	0.2	1.0	0.0248	0.0008	0.0179	0.0010	0.0024	0.0008	0.0025	0.0254	0.0021	0.0008	0.0021	0.0018
500	2.0	0.2	3.5	0.0348	0.0021	0.0200	0.0045	0.0447	0.0015	0.0396	0.2737	0.0177	0.0022	0.0151	0.0471
500	2.0	0.4	0.2	0.0301	0.0005	0.0190	0.0005	0.0006	0.0005	0.0006	0.0005	0.0005	0.0005	0.0005	0.0005
500	2.0	0.4	1.0	0.0282	0.0009	0.0190	0.0010	0.0029	0.0008	0.0027	0.0015	0.0014	0.0008	0.0016	0.0009
500	2.0	0.4	3.5	0.0363	0.0023	0.0211	0.0042	0.0499	0.0000	0.0553	0.2905	0.0056	0.0025	0.0117	0.0046
500	2.0	0.5	0.2	0.0307	0.0005	0.0192	0.0005	0.0008	0.0005	0.0006	0.0005	0.0005	0.0005	0.0005	0.0005
500	2.0	0.5	1.0	0.0273	0.0009	0.0193	0.0011	0.0049	0.0003	0.0036	0.0016	0.0010	0.0009	0.0013	0.0009
500	2.0	0.5	3.5	0.0349	0.0023	0.0216	0.0043	0.0417	0.0000	0.0480	0.2500	0.0063	0.0026	0.0103	0.0042
500	3.0	0.0	0.2	0.0258	0.0004	0.0190	0.2030	0.0005	0.0004	0.0005	0.1042	0.0005	0.0004	0.0005	0.1042
500	3.0	0.0	1.0	0.0226	0.0007	0.0188	0.2814	0.0023	0.0007	0.0025	0.0593	0.0023	0.0007	0.0025	0.0593
500	3.0	0.0	3.5	0.0311	0.0021	0.0197	0.2736	0.0340	0.0021	0.0371	0.0331	0.0340	0.0021	0.0371	0.0331
500	3.0	0.2	0.2	0.0272	0.0004	0.0186	0.0004	0.0005	0.0004	0.0005	0.0007	0.0005	0.0004	0.0005	0.0007

Variance				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
500	3.0	0.2	1.0	0.0248	0.0008	0.0180	0.0010	0.0024	0.0008	0.0025	0.0254	0.0022	0.0008	0.0022	0.0018
500	3.0	0.2	3.5	0.0348	0.0021	0.0200	0.0044	0.0447	0.0016	0.0393	0.2737	0.0150	0.0021	0.0192	0.0017
500	3.0	0.4	0.2	0.0282	0.0005	0.0187	0.0005	0.0005	0.0005	0.0006	0.0005	0.0005	0.0005	0.0005	0.0006
500	3.0	0.4	1.0	0.0262	0.0008	0.0191	0.0010	0.0028	0.0008	0.0027	0.0015	0.0015	0.0008	0.0020	0.0009
500	3.0	0.4	3.5	0.0359	0.0022	0.0206	0.0042	0.0495	0.0000	0.0541	0.2898	0.0155	0.0023	0.0232	0.0042
500	3.0	0.5	0.2	0.0273	0.0005	0.0185	0.0005	0.0006	0.0005	0.0006	0.0005	0.0005	0.0005	0.0005	0.0005
500	3.0	0.5	1.0	0.0236	0.0009	0.0186	0.0011	0.0045	0.0003	0.0035	0.0016	0.0010	0.0009	0.0016	0.0009
500	3.0	0.5	3.5	0.0335	0.0022	0.0210	0.0044	0.0400	0.0000	0.0460	0.2500	0.0140	0.0023	0.0208	0.0042

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

CBS-CG: Cubic B-spline using control group.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.21 Mean Squared Error of Switching Effect Estimates by Methodology as Switching Time Approaches 0 (Sample Size per Group = 100)

MSE				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
100	1.4	0.0	0.2	0.0540	0.0019	0.0295	1.4012	0.0025	0.0019	0.0027	1.5448	0.0025	0.0019	0.0027	1.5448
100	1.4	0.0	1.0	0.0398	0.0036	0.0256	1.3549	0.0100	0.0036	0.0098	1.5441	0.0100	0.0036	0.0098	1.5441
100	1.4	0.0	3.5	0.0453	0.0088	0.0248	1.3068	0.1041	0.0088	0.1021	1.4611	0.1041	0.0088	0.1021	1.4611
100	1.4	0.2	0.2	0.0540	0.0027	0.0289	0.0028	0.0030	0.0031	0.0027	0.0249	0.0028	0.0027	0.0025	0.0133
100	1.4	0.2	1.0	0.0469	0.0049	0.0267	0.0792	0.0100	0.0121	0.0099	0.5733	0.0077	0.0051	0.0073	0.1990
100	1.4	0.2	3.5	0.0547	0.0116	0.0279	0.3540	0.1362	0.0260	0.1559	1.0916	0.1191	0.0147	0.0977	0.9327
100	1.4	0.4	0.2	0.0599	0.0034	0.0285	0.0036	0.0023	0.0050	0.0026	0.0050	0.0018	0.0033	0.0021	0.0035
100	1.4	0.4	1.0	0.0469	0.0064	0.0280	0.0075	0.0117	0.0276	0.0122	0.1143	0.0041	0.0072	0.0058	0.0080
100	1.4	0.4	3.5	0.0635	0.0129	0.0298	0.0205	0.1865	0.0381	0.2052	0.6591	0.1184	0.0244	0.0926	0.3280
100	1.4	0.5	0.2	0.0657	0.0048	0.0304	0.0049	0.0018	0.0072	0.0031	0.0067	0.0016	0.0047	0.0022	0.0042
100	1.4	0.5	1.0	0.0486	0.0067	0.0298	0.0081	0.0139	0.0340	0.0151	0.0527	0.0030	0.0081	0.0052	0.0084
100	1.4	0.5	3.5	0.0635	0.0146	0.0324	0.0173	0.1673	0.0396	0.1786	0.4906	0.1465	0.0288	0.1138	0.1711
100	2.0	0.0	0.2	0.0532	0.0019	0.0300	1.4333	0.0024	0.0019	0.0026	1.5864	0.0024	0.0019	0.0026	1.5864
100	2.0	0.0	1.0	0.0388	0.0034	0.0247	1.3395	0.0090	0.0034	0.0100	1.5292	0.0090	0.0034	0.0100	1.5292
100	2.0	0.0	3.5	0.0426	0.0081	0.0280	1.3506	0.0969	0.0081	0.0865	1.5226	0.0969	0.0081	0.0865	1.5226
100	2.0	0.2	0.2	0.0558	0.0019	0.0306	0.0020	0.0024	0.0026	0.0023	0.0151	0.0021	0.0020	0.0022	0.0130
100	2.0	0.2	1.0	0.0429	0.0037	0.0260	0.0529	0.0103	0.0119	0.0094	0.5538	0.0061	0.0039	0.0066	0.1138
100	2.0	0.2	3.5	0.0509	0.0086	0.0291	0.3538	0.1441	0.0266	0.1575	1.0900	0.0875	0.0106	0.0727	0.7697
100	2.0	0.4	0.2	0.0663	0.0022	0.0304	0.0023	0.0028	0.0038	0.0022	0.0043	0.0019	0.0022	0.0018	0.0031
100	2.0	0.4	1.0	0.0505	0.0039	0.0247	0.0051	0.0124	0.0269	0.0109	0.0823	0.0044	0.0042	0.0063	0.0070
100	2.0	0.4	3.5	0.0629	0.0090	0.0298	0.0185	0.1968	0.0389	0.1880	0.6556	0.0655	0.0143	0.0540	0.1561
100	2.0	0.5	0.2	0.0756	0.0027	0.0307	0.0027	0.0026	0.0048	0.0022	0.0048	0.0017	0.0027	0.0018	0.0026
100	2.0	0.5	1.0	0.0563	0.0043	0.0253	0.0056	0.0157	0.0328	0.0135	0.0522	0.0044	0.0046	0.0058	0.0071
100	2.0	0.5	3.5	0.0655	0.0092	0.0283	0.0165	0.1620	0.0399	0.1722	0.4774	0.0822	0.0159	0.0586	0.0524
100	3.0	0.0	0.2	0.0532	0.0019	0.0300	1.4333	0.0024	0.0019	0.0026	1.5864	0.0024	0.0019	0.0026	1.5864
100	3.0	0.0	1.0	0.0388	0.0034	0.0247	1.3395	0.0090	0.0034	0.0100	1.5292	0.0090	0.0034	0.0100	1.5292
100	3.0	0.0	3.5	0.0426	0.0081	0.0280	1.3506	0.0969	0.0081	0.0865	1.5226	0.0969	0.0081	0.0865	1.5226
100	3.0	0.2	0.2	0.0557	0.0019	0.0305	0.0020	0.0024	0.0025	0.0023	0.0150	0.0021	0.0019	0.0022	0.0131

