EVALUATION OF TRANSPLANT BENEFITS WITH THE U.S. SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS BY SEMIPARAMETRIC REGRESSION OF MEAN RESIDUAL LIFE

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Kidney transplantation is the most effective renal replacement therapy for end stage renal disease patients. With the severe shortage of kidney supplies and for the clinical effectiveness of transplantation, patient's life expectancy post transplantation is used to prioritize patients for transplantation; however, severe comorbidity conditions and old age are the most dominant factors that negatively impact post-transplantation life expectancy, effectively precluding sick or old patients from receiving transplants. It would be crucial to design objective measures to quantify the transplantation benefit by comparing the mean residual life with and without a transplant, after adjusting for comorbidity and demographic conditions. To address this urgent need, we propose a new class of semiparametric covariate-dependent mean residual life models. Our method estimates covariate effects semiparametrically efficiently and the mean residual life function nonparametrically, enabling us to predict the residual life increment potential for any given patient. Our method potentially leads to a more fair system that prioritizes patients who would have the largest residual life gains. Our analysis of the kidney transplant data from the U.S. Scientific Registry of Transplant Recipients also suggests that a single index of covariates summarize well the impacts of multiple covariates, which may facilitate interpretations of each covariate's effect. Our subgroup analysis further disclosed inequalities in survival gains across groups defined by race, gender and insurance type (reflecting socioeconomic status).

1. Introduction. About 15% of American adults have chronic kidney disease (Saran et al., 2016), suffering worsened kidney functions with less fluid filtrated by the glomerular, and losing kidney functions gradually but permanently over the cause of months or years. According to the glomerular filtration rate (GFR), chronic kidney disease is classified into five stages, where stage four (GFR between 15 and 29 ml/min/1.73m^2) and stage five (GFR less than 15 ml/min/1.73m^2) kidney diseases are considered to be end stage renal disease (ESRD), one of the most lethal diseases globally (Ferri, 2017; Feng et al., 2019). In the U.S., more than 600,000 individuals are living with ESRD, about 100,000 new ESRD cases are diagnosed and 50,000 deaths occur each year (Salerno et al., 2021).

The most common treatment for ESRD is renal replacement therapy, including dialysis and kidney transplant. As dialysis only provides partial kidney functions, dialysis patients tend to have shorter survival than those receiving kidney transplants, which often lead to a longer and a better quality of life (Evans et al., 1985; Wolfe et al., 1999; Liem et al., 2007). Due to severe shortages in kidney supplies, however, there are far more ESRD patients who need kidney transplants than donors available in the U.S. (Tonelli et al., 2011). For example, the

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U.S. Scientific Registry of Transplant Recipients (SRTR) reports that among 247,123 patients awaiting kidney transplants during 2011-2018, only 139,270 patients actually received one, leaving the remaining 107,853 still waiting (Hart et al., 2021).

Currently, decisions on patients' priority of receiving kidney transplants are based on the Estimated Post-Transplant Survival (EPTS) score, which predicts a patient's life expectancy post transplantation by using a Cox model with age, diabetes status, prior solid organ transplant and time on dialysis as predictors (Time, 2012). Pre-existing conditions such as diabetes, prior solid organ transplants and long dialysis vintage are associated with shorter survival (Cosio et al., 1998; Meier-Kriesche et al., 2000; Kasiske et al., 2001); thus patients with these conditions tend to have a lower priority for transplantation (Cosio et al., 1998; Molnar et al., 2011). On the other hand, younger age is found to be associated with better outcomes and younger patients are likely to have a higher priority for transplantation. Thus, age and severe comorbidity conditions have effectively become the most dominant factors when deciding on who to receive transplants, which may preclude older and sicker patients from benefiting from transplantation (Jassal, Schaubel and Fenton, 2005; Gore et al., 2009; Weng et al., 2010). A more comprehensive system, however, should give a higher priority to those who would benefit more from transplantation among patients with similar conditions, and in the meantime triage candidates who may gain little or even suffer a loss in life expectancy. We propose to quantify the transplant benefit by comparing the improvement of the patient's expected residual life with and without transplantation. The expected residual life characterizes the mean of the remaining survival time given that a patient has survived up to a certain time (Hall and Wellner, 1981). Compared to overall survival, the residual life expectancy provides a real time assessment of transplant benefits at any given time when a kidney becomes available (Lin, Fei and Li, 2016). As demographic and clinical conditions may be confounders affecting survival and should be adjusted for when assessing transplant benefits (Cosio et al., 1998; Carrero et al., 2018), we aim at modeling and evaluating a patient's potential residual life expectancy with or without transplant, based on the patient's covariate profile.

Much work on mean residual life models has been sparked by Oakes and Dasu (1990). For example, Maguluri and Zhang (1994) proposed a univariate proportional mean residual life model; Oakes and Dasu (2003) established the theoretical properties of the methods in Oakes and Dasu (1990); Chen and Cheng (2005) estimated the coefficients of covariates in a proportional mean residual life model by a partial-score approach, analogous to the partial likelihood approach; Chen et al. (2005) employed the inverse probability weighting approach for inference; Müller and Zhang (2005) extended the mean residual life model to incorporate time-varying covariates; Chen and Cheng (2006) proposed an extended Buckley-James estimator to estimate a linear residual life model and Chen (2007) further proposed an additive mean residual life model. These works inspired median and quantile residual life models; see for example, Jeong, Jung and Costantino (2008); Jung, Jeong and Bandos (2009); Ma and Yin (2010) and Ma and Wei (2012). However, all these works imposed parametric dependency of residual life on covariates as well as how long the patient has lived up to transplantation (or "alive time" hereafter). Violations of the model assumptions will lead to biased estimates and incorrect inferences (Chen, 2007; Chen et al., 2005). Our preliminary analysis of the kidney transplant data from SRTR indicates that the mean residual life depends on alive time and patients' other covariates, such as treatment history, commorbidty conditions and demographics, through a complicated form which is challenging to model parametrically.

We propose a new class of semiparametric mean residual life models, with the goal of detecting the effects of patients' covariates on the residual life and identifying the patients who may benefit most from transplantation. Our model does not impose any parametric assumptions on the mean residual life function and, thus, the hazard function, and extends the

model in Ma and Zhu (2012) and Ma and Zhu (2013) to accommodate censoring in response. Moreover, given multiple covariates, we also propose a flexible dimension reduction method to achieve a parsimonious model for efficiency and interpretability. To derive the estimators, we employ a semiparametric method, in combination with a martingale treatment as in Zhao, Ma and Lu (2022), to derive a semiparametrically efficient estimator (Bickel et al., 1994) for the effects of covariates and an asymptotically normally distributed nonparametric estimator of the mean residual life function. We apply the proposed method to analyze the SRTR kidney transplant data and quantify transplantation gains by using the residual life expectancy. Our analysis suggested that a single index of covariates summarize well the impacts of multiple covariates, which may facilitate interpretations of each covariate's effect. Our subgroup analysis further disclosed inequalities in survival gains across groups defined by race, gender and insurance type (reflecting socioeconomic status). The results may inform the priority rules for kidney transplantation.

This paper is organized as follows. Section 2 proposes the mean residual life model, and Section 3 derives the estimators for the proposed model and discusses their properties. We assess the finite sample properties of the methods by simulation studies in Section 5 and apply it to analyze the kidney transplant data in Section 6. We conclude the paper with some discussions in Section 7. We defer the regularity conditions and technical properties to the Supplementary Materials.

2. Semiparametric regression of mean residual life. Denote by T the potential time lag from being waitlisted for transplantation (i.e., became eligible) to death in the absence of censoring and by $\mathbf{X} \in \mathcal{R}^p$ the baseline covariates, such as age, diabetes status, and prior solid organ transplant, measured at the waitlisting time. Denote by W the time lag from waitlisting to hypothetical transplant time that would have occurred in the absence of censoring. Our focus is to model the difference of the mean residual life with and without transplant at any time point t, given $\mathbf{X}$ and W observed up to t.

Let the indicator function $I(W \leqslant t)$ describe the time-dependent transplant status, with $I(W \leqslant t) = 0$ and 1 corresponding to "Non-transplant" and "Transplant" at time t, respectively. Following the missing data literature, we use $WI(W \leqslant t)$ to indicate the value of W *only* when the transplant occurs before t. Given the history of transplantation status up to time t, i.e., $\{I(W \leqslant t), WI(W \leqslant t)\}$, we specify that the conditional hazard at t depends only on the transplantation information at t, that is,

$$\begin{aligned} &\lim_{h \to 0^+} h^{-1} P\{t \leqslant T \leqslant t + h \mid T \geqslant t, \mathbf{X}, I(W \leqslant t), WI(W \leqslant t)\} \\ &= \lambda\{t, \mathbf{X}, I(W \leqslant t), WI(W \leqslant t)\} \\ &= \lambda_T(t - W, \mathbf{X}, W) I(W \leqslant t) + \lambda_N(t, \mathbf{X})\{1 - I(W \leqslant t)\}, \end{aligned} \tag{1}$$

where the subscripts "$_T$" and "$_N$" respectively stand for "Transplant" and "Non-transplant." Within the non-transplant group by time t, i.e. $W > t$, the hazard function depends on the time and covariates only; at and after transplantation, i.e. $W \leqslant t$, the hazard function is to be reset and is a function of $t - W$ (the time lag since transplantation) because of immediate surgical risks (Humar and Matas, 2005; Hernandez et al., 2006) and long term benefits of receiving functional organs (Lin, Fei and Li, 2016). Additionally, W is considered as an influential factor in λ_T because, for example, there is a clear survival advantage in favor of preemptive kidney transplantation (Liem and Weimar, 2009).

