Supplementary Online Content


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This supplementary material has been provided by the authors to give readers additional information about their work.
Supplemental Methods

Prior to implementing a marginal structural model using inverse probability of treatment and censoring weighting, a logistic regression analysis was used to estimate the probability (propensity) of a patient initiating treatment with PD on day 90 using all relevant baseline covariates including, via stepwise regression, any significant two-way interactions among these covariates. How well the logistic regression model predicts modality selection was assessed using the concordance index, c. Additional analyses were also undertaken to demonstrate that PD and HD patients with similar propensity scores (PS) were comparable with respect to all baseline covariates. Specifically, the PS were divided into quintiles and odds ratios were computed to determine if the odds of being treated with PD and HD were the same across all measured covariates within each quintile. Given the proximity of estimated odds ratios to a value of 1.00 within each of the PS quintiles, Mantel-Haenszel estimates of a common odds ratios across quintiles were computed to assess the assumption of conditional independence ("conditional randomization") between PD and HD given the PS’s (supplemental data, Figures 1-3). Box plots were also computed to compare the degree of overlap in PS’s between the two modalities within quintiles (supplemental data, Figure 4).

In addition to inverse weighting by the probability of treatment selection using the PS, marginal structural models for survival analysis also typically adjust for possible informative censoring using inverse probability of censoring weights. To determine the need for such adjustment, we compared the rate of transplantation among PD versus HD patients using a non-proportional hazards model adjusting for all measured baseline characteristics. The results
of that analysis reveal time-dependent hazard ratios that show the adjusted rate of
transplantation is significantly higher among patients who initiate dialysis on PD versus HD
indicating a need to also weight by the inverse probability of censoring (supplemental data,
Figure 5). To compute inverse probability of censoring weights, a piecewise exponential non-
proportional hazards (NPH) model was used to estimate each patient’s probability of remaining
transplant–free (uncensored with respect to transplantation) within each 6-month interval.
Likewise, a piecewise exponential NPH model was used to estimate each patient’s probability of
remaining censored-free with respect to dropout to alternative forms of dialysis other than PD
and HD (i.e., to home hemodialysis or “other” PD). These two censoring mechanisms were then
combined with the estimated PS’s to form a set of inverse probability of treatment and
censoring weights in a fashion similar to that described by van der Wal et. al. in a prospective
cohort study comparing PD and HD mortality among 1,800 patients from the Netherlands.

In computing inverse probability of treatment and censoring weights, we used stabilized
weights as described by Robins et al. With this approach, the inverse probability of treatment
weight is computed as the marginal propensity score (the observed proportion of patients
selected to PD) divided by the modeled propensity score from logistic regression to form a
stable inverse probability of treatment weight, \( w_{PD} \). Likewise, stable weights for inverse
probability of censoring for transplantation, \( w_{XPLANT} \), and inverse probability of censoring for
dropout to other dialysis, \( w_{DROP} \), were computed within each 6-month interval. The IPTCW
weights within each 6-month interval of follow-up is then computed as the product of these
individual stabilized weights, i.e., \( w(t) = w_{PD} \times w_{XPLANT} \times w_{DROP} \). The use of stabilized
weights typically mitigates the influence that a few patients with extremely low propensity
scores can have in an IPW analysis\textsuperscript{1-3}. We examined the distribution of these stable weights (supplemental data, Tables 1-2) and the fact that the mean weights were all near 1.00 and that the range of these weights were reasonably narrow provides evidence that these models were neither mis-specified nor in violation of the assumption of experimental treatment assignment as required for valid inference under inverse probability of weighting methods\textsuperscript{3-4}. Moreover, based on the very narrow range of the censoring weights due to dropout to home HD or “other” PD, there appears to be little evidence of selection bias among patients who switch to either home HD or “other” PD. The IPTCW-based adjusted patient survival for PD versus HD for the entire study period was compared to the IPTW-based adjusted patient survival wherein we exclude weighting by the inverse probability of censoring. The results, while very similar, do reflect a small but important correction for time-dependent selection-bias resulting primarily from the differential transplantation rates among PD and HD patients (supplemental data, Figures 5-6).