MSE				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
100	3.0	0.2	1.0	0.0428	0.0037	0.0261	0.0528	0.0103	0.0119	0.0093	0.5540	0.0062	0.0037	0.0068	0.1120
100	3.0	0.2	3.5	0.0509	0.0086	0.0292	0.3539	0.1441	0.0265	0.1552	1.0909	0.0806	0.0087	0.0738	0.6639
100	3.0	0.4	0.2	0.0638	0.0020	0.0297	0.0021	0.0029	0.0037	0.0020	0.0041	0.0020	0.0020	0.0018	0.0032
100	3.0	0.4	1.0	0.0495	0.0038	0.0255	0.0048	0.0125	0.0269	0.0115	0.0813	0.0048	0.0038	0.0069	0.0061
100	3.0	0.4	3.5	0.0631	0.0087	0.0299	0.0186	0.1968	0.0388	0.1898	0.6639	0.0732	0.0090	0.1100	0.0967
100	3.0	0.5	0.2	0.0706	0.0022	0.0307	0.0023	0.0033	0.0046	0.0021	0.0048	0.0021	0.0022	0.0017	0.0030
100	3.0	0.5	1.0	0.0569	0.0039	0.0263	0.0053	0.0158	0.0325	0.0133	0.0503	0.0048	0.0039	0.0067	0.0060
100	3.0	0.5	3.5	0.0649	0.0085	0.0295	0.0124	0.1620	0.0399	0.1708	0.4904	0.0737	0.0089	0.1442	0.0298

MSE: Mean squared error

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

CBS-CG: Cubic B-spline using control group.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.22 Mean Squared Error of Switching Effect Estimates by Methodology as Switching Time Approaches 0 (Sample Size per Group = 200)

MSE				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
200	1.4	0.0	0.2	0.0298	0.0009	0.0210	1.3923	0.0010	0.0009	0.0012	1.5459	0.0010	0.0009	0.0012	1.5459
200	1.4	0.0	1.0	0.0296	0.0018	0.0217	1.3332	0.0055	0.0018	0.0052	1.5318	0.0055	0.0018	0.0052	1.5318
200	1.4	0.0	3.5	0.0354	0.0052	0.0230	1.2517	0.0609	0.0052	0.0597	1.4669	0.0609	0.0052	0.0597	1.4669
200	1.4	0.2	0.2	0.0371	0.0011	0.0216	0.0011	0.0014	0.0016	0.0013	0.0021	0.0015	0.0011	0.0014	0.0018
200	1.4	0.2	1.0	0.0364	0.0022	0.0226	0.0147	0.0066	0.0093	0.0066	0.2300	0.0053	0.0024	0.0053	0.0392
200	1.4	0.2	3.5	0.0386	0.0059	0.0228	0.1056	0.0904	0.0233	0.0889	0.9315	0.0590	0.0103	0.0517	0.6115
200	1.4	0.4	0.2	0.0481	0.0017	0.0254	0.0018	0.0016	0.0037	0.0016	0.0033	0.0016	0.0017	0.0015	0.0015
200	1.4	0.4	1.0	0.0398	0.0026	0.0233	0.0036	0.0083	0.0290	0.0087	0.0299	0.0041	0.0040	0.0044	0.0037
200	1.4	0.4	3.5	0.0436	0.0070	0.0273	0.0110	0.1115	0.0393	0.1094	0.5236	0.0780	0.0232	0.0624	0.1029
200	1.4	0.5	0.2	0.0519	0.0024	0.0261	0.0025	0.0013	0.0057	0.0019	0.0041	0.0016	0.0023	0.0016	0.0023
200	1.4	0.5	1.0	0.0421	0.0035	0.0266	0.0047	0.0097	0.0370	0.0107	0.0338	0.0024	0.0060	0.0053	0.0047
200	1.4	0.5	3.5	0.0438	0.0082	0.0283	0.0113	0.0958	0.0400	0.1029	0.3800	0.0785	0.0296	0.0720	0.0622
200	2.0	0.0	0.2	0.0305	0.0009	0.0204	1.3729	0.0011	0.0009	0.0013	1.5433	0.0011	0.0009	0.0013	1.5433
200	2.0	0.0	1.0	0.0299	0.0018	0.0220	1.2783	0.0056	0.0018	0.0057	1.5262	0.0056	0.0018	0.0057	1.5262
200	2.0	0.0	3.5	0.0363	0.0050	0.0226	1.2331	0.0556	0.0050	0.0589	1.4346	0.0556	0.0050	0.0589	1.4346
200	2.0	0.2	0.2	0.0339	0.0009	0.0196	0.0009	0.0011	0.0013	0.0011	0.0019	0.0010	0.0009	0.0011	0.0018
200	2.0	0.2	1.0	0.0362	0.0019	0.0228	0.0021	0.0059	0.0091	0.0053	0.2060	0.0045	0.0019	0.0050	0.0368
200	2.0	0.2	3.5	0.0402	0.0051	0.0234	0.1183	0.0799	0.0239	0.0773	0.9440	0.0547	0.0062	0.0613	0.3097
200	2.0	0.4	0.2	0.0461	0.0010	0.0216	0.0010	0.0014	0.0022	0.0010	0.0018	0.0011	0.0010	0.0010	0.0010
200	2.0	0.4	1.0	0.0436	0.0019	0.0231	0.0020	0.0075	0.0264	0.0068	0.0411	0.0029	0.0020	0.0048	0.0030
200	2.0	0.4	3.5	0.0494	0.0057	0.0247	0.0095	0.0985	0.0395	0.1030	0.5351	0.0439	0.0095	0.0580	0.0330
200	2.0	0.5	0.2	0.0558	0.0011	0.0233	0.0011	0.0014	0.0031	0.0011	0.0023	0.0009	0.0011	0.0012	0.0013
200	2.0	0.5	1.0	0.0469	0.0019	0.0221	0.0023	0.0104	0.0343	0.0082	0.0283	0.0026	0.0021	0.0048	0.0024
200	2.0	0.5	3.5	0.0506	0.0055	0.0253	0.0095	0.0821	0.0400	0.0950	0.3756	0.0420	0.0114	0.0596	0.0244
200	3.0	0.0	0.2	0.0305	0.0009	0.0204	1.3729	0.0011	0.0009	0.0013	1.5433	0.0011	0.0009	0.0013	1.5433
200	3.0	0.0	1.0	0.0299	0.0018	0.0220	1.2783	0.0056	0.0018	0.0057	1.5262	0.0056	0.0018	0.0057	1.5262
200	3.0	0.0	3.5	0.0363	0.0050	0.0226	1.2331	0.0556	0.0050	0.0589	1.4346	0.0556	0.0050	0.0589	1.4346
200	3.0	0.2	0.2	0.0338	0.0009	0.0195	0.0010	0.0010	0.0013	0.0011	0.0018	0.0010	0.0009	0.0011	0.0019