A naive mean residual life (Maguluri and Zhang, 1994) would have been computed as $E(T - t \mid T \geqslant t, \mathbf{X}, W)$. However, the conditioning part of this expectation looks beyond t for a prospective $W > t$, which is problematic as a patient would be guaranteed to survive at least up to W when $W > t$, coinciding with the notion that one cannot directly use time

dependent treatment or, more broadly, "internal" time dependent covariates to predict survival (Kalbfleisch and Prentice, 2011). Instead, at each time t, we compute the mean residual life based on the hazard (1) that strictly conditions on the information available by then, that is,

$$\begin{aligned} &E(T-t \mid T \geqslant t, \mathbf{X}, I(W \leqslant t), WI(W \leqslant t)) \\ &= e^{\Lambda_T(t-W,\mathbf{X},W)} \int_{t-W}^{\infty} e^{-\Lambda_T(s,\mathbf{X},W)} ds I(W \leqslant t) + e^{\Lambda_N(t,\mathbf{X})} \int_t^{\infty} e^{-\Lambda_N(s,\mathbf{X})} ds \{1 - I(W \leqslant t)\}, \end{aligned} \tag{2}$$

and will draw inference based on this valid model. Here, $\Lambda_N(t,\mathbf{X}) = \int_0^t \lambda_N(s,\mathbf{X})ds$ and $\Lambda_T(t,\mathbf{X},W) = \int_0^t \lambda_T(s,\mathbf{X},W)ds$ are the two cumulative hazard functions. This model uses the "baseline" information at time t only (i.e., no look beyond t) to project future survival. See details in Section 1 of the Supplementary Material.

For ease of notation, we rewrite as (2) as $m\{t,\mathbf{X},I(W \leqslant t),WI(W \leqslant t)\} = m_T(t - W,\mathbf{X},W)I(W \leqslant t) + m_N(t,\mathbf{X})\{1 - I(W \leqslant t)\}$, where

$$m_T(t,\mathbf{X},W) = e^{\Lambda_T(t,\mathbf{X},W)} \int_t^{\infty} e^{-\Lambda_T(s,\mathbf{X},W)} ds$$

and

$$m_N(t,\mathbf{X}) = e^{\Lambda_N(t,\mathbf{X})} \int_t^{\infty} e^{-\Lambda_N(s,\mathbf{X})} ds,$$

which may facilitate evaluation of the benefits of transplant at any given time. Particularly, $m_T(t-W,\mathbf{X},W) - m_N(t,\mathbf{X})$ quantifies the gain (or loss) of life expectancy of patients at t with a transplant given at $W < t$ compared with those who would never receive a transplant; candidates with close to zero or a negative value of $m_T(t-W,\mathbf{X},W) - m_N(t,\mathbf{X})$ would benefit little from organ transplantation and would have lower priorities in the waiting list (Chadban et al., 2020). This formulation suits the organ transplant setting: the severe shortage of organs restricts the sources of donations and obliges us to compare the situation where an immediate donation is received with the situation where donation is impossible at all.

To ensure estimability, we make a complete follow-up assumption (Tsiatis, 1990; Chen et al., 2005; Chen and Cheng, 2005; Sun and Zhang, 2009), that is, the failure time T is supported on a finite range $(0,\tau)$ with $\tau < \infty$, where in practice τ is the maximum follow-up time; we relax this assumption in Supplement 5. We further assume the covariates $\mathbf{X}$ affect T via index $\boldsymbol{\beta}$, where $\boldsymbol{\beta} \in \mathcal{R}^{p\times d}$ is the coefficient matrix with $d \leqslant p$. Then (1) and (2) can respectively be expressed as

$$\begin{aligned} &\lambda\{t,\mathbf{X},I(W \leqslant t),WI(W \leqslant t)\} \\ &= \lambda_T(t-W,\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X},W)I(W \leqslant t) + \lambda_N(t,\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})\{1 - I(W \leqslant t)\}, \end{aligned} \tag{3}$$

$$\begin{aligned} &m\{t,\mathbf{X},I(W \leqslant t),WI(W \leqslant t)\} \\ &= m_T(t-W,\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X},W)I(W \leqslant t) + m_N(t,\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})\{1 - I(W \leqslant t)\}, \end{aligned} \tag{4}$$

where $\lambda_T, \lambda_N, m_T$ and m_N are unspecified positive functions, which need to be estimated. The model stipulates that the conditional mean of $T - t$ depends on $\mathbf{X}$ via its d indices, formed by projecting $\mathbf{X}$ to the columns of $\boldsymbol{\beta}$, and the waiting time W. When $d = 1$, the model reduces to a single index model in terms of $\mathbf{X}$; when $1 < d < p$, it corresponds to a dimension reduction structure; when $d = p$, the model is completely nonparametric. Our analysis first focuses on a fixed d, followed by selecting d in a data driven fashion as discussed in Section 6. Model (4) is general: it includes the proportional mean residual life model, i.e., $m\{t,\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X},I(W \leqslant t),WI(W \leqslant t)\} = m_0(t)\exp(\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})$

(Oakes and Dasu, 1990) as a special case by specifying $m_N\{t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}\} = m_0(t)e^{\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}}$, $m_T\{t - W, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W\} = m_0(t)e^{\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}+\alpha W}$ with $\alpha = 0$, and $d = 1$; it reduces to the additive model $m_0(t) + \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}$ (Chen, 2007) by specifying $m_N\{t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}\} = m_0(t) + \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}$, $m_T\{t - W, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W\} = m_0(t) + \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X} + \alpha W$ with $\alpha = 0$, and setting $d = 1$. By allowing d to be larger than 1, model (4) extends these classical models by allowing more flexible forms such as $m\{t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, I(W \leqslant t), WI(W \leqslant t)\} = m_0(t)\{\sum_{k=1}^{d} \exp(\boldsymbol{\beta}_{\cdot,k}^{\mathrm{T}}\mathbf{X})\}$ and $m\{t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, I(W \leqslant t), WI(W \leqslant t)\} = m_0(t) + \sum_{k=1}^{d} \boldsymbol{\beta}_{\cdot,k}^{\mathrm{T}}\mathbf{X}$, where $\boldsymbol{\beta}_{\cdot,k}$ is the kth column of $\boldsymbol{\beta}$. These special cases implicitly assume that transplant or the timing of transplantation does not impact survival.

We further assume that T is subject to random right censoring so that $C \perp\!\!\!\perp T \mid W, \mathbf{X}$, where C is the censoring time and we observe $Z = \min(T, C)$ and $\Delta = I(T \leqslant C)$. In our dataset, W (or transplant) can only be observed while the patient is still at risk, that is, before death or censoring occurs. We assume the observed $\{\mathbf{X}_i, Z_i, \Delta_i, I(W_i \leqslant Z_i), W_i I(W_i \leqslant Z_i)\}$, $i = 1, \ldots, n$ be independently and identically distributed realizations of $\{\mathbf{X}, Z, \Delta, I(W \leqslant Z), WI(W \leqslant Z)\}$. This notation stipulates that W is subject to censoring due to Z, with an indicator of $I(W \leqslant Z)$. To make (4) identifiable and estimable, we fix the upper $d \times d$ block of $\boldsymbol{\beta}$ to be $\mathbf{I}_d$, and estimate the lower $(p - d) \times d$ block of $\boldsymbol{\beta}$. Corresponding to the upper and lower parts of $\boldsymbol{\beta}$, we write $\mathbf{X} = (\mathbf{X}_u^{\mathrm{T}}, \mathbf{X}_l^{\mathrm{T}})^{\mathrm{T}}$, where $\mathbf{X}_u \in \mathcal{R}^d$ and $\mathbf{X}_l \in \mathcal{R}^{p-d}$.

3. A semiparametrically efficient estimator. Denote the conditional survival function, cumulative hazard function, hazard function and probability density function of the censoring time C by $S_c(z, \mathbf{X}) = \mathrm{pr}(C \geqslant z \mid \mathbf{X})$, $\Lambda_c(z, \mathbf{X}) = -\log S_c(z, \mathbf{X})$, $\lambda_c(z, \mathbf{X}) = \partial\Lambda_c(z, \mathbf{X})/\partial z$ and $f_c(z, \mathbf{X}) = -\partial S_c(z, \mathbf{X})/\partial z$ with $z < \tau$, where $0 < \tau < \infty$ is the upper bound of the follow-up time. Let $p(\mathbf{X}) \equiv \mathrm{pr}(C = \tau \mid \mathbf{X})$, and it follows that $S_c(\tau, \mathbf{X}) = f_c(\tau, \mathbf{X}) = p(\mathbf{X})$, and $\lambda_c(\tau, \mathbf{X}) = 1$. Here, $\lambda_c(z, \mathbf{X})$ and $f_c(z, \mathbf{X})$ are absolutely continuous on $(0, \tau)$, but with a discontinuity point at τ.