Lastly, as a check on the sensitivity of using inverse probability of treatment and censoring weighting, we compared the results from our NPH marginal structural model using IPTCW to results from a stratified NPH model in which sub-classification according to quintiles of the PS’s were used as a means for reducing sensitivity to unusually low PS’s (e.g., Schafer and Kang\textsuperscript{5}). This was performed for the entire study population. A comparison of the time-dependent hazard ratios between these two methods yielded qualitatively similar results (supplemental data, Figure 7) suggesting our analyses based on the use of stable inverse probability of treatment and censoring weights is reasonably robust. The advantage of our approach over the use of sub-classification on PS’s is that we can readily compute adjusted
cumulative hazard functions from which adjusted population survival curves can be computed. In addition, our approach allows us to adjust for any time-dependent selection bias associated with censoring due to transplantation or dropout. We know of no such approach using the method of sub-classification or stratification.

In summary, while the use of inverse probability weighting (IPW) appears somewhat complex, it may be thought of as an extension of the commonly used method of direct-standardization\(^7\). Indeed, when one is faced with controlling for one or two confounding factors, the two methods are identical\(^7\). However, the use of IPW allows for greater complexity including the use of continuous confounding covariates – something direct standardization is unable to handle.

**References**


Supplemental Table 1: Descriptive statistics of inverse probability of treatment stabilized weights.

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Supplemental Table 2: Descriptive statistics of inverse probability of censoring stabilized weights

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Legends for Supplemental Figures

**Supplemental Figure 1:** Common odds ratio and 95% confidence intervals across propensity score quintiles according to baseline demographics.

**Supplemental Figure 2:** Common odds ratio and 95% confidence intervals across propensity score quintiles according to baseline clinical characteristics.

**Supplemental Figure 3:** Common odds ratio and 95% confidence intervals across propensity score quintiles according to baseline laboratory characteristics.

**Supplemental Figure 4:** Box plots to evaluate the overlap of propensity scores between incident HD and PD patients in the overall cohort, and in the five quintiles of propensity scores.

**Supplemental Figure 5:** Adjusted time-dependent transplant hazard Ratios and 95% confidence intervals over time.

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**Supplemental Figure 7:** Adjusted time-dependent hazard ratios and 95% confidence intervals comparing inverse probability of treatment and
censoring weighing to a non-proportional hazards model stratified by quintiles of the propensity scores in incident dialysis patients in the United States from 1996-2004.
Supplemental Figure 1

Common Odds Ratios (95% CI) According to Baseline Demographics

Odds Ratio (PD:HD)
Supplemental Figure 2

Common Odds Ratios (95% CI) According to Clinical Characteristics (Baseline)
Supplemental Figure 3

Common Odds Ratios (95% CI) According to Baseline Labs

Common Odds Ratio Across All patients

Risk Factors: Hgb, BUN, Albumin

Odds Ratio (PD:HD)

Common Odds Ratio Across PS Quintiles

Risk Factors: Hgb, BUN, Albumin

Odds Ratio (PD:HD)
Evaluation of Overlap in Propensity Scores Between Modalities

Supplemental Figure 4
ITT Adjusted Transplant Hazard Ratios

Population = Overall

Hazard Ratio (PD:HD)

Interval Follow-up
Effect of Inverse Probability of Treatment Weighting versus Inverse Probability of Treatment and Censoring Weighting

Supplemental Figure 6
Comparison of Inverse Probability of Treatment and Censoring Weighting versus Sub-classification on Propensity Scores

ITT IPTCW – Adjusted Hazard Ratios
Population = Overall

ITT PS – Stratified Hazard Ratios
Population = Overall

Supplemental Figure 7