MSE				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
200	3.0	0.2	1.0	0.0363	0.0019	0.0228	0.0021	0.0059	0.0091	0.0053	0.1961	0.0045	0.0019	0.0047	0.0367
200	3.0	0.2	3.5	0.0403	0.0052	0.0233	0.1185	0.0799	0.0238	0.0773	0.9321	0.0539	0.0051	0.0737	0.1773
200	3.0	0.4	0.2	0.0452	0.0010	0.0210	0.0010	0.0015	0.0022	0.0010	0.0017	0.0011	0.0010	0.0011	0.0010
200	3.0	0.4	1.0	0.0430	0.0019	0.0228	0.0020	0.0076	0.0265	0.0067	0.0410	0.0032	0.0019	0.0050	0.0023
200	3.0	0.4	3.5	0.0474	0.0054	0.0244	0.0090	0.0985	0.0396	0.1018	0.5462	0.0464	0.0054	0.0658	0.0256
200	3.0	0.5	0.2	0.0541	0.0010	0.0225	0.0010	0.0018	0.0028	0.0010	0.0021	0.0011	0.0010	0.0010	0.0012
200	3.0	0.5	1.0	0.0457	0.0019	0.0227	0.0022	0.0108	0.0341	0.0080	0.0277	0.0029	0.0019	0.0048	0.0022
200	3.0	0.5	3.5	0.0493	0.0053	0.0243	0.0092	0.0821	0.0400	0.0936	0.3794	0.0435	0.0053	0.0594	0.0154

MSE: Mean squared error

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

CBS-CG: Cubic B-spline using control group.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Table A.23 Mean Squared Error of Switching Effect Estimates by Methodology as Switching Time Approaches 0 (Sample Size per Group = 500)

MSE				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
500	1.4	0.0	0.2	0.0263	0.0004	0.0191	1.3851	0.0005	0.0004	0.0005	1.4805	0.0005	0.0004	0.0005	1.4805
500	1.4	0.0	1.0	0.0241	0.0008	0.0190	1.2753	0.0029	0.0008	0.0028	1.4936	0.0029	0.0008	0.0028	1.4936
500	1.4	0.0	3.5	0.0313	0.0022	0.0206	1.2957	0.0415	0.0022	0.0398	1.5268	0.0415	0.0022	0.0398	1.5268
500	1.4	0.2	0.2	0.0283	0.0005	0.0195	0.0006	0.0007	0.0009	0.0006	0.0010	0.0007	0.0005	0.0006	0.0007
500	1.4	0.2	1.0	0.0303	0.0009	0.0184	0.0012	0.0030	0.0083	0.0030	0.0066	0.0031	0.0012	0.0031	0.0017
500	1.4	0.2	3.5	0.0339	0.0025	0.0194	0.0047	0.0508	0.0258	0.0496	0.7920	0.0262	0.0088	0.0220	0.2258
500	1.4	0.4	0.2	0.0324	0.0007	0.0214	0.0007	0.0011	0.0026	0.0008	0.0017	0.0020	0.0007	0.0008	0.0007
500	1.4	0.4	1.0	0.0359	0.0013	0.0213	0.0017	0.0036	0.0306	0.0040	0.0181	0.0025	0.0026	0.0026	0.0013
500	1.4	0.4	3.5	0.0407	0.0032	0.0239	0.0053	0.0613	0.0399	0.0663	0.4000	0.0236	0.0246	0.0212	0.0087
500	1.4	0.5	0.2	0.0410	0.0008	0.0233	0.0009	0.0019	0.0040	0.0008	0.0022	0.0029	0.0008	0.0008	0.0009
500	1.4	0.5	1.0	0.0345	0.0015	0.0215	0.0020	0.0049	0.0386	0.0055	0.0283	0.0020	0.0040	0.0020	0.0014
500	1.4	0.5	3.5	0.0387	0.0037	0.0241	0.0070	0.0706	0.0400	0.0744	0.2439	0.0228	0.0332	0.0237	0.0116
500	2.0	0.0	0.2	0.0255	0.0004	0.0189	1.3403	0.0005	0.0004	0.0005	1.4664	0.0005	0.0004	0.0005	1.4664
500	2.0	0.0	1.0	0.0226	0.0007	0.0190	1.2123	0.0025	0.0007	0.0027	1.5146	0.0025	0.0007	0.0027	1.5146
500	2.0	0.0	3.5	0.0309	0.0021	0.0197	1.2341	0.0351	0.0021	0.0384	1.5457	0.0351	0.0021	0.0384	1.5457
500	2.0	0.2	0.2	0.0274	0.0004	0.0184	0.0004	0.0005	0.0008	0.0005	0.0008	0.0005	0.0004	0.0006	0.0007
500	2.0	0.2	1.0	0.0253	0.0008	0.0179	0.0010	0.0025	0.0079	0.0025	0.0273	0.0024	0.0008	0.0026	0.0020
500	2.0	0.2	3.5	0.0345	0.0021	0.0202	0.0044	0.0472	0.0258	0.0424	0.8061	0.0211	0.0036	0.0188	0.0467
500	2.0	0.4	0.2	0.0330	0.0005	0.0188	0.0005	0.0009	0.0018	0.0006	0.0012	0.0005	0.0005	0.0006	0.0006
500	2.0	0.4	1.0	0.0304	0.0008	0.0189	0.0010	0.0041	0.0278	0.0033	0.0169	0.0016	0.0010	0.0026	0.0010
500	2.0	0.4	3.5	0.0364	0.0023	0.0214	0.0042	0.0659	0.0400	0.0730	0.3679	0.0111	0.0076	0.0166	0.0066
500	2.0	0.5	0.2	0.0376	0.0005	0.0191	0.0005	0.0008	0.0027	0.0006	0.0017	0.0006	0.0005	0.0006	0.0006
500	2.0	0.5	1.0	0.0354	0.0009	0.0192	0.0011	0.0063	0.0365	0.0046	0.0250	0.0013	0.0011	0.0024	0.0010
500	2.0	0.5	3.5	0.0368	0.0023	0.0220	0.0043	0.0740	0.0400	0.0792	0.2545	0.0119	0.0105	0.0160	0.0061
500	3.0	0.0	0.2	0.0255	0.0004	0.0189	1.3403	0.0005	0.0004	0.0005	1.4664	0.0005	0.0004	0.0005	1.4664
500	3.0	0.0	1.0	0.0226	0.0007	0.0190	1.2123	0.0025	0.0007	0.0027	1.5146	0.0025	0.0007	0.0027	1.5146
500	3.0	0.0	3.5	0.0309	0.0021	0.0197	1.2341	0.0351	0.0021	0.0384	1.5457	0.0351	0.0021	0.0384	1.5457
500	3.0	0.2	0.2	0.0275	0.0004	0.0185	0.0004	0.0005	0.0008	0.0005	0.0009	0.0005	0.0004	0.0006	0.0007

MSE				Common				Varying(A)				Varying(B)			
n	C_L	β	ρ_S	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG	CBS-CG	PAFT	CBS-OG	PM-OG
500	3.0	0.2	1.0	0.0253	0.0008	0.0181	0.0010	0.0024	0.0079	0.0025	0.0274	0.0024	0.0008	0.0025	0.0020
500	3.0	0.2	3.5	0.0345	0.0021	0.0202	0.0044	0.0472	0.0259	0.0418	0.8059	0.0168	0.0021	0.0213	0.0051
500	3.0	0.4	0.2	0.0320	0.0005	0.0185	0.0005	0.0011	0.0017	0.0006	0.0012	0.0007	0.0005	0.0006	0.0006
500	3.0	0.4	1.0	0.0292	0.0008	0.0191	0.0010	0.0041	0.0274	0.0032	0.0166	0.0016	0.0008	0.0028	0.0010
500	3.0	0.4	3.5	0.0364	0.0022	0.0208	0.0041	0.0657	0.0400	0.0706	0.3628	0.0171	0.0023	0.0262	0.0056
500	3.0	0.5	0.2	0.0372	0.0005	0.0184	0.0005	0.0014	0.0024	0.0006	0.0016	0.0007	0.0005	0.0006	0.0006
500	3.0	0.5	1.0	0.0330	0.0008	0.0185	0.0011	0.0065	0.0360	0.0044	0.0243	0.0010	0.0008	0.0026	0.0011
500	3.0	0.5	3.5	0.0365	0.0022	0.0213	0.0044	0.0731	0.0400	0.0782	0.2547	0.0151	0.0024	0.0248	0.0059

MSE: Mean squared error

Common: Type where the switching effect remains constant over time.