To estimate $m_T(t - W, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W) - m_N(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})$, which quantifies the gain (or loss) of mean residual life after t with transplant given at $W \leqslant t$, we need to estimate $\boldsymbol{\beta}$ and the functionals of m_T and m_N, for which we consider a likelihood-based approach.

Under independent censoring, the joint partial probability density function [for mixed random variables (Casella and Berger, 2001)] of $\{\mathbf{X}, Z, \Delta, WI(W \leqslant Z)\}$, conditional on a random variable $I(W \leqslant Z)$, is

$$
\begin{aligned}
&f_{\mathbf{X},Z,\Delta,WI(W\leqslant Z)\mid I(W\leqslant Z)}\{\mathbf{x}, z, \delta, wI(w \leqslant z) \mid I(w \leqslant z)\} \\
&= \{\lambda_T(z - w, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{x}, w)\}^{\delta} e^{-\int_0^w \lambda_N(s, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{x})ds - \int_w^z \lambda_T(s-w, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{x}, w)ds} \lambda_c(z, \mathbf{x})^{1-\delta} e^{-\int_0^z \lambda_c(s,\mathbf{x})ds} \\
&\quad \times f_{\mathbf{X},W\mid W\leqslant Z}(\mathbf{x}, w) I(w \leqslant z) \\
&\quad + \{\lambda_N(z, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{x})\}^{\delta} e^{-\int_0^z \lambda_N(s, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{x})ds} \lambda_c(z, \mathbf{x})^{1-\delta} e^{-\int_0^z \lambda_c(s,\mathbf{x})ds} f_{\mathbf{X}\mid W>Z}(\mathbf{x})\{1 - I(w \leqslant z)\},
\end{aligned}
\tag{5}
$$

where the last equality stems from (1)–(3). We do not need to specify the distribution of $\mathbf{X} \mid W > Z$ or the joint distribution of $\mathbf{X}, W \mid W \leqslant Z$ as our ensuing estimation is conditional on the observed W, $\mathbf{X}$ and $W \leqslant Z$.

We view the probability function in (5) as a semiparametric model where all unknown components, except for $\boldsymbol{\beta}$, are infinite dimensional nuisance parameters. The parameters $\boldsymbol{\beta}$ are parameters of interest with a finite dimension. We will estimate $\boldsymbol{\beta}$ by using a geometric approach, which avoids decomposing $\lambda(\cdot)$ to be $\lambda_*(z)e^{\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}}$ as in a proportional hazards model. This entails more flexibility for the model.

Let $Y(t) = I(Z \geqslant t)$ and $N(t) = I(Z \leqslant t)\Delta$ be the at-risk and counting process, respectively. Define the filtration $\mathcal{F}_t = \sigma\{N(u), Y(u), \mathbf{X}, I(W \leqslant u), WI(W \leqslant u), 0 \leqslant u < t\}$, and

let $M(t) = N(t) - \int_0^t Y(s)\lambda\{s, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, I(W \leqslant s), WI(W \leqslant s)\}ds$ be the martingale with respect to $\mathcal{F}_t$.

3.1. *Construction of Efficient Score Functions.* Given the regular score by differentiating the joint partial probability density function (5) with respect to $\boldsymbol{\beta}$, an efficient score, as derived in Supplementary 2.1, is

$$\begin{aligned}
&\mathbf{S}_{\text{eff}}\{\Delta, Z, {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}, I(W \leqslant Z), WI(W \leqslant Z)\} \\
&= \int_0^\infty \left\{ \frac{\mathbf{m}_{12}\{s, {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}, I(W \leqslant s), WI(W \leqslant s)\}}{m_1\{s, \boldsymbol{\beta}_0^{\mathrm{T}}\mathbf{X}, I(W \leqslant s), WI(W \leqslant s)\} + 1} - \frac{\mathbf{m}_2\{s, {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}, I(W \leqslant s), WI(W \leqslant s)\}}{m(s, {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}, I(W \leqslant s), WI(W \leqslant s))} \right\} \\
&\quad \otimes \left[\mathbf{X}_l - \frac{E\left\{\mathbf{X}_l S_c(s, \mathbf{X}) \mid {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}\right\}}{E\left\{S_c(s, \mathbf{X}) \mid {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}\right\}} \right] dM\{s, {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}, I(W \leqslant s), WI(W \leqslant s)\},
\end{aligned} \tag{6}$$

where $m_1(s, \mathbf{v}, \cdot, \cdot) \equiv \partial m(s, \mathbf{v}, \cdot, \cdot)/\partial s$, $\mathbf{m}_2(s, \mathbf{v}, \cdot, \cdot) \equiv \partial m(s, \mathbf{v}, \cdot, \cdot)/\partial \mathbf{v}$, $\mathbf{m}_{12}(s, \mathbf{v}, \cdot, \cdot) \equiv \partial \mathbf{m}_2\{s, \mathbf{v}, \cdot, \cdot\}/\partial s$, and $\mathbf{X}_l$ is the lower $p - d$ components in $\mathbf{X}$.

3.2. *Construction of Semiparametrically Efficient Estimator of $\boldsymbol{\beta}$.* A consistent estimating equation can be obtained from $E[\mathbf{S}_{\text{eff}}\{\Delta, Z, \mathbf{X}, I(W \leqslant Z), WI(W \leqslant Z)\} \mid \mathbf{X}] = \mathbf{0}$ as the integrand in the above integral is predictable and $M\{s, \boldsymbol{\beta}_0^{\mathrm{T}}\mathbf{X}, I(W \leqslant s), WI(W \leqslant s)\}$ is a martingale. Hence, to preserve the mean zero property and to simplify the computation, we can replace the part in the form of $\mathbf{m}_{12}/(m_1 + 1) - \mathbf{m}_2/m$ within the curly brackets in (6) by an arbitrary function of s, ${\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}$, $I(W \leqslant s)$, and $WI(W \leqslant s)$, say $\mathbf{g}\{s, {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}, I(W \leqslant s), WI(W \leqslant s)\}$, and still obtain

$$\begin{aligned}
&E\left(\int_0^\infty \mathbf{g}\{s, {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}, I(W \leqslant s), WI(W \leqslant s)\} \right. \\
&\left. \otimes \left[\mathbf{X}_l - \frac{E\left\{\mathbf{X}_l S_c(s, \mathbf{X}) \mid {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}\right\}}{E\left\{S_c(s, \mathbf{X}) \mid {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}\right\}} \right] dM\{s, {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}, I(W \leqslant s), WI(W \leqslant s)\} \right) = \mathbf{0}.
\end{aligned}$$

This provides a richer class of estimators than the estimator based on $\mathbf{S}_{\text{eff}}$ alone. For example, assigning a simple $\mathbf{g}\{s, {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}, I(W \leqslant s), WI(W \leqslant s)\}$ yields a useful estimating equation whose solution is consistent and often easy to get due to its simplicity. It is usually adopted as an initial value for the efficient estimator proposed later to avoid local solutions in the finite sample situations.

The fraction within the square brackets in (6) satisfies, when $t \leqslant \tau$,

$$\frac{E\left\{\mathbf{X}_l S_c(t, \mathbf{X}) \mid {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}\right\}}{E\left\{S_c(t, \mathbf{X}) \mid {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}\right\}} = \frac{E\left\{\mathbf{X}_l Y(t) \mid {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}, I(W \leqslant t), WI(W \leqslant t)\right\}}{E\left\{Y(t) \mid {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}, I(W \leqslant t), WI(W \leqslant t)\right\}}; \tag{7}$$

see Supplement 2.1.2 for further discussion at the tail when $t > \tau$. We then verify that

$$E\left(\int_0^\infty \mathbf{g}\{s, {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}, I(W \leqslant s), WI(W \leqslant s)\} \otimes \left[\mathbf{X}_l - \frac{E\left\{\mathbf{X}_l S_c(s, \mathbf{X}) \mid {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}\right\}}{E\left\{S_c(s, \mathbf{X}) \mid {\boldsymbol{\beta}_0}^{\mathrm{T}}\mathbf{X}\right\}} \right] dN(s) \right) = \mathbf{0}. \tag{8}$$