Varying(A): Type where the switching effect decreases over time.

Varying(B): Type where the switching effect decreases by interval.

n: Sample size per group; C_L: Maximum follow-up time; β: Treatment effect; ρ_S: Switching time shape parameter

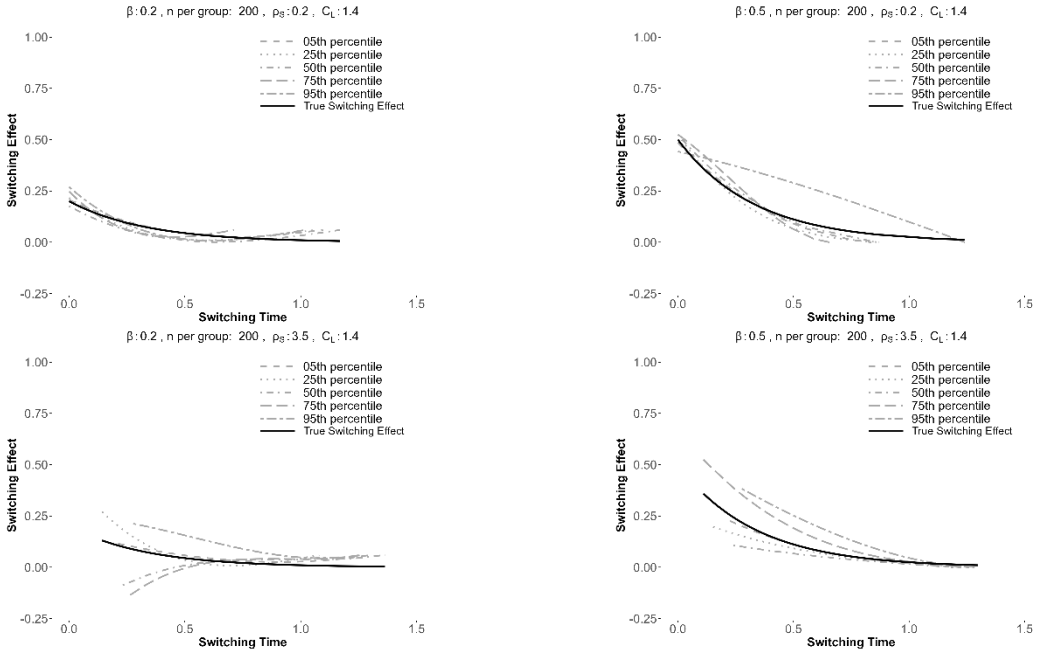
CBS-CG: Cubic B-spline using control group.

PAFT: Proposed accelerated failure time model.

CBS-OG: Cubic B-spline using overall group.

PM-OG: Piecewise model using overall group.

Appendix IV

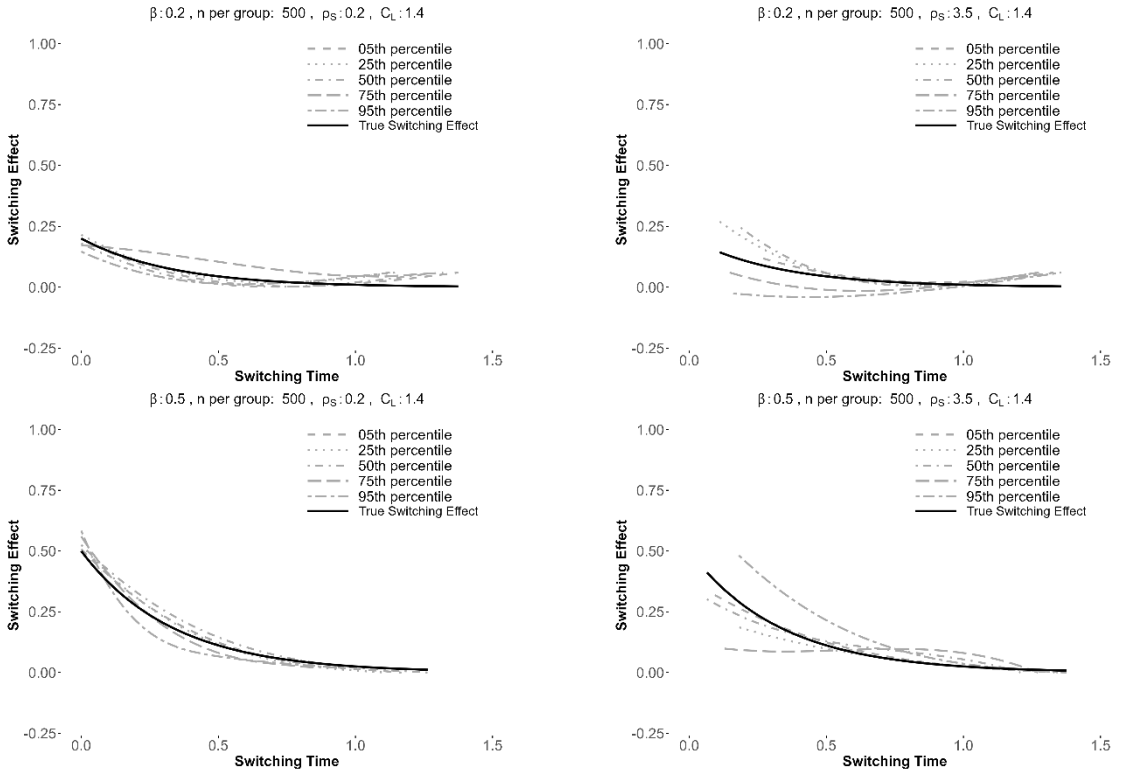


$\rho_S = 0.2$

$\rho_S = 3.5$

$\beta = 0.2$ $\beta = 0.5$

Figure A.1 Fit Results of the Varying Type A by CBS-CG at the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE (n per group = 200, C_L= 1.4)



$\rho_S = 0.2$

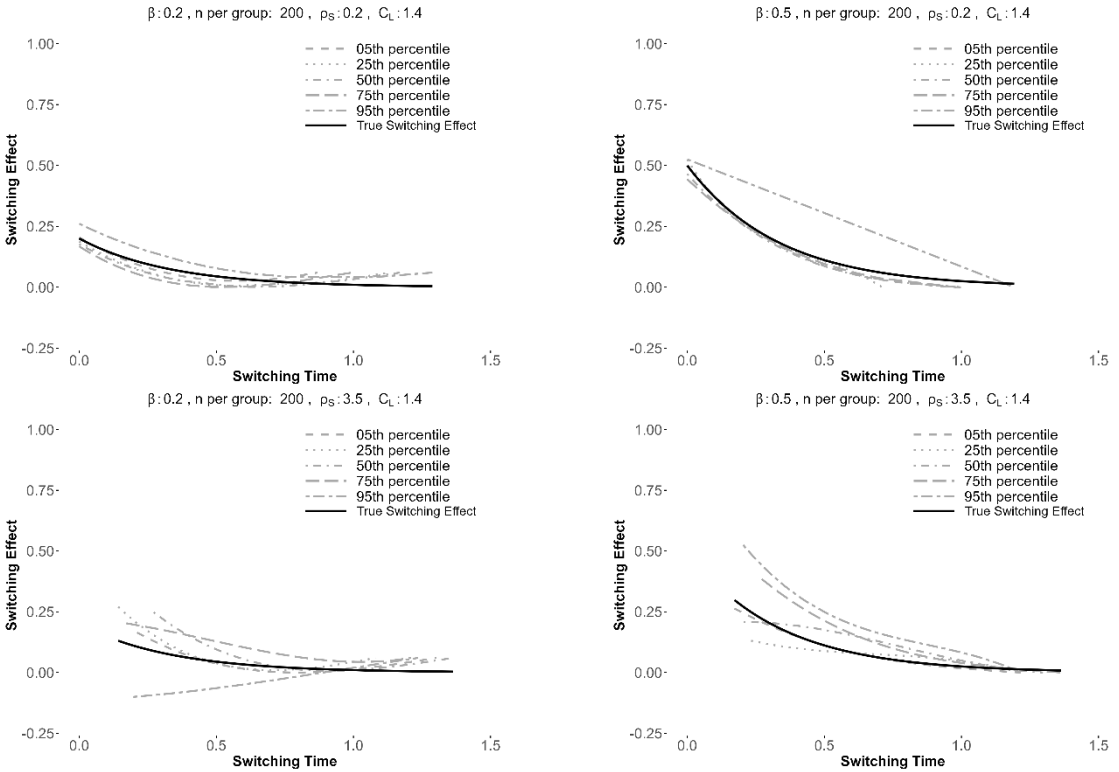
$\rho_S = 3.5$

$\beta = 0.2$ $\beta = 0.5$

Figure A.2 Fit Results of the Varying Type A by CBS-CG at the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE (n per group = 500, C_L= 1.4)

$\rho_S = 0.2$

$\rho_S = 3.5$

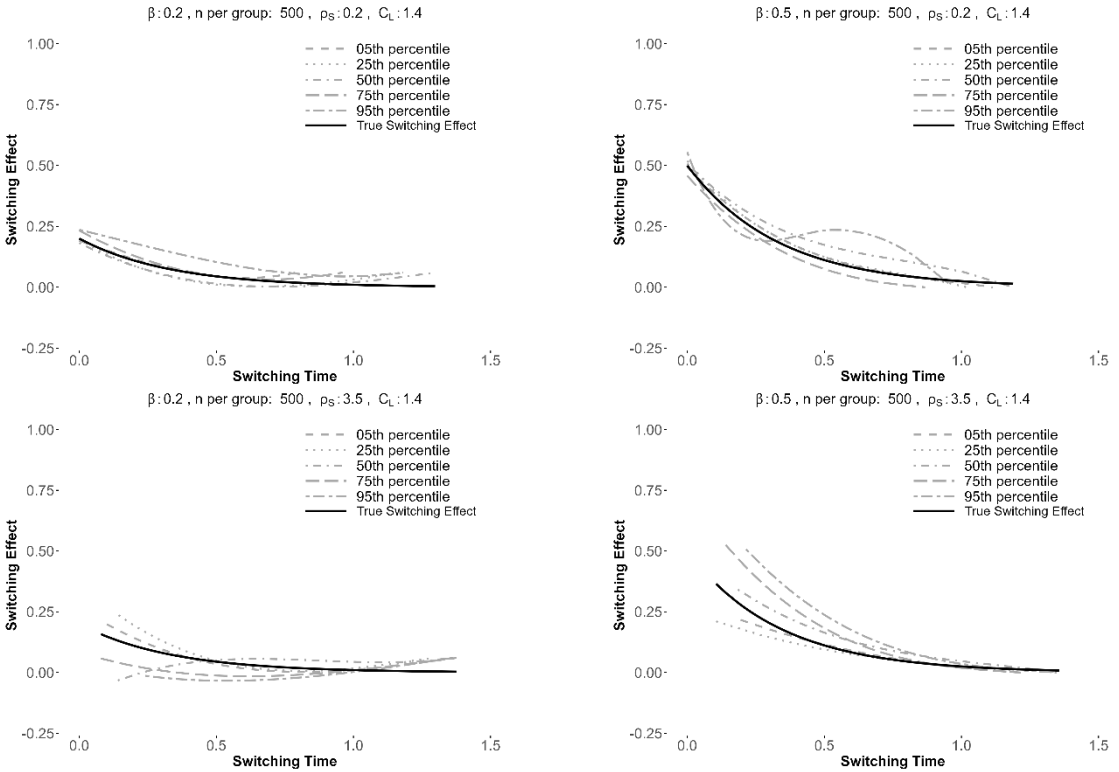


$\beta = 0.2$ $\beta = 0.5$

Figure A.3 Fit Results of the Varying Type A by CBS-OG at the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE (n per group = 200, C_L= 1.4)

$\rho_S = 0.2$

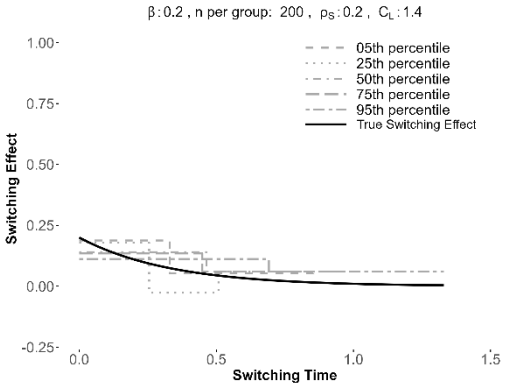
$\rho_S = 3.5$

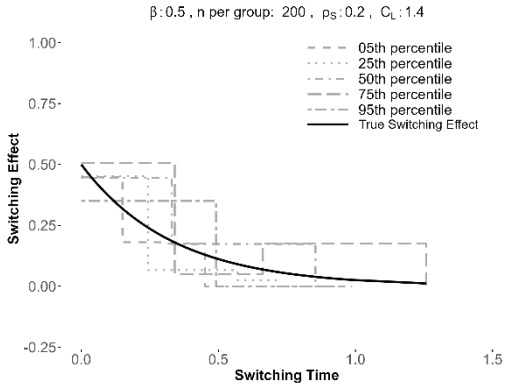


$\beta = 0.2$ $\beta = 0.5$

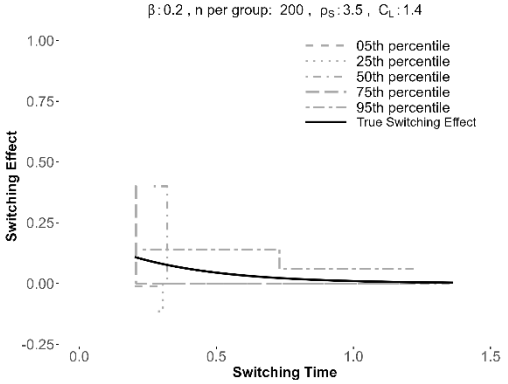
Figure A.4 Fit Results of the Varying Type A by CBS-OG at the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE (n per group = 500, C_L= 1.4)