Note that (7) and (8), proved in Supplement 2.1.2, imply that we can construct estimating equations that depend on the transplantation status as follows:

$$\sum_{i=1}^{n}\Delta_i \mathbf{g}\{Z_i, \boldsymbol{\beta}_0{}^{\mathrm{T}}\mathbf{X}_i, I(W_i \leqslant Z_i), W_i I(W_i \leqslant Z_i)\} \otimes \left[\mathbf{X}_{li} - \frac{\widehat{E}\left\{\mathbf{X}_{li}Y_i(Z_i) \mid \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_i, I(W_i \leqslant Z_i), W_i I(W_i \leqslant Z_i)\right\}}{\widehat{E}\left\{Y_i(Z_i) \mid \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_i, I(W_i \leqslant Z_i), W_i I(W_i \leqslant Z_i)\right\}}\right] = \mathbf{0}, \tag{9}$$

where $\mathbf{g}(\cdot)$ is any non-random function and $\widehat{E}\left\{Y_i(Z_i) \mid \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_i, I(W_i \leqslant Z_i), W_i I(W_i \leqslant Z_i)\right\}$ and $\widehat{E}\left\{\mathbf{X}_{li}Y_i(Z_i) \mid \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_i, I(W_i \leqslant Z_i), W_i I(W_i \leqslant Z_i)\right\}$ are given in Supplement 2.2.1. Here, $\widehat{E}\{Y_i(Z_i) \mid \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_i, I(W_i \leqslant Z_i), W_i I(W_i \leqslant Z_i)\} \equiv \widehat{E}\{Y_i(t) \mid \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_i, I(W_i \leqslant Z_i), W_i I(W_i \leqslant Z_i)\}|_{t=Z_i}$ and similarly for the other terms.

As such, we obtain the efficient estimator of $\boldsymbol{\beta}$ by solving

$$\sum_{i=1}^{n}\Delta_i \left[\frac{\widehat{\mathbf{m}}_{12}\{Z_i, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_i, I(W_i \leqslant Z_i), W_i I(W_i \leqslant Z_i)\}}{\widehat{m}_1\{Z_i, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_i, I(W_i \leqslant Z_i), W_i I(W_i \leqslant Z_i)\} + 1} - \frac{\widehat{\mathbf{m}}_2\{Z_i, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_i, I(W_i \leqslant Z_i), W_i I(W_i \leqslant Z_i)\}}{\widehat{m}\{Z_i, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_i, I(W_i \leqslant Z_i), W_i I(W_i \leqslant Z_i)\}}\right] \otimes \left[\mathbf{X}_{li} - \frac{\widehat{E}\left\{\mathbf{X}_{li}Y_i(Z_i) \mid \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_i, I(W_i \leqslant Z_i), W_i I(W_i \leqslant Z_i)\right\}}{\widehat{E}\left\{Y_i(Z_i) \mid \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_i, I(W_i \leqslant Z_i), W_i I(W_i \leqslant Z_i)\right\}}\right] = \mathbf{0}, \tag{10}$$

where $\widehat{m}_1(t, \mathbf{v}, \cdot, \cdot)$, $\widehat{\mathbf{m}}_2(t, \mathbf{v}, \cdot, \cdot)$, $\widehat{\mathbf{m}}_{12}(t, \mathbf{v}, \cdot, \cdot)$ are estimators for the derivatives of $m(t, \mathbf{v}, \cdot, \cdot)$ with respect to the first two elements given in Supplement 2.2.1. The results on efficiency are given in Theorem 2.

3.3. *Nonparametric Estimation of Mean Residual Life Functions.* We estimate $m\{t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, I(W \leqslant t), WI(W \leqslant t)\}$ nonparametrically via $\widehat{\Lambda}_T\{t - W, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W\}I(W \leqslant t) + \widehat{\Lambda}_N\{t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}\}\{1 - I(W \leqslant t)\}$ based on a kernel smoothed version of the Nelson-Aalen estimator (Ramlau-Hansen, 1983; Andersen et al., 1993). For any t, W (such that $W < t$), and $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}$, the estimators, $\widehat{\Lambda}_T\{t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W\}$ and $\widehat{\Lambda}_N\{t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}\}$, have the forms of

$$\widehat{\Lambda}_T(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W) = \sum_{i=1}^{n}\int_0^t \frac{I(W_i \leqslant s)K_h(\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_i - \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W_i - W)}{\sum_{j=1}^{n} Y_j(s)I(W_j \leqslant s)K_h(\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_j - \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W_j - W)}dN_i(s),$$

$$\widehat{\Lambda}_N(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}) = \sum_{i=1}^{n}\int_0^t \frac{I(W_i > s)K_h(\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_i - \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})}{\sum_{j=1}^{n} Y_j(s)I(W_j > s)K_h(\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}_j - \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})}dN_i(s),$$

with a multivariate kernel function $K_h(u_1, u_2, ..., u_q) = \prod_{i=1}^{q} K(u_i/h_i)/h_i$, where $h = (h_1, \ldots, h_q)$ is a bandwidth vector and $K(\cdot)$ is a standard univariate kernel function satisfying $K(u) \geqslant 0$ and $\int_{-\infty}^{\infty} K(u)du = 1$ (Wand, 1994).

Following Maguluri and Zhang (1994), we obtain

$$\begin{aligned}\widehat{m}_T(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W) &= e^{\widehat{\Lambda}_T(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W)}\int_t^{\infty} e^{-\widehat{\Lambda}_T(s, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W)}ds; \text{when } W \leqslant t;\\ \widehat{m}_N(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}) &= e^{\widehat{\Lambda}_N(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})}\int_t^{\infty} e^{-\widehat{\Lambda}_N(s, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})}ds; \text{when } W > t.\end{aligned} \tag{11}$$

It is worth noting that when computing $\widehat{\Lambda}_T(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W)$ or $\widehat{m}_T(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W)$, we use only the transplanted observations, whereas when computing $\widehat{\Lambda}_N(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})$ or $\widehat{m}_N(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})$, we use the full data but censor those who have received the transplant at the transplantation time.

4. Asymptotic properties and semiparametric efficiency. We develop a series of theorems and establish that the estimators of $\boldsymbol{\beta}$ are $\sqrt{n}$-consistent, asymptotically normally distributed and semiparametrically efficient, and the nonparametric estimators, $\widehat{m}_T(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W)$ and $\widehat{m}_N(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})$ in (11), are asymptotically normally distributed. We defer the required conditions, lemmas and all the proofs to the Supplementary Material.

Theorem 1. *Under the regularity conditions in Supplement 4.1, $\widehat{\boldsymbol{\beta}}$, the estimator obtained by solving (9) or (10), is consistent, i.e. $\widehat{\boldsymbol{\beta}} - \boldsymbol{\beta} \to \mathbf{0}$ in probability when $n \to \infty$.*

Theorem 2. *Under the regularity conditions in Supplement 4.1, the estimator, $\widehat{\boldsymbol{\beta}}$, obtained by solving (9) or (10) satisfies $\sqrt{n}(\widehat{\boldsymbol{\beta}} - \boldsymbol{\beta}) \to N(\mathbf{0}, \mathbf{A}^{-1}\mathbf{B}\mathbf{A}^{-1^{\mathrm{T}}})$ in distribution when $n \to \infty$, where $\mathbf{A}$ and $\mathbf{B}$ are given in Supplement 4.4.*

Further, the estimator, $\widehat{\boldsymbol{\beta}}$, obtained by solving (10) is semiparametrically efficient and satisfies

$$\sqrt{n}(\widehat{\boldsymbol{\beta}} - \boldsymbol{\beta}) \to N\{\mathbf{0}, (E[\mathbf{S}_{\text{eff}}^{\otimes 2}\{\Delta, Z, \mathbf{X}, I(W \leqslant Z), WI(W \leqslant Z)\})^{-1}\}$$

in distribution, where $\mathbf{S}_{\text{eff}}\{Z, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, I(W \leqslant Z), WI(W \leqslant Z)\}$ is given in (6).

Theorem 3. *Under the regularity conditions in Supplement 4.1, the nonparametric estimators $\widehat{m}_N(t, \widehat{\boldsymbol{\beta}}^{\mathrm{T}}\mathbf{X})$ and $\widehat{m}_T(t, \widehat{\boldsymbol{\beta}}^{\mathrm{T}}\mathbf{X}, W)$ satisfy*

$$\sqrt{nh}\left\{\widehat{m}_N(t, \widehat{\boldsymbol{\beta}}^{\mathrm{T}}\mathbf{X}) - m_N(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})\right\} \to N\{0, \sigma_N^2(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})\}$$

$$\sqrt{nh}\left\{\widehat{m}_T(t, \widehat{\boldsymbol{\beta}}^{\mathrm{T}}\mathbf{X}, W) - m_T(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W)\right\} \to N\{0, \sigma_T^2(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W)\}$$

in distribution for all t, W (such that $W < t$) and $\mathbf{X}$, where $\sigma_N^2(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})$ and $\sigma_T^2(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W)$ are given in Supplement 4.5.

5. Simulation. The section features four simulation studies for evaluating the finite sample performance of our method. For comparisons, we additionally implement a semiparametric proportional mean residual life model, denoted as "PM" (Chen and Cheng, 2005), which implicitly assumes $d = 1$.