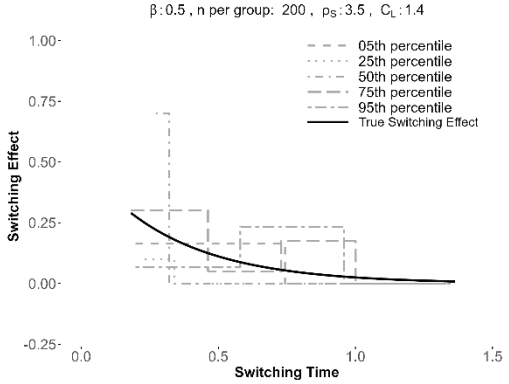
$\rho_S = 0.2$





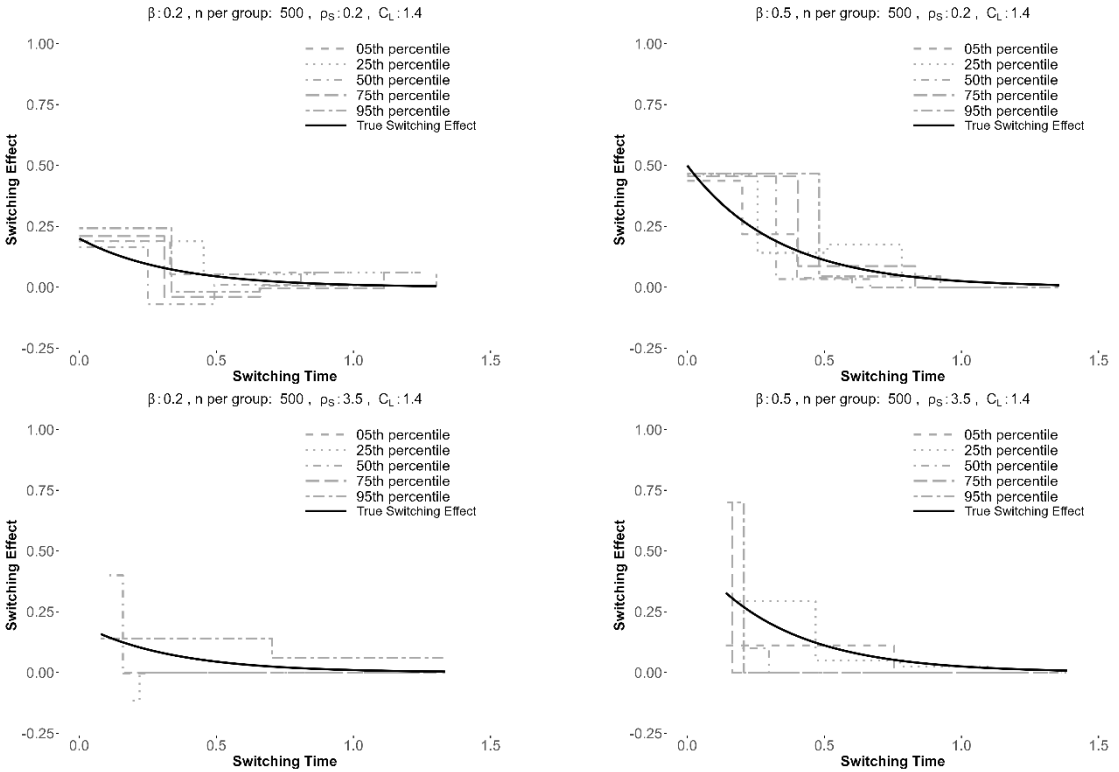
$\rho_S = 3.5$





$\beta = 0.2$ $\beta = 0.5$

Figure A.5 Fit Results of the Varying Type A by PM-OG at the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE (n per group = 200, C_L= 1.4)

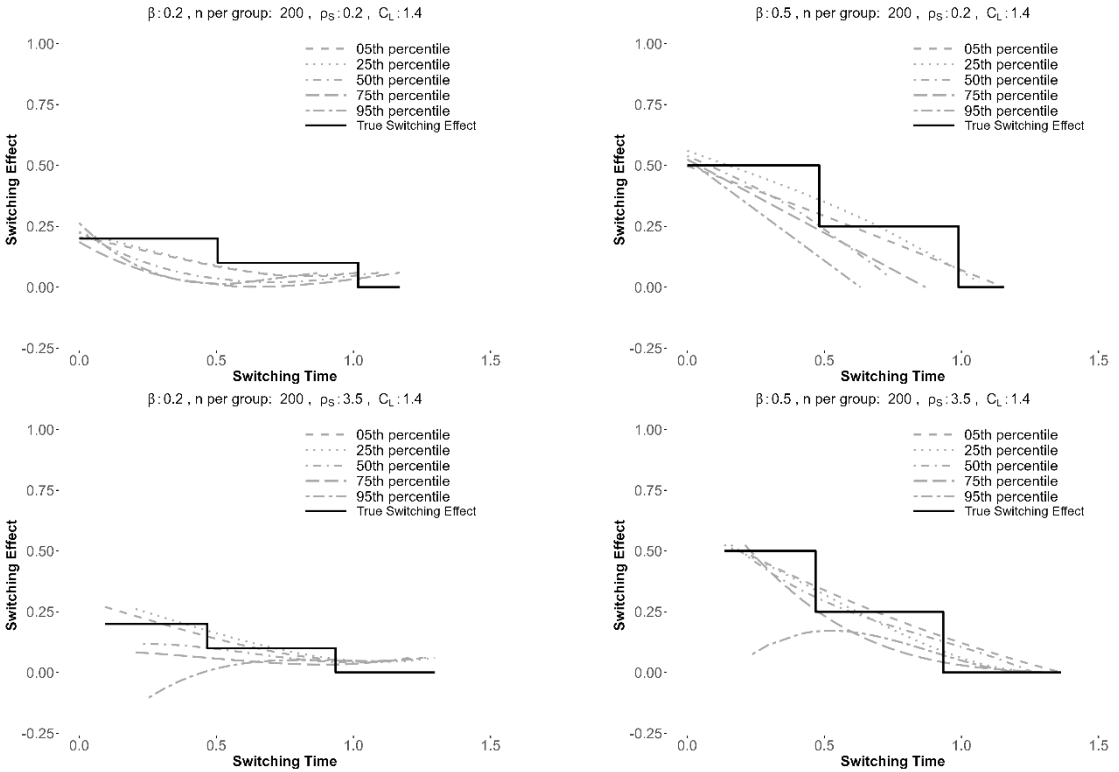


$\rho_S = 0.2$

$\rho_S = 3.5$

$\beta = 0.2$ $\beta = 0.5$

Figure A.6 Fit Results of the Varying Type A by PM -OG at the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE (n per group = 500, C_L= 1.4)

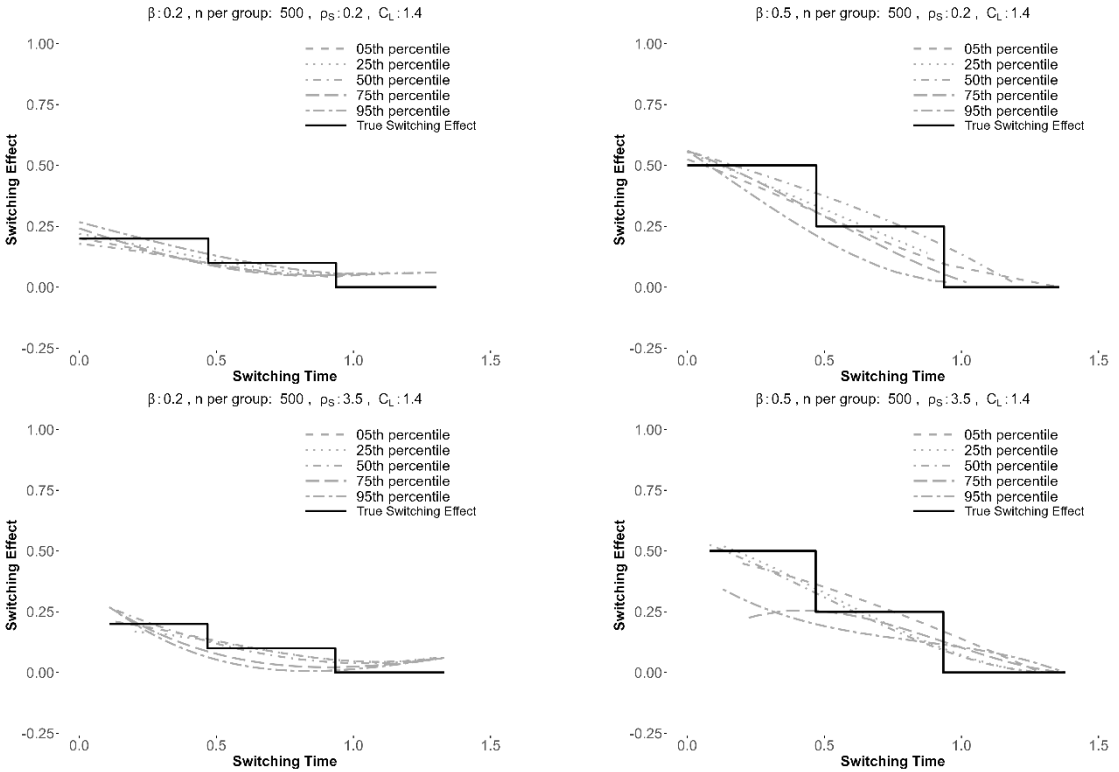


$\rho_S = 0.2$

$\rho_S = 3.5$

$\beta = 0.2$ $\beta = 0.5$

Figure A.7 Fit Results of the Varying Type B by CBS-CG at the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE (n per group = 200, C_L= 1.4)