Study 1: We generate event times with hazard functions of $\lambda_N(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}) = te^{\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}}$ and $\lambda_T(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W) = \frac{10e^{\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}+W}+1}{t+1}$ so that the true mean residual life is

$$m_N(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}) = e^{\frac{t^2}{2e^{\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}}}}\Phi\left(-\frac{t}{\sqrt{e^{\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}}}}\right)\sqrt{2\pi},$$

$$m_T(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W) = \frac{t+1}{10e^{\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}+W}},$$

where Φ is the cumulative distribution function of the standard normal distribution. Each component of $\mathbf{X}$ is generated independently from the standard normal distribution and W is generated independently from a uniform distribution over $[0, 10]$. We consider $d = 1, p = 9$ and set the true parameters to be $\boldsymbol{\beta} = (1, -0.6, 0.0, -0.3, -0.1, 0.0, 0.1, 0.3, -0.5)^{\mathrm{T}}$. The sample size is $n = 300$ and we randomly assign one third of samples to take the transplant.

Study 2: We generate event times with hazard functions of $\lambda_N(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}) = \frac{2t}{e^{\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}}+t^2}$ and $\lambda_T(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}, W) = \phi\{\ln(t) - 3 - W/100 + 0.1(1 - \sqrt{2}\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})^2\}/t[\Phi\{-\ln(t) + 3 + W/100 -$

$0.1(1-\sqrt{2}\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})^2\}]$ so that the true mean residual life is

$$m_N(t,\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}) = \left(1+\frac{t^2}{e^{\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}}}\right)\left\{\frac{\pi}{2}-\tan^{-1}\left(\frac{t}{e^{\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}}}\right)\right\},$$

$$m_T(t,\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X},W) = \Phi\left\{-\ln(t)+3+W/100-0.1(1-\sqrt{2}\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})^2\right\} \times\int_t^\infty \frac{1}{\Phi\{3+W/100-\ln(s)-0.1(1-\sqrt{2}\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})^2\}}ds,$$

where ϕ is the probability density function of the standard normal distribution. Each component of $\mathbf{X}$ is generated independently from the standard normal distribution and W is generated independently from uniform distribution over $[0,200]$. We consider $d=1,p=9$ and set the true parameters to be $\boldsymbol{\beta}=(1,-0.6,0,-0.3,-0.1,0,0.1,0.3,-0.5)^{\mathrm{T}}$. The sample size is $n=1,000$ and we randomly assign one third of samples to take the transplant.

Study 3: The hazard functions are $\lambda_N(t,\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}) = t^{2/5}\sum_{i=1}^d e^{\boldsymbol{\beta}_i{}^{\mathrm{T}}\mathbf{X}}$ and $\lambda_T(t,\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X},W) = t^{7/5}W\sum_{i=1}^d e^{\boldsymbol{\beta}_i{}^{\mathrm{T}}\mathbf{X}}$, with the corresponding mean residual lives of

$$m_N(t,\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}) = e^{\frac{5}{7}t^{7/5}\sum_{i=1}^d e^{\boldsymbol{\beta}_i{}^{\mathrm{T}}\mathbf{X}}}\int_t^\infty e^{-\frac{5}{7}s^{7/5}\sum_{i=1}^d e^{\boldsymbol{\beta}_i{}^{\mathrm{T}}\mathbf{X}}}ds,$$

$$m_T(t,\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X},W) = e^{\frac{5}{12}t^{12/5}\sum_{i=1}^d e^{\boldsymbol{\beta}_i{}^{\mathrm{T}}\mathbf{X}}}W\int_t^\infty e^{-\frac{5}{12}s^{12/5}\sum_{i=1}^d e^{\boldsymbol{\beta}_i{}^{\mathrm{T}}\mathbf{X}}}ds.$$

Each component of $\mathbf{X}$ is generated independently from the standard normal distribution. The waiting time W is generated independently from a uniform distribution over $(0,1)$. We consider $d=2,p=6$ and set the true parameters to be $\boldsymbol{\beta}=(\boldsymbol{\beta}_{\cdot 1},\boldsymbol{\beta}_{\cdot 2}) = ((1,0,-0.65,-0.5,-0.25,0.25)^{\mathrm{T}},(0,1,-0.5,0.5,-0.4,0.25)^{\mathrm{T}})^{\mathrm{T}}$. The sample size is $n=2,000$ and we randomly assign around one third of samples to take the transplant.

Study 4: This setting mimics the real data application. The hazards are set to be

$$\lambda_N(t,\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}) = \frac{1}{200}e^{t/200+\arctan(\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})+\pi/2}-\frac{1}{200},$$

and

$$\lambda_T(t,\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X},W) = \frac{1}{300}e^{t/300+\arctan(\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}-W/5+10)+\pi/2}-\frac{1}{300},$$

with the corresponding mean residual lives of

$$m_N(t,\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}) = 200e^{-t/200-\arctan(\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X})-\pi/2},$$

$$m_T(t,\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X},W) = 300e^{-t/300-\arctan(\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X}-W/5+10)-\pi/2}.$$

We consider $d=1,p=9$ and set the true parameters to be $\boldsymbol{\beta}=(0.4,1,-0.4,-1.50,-1.1,1.4,-0.1,-0.7)^{\mathrm{T}}$. The transplantation time W is generated from the uniform distribution on $(0,\max(T_N))$. The sample size is $n=2,000$ with a censoring rate of 26%, and about half of the samples receive the transplantation during followup. Study 4 mimics the features of real data that the mean residual life functions are decreasing gradually as t increases. The transplant group accounts for W: the improvement $m_T(t-W,\mathbf{X},W)-m_N(t,\mathbf{X})$ is negative when W is close to 0, and approaches 0 positively as W increases.

TABLE 1

Results of **Study 1**, *based on 1000 simulations with sample size 300. "Prop." is the semiparametric method, "PM" is the proportional mean residual life method. "emp sd" is the sample standard deviation of the corresponding estimators; "est sd" is the estimated standard deviation; "CP" is the estimated coverage probability of confidence intervals.*

		β_2	β_3	β_4	β_5	β_6	β_7	β_8	β_9
	truth	-0.6	0.0	-0.3	-0.1	0.0	0.1	0.3	-0.5
		No censoring							
Prop.	point estimate	-0.597	0.002	-0.290	-0.096	0.000	0.073	0.302	-0.504
	emp sd	0.229	0.442	0.180	0.438	0.437	0.437	0.171	0.206
	est sd	0.164	0.474	0.166	0.470	0.474	0.469	0.166	0.165
	CP(%)	88.8	96.2	94.4	96.0	95.8	96.1	94.9	91.2
PM	point estimate	0.442	-0.978	5.697	-20.47	0.986	-13.60	5.893	-3.780
	emp sd	57.8	95.11	155.9	583.0	36.7	352.5	212.5	156.5
		20% censoring							
Prop.	point estimate	-0.590	-0.003	-0.289	-0.086	0.007	0.101	0.289	-0.486
	emp sd	0.178	0.379	0.153	0.373	0.379	0.368	0.148	0.165
	est sd	0.156	0.406	0.146	0.404	0.407	0.406	0.145	0.152
	CP(%)	92.8	96.7	94.1	96.7	97.1	96.9	95.6	94.8
PM	point estimate	-0.774	0.067	-0.236	-0.027	0.150	0.176	0.339	-0.577
	emp sd	2.235	3.794	1.380	3.693	5.911	3.563	1.570	3.981
		40% censoring							
Prop.	point estimate	-0.518	0.020	-0.260	-0.079	0.020	0.088	0.266	-0.434
	emp sd	0.168	0.368	0.136	0.368	0.387	0.362	0.142	0.159
	est sd	0.149	0.392	0.140	0.396	0.391	0.389	0.140	0.144
	CP(%)	89.0	96.9	94.7	97.4	96.0	96.2	94.9	89.9
PM	point estimate	7.493	-7.316	-1.349	9.838	-21.588	-19.11	2.057	5.720
	emp sd	262.6	160.8	116.7	367.1	570.9	762.8	63.4	185.9

The results for the estimation of $\boldsymbol{\beta}$ under Study 1 are given in Table 1, with three censoring rates, 0%, 20% and 40%. The proposed method has much smaller biases and standard deviations, whereas "PM" is biased with larger standard deviations. The performances of all of the estimators deteriorate when the censoring rate increases, though our method still outperforms the others. We also demonstrate the true and error plots in Figure S1–S3, demonstrate that our method fare well for estimating $m(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{x})$ when t and $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{x}$ are not too extreme. The contour plots reveal that bias increases as censoring rate increases and the estimation deteriorates when t is large. These results show an overall satisfactory performance of our semiparametric method. Figure S1–S3 reveals that the performance of our method is better when t is in the interior of the range because more observations are available for the local estimation, as opposed to a larger t with fewer observations available. In contrast, regardless of the magnitude of t, the mean residual life function estimated by "PM" is severely biased, as shown in the last two rows from Figure S1–S3. This is because this model assume a pre-determined functional form of the mean residual life, which in this case is misspecified.

Tables 2 and 3 report the results of Studies 2 and 3 related to $\widehat{\boldsymbol{\beta}}$, respectively. We also provide the error plots of $\widehat{m}(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{x}) - m(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{x})$ in Study 2 using a contour plot in Figure S4–S6. The proposed method performs better than the competitor. For Study 3, we provide the error plots of $\widehat{m}(t, \boldsymbol{\beta}_1{}^{\mathrm{T}}\mathbf{x}, \boldsymbol{\beta}_2{}^{\mathrm{T}}\mathbf{x}) - m(t, \boldsymbol{\beta}_1{}^{\mathrm{T}}\mathbf{x}, \boldsymbol{\beta}_2{}^{\mathrm{T}}\mathbf{x})$ fixed at $\boldsymbol{\beta}_1{}^{\mathrm{T}}\mathbf{x} = 0$ and $\boldsymbol{\beta}_2{}^{\mathrm{T}}\mathbf{x} = 0$ in Figure S7 and S8. Similar to the conclusion in the first simulation study, the performance of estimating $\boldsymbol{\beta}$ by our proposed estimator is satisfactory. The performance of the mean residual life estimation is better when t is smaller, deteriorates when t and $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{x}$ becomes extreme, and is better for smaller censoring rates.

The results for Study 4 are presented in Table 4 which displays the estimated vector $\widehat{\boldsymbol{\beta}}$ for both methods. Notably, the PM method exhibits a significantly larger bias compared to

TABLE 2

Results of **Study 2**, *based on 1000 simulations with sample size 1000. "Prop." is the semiparametric method, "PM" is the proportional mean residual life method. "emp sd" is the sample standard deviation of the corresponding estimators; "est sd" is the estimated standard deviation; "CP" is the estimated coverage probability of confidence intervals.*

		β_2	β_3	β_4	β_5	β_6	β_7	β_8	β_9
	truth	-0.60	0.00	-0.30	-0.10	0.00	0.10	0.30	-0.50
		No censoring							
Prop.	point estimate	-0.611	0.002	-0.308	-0.101	-0.005	0.101	0.310	-0.505
	emp sd	0.140	0.106	0.114	0.104	0.106	0.104	0.114	0.127
	est sd	0.135	0.118	0.122	0.118	0.118	0.118	0.122	0.129
	CP(%)	95.0	97.4	97.5	98.1	97.4	97.6	97.3	95.8
PM	point estimate	-0.601	0.003	-0.301	-0.099	0.006	0.096	0.300	-0.506
	emp sd	0.069	0.083	0.073	0.074	0.083	0.088	0.097	0.084
		20% censoring							
Prop.	point estimate	-0.596	0.003	-0.306	-0.100	0.001	0.094	0.303	-0.499
	emp sd	0.140	0.116	0.126	0.113	0.109	0.110	0.123	0.137
	est sd	0.135	0.119	0.123	0.119	0.119	0.119	0.123	0.130
	CP(%)	94.7	95.8	94.4	96.5	97.0	96.1	96.0	94.5
PM	point estimate	-0.604	0.000	-0.305	-0.114	-0.023	0.092	0.299	-0.501
	emp sd	0.146	0.380	0.121	0.355	0.373	0.384	0.132	0.133
		40% censoring							
Prop.	point estimate	-0.596	0.001	-0.300	-0.098	-0.004	0.098	0.295	-0.498
	emp sd	0.156	0.129	0.136	0.131	0.125	0.127	0.140	0.148
	est sd	0.147	0.129	0.134	0.130	0.129	0.130	0.134	0.142
	CP(%)	95.1	95.0	95.4	94.8	95.9	95.6	93.5	93.9
PM	point estimate	-0.553	0.495	-0.242	0.220	0.114	-0.216	0.379	-0.565
	emp sd	1.805	15.895	2.105	10.373	4.706	10.316	2.535	1.833

TABLE 3

Results of **Study 3**, *based on 1000 simulations with sample size 2000. "emp sd" is the sample standard deviation of the corresponding estimators; "est sd" is the estimated standard deviation; "CP" is the estimated coverage probability of confidence intervals.*

	β_{31}	β_{41}	β_{51}	β_{61}	β_{32}	β_{42}	β_{52}	β_{62}
truth	-0.65	-0.50	-0.25	0.25	-0.50	0.40	-0.40	0.25
	No censoring							
point estimate	-0.662	-0.551	-0.237	0.253	-0.492	0.465	-0.407	0.251
emp sd	0.152	0.117	0.136	0.129	0.169	0.121	0.137	0.129
est sd	0.139	0.125	0.145	0.146	0.147	0.131	0.152	0.154
CP(%)	91.3	93.4	95.5	96.1	89.9	93.5	96.6	97.8
	20% censoring							
point estimate	-0.608	-0.401	-0.252	0.238	-0.480	0.301	-0.363	0.236
emp sd	0.105	0.097	0.097	0.091	0.110	0.098	0.098	0.090
est sd	0.103	0.094	0.107	0.107	0.108	0.098	0.111	0.112
CP(%)	93.4	81.2	94.9	96.1	93.1	81.8	95.9	98.0
	40% censoring							
point estimate	-0.587	-0.420	-0.234	0.227	-0.456	0.316	-0.357	0.228
emp sd	0.084	0.071	0.080	0.073	0.089	0.082	0.078	0.074
est sd	0.092	0.083	0.092	0.093	0.098	0.087	0.097	0.098
CP(%)	93.3	87.3	97.5	97.7	95.2	85.4	97.3	98.1

our method. We also assess the error of $\widehat{m}_T(t-w, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{x}, w) - \widehat{m}_N(t, \boldsymbol{\beta}^{\mathrm{T}}\mathbf{x})$ using a contour plot in Figure S9. Our proposed method outperforms the competitor across various scenarios. This difference in performance is particularly evident when $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{X} > 0$, where the PM method struggles to accurately estimate the mean residual life function of the transplanted objects.

This discrepancy can be attributed to the PM method's limited ability to handle the nonlinear structure inherent in the mean residual life function.

Finally, we have assessed the use of the Validated Information Criterion (VIC) (Ma and Zhang, 2015) for determining the number of indices, d, of the dimension reduction model in these 4 study settings; the d with the smallest VIC value would be selected. In Study 1, VIC selects d with an accuracy of 100% under all the three censoring rates, whereas the accuracies of selecting d via VIC are 97.1%, 100% and 100% in Study 2 and are 100%, 99.8% and 99.8% in Study 3, respectively corresponding to the censoring rates of 0%, 20% and 40%. Moreover, the accuracy of determining d via VIC in Study 4 is 97.8%. These high accuracies validate the utility of using VIC to select d across the examined settings.

TABLE 4

Results of **Study 4***, based on 1000 simulations with sample size 2000. "emp sd" is the sample standard deviation of the corresponding estimators; "est sd" is the estimated standard deviation; "CP" is the estimated coverage probability of confidence intervals.*

		β_2	β_3	β_4	β_5	β_6	β_7	β_8	β_9
		0.4	1	-0.4	-1.50	-1.1	1.4	-0.1	-0.7
Prop.	point estimate	0.409	0.912	-0.396	-1.263	-0.945	1.344	-0.109	-0.606
	emp sd	0.300	0.638	0.427	1.191	0.647	0.647	0.312	0.478
	est sd	0.279	0.776	0.473	1.225	0.769	0.763	0.467	0.519
	CP(%)	90.3	96.5	97.5	94.8	95.7	97.4	97.6	92.0
PM	point estimate	0.646	0.950	0.205	-0.776	-0.303	0.790	1.557	-0.090
	emp sd	22.847	6.882	2.545	3.545	1.879	4.259	8.725	1.556

6. Analysis of the Kidney Transplant Data. We apply the proposed method to analyze a kidney transplant data set from the U.S. Scientific Registry of Transplant Recipients (SRTR) mentioned in the introduction. Briefly, the registry is maintained by the United Network for Organ Sharing and Organ Procurement and Transplantation Network (UNOS/OPTN) and includes all waitlisted kidney transplant candidates and transplant recipients in the U. S. (`https://unos.org/`). For assessing possible benefits of transplantation, we use the residual life to estimate how much longer a patient can survive if she or he receives a transplant than otherwise.

To avoid confounding cohort effects and also to have a sufficiently long followup, we focus on the patients who were waitlisted in the same year of 2011. There were 43,140 patients in this cohort with an average followup of 907 days after waitlisting. During the followup, a total of 22,183 patients received kidney transplants. The response variable is the survival time in days (T_i) starting from waitlisting. Among patients who got a transplantation, 5.86% of the observations were censored, and the censoring rate was 26.43% among those without a transplantation. The covariates $\mathbf{X}$ included in our analysis were gender (X_1), race (X_2), max cold ischemia time (X_3), insurance coverage (X_4), body mass index (X_5), diagnosis type (X_6), peak PRA/CPRA (X_7), previous malignancy status (X_8) and diabetes indicator (X_9), all of which were used for computing the EPTS score (Time, 2012). The waiting time W is also considered in our model as proposed in (1) and (2). Our analytical goal was to use model (2) to quantify the potential residual life increment if a patient receives a kidney transplant given the covariate profile. The model mimics a real waitlisting to transplantation process by stipulating that all of the patients started by belonging in the non-transplant group, while those who got a transplantation were viewed as censored at transplantation; once transplanted, a patient would switch his or her membership to join the transplant group.