$\rho_S = 0.2$

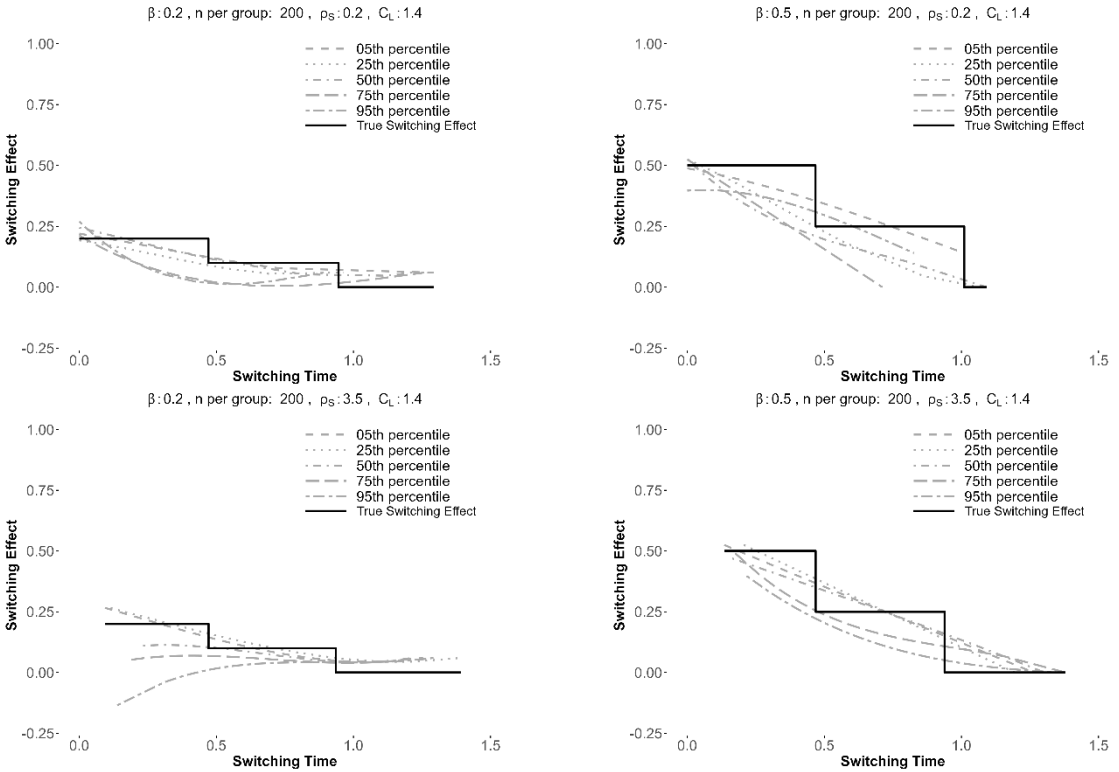
$\rho_S = 3.5$

$\beta = 0.2$ $\beta = 0.5$

Figure A.8 Fit Results of the Varying Type B by CBS-CG at the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE (n per group = 500, C_L= 1.4)

$\rho_S = 0.2$

$\rho_S = 3.5$

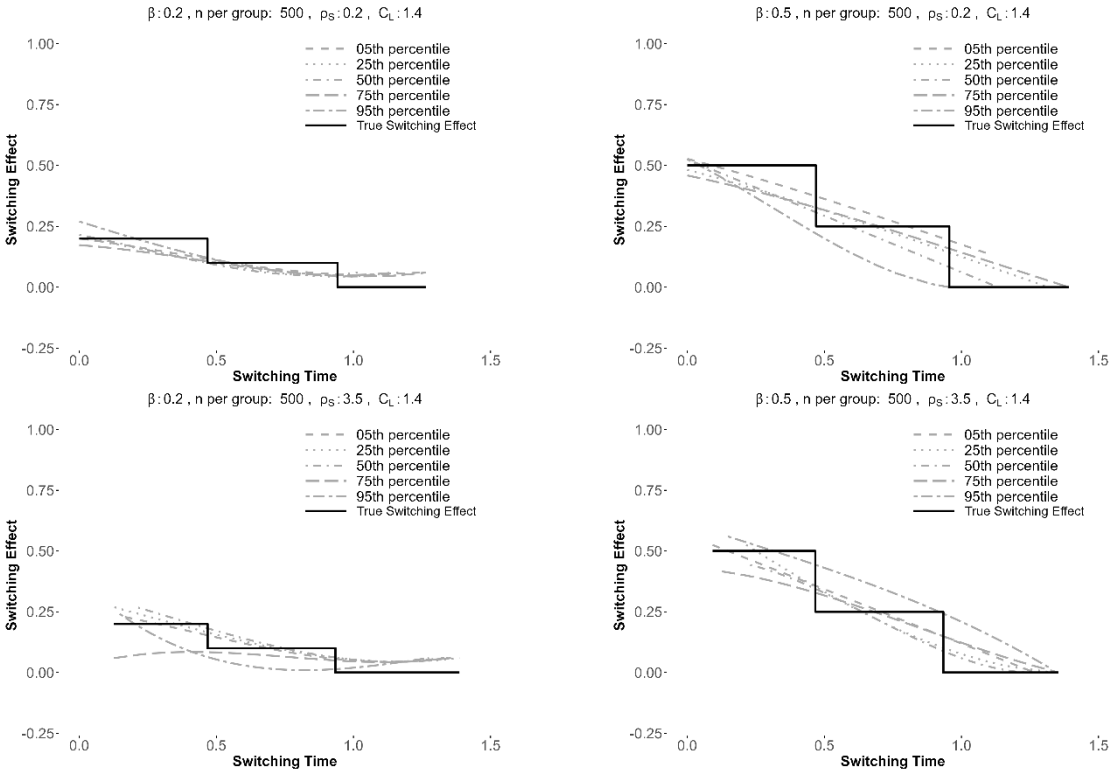


$\beta = 0.2$ $\beta = 0.5$

Figure A.9 Fit Results of the Varying Type B by CBS-OG at the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE (n per group = 200, C_L= 1.4)