To proceed, we first determine the number of indices d using VIC (Ma and Zhang, 2015). In our analysis, $d = 1$ is chosen with the smallest VIC $= 143.66$, indicating a single index is

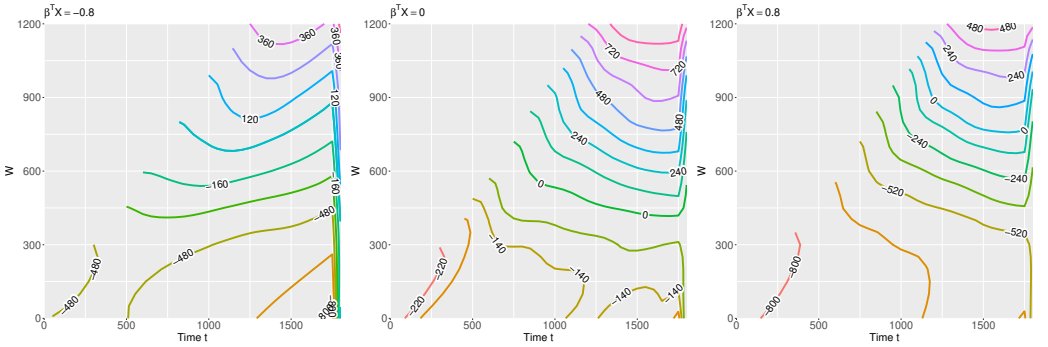

Fig 1: Mean residual life improvement from UNOS/OPTN data. Panels from left to right: $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{x} = -0.8, 0, 0.8$.

sufficiently informative; see Table 5. Subsequently, we normalize the index vector by fixing the first component (gender) at 1, and report 8 coefficient estimates. All of the covariates, except for the max cold ischemia time (X_3) and the body mass index (X_5), have significant effects on the mean residual life, which agrees with the previous studies (Friedman et al., 2003; Webster et al., 2017).

The max cold ischemia time (X_3) that refers to the tolerable amount of time from when a kidney is removed from the donor to the time it is transplanted into the recipient. Although the max cold ischemia time reflects the patient's physiological conditions indirectly, it is not as significant as the real cold ischemia time in determining the post-operative risk (Iida et al., 2008; Kayler et al., 2011). BMI (X_5) is commonly suggested as a "paradox" risk factor in the literature (Kalantar-Zadeh et al., 2005; Ahmadi et al., 2016). A popular explanation is that the BMI cannot differentiate between fat and muscle, thus high BMI patients may gain a survival advantage (Beddhu, 2004; Mafra, Guebre-Egziabher and Fouque, 2008).

On the other hand, race (X_2) and insurance coverage (X_4) have significant impacts on survival. It has been widely accepted that race and insurance coverage are highly correlated with patients' socioeconomic status, which plays an crucial role in the choice of chronic kidney disease treatment, especially for the end-stage patients(Lewis et al., 2010; Muntner et al., 2012; Nicholas, Kalantar-Zadeh and Norris, 2013; Webster et al., 2017). The other significant variables are also known risk factors for the ESRD mortality in the literature (Kauffman et al., 2005; Mehdi and Toto, 2009; Kayler et al., 2011; Pyram et al., 2012; Lim, Chapman and Wong, 2015).

Given a patient with characteristics $\mathbf{x}$, alive at time t, and waiting time w, $\widehat{m}_T(t - w, \widehat{\boldsymbol{\beta}}^{\mathrm{T}}\mathbf{x}, w) - \widehat{m}_N(t, \widehat{\boldsymbol{\beta}}^{\mathrm{T}}\mathbf{x})$ provides an estimate of the patient's mean residual life improvement after receiving a kidney transplant at w. Because the difference is a function of t, $\widehat{\boldsymbol{\beta}}^{\mathrm{T}}\mathbf{x}$ and w, we present the difference using various plots. Figure 1 plots contours that change with t and $\widehat{\boldsymbol{\beta}}^{\mathrm{T}}\mathbf{x}$ at several fixed w values.

TABLE 5

Parameter estimation of the kidney transplant data. "est." is the estimation of parameter, "s.d." is the estimated standard deviation of $\widehat{\boldsymbol{\beta}}$.

	$\widehat{\boldsymbol{\beta}}_2$	$\widehat{\boldsymbol{\beta}}_3$	$\widehat{\boldsymbol{\beta}}_4$	$\widehat{\boldsymbol{\beta}}_5$	$\widehat{\boldsymbol{\beta}}_6$	$\widehat{\boldsymbol{\beta}}_7$	$\widehat{\boldsymbol{\beta}}_8$	$\widehat{\boldsymbol{\beta}}_9$
est.	-0.097	-0.003	-0.174	-0.029	-0.119	0.030	-0.162	0.004
s.d.	0.011	0.007	0.010	0.007	0.009	0.005	0.016	0.011
p-value	0.000	0.866	0.000	0.073	0.000	0.000	0.000	0.008

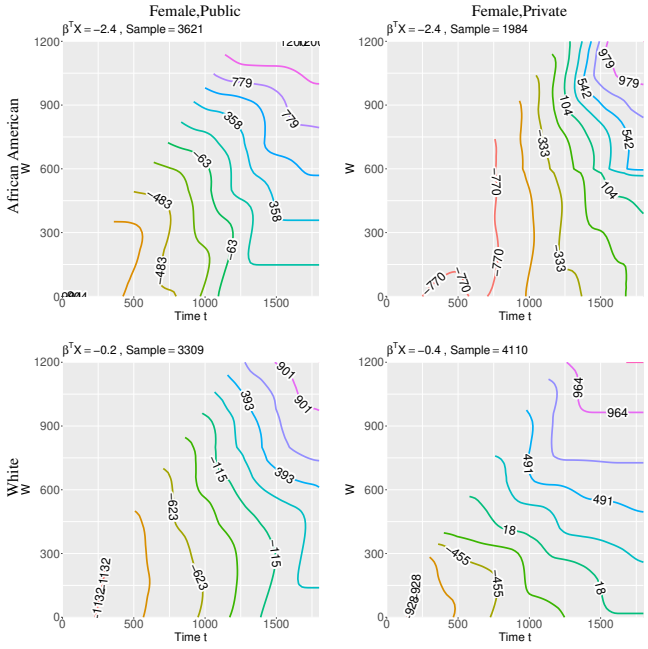

Fig 2: Mean residual life improvement from UNOS/OPTN data. Representative strata by Race, Gender, and Insurance Status with minimum $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{x}$ per stratum.

Several important observations can be made. First, with the waiting time being close to 0 in each panel of Figure 1, kidney transplant led to less survival gains compared to dialysis treatment, possibly because patients transplanted without waiting were likely to be high-risk patients and postoperative complications, such as cardiovascular and urological complications, increase mortality risk among them (Rahnemai-Azar, Gilchrist and Kayler, 2015; den Dekker et al., 2020). Second, as the waiting time w increases, kidney transplant could result in a reasonably larger improvement compared to dialysis. This is because these patients tended to be more stable, allowing kidney transplant to provide a notable survival advantage (Ingsathit et al., 2013; Schold et al., 2014; Bui, Kilambi and Mehrotra, 2019). Moreover, with t and w fixed, complex relationships existed between the patient's index value $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{x}$ and the survival improvement. The improvement is larger at $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{x} = 0$ than that at $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{x} = -0.8, 0.8$. It is very likely that large or small values of $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{x}$ were resulted by extreme health conditions which led to the worse improvement. Thus, this index in general measured patients' overall health condition.