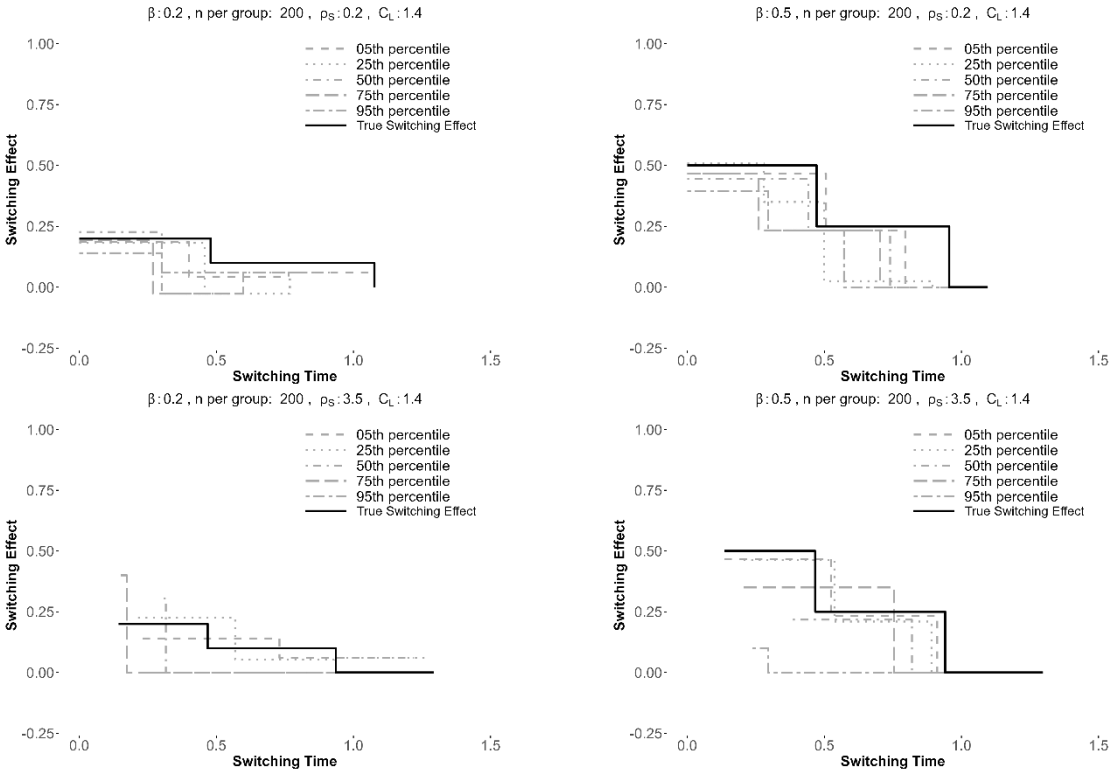
$\rho_S = 0.2$

$\rho_S = 3.5$



$\beta = 0.2$ $\beta = 0.5$

Figure A.10 Fit Results of the Varying Type B by CBS-OG at the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE (n per group = 500, C_L= 1.4)



$\rho_S = 0.2$

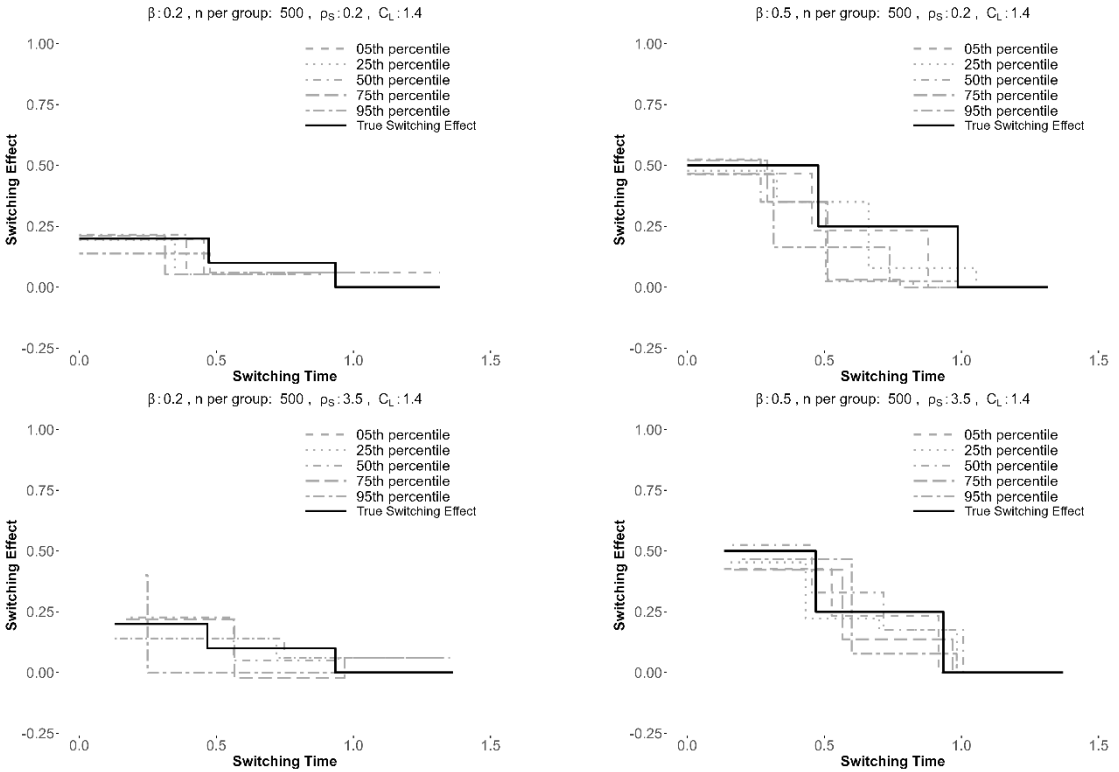
$\rho_S = 3.5$

$\beta = 0.2$ $\beta = 0.5$

Figure A.11 Fit Results of the Varying Type B by PM-OG at the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE (n per group = 200, C_L= 1.4)

$\rho_S = 0.2$

$\rho_S = 3.5$



$\beta = 0.2$ $\beta = 0.5$

Figure A.12 Fit Results of the Varying Type B by PM -OG at the 5th, 25th, 50th, 75th, and 95th Percentiles of the MSE (n per group = 500, C_L= 1.4)

국문요약

무작위 임상시험에서 가속 실패 모형 기반 시간 변동 치료전환 효과를 보정한 치료효과 추정

본 연구는 치료 전환이 허용되는 무작위 임상시험에서 치료 효과를 정확하게 추정하기 위한 방법론을 제안한다. 가속 실패 시간(Accelerated Failure Time, AFT) 모델은 편향을 초래할 가능성이 있으며, 치료 전환 효과를 보정하기 위한 Rank Preserving Structural Failure Time Model(RPSFTM)은 일관적인 치료 효과(common treatment effect)를 가정하는데, 이는 다소 비현실적인 가정이다.

이러한 한계를 해결하기 위해, 본 연구는 두 집단 간의 시변 치료 전환 효과(Time-Varying Switching Effect, TVSE)를 모델링할 수 있는 유연한 프레임워크를 제안한다. 구체적으로, 본 방법론은 대조군에서 실험군으로의 치료 전환 효과를 부여한 full likelihood 접근법을 채택하였으며, TVSE를 적합하기 위해 3차 B 스플라인(cubic B-spline)과 조각 상수 함수(piecewise constant function)에 기반한 방법론을 도입하였다.

시뮬레이션 연구 결과, 새로운 방법론은 치료 효과를 추정하는 데 있어 기존 방법론에 비해 일관되게 우수한 성능을 보였다. 새로운 방법론은 기존 방법론보다

훨씬 작은 편향, 안정적인 분산, 신뢰구간이 적절하게 구성되어 그 견고함을 입증하였다.

새로운 방법론은 국민건강보험공단 노인 코호트 DB를 활용하여 만성신장질환(CKD)을 앓고 있는 환자에서 혈관 접근법(중심정맥카테터(Central Venous Catheters, CVC)에서 자가 동정맥루(Arteriovenous Fistulas, AVF)로 전환)의 생존 결과를 추정하는 데에도 적용되었다. 제안된 방법론으로부터 도출된 생존 추정치는 기존의 AFT 모델을 통해 얻어진 결과보다 AVF 환자의 생존 예후가 더 크게 개선되는 것으로 나타났다. 이러한 결과는 시뮬레이션 결과와 일치하며, 새로운 방법론이 기존 접근법에 비해 가지는 장점을 강조한다.

결론적으로, 새로운 방법론은 치료 전환이 허용되는 임상시험에서 진정한 치료 효과를 추정하는 데 있어 상당한 이점을 제공한다. 그러나 실제 임상시험에 적용할 때에는 자료를 면밀히 검토하고, 기존 방법의 결과와 함께 제시하여 보다 포괄적이고 견고한 결론을 도출할 것을 권장한다.

핵심되는 말: 치료전환, 시간변동 전환효과, 가속실패시간모형, 3차 B 스플라인, 조각 상수 함수