Figure 2–4 further reveal the mean residual life improvement stratified by gender (X_1), race (X_2), and insurance coverage (X_4) at different values of $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{x}$. Several inequalities are noteworthy. First, patients with private insurance performed better than those with public insurance in most of cases, possibly due to socioeconomic status differences and the affordability for disease maintenance and treatment (Goldfarb-Rumyantzev et al., 2006; Nicholas, Kalantar-Zadeh and Norris, 2015). Second, the life gains were not very similar across male and female patients, especially the patterns differed between them. Females tended to have life gains positively related to the index; in contrast, males tended to have higher residual life gains at small absolute index. It is likely that heterogeneous kidney disease progression rates and lifestyles might lead to the pattern discrepancy (Baylis, 2009; Okada et al., 2014; Pscheidt et al., 2015), though the negligible difference in quantity between genders exemplified the "canceled survival advantage between genders" phenomenon (Øien et al., 2006;

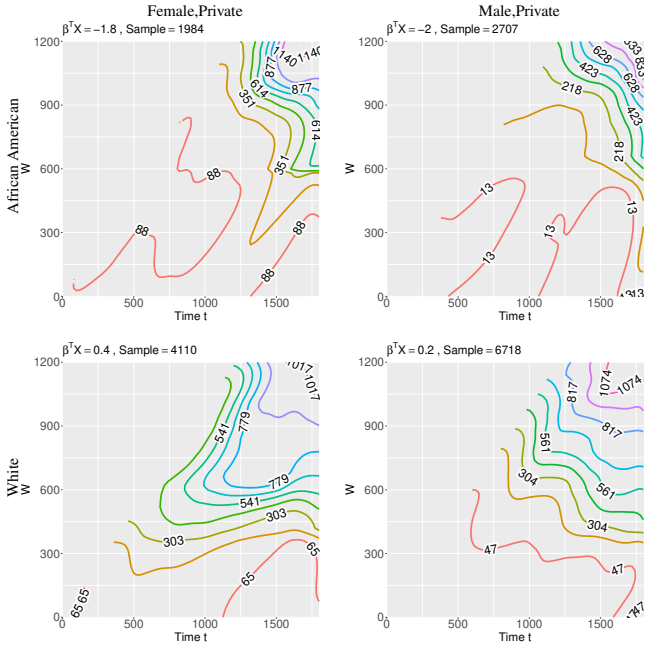

Fig 3: Mean residual life improvement from UNOS/OPTN data. Representative strata by Race, Gender, and Insurance Status with median $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{x}$ per stratum.

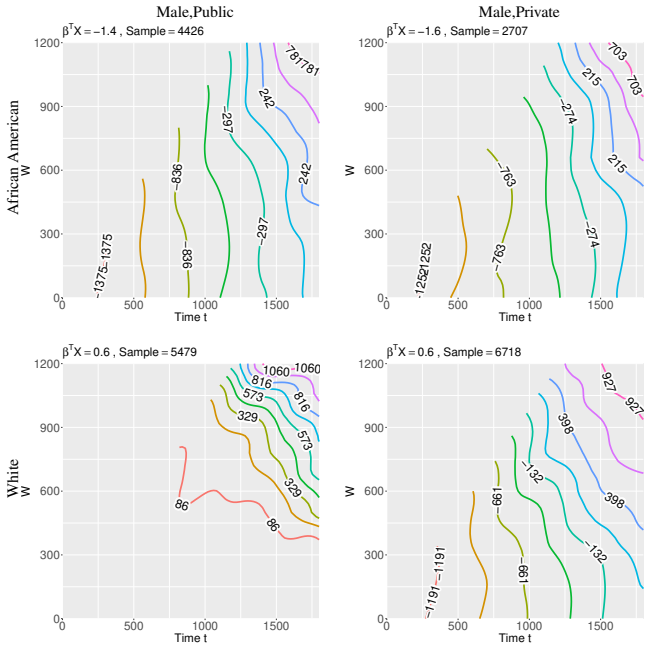

Fig 4: Mean residual life improvement from UNOS/OPTN data. Representative strata by Race, Gender, and Insurance Status with maximum $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{x}$ per stratum.

Carrero, 2010; Cobo et al., 2016). More detailed illustrations can be found in Figure S10–S12.

Survival gains of African Americans with public insurance were not monotonically related to the index regardless of gender given t; further, it was observed that African American females experienced greater life expansion compared to their male counterparts. Interestingly, we found the survival gains of African Americans were comparable with those of non-Hispanic Whites, even though these two racial groups had very different mortality among the general population (Lewis et al., 2010). However, the African American groups exhibited markedly different indices compared to the non-Hispanic white groups, possibly due to lifestyles and lack of access to healthcare among those groups (Kasiske, London and Ellison, 1998; Nicholas, Kalantar-Zadeh and Norris, 2013; Fedewa et al., 2014).

The Hispanic patients displayed consistent patterns in relation to their insurance type. Notably, there was minimal improvement in life gains when w was less than 500 and when $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{x} > -1.2$. However, at $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{x} = -1.8$, life gains showed a notable increase as w increased. The most significant decrease in life gains was observed under specific conditions: when t and w were small, and $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{x} < -1.5$. These trends held true for both genders and across different insurance types.

Among the Asian patients, a distinct pattern emerged in life gains with respect to t and w. Initially, life gains exhibited a rising trend, followed by a subsequent decline, with fluctuations observed along these dimensions. However, when $\boldsymbol{\beta}^{\mathrm{T}}\mathbf{x} < 0$, the alterations in life gains were less pronounced. Remarkably, the impact of insurance type on survival outcomes varied between genders. For the female patients, the choice between private and public insurance did not yield significantly divergent survival gains. Conversely, among the male patients, private insurance demonstrated a better outcomes when compared to public insurance.

7. Discussion. Addressing a severe shortage of organs that are needed to sustain ESRD patients' life, this work aims to design a feasible strategy to increase the potential efficiency brought by each available kidney. Instead of evaluating the patients' expected survival time, as is done in the literature, we consider the potential residual life prolonged by kidney transplant. By comparing patients' expected residual life with and without transplant, we use their difference to gauge the potential benefit gained from the transplant; patients with larger differences may have a higher priority for organ allocations than those with smaller values. As the primary purpose of the project is to improve the donor distribution strategy by assessing the post-transplantation performance, particularly with very limited organ donations, rendering the measurement of the entire lifespan is likely to be more pertinent (Assfalg et al., 2020) than focusing solely on a limited portion of future life, which the restricted mean survival time (RMST) is designed for. In addition, the choice of the length of the follow up window may complicate the organ distribution strategy. Therefore, we opt for the proposed model which is established on the premise of improving the overall residual life.

A natural extension of our model is to compute the causal effect between two groups. In the absence of a strong confounder "age", it is impossible to draw causal conclusion in this study. However, our comparison between two groups has a capability to analyze the causality as long as all confounders are included. On the other hand, our model compares the transplant cohort to a special case of the nontransplant cohort in which the transplantation would never happen in the future. A more general model will be studied in the future that transplant occurred at any time. Therefore, excepting comparing the mean residual life, many other quantities such as all-cause survivals and hazard ratio will be considered (Aalen, Cook and Røysland, 2015; Andersen, Syriopoulou and Parner, 2017; Syriopoulou, Rutherford and Lambert, 2020).

Our semiparametric regression model of mean residual life relaxes the parametric assumptions on the dependence of mean residual life on covariates and how long a patient has lived. To strike a balance between interpretation and flexibility, our procedure enables one to reduce the covariate dimensions from p to d: when $d = 1$, the model falls to the single index

model, while $d = p$ corresponds to a completely nonparametric model. We suggest to use the Validated Information Criterion (Ma and Zhang, 2015) to choose d, which seems to fare well in practice.

In our model, both the transplant and non-transplant groups are characterized by the same set of indices denoted as $\boldsymbol{\beta}$ throughout the study. An alternative would be to conduct separate estimation processes to distinguish the effects of these indices on different transplantation statuses. While our method can accommodate this suggestion by applying the model separately to each group, this separation approach may imply independent progressions for the same patient before and after the transplant. This may be beyond the scope of our primary objective of consistently quantifying survival improvements. To estimate the mean residual life enhancement attributable to inherent factors which reflect patient functional status, we intend to treat each patient's progression as a cohesive whole. This seems reasonable in the realm of kidney transplantation as studies showed that transplant does not interact significantly with patients' pre-operative functional status and is "associated with substantial improvement in all stages of functional capacity" (Ali et al., 2021).

To ensure estimability, we have assumed the complete follow-up condition, which is reasonable in clinical studies with high event rates and long followup (Sun, Song and Zhang, 2012), such as in studies with advanced stage cancer patients (Chen et al., 2005) and ESRD patients (Mansourvar, Martinussen and Scheike, 2016). Our data example features renal failure patients with a long followup, which may satisfy the assumption. We also acknowledge that, while the complete follow-up condition is a common assumption (Chen et al., 2005; Chen and Cheng, 2005; Tsiatis, 1990; Sun and Zhang, 2009), it incurs some limitations. For example, Ying (1993) pointed out that this assumption implies that the knowledge of the support is obtained in advance to assure a reasonable maximum followup time τ. Sun, Song and Zhang (2012), Chen and Cheng (2006) and Mansourvar, Martinussen and Scheike (2015) proposed various ways of selecting a reasonable τ, all requiring certain pre-knowledge. Due to these limitations, in Supplement 5, we further relax the complete followup condition, where we allow an unbounded support for the event time and only require a tail condition on the distribution similar to but weaker than the sub-Gaussian type. Finally, we are aware that the kidney transplant data from the U.S. SRTR may represent a biased sample, that is, the included patients were those with access to transplantation. In order to make results generalizable to a more general population, it is vital to take the probability of accessing transplantation into account. Estimation of this probability, however, is challenging because of many tangible and intangible factors involved in the process (Axelrod et al., 2008; Weng et al., 2010; Kucirka, Purnell and Segev, 2015; Carrero et al., 2018). More research is warranted.